

GW RESEARCH DAYS

— TUESDAY, MARCH 31, 2015

THE GEORGE WASHINGTON UNIVERSITY

WASHINGTON, DC



GW RESEARCH DAYS

2015

ANNUAL RESEARCH DAY

TUESDAY, MARCH 31, 2015

MARVIN CENTER

800 21ST STREET, NW, 3RD FLOOR

- | | |
|----------------------|--|
| 8:30-10:00 a.m. | Registration and Breakfast (<i>Grand and Continental Ballrooms</i>) |
| 8:30-10:00 a.m. | Posters Setup (<i>Grand and Continental Ballrooms</i>) |
| 9:00 a.m.-2:00 p.m. | Research Days Vendor Showcase (<i>Grand and Continental Ballrooms</i>)
http://research.gwu.edu/research-days-2015-vendor-showcase |
| 10:00 a.m.-1:00 p.m. | Poster Presentations and Judging (<i>Grand and Continental Ballrooms</i>) |
| 1:00-2:30 p.m. | Poster Removal (<i>Grand and Continental Ballrooms</i>) |

RESEARCH DAYS 2015 WEBSITE

ONLINE - [HTTP://RESEARCH.GWU.EDU/RESEARCH-DAYS-2015](http://RESEARCH.GWU.EDU/RESEARCH-DAYS-2015)

- | | |
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| 5:00-5:15 p.m. | Poster Winners Announced Online |
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BUSINESS



SCHOOL OF BUSINESS

Evolution of Two Iconic Toy Brands

Two iconic toy brands, Tonka and Barbie, grew in popularity after their establishment in mid 1900s. The research stems from within the respective companies themselves and external marketplaces with their corresponding consumers. Individual analysis of the changes and why they happened will be utilized to understand the evolution of these two individual brands. Both brands have faced dramatic changes in their popularities and appearances due to the advancement in technology, in addition to other consequences caused by globalization and cultural differences.

STATUS

Student - Undergraduate

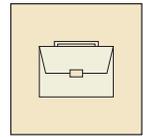
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SCHOOL OF BUSINESS

Bills of Exchange: Evolution of a New Currency across Europe

Beginning in approximately 1500 AD a price revolution began to occur throughout Europe when prices were increasing by a significant amount across the continent, while there was no simultaneous nor proportionate increase in precious metal based coins. At the start of the Price Revolution coins were the most common form of money used. Therefore, something else led to the drastic increase in prices.

Italians were the first country to dominate banking in Europe. Over time the Germans and Dutch also became influential in banking. One important financial innovation were bills of exchange, a method of transferring purchasing power across currencies, which became useful at fairs where merchants were trading. By facilitating a liquid currency exchange market, exchange bills allowed merchants to transfer purchasing power across currencies and countries over time. Fairs were located in places such as Italy, Champagne, Bruges, Antwerp, and Amsterdam. One major difference in the bills was that in the North they were transferrable amongst recipients, but that was not the case in the Southern Europe.

Through literature review, it is apparent that bills of exchange are private market phenomena. During this time period banks were developing in Northern cities, such as Hamburg and Amsterdam. This has led us to consider the relationship between the bills within private markets and bank development. Are these complements, substitutes? Both? Does the development of these banks explain the differences in bill of exchange usage across Europe? Or were they other underlying issues. These are important questions in the continuation of our research.

Looking forward there is much more research, specifically quantitative, that needs to be done. We hope to track down bills of exchange through archives and potentially notarial records from this time period. A major hurdle is understanding where these can be found, if they are in family bank records or in notary records. Secondly, we look to further understand how bills of exchange were used over time and if they were used differently across the European continent.

STATUS

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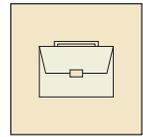
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BUSINESS



SCHOOL OF BUSINESS

International Transferable Best Practices in Sustainable Healthcare

Each year, the healthcare industry creates a significant amount of waste and contributes to a large portion of greenhouse gas emissions across the globe. Developments in sustainability enable healthcare stakeholders to decrease their environmental footprint via energy efficiency, sustainable procurement, waste management, recycling programs, telecommunication, and other best practices. Research shows that green healthcare systems not only benefit the environment, they also save money to both healthcare systems, and ultimately the consumer, and provide a better atmosphere for both patients and employees. Often, healthcare systems may realize some of the positive implications of green best practices, yet do not know where to begin in regards to implementation. Practitioners may feel that the costs are too high, or employees will not be receptive to change. Through an analysis of case studies, scholarly articles, current news, and interviews and surveys with healthcare professionals and experts, this project analyzes the best practices in sustainable healthcare. Looking at best practices across the globe provides an international perspective, and ultimately enables identification of transferable tactics that can easily be implemented internationally. Research is conducted considering the engagement of various stakeholders, including healthcare operators, patients, healthcare employees, suppliers, and government. Future sustainable healthcare trends suggest the industry requires greater collaboration between key stakeholders to truly understand what each party can provide, and how each party will benefit from new initiatives in sustainable healthcare.

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BUSINESS



SCHOOL OF BUSINESS

How does managerial activism affect corporations?

We examine the effects of managerial activism in the corporate sector. We find that firms with active managers have weaker corporate governance that gives more power to managers and also have high managerial compensations. These firms are also targeted more by shareholders and institutions. Yet, firms with active managers do not destroy value and are relatively more socially responsible. Using a natural experiment on managerial activism, we find that shareholders consider events that give more power to managers as value decreasing. However, operating performance of these firms is comparable to their peers. Overall, managerial activism gives more power and pay to managers, but managers act in the interest of the firm, possibly balancing the effects of shareholder activism

STATUS

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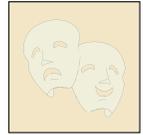
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CREATIVE ARTS



COLUMBIAN COLLEGE OF ARTS & SCIENCES

A Place at the Table: The Role of Historic Sites in Gentrifying Neighborhoods Our Stories: Shaw through the 1970s

Washington, DC is experiencing massive population growth and skyrocketing property values in each of its neighborhoods. The influx of affluent, typically White residents and the moving out of long-time, typically Black residents has caused anger and frustration that is palpable across the District. The proposed exhibition in this thesis challenges museums and historic sites to reexamine their function and role in transitioning or gentrifying neighborhoods in order to address this rising tension.

Located in the Shaw, one of DC's oldest African American (and most recently gentrified) neighborhoods, the proposal details the inaugural exhibition to be held at the newly restored Carter G Woodson Historic House. Exploring daily life in Shaw during the 1970s establishes the historic house as a living, active neighborhood museum, dedicated to preserving Shaw's at-risk history. The exhibition intends to facilitate multigenerational dialogue by engaging past and present residents as well as students and alumni of Howard University in active memory sharing. By engaging site-specific interpretation and community involvement heritage sites, such as the Carter G Woodson House, can have a place at the table in constructing or reconstructing public life in transitioning and gentrifying neighborhoods.

This proposal addresses challenges in site, audience, and topic history by utilizing precedents of similar projects or museums, interviewing long-time residents, and engaging neighborhoods organizations and stakeholders. The exhibition reflects the evolving story of the neighborhood, while the historic house acts as a more permanent container of the past that does not ignore the present in which it sits.

STATUS

Student - Graduate

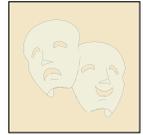
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CREATIVE ARTS



COLUMBIAN COLLEGE OF ARTS & SCIENCES

Exploring Race and Gender in Kara Walker's Art

The advent of the feminist and civil rights movements in late 20th century America prompted an explosion of experimental art that addressed politically charged issues of race, gender, and sexuality. These same issues were molding a new age of thinkers that challenged the traditional academic canon and inspired artists to push beyond the constraints of classical art forms. African American artist Kara Walker (b. 1969) has continued this new tradition of transcending boundaries with her highly provocative silhouette installations centered on slave life in the pre-Civil War South. Walker's work plays with unconventional artistic approaches and masterfully enriches them with historical context and awareness to the unspoken tragedy of such a history. Walker's work joins that of other influential African American artists such as Faith Ringgold and Renee Cox in exposing gender inequality and the socially defined sexual culture of women in history, especially that for women of color. Walker's most recent piece, "Sugar Sphinx" is a hotbed of political debate that encapsulates not only black history but also the tainted history of America's white oppressors. A traditional model of a slave woman crafted out of bleached white sugar and displayed in an abandoned Domino Sugar Factory in Brooklyn, New York, "Sugar Sphinx" is a temporal artwork that is confrontational both in its physical size and subject matter. In creating this piece, Kara Walker is able to effectively and profoundly weave together ideas concerning the economic status and weight of slaves, the untapped realm of female sexuality, and the dual temporal and permanent nature of race and gender in society.

STATUS

Student - Undergraduate

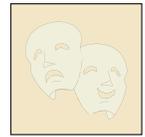
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CREATIVE ARTS



COLUMBIAN COLLEGE OF ARTS & SCIENCES

Picasso's Les Demoiselles d'Avignon: Female Sexuality & Colonialism

Artist Pablo Picasso, along with his peer Georges Braque, began and led the Cubist Movement in Paris, France from 1907 to 1914. In this short period, these artists transformed how formalized imagery could be manifested visually and contextually. Cubism rejected the concept that art should mimic nature; instead, it emphasized an expression of an artist's sense of reality. Picasso pivotally demonstrated this in his painting *Les Demoiselles d'Avignon*, as he explored burgeoning topics concerning female sexuality and colonialism. Specifically, the painting addressed female sexuality through its composition of five female prostitutes. This content is significant because at the time such women were criticized for their promiscuity, despite serving men of the bourgeoisie. Thus, Picasso's imagery provoked a valuable discourse on moral hypocrisy and societal privilege. Comparatively, Picasso acknowledged Primitivism and African Art in *Les Demoiselles d'Avignon* through literal appropriation of abstract forms that showcased geometric forms, shallow space, and contrasting viewpoints. It is especially important to recognize the African forms within *Les Demoiselles d'Avignon* because at the time strong cultural tensions existed between Europeans and Africans. Ultimately, Picasso's appropriation and augmentation of Primitivism and African Art in his work influenced the direction and foundation of the Cubist Movement. Cubists discovered a new way of seeing, being, and acknowledging life through cultural exploration and a rejection of society's conventions and traditions.

STATUS

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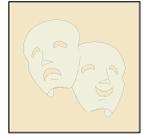
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CREATIVE ARTS



ELLIOTT SCHOOL OF INTERNATIONAL AFFAIRS

The Role of the Performing Arts within International Development: A Study on The Bokamoso Youth Center, Winterveld, South Africa

South Africa's 1959 Promotion of Bantu Self-Government Act forcibly removed more than 3.5 million black South Africans from their homes into black ghettos or "Bantustans" as they were called during the apartheid regime. These Bantustans suffered from massive underdevelopment and utter poverty, and although the regulations and laws of apartheid have been abolished, the economic and developmental effects remain. One Bantustan in particular where poverty still reigns rampant is in Winterveld, a small community in the Gauteng province near Pretoria. While a majority of development projects from Non Governmental Organizations and private sector business in Winterveld have failed, community led initiatives that incorporate the performing arts have been thriving and have served as a source of hope and solace for youth in the area.

The object of this study is to analyze the role that the performing arts, and music in particular, plays in the lives of youth within Winterveld and in turn how that aids in the development of South Africa as a whole. Through a series of interviews, research studies based on various community engagement and self-efficacy scales, and extensive research on the performing arts, it is clear that the performing arts, create an environment that aids in the advancement of one's social, emotional, and physical well-being and serves as a springboard to higher self-esteem and in turn personal growth and development.

The Bokamoso Youth Center, serves as that springboard to the Winterveld community. Through song, dance, and acting, students at the Bokamoso Youth Center gain access to resources and unlock internal confidence that propels them through poverty to college and careers integral to success. While the results produced in this study deal specifically with the Bokamoso Youth Center and how the performing arts aids in the development of Winterveld, it lays the foundation for further research to show how music and the performing arts can be an integral component of International Development.

STATUS

Student - Undergraduate

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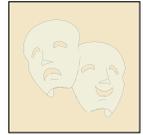
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CREATIVE ARTS



COLUMBIAN COLLEGE OF ARTS & SCIENCES

(Re)Designing The Museum: Participatory Art and the Importance of Visitor (Re)Engagement

Is there a “right” way to look at art? The traditional art museum model is static – one where the status quo reigns. New ways of approaching art exhibitions is an uncultivated area. (Re) Designing The Museum: Participatory Art and the Importance of Visitor (Re)Engagement is an exhibition proposal that looks to provide a unique art museum experience; one where the will visitor discover new ways to engage with and look at artworks within an exhibition. The exhibition, pARTicipate: A Guide to Looking at Art, will include modern and contemporary art works that engage the visitor through the categories of ideas, people, objects, and physical. This art exhibition will examine traditional modes of displaying art works and look to reassess the conventional art viewing experience. Aimed to engage members of the millennial generation, pARTicipate analyzes social constructs of this demographic to create a better designed and more relevant museum experience. Interactive components such as writing on the walls, creating object labels, or changing the wall color will encourage the visitor’s role to shift from passive to active.

Taking place at the newly constructed Whitney Museum of American Art, pARTicipate will be the inaugural exhibition to celebrate the opening of their new building. As a permanent collection installation, this show will use a non-traditional approach to reassess and redefine conventional uses of space, graphics, and overall tone within the art museum, creating an exhibition that aims to re-engage the visitor.

STATUS

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CREATIVE ARTS



COLUMBIAN COLLEGE OF ARTS & SCIENCES

Day One: An Exploration of Culture

Throughout my studies at the George Washington University, one particular idea has stuck with me, the concept of societal and national culture, as presented by Will Kymlicka. In his book *Multicultural Citizenship*, he delves into a discussion of how different cultures interact together in democratic countries, with a particular focus on those that have large populations of immigrants. One of his theories I found particularly interesting, as the granddaughter of immigrants, is that those who participate in multiple cultures, through language, cannot ever be fully integrated into only one of those cultures. This concept, while unnerving for someone who speaks multiple languages at home and often feels split between two cultures, made logical sense. I had spent the majority of my life never truly being a member of the hispanic community in Miami, Florida where I grew up, but never truly being a member of the American community either; I understood Kymlicka's assertion on a personal level. Then I met the Ambassadors of the Bokamoso Youth Center from Winterfeldt, South Africa who were mostly of different cultures, but united in order to be a representation of South Africa itself.

South Africa is a nation of cultural plenty; eleven official languages that define cultural lines, each accompanied by a variety of shared foods, arts and, experiences, each different than the last. These diverse experiences and practices have shaped the lives of the individuals in the country for centuries and continue their influence to this day. As the modern global community has begun to shape the more traditional local ones, how these cultures have influenced the lives of those that practice them have transformed, particularly with younger generations who have increased access to other cultures through the Internet. But, my personal experiences with the Bokamoso Youth hinted something more, that culture, though inherently connected to language in their society, can change in a way that doesn't dilute the traditions and wisdoms of its original form. This documentary will focus on following the lives of three people from the Bokamoso Youth Center, and interweave interviews with various others, in order to analyze the application of Kymlicka's theories to a land with an abundance of robust cultures in "Day One, an Exploration of Culture".

STATUS

Student - Undergraduate

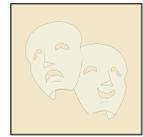
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CREATIVE ARTS



COLUMBIAN COLLEGE OF ARTS & SCIENCES

The New Media of Modernism: Photographs and Posters Dismantle Artistic Hierarchies

In Montmatre Paris at the crossroads of a busy, commercial intersection sits the Moulin Rouge, center of late nineteenth-century entertainment and the focus of many advertising posters by Henri Toulouse-Lautrec and Jacques Cheret. These sophisticated, experimental posters quickly moved from utilitarian advertising functions to the center of the avant-garde art scene. The works reflected new technological advances and they blurred or even removed the division between "high" and "low" art. Their content suggested the disintegration of existing societal hierarchies; popular culture became the focus for the experimental artists living and working in Montmatre. The object of this study is to suggest parallels between these artistic innovations and today's Instagram photography and Vine videography. When new styles of art and new media for conveying these stylistic developments emerge, a paradigm shift must occur to understand these phenomena. Toulouse-Lautrec's and Jacques Cheret's ways of approaching movement and art reflected a departure from objective reality and their work established a more subjective reality that, paradoxically as it may seem, is more real to the viewer on the street. I propose that new technological advances in iPhone applications and the internet serve as new media sites for today's artists. In examining the works of Man Ray and Henri Cartier-Bresson in photography, as well as Henri Toulouse-Lautrec and Jacques Cheret in poster-making, one can see the gradual acceptance of these two media forms and it may provide the modern viewer a lens through which we can examine contemporary media forms.

STATUS

Student - Undergraduate

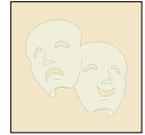
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CREATIVE ARTS



COLUMBIAN COLLEGE OF ARTS & SCIENCES

Monet's "Floating World" : A Bridge Between Japanese Ukiyo-e Painting and French Impressionism

People with some knowledge of Monet's work will be familiar with the Japanese bridge that frequently appears in many of his paintings, and those who have been to Monet's garden at Giverny may also recall the vast collection of Japanese Ukiyo-e ("paintings of the floating world") in his living room. When I visited Giverny's gardens this past summer, I was immediately reminded of past sensory experiences. The garden arrangement looked familiar to ancient Chinese designs, where the landscape views never the same from one place to another; and the variety of flowers appears closer to a Japanese setting. This parallel world experience gave me the incentive to examine Monet's paintings and the Japanese Ukiyo-e, and through research and analysis of the two subjects, I found the intersection of eastern and western cultures was not merely a coincidence. Monet found a perfect way to blend Japanese elements into his work, and his personal experiences created an inevitable bridge between him and the Japanese culture. Monet never lived too far from water, thus water appears frequently in his paintings. And for an island country like Japan, water is almost an indivisible part of its culture. In later stages of Ukiyo-e paintings water appears largely as the setting. Moreover, the use of color suggests how Monet absorbed characteristics of Ukiyo-e and incorporated them within his own paintings. If we look at the main color used in Monet's Water-Lilies series, one can see how the changes of different levels of blue were manipulated. Compare that to Thirty-six Views of Mount Fuji, although the style of the two is very much distinguished, the similarity of the technique is obvious. Rather than state Monet was influenced by Ukiyo-e, it is more appropriate to describe this strong linkage as a sensory resonance across cultures.

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EDUCATION



GRADUATE SCHOOL OF EDUCATION & HUMAN DEVELOPMENT

Expanded Learning Time: Case Studies in Four States

Many low-performing schools across the nation have expanded learning time (ELT) in response to federal requirements for the School Improvement Grant (SIG) program or under the conditions of the Elementary and Secondary Education Act (ESEA) waivers. The waivers allow greater flexibility to redirect federal 21st Century Community Learning Center (21st CCLC) funds toward ELT. Yet, there is little research on how schools are meeting the federal requirements or if ELT has impacted school culture or student outcomes. The purpose of this study was to investigate and better understand implementation of federal ELT initiatives with particular emphasis on schools designated by states as the lowest-achieving under the federal programs to inform future federal policy decisions. A multiple-case study design allowed data analysis to occur within and between three levels of education governance: the state education agency, the district, and the school. Purposefully selected case study states met the following criteria: they were implementing a SIG program, had received an ESEA waiver, and had requested to waive the requirements of the 21st CCLC program. Four states, Connecticut, Colorado, Oregon, and Virginia were selected and participated in the study. Using semi-structured interview protocols, researchers interviewed 13 state education officials, 18 district leaders, and 18 school leaders. To extract themes from the school-, district-, and state-level data, researchers independently reviewed and coded transcripts and relevant documents in Nvivo. Researchers compared codes and developed final coding matrices for each case. All cases were member checked by study participants. Researchers found that case study schools were meeting the federal requirements for ELT, but that implementing ELT is costly, and with the short-term nature of federal grants some schools may face sustainability issues. Researchers also found: sites varied in their implementation of ELT; school leaders could not attribute improved student outcomes directly to ELT due to reforms being implemented simultaneously; education leaders felt that increasing quality of instruction was as or more important than increasing quantity; and few schools were taking advantage of the 21st CCLC flexibilities. This research has several implications for implementing ELT initiatives: schools need more flexibility than is currently given under the federal programs studied to design ELT strategies suited to their context; ELT policies should place a priority on additional time for teacher collaboration and professional development as well as student instruction; and any long term efforts to improve low-performing schools will require reliable funding sources for ELT and other required reforms.

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EDUCATION



SCHOOL OF ENGINEERING & APPLIED SCIENCE

A Risk Assessment Tool for Mobile Identity and Access Management Systems during Disaster Response

First responders to natural disasters can assume the responsibilities of distinctly different roles spanning medical, law enforcement, and volunteer professions. Their identity and related attributes must be correctly defined and discoverable in any system designed for working with disaster data that may contain sensitive information such as health care records and official use only data to ensure that only authorized users access this information. The problem is further exacerbated by lack of federal or industry-proven identity management standards for mobile devices as they are becoming more relied upon these days. Many frameworks have been proposed to address the dynamic nature of identity management during disaster response but none systematically analyze security and privacy risks in terms of confidentiality and integrity. This research seeks to develop a first order risk assessment tool identifying a core set of design factors to assess a systems ability to mitigate security and privacy risks that also accounts for the mobile aspects of the system.

STATUS

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EDUCATION



COLUMBIAN COLLEGE OF ARTS & SCIENCES

Washington D.C. as a Latin Classroom: Modern City, Ancient Lessons

During my final year at GW, I wanted to complete a Senior Project that could encapsulate my experiences with the Classics Department, including both my academic courses and my internship at School without Walls (SWW). Since I want to be a Latin teacher, I set out on a project to further my understanding of both Latin pedagogy and the relevance of the ancient world to our modern American world. Over the past six months I have written, edited, and will pilot a supplementary curriculum to a Latin III/Third semester class that incorporates Washington, D.C. in a way that encourages comparisons between the ancient and modern worlds. My curriculum, or “workbook,” includes five units that revolve around a theme relevant to both ancient Rome and modern Washington D.C. Each unit contains worksheets for a site visit, Latin vocabulary, Latin passages for translation, reading about the theme, and an outline of key concepts and figures. This type of project is important to Latin classrooms because it encourages comparisons between Washington D.C. and Rome, teaches Latin students about the larger classical world, shows students how the material they study is relevant to the modern world, and allows them to further translation skills and critical thinking skills in a way that is fun and that will inspire students to continue their study of Latin. While many Latin teachers in the D.C. area have thought about the topic, there are no resources of the kind I have created. I will be testing out one of the five units at School without Walls the week of March second, and therefore would be able to present about how effective my project was at achieving those goals, and where I can make improvements to the curriculum.

STATUS

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EDUCATION



COLUMBIAN COLLEGE OF ARTS & SCIENCES

Learning Style Progression and Success Among Students in a Learning Assistant Program-based Biology Classroom

The Learning Assistant (LA) Program was first brought to the George Washington University during the fall semester of 2012, implemented in a select few introductory science courses, including biology and chemistry. Since then, the program has expanded in both number of classrooms and disciplines, pervading traditional lecture halls and more interactive classrooms alike. The LA Program places several undergraduate students into a large lecture as facilitators, while simultaneously requiring them to take a graduate level class on the successful and more interactive styles used in education. The LAs apply these practices by splitting the class into smaller discussion groups. Through this program, students have the opportunity to learn material more intimately and actively, thus providing a unique way to learn the sciences and promote interest in the topic at hand. Now in the Program's fourth semester, the purpose of this study is to determine whether the LA Program is successful in its attempt to provide students with a better understanding of science, by ensuring their learning goes beyond memorization and can successfully be used to analyze and change their perspectives of future studies. The study aims to determine this by conducting a series of surveys and focus groups to analyze student work. The goal of these measures is to determine if the students grow in learning style according to the material they learn over the course of one semester, both subjectively and objectively. Should this prove successful, the LA Program has the potential to change the course of education, both in and outside of science disciplines.

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GRADUATE SCHOOL OF EDUCATION & HUMAN DEVELOPMENT

Model Ka band High Throughput Satellite System SNIR

The proliferation of communications traffic led by Internet access, multimedia services demand and globalization has resulted in spectrum congestion which pushes steadily the frequency bands of communications satellites up, from L, S and Ku bands to Ka and V bands. Crossing the 10GHz frequency limit however gives rise to significant signal fading induced by the troposphere layer of the geostationary satellite channel.

In contrast to past Ka band communications satellite systems where spot beams were used for focused coverage, current dedicated Ka band systems deploy spot beams for throughput increase of multiple times by employing frequency reuse among the beams. This however results also in much intra-system co-color interference in the high throughput systems (HTS) in addition to troposphere layer induced fading in Ka band.

This research presents a probability model of the Ka band HTS satellite channel including major channel induced impairment. The empirical land mobile satellite signal-to-noise-plus-interference ratio (SNIR) model is examined for the Ka band spot beam uplink and developed into the SNIR probability density function (pdf) of the uplink accordingly. The development brings about flexibility in operational scenario representation and numerical solution implementation feasibility. Results from Matlab numerical solutions to the model and simulation validation in selected operational scenarios are then given to illustrate the wide range applicability of the developed model.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Design and Acoustic studies of Phase Shift Nanodroplets

Recent efforts in the area of developing extravascular contrast agents for diagnostic and therapeutic applications has led to development of phase shift nanodroplets. Phase shift nanodroplets (PSNDs) consist of a liquid perfluorocarbon core in an encapsulating shell. These nanoscale agents undergo phase transition and hence vaporized into highly echogenic bubbles once they are exposed to sufficient acoustic energy. In this study, we demonstrate formation of lipid-coated nanodroplets based upon condensation of lipid-coated microbubbles containing low boiling point decafluorobutane (DFB). Our droplets are routinely on the order of 300-400 nm range and once vaporized yield microbubbles of 5-6 times bigger according to ideal gas law expansion predictions. Acoustic droplet vaporization (ADV) of the generated phase shift nanodroplets are investigated both optically, using a light microscope, and acoustically in our experimental setup. The acoustic droplet vaporization threshold of our droplets at 10 MHz is around 4 MPa which yields a mechanical index within FDA approved ranges. Since we are using low boiling point perfluorocarbon as the core, low activation energy is required compared to other PSND compounds which minimize the potential for bioeffects in human. Thus, Decafluorobutane nanodroplets may present a new means to safely extend ultrasound imaging beyond the vascular space. Finally, since the ultimate goal of these nanodroplets is for in vivo applications where they will be exposed to different temperatures, pressures and blood viscosity, therefore ADV threshold dependence on these ambient parameters is studied.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Exploration of Energy Efficient and Environmentally Friendly Magnetic Refrigeration System

In contrast with conventional vapor-compression refrigerator systems that work based on compression and evaporation of gas, magnetic refrigeration systems work based on magnetizing and demagnetizing a magnetic material (refrigerant). Magnetic refrigeration is a good candidate for reducing our energy consumption. Magnetic refrigeration is an emerging energy efficient and environmentally friendly refrigeration technology with the following desirable characteristics: (i) it does not use ozone depleting chemicals (CFCs), hazardous chemicals (NH₃) or greenhouse gases (HCFCs and HFCs); (ii) the cooling efficiency of magnetic refrigeration is significantly higher than conventional cooling technology compressor-based techniques; and (iii) the magnetic refrigerator can be built more compactly and generates much less noise make it more suitable for critical applications such as military use.

Magnetic refrigeration exploits a property of magnetic materials called the magnetocaloric effect (MCE): the temperature of ferromagnetic materials is observed to rise upon the application of a magnetic field and fall upon its removal. The heating and the cooling of a magnetic material in response to a changing magnetic field is similar to the heating and the cooling of a gaseous medium in response to an adiabatic compression and expansion in a conventional refrigeration system.

A novel experimental test system with fully-controlled magnetic field, temperature, and time capabilities has been designed and implemented to study the effect of the system's parameters on a reciprocating Active Magnetic Regenerator (AMR) near room temperature. This study focuses on the methodology of a single stage AMR operating conditions (such as frequency, flow rate, flow duration, and displaced ratio) to get a higher temperature span near room temperature.

In contrast to the common belief in the scientific community, the results of this study introduced a new approach of interpreting the ΔT_{ad} measurements emphasizing on the reversibility of the magnetocaloric effect. Also a new parameter "Cooling Factor" has been proposed in order to provide a better understanding of magnetic refrigeration system performance in a given temperature range. In addition the optimal operating conditions of our advanced in-situ magnetic refrigeration system (such as operating frequency, heat transfer fluid flow rate, flow duration, and displaced volume ratio) has been investigated in order to obtain the maximum cooling performance. It is expected that such optimization will permit the design of a more efficient, high performance, and commercially feasible magnetic refrigeration system.

STATUS

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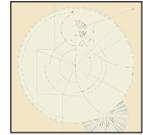
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Impact of Zero-Emission Vehicles on Air Quality and Human Health in Urban Environments

INTRODUCTION:

Electric and hybrid-electric vehicles bear significant potential for a cleaner transportation sector. In recent years, the electrification of the transportation sector has been identified as one critical component emerging conversation of the electric grid [1]. Hypothesized penetration of electric vehicles (EVs) in the automobile market shows full replacement, demonstrating a growing computable concentration of pollutant matter due to EVs supplanting the decreasing concentration due to gasoline vehicles (GVs). The air quality alterations relate to potential effects on the human health, validated with corresponding biological methods. The objective of this project was to investigate and harvest the emission reduction potential in relation to impacts on urban environments. Here we show that with projected adoption replacement of electric vehicles from gasoline vehicles, both local air quality in the metropolitan area of Washington D.C. and the human health of Washington D.C.'s population will quantitatively improve. Our results demonstrate the potential of crosslinking EV adoption with air quality and agreeing health impacts to examine environmental impact.

METHODS:

Our approach first utilized the Bass model to predict the rate of adoption based on a replacement scenario for GV in Washington D.C. for the next 50 years. The Bass model is a non-parametric conditional likelihood model that uses three inputs to forecast the annual number of buyers of a new technology: the maximum market size (m); a coefficient of innovation or number of first-time buyers (p); and a coefficient of likelihood of additional consumer adoption or coefficient of imitation (q) [2]. The Bass model is formalized:

(1) Differentiating and integrating (1) yielded variations of (1), generating a predicted diffusion process. Power mix determination and subsequent power plant emission rate utilized the Geographical Information System (GIS) mapping and two versions of the air dispersion models to estimate the amount of pollutants travelling back to the studied area. Electric vehicles were modelled as point source power plants (their energy suppliers) with the Gaussian Plume Model while gasoline vehicles were considered as line sources with the line source Gaussian model [3]. These models accepted necessary information from Energy Plus sources, generating meteorological input, and combined with power-plant specific inputs to produce concentrations of specified pollutant. The Gaussian Plume model can be computed with:

(2) where C is the concentration of a pollutant at any point (x, y) , Q is the pollutant emission rate (g/m^3), u is the average wind speed at the source level at stack height (m/s), σ_z/σ_y are the vertical/horizontal dispersion coefficients or the standard deviations at z/y axes (m), H is the effective stack height [4]. The line source model can be computed with:

(3a) (3b) The line source model computes the concentration of a pollutant ($\mu g/m^3$) at a point $(X-r, Y_r)$, from line source top and bottom endpoints Y_2 and Y_1 . The dispersion coefficient is calculated using the effective horizontal (x_{eff}) distance (m), or $x/\cos(\theta)$, where θ is the wind angle in radians. The calculation of t_i accounts for error in the model's vertical sensitivity. Visual Basic, Java, and R simulated the dispersion model and generated both raw data and geo-spatial pollutant concentration maps, as a function of technology adaption and replacement. Incidence rate models then allowed estimation of various health impacts, defined by:

(3) here, y_0 is the baseline prevalence of illness per year, β is the coefficient of the concentration change, C exposure is the exposure-related concentration, and P , Population, is the number of persons exposed [5]. For each pollutant, y_0 and β vary.

RESULTS AND DISCUSSION:

The electric vehicle forecast was created using (1), utilizing the logic of the Bass Model. Historical sales are in general the best source for generating accurate forecasts. The department of Energy (DOE) had recently released all EV sales data from December 2013 to August 2014, yielding values of p and q using nonlinear squares procedure [6]. According to the Department of Transportation, in 2010, which is the year where the first EVs debuted in the US market, 159,920 GV had been registered in Washington DC [7]. Therefore, the maximum market size, m , is 159,920. The respective gray and green areas account for error in calculation and for variance in the p and q parameters. According to Figure 1, the peak of new EV users occurs in

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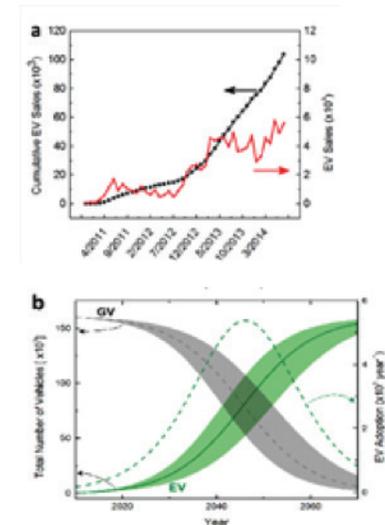
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Figure 1



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ENGINEERING

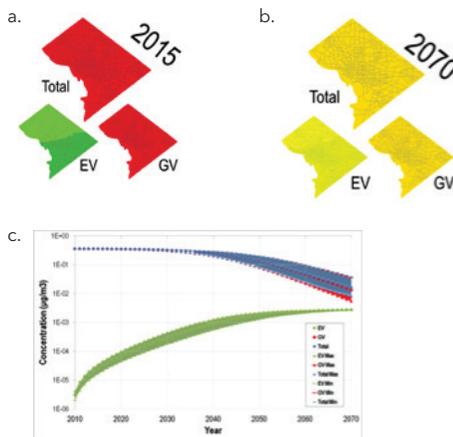


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2047, where 79,959 thousands (cumulative) drivers have purchased one EV. In addition, in the number of EV adopters will equal to the number of GV users (point of intersection). In order to evaluate the concentration levels of various pollutants, emitted from power plants, due to the EV charging, the Gaussian Plume model was used. Combining such with GIS systems resulted in heat-map representations of concentration in the metropolitan area, green indicating lower (healthier) levels of PM2.5 and maroon

Figure 2.

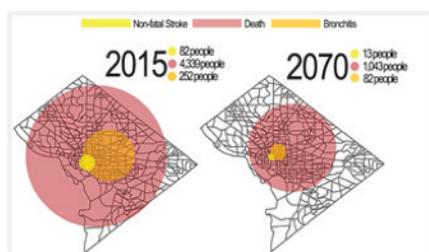
(a). Concentration of PM2.5 in Washington D.C. in 2015, (b). 2070.
 (c). Pollution comparison indicating higher (more toxic) levels of PM2.5.



Figures 2a and 2b provide a brief look at concentration changes from 2015 and 2070, a snapshot at the health of Washington D.C. air due to vehicle emissions. In 2015 there is a five orders of magnitude difference between concentration due to EVs and GVs. By 2070, there is a 907 times increase in annual concentration of PM2.5 due to electric vehicles. There is a 26 times decrease in annual concentration of PM2.5 due to gasoline vehicles. The order of magnitude difference between the two concentrations decreases to one-third from five. It is evident overall Net concentration decreases, but continued modelling of EV use and potential growth in number of vehicles may attribute to a rise in pollution to original 2015 levels. It must be noted neither predicted Corporate Average Fuel Economy (CAFE) standards as anticipated by future federal administrations or transitions to cleaner coal and/or renewable resources as potential power plant replacements were included. Such distinguishable scenarios will be included in future research.

Chronic PM2.5 exposure affects both the respiratory and cardiovascular systems. All-cause mortality, chronic bronchitis, and nonfatal stroke were included as three exposure-related incidences that can be modelled by (3). The current population of Washington D.C. of 646,449 persons was held constant for the 65-year span. Figure 3 is a map of

Figure 3. Health impacts for 2015 and 2070 due to PM2.5 exposure.



Washington DC where the different sized/colored dots signify magnitude and type mortality and morbidity types. The growth in EV vehicle number correlates to a decrease in computed health impact: mortality decreases from 4,339 to 1,043 people, bronchitis cases decrease from 252 to 82 people, and nonfatal stroke instances decrease from 82 to 13 people. The city will be 4 times healthier in 2070 than in 2015 with the replacement of GVs by EVs. The number of those people suffering Washington DC will be healthier with the use Electric Vehicles instead of Gasoline Vehicles.

CONCLUSION:

The main objective of this research is to determine the concentration levels of various pollutants, emitted from power plant stacks, due the increased electricity demand of the growing EV penetration, and how such affects the living environment and health conditions of urban population. It can be concluded that the substitution of gasoline vehicles with electric vehicles in the Washington D.C. urban area contributes to an overall healthier population. However, potential future EV growth, leads to stagnation of decreasing total concentration amounts, approximately in the year 2058. This implicates that by the year 2058, substantial advances must be made in EV battery capacity, a shift from fossil fuels to renewable energies, and improvements in fuel standards must be in place to compensate for the rising concentration due to EVs. Applications of human health affects due to chronic PM2.5 exposure can be extended to various other pollutants, GV-to-EV replacement scenarios, and additional areas of the United States to provide comprehensive conclusions. Future applications include an air pollution dispersion mobile application, where users can investigate the concentrations of pollutants due to the transportation sector in their immediate area. Our research work is fundamental in that expansion to the whole to the United States can contribute to the development of analytical tools and information awareness for future sustainable urban planning, guidance on environmental justice, supposed delineation on smart-grid solutions such as demand-response programs, as well as marketable applications for real estate value.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

3D Printed Microchannels to Create Networks of Endothelial Cells for the Development of a Tissue Engineered Blood Vessel

Cardiovascular disease is the leading cause of death in western nations. Coronary bypass surgery is often performed to treat patients with this disease, but the number of suitable vessels available for this procedure is limited. Vascular tissue engineering (TE) is a developing field which seeks to provide readily available and off-the-shelf alternatives to traditional vascular auto and allografts. Still, remodeling vascular tissue presents a formidable challenge due to the multi-cellular composition, tissue architecture, and various physical and mechanical properties of native vessels. 3D printing has recently emerged as a promising new fabrication technique for scientists and engineers to more precisely control the design of complex structures, such as those found in the vasculature. The focus of this research is to apply 3D printing techniques to fabricate a biomimetic tissue engineered blood vessel for coronary bypass surgeries.

Blood vessels are multi-layered systems with two major cell types: endothelial cells (ECs) and smooth muscle cells (SMCs). ECs line the inner lumen of blood vessels and serve to prevent thrombosis. SMCs surround the EC lining in multiple layers and control the vasoactivity of the construct. The unique alignments of both of these cells contribute to their individual functionality. Specifically, ECs orient themselves in the direction of blood flow, whereas SMCs align circumferentially around the vessel wall. It is the aim of this study to employ stereolithography (SL) printing techniques to fabricate a biocompatible polymer scaffold with channeled architectures to properly align vascular cells in their native orientations. We demonstrate the ability of SL printing techniques to create carefully-aligned poly(ethylene glycol) (PEG)-based hydrogel composite microchannels and quantify the extent of EC attachment and proliferation on their surfaces. Ongoing work is being performed to show the ability of these constructs to support multiple vascular cell types in a multi-layered structure. These cell-seeded polymer sheets will later be rolled up into tubular constructs and mounted in a perfusion bioreactor to improve the cell functionality and mechanical properties of the vascular graft. Overall, this technology shows great potential for 3D printing blood vessels to provide additional off-the-shelf vascular graft options for patients in need.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Flow over a surface-mounted obstacle in steady and unsteady flow

Flow separation over a surface-mounted hemispheroid is prevalent in countless applications, both under steady (constant velocity) and unsteady flow over the protuberance. Previous studies of 3D separation have been limited to steady flow. In biological and geophysical flows, pulsatile conditions are much more commonly observed, yet this combination of parameters so far hasn't been studied. Primarily motivated by previous studies of the flow conditions observed in various geometric human vocal fold pathologies, our research aims to fill this gap in the knowledge of 3D flow separation. This is achieved by characterizing surface pressure fields and velocity fields, focused primarily on the vortical flow structures and dynamics which occur around a hemispheroid in pulsatile flow conditions. As part of this study, surface pressure and two-dimensional, instantaneous and phase-averaged, particle image velocitremy data in steady and pulsatile flow are presented and compared. Flow separation over a surface-mounted hemispheroid is prevalent in countless applications, both under steady (constant velocity) and unsteady flow over the protuberance. Previous studies of 3D separation have been limited to steady flow. In biological and geophysical flows, pulsatile conditions are much more commonly observed, yet this combination of parameters so far hasn't been studied. Primarily motivated by previous studies of the flow conditions observed in various geometric human vocal fold pathologies, our research aims to fill this gap in the knowledge of 3D flow separation. This is achieved by characterizing surface pressure fields and velocity fields, focused primarily on the vortical flow structures and dynamics which occur around a hemispheroid in pulsatile flow conditions. As part of this study, surface pressure and two-dimensional, instantaneous and phase-averaged, particle image velocitremy data in steady and pulsatile flow are presented and compared. Coherent vortical flow structures have been identified by measure of their swirling content. This is analysis has revealed a novel set of flow structures completely dependent on the pulsatile forcing function. This is analysis has revealed a novel set of flow structures completely dependent on the pulsatile forcing function.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

3D Printed Bioactive Scaffolds for Osteochondral Regeneration

STATEMENT OF PURPOSE:

Osteoarthritis (OA) is clinically defined as the progressive degeneration of hyaline cartilage within articulating joints leading to structural and functional failure at the interface. Reduced joint mobility and severe pain due to articular cartilage and subchondral bone (collectively known as osteochondral tissue) damage is common to patients suffering from OA. Current treatment methods used to address these defects include autografts, allografts, and mosaicplasties which contain their own inherent limitations, including donor site morbidity, infection, poor tissue integration, and insufficient neovascularization. Therefore, the objective of this work is focused on the manufacture of three-dimensional (3D) bioactive nanocomposite scaffolds for osteochondral tissue regeneration.

METHODS:

For the current work, a porous and highly interconnected poly(ethylene glycol) diacrylate (PEG-Da) hydrogel scaffold containing graded nanocrystalline hydroxyapatite (nHA) was fabricated via our novel table-top stereolithography 3D printer based on the open-source Solidoodle platform. Various in-fill densities (40% - 80%) of 60wt% PEG-Da in PEG were evaluated for cell adhesion. Three-layer scaffolds were fabricated with increasing nHA concentration (20%, 10%, 0%) of the best performing in-fill density. In addition to osteoconductive nHA, transforming growth-factor $\beta 1$ (TGF- $\beta 1$) was incorporated within the smooth articulating cartilage layer (top) at a concentration of 10 ng/mL. Wet co-axial electrospraying was employed to fabricate poly(lactic-co-glycol acid) core-shell nanospheres for sustained delivery. Human bone marrow-derived mesenchymal stem cells (MSCs) were seeded onto control and graded scaffolds and evaluated for adhesion, proliferation and osteochondral differentiation in vitro.

RESULTS:

The current work has focused on the development a novel 3D printed bioactive nanocomposite scaffold for osteochondral tissue regeneration. CAD models with optical and scanning electron micrographs of fabricated control and graded nHA scaffolds illustrate good integration between the respective layers producing a highly porous osseous tissue-like porous structure combined with a smooth articular cartilage top layer. In addition, through with the incorporation of the developed sustained release nanospheres we have shown the capacity of extended bioactive factor release when compared to bare incorporated growth factor.

Mesenchymal stem cell proliferation illustrates the capacity of nanocomposite 3D scaffolds to induce increased cell proliferation wherein expedited cell differentiation can be facilitated. Confocal microscopy images of MSCs seeded upon the porous structure illustrate the effectiveness of incorporated nHA in the promotion of cell spreading and adhesion.

In addition, two-week morphogenetic differentiation demonstrated the efficacy of early (glycosaminoglycan) (Figure 6) and late-stage chondrogenic (Type II collagen) and late-stage osteogenic (extracellular calcium) biological markers.

CONCLUSIONS AND FUTURE WORK:

The current work illustrates the efficacy of our current 3D printing technology for efficient fabrication of the novel nanocomposite hydrogel materials with good spatiotemporal control of morphogenetic nanomaterials. In addition, tissue-specific growth factors illustrated a synergistic effect leading to increased cell adhesion and directed MSC differentiation. Mechanical testing illustrated improved strength with the incorporation of reinforcing bioactive nano ceramics.

STATUS

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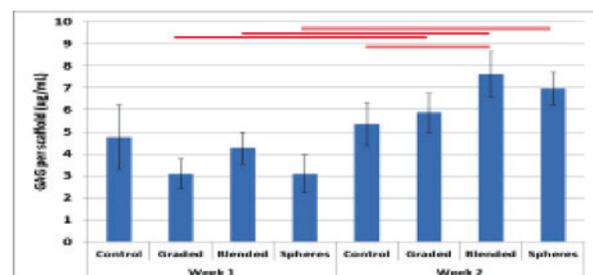
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Figure 6





SCHOOL OF ENGINEERING & APPLIED SCIENCE

Vital Ring: a Wearable Wireless Multiple-Lead ECG Sensor

Electrocardiogram (ECG) is an important tool widely used in the clinical diagnostic of heart diseases. It can be used to diagnose symptoms of myocardial infarction, pulmonary embolism, etc. [1] Among those symptoms, detection and early warning of the potential of heart attack such as myocardial infarction can be crucial in daily life for patients, especially those who live alone, because once happened, it need to be taken immediate care of. Unfortunately, the traditional equipment currently used in the hospital cannot fulfill this real-time on-demand monitoring requirement. To address this problem, the wearable ECG monitoring system comes into play.

Recently, wearable healthcare devices have attracted considerable interest both in the academic and industry. The important role ECG playing in the heart disease diagnostic and the convenient noninvasive way of measurement makes it an ideal candidate to be converted to wearable healthcare device, and have already draw many researchers' attention. Y. Chi and G. Cauwenberghs at UCSD have demonstrated a wireless ECG/EEG monitoring system using noncontact electrodes. [2] The gel free noncontact electrodes make the wearing of the device more comfortable and cleaner. However, their electrodes are rigid which makes it less compatible to soft human bodies. Moreover, it is uncomfortable to wear several hard electrodes of noticeable sizes. AliveCor® developed a single-lead ECG monitoring system in the smartphone case format, which can monitor the ECG at fingertip and displays on the smartphone screen. This system has gotten FDA approval, which confirms the possibility to achieve a wearable ECG system. Unfortunately, single-lead ECG measurements, which apply to all existing systems, cannot be used to diagnose myocardial infarction. The phone case format makes it convenient to carry around, but, on the other hand, limits it to single-lead measurement only. IMEC® developed a long term multiple-lead ECG monitoring patch, which can be attached to the upper body and last as long as one month. The only drawback is the usage of conduction gel, which is commonly used in the traditional ECG. The sticky gel is difficult to keep clean. Moreover, it can cause allergy to some patients [3]. The IMEC system uses Bluetooth Low Energy (BLE) to transfer data, which is suited for wearable healthcare equipment because of the low energy consumption and sufficient transfer rate. However, a dedicated BLE data transfer base device in their device is not necessary, because there are many BLE enabled devices available now, such as smartphones and laptops. Using a smartphone to communicate with these wearable devices is convenient, because people carry smartphone around and the smartphone has the ability to further analyze the data, to transfer the data to the physicians, and/or to upload the data to a database.

In this work, we propose and demonstrate a wearable ECG monitoring system capable of providing on-demand multiple-lead ECG signals in the format of a flexible finger ring. Such extreme form factor is enabled by a novel soft electronics/microfluidics co-packaging technique recently developed by us [4]. The flexibility is a key advantage to achieve a comfortable device, and also provides certain durability during impact. We will also use dry electrodes to eliminate the skin reaction issue and the clean issue mentioned before. We will use BLE to transfer the data to smartphone or laptop for further analysis of the data.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Integrating 3D Bioprinting and Cold Atmospheric Plasma for Cartilage Regeneration

Cartilage tissue is hard to regenerate naturally due to its extremely poor regenerative capacity, avascular nature, and complex stratified structure. In this project, we combined the 3D bioprinting method of stereolithography with cold atmospheric plasma (CAP) treatment to create complex poly (ethelene glycol) diacrylate: (poly ethelene) glycol (PEG-DA:PEG) hydrogel scaffold structures that guide the regenerative process. Three scaffold geometries were printed and seeded with human bone marrow mesenchymal stem cells (hMSC) for a four hour adhesion study: square cross-hatch, graded cross-hatch and hexagonal infill. The cross-hatch designs proved to be the best two geometries and were then selected to undergo a five minute CAP treatment for biomimetic surface modification. They were then cultured in complete stem cell media for a 1, 3 and 5 day proliferation study and chondrogenic stem cell media for a two week differentiation study. CAP treated scaffolds showed increased cell proliferation over non-treated scaffolds. During differentiation, CAP treated scaffolds facilitated Type II Collagen production only in week one and did not have a sizable effect on glycosaminoglycan (GAG) production. Therefore we conclude for pore geometries, that since the size of the cross-hatch pores appears to be smaller than the hexagonal pores, our data is consistent with the statement that the ideal size range is ~300 um for hMSC growth shown in other studies. As for the CAP treatment, since it is only a surface modification of a biodegradable hydrogel and PEG degrades both through surface erosion and bulk degradation through hydrolysis, the retention of the surface charge is short and therefore the short-term experiments would tend to perform better.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Development of 3D Printed hydrogel scaffold with core-shell nanoparticles for nerve regeneration

Neural tissue engineering is being explored in an effort to develop artificial nerve scaffolds to overcome the limitation of autologous transplantation. Particularly, advancement in both 3D scaffold fabrication strategies and nanotechnology has inspired this field into a new era. Nerve scaffolds can be fabricated by various methods. Amongst them, 3D printing techniques have drawn great interest because they can prepare scaffolds with highly controlled spatial architecture to meet the customized requirements. In addition to the customized architecture, drug delivery system is highly encouraged to incorporate in nerve scaffolds. An effective neurogenic factor delivery system can successfully facilitate neurite outgrowth and tissue regeneration. Since many human neural tissue extracellular matrix components are nanometer in dimension, nanoparticles are considered a robust neurogenic factor delivery device for enhancing nerve regeneration. Therefore, in this study, we developed a novel nerve scaffold by integrating 3D printing technique and nanoparticle drug delivery system. In particular, poly lactic-co-glycolic acid (PLGA) core-shell nanoparticles with encapsulated BSA (Bovine serum albumin, a model bioactive factor) were fabricated via a coaxial electrospaying technique. Then, the nanoparticles were embedded inside poly (ethylene glycol) diacrylate (PEG-DA) hydrogel solution and printed by a SL based 3D bioprinter. SL printed scaffolds were designed as square pattern with small, medium, and large and small pores geometry (corresponding to 44%, 56%, and 68% porosity) using computer aided design software. For the nanoparticles embedded scaffolds fabrication, lyophilized nanoparticles were blended with printable solution by ultrasonication in concentrations of 0.1%, 0.5%, and 1%, respectively. PC-12 cells (ATCC) were seeded onto prewetted scaffold and evaluated for adhesion and proliferation study. Preliminary results illustrated the uniform morphologies of nanoparticles and printed scaffolds. 4 h cell adhesion study showed the scaffolds with 68% porosity can significantly improve cell attachment compared to other two groups. Then three more groups of scaffolds (68% porosity) with different concentration of BSA/PLGA nanoparticles were prepared for proliferation study. Compared to control group, PC-12 cells proliferate significantly on scaffolds with nanoparticle. Current 3D printing technology allows fabrication of nerve scaffolds with controlled porous structure. Meanwhile, bioactive factor nano delivery system was effectively incorporated inside scaffolds and improved neural cell adhesion and proliferation, thus promising for improved neural regeneration.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Dynamics of a Viscoelastic drop

Emulsions of drops make up many important liquids. For example blood, crude oil, milk and paint. Understanding their flow properties is essential. Based on the behavior of a single drop, coarse-grained models for bulk properties can be used to great advantage. Studying a single drop allows to isolate and understand the physics behind their behavior. In the present work, a viscoelastic drop is suspended in a Newtonian fluid. The deformation of the drop under time periodic flows is investigated numerically.

The numerical method used is a finite-difference front-tracking operator split projection method for solving the multiphase incompressible Navier-Stokes equations with viscoelasticity described by a finitely extensible nonlinear elastic model (FENE -MCR). The implementation can be used to model a combination of viscoelastic and Newtonian phases. The drops are subjected to Oscillating planar Extensional Flow (OEF) and Rotating planar Extensional Flow (REF) as these have been proposed in literature as useful flows to study micro-rheological behavior. The effect of elasticity is systematically studied.

The important forces in this scenario are due to inertia, surface tension, viscous stress and polymeric stress. Viscoelasticity supports shear wave propagation and this is evident in the results. When the forcing frequency matches the resonance frequency of the system, increased deformation has been observed. The results also indicate that viscoelasticity causes the drop to stretch along the stagnation line. This does not happen for a purely viscous drop and has not been reported previously in literature.

The drop resonance due to viscoelasticity means that, at the right frequency, viscoelastic drops may break up more easily than Newtonian drops under otherwise similar conditions. This, while being of fundamental interest, is also relevant for several practical applications.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Characterization and Application of Layered Transition-Metal Dichalcogenides as Broadband Absorber and Excitoplasmonic Sensor

Material characterization of monolayer molybdenum disulfide (MoS₂) is studied. Optical image and Atomic force microscope (AFM) characterizations indicate the morphology and thickness of as-grown film on SiO₂/Si substrate. Raman signal and photoluminescence spectrum at different points of individual crystallites reflect the crystalline quality and optical properties of the sample. In our experiment of Raman scanning, we measure the A_{1g}/E_{12g} peak intensity ratio of 1.54, which indicates that there could have native defects such as interstitials and vacancies present in the sample. Overall material can be summarized to be of high chemical purity but with native defects and good crystalline. The developed permittivity model is introduced to represent the monolayer MoS₂ under different biasing conditions for the design and simulation of MoS₂ based devices. Future nano-excitoplasmonic sensor devices will most likely be based on strong excitonic atomically thin layered chalcogenides material supported with plasmonic structure of the device. Simulation results of the structure comprising monolayer MoS₂ under both bias and unbiased condition on top of a plasmonic structure reveals the application in excitoplasmonic sensor. Furthermore we discuss the implementation of monolayer MoS₂ in a finite Bragg stack geometry of alternate high- and low- index films as MoS₂ and SiO₂, respectively, which can be used as efficient (~95 % of average absorption), broadband (entire visible spectrum) and nearly polarization-independent absorbers towards application in photovoltaic cell.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Three Dimensional Printing of Gradient Scaffolds to Bridge the Gap Between Bone and Cartilage for Osteochondral Defect Repair

Osteoarthritis (OA) is a degenerative joint disease with symptomatic joint pain and dysfunction.¹ In 2005, 47.8 million Americans were diagnosed with OA; this number is expected to grow to 67 million by 2030. Of this increasing population, 33% will be workforce contributors aged between 45 and 64 years.² This condition adversely affects patient quality of life and indirectly impacts economic productivity through reduced contribution to the work force and increased disability compensation. In addition, the increasing national obesity epidemic may prove a substantial contributing factor not currently included in the 2030 prediction.² Increased weight may lead to increased joint loading thus inducing or further exacerbating acute trauma and progressive degeneration.

Pathologically, joint degeneration is caused by gradual loss of cartilaginous tissue at the joint surface. Existing minimally-invasive methods of treatment or mitigation of disease progression exist, but in most severe cases, all treatments eventually lead to total joint arthroplasty. Tissue engineering (TE), however, holds great promise for developing methods of repairing damaged tissue. TE applies the principles of engineering and life sciences for the development of biological substitutes that restore, maintain, or improve tissue function.³ For joint repair, cells can be harvested from the patient, seeded and grown upon a three dimensional (3D) scaffold in vitro, and transplanted back into the patient after desired cellular differentiation. The challenge with such scaffolds at joint surfaces is the diverse nature of bone and cartilage extracellular composition and mechanical properties, specifically at the osteochondral interface.

This research hypothesizes that a gradient 3D scaffold, where pore size varies over the scaffold thickness, will have the ability to meet the needs of the bone and cartilage regions, as well as, the osteochondral interface. Successful gradient differentiation over the thickness of the scaffold would indicate an ability of this implant to promote bone, cartilage, and osteochondral repair and growth in vivo.

Fused Deposition Modeling (FDM) of High Impact Polystyrene (HIPS) created the scaffold molds. A PEG/PEGDA hydrogel solution filled each mold and cured under ultraviolet light until firm. Heated sonication in a Dilimonene, ultrapure water solution, assisted in leeching the HIPS out of the hydrogel leaving a porous, channeled scaffold of PEG/PEGDA.

After leeching, the scaffolds were sterilized under UV light for 30 minutes. Cell adhesion was executed by covering each scaffold with a solution of mesenchymal stem cells (MSC) in media for four hours. After four hours the scaffolds were removed from the solution and cells lifted with Trypsan. These cells were then counted using a spectrometer to determine cell adhesion values for each scaffold.

The biphasic and triphasic scaffolds both outperformed the homogenous scaffolds and the control significantly. We expected these two scaffolds to perform well because they both have high pore density; however, we also expected homogeneous scaffold 4 to have a similar performance because it too has a high pore density. This result indicates that pore density is likely less important than pore distribution. Scaffold 4 and 2 have uniform distribution of pores. Scaffold 4/2 and 4/3/2 are discontinuous at the phase boundaries. This indicates that the cells in the continuous models (4 and 2) are traveling through the channels to the other side of the scaffold without getting trapped or adhering within. The discontinuous scaffolds promote cell captivation forcing transport throughout the scaffold. This is causing more cells to become trapped within the scaffold, attaching to the scaffold walls within the pores, rather than traveling straight through the channels without adhering at all.

Each scaffold also went through compression testing. The homogeneous sample with smaller spacing, contributing to a larger number of total pores, and the biphasic sample had the lowest peak stresses. The triphasic sample had the largest peak stress of all of the samples, even with a considerable pore density. This is likely due to the misalignment of pores created by the middle layer. This misalignment reduces crack propagation in the sample and allows it to carry a larger load than those with increased pore alignment. The modulus of elasticity results did not follow the stress results. The homogeneous sample with the lowest porosity outperformed all other samples, however, the improved performance was not statistically significant compared to the triphasic sample. This is likely due to the compressive deformation. More evaluation is required to determine significance of porosity and pore distribution on deformation.

The initial adhesion results show promise for improved cell adhesion in scaffolds with discontinuous pore distribution. Mechanical testing indicates improved strength with a discontinuous pore distribution, however more investigation of the effects of scaffold deformation is necessary to improve the modulus of elasticity. Moving forward, cell proliferation and differentiation tests are necessary to determine how time impacts scaffold performance. For differentiation testing nanoparticles and/or growth factors will be introduced to promote a bi or tri-phasic differentiation in support of the diverse bone, osteochondral, cartilage region these scaffolds intend to support.

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ENGINEERING



SCHOOL OF ENGINEERING & APPLIED SCIENCE

Creating Automated Instructional Tools for Adult Literacy Education

According to the American Library Association, 14% of adults in the United States cannot “search, comprehend, and use continuous texts” [1]. Current government and philanthropic funding only indirectly helps 3 of these nearly 30 million individuals. There is therefore a significant opportunity for the development of technology to help improve literacy rates. Little research has yet been done on either the design of software for low-literacy users or its long-term impact. The goal of the CAPITAL project is to make high quality learning resources accessible to users of all literacy levels. The project aims to automatically create exercises based on instructor specified parameters that will help users improve their reading skills using a smartphone application, CAPITAL Words. Design choices needed to be made to cater to the unique needs of low-literacy users. We eliminated nearly all text, relying instead on minimalistic pictorial representations in our app to convey instructions.

We tested our app in order to evaluate our software both on the intuitiveness of its design, and on its general learnability. 15 total students from the Washington Literacy Center participated in a guided think-aloud exploration of the app. Students were presented with a 5- minute video which outlined the purpose of our software and how to think aloud. Their successes and failures were tallied for each task:

1. Enter designated Course
2. Take Lesson
3. Answer each question
4. Re-enter previously-completed Lesson.

At no time would we answer questions or provide hints for how to accomplish a task, and only would interfere if the student explicitly “gave up” after repeated failures. Following the test, each student was given an anonymous survey addressing overall perceptions of the app.

Ultimately, the think-aloud study proved that the application was intuitive enough that users were able to navigate exercises. The learnability results show that subjects can learn to use the software and have success over time. Additionally, the feedback from the students in the post-test survey was overwhelmingly positive in their want to use the app after the study and ease of use. Currently, the application is deployed on six subjects’ personal devices. Their progress is being monitored using the online instructor interface. The next step in the CAPITAL project is designing to algorithmically generate questions from a reading passage. The focus on CAPITAL Passages questions will be on comprehension of the reading material, as opposed to CAPITAL Word’s emphasis on pronunciation.

[1] “Outreach Resources for Services to Adult New and NonReaders.” American Library Association, n.d. Web. 13 Nov. 2014.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Spiral Solar Cell

Recent investigations of semiconducting two-dimensional (2D) transition metal dichalcogenides have provided evidence for strong light absorption relative to its thickness attributed to high density of states. Stacking a combination of metallic, insulating, and semiconducting 2D materials enables functional devices with atomic thicknesses. While photovoltaic cells based on 2D materials have been demonstrated, the reported absorption is still just a few percent of the incident light due to their sub-wavelength thickness leading to low cell efficiencies. Here we show that taking advantage of the mechanical flexibility of 2D materials by rolling a molybdenum disulfide (MoS₂)/graphene (Gr)/hexagonal boron nitride (hBN) stack to a spiral solar cell allows for solar absorption up to 90%, without the need to contact each layer separately. The optical absorption of a 1 μm -long hetero-material spiral cell consisting of the aforementioned hetero stack is about 50% stronger compared to a planar MoS₂ cell of the same thickness; although the volumetric absorbing material ratio is only 6%. A core-shell structure of the spiral exhibits enhanced absorption and pronounced absorption peaks with respect to a spiral structure without metallic contacts. The overall efficiency of the core-shell cell is estimated about 15%. We anticipate these results to provide guidance for photonic structures that take advantage of the unique properties of 2D materials in solar energy conversion applications.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

A Compressible High-Order Unstructured Spectral Difference Code for Stratified Convection in Rotating Spherical Shells

We present a novel and powerful Compressible High-ORder Unstructured Spectral-difference (CHORUS) code for simulating thermal convection and related fluid dynamics in the interiors of stars and planets. The computational geometries are treated as rotating spherical shells filled with stratified gas. The hydrodynamic equations are discretized by a robust and efficient high-order Spectral Difference Method (SDM) on unstructured meshes. The computational stencil of the spectral difference method is compact and advantageous for parallel processing. CHORUS demonstrates excellent parallel performance for all test cases reported in this paper, scaling up to 12,000 cores on the Yellowstone High-Performance Computing cluster at NCAR. The code is verified by defining two benchmark cases for global convection in Jupiter and the Sun. CHORUS results are compared with results from the ASH code and good agreement is found. The CHORUS code is transformative and creates new opportunities for simulating such varied phenomena as multi-scale solar convection, core convection, and convection in rapidly-rotating, oblate stars.

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Electrospinning of Highly Reactive Pd-Carbon Nanofiber Catalysts for Hydrogenation of Waterborne Contaminants

Palladium (Pd)-based catalytic reaction holds great promise to remove a broad range of persistent waterborne contaminants, and it promotes advanced water treatment as well as water reuse. Nanoparticulate Pd is always used for catalytic reactions due to their large surface area to volume ratio and enhanced reactivity. Immobilization of Pd nanoparticles onto a support is essentially important because it improves the reusability and recyclability of the catalytic precious metal, maintains high nanoparticle dispersion in reaction, and enhances catalytic reactivity through a strong support-metal interaction. Carbon nanofibers (CNFs) are an ideal support for Pd catalysts because of their large surface area, little to no micropores, versatile surface functional groups, and economical feasibility. These properties enable increased Pd dispersion and minimized mass transfer limitations to promote catalytic reactivity significantly.

To create hydrophilic functional groups on CNF surface for a better Pd dispersion, concentrated strong acids (e.g., HNO₃, H₂SO₄) are always used to etch CNF surface at an elevated temperature. However, this method is costly, time consuming, energy intensive, difficult for handling, and non-sustainable due to acidic waste generation. We aim to develop an in situ Pd loading method for the CNF support without pretreatment.

Electrospinning is a versatile and industrial viable approach for a mass-production of CNFs. Briefly, a polyacrylonitrile (PAN) solution is withdrawn from a blunt needle under a high electric field (usually kV/cm), and produced ultrathin nanofibers self-assemble as a non-woven membrane. The as-electrospun polymeric nanofibers are annealed at an elevated temperature to convert to the CNFs. Pd-loaded CNFs is able to be produced by electrospinning a mixture of Pd salt (e.g., Pd acetylacetonate (Pd(acac)₂)) and PAN solution; however, the majority of formed Pd nanoparticles are embedded in CNFs. These Pd nanoparticles show little to no catalytic activity because of limited exposure to contaminants during reduction.

The objective of this research is to electrospin Pd-loaded CNFs with enhanced Pd exposure and reactivity for waterborne contaminant removal. Terephthalic acid (PTA) was used as a porogen because it sublimates in the annealing process and creates macropores. Pd-loaded CNFs with PTA showed an enhanced catalytic reactivity (reduction rate constant of 0.0181 L min⁻¹ (g catal.)⁻¹). Without the presence of PTA, the formed Pd-loaded CNFs did not show any catalytic reactivity. Selection of Pd acetate as the precursor produced a highly reactive Pd/CNFs catalyst, and the reduction rate constant was 0.614 L min⁻¹ (g catal.)⁻¹, which was 33.9-fold increase compared with PTA sample. This pioneer study is innovative because it provides a facile synthesis strategy for the production of highly reactive Pd-loaded CNFs.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

System and Material Parameter Effects on Thermoelectric Power Generation in a Tankless Water Heater

One of the major causes of inefficiency in energy systems is heat loss. Similar to other combustion systems, there is a large amount of heat loss in water heaters. Water heater is a kind of heat exchanger in which water and gas flow through and over the pipes respectively. When natural gas is burned to heat water, the outlet gas temperature is very high and notable amounts of unused heat are still available to harvest. The large temperature gradient between gas and water in water heaters is ideal for thermoelectric cogeneration. Thermoelectric module can turn a temperature difference into electricity by exploiting the flow of electrons from a warmer area to a cooler one. Thus, they can theoretically turn wasted heat into a power source. They are an attractive cogeneration solution because they are light, silent, and have no moving parts. In this study, the performance of a system comprised of a water heater and thermoelectric generator is investigated and the goal is to optimize the thermoelectric power generation by investigating both system and material parameters. There is a distinction between increasing the thermoelectric efficiency by varying the thermoelectric properties and whole system efficiency. Many researches have been done to increase thermoelectric efficiency merely by improving material properties; however, this work is important because it determines the effects of system parameters as well. The finite volume method is used as simulation technique. Thermoelectric module is modeled as a ring shape structure and is attached to the internal wall of the pipe. Results demonstrate that thermoelectric module power output increases the most when the pipes are arranged horizontally in parallel rather than vertically stacked. Doubling the convection coefficient can increase the electrical power output by 50%. It is concluded that among all the investigated parameters, reduction of thermal conductivity (a material parameter) causes in the highest increase in output power while thermal interface materials (a system parameter) can severely limit it.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Achieving Sustainable Water Treatment: Graphitic Carbon Nitride for Persistent Waterborne Contaminant Removal with Visible Light Irradiation

Solar-energy-enabled photocatalysis is a sustainable technology to destruct persistent environmental pollutants. Graphitic carbon nitride (g-C₃N₄) has emerged as a novel polymeric photocatalyst because of its capability to utilize visible light, low cost, great stability, and no toxicity, however its application in environmental remediation is largely underexplored. Preliminary results indicate that urea-based g-C₃N₄ has the highest reactivity in phenol degradation under visible light irradiation (>400 nm) compared to counterparts from melamine, dicyandiamide, and thiourea (1st order rate constant of 0.026 min⁻¹ vs. 0.003-0.004 min⁻¹). Microscopic characterization shows an increased surface area and carbon doping in urea-based g-C₃N₄ improves charge separation, visible light utilization, and corresponding reactivity. However, the extreme low urea-to-g-C₃N₄ yield (1-5 wt %) compromises catalyst practicality. We next developed a supermolecule-based g-C₃N₄ from melamine, cyanuric acid, and barbituric acid with significantly improved yield (25-30 wt %) and similar reactivity compared to urea-based g-C₃N₄ in phenol degradation (0.027 min⁻¹). This method is superior because it is highly tunable to produce g-C₃N₄ with an enlarged surface area and an optimum carbon doping level. This study paves a new avenue for application of a new visible-light-responsive photocatalyst for persistent contaminant removal, and addresses challenges in sustainable water treatment and water-energy nexus.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Enhanced Stem Cell Functions on Cold Atmospheric Plasma Treated Composite Cartilage Scaffolds

Articular cartilage connects diarthrodial joints, lubricates surface between bones, transfers and withstands repetitive load over the lifetime, which is prone to degeneration by various diseases, trauma and injuries. Once degeneration takes place, the avascular structure of human cartilage makes the self-healing extremely challenging. Therefore, the main objective of this study is to fabricate a biomimetic cartilage scaffold by integrating electrospinning and cold atmospheric plasma (CAP) techniques. Particularly, CAP is an ionized gas with various electrons, positive/negative ions, and excited molecules. It was utilized to create a more biomimetic and biocompatible surface of the electrospun cartilage scaffold. For this purpose, a polycaprolactone (PCL) scaffold with randomly distributed microfibers was electrospun. Poly(lactic-co-glycolic) acid (PLGA) was employed to fabricate bioactive factor loaded microspheres using a water/oil/water double emulsion solvent extraction method and deposited into electrospun fiber mat. The composite scaffolds were further modified using CAP for 0, 1, 3 and 5 min. Scanning electron microscopy results illustrated the electrospun fibers had uniform diameter distribution and microspheres were homogenously embedded inside the scaffold. The human bone marrow mesenchymal stem cell (MSC) experiments showed that the cartilage scaffold with bioactive factor loaded PLGA microspheres can sustainably improve MSC growth after 7 days. Furthermore, CAP modified composite scaffolds had enhanced cell proliferation after 5 days culture. It is ascribed to both the improvement of hydrophilicity and adhesion-mediating proteins adsorption (vitronectin) on CAP modified scaffolds. The enhanced stem cell response rendered by CAP treatment and microspheres makes our scaffold promising for improved cartilage regeneration.

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Improving the Cost-Effectiveness of Inpatient Cardiac Monitoring

The utilization of telemetry services has been characterized by immense practice variation and is rife with overuse. Such programs are expensive, labor intensive, and are used ubiquitously; however, studies have shown that arrhythmia detection technology affects clinical management in only 3.4% to 12.7% of patient cases. In fact, estimates show that the typical 400-bed hospital could slash costs by \$250,000 annually by reining in undue utilization of cardiac monitoring. By scaling back the discretionary use of these services, health care costs can be reined in without impairing patient outcomes and other measures of quality. As a result, the Choosing Wisely Campaign and the Society of Hospital Medicine is targeting unnecessary inpatient use of cardiac monitoring.

The George Washington University Hospital is ripe for a quality improvement initiative to counter the excessive use cardiac monitoring services. In the week of February 9, 2015, the non-ICU telemetry division reported peak utilization at 86 patients per day. Subsequent weeks demonstrated that utilization levels oscillated between 50-60 patients on a daily basis.

The quality improvement plan entailed the use of a checklist to reduce practice variation in telemetry services by the inpatient medicine ward teams. The checklist contained all of the indications for telemetry and levels of evidence behind each indication. This checklist was replicated from guidelines published by the American Heart Association in 2004 and have been replicated at the University of Pennsylvania and Christiana Care Health System.

Since physicians authorize orders for telemetry services, the checklist strategy focused on doctors, specifically internal medicine residency house staff who usually admit and care for patients. Each week, new incoming medicine residents were sent emails of the checklist and were asked to make decisions on cardiac monitoring that were consistent with checklist indications. In addition, the on-call night float resident would personally deliver a paper copy of the checklist to the daytime on-call team in order to stress the importance of curbing unnecessary use of telemetry. This initiative lasted for 3 weeks and utilization data was collected at the end of the 3 weeks to assess the impact of the intervention.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

2D and 3D Microimaging Approaches for Identifying Biomarkers in 22q11/DiGeorge Syndrome Mouse Model

DiGeorge Syndrome/22q11 (LgDel) deletion is a genetic developmental disorder that compromises craniofacial development. Individuals with DiGeorge Syndrome often have feeding and swallowing difficulties (dysphagia) due to the abnormal coordination or development of the caudal cranial nerves. This project focused on validating a mouse model for studies of dysphagia in 22q11DS by crossing a ChAT-GFP reporter line with 22q11 deletion mouse. ChAT is a well-established marker for cranial motor neurons. The resulting 22q11/ChAT-GFP was used to search for abnormalities in the caudal cranial motor neurons. We established a workflow to acquire complex image data from cranial motor nuclei, structure this data, and analyze outcomes, including the size and density of GFP-labeled cells. ChAT-GFP; LgDel animals were identified by PCR genotyping. The brainstems were prepared and cut into 100µm thick serial sections using a vibratome. Images were captured as stitched 2D and 3D image series using linear spectral unmixing to eliminate excessive autofluorescence. Images were stitched using software to generate a single image set. The 2D and 3D data sets were then analyzed using Volocity and Imaris image visualization and analysis software. A protocol to separate individual cell bodies based on cell size was designed and validated. This approach allowed for the analysis of morphology, size, and volume of the hypoglossal, facial and other cranial motor neurons. This study resulted in the successful generation of a novel mouse model by crossing the LgDel mouse with the ChAT/GFP reporter line. In addition, the combination of using 2-D registrations as well as optically sectioned 3-D registrations helped to effectively visualize the neurons with high resolution. Furthermore, the analysis showed that motor neuron cell size could serve as a biomarker for the severity of the deletion outcome. Cell size difference may be related to the passive membrane properties alterations and excitability changes, which in turn may result in abnormal innervations of the targeted muscles. The many techniques used in this study support and validate the use of LgDel/ChAT/GFP mouse model as well as confirm the utility of spectral imaging to produce high contrast images that specifically address the identification of biomarkers in the cranial motor nuclei.

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Effectiveness of Voice Intensive Program for Transgender (VIP-TG) for Nine Male-to-Female Speakers

BACKGROUND:

People who are transgender seek services from speech-language pathologists to change their interpersonal communication to achieve congruency with their genuine gender and desired presentation. Acoustic and voice quality changes after therapy have resulted in desired gender perception outcomes. Patel, Bless, & Thibeault (2008) suggest voice quality of dysphonic speakers could be improved with intensive therapy format; this study aims to apply their hypothesis in voice therapy for male-to-female transgender (MTF) people. We hypothesized that our 4-hour Voice Intensive Program for Transgender (VIP-TG) for MTF people, which focuses on evidenced-based therapy targets of pitch elevation, oral resonance, and intonation, would achieve positive outcomes in a short amount of time.

METHODS:

The VIP-TG followed a standardized therapy protocol, modified to an appropriate goal level for each participant. Treatment utilized a physiologic approach to voice therapy, achieving optimal voice quality through altering the physiology of voice production while targeting behaviors (pitch elevation, oral resonance, and intonation) that are evidenced to improve perception of voice femininity. Nine participants were assessed pre/post the VIP-TG workshop. Assessment included acoustic measures (sustained vowels and habitual pitch in reading and conversation), perceptual ratings (overall femininity and likability of voice, CAPE-V: voice quality of participant's voice including overall severity, roughness, breathiness, strain, loudness, and pitch), and self-rating measures (Transsexual Voice Questionnaire-Male to Female [Dacakis, et al. 2013] and self-perception of voice). Further, the relationships between participant characteristics and treatment gains were tested.

RESULTS:

Aggregate data was examined using medians and non-parametric statistics. F0 during production of vowels and conversation significantly increased following the VIP-TG. Increases in SFF appear to be due to elevation of lowest frequency, as highest frequency did not change significantly. Changes in formants did not reach level of significance. Time presenting full time in the female role and amount of previous voice treatment were significantly and inversely related to gains in this program. All participants' self-ratings of satisfaction with their voice, voice femininity, and voice likeability increased significantly after the VIP-TG. All participants gave a positive evaluation of the program and indicated it was a beneficial format.

CONCLUSION:

A 4-hour intensive voice treatment program targeting pitch, resonance, and intonation can improve acoustic and perceptual correlates of femininity for MTF speakers. This service delivery method may be best suited for those beginning their voice change journey. Future research is warranted to extend findings and determine maintenance of treatment gains resulting from this new service delivery method.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Phthalate exposure affects normal cardiac physiology in human stem cell-derived cardiomyocytes and excised rat hearts

The ubiquitous use of plastics in objects ranging from packaging materials to medical equipment has raised concerns due to continuous human exposure to plasticizers. Of particular concern is diethylhexyl phthalate (DEHP), a plasticizer that is used in the production of flexible polyvinyl chloride (PVC) products. Because DEHP is not covalently bound to PVC it can leach out of medical equipment upon contact with water, blood, and saline solutions. Studies show that a large proportion of both adults and children are routinely exposed to DEHP. Exposure levels are dramatically higher in patients with treatments requiring repeated use of IV bags and tubing.

DEHP belongs to a class of compounds known as endocrine disrupting compounds (EDCs) that can cause dysfunction to hormonally regulated body systems such as the cardiovascular system. Recent epidemiological studies have drawn links between urinary EDC levels and cardiovascular disease. This study sought to find direct evidence linking DEHP exposure and adverse effects in human cells and excised hearts.

The effects of DEHP on calcium handling and intercellular connectivity were studied using monolayers of human embryonic stem cell-derived cardiomyocytes treated with clinically-relevant DEHP concentrations ranging from 5 to 50 $\mu\text{g}/\text{mL}$. The cells contained an endogenous gCAMP calcium sensor and calcium transients were recorded using a Zeiss confocal imaging system. DEHP exposure for 24 to 72 hours promoted after contractions, decreased transient amplitudes, diminished intercellular connectivity, altered connexin-43 expression, and negatively impacted cellular ability to adjust to higher pacing frequencies.

Because alterations in calcium handling directly affect cardiac contractility the acute effects of DEHP exposure on mechanical function of excised hearts was also assessed. A Langendorff setup was used and a latex balloon catheter was inserted into the left ventricle (LV) to measure LV pressure and contractility. Electrodes were positioned next to the two atria and at the apex of the heart to acquire ECG signal. A pacing electrode was placed between the right ventricle and apex of the heart. High concentrations of DEHP led to significant increases in diastolic pressure, resulting in a 73 percent decrease in LV developed pressure.

Future studies are necessary to determine DEHP's lowest observed adverse effect level on mechanical function in excised hearts. Our current findings indicate that DEHP affects normal cardiac physiology at both the cell and organ levels. DEHP remains a public health concern warranting additional studies that investigate the effects of phthalate exposure on cardiac function, especially in vulnerable patient populations.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Identifying the essential region of a putative, small RNA in *Mycobacterium tuberculosis*

Toxic radicals, such as reactive oxygen species (ROS) and reactive nitrogen intermediates (RNI), are produced by macrophages to kill invading microorganisms. However, *Mycobacterium tuberculosis* (Mtb) is one of few bacteria able to survive within the harsh environment of the human alveolar macrophage. Bacteria utilize numerous mechanisms to adapt to environmental stress. To date, more than 90 sRNAs have been identified in *E. coli* that play a regulatory role in growth and survival. While several genes and gene products involved in Mtb stress regulation have been described, sRNAs have yet to be characterized. Our lab has evidence that a sRNA exists and affects Mtb growth. Specifically, we have identified a 30-nucleotide sequence, termed small anti-stress RNA (SasR), from Mtb that enhances the growth kinetics and survival of Mtb as well as recombinant *E. coli* and *Salmonella*. We previously demonstrated that recombinant *E. coli* containing SasR confers up to 5 logs greater survival to both *E. coli* and *Salmonella* in the presence of 1.5 mM hydrogen peroxide (H₂O₂, a form of ROS) compared to the same hosts containing the vector control. To determine if SasR functions in Mtb, an in-frame deletion of SasR was previously generated via homologous recombination and demonstrated altered growth characteristics. For example, wildtype Mtb colonies were significantly larger than a SasR mutant and at 22 days of incubation the null mutant demonstrated two logs less growth compared to wildtype Mtb and a complemented SasR mutant. The goal of the current study was to identify the functional region of SasR by generating mutations altering the SasR RNA secondary structure. The phenotypes were tested using recombinant *E. coli* H₂O₂ survival assays. Our results demonstrate that mutants vary in their ability to grow and survive. For example, a mutation (GT break) that adds a loop to the secondary structure is significantly ($p < 0.05$) less able to survive in the presence of 1.5 mM H₂O₂, suggesting that the RNA structure is critical for function. Although the mutations generated in this study had an effect on survival, none of the mutations abolished the survival phenotype. Hence, additional SasR mutations will be generated and tested for function in recombinant *E. coli*. Moreover, future studies will be carried out to further characterize SasR's regulatory mechanism in Mtb. In conclusion, these findings provide evidence of a putative, novel regulatory mechanism in Mtb and may contribute to the overall understanding of *M. tuberculosis* growth and persistence.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

The Developmental Function of WBP2NL, a Novel Maternal mRNA

During embryonic development, cells acquire different fates to become the various organs of the body. In many animals, cell fate choices are influenced by the inheritance of mRNAs and proteins from the oocyte. These are called maternal determinants. In an effort to discover novel maternal determinants of ectodermal fate, the Moody lab used a microarray screen to identify maternal mRNAs that are enriched in the animal pole cells of the frog, *Xenopus laevis*. Fate map studies show that the ventral-animal cells will become the epidermis (skin) whereas the dorsal-animal cells will become the nervous system. One of the newly identified maternal mRNAs encodes a protein called WBP2NL. Our laboratory showed that when this protein is prevented from being expressed, several neural gene expression patterns are changed, suggesting that WBP2NL is required for nervous system development. We next asked whether increasing the expression of this protein in the embryo changes cell fate. First, we tested whether overexpressing the wild-type protein induces or represses genes that are specifically expressed the neural plate, mesoderm, endoderm or epidermis. This was accomplished by microinjecting mRNA into the dorsal-animal cells at the 8-cell stage and processing the embryos by in situ hybridization after gastrulation. Our data show that expressing wild-type WBP2NL in the neural plate lineage weakly induces an epidermis gene (Keratin) and strongly induces two neural crest genes (FoxD3, Zic2). It also represses two genes that are expressed in the neural plate and cranial sensory placodes (Sox11, Irx1). To determine exactly part of the protein causes these effects, we made five mutant versions of WBP2NL. We used polymerase chain reaction techniques to synthesize five complementary DNA (cDNA) strands that contain each mutation. The mutant cDNAs were cloned into an expression bacteriophage vector (pCS2+) using standard molecular biological techniques, and transfected into bacteria to amplify the DNA. We then isolated the DNA and sequenced it to confirm we made the correct mutations. We designed mutations that code for regions that may be involved in the protein's ability to bind to the nuclear membrane and/or trigger 2nd messenger cascades. The mRNAs that code for the mutant proteins are currently being microinjected and gene expression patterns analyzed. Since WBP2NL is highly conserved across all vertebrates, including humans, our research may be important for learning how to manipulate embryonic stem cells for neural replacement therapies.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

The potential role of SMCR7L in embryonic neural development in *Xenopus*

In the developing embryo, the adult organs arise from three germ layers: endoderm, mesoderm and ectoderm. The endoderm gives rise to the gut, lungs, pancreas, and liver; the mesoderm gives rise to the bones, muscles, heart and blood; the ectoderm gives rise to the epidermis (skin) and the nervous system. Prior to germ layer formation, the embryo is composed of cells, called blastomeres, that differentially contribute to the germ layers. The blastomeres located in the animal region inherit maternal mRNAs from the fertilized egg, and later give rise to the ectoderm. The dorsal-animal blastomeres give rise to the nervous system and the ventral-animal blastomeres give rise to the skin. Previous work from the Moody laboratory indicates that maternal factors bias dorsal-animal blastomeres to form neural tissue. To identify novel factors that may be involved in this process, we used a microarray expression assay to identify maternal mRNAs that are highly enriched in animal blastomeres and are later expressed in the nervous system (Grant et al., 2015, *Devel. Dyn.* 243: 478-496). In this project, we tested whether one of these maternal mRNAs, called SMCR7L, plays a role in early nervous system formation by loss-of-function and gain-of function manipulations and assaying germ layer gene expression by in situ hybridization. First, reducing the level of endogenous SMCR7L protein (loss-of-function) caused a loss of neural and epidermal genes; these cells were not converted to a mesoderm or endoderm. Second, we increased the level of SMCR7L protein by microinjecting mRNAs into dorsal-animal blastomeres (gain-of-function). Preliminary experiments demonstrate that neural crest genes are reduced; neural crest cells give rise to the peripheral nervous system. However, no effects were observed on epidermal, neural plate, mesoderm or endoderm genes. These experiments are being repeated with higher doses of mRNA to ascertain whether phenotypes are observed with higher protein levels. In addition, we analyzed the protein structure of SMCR7L and found a MAB 21 domain at the carboxy-terminus; this domain has been implicated in neural development in the nematode. We have made two deletion mutations of this domain and are in the process of testing whether these mutant proteins cause abnormalities in neural development. These experiments will determine whether SMCR7L plays a role in the development of the nervous system. It is important to identify factors that promote neural fate in embryonic cells because these factors may promote the formation of new neural cells after damage.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Mesenteric Venous Thrombosis (MVT)

Mesenteric venous thrombosis (MVT) is a rare diagnosis that represents 1 in 5,000 to 15,000 inpatient admissions and 6 to 9 percent of cases of acute mesenteric ischemia. Thus, the diagnosis requires a high clinical index of suspicion. The symptomatic presentation of MVT tends to be acute in nature (60-80 percent of cases) and usually manifests as evolving abdominal pain over the course of 6 to 14 days. The abdominal pain is often located in the mid-abdomen and occurs out of proportion to physical exam findings. The mean age at presentation is 40 to 60 years, and males are more commonly affected. Symptoms that are typically associated with MVT include nausea, emesis, anorexia, fever, constipation, diarrhea, and - if ischemia is prolonged - gastrointestinal bleeding. Diagnosis is made by abdominal CT imaging with contrast, which has an accuracy of 90 percent. Treatment consists of anticoagulation with warfarin after appropriate enoxaparin or heparin bridging. Use of the novel factor Xa anticoagulants have not been evaluated by formal studies of MVT patients.

Thrombophilia and malignancy - especially myeloproliferative disorders like polycythemia vera, essential thrombocythemia, and myelofibrosis - collectively account for 40 percent of MVT cases. Consequently, a hypercoagulability and malignancy workup is crucial to identify the etiology of MVT. Abdominal imaging should reveal any local abdominal malignancies near the mesenteric veins that could trigger thrombosis. Hypercoagulability testing should consist of assays for prothrombin gene mutation, factor V Leiden, protein C and S, and antithrombin III levels. Ideally, blood should be drawn prior to initiation of anticoagulation for thrombophilia testing. JAK2 and BCR-abl genetic mutations should also be tested for identification of any occult myeloproliferative disease.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Age Differences in Spectral Measures of Male Voices

INTRODUCTION:

The aging population is the fastest growing segment of the population. In 2011 there were an estimated 41.4 million adults over age 64. By 2060 this number is expected to grow to 92 million older adults (Administration on Aging, 2012).

Research has documented the various changes that occur in an individual's vocal quality throughout the aging process. Common perceptual characteristics associated with the aging male voice include reduced loudness, increased pitch, hoarseness, roughness, and breathiness (Kendall, 2007; Ramig et al., 2001). With the growing aging population, the incidence of vocal disorders is estimated to be between 12-35% (Bradley et al., 2014). In order to accurately diagnose and treat vocal disorders of the aging population, it is important to understand the normal aging voice (Ramig, et al., 2001). One step in this process is to determine normative values for objective measures that strongly correspond to perceptions of vocal quality. Objective measures collected from the frequency spectrum of the acoustic signal (i.e., spectral measures) are becoming more widely researched because they have been shown to correlate well with perceptions of breathiness and overall vocal quality in connected speech (Heman-Ackah et al., 2002).

PURPOSE:

This study compares voices of 20 younger males and 20 older males using spectral characteristics known to correspond to listener perception of voice. Differences in these values would provide rationale for establishing normative values for these measures for different age groups.

METHODS:

Twenty male speakers, ages 20-40 years, and twenty male speakers, ages 60-80 years participated. Audio samples of the men sustaining a vowel, reading sentences, and reading a passage were recorded using the Computerized Speech Lab (Kay-PENTAX, NJ). Spectral measures of Cepstral Peak Prominence (CPP), fundamental frequency of CPP (CPP F0), and low frequency energy-verses-high frequency energy ratio (L/H Ratio) were collected using Voice Sauce program. A MANOVA was used to compare the two age groups.

RESULTS:

Preliminary results confirm significant differences in CPP values between younger and older males for vowels and some sentences. Older males had lower CPP values, indicating a worse vocal quality. Differences in CPP F0 and L/H Ratio values did not reach significance, but at the trend level, older men had higher CPP F0 (i.e., higher pitch) and lower L/H Ratios (i.e., poorer vocal quality), as expected.

CONCLUSION:

As spectral measures are increasingly used in voice assessment, development of age-based normative values is indicated.

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Clinical Significance of the BRAF V600E mutation in Erdheim Chester Disease; a Systematic Review of Cases Seen at the NIHCC

Erdheim-Chester Diseases (ECD) is a very rare non-Langerhans cell histiocytosis of unknown origin and pathogenesis. It has been reported mainly in adults, and childhood cases are rare. Family studies have not been performed due to the rarity and sporadic nature of the disease. The clinical characteristics of ECD range from asymptomatic to multisystemic involvement. ECD commonly affects the bones, kidneys, retroperitoneal space, skin and brain. After diagnosis, the disease progresses rapidly unless treatment is started. Without treatment, ECD is fatal, causing severe lung disease, chronic renal failure, cardiomyopathy and other complications. The diagnosis of ECD relies upon imaging studies and specific pathologic findings in biopsies of affected organs, i.e., fibrosis and infiltration of the affected tissues with foamy histiocytes, lymphocytes, and plasma cells. Immunohistochemistry reveals cells positive for CD68 (a macrophage marker) and negative for CD1a (Langerhans-cell marker) and S-100 (protein marker). There is no approved treatment for ECD, although chemotherapy, radiation, stem cell transplantation, alpha-interferon, steroids, monoclonal antibodies and sirolimus have been proposed. A systemic proinflammatory cytokine signature has been described which has encouraged the use of interferon over other treatments. Symptomatic improvement has been reported with some of these therapies, but death within a few years after diagnosis remains the expected outcome. BRAF, a gene normally involved in regulating cell division and differentiation, has been found to be mutated in some patients with ECD. This mutation is known as V600E, since the 600th codon of this amino acid sequence changes from a Valine (V) to Glutamic Acid (E). As a result, it has become a gene of interest for current research. Our team is currently looking into the location of ECD-related lesions in each patient (which organs are involved, what type of lesion etc.) in relation to whether or not that patient has a mutation in the BRAF gene.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Subventricular Zone of the Developing Gyrencephalic Brain Under Normal Physiological Conditions and After Hypoxia

The majority of children with congenital heart disease (CHD) suffer from neurodevelopmental delay as a consequence of their CHD. However, the majority of children after CHD repair now suffer significant neurological impairments or behavioral problems. Reduced oxygen delivery due to cardiac anomalies in utero results in sub-normal cortical development. Chronic exposure to hypoxia alters neuronal/glial cell development. Thus, optimal treatment requires new therapies aimed at regenerating injured cells.

Alterations of neural stem/progenitor cells of the SVZ may represent a major cellular mechanism underlying sub-normal cortical development in CHD. Our future study will define alterations in the migration and differentiation of SVZ cells after hypoxia using our MRI-based cell tracking and fate analysis.

Neural stem/progenitor cells retain their mitotic and differentiation potential, as the brain is able to replenish damaged neurons and glial cells. The largest source of these cells is the subventricular zone (SVZ). However, the structural and cellular properties of the well-studied rodent SVZ are very different from its human counterpart. Because of obvious technical and ethical hurdles, the contribution of the SVZ to development of the gyrencephalic human brain and the response of these cells to pathological environments remain poorly understood. This prevents advancing regenerative treatments for neonatal hypoxic brain damage. Thus, development of human-like SVZ neural stem/progenitor cells needs to be defined in the gyrencephalic brain under normal and pathological conditions.

The developing porcine brain displays features that are similar to the human brain, including gyrencephalic, rather than smooth, cortex and a similar progression in white matter maturation. Our current results demonstrate that in early postnatal period: i) the anatomical and cellular characteristics of the porcine SVZ closely resemble their human counterpart; ii) the dorsolateral-SVZ contains the highest number of NSPCs and is a predominant proliferative region; and iii) during normal development, porcine SVZ neural stem/progenitor cells migrate into the cortex. Thus, we hypothesize that the SVZ contributes to gyrencephalic cortical development. To define both areas of migration and differentiation potential of SVZ cells, we used MRI-based cell tracking and fate analysis of porcine SVZ cells, which has never succeeded in gyrencephalic animals.

We also established a hypoxic injury paradigm in piglets. Macro-structural alterations of the developing porcine brain, due to prolonged hypoxia, are very similar to those observed in CHD newborns. We, therefore, hypothesize that this novel animal model shares mechanisms underlying sub-normal cortical development in CHD. In present study, gyrification index was analyzed to define its relevance to volumetric growth disturbances observed in CHD patients.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Engineered Cardiac Fibers - Biological Pump to Aid Venous Flow

BACKGROUND:

Chronic venous disease, also known as Chronic venous insufficiency (CVI), prevalent worldwide, is a disease affecting 40% of adults in the Western world. It occurs most commonly from distention of veins, the progressive degradation of the venous valves, or a combination of both. A new field of tissue engineering aims to develop external cuffs of engineered heart tissue (EHT) using harvested cardiomyocytes to wrap them around vein segments with incompetent valves, as there is an unmet need to further develop novel approaches to treat chronic venous insufficiency and associated conditions.

METHODS AND RESULTS:

Saphenous veins from the lower limb of pigs, rabbits and rats were dissected immediately after the animal was euthanized. Several methods to create a venous pump were explored. They involved casting rat neonatal cardiomyocytes in fibrin and collagen hydrogel scaffolds to be used for wrapping the vessel of interest. The type of 3D matrix, cell-plating density, size of the molds, and different mechanical strain schedules were tested for their ability to create maximum contractility to promote ideal unidirectional flow and/or internal hydrostatic pressure.

CONCLUSIONS:

Recent advances in tissue engineering allows the possibility of the creation of biological mini pumps with varied properties, including density, geometry, strength and rate of spontaneous contractions. These findings merit further experimentation of this approach, particularly to make progress on minimizing matrix degradation and maximizing cell viability and their spontaneous contractions.

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Building from Experience: Creating Sustainable Bridges Between Emergency Medicine Researchers and Invested Public Health Agencies

INTRODUCTION:

Emergency Medicine-Public Health Partnerships (EM-PHPs) arising from shared expertise in healthcare can potentially be leveraged to target high-risk populations with preventive measures, increase secondary and tertiary interventions, improve public health outcomes and reduce healthcare costs.

METHODS:

To examine current EM-PHPs, we conducted a comprehensive review of EM based public health initiatives and assessed US federal funding for these projects using a comprehensive, two-pronged systematic review of EM-PHPs. Projects were selected using inclusion criteria to identify relevant emergency medicine and public health studies, occurring in the ED from the PubMed database and NIH RePORTER. A standardized abstraction tool was used to construct a database for examination of funding trends.

RESULTS:

102 projects met the inclusion and exclusion criteria. Of these, 42 studies were categorized as drug screening or treatment that also received the most overall funding. 31 projects focused on infectious disease, 10 on chronic disease, and 10 on injury prevention. Trends over the years show the earliest projects funded were injury prevention and drug screening/treatment.

CONCLUSION:

Our findings reveal that funding has decreased overall since 2008, which has an important impact on developing collaborative partnerships between EM and public health investigators. In conclusion, public health initiatives in the ED are highly dependent upon partnerships and funding from federal agencies. Declining levels of funding and support for these initiatives may potentially have a negative impact on future endeavors.

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Surgical Cardiac Denervation Therapy for Treatment of Congenital Ion Channelopathies in Pediatric Patients

BACKGROUND:

Congenital ion channel disorders, including congenital long QT syndrome (LQTS), cause significant morbidity in pediatric patients. When medication therapy does not control symptoms or arrhythmias, more invasive treatment strategies may be necessary. This study examines our institution's clinical experience with surgical cardiac denervation therapy for management of these arrhythmogenic disorders in children.

METHODS:

An institutional review board-approved retrospective review identified ten pediatric patients with congenital ion channelopathies who underwent surgical cardiac denervation therapy at a single institution between May 2011 and April 2014. Eight patients had a diagnosis of congenital LQTS, two patients were diagnosed with catecholaminergic polymorphic ventricular tachycardia (CPVT). All patients underwent sympathectomy and partial stellate ganglionectomy via video-assisted thoracoscopic surgery (VATS).

RESULTS:

Six of the ten patients had documented ventricular arrhythmias preoperatively, and 70% of the patients had preoperative syncope. The corrected QT interval decreased in 75% of patients with LQTS following sympathectomy. Postoperative arrhythmogenic symptoms were absent in 88% of congenital LQTS patients, but both patients with CPVT continued to have symptoms throughout the duration of follow-up. All patients were alive after a median follow-up period of 10 months.

CONCLUSIONS:

Surgical cardiac denervation therapy via VATS is a useful treatment strategy for congenital LQTS patients who fail medical management, and its potential benefit in the management of CPVT is unclear. A prospective comparison of the efficacy of surgical cardiac denervation therapy and implantable cardioverterdefibrillator use in congenital ion channelopathies is timely and crucial.

KEYWORDS:

Congenital long QT syndrome, congenital ion channel disorders, surgical cardiac denervation therapy, sympathectomy, stellate ganglionectomy

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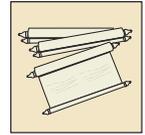
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Bridging the Gap Between Arts and Sciences: Using Psychology to Explain the Mysteries of Picasso's Les Demoiselles d'Avignon

Pablo Picasso, a famous painter and contributor to modern art thanks to his groundbreaking creation of the Cubist movement, shocked his audience in 1907 with his unquestionably disturbing and thought-provoking debut of Les Demoiselles d'Avignon. At the time, nobody knew how or why Picasso created such an unsettling painting - a question still left unanswered to this day. The fields of science and art history hardly ever collaborate, and this lack of partnership leads to many interstices between the fields that have various opportunities for discovery. This paper explores Sigmund Freud's psychoanalytic theories and how they help explain Picasso's thoughts behind his shocking, disturbing, and arguably most famous painting, Les Demoiselles d'Avignon. Within the same decade that Freud's famous ideas of psychoanalytic theory, specifically repression, were gaining popularity around Europe, Picasso was an emerging artist in Paris. Certain actions and words of Picasso hint at Freud's theories as sources of influence for Les Demoiselles d'Avignon. Perhaps this connection between psychoanalytic theory and art history provides some answers to the many questions raised by Les Demoiselles d'Avignon, and can lead us to finding more answers behind this puzzling work of art.

STATUS

Student - Undergraduate

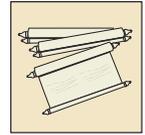
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Changing Duty: Female Roles and Responsibilities in Three Versions of *Coriolanus*

In William Shakespeare's relatively obscure Roman tragedy, *Coriolanus*, the title character's mother Volumnia must choose between her familial obligations and her community responsibilities. Her dilemma ties into the ancient Roman concept of *pietas* - duty or responsibility to the family, the community, and the divine - that governed almost every aspect of Roman life. Shakespeare's appropriation of the classical Greco-Roman biographer Plutarch's *Life of Coriolanus* retains the Roman understanding of *pietas* while expanding Volumnia's presence and influence. Over 400 years later, Ralph Fiennes' 21st-Century film *Coriolanus* reinterprets Volumnia and *pietas* for modern audiences. This study examines the three *Coriolanuses* to explore their representations of a woman's roles and responsibilities in her family, her community, and her faith. Although many scholars have explored the connections between Plutarch's *Life of Coriolanus* and Shakespeare's *Coriolanus*, the three works mark out a trans-temporal trajectory that invites and rewards examination through the lens of *pietas*. Through textual and historical research, the study finds that Plutarch's quickly sketched Volumnia generally, if imperfectly, adheres to ancient Roman ideals for the three facets of female *pietas*. Further textual analysis shows that Shakespeare challenges the ancient Roman and early modern ideas about the proper balance of feminine responsibilities through his unorthodox and overzealous but powerful and persuasive Volumnia. The investigation contextualizes this adaptation through its archival research into early modern understandings of female roles and responsibilities. Finally, the project explores Fiennes' film with performance studies methods, finding a Volumnia who persistently navigates the patriarchal *pietas* system of an oppressive Rome. Through this trans-temporal examination, the study concludes that the three works' depictions of Volumnia's *pietas* create a trajectory from unusual devotion through unconventional responsibility to unflinching commitment. The analysis suggests that the three *Coriolanuses* reveal literary-historical trends and offer insight into how a person comes to terms with obligations to the family, the community, and the divine.

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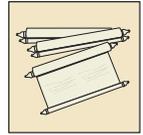
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Curricular Peer Mentoring in First-year German Classes: A Pilot Study

Curricular peer mentoring is a form of peer learning that involves more experienced students helping other students enrolled in a specific course through interactive engagement with the material. In recent decades, focus on student-centered learning models has resulted in increased attention to peer-assisted learning as a way of promoting student ownership and enjoyment of the learning process. A curricular peer mentoring program was piloted in fall 2014 at The George Washington University in the German program, in which six advanced German students, recently returned from a study abroad or internship experience in a German-speaking country, facilitated peer learning by serving as "Learning Assistants" (LAs) in the introductory level German language classes. These LAs provided individual and group assistance, modeled tasks, facilitated collaborative learning and encouraged students to become more involved in their learning. End-of-semester surveys were administered to the LAs, First-year Germans students and their instructors in order to identify perceived and experienced benefits of the peer learning program to all participants, as well as general satisfaction with the program. Survey data suggests that the overall response to the program was positive. Student and LA responses indicate that students benefited most through the peer relationship shared by LAs and students, which results in lowered anxiety and motivation to pursue further studies. The nature and impact of the "near-peer" relationship is examined in greater depth, especially with regard to the ways in which LAs served as model for students both in the short-term, through demonstration of concrete tasks students themselves were then expected to perform, and the long-term, as advanced speakers of the language with personal experience living abroad.

STATUS

Student - Undergraduate

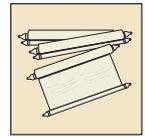
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Big ideas, tiny spaces, and the resurgence of micro housing in 21st century America

In the past decade, tiny apartments have emerged in American cities. This micro housing boom, referring to homes whose area is 300 square feet or less, has been covered by traditional publications like *The New Yorker* and the *Washington Post*, and by new media including *The Hairpin* and *The Morning News*. Despite varied coverage, micro housing is frequently treated a-historically, linked only to contemporary events like the Great Recession and housing bubble. By researching scholarship on old alley dwellings and tenement housing in Washington, DC and New York City, I sought to ground this contemporary phenomenon in urban history. After reading histories of old forms of micro housing, their demographics, reasons for living in tiny dwellings, and making site visits to remaining alley dwellings and tenements, I connected these old forms to their modern successors. Today's micro housing occupants are not the working class minority families of previous centuries. Most are young, white, middle class professionals, whose desires to return to the center city and live "minimally" have led them to accept small spaces in desirable neighborhoods. Micro housing is growing in popularity as its proponents push for its greater legal and social acceptance. Understanding micro housing's roots will help city leaders and scholars proactively plan for further development, so modern micro housing does not suffer the problems of its predecessors.

STATUS

Student - Undergraduate

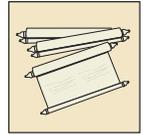
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Reintegration after International Volunteer Service

As international volunteer service gains momentum with many high school and university programs, more research is needed about the process of preparing for re-entry. Reintegrating into one's home society can be difficult and overwhelming without the proper preparation, and many service programs do not adequately prepare their participants for this difficult transition. This study examines how international volunteer service participants reintegrate back into their home societies after serving abroad. Data was gathered through interviews with returned international volunteer service participants at The George Washington University. The results of the study show that reintegrating back into one's home society was more overwhelming and stressful than the culture shock experienced at the beginning of the trip for many participants. The research identifies a need for international volunteer service organizations to reevaluate how they approach the end of their trips and to hold conversations with and trainings for their participants.

STATUS

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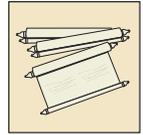
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Frequency and Uses of Religious Rhetoric in Presidential Speech: A Focus on Inaugural and State of the Union Addresses

Religious rhetoric, including explicit and indirect reference to the Deity or Scripture, has been a rhetorical tool wielded by American presidents from George Washington to the current day. This paper reports a content analysis of every presidential Inaugural and State of the Union address in American presidential history seeking to both quantify the frequency of religious rhetoric and categorize in which ways they are used. Religious references were categorized into five categories of use: Perfunctory/general, Personal, America as a God-favored nation, Policy-specific, Value(s)-specific. Initial research identified another common phenomenon in the speeches: religious-like hero worship for the Founding Fathers, earlier presidents, and even the Constitution itself. It is almost of a religious fervor as if the creators of the Constitutions and forgers of independence were the equal of the Biblical patriarchs. This occurrence is too coded for in a similar way God references are. References to the Founding Fathers, Founding Documents, or the American Revolution are categorized in the following five categories: General, Personal, America as an International Example, Policy Specific, Value(s) promotion. The frequency and prevalence of religious and religious-like rhetoric in Inaugural and State of the Union addresses reinforce Robert Bellah's (1967) concept of "civil religion," defined as a nonsectarian force that gives America's political realm a religious dimension.

STATUS

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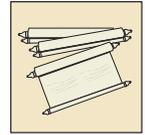
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Is there a right way to run? The influence of ground stiffness on habitual barefoot running form

Our ancestors have been running barefoot for millions of years, and began wearing shoes only recently, perhaps 30kya. To understand how people ‘naturally’ run when barefoot, biological anthropologists turned to researching how habitually barefoot people run today. They studied habitually barefoot people because evidence shows that wearing shoes influences how foot anatomy develops during growth. These studies, however, have had conflicting results. Some studies indicate that habitually barefoot runners typically land on the balls of their feet (forefoot strike), not on their heels (heel strike), and suggest that this is a healthier and “natural” way to run because it may reduce jarring impact forces. However, other studies found that habitually barefoot runners typically heel strike, and hypothesized that one of the main factors influencing foot strike patterns may be the stiffness or compliance of the ground itself, so that people may alter their footfall patterns to accommodate the stiffness of the ground. This study tests the ground compliance hypothesis by collecting data on foot motions in 20 men and 10 women from the habitually barefoot Daasanach people in northern Kenya, to provide a more complete understanding of whether there is any “natural” way to run. In this experiment we explicitly analyzed the effects of substrate stiffness (soft, medium and hard) and speed on running strike patterns, something that had not been done in prior studies. Preliminary results indicate that habitually barefoot people do not change their foot strike angle when running on substrates of different compliances, as long as they are running at the same speed. However, speed does affect foot strike angles on all three surfaces, as the majority of the people we studied transitioned from a rearfoot strike to a midfoot strike at higher speeds. Our results indicate that speed, but not substrate, influences running form, and they shed important new light on debates over variations in running form among habitually barefoot people.

STATUS

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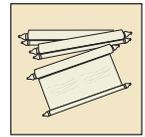
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HUMANITIES



COLUMBIAN COLLEGE OF ARTS & SCIENCES

Mental Health Programming at Universities: Looking Beyond the Counseling Center

In recent years, the prevalence and awareness of mental illness has become an important topic of discussion, particularly on college campuses. There has been a drastic increase in the number of students requiring mental health resources and research has shown that university counseling centers cannot keep up with the need for services. The purpose of this study is to explore how universities are addressing mental illness beyond the counseling center. This study includes nine interviews from students, student leaders, and administrators from the George Washington University. Student leaders and administrators were asked about the types of programming and services they are involved with and how this addresses mental illness on campus. Students were asked about their knowledge of services on campus and whether or not they see the university's current programs (both formal and informal) as useful. The results show that, outside of the counseling center, there are numerous mental health resources offered at GWU with many of them initiated by students themselves. Students and administrators understand the importance of offering quality and supportive programs to all students, especially those who are struggling. Additionally, many of the initiatives currently offered have been implemented within the past two years, thus demonstrating the recent increase in the importance of mental health resources on college campuses. This study offers insights into how one institution is bridging the gap between available counseling services and student need.

STATUS

Student - Undergraduate

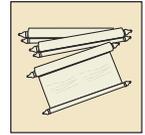
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Intersectional Feminism in Antiquity: The Parallel Lives and Deaths of Sophonisba and Cleopatra VII

My project uses contemporary feminist and race studies theory to analyze and compare the representations of two North African queens who committed suicide to avoid capture by Rome: Sophonisba and Cleopatra. By examining ancient literary sources and material culture, my research brings to light the history of a forgotten princess whose story is illuminated all the more brightly in the context of one of Egypt's most notorious rulers. The Carthaginian Sophonisba was married to two Numidian kings, Syphax, an ally of Carthage, and Masinissa, an ally of Rome, before committing suicide to avoid the infamy of defeat. While her husbands play important roles in histories of the Punic Wars, Sophonisba is seldom even mentioned by name. Though extremely little is known about her today, the precedent she set influenced representations of Cleopatra VII of Egypt, and vice versa. Like Cleopatra, Sophonisba committed suicide to preserve both her honor and that of her country—an act that was valued and respected in Roman literature and society.

Indeed, Cleopatra and Sophonisba challenged Roman understandings of foreignness and femininity by wielding influence over international politics and by proudly committing suicide, although Sophonisba's relative lack of autonomous political power positioned her as less of a prominent foreign threat than Cleopatra. Both queens were initially understood to be troublesome because of their perceived sexuality, their gender, and their foreignness, but ultimately, Cleopatra was demonized to a far greater extent. Moreover, the Punic Wars were an explicitly foreign set of conflicts between Rome and Carthage, but Cleopatra's death allowed Roman writers to capitalize on her Egyptianness and make the important narrative shift of reframing a civil war between rival Roman political factions as a foreign one against Egypt.

In comparing Cleopatra and Sophonisba as case studies, I employ an interdisciplinary methodology that reexamines ancient literature through a contemporary feminist perspective. My background in women's studies and classical studies has provided me with the theoretical and methodological tools to expose important patterns in ancient literature by giving Sophonisba more attention than most previous scholars have and analyzing her story in a broader gendered historical context. This project is significant because it not only centers women of color, but also assertively brings to the forefront issues of language, representation, and agency in the context of ancient colonial power to demonstrate the factors that determined Roman representations of these two North African queens.

STATUS

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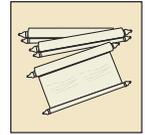
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We Are Making a New World: The Great War Work of Paul Nash

Paul Nash (1889-1946) is best known as a leading English surrealist painter, but he began his career and gained early fame as one of the ninety officially commissioned British “war artists” of the First World War. The purpose of this study is to assess Nash’s role as an official artist and to consider the effects of the war on his personal development as a painter and art theorist. In order to bring Nash’s personal reactions and opinions to bear on the public record left by his officially commissioned paintings, his private papers housed in the Tate Gallery Archives were considered in conjunction with his paintings that were displayed by the Imperial War Museum during the First World War Centenary. Key paintings used in the study include “The Menin Road,” “We Are Making a New World,” and “Spring in the Trenches: Ridgewood, 1917.” The research displays Nash’s steady progression from an enthusiastic and optimistic soldier with a passion for landscapes into a disillusioned and disturbed individual expressing his horror at the realities of the Great War. Early evidence of Nash’s surrealist style invites obvious connections with his own later post-war experiences of shell shock and subsequent hospitalization. Although this research establishes a basis for the experimental and sometimes shocking projects that Nash undertook later in his career, it also reveals his devotion to the tradition of English landscape painting. Despite the fact that Nash is often categorized as a modernist, the persistent presence of the landscape tradition in his work reveals a tension that questions the myth of modern progress while simultaneously questioning the validity of the British tradition. Ultimately, this study reveals Nash’s war paintings in their personal and cultural context, and provides a new lens through which to consider the early career of arguably the most significant surrealist painter of his generation.

STATUS

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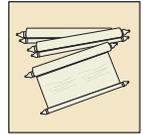
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Understanding the Impact of Volunteer Management Practices on Volunteer Retention within the Nonprofit Sector

Volunteer retention, defined as the proportion of volunteers who return the next year to volunteer with the same organization, has steadily remained a problem in the nonprofit sector. Data show that about one third of volunteers tend to drop out of service each year. To address volunteer retention, focus is on the process of volunteer management in an effort to effectively recruit, satisfy, and retain volunteers within the nonprofit sector. However, little research has been able to identify the impact of these practices. The purpose of this study is to answer the question of how the implementation of best practices for volunteer management affects volunteer retention. In order to address this purpose, a mixed methods approach was designed. First, 294 nonprofit organizations around the U.S. completed a self-audit survey. Data analysis identified trends within current volunteer management practices. To explore the trends, six survey respondents, whose organizations had a volunteer coordinator, participated in qualitative interviews. These interviews were then coded for various themes in the data. Findings revealed themes relating to the beneficial role of the volunteer coordinator and how different organizational factors impact a nonprofit's ability to manage volunteers. Findings also highlight that nonprofits struggle with two primary best practices (1) Strategic Planning with the Board of Directors and (2) Measuring Outcomes and Evaluating the Process. Such results can be utilized to not only highlight the significance of best practices in the context of volunteer retention, but to further develop these best practices to be more accommodating to the diverse field of nonprofits.

STATUS

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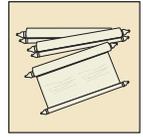
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Defining “Child Prostitution”: Exploring the Influence of Language on Perceptions of the Commercial Sexual Exploitation of Child

Each year, an estimated one million children enter into prostitution across the globe (Willis & Levy, 2002). The secrecy and illegality of this crime provides a cloak for its perpetrators and causes the issue to have a lack of credible research and understanding, especially in the United States. An Australian study on the power of language in media reported that child prostitution is often reported more closely to adult prostitution than child sex abuse (Goddard, De Bortoli, & Saunders, 2005). Recently, academics shifted the language they use to describe the issue from “child prostitution” to “the commercial sexual exploitation of children” (CSEC) due to research indicating that the first term placed blame on the child involved. The affects of the shift on perceived notions of the prostitution of children have not been studied. This research interviewed 10 George Washington University students on their perceptions of child prostitution with particular attention on the role of language. Results from this study find that university students generally get their idea of child prostitution from the media and other cultures outside of the United States. Additionally, students felt that greater awareness for the issue needs to exist in order to create meaningful change. Students were split when it came to whether “child prostitution” or “the commercial sexual exploitation of children” was a better term for the issue, but most viewed them as synonyms. This study invites further research regarding awareness about the prostitution of children in the United States.

STATUS

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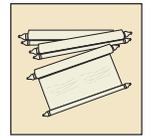
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HUMANITIES



COLUMBIAN COLLEGE OF ARTS & SCIENCES

The Role of Physical Activity in Youth Mentorship Programs

Youth mentoring is an increasingly popular social intervention and effective strategy for creating supportive relationships. In American society, there's an estimated three million youth in formal one-to-one relationships with a mentor (Rhodes & DuBois, 2008). Recently, physical activity based mentorship programs are emerging as a subtype of mentoring to promote positive youth development while incorporating exercise. It is important to study how physical activity can offer unique contributions and be used as a tool for strengthening youth mentorship programs for both mentors and mentees. In order to understand the how to make this practice most effective, the researcher conducted qualitative interviews with five mentors from physical-activity based programs. Questions regarded how the physical activity affected the mentor's experience with the program, including the mentor-mentee relationship and perceived outcomes. The results of this study show that the physical activity strengthened the mentor-mentee relationship, promoted mentee-mentee bonding, and provided unique health and social benefits for both mentors and mentees. This research identifies the importance of incorporating physical activity into curriculums for youth mentorship programs in the future.

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Fighting Unconventional Wars Unconventionally: The Problematic Use of India's Counterinsurgency Strategy to the Naxalite Threat

Since Independence in 1947, India has been forced to combat innumerable insurgencies, rebellions, and terrorist organizations. In light of the sectarian, racial, regional, linguistic, social, economic, and political differences that exist throughout the country, this is unsurprising. While most attention is focused on the ongoing conflict with Pakistan, India's experience with internal security challenges has posed as great a threat to its stability. To examine these issues, this study proceeds in three sections. First, the study outlines the mixed success of India's strategy in combating insurgencies in Punjab, Kashmir, and the northeast frontier. Parts of this strategy include a unique willingness to address the political demands posted by the separatists—short of granting independence—and active engagement with moderate elements of the target populations. From a security standpoint, India has turned Western counterinsurgency doctrine on its head by using time against the insurgents, flooding an area with security personnel and willingly absorbing losses while engaging in brutal paramilitary campaigns. Second, this study analyzes the emerging threat posed by the Maoist insurgency in India's central states. The small militant communist movement in India, which began in the 1970s, took a dramatic turn in 2004 when the two largest Maoist factions formed the Communist Party of India - Maoist ("CPI-M"). The well-organized CPI-M, or Naxalites, has since exploded on the scene, spreading to at least eight states. The CPI-M has conducted hundreds of attacks each year resulting in tens of thousands of casualties. This study explores why the Maoist insurgency poses a threat unlike any that India has ever faced. Instead of combatting separatist insurgencies that are trying to break from the state, Indian security forces face an enemy with no real religious or ethnic homogeneity, working towards the wholesale destruction of the state. Third, this study uses both qualitative and quantitative analysis to compare India's history of combatting separatist insurgencies with its current experience with the Naxalites. It also evaluates the successes and failures of the methods India is currently employing against the Naxalite threat. This study concludes with two main conclusions for policy makers: 1) the current counterinsurgency strategy and tactics of the Indian security forces are failing to sufficiently address the threat posed by CPI-M; and 2) in order to address the crisis, the Indian government must place a more significant emphasis on establishing a coherent "unity of effort" between security and development actors at all levels of government.

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Education and Urban Refugees: The Gaps and Potential in Current Policy

The Syrian crisis presents a new kind of refugee crisis to the international community, combining different challenges that have been seen separately in other situations. As of February 16th, 2015, the United Nations High Commissioner for Refugees (UNHCR) reports that there are 3,814,468 persons of concern in the Syrian Refugee crisis (UNHCR). A report from the International Rescue Committee shows that one-hundred percent of registered Syrian refugees in Lebanon and eighty percent in Jordan live in cities (International Rescue Committee). With the challenges of urbanization, limited resources, and ongoing conflict combined, NGOs and IGOs have to work to create a new paradigm for refugees, as more refugees move into the city and away from camps. The vast majority of UNICEF and UNHCR protocol is based on the policy that the refugee camps are the primary 'sphere of influence' for organizations such as UNHCR and UNICEF. This paper examines the approaches traditionally used by UNICEF and UNHCR to help refugees to receive education, and how these methods have played out in past and current situations. Then it examines the particular challenges faced by UNICEF and UNHCR in helping urban refugees. After this, it examines the historical context of urban refugees, and their experiences previously in Nairobi, Kenya. Finally, this paper suggests that, to best serve urban refugees in Lebanon and Jordan, programs of registration must first be implemented, and specific measures must be taken by local governments in schools to count the number of refugee children in order to ensure that as many children as possible are receiving the education that they deserve. This is not a complete solution, but rather a gateway solution that fills in the first gaps so that more methods of evaluation can be used.

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KDU-CSL in the Czech Republic: Historical Development to Current Platform

With over 60% of Czechs claiming to have no religious affiliation and citizens ranking the “importance of God” lower than any other country in Europe, the Czech Republic is often labeled the most secular country in the world. Despite this environment, a Christian Democratic political party, the KDU-ČSL, has been able to have a significant impact on the country. The party is small, but its participation in governing coalitions has given it a role in policymaking. The party’s moderate position has allowed it to join coalition governments dominated by parties across the political spectrum, and it has been able to push through key legislation on abortion and church property restitution. The KDU-ČSL has also shown great resilience. It was able to join the interwar period coalition government of Czechoslovakia, despite strong anti-Catholic sentiment caused by Catholicism’s association with Austria-Hungary. After the fall of communism, the party was again able to join the government, despite public distrust caused by the party’s former ties with the communist government. Europe is becoming more and more secularized, with religious views across the continent beginning to resemble those in the Czech Republic. If this trend continues, the influence of religion on politics will probably be through small but strategic parties like the KDU-ČSL. The KDU-ČSL provides an example of a party that ties itself to Christian values while maintaining a moderate position on the political spectrum, avoiding nationalism and the extreme right. This paper analyzes historical trends in the development of Christian Democracy and how the KDU-ČSL’s development and platform have been impacted by the Czech historical experience of religion in politics.

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The Himalayan Tsunami: A Review Of The June 2013 Uttarakhand Disaster And The State's Disaster Management Policies

On June 16, 2013, the state of Uttarakhand experienced one of the worst natural disasters in India since the 2004 Boxing Day tsunami. A series of extreme weather occurrences created a chain reaction of events that led to flash flooding in the Kedarnath area and other nearby villages. Weeks after the disaster, it was revealed that the state of Uttarakhand did not have a warning system in place or a disaster management plan. This project reviewed the management of the disaster and the changes that occurred in the 17 months afterward. Research is centered around the Rudraprayag district, with a specific focus on Kedarnath - one of the worst hit areas. This study was done with the help of Goonj, an Indian NGO that provides resources and aid to the underprivileged. Interviews with aid workers and flood victims were conducted to gain a firsthand perspective of the disaster and its lasting impact on the area. The results of this fieldwork revealed that survivors are still struggling with trauma and unemployment, while the government works towards installing a warning system and implementing a new disaster management plan.

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Dismantling the FDLR: Towards a Comprehensive Strategy

The FDLR (Democratic Forces for the Liberation of Rwanda) is among the most active foreign armed groups operating in the Democratic Republic of the Congo that is both long-established and hard to be eradicated. Its full dismantlement has crucial implication on long-term peace and stability of the country and the region, given the group’s special history with Rwanda and demonstrated resilience. Towards this end, this paper proposes a dual approach consisted of demilitarization and reconciliation. Demilitarization requires political, security, and economic processes to reduce incentives for violence, while the restoration of justice and the storytelling of history are essential to reconciliation. As the paper concludes, future success hinges upon two conditions: the easing of insecurity and ethnic tension in a wider context, and the cautious utilization of the FDLR’s internal tension.

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A Disjointed Effort

This research project was designed to investigate the extent to which the reintegration process for those returning from the rebel group, the Lord's Resistance Army (LRA), has been coordinated and facilitated by the Government of Uganda and NGOs at the present time. The LRA terrorized northern Uganda for more than 20 years before moving to neighboring Central Africa Republic and Democratic Republic of Congo. Although the LRA has left the country, northern Uganda still faces many post-conflict challenges. One major obstacle to peace in northern Uganda is the rehabilitation and reintegration of those returning home from the LRA.

This research was completed through examining current government initiatives, NGO initiatives, and the current coordination between the two sectors. Special emphasis was given to the role of the Government of Uganda specified in the Ugandan Peace, Recovery, and Development Plan. This study discovered that the Government of Uganda has neglected to take a leadership role on the issue of reintegration. Rehabilitation and reintegration of those returning from the LRA has been almost completely left in the hands of development partners including NGOs. It was determined that a partnership between the government and NGOs is necessary in a post-conflict situation, but the Government of Uganda should take a more leading role in facilitating and coordinating reintegration initiatives within the country.

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Shared Grievances, Divided Response: The Impact of Ethno-National Discourse on Collective Youth Action in Bosnia and Herzegovina

Twenty years after wars of secession tore apart the former Yugoslavia, Bosnia and Herzegovina (BiH) remains politically, socially and territorially divided among the three main ethno-national groups: Bosniaks (Bosnian Muslims), Bosnian Serbs, and Croats. Through a series of qualitative interviews with young activists and students in BiH, this research explores the influence of divided ethno-national discourse on Bosnian youth, ages 18-30, and how ethno-national divisions affect cooperation among these groups to address shared socio-political grievances in BiH today. These findings reflect youth perspectives on three central questions: what are the main socio-political issues facing young people in BiH today; how do youth mobilize to address these issues; and how does divided ethno-national identity among young people in BiH affect inter-ethnic collaboration in finding solutions to these problems? Youth perspectives on these issues in BiH provide insight into generational identifications within a broader post-conflict context. Understanding youth collaboration in addressing shared socio-political concerns, and different views on why this cooperation does or does not occur, provides a deeper understanding of the complex components of Bosnian youth identity, particularly the intersection of generational and ethno-national identities. These findings in turn offer insight into the capacity for cooperation between divided youth in post-conflict societies and how structural divisions affect their ability to work together towards shaping the future for the next generation.

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The Impact of Popular Definitions of Democracy on Democratic Legitimacy in Select African Countries

The 1990s saw many democratic transitions in Africa, which produced mixed results. Although surveys like Afrobarometer ask questions about democratic legitimacy and the meaning of democracy, current scholarship fails to contextualize the democratic legitimacy in light of varying definitions. How do variations in popular definitions of democracy impact democratic legitimacy? To answer this question, I analyze Afrobarometer data from thirty-three African countries from 2011-2012. I construct indices to measure preference for definitions focusing on political inputs (political structure and civil rights) and outputs (governance quality and socioeconomic guarantees), as well as belief in democratic legitimacy. I then regress input-oriented definitions against democratic legitimacy. I find a significant relationship between preference for input-oriented definitions of democracy and belief in democratic legitimacy, even when controlling for other factors traditionally thought to impact democratic legitimacy. South Africa serves as a case study to consider this relationship at the individual level. I explore theoretical causal mechanisms for this relationship, both generally and in reference to South Africa specifically.

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Beyond Capabilities: Investigating China's Military Strategy and Objectives in Cyberspace

United States government officials and policy makers regularly warn that China will launch destructive cyberattacks against critical US civilian infrastructure, including electrical grids, water supply stations, and transportation networks. However, such predictions are based on analysis that emphasizes China's cyberwarfare capabilities, while ignoring the country's cyberwarfare strategy and objectives. While China may possess the capacity to carry out devastating cyberattacks, do they want to? Accurately predicting Chinese cyberattacks requires a holistic analysis that considers not just China's capabilities, but its strategy and objectives as well. This paper relies on journal articles produced by senior military officials at China's Academy of Military Science to uncover, organize, and ultimately distill Chinese cyberwarfare strategies and objectives. In addition, secondary analysis conducted by western military experts on China and intelligence gathered by the US government help identify key trends and anomalies found in the primary sources. In reviewing these documents, it becomes clear that Chinese cyberwarfare strategy calls for cyberattacks to be used during military conflicts in a preemptive manner to disrupt enemy communications and logistics networks. It does not call for the destruction of civilian infrastructure during peacetime. Framing China's cybersecurity threat within a broader context of strategy and objectives reveals that the country may not be the most likely perpetrator of future destructive cyberattacks. This discovery has significant implications for current US national security policy, which is heavily focused on confronting a major Chinese cyberattack.

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A Preliminary Analysis of Sex Education for High School Students in Mainland China

Sex education in schools is becoming an increasingly accepted solution globally to addressing public health crises to empower young people with the skills and knowledge they need to make decisions that are good for their mental and physical health. With this background, a survey was distributed to sixteen Chinese students in the United States who attended high school in Mainland China anytime between the years 2005 and 2014. The survey responses as well as primary and secondary research of Chinese textbooks, teachers manuals, academic studies and newspaper articles are used to conduct a preliminary analysis of the sex education high school students receive in Mainland China. This paper identifies the arguments for comprehensive sex education in Chinese high schools including, but not limited to, rising STI, HIV and abortion rates among Chinese youth. Findings include that conservative dissent, teacher training, and the college entrance exam system all pose significant challenges to the sex education movement in Mainland China. Alternative methods for addressing the lack of sex knowledge among Chinese adolescents are examined. I conclude with additional findings from two other academic studies, recommending further study on the movement for sex education in Mainland China.

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Perceptions of Gender Roles and Property Rights: Analyzing Policy as a Mechanism for Safeguarding Women’s Land Rights in Liberia

In May 2013, the Liberian government reformed its land management system by introducing the country’s first Land Rights Policy. The goal of the document is to clearly define various land categories and identify individual property rights. The policy also attempts to specifically outline land rights as they apply to women in Liberia. However, since gender roles are strongly connected to historical and cultural norms, policy alone is not always sufficient in securing equal access for men and women. In Liberian society, land access and personal livelihood are heavily contingent on gender identity. Historical prominence and cultural acceptance of men as laborers reinforce control over land by male household heads, at the expense of women’s autonomy. This thesis closely analyzes the 2013 Liberian Land Rights Policy from a gender perspective and provides a historical synopsis of property ownership and gender roles in Liberia to evaluate whether policy is an effective mechanism for safeguarding women’s land rights in the country. An analysis of historical documents, oral histories, and surveys will illustrate the social and economic necessity and feasibility of adequately safeguarding Liberian women’s land rights. This topic is important to the socioeconomic advancement of women in Liberia because effective land rights policies positively increase women’s access to sustainable livelihoods, food security, and economic independence. This research finds that through a stronger implementation of gender equality principles and changes in social and cultural perceptions of gender roles and property rights the Liberian government can effectively safeguard women’s land rights.

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An American Embassy in Iran

After announcing the reestablishment of diplomatic relations between the United States and Cuba following a fifty-year hiatus, President Barack Obama was asked about the possibility of achieving the same objective with the Islamic Republic of Iran prior to the end of his term. His response, "Never say never."

Relations between the United States and Iran abruptly broke as a result of the infamous takeover of the American embassy in Tehran by revolutionary students. Despite the strong alliance shared by both nations under the leadership of the shah, Mohammad Reza Pahlavi, the emergence of a new Islamic government redefined the interests of the American-Iranian relationship that led to the permanent end of diplomatic relations.

Over the past thirty-five years since relations were broken, both the United States and the Islamic Republic of Iran have expressed a sporadic desire to improve relations. President George H.W. Bush (1989-1993) spoke that "goodwill begets goodwill"—a phrase aimed at Iran to build trust and cooperation. Under President Mohammad Khatami (1997-2005), Iran advocated for a "dialogue among civilizations," largely intended to reconstruct the Western perception of Iran and especially reach out to the United States.

This paper advocates that the United States should work to reopen its embassy in Iran as a means of improving diplomatic relations between the two countries. The research behind this argument comes from interviews conducted with six former US Ambassadors. Throughout these interviews, four themes persisted in the role ambassadors play, whether appointed to friendly or adversarial nations: consulting foreign governments for their perspective, presenting US policy to foreign nations and governments, clarifying misinterpreted actions for both the foreign government and for Washington, and building rapport with foreign leaders. Incidentally, these four patterns are strongly lacking in the current American-Iranian relationship. This paper will also discuss why other forms of diplomacy, such as summits, are beneficial but insufficient to achieve the work that ambassadors do.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

The Politics of Privatization: Electoral Competition and Public Sector Privatization in India

Why do some democratic governments privatize their public sector more rapidly than others, and why do they pick different methods of privatization? Privatization has been shown to be beneficial for economic growth and development. However, critics argue that privatization negatively impacts worker wages, working conditions, and increases inequality. Privatization is controversial and yet, it is an extremely widespread phenomenon. Since 2009, over \$1.1 trillion worth of public sector enterprises (PSEs) have been sold, more than any other time since 1979.

In addition, governments also employ alternate methods of privatization. While the sale of public companies has been booming, we have also seen the rise of public-private partnerships (PPPs). PPPs are long-term contracts between the public and the private sector to deliver public goods and services. According to the World Bank, they are used today in 134 developing countries, and account for 15 to 20 percent of the total investment in infrastructure.

So what explains the variation in levels and methods of privatization? My dissertation tests the relationship between the politics of elections and privatization, using evidence from India at the national and state levels since 1991.

I argue that while discouraging some forms of privatization, democratic competition encourages others. Competition reduces the likelihood of the sale of PSEs, because selling public companies is controversial and unpopular with public sector workers. Politicians fear losing their seat, and consequently, refrain from privatizing through the sale of PSEs.

Conversely, competitive elections increases the likelihood of privatization through PPPs. PPPs improve the quality and delivery of public goods like roads, airports, hospitals etc. They do not face opposition from public sector workers, and receive strong support from business groups and international institutions like the IMF. So while competition makes privatization through the sale of public companies less likely, it makes privatization through PPPs more likely.

Using evidence from India, my project tests these claims using a mixed methods research design. It tests the relationship between politics and privatization statistically, using data collected through fieldwork in India between 2012-2014. I also conduct case studies at the national level, and in three states in India. The project generates a comprehensive, original database of privatization in India., and addresses the debate on the relationship between democracy and development. I find that while democracy makes some economic policies harder to implement, it might make alternate economic policies easier.

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Can Our Gods Bring Us Together? The Need for Ethno-Religious Peacebuilding in Sri Lanka

In 2009, the Sri Lankan government ended a thirty-year civil war between the Buddhist Sinhalese majority and Hindu Tamil minority that propagated increasing polarization toward ethnic and religious identity while smaller Muslim and Christian communities fell into the crossfire. After a brutal final battle between the Liberation Tigers of Tamil Eelam and the Sri Lankan Armed Forces, the leader of the Tamil Tigers was killed and the government gained full control of the island for the first time in over ten years. Tens of thousands of Sri Lankans were caught in the middle of the conflict and became victims of gross human rights violations. There has been little to no national reconciliation or government reformation and the minority rights grievances that started the civil war have been left largely unaddressed. Recently there has been a striking increase in religious violence, especially against the Christian and Muslim communities. The current alliance that controls parliament is dependent on two Sinhalese Buddhist nationalist political parties to maintain control and thus stifle any national reconciliation. While many scholars have analyzed the role religion played in propagating the conflict, little has been written on the potential for religion to be used as a tool to bridge gaps and build a pluralistic Sri Lankan society. Through interviews with local and international peacebuilding organizations, officials and diaspora communities, this research analyzes what role interreligious programming plays in peacebuilding initiatives throughout the island nation. While specifically addressing the Buddhist, Hindu, Muslim and Christian communities, interreligious peacebuilding programs are able to build stronger relationships between disparate communities and move toward reconciliation. Understanding the limitations of liberal western peacebuilding, interreligious peacebuilding has the unique backing of religious faith to support such initiatives. With the promising election of President Sirisena in early 2015, Sri Lanka has potential to address minority rights for the first time since the end of the civil war. Interreligious peacebuilding is crucial to bring the electorate thus the legislative branch in line with the executive's beliefs and begin a national reconciliation process. Successful interreligious peacebuilding in Sri Lanka has the potential to be a valuable model for peacebuilding when addressing ethno-religious conflicts across the globe.

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Occupational Health Risk Factors for Schistosomiasis: Systematic Review and Analysis

Schistosomiasis is a neglected tropical disease caused by a parasitic flatworm which afflicts over 200 million people in the poorest regions of seventy-four countries in Africa, South America, Southeast Asia, and the Middle East. Carried by snails living in fresh, stagnant water, the parasite penetrates human skin upon contact, causing the victim to suffer a range of symptoms including severe pain, diarrhea, blood in the urine, and eventual death. Despite its prevalence, schistosomiasis is preventable, treatable, and curable once a control program is implemented. Substantial reduction of schistosomiasis would relieve suffering and produce many socio-economic benefits, including higher productivity and higher school attendance rates. Disease transmission is directly tied to the environment, and those in certain occupations are at particularly high risk, including agricultural workers, irrigation workers, fishermen, miners, and people carrying out domestic tasks due to direct contact with unsafe water. The objective of this study was to examine which occupations yield the highest risk factors for acquiring schistosomiasis. Conducting a systematic review and analysis, I will ultimately select about thirty peer-reviewed studies from Scopus, Web of Science, and Medline based on specific inclusion criteria. All relevant evidence from the systematic review will likely conclude that certain occupations result in an increase in risk of schistosomiasis, and that a comprehensive approach to prevention and treatment is integral in community health and development in poor, rural areas. Prevention and control programming for schistosomiasis should focus on at-risk occupations, including targeting water-resource management, irrigation systems management, and agricultural management, in order to stop the occupation-specific transmission of the disease, which leads to higher schistosomiasis rates in endemic communities.

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Learning to Share the Pie: Civil-Military Negotiation over the Defense Budget

After over a decade of war, the United States military faces difficult choices. Much like other drawdowns, the Department of Defense (DoD) must determine the appropriate size and scope of a presumably smaller force. Yet as the military maintains a range of capabilities, appropriate levels of readiness, and technological edge, the Pentagon confronts a daunting fiscal environment characterized by shrinking budgets. As a result, the competition between the four services for their share of the defense budget intensifies. DoD's internal budget dynamics outlined in the Planning, Programming, Budgeting, and Execution (PPBE) process require each service to submit proposals to the Office of the Secretary of Defense prior to their inclusion in the President's Budget. Each service makes an independent assessment of what programs require funding in order to execute the defense strategy. Fearing deep cuts, the services justify extraneous programs to maintain their share of the pie. Given this incentive structure, there are deep discrepancies between the "theory" codified in manuals for military programmers and the "practice" by which senior officials develop the budget. Drawing upon a series of interviews with government officials, military personnel, and academics, I explain the process by which the military services reconcile the difference between the desirable force and the feasible force. Efforts to resolve this divergence are constrained by five issues: an unrealistic timeline ("timeline"), a stove-piped analytic system to model scenarios prior to budget discussions ("analytics"), a lack of civilian oversight to piece together the splintered service budget submissions ("shards"), a preference by the services to preserve their individual equities at the expense of the defense strategy ("parochialism"), and a reliance on external funding supplies, primarily Overseas Contingency Operations funding ("dependence"). Until these constraints are addressed, DoD cannot budget properly for the future security environment and is forced, therefore, to endure additional and unnecessary risk.

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Experimental Determination of Optical Band Gaps for Soot in Nitrogen-diluted, Ethylene/Air Non-premixed flames

In order to most effectively mitigate the negative effects of combustion processes the chemical and physical processes need to be well understood. While the general mechanism of soot formation is agreed upon, the size at which soot precursors transition from chemical to physical growth is highly contested in the combustion community. In this work, visible light extinction was measured throughout a nitrogen-diluted, ethylene/air, non-premixed flame system. Using Tauc/Davis-Mott analysis, this data was used to determine the optical band gap, E_{opt} , as a function of flame position. Observed optical band gaps span the range from 1.85eV to 2.35eV, where lower band gaps are observed in regions of the flame with the largest soot concentration. Comparing these results to previously published computational results from our lab relating calculated HOMO-LUMO gaps for a variety of D2h PAH molecules to the number of aromatic rings in the structure, showed that the observed optical band gaps are consistent with PAHs between 10 and 20 rings in size or a conjugation length between 0.85 and 1.15nm. The average OBG measured throughout the flame system correlates to a species with 14 aromatic rings and a conjugation length of 0.97nm, something about the size of circumpylene. This result agrees with the hypothesis that PAH condensation begins at modest molecular size. Future experiments aim to extend the spectral range and add scattering measurements, in order to gain additional information about the physical structure and chemical make-up of soot as a function of flame position.

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Characterizing Candidate Genes for Giant Sperm in *Drosophila melanogaster*

Reproductive traits are important in ensuring fitness, and they tend to evolve rapidly. Sperm, in particular, is the most variable cell type in the animal kingdom. Although much is known about the genetics of spermatogenesis as a general process, little is known about the genetics of variation in sperm length. One component of sperm shape that is frequently variable among species is length, which is important in sperm competition and can contribute to reproductive isolation and male-female coevolution. The Manier lab previously investigated the genetic basis of sperm length in *Drosophila melanogaster* and found 300 protein coding genes that may be involved in sperm length. A subset of these genes, *crossveinless c* and *Stat92E*, was assessed using mutant lines. These genes are important for open tracheal system development, and *Stat92E* is also important for post-embryonic organ morphogenesis. The tracheal system, a branched network of tubes throughout the body, is the location of gas exchange. Sperm length was assessed by collecting newly emerging males as adults from pupal cases and dissecting their testes. Sperm from dissected testes were imaged and measured, and a statistical t-test was used to compare the mutant lines to appropriate wild type flies. Results found that mutant flies that lack proper function of *crossveinless c* have sperm that are longer than control wild type flies, suggesting that this gene plays a role in negatively regulating sperm length. In other words, *crossveinless c* functions to keep sperm shorter than they would otherwise be without it, such that when its function is disrupted, sperm become longer. On the other hand, results found that *Stat92E* is significantly shorter than control wild type sperm, suggesting that this gene is involved in positive regulation of sperm length. Future studies will investigate the roles of these genes during spermatogenesis using developmental, cellular, and molecular methods.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Measurement Device for Rolling Objects

This study was inspired by an assignment during a lab session in the intermediate physics laboratory. The class was tasked with calculating the moment of inertia for a uniquely shaped object that was to be created in the machine shop. That calculation was used to approximate the time required for the object to roll down a short incline. In all cases, the estimates showed that one would have to be able to measure the time of the roll to the hundredths of a second. Any length of time longer and the accuracy of the predictions and calculations would not be able to be verified. The lab was not set up with any equipment capable of obtaining this measurement with the required precision so new equipment had to be created in order to measure the time required to roll down the incline. Using an Arduino microcontroller, two pressure sensors, an accelerometer, a gyroscope, an eight foot long board, and over 300 lines of custom source code, a device was created that gave the precision and accuracy required. Further, it automatically calculates the angle of its inclination so multiple angles of inclination can be used to get a more robust set of data. The ramp was tested with simple objects and known moments of inertia - a hoop and a solid cylinder—in order to determine its accuracy and precision. The ramp successfully and repeatedly measures the roll time of objects to within two hundredths of a second. With the level of precision and accuracy afforded by the ramp, all calculations and estimates of roll times can be measured and verified.

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Developing an in vivo Model for Amylin Toxicity in the Nervous System

Type II Diabetes Mellitus (DM) is a prevalent metabolic disease that affects over 25 million people in the U.S. alone. The disease is characterized by the body's inability to regulate glucose levels in the blood. Normally, blood glucose is regulated via the pancreatic hormones, insulin and amylin, which are cosecreted. However, in patients with Type II DM, the body becomes resistant to the regulatory effects of insulin. In addition, the pancreatic cells which produce amylin and insulin die off. This process of cell death is largely influenced by amylin derivatives, or amyloids. Amyloids are also found to have toxic effects in the central nervous system where a mechanism of pathology is not yet defined. The goal of this research is to produce an in vivo model for amylin toxicity in the nervous system using a transgenic strain of *Caenorhabditis elegans*.

The first step of this project was to create the transgenic strain of *C. elegans*. This was achieved by injecting the *C. elegans* germ-line with a plasmid carrying the human amylin gene. The plasmid was made so that the human amylin gene would be expressed via a heat-inducible promoter. To demonstrate that the strain expresses the human amylin gene, western blots were performed after heat induction. The next step in the proteomic analysis of this transgenic strain will be the immuno-isolation of amylin hetero complexes. In addition RNA sequencing of the transgenic strain after heat induction will be performed. Behavioral and anatomical characterization of defects due to human amylin expression is another major aspect of this study. By performing behavioral assays and examining neuronal mapping we have quantified the deleterious effects of amylin expression in the nervous system of *C. elegans*.

Concordantly, all experiments performed on the human amylin transgenic strain have been conducted on a rat amylin transgenic *C. elegans* mutant. Unlike human amylin, rat amylin does not form amyloids, although the two are homologous. The rat amylin-expressing strain serves as a control for the expression of a foreign protein in *C. elegans*. Thus far, studies have shown that neurodegenerative effects have only manifested in the human amylin, not the rat amylin, transgenic strain.

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Characterizing the effect of a dimeric structure of MID1's Bbox1 Domain

MID1 is an essential protein for proper development of the midline region of humans during embryogenesis. When MID1 is mutated, males are born with X-linked Opitz G/BBB syndrome, which is midline defects that includes cleft lip and palate, wide spaced eyes, and defects with many organs along the midline. Bbox1 is the second domain among MID1's seven domains. Previous results have shown that Bbox1 either has a similar function as the RING Domain, which is as an E3 ligase, or it increases the RING domain E3 ligase activity, serving as an E4 ligase. It is well known that protein's structure determines its function. My project investigates the dimer structure of Bbox1 and the role this has in dictating these two functions of MID1. My project involves establishing protein expression and protein purification protocols so that we can identify the dimeric structure and its properties by NMR spectroscopy. I will also study how mutations associated with XLOS affects the dimer structure of MID1.

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An Open-Path Tunable Diode Laser Sensor for Simultaneous Measurement of Methane and Carbon Dioxide

Melting arctic permafrost is a large carbon source which releases key greenhouse gases (GHG) into the atmosphere. In a collaboration between NASA Goddard Space Flight Center, the University of Alaska-Fairbanks, and the George Washington University a study of the feedbacks to climate change caused by melting permafrost has been initiated. An array of ground experiments at three unique permafrost sites will record permafrost depth, structure, meteorological data, and emissions of key greenhouse gases during a springtime permafrost melt. Ground data will be linked to climate models and landscape structure from satellite imagery to gauge the magnitude of the feedbacks.

GWU will perform high-sensitivity ground-level measurements of carbon dioxide and methane. Currently, we are developing a low-power and portable open-path instrument which builds on our laboratory's previous experience with deployment of multi-laser, multi-species sensors. Spectral simulations suggest that at ambient levels of CO₂ and CH₄ (400 and 2 ppmV, respectively) we will observe \approx 1% absorption over a 200 meter path. Prior work in our laboratory suggests that a signal-to-noise ratio (SNR) in excess of 100 will be achievable at these absorption levels using sweep averaging or other techniques. Here we report on the progress of the sensor's construction with a focus on the design of the laboratory prototype.

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Discovering mechanics problems with dependent responses in a MOOC

We searched for pairs of problems that students answer similarly in the MIT's MOOC 8.MReVx. We plan to use such pairs, or groups of pairs, to identify skills that students actually use to solve problems. To avoid false dependencies that arise when skillful (unskillful) students answer both problems correctly (incorrectly), we divided the students into ability-based groups using three sorting methods: skill from Item Response Theory, success rate on attempted problems, and success rate on all problems. The results show similar trends for all three methods, with each method yielding consistent numbers of dependent problem pairs well above chance. We will discuss our findings, implications for instruction, as well as our plans to cluster the pairs of problems and identify the types of skills associated with each cluster.

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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Comparison of Analysis Frameworks, AcquRoot and GoAT

Nuclear physics experiments create a large volume of data which can only be processed efficiently using computer software. Typical data analysis frameworks need to convert raw pulse heights from experiments and represent it in physical quantities such as the time and energy of a particles detection. Using the position of the detectors and timing and energy information, the particle can also be tracked and identified. Within the A2 collaboration at the MAMI accelerator, in Mainz, Germany, AcquRoot has been the analysis framework utilized for a long time. It is based on the CERN ROOT toolkit, an object oriented software package, designed for high energy physics. However, because of the complexities of AcquRoot a new analysis framework, GoAT (Generation of Analysis Trees), was developed recently as an extension to AcquRoot. It allows for easier interfacing and reduces the time required to change criteria/physics on an event-by-event basis. Although GoAT has been tested using real data it has yet to be benchmarked thoroughly against AcquRoot. In order to see any significant differences between the two systems, this project will analyze simulated data consisting of proton Compton scattering (with a photon incident energy of 50-400 MeV) and identifying these events within AcquRoot and GoAT. A comparison of the two outputs will be achieved by looking at the physical properties of the reaction such as missing mass of proton. The comparative efficiency will then be calculated thereby giving a basis for comparing the two frameworks.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Characterizing the MID1 Fibronectin Type III Domain Through NMR Studies

MID1 is a microtubule-associated protein that plays a key role in regulating the cellular concentration of Protein Phosphatase 2A (PP2A) and Alpha-4 through the ubiquitination pathway. MID1 facilitates the transfer of ubiquitin, a specific protein tag, to target a protein for degradation. Mutations in MID1 are linked to X-Linked Opitz G Syndrome (XLOS), a developmental disorder characterized by abnormalities along the midline of the body that include cleft lip, agenesis of the corpus callosum, and various organ complications. To understand MID1 function and its role in causing XLOS, a comprehensive investigation of the structural components of the MID1 domains is necessary.

The Fibronectin Type III (FNIII) domain is located within the C-terminal region of MID1 and its structure and function, as a part of MID1, are unknown. Three point mutations within this domain (P441L, G452S, and V463F) are found in XLOS patients. My research focuses on using three-dimensional Nuclear Magnetic Resonance (NMR) spectroscopy to determine the MID1 FNIII structure and further understand how it interacts with other MID1 domains and contributes to the overall function of MID1, including its enzymatic activity. Here I present and compare the structures of the three FNIII mutations and the wild-type FNIII. This understanding could help us clarify how FNIII functions and its role in XLOS.

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Phenology of Black Cherry and Eastern Tent Caterpillars: Understanding Synchrony and its Effects on Plant Quality

This study quantifies the degree of synchrony between black cherry (*Prunus serotina*) and its specialized herbivore, the eastern tent caterpillar (ETC; *Malacosoma americanum*), as well as observes the effect of defoliation by ETCs on subsequent phenological events such as flowering, fruit production and leaf senescence. ETCs are spring feeders that rely upon synchronizing their hatching with bud burst of black cherry to survive, and if environmental factors are ill-suited during hatching, larvae often die before completing development. The knowledge of baseline levels of synchrony is necessary to forecast the effects of climate change on ETCs. Additionally, life cycle events of black cherry trees can be altered by interactions with ETCs, with potential resulting changes in foliar phenology and chemistry having direct effects on the host plant and indirect effects on subsequent herbivores encountering the plant.

Phenological events of black cherry trees (bud burst, leaf elongation, leaf senescence) and eastern tent caterpillars (hatching) were monitored starting in February 2014 in a common garden at The George Washington University. Eighty trees were monitored throughout the study, half belonging to the test group (with local ETC egg masses) and half to the control group (lacking ETC egg masses).

While there was some variation among trees and egg masses in budburst and egg hatch phenology, most plant-herbivore pairs had caterpillar hatch dates that lagged slightly behind bud burst. With a few day delay, the presence of adequate food for ETCs was assured, supporting caterpillar development. However, the relatively small size of experimental trees resulted in very high levels of defoliation by ETCs in the experimental trees. The defoliation of black cherry by ETCs and the subsequent re-growth of foliage show the ETCs significant impact on subsequent phenological events of black cherry trees, including a lack of flowering, fruiting, and a major shift in leaf senescence in the ETC-defoliated trees relative to the controls.

The results of this study suggest that the current levels of asynchrony displayed in this experiment are not significant enough to threaten species survival, although further climate change may further increase the asynchrony. ETC phenological phases coincided closely enough with black cherry phases to ensure the presence of a food source during growth. The impact of defoliation on black cherry trees was found to be significant, as their subsequent phenological phases were either significantly altered or absent, highlighting the intense selection pressure that this specialist herbivore has on its host plant.

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Characterization of the sodium calcium exchanger mutant *ncx-6* and *ncx-1* in *Caenorhabditis elegans*

The genes *ncx-1* and *ncx-6* belong to the Sodium Calcium Exchanger family and are responsible for calcium regulation. Sodium Calcium Exchangers are expressed in human cardiac sarcolemma, the brain, kidneys, liver, pancreas, skeletal muscle, placenta, and the lung. The NCX proteins play an important role in development and pathogenesis.

The *ncx-6* gene belongs specifically to the Ca²⁺/Cation exchanger (CCX) branch. The human equivalent to the Ca²⁺/Cation exchanger is the Na⁺, Li⁺/Ca²⁺ exchanger (NCLX). NCLX proteins are broadly expressed in excitable cells, and localize to the mitochondrion. NCLX regulates a wide variety of cellular responses and dysfunction has been linked to Parkinson's disease, Alzheimer's disease, and cardiac arrhythmia, which is a leading cause for strokes and death associated with heart failure. Mutations in the *ncx* genes are not well understood since the viability rate of mutants is low. However, *Caenorhabditis elegans* mutants have been found to be viable and thus *C. elegans* represent a powerful new model organism for the investigation of sodium calcium exchangers. Here, we describe our characterization of a *C. elegans ncx-6* and *ncx-1* mutation. The causative lesion within the *ncx-6* and *ncx-1* genes in our mutants is defined by a premature stop codon and may represent a genetic null. We show that *ncx-6* is expressed in a subset of cephalic primary sensory neurons and find that *ncx-6*^{-/-} mutants exhibit defective sensory behavior. *Ncx-1* is shown to be expressed in the AIY interneuron within the inter neuron pair in the cephalic ganglion.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Muscle architecture and myosin profile of the cypriniform palatal organ

Cypriniformes is thought to have evolved 250-350 million years ago and the group has grown to include more than 3,000 species that are characterized by a number of feeding novelties. These feeding structures include: a unique arrangement of the pharyngeal jaws in which the lower pharyngeal jaws are greatly enlarged, loss of oral teeth and a stomach, and a new ossification of the cranial skeleton that aids in jaw protrusion. Such novelties have most likely contributed to the successful evolutionary diversification of this group. This study specifically focuses on a muscular structure located on the roof of the buccopharyngeal cavity known as the palatal organ. This palatal organ is attached laterally to the branchial arches and is covered with a taste bud-studded epithelium. There has been very little research into the structure and function of this palatal organ across cypriniform species, with no research on the specific myosin composition constituting the palatal organ. Through histological and immunoblotting techniques we were able to investigate the anatomical and physiological characteristics of the palatal organ muscle fibers in ten species. There are pronounced differences in both the architecture and diameter of the muscle fibers. Immunoblotting, used to identify the specific make-up of the myosins, revealed that there are significant differences in the myosins that comprise the palatal organ. Such differences in both anatomy and physiology of the muscle fibers suggests that there may be important differences in function of the palatal organ between cypriniform fishes. Although previous researchers have dismissed the palatal organ as a vestigial feeding structure in the majority of these fishes, we have concluded that this palatal organ likely serves a role during feeding. These differences in muscle fiber diameters, composition, and arrangement all signify the importance of this muscular structure within cypriniform feeding mechanisms and that this structure has evolved to serve different functions within each species. Future research includes using electromyography to observe different cypriniform species while feeding to determine if these anatomical and physiological differences correspond to specific differences in function.

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A Molecule based reaction-transportation model explains the oscillatory migration of Zyxin-Depleted human fibrosarcoma cell

Cell migration is essential in biology, and it is closely related to biological functions such as wound healing, immune responses and cancer cell metastases. Without chemical or physical gradients, cells migrate randomly. Recently, the Wirtz lab discovered the large scale periodic cell migration of Zyxin-depleted human fibrosarcoma cells with period longer than 2 hours. These cells exhibit distinct regular oscillatory migration patterns in three-dimensional ECM and along one-dimensional chambers. Here, we present a reaction-transportation model based on a coarse-grained molecular picture of the process. Migrating cells have well-defined polarity and microtubules are known to play important roles. By explicitly incorporating these two facts in a reaction-transportation framework, we successfully reproduced the experimentally observed periodic migrating patterns. Our results suggest that, although diffusion and motor-based active material transportation (convection) both exist in cell, the periodic switching of cell's polarity is mainly due to the motor-based convection. Surprisingly, we discovered two distinct oscillatory phases: in the first phase, the polarization factors undergo simple and fast end-to-end oscillation, which would not lead to the observed large scale periodic migration; whereas in the second phase, the polarization factors not only oscillate between two cell ends but also generate vortex-like local patterns at either ends. These vortex-like patterns greatly elongate the period of the oscillation, which effectively stabilizes the migration in either direction, leading to the large scale oscillatory migration. Based on our model, the cell length dependencies of various oscillatory characteristics have been predicted for future experimental verification. The identified two oscillatory phases may provide useful insights to the general picture of how cells alter direction during rather persistent migration, and the developed reaction-transportation model provides a general framework for studying the long-range cytoplasmic translation dynamics of any molecules.

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Uncovering Metabolic Changes in Single *Drosophila melanogaster* infected by Nematode Parasites using Capillary Electrophoresis Mass Spectrometry

INTRODUCTION:

Host-pathogen interactions are the underlying cause of several infectious diseases, including ~20% of global deaths caused by incurable infections. The etiology of these diseases and development of treatments is dependent on understanding host-pathogen interactions at the molecular level; however, this requires analytical techniques that are sensitive, selective, and adoptable to constrained volumes/amounts of material available in host-pathogen models. Here, we use volume-limited capillary electrophoresis-mass spectrometry (CE-MS) to identify metabolites produced in single larvae of the fruit fly (*Drosophila melanogaster*) during infection with the soil nematodes (*Steinernema carpocapsae*) that live in symbiosis with the bacteria *Xenorhabdus*. We demonstrate that CE-MS is able to detect metabolic changes in the host upon infection with the nematode parasites and their associated bacteria.

METHODS:

Three types of single *Drosophila* larvae were studied: (i) uninfected larvae (negative control); (ii) larvae infected with the nematodes lacking the bacteria (axenic nematodes); and (iii) larvae infected with the nematodes carrying the bacteria (symbiotic nematodes). Metabolites of these specimens were extracted in 50% methanol (0.5% acetic acid) after centrifugation of cell debris. A 10 nL-volume of the extract was injected into our CE-MS system, and metabolites were separated in a fused silica capillary (40/105 μm ID/OD, 90 cm length) at 1,950 V potential in 1% formic acid. Metabolites were ionized by a CE-electrospray source and identified by a quadruple time-of-flight tandem mass spectrometer operated at 40,000 (FWHM) resolution.

PRELIMINARY DATA:

Before measuring the *Drosophila* larval extracts, the analytical performance of the CE-MS instrument was thoroughly evaluated using chemical standards. For octopamine and tyramine, classical neurotransmitters of the fly brain, the lower limit of detection was ~10 nM (60 amol) and the quantitative reproducibility was ~25% relative standard deviation. These figures of merit were appropriate to measure endogenous metabolites in single *Drosophila* larvae.

Using the CE-MS platform, we detected more than 100 different molecular features in individual *Drosophila* larval extracts, indicating complex chemical composition in the host. A total of 35 of these features were confidently identified as different metabolites by comparing accurate masses and tandem mass data to metabolomic databases (Metlin and KEGG). Among the identified metabolites were amino acids, energy carriers, and nucleotides.

To characterize molecular features during the infection process, normalized metabolite abundances were compared three-ways, between the uninfected control *Drosophila* larvae, larvae infected with axenic nematodes, and larvae infected with symbiotic nematodes. Cycloleucine was measured in comparable amounts between all the extracts, and the uninfected larvae and those infected with axenic nematodes gave comparable ion signal for valine, glycine, aspartic acid, and histidine. In contrast, threonine, proline, and alanine were detected in higher ion counts in the uninfected larvae. Larvae infected by axenic nematodes contained more histamine and creatinine, and larvae infected with symbiotic nematodes were richer in cysteine. Using a higher number of biological replicates, we anticipate to identify metabolic processes with high statistical significance.

Although the biological reason for these observed differences is yet unknown to us, they certainly indicate that infection has an impact on the metabolome of the host. The results and analytical approaches described here can be extended to other sample types where sensitive metabolic detection is required at the low nanomolar level.

NOVEL ASPECT:

Using a volume-limited CE-MS platform, we uncover metabolic changes in *Drosophila* larvae during pathogenic interactions.

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Modeling of Quantum Efficiency and Electron Spin Polarization from strained NEA GaAs Photocathodes

Photoemission from strained GaAs activated to negative electron affinity (NEA) is a main source of polarized electrons for modern nuclear-physics and particle-physics facilities. Future experiments at advanced electron colliders will require highly efficient polarized electron beams, which could provide high polarization and luminosity. This sets new requirements for photocathodes in terms of high quantum efficiency (QE) ($\gg 1\%$) and spin polarization ($\sim 85\%$). Despite the many years of experience in this field, there are such important processes as electron-phonon interactions near the surface that must be studied in depth. Detailed Monte Carlo simulation and modeling of physical processes in photocathodes is important for optimization of their design in order to achieve high QE and reduce depolarization mechanisms. The purpose of the present work was to develop a semi-phenomenological model, which could predict photoemission and electron spin polarization from NEA GaAs photocathodes. Influence of the presence of quantum heterostructures on the diffusion length was studied. Simulation results were compared to the experimental results obtained at Thomas Jefferson National Accelerator Facility, Newport News, VA (Jefferson Lab).

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Calnexin interaction with ABCA1 is impaired in HIV infection and Tangier disease

IV-1 infection is associated with an increased risk of developing atherosclerosis. Studies have demonstrated that this results from impairment of cholesterol transporter ATP-Binding Cassette A1 (ABCA1). In normal cholesterol transport, ABCA1 mediates the efflux of cholesterol to lipid-poor apolipoproteins, which then form high-density lipoproteins (HDL). HDL is responsible for transporting cholesterol from body tissues to the liver, where it is removed from the blood. Nonfunctioning ABCA1 results in a buildup of cholesterol within the cell and leads to the development of foam cells that accumulate to cause atherosclerosis. HIV protein Nef binds to the endoplasmic reticulum (ER) chaperone calnexin, a protein responsible for the folding and maturation of ABCA1. ABCA1 then exhibits weaker binding to calnexin and is unable to undergo transport from the ER to the cell membrane. In this study, confocal microscopic techniques were used to demonstrate ABCA1 retention in the ER in HIV-infected macrophages. Upon further investigation, it was found that this phenomenon is present in images of cells transfected with ABCA1 mutations, Q597R and R587W, characteristic of Tangier disease, a genetic disorder characterized by significantly reduced levels of HDL in blood. We hypothesized that these mutations were responsible for weakened interaction between calnexin and ABCA1, similar to the mechanism engaged by Nef in HIV-infected cells. However, results demonstrated that ABCA1 mutants bind more strongly to calnexin than the wild type ABCA1. We therefore conclude that an optimal level of ABCA1-calnexin binding is necessary for normal cholesterol efflux; both increased and decreased binding affinity retains ABCA1 in ER and affect cholesterol efflux. Further study will test whether Nef, by decreasing interaction between Q597R and R587W ABCA1 mutants with calnexin, can reverse retention of mutant ABCA1 in ER and rescue cholesterol efflux. A positive result would suggest a new therapeutic approach for treating Tangier disease by Nef-mimicking peptides.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Improving the Utility of Seasonal Outlooks of Anomalous Precipitation for California

California's population grew by over 10 million from 1980 to 2000 and is expected to reach a total of 48 million by 2030. This will create additional strain on a water supply already stretched by severe, prolonged droughts that are expected to become more frequent in the region as the global climate changes. The ability to anticipate precipitation for the coming seasons can help water resource managers make decisions and mitigate the effects of severe drought or flood events. Due to the need for better predictive abilities for water resources, this project aimed to improve the utility of seasonal climate outlooks through analysis of past climatic signals. Compared to forecasts with shorter lead times, 90-day to two-year seasonal forecasts have the least level of skill and are often considered the most challenging to predict. Therefore, this project incorporated National Oceanic and Atmospheric Administration (NOAA) Climate Data Records (CDRs), National Aeronautics and Space Administration (NASA) satellite data, and in-situ data to understand and identify the climatic indicators that lead to anomalous seasonal precipitation (i.e. extremely wet or dry seasons). The precipitation anomalies were defined via in-situ precipitation data from the National Climatic Data Center's Global Historical Climatology Network in California Climate Divisions 2 and 5. This project identified climatic patterns that influence the recurrence of anomalously high or low precipitation. A secondary result of this project was a compilation of information from end-users that describes the degree to which NOAA CDRs and NASA earth observations are used operationally. Results of this project will potentially aid California resource managers and policy-makers in preparing for, and mitigating, the impacts of future extreme events.

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Divergent Angiotensin Receptor Signaling in a mouse model of Post-Traumatic Stress Disorder (PTSD)

Independent of their beneficial effects on hypertension and cardiovascular related disease, angiotensin receptor type 1 (AT1R) blockers can improve stress-related symptoms (Saavedra JM et al., 2012). AT1R receptor-mediated actions can be counteracted directly or indirectly by the angiotensin receptor type 2 receptor (AT2R). Our recent studies in a mouse model of PTSD have shown that AT1R blockade increases the extinction (learned inhibition) of a traumatic fear memory and that AT1R mRNA expression is reduced in fear related brain regions of losartan treated animals (Marvar et al., 2014). These data imply that downstream AT1 signaling events maybe important in consolidation of fear memory extinction. Therefore we investigated the acute effects of AT2R inhibition on fear memory and baseline anxiety. Methods: We performed classical Pavlovian fear conditioning pairing auditory cues with foot shocks and examined fear extinction behavior and cardiovascular responses in the presence of the AT2R antagonist PD 123319. Results: Twenty-four hours following fear conditioning, PD 123319 (15 mg/kg IP) was administered prior to fear memory extinction. The PD treated group exhibited significantly less freezing behavior ($F_{10, 300} = 1.9$; $p < 0.05$) during fear expression and contrary to our previous results with the AT1 antagonist losartan, there was no effect during extinction retention, an index of long-term fear memory. Moreover, qPCR data revealed that mRNA expression of the traditional renin angiotensin pathway gene, angiotensin converting enzyme (ACE) is elevated following fear conditioning in the mouse brain, whereas non-traditional pathways are unaltered. Conclusion: These data indicate that AT1R and AT2R may have divergent effects on short and long-term fear memory formation. Further studies are required to understand the differential regulation of angiotensin receptor signaling in PTSD.

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The expression pattern of NMDA and AMPA receptor subunits in the neocortex and striatum in primates

Metabolic strategy and accompanying synaptic reorganization differ significantly among species. Our previous results indicate that there is differential metabolism in neuronal synaptic terminals that evolved among different primate lineages to meet the energy requirements at the subcellular level in neocortical cells. Therefore these metabolic changes might be associated with modifications in the molecular composition in post-synaptic specialization for elevated neuronal activity and plasticity. Also, because the prefrontal cortex is highly associated with the control of cognition and in the course of evolution, undergoes more expansion than rest of the brain, we aimed to examine the hypothesis that an acceleration of changes in the molecular framework of the PSD, in particular ionotropic glutamate receptor complexes, were associated with the evolution of prefrontal cortex in primates. We examined the expression level of NMDA receptor subunits (NR1, NR2A/B) and the AMPA receptor subunit (GluR2) in the neocortex and striatum in primates using quantitative Western blotting analysis of synaptosomal fractions. Quantitative Western blot analysis demonstrated that the expression of the GluR2 subunit of the AMPA receptor in the prefrontal cortex of haplorhines (i.e., monkeys, apes, and humans) was elevated by 42% as compared to strepsirrhines (i.e., lemurs and lorises), being most pronounced in chimpanzees and humans (70% greater than in strepsirrhines). In the striatum there were no significant differences in synaptosomal expression of ionotropic glutamate receptor subunits protein levels between groups. Our findings show that additional changes in glutamate metabolism took place in prefrontal cortex on the human evolutionary lineage.

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Effect of endosymbiotic microbes on the immune response of *Drosophila melanogaster* to nematode parasites and their mutualistic bacteria

Despite impressive advances in the broad field of innate immunity, our understanding of the participation of endosymbionts in the host immune response to pathogenic infections remains incomplete. Particularly understudied is the role of endosymbiotic bacteria in host defense against nematode parasites and their mutualistic bacteria. The interaction between *Steinernema carpocapsae* nematodes and their mutualistic bacteria, *Xenorhabdus nematophila*, with *Drosophila melanogaster* flies and their endosymbiotic bacteria, *Wolbachia* and *Spiroplasma*, represent an excellent model in which mutualistic and pathogenic processes can be studied simultaneously. In my research I have infected three different strains of *Drosophila* (one carrying *Wolbachia* and *Spiroplasma* together, one carrying *Wolbachia* only, and one carrying no endosymbionts) with the *Steinernema* nematodes containing (symbiotic nematodes) or lacking (axenic nematodes) *Xenorhabdus* bacteria and monitored the survival rates of the infected *Drosophila* larvae at several time points post infection. I have found that *Drosophila* strains carrying both *Wolbachia* and *Spiroplasma* succumbed significantly faster to infection by *Steinernema* axenic nematodes compared to the other two *Drosophila* strains. These results imply that the presence of both endosymbionts in *Drosophila* confer a negative effect on host anti-nematode immune response. Results from this project will generate novel insights into the potential role of endosymbionts as host immune regulators and may expose a currently unknown layer of the innate immune system. From the practical point of view and given that host innate immune responses are broadly conserved, results will potentially contribute towards the development of novel means for the efficient control of parasitic nematodes of humans.

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Rho meson resonance in pipi scattering channel

There are four kinds of fundamental forces in the universe, the strong force, the weak force, the electromagnetic force and gravitational force. The strong force will play a determinant role in hadron-hadron interaction. Meson is one kind of hadron which is also governed by strong force and built up by two quarks. The popular theory right now to describe strong interaction and strong force is Quantum Chromodynamics. In this study, we start from the first principal (Quantum Chromodynamics) and focus on rho meson resonance in two pion scattering channel (which mean two pion with back to back momentum collide into one intermediate particle we called rho meson). We employ the Quantum Chromodynamics theory onto several size of lattice which can be simulated in supercomputer cluster with Monte-Carlo simulation method and compute the rho meson parameters.

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Developing a Method for Rearing *Drosophila melanogaster* Fruit Flies That Lack a Gut Microbiota

The microbial community (microbiota) inhabiting the gut can play an important role in many biological processes including immune function, cognition, and metabolism. In this study, the model organism, the fruit fly (*Drosophila melanogaster*), is used to investigate the link between the gut microbiota and cognitive function using abiotic flies, which lack a gut microbiota. The goal of this study is to develop a protocol for rearing abiotic flies that will be tested for cognitive function in the future. To rear abiotic flies, eggs from wild type flies were collected, sterilized, and raised on sterile food media all within a laminar flow hood, which provides a sterile environment. In each generation, DNA is extracted from flies and genetically assayed for presence of bacteria by attempting to amplify the bacterial gene for the 16S rRNA. If we fail to amplify this bacterial gene, as visualized using agarose gel electrophoresis, we can be assured our flies are sterile. Control flies are used as a positive control to verify that the genetic test is working properly. Based on preliminary trials, I have obtained a survival rate of approximately 11% for sterilized eggs. The goal of subsequent experiments will be to increase this survival rate and to determine the effect of the gut microbiota on cognitive function in *D. melanogaster*.

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Global Analysis of Snake Ecomorphology: A Preliminary Study

Ecomorphology is the study of the relationship between the ecological role of an individual and its morphological adaptations. Previously, there have been some attempts to quantify these snake ecomorphotypes depending on what type of predator they are, such as forage or ambush. There have also been other attempts to classify ecomorphotypes of snakes based on what habitat they are found in, such as in trees or aquatic environments. But what makes an arboreal snake arboreal or a terrestrial snake terrestrial? Our aim is to compare and quantify ecomorphotypes around the globe starting with species from 3 regional assemblages compared over 150 specimens.

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Marker versus shotgun-based metagenomics for clinical pathology

Technological improvements in High-Throughput Sequencing (HTS) have led to an increased use of HTS in pathogen detection and have raised questions about its ability to inform the diagnosis of patients with infectious diseases. Currently, diagnoses of these patients are obtained using culture techniques, which are inherently biased because some pathogens are unculturable. The purpose of this study is to evaluate the ability of two HTS methods, 16S rRNA marker sequencing (16S) and shotgun sequencing, to recover the diagnosis obtained by traditional culture methods. Samples from six patients in the GWU Hospital with Ventilator-Associated Pneumonia (VAP) were cultured using standard protocols and sequenced using 16S and shotgun sequencing. Both sets of sequences were analyzed using a taxonomic profiler. The taxonomic profiler mapped the 16S sequences to 'The All-Species Tree of Life' Project 16S database and the shotgun sequences to a subset of the NCBI nr nucleotide database containing bacterial, fungal, and viral sequences. The shotgun sequencing was able to recover the culture diagnosis down to the species level as the top hit for five of the six patients while the 16S sequencing was only able to recover the culture diagnosis at this level for two of the six patients. However, the shotgun sequencing took on average 22 hours and 41 minutes to map while the 16S sequences took on average less than 9 minutes to map. These results indicate that shotgun sequencing shows greater potential to match the culture diagnosis of patients with VAP than 16S sequencing, but technological improvements at both the sequencing and mapping stages are necessary to decrease the overall turnaround time.

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Species Diversity and Composition across and Ecotone at the Dyke Marsh Wildlife Preserve

Ants are a valuable indicators of biodiversity within and among habitats. In this study, we wanted to use ants to understand the difference in diversity across an ecotone in the local DC-area. An ecotone is defined as an area where two distinctly different habitats intersect, and in this study we focus on an ecotone across oak forest and marsh habitats. We worked with National Park Service collection material taken using a malaise trap at six different locations across three habitat types. Two locations were located in a forest habitat, two in a marsh habitat, and two in the ecotone of the marsh and forest. From the collections, which took place over a two year period in 1998 and 1999, we sorted the ants into morphospecies and identified the ants to genus. These data will be used to address differences in species richness and composition of ant communities across the ecotone. More specifically, we are testing whether there are consistent differences in abundance and diversity of different ant genera across the ecotone, potentially informing our general understanding of how these habitat transitions impact diversity. Our preliminary analysis support a decline in total species richness, richness of well-represented genera, and ant abundance across the ecotone. These finding will potentially serve as a foundation for better understanding how the availability of resources like food and nesting sites impact the different ant taxa. These studies are also contributing to the overall biodiversity inventory studies of the National Parks Service in the DC area parks.

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Establishing an in vitro tissue culture system to investigate spermatogenesis

Reproductive traits are fundamentally important factors of reproductive success. Sperm traits, in particular, vary widely among even closely-related species and in ways that influence the outcome of sperm competition between rival males. Fruit flies of the genus *Drosophila* produce some of the longest sperm known, ranging from 0.3 mm in *D. persimilis* to 5.8 cm in *D. bifurca*, 20 times longer than the size of the fly. In the genetic model *D. melanogaster*, longer sperm outcompete shorter sperm during sperm competition, yet virtually nothing is known about the genetic basis of sperm length. The process of sperm production, or spermatogenesis, has been investigated by many biologists, but the exact processes and mechanisms that produce variation in sperm traits remain poorly understood. This study aimed to develop a protocol for an in vitro tissue culture system that facilitates controlled study of the process of spermatogenesis. In *D. melanogaster*, 64 sister spermatids develop together within an enclosed cyst, until individualized mature sperm separate and are stored for use. Previous research in another lab reported success in observing spermatid elongation in vitro. This study reports successful elongation of *D. melanogaster* spermatogenic cysts in culture. Cysts were extracted from the testes of wild type pupae using standard sterile technique, and placed in tissue culture media. Surviving cysts were observed for elongation at 24 hour intervals. Future investigation will quantify rates of cyst elongation in populations of *D. melanogaster* and in closely related species that vary in sperm length to determine if elongation rates differ for males with different sperm lengths. The development of a viable tissue culture system will be useful for future studies that will examine the effect of various genes on spermatogenesis and will allow comparison of spermatogenic dynamics within and across species.

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The influence of climate on spider size in the southeastern USA

The orchard spider *Leucauge venusta* is a common species of orb-weaving spider found in North and South America. We collected 248 adult female specimens from 54 sites in the southeast United States, observing variation in body size. Using GIS data from the BioClim data set, we tested for a correlation between body size and climatic variables, namely temperature. We determined there was a converse Bergmann cline, with larger spiders occurring at lower latitudes where the climate is warmer and wetter. These results are consistent with mechanisms including longer growing seasons, larger prey, and increased competition in warmer areas.

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Hollow Carbon Nanosphere/Germanium Composites for use as Li-Ion Battery Anode

The Li-ion battery is the most widely used rechargeable battery for powering portable electronics. Because Li metal is unsafe to charge and discharge, Li-ions are a good alternative. Graphite is one material that can store Li-ions and it operates at a similar electrochemical potential to Li metal making it a good anode material without the risk of battery fires. However, graphite is currently the limiting factor to the battery in both charge rate and capacity. Diffusion of Li-ions into graphite, by intercalation, depends on the size of the graphite particles, which are microns in diameter. Our project seeks to replace graphite with graphitic hollow carbon nanospheres (HCNS). An HCNS has a diffusion path length of ~50 nm vs. ~10,000 nm of a graphite particle which allow Li-ions to intercalate at a significantly faster rates from hours down to minutes. HCNS cycles with minimal capacity fade and a long-term Coulombic efficiency of >99.9%. Additionally, HCNS can operate with inexpensive low-melting electrolytes at temperatures as low as -40°C.

Despite the advantageous properties of HCNS it has a lower gravimetric capacity than graphite (~190 mAh/g vs 372 mAh/g). HCNS is synthesized by graphitizing cellulose using nickel catalyst, but when replaced by a cobalt catalyst we observed an increase in capacity (~235 mAh/g). Utilizing HCNS as a support material for other Li-ion alloy compounds can further increase the capacity. Germanium is one such material; it has a capacity of 1385 mAh/g and high Li-ion diffusivity but undergoes a large volumetric expansion upon alloying. This makes it impractical as an anode material by itself, but stable performance was observed when we combined Ge with HCNS. Early results show very stable cycling at around 600 mAh/g that could lead to a Li-ion battery with a much larger gravimetric capacity and a rapid charge rate that what is available today.

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Radiative corrections to the elastic e-p and mu-p scattering in Monte Carlo simulation approach

In this paper, we calculated exactly lepton mass corrections for the elastic e-p and mu-p scatterings using the ELRADGEN 2.1 Monte Carlo generator. These estimations are essential to be used in the MUSE experiment that is designed to solve the proton radius puzzle. This puzzle is due to the fact that two methods of measuring proton radius (the spectroscopy method, which measures proton energy levels in hydrogen, and the electron scattering experiment) predicted the radius to be 0.8768 ± 0.0069 fm, whereas the experiment that used muonic hydrogen provided the value that is 5% smaller. Since the radiative corrections are different for electrons and muons due to their mass difference, these corrections are extremely important for analysis and interpretation of upcoming MUSE data.

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Optimizing Light Detection in an Active Polarized Target: Hardware and Simulation Developments

Nuclear Physics experiments typically consist of a target containing the substrate to be investigated surrounded by a detector system. A beam of particles is then fired at the target and the resulting scattered particles, ejected from or created in the target, are identified and tracked. These experiments allow extraction of information about particles to study their behavior and structure. In certain circumstances, the target is required to polarize the substrate as well as contain it. This requires the implementation of large magnetic fields and extreme cryogenic temperatures to retain polarization.

The Mainz Frozen Spin Target (FST), used with the Crystal Ball and TAPS spectrometer system at the MAMI accelerator in Mainz, Germany, is a cutting edge example of such a system. Nuclear physics experiments, such as measurements of Compton Scattering on the proton (a two-body inelastic collision between a photon and a proton), can be reliably conducted using the Frozen Spin Target. Compton Scattering measurements allow extraction of the nucleon polarizabilities and fundamental properties of the proton, which give information on its internal structure and binding. However, the nature of the target material requires that one detect the outgoing proton in order to gather a clean data sample. At the same time, the necessary magnetic and cooling infrastructure result in a high energy threshold for outgoing proton detection in the surrounding calorimeter.

By detecting the particles within the target material itself, that threshold of detection would be substantially lowered. This would allow an extension to the angular and energy range over which Compton Scattering events can be reconstructed. Thus, the Active Polarized Target (APT) was developed. The purpose of this research project was to optimize light detection in the APT by finding the best target wrapping material. Additionally, computer simulation was used to further investigate the potential of the APT. The results from the hardware experiments and the simulations will be discussed.

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Characterizing Pulses Observed in Gamma-ray Bursts (GRBs)

Gamma-ray Bursts are the most powerful and possibly the most distant explosions ever observed. An understanding of the physical mechanism(s) that drive these events would motivate their use as 'distance' measures to probe the ancient universe. GRBs are also expected to be significant sources of gravitational waves, cosmic rays and neutrinos and could prove to be excellent laboratories for the study of general relativity and the production of elementary particles at very high energies. GRB light curves exhibit high levels of complexity that have hindered studies based on physical models. However, recent studies have shown that the GRB emission is composed of pulsed radiation with the pulses exhibiting relatively robust temporal and spectral properties. Resolving GRB light curves into pulses is an essential first step towards connecting physical models to observations. We describe a sophisticated pulse-extraction code and present preliminary results for a sample of GRBs.

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Relationship Between MID1 B30.2 domain and Huntington's Disease

MID1 is a microtubule-associated protein belonging to the tripartite motif (TRIM) family, and functions as an E3 ligase in the ubiquitination pathway, which tags proteins for degradation. Mutations with MID1 are widely known to be associated with the X-linked Opitz BBB/G syndrome, a developmental disorder characterized by malformation of the ventral midline with symptoms such as cleft lip and/or palate, mental retardation, and organ complications along the midline of the body. Our research focuses on one of the C terminal domains of MID1, specifically the B30.2 domain and its association with Huntington's disease.

Huntington's disease is a hereditary neurological disorder that over time, cause the progressive loss of nerve cells in the brain, impacting movement, cognition, emotions, and behavior. The disease is attributed to the translation of expanded CAG repeats into abnormally long polyglutamine stretches that lead to protein misfolding and aggregation. The B30.2 domain binds with the CAG repeats and is involved promoting the translation of the protein that causes Huntington's disease. Other studies have shown that B30.2 binds to CAG repeats through protein-RNA binding studies with polyacrylamide gels. The overall structure and function of B30.2 is still unknown. We are trying to determine the structure of B30.2 by three-dimensional Nuclear Magnetic Resonance (NMR) spectroscopy. My research focuses on purifying and identifying conditions that will keep the B30.2 domain soluble and stable for 2-3 weeks so that we can acquire NMR data.

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Effect of Arctic Urban and Industrial Development on Land Surface Temperature: a case study for the Norilsk Region, Russia

Urbanization and industrial development have significant impacts on regional climate that in turn controls settlement patterns and socio-economic processes. Urban heat island (UHI) effect is a well-known feature that has been extensively studied in low and mid latitude regions. However, the impacts of urbanization on Arctic climate and natural environment are yet to be understood. In this study, we have analyzed the anthropogenic influences on regional land surface temperature for Norilsk region, Russia. Norilsk industrial region is located in the Central Siberia at 70N latitude. The regional population of approximately 200,000 is concentrated in four distinct urban areas. The region is characterized by highly developed industrial and transportation infrastructure. We have used a combination of MODIS- and AATSR-derived Arctic Land Surface Temperature products available at 1 km spatial and weekly to monthly temporal resolution, LANDSAT imagery, and detailed city- and regional- level GIS layers to examine the characteristic seasonal LST signatures, related to several representative assemblages of Arctic urban and industrial infrastructure in order to quantify anthropogenic influence on regional surface temperature.

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Towards Comprehensive and Untargeted Proteomics on Single Cells for the 16-cell *Xenopus* Embryo using μ CE-ESI-MS/MS

Characterization of cell-to-cell heterogeneity in the developing embryo helps the understanding of developmental diseases and the design of targeted therapeutics, but requires new technologies capable of measuring broad type of molecules in single cells. Particularly needed are approaches to monitor the expression of proteins in single cells as these biomolecules are known to coordinate different stages of embryonic development. Here we present the advancement of mass spectrometry based technology and corresponding bottom-up workflow for the proteomic analysis of individual embryonic cell (blastomere). In this study we used 16-cell South African clawed frog (*Xenopus laevis*) embryo, the popular model in cell and developmental biology.

In preparation for single-cell measurements, we first developed a bottom-up proteomic workflow for mass-limited samples to increase the confidence and number of protein identifications. Using whole-embryo lysates, the steps of sample preparation, peptide separation, data acquisition, and bioinformatics were evaluated. With the resulting workflow, we were able to identify ~340 different protein groups using only ~20 ng of proteins from the embryo. The combination of two different databases, *Xenopus laevis* Uniprot canonical and isoform and Phrog, increased the number of identified proteins to ~390, and the incorporation of a dual search engine strategy via Sequest HT and MS Amanda extended identifications to ~430 different proteins (<1% FDR). As our volume-limited μ CE-ESI-MS/MS system was able to measure ~20 nL of extract, it was possible to analyze each blastomere extract in technical duplicates, which in turn further enhanced identifications to ~480 different protein groups.

The resulting strategy enabled the proteomic interrogation of individual blastomeres isolated from the 16-cell embryo. As proof of principle, we selected the D11, V11 and V21 blastomeres, which reproducibly give rise to different tissue types. For each blastomere, μ CE-ESI-MS/MS succeeded in identifying ~700 different protein groups, amounting to the identification of a total of ~1,700 different protein groups across 3 biological and 2 technical replicates. Closer inspection of the data revealed that ~20% of these proteins were uniquely identified in each type of blastomere, suggesting proteomic differences between the D11, V11, and V21 blastomeres.

The number of proteins identified here is substantial considering the mass- and volume-limited nature of embryonic cells. Detection of blastomere type-specific proteomic differences in the early, only 16-cell embryo provides new insight into embryogenesis. It also sets the stage for quantitative experiments, promising a new means for uncovering spatial and temporal changes in the developing embryo during states of health and disease.

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Pollution in Stone Town's Coastal Waters: An Assessment of Environmental Influences on Fecal Contamination

Preserving the integrity of Tanzania's coastal regions is essential to the well being of the areas' natural resources, as well as the people that depend on them.¹ In recent years, coastal regions have been vital to Tanzania's economy; coastal tourism and aquaculture have become extremely important sources of revenue for the country.² However, these resources have been compromised by untreated sewage that is regularly deposited into the country's coastal waters, an issue that has been caused and exacerbated by non-existent or largely inadequate waste management systems.³ Tanzania's urbanized areas, including Zanzibar Town on Unguja, are struggling to deal with the large amounts of waste generated by growing populations and increasing tourist industries.⁴

In 2010, the waters surrounding Stone Town, a subsection of Zanzibar Town, were found to be highly polluted by fecal waste.⁵ When found in recreational water, enterococci bacteria acts as an indicator of fecal pollution and alludes to the possibility of pathogens that cause intestinal diseases.⁶ Using the membrane filtration method, concentrations of enterococci bacteria were quantified from two sites in Stone Town, Africa House and the Port, in order to determine whether fecal pollution had lessened or worsened four years after the original measurements. Additionally, several environmental components of the coastal area, particularly tides, were tested to deduce how they influenced enterococci levels.

Results suggest that the fecal pollution at both sites has worsened and continues to pose a serious risk to public health. Spring and neap tides had a significant impact on enterococci concentrations at Africa House. However, it is unclear how tidal fluctuations influenced enterococci concentrations at the Port. If measures are not taken in the future to improve the pollution in Stone Town's coastal waters, there could be serious consequences to the local economy and the community's well being.

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A Recombinant Sp185/333 Immune Protein from the California Purple Sea Urchin binds to phosphatidic acid

The purple sea urchin, *Strongylocentrotus purpuratus*, possesses a sophisticated innate immune system that functions without adaptive immune capabilities and responds to pathogens effectively by expressing the highly diverse Sp185/333 gene family. The upregulation in gene expression in response to immune challenge and the sequence diversity of Sp185/333 cDNAs suggest that the encoded proteins have immune functions. Individual sea urchins can express more than 260 distinct Sp185/333 proteins and the diversity of Sp185/333 proteins indicates that different versions may have different functions. Although the deduced proteins display sequence diversity, they share an overall organization and structure including a hydrophobic leader sequence, a glycine-rich N-terminal region with a RGD motif (integrin binding), a histidine-rich region, and a C-terminal region. The predicated amino acid sequence suggests that Sp185/333 proteins may be intrinsically disordered proteins (IDPs). Sp185/333 proteins are associated with the membranes of perinuclear vesicles in four types of phagocytes (polygonal, discoidal, small and medium) and the plasma membrane of small phagocytes. Yet the membrane association is unexpected due to the lack of transmembrane regions and conserved GPI linkages based on bioinformatic predictions. To understand how Sp185/333 proteins associate with phagocyte membranes, membrane lipid strips were used to test whether a recombinant Sp185/333 (rSp0032) would bind to phospholipids, and results show that rSp0032 binds to phosphatidic acid (PA). PA is a minor lipid constituent of cell membranes and a precursor molecule involved in the formation of other phospholipids responsible for some immune-related functions, such as endocytosis, exocytosis, phagocytosis, vesicle formation, Ca²⁺ regulation, and signal transduction. Synthetic liposomes composed of PA and phosphatidylcholine (PC) were made to examine binding and interactions of rSp0032 to PA by Fluorescence Resonance Energy Transfer (FRET) analysis, leakage assay, circular dichroism (CD), and confocal microscopy. Results show that rSp0032 binds to PA in liposomes, its secondary structure changes in the presence of PA, and it induces liposome membrane instability causing budding, lysis, fusion and invagination. These results provide new clues as to how Sp185/333 proteins associate with cell membranes.

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Infection strategies of the bacterial pathogen *Photobacterium*

Bacterial pathogens have evolved a fascinating way of communicating amongst themselves in order to reach their overall goal, which is to eventually eliminate their host. They do this through Quorum Sensing, a response system that depends on the population density of bacteria in order to activate chemical signal molecules called autoinducers that promote bacterial virulence, bioluminescence, antibiotic production and other factors. Our investigation on bacterial cooperation involves the gram-negative pathogenic bacteria *Photobacterium asymbiotica* and *Photobacterium luminescens*. The first is an emerging human bacterium that also infects insects, while the second is only pathogenic to insects. Using two different insect cell lines from *Drosophila melanogaster* and *Spodoptera frugiperda*, we have initiated a study to understand bacterial communication and pathogenesis of the two bacterial species against insect cultured cells. Such studies will potentially provide information on the strategies that these pathogens employ to infect host cells, which will in turn result in the identification of novel host defense mechanisms.

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Maternally Expressed Genes Can Determine Neural Fate

In many organisms, important developmental events are regulated by mRNAs that are synthesized in the oocyte and locally stored for use after fertilization during embryonic development; these are called maternal factors. In the frog, *Xenopus laevis*, several maternal mRNAs are highly enriched in the animal blastomeres that give rise to the ectoderm. Four of these localized mRNAs encode for transcription factors that have important roles in the formation of the neural plate after gastrulation (Sox11, Gem, Zic2, and FoxD4L1). In this study we tested whether these transcription factors also have a function before the induction of the neural plate using a culture system that removes cells from the embryonic environment prior to the onset of embryonic (zygotic) gene transcription. Expressing each of these mRNAs ectopically in isolated ventral blastomeres that give rise to the epidermis (skin) stimulated expression of zygotic neural genes. Over-expressing the mRNAs in isolated dorsal blastomeres that normally give rise to neural plate caused an increase in the expression of zygotic neural genes. Moreover, reducing endogenous expression of Foxd4L1 or Zic2 in dorsal cells caused a decrease in the expression of zygotic neural genes. These series of experiments indicate that all four of these maternally derived transcription factors promote a neural fate prior to the induction of the neural plate. Finally, we identified the homologous mouse and human genes and expressed them in isolated dorsal and ventral cells. Data to date indicate that some of the functions of these maternal transcription factors have been evolutionarily conserved. Understanding how cells in the embryo become part of the neural plate will provide critical information about how to create and manipulate neural stem cells for therapeutic uses.

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Development of Capillary Electrophoresis Mass Spectrometry for the Metabolic Investigation of Single Embryonic Cells of *Xenopus laevis*

Single-cell mass spectrometry (MS) empowers metabolic investigations at the cellular level. To enhance measurement of complex biological samples, new single-cell MS technologies with improved detection sensitivity and metabolite coverage are required. Here, we develop our custom-built capillary electrophoresis electrospray ionization (CE-ESI)-MS platform and apply it to characterize metabolites in single embryonic cells (blastomeres) of the South African clawed frog (*Xenopus laevis*), a model organism in developmental biology. We demonstrate that the analytical performance of our single-cell CE-ESI-MS is sufficient to confidently identify and quantify more than 30 different metabolites in blastomeres of the 16-cell embryo, affording fundamental insights to early embryogenesis.

We present an analytical workflow based on our CE-ESI-MS platform, to identify metabolites in single blastomeres of *Xenopus*. The platform was systematically characterized for performance using chemical standards under various separation conditions. The limit of detection for acetylcholine standard was 10 nM, or 60 amol, and quantitation was linear up to 1 μ M. In addition, the system provided reproducible separation and reliable detection sensitivity. These performance characteristics were sufficient to measure metabolites extracted from single blastomeres in the 16-cell embryo.

Using this single-cell MS technology, we successfully identified and quantified a total of 40 metabolites with high confidence to include amino acids (e.g. lysine, threonine), neurotransmitters (e.g. acetylcholine, γ -aminobutyric acid), energy carriers (e.g. creatine, carnitine, and acetylcarnitine), and cell growth factors (e.g. spermidine, putrescine, and S-adenosylmethionine). Furthermore, this single-cell MS system detected variation in the biochemical composition of single blastomeres isolated from the ventral and dorsal regions of the embryo. For example, higher levels of spermidine, arginine, and glutamine were observed in the ventral blastomeres whereas the dorsal blastomeres, which contribute significantly to the development of nervous system tissue, were abundant in γ -aminobutyric acid and the neurotrophic factor serine. This information is essential to assess functional variation between individual cells.

In conclusion, these results demonstrate the utility of single-cell CE-ESI-MS for the identification and quantitation of a range of metabolites during early embryo development. We anticipate this single-cell MS technology to deliver discoveries in developmental biology.

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Macroscopic Velocity Amplification in Stacked Disks

When a small sphere rests atop a larger sphere (for example, a basketball with a tennis ball balanced on top), and both are released from a height, the resulting “velocity amplification” of the small sphere when the pair rebound from a hard floor, is a staple of the physics demonstration toolkit--usually impressive, sometimes dangerous. While this phenomenon has been studied in the literature in some detail, we set out to explore this effect by constructing a device involving stacked disks falling in a plane, fashioned after an online design by Wayne Peterson of Brigham Young University. When two disks, stacked edge to edge atop one another and confined to a vertical plane, are dropped, the top disk rebounds to a much greater height than it started from, as expected. In this talk, we report on experiments conducted by dropping the disks and recording the heights to which they rise on rebound, and the comparison of these results with some theoretical predictions and computer simulations.

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Land Cover and Permafrost Change Mapping Using Landsat Dense Time Stacks and Quickbird Imagery

Climate change is especially pronounced in the Arctic having exceeded natural climate variability. Discontinuous permafrost regions such as our study areas near the city of Igarka, Russia are at the frontier of these changes. River runoff is impacted by a variety of physical properties at various scales. Annual discharge into the Arctic Ocean from Northern Eurasia has reached a new historical maximum as of 2007. Winter discharge contributes 70% of the increase in annual discharge from 1936 to 2010. This work contributes to a larger ongoing project investigating ground-ice melt water's contribution to increased river runoff for five small to medium watersheds into the Yenisei River. Discontinuous permafrost areas are characterized by land covers indicative of permafrost conditions making satellite imagery an important tool for assessment of environmental change in remote areas. This can be particularly challenging in the Arctic with the consistently high cloud cover and heterogeneous landscapes. This work highlights a successful way of dealing with such issues with a modified version of the emerging methodology called "dense time stacking". The method was applied to Landsat imagery and the later stack was validated with Quickbird imagery also used to focus on one of the Little Graviyka watershed. The resulting map products prove this to be effective within the Arctic for both temporally and spatially multiscalar land cover and permafrost mapping.

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Capillary Electrophoresis Mass Spectrometry for Differentiating Single Cells in the frog (*Xenopus laevis*) Embryo

Characterization of the metabolome, the whole suit of metabolites expressed by embryonic cells, is key to understanding healthy embryo development. However, this calls for novel analytical technologies, mainly those that are highly sensitive, selective to diverse types of biomolecules, and compatible with extremely small sample volumes afforded by single cells. We report here a new approach based on single-cell mass spectrometry (MS) to enable profiling of metabolites in single embryonic blastomeres (or cells) of the South African clawed frog (*Xenopus laevis*), the favorite model in cell and developmental biology. We use this information to find, for the first time, cell-type specific metabolic differences in the early developmental stage of the embryo.

Our recently developed technology combines microsampling and volume-limited capillary electrophoresis-electrospray ionization-MS (CE-ESI-MS). CE-ESI-MS achieved a low limit of detection (LOD) below 10 nM (60 amol) for acetylcholine among other compounds. This LOD is sufficiently low to enable the measurement of endogenous metabolite levels. Three different types of embryonic cells with different tissue fates in a developed embryo were identified and microdissected from 16-cell *Xenopus* embryos. Subsequently, their metabolomes were extracted and 10 nL of the extracts were measured by CE-ESI-MS. Metabolomic profiling revealed more than 80 different small molecules that were consistently measured in the three different cell-types, 40 of which were identified as metabolites with high confidence. Multivariate and statistical analysis of the metabolomic data revealed differential clustering between the three cell-types which were from the ventral, dorsal, and vegetal regions of the embryo.

The discovery that embryonic cells have unique metabolomes this early during development is surprising, and demonstrates that single-cell MS raises a new opportunity for investigating biochemical processes that underlie embryonic development. This remarkable finding has prompted several fundamental questions that when addressed will help us elucidate basic characteristics and/or processes governing these single-cells during division. For instance, it would be interesting to know processes that underlie the differential levels of abundance of metabolites in each cell this early during embryogenesis.

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Annotation of Contig22 of 3L in *Drosophila biarmipes*

This project is part of a larger effort through the Genomics Education Partnership centered at Washington University in St. Louis examining the evolution of the tiny fourth or "dot" chromosome in *Drosophila*. The dot chromosome contains approximately 80 genes. DNA actively transcribes these genes; however, the structure is consistent with DNA domains that are typically silent and not expressed. The dot chromosome, therefore, has an intermediate structure and function combination. The project aims to understand how the material can still be active if it is structurally silent. The 3L chromosome is being annotated as a control for comparison. *Drosophila biarmipes* is a species that has not been previously sequenced. There is a need to determine the structure by annotation of the dot chromosome in a large number of species. Annotation of these regions in comparison to the dot chromosome may shed light into its DNA sequence organization, gene regulation, and chromatin packaging. My project was to annotate contig22 of 3L in *Drosophila biarmipes*. A contig is a set of overlapping DNA fragments that have been assembled to form a continuous sequence of DNA. These DNA fragments are often assembled by computer and need to be verified through the process of annotation. Based on the Genscan predictions, contig22 was estimated to have 6 genes; however, only 2 genes were discovered to be homologous with *Drosophila melanogaster* with one gene potentially non-homologous to *D. melanogaster*.

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Development of a Neutron Detector

The Mainz A1 spectrometers perform high precision measurements to investigate the structure of the nucleus and its constituents. Previous knowledge of the neutron form factor (FF) is limited due to poor detection efficiencies. Our goal is to create a neutron detector with an efficiency better than 80%, leading to the improvement of the measurements of the neutron electric FF and reducing systematic uncertainties.

This new detector would also open up the possibility to study nonmesonic two-body weak decays. The neutron detector should have a large active detector volume, a high detection efficiency (>80%), a good resolution (<0.5 ns), and must be low in cost. The proposed design of the detector follows a modular concept with an active detector volume of approximately one cubic meter. In order to allow high beam currents and their resulting high rates, this detector will be highly segmented using 32 crossed layers consisting of 64 bars, utilizing solid and liquid organic scintillators, with dimensions (15 x 30 x 960) mm³ channels have to be read out via WLS fibers using silicon multi pixel photon counters (MPPC).

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Trait-mediated competition in *Temnothorax*

Inter- and intraspecific competition is an integral part of ant communities. The majority of existing research has focused on competition in the field but competition under experimental conditions remains poorly studied. The goal of this research was to study the interactions between colonies of *Temnothorax* in an experimental set-up emulating the dispersion conditions found in nature. Colony density in the field varied from 1 colony in a square meter to 8 colonies in a single square meter. Most of the experiments contained two colonies placed in the experimental arena along with 34 empty nests. Mortality occurred in each of the experiments, but colony extirpation did not occur. Our analyses suggest a “war of attrition” model that shows that a larger number of combatants is linked to a higher level of mortality.

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Investigating the role of center divider in spermatogenesis and in development of the female reproductive tract in *Drosophila*

Sperm cells, which are the most variable cell type in the animal kingdom, function based on their structure, which in turn impacts reproductive success. At the same time, sperm morphology is often correlated and coevolves with aspects of the female reproductive tract. Fruit fly species related to the genetic model organism, *Drosophila melanogaster*, have some of the longest sperm known, up to 5.8 cm, while the female's sperm storage organ, the seminal receptacle (SR), can reach 8 cm. In *D. melanogaster*, a genetic screen previously identified candidate genes involved in sperm length variation, including center divider (*cdi*), which is expressed in male testes. Interestingly, silencing *cdi* has no effect on sperm length, but causes SRs to become longer. The goal of this study was to further characterize the role of this gene by localizing where the *cdi* protein is being expressed in the SR during development. The use of transgenic flies, in which *cdi* protein expression is associated with green fluorescent protein (GFP), allowed for the visualization of *cdi* expression in the developing SR. Female reproductive tracts were dissected at different time points during SR development and the location of *cdi* expression, based on the presence of GFP, was documented.

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Colobus angolensis palliatus and Their Tree Utilization: Use vs Availability

During November of 2014, I studied a troop of *Colobus angolensis palliatus*, inhabiting a small isolated section of the Sagara Forest known as the Mikunguni Forest. I studied the behavioral habits of the troop and their utilization of tree species in their environment. I was in the field from 7:00am-1:00pm for 14 days collecting data. I recorded the frequency of behaviors and the tree species in which they performed these behaviors. After by 14 days of data I conducted a survey of the forest to note the composition of the forest at or above my mean DBH of 83cm (20-208) for trees the monkeys utilized in the previous study days. I found that the behaviors, resting and feeding, are not independent of tree species $p=2.0057E-204$ with an alpha: 0.05. The *Colobus angolensis palliatus* have an affinity for certain tree species for these two behaviors.

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Resistance to a model of Parkinson's Disease in Learning Mutants of *Drosophila Melanogaster*

Approximately one million people throughout the world are diagnosed with Parkinson's disease. One suspected mechanism for modeling Parkinson's concerns the Proteasome System, a protease involved in protein degradation. If the proteasome does not function properly, malformed proteins tagged for degradation build up and cause protein aggregation, leading to cell death in the nervous system. In the lab, we wanted to support previous research that the inhibition of the proteasome in *Drosophila Melanogaster* by the protein MG-132 models Parkinson's. We hypothesized that unlike normal *Drosophila*, the learning mutants *Dunce* and *Rutabaga* *Drosophila* are more resistant to neurodegeneration because of their impaired synaptic strengthening and resistance to excitotoxicity. To measure neurodegeneration, we tested the locomotion of *Drosophila* in plastic vials using a negative geotaxis assay. The vials were divided into three heights: <2 cm, > 2cm, and >6 cm. Thirty minutes after leaving the incubator, the number of *Drosophila* in each region was counted. Cell viability was measured using an MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) absorbance assay. Mortality was measured daily, and a Kaplan Meier statistical analysis was done. The results showed that the normal *Drosophila* were not resistant to neurodegeneration, and had a strong mortality rate over the course of eight days. The negative geotaxis assay results showed an impaired locomotive ability in treated normal *Drosophila*. In both tests the learning mutants resisted the effects of MG-132. The MTT absorbance assay values were not significant. It was concluded that MG-132 models Parkinson's in *Drosophila*, and that the learning mutants are resistant to neurodegeneration.

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The Interaction between *Aphis craccivora*-tending *Formica subsericea* and *Epargyreus clarus*

Previous research in behavioral ecology has shown that simply the presence of predators can be enough to impact the abundance, behavior and composition of prey communities. This study examines this "ecology of fear" phenomenon, examining how the ontogenetic stage of a prey species (the shelter-building caterpillar, *Epargyreus clarus*) influences its interactions with a common ant predator (*Formica subsericea*) that tends the aphid, (*Aphis craccivora*) on black locust (*Robinia pseudoacacia*). In the summer of 2014, six plants of *R. pseudoacacia* planted in the Patuxent Research Refuge in Patuxent, MD were utilized. Branches that contained *F. subsericea* tending *A. craccivora* aphids were identified on each tree and caterpillars of *E. clarus* of various instars were placed at varying distances along these branches (n=43). Control branches were also established on these trees on which *F. subsericea* were excluded through the use of Tanglefoot® (n=25). Both control and ant treated branches were observed for 30 minutes at placement and checked regularly in the weeks after that in order to measure caterpillar survival. Additionally a select number of focal caterpillars were observed for longer periods of one to two hours following their placement. Caterpillars on ant branches displayed faster times to shelter initiation. Additionally early instar caterpillars on ant branches displayed significantly faster times to shelter initiation than did their control counterparts. Late instars, however, were not affected by ant presence. Overall survival on ant treated versus control branches was not significantly different. Taken together, these results indicate that despite having little effect on the actual survival of *E. clarus*, *F. subsericea* still impact the caterpillars' behavior, particularly for early instars and may influence other aspects of fitness (e.g., growth rate or development time) that were not measured in this study.

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The Effects of Climatic Trends, Variability, and Rates of Change On Mammalian Brain Evolution

Explanations for the dramatic brain size increase observed in the hominin lineage have inspired a wide variety of competing explanations for this hallmark evolutionary event. Large-scale climatic hypotheses have traditionally focused on either 1) the effects of consistent trends towards cooler temperatures, aridity, or increasing proportion of C4 vegetation, or 2) increasing variability in these climatic variables. However, this assumes a false dichotomy between these models of climatic selection when it is far more likely that these interrelated types of global climatic change are neither mutually exclusive nor the only factors that drove hominin encephalization. Furthermore, almost all tests of these hypotheses to date have investigated hominin specimens to the exclusion of other mammalian taxon. The present study sought to quantify the relative contribution of consistent trends, variability, as well as rates of climatic change across a wide variety of hominid and non-hominid mammalian species in order to more comprehensively understand the effects of global climate on brain size as a general principle of mammalian evolution. Results revealed that climatic Variability, Trend, and Rate (in terms of both temperature and vegetation) have all served as indirect drivers of mammalian brain expansion, albeit not for every mammalian taxa at every point in time. Furthermore, hominin cranial capacity was most strongly correlated with climatic trends towards global cooling. These results indicate that global-scale climatic variables played significant and not necessarily mutually exclusive roles in hominin and non-hominid mammal brain evolution.

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The effect of knocking down the gene center divider on sperm and seminal receptacle length in *Drosophila melanogaster*

Sperm length plays an important role in reproductive success in various species, but the genetic basis of sperm length variation is poorly understood. The fruit fly, *Drosophila melanogaster*, is an excellent model organism in which to study this trait because sperm in the *Drosophila* genus are among the longest recorded, ranging from 0.3 mm to 5.8 cm in length. Sperm length in this group is also positively correlated with length of the female's sperm storage organ, the seminal receptacle (SR). One possible genetic mechanism for this male-female correlation is that a subset of genes controlling sperm length may also influence SR length. Research in our lab has previously identified over 300 candidate genes that may influence sperm length in *D. melanogaster*. This study focuses on whether disrupting the function of one of these genes, center divider (*cdi*), causes a change in length of sperm in males or the SR in females. Disruption of *cdi* gene expression does not alter sperm length, but it does result in longer SRs. One explanation for this result is that there is functional redundancy of *cdi* in spermatogenesis such that another gene can take over its function if it is silenced. These results highlight potential differences in gene function and developmental pathways in males and females. In future studies, we will explore the role of other genes in spermatogenesis using the RNAi knockdown system, as well as try to characterize in more detail how these genes function in spermatogenesis compared to development of the SR.

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Synthesis of β -Substituted FR900098 Derivatives as Inhibitors of Mtb Dxr

Tuberculosis (TB) is the second leading cause of death due to an infectious agent. The causative agent of TB is a bacteria known as, *Mycobacterium tuberculosis* (Mtb). In recent years there has been an increase in cases of drug-resistant and extensively drug-resistant TB. In addition to this, there is high comorbidity of TB with HIV. As a result there is now, more than ever, a serious need for new medicines to treat TB. The target pathway that we have chosen to pursue is the non-mevalonate pathway (NMP) of isoprene biosynthesis. Within that pathway we have chosen to inhibit the enzyme, 1-deoxy-D-xylulose-5-phosphate reductoisomerase (Dxr) as it is essential for Mtb survival but absent in humans. FR33289 is a β -hydroxy substituted phosphonate that has been shown to inhibit Dxr in *Plasmodium falciparum* (Pf), the causative agent of malaria. We are interested in assessing the effectiveness of FR33289 and other β -substituted FR900098 derivatives as inhibitors of Mtb Dxr and intact Mtb cells. We describe here our novel synthetic methods for obtaining FR33289 and other β -substituted derivatives as well as their evaluation against whole cell Mtb and Mtb Dxr.

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Functional characterization of Thioester-containing proteins in the *Drosophila* anti-bacterial immune response

The fruit fly *Drosophila melanogaster* is an outstanding model to study the complexities of host-pathogen interactions and innate immune defense mechanisms. Flies elicit specific immune responses against different types of microbes. Thioester-containing proteins (TEPs) are conserved throughout the animal kingdom. TEPs participate in recognition and opsonization of bacteria and parasites in mosquitoes but their immune function in *Drosophila* is currently unknown. We have started to characterize the function of TEPs in the immune response of *Drosophila* against infection by the insect pathogenic bacteria, *Photorhabdus luminescens* and the emerging human pathogen, *Photorhabdus asymbiotica*. We infected TEP loss-of-function mutants and their genetic background controls with *P. luminescens* and *P. asymbiotica* bacteria and observed significant differences in their ability to survive infection by each *Photorhabdus* species. Infection of genetic background controls with each *Photorhabdus* species induced expression of TEP genes to different levels. In addition, immune signaling pathways were differentially activated in TEP mutant flies suggesting that TEP gene expression strongly interferes with immune signaling activation in response to *Photorhabdus* infection. Current results imply that expression of certain TEP genes in *Drosophila* likely participates in the immune response against *Photorhabdus*. Future functional assays using TEP mutant flies infected by either *Photorhabdus* species is expected to uncover the exact anti-bacterial function of TEP molecules in *Drosophila*, including novel antibacterial defense mechanisms in *Drosophila* that may function in other insects. Outcomes may have direct or indirect repercussions on human health because of insects acting as disease vectors.

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Bumble Bee Foraging and the Evolution of Novel Social Traits

The evolution of social cooperative groups requires massive modification of ancestral solitary behaviors to enable new behaviors required for social coordination. How have ancestral physiological regulatory mechanisms been co-opted to make current social phenotypes? We used bumblebees to test a hypothesis for the evolution of specialized foraging behavior among social insect workers. The reproductive groundplan hypothesis (RGPH) proposes that specialized pollen and nectar foraging evolved through repurposing ancestral reproductive pathways: ancestral solitary bees forage for pollen (protein) when developing eggs, and carbohydrates (nectar) at other times. Ovary state influences sensory sensitivity, which drives pollen or nectar preference, linking reproductive physiology with foraging behavior. In highly social honey bees, this ancestral regulatory mechanism is used by non-reproductive workers for pollen or nectar foraging specialization. We show that bumblebee foragers also specialize on pollen or nectar. We then test two specific predictions of the RGPH using bumblebees. First, pollen foragers should have larger ovaries than nectar foragers. Second, pollen foragers should show higher sensory sensitivity to sucrose as measured by the proboscis extension response (PER). We report foraging specialization, ovary measurements, and PER data for three colonies of bumblebees.

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The role of proteolytic compartments in human amylin turnover and toxicity

Amylin, also known as islet amyloid polypeptide (IAPP), is a 37 amino acid hormone produced and co-secreted with insulin from pancreatic β -cells. IAPP is also expressed in pancreatic islet δ -cells in gastrointestinal tract of rat, mouse, cat, and human, as well as in sensory neurons of rat and mouse. Although the exact hormonal function of amylin is still unclear, it has been proposed that amylin controls food intake and energy homeostasis. Amylin primarily regulates nutrient fluxes by acting as a potent satiation signal that reduces secretion of gastric juices and the hormone glucagon, and also reduces the rate of gastric emptying. Toxic human amylin oligomers and aggregates are implicated in the pathogenesis of type 2 diabetes mellitus (T2DM). Although recent studies demonstrated a causal connection between amylin uptake and toxicity in pancreatic cells, the mechanism of amylin's clearance and proteolytic compartments regulating its turnover and toxicity are yet to be determined. Using pancreatic rat insulinoma (RINm5F) beta-cells and human islets as model systems, we show that human amylin, following its internalization, first accumulates in the cytosol followed by its redistribution (translocation) into nucleus, mitochondria and lysosomes which keeps the net cytosolic amylin content low. Our immunoprecipitation studies show that human amylin interacts with 20s proteasome resulting in a decrease in its proteolytic activity. Cytosolic amylin was largely absent from Golgi complex, and did not co-localize with aggresomal markers, heat shock proteins (HSP) 70 and 90, and tubulin. A small amount of internalized amylin was found in the mitochondria. In agreement with colocalization studies and immunoprecipitation results, inhibition of proteolytic activity significantly increased intracellular amylin content and toxicity. Our results suggest a pivotal role for proteasomes, and to lesser extent lysosomes, in amylin's proteostasis and detoxification in pancreatic cells.

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Power of Quantum Computing Algorithms

Algorithms based on the properties of quantum physics can facilitate enormous computations that would be unthinkable on a classical computer. Analysis of quantum algorithms involves several areas of mathematics and computer science, including linear algebra, complex analysis, and computational complexity theory. Our goal is to analyze two famous quantum algorithms: the Deutsch-Jozsa algorithm and Grover's search algorithm. Using techniques of algorithm analysis, we can calculate the time complexity of each quantum algorithm and compare it with the time complexity of its corresponding classical algorithm. These algorithms are probabilistic. From these comparisons it will be clear that the quantum algorithms run much faster than their classical counterparts. If a quantum computer that can harness the power of these algorithms is built, it will have a revolutionary impact on computing and our world.

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Application of Cellular Analysis of Hemocytes in *Apis mellifera* During Bacterial Infection

The European honeybee, *Apis mellifera*, is vital to agriculture because it is a versatile pollinator of many different crops. In the past decade, though, pollinator populations in general have been in decline. Honeybee decline is associated with Colony Collapse Disorder which is characterized by sudden and unexplained losses of hives and may be related to a number of causes including disease, pesticides, and environmental stresses. The goal of this experiment was thus to identify an effective way of measuring general immune activity in honey bee hemocytes in a low budget and visible fashion. Insects rely on hemolymph, containing hemocytes, for both the delivery of nutrition and for immune activity. In this experiment, bees were exposed to artificial bacterial infection with *E. coli* in order to characterize the cellular immune response in newly hatched honey bees. The delicate nature of honey bee hemocytes and the discrepancies within the literature of the types of hemocytes in bees necessitated the development of new extraction technique to maintain cell shape as well as a strategy for differentiating the cell types. Trials of different extraction techniques showed that the use of a 31g sterile needle was most effective for extraction and the use of a single nuclear stain, Giemsa, was most effective for cell differentiation counts under a light microscope. Results indicate that healthy, newly hatched worker bees infected with *E. coli* have significantly more hemocytes in the isolated hemolymph samples than bees not infected with *E. coli*. However, there is no significance in the type of hemocytes in the hemolymph, although there is notably a high count of prohemocytes and plasmatocytes in the hemolymph as compared to other types. Understanding the total cell count and differential cell count offers insight into the movement of immune cells and can help further research into the effects that pesticides, environmental triggers, and other diseases may have on the overall health of bee populations.

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Testing the Normalization of Compton Scattering Data

The investigation of proton polarizabilities using Compton Scattering allows us to study the internal structure and dynamics of the proton. The most commonly studied property of Compton Scattering is the reaction cross section, a measure of the reaction probability. In order to measure this, many aspects of the experiment have to be closely controlled and calibration measurements have to be made. To ensure the accuracy of detection, we can calculate the reaction cross section of a more probable and, therefore, a higher statistics reaction. In this case, the reaction is pion photoproduction. We will analyze both real and computer generated data of both reactions in order to calculate the cross sections of pion photoproduction and Compton scattering on the proton. Comparing the pion photoproduction cross section to the known values, allows a cross check of the various normalization factors required in the calculation of the Compton scattering cross section. With this information, we can calculate and compare both cross sections, thus establishing the detector efficiency.

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Drosophila flies and Steinernema nematodes: A new model for immunity and parasitism

Drosophila melanogaster, the common fruit fly, is an important model host to study the insect innate immune system, which shares homology with that of humans. Most work on understanding the immune system of flies has been done with microbes and hence knowledge of immune function against parasitic nematode infections is lacking. *Steinernema carpocapsae* nematodes form mutualistic relationship with the insect pathogenic bacteria, *Xenorhabdus nematophila*. This partnership renders the nematode highly pathogenic. We have recently developed a method to separate these two partners allowing us to study the *Drosophila* immune response against infection by symbiotic nematodes (carrying bacteria) and axenic nematodes (lacking bacteria). Survival results for larvae infected by symbiotic and axenic nematodes have revealed that both types of nematodes are equally pathogenic to *Drosophila* larvae. These results imply that the presence of *Xenorhabdus* bacteria does not increase nematode pathogenicity. We are in the process of performing a transcriptome study in *Drosophila* to identify and functionally characterize those genes that are involved in anti-nematode immune defense. Results from this project will potentially uncover the molecular basis of nematode-insect interactions and shed light on the host immune defense against parasitic nematode infections.

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The degree profile and weight in Apollonian networks and k-trees

We investigate the degree profile and total weight in Apollonian networks. We study the distribution of the degrees of vertices as they age in the evolutionary process. Asymptotically, the (suitably-scaled) degree of a node with a fixed label (timestamp) has a Mittag-Leffler-like limit distribution. The degree of nodes with intermediate age (growing, but not too fast, label) have different asymptotic distributions, influenced by their labels. The very late arrivals have a degenerate distribution. The result is obtained via triangular Polya urns. Also, via the Bagchi-Pal urn, we show that the number of terminal nodes asymptotically follows a Gaussian law. We prove that the total weight of the network asymptotically follows a Gaussian law, obtained via martingale methods. Similar results carry over to the sister structure of the k-trees, with minor modification in the proof methods, done mutatis mutandis.

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Associative Learning Response in Honeybees (*Apis mellifera* L.): Impaired by Sub-lethal Exposure to Imidacloprid

Our results demonstrate that neonicotinoids have an adverse effect on the cognitive abilities of honeybees and thus may play a role in Colony Collapse Disorder (CCD). In the present study, we show that honeybees' associative learning response to conditioning with lemongrass vapor is weakened within 60 minutes by oral exposure to lethal (LD50) and sub-lethal dosages (.05% and 5-10% LD50) of imidacloprid. We used classical conditioning of the proboscis extension reflex (PER) in honeybees with lem-ongrass vapor as the conditioned stimulus and sugar water as the unconditioned stimulus. Our objective was to condition honeybees to lemongrass vapors in four conditioning trials and test their olfactory learning performance in a classical choice experimental set-up, using a choice chamber with lemongrass vapor or pure air fanned through each of two half-chambers. We compared the mean percentage of successfully exhibited conditioned response between honeybees treated with different concentrations of imidacloprid. There is significant evidence that imidacloprid impairs the associative memory of honeybees at imidacloprid dosages of .05% and 5-10% LD50. By contrast, there is no evidence indicating that neither imidacloprid dosage nor digestion time reduces the amount of time bees spend in choosing to enter either half-chamber. The observations from this study may help explain how sub-lethal dos-ages of neonicotinoids cause the disappearance of honeybees from their hives.

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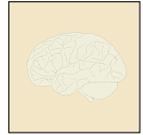
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Grandmothering in Wild Chimpanzees: Evolutionary Implications for Reproductive Fitness

Human females, unlike the majority of other mammals, live long past their child-bearing years. One explanation for this longevity, the grandmother hypothesis, suggests that post-fertile females enhance their own fitness by investing in the reproductive success of their offspring and survival of their grandoffspring. Grandmothers can provision food, carry, groom, and otherwise effectively alloparent their grandchildren. While studies in a variety of other species have investigated the grandmother effect with mixed results, this hypothesis has never been addressed in human's closet living relatives, including the chimpanzee. Female chimpanzees typically disperse and settle in new communities before reproducing; therefore it is rarely possible for grandmothers and grandoffspring to interact. However, at Gombe National Park, Tanzania, ~50% of females stay and reproduce in their natal community, which provides the unique opportunity to observe chimpanzee grandmothers with their grandoffspring. In this study, we used 35+ years of behavioral and demographic data from Gombe National Park, Tanzania to test for evidence of the grandmother effect in wild chimpanzees (*Pan troglodytes schweinfurthii*). We found that direct interactions, such as grooming and playing, between grandmothers and their grandoffspring were extremely rare and although grandmothers did continue to behaviorally invest in their adult daughters via grooming, grandmother presence in the community was not related to grandoffspring survival to ages 1, 5, or 12 years. These results indicate that given the opportunity, chimpanzee grandmothers do not directly invest in or influence the survival of their grandoffspring. Thus, behavioral changes during hominin evolution beyond dispersal patterns, such as food availability and foraging strategies, likely selected or allowed for grandmothers to invest in their grandoffspring.

STATUS

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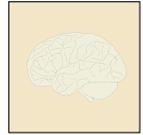
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Preparing Everyone for Disasters: The relationship between demographics and emergency preparedness

Natural and human made disasters disproportionately affect individuals of lower socioeconomic status, those with disabilities, and the elderly. One way to offset the consequences of disasters is through preparedness. This study seeks to evaluate the effectiveness of the Red Cross's emergency preparedness presentations in the National Capital Region of the Red Cross. The Red Cross is collaborating in this research because of their desire to reach diverse populations and in order to maintain high standards in effecting change in emergency preparedness for all. There is little published evidence of the effectiveness of such presentations to date. Trained Red Cross volunteers routinely present emergency preparedness presentations when requested by community organizations. Participants in this study (N=approximately 160 to date) completed brief surveys before and after four presentations to members of Rotary, a Baptist Church, and two Senior Living Centers. They were compensated \$5 for their time. This pre-post evaluation design included measures of demographics (e.g., race, gender, income) and emergency preparedness behaviors (20 items measuring behaviors recommended by FEMA and the National Red Cross - in three domains - "build a kit," "make a plan," and "be informed"). Analyses examined the degree to which demographic characteristics affected whether participants planned to implement the Red Cross's recommendations for emergency preparedness. This study will help us understand the role of demographic factors in preparedness and increase their effectiveness in the future.

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Using Synthetic Controls to Estimate the Effect of the 2010 World Cup on South African Tourism

Using the 2010 World Cup as a case study, this paper will estimate the mega-event's effects on the South African tourism industry. A mega-event has the ability to draw fans from around the world to a host country, generating opportunity for an expansion in its tourism industry. This study will utilize the data-driven statistical method 'synthetic controls,' in order to create a weighted average of foreign tourist arrivals in control countries to estimate the number of foreign tourist arrivals in South Africa. By comparing South Africa to control countries without mega-events, this method will enable the present study to isolate the effects of the 2010 World Cup on the South African tourism industry.

STATUS

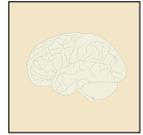
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Social ostracism predicts BMI, emotional eating, lower self-esteem, and lower self-compassion among college women

Prior research suggests that ostracism (social exclusion or rejection) negatively impacts wellbeing, including risky health behaviors and concepts of the Self (Bastian & Haslam, 2010). Past studies have explored the effects of ostracism on eating, but have not explored how individual differences in dietary concern may moderate the effects of ostracism on maladaptive eating (Oaten, Williams, Jones, & Zadro, 2008). The current study examined preliminary associations between ostracism, maladaptive eating patterns, and constructs found to be related to ostracism, such as self-esteem (Buckley, Winkel, & Leary, 2004; Salvy et al., 2011). 133 undergraduate women completed an online survey as part of an ongoing study assessing daily health habits. Bivariate correlations revealed a marginally significant positive relationship between self-reported ostracism and BMI (Body Mass Index) ($r = .15, p < .08$). Regression analyses controlling for BMI also revealed that women who experience more ostracism also report: more emotional eating ($\beta = .24, p < .004$), lower dietary concern ($\beta = -.20, p < .03$), and lower self-esteem ($\beta = -.48, p < .001$). On the other hand, individual differences in trait self-compassion ($\beta = -.25, p < .004$), and propensity to practice spontaneous self-affirmation ($\beta = -.20, p < .03$) are negatively related to ostracism. Furthermore, dietary concern interacted with ostracism experiences to predict emotional eating ($\beta = .18, p < .04$): for women high dietary concern, ostracism significantly predicted more emotional eating ($\beta = .23, p < .002$); this pattern did not hold for individuals low in dietary concern ($p = .19$). Though directionality cannot be determined from cross-sectional data, results provide preliminary evidence for the negative impacts of ostracism on eating-related outcomes – particularly for women high in dietary concern. Future studies are planned to examine the causal relationships between ostracism, eating outcomes, and the moderating roles of self-compassion and dietary concern.

STATUS

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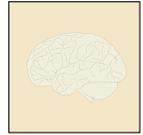
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A Bipartisan Political Personality Profile

On the eve of the 2014 midterm congressional elections in the United States, the American people ranked the war with ISIS as only the sixth most important campaign issue and the Ebola outbreak as a distant seventh. Instead, breaking Washington gridlock was identified as the most pressing electoral problem. If partisan polarization is responsible for this state of affairs, how can the electorate recognize candidates for Congress who will actually work to foster bipartisan political engagement and dialogue? How can they cut through campaign rhetoric to identify aspirants to office that will behave as if governing, rather than gridlock, is good politics?

Characterized across party lines as a “compromiser who operates above the partisan fray,” retired Congressman Lee H. Hamilton is examined as a possible archetype of the bipartisan political personality. A profile is constructed using automated operational code and leadership trait analysis. It is tested against and validated by third person reflections of the subject and by the tenor of the subject’s own public written and verbal communications.

Though the results are intuitive in part, little or no prior research exists regarding a bipartisan personality and thus questions are generated for future research which should include an expanded subjects pool. Consequently, the profile offered forth is intended merely to begin a conversation that might conclude with an electorate better informed about how to evaluate candidates on the most pressing campaign issue of the day.

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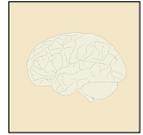
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The Conceptualization of Environmentalism in Sagara

My study focused on the perceptions of “environmentalism” in Sagara, Tanzania and attempted to compare Sagaran concepts to those of a more Western model. My study also identified the “actors” that taught Sagarans about the environment. After finding that Sagarans held a strong resource conservation focus in their responses, I then focused on the details of their resource use to see whether what they have been taught about conservation has been actualized in their daily life. I predicted to find that Sagarans have a much more generalized and resource conservation focused definition of “environmentalism” and that their patterns of resource use would not necessarily fit into what they had been taught about conservation. I conducted the study in Sagara, a small village in the West Usambara Mountains from April 7th - 25th, 2014. My sample frame was limited to adult residents of Sagara Village and members of organizations that have interacted with Sagara Village over the past 25 years. My sample population was “mothers” and three key-informant interviews with Sagara’s village chairman, a representative from Tanzania Forest Conservation Group (TFCG), and a primary school teacher. I gathered my data through two sets of semi-structured interviews, three focal groups, and three key informant interviews. Each set of semi-structured interviews had 50 respondents (n1 = 50) (n2 = 50) while each of the three focal groups had 5 respondents for a total of 15 respondents (n3 = 15). I found that my predictions were accurate in that there was a definitive focus on resource conservation in the respondents’ perception of “environmentalism”. I also found that formal teachers of the environment, such as the government, school, and TFCG more successfully transferred knowledge about the environment than families, an informal educator. However, I found that the government and the local school were both heavily influenced by TFCG teachings themselves, and therefore all taught similar aspects of “environmentalism” such as wood and water conservation. This was in contrast to family teachings which focused more around cultivation and agriculture. Lastly, it was shown that even though many respondents were aware of the teachings of TFCG, the government, and school (proving successful knowledge transfer), the actualization of these teachings proved to be lacking. The resource use habits of many Sagarans proved to, oftentimes, contradict their own definitions of “environmentalism”, taught to them by the actors previously mentioned. Overall, I found that perceptions of “environmentalism” in Sagara village greatly differ from those in the Western world, and that although TFCG has been successful in teaching Sagarans about the topic, residents of Sagara village have not necessarily put into action what they have learned.

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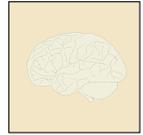
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Microfinance In America: Assessing the Efficacy of Training and IDAs in Contributing to Microloan Repayment

Though it is most well known for its use in international development, microfinance (also known as microlending or microcredit) has become an increasingly prominent tool used by private-sector charities and non-profit community development organizations in the United States. Today there are nearly 500 microfinance organizations serving low-income entrepreneurs throughout the country, with an estimated \$529 million in loans outstanding. This paper adds to the limited discourse examining the determinants for borrowers' success by assessing the impact of business training and savings support on loan repayment outcomes. Research focuses specifically on data from the Women's Initiative for Self Employment (WISE), a California-based microfinance organization that operated from 1988 to 2014, provided by the Field Institute. By testing the hypotheses that WISE's training initiatives and use of Individual Development Accounts (IDAs) are negatively correlated with loan default, we hope to determine whether these factors have a positive impact on microlenders and borrowers.

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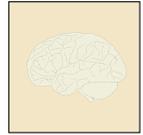
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Reciprocal Effects: An examination of the relationship between post-job-loss stressors and internalizing

INTRODUCTION:

To better understand the effects of post-job-loss stressors on internalizing, we examined 426 recently unemployed individuals, collecting data on stressors and symptoms five times over the six months following job loss. Given the high co-occurrence of depression and anxiety, we analyzed the overlapping variance of these two conditions in a latent construct that we termed internalizing. To test the dynamic interplay between stress and internalizing, we examined a reciprocal effects model. This model, combining both the stress effects and stress generation models, specifies the hypothesis that stress predisposes an individual to internalizing, and that internalizing may foster an increase in stressors. While some research has supported the stress effects model following job loss, we could not find any research examining the stress generation model within a job loss context.

METHODS:

With the help of state unemployment agencies, we recruited 426 individuals who had recently lost their job, and interviewed them within seven weeks of job loss. We administered the CES-D, the Penn State Worry Scale, Brief Social Phobia Scale, and a checklist of stressful events that commonly occur in the aftermath of job loss. We repeated these interviews four times, for a total of five assessments across six months.

RESULTS:

Internalizing was modeled with a latent variable loading on depression, worry, and social anxiety. To help distinguish temporal priority of job loss stress and internalizing, we employed a multilevel autoregressive model. We chose the time frame of 6 weeks because past research has suggested this period as appropriate for observing an increased risk of major depression following job loss.

Results supported both stress effects and stress generation models, suggesting a reciprocal effects model may best explain the interplay between job loss stress and internalizing.

DISCUSSION:

Given support for both the stress effects and stress generation, we believe that the reciprocal effects model best represents the relationship between job loss stress and the common component of anxiety and depression. This suggests that job loss may trigger a cyclical stress response that elicits future stressors unrelated to the original job loss event. To prevent this cyclical response, it may be important to intervene before job loss triggers internalizing, thus cutting the cycle before it can cascade into a more self-perpetuating pattern.

STATUS

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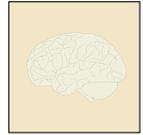
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Time Course of Learning

This experiment was performed to compare the process of learning for integrated and unintegrated information. While scholars have studied the time course of learning word-lists and expository individually, this study investigated process of learning in the two types of information together. Participants were asked to memorize randomly paired nouns over five time blocks and learn the specific nuances of a short story over five time blocks. The five time blocks were the same for each condition. Analysis of the results of tests administered after each block suggests we handle these integrated and unintegrated information differently. Our study found that after one exposure of either a list of randomly paired nouns or difficult piece of literature, participants ($n = 20$) performed at about 42% accuracy in both tasks. After the second exposure, test accuracy increased to 63% for word-pair learning but only 45% for expository text learning. From this point forward, the word-pair learning occurred at a linear rate but the expository text learning occurred at a power function-where approximately 95% accuracy occurred at the fifth and fourth blocks respectively. While the sample size of this investigation is small, the results propose different trajectories in integrated and unintegrated knowledge acquisition. Further replications will enhance the results and implications of the present study.

STATUS

Student - Undergraduate

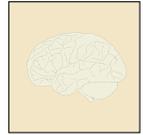
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International Trade and Civil War in Latin America

In recent years, scholars have conducted large-N empirical examinations of global civil war and trade data in order to understand the relationship between civil war and international trade. Often, scholars seek to elaborate theoretical arguments about whether or not dependence upon international trade flows makes a country more or less likely to engage in civil war, and to evaluate the Kantian “liberal peace theory.” This paper seeks to add to that body of research at the intersection of conflict and trade studies by focusing on civil war and international trade flows in a specific region that has seen 78 civil conflicts in the last two hundred years: Latin America. This paper will utilize a gravity model methodology to measure the impact of the presence of civil war on bilateral trade among Latin American countries between 1870 and 2009. Additionally, the paper will attempt to separate the overall impact of civil war on bilateral trade into its explanatory components by categorizing the aims of civil war participants, in order to determine which types of civil war are empirically the most impactful on bilateral trade. The findings of this paper suggest that civil war has a negative impact on bilateral trade among Latin American countries, and that civil wars for central control are more negatively impactful than civil wars over local issues.

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A Study of Flow and its Effects on Quality of Performance of Jazz Musicians

As defined by Csikszentmihalyi (1990), flow is the state of concentration where time flies, and a worker is at his or her most-productive best. The concept of flow, similar to notions of being in the zone or in the groove, is an ideal explanation as to what jazz musicians experience during a performance. The only research similar to this topic is from a study by De Manzano (2010), who looked at the flow experience of individual pianists. The study featured 21 professional classical pianists who were asked to manually classify their flow experience while playing the piano.

This study will build upon the concept of individual “flow” as defined by Csikszentmihalyi (1990) to the group level. In this study, jazz musicians of varying levels of expertise will perform individually, as well as in groups of 4. The participants will be told that this study will test their musicianship, by playing a specific, standardized jazz standard. All performances will be video recorded, with audio, in order to play back for reference. After the performances are completed, both the video recording and surveys will be reviewed following predetermined scales, which will measure specific variables—creativity through Teresa Amabile’s study, and quality of performance and expertise through a scale influenced by the GW Jazz faculty grading rubric.

This study will aim at identifying some of the pre-requisites for “flow”, the state of work where “time flies”, and the worker is at his most-productive best, in order to help isolate what attributes to the quality of a jazz performance. This knowledge, in turn, could be used to better performance practice for musicians, and be replicated in other professional contexts and settings as well.

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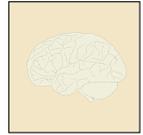
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Transpersonal Efficacy in Virtual Teams

Transpersonal efficacy (Emich, 2012) has recently emerged as an important predictor of team performance. Based in social cognitive theory, transpersonal efficacy can be conceptualized as an individual's confidence in another's ability to successfully perform a task. Emich found that team members work much harder when they perceive their teammates to have strong abilities, but when people are not confident in their teammates' abilities, they are less likely to put in all of their effort.

To expand the nomological network of transpersonal efficacy, it is important to understand how it develops and whether its effects on performance will generalize to diverse team types. Critically, we seek to explore how transpersonal efficacy develops in virtual teams. Given that teams who interact virtually for at least part of their work are now the norm, it is essential to understand how members of these teams collect information about each other to form efficacy judgments.

Results showed that transpersonal efficacy was positively correlated with task interdependence, organizational citizenship behaviors, normative commitment, and negatively correlated with task, relationship, and process conflict. However, transpersonal efficacy did not significantly correlate with virtuality, as was hypothesized.

Transpersonal efficacy is still a significant predictor of all of these outcomes when collective efficacy is included in the model, showing that the two constructs are distinct. Transpersonal efficacy adds to our understanding of teamwork dynamics that impact work behaviors, and its effects should continue to be investigated through further research.

STATUS

Student - Undergraduate

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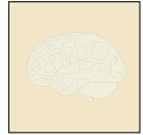
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ELLIOTT SCHOOL OF INTERNATIONAL AFFAIRS

The Pink Engineer: Barbie’s Identities in Conflict and Resulting Efficacy as a STEM Role Model

Recent education policy has put an emphasis on the importance of engaging girls in the fields of science, technology, engineering, and mathematics (STEM). Women continue to be underrepresented in these careers, which produce continuous job growth and provide higher incomes, and initiatives to engage female students in STEM studies emphasize the need for female role-models in these careers. The Mattel company has vocally produced their most successful toy, the Barbie doll, as a female role model girls from very young ages can see in STEM and other male dominated fields. Contrary to their intended message, research shows that adolescent and preadolescent girls presented with stereotypically feminine STEM roles models predict fewer job opportunities for themselves or are dissuaded from pursuing them. One study that specifically examined girls’ play with a fashion and career doctor Barbie versus play with non-sexualized female doll (Mrs. Potatohead) reported that young girls predicted they could participate in fewer male-dominated jobs after play with either Barbie doll than those who had not.

While the Barbie doll has always been marketed with the message that girls can achieve anything they dream of, her hyper-feminine image reinforces the stereotypical female identity. This research focuses on three separate career Barbie dolls in STEM fields (Zoo Doctor Barbie, Newborn Baby Doctor Barbie, and Computer Scientist Barbie) to examine how the Barbie doll’s hyper-feminine image may create conflict between the doll’s female and scientific identities. Observations made about the dolls’ outfits and accessories implied that, while neither image is intended to subordinate the other, the stereotypical portrayal of the feminine ideal always seems to trump the career image. In each example, the doll is sold in stereotypically feminine colors and form-fitting clothing, which lowers her perceived capability in male dominated careers for some and creates an unattainably perfect female role model for others. The doll is also paired with baby dolls or animals, pairing the dolls’ scientific image with that of a nurturer, a typical gender role for women, further emphasizing the female identity. Barbie cannot be an effective role model, as the doll’s stereotypical femininity renders it unbelievable or too perfect for girls to attain.

With an increase in the gender marketing of toys in the recent decades, examining the Barbie doll, arguably the figurehead of girls’ toys, shows how the stereotypically feminine images implicitly teaches girls, from an early age, career limitations.

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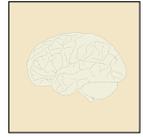
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Buzzfeed User-Generated Content’s Impact on Attitudes Toward Depression

Depression is a serious mental illness with 1 in 20 Americans age 12 and up reporting they have experienced depression (Pratt and Brody, 2006). Prior studies have suggested news and entertainment content focused on mental illness may reinforce stigma surrounding depression and mental illness. Considerable research has demonstrated that how media frames a problem influences attitudes toward that problem (Entman, 1993, Chong and Druckman, 2007). This study examines the potential effects of a very different type of content - user-generated content- appearing on new news sites. For example, online organizations like the website BuzzFeed give individuals the ability to tell their own stories. The study answers whether reading the personal story of a person suffering from depression might increase sympathy and acceptance toward people with depression compared to a traditionally styled media account of the illness.

400 participants were randomly assigned to one of four treatment groups. The first treatment group read a user-generated, first person account of experiencing depression. The second treatment group read a reporter-written story featuring a depressed person’s experiences with the illness. The third treatment group read a fact-based story in the “listicle” form BuzzFeed often uses. The fourth group was the control group and received a story about Uber. All treatment groups also read a filler story about a southern university cutting its football program. After reading the stories, participants answered a survey about their attitudes toward people with depression. A Comparison of attitudes across treatment groups helps determine whether user-generated content (which frames depression in a very personal way) increases sympathy and decreases stigma toward people with depression.

Currently, the research is in progress. The results may help communication and public health professionals design stronger depression awareness campaigns that encourage people to seek treatment and lower stigma surrounding the illness.

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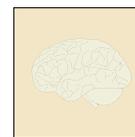
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

How do Stakeholders Influence EPA's Chemical Risk Values?

The objective of this research is to understand how external peer reviews and interagency comments impact EPA's final toxicological assessments of chemicals. The Environmental Protection Agency (EPA) conducts risk assessments to characterize the nature and magnitude of health risks to humans and wildlife from chemical contaminants. In the early 1980s, EPA released the Integrated Risk Information System (IRIS), a human health assessment database, which evaluates information on health effects that result from exposure to environmental contaminants. The data in IRIS is considered the best information available to the government regarding risks associated with chemicals found in commerce. In developing each toxicological assessment, EPA's 26-month process includes opportunities for external peer reviews and interagency consultations. The IRIS process has been criticized and subsequently altered at various points in its history. Prior to 2009, interagency comments regarding IRIS's toxicological assessments were not made publicly available. In response to fervent criticism, EPA updated its IRIS assessment process to make interagency comments available to the public. This study reviews the external peer review and interagency comments for 11 of the 41 chemical assessments published since 2009 that have disclosed and archived all interagency science consultation and discussion and external peer review comments. Key terms were culled and analyzed from the Science Advisory Board meetings and Responses to General Charge Questions for the 11 chemicals. In addition, interagency comments were evaluated to determine if Agencies supported the external peer review comments. We find that when a majority or plurality of external peer-reviewers and agencies agree on a portion of the draft IRIS report, EPA makes alterations in its final toxicological assessment to respond to these recommendations. This research is the first stage in developing a delimited survey style for external peer and interagency review to streamline the EPA's IRIS database process.

STATUS

Student - Graduate

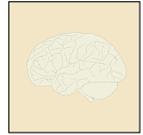
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Outside Interests in U.S. Congressional Elections: Analyzing the Strategies and Impact of the Club for Growth

The purpose of this research is to investigate the electoral strategies employed by the conservative interest group The Club for Growth in order to elect candidates that adhere to their preferred fiscal policies. The study focuses on two questions, the first being how the Club allocates its campaign donations during each election cycle, and the second being how successful the Club for Growth is in ensuring that the candidates it favors win their elections. By compiling data on the Club's choice of candidates as well as the outcomes of their Congressional races, I seek to test my hypotheses that the candidates the Club favors tend to be more fiscally conservative than most Congressional Republicans, and that the districts that are targeted tend to be more conservative than the nation as a whole.

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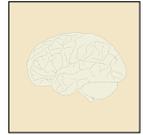
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Revisiting Organizational Constraints: A Qualitative and Quantitative Study on Perceived Organizational Barriers

Organizational constraints are features of a work environment that inhibit the expression of abilities and motivation required for effective performance. Organizational constraints are one of the most stressful situations encountered by employees in the workplace and can prevent employees from successfully completing job tasks and duties. The current study aims to update Peters & O'Connors (1989) organizational constraints taxonomy, identify employee reactions to modern organizational constraints (i.e. outdated equipment, bandwidth issues) based on their productive or counterproductive nature, and examine how employees utilize technology to overcome job-related barriers in the workplace. A survey design study collecting both qualitative and quantitative methods was launched on Amazon's Mechanical Turk (mTurk) portal. Participants (n=250) provided examples of constraints encountered in the workplace and their reactions to these experienced constraints. Current findings suggest organizational constraints can be classified into three domains: individual, organizational, and technological. Results also show employees utilize technology in the workplace to overcome constraints that hinder job performance (i.e. using personal devices to access information blocked by the organization). Findings build on the organizational constraints literature by developing a classification of workplace barriers as perceived by employees, allowing researchers and managers alike to identify issues within an organization. Incorporating employees reactions into this classification will provide insight into how organizations can best develop and remove barriers to aid in expression of productive employee behavior.

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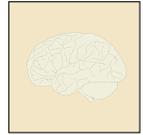
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ELLIOTT SCHOOL OF INTERNATIONAL AFFAIRS

Social Media and Contentious Politics: Tunisia 2010-2013

How do social media contribute to groups engaged in contentious politics within a domestic environment? While many have examined the influence of social media on the Arab revolutions of 2010-2011 from an international perspective, there are fewer studies examining the impact of social media within a national environment after these events. Through interviews with a group of 40 Tunisians, many of them active in contentious politics from 2010-2013, this research identifies what sources initially informed the group members of a movement as well as the sources that ultimately pushed them to become active. While information gleaned via social media certainly played a role in the decisions of many interviewees to join the movements examined in this research – unsurprising, given the high rates of internet use within the group – social media were often cited as less trustworthy than other sources and were more likely to inform the respondents of a movement’s existence than to push them to act. While these findings are not unexpected, they do require that future efforts examining the role of social media in contentious politics within a country’s borders differentiate how different types of sources are viewed by potential supporters and how they might contribute to mobilization in different ways.

STATUS

Student - Graduate

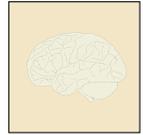
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Taxing Inequality: An examination of redistributive taxes and inequality in OECD countries

This paper focuses on the relationship between economic inequality, as measured by the Gini coefficient, and the relative prevalence of redistributive taxes within a country. Using a fixed time and entity effects panel of three years and more than thirty OECD countries, the study examines this relationship to focus on the ability of countries to directly impact income inequality through tax policy. The paper seeks to determine, moreover, if there is a relationship between these tax rates and the inequality measures.

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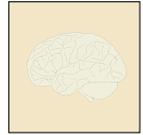
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Conflict and Urbanization: The Case for Sierra Leone

This paper seeks to examine the impact of civil conflict on rural-urban migration. Standard theory suggests that urbanization and industrialization are precursors to development. Recent literature though, has pointed to a group of countries, mainly in Sub-Saharan Africa, where rapid urbanization has transpired without industrialization and has been associated with stagnation or negative growth (Gollin, Jedwab and Vollrath, 2014; Annez and Buckley, 2009; Fay and Opal, 2000). This evidence suggests that push factors, as supposed to pull ones, are driving rural-urban migration. Using census data from Sierra Leone this paper studies the effect of one potential push factor, conflict.

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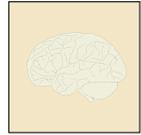
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Popping pills: How favorable social norms and prototypes impact undergraduates' willingness and intentions to use non-medical prescription stimulants (NPS) over the course of an academic semester

Non-medical prescription stimulant (NPS) use is a growing problem in the U.S. with 1.4 million users nationwide, most of which are young adults aged 18 to 25 (NIDA, 2013). Since the average age of initiation is 21, undergraduates are especially at-risk for experimentation and addiction (SAMSHA, 2014). In fact, Garnier-Dykstra et al. (2012) found that 62% of undergraduates had been offered NPS and 31% had used within 4 years.

Academic and social pressures might motivate students to engage in NPS use (i.e., Adderall). Perceived academic benefits of use include increased alertness and concentration, which are believed to aid in studying (Stock et al., 2013). Alternatively, the social atmosphere can encourage recreational use: partying and getting high (NIDA, 2013). The college environment is capable of promoting potentially harmful social norms about NPS use. Norms can be based on both perceptions of how many other students use (descriptive norms) and what behaviors meet other's approval (injunctive norms).

Social norms are a central construct in the Prototype-Willingness (PW) model of health behavior (Gerrard et al., 2008). This model also includes prototypes (e.g., favorable images of the typical NPS user), which predict willingness to engage in risky health behaviors. Although past research found positive relations between favorable descriptive norms, prototypes of NPS users, and willingness to use (Stock et al., 2013), no study has examined changes in NPS willingness, intentions, and actual use during an academic semester.

A longitudinal two-part survey was distributed to 401 undergraduates (78% Caucasian; 277 females) to examine cognitive predictors (norms and prototypes) of NPS willingness, intentions and use over time.

Regressions were conducted to test whether T2 descriptive and injunctive norms, and favorable prototypes of NPS users, predicted T2 willingness and intentions to use NPS while controlling for corresponding T1 variables. Likewise, we examined whether T2 willingness/intentions predicted T2 use. Gender, year in school, past substance and NPS use were entered as covariates.

Results revealed that descriptive ($\beta=.115, p<.012$) and injunctive norms ($\beta=.193, p<.001$) significantly predicted willingness. However, only injunctive norms predicted intentions to use NPS ($\beta=.269, p<.001$). Prototypes predicted both willingness ($\beta=.118, p<.001$) and intentions ($\beta=.096, p<.027$). Following the PW model, both willingness and intentions ($\beta=.401; \beta=.281; ps <.001$) predicted greater NPS use at T2.

Our findings have important prevention/intervention implications. Exposing students to negative prototypes of NPS users and norms that do not favor use may decrease the willingness, intentions, and use of NPS on college campuses.

STATUS

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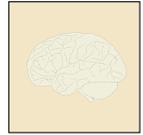
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Exploring How International Service Volunteer Preparation Aligns With the Actual Service Experience

Each year, 1.6 million people volunteer to serve internationally, however the level of preparation these volunteers receive varies. If volunteers experience improper preparation, it can lead to various negative consequences for the volunteers and for the people they are serving in the host communities. The purpose of this study is to examine how preparation received prior to the international service aligned with the actual service experience of volunteers, as well as how volunteers felt their service was perceived by the people within the host communities. Five individuals were interviewed for the study. The individuals were all college students who participated in various international service programs. Through the interviews, the findings were mixed in relation to volunteers' feelings about their preparation. While some individuals felt that they were adequately prepared for their service trips, others felt that they lacked the cultural competency or maturity necessary for such service trips. The individuals' views of how the people and host communities viewed their service also yielded a range of results. Some participants felt that the people and communities were grateful for the service they were receiving, while other participants stated that they thought the people from the host communities felt exploited by foreigners in their homes. Those participants who read up and familiarized themselves with the culture of the community they would be traveling to felt more prepared than those participants who did no prior studying or reading. Yet, the varied findings make it difficult to generalize service participants' thoughts on their preparation and how the people and communities perceive their service. There are no consistent preparation programs in international volunteer programs and given this, there are a range of experiences that are greatly shaped by both the participants and host communities.

STATUS

Student - Undergraduate

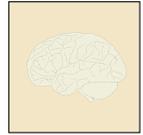
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ELLIOTT SCHOOL OF INTERNATIONAL AFFAIRS

Hashtagging Sandy: How are the psychological effects of natural disasters expressed in social media?

In the wake of crisis, humans innately succumb to particular set of emotions, allowing psychologists to develop a pattern for their responses to trauma. While subjective, a general cycle of emotions can be broken down into three stages: anticipation, experience, and recovery. This study examines this traditional psychological theory and its application to current events through the October 2012 disaster, Hurricane Sandy, and how it was expressed through social media. Presenting the timeline of trending topics and hashtags as exhibits, the investigation asks: to what extent did social media act as an outlet to express the psychological effects of natural disasters? Using the psychological stages to trauma recovery, as described by Herman (2002), and Quarantelli and Dynes (1977), as methods, this study finds that a similar pattern of human response and cycle of emotions was captured on Twitter during Hurricane Sandy. During this computerized era, this investigation examines relevant information regarding the hybridization of traditional psychology and new technology.

STATUS

Student - Undergraduate

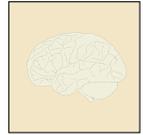
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ELLIOTT SCHOOL OF INTERNATIONAL AFFAIRS

Informal Education of Patriotism in Rwanda: The Case of Ingando and Itorero ry'igihugu

Ingando and Itorero are two modern compulsory education programs designed to teach and promote national unity and reconciliation in Rwanda. Although there is much research to date in regards to the ways in which these programs could be used as political tool there is no available research that actually includes the curriculum itself. Through interviews and curriculum analysis, this study seeks to address the omissions in the modern history curriculum in both Itorero and Ingando, while also comparing the current Itorero program it its pre-colonial predecessor. It found that the many of the omissions were in the lack of Post-Genocide history material, and that the current Itorero program was well aligned with its predecessor.

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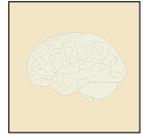
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GRADUATE SCHOOL OF EDUCATION & HUMAN DEVELOPMENT

Using group counseling to improve self-esteem, school adjustment and academic performance of middle school ESL students

American public schools have been serving an increasing number of English as a Second Language (ESL) students. Several authors have articulated the ways that school counselors could better connect with ESL students, immigrant youth and international student. A limited number of authors have acknowledged the significance of serving ESL students in school counseling programs. Previous research has demonstrated that school counselors can have a positive impact on ESL students by intentionally interacting and connecting ESL students and teachers. This study will be conducted as a pilot study and provide additional data to determine the efficacy of this group intervention to improve ESL students' self-esteem, school adjustment and academic performance. This study add evidence for school counselor group intervention with ESL students and future research could be built upon the results of this study. An evidenced-based group counseling intervention, which combines both counseling and psychoeducational group strategies, will be conducted weekly for 12 sessions during the second semester of the 2014-2015 school year at the Columbia Heights Educational Campus. The student participants in this study will be considered at-risk and from an economically disadvantaged background and will come from the overall ESL population within CHEC. Selected students will be assigned to either a treatment or control group. Both 6th grade and 8th grade ESL students will be randomly selected to participate in different groups. It is expected that the group interventions will promote academic and personal-social development. Findings from the measurements in this study will be analyzed to determine the variables, which are positively correlated with the group intervention and academic success. These findings will provide implications for future interventions. Finally, gains in the students' overall Grade Point Average will be good indicators that demonstrate the success of this project as well as their reflective and structure writing activities.

STATUS

Student - Graduate

AUTHORS

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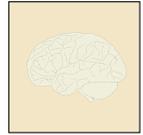
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Healing Hidden Wounds: Identifying Current and Future Treatment Options for Those Living with PTSD in Rwanda

As defined by the DSM 5, Post Traumatic Stress Disorder (PTSD) is a diagnosable mental health condition, occurring after a serious encounter with trauma and causing significant physiological and cognitive effects. The prevalence of PTSD in Rwanda is estimated at about 26.1%, and this may be largely attributed to the 1994 Rwandan genocide. Given such a high PTSD occurrence, it becomes necessary to understand current PTSD and trauma treatment practices offered in Rwandan public hospitals and private institutions. This qualitative study included interviews conducted within Rwanda from relevant professionals working in the field of mental health, including psychiatrists, mental health nurses, mental health policy makers, University of Rwanda professors, and representatives from significant non-governmental organizations. Findings suggest that there remains an overemphasis on medication within government institutions, and patients may not receive individualized and appropriate mental health care. This trend can be attributed to the small number of mental health professionals currently employed in Rwanda, creating an environment in which treatment is rushed and often placed in the hands of psychiatric nurses; however, a recent increase in training programs designed for mental health professionals should alleviate some of this burden. The collected research also suggests that community-based interventions offered by non-government organizations that offer simple forms of counseling may provide a critical piece of trauma treatment. Finally, while the Rwandan Mental Health Draft Bill addresses patients' rights to treatment, a secondary analysis of the bill suggests that it focuses exclusively on civil rights for those facing mental illnesses, neglecting to include more medical language, such as the necessary balance between medicine and psychotherapy in treatment. This research indicates a serious disparity between medicinal use and psychotherapy in trauma treatment, and government medical institutions may consider working in greater collaboration with non-government organizations providing trauma treatment, as their work demonstrates the benefits of community-based, holistic care. Further research is necessary in order to more quantifiably determine the effectiveness of techniques utilized by such non-governmental organizations, as well as exploring the long-term benefits of new education programs to train future mental health care workers.

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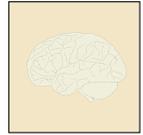
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

How Rugby Shapes the Self-Identity of Female Players

The sport of rugby promotes gender equality on the field by having the same rules, field size, and ball size between men and women's team. Off the field, however, male and female rugby players experience different perceptions and stereotypes. For example, females players are often negatively stigmatized by outsiders such as family members, friends and strangers, as aggressive, lesbian, or masculine; whereas, males have similar perceptions of being masculine and aggressive, but it is appropriate for males to be perceived this way according to Howe (2003). These gender-based perceptions of players create biases that contribute to the identity and image of a player. The purpose of this study is to gain a better understanding of the social nature of rugby and to examine how the sport shapes self-identity for players. The literature review focuses on the culture of rugby, identities for female athletes as well as showing how the impact of rugby on women is unexplored. The research is conducted by semi-structured interviews with nine female participants who have played or are currently playing in the Washington, D.C. area. The data was coded and analyzed to see the major themes on how rugby serves in shaping their identity. The major results of analysis show that strangers react with surprise when the participants physically contradicted the perceived stereotypes about rugby players, but those reactions do not affect one's identity. The results also show players are more likely to have higher self-confidence that is shown outside of rugby, which goes against all of the negative perceptions that she encountered as well as have a deep bond to teammates that shapes her identity. The findings from this study offer new data that contradicts the literature regarding how much stereotypes and peers perceptions affect rugby players' sense of identity.

STATUS

Student - Undergraduate

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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Ambiguous Loss: Missing Migrants along the US-Mexico Border

In the 1990s through the 2000s, increased border security measures were enacted to deter potential unauthorized migrants from crossing the border (Dunn, 2009). These measures deliberately caused migration flows to shift into the most dangerous, remote parts of the border, thereby creating an even higher risk during unauthorized border crossings. This policy was enacted with the hope that the risk would outweigh any reward. To date, reports of exact numbers of migrant deaths along the border are inconclusive. In many cases, the missing are unreported or authorities are unable to link recovered remains to missing persons reports. Nevertheless, academic research indicates that border control measures are not a successful deterrent, and instead many migrants are dying to cross the border (Eschbach et al, 1999). The Colibrí Center for Human Rights in Tucson, Arizona works to connect missing person reports with unidentified remains brought to the Pima County Office of the Medical Examiner. Utilizing data collected by the Colibrí Center, this study illustrates demographic information on the missing. Nationality, age, time of disappearance, and sex are examined and the impact of disappearances on family members and communities are contextualized through a theoretical understanding of ambiguous loss (Boss, 2000). Additionally, demographic information on the missing is compared with data on unidentified remains from the Office of the Medical Examiner and on apprehension rates from the United States Border Patrol. This research contributes to the systematic documentation of missing migrants and migrant deaths along the US-Mexico border and aims to raise awareness of the detrimental impact current immigration policies have on not only migrants but also families and communities throughout Mexico and Central America.

STATUS

Student - Undergraduate

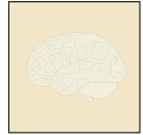
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Campaign Messaging and Engagement on Twitter in the 2014 U.S. Senate Elections

In a very short period of time, Twitter has become an inescapable, and arguably crucial, part of many people's lives. Twitter, and social media in general, has changed the way individuals communicate with one another and this trend has worked its way into the political sphere. In 2014, all but one candidate for the U.S. Senate had a Twitter account associated with their campaigns, demonstrating the broad reach of the platform. Twitter is also constantly evolving, so it is important after each election to reevaluate how candidates are using the platform to communicate with voters and determine whether candidates are applying old campaign techniques to new technology, or developing new techniques altogether. Past research and campaign strategists suggest that Twitter provides a unique opportunity for candidates to engage with voters and start a true conversation with them. However, preliminary analysis of the tweets of 2014 U.S. Senate candidates reveals that instead of taking full advantage of this opportunity for engagement, candidates use Twitter for more superficial engagement, using it to update their followers on campaign activities and encouraging them to vote. Additionally, differences in usage exist between safe and unsafe candidates. Safe candidates are more likely to promote their own views, while unsafe candidates are more likely to be more innovative in their attempts to engage with voters.

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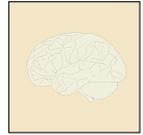
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The Role that Religious Leaders Play in Mental Health Care Access in African American Communities

African American communities have significantly lower mental health care use rates than other ethnic communities. Previous research links low mental health care use to financial barriers as well as increased stigma, lack of healthcare and the absence of African American mental health care providers. Research also demonstrates the centrality of the Black church in African American communities. The purpose of this study is to analyze what role, if any, African American religious leaders play in mental health care access in African American communities. The researcher gathered data through qualitative interviews with 3 Christian pastors of predominately African American churches in Washington, DC. Interview questions focused on referral, training, parishioner and pastor attitudes towards mental health care and mental health professional-church collaboration. Results demonstrated the distinct ways in which religious leaders in African American communities influence behavior and attitudes towards mental health among parishioners. Results indicated strong referral to mental health professionals, a lack of mental health training, comfort with typical pastoral counseling duties, such as marriage and family counseling, receptivity to mental health professional-church collaboration and changing attitudes towards mental health among parishioners. The research adds understanding to current literature about the way religious leaders view mental health and mental health professionals as well as how they assist parishioners in getting the care they require. The findings also indicate opportunities for collaboration between mental health professionals and the church to best meet the needs of African American individuals.

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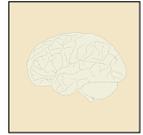
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Crossing Borders: Marx's Concept of Alienation and the Plight of Undocumented Immigrant Women Farm Workers in the 21st Century

Drawing on secondary data analysis, this paper is a theoretical exploration of the lives of Latina farm workers from the perspective of the concept of alienation. Most research on Latina farm workers focuses on the exploitative material conditions under which they labor. In this paper, I want to explore an overlooked facet of their experience: what Marx identifies as alienation. The loss of dignity in the workplace among undocumented minority women leads to alienation which results from their gender, race, and undocumented status. Alienation is a condition produced by capitalist arrangements of production that deny the worker the possibility of full personhood through productive collective labor. The estrangement of undocumented women farm workers' labor lies the facts that they cannot enjoy the fruits of their labor, that they have no control over their body and time, that they must compete with other workers rather than work cooperatively, and the value of the work they do is devalued by the sub-living wage this competition forces them to settle for. Latina farm workers begin to feel alienated when they cease to enjoy their participation in the workforce as a free activity and they become another commodity through which production must be maximized. Women farm workers face alienation in their occupations since they must produce for the market for their own survival. Moreover, women farm workers may face extra challenges when they are on the fields such as physical, verbal, and sexual abuse. According to Human Rights Watch (2012), undocumented women farm workers are reluctant to report any abuse for fear of deportation or losing their jobs.

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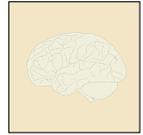
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

The Premium Overlap Puzzle: Evidence from the Federal Health Exchange

This paper explores the distribution of health insurance premiums for plans sold in the first two years of the Affordable Care Act's federal health exchange. In particular, the focus is on why plans with less generous coverage may cost more than plans with greater coverage (this is termed "premium overlap."). The author finds that the prices of comparable health insurance plans converge over time, with fewer plans' premiums "overlapping" into other metal tiers. The paper considers the effect of firm experience in offering these new insurance plans by exploiting the information asymmetry induced by new (and thus inexperienced) entrants to the health insurance market in the second year of the exchange. The conclusion is that firm inexperience in the market generates premium overlap, and that market equilibration leads to more competitively priced plan options for consumers. Further, the paper finds that new entrants systematically "over-price" their premiums, pulling up the average premium across tiers.

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Use of Inner Speech Affects Executive Functioning Performance and is Moderated by the Presence of Autistic Traits

Since Vygotsky's (1962) seminal work, a link has been drawn between inner speech and problem-solving abilities. A growing body of work corroborates these early observations in that use of inner speech facilitates problem solving in executive functioning tasks. Here, we show that interfering with inner speech via Articulatory Suppression (AS; i.e., speaking aloud to the beat of a metronome) in healthy adult controls (N=31; 11 male, mean age 20.9 years) detrimentally affects performance on the Tower of London (TOL), an executive functioning task, relative to a control Foot Tapping (FT; i.e., tapping one's foot to the beat of a metronome) condition. Specifically, participants made more extraneous moves in the TOL task in the AS condition, relative to the FT condition. There is also growing evidence in the extant literature that individuals with autism spectrum disorder do not utilize inner speech to the same degree as typically developing control subjects in the service of problem solving. Therefore, we also administered a self-rating measure of autistic traits (i.e., the Social Responsiveness Scale-2, Adult form) to these healthy adult controls to examine whether there was an association between the interfering effects of AS (vis-à-vis FT) and presence of autistic traits. We classified the extraneous number of moves needed to complete the TOL task under the AS condition relative to the FT condition as the Articulatory Suppression Disadvantage, a metric whose value corresponds to the extent to which AS interferes with inner speech. We found this metric to be significantly correlated with self-ratings of autistic traits. Taken together, these findings indicate that inner speech is a key contributor to executive functioning and that the presence of autistic traits moderates this relationship. This work will be extended to samples of individuals with autism spectrum disorder in the hopes of identifying a key treatment target for future intervention studies.

STATUS

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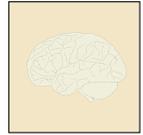
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Psychological Factors Related to Emergency Preparedness

Natural and human made disasters have considerable consequences for individuals' well-being and property. One way to stem the effects of these disasters is through emergency preparedness organizations are trying to educate the public about preparedness through community presentations. Our research aims to assess the effectiveness of psychological factors, for example, self-efficacy and perception of threat, on emergency preparedness for participants attending Red Cross Emergency Preparedness presentations in the Virginia, Maryland, and DC area. To date, roughly 160 participants have attended and completed pre and post surveys at Red Cross preparedness presentations in the greater Washington DC area. Measures on the survey include past exposure to disasters, perception of threat of disasters, self-efficacy for emergency-preparedness, distress, emergency preparedness behaviors, and demographic questions. Participants were sampled at four different locations, including a Rotary Club, Church, and two senior living homes in DC, MD, and VA. We are continuing to collect and code data, including results from a follow-up survey administered 30 days after each presentation. The results of our research on safety, preparedness, and self-efficacy have the potential to provide recommendations to improve emergency preparedness presentations, such as those provided by the Red Cross. They may also provide insights in regards to encouraging preparedness for individuals and households in general.

STATUS

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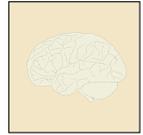
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Going Grün in the Swiss Alps

The world's mountains are of significant importance to humanity. Not only are they home to 22% of the world population, but they also provide water to over 3.5 billion people. Mountain environments are rich in resources and biodiversity and are sources of popular sports such as hiking, climbing, and skiing. Unprecedented levels of climate change are altering the natural resources available to humans, forcing us to rethink how we use them. There is certainly no shortage of research on the impact of climate change on high altitude environments, however, there exists a gap in interdisciplinary mountain research. A conference on Global Change and the World's Mountains held in Perth, Scotland, in 2010, found that most studies focus on either human or environmental systems but only 6% covered social-environmental relationships. This paper seeks to help fill that gap by analyzing both environmental and human development in the Jungfrau region of the Bernese Alps in Switzerland. It is a compilation of previous studies, data analysis, and stakeholder interviews taken during field research. The first section of the paper covers the physical evolution of the Swiss Alps, including the influence of glaciers, snow, and climate variability on the environment. The second section discusses human development in the region, focusing on the transition from an agricultural-based economy to a tourism-based economy. The third and final section explores the relationship between humans and the environment and how climate change could possibly impact it in the future. The Jungfrau region is the most glaciated region of the European Alps and therefore has some of the longest records of mountain research, making it an ideal location to study changing physical and human landscapes over time.

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Student - Undergraduate

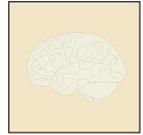
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Exploring the Lag in Visual Acuity as we Age Through use of an Object Based Attention Task

Interacting with a visual environment requires our attention to be shifted rapidly in order to select relevant information for further processing. The theory of Object Based Attention (OBA) posits that when attention is directed to an object, shifts within an object are initiated and executed faster than equidistant shifts to a different object. While object-based attention has been successfully demonstrated in young adults, whether this advantage hold with age remains an open question. In this experiment, the theory of OBA was tested in two age demographics: college age students (18-24) and senior adults (65+). By using the paradigm established by Egly, Driver, and Rafal (1994), we were able to measure the speed and accuracy of an attention switch within and between objects. The results from both groups replicated the trends from the original OBA experiment, as evidenced by faster switches in attention within an object, and slower attention switches to different objects. Age, however, did play a factor in reaction time. The older demographic took, on average, 200ms longer to react to the target in both the occluder bar and no occluder bar versions of the experiment. The findings from this experiment are evidentiary of a lag in visual attention astuteness that accompanies an aging brain. This can be due in part to a more delicate level of attentiveness or in part due to slowing neural connections. Although this experiment cannot parse out the exact reason for this delay in reaction time, we still see that shifting attention in a visual environment continue to be influenced by the objects within it even as we age.

STATUS

Student - Undergraduate

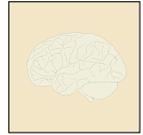
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Using Satellite Imagery to Quantify Spatial Features of Urban Areas and their Relationship to Census Data in Accra, Ghana

Mapping urban areas via satellite imagery is an important task for detecting and anticipating land cover and land use change at multiple scales. As developing countries experience substantial urban growth and expansion, remotely sensed based estimates of population and quality of life indicators can provide researchers and aid workers timely and spatially explicit information for planning and development. In this study, we use commercial high spatial resolution satellite imagery, in combination with fine resolution census data, to determine if remotely sensed data is an effective and appropriate means of identifying spatial patterns of quality of life in Accra, Ghana. Traditionally, spectral characteristics are used on a per-pixel basis to determine land cover; however, in this study, we test a new methodology that quantifies spatial characteristics of urban areas using a variety of spatial features observed in the imagery. Spatial features, such as Line Support Regions (LSR) and PanTex, focus on extracting structural and textural patterns of built-up areas, such as roads, buildings, and building shadows. Information derived from aggregating the descriptive statistics of these spatial features at the neighborhood level are then compared to census derived quality of life indicators including information about housing and employment. The Normalized Difference Vegetation Index (NDVI) is also computed for comparative analysis between spatial and spectral features. Results indicate that the strongest correlations are between LSR and lighting source and literacy rates, PanTex and immigration and employment variables, and NDVI and housing and slum variables. Final results from this study will be used to determine if this methodology provides a new and improved way to measure a city structure in developing cities, and differentiate between residential and commercial land use zones, as well as formal and informal housing areas.

STATUS

Student - Graduate

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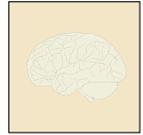
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Balancing Conservation and Development: A Case Study of Economic Efficiency in Queen Elizabeth National Park, Uganda

This study is a comprehensive analysis of Queen Elizabeth National Park's revenue, expenditures, and economic sustainability. Queen Elizabeth National Park is located in Kasese, Uganda, in the southwest of the country. It is the most visited park in Uganda, welcoming over 34,000 visitors annually and publically generating more than \$1,705,000 US per year from tourists. Three weeks were spent in the field at Queen Elizabeth National Park, and three weeks in the capital city of Kampala, Uganda to aggregate statistics, literature, and to conduct interviews with all stakeholders to analyze the park's economic efficiency. The study includes data on stakeholder incentives and interests, community relations, resource extraction, economic appraisals of wildlife, and accountability. The research ultimately concluded that while Queen Elizabeth is currently profitable, it is not yet reaching its full potential for either conservation or revenue generation, largely due to conflicting stakeholder interests and the results of miscommunication. Queen Elizabeth is unique in that it has historic, human community enclaves scattered within park boundaries, but relations between these communities and the local government authorities remain volatile. As such, the park is representative of the greater whole of Uganda's tourism industry by not playing the larger role in national economic development that it could be. Several closing recommendations to increase efficiency, productivity, and sustainable conservation within the park and to expand Queen Elizabeth National Park's impact on national development are included.

STATUS

Student - Undergraduate

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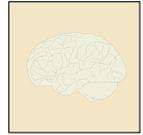
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Gender Assumptions, Public Trust, and Media Framing: The impact of media-constructed gender performance on voter trust

This research examines how conflict between voter assumptions and media framing of a political candidate's gender performance impacts voter trust in the candidate. Media shape public opinion and play a significant role in the construction of identity. Assuming that gender is a social construction rather than a fixed characteristic, the media also have a unique ability to influence voters' perception of a candidate's gender performance through framing. Additionally, existing research suggests that the Republican and the Democratic Parties are linked cognitively with ideas about gender, with people often associating the Republican Party with masculine characteristics and the Democratic Party with feminine characteristics. Building upon these conclusions, this study considers whether conflict between media representation and voter assumptions leads to lower levels of trust in a candidate whose gender is framed as conflicting with the underlying gendered assumptions of their party. In an experiment, subjects will answer a questionnaire to measure their trust in a hypothetical political candidate after reading one of six constructed news stories that are identical aside from variation of the candidate's media framed gender performance and political party. Expected conclusions suggest that voters have higher levels of trust in a political candidate when media coverage frames the candidate's gender performance as masculine, for a Republican candidate, and feminine, for a Democratic candidate. This study expands the current conversation about media and gender to look beyond a candidate's sex and consider the media's role in constructing and reinforcing a candidate's gender performance. It also provides a foundation for future study about the media's power to shape public perception of candidates and, by extension, the electoral process.

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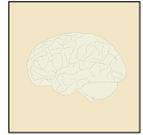
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The Impact of Linguistic Apartheid on Development in Haiti

From 1625 to 1789, France ruled French Saint-Domingue in what would later become the nation of Haiti as a result of the Haitian Revolution. Today, the remnants of Haiti's colonial past is illustrated in a language divide that can be traced back to French colonialism. Although Creole was dominant during French rule, the elites and upper class citizens promoted the use of French to distinguish themselves from citizens of lower classes. Thus, Creole became associated with "second-class citizens." Today, Creole is the only language spoken and understood by 90-95% of Haitians while the remaining population is fluent in both French and Creole. Even though Creole and French are both official languages under Haitian law, French has been historically used as Haiti's primary official language. This condition is considered a form of "linguistic apartheid" in which Haitians who only speak Creole are denied access to many public services that are conducted in French. Since the devastating earthquake in Haiti in January 2010, international agencies and governments have pledged billions of dollars to assist in post-disaster and nation building efforts. This paper will examine the impact of the language dichotomy between French and Creole on development efforts in Haiti following the 2010 earthquake, specifically in the areas of law, education, and health care. Through an analysis of Haitian history and public policy and a series of interviews with development experts and Haitian professionals, I will present potential correlations that may exist between the Haitian language dichotomy and the effectiveness of post-disaster and nation building efforts in the nation.

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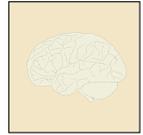
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Combating Slacktivism: Engaging social media in veteran and military support non-profit organizations

Social media has forever altered how the world communicates. Over the past decade, the sectors of commerce, government, and non-profit have begun to change their outreach strategies to include social media. Yet even as the internet has become an intricate part of society, organizations are constantly faced with a challenge to better engage their audiences. "Slacktivism" refers to the trend in which social media users perform online displays of support, but do not make any further effort to engage in action. The purpose of this study was to explore how non-profit professionals are using social media to engage constituents, volunteers, advocates, and donors. Specifically, this study focused on how non-profit organizations that support military members, veterans, and their families use social media to recruit volunteers, gain fiscal support, and promote advocacy. Findings address how non-profit communication leaders are approaching social media strategies in their efforts to uphold their organization's mission. Six non-profit organization professionals in the Maryland, Virginia, Washington, D.C. area, whose missions support active duty military, veterans, or their dependents and who also use social media in their communication strategies, participated in Qualitative interviews. Data analysis revealed themes relating to organization visibility and responsibilities, engagement through emotional content, and professional approaches to social media. Slacktivism is being combated through either the organization's strategic plan, or by an organic community of already engaged social media users, but according to this research, social media is used with the hope to better amplify the organization's work to change the lives of veterans and their families.

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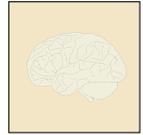
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Regulatory Gridlock: Does the ossification of rulemaking exist?

The United States government is often characterized by gridlock. While some argue that the Framers intended this gridlock, critics complain that it prevents government from making necessary policy changes. Although researchers often focus on stalemate within the legislature, gridlock can occur in the executive branch as well. For example, it regularly takes government agencies such as the Department of Transportation and Environmental Protection Agency many years to write regulations, a reality that has been dubbed the “ossification” of rulemaking. Is it in fact the case, however, that the regulatory process is ossified?

Previous research on ossification has been limited in two primary respects: (i) A focus on a broad set of rules that fails to account for the impact of controversial rules; and (ii) Lack of a measure that reflects the overall time it takes for an agency to promulgate a rule. As a result, this study uses a more appropriate dataset that focuses on economically significant rules and different parameters to better determine the total time it takes an agency to promulgate a rule.

My findings, which include the calculated averages for each agency, show that it is difficult to determine whether ossification exists in the rulemaking process because of the varied length of time. Instead, my results indicate the need to further investigate why observed rules vary significantly in the time it takes to issue them. An elongated rulemaking process has serious implications for Americans because the rules made by agencies arguably impact the structure and quality of our lives to a great degree. This implicative nature is directly exemplified by both the financial crisis in 2008 and the Gulf Oil Spill in 2010, where failures to act, or to act quickly, in the regulatory system may be at least partly to blame.

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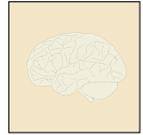
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Knowledge and consumption of organic food in Valle de Azapa, Chile: A case study

The organic market in Chile is heavily export based and includes a low internal demand for organic products. However, in other, more developed countries of North America and Europe, the internal demand for organics is high and knowledge of such products is widespread. Thus, consumers are generally aware of their right to a choice between organic and non-organic food. The global demand for organic products is expected to increase in the next 15 years. However, an increase can only exist in Chile with increased knowledge of organics. The object of this study is to determine what, if anything, the people of Valle de Azapa, Chile—one of the country's most productive agricultural regions—know about organic agriculture, and to understand their preferences of cultivation and purchase of agricultural goods to determine the difference and the choice between organic and non-organic alimentation. Data was gathered from a survey of 14 people residing in Valle de Azapa, Chile. The survey included 24 close-ended questions and 6 open-ended questions. Interviews with an organic olive farmer and a nutritionist were conducted. Participants were not given any prior information or definitions of terms that appeared in the questionnaire. All surveys and interviews conducted in this study adhered to a code of ethics to protect the anonymity of all participants. Participants in this study spanned all gender, socioeconomic and educational distinctions. Respondents either did not know what an organic product is or responded with an incorrect definition, which indicated confusion and limited understanding of organic products. Therefore, their responses with respect to their consumption and the availability of such products generally corresponded to erroneous definitions. This suggests that the majority participants do not consume organic products. No correlation between socioeconomic or educational levels and the understanding of organic products was determined in this study. The study concluded that the people of Valle de Azapa, Chile do not have adequate knowledge of or familiarity with organic products, for which the lack of information and education about such products is responsible. It is recommended that the government of Chile incorporate a program that teaches Chileans what comprises a healthy agricultural product and the toxic side effects of consuming food contaminated with synthetic pesticides to increase the demand for organics. Farmers and agricultural companies must also be held accountable by practicing organic farming techniques.

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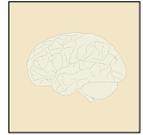
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Barriers to Communication Between Military Deployed Parents and Their Families

Our research is part of an investigation of distance communication between deployed parents and their families. Distance communication refers to communication by phone, email, social networks (e.g., Facebook), text messages, video chatting (e.g., Skype), or mail. Since deployed parents are away for long periods of time, it is important to know to what extent they communicate with their families and how they maintain contact. It is especially important to know what barriers exist to good communication so as to inform those in a position to make communication easier. We analyzed open-ended responses from a survey of deployed parents and a parallel survey of their stay at home partners. Our goal was to clarify what methods of communication worked best for their family, what worked best for their children, what were the problems that made it difficult for them to communicate, and, if no barriers existed, which method of communication they would prefer to use. The objective of our research is to enrich our interpretation of responses to structured questions about family communication. For our analysis we used two methods for reviewing the open-ended questions asked: 1. We read the responses of 163 deployed parents and 281 of their partners and categorized their responses in terms of communication barriers (e.g., time difference, cost, privacy, age of children, and amount of time given to communicate). 2. We used Nvivo to count the frequency of key terms selected based on our prior reading of the survey questions and answers. The previous analysis of the structured questions told us about the different modalities of communication, communication satisfaction, and frequency of communication. Our analysis of the open-ended questions provides further insight into the underlying reasons for these findings and shows that different people use the same methods for different reasons.

STATUS

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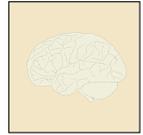
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

The Role of the Left Frontal Cortex in Phonological Selection During Sentence Production

An important aspect of language production is the selection and sequencing of phonological representations; the mental representations of sounds that make up a word. Earlier evidence for the involvement of the left frontal cortex (LFC) in selection and phonological processing motivated us to examine the function of this cortical region in phonological selection. The results from this fMRI experiment showed differences in activation during sentence production involving phonologically overlapping and non-overlapping words; this means when the initial sounds were similar (e.g. "prince" and "priest") or different (e.g. "prince" and "surfer"). The results from this experiment agree with previous neurolinguistic evidence that suggests a role for the posterior LFC in phonological selection. There was no effect observed in the anterior LFC. These results support the involvement of LFC in sentence production and provide a technical explanation as to why damage to the posterior LFC might disrupt sentence production in aphasia.

STATUS

Student - Undergraduate

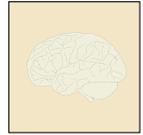
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Malathi Thothathiri

SOCIAL SCIENCES



COLUMBIAN COLLEGE OF ARTS & SCIENCES

And the dish ran away with the spoon: A study of spoon attrition rates in contemporary America

How likely would you be to take a spoon if others did little to track it down? Tsebelis and others have argued that non-observation of human behavior is often a catalyst for fiddling with assumed social contracts to accomplish private objectives (Tsebelis 1990). Many Game Theory models demonstrate this phenomenon, noting that actions can differ substantially depending on a person's perception of overall public good as well as whether that person believes he or she is being observed (Andreozzi 2004; Pradiptyo 2007). In communal spaces such as work-place kitchens, normally compliant coworkers may jump at subconsciously overbearing incentives to moonlight as defectors from the common good. We model this behavior using spoons. We placed 24 spoons in each of 5 kitchens in the MPA building on GW campus and tracked the attrition rate each week. Halfway through the study we placed signs in two of the kitchens asking for the return of missing spoons. Initial results show swift spoon attrition that was only marginally mitigated by the signs. Although results may do little to waylay endogeneity concerns, this novel affirmation of seemingly defunct communal interactions supports the theories discussed above.

STATUS

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ELLIOTT SCHOOL OF INTERNATIONAL AFFAIRS

Commercial Bank Profitability in the Oil and Non-Oil Economies of the Middle East

In my thesis, I would like to explore whether the size, profitability of oil sectors of various Middle Eastern and their respective economic dependence on the commodity affect, in a positive way, the profitability of commercial, Islamic, and investment banks in the MENA countries. Presumably, energy dependence should have both the impact of increasing bank liquidity and providing a low-tax environment that is favorable for trade and finance. Specifically, I would like to examine the independent factor - size and profitability of the oil sector in the economies of various Middle Eastern countries, some of which are oil-producing countries, and its subsequent effect on the dependent factor in my study, bank performance as measured by ROA (profits/total assets) BTP/TA, and ROE.

As oil forms a large part of external and government income in MENA, I would expect that the oil index assigned to each country (on the basis of absolute production capacity, exports and percentage of economy which the oil sector comprises) to have a positive relationship with banking profitability within each of the countries. I believe that energy endowments tend to spur foreign direct investment that would tend to inhibit liquidity in non-oil producing economies and work to accelerate performance indicators in the oil countries. This would primarily concentrate on the period from 2000-2014 in nineteen Middle Eastern countries in three classes: members of the top 25-oil producing states in the world, semi-oil economies (countries with less substantial, though small, amounts of oil) and non-oil economies (economies with little to no oil reserves). There may also be implications in terms of the effect which oil reliance has in terms of state-managed versus private banks, which would be a discussion in terms of oil-producing economies and their respective banking profitability.

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STATUS

Student - Undergraduate

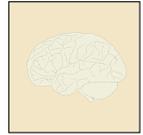
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Elizabeth Whiting

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SOCIAL SCIENCES



COLUMBIAN COLLEGE OF ARTS & SCIENCES

How to Successfully Integrate Females into Combat Roles in the U.S. Military

As an institution where feedback might not always be encouraged, the military presents researchers an opportunity to learn first-hand what soldiers, both male and female, feel are the most prevalent and significant obstacles to females' successful integration into combat roles. The research proposes a survey and in-depth interviews with soldiers of varying rank and branch of U.S. military to observe what the soldiers themselves believe to be the main challenges with respect to females serving in infantry or special-ops. The survey and interviews specifically focus on (1) physical training, (2) culture of the military (masculinization of female soldiers and leaders' implicit and explicit values), and (3) branch of the military as they might correlate with (1) a soldier's perception of safety, (2) unit cohesion, (3) perception of "right" to be in a combat unit, and (4) his/her satisfaction with military experience.

STATUS

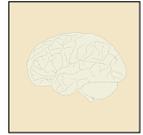
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Nils Olsen



COLUMBIAN COLLEGE OF ARTS & SCIENCES

Improving Real-Time Employment Estimates: A State-Space Signal Extraction Approach

The need for accurate real-time measures of economic indicators is crucial to understanding the broader state of the macroeconomy. Payroll employment is a salient indicator of the health of an economy, guiding decisions in both the private and public sectors. Studies have shown that payroll employment data that are initially released by the U.S. Bureau of Labor Statistics (BLS) are not accurate and require significant revisions. The BLS releases other measures of employment based on different sample sizes and methodologies that do not undergo the same revision process as payroll employment. This paper proposes a signal-extraction forecasting model that estimates the revised value of payroll employment. This is similar to a framework proposed by Aruoba et al (2013) for GDP. The model proposed in this paper successfully produces a value of payroll employment that is closer to revised figure and is easy for policymakers and market observers to apply.

STATUS

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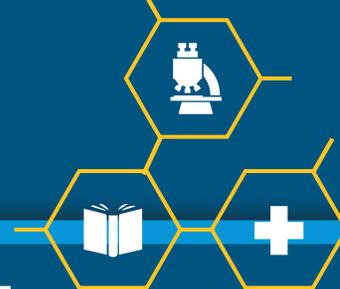
GW RESEARCH DAYS

— WEDNESDAY, APRIL 1, 2015

HEALTH & MEDICINE RESEARCH DAY

THE GEORGE WASHINGTON UNIVERSITY

WASHINGTON, DC



GW RESEARCH DAYS

2015

HEALTH & MEDICINE RESEARCH DAY

WEDNESDAY, APRIL 1, 2015

MARVIN CENTER

800 21ST STREET, NW, 3RD FLOOR

8:00-9:00 a.m. **Posters Setup**
(Grand and Continental Ballrooms)

LISNER AUDITORIUM

730 21ST STREET, NW

8:00-9:00 a.m. **Registration and Breakfast**

9:00-9:05 a.m. **Welcome & Introduction of Keynote Address**

Jeffrey S. Akman, MD
Vice President for Health Affairs and Dean,
School of Medicine and Health Sciences

9:10-10:00 a.m. **Keynote Address**

Philip E. Bourne, PhD
Associate Director for Data Science
National Institutes of Health
"Biomedicine in the Digital Era,
An NIH Perspective"

10:00-10:05 a.m. **Introduction of Keynote Address**

Lynn R. Goldman, MD, MS, MPH
Michael and Lori Milken Dean
Milken Institute School of Public Health
Professor of Environmental and
Occupational Health

10:05-10:55 a.m. **Keynote Address**

Julie Segre, PhD
Senior Investigator
National Human Genome Research Institute,
NIH Chief, Translational and Functional
Genomics Branch Head, Microbial
Genomics Section
"Tracking Hospital Transmissions of
Antibiotic-Resistant Bacteria in the
Genomic Era"

10:55-11:15 a.m. **Coffee break**

11:15 a.m.-12:00 p.m. **Panel Discussion: "Immunology and Big Data in Health and Medicine"**

Moderator: Tim McCaffrey, PhD
Professor of Medicine and Microbiology,
Immunology, and Tropical Medicine, Director,
Division of Genomic Medicine, School of
Medicine and Health Sciences

Philip E. Bourne, PhD
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Eric Hoffman, PhD
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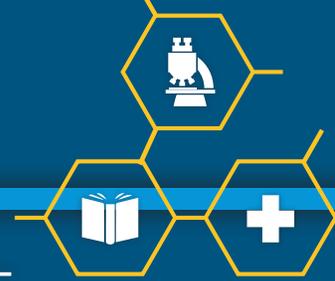
MARVIN CENTER

800 21ST STREET, NW , 3RD FLOOR

12:30-2:00 p.m. **Distribution of Box Lunches**
(MC 309)

12:30-3:00 p.m. **Poster Presentations and Judging**
(Grand and Continental Ballrooms)

3:00-4:30 p.m. **Award Ceremony and Oral Presentations**
(includes 10 min presentations by winners of oral
competition awards from each School) (MC 309)



GW RESEARCH DAYS

APRIL 1, 2015

3:00–4:30 p.m.

AWARD CEREMONY

SCHOOL OF MEDICINE AND HEALTH SCIENCES, DONALD H. GLEW PRIZE

Moderator: **Robert H. Miller, PhD**
*Senior Associate Dean for Research,
School of Medicine and Health
Sciences*

Zachary Kendrick:
*"Type 2 diabetes associated beta-
adrenergic receptor polymorphisms
are independently associated with BMI
and physical activity in college-age
populations"*

INSTITUTE FOR BIOMEDICAL SCIENCES

Moderator: **Linda Werling, PhD**
*Associate Dean for Graduate Studies,
School of Medicine and Health
Sciences; Director, Institute for
Biomedical Sciences*

Marine Bouyssi-Kobar:
*"Cerebral Perfusion and Brain Injury in
the Very Preterm Infant"*

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Cassandra A. Phillips:
*"Fast Food: a Source of Exposure
to Phthalates and Bisphenol A in a
Nationally Representative Sample"*

SCHOOL OF NURSING

Moderator: **Dr. Joyce Pulcini**
*Professor, Director, Community and
Global Initiatives, School of Nursing*

Elzbieta Kmiecik, MSA, RN:
*"Impact of Implementing the Geriatric
Resource Nurse Model on Fall and
Hospital Acquired Pressure Ulcer Rates,
and Length of Stay"*

RESIDENT ORAL PRESENTATION

Moderator: **Robert H. Miller, PhD**

Ivy Haskins, MD (Clinical Science):
*"VTE (Venous Thromboembolism) and
Bariatric Surgery"*

GRADUATE MEDICAL EDUCATION RESEARCH COMPETITION WINNERS

Case Report:
Niharika Tipirneni, MD
*"Swyer-James-MacCloed and Post-
Pneumonectomy Syndromes"*

Basic Science:
Raul Sebastian Laines, MD
*"Gene therapy–Stem Cell Derived
Angiogenic Cell Infusion for Wound
Healing"*

Quality Improvement:
Johnny Mai, MD
*"Cause Analysis of Risk Factors
Associated With Burn During Monopolar
Cautery Assisted Tonsillectomy"*

2015 DORIS DEFORD SPECK AND GEORGE SPECK, MD ENDOWED PRIZE

Presenter: **Robert H. Miller, PhD**

Andrew D. Kerkhoff:
*"The predictive value of anemia for
tuberculosis among HIV-infected patients
requiring hospitalization in Cape Town,
South Africa"*

2014 ELAINE H. SNYDER CANCER RESEARCH AWARD

Presenter: **Robert H. Miller, PhD**

Yang Liu, PhD
*Bosworth Chair for Cancer Biology;
Director, Center for Cancer and Immunology
Research*

2015 DISTINGUISHED RESEARCHER AWARD

Presenter: **Robert H. Miller, PhD**

Anthony-Samuel LaMantia, PhD
*Professor, Pharmacology and Physiology;
Director, GW Institute for Neuroscience*

POSTER AWARD WINNERS ANNOUNCED

School of Medicine and Health Sciences
Institute for Biomedical Sciences
Biomedical Engineering
Milken Institute School of Public Health



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BASIC BIOMEDICAL SCIENCES



COLUMBIAN COLLEGE OF ARTS & SCIENCES

Scaffold assembly based on genome rearrangement analysis

Advances in DNA sequencing technology over the past decade have increased the volume of raw sequenced genomic data available for further assembly and analysis. While there exist many algorithms for assembly of sequenced genomic material, they often experience difficulties in constructing complete genomic sequences. Instead, they produce long genomic subsequences (scaffolds), which then become a subject to scaffold assembly aimed at reconstruction of their order along genome chromosomes. The balance between reliability and cost for scaffold assembly is not there just yet, which inspires one to seek for new approaches to address this problem.

We present a new method for scaffold assembly based on the analysis of gene orders and genome rearrangements in multiple related genomes (some or even all of which may be fragmented). Evaluation of the proposed method on artificially fragmented mammalian genomes demonstrates its high reliability. We also apply our method for incomplete anophelinae genomes, which expose high fragmentation, and further validate the assembly results with referenced-based scaffolding. While the two methods demonstrate consistent results, the proposed method is able to identify more assembly points than the reference-based scaffolding.

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BASIC BIOMEDICAL SCIENCES



SCHOOL OF MEDICINE & HEALTH SCIENCES

Development of a Method Quantifying Fibrosis in Wedge Liver Biopsies with Non-Alcoholic Fatty Liver Disease (NAFLD)

Non-alcoholic Fatty Liver Disease (NAFLD) is the most common chronic liver disease in the U.S. with prevalence of near 90% in patients with Morbid Obesity (MO), complicated by Non-Alcoholic Steatohepatitis (NASH) with progressive fibrosis and cirrhosis in 35%. Currently, liver biopsy fibrosis is detected by pathologist-interpretation of Masson Trichrome (MT) stain to determine stage of disease (0= no fibrosis, 1= pericentral or portal fibrosis, 2= pericentral and portal fibrosis, 3= bridging fibrosis, 4= cirrhosis). More sensitive and quantitative methods for specific measurement of collagen using Sirius Red (SR) stain are described for liver core biopsies in hepatitis, but the method is not standardized and it has not been applied to wedge biopsies from patients with NAFLD, the subject of this report.

METHOD DESCRIPTION:

17 wedge liver biopsies from patients with NAFLD (mean BMI 46, mean age 47) were categorized into stage 0 (n=5), stage 1-2 (n=4), stage 3 (n=4) and stage 4 (n=4) using pathologist-interpretation of MT. Additional tissue sections were stained with SR and scanned into digital slides using Aperio Scanscope (20X). A grid (ImageScope) was applied to the digital slides at 0.3X to demarcate fields of 0.9 mm². A randomized, standardized approach selected fields for image capture at 10X, avoiding capsule, septal areas and artifacts. Collagen proportional area for SR (CPAs) was measured by an average of 10 image fields using image analysis (Image J).

RESULTS:

CPAs showed a statistically significant increase with MT stage of disease on biopsy (0= mean 2.44 ± 1.33 , 1-2= mean 3.27 ± 1.44 , 3= mean 4.02 ± 3.75 , 4= mean 8.15 ± 5.33), $p < .001$. Spearman correlation coefficient of CPAs and MT was 0.5. Results of CPAs were significant between no fibrosis and any fibrosis, $p < .001$ and between stage 4 cirrhosis and lesser stages of fibrosis (1-3), $p < .001$. One slide from a stage 3 biopsy was analyzed to determine the variability of CPAs using 9 mm² (10 image fields) vs 36 mm² of tissue, showing a 9% coefficient of variation, suggesting 10 image fields were adequate to determine CPAs.

DISCUSSION/ CONCLUSIONS:

Results using the standardized method described here for measuring CPAs in NAFLD wedge liver biopsies shows promise as a more objective and quantitative measure of fibrosis than MT, with potential for greater sensitivity and precision in detection that might be advantageous in determinations of disease progression and in studies of fibrogenesis in NAFLD and NASH.

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BASIC BIOMEDICAL SCIENCES



INSTITUTE FOR BIOMEDICAL SCIENCES

Single-locus resolution of transposable element expression using RNA-seq

BACKGROUND:

Transposable elements constitute nearly 50% of the human genome and are known to be important in genome maintenance and evolution. However, less is known about the genome-wide transcriptional activity of these elements and their role in disease. Recent innovations in next-generation RNA sequencing (RNA-seq) promise to facilitate high-throughput characterization of transposable element expression, although these possibilities are hindered by the highly repetitive nature of transposable elements. Repetitive sequences pose a challenge for short read mapping tools, and existing approaches for estimating transcript abundance are inaccurate when repeat content is high.

RESULTS:

We present a novel approach for accurately quantifying the abundance of transposable element transcripts using RNA-seq. Our method accounts for the highly repetitive sequence structure of transposable elements using a previously described Bayesian read reassignment algorithm. We implement this method, originally intended for metagenomic strain identification, within the context of RNA-seq gene expression experiments. We evaluate the performance of our approach compared to existing methods using simulated data, and apply these methods to RNA-seq data from HIV-1 infected human CD4+ T cells.

CONCLUSIONS:

Our results show that our approach can accurately quantify transposable element transcript abundance at the resolution of a single genomic locus. We find that our approach has better sensitivity compared to the existing methods tested. We report the detection of many transposable element transcripts that are differentially expressed in HIV-1 infected cells compared to mock infected cells, including transcripts originating from HERV-K HML-2 and HML-6 proviruses.

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BASIC BIOMEDICAL SCIENCES



INSTITUTE FOR BIOMEDICAL SCIENCES

Understanding the mechanism of amylin mediated cytotoxicity in the pancreatic β cells

Type 2 diabetes mellitus (T2DM) is a multifactorial metabolic disorder, characterized by insufficient insulin secretion, insulin resistance and accumulation of insoluble amyloid aggregates, primarily composed of pancreatic hormone amylin. Amylin or Islet amyloid polypeptide (IAPP) is a 37 amino acid hormone, co-secreted with insulin from the pancreatic β cells. In contrast to the human IAPP, rat IAPP is non-amyloidogenic due to the presence of three proline residues in its amino acid sequence and was used as a negative control to human amylin aggregation in our studies. Both extracellular and intracellular human IAPP aggregates have been implicated as a causal factor for the pancreatic β cell loss during T2DM. Amylin aggregation in the pancreas is slow, progressive event that ultimately lead to distraction of the islet β cells and insulin deficiency. However these conditions are difficult to recapitulate in the experimental system. Hence the development of robust cellular model system that can mimic amylin aggregation and cytotoxicity in situ and can also offer easy experimental manipulations was the goal of this study. To achieve this goal, we used lenti virus mediated gene delivery strategy to overexpress FLAG tagged, prepro cytotoxic human IAPP and non-toxic rat IAPP, in two rat pancreatic insulinoma β cell lines: the RIN-m5f and the INS-832/13. Western blot analyses and amylin specific ELISA confirmed the overexpression of the human and rat IAPP in both the RINm5f and the INS 832/13 cell lines. Light microscopy revealed 60% and 20% transduction efficacy in the RIN-m5f and INS-832/13 cells respectively, using human IAPP lenti virus. Confocal microscopy confirmed the biochemical and light microscopy data by showing diffused cytoplasmic and perinuclear expression patterns of the human IAPP in both RIN-m5f and INS-832/13 cells. Contrary to our expectations, expression of pro human IAPP did not induce significant cytotoxicity in the RIN-m5f cells, indicating existence of an unidentified protective mechanism which protects this cell from amylin insult. Immunoprecipitation (IP) followed by western blot confirmed detectable human IAPP accumulation after 48 hours of transduction in both cell lines. Ability to pool down human amylin by IP together with mass spectrometric studies allows us to detect the molecular composition of the human amylin-protein complex in these cells. This in turn will help us to identify the regulatory proteins involved in the amylin turnover and toxicity in pancreatic β cells, which is important for understanding the etiology of T2DM and its prevention.

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BASIC BIOMEDICAL SCIENCES



INSTITUTE FOR BIOMEDICAL SCIENCES

Commonly affected canonical pathways in dystrophin deficiency: Cross species comparison

OBJECTIVE:

To identify commonly shared pathways in three different models of DMD (human, mouse, and dog)

BACKGROUND:

Animal models are generally used to understand the disease pathogenesis as well as to assess therapeutic efficacy in preclinical studies. Predictive power of animal models often depends on the commonly shared molecular pathways between patients and animal models. Systematic comparison of affected pathways between DMD patients and animal models (GRMD Dog and Mdx mouse) of dystrophin deficiency would significantly help to predict human outcomes.

DESIGN/METHODS:

We performed cross species comparison of the skeletal muscle mRNA profiles in presymptomatic and symptomatic phases of the disease in DMD children, GRMD dogs and mdx mice.

RESULTS:

Bioinformatic analysis revealed alteration in mitochondrial, protein ubiquitination, nitric oxide, insulin, PKA and ILK signaling during the presymptomatic phase of the disease. Pathways that are shared in the symptomatic phases of the disease include immunological (e.g., cytokine, complement integrin), vascular (E.g., VEGF, Ephrin, Rho GTPase) and fibrotic pathways.

CONCLUSIONS:

We are in the process of identifying drug targets and candidate drugs that modulate these pathways. These results suggest that dystrophin deficiency leads to alteration in several pathways in all three species. Understanding the contribution of these pathways would help to design future therapeutics for DMD.

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BASIC BIOMEDICAL SCIENCES



INSTITUTE FOR BIOMEDICAL SCIENCES

Dystrophin expression is variable in mdx mice after short-term morpholino treatment

BACKGROUND:

Currently, exon-skipping using antisense oligonucleotides, is one of the most promising therapies for Duchenne muscular dystrophy (DMD). Exon-skipping using phosphorodiamidate morpholino oligomers (PMO) efficiently restored a shorter, but functional dystrophin protein in both animal models and DMD boys. However, restoration of de novo dystrophin did not correlate with muscle function improvement in the recent Phase III clinical trials. These findings raised concern whether dystrophin can be used as a surrogate biomarker to determine efficacy of exon-skipping treatment.

OBJECTIVE:

To define the expression pattern of de novo dystrophin in various muscle groups after exon skipping in a murine (mdx) model of DMD. In addition, to compare three quantification methodologies to assess de novo dystrophin protein after exon-skipping treatment. Here, we hypothesize that the previously observed lack of correlation between dystrophin rescue and muscle function after exon skipping is due to the inherent variability of dystrophin expression in different muscle groups as well as the inheritably different nature of methods to detect de novo dystrophin production.

DESIGN/METHODS:

After a short-term (1 month) single high dose (800 mg/kg) intravenous PMO treatment, muscle samples from mdx mice (n=6) and saline control wild type mice (n=2) were processed for dystrophin quantification by immunohistochemistry, western-blotting and mass spectrometry.

RESULTS:

The data presented here shows a single administration of a high dose of PMO results in a measurable amount of dystrophin protein, however expression is variable between all muscles of individual animals as well as between the same muscles of different mice. There are no patterns of which muscles preferentially are "hot" with expression of dystrophin adding to the complexity of the treatment. In addition, results from the three quantification methods showed highest Spearman correlation between IF and WB at 0.4997 and lowest correlation between IF and MS at 0.3281.

CONCLUSIONS:

These findings provide further evidence for clinical trials demonstrating that after PMO treatment dystrophin restoration is not homogeneous or preferential to any specific muscle. Correlation analysis between the dystrophin detection methods highlight that complementary methods (preferably MS and WB) are needed for more realistic and robust detection/quantification of de novo dystrophin after exon-skipping.

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BASIC BIOMEDICAL SCIENCES



SCHOOL OF MEDICINE & HEALTH SCIENCES

Rescue of the temperature-sensitive, autosomal-recessive mutation R298S in the sodium-bicarbonate cotransporter NBCe1-A characterized by a weakened dimer and abnormal aggregation

BACKGROUND:

Band keratopathy, an ocular disease that is characterized by hypercalcemia and opaque bands across the cornea, has been associated with kidney disease. Type-II renal tubular acidosis (RTA), a condition in which the kidneys fail to recover bicarbonate (HCO_3^-) in the proximal tubule of the nephron, results in HCO_3^- wastage in the urine and low blood pH. The development of these diseases is associated with autosomal-recessive mutations in the Na⁺-coupled HCO_3^- cotransporter NBCe1-A located at the basolateral membranes of either cell type.

METHODS:

We provide insight into the devastating R298S mutation found in type-II RTA-afflicted individuals using confocal-microscopy imaging of fluorescently-tagged NBCe1-A and NBCe1-A-R298S molecules expressed in human corneal endothelial and proximal tubule cells and from in-depth biophysical studies of their cytoplasmic N-terminal domains (Nt and Nt-R298S), including Nt crystal structure, melting-temperature, and homodimer dissociation constant (KD) analyses.

RESULTS:

We illuminate and rescue trafficking defects of the R298S mutation of NBCe1-A. The KD for Nt monomer-dimer equilibrium is established. The KD for Nt-R298S is significantly higher, but immeasurable due to environmental factors (pH, temperature, concentration) that result in dimer instability leading to precipitation. The crystal structure of Nt-dimer shows that R298 is part of a putative substrate conduit and resides near the dimer interface held together by hydrogen-bond networks.

CONCLUSIONS:

The R298S is a temperature-sensitive mutation in Nt that results in instability of the colloidal system leading to abnormal aggregation.

GENERAL SIGNIFICANCE:

Our findings provide new perspectives to the aberrant mechanism of certain ocular pathologies and type-II RTA associated with the R298S mutation.

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BASIC BIOMEDICAL SCIENCES



SCHOOL OF MEDICINE & HEALTH SCIENCES

COL5A1 variant is associated with body composition and physical activity in males

INTRODUCTION:

Studies have shown that the desire to exercise may be modulated genetically, in addition to environmentally. Certain genetic variants have been associated with a decreased level of physical activity and increased levels of muscle damage after exercise. Muscle's response to exercise likely plays a large role in an individual's desire to exercise and proper collagen function is vital for muscle development and usage. COL5A1 and COL6A3 encode collagen V and VI respectively, which are vital for proper extracellular matrix structure in skeletal muscle. We hypothesize that this decrease in muscle health may discourage physical activity, thus resulting in a more sedentary lifestyle and associated health complications such as less muscle mass and higher fat mass. We chose to look at variants in two genes that play a role in extracellular matrix support, COL5A1 and COL6A3 (variants rs227069 and rs12722, respectively). The purpose of this study is to investigate the association between these genes, voluntary physical activity and body composition.

METHODS:

We genotyped 116 healthy Caucasian individuals from the Bone and Muscle Cohort. Participants were assessed for various morphometric measurements. Physical activity level was measured using the International Physical Activity Questionnaire. Genotyping was performed using a taqman allelic discrimination assay. These data were statistically analyzed to compare genotypes with apparent phenotype.

SIGNIFICANT RESULTS:

The COL5A1 variant (rs12722) was associated with lean mass ($p=0.0025$), body fat percentage ($p=0.0274$) and physical activity ($p=0.0007$) in males. The COL6A3 variant (rs2270669) was not found to be associated significantly with physical activity or any morphometric measurements from the cohort. Neither the COL5A1 variant nor the COL6A3 variant was associated significantly with bone mineral density and neither variant was statistically significant in females.

DISCUSSION:

To our knowledge, this is the first study that suggests a link between COL5A1 and body composition and physical activity in males. We found that the rs12722 variant is strongly correlated with physical activity in males ($p=0.0007$). Coincidentally, we also found that COL5A1 has an impact on lean body mass and fat percentage. It is possible that those with a mutation in this gene may suffer from increased muscle discomfort after exercise, thus conditioning them to exercise less. This muscle damage is characterized by temporary soreness and decrease in strength, which may in turn discourage continued physical activity. This lack of exercise may lead to a lower lean body mass and higher body fat percentage.

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A short nucleotide sequence that enhances the growth kinetics and density of recombinant bacterial cells in vitro

A short, 30 nucleotide DNA sequence was identified that when cloned into recombinant gram-negative bacteria of different genera and species (*Escherichia coli* and *Salmonella typhimurium*) confers significantly ($p < 0.05$) enhanced growth. For example, when the sequence is cloned into a high-copy plasmid (pBluskript - pBS) and transformed into various *E. coli* cloning strains (DH5-alpha and HB101), up to 1 log higher growth within 3 hours and 2 logs more growth within 4 hours is observed at both a pH of 7.0 and pH of 5.0 compared to the same recombinant bacterial strains containing the empty pBS vector. When cloned into a low-copy vector (pACYC177), enhanced growth of *E. coli* by at least 2 logs after 4 hours of incubation at 37°C was observed. Moreover, introduction of the 30-nucleotide sequence into the pET21 protein expression vector increased the production of β -galactosidase from the lacZ gene in *E. coli* when compared with a recombinant *E. coli* transformed with pET21 containing the lacZ gene but lacking the 30-nucleotide insertion. The increased production of β -galactosidase is likely due to the enhanced growth of the recombinant *E. coli* containing the short sequence. A similar effect was observed when the sequence was introduced into several species of the Gram-positive *Mycobacterium* genus, including *M. bovis*, *M. tuberculosis* and *M. smegmatis*. For example, recombinant *M. tuberculosis* transformed with a high copy number plasmid containing the sequence grew to 2 log higher density after 22 hours incubation at 35°C compared to wildtype. These data demonstrate that incorporation of the 30-nucleotide sequence into cloning and expression vectors may shorten the time necessary to perform various molecular manipulations (e.g., gene cloning), and could potentially be used as a biotechnology tool in commercial applications, such as the production of recombinant proteins and vaccines.

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Regulation of cyclic AMP synthesis by anthrax edema factor by p21-activated protein kinase 1

PAK1, p21-activated protein kinase 1, plays an important role in cell signaling, motility, morphology, and differentiation. Our goal was to investigate the role of PAK1 in the regulation of cyclic AMP synthesis. Anthrax edema factor (EF), is a bacterial adenylate cyclase toxin responsible for disruption of cellular homeostasis by increasing intracellular cyclic AMP levels in a calcium-independent but calmodulin-dependent manner. To identify the role of PAK1, EF was treated with various combinations of calcium, calmodulin, and PAK1 in vitro at 30°C for 10 min. Synthesis of cyclic AMP from ATP by EF was then assayed in triplicate using high performance liquid chromatography. Peaks on chromatogram were processed by the integration software to calculate the levels of ATP and cyclic AMP. Results showed a statistically significant increase in cyclic AMP synthesis by EF in the presence of PAK1 and average stimulation was around 20%. Inhibitors of PAK1 protein kinase activity had no effect on stimulation suggesting that PAK1 acts as a scaffold that enhances activity of EF-calmodulin complex in the presence of calcium. Intact COS-7 cells were infected with a mixture of protective antigen and EF and treated with various pharmacological inhibitors or activators of PAK1. Data indicate that EF-dependent synthesis of cyclic AMP is suppressed in cells by compounds that are known to affect scaffolding function of PAK1. Thus, PAK1 is an important regulator of cyclic AMP synthesis and a potential therapeutic target in the treatment of exposure to anthrax pathogen.

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What influences Postoperative Spine infections with MRSA the most?

INTRODUCTION:

Postoperative spine infection is a well-known complication. The purpose of this study was to determine the efficacy of Vancomycin powder and Intravenous (IV) prophylactic Vancomycin in treatment of spine infection with Methicillin-resistant Staphylococcus aureus (MRSA) in presence of different metals.

METHODS:

54 rabbits underwent a posterior L5-L6 approach. 12 rabbits had no metal implants(4 sham, 4 MRSA and 4 MRSA +Vanco). 42 rabbits had 4 cm wire of different metals was placed around the L5 and L6 spinous processes. 6 rabbits each with MRSA and Stainless Steel, Titanium or COCr. 6 rabbits each with MRSA + Vanco with Stainless Steel, Titanium or COCr . 6 rabbits with MRSA, Stainless Steel and IV Vanco. The implant was inoculated with 100 μ L MRSA containing 106 colonies. 40 mg of Powder Vancomycin was placed in the wound prior to closure. The dose of IV Vancomycin was 15mg/kg. The metal implants and the infected tissue was analyzed separately for infection by calculating Colony forming units by plating on Oxacillin or blood agar plates. Proportions of infected rabbits were compared using chi-square tests, and compared between groups using Cochran-Mantel-Haenzsel tests. CFU counts for the tissue and implant were compared using Wilcoxon rank sum tests.

RESULTS:

The proportions of rabbits with infection were significantly higher in rabbits with no Vancomycin compared to powder Vancomycin ($p < 0.001$ for tissue-ox, tissue-blood, implant-ox, and implant-blood). Cobalt chrome (CoCr) had higher rates of residual infection with Vancomycin powder than Titanium (Ti) and Stainless Steel (SS) ($p = 0.040$). In rabbits with SS, the proportions of infection rabbits differed significantly among Vancomycin types (none, powdered, or IV). Rabbits treated with powdered Vancomycin powder had with a significantly lower proportion of infection ($p = 0.015$ for tissue-ox). Rabbits with SS implants treated with Vancomycin powder had a lower infection rate than those treated with IV Vancomycin, although this difference was not statistically significant ($p=0.557$).

CONCLUSION:

Vancomycin powder is successful in eradicating infection with MRSA without metal and reducing it significantly in the presence of metal. CoCr had more residual infection in the tissues when compared to SS and Ti. SS had similar residual infection as Ti. The Vancomycin powder appears to be more effective in eliminating the infection than prophylactic IV Vancomycin.

CLINICAL RELEVANCE:

This rabbit model shows that Vancomycin powder is effective in treating MRSA infection. It is an excellent tool to prevent postoperative MRSA infection following surgery.

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Mitochondrial regulation of F-actin facilitates repair of injured muscle cell membrane

Production of mechanical force by skeletal muscle contraction is the basis for animal motility. At the cellular level, force generation requires energy produced by mitochondria, which facilitates activity of actin and myosin resulting in muscle contraction. The mechanical strain during this force generation can result in injury to the cell membrane of skeletal muscle cells - myofibers. Unless rapidly repaired, injury to the cell membrane results in death of the myofiber. We recently identified mitochondria are required for the repair of injury to the myofiber cell membrane. However, the mechanism by which mitochondria play such a role is not understood. Here, we carried out real-time imaging of the spatial and temporal changes in mitochondria and cytoskeleton after injury to individual muscle cells. Using pharmacological inhibitors we investigated the role of mitochondrial activity and actin dynamics in the repair of injured cell membrane. We find cell membrane injury causes loss of F-actin at the site of injury. The F-actin needs to be resynthesized at the injury site for the cell membrane to repair. Functional mitochondria are necessary for actin build-up at the site of injury. Injury-triggered increase in cytoplasmic calcium is taken up by mitochondria, through the mitochondrial calcium uniporter (MCU). Inhibition of MCU or its genetic deletion causes cells to repair poorly from focal injury. Uptake of calcium by the mitochondria increases oxidative phosphorylation and production of superoxide. A block in superoxide production, but not ATP production, compromised repair of injured cells. Concordantly, increasing mitochondrial superoxide production promoted F-actin build up and improved repair of the injured membrane. These data demonstrate calcium-triggered superoxide production by the mitochondria regulates repair of injured plasma membrane. Thus, our study identifies new roles of mitochondria and actin in skeletal muscle physiology.

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Ensemble Models of Nucleosome Arrays Constrained by Small-Angle X-ray Scattering

Chromatin conformation and dynamics remains unsolved despite the fundamental role of the chromatin in genetic functions such as transcription, replication, and repair. At the molecular level, chromatin can be viewed as a linear array of nucleosomes, each consisting of 147 base pairs (bp) of dsDNA wrapped around a protein core and connected by 10 to 90 bp of linker dsDNA. Using small-angle x-ray scattering (SAXS), we have investigated how the conformations of model nucleosome arrays in solution are modulated by ionic condition as well as the effect of linker histone proteins. To facilitate ensemble modeling of these SAXS measurements, we have developed a DNA Monte Carlo move module allowing the generation of tens of thousands of all-atom nucleosome array structures. Such ensembles, filtered by SAXS measurements, provide valuable solution structure information of short chromatin fragments.

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Barcoded Molecular Tags to Identify Genetic Determinants of E. coli Colonization Efficiency in Mice

BACKGROUND:

E. coli colonization of the GI tract is critical for the development of a normal gut microbiome; as the predominant facultative anaerobe in the human GI tract, E. coli reduces oxygen levels for the anaerobes which comprise >90% of gut microbiota. However, the mechanisms that govern E. coli colonization remain unclear, and studies of colonization in physiologic settings have been hampered due to colonization resistance, which necessitates the use of antibiotics or gnotobiotic mice.

METHODS:

We developed a new technology, In Vivo Gastrointestinal Evaluation Technology (IGET), which tags and tracks live bacteria in an intact mouse GI tract. IGET uses a set of plasmids, each with a unique DNA barcode and the thyA gene to enable plasmid stabilization in thyA⁻ bacteria without antibiotic selection. We transformed each of 5 E. coli strains (MG1655, CLRN2, DH5 α , JC1, JC3) with a unique IGET plasmid, and inoculated them into the GI tracts of mice. Colonization levels were tracked for 10 weeks by running qPCR on fecal DNA. We assayed each strain for growth rates and immunogenicity, and sequenced each genome to identify which genetic factors improved E. coli colonization in the mouse GI tract.

RESULTS:

IGET tracking showed JC3 stably colonizing the mouse GI tract at levels much greater (>10⁸ plasmids/g feces) than observed in the other four strains. MG1655 also successfully colonized the GI tract, but at lower levels (~10⁵ plasmids/g feces) than JC3. All other strains failed to stably colonize the GI tract. Colonization ability was unrelated to neither intrinsic growth rates nor immunogenicity. Genomic analysis revealed that JC3 contains genes to use additional carbon sources, and lacks genes for flagella synthesis.

CONCLUSIONS:

This study expands upon previous studies, which found that the ability to use additional carbon sources and the absence of flagella improve colonization. These experiments also demonstrate that IGET can distinguish between good and bad colonizers over long timeframes in individual animals, and thus represents a new technology for evaluating what factors promote or inhibit colonization.

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Soluble CD14 associates with overall mortality, cardiovascular disease and progression of chronic kidney disease

CD14 plays a key role in the innate immunity as pattern-recognition receptor of endotoxin. Recently, plasma soluble CD14 (sCD14) has been associated with overall mortality in hemodialysis patients. The influence of renal function on plasma sCD14, however, is unknown, as well as its relationship with adverse outcomes in CKD. We performed a prospective study in 499 patients with CKD stage 1-5 and measured plasma levels of sCD14 and endotoxin. There was a significant correlation between plasma sCD14 and renal function (ρ -0.34, $P < 0.0001$) with higher levels of sCD14 observed in patients with lower eGFR. Plasma sCD14 was predictive of overall mortality, even after adjustment for renal function, Framingham risk factors, markers of mineral bone metabolism, as well as nutritional and inflammatory parameters (HR per SD increase of 1.899, P 0.0006). After adjustment for the same risk factors, plasma sCD14 was also a borderline significant predictor of cardiovascular disease (HR 1.299, P 0.05). Although plasma sCD14 associated with CKD progression in fully adjusted models (HR 1.238, P 0.04), significance was lost in a subgroup with availability of 24h proteinuria (P 0.11). There was neither correlation between plasma endotoxin and sCD14 (ρ -0.06, P 0.20), nor did endotoxin independently associate with adverse outcome during follow-up. Thus, plasma sCD14 is elevated in patients with more advanced CKD and associates with overall mortality, cardiovascular disease and CKD progression. The pathophysiological role of sCD14 in patients with renal dysfunction requires further investigation.

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Detection of genetically distinct subclones: a novel NGS algorithm with high spatial and genetic resolution

Despite the large number of genome data banks, reference sequences are not always the best match for high-throughput analysis. This is especially true in studies of intratumor heterogeneity where increased mutation rates are observed; the use of a reference genome can complicate the interpretation of the results. Current techniques attempt to circumvent this obstacle by applying de novo assembly algorithms, but the process is slow and often without viable results. Here, we introduce a new technique to decrease the dependency of these pipelines on reference sequences. Our clone discovery algorithm takes advantage of existing alignment data and correlates distant mutations, reported by an alignment algorithm. The algorithm makes no statistical assumption; it extracts information from the overlapping alignments in a step-wise fashion, using reference coordinates of aligned reads. Due to the randomness of noise, the algorithm can be very sensitive and identify clones of low frequency.

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miR-671-5p, a novel biomarker for predicting ADH outcome following CNB procedure

Successful breast cancer treatment relies on early and accurate pathological diagnosis. Breast cancer progression involves stepwise transition from atypical ductal hyperplasia (ADH), to ductal carcinoma in situ (DCIS) and then to invasive ductal carcinoma (IDC), although not necessarily always in this linear fashion. Core needle biopsy (CNB) is the standard technique for initial histological diagnosis for breast lesions following mammography. However, it is less reliable for differentiating between ADH and advanced lesions (DCIS and/or IDC), resulting in misdiagnosis or unnecessary additional invasive procedures. Therefore, novel molecular biomarkers are needed. miRNAs are small, single-stranded non-coding RNAs that control gene expression and therefore play an important role in cancer development and progression. Their accessibility makes miRNAs attractive in the era of personalized tumor classification and treatment. In this study, we analyzed miR-671-5p expression in patients with confirmed ADH diagnosis and advanced lesion diagnosis following CNB and surgical excision procedures. In addition, we used normal and ADH cell lines to elucidate the functional role of miR-671-5p in early breast cancer progression. Our objective was to analyze and validate miR-671-5p as a potential biomarker for differentiating ADH and advanced lesion diagnoses following the CNB. The FFPE tissue blocks were retrieved from the tissue repositories of the Armed Forces Institute of Pathology, The George Washington University Hospital and Peking University School of Oncology, Beijing Cancer Hospital & Institute with IRB approvals, and were subject to microdissection. The 21PT, representing ADH cells, and normal mammary epithelial, H16N2 from the same patients, were maintained in culture in α -MEM. Total RNA was isolated using either the RecoverAll Total Nucleic Acid Isolation kit or Trizol reagent following the manufacturer's instructions. miRNA qRT-PCR analysis was performed using Taqman miRNA Reverse Transcript Kit. The mean quantity values of the miRNA expression were normalized by U6 snRNA. Statistical analysis was performed using paired t-test. Down-regulated miR-671-5p expression was detected in 94.7% of advanced lesion (DCIS and/or IDC) cases (18/19) ($p < .05$), compared in 47.5% of ADH cases (9/19) ($p > .05$), both in comparison of their matched normal controls. To explore the role of miR-671-5p in ADH precancerous lesion, we transfected miR-671-5p into both H16N2 (normal) and 21PT (ADH) cell lines. We found that forced expression of miR-671-5p resulted in significantly decreased proliferation in both cell lines. These data suggest that miR-671-5p is a novel tumor suppressor in breast carcinogenesis, and could potentially be used as a companion prognostic tool following ADH diagnosis by CNB.

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CXCL5 and POSTN are involved in the phenoconversion of fibroblasts to myofibroblasts in Chronic Rhinosinusitis.

RATIONALE:

Chronic rhinosinusitis (CRS) is one of the most prevalent and costly diseases in children. The sustained chronic inflammation results in sinonasal epithelium remodeling, including subepithelial fibrosis, extracellular matrix (ECM) accumulation and submucosal gland hyperplasia/hypertrophy (SMGHH). SMGHH is thought to be responsible for mucus hypersecretion and disease morbidity. However, the mechanisms that lead to SMGHH are not established. Data (manuscript in preparation) has shown that a) fibroblasts isolated from CRS sinus mucosa, as well as CRS fibroblast-conditioned media, increase glandular formation and mucous hyperproduction, and b) elevated expression and secretion of myofibroblast-associated proteins occurs in CRS fibroblasts. Myofibroblasts are activated fibroblasts, which secrete excessive ECM proteins, including periostin (POSTN) that promotes glandular epithelial cell proliferation and migration in prostate tissues. CXCL5, a chemokine, promotes differentiation of prostate fibroblasts into myofibroblasts. We have previously shown that CXCL5 is markedly upregulated in pediatric CRS sinus mucosa (Wu, X. et al, 2009). Taken together, this led to our hypothesis that CXCL5 increases the activation of sinonasal fibroblasts to myofibroblasts to increase ECM expression/secretion, which in turn promotes sinonasal epithelial cell proliferation and differentiation that ultimately leads to SMGHH in CRS.

METHODS:

Tissues from 5 CRS and 5 non-CRS patients were evaluated by microscopy and immunostaining. Primary sinonasal fibroblasts from normal pediatric patients exposed to CXCL5 for 72 h were evaluated morphologically by immunostaining. mRNA expression of α SMA, COL1A1, TGF β 1 and POSTN were assessed at 2 h intervals over an 8 h exposure of primary non-CRS fibroblasts to CXCL5 by real time qRT-PCR. HNE acinar cells were exposed to POSTN in 3D acinar cultures and changes in the diameter of acini were measured with Image J (NIH) software.

RESULTS:

Dramatic fibrosis and increased myofibroblasts were observed in the basal lamina of sinus tissues from pediatric CRS patients. CXCL5 exposed fibroblasts underwent myofibroblast phenoconversion as evidenced by the increased expression of α SMA with increasing concentrations of CXCL5. mRNA analyses show that myofibroblast associated genes -- α SMA, COL1A1, TGF- β 1 and POSTN -- are significantly increased 2-6 fold above basal levels in CXCL5 exposed fibroblasts by 4 h and maintained for 8 h. Myofibroblast phenoconversion (monitored by expression of α SMA) was also observed following exposure of non-CRS fibroblasts to POSTN, suggesting a forward feedback loop whereby POSTN, which is secreted by sinus fibroblasts, can also induce sinus fibroblast differentiation to myofibroblasts. In addition, POSTN increased HNE acinar epithelial proliferation, leading to glandular hyperplasia/hypertrophy.

CONCLUSIONS:

CXCL5 increases the activation of sinonasal fibroblasts to myofibroblasts to increase POSTN expression/secretion, which in turn promotes sinonasal epithelial cell proliferation and differentiation that ultimately leads to SMGHH in CRS.

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Differential responses of epithelial cells from bladder and biliary tract to eggs of *Schistosoma haematobium* and *S. mansoni*

BACKGROUND:

More than 200 million people are afflicted with schistosomiasis; infection with *Schistosoma japonicum* and *S. mansoni* causes hepatointestinal schistosomiasis and *S. haematobium* causes urogenital schistosomiasis (UGS). UGS is associated with hematuria, major bladder wall pathology and hydronephrosis leading to kidney damage, whereas chronic deposition of eggs of *S. haematobium* frequently leads to squamous cell carcinoma of the bladder. Notably among these diverse forms of schistosomiasis, UGS is classified as a group 1 carcinogen by the International Agency for Research on Cancer. However, the cellular and/or molecular mechanisms linking UGS with carcinogenesis have yet to be defined.

OBJECTIVES/METHODS:

We investigated the effects of co-culture with eggs of *S. haematobium* on epithelial cell lines, HCV29 established from human bladder urothelium and H69 from the human cholangiocytes. Cell growth of HCV29 and H69 cultured with *S. haematobium* and *S. mansoni* eggs was monitored using the xCELLigence real time cell assay (Acea Biosciences); xCELLigence monitors conductivity across electrodes lining the tissue culture well. Gene expression analysis of the cells was also undertaken, specifically on gene networks and pathways involved in oncogenesis and in epithelial to mesenchymal transition.

RESULTS:

Schistosome eggs promoted proliferation of HCV29 urothelial cells: ~27% and ~14% more proliferation in cells exposed to *S. haematobium* or *S. mansoni* eggs, respectively than control cells. Proliferation to *S. haematobium* eggs was more pronounced than to eggs of *S. mansoni*, which is noteworthy given that eggs of *S. haematobium* transverse the urothelium to exit in the urine (whereas *S. mansoni* eggs transverse the gut to complete disease transmission). By contrast, both eggs of both schistosomes induced cell death of the cholangiocytes. Tumor suppressors, e.g. P53, and metalloprotease inhibitors were down regulated in cells exposed to *S. mansoni* and *S. haematobium* eggs. *S. mansoni* eggs up regulated cell cycle regulators, e.g. E2F1 transcription factor, and the cell invasion-related proto-oncogene SH3PXD2A. *S. haematobium* eggs down regulated desmosomal proteins involved in cell-cell junctions and the platelet-derived growth factor receptor that plays a role in the migration of vascular smooth muscle cells and formation of the neointima at vascular injury sites.

CONCLUSIONS:

Proliferative changes appeared to depend not only on the species of schistosome, but also on the organ system origin of the epithelial cells. Deeper study of cellular and/or molecular mechanisms linking the UGS and the development of bladder cancer can be expected to aid discovery of new interventions for this neglected tropical disease-related cancer.

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Identification of RNA biomarkers for diagnosis of acute appendicitis

Acute appendicitis is one of the leading causes of non-injury related abdominal pain in patients presenting to the ER. Computed tomography (CT) is the gold standard for diagnosis of appendicitis, with a sensitivity of 93.2% and PPV of 97.6%. However, in addition to a high healthcare cost per procedure, CT carries significant radiation exposure, which is a serious concern for children and reproductive age women. Accurate, rapid diagnostic tests are needed to help utilize CT scanning more appropriately and provide an alternative diagnostic solution for situations where CT is unavailable. Blood from ER patients with surgically confirmed appendicitis, abdominal pain from other causes, and lower respiratory infections was collected and genome-wide expression profiling was used to identify RNA biomarkers. Using a combined t test probability of <0.05 and >2 fold change, thirty-seven differentially expressed gene transcripts were identified in the appendicitis group. The transcripts tended to fall into infection-related, inflammation-related, and ribosomal processing gene families. Surprisingly, infection-related transcripts were the lowest in the appendicitis group, suggesting that the host's immune cells are not directly in contact with the pathogen itself. The biomarkers were further evaluated in an ex vivo model of LPS stimulation of lymphocyte gene expression. Altogether, the panel of genomic biomarkers may be used for a rapid peripheral blood-based diagnostics of acute appendicitis.

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Clonal Evolution and Anatomical Heterogeneity of Childhood Brainstem Gliomas

Diffuse Intrinsic Pontine Gliomas (DIPGs) are infiltrative, high-grade childhood brainstem tumors, with a peak onset of 6 to 9 years of age. While comprising of only 10-20% of pediatric brain tumors, DIPGs are the main cause of death amongst childhood brain cancers. DIPG originates in the pons and diffuses throughout the brainstem, with the potential of extending to distant locations within the cerebral cortex. However, there are no published studies characterizing potential clonal evolution of tumor cells within the brainstem or cortex. Although mutations in histone 3 (h3) genes have been shown to be involved in up to 80% of primary DIPGs, the molecular characterization of metastatic tumor cells has not been described.

To address this, we analyzed primary and extended tumors with regard to brain anatomical locations. Eight DIPG whole brains, collected at autopsy, were used to study tumor extension. A total of 20 specimens per brain, representing various anatomical brain locations including frontal lobe, thalamus, hippocampus, lateral ventricles, and cerebellum were isolated (a total of 160 specimens). Our analyses included immunohistochemical studies, targeted mutation analysis, as well as mRNA and methylation profiling. Generated data were analyzed using R script software.

Methylation analysis indicated clustering of our DIPG cohort with a larger cohort (n= 9) of childhood cancers carrying h3 mutations. Brainstem specimens (n= 3) exhibited a distinct methylation pattern, when compared to normal samples obtained from cerebral cortex, and cerebellum. mRNA profiling showed patterns of gene expression unique to anatomical rostral/caudal orientation within the brainstem. Targeted mutation studies identified the presence of tumor cells harboring h3 mutation throughout the brain. Furthermore, histologic examinations revealed the presence of up to 8% mutant cells in brain regions deemed 'normal' by either pathological examination, or mutation analysis.

Our study is the first to describe tumor extension and metastasis, within whole brains in DIPGs. Understanding molecular characteristics of primary and extended tumors will lead to the establishment of targeted therapy for children with DIPG.

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Intestinal Selection of Immunogenic Antigen: An In Vivo Screen for Immunogenicity of Antigens Surface Expressed on *E. coli*

Previous vaccine technologies have selected antigens arbitrarily or used a whole immunogen, without a systematic effort to identify antigens of maximum immunogenicity. Despite recent advances in vaccinology, a method for rapid and efficient identification of optimally immunogenic antigens would greatly enhance vaccine development. We developed a novel in vivo antigen identification technology: Intestinal Selection of Immunogenic Antigen (ISIA). ISIA interrogates an intact mouse gut immune system to compare the immunogenicity of selected test proteins expressed on the surface of commensal *E. coli* that stably colonize the gut. ISIA employs a plasmid containing a DNA barcode for in vivo bacterial population identification and quantification, and a Gram-negative autotransporter expression cassette for surface expression of test proteins. We orally inoculated mice with *E. coli* transformed with a set of plasmids, each encoding a unique DNA barcode and corresponding test protein, to study the interaction of these test proteins with the gut-associated lymphoid tissue (GALT). Test proteins included *Helicobacter pylori* UreaseA, mouse erythropoietin, AAmixshort, and a no expression control. qPCR showed *E. coli* populations expressing immunogenic test proteins were eliminated from the GI tract, while *E. coli* expressing non-immunogenic or no test protein colonized stably for >8 weeks. Mice showed significant levels of serum IgG+IgM, fecal IgA, and IFN-gamma production specifically against immunogenic UreaseA. Mice did not produce significant humoral or cell-mediated immunity against non-immunogenic AAmixshort. ISIA employs an intact, living gut immune system, to distinguish between immunogenic and non-immunogenic test proteins expressed on the surface of *E. coli*. This system can potentially identify optimally immunogenic vaccine antigen candidates for downstream therapeutic development.

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Comparative Analysis of Airway Secretions in Autosomal Dominant Hyper-IgE Syndrome

RATIONALE:

Autosomal dominant Hyper IgE Syndrome (AD-HIES), is a rare, life-shortening multisystem disorder caused by mutations in the signal transducer and activator of transcription 3 (STAT-3) gene that involves the skin, lungs, connective tissue, and vasculature. AD-HIES patients have recurrent pneumonias, skin infections, eczema, and connective tissue abnormalities. The airway mucus appears thicker and more tenacious than secretions from patients with cystic fibrosis (CF) or asthma, but the composition had not been delineated. We hypothesize that proteomic analysis of airway secretions will identify disease-specific pathologic proteins.

METHODS:

Twelve airway specimens from 9 AD-HIES subjects were collected via bronchoscopy or expectorated sputum. Samples were dissolved in RIPA buffer and separated by LDS-PAGE. Proteins were identified after in-gel digestion and extraction using LC-MS analysis. Proteins in all 12 subjects with a peptide probability >0.98 and >2 spectral counts were analyzed based on biological processes (Panther Database) and cellular networks (Ingenuity Pathways). Proteins were compared to three previously published on bronchoalveolar lavage fluid from normal and CF patients to BALF from 3 asthmatic patients (inflammatory control) at CNMC.

RESULTS:

Of the 437 total proteins identified, 62 were present in all 12 AD-HIES samples. The predominant biological processes of all these 62 proteins were immune system, response to stimulus, and metabolic and cellular processes. The major network associated with these proteins were "neurological disease, cellular assembly and organization, cancer." Of these 62 proteins, 47 were present in normal, 52 in CF, and 53 in asthmatic BALF. Two immunoglobulin-1 proteins were found in all AD-HIES but not in normal, CF, and asthmatic samples. Four proteins were absent in all AD-HIES samples but present in normal and disease controls, surfactant A1 and B (up-regulated by STAT3 when there is lung injury), cofilin (involved in actin filament disassembly; implicated in up-regulation of STAT3 activity) and fetuin A (inhibitor of soft tissue calcification).

CONCLUSION:

Proteomic analysis provides a detailed approach to describe AD-HIES airway secretions. Comparative analysis of these secretions suggests they largely consist of immune response proteins and may lack specific proteins in normal and disease controls. Future studies may help delineate the role of STAT3 function in regulation of these proteins.

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A Proteomic Approach to Decreasing Mucus Production in the Airways of Patients with Cystic Fibrosis

Chronic pulmonary infections by bacterial pathogens, especially *Pseudomonas aeruginosa* (PA), and mucus hypersecretion/overproduction are the major causes of morbidity and mortality in cystic fibrosis (CF) patients. Mucosal secretions provide a barrier that protects the apical surfaces of lung epithelium against bacterial and environmental challenges. These apically secreted proteins mediate innate immune responses and may be deficient in CF as they have been reported to exhibit altered anti-microbial activity and exhibit innate immune dysfunctions. Our lab has recently used an in vitro model of differentiated human bronchial epithelial (HBE) cells from CF and non-CF individuals and Stable Isotope Labeling with Amino Acids in Cell Culture (SILAC) to quantitatively compare the CF and non-CF proteins secreted apically at homeostatic conditions. Inherent differences in innate immunity, proteases, extracellular matrix, and mucin glycoproteins are seen in the constitutive apical secretions of CF lung epithelial cells (1). We hypothesized that CF lung epithelial cells would also exhibit an altered apical secretome compared to non-CF cells following a bacterial challenge with PA that would provide insight into how mutated CFTR sets the stage for an aberrant response to infection.

EXPERIMENTAL APPROACH AND RESULTS:

CF and non-CF life-extended HBE cells cultured at air liquid interface (ALI) were exposed either to 1 ml of control media or 1 ml of MPAO1 strain of PA at a concentration of 5×10^8 CFU/ml for one hour. The PA samples were diluted from a frozen stock that had previously been shown to induce host defense gene expression in normal life extended HBE-ALI cells. Apical secretions were collected 24 hours following exposure. The peptides present were identified using shotgun proteomics, consisting of peptide digestion followed by mass spectrometry. Significant proteome differences between CF and non-CF secretions following exposure to control media corroborated recently published data (1). However, no significant differences were seen with PA exposure in either the CF or non-CF group, perhaps indicating a lack of cellular response or secretion to the bacterial challenge used. To test the exposure conditions and viability of the PA stock, A549 lung epithelial cells, which exhibit alterations in mRNA levels following a 1 h PA exposure (2) were exposed to PA and secretions evaluated by shotgun proteomics. However, significant protein differences again were not observed. The exposure time (1 h) may have been too short, the PA concentration too low, or the PA frozen stock unviable. These concerns will be addressed in future experiments. Additionally, a SILAC standard of epithelial lung secretions will be generated and added to CF and non-CF secretions to allow quantitative comparisons (3).

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- (2) Hawdon NA, Aval PS, Barnes RJ, Gravelle SK, Rosengren J, et al. (2010) Cellular responses of A549 alveolar epithelial cells to serially collected *Pseudomonas aeruginosa* from cystic fibrosis patients at different stages of pulmonary infection. *FEMS Immunol Med Microbiol* 59: 207-220
- (3) Deeb SJ, D'Souza RCJ, Cox J, Schmidt-Supprian M, & Mann M (2012) Super-SILAC Allows Classification of Diffuse Large B-cell Lymphoma Subtypes by Their Protein Expression Profiles. *Molecular & Cellular Proteomics* : MCP, 11(5), 77-89. doi:10.1074/mcp.M111.015362

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Elucidating molecular diagnostics for myopathies using targeted and exome sequencing technologies.

OBJECTIVE:

To use next-generation sequencing technologies to provide molecular diagnostics for patients with previously undiagnosed myopathies.

BACKGROUND:

Molecular diagnostics in the genetic myopathies often requires testing of the largest and most complex transcript units in the human genome (DMD, TTN, NEB). Iteratively targeting single genes for sequencing traditionally has entailed high costs and long turnaround times. Exome sequencing is beginning to supplant single targeted genes, but there are concerns regarding coverage and needed depth of the very large and complex genes that frequently cause myopathies.

METHODS:

We tested a highly parallel targeted approach, using a 45 gene emulsion PCR myopathy panel, with subsequent next-generation sequencing on the Illumina platform in 95 undiagnosed patients. We compared the targeted re-sequencing approach to whole exome sequencing for 12 of these patients studied.

RESULTS:

We detected likely pathogenic mutations in 34% of patients (33 out of 95), with a relatively high frequency of likely pathogenic titin gene mutations. Mutation detection was similar in both methods; however we found that distribution of reads and number of dropouts for individual exons was more variable in the targeted panel data compared to exome.

CONCLUSIONS:

Given that costs of highly parallel re-sequencing and whole exome sequencing are similar, and that exome sequencing now takes considerably less laboratory processing time than targeted re-sequencing, we conclude that whole exome approaches will likely become the standard approach for molecular diagnostics.

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Thymosin β 4 protects against Ethanol-LPS induced Liver Injury in the Mouse Model by Inhibiting Oxidative Stress, Activation of NF κ B signaling and Pro-inflammatory Cytokine Production, and Fibrogenesis

BACKGROUND AND RATIONALE:

Alcohol induced liver disease (ALD) is a leading cause of death worldwide. Based on the well accepted two-hit model for ALD, chronic ethanol (EtOH) and lipopolysaccharide (LPS) generated endotoxins activate nuclear factor Kappa B (NF κ B) in the Kupffer cells that up regulates tumor necrosis factor alpha (TNF α), and interleukin 1 beta (IL1 β), the potent pro-inflammatory cytokines that propagates liver inflammation. Moreover, in the hepatocytes, ETOH is oxidized to its toxic metabolite, acetaldehyde by alcohol dehydrogenase (ADH) and cytochrome P450 2E1 (CYP2E1) leading to the generation of reactive oxygen species (ROS), resulting in oxidative stress and the activation of hepatic stellate cells (HSC) causing the up regulation of fibrogenic genes, platelet derived growth factor β -receptor (PDGF β R), α -smooth muscle actin (α SMA); extracellular matrix (ECM) protein, collagen I (Col1); and epigenetic repressor gene, methyl-CpG binding protein 2 (MeCP2). In contrast, adipogenic genes, peroxisome proliferator-activated receptor γ (PPAR γ), and sterol regulatory element-binding protein 1c (SREBP1c) are suppressed resulting in the transdifferentiation of HSC from quiescent lipid storing phenotype to activated myofibroblastic phenotype. Thymosin β 4 (T β 4), a bioactive peptide, is reported to prevent inflammation and fibrosis in many extra-hepatic tissues. Therefore, in this study, the protective role of T β 4 in EtOH-LPS induced oxidative stress, inflammation and fibrogenesis was investigated.

METHODS:

The two-hit EtOH-LPS mediated liver injury was induced in the in vivo mouse model using chronic 5% ETOH fed in a liquid diet for 8 weeks as well as a single i.p. dose of ETOH (3.2g/kg body wt.) and LPS (2mg/kg body wt.), 6h prior to the experiment. T β 4 (1mg/kg body wt.) was administered as a daily i.p. dose for 1 week. The above mentioned genes and their products were measured using quantitative RT-PCR and Western blotting, respectively. Effect on oxidative stress was determined using ROS and glutathione (GSH) fluorescent assays.

RESULTS:

T β 4 protected against EtOH-LPS induced oxidative stress by decreasing the levels of ROS and increasing the levels of the anti-oxidant, GSH. T β 4 protected against EtOH-LPS induced liver injury by inhibiting the activation of NF κ B by blocking the phosphorylation of the inhibitory protein I κ B and thereby prevented the up regulation of TNF α , and IL1 β and consequent liver injury. T β 4 also prevented the activation of HSC by suppressing the up regulated MeCP2, that coordinately reversed the down regulated adipogenic genes (PPAR γ and SREBP1c) and the up regulated fibrogenic genes (α SMA, PDGF β R and Col1).

CONCLUSION:

These data suggest that T β 4 may have therapeutic potential as an anti-oxidant, anti-inflammatory and anti-fibrogenic agent for the treatment of ALD.

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Molecular Mechanisms Underlying Congenital Heart Defects in a Hectd1 Mutant Mouse Line

Congenital heart defects (CHDs) are the most common birth defect in the United States. While it is known that CHDs are caused by a combination of genetics and environmental factors, the genetic component and how these interact with environmental factors are not well understood. A CHD genetic screen in mouse (Yu et al. 2004) identified a mutation in Hectd1 causing heart defects including abnormal aortic arches and ventricular septal defects (VSDs). Data from the Zohn lab indicates that Hectd1 is involved in retinoic acid (RA) signaling, a signaling pathway that is vital for proper heart development. Thus we will investigate the hypothesis that CHDs in Hectd1 mutants are due to reduced RA signaling. To address this hypothesis, we will characterize congenital heart defects in our Hectd1 mutant mouse model and elucidate the molecular pathways underlying these defects. Histological techniques were used to determine the pattern of Hectd1 expression during heart development and categorize developmental defects in the hearts of Hectd1 mutants. To understand the underlying developmental programs disrupted in Hectd1 mutants, immunohistochemistry and in situ hybridization techniques were used to visualize changes in the expression patterns of key genes controlling heart development. Hectd1 is expressed throughout heart development in the developing arteries, atria, and ventricles. Thus Hectd1 can potentially regulate heart development by acting in many cell types and at multiple developmental stages. Hectd1 mutants show thin myocardial walls, hypoplastic ventricles, and abnormal aortic arteries. Hectd1 mutants also show changes in expression of several heart-specific markers important for ventricular and aortic artery development. All of these defects are consistent with reduced RA signaling. Future work will determine if reduced RA signaling in Hectd1 mutants results in CHDs. Towards this goal we will utilize a novel allelic series of Hectd1 mutant mouse lines, RA reporter mice and a variety of molecular and genetic techniques.

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miR-671-5p inhibits epithelial-to-mesenchymal (EMT) transition by downregulating FOXM1 expression in breast cancer

MicroRNAs (miRNAs) are small, single-stranded non-coding RNAs that control gene expression. miRNAs function as either tumor suppressors or oncogenes, and play a critical role in cancer initiation and progression by regulating target genes. Our previous studies showed that miR-671-5p was deregulated during breast cancer progression. Here, we identified miR-671-5p as a tumor suppressor, which exerts its function by targeting Forkhead Box M1 (FOXM1), an oncogenic transcription factor, in breast tumorigenesis. We found that expression of miR-671-5p was decreased significantly in ductal carcinoma in situ (DCIS) and invasive ductal carcinoma (IDC) compared to normal and atypical ductal hyperplasia (ADH) in microdissected formalin-fixed, paraffin-embedded (FFPE) tissues. FOXM1 was predicted as one of the direct targets of miR-671-5p, which was subsequently confirmed by luciferase assays. The forced expression of miR-671-5p in breast cancer cell lines downregulated FOXM1 expression, resulting in decreased proliferation and invasion. Notably, overexpression of miR-671-5p caused a shift from epithelial to mesenchymal transition (EMT) to mesenchymal-to-epithelial transition (MET) phenotypes in MDA-MB-231 breast cancer cells, and induced S-phase arrest. Moreover, miR-671-5p sensitized breast cancer cells to cisplatin, 5-fluorouracil (5-FU) and epirubicin exposure. Host cell reactivation (HCR) assays showed that miR-671-5p reduces DNA repair capability in post-drug exposed breast cancer cells. Our data defined, for the first time, a role for miR-671-5p as a tumor suppressor miRNA in breast cancer involving cell proliferation, invasion, cell cycle arrest, EMT and chemotherapeutic sensitivity by directly targeting FOXM1. Therefore, miR-671-5p may serve as a novel therapeutic target in the management of breast cancer.

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Novel Delta-9,11 Glucocorticoid (GC)-Analogue (VBP15) Improves Mitotic Asynchrony in Human Asthmatic Bronchial Epithelium

BACKGROUND:

VBP15 is a novel anti-inflammatory compound synthesized based on the lazeroid steroidal backbone that maintains classical inhibition of NF κ B-mediated inflammation, with a much-reduced capacity to cause deleterious effects associated with chronic glucocorticoid use (e.g. growth delay and adrenal suppression). We have previously shown that VBP15 inhibits allergic pulmonary inflammation in an animal model. In our current work we investigated whether VBP15 also mitigates airway epithelial asynchrony and improves epithelial regeneration after in vitro mechanical injury in a model of asthmatic human bronchial epithelia lacking inflammatory cells.

METHODS:

Non-asthmatic and asthmatic primary differentiated (air-liquid interface (ALI) airway epithelia were exposed to VBP15, dexamethasone (DEX) or vehicle following mechanical injury at different time points. Basolateral cytokine secretions (TGF- β 1, IL-10, IL-13, and IL-1 β) were analyzed using cytometric bead assays and wound regeneration/mitosis examined by bright-field microscopy visualization and flow cytometry using BrdU+ staining.

RESULTS:

VBP15 improved mitotic synchrony of proliferating cells (G1/G0, S, G2/M) and enhanced wound regeneration in asthmatic epithelia compared to untreated asthmatic cultures. VBP15 also significantly reduced the basolateral secretion of pro-inflammatory (i.e. IL-1 β) and pro-fibrotic cytokines (i.e. TGF- β 1) in ALI-differentiated asthmatic epithelia following in vitro mechanical injury ($p < 0.05$).

CONCLUSION:

VBP15 improves mitotic asynchrony, abnormal repair and injury-induced pro-inflammatory and fibrogenic responses in asthmatic bronchial epithelium with efficacy comparable to classical GCs. These findings suggest that VBP15 might be a potential alternative to conventional GC therapy in asthma and other respiratory conditions that involve abnormal repair and remodeling of the lung.

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Superresolution imaging of viral protein clustering on the outer mitochondrial membrane

BACKGROUND:

Congenital infection with human cytomegalovirus (HCMV) is the leading viral cause of birth defects in developed countries. One of the first products encoded by HCMV is the viral mitochondrial-localized inhibitor of apoptosis (vMIA) that is critical for its growth. vMIA is synthesized at the endoplasmic reticulum (ER), from where it traffics sequentially to the mitochondrial-associated membrane (MAM) to the outer mitochondrial membrane (OMM). vMIA causes calcium efflux from ER stores. vMIA also prevents mitochondrial-mediated apoptosis, regulates ATP synthesis, and augments mitochondrial biogenesis. vMIA localizes predominantly on the OMM whose close proximity to the MAM and ER allows for coordinated responses. We recently found that vMIA is organized in nanometric clusters of ~100 nm on the OMM, similar to other mitochondrial proteins.

OBJECTIVE:

We examined the vMIA sequences necessary for its trafficking and clustered organization at the OMM.

DESIGN/METHODS:

vMIA-HHB has a mutant leader whose hydrophobicity is higher than that of wild-type vMIA (hydropathy scores of 2.600 and 1.289, respectively). HHB mutant is defective in OMM trafficking. vMIA-CBDII has a mutant cholesterol binding domain (CBD) and cannot associate with MAM lipid rafts but efficiently traffics to the OMM. Confocal microscopy, superresolution multifocal structured illumination microscopy (MSIM), and fluorescence-lifetime imaging microscopy (FLIM), which measures protein interactions at <10 nm, were used to study clustering of fluorescent protein tagged vMIA wild type and mutant proteins.

RESULTS/DISCUSSION:

Using MSIM imaging, we verified that vMIA HHB mutant traffics through the secretory apparatus rather than to the OMM. In contrast, vMIA-CBDII mutant traffics efficiently to the OMM similar to the wild type vMIA. Further, we observed clustering of wild type vMIA-enhanced green fluorescent protein (EGFP) on the OMM of transiently transfected HeLa cells. MSIM and confocal microscopy also showed that the vMIA mutants, HHB and CBDII mutants are partially defective in clustering compared to wild type vMIA. These results were independently verified using FLIM, which found clustered organization of wild type vMIA on the OMM, whereas the mutants were partially defective in clustering. Study of vMIA clustering will provide insight into how functional complexes are formed and organized at the OMM.

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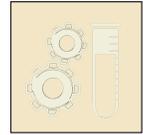
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3D Printed Microchannels to Create Networks of Endothelial Cells for the Development of a Tissue Engineered Blood Vessel

Cardiovascular disease is the leading cause of death in western nations. Coronary bypass surgery is often performed to treat patients with this disease, but the number of suitable vessels available for this procedure is limited. Vascular tissue engineering (TE) is a developing field which seeks to provide readily available and off-the-shelf alternatives to traditional vascular auto and allografts. Still, remodeling vascular tissue presents a formidable challenge due to the multi-cellular composition, tissue architecture, and various physical and mechanical properties of native vessels. 3D printing has recently emerged as a promising new fabrication technique for scientists and engineers to more precisely control the design of complex structures, such as those found in the vasculature. The focus of this research is to apply 3D printing techniques to fabricate a biomimetic tissue engineered blood vessel for coronary bypass surgeries.

Blood vessels are multi-layered systems with two major cell types: endothelial cells (ECs) and smooth muscle cells (SMCs). ECs line the inner lumen of blood vessels and serve to prevent thrombosis. SMCs surround the EC lining in multiple layers and control the vasoactivity of the construct. The unique alignments of both of these cells contribute to their individual functionality. Specifically, ECs orient themselves in the direction of blood flow, whereas SMCs align circumferentially around the vessel wall. It is the aim of this study to employ stereolithography (SL) printing techniques to fabricate a biocompatible polymer scaffold with channeled architectures to properly align vascular cells in their native orientations. We demonstrate the ability of SL printing techniques to create carefully-aligned poly(ethylene glycol) (PEG)-based hydrogel composite microchannels and quantify the extent of EC attachment and proliferation on their surfaces. Ongoing work is being performed to show the ability of these constructs to support multiple vascular cell types in a multi-layered structure. These cell-seeded polymer sheets will later be rolled up into tubular constructs and mounted in a perfusion bioreactor to improve the cell functionality and mechanical properties of the vascular graft. Overall, this technology shows great potential for 3D printing blood vessels to provide additional off-the-shelf vascular graft options for patients in need.

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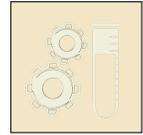
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Simulation of the effect of plasma species on tumor growth and apoptosis on a three-dimensional microscopic scale

Plasma oncology is an emerging field that seeks to understand the effects of cold atmospheric plasma on cancer cells. It has been shown in literature that cold atmospheric plasma therapy, when applied to cancer cells, initiates the apoptotic pathway and leads to a sharp decrease in cell viability. Consequently, and equally as important, when the same conditions are applied to non-cancerous cell lines, research finds very low amounts of apoptotic signaling. Currently, this field aims to understand the mechanism using in vivo and in vitro techniques, but it is important to turn to in silico modeling techniques to further this field of study. This research project utilizes a computer model to simulate the interactions of tumor cell populations with cold plasma species, which can be used predict the non-intuitive progression of tumor cell apoptosis after exposure to cold atmospheric plasma. The model makes use of a three-dimensional hybrid discrete-continuum model to show the apoptotic effect a tumor volume undergoes when treated with particular chemical species from the cold atmospheric plasma. The continuum model is governed by Fick's Second Law of Diffusion to represent the diffusion of cold atmospheric plasma species through a tumor volume. The discrete model utilizes Voronoi polyhedrons to represent a tumor cell physically and mathematically, and it implements stochastic functions to govern the progression of tumor cells. The simulation results show that the treated tumor death, irrespective of tumor volume, follows an exponential decay and that the untreated tumor growth follows an expected growth pattern. By comparing treated and untreated tumors of varying sizes, measured spatiotemporal data can also be used predict trends of tumor evolution. Thus, the model introduces a possible paradigm shift in cancer therapy as it provides key insight into the development of a personalized cancer treatment system using the cold plasma modality.

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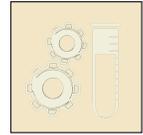
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Ultrasound Stimulation of Insulin Release From Pancreatic Beta Cells

BACKGROUND, MOTIVATION AND OBJECTIVE:

Type 2 diabetes mellitus is a complex metabolic disease that has reached epidemic proportions. Controlling type 2 diabetes is often difficult. Many patients are poorly compliant with lifestyle changes, and pharmacological management often requires complex therapy with multiple medications, and loses its effectiveness over time. Thus, new modes of therapy are needed that will directly target the underlying causes of impaired glucose homeostasis. Our research objective is to study a novel, nonpharmacological approach that utilizes the application of ultrasound energy to augment insulin release from pancreatic beta cells.

STATEMENT OF CONTRIBUTION/METHODS:

Our experiments have focused on determination of effectiveness and safety of ultrasound application in stimulation of insulin release from pancreatic beta cells. ELISA insulin release assay has been used to determine and quantify the effects of ultrasound on insulin release in cultured beta cells. Effects of ultrasound on cell viability have been assessed by employing trypan blue staining for samples collected for up to 30 minutes after treatment. Cells have been exposed to ultrasound with varying center frequencies of 400 kHz to 1 MHz and intensities of 0.1 to 1 W/cm² for 5 minutes. Insulin was previously shown to be released in a calcium-dependent manner in response to changes in blood sugar levels. Therefore, we are also looking to evaluate extracellular calcium influx as a potential mechanism for enhanced ultrasound-induced insulin release. An experimental setup was designed for real-time ratiometric imaging of calcium transients during our ultrasound treatments. Insulin release and cell viability results will be correlated as a function of temperature increase and non-thermal activity as measured experimentally and simulated using PZFlex modeling software.

RESULTS/DISCUSSION:

Our preliminary data indicated that application of therapeutic ultrasound may lead to increase of insulin secretion from beta cells while maintaining cell viability. Cell viability was not significantly affected during and for up to 30 minutes after treatment in trypan blue studies. Effects of ultrasound on beta cell function are currently being studied for a wide range of ultrasound parameters as to find the exposure inducing optimized insulin release from beta cells. If shown successful our approach may eventually lead to new methods in the treatment of diabetes and other secretory diseases. Our future studies will focus on application of ultrasound to the pancreas in an in vivo animal model to determine whether it would be possible to stimulate beta cells without stimulating other endocrine and exocrine cells of the pancreas.

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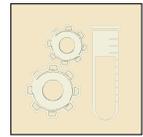
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3D Printed Bioactive Scaffolds for Osteochondral Regeneration

STATEMENT OF PURPOSE:

Osteoarthritis (OA) is clinically defined as the progressive degeneration of hyaline cartilage within articulating joints leading to structural and functional failure at the interface. Reduced joint mobility and severe pain due to articular cartilage and subchondral bone (collectively known as osteochondral tissue) damage is common to patients suffering from OA. Current treatment methods used to address these defects include autografts, allografts, and mosaicplasties which contain their own inherent limitations, including donor site morbidity, infection, poor tissue integration, and insufficient neovascularization. Therefore, the objective of this work is focused on the manufacture of three-dimensional (3D) bioactive nanocomposite scaffolds for osteochondral tissue regeneration.

METHODS:

For the current work, a porous and highly interconnected poly(ethylene glycol) diacrylate (PEG-Da) hydrogel scaffold containing graded nanocrystalline hydroxyapatite (nHA) was fabricated via our novel table-top stereolithography 3D printer based on the open-source Solidoodle platform. Various in-fill densities (40% - 80%) of 60wt% PEG-Da in PEG were evaluated for cell adhesion. Three-layer scaffolds were fabricated with increasing nHA concentration (20%, 10%, 0%) of the best performing in-fill density. In addition to osteoconductive nHA, transforming growth-factor $\beta 1$ (TGF- $\beta 1$) was incorporated within the smooth articulating cartilage layer (top) at a concentration of 10 ng/mL. Wet co-axial electrospraying was employed to fabricate poly(lactic-co-glycol acid) core-shell nanospheres for sustained delivery. Human bone marrow-derived mesenchymal stem cells (MSCs) were seeded onto control and graded scaffolds and evaluated for adhesion, proliferation and osteochondral differentiation in vitro.

RESULTS:

The current work has focused on the development a novel 3D printed bioactive nanocomposite scaffold for osteochondral tissue regeneration. CAD models with optical and scanning electron micrographs of fabricated control and graded nHA scaffolds illustrate good integration between the respective layers producing a highly porous osseous tissue-like porous structure combined with a smooth articular cartilage top layer. In addition, through with the incorporation of the developed sustained release nanospheres we have shown the capacity of extended bioactive factor release when compared to bare incorporated growth factor.

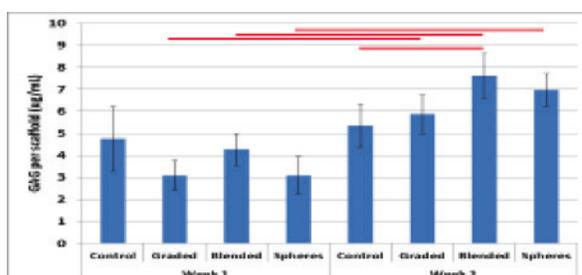
Mesenchymal stem cell proliferation illustrates the capacity of nanocomposite 3D scaffolds to induce increased cell proliferation wherein expedited cell differentiation can be facilitated. Confocal microscopy images of MSCs seeded upon the porous structure illustrate the effectiveness of incorporated nHA in the promotion of cell spreading and adhesion.

In addition, two-week morphogenetic differentiation demonstrated the efficacy of early (glycosaminoglycan) (Figure 6) and late-stage chondrogenic (Type II collagen) and late-stage osteogenic (extracellular calcium) biological markers.

CONCLUSIONS AND FUTURE WORK:

The current work illustrates the efficacy of our current 3D printing technology for efficient fabrication of the novel nanocomposite hydrogel materials with good spatiotemporal control of morphogenetic nanomaterials. In addition, tissue-specific growth factors illustrated a synergistic effect leading to increased cell adhesion and directed MSC differentiation. Mechanical testing illustrated improved strength with the incorporation of reinforcing bioactive nano ceramics.

Figure 6:



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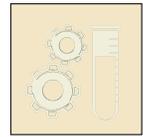
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Measuring Physiological Response of Bisphenol-A on Cardiac Excitation-Contraction Coupling

Biomonitoring studies indicate that 90% of the population is routinely exposed to Bisphenol-A (BPA), a compound commonly found in household plastics. Environmental exposure varies between 1- 100 nM, while clinical and industrial exposure can reach 10 μ M. Epidemiological studies have shown an association between increased BPA exposure and cardiovascular diseases. We aimed to test the direct effects of BPA on cardiac function using a Langendorff-perfusion model. Excised female rat hearts were treated with 1 nM-10 μ M BPA and the resulting effects on cardiac mechanical function and calcium handling were monitored. For calcium imaging, excised hearts were treated with Blebbistatin to arrest mechanical function, and then stained with Rhod-2, a calcium indicator dye. Epicardial calcium transients were recorded using an Andor CCD camera equipped with wavelength specific filters (570 \pm 30 nm), and an LED spotlight (535 nm) was used for dye excitation. Calcium transients were initiated at various pacing frequencies (5Hz, 6.6Hz, and 9Hz). To assess the effect of BPA on the mechanical function of the heart, a latex balloon was inserted into the left-ventricle to quantitate left-ventricular developed pressure (LVDP) and maximum contractility. At high pacing frequencies, BPA decreased LVDP by 16% at 1 nM, 24% at 100nM and 36% at 10 μ M, while the maximum contractility decreased by 23% at 100 nM and 33% at 10 μ M. We conclude that alterations to mechanical function and calcium handling are a sensitive parameter for assessing BPA cardiac toxicity. Our findings indicate that further studies are necessary to clarify the complete extent through which BPA affects cardiovascular function.

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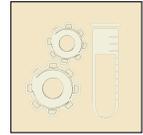
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Vital Ring: a Wearable Wireless Multiple-Lead ECG Sensor

Electrocardiogram (ECG) is an important tool widely used in the clinical diagnostic of heart diseases. It can be used to diagnose symptoms of myocardial infarction, pulmonary embolism, etc. [1] Among those symptoms, detection and early warning of the potential of heart attack such as myocardial infarction can be crucial in daily life for patients, especially those who live alone, because once happened, it need to be taken immediate care of. Unfortunately, the traditional equipment currently used in the hospital cannot fulfill this real-time on-demand monitoring requirement. To address this problem, the wearable ECG monitoring system comes into play.

Recently, wearable healthcare devices have attracted considerable interest both in the academic and industry. The important role ECG playing in the heart disease diagnostic and the convenient noninvasive way of measurement makes it an ideal candidate to be converted to wearable healthcare device, and have already draw many researchers' attention. Y. Chi and G. Cauwenberghs at UCSD have demonstrated a wireless ECG/EEG monitoring system using noncontact electrodes. [2] The gel free noncontact electrodes make the wearing of the device more comfortable and cleaner. However, their electrodes are rigid which makes it less compatible to soft human bodies. Moreover, it is uncomfortable to wear several hard electrodes of noticeable sizes. AliveCor® developed a single-lead ECG monitoring system in the smartphone case format, which can monitor the ECG at fingertip and displays on the smartphone screen. This system has gotten FDA approval, which confirms the possibility to achieve a wearable ECG system. Unfortunately, single-lead ECG measurements, which apply to all existing systems, cannot be used to diagnose myocardial infarction. The phone case format makes it convenient to carry around, but, on the other hand, limits it to single-lead measurement only. IMEC® developed a long term multiple-lead ECG monitoring patch, which can be attached to the upper body and last as long as one month. The only drawback is the usage of conduction gel, which is commonly used in the traditional ECG. The sticky gel is difficult to keep clean. Moreover, it can cause allergy to some patients [3]. The IMEC system uses Bluetooth Low Energy (BLE) to transfer data, which is suited for wearable healthcare equipment because of the low energy consumption and sufficient transfer rate. However, a dedicated BLE data transfer base device in their device is not necessary, because there are many BLE enabled devices available now, such as smartphones and laptops. Using a smartphone to communicate with these wearable devices is convenient, because people carry smartphone around and the smartphone has the ability to further analyze the data, to transfer the data to the physicians, and/or to upload the data to a database.

In this work, we propose and demonstrate a wearable ECG monitoring system capable of providing on-demand multiple-lead ECG signals in the format of a flexible finger ring. Such extreme form factor is enabled by a novel soft electronics/microfluidics co-packaging technique recently developed by us [4]. The flexibility is a key advantage to achieve a comfortable device, and also provides certain durability during impact. We will also use dry electrodes to eliminate the skin reaction issue and the clean issue mentioned before. We will use BLE to transfer the data to smartphone or laptop for further analysis of the data.

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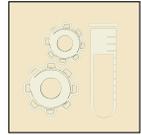
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Surface thermal pattern analysis and its relationship with the breast cancer: an infrared imaging approach

Although the mammogram remains the gold standard for breast cancer screening and evaluation, the required radiation and need for physical compression continuously motivate the seeking of complementary modalities. Tumor growth causes angiogenesis, which is the growth of new blood vessels to supply the tumor. The consequent increased blood flow causes the temperature to increase around the tumor. Previous theoretical and simulation studies in our lab have shown that certain relationships exist between the presence of a tumor and increased localized surface temperature. In this study, infrared images are used for the thermal pattern analysis. Volunteer human subjects were imaged in a controlled environmental setting and a series of infrared images were obtained. Software was developed for quantitative analysis and visualization of the obtained images. To eliminate the effect of inherent noise and blurring, a total-variation based restoration method was used, incorporating both spatial and temporal consistency. After the pre-processing procedure, we used local thresholding and region growing to delineate the region with the elevated temperature. Edge detection was also used as a complementary method to identify region(s) of elevated temperature. The contralateral breast was used as a control, since bilateral cancer occurs in fewer than 4% of cases. Reference points (center position of the nipple region) were selected automatically by using the Hough transform. The region in the contralateral breast that corresponds to the region identified in the subject breast was found by calculating the angles and distances to those reference points. For future research, images with positive or negative diagnoses will be obtained with the collaboration of clinicians. An analytical method will be developed for evaluating the infrared images and for assessing the effectiveness of an infrared-based modality as an adjunct to mammograms.

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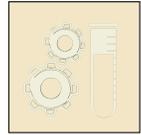
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Shortening of Action Potential Duration with Increased Work in Contracting Rabbit Heart

Coronary heart disease (CHD), also known as ischemic heart disease, causes approximately half of all deaths from cardiovascular causes and is the number one cause of death among both males and females. The ischemic tissue that results from coronary blockage in CHD does not receive the oxygen or fuels to maintain normal cardiac function. Patients with ischemic heart tissue could experience serious and potentially fatal deficits in cardiac function with rapid increases in heart rate, as occurs in exercise. When undiagnosed, this condition is especially dangerous.

Optical mapping with voltage sensitive dyes tracks electrical changes, such as cardiac action potentials (APs). Action potential duration (APD) is calculated from the APs recorded from the epicardial surface. Shortening of the APD indicates ischemia and is a valuable metric to evaluate electrical changes in the heart. Ratiometric optical mapping of a contracting heart offers a unique and novel method of obtaining electrical signals while more closely mimicking energy consumption in vivo. Typical optical mapping preparations require a mechanical uncoupler; however, work demand is significantly less when contraction is inhibited.

Hearts from New Zealand white rabbits were excised and cannulated in Langendorff mode and bi-ventricular working heart mode. AP measurements were taken in both modes and the order was randomized. Hearts were perfused with modified Krebs-Henseleit solution and oxygenated. $20\mu\text{M}$ of the voltage-sensitive dye Di-4-ANEPPS binds to the phospholipid membrane and exhibits a change in fluorescence with changes in voltage. 0.8mm black dots were applied to the left ventricular epicardium for motion tracking. Excitation LEDs at 450nm (royal blue) and 505nm (cyan) were placed in a randomized bundle and the singular output aimed at the epicardial surface. Excitation lights were cycled in rapid sequence for ratiometry measurements. A charge-coupled device (CCD) camera captured the images and emitted light at 490 frames per second. Pressure transducers measured aortic pressure, left atrial preload, and LVDP.

Using this novel method in contracting rabbit hearts demonstrated demand-induced ischemia at higher pacing rates. This effect was more pronounced in bi-ventricular mode as compared to Langendorff. In Langendorff mode, the APD was 137.67 ± 4.29 ms, 113.44 ± 7.89 ms, and 106.44 ± 0.44 ms when paced at 330ms (normal sinus rhythm), 220ms, and 170ms cycle lengths, respectively. In bi-ventricular working heart mode, the APD was 106.56 ± 13.03 ms, 78.00 ± 2.33 ms, and 69.33 ± 0.77 ms when paced 330ms, 220ms, and 170ms cycle lengths, respectively. The result that APD shortens with increasing heart rate indicates demand-induced ischemia.

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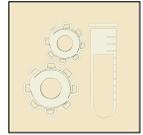
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BIOMEDICAL ENGINEERING



SCHOOL OF ENGINEERING & APPLIED SCIENCE

Characterization of Material Properties of Synthetic Vocal Models

Voice disorders afflict about 30% of the population at some point in their lives, and as many as 60% of those who use their voices extensively, e.g. teachers and singers. Additionally, voice disorders account for substantial economic impact of about \$2 billion annually in the US alone. Human speech, specifically the vowel sounds, is produced by the vocal folds (VFs). The VFs are constructed of complex layers of tissue comprised primarily of 3 distinct layers. Each of these tissue layers possesses specific material properties arising from varying amounts of collagen and elastin fibers present. Synthetic VFs can be fabricated using silicone in order to mimic human VF properties to facilitate studies of human phonation, structural dynamics, and acoustics. The material properties of these artificial VF models should replicate in-vivo properties because material properties affect aerodynamic and elastic forces, tissue deformation, and oscillation. A full characterization of silicone vocal fold models has been undertaken in order to develop valid fabrication guidelines and procedures to produce synthetic VFs that faithfully mimic human vocal folds. Ultimately, the goal is to relate material properties to the tissue forces and deformation that occur when the VF models oscillate.

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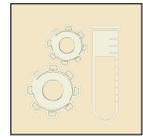
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Deterministic Trapping of Single Cells on a Microfluidic Chip

Individual cells within clonal populations can exhibit wide variations in genetic expression and phenotypic behavior. Certain types of cells are very rare (e.g. circulating tumor cells) or difficult to culture (e.g. stem cells) yet are of significant biological interest. These challenges necessitate technologies that can facilitate single cell analysis. In this work, microfluidic technology is employed to develop a small footprint device for the capture and isolation of individual cells from a bulk sample. In microfluidic devices, cell capture is often achieved by means of trapping. While many microfluidic trapping techniques exist, hydrodynamic methods are particularly attractive due to their simplicity and scalability. However, current design guidelines for single cell hydrodynamic traps predominantly rely on flow resistance manipulation or qualitative streamline analysis without considering the target particle size. This lack of quantitative design criteria from first principles often leads to non-optimal probabilistic trapping. To address this problem, an analytical design guideline was developed for deterministic single cell hydrodynamic trapping through the optimization of streamline distributions under laminar flow with cell size as a key parameter. The theory was that by adjusting the streamline boundary threshold distance equal to the particle radius, deterministic trapping could be achieved. Finite element modelling was used to determine the design parameters necessary for optimal trapping. The simulation results were subsequently confirmed with on-chip microbead and white blood cell trapping experiments. Using this guideline, an example optimized design was demonstrated to achieve 100% capture efficiency for a given particle size. This new development takes the guesswork out of single cell trapping is expected to be of great value to scientists working with rare and limited cell samples.

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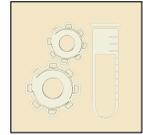
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

The Role of Blood Rheology and Flow Measurements in a Curved Artery in plastico Model

BACKGROUND:

Blood is a complex fluid comprised of platelets, red blood cells, leukocytes, and numerous other particulates. In physiological flows, blood has often been modeled as a Newtonian fluid wherein a linear stress and strain rate relationship exists. This assumption has been used in numerous previous studies related to the core regions of large-diameter, curved blood vessels, e.g. the carotid artery. Non-Newtonian, more specifically shear-thinning, fluid decreases in viscosity as shear rate increases; toothpaste is an example of such a fluid [1-3]. The complex material composition of blood results in non-Newtonian fluid behavior, prompting further exploration.

MOTIVATION AND OBJECTIVE:

Atherosclerosis, a leading cause of death in the developed world, is associated with plaque build-up in the near wall regions of curved arteries. The objective of this study is to create a realistic, complex, blood-analog fluid with shear-thinning properties to facilitate non-invasive cardiovascular flow measurements in a model artery.

METHODS:

The following experiments were used to characterize various blood-analog fluids created in the laboratory:

1. Rheological measurements: Kinematic viscosity and mechanical responsiveness tests were performed using an Ubbelohde viscometer and rheometer (DHR-series), respectively.
2. Hydrodynamics measurements: Pressure and flow rate time-series data were acquired using a pressure catheter mounted on a hemostasis valve and an ultrasonic flow rate sensor.
3. Optical property: Refractive indices of the fluid were measured using a refractometer (Atago-PALRI) to match it with that of an acrylic curved artery model for non-invasive, laser-based flow diagnostics. [5-6]

RESULTS:

Comparisons were made between a (viscoelastic, shear-thinning) non-Newtonian blood-analog fluid containing Xanthan gum (an inexpensive powder used in foods) and a Newtonian (Glycerol/Water) blood-analog fluid [3]. Rheological data agreed well with the published viscosity of blood, and rheometric tests determined a shear-thinning fluid was successfully created (Table 1). Hydrodynamics measurements showed that under carotid artery inflow conditions, flow rate variations were similar, while pressure variations were masked by large phase shifts with flow rate and lower values in the Newtonian case (Fig. 1).

CONCLUSION:

A realistic, non-Newtonian blood-analog fluid was created with accepted values of blood viscosity and refractive indices that facilitate non-invasive optical measurements. Based on hydrodynamics measurements, of pressure, flow rate and velocity, it is clear that the non-Newtonian aspects of blood analog fluids need to be examined more thoroughly. For deeper insights into the effects of non-Newtonian, shear-thinning properties in physiological flows, extensive experiments are under way using particle image velocimetry (PIV) and Laser Doppler velocimetry (LDV) techniques.

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Figure 1:

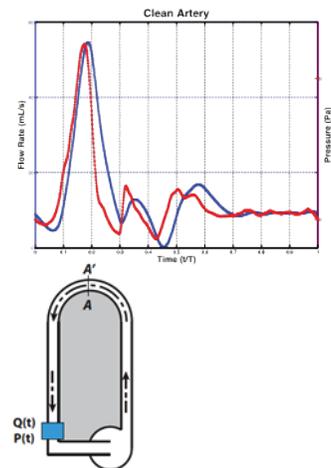
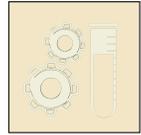


Table 1:

Chemical components/ Property	Newtonian (N)	Non-Newtonian (NN)
Glycerol	20.00 %	21.02 %
Saturated NaI	79.00 %	-
NaI	-	22.57 %
DI Water	1.00 %	56.38 %
Xanthan Gum [3]	-	.03 %
Kinematic viscosity (Ubbelohde, v: mm ² /s)	3.59 (± 0.0563%)	n/a
Kinematic viscosity (Rheometer, v: mm ² /s)	3.27 (± 0.0141%)	4.93*
Refractive Index	1.4932	1.4949
Refractive index of acrylic test-section: 1.490-1.492**		



SCHOOL OF ENGINEERING & APPLIED SCIENCE

3D Bioprinted Polymer / Nanocrystalline Structures with Microchannels for Vascularized Bone Growth

Critical sized bone defects resulting from traumatic injury, cancer, degenerative diseases, or birth defects present a crucial clinical problem. In this study, we will integrate 3D bioprinting and nanomaterials to create a novel vascularized bone scaffold. A series of microstructured scaffolds containing both a bone matrix and a microvascular network were designed and 3D printed. The size of the bone microstructure was kept constant (i.e., 350 μm hexagonally shaped pores alternating with dense linear patterns, layer by layer, to adequately restrict fluid perfusion through the bone network itself). The sizes of the microvascular network were 500 μm (large vascular) and 350 μm (small vascular). Printed scaffolds were then conjugated with nanocrystalline hydroxyapatite (nHA, bone minerals). Young's modulus compiled from mechanical compression data showed the scaffold with a smaller microvascular network has higher mechanical stiffness and more bone-like properties. Human bone marrow derived mesenchymal stem cell (hMSC) 4 h adhesion and 1, 3 and 5 day proliferation were investigated in vitro. The 4 h cell adhesion result demonstrated that 3D printed scaffolds with a smaller microvascular network and nHA had the greatest cell adhesion. In addition, 5 day hMSC proliferation result also showed an excellent cell growth on all scaffolds, with the greatest increase on small microvascular nHA scaffolds, at one and five days. Further study will focus on co-culturing hMSCs and endothelial cells in the bone scaffold for improved osteogenesis and bone formation.

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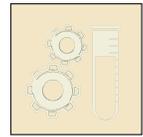
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Self-Oscillating Vocal Fold Model Mechanics: Healthy, Diseased, and Aging

BACKGROUND/MOTIVATION:

Whether it is a cry of hunger or shout of pain, the human voice is primitively used as a tool for basic survival. Voiced speech is produced when a critical lung pressure is achieved, forcing air through the vocal folds which are two bands of complex muscle and tissue layers stretched across the airway. Certain types of growths on the vocal fold (VF) surfaces, such as nodules and polyps, can result from the repeated and prolonged collision between the tissues of opposing VFs, and can be devastating to one's daily life. Approximately 30% of people will suffer from a voice disorder at some point in their lives with this probability doubling for those who rely heavily on their voice for work, such as teachers and singers. Voice disorders in teachers alone have been estimated to have an annual societal economic impact of \$2.5 billion in the United States.

OBJECTIVES:

The objective of this research is to study and improve synthetic vocal fold models by evaluating the ability of the models to replicate physiological VF motion and characteristic parameters of human speech within a life-size experimental setup, and compare the experimental results with clinical results from the GWU Department of Speech and Hearing Sciences.

Replicating physiological properties of human VFs will enable bench-top scientific speech investigations that can eventually be customized based on patient parameters and geometries. Ultimately, this will improve understanding of and care for those who suffer from a voice disorder by advancing the understanding of resulting flow features, progression of pathological conditions, and medical techniques.

METHODS:

Synthetic VF models are fabricated both with and without a polyp-like structure, to exhibit material properties representative of the different layers of human VFs. These VF models are evaluated experimentally in a vocal tract simulator to replicate physiological conditions. Pressure measurements are acquired along the vocal tract, and high-speed images are captured at varying flow rates. Clinically relevant parameters are calculated from the volume-velocity output of a circumferentially-vented mask (Rothenberg mask) and compared to clinical patient data to facilitate understanding of the characteristics of healthy and damaged VFs.

RESULTS:

Using a custom MATLAB algorithm, all tested VF models were found to oscillate at fundamental frequencies within the range of physiological values. Further, the healthy and diseased two-layer VF models were found to have mean speed quotient values within the range of accepted and expected speed quotient values. The high-speed images for all VF models were analyzed using a videokymography line-scan technique that has been used to examine VF motion and mucosal wave dynamics in vivo.

CONCLUSIONS:

The silicone sample ratios used to generate our synthetic VF models resulted in modulus of elasticity values within the range of physiological values, and allowed for repeatable use in our experiments; therefore, we concluded that silicone is effective for modeling physiological VFs. This conclusion is further supported with our fundamental frequency, kymograph, and clinical speech parameter results. The kymograph and CV mask results show that the wool additive and two-layer VF models more accurately replicate physiological characteristics of vocal folds.

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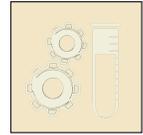
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

3D-printed, in vitro Bone Models for the Study of Breast Cancer Metastasis

Breast cancer is the second leading cause of cancer deaths in women in the United States. In most cases, death results from metastasis instead of the primary tumor. Uncertainty of the metastatic mechanism hinders development of new treatments. Studying the very early stages of breast cancer metastasis is very difficult and the current methods of testing with 2D culture do not accurately recapitulate the natural 3D microenvironment of cells. Additionally, since cells cultured in 2D can behave very differently from cells cultured in 3D, the validity of results obtained from 2D culture can be impaired. To address these issues, in this study, novel 3D-printed bone-like scaffolds were developed using a standard UV-stereolithography printer to efficiently evaluate breast cancer cell (MDA-MB-231) bone invasion in a biomimetic bone microenvironment. The printable resin consisted of polyethylene glycol (PEG) and polyethylene glycol diacrylate (PEGDA) in a 40%/60% w/w ratio mixed with photoinitiator and varying amounts of nano-hydroxyapatite (nHA, a biomimetic bone mineral). Square scaffold patterns were designed by CAD, and pore size of the patterns was varied (small, medium, and large) in order to determine optimal scaffold geometry. Scanning electron microscopy revealed all scaffolds were printed successfully with well-defined morphology. Our results demonstrated that scaffolds with medium pore size presented better cell adhesion than the other 3D printed scaffolds and 2D culture. Afterward, medium pore size scaffolds were made with 0%, 2%, 5% and 10% w/w nHA for proliferation studies. The highest nHA content (10%) scaffolds displayed the best cell proliferation, with significant improvements from other scaffolds at 3 and 5 days. In addition, confocal microscopy imaging of the scaffolds corroborated the proliferation results. Consequently, we have developed a viable, biomimetic, easy-to-manufacture bone scaffold that can be used for the 3D in vitro study of breast cancer bone metastasis.

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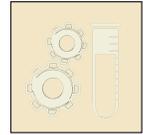
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Permeabilization of Cell Membrane in the Presence of Encapsulated Microbubbles for Drug Delivery

Encapsulated microbubbles were initially developed as contrast enhancing agents for ultrasound imaging. They contain a gas core encapsulated by a shell layer of lipid or protein. The shell stabilizes them against dissolution in the bloodstream. Currently, ultrasound contrast agents are used not only to image the blood pool and tissue, but also in therapeutic applications such as drug delivery and gene therapy. Contrast agents can carry and transport drugs or genes on or within their shells to the desired site within the body. Physicochemical interactions can be used to increase the specificity of microbubbles targeting while limiting the toxicity of the drug to healthy tissues. Upon arriving at a target, microbubbles are motivated by ultrasound waves, leading to violent collapse. These violently collapsing bubbles release the drug/gene and also cause the cell membrane to perforate in a process known as sonoporation. The perforation of cell membrane allows large molecules and drug to pass easily through the membrane to reach the unhealthy tissue, and hence to facilitate the uptake of drug. As an example, imagine the drug delivery into brain. The only way to deliver drug into the brain is through blood brain barrier. The ultrasound in the presence of contrast agent can increase the permeability of the barrier resulting in the uptake of drug into the brain.

The objective of this work is to study the sonoporation numerically as the process is currently very difficult to be understood experimentally. The boundary element method has been used for our numerical simulation as it is a very powerful technique to study bubble collapse near membrane. It is worth mentioning that the encapsulation of the microbubble affects the dynamic boundary conditions. In this study the encapsulation is modelled using a strain softening model named exponential elasticity model developed by our group, and it has been added to the boundary element code for the first time.

When collapsing microbubbles are in the vicinity of cell membranes, we are showing that the collapse can result in the formation of liquid microjet travelling at high speed toward the membrane. Also we are showing that the fluid near the jet impinges the cell membrane with a high velocity resulting in high shear stress. The high shear stress along with the formation of jet ruptures the cell membrane transiently and therefore facilitates the uptake of drug into tissue through the pores of the membrane.

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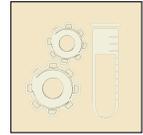
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Enzyme-Dependent Fluorescence Recovery after Photobleaching (ED-FRAP) in a whole heart.

Enzymes has been widely studied due to the fact that they act as important biological catalyst in many cellular processes, making them essential molecules for the proper understanding of organic processes. Due to the key role in cell metabolism and its involvement in many redox reactions, we have focused in the present study in the recovery of the reduce form of nicotinamide adenine dinucleotide (NADH). During aerobic energy metabolism, electrons are harvested from fuels and reduce NAD^+ to NADH. NADH is subsequently oxidized back to NAD^+ as these electrons are used to produce ATP, which is the source of most of the endogenous NADH fluorescence that can be detected in intact cardiac myocytes. Thus, NADH can be monitored by exciting the cardiac epithelium with UV light and changes in the amplitude of the signal indicate a change in the balance between NADH production and utilization. Previous work in cells and isolated mitochondria has demonstrated the efficacy of bleaching the NADH fluorophore and using the rate of recovery to determine the rate of NADH production alone. The goal of the present work is to expand this technique to intact, whole hearts using new LED technology in order to evaluate its enzymatic activity according to different conditions. Hearts from adult Sprague-Dawley rats were excised, cannulated via the aorta, and Langendorff perfused with oxygenated Tyrode's solution. Two 365nm UV LED sources were used to excite epicardium: one low power light (1.5mW) for continual imaging and one high intensity light (500mW) for bleaching. The light was focused on an area of approximately 7.01 mm². Lights were controlled using a custom LabVIEW program and the emitted signal was filtered at 475 ± 25 nm and captured using a CCD camera. There is a dependency of the depth of photobleaching and regeneration capacity with respect to the energy delivered to the heart. With energies imparted between 3.9 and 39 mJ during bleaching there was a decrease in amplitude from 4% to 9% respectively with a recovery related to the amount of photobleaching including the recovery time. With the application of ED-FRAP it is possible to obtain a great insight of cellular metabolism in the whole heart under different circumstances that could benefit or not its performance.

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Graduate Student

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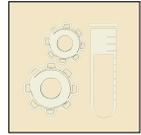
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Vortex core line tracking in a curved artery model under the physiological pulsatile flow using Particle Image Velocimetry

Investigations of secondary flow morphologies in curved pipes have been of interest for many years. Curvature-related vortical structures that produce secondary flows appear in cross-sectional planes of curved pipes. Such secondary flow vortical structures which alter energy transport have the potential to affect shear stresses in the flow and near-wall regions, and hence impact hemodynamics, drug delivery, concentration of various blood-borne particles and platelet activation. Moreover, blood is a complex material, composed of plasma, blood-borne particulates e.g. red blood cells (RBCs), leukocytes, and is a non-Newtonian, viscoelastic fluid. Therefore, the investigation of hemodynamic flow structures (i.e. vortices) associated with non-Newtonian fluid motion in curved arteries are expected to provide realistic insights into pathophysiological cardiovascular flows.

Most of the previous investigations of secondary flow structures were limited to 1) assumption of blood with Newtonian working fluid, 2) steady inflow condition rather than pulsatile flow and 3) cross-sectional planes at specified angles in the curved artery test-section. However, the current study is directed towards capturing secondary flow structures in several cross-sectional planes as well as axial planes under physiological pulsatile inflow condition, obtained from carotid artery flow rate. A non-Newtonian, viscoelastic working fluid having characteristics similar to blood with 40% hematocrit was prepared and used as a blood-analog fluid. A non-invasive method named Particle Image Velocimetry (PIV) is used to obtain velocity field with high resolution. The results revealed that due to separation of flow from inner wall vortical structures exist along the primary flow direction in the curved artery model between $\sim 5^\circ$ - 40° angular locations. These vortices differ from the Dean-, Lyne- and Wall-type (D-L-W) vortices in secondary flow and have not been previously reported. Downstream of 40° location secondary flow (D-L-W) vortices persist.

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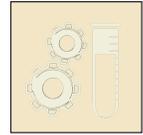
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Ultrasound-enhanced Drug Delivery for Treatment of Parasitic Diseases in the Eye

OBJECTIVE:

Infectious keratitis is a sight threatening rapidly progressive condition with an explosive onset associated with stromal inflammation and necrosis. Keratitis caused by fungi and parasites is difficult to treat and can result in loss of vision and blindness requiring corneal transplantation. Our main objective is to determine whether therapeutic ultrasound can be used in a safe and effective manner to improve treatment of parasitic and fungal keratitis leading to faster healing times and better outcomes in terms of vision preservation.

METHODS:

In vitro experiments were performed in a standard diffusion cell setup utilizing excised corneas of New Zealand White rabbits. The corneas were exposed to a 0.02% topical solution of Polyhexamethylene biguanide (PHMB), a compound used in the treatment of the treatment of Acanthamoeba keratitis. PHMB has average molecular weight of 2400 g/mol and is a hydrophilic compound with a high solubility in water (>40% w/w). Ultrasound was applied at frequency of 400 kHz and intensity of 0.8 W/cm² for 5 min (since these parameters were found optimal in our previous studies with steroid drugs). Heating bath was used to keep the corneas at the baseline temperature of 34 °C (physiological temperature). Temperature was measured intermittently with a thin thermocouple in the proximity of the cornea during ultrasound application. After the experiment, amounts of the drug that penetrated through the cornea was determined using a spectrophotometer, and these quantities were utilized to find corneal permeability to PHMB after ultrasound- and sham-treatment. Histological studies were performed to determine changes in the cornea due to ultrasound application.

RESULTS:

The concentration of PHMB in the receiver compartment of the diffusion cell was 2.85 ±0.87x10⁻⁵ % in the sham-treated cases and 16.32±5.99x10⁻⁵ % in ultrasound-treated cases. The PHMB delivery increase through the cornea due to ultrasound application appeared to be 5.7 times. The corneal damage due to ultrasound application was limited to the surface layers of the corneal epithelium. The measured temperature increase during ultrasound application was up to 2 °C.

CONCLUSIONS:

Our long-term goal is to develop an inexpensive, convenient, and minimally-invasive ultrasound method that can be applied in an outpatient clinic and eventually at home to facilitate delivery of medications into diseased eye tissues.

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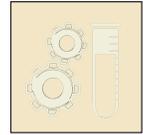
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

Identification and Enumeration of Lymphocytes Expressing Human CD4 Antigen in Whole Blood Using a Microfluidic Device

MOTIVATION:

Counting the number and percentage of CD4+ T cells in blood is an important criterion for categorizing HIV-related clinical conditions, such as AIDS. Methods to quickly and cheaply test for HIV are important for decreasing the rate of transmission and improving the quality of care for various states of progression. A simple, handheld CD4 cell counter would be instrumental in enabling faster diagnosis of HIV/AIDS at the point-of-care.

DESIGN:

A microfluidic device was designed and fabricated in poly-di-methyl-siloxane (PDMS) to hydrodynamically capture lymphocytes in single cell trap arrays. Testing of a previous CD4 specific device led to the newest version of this design, which uses a filter, passive retention traps and applies a streamline trapping method to arrays. The ordered array design allows for simple enumeration and observation, and is sized to capture and retain all white blood cell populations. The design was also simulated in COMSOL Multiphysics to recreate the observed phenomena of biological cell trapping and ensure deterministic trapping.

EXPERIMENTATION:

To test the device, whole blood samples ($< 10 \mu\text{L}$) were collected and processed to lyse and remove red blood cells as well as fluorescently label the CD4+ cells. An inverted microscope with software was used to record fluorescent and bright-field images of the captured cells at intervals in the channels of the device. These images were then input into a MATLAB algorithm to enumerate the captured CD4+ cells from the blood sample. Counts of fluorescent regions were produced and corresponded with cells seen in the bright-field images.

RESULTS:

Our results have shown that it is possible to capture and count CD4+ T-cells using a microfluidic trapping device. Size differentiated hydrodynamic trapping was effective in capturing CD4+ cells in the device and showed negligible cell loss during the experiment. Additionally, array applications of streamline trapping theory for multiple trap sizes can be greatly simplified to only a few representative simulations.

CONCLUSION:

This research indicates the design's potential to determine the possibility and progression of HIV/AIDS in a subject, so that the disease can be treated accordingly. The design potentially has the application of prolonged observation of all white blood cell populations and can be generalized to other diagnostic applications such as capturing schistosoma haematobium eggs from urine. Further modifications of the device to include blood sampling and processing procedures may allow this design to form the basis of a lab-on-a-chip portable HIV test.

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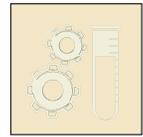
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SCHOOL OF ENGINEERING & APPLIED SCIENCE

miR-141 Regulates CDC25A Expression in MCF7 Breast Cancer Cells

Breast cancer is the most common cancer among women besides skin cancer, with about 232,570 new cases each year, and a one in eight chance of developing breast cancer in a woman's lifetime. The objective of this study was to elucidate the role of miR-141 in breast cancer development and progression. We aimed to identify potential target genes of miR-141, and its relevant molecular pathways in breast tumorigenesis. miRNAs are non-coding RNA molecules, about 18-24 nucleotides in length that silence protein-coding gene expression by binding to complementarity sequences of target genes. As a result of the prominent role miRNAs play in gene expression, miRNAs have been linked to cancer development and progression. From our recent studies, we found that certain miRNAs, including miR-141, are differentially expressed during breast cancer progression. miR-141 expression was analyzed in five different breast cancer cell lines. Next, bioinformatics techniques were used to identify possible downstream target genes for miR-141. The list of potential targets to be analyzed was narrowed down based on the function of the genes in relation to cancer progression. MCF7 breast cancer cells were seeded and transfected with miR-141 mimic or inhibitor, to promote or inhibit miR-141 expression, respectively. qRT-PCR was performed to test the relative expression of miR-141 in order to confirm successful transfection of miR-141 mimic or inhibitor. Among the 10 target genes we tested, CDC25A had the most significant change in expression. Dual-luciferase reporter assay is being employed to confirm the specificity of miR-141 in binding to CDC25A. We found miR-141 expression is lower overall in triple negative breast cancer (TNBC) cell lines, MDA-MB-231 and HS578T, and higher in non-TNBC cell lines, MCF7 and T47D, when compared to control cell line MCF10A. CDC25A, a suspected oncogene, was downregulated in miR-141 overexpressed cells when compared to the control. CDC25A was upregulated in MCF7 cells when transfected with miR-141 inhibitor. Our data suggest that miR-141 directly binds to and regulates CDC25A expression. Overexpression of miR-141 decreases the expression of CDC25A, which would inhibit cell proliferation and possibly increase apoptosis. Therefore, miR-141 could serve as a potential target for breast cancer management.

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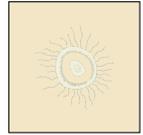
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Increase in contrast enhancement after chemoradiotherapy for glioblastoma predicts worse overall and progression-free survival

PURPOSE/OBJECTIVES:

Assessment of treatment response and progression is suboptimal in glioblastoma (GBM). In the context of pseudoprogression, radiographic change is a challenging parameter to assess. Based on unpublished data from Gzell et. al., a novel method for measurement of contrast enhancement demonstrates promise in predicting survival. We aim to determine if early measurement of radiographic change post-CRT using multiple methods is predictive for overall survival (OS) and progression free survival (PFS).

MATERIALS/METHODS:

Patients >17 years with primary GBM who received CRT at our institution between 2007-14, and had sequential post-CRT gadolinium-enhanced T1 weighted (T1+C) MRIs within our PACs, were identified. Inclusion criteria for analysis were: initiation on concurrent CRT, presence of 1 and 3 month post-CRT T1+C MRIs, absence of clinical or radiographic progression by 3 months post CRT, and no treatment with bevacuzimab prior to 3 months post-CRT. For the 29/97 eligible patients, post-operative (PO), 1 month and 3 month post-CRT T1+C MRIs were imported into Pinnacle for analysis. We quantified bi-directional product (BP), volume of the post-surgical cavity including surrounding enhancement (Vol), and volume of T1+C enhanced rim (Rim)with the cavity subtracted. We first sought to determine if a 25% increase between PO and 1 or 3 month T1+C MRIs was predictive of worse OS and PFS for each technique. If significant, we planned to determine if a 5% increase, or any increase were also predictive.

RESULTS:

Median age was 61.8 years. Median OS and PFS were 18.6 and 11.7 months. A relative increase in Rim volume of 25% at 3 months was a poor prognostic factor for OS (15.2 vs 31.3 months $p=0.001$) and for PFS (10.0 vs 15.5 months $p=0.011$). Even at 1 month, Rim increase of 25% was a poor prognostic factor for OS and for PFS. Vol and BP change did not statistically significantly predict OS. Rim increase of only 5% at 1 month predicted for worse OS (15.2 vs 26.9 months $p=0.010$). Further, at 1 month, any increase in Rim enhancement was associated with worse OS (15.2 vs 21.3 months $p=0.025$).

CONCLUSIONS:

Even minor change in the relative amount of enhancement surrounding the post-surgical cavity is an early prognostic factor for OS and PFS. Changes of Vol or BP were not significant predictors of OS. These findings suggest that either a lack of early response or underappreciated progression portends a significantly worse prognosis and raises the question of whether salvage therapies should be considered earlier in these patients.

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New feature of accelerated aging in xeroderma pigmentosum adults: Premature menopause

Xeroderma pigmentosum (XP) is a rare autosomal recessive disorder of DNA repair that has features of premature aging. Acute burning on minimal sun exposure is present in about half of the patients. XP patients characteristically develop freckle-like pigmented lesions on sun exposed skin before age 2 years. Continued sun exposure of XP children results in poikiloderma, a sign of accelerated photo-aging. XP patients have a 10,000-fold increase in melanoma and non-melanoma skin cancer which develops 33 to 60 years earlier than in the general population, another feature of premature aging. About 25% of the XP patients develop severe progressive neurological degeneration. Serial audiograms documented accelerated hearing loss in most XP patients including patients with mutations in the XPC gene who do not have severe neurodegeneration. We recently identified a new feature of accelerated aging in XP. We analyzed our 40 year follow-up study of 54 women with XP. We found that 9 of 12 menopausal women experienced cessation of menses before 40 years of age. The median age of XP women at menopause (31.5 yr) was about 20 years younger than in the general population (52.9 yr). Further, they all had mutations in the XPC gene. These results suggest that the ovaries sustain DNA damage and DNA repair plays a role in maintenance of normal ovarian function. We had not seen this premature menopause previously and suggest that it is being revealed as more XP patients survive into adulthood.

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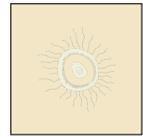
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Obstructive voiding symptoms following stereotactic body radiation therapy for prostate cancer

BACKGROUND:

Obstructive voiding symptoms (OVS) are common following prostate cancer treatment with radiation therapy. The risk of urinary retention (UR) following hypofractionated radiotherapy has yet to be fully elucidated. This study sought to evaluate OVS and UR requiring catheterization following SBRT for prostate cancer.

METHODS:

Patients treated with SBRT for localized prostate cancer from February 2008 to July 2011 at Georgetown University were included in this study. Treatment was delivered using the CyberKnife® with doses of 35 Gy-36.25 Gy in 5 fractions. UR was prospectively scored using the CTCAE v.3. Patient-reported OVS were assessed using the IPSS-obstructive subdomain at baseline and at 1, 3, 6, 9, 12, 18 and 24 months. Associated bother was evaluated via the EPIC-26.

RESULTS:

269 patients at a median age of 69 years received SBRT with a median follow-up of 3 years. The mean prostate volume was 39 cc. Prior to treatment, 50.6% of patients reported moderate to severe lower urinary track symptoms per the IPSS and 6.7% felt that weak urine stream and/or incomplete emptying were a moderate to big problem. The 2-year actuarial incidence rates of acute and late UR \geq grade 2 were 39.5% and 41.4%. Alpha-antagonist utilization rose at one month (58%) and 18 months (48%) post-treatment. However, Grade 3 UR was low with only 4 men (1.5%) requiring catheterization and/or TURP. A mean baseline IPSS-obstructive score of 3.6 significantly increased to 5.0 at 1 month ($p < 0.0001$); however, it returned to baseline in 92.6% within a median time of 3 months. Late increases in OVS were common, but transient. Only 7.1% of patients felt that weak urine stream and/or incomplete emptying was a moderate to big problem at two years post-SBRT ($p = 0.6854$).

CONCLUSIONS:

SBRT treatment caused an acute increase in OVS which peaked within the first month post-treatment, though acute UR requiring catheterization was rare. OVS returned to baseline in > 90% of patients within a median time of three months. Transient Late increases in OVS were common. However, less than 10% of patients felt that OVS were a moderate to big problem at two years post-SBRT.

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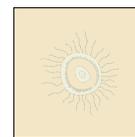
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Development of a novel Prussian blue nanoparticle-backpacked immunotherapeutic tool for improved anti-tumor efficacy

Adoptive immunotherapy with genetically modified T cells has shown great promise in the treatment of leukemia, but little efficacy against solid tumors. While T cells can home to the site of disease, they are rendered impotent by the inhospitable immunosuppressive tumor microenvironment. Although efforts to improve their resistance against immunosuppressive mechanisms are underway, we posit that the coupling of anti-tumor effector agents onto the T cells may be a better alternative. Essentially, these anti-tumor effectors will be linked to the T cells, using them as vehicles to arrive at cancer sites. Nanoparticles, for instance, are especially useful anti-tumor effectors as they can both mediate local photothermal ablation and can carry additional antitumor molecules that can improve the T cell efficacy.

We therefore aim to develop a platform that allows for the fabrication of this nanoparticle-T cell coupled construct. We hypothesize that nanoparticles can backpack onto T cells and can use these cells' innate homing ability to exert effects on tumor sites.

We have developed a biodegradable nanoparticle - Prussian blue - that can be easily biofunctionalized and can mediate photothermal effects against tumors. We will use NHS-ester crosslinking to attach these particles ("backpacking") onto different T cells (genetically modified, antigen-specific, immortalized), verify maintenance of T cell function (particularly homing) post-backpacking, and demonstrate improved efficacy of genetically modified T cells with backpacking nanoparticles against solid tumors in murine models.

Our preliminary findings suggest successful coupling, or "backpacking", of Prussian blue nanoparticles (98 ± 20 nm diameter) onto immortalized T cells through NHS-ester crosslinking. These backpacked T cells achieved stable conjugation (average zeta potential = -40 mV), and were able to perform photothermal therapy to ablate tumor cells (cell viability decreased by 49.5%, $p=0.04$) equally as effectively as the nanoparticles alone ($p>0.05$). The results thus serve as a springboard for future studies backpacking Prussian blue nanoparticles onto primary genetically modified T cells and in vivo examination of improved anti-tumor efficacy.

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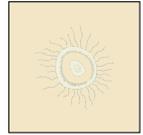
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Assessment of activation of NF- κ B pathway in colorectal carcinoma cell lines with lipopolysaccharide

Colonic epithelial cells are constantly exposed to lipopolysaccharide (LPS) due to the presence of Gram-negative bacteria in the intestinal flora. These bacteria rarely stimulates the colonic epithelial cells directly when this epithelium is intact. When a patient has colorectal carcinoma (CRC), LPS is still present but its effects on the cancerous cell lines is still unknown. During resection of colonic cancers the epithelial barrier is broken and all its cells (neoplastic and non-neoplastic) are exposed to high level of LPS form the residential bacteria and inflammatory signals ensue.

This study was meant to examine the role of LPS stimulation on colorectal carcinoma epithelial cell lines and in particular its level of activation of the NF- κ B pathway. The level of activation was measured after stimulating six established CRC cell lines (HCT-116, Ht-29, SW480, CaCo, Colo-205, and LoVo) with LPS, or serum free medium for the controls, at four different time points including at 1 hr, 45 min., 30 min., and 15 min. In order to establish level of activity of the NF- κ B pathway we measured the ratio phosphorylated:non phosphorylated form of I κ B, a protein that in basal conditions keeps NF- κ B inactive in the cytoplasm. Once the pathway is active, the protein is phosphorylated (p-I κ B) and frees the transcription factor to translocate to the nucleus and initiate the gene transcription of inflammatory related genes

Cell lysates were properly collected with a specific protein lysate buffer and the ratio of proteins was established by measuring both I κ B and p-I κ B by western blot. We came to find that the pathway was differently activated across the six cell lines, suggesting that different CRC types with different behaviors, as is being described by different research groups. An inflammatory-related subtype could be represented by those cell lines that are activated with the bacterial endotoxin. These types could be addressed from research and therapeutic stand points, with a better knowledge of genes and proteins expressed upon inflammatory activation. These are the next steps in our study.

STATUS

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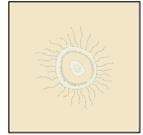
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Rnaseh2c and Emp1 are candidate metastasis susceptibility genes in breast cancer

Breast cancer is the second leading cause of cancer-related female deaths in the United States, the majority of which are due to distant metastases. Therefore, elucidating the mechanisms that drive metastasis is critical to improving patient outcome. Using a strategic mouse breeding scheme combined with quantitative trait loci and microarray analyses, we identified candidate metastasis susceptibility genes Rnaseh2c and Emp1. Rnaseh2c encodes a scaffolding subunit of Ribonuclease H2 which removes RNA from RNA:DNA heteroduplexes such as those generated during replication and transcription. Though mutations in this gene are known to cause the neurological autoinflammatory disorder Aicardi-Goutières Syndrome, Rnaseh2c has not previously been linked to cancer. Epithelial membrane protein 1 (Emp1) is thought to function in cellular adhesion and signaling. Human single nucleotide polymorphisms (SNPs) associated with breast cancer outcome identified in a cohort of 5000 Chinese breast cancer patients revealed an association between EMP1 expression and distant metastasis-free survival. Overexpression of Emp1 in several cancer cell lines has been shown to result in increased apoptosis, decreased motility and invasion, and reduced VEGFC expression. In order to investigate the roles of these genes in metastasis, we separately knocked down Rnaseh2c and Emp1 in mouse mammary cell lines using siRNAs. We observed fewer pulmonary metastases and reduced tumor burden in spontaneous metastasis assays in vivo, suggesting both genes promote tumor progression. Knockdown of Rnaseh2c also reduced motility in vitro. Interestingly, treatment of Rnaseh2c knockdown cells with doxorubicin neither altered cell cycle progression nor promoted p21 expression, suggesting that reduction of Rnaseh2c expression does not prompt a p53-mediated DNA damage response. Current experiments are examining the effect of gene overexpression on metastasis in vivo. Future studies will focus on determining whether the effect of Rnaseh2c on metastasis is through the RNase H2 complex, and if Emp1 functions through a known signaling pathway. Elucidating how differential expression of these metastasis susceptibility genes impacts metastasis can contribute to both the development of novel metastasis biomarkers and therapeutic targets.

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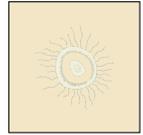
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Downregulation of polycomb group protein BMI1 and breast cancers stem cell phenotype by PLK1 inhibition

The polycomb group protein BMI1 is an important regulator of cancer stem cell (CSC) phenotype and is often overexpressed in cancer cells. Its overexpression leads to increase in CSC fraction and therapy resistance in tumors. BMI1 functions via polycomb repressive complex 1 (PRC1) -mediated gene silencing and also via PRC1-independent transcriptional activities. At present, very little is known about the therapy reagents that can efficiently inhibit BMI1 expression, and the CSC phenotype. Here, we report that the polo-like kinase 1 (PLK1) regulates BMI1 expression, and that its inhibition can efficiently downregulate BMI1 expression and PRC1 activity, and induce premature senescence in breast cancer cells. Next, we show that the PLK1 inhibition suppresses breast cancer stem cell (BCSC) phenotype and BMI1 overexpression restores BCSC phenotype in breast cancer cells. We also show that the exogenous BMI1 overexpression mitigates anti-oncogenic effects of PLK1 inhibition and overcomes senescence induction by PLK1 inhibitors. We further show that PLK1 inhibition downregulates BMI1 and BCSC phenotype by upregulating the miRNA-200c/141 cluster, which encodes miR-200c and miR-141, both of which are known to posttranscriptionally downregulate BMI1 expression. Thus, our data suggest that PLK1 inhibitors can be successfully used to inhibit growth of tumors in which PcG protein BMI1 is overexpressed or the PRC1 activity is deregulated.

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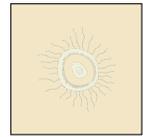
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The Effect of Mechanical Stimulation on PC3, LNCap and HT-29 Cancer Lines

In the United States, prostate cancer is the most common internal tumor in men, and the second leading cause of cancer related deaths. Prostate carcinomas preferentially metastasize to secondary sites in the bone, particularly to the spine. Once this metastasis occurs quality of life is drastically decreased and an ominous prognosis is generally forthcoming. The ultimate aim of this research is a therapy to prevent or delay the metastasis.

In order to identify and further understand the mechanisms of prostate cancer metastasis, this study focused on the metastatic effects of mechanical stress, induced in vivo as a result of exercise. Human prostate cancer: PC3 and LNCap, and human colon cancer: HT-29, were cultured and maintained at 37°C in a humidified atmosphere. Once the cells reached confluence, they were seeded onto two groups of slides. One group was subjected to mechanical stimulation, while the control group was isolated from all vibration and other mechanical movement.

After 24 hours, the medium in each group was collected and filtered. The produced growth factors were added to cultured mesenchymal cells, MLO-Y4 osteocytes, and monocytes. The subsequent effect of the cytokines on these basal was analyzed using measurements of migration and growth. As statistical analysis revealed the data to have a skewed distribution, non-parametric testes were selected. Using the Mann-Whitney U test (n=4-5), there was statistical significance at $p < 0.05$. It was shown that there was an increase in growth of mesenchymal cells in contact with medium from the stimulated PC3 line and an increase in migration of mesenchymal cells in contact with the stimulated LNCap line. The same distribution, with an increase in migration occurred when the mediums were added to Raw monocytes. When the mediums were added to the MLO-4Y osteocytes, there was a decrease in migration from PC3 and HT-29 cells that had not undergone mechanical stimulation.

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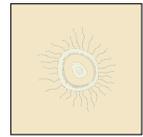
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SCHOOL OF MEDICINE & HEALTH SCIENCES

High-Quality Variant Calling in Targeted Exome Sequencing in Cancer

The advent of next-generation DNA sequencing technologies has allowed for the genomic profiling of cancers at an unprecedented depth. Targeted sequencing panels that assay a small number of genes with known therapeutic indicators are both fast and inexpensive. However, the resulting data presents unique challenges for the downstream analysis. We used the Fluidigm Access Array System to design 321 amplicons targeting 17 genes. We applied this panel to a set of 323 samples (without corresponding normal) of several cancer types, and sequenced the resulting PCR products on the Illumina HiSeq platform. The conventional analytical pipeline of preprocessing, read mapping, and variant calling proved inadequate, resulting in false variants and the failure to discover true variants in the tumor samples.

We created a pipeline that began by making use of the limited amplicon size and known PCR primer sequences to join and trim the paired-end reads in the preprocessing step. Failing to remove the primer sequences masked the correct origin of reads that were derived from similar regions elsewhere in the genome, such as pseudogenes, causing false variants to be called in our target regions. However, reads with primers removed in our pipeline were more likely to map to multiple places in the genome. Rather than eliminating all such multi-mapping reads, where possible we used the characteristics of the amplicons to distinguish the reads that were likely derived from our regions of interest. Variant calling resulted in a set of single nucleotide polymorphisms (SNPs), small indels, and short haplotypes. Again utilizing the features of our amplicon-based data, we were able to discover a set of variants resulting from larger indels (7-38bp), most of which were missed using the conventional analytical approach.

STATUS

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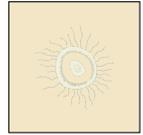
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Incidence and characterization of pure non-urothelial cancers over a 10 year period

BACKGROUND:

Urothelial carcinoma makes up the most common histology in the bladder as well as the upper tract. For bladder cancer, urothelial carcinomas make up over 90% of the histology. Urothelial cancers may also occur other than a pure form, with mixed or variant histology that includes squamous, glandular, sarcomatoid, micropapillary, small cell and plasmacytoid.¹ Finding a non-urothelial component predicted for worse survival in both overall and recurrence-free survival in a multivariate analysis when histologic type was compared (pure urothelial versus urothelial with mixed histologic features). Furthermore, findings of mixed urothelial with divergent variants also portends for a higher grade, with worse outcomes for recurrence and progression.^{2,3} In addition, patients with non-urothelial primary bladder cancer, such as pure squamous cell carcinoma, small cell carcinoma, pure bladder sarcoma or pure adenocarcinoma, are also known to have typically worse outcomes.^{4,5} However, the overall characterization of this group of patients is rare. There are no randomized clinical trials evaluating treatment modalities for non-urothelial cancers and current treatment is based on data extrapolation from case studies.

METHODS:

We seek to determine retrospectively the incidence and characterize the patterns of presentation, treatment, and outcomes of patients who presented with pure non-urothelial cancers at the George Washington University Hospital over a 10-year period. We will obtain the information from the Cancer Center Tumor Registry Data.

ANTICIPATED OUTCOMES:

The aim of the project is to identify characteristics of patients with non-urothelial bladder cancers and may have potential implications in the early detection and treatment of the disease, which may lead to improved survival.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Evaluation of lymph node density and number of nodes positive in treatment outcome of head and neck squamous cell carcinoma

BACKGROUND:

Head and neck squamous cell carcinoma (HNSCC) affects approximately fifty thousand people in the US a year and is currently staged by the AJCC TNM staging system. Recent studies have supported the use of other prognostic tools alongside TNM staging in predicting survival outcomes for these HNSCC patients, including lymph node density (LND), which is the ratio of positive lymph nodes to the total lymph nodes removed during treatment, and number of nodes positive (NNP). In this study, we evaluate LND and NNP in predicting survival of HNSCC patients at different HNSCC surgical subsites.

METHODS:

We collected the records of 10,566 oral cavity, pharyngeal, and laryngeal cancer patients from the Surveillance, Epidemiology, and End Result Program (SEER) who underwent neck dissection from 2004 to 2011 for the evaluation of regional lymph nodes. Chi-square was used to examine associations between outcomes and predictors. Multivariate cox regression was used to examine times-to-event, adjusting for age, sex, race, AJCC6 category, tumor site, and radiation use. Analyses were done for overall survival (OS) and disease-specific survival (DSS).

RESULTS:

Overall survival. After adjusting for covariates, NNP was significantly associated with time to death. Having 1 NNP had similar time to death as having 0 NNP ($P=0.42$, $HR=1.06$), but as nodes positive increased above 1 NNP, the likelihood of death increased in a linear fashion: 2-3 NNP ($P=.0001$, $HR=1.32$), 4-6 NNP ($P<.0001$, $HR=1.86$), and 6+ NNP ($P<.0001$, $HR=2.83$). LND was significantly associated with time to death as well. Higher LND was associated with reduced time to death, although the association was not linear: 0-0.6 LND ($P=0.25$, $HR=1.09$), 0.6-.189 LND ($P<.0001$, $HR=1.48$), .189-1 LND ($P<.0001$, $HR=2.07$), 1 LND ($P=0.12$, $HR=1.48$).

Disease-specific survival (DSS). NNP was significantly associated with DSS, with increasing NNP having a linear increased risk of death: 1 NNP ($P=0.29$, $HR=1.10$), 2-3 NNP ($P<.0001$, $HR=1.41$), 4-6 NNP ($P<.0001$, $HR=2.15$), 6+ NNP ($P<.0001$, $HR=3.27$). LND was also significantly associated with DSS but the association was somewhat weaker than for NNP: 0-0.6 LND ($P=0.19$, $HR=1.12$), 0.06-.189 LND ($P<.0001$, $HR=2.33$), .189-1 LND ($P<.0001$, $HR=2.33$), 1 LND ($P=.0041$, $HR=1.64$).

CONCLUSION:

Both LND and NNP are significant predictors in overall and disease specific survival in HNSCC patients, where patients with 0-1 NNP and the lowest LND had the lowest death rates. The non-linear relationship of LND needs to be explored. Furthermore, future comparisons need to be made with TNM pN staging via HNSCC subsite analysis.

STATUS

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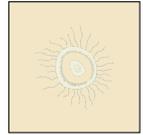
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Gene expression markers from inflammation-dependent and independent metastatic lesions in patients with advanced melanoma

IL-18, an immunostimulatory cytokine, has antineoplastic properties that has shown significant promise in preclinical animal models and phase I clinical trials in stimulating the immune system to combat certain cancers.³ For this reason, exogenous IL-18 has been proposed as adjuvant therapy against melanomas, although demonstrated limited efficacy in a phase II study in patients with metastatic melanoma.^{1,2,5} Additionally, it has been associated with elevated serum levels in patients with various cancer types, and linked to cancer progression and metastatic recurrence.^{1,4,5,6,7} Thus, the role of IL-18 in cancer pathogenesis, melanoma included, remains unclear. The aim of the study was to identify IL-18-dependent genes in metastatic human cell lines, and to verify their expression levels in primary and metastatic lesions from patients with melanoma. Total RNA was purified from untreated and IL-18-treated A375 melanoma cell lines, and hybridized to custom-made 36K-oligonucleotide microarrays. The gene expression profile of melanoma cells in response to recombinant IL-18 was determined through non-supervised analyses of hierarchical groups with Cluster and Tree View programs. We found 50 overexpressed and 26 underexpressed genes in the A375 cell line. Interestingly, from the list of overexpressed genes, we found 7 genes (IQCE, PFAS, PPAT, PTPLAD1, UBE2C, UMPS, ZBTB9) to be similarly overexpressed by metastatic melanoma, and 3 of these genes (IQCE, PFAS and PTPLAD1) were subsequently found to be overexpressed in more than 90% of 19 cutaneous primary melanoma lesions that included both low and high Breslow index lesions. The clinical significance of these signature genes was demonstrated by their remarkable expression in lesions from melanoma patients despite being obtained from IL-18-treated cultured human melanoma cell lines. These findings suggest that some of these IL-18-dependent signature genes are already operating in early stage melanomas. Furthermore, we found that specific IL-18-dependent genes were expressed by cutaneous metastasis and only one third of lymph node metastasis, suggesting that expression level of these genes also changed according to body location and may have organ site-specific regulation.

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STATUS

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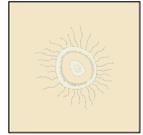
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Volumetric Analysis of CyberKnife Treatment

INTRODUCTION:

Recent studies have demonstrated diminished cognitive function, worse quality of life, and no overall survival benefit from the addition of adjuvant whole brain radiation therapy (WBRT) to stereotactic radiosurgery (SRS) in the management of brain metastases. This study analyzes the treatment outcome of SRS based on the total tumor volume compared to the absolute number of lesions.

METHODS:

A retrospective analysis of hospital records at Virginia Hospital Center for patients with brain metastases who underwent CyberKnife treatment between June 2008 and June 2014 was performed. Previous treatment history, metastatic tumor dimensions, and outcomes were recorded. Predictors of neurological defects, local tumor progression, and overall survival were assessed with univariate and multivariate analysis.

RESULTS:

We identified 127 adult patients (33% male) with a median age of 61.5 years and a median follow-up of 6.1 months. Worsening neurological defects showed an association with an increased number of lesions ($p < .02$), age ($p < .05$), and a total tumor volume greater than the median volume of 7cc ($p < .05$). For local tumor progression, patients who have received WBRT were less likely to progress (.74, 95% CI .49, 1.10), while those who received chemotherapy (1.48 95% CI 1.00, 2.24), or surgery (1.40 95% CI .88, 2.16) without WBRT were more likely to progress. The number of lesions treated with CyberKnife radiosurgery ($p < .05$) was the only negative factor associated with patients' survival.

CONCLUSION:

Our data suggest that a total tumor volume limit of 7cc correlates with worse neurologic outcomes following CyberKnife radiosurgery. In addition, WBRT appears to have a role in improved survival for patients with increased tumor burden. A prospective study is warranted to validate these findings.

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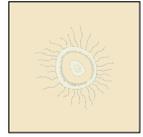
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Head and Neck Cancer: Evaluating timeliness of care and the impact of Cancer Care Coordination

Effective head and neck cancer care requires a multidisciplinary approach and therefore well-managed coordination between specialties and patient's to ensure timely delivery of care. There is scarce research on the effect that delays in the treatment of head and neck cancer has on patient outcomes. Patient navigation is a concept that has seen much success when applied in breast and colon cancer settings. It promises to be of much benefit to head and neck cancer patients as well.

The aims of this study are to determine how delays in the treatment of head and neck cancer affect patient outcomes and how a cancer care coordinator (CCC) will improve timeliness of care, patient compliance and outcomes. We measured specific time intervals in the treatment process of H&N cancer following pathological diagnosis, before and after the hiring of a CCC. This data was further divided by cancer stages I/II and stages III/IV. A Total of 182 patients were identified with head and neck cancer diagnosis after December 31, 2006. There were 125 patients in the Pre-CCC group and 57 patients in the Post-CCC group.

The overall means and standard deviations were calculated between the two cohorts based on three parameters: 1) Time from pathological diagnosis to initiation of treatment, 2) time from surgery to the start of post-operative chemotherapy and/or radiation, and 3) time from initiation of radiation to its completion or discontinuation. The overall numbers in the above groups were 1) 48 vs. 50, SD: 11.5 and 6.5 ($p=0.17$); 2) 71 vs. 76 SD: 83 and 0.5 ($p=0.80$); 3) 58 and 59 SD: 2 and 8.5 ($p=0.35$).

The results for Stage I/II were the following for Pre CCC and Post CCC: 1) 46.22 and 38.18 ($p=$ not sig); 2) 64.7 and 38.5 ($p=$ not sig); 3) 52 and 44.5 ($P=0.0187$ with 95% CI of 1.37 to 13.62). Results for Stage III/IV were: 1) 44.62 and 35.93 ($p=0.0002$ with 95% CI 4.25 to 13.12); 2) 71.94 and 67 ($p=$ not sig); 3) 59.1 and 60.9 ($p=$ not sig).

With this data we see that the role of the CCC is critical in improving the timeliness of the diagnostic and therapeutic process in this population. These results add strong evidence to the limited existing literature on the necessity of patient navigation for the multidisciplinary approach of head and neck cancer care.

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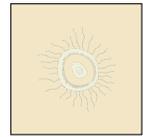
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Characterization of differences between prostate cancer (PCa) patients presenting as de novo versus primary progressive (PP) metastatic disease

BACKGROUND:

In 2014 alone, 29,480 men were projected to die of Prostate Cancer. Approximately 4% are metastatic on presentation (de novo, dn) while a subset of men progress on to metastatic disease during the course of their disease (primary progressive, pp). We sought to characterize and compare differences in disease characteristics and outcomes between those who present as dn vs pp metastatic disease in our institution.

METHODS:

A retrospective chart review of dn vs pp metastatic patients for the past 2 years was undertaken. Characteristics such as demographics, Gleason score, duration of hormone sensitivity, sites of metastasis, and treatment, were obtained. T-test and Fisher's exact test were used to test differences in patient and disease characteristics between dn and pp metastatic patients.

RESULTS:

Preliminary results on 10 de novo and 13 primary progressive patients are presented herein. Statistically significant differences were noted for median age at diagnosis: de novo 66.5 years of age (63-71) vs primary progressive 58 years of age (54-63), $p = 0.05$; Median duration of hormone sensitivity: de novo 149.5 days (130-212) vs primary progressive 1159 days (1022-1682), $p = 0.0002$; Median Gleason Score: de novo 9 (6-10) vs primary progressive 8 (6-9), $p = 0.002$. Although there was a tendency towards higher mean and median of PSA levels at metastasis for the de novo (232.05 and 52.20 ng/ml, respectively) vs primary progressive (78.88 and 10.20 ng/ml, respectively), the difference was not statistically significant ($p = 0.28$). There was also non-significant trends for the de novo group to be more likely to have a lymph node metastasis (70%, $p = 0.40$) and Caucasian (62%, $p = 0.16$) compared to the primary progressive group (46% lymph node metastasis, 23% Caucasian).

CONCLUSION:

While the reported samples are small, our data reveals a potential difference in disease aggressiveness in those presenting with de novo metastatic cancer with higher-risk disease and shorter time to castration resistance. Further data collection is underway and a prospective trial assessing the difference molecularly between both groups is planned to confirm these findings.

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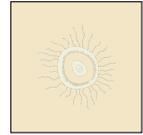
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Identification of Patients with Inflammation-Dependent Head and Neck Squamous Cell Carcinoma Profile

While the genetic changes that occur within cancer cells themselves, such as activated oncogenes or dysfunctional tumor suppressors, are responsible for many aspects of cancer development, they are not sufficient. Tumor progression is dependent on ancillary processes involving cells of the tumor microenvironment that are not necessarily cancerous themselves. Host cytokines and growth factors play key roles in both inflammation and tissue regeneration but also in cancer by promoting proliferation, angiogenesis and immune suppression. Tissue vasculature is a vital part of its microenvironment, supplying oxygen, nutrients, and growth factors to rapidly dividing cancer cells and providing a mechanism for metastatic spread.

Recently, there have been increasing clinical and experimental evidences on the carcinogenic and prometastatic role of inflammation in Head and Neck Squamous Cell Carcinoma (HNSCC). The link between cancer and inflammation has been further substantiated with studies that show the triggering of Toll Like Receptor 4 by inflammatory agents, such as bacterial endotoxin lipopolysaccharide (LPS), which in turn increases experimental metastasis by causing tumors to have an increased NF- κ B translocation leading to more efficient neovascularization, immune resistance and growth (Szczipanski et al., 2009). In particular, it has shown that an inflammatory microenvironment induces tumor expression of COX-2 mRNA/ proteins resulting in an increase of proangiogenic factor secretion VEGF (Galo et al., 2001). While current research has established the link between HNSCC metastasis and inflammatory agents, novel biomarkers are needed for clinical validation purposes, and specially for identifying which patients have HNSCC cancers that are using inflammatory factors to invade and metastasize.

My initial goal focused on culturing a human HNSCC lines that would be used in later parts. Part one of the project, conducted by Dr. Vidal, consisted of investigating the stromagenic and angiogenic cytokines involved in an experimental metastasis model of hepatic colonization. In this study, PAM 212 and PAM LY-2 murine Squamous Cell Carcinoma cell lines were intrasplenically injected in Balb/c mice. Anti-murine CD31, anti-alpha actin smooth muscle and ant-ki67 antibodies were used to identify angiogenesis, stromagenesis and tumor cell proliferation.

The results showed that differential stromagenic and angiogenic cytokine patterns and endogenous oxidative stress balance were associated with replacement/invasive-type and pushing/expansive-type hepatic metastasis growth mechanisms of Squamous Carcinoma cells. These results suggest different molecular targets for therapeutic innovation against the two reported hepatic metastasis mechanisms.

STATUS

Medical Student

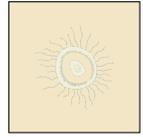
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INSTITUTE FOR BIOMEDICAL SCIENCES

Exon skipping as a mechanism for health disparities in African American prostate cancer

BACKGROUND:

Prostate cancer is the second highest cause of male cancer-related deaths in the United States. In addition to widespread prevalence, prostate cancer also exhibits dramatic race disparities. Prostate cancer risk, incidence, and mortality are greatly increased in African American (AA) men compared to European American (EA) counterparts. Increasing evidence suggests that, after accounting for epidemiological factors, a remaining component of this disparity is due to intrinsic genetic and biological factors. One possible mechanism for this health disparity is differential regulation of splicing factors, leading to disparate patterns of alternative splicing of genes in key oncogenic pathways.

PURPOSE:

In this study, we investigate the role of differential expression of splicing factors and exon skipping in the receptor tyrosine kinase family on prostate cancer health disparities.

RESULTS:

Microarray and RT-qPCR data revealed differential expression of serine/arginine rich (SR) splicing factor family members in AA patient samples compared to EA. The increased expression of SR splicing factors in AA prostate cancer specimens was confirmed via immunohistochemistry. We then identified FGFR3, a member of the known oncogenic family of receptor tyrosine kinases, as a candidate for differential alternative splicing. Exon profiling of the FGFR3 gene confirmed exon 14 skipping in AA but not EA specimens. Computational analysis of the intronic sequences flanking exon 14 identified cis-acting binding site sequences for the SR family of splicing factors. Finally, functional assays in cell lines confirmed that the short isoform of FGFR3 confers an oncogenic advantage.

CONCLUSION:

We have shown that AA prostate cancer patient specimens have increased expression of specific splicing factors compared to EA specimens. We have identified an oncogene of interest, FGFR3, which undergoes exon skipping that is specific to AA cancers. In cell lines, this shorter isoform of FGFR3 leads to an increased oncogenic phenotype based on invasion and proliferation assays. Thus, differential expression of splicing factors and exon skipping in FGFR3 may be one mechanism contributing to the increased aggressiveness of prostate cancer in AA patients.

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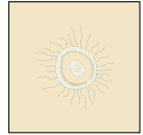
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Pan-cancer variome DNA functional elements: explaining variation through regulation

Sequencing technology has rapidly improved in recent years, decreasing the expense of the technology and enabling identification of single nucleotide variations (SNVs) in different cancer lines. These findings are widely studied, driven by a coherent effort to unify the fragmented information generated into comprehensive databases. DNA functional elements are biochemically active DNA regions which occur outside of coding elements. They have been found widely throughout the genome – up to 80% as estimated by the ENCODE project – and biologists are realizing that regulatory elements account for at least some of the biological complexity of life. In this study, we investigate the frequency of variation found in tissue-independent DNA functional elements. 14 different functional elements were used in this study. Out of 1 651 364 cancer related SNVs that matched one or more of 5 680 308 bases of total DNA elements collected, we identified a number of variations that significantly affect a broad range of DNA functional elements and variation that occur more often than would be expected by random chance. Pan-cancer analysis across several different cancer types led to the identification of SNVs located in functional elements found in 3 or more cancer types.

STATUS

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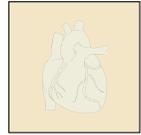
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Gender Difference in Healthcare Costs in the Emerging Adult Congenital Heart Disease Population

BACKGROUND:

It is important to understand the factors that drive costs as patients with congenital heart disease (CHD) transition from pediatric to adult health care. Gender differences in the prevalence and complexity of CHD are expressed throughout life, but it is unknown if this is reflected in healthcare costs during the transitional years.

METHODS:

California State Inpatient Databases 2005-2009 were used to conduct a retrospective study on inpatient admissions of CHD patients 10-29 years old. This population was divided into three study groups: (1) all male admissions (AM), (2) all female admissions (AF), and (3) female admissions unassociated with reproductive health codes.

RESULTS:

Female admissions without associated reproductive diagnostic codes were fewer than male admissions, but the admissions for all females exceeded that of in the twenties. Males with CHD have higher inpatient admission costs than their female counterpart ages 10-29, but this cost difference narrows in the twenties. During the twenties, males have lower hospital admissions and higher mortality than females. Males also have more emergency admissions at ages 10-24 and longer length of stay (LOS) at ages 15-29. At all age groups, males have higher percentages of no insurance and unknown insurance.

Females ages 10-29 have statistically significantly more admissions for atrial septal defect (ASD). Males ages 15-29 have statistically significantly more admissions for CHD surgery, arrhythmia/ congestive heart failure (CHF), and trauma; males ages 15-24 have statistically significantly more admissions for catheterization/ electrophysiology studies. The cost impact for several factors were not statistically significant, except for LOS where males cost \$3296.677 and females cost \$42140.117 ($p = 0.0441$).

CONCLUSION:

The driver of healthcare utilization and costs is the gender-specific presentation of CHD. Females have lower inpatient costs than males, despite unilateral reproductive costs and more admissions in their twenties. Females generally have significantly more ASD admissions, fewer emergency admissions, and shorter LOS, all of which are associated with lower total admission costs.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Are Guidelines Effective In Increasing Awareness And Detection Of Peripheral Arterial Disease (PAD)?

BACKGROUND:

Peripheral arterial disease (PAD) represents atherosclerotic disease in the large-vessel arterial beds excluding the coronary and cerebral circulation. PAD is asymptomatic in 50% of patients which often delays diagnosis. Early recognition can minimize complications such as limb loss and prevent cardiovascular complications, a major cause of morbidity and mortality in these patients. AHA/ACCF guidelines released in 2005 and 2011 have focused on augmenting PAD surveillance. The goal of this study is to evaluate the response to guidelines by measuring new diagnoses of PAD from 2006-2013 at an urban, university medical center.

METHODS:

Medical records of patients newly diagnosed with peripheral arterial disease from 2006-2013 were evaluated under the premise of intuitional IRB. There were no exclusion criteria. Patient age, gender, and ethnicity were obtained. An anonymous database which maintained patient confidentiality was created with new diagnoses of PAD grouped by their respective months and years.

RESULTS:

Medical records of 758,927 patients were surveyed for the diagnosis of PAD. The total patients seen increased annually, from 74,666 patients in 2006 to 126,683 patients in 2013. Average age of the patient population increased (47.234 years-49.374 years) over the eight year period. 5,242 patients (2628 males, 2614 females) were diagnosed with PAD. The incidence of PAD increased from 2006-2009 (0.00715-0.00860) and decreased from 2009-2013 (0.00860-0.00429). The average age at diagnosis did not follow a linear trend but increased from 65.227 years to 69.864 years from 2009-2013.

CONCLUSION:

Individuals with peripheral arterial disease (PAD) have higher morbidity and mortality due to cardiovascular causes. This study is of interest because despite a growing, aging patient population and a recommended earlier age of surveillance, the findings show an overall decline in incidence of PAD and an increasing age at diagnosis from 2006-2013. Suspected lack of guideline awareness, dearth of primary care literature about PAD, and insufficient diagnostic experience among primary care physicians may explain these findings. Further research about guideline efficacy and physician awareness of PAD should be performed.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Feasibility of Synthetic High-Fidelity Ventricular Septal Defects (VSD) Models for Stimulation and Education

OBJECTIVE:

Although simulation-based education is now commonly utilized in medicine, its use in the instruction of congenital heart disease remains limited. The objective of this study is to evaluate whether heart models created with three-dimensional printing technology can be effectively incorporated into a simulation-based congenital heart disease and critical care training curriculum for pediatric resident physicians.

DESIGN:

Utilizing heart models created with a three-dimensional printer, pediatric residents participated in a 60-minute simulation seminar with three consecutive components: (1) didactic instruction on ventricular septal defect anatomy; (2) didactic/simulation-based instruction on echocardiographic imaging of ventricular septal defects and anatomical teaching/operative simulation of ventricular septal defect repair; (3) simulation-based instruction on postoperative critical care management of ventricular septal defects.

SETTING:

Academic, free-standing, children's hospital with quaternary care referrals.

PARTICIPANTS:

Twenty-three pediatric resident physicians.

OUTCOME MEASURES:

Subjective, Likert-type questionnaires assessing knowledge acquisition, knowledge reporting, and structural conceptualization of ventricular septal defects.

RESULTS:

Three-dimensional printing technology was successfully utilized to create heart models of five common ventricular septal defect subtypes. After using these models in a simulation-based curriculum, pediatric residents were found to have improvement in the areas of knowledge acquisition ($P = .0082$), knowledge reporting ($P = .01$), and structural conceptualization ($P < .0001$) of ventricular septal defects, as well as improvement in the ability to describe and manage postoperative complications in ventricular septal defect patients in the critical care setting.

CONCLUSIONS:

The utilization of three-dimensional printing in a simulation-based congenital heart disease and critical care training curriculum is feasible and improves pediatric resident physicians' understanding of a common congenital heart abnormality.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Seasonal Pattern in Births of Patients Born With Congenital Heart Diseases

The most common congenital anomalies are of cardiovascular origin. While the etiology of many congenital heart diseases (CHDs) remains elusive, it is generally understood that the disruption of embryological processes leading to the emerging phenotypes are often multi-factorial in nature and frequently occur in seasonal clusters. The proportion of CHDs that may be preventable through changes in the fetal environment remains unclear. Current literature on this subject is often dated, occasionally inconsistent, and does not necessarily elucidate whether there are any potential developmental links between the observed defects. To address these challenges we have used statistical measures that may be more appropriate for investigating seasonal patterns and grouped lesions based on related anatomy. The objective of our investigation was to determine whether seasonal patterns could be observed for patients born with CHDs and explore such variations across major anatomical types. All patients who underwent cardiac surgery for a CHD at The Hospital for Sick Children between 2002 and 2011 were included (N=3775). Seasonal variation was significantly associated with anatomical types of CHD. Left heart lesions and septal defects (N=1,716) peaked in November and October, while excess cases of right heart lesions (N=463) were noted in September. Finally, abnormalities of the great arteries and the aorta (N=742) were associated with a peak in December and March through May. It is known that a number of core cardiac transcription factors function in a complex transcriptional network in which factors can regulate each other's expression in a highly structured and coordinated fashion. Clustering of seasonal patterns noted across major anatomic groups may therefore suggest involvement of related network of genes for each of the anatomical groups. Furthermore, there may be a developmental link with environmental influences or possible gene-environment interactions.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Use of 3-d echocardiography and cardiac magnetic resonance in Mitral Valve Prolapse

Mitral valve prolapse (MVP) is the bulging of the mitral valve into the left atrium during ventricular systole. It is a common disorder that is prevalent in approximately 2 to 3 percent of the general population. Patients with MVP range from being asymptomatic to having severe complications such as congestive heart failure, endocarditis, mitral regurgitation, arrhythmias and sudden death. Depending on the severity of symptoms, patients may be treated pharmacologically, or by surgical repair/replacement of the mitral valve. The integrity of the mitral valve depends on the interactions between the annulus, the anterior and posterior leaflets of the mitral valve, chordae tendonae, papillary muscles, and left ventricle. MVP may also be caused by abnormal thickening of the valve due to excessive proliferation of fibroblasts in the cardiac muscle called myocardial fibrosis. Determining myocardial fibrosis is critical because the presence of preoperative fibrosis is associated with worse postoperative outcomes in patients with chronic mitral regurgitation undergoing mitral valve repair.

MVP is predominantly diagnosed using 2-dimensional echocardiography to examine the various components that make up the mitral valve apparatus. Use of 3-dimensional echocardiography and cardiac magnetic resonance (CMR) is useful for clinicians. 3D echocardiograms improve the understanding of the mitral valve anatomy, function and pathology. It helps assess the severity of mitral stenosis or regurgitation, chordal rupture, and the geometry and volume of the valve. CMR is a noninvasive imaging tool that provides quantitative data in valve morphology, velocity of blood flow, abnormal traction and excursion of the papillary muscle, and extent of myocardial fibrosis of the mitral valve. Although the use of 3-dimensional echocardiography and cardiac magnetic resonance (CMR) in MVP are valuable, their usage has not been clearly defined. This paper will investigate the use of 3-dimensional echocardiography and CMR imaging for diagnosing and characterizing MVP, and identifying patients with myocardial fibrosis.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Truncated protein MyBP-C allelic expression in hypertrophic cardiomyopathy by Multiple Reaction Monitoring Mass Spectrometry

BACKGROUND:

Mutations in the MYBPC3 gene, encoding the myosin binding protein C (MyBP-C) are a leading cause of hypertrophic cardiomyopathy (HCM). It is commonly believed that a premature termination codon mutation leads to haploinsufficiency; however, specific allelic variant expression has not been conclusively determined. The MYBPC3 mutation phenotype is variable and the molecular mechanisms dictating severity of disease are unknown. We hypothesize that some disease variability may be due to the extent the truncated protein incorporates, and seek to measure the quantity of mutant protein.

OBJECTIVE:

To determine the feasibility in detecting MyBP-C quantities in myomectomy samples with MYBPC3 mutations by MRM mass spectrometry.

DESIGN/METHODS:

Tissue banked donor control (n=3) and HCM (n=3) human heart tissue from genotyped individuals were snap frozen and stored at -80. The individuals had the same premature termination codon mutation 2827C>T. Proteins were extracted by 8M Urea, 0.1M Tris-HCl (pH 8.5). The myofilaments was trypsinized (FASP kit, Expedeon). The peptides were desalted with C18 mini-spin columns (Pierce) and reconstituted in 0.1% Formic Acid, 5% Acetonitrile prior to LC-MS/MS (AB SCIEX QTRAP 6500).

RESULTS:

Transitions were selected to quantify N and C terminus domains of MyBP-C. These signals were normalized against α -sarcomeric actin. The C-terminus of MyBP-C of HCM samples expressed 49.2% (p=0.0013) when compared to control samples. These results were consistent with the Western Blot analysis using an anti-MyBP-C that recognizes an N-terminus domain, in which the HCM samples contained 47% MyBP-C (n =3 vs n =3, t-test p=0.005) compared to control.

CONCLUSIONS:

The HCM samples showed a decrease by approximately 50% in MyBP-C as compared to the control samples when normalized against actin. These results suggest complete haploinsufficiency in these particular HCM samples. Studies looking into mutant specific allele expression for other HCM causing mutations (MYH7) are underway.

STATUS

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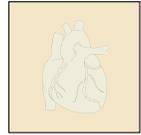
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Cardioprotective Efficacy of Mg-supplementation during HAART Therapy

INTRODUCTION:

Efavirenz (EFV) and Ritonavir (RTV) are first line anti-HIV agents, but their use may increase risk of co-morbid toxicity and cardiac dysfunction.

METHODS:

We compared oxidative stress, altered lipid metabolism, eNOS status and cardiotoxicity of EFV vs RTV treatment (75 mg/kg/day by gavage) in Lewis-Brown Norwegian rats (160g) up to 8 weeks and assessed effects of dietary magnesium supplementation (Mg-Sup: 6-fold higher MgO). Cardiac functional and pathological changes were monitored by in situ echocardiography and by histochemistry.

RESULTS:

EFV enhanced plasma triglyceride (TG) during week 1 whereas RTV enhanced plasma TG and cholesterol levels early on (8 days) up to 8 weeks (40-80%; $p < 0.01$). Mg-Sup completely (100%) suppressed RTV- or EFV-induced lipid abnormality. Blood neutrophils from EFV- and RTV-treated rats displayed 6-fold and 3.3-fold higher basal superoxide activity ($p < 0.01$) and plasma 8-isoprostane levels rose 2.8- and 2.3-fold ($p < 0.05$) at 5 weeks compared to vehicle controls. RBC GSSG/GSH ratios were increased 2.8- and 3.2-fold by RTV and EFV ($p < 0.025$). RTV down-regulated eNOS mRNA and protein 30-60%; but both EFV & RTV decreased plasma nitrite level by ~50% ($p < 0.025$). Mg-Sup substantially (>75%, $p < 0.025$) attenuated all these oxidative indices and nitrite levels. At 5 weeks, both drugs caused significant decreases in shortening fraction ($p < 0.05$) and mitral valve E/A ratio ($p < 0.05$). At 8 wks, RTV caused a greater decline (14%) in shortening fraction versus EFV (10%). Both drugs decreased left ventricular posterior wall thickness in diastole (LVPWd: 8.5-10%) and systole (LVPWs: 11-12%), indicative of progression toward dilated cardiomyopathy ($p < 0.05$). Mg-Sup attenuated RTV-induced declines in systolic and diastolic function (>70%; $p < 0.05$) and lessened LVPWs wall thinning (8 wks: by 75%, $p < 0.01$). Partial protection (~ 50%) by Mg-Sup was observed in EFV-treated rats. Histochemical analysis showed prominent WBC (CD 11b+) infiltration and fibrotic staining in the vascular and peri-vascular area of the 8 wk EFV ventricles; both were attenuated by Mg-Sup.

CONCLUSION:

Prolonged use of EFV and RTV caused enhanced oxidative stress, hyperlipidemia, eNOS downregulation, systolic and diastolic dysfunction and cardiac pathology. This study demonstrates the benefits of magnesium supplementation against HAART-induced cardiac toxicities (Supported by NIH-R21NR012649, NIH R21HL125038).

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CARDIOLOGY/CARDIOVASCULAR RESEARCH



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To Determine the Individual Effect of Age, Duration of Diabetes, BMI, and HbA1c on Arterial Stiffness in Patients with DM type 2 Diabetes

Arterial Stiffness (AS) has been used as a measure of vascular health. However limited number of studies exists to determine which parameter of a patient has more effect on AS measures. The indices for measuring AS we used are Augmentation Index (Ag), Augmentation Index adjusted for heart rate⁷⁵ (AgI-75), augmentation pressure (AP) and Pulse Wave Velocity (PWV). We used The Pearson product-moment correlation as a statistical method for analysis. We analyzed 18 patients to understand which of the above parameters have most effect on AS. AI, AI-75, AP and PWV. Only one time point was taken for this study. Patients enrolled were subjects with DM \leq 8 years, age 40-70, with HbA1C of 6-9 and BMI 25-39.9. We enquired: a) whether age or year of DM has more impact on the AS and; b) whether BMI or HBA1c level has more impact on AS.

RESULTS:

a) AI and PWV c-f from the group of patients with DM duration of 0-4year (P correlation (Pc) =0.83; 0.93 n= 10) has linear relationship with age. AI and age has a linear relationship Pc=0.75; n=18 with DM duration 0-8yrs; b) relationship between AP and age is linear, Pc = 0.82; n=18; c) PWV c-r and year of DM in the group of people age 40-55 has a linear relationship with Pc = 0.93; n=5; d) HbA1c has direct effect on AI 75 in the patients with BMI 25.0-29. Pc = 0.89; n= 18; d) HbA1c has linear impact on PVW c-f in the patients with BMI 25.0-29.9. Pc= 0.96; n=4. We conclude that: a) Arterial stiffness measures in diabetes subjects appear to be reliable and reproducible using multiple measurement indices. B) PWV appears to be more informative than PWA, b) age can affect AS more than duration of DM; c) Level of HbA1c has more effect on AS than BMI, particularly in patients with BMI 25.0-29.9.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Rate Control of Atrial Arrhythmias Can Be Achieved by Selective Cardiac Neurostimulation

INTRODUCTION:

Atrial arrhythmias (AA) occur in 40% of patients recovering from open-heart surgery (OHS). Pharmacologic treatment has been the main strategy for the control of post-operative AA, but is associated with hypotension, pro-arrhythmia and myocardial dysfunction. There is a need for a reversible, modulated solution to rate control. We demonstrated the efficacy of vagal stimulation at inferior right fat pad (FP) to slow the ventricular response (VR) of atrial fibrillation (AF) and junctional ectopic tachycardia (JET). We hypothesized that the VR response to AA could be improved by alterations in 1) the site of stimulation (anterior right FP vs. inferior right FP), 2) site within the two FP regions tested, and 3) whether there was a relationship between stimulation voltage (V) and electrophysiologic effect.

METHODS:

Eight mongrel dogs, age 8.7 ± 3.9 months and weighing 21.5 ± 2.5 kg, underwent OHS replicating tetralogy of Fallot repair. Stimulation of the anterior right (AR) and inferior right (IR) FP was used to control the VR of AF and JET. A 7-pole electrode was sutured to the AR and IR FP and used to deliver stimulation therapy. Tested parameters included: 1) FP site, 2) stimulation pole configuration, and 3) stimulation (1-25) V on the VR to AF and JET. Stimulation frequency was 30 Hz, and pulse width was 0.15 msec.

RESULTS:

- 1). The inferior right FP was more effective in slowing the VR response to AF (-0.43 ± 0.18 vs. -0.18 ± 0.11 %, $p=0.03$) and JET (-0.16 ± 0.06 vs. 0.0 ± 0.0 , $p=0.06$.)
- 2). Selective site stimulation within a FP region could augment the effect of stimulation during AF (-0.48 ± 0.21 (maximum effect) vs. 0.0 ± 0.0 % (least effect), $p=0.01$).
- 3). FP stimulation at increasing V demonstrated a voltage-dependent effect (-0.12 ± 0.19 (low V) vs. -0.63 ± 0.21 (high V) %, $p=0.01$).

CONCLUSIONS:

Selective site stimulation within a FP region and optimizing the voltage output enhanced the efficacy of VR slowing during post-op AA. Stimulating multiple sites of the IR FP using combinations of electrodes allowed for maximal slowing of VR. The IR FP was more effective in decreasing VR during AF, suggesting its role in control of AV node conduction. The AR FP had little effect on JET compared with the IR FP, suggesting differences in mechanism of action between the two regions. FP stimulation may be a novel therapeutic option for rate-control of post-op arrhythmias.

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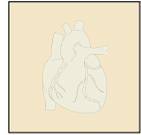
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CARDIOLOGY/CARDIOVASCULAR RESEARCH



SCHOOL OF MEDICINE & HEALTH SCIENCES

Assessing Adherence to the 2013 ACC/AHA Guidelines on the Treatment of Blood Cholesterol

INTRODUCTION:

The American College of Cardiology and American Heart Association released new clinical practice guidelines for the treatment of blood cholesterol in November 2013. The new guidelines emphasize statin therapy and are significantly different from the Adult Treatment Panel (ATPIII) guidelines that have been followed for the past decade.

OBJECTIVES:

1) To assess physicians' knowledge of the new guidelines. 2) To assess physicians' adherence to the guidelines in clinical practice.

METHODS:

A six-item online survey with case presentations and general questions pertaining to the guidelines was administered to residents, fellows, and faculty at the George Washington University Medical Faculty Associates. Voluntary responses were collected. A chart review of patients seen by cardiology and internal medicine faculty over a one-week period in June 2014 was conducted. Charts were scored for application to the new guidelines.

RESULTS:

70 survey responses were collected. Cardiology faculty scored highest on the survey (75% correct), followed by cardiology fellows (67% correct), internal medicine faculty (62% correct), and internal medicine residents (57% correct). 123 cardiology charts and 125 internal medicine charts were reviewed. 63% of cardiology patients and 62% of internal medicine patients received treatment in accordance with the new guidelines. Cardiology faculty were most likely to follow guidelines for patients with clinical atherosclerotic cardiovascular disease (ASCVD), whereas internal medicine faculty were mostly likely to follow guidelines for patients with an estimated 10-year ASCVD risk of 7.5% or greater. Physicians in both departments were least likely to follow the guidelines for patients with diabetes.

DISCUSSION:

Six months after the release of the new ACC/AHA guidelines for the management of blood cholesterol, about a third of physicians are not familiar with the new guidelines and are not applying them to clinical practice.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Atrial Fibrillation, Catheter Ablation, Inflammation, and Recurrence

Atrial fibrillation (AF) is a rapid and irregular heart rhythm originating in the atrium and resulting in an uncoordinated flow of blood through the heart. AF is present in about 1-2% of the general population in the US and is an important topic of study as it can have potentially life threatening consequences due to the associated thromboembolic risks. It has been shown that catheter ablation is a promising treatment option for AF refractory to medications, and that it maintains sinus rhythm, improves quality of life, and reduces hospital readmission rates more than continued drug therapy (level 2 [mid-level] evidence). Catheter ablation is a procedure in which a catheter is seeded through a vein and into your heart, where small bursts of radiofrequency energy are released to destroy abnormal heart tissue producing arrhythmias. This study aimed to identify specific inflammatory markers that predicted the recurrence of AF following catheter ablation. This study is still in the preliminary stage that involves identifying the relevant biomarkers based on compiling and analyzing previous literature on the subject matter. The hypothesis is that AF recurrence can be inflammatory dependent or inflammatory independent, depending on the patient. In being able to identify inflammatory dependent recurrence in patients the hope is that this can guide ablation recommendations and avoid unnecessary surgeries in the future. Based on currently available literature, the most intriguing pre-ablation biomarkers for predicting late AF recurrence are C reactive protein (CRP), the neutrophil-to-lymphocyte ratio (NLR), matrix metalloprotein 2, TNF-alpha 1, endothelin 1, big endothelin-1, and monocytic CD-36. These markers are baseline serum levels prior to ablation that showed significant predictive value for AF recurrence following ablation. The post-ablation markers useful for predicting recurrence include CRP, myeloperoxidase, and NLR based on available literature. The future direction of the study is to use this comprehensive panel of biomarkers in clinic to predict recurrence of AF in patients post-ablation in order to determine its usefulness.

Full list of references available upon request.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Kidney plasmacytoid dendritic cells display distinct cell markers and may explain tolerance induction by kidney allografts

Prolonging heart allograft acceptance and eventual long-term tolerance is an important area of research as the number of patients with conditions requiring heart transplantations increase. Recent studies in pigs and non-human primates (NHPs) have demonstrated that co-transplantation of kidney and heart allografts from the same donor leads to the acceptance of the heart allograft. Additionally, murine studies have demonstrated the spontaneous acceptance of full MHC-mismatched kidney allografts. This observation has led our lab to a renewed interest in identifying the underlying mechanisms behind this apparent systemic tolerization by the kidney and the role of kidney pDCs in this process. Studies surrounding pDCs have suggested their role in immunoregulation through the release of type I interferons, antigen presentation, and cell-cell interactions. More importantly, immature pDCs, characterized by B220+/CD11c+/CCR9+/SiglecH+, have been shown to participate in regulatory and deletional tolerance through robust conversion of naïve CD4+ T-cells into induced FoxP3+ regulatory T-cells (Tregs) and the deletion of antigen-reactive thymocytes, respectively.

Interestingly, we have observed distinctive characteristics between pDCs isolated in the kidney from those isolated in the bone marrow. In a mixed-chimeric NHP tolerant to heart and kidney allografts, we found that pDCs from the tolerant kidney were BDCA2hi (cell surface marker unique to pDCs in primates) in contrast to bone marrow pDCs in naïve NHPs, which were BDCA2low. Similarly, naïve kidney pDCs in DBA/2 mice were found to be B220low and PDCA1low (cell surface marker unique to pDCs in mice), whereas naïve DBA/2 bone marrow pDCs were B220hiPDCA1hi. Furthermore, isolated DBA/2 kidney pDCs cultured with naïve B6 T-cells, IL-2, and TGF- β were found to convert naïve CD4+ T-cells into FoxP3+ Tregs.

The observed distinctness in kidney pDCs may be evidence of the kidney pDC's ability to induce tolerance and may provide an explanation for heart allograft acceptance in the context of heart/kidney co-transplantation in NHPs, as well as spontaneous kidney allograft accept in mice. While currently we are obtaining more data to understand these observations, we are convinced that kidney pDCs have inherently different properties that contribute to inducing tolerance in NHP and mice.

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Poly-ADP Polymerase (PARP) inhibition enhances the healing of diabetic and ischemic wounds

BACKGROUND:

Diabetes and arterial occlusive disease are two major risk factors that contribute to chronic, non-healing wounds. Our previous experiments showed that ischemic/diabetic wounds exhibited markedly increased PARP activity compared to normal (non-diabetic/non-ischemic) wounds but the exact mechanism of PARP behind impaired healing of ischemic/diabetic wounds is not well understood.

OBJECTIVE:

This study further investigates the role of PARP activity in the healing of diabetic/ischemic wounds.

METHOD:

Diabetic/ischemic wound healing was studied using an in-vitro scratch wound assay using HUVECs and an established murine model where mice were made diabetic and ischemic by streptozocin injection and femoral artery ligation, respectively. Subsequently, a full thickness wound is made on the ventral surface of the thigh. One group was treated with a PARP inhibitor (PJ34) and another group was treated with vehicle. In addition, the effect of PARP deletion was tested using PARP KO mice and the wound healing was compared to background wild type mice. Daily digital photographs were taken to monitor healing which was calculated as percent healing of the original wounds. Tissues were collected at different time points for molecular analysis. PARP activity and angiogenesis marker VEGFR2 were measured using Western Blot. Angiogenesis assays were performed using 2D angiogenesis assay and aortic ring sprouting assay.

RESULTS:

PARP inhibition enhanced HUVEC migration in the in vitro scratch wound assay ($344.56 \pm 39.75\mu\text{m}$ vs. $250.49 \pm 35.13\mu\text{m}$ in control group after 24 hours, $p < 0.05$). Treatment with PARP inhibitor also promoted wound healing in the murine model. At day 7, treated group showed $68.7 \pm 11.3\%$ healing compared to $56.4 \pm 25.5\%$ in control group, $p = 0.05$. Similarly, PARP1-knockout mice healed faster than WT mice at day 7 ($71.6 \pm 10\%$ vs. $57.1 \pm 20\%$, respectively, $p = 0.05$). PARP inhibition enhanced angiogenesis evidenced by higher level of VEGFR2 in the wounds at day 4 and significantly more tube formation and sprouting in 2D angiogenesis assay and aortic sprouting assay, respectively.

CONCLUSION:

PARP inhibition enhances ischemic/diabetic wound healing and one mechanism behind this beneficial effect is improved angiogenesis. Further investigation of the role of PARP in wound healing is needed before the therapeutic potential of PARP inhibition could be applied to patients in the clinic.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Venous Valve Leaflet Visualization

Autologous stem cell-derived cardiomyocytes have been shown to grow into beating cuffs of cardiac tissue by Sarvazyan et al. This innovation has potential medical implications for those who suffer from chronic deep vein insufficiencies where an engineered cardiac cuff could be implanted around a failed venous segment to aid in reestablishing adequate blood flow back the heart. This study aims to visualize venous valves in both an in vivo and ex vivo environment in order to better assess the optimal placement and effectiveness of implanted cardiac constructs to alleviate venous insufficiency. Several animal models were used to visualize valve movement including rabbit, rat, and pig. The lower extremities were dissected to reveal the great saphenous vein. Valves were visualized in vivo by coercing blood distally against the valve until the bulge in the venous sinus was found indicating the presence of a valve. That segment was then excised and cannulated in order to perform perfusion studies. A dyed solution of 1x PBS was flushed through the venous segment using a bidirectional peristaltic pump. Images of valve movement were taken using a stereoscope and eyepiece camera. All the veins that were examined showed competence in vivo as expected. However, the saphenous vein lost valve function when excised from the connective tissue sheath that encases it. This suggests that the sheath is important in limiting the compliance of the vessel and maintaining valve patency. Similarly in diseased veins, it may be beneficial to implant cardiac cuffs directly surrounding an incompetent valve. In this manner, the cuff acts as an encasing sheath to maintain compliance as well as provide contraction waves to propel blood toward the heart.

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CARDIOLOGY/CARDIOVASCULAR RESEARCH



SCHOOL OF MEDICINE & HEALTH SCIENCES

Validation of a novel risk assessment model for sudden cardiac death in hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is a common inherited condition that can cause sudden cardiac death in young adults. It is important to identify these individuals early on and treat them with implantable cardioverter defibrillators (ICDs) to prevent the likelihood of sudden cardiac death. Validation of current algorithms suggests that many patients are treated with inappropriate prophylactic ICD implantation. The goal of this project was to validate a novel model for which individualized risk assessments for sudden cardiac death could be produced to improve the treatment of patients with HCM. Data was gathered from the electronic medical record system of a large, urban hospital and pooled with data from other participating US and European sites. The data is currently still under analysis and therefore, a summary of the findings thus far will be presented.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Takotsubo with a Twist

A 48 year-old premenopausal woman with hypertension presented to the emergency room with 2-days of worsening dyspnea in the context of two weeks of non-productive cough. She was tachycardic at 120 beats per minute, hypertensive at 146/98 mmHg, tachypneic at 30 breaths per minute, and hypoxic on room air with pulse oximetry showing 65% arterial oxygen saturation, requiring non-invasive positive-pressure ventilation. Chest X-ray showed pulmonary edema. Twelve-lead electrocardiogram showed sinus tachycardia, Mobitz-I heart block, and prolonged corrected-QT-interval at 581 milliseconds. Pro-brain natriuretic peptide (pro-BNP) was elevated at 2,860 pg/mL. Throat swab was positive for Influenza A. She was admitted for monitoring and diuresis. Echocardiogram suggested takotsubo cardiomyopathy (TCM) with left ventricular apical akinesis, hyperdynamic bases, and ejection fraction of 45%. Telemetry showed premature ventricular complexes, occasionally falling on T-waves given the prolonged QT interval, triggering runs of increasingly frequent polymorphic ventricular tachycardia (Torsades de pointes). Isoproterenol administration failed to reverse the Mobitz-I pause-associated prolonged QT-interval, necessitating sedation and intubation to suppress the ectopy. A transvenous pacemaker was inserted to overdrive pace through the ventricular tachycardia, however a 3-minute episode of Torsades de pointes occurred with hemodynamic compromise requiring chest compressions. Ventricular ectopy resolved with diuresis, but Mobitz-I persisted. Left heart catheterization showed no obstructive coronary artery disease. Myocardial biopsy revealed no inflammation. She was diagnosed with TCM. She received a bi-ventricular implantable cardioverter-defibrillator for secondary prevention and persistent Mobitz-I. She was discharged on metoprolol succinate, furosemide and magnesium supplementation. Three-month follow-up echocardiogram showed normalization of left ventricular motion and systolic function.

TCM, or stress-induced cardiomyopathy, is a well-recognized syndrome with a 0.02% prevalence across all US admissions. It is an increasingly diagnosed condition typically seen in postmenopausal female smokers >55 years old with significant emotional or physiologic stress states. Treatment is generally supportive, with diuresis and medical management similar to other causes of systolic heart failure. It carries a favorable prognosis; most patients enjoy full resolution of their cardiomyopathy. Acutely, however, it can be associated with potentially lethal electrical instability, which should be anticipated and addressed when present. One study demonstrates 26% prevalence of cardiac arrhythmia in TCM - 4.2% of which were ventricular in origin - and increased mortality. While such arrhythmias are usually not missed in hospital settings, attention to detail and proper triaging of patients at risk of catastrophic consequences (such as this patient) help avoid long-term irreversible consequences in an otherwise reversible syndrome.

STATUS

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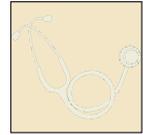
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Re-expansion pulmonary edema

INTRODUCTION:

Re-expansion pulmonary edema (RPE) is a rare complication of therapeutic thoracentesis. Unfortunately, there is no definitive treatment modality for RPE. The high mortality rate, reported up to 21%, presses the issue for finding adequate prevention and treatment. Here we report a new management modality that is very useful for a patient with RPE.

CASE REPORT:

An 80-year-old man with a history of hypertension, atrial fibrillation, congestive heart failure with preserved ejection fraction, and sacral decubitus ulcer, who was admitted for surgical debridement of his ulcer. He developed hospital-acquired pneumonia and was resolved with antibiotics and aggressive hydration. He became hypoxic, and his chest imaging revealed bilateral pleural effusions refractory to diuresis. He underwent right-sided thoracentesis with removal of 2.5 liters of transudative fluid. He immediately improved, and his chest x-ray post-thoracentesis showed a significant reduction in the right pleural effusion. Later that night, the patient developed dyspnea and hypoxia. Lung auscultation revealed new crackles on the right side extending to the apex. Repeated chest x-ray showed diffuse right-sided infiltrates, consistent with re-expansion pulmonary edema. We started him on BiPAP ventilation as well as diuresis. Repeated imaging within five hours demonstrated a significant reduction in the pulmonary edema, and his clinical condition improved markedly. He was transitioned to supplemental oxygen via nasal cannula at 2L/min within 24 hours.

DISCUSSION:

RPE occurs due to increase permeability of pulmonary capillary vessels secondary to rapid reduction in the pleural cavity pressure and sudden lung expansion. The severity of the intra-pleural negative pressure is thought to contribute to the risk of developing RPE. A recent study has proved a correlation between the amount of volume removed from the pleural cavity and the chance of developing RPE. Treatment for RPE is supportive, with oxygen supplementation and diuresis. However, we found dramatic clinical and radiological changes after applying BiPAP and thereby increasing the intra-pleural pressure.

CONCLUSION:

Clinicians should be encouraged to place patients who develop RPE on BiPAP for six to twelve hours to prevent worsening of pulmonary edema. As presented in our case, this management modality had desirable outcomes in as little as five hours. Further studies require to assess the effectiveness of BiPAP to decrease the progression and mortality of RPE.

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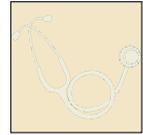
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An Uncommon Cause of Altered Mental Status

CASE PRESENTATION:

A 73-year-old man with a history of hypothyroidism and alcohol abuse was transferred from his nursing home to the Emergency Department with four weeks of progressively worsening mental status, paranoia, and hallucinations. Staff from his nursing home reported that he had been receiving levothyroxine as prescribed, he had not started any new medications, and he had no access to alcohol. Vitals were remarkable for a heart rate of 115 and a respiratory rate of 23. He was confused and agitated, but had a normal cardiovascular and pulmonary exam, on neurologic exam he had no nystagmus or asterixis. Labs on admission were significant for an ammonia level of 61 and elevated liver function tests with AST of 42 and an ALT of 43. TSH was 4.19 on admission. CBC, electrolytes, Vit. B12, urine toxicology screen, urinalysis, chest film, and head CT were all without significant abnormalities.

He was treated for presumptive hepatic encephalopathy with lactulose and rifaximin. Even though he did not have nystagmus, he was still treated for possible Wernicke's encephalopathy with IV thiamine. His mental status did not improve. On hospital day five, he developed myoclonic jerks in his legs bilaterally and in his right arm. EEG was performed and showed background and bifrontal slowing consistent with a moderate encephalopathy. In addition, periodic lateralized epileptiform discharges (PLEDS) were noted on the left. PLEDS are commonly associated with partial seizures in the context of acute insults such as vascular lesions or infections. MRI of the brain showed mild volume loss, mild nonspecific white matter changes, presumed microangiopathy and old lacunar infarct within the right thalamus. Examination of the CSF fluid revealed a leukocyte count of 2 (lymphocytes), RBC 0, glucose 74, protein 40, and negative gram stain.

Encephalopathy and myoclonic jerks persisted and on hospital day ten, his respiratory status began to decline. A subsequent chest film showed an infiltrate, and he was started on treatment for aspiration pneumonia. His breathing became more labored and he was transferred to the ICU where he was intubated for airway protection. A full course of antibiotics for aspiration pneumonia was completed without improvement. Mental status worsened in the ICU, he became unresponsive to voice or physical stimuli. Serum TSH was increased to 10.19 and his dose of thyroid replacement was increased without improvement in clinical status. Patient was trialed on multiple anti-epileptic medications without response. Repeat LP was performed and was unrevealing; CSF studies for paraneoplastic antibodies, RPR/VDRL, and HIV were all negative. Repeat EEG showed repeated generalized sharp slow wave complexes at 1-2Hz, a finding associated with non-convulsive status epilepticus, severe hepatic or renal encephalopathy or Creutzfeldt-Jakob disease.

At this point, the differential diagnosis included Hashimoto's encephalitis—with elevated TSH values, elevated thyroglobulin antibody level, and elevated thyroperoxidase—versus Creutzfeldt-Jakob disease (CJD).

A five-day trial of high-dose IV steroids was initiated for empiric treatment of Hashimoto's Encephalitis. His condition did not improve and his family decided to withdraw care. He expired two days later, one month after being transferred to the ICU. Post-mortem, CSF levels of 14-3-3 and tau proteins were found to be highly elevated. Thus, his post-mortem diagnosis was CJD. The patient's family declined autopsy.

DISCUSSION:

Altered mental status (AMS) is a common presentation in Emergency Departments as well as inpatient Medicine and Neurology services. This case is an example of a rare cause of AMS with no known treatment. The diagnosis was established only after more common metabolic, toxicologic, cardio-pulmonary, vascular, neurologic, and infectious causes had been ruled out. CSF tau level carries a positive predictive value of 86% for CJD, which—curiously, like Hashimoto's encephalitis—can also present with elevated thyroid autoantibodies.

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The Use of Robotic and Laparoscopic Surgical Stapling Devices during Minimally Invasive Colon and Rectal Surgery - A Comparison.

PURPOSE:

To date there exists no published study examining the safety and efficacy of the EndoWrist 45 (Intuitive Surgical, Inc.) robotic stapler. We compared outcomes between the robotic stapler and comparable laparoscopic staplers in patients who underwent robotic-assisted colon and rectal procedures.

METHODS:

We conducted a retrospective review of 93 patients who underwent robotic-assisted colorectal surgery at a single institution from 2012 to 2014. Surgeries included left, sigmoid, sub-total and total colectomies as well as low-anterior rectal resections. Indications were malignancy, diverticular disease and inflammatory bowel disease. Pre-operative demographics, intra-operative data, and post-operative outcomes were examined. Student's t-test was used to analyze continuous variables; Fischer's exact test was used for categorical variables.

RESULTS:

45mm laparoscopic staplers were used in 58 cases, while the 45mm robotic stapler was used in 35 cases. There was no statistically significant difference in age ($p=0.651$), gender ($p=0.832$) or BMI ($p=0.204$) between the two groups. Additionally, there was no difference in estimated blood loss ($p=0.524$), operative time ($p=0.769$), length of hospital stay ($p=0.895$) or overall complication rate ($p=0.778$). The robotic stapler group had two anastomotic leaks, while the laparoscopic stapler group had six ($p=0.705$). There were, however, significantly more laparoscopic stapler fires (2.69) required per patient than robotic stapler fires (1.86) ($p=0.001$). The stapler cost per patient for the laparoscopic stapler group was \$631.45 vs. \$473.28 for the robotic stapler group ($p=0.001$).

CONCLUSION:

This is the first study of its kind to evaluate the robotic stapler. Advantages of the robotic stapler include a large range of motion and 90 degrees of articulation, which may provide a benefit when using the stapler in confined spaces such as the pelvis. Our data indicates that the robotic stapler has a comparable level of safety and efficacy as a 45mm laparoscopic stapler, and that it is more cost effective.

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Interferon gamma is elevated in wound fluid from hidradenitis diseased skin compared to wound fluid from chronic wounds

Hidradenitis suppurativa (HS) is a chronic recurrent inflammatory disease of apocrine glands in which patients develop debilitating recurrent inflammatory nodules, sinus tracts and abscesses. The immune triggers for this disease are unknown. The purpose of this study was to utilize wound fluid specimens from subjects enrolled in the WE-HEAL study to identify key inflammatory cytokines and growth factors which are dysregulated in patients with HS compared to patients with chronic wounds.

METHODS:

The WE-HEAL Study is a biospecimen and data repository for studying chronic wounds approved by the George Washington University IRB (041408). Wound fluid specimens are collected using the Levine technique and are processed immediately upon collection.

HS wound fluid specimens were available on 7 patients. Chronic wound fluid specimens were selected from 6 age, sex and race matched patients as a control group. The Meso Scale Discovery V-Plex cytokine panel 1 and the V-plex proinflammatory panel 1 (MSD, Rockville, MD) were used to analyze proinflammatory cytokines in the fluid specimens. For the proinflammatory panel a 10 fold dilution was used and for cytokine panel-1 a 20 fold dilution was used. Samples were run in duplicate and processed according to the manufacturer instructions.

RESULTS:

Levels of interferon-gamma (IFN- γ) were significantly elevated in the HS specimens compared to the control subjects with chronic wounds (1402 ± 1518 compared to 28.93 ± 28.95 , $p = 0.048$). The other cytokines analyzed were similar in the HS samples and chronic wound samples. Interferon-gamma is known to play a critical role in mediating innate and adaptive immunity. Particularly relevant to HS, as an activator of macrophages Interferon gamma is a crucial molecule in the development of granulomas. Released by macrophages, IFN- γ causes activation of TH1 cells, and further activation of macrophages facilitating intracellular killing of bacterial and resulting in macrophages transitioning to a fibroblast phenotype thus walling off granulomatous pockets of infection.

CONCLUSIONS:

This study found significantly elevated levels of IFN- γ in HS wound fluid specimens compared to chronic wounds. This finding supports the hypothesis that IFN- γ is a crucial molecule in the development and perpetuation of HS.

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Pernicious Anemia: A Rare Cause of Pancytopenia and Hemolysis

A 48 year-old woman with past medical history of Graves' disease and vitiligo was referred to the emergency department after she presented to clinic with worsening dizziness and generalized malaise over several weeks. She had been lost to follow up and reported not taking any medications. She denied melena, hematochezia, numbness, paresthesias, dyspepsia, chest pain, or shortness of breath. Aside from a mildly low blood pressure of 93/58, vital signs and physical exam were unremarkable. Initial labs revealed pancytopenia with white blood cell count (WBC) of 4.0 (4.8-10.8), hemoglobin (Hgb) 3.8 g/dL (12-16), and platelets 64,000 (130-400). Further work-up before red blood cell transfusion was remarkable for evidence of hemolysis on peripheral blood smear, haptoglobin <10 (45-165), fibrinogen 149 (200-400), and lactate dehydrogenase (LDH) 9231 (140-280). Significantly, vitamin B12 was low at <159.0 pg/mL (200-800), serum methylmalonic acid was high at 8180 nmol/L, and intrinsic factor antibody was positive, which confirmed the diagnosis of pernicious anemia. The patient was started on intramuscular B12 injections and her pancytopenia, hemolysis as well as symptoms quickly improved.

Pernicious anemia is an autoimmune disease causing destruction of both gastric parietal cells and the autoantibody inactivation of intrinsic factor leading to malabsorption of vitamin B12. Deficiency of vitamin B12 impairs DNA synthesis, and therefore early recognition and treatment is vital in preventing irreversible cellular damage. Our patient did not have the commonly associated megaloblastic anemia, but instead presented with pancytopenia and hemolysis. This has been reported in a few cases of B12 deficiency and is thought to be due to ineffective hematopoiesis leading to production of immature cells at risk for cell lysis.

This case highlights the importance of recognizing pernicious anemia as a rare cause of pancytopenia and hemolysis. Early testing should be encouraged as the treatment is simple and procures a good prognosis.

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The effect of different crystalloid solutions administered intraoperatively on transplant function in patients undergoing kidney

Each year thousands of patients undergo kidney transplants. Although past research has suggested that Normal Saline may be inferior to balanced solutions in normalizing function post-surgery, current studies lack significant evidence to establish whether the choice of fluid therapy solution used- Normal Saline, Ringer's Lactate, or Plasma-lyte- leads to differences in kidney transplant outcomes. This study is the first to investigate the link between type of intraoperative solution used and kidney function post-transplant. Data was pulled from the UCSF Dept. of Anesthesia- PICIS Database containing records for 2500+ kidney transplant patients including: Patients' demographics and perioperative data such as age, gender, BMI, ASA classification, comorbidities and intraoperative fluid management including blood transfusion and type and amount of crystalloids used. The data was matched to records from the TITUS Transplant Database containing pre-transplant and outcome data including: types of donor kidneys, cold ischemia time, immunosuppression regimen, need for postoperative dialysis, length of hospital stay, postoperative creatinine, postoperative potassium, major infection, ICU admission and mortality. Results are currently being analyzed to determine the impact of choice of intraoperative solution on the primary outcome data variables: DGF and 1 year creatinine values. Delayed Graft Function (DGF) is a major predictor for kidney transplant failure. Clinical significant differences in DGF occurrence among the 3 crystalloid solutions could impact which of the 3 crystalloid solutions are more commonly used intraoperatively during kidney transplants and subsequently improve outcomes for future kidney transplant recipients.

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Delayed traumatic aortic pseudoaneurysm formation causing vertebral body erosion and back pain: case report and literature review

Aortic pseudoaneurysm is a known, yet rare, cause of chronic back pain, usually due to compression of the adjacent neurovasculature. Additionally, it is uncommon for patients with pseudoaneurysms of the abdominal aorta to present in a delayed fashion after initial traumatic injury. We present an unusual case of a 66 year old male patient presenting with isolated progressive axial back pain in which a pseudoaneurysm of the aorta eroded the adjacent L1 vertebral body. This pseudoaneurysm was thought to be secondary to a gunshot wound with retained ballistic fragment that occurred 27 years prior. The patient was treated initially with an endovascular coiling of the pseudo aneurysm with complete resolution of pain symptoms. Approximately 1 month post-op, the patient re-presented with back pain with evidence on angiography of residual filling in the neck of the pseudoaneurysm. The patient was then treated with an open aortic bypass followed by endovascular placement of a covered stent across the opening of the pseudoaneurysm. The treatment led to complete resolution of the patient's back pain that is stable on extended follow-up. Less invasive imaging modalities such as Doppler flow or CT Angiography have seen an increased use for initial diagnosis of aortic pseudoaneurysms. Endovascular repair, including coil embolization, of these pseudoaneurysms has led to a marked decrease in morbidity and mortality of these patients.

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Proximal Sessile Serrated Adenomas May Occur More Frequently in Whites

PURPOSE:

Colorectal cancer causes significant morbidity and mortality in the United States. Sessile serrated adenomas may have significant malignant potential, with reports suggesting that 20-30% of all colon cancer may arise from these lesions. Sessile serrated adenomas occur more frequently in the proximal colon. However, the prevalence and risk factors for these lesions have been incompletely elucidated. This study evaluated the prevalence of proximal sessile serrated adenomas occurring in individuals undergoing colonoscopy at an urban university medical center.

METHODS:

Medical records of consecutive patients undergoing a colonoscopy during a 5-year period by a university gastroenterologist were reviewed. Patients' gender, ethnicity (white, African American, other ethnicity or ethnicity not documented), and proximal sessile serrated adenomas were obtained. There were no exclusion factors. A database, maintaining patient confidentiality, was created. Statistical analysis was performed using Fisher's exact test with significance set at $p < 0.05$. The study was approved by the university Institutional Review Board.

RESULTS:

Eight hundred ninety-seven screening colonoscopies were performed. Three hundred twenty-three (36%) individuals (157 female, 166 male) had a proximal adenomatous lesion. One hundred sixty-one of the 323 (49.8%; 74 females, 87 males) of the proximal adenomatous lesions were a sessile serrated adenoma. There was no significant difference in the rate at which proximal sessile serrated adenomas ($p = 0.3739$) were found based upon gender. In the 161 individuals with sessile serrated adenomas, 103 (64%) were white, 42 (25%) African American, and 16 (10%) were of other ethnicities or their ethnicity was not documented. Significantly more ($p = 0.0001$) proximal sessile serrated adenomas were identified in whites compared to African Americans.

CONCLUSION:

Sessile serrated adenomas are reported to occur more frequently in the proximal colon. However, the prevalence and risk factors for development are incompletely known. This study revealed that approximately 50% of proximal adenomatous lesions in this study group were sessile serrated adenomas. Additionally, whites more frequently had proximal sessile serrated adenomas compared to African Americans. While this study may be limited based upon evaluation of colonoscopies performed by 1 gastroenterologist at a single institution, it emphasizes the importance of further studies being conducted that evaluate the prevalence and risk factors for proximal sessile serrated adenomas.

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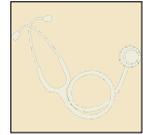
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Relationships of Rectus Femoris Muscle Size and Echotexture to Functional Mobility in Children with Cerebral Palsy

Approximately 50% of individuals with CP who walk independently during childhood lose this ability in adulthood (1). Knee extensor muscles, such as the rectus femoris (RF), are important for maintaining an upright posture during gait. In healthy muscle, ultrasound (US) waves are transmitted through organized tissue. In diseased muscle, sound may be reflected at areas of increased fibrosis, fatty infiltration, inflammation, or necrosis (2).

The objective of this study was to use ultrasound to determine whether there is a relationship between muscle size/structure and functionality measures in children with CP. In this study, we used US to analyze muscle echotexture, which refers to the speckle pattern produced as sound propagates through tissues.

Participants in this study included 22 children (mean age = 10.6) with a diagnosis of spastic bilateral CP due to a peri-ventricular white matter injury. Children were excluded if they had received baclofen, surgery to the lower extremities in the past year, or any major surgery within the past 6 months. Ultrasound images were collected at 50% muscle length on the leg ipsilateral to the non-dominant upper extremity. Statistical echotexture analysis was performed using a region of interest for both the contracted and relaxed muscle states. Quantitative methods were used to estimate the statistical properties of the speckle to understand the underlying tissue microstructure. All outcome variables were analyzed using SPSS. Pearson product-moment correlation coefficients (r) were used to assess relationships between variable pairs ($p < 0.05$).

Our results demonstrate that an increased echotexture value is correlated with gait function: an inverse relationship was found between RF echotexture during relaxation and self-selected gait speed. Statistically significant relationships ($p < 0.05$) were also found between RF muscle size (cross-sectional area and thickness) and several measures of functionality, including free and fast cadence on an elliptical device, scores on the PODCI and PEDI questionnaires, and knee extensor strength.

Evidence from pre- and post- strengthening interventions have demonstrated an increased muscle size on ultrasound, however, changes in echotexture have not been examined. In muscles of children with CP, the total amount of collagen is increased and is correlated with severity of the disease (3). These changes in muscle structure may cause the US image to appear more echogenic (brighter) and to have an increased echotexture due to a disorganized muscle structure.

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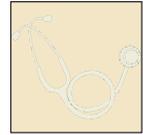
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Serotherapy with Alemtuzumab but not ATG is Associated with Increased Adenovirus Infection in Pediatric Recipients of Cord Blood

Hematopoietic stem cell transplantation (HSCT) is curative for a number of malignant and non-malignant conditions in children. Unrelated cord blood transplant (UCBT) is an established graft source for HSCT. Pre-transplant serotherapy has been used in UCBT pre-transplant to immunosuppress the host as well as to potentially reduce the incidence of graft-versus-host disease (GVHD). The benefit of this approach remains unknown though. The use of serotherapy agents such as anti-thymocyte globulin (ATG) and alemtuzumab may be associated with delayed immune reconstitution, leading to increased viral reactivation. We studied the impact of serotherapy along with other factors on viral reactivation, GVHD (grades 2-4), and transplant-related mortality (TRM) at 100 days. The statistical analysis used was chi-squared analysis, and Kaplan-Meier cumulative incidence along with log rank tests. This retrospective study consisted of 47 consecutive UCBT recipients (between years 2006-2014). Patients had a median age of 3 years (range 0-17) and had the following diagnoses: leukemia (n = 19), immunodeficiency (n = 10), hemoglobinopathy (n = 7), bone marrow failure syndrome (n = 5), metabolic disorder (n = 3), histiocytic disorder (n = 2), other (n = 1), conditioning type [myeloablative (n = 21) and non-myeloablative (n = 26)], cell dose [median = 6.15×10^7 ($0.9 - 18.9 \times 10^7$)], serotherapy [no serotherapy (n = 17), ATG (n = 15), and alemtuzumab (n = 15)], and HLA matching. Amongst all these variables, underlying diagnosis was the only category to have a relationship with acute GVHD, with leukemia being associated with more acute GVHD ($p = 0.048$). In relation to viral reactivation the type of conditioning had strong evidence of relationship with non-myeloablative conditioning on CMV ($p = 0.044$) and myeloablative conditioning on EBV ($p = 0.046$). We also found that the alemtuzumab type of serotherapy used had strong evidence of a relationship to the reactivation of ADV ($p = 0.044$).

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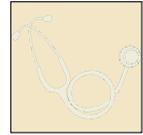
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Are repeat outpatient ketamine infusions associated with cognitive dysfunction?

INTRODUCTION:

Outpatient ketamine infusions can be effective in relieving severe neuropathic pain for a period of weeks or months. The NMDA receptor is involved in learning and memory and antagonists such as ketamine may be associated with cognitive impairment. The objective of this study is to investigate whether repeat outpatient ketamine infusions are associated with cognitive dysfunction as measured by the Manos 10-point clock test, a validated screening tool for cognitive dysfunction.

METHODS:

With IRB approval, patients undergoing repeat outpatient ketamine infusions were asked to complete a Manos 10 point clock test before and after each ketamine infusion and on the follow up clinic visit 2 to 4 weeks after the last infusion. The clock is scored using the Manos 10 point clock drawing criteria. Intact cognition was a score of 10, probable cognitive deficit, less than 8, and severely impaired at less than 4.

Statistical analysis was done in two parts. In the first part we assessed each episode individually based on pre and post scores from each of the three infusions for that episode. A mean score chart was drawn to see the trend of the data, followed by a repeated measure two-way Anova that tested the significance of the difference in the means, and finally the GEE (general estimating equation) was used to detect which factors contributed significantly. For the second part we assessed the episodes against one another. A plot of the mean score of the pre and post tests for each episode was drawn, followed by a two-way measured ANOVA test and GEE model that was applied on episodes and pre-post test to check if the episode effect is significant.

RESULTS:

Each patient was given ketamine infusions for 3 consecutive days constituting one episode. These episodes were repeated 4 to 16 weeks apart. Data from 22 patients, who collectively had 91 repeat episodes, were collected. We examined the association of pre and post infusion clock scores within each day of infusion and found no significant difference in scores among the three days in each episode. We also examined post infusion clock scores over multiple episodes and found no difference in mean clock scores amongst each of the first three episodes, with the fourth episode showing a statistically significant difference that is attributable to outliers within that data set.

CONCLUSION:

Ketamine use may be associated with decreased cognition. In our study, patients with neuropathic pain receiving repeat outpatient ketamine infusions did not demonstrate cognitive dysfunction as tested with the Manos10-point clock scale.

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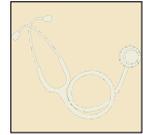
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Effectiveness of Phenobarbital and Levetiracetam in Treating Neonates with Hypoxic-Ischemic Encephalopathy: A Retrospective Study

OBJECTIVES:

To report the use and effectiveness of anti-epileptic drugs (AEDs) to treat seizures in neonates with hypoxic-ischemic encephalopathy (HIE).

METHODS:

We reviewed medical records of 79 consecutive full-term newborns with hypoxic-ischemic encephalopathy and treated with a hypothermia protocol within six hours of birth. We analyzed the association of AEDs with seizure burden and survival using Fisher's exact and Wilcoxon rank-sum tests.

RESULTS:

Within 24 hours of admission to the NICU, 45/79 (57%) had at least one video-EEG confirmed seizure. Of those with seizures, 17 (38%) were treated with phenobarbital (PHB) only, 12 (27%) were administered levetiracetam (LEV) only, and 14 (31%) were treated with both PHB and LEV. The choice of LEV versus PHB was physician-dependent and likely biased. The death rate among the PHB group (47%) was significantly higher than the LEV group (8%), and statistically significant ($p = 0.043$), likely indicating a higher burden of disease among PHB recipients. Neonates that started PHB treatment versus those treated with LEV had a significantly longer median duration to seizure cessation ($p = 0.048$). In addition, those treated with a combination of LEV and PHB had significantly longer latency to seizure freedom than those treated with LEV only ($p = 0.005$). Neonates that received PHB had a median latency of 67 hours (IQR 24-86.5), those treated with LEV had a median latency of 20.7 hours (IQR 0-54.5), and those administered both drugs had a median latency of 85.4 hours (IQR 48-118.9)

CONCLUSIONS:

In the absence of a definitive trial comparing PHB to LEV, most practitioners continue to favor phenobarbital as the antiepileptic drug of choice for treatment of neonatal seizures. Our study suggests that LEV may be a viable and perhaps even superior alternative to PHB for treatment of neonatal seizures. However, this study is limited by a relatively small sample size and a lack of randomization, and may be confounded by physicians choosing PHB for neonates who are inherently more difficult to treat. Further study is needed to adjust for this potential bias, and more broadly, a double-blind randomized noninferiority trial comparing LEV and PHB would definitively settle this debate.

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Social Impact of Facial Infantile Hemangiomas on Preteen Children

IMPORTANCE:

Involuted infantile facial hemangiomas (IH) may adversely affect social skills in children.

OBJECTIVE:

To assess the social impact of involuted facial IH in preteen children.

DESIGN:

Observational, cross-sectional study of social anxiety and skills in preteens diagnosed with facial IHs during infancy using following psychiatric scales:

1. Social Anxiety Scales for Children-Revised (SASC-R, completed by subjects) with domains of:

FNE: Fear of Negative Evaluation

SAD-New: Social Avoidance/Distress in New Situations

2. Social Competency Inventory (SCI, completed by parents) with domains of:

Prosocial Behavior

Social Initiative

Setting: Academic institution and a community dermatology practice

PARTICIPANTS:

144/236 parents of preteen, school-age subjects with a history of facial IH were reachable by telephone and mailed study packets. 30/144 returned completed questionnaires.

Intervention: Demographic, clinical details and questionnaire responses were collected and questionnaire scores were compared with established normative data.

RESULTS:

Subjects' mean age was 10.0 years (5.4-12.9) with a 2:1 female:male ratio. 83% had a single IH and the remaining had multiple with at least one IH in a cosmetically sensitive area. The periocular region was the most common site of IH, followed by the cheek, nose, lip/perioral, and ear. 19 subjects had prior treatment for their IH.

SASC-R:

Social anxiety of subjects was not increased over normative data however subjects that did not receive IH treatment had significantly greater anxiety for new situations compared to those subjects that did receive treatment (SAD-New mean 15.6 vs. 11.5 $p=0.0245$).

SCI:

Prosocial Orientation of subjects was similar to normative data (3.96 vs. 3.89, $p=0.501$) however social initiative tended to be poorer in subjects compared to normative controls (mean 3.81 vs. 4.03 $p = 0.065$). Furthermore social initiative was significantly poorer in untreated subjects vs. treated subjects (mean 3.45 vs 4.03 $p = 0.006$).

CONCLUSIONS:

Preteen children with involuted, untreated facial IH have higher social anxiety in new situations and decreased social initiative compared to children who receive treatment for their facial IH. These effects may adversely affect peer relationships and persist as social inadequacies in adolescence and adulthood.

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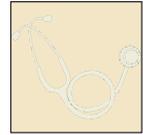
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The Role of Imaging in the Diagnosis, Grading and post operative Management of Patients with Otospongiosis

BACKGROUND INFORMATION/PURPOSE:

Temporal bone imaging is an important part of the diagnosis of otospongiosis. Moreover it is also an important branch point in the clinical decision making process to do with the treatment of otospongiosis, specifically before and after surgical intervention. The purpose of this poster is to describe the ways in which high-resolution temporal bone imaging can help to inform the ongoing surgical management of otospongiosis after diagnosis has been made.

EDUCATIONAL GOALS/TEACHING POINTS:

- Pathophysiology and clinical aspect of otospongiosis
- Imaging of otospongiosis
- Grading of disease
- Differential diagnosis
- Treatment
- Post operative imaging, including complications and surgical failure.

Key Anatomic or Pathophysiologic Issues, Imaging Findings or Imaging Technique:

High-resolution CT of the temporal bone provides detailed visualization of the anatomy relevant to the differential diagnosis of otospongiosis: the oval window, round window, facial nerve canal, middle ear ossicular chain, jugular bulb, labyrinth (cochlear including the spiral ligament, semi-circular canals) and otic capsule. This allows sub-differentiation of otospongioses in terms of grading, and by location: stapedio-fenestral, retrofenestral/cochlear, peri-cochlear/fissular, with or without round window involvement; as well as differentiation of primary and secondary stapes surgery failure by etiology:

- Round window obliteration
- Tympanosclerosis
- Superior semicircular canal dehiscence
- Perilymphatic fistula
- Incus/malleus fixation; and
- Subluxation/dislocation
- Bone regrowth at the oval window
- Lysis of the incus.

CONCLUSION:

Beyond diagnosis, high-resolution temporal bone imaging is an important part of the clinical decision making process for the management of otospongiosis before and after surgical intervention.

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A Phenomenological Study of Developing Competency in Thyroid Surgery

OUTCOME OBJECTIVES:

The Accreditation Council for Graduate Medical Education and Resident Review Committee has guidelines on assessing surgical qualifications. To help educators understand this better, this qualitative study will:

1. Explore the resident's perspective on gaining experience and achieving competency in thyroid surgical procedures.
2. Document the learning methods residents use to gain thyroid surgery experience.

METHODS:

From 2012-2014, 14 chief residents (otolaryngology or general surgery) from local teaching hospitals were interviewed. These semi-structured interviews were recorded, transcribed, and then broken up into codes utilizing Moustakas' analysis. The codes were then used to develop a comprehensive list of master themes regarding the achievement of competency in thyroid surgery. Epoche, debriefing, investigator triangulation, reciprocal coding of transcripts, member checks, and thick, rich description established data trustworthiness.

RESULTS:

Surgical specialty residents experience and learn thyroid surgery in five related but different learning experiences:

1. Self-directed learning is significant during residency.
2. Repetition with graduated autonomy is key.
3. Effective mentors are competent surgeons who challenge residents and use positive teaching techniques.
4. Residents employ active learning through the "see one, do one, teach one" philosophy.
5. Learning from complications is of importance to residency training.

CONCLUSION:

This study demonstrates how residents progress in approaching competency in thyroid surgery. Adult learning strategies are preferred, and programs should incorporate tailored techniques in order to meet the individual needs of their residents. A more in depth study should be continued to more precisely measure achievements and milestones throughout residency.

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Advances in Semen Analysis Used in Epidemiological Research

Male factor infertility accounts for 25 to 30% of all cases of infertility and contributes, in combination with female factors, another 30%. The prevalence of male factor infertility indicates its importance in the field of epidemiological research, which involves characterizing the fertility status of a male population. The WHO laboratory manual for the examination and processing of human semen provides guidelines for performing semen analysis and studies on male infertility in clinical treatment and research laboratory settings. However, within these guidelines there are several options within the outlined protocols that are available for investigators performing epidemiological research.

This article identifies the strengths and weaknesses of specific guidelines in the WHO manual and makes recommendations for investigators interested in performing epidemiological research on male infertility.

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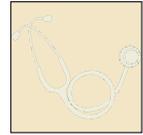
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The effect of obstructive sleep apnea on sexual function in men

INTRODUCTION:

Men with obstructive sleep apnea (OSA) are more likely to suffer from decreased erectile and sexual function compared to matched controls. The effect of OSA on each specific domain of erectile function is less clear, as is which domains of erectile dysfunction improve with CPAP treatment.

METHODS:

Prospective observational single-centre study. Men 21 years or older, with a regular sexual partner, diagnosed with OSA by polysomnography, were enrolled prior to starting CPAP treatment. Baseline sexual function was determined by a self-administered gender-specific, validated sexual function questionnaire; the International Index for Erectile Function (IIEF). The IIEF consists of 5 domains: erectile function, orgasmic function, sexual drive, intercourse satisfaction and overall satisfaction. Patients were classified as having either mild (AHI 5-15), moderate (AHI 15-30) or severe sleep apnea (AHI >30), and their sexual function scores were compared with ANOVA one-way variance for independent samples. Baseline IIEF scores were compared with post- CPAP treatment scores using the paired two sided t-test. P values of less than 0.05 were considered significant.

RESULTS:

Twenty-nine men were enrolled. The mean age was 45.7 ± 11.2 years and BMI was 34.4 kg/m^2 . The average apnea-hyponea score (AHI) was 36.1 ± 21.4 events/ hr. When stratified according to AHI, men in the mild, moderate and severe apnea groups had no significant difference in age or BMI, nor in the domains of erectile dysfunction, except in the domain of sexual desire, where their scores were 9.0 ± 2 ; 7.9 ± 1.4 and 5.8 ± 2.7 ; $p = 0.04$ respectively. Nine men completed follow-up surveys (median follow-up time 133 [111-509] days). Following treatment with CPAP, there was a significant improvement in the domain of orgasmic function only (7.0 ± 3.0 to 9.8 ± 0.7 ; $p = 0.03$).

CONCLUSION:

Men with OSA may suffer from erectile dysfunction, although the severity of their OSA does not correspond with the severity of erectile function. Treatment with CPAP can be beneficial in improving orgasmic function in this small cohort. Knowledge of improvement of sexual function and libido with CPAP treatment for men could strengthen the notion that sleep apnea-induced sexual dysfunction is reversible.

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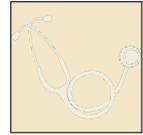
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CHILDREN'S NATIONAL MEDICAL CENTER

Long-term Coarctation of Aorta

INTRODUCTION:

Coarctation of aorta occurs is the sixth most common cardiovascular defect, accounting for 5% of all congenital heart defects. The location of the lesion in relation to the aorta is important in the specific diagnosis and subsequent therapy of the coarctation. The surgical approach is determined by patient age, extent of stenosis, and coexisting cardiovascular lesions. We present a case of long segment aortic coarctation for repair through right thoracotomy.

CASE DESCRIPTION:

A 2 year old, 8 kg male with a double aortic arch, presented for redo aortic coarctation repair. CT angiogram showed a hypoplastic left aortic arch with extreme stenosis below the level of the left subclavian which was clipped during his prior operation. Cardiac catheterization indicated a patent transverse aortic arch to the left subclavian and flow between the left subclavian and thoracic aorta between surgical clips. After routine induction of anesthesia and placement of invasive lines, the patient was positioned for a right thoracotomy. A 10mm ring-reinforced Gortex graft was used to connect the ascending aorta to the descending thoracic aorta. Mild hypothermia (34-35 degrees Celsius) was maintained throughout the repair with a total clamp time of 44 minutes.

DISCUSSION:

Paraplegia is one of the most serious long-term complications of coarctation repair; it occurs in 0.5-1.5% of cases and is secondary to diminished spinal cord blood flow during the cross clamp. In this case, spinal cord protection was of utmost importance because a long segment interruption of descending aorta needed repair. Minimizing clamp time along with moderate hypothermia has been shown to protect the adult spinal cord from injury. Most of the adult literature suggests that clamp times greater than 20 minutes leads to a progression of cell death. However, the anatomical differences between the pediatric spine and its adult counterpart are significant. Techniques, such as insertion of a lumbar drain to decompress the spinal column and promote perfusion, may not be feasible in the pediatric patient. In the case presented here, no gross clinical signs of neurologic injury occurred with the use of moderate hypothermia alone for spinal cord protection, despite a longer aortic cross clamp time. This could be due to the presence of collateral circulation that may have developed due to the significant stenosis that was present over a prolonged period of time. However, the question remains whether other monitoring, such as SSEP or somatic NIRS, should be employed to help confirm appropriate intraoperative spinal cord perfusion. Further studies to examine the utility of these monitoring modalities is warranted, as well as what benefit, if any, other protective methods may provide. Possible therapies to investigate include use of barbiturates to decrease oxygen consumption, low dose anticoagulation, or cardiac bypass.

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Blood, Brain and Now Bone - Learning More About an Often Overlooked Pathogen

INTRODUCTION:

Arcanobacterium haemolyticum (previously *Corynebacterium haemolyticum*), a facultative anaerobe, Gram positive rod was first isolated from United States servicemen and indigenous populations of the South Pacific in 1946. Early reported cases detailed *A. haemolyticum* as a causative pathogen for exudative pharyngitis (most commonly in adolescents) and cutaneous infections. Osteomyelitis caused by *A. haemolyticum* has been described in less than five cases in the literature. Here, we describe our experience in diagnosing patient with osteomyelitis caused by *A. haemolyticum*.

CASE REPORT:

A 30-year-old man with a history of peripheral neuropathy, diabetic foot ulcers, methicillin-resistant *S. aureus* osteomyelitis and amputation of the left second distal phalanx, who presented with a malodorous and painful plantar ulcer. Physical exam showed erythematous, edematous distal left foot and 3cm x 0.5cm x 2mm plantar ulcer with necrotic tissue and serosanguinous drainage. Labs revealed elevated inflammatory markers. Left foot X-ray showed previous amputation of second distal phalanx, soft tissue swelling and indistinctness of the cortex of the 3rd distal phalanx, consistent with osteomyelitis. He underwent intraoperative debridement and resection of the distal second metatarsophalangeal joint. Intraoperative wound and bone cultures grew aerobic gram-positive bacilli with few diphtheroids. Histochemical analyses confirmed *Arcanobacterium haemolyticum* three days from the procedure. He was discharged home on a six-week course of IV clindamycin with wound VAC.

DISCUSSION:

A. haemolyticum infections can be separated epidemiologically into two distinct subsets. Healthy adolescents presenting with upper respiratory tract infections and immunocompromised patients presenting with systemic serious infection. It is often overlooked or misdiagnosed due to its slow growth and features similar to other pathogens. Initial microbiology reads that show mixed flora, including gram-positive rods and diphtheroid bacilli, are part of the normal flora of the skin. *A. haemolyticum*'s distinct colony features typically are only seen after 72 hours of incubation.

CONCLUSION:

Gram-positive organisms, including *Staphylococcus aureus*, β hemolytic *Streptococcus*, and coagulase-negative *Staphylococcus* are the most common cause of osteomyelitis. *A. haemolyticum* is another gram-positive organism and the causative agent of osteomyelitis that is less commonly known. However, differentiation of *A. haemolyticum* from other gram-positive organisms is essential for proper management and appropriate antibiotic treatment.

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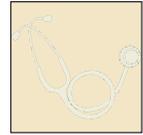
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The Impact of Paravertebral Blocks on Rib Fractures and Survival

INTRODUCTION:

Paravertebral blocks are an underutilized modality of pain control that should improve survivability in trauma patient population.

METHODS:

Using 35,058 patients identified in the 2008 NTDB with ≥ 3 rib fractures or a sternal fracture, we created a model of expected death rates based on patient characteristics such as demographics (age, sex, race); rib fracture variables (number of ribs fractured, whether open or closed, sternum fracture, "flail-chest"); whether penetrating, blunt, burn, or other injury type; and injury severity scores (GCS, ISS). A logistic regression model developed from the NTDB sample predicted the outcomes of the patient sample. An algorithm determined a risk assessment and compared this model with paravertebral catheter usage for death and total hospital los > 3 days. An ordinal risk variable was created using 6 groups (10th, 25th, 50th, 75th, and 90th percentiles). This risk score calculator was used to compute risk scores all GW trauma patients with ≥ 3 rib fractures or sternal fractures.

RESULTS:

The distribution of death rates for patients with and without PVB was analyzed, stratified by risk category. Pts with a highest two risk stratified death rates who received a PVB had a much lower than expected death rate. The length of stay in the hospital was significantly higher in the highest risk stratified group who received PVBs.

CONCLUSION:

Although increases their hospital length of stay, Pts in the highest risk stratified groups of with ≥ 3 rib /sternal fractures had an improved survival with use of paravertebral blocks.

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Four Rods Prevent Rod Breakages and Pseudarthrosis in Pedicle Subtraction Osteotomies

STUDY DESIGN:

This study was a retrospective, radiographic review of consecutive pedicle subtraction osteotomies performed at two centers. The difference in technique between the two centers was the use of 2 rods vs. 4 rods.

OBJECTIVE:

The purpose of this study was to assess two methods of posterior instrumentation (2 rods vs. 4 rods) used in the surgical technique when performing the pedicle subtraction osteotomy (PSO).

SUMMARY OF BACKGROUND DATA:

The PSO has been widely used to treat sagittal plane deformities. Non-unions and rod breakages are well-known complications of pedicle subtraction osteotomies. Multiple rods appear to help in osteotomy closure and prevent rod breakage.

METHODS:

Group 1 using 4 rods had 29 pts and Group 2 using 2 rods had 20 pts that were analyzed. The clinical as well as the radiographic data was reviewed. Statistical methods used were two-sample t-tests and Fisher's Exact Test.

RESULTS:

The mean preoperative Sagittal Vertical Axis ($p=0.014$), Center Sacral Vertical Line ($p=0.004$), and Pelvic Incidence + Thoracic Kyphosis+ Lumbar Lordosis ($p=0.033$) were larger for Group 1. Preoperative to postoperative radiographic measurements did not differ including the PSO angle between institutions. Pseudarthrosis of 25% with 2 rods was greater than 3.4% with 4 rods ($p = 0.035$). Rod breakage was 25% with 2 rods and 0% with 4 rods ($p = 0.008$). The broken rods were Stainless Steel (diameters 5.5 mm & 6.35 mm) and Cobalt Chrome (diameters 5.5 mm, 6.0 mm & 6.0 mm). The patient with a pseudarthrosis from Group 1 had an infection and developed a pseudarthrosis after rod removal. Rates of other major and minor complications did not differ significantly.

CONCLUSION:

Both techniques can be successful in correcting sagittal plane deformity. The novel four-rod technique is more successful in preventing non-unions and rod breakages compared two rods.

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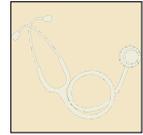
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Progressive Supranuclear Palsy Treatment- A Systematic Review

INTRODUCTION:

Progressive Supranuclear Palsy (PSP) is an uncommon neurodegenerative disease associated with postural instability, falling, and memory loss. Because of clinical similarities, it is often classified as atypical Parkinson's disease. PSP may present abruptly with a relatively rapid decline, leading to death in a few years. Different therapeutic approaches have been suggested for PSP, but their efficacy is unclear. To our knowledge, there has been no systematic review of PSP treatment.

OBJECTIVE:

To determine the effectiveness PSP treatments.

METHODS:

A systematic review of published literature was completed. We searched using PubMed and SCOPUS for related articles. The search terms are listed in the Table. To maximize sensitivity, we also searched "gray" literature. Our initial inclusion criteria were: English, published after January 1, 1994, provides data on a treatment intervention for PSP patients, and had measurable outcomes.

Articles were then excluded if they had: no comparison group; no clear, defined interventions; outcome(s) that were not objective (we allowed opinion/observations recorded by the patient or a family member); and outcome assessors not blinded to the intervention. The control population needed to have an intervention similar to the experimental intervention (an attention sham).

We then grouped the remaining articles according to the therapeutic domain: ophthalmic treatment, physical therapy, intra/trans cranial procedures and medications.

RESULTS:

The initial search obtained 617 publications. Of these, 28 met our inclusion criteria. These were grouped by therapy: 2 dealt with an ophthalmic interventions; 3 with a PT/rehabilitation intervention; 4 with some intracranial procedures; and 17 dealt with medications. 2 dealt with 2 or more types of intervention. Of these, none remained after application of our exclusion criteria. A meta-analysis was not possible. Authors' conclusions: No therapy has been established as efficacious for PSP. Studies of one medication, Co-Q 10, have been encouraging, and a study is currently active. An approach using physical therapy (balance training) and eye movement rehabilitation found some benefit in gait and general mobility, but there was no adequate control and the overall benefit to patients (falls, quality of life, hospitalization, etc.) was not evaluated.

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The Prevention of Delirium and Complications Associated with Surgical Treatments

INTRODUCTION:

Postoperative delirium is one of the most common complications of major surgery, affecting 10-70% of surgical patients 60 years and older. Delirium is an acute change in cognition that manifests as poor attention and illogical thinking and is associated with longer intensive care unit (ICU) and hospital stay, long-lasting cognitive deterioration and increased mortality. Ketamine has been used as an anaesthetic drug for over 50 years and has an established safety record. Recent research suggests that, in addition to preventing acute postoperative pain, a subanaesthetic dose of intraoperative ketamine could decrease the incidence of postoperative delirium as well as other neurological and psychiatric outcomes. However, these proposed benefits of ketamine have not been tested in a large clinical trial.

METHODS:

The Prevention of Delirium and Complications Associated with Surgical Treatments (PODCAST) study is an international, multicentre, randomised controlled trial. 600 cardiac and major non-cardiac surgery patients will be randomised to receive ketamine (0.5 or 1 mg/kg) or placebo following anaesthetic induction and prior to surgical incision. For the primary outcome, blinded observers will assess delirium on the day of surgery (postoperative day 0) and twice daily from postoperative days 1-3 using the Confusion Assessment Method or the Confusion Assessment Method for the ICU. For the secondary outcomes, blinded observers will estimate pain using the Behavioral Pain Scale or the Behavioral Pain Scale for Non-Intubated Patients and patient self-report.

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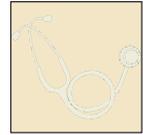
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Genetic Variation in Neuromedin U Influences Lean Body Mass and Bone Morphometry in Men

PURPOSE OF STUDY:

Neuromedin U (NMU) is a highly conserved hypothalamic neuropeptide that regulates food intake, body weight, glycemic control, energy homeostasis, and is thought to have an effect on the stress response, inflammatory diseases, and the biological clock^{1,2}. NMU aids in the formation of bone by acting on osteoblast beta-2-adrenergic receptor (ADR β 2), which regulates cell proliferation in bones³. Understanding genetic differences in how NMU affects bone development and metabolic functions may be important for creating strategies to maximize childhood bone development and prevent osteoporosis later in life. This study aimed to determine if there is a relationship between genotype for the chosen single nucleotide polymorphisms (SNP) of the NMU gene, rs6827359, rs12500837, and rs9999653, and bone health by examining their association with bone mineral density (BMD) and bone mineral content (BMC) in healthy individuals.

METHODS USED:

The Bone Health (BH) cohort included healthy African American children aged 5 to 9 years. The Muscle and Bone (MB) cohort included healthy college aged participants. Dual energy x-ray absorptiometry scans were obtained using the Hologic QDR Discovery A Densitometer. Genotyping was performed using the Taqman allele discrimination assay.

MB: Total body BMD, lumbar bone mineral density, total body BMC, and lumbar BMC were significantly associated with variations in rs6827359. Variations in rs12500837 were found to be significantly associated with lean mass in males. BH: Lumbar BMD, lumbar BMC without head, and total body BMD were associated with variants in rs12500837.

CONCLUSIONS:

Osteoporosis is the most common bone disorder in the western world and is a significant cause for morbidity and mortality. We have demonstrated that variations in the NMU gene are associated with better BMD and BMC primarily in men. Further exploration into how these genetic variants influence bone development may be important for maximizing bone health.

SIGNIFICANCE:

This study demonstrates that genetic variations in the NMU gene are associated with higher BMD and BMC primarily in men. Future research into the influence of NMU on bone development may lead to more effective treatment strategies to prevent the debilitating bone diseases that affect millions of Americans such as osteoporosis.

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Dose-response of intrathecal morphine post-cesarean

Most women undergoing elective cesarean delivery in the United States receive spinal anesthesia, including a dose of intrathecal (spinal) morphine for postoperative analgesia. However, the appropriate dose of morphine is unclear. In an era of “multimodal analgesia” including routine non-steroidal anti-inflammatory medications, the required dose of morphine may be significantly less than the 200-300 µg common a decade ago. We have performed a 2-center, prospective, randomized, blinded trial comparing three doses of intrathecal morphine, combined with routine intravenous (IV) ketorolac, in 144 healthy women undergoing elective cesarean delivery.

METHODS:

Subject patients received spinal or combined spinal-epidural anesthesia with an intrathecal injection of 12 mg hyperbaric bupivacaine, 15 µg fentanyl and a dose of 50, 100, or 150 µg morphine in a volume of 2.2 ml. Patients received 30 mg ketorolac IV before leaving the operating room, and 15 mg IV every 6 hours for the duration of the study (24 hours). All received additional postoperative analgesia in the form of self-administered IV morphine. The primary endpoint was total IV morphine administered over 24 hours.

RESULTS:

There were no differences between dose groups (or institutions) in IV morphine use over 24 hours, or for the first 12 hours. Visual analog scale scores for pain, nausea/vomiting or overall satisfaction did not differ. There was slightly less pruritus at 6 and 12 hours in the 50 µg group compared to the two larger dose groups; this difference was not present at 18 and 24 hours, and there was no difference in the percentage of patients in each group who required treatment of nausea or pruritus. There were no instances of respiratory depression or significant sedation.

CONCLUSION:

There do not appear to be important differences in analgesia or side effects in the dose range of intrathecal morphine utilized, 50-150 µg.

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Factors associated with non-accidental trauma evaluation among patients <36 months old presenting with femur fractures

PURPOSE:

In 2009 the AAOS published practice guidelines on the treatment of pediatric diaphyseal femur fractures recommending a non-accidental trauma (NAT) work-up on all patients presenting <36 months of age. A previous study suggested poor clinical compliance (48%) with this recommendation. We assessed factors associated with a NAT evaluation for femur fractures in this population to determine areas for improvement in compliance with this guideline.

METHODS:

We performed a retrospective review of patients presenting to a single pediatric tertiary care hospital with a diaphyseal femur fracture between 2007 and 2012, <36 months old. Medical records were reviewed for documentation of an NAT evaluation, patient characteristics, presence of other fractures or injuries, and hospital of presentation. Radiographs were reviewed for fracture pattern. T-tests (for age) and Chi-square tests (for all other variables) were used to assess for differences overall and before and after CPG publication.

RESULTS:

During the study period, 281 children <36 months presented with femur fractures; 41% of these patients underwent evaluation for NAT. Over the study period, the following factors were significantly associated with receipt of the NAT evaluation: younger age ($p<0.001$), transfer from an outside facility ($p=0.03$), and identification of another fracture ($p=0.004$). Prior to publication of the CPG, non-white patients were much more likely to undergo NAT evaluation compared with white patients (43% vs 19%; $p=0.01$). After publication, this differential disappeared (43% vs 47%; $p=0.69$). Fracture pattern and patient gender did not influence receipt of NAT evaluation.

CONCLUSION:

In general we found poor utilization of NAT evaluation for patients presenting with femur fracture < 36 months old. Despite CPG publication, only modest improvements in this evaluation occurred over time, with less than half of all patients being evaluated. Patients transferred from other institutions, presenting with concomitant fractures, and very young children were more likely to undergo NAT evaluation, indicating patients with isolated femur fractures and older children should be focused on to improve compliance with this CPG. Interestingly we found an improvement in the utilization of NAT for white patients following the CPG publication, indicating a possible correction of racial bias in initiation of NAT evaluation.

SIGNIFICANCE:

Evaluation of children < 36 month old for NAT following presentation of a femur fracture is severely inadequate. Older patients, those presenting initially to tertiary care centers, and those with isolated injuries are at greatest risk for non-evaluation. The implementation of this CPG may have improved racial bias in the use of NAT evaluation.

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A very rare cause of pancytopenia.

INTRODUCTION:

Levetiracetam (Keppra) is a pyrrolidone derivative and acts as an anti-epileptic medication by modulating neurotransmitter release. Pancytopenia is a very rare adverse effect caused by levetiracetam. There are fewer than four case reports in the medical literature discussing the association between levetiracetam and pancytopenia. The pathogenesis behind this relationship is unclear. Therefore, this case will serve to spread awareness of a rare cause of pancytopenia and to hypothesize how this medication causes pancytopenia.

CASE REPORT:

A brain MRI of a 79-year-old female with a medical history of hypertension, Type II diabetes, and CVA revealed a right temporoparietal mass. She was started on dexamethasone prior to surgery due to the extensive amount of vasogenic edema. She underwent a temporal craniotomy with resection of the mass and was started on levetiracetam as seizure prophylaxis. Postoperatively, her blood count remained stable. She was on levetiracetam, dexamethasone, pantoprazole, and enoxaparin as prophylaxis. She was noted to have an episode of melena and anemia on the fifth day postoperatively, which resulted in a transfusion of two units of blood with an appropriate response. No acute gastroenterological intervention was deemed necessary. The patient was also noted to develop thrombocytopenia and leukopenia. Thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, and heparin-induced thrombocytopenia were ruled out. Pantoprazole and enoxaparin were discontinued without any improvement in cell counts. The patient received a total of five units of platelets due to a platelet count of less than 100,000. Levetiracetam was changed to lacosamide on day ten post-operative, and dexamethasone was continued without change. Within 24 hours of discontinuing levetiracetam, the platelet counts improved and continued to trend upward. A noticeable increase in white blood cells and hemoglobin were seen five days after that.

DISCUSSION:

Levetiracetam was approved by FDA for partial seizure, myoclonic seizure, and generalized tonic-clonic seizure. It is used off-label as seizure prophylaxis. This medication is associated with a few side effects that include behavioral changes, headache, drowsiness, and weakness. Hematologic adverse effects are rarely caused by this therapy. These effects include anemia, thrombocytopenia, and leukopenia. Our patient developed pancytopenia induced by levetiracetam and was resolved after we discontinued this medication. Her hemolysis profile and blood smear did not reveal any signs of hemolysis. Therefore, we hypothesize that levetiracetam induces pancytopenia by causing bone marrow suppression.

CONCLUSION:

Clinicians should be aware that levetiracetam induces severe pancytopenia. We should consider changing levetiracetam to lacosamide in patients who develop pancytopenia with negative hemolysis profile. Further studies need to understand how levetiracetam induces bone marrow suppression and to find a blood test for diagnosis.

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Effects of a randomized health care transition care coordination intervention on perception of chronic illness care and readiness to transition

BACKGROUND:

Care coordination has been reported to be effective in facilitating health care transition (HCT) from pediatric to adult care. No studies have examined the effects of HCT care coordination compared to a robust control group in real time. In this study we report longitudinal perception of chronic illness care and transition readiness data from a randomized HCT care coordination intervention trial for youth with special health care needs.

METHODS:

210 participants ages 16-22 years old (mean age 18.9 +/-1.7 years) were enrolled in a randomized controlled HCT care coordination intervention and were recruited from a large urban academic adolescent health clinic located in a pediatric tertiary referral health system. Following enrollment and baseline data collection, 105 participants were randomized to the HCT care coordination intervention group, and the other 105 were randomized to the control group. All participants were interviewed at 0, 6 and 12 months completing the Patient Assessment of Care for Chronic Conditions (PACIC) which assesses five domains (patient activation, delivery system design, decision support, goal setting, problem solving, and follow-up/coordination), the Client Perceptions of Coordination Questionnaire (CPCQ) assessing perception of patient-centered care and care coordination, and a self-rating on a scale of 1-10 how ready they feel to transfer to adult care. We compared responses in intervention and control participants using contingency table analyses and relied on chi square tests to identify differences that were unlikely to have occurred by chance.

RESULTS:

At baseline there were no statistical differences in PACIC, CPCQ or readiness scores when comparing the intervention to control group. At 6 months, no differences were observed in the PACIC scores, while intervention participants rated quality of chronic illness care higher ($p=0.065$) and reported less conflicting advice from providers ($p=0.018$) than the control group. At 12 month follow-up there were significant differences seen in the PACIC as patient activation ($p=0.015$), goal setting ($p=0.034$), problem solving ($p=0.009$) and coordination/ follow-up ($p=0.016$) all rated statistically significantly higher in the intervention than control group. At 12 months, intervention participants reported more often receiving the services they thought they needed ($p=0.03$), were less confused about the role of providers ($p=0.012$) and reported more frequent discussions with providers about future care ($p=0.05$) than control participants. There were no differences in self-rating of transition readiness between the two groups throughout the study period.

CONCLUSIONS:

This HCT care coordination intervention improved many aspects of quality of chronic illness care for participants. Self-assessment of readiness was not impacted by this intervention. Future studies need to assess medical outcome and cost data to see if these perceptions of improved quality of care translate to better HCT outcomes.

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Case Report: May-Thurner syndrome in pregnancy, and the risk of phlegmasia cerulea dolens

CASE:

A 37-year-old, 21 weeks pregnant, female presented with left lower extremity swelling and pain. She was found to have a deep vein thrombosis (DVT) and subsequently underwent a CT angiogram revealing a pulmonary embolus. The patient was treated for the DVT and PE with therapeutic low-molecular weight heparin. The pain and edema in her left leg, however, worsened significantly over the course of several days, and there was concern for phlegmasia cerulea dolens (PCD), an uncommon complication of acute massive thrombosis occluding the major veins of an extremity. PCD is characterized by significant swelling, pain, edema, and cyanosis of the extremity, with risk for limb ischemia and gangrene, and potential need for amputation. In our patient, a repeat LE Doppler revealed massive thrombus occluding the left common femoral vein and extending to the left popliteal vein. Due to the patient's pregnancy, thrombolysis and thrombectomy (otherwise the treatments of choice) were contraindicated. Using a conservative approach by Interventional Radiology, catheter tunneling through the extensive clot was done to recanalize the vessel. The procedure revealed that the patient had a rare anatomical finding known as May-Thurner syndrome (MTS). MTS, also known as iliac compression syndrome, is the result of extrinsic compression of the left common iliac vein by the right common iliac artery.

The combination of MTS and pregnancy, both independent risk factors for DVT, were most likely responsible for the extensive clot burden in our patient, leading to the rare complication of PCD.

This case report describes the clinical presentation and pathophysiology of May-Thurner Syndrome, including the risk of phlegmasia cerulea dolens, and discusses the management approach of PCD in the unique situation of a gravid patient with contraindications to thrombectomy and thrombolysis.

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A Dizzying Case

A 21 year old Serbian male with no past medical history presented our hospital with one month of headache, dizziness, and worsening ataxia with falls.

The patient had a prolonged stay given his worsening ataxia and requirement for rehabilitation with a tentative diagnosis of post-viral cerebellitis. After transfer to an onsite rehabilitation center, he was re-admitted for progressive symptoms and infectious, paraneoplastic and rheumatologic studies were negative. Three weeks into the admission, a detailed physical exam revealed a right testicular mass. At that time, the patient recalled testicular swelling and pain eighteen months prior, which resolved spontaneously without seeking medical attention. Ultrasound performed at bedside confirmed a testicular mass, but serum AFP and beta-HCG levels were negative. He was restarted on methylprednisolone, given IVIG, and underwent an orchiectomy resulting in gradual improvement in his symptoms. Pathology and staging revealed a pure T1 teratoma. He continued to improve with steroids and physical rehabilitation and he returned to Serbia to continue surveillance treatment.

The final diagnosis of his neurologic symptoms was seronegative paraneoplastic cerebellar degeneration. The sensitivity of checking paraneoplastic antibodies is only 50-60%, explaining our negative workup. Very few case reports have identified teratomas as a cause of paraneoplastic syndromes, but screening imaging studies including testicular ultrasound are recommended when suspicion for these syndromes is high. Furthermore, this case highlights the importance of doing a detailed physical exam, as patients can present atypically for the primary disease.

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Susceptibility to Obesity and Bone Mineral Density in Young African American Populations

Given the disparate effects of obesity on Europeans and African Americans, it is crucial to generate a better understanding of the genetic influences on obesity within the AA pediatric population. Monda et.al recently published a genome-wide association study identifying six SNPs associated with BMI, which were selected for genotyping in our pediatric AA cohorts to examine the relationship between genetic risk variants for obesity and bone mineral density (BMD).

This study includes AA children, ages 5 to 9 years. Case patients had an isolated and radiographically demonstrated forearm fracture and control patients had no self-reported history of a prior bone fracture. Dual energy x-ray absorptiometry scans were obtained. Phenotypes analyzed included lumbar BMD and bone mineral content. DNA was isolated using the Puregene Blood DNA purification kit. Genotyping was performed using the Taqman allele discrimination assay and called using the Applied Biosystems 7900HT Real-Time PCR system. Each phenotype was tested for an association with each SNP. The six SNPs and bone mineral density height adjusted z-score were analyzed using ANOVA/ANCOVA models as appropriate.

Of the obesity-related SNPs, we found a statistically significant association between Lumbar BMD (height adjusted z-score without head) and SNPs rs974417, and rs10261878. In these SNPs, participants showed higher lumbar BMD z-score. In some studies, obesity has been associated with increased bone mass in some, but results and mechanisms are inconclusive. In our BH cohort, we have shown those children with susceptibility to obesity to have already possessed higher lumbar BMD z-scores. This may indicate that increased BMD associated with obesity is more than just the mechanical loading of bone through excess weight, since the risk alleles confer both susceptibility to obesity and increased BMD z-scores.

Our study is one of few that have reported genetic studies of BMD determination in childhood, especially in AA population. It is crucial to understand these genetic differences on obesity. This will offer the possibility of better intervention and treatment options in the future.

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Sex Differences in the Association between Neck Circumference and Asthma

Studies evaluating the association between obesity and poor asthma control/quality of life commonly utilize body mass index (BMI) as the anthropomorphic measure of adiposity, despite its recognized limitations and the existence of alternative measures. For example, neck circumference (NC) has been shown to better indicate visceral adiposity than BMI. The objective was to examine the association between higher NC and worse asthma control/quality of life in youth with asthma, with particular attention to male-female differences. The Asthma Severity Modifying Polymorphisms (AsthMaP)-2 Project is an observational study of youth (ages 6 to 20 years, inclusive) with physician-diagnosed asthma. NC was measured, stratified according to age- and sex-specific cutoffs, and associated with asthma control (via Asthma Control Test [ACT] scores) and quality of life (via Integrated Therapeutics Group [ITG] - Asthma Short Form scores). The cohort included 116 youth at the time of these analyses. The mean \pm SD age was 11 ± 4 years, and 53% were male. The mean BMI percentile was at the 72nd \pm 28 percentile. Criteria for high neck circumference (NC) were met (i.e. above predefined age- and sex-specific cutoffs) in 31 (27%) participants. The results demonstrated that compared to males with a low NC, males with high NC had significantly worse asthma control and lower quality of life, as indicated by lower ACT and ITG scores, respectively. Similarly, female participants with high NC trended toward lower ACT scores than low NC females, but this and ITG scores were not significantly different. The proportion of variability in scores among females explained by BMI percentile was very small. Conversely, for males, the proportion of variability in these scores explained by adding NC to BMI percentile was significantly larger than BMI percentile alone: Among male youth with asthma, high NC was associated with worse asthma control and quality of life. Combined use of NC and BMI percentile explained asthma control and quality of life better than BMI alone for males. Future studies of asthma should include measurement of NC and other anthropogenic measures of regional adiposity to clarify sex differences in asthma.

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Change in wound fluid cytokine profile as chronic wounds transition from recalcitrant to healing phase

Normal wound healing involves four phases: hemostasis, inflammation, proliferation and remodeling, which progress sequentially regardless of wound etiology. Chronic wounds are arrested in the inflammatory phase and are unable to transition to the proliferation phase. Interactions between pathways contributing to the inflammatory state in chronic wounds are poorly understood. The purpose of this study was to utilize wound fluid specimens collected through the WE-HEAL Study to investigate whether wound fluid cytokine profiles change as a wound transitions to the healing phase.

METHODS:

The WE-HEAL Study is a biospecimen and data repository for studying chronic wounds approved by the George Washington University IRB (041408). In this study, the primary outcome is % change in wound surface area per week. Reduction >10% per week is considered healing. Wounds that are not shrinking by >10% per week are considered recalcitrant. Wound fluid specimens are collected using the Levine technique and are processed immediately upon collection.

Two patients with paired wound fluid specimens were selected for this study. In subject 1, specimen 1 was collected when the wound was recalcitrant and specimen 2 was collected when the wound was in the healing phase. In subject 2, both specimens were collected when the wound was in the recalcitrant phase. The Meso Scale Discovery V-Plex cytokine panel 1 and the V-plex proinflammatory panel 1 (MSD, Rockville, MD) were used to analyze proinflammatory cytokines in the wound fluid specimens. For the proinflammatory panel a 10 fold dilution was used and for cytokine panel-1 a 20 fold dilution was used. Samples were run in duplicate and processed according to the manufacturer instructions.

RESULTS:

Specimens from the persistently recalcitrant wound showed induction of proinflammatory cytokines and elevation of IL10 and IL7 which are known to be involved in the downregulation of the immune response. In contrast, the wound which transitioned to the healing phase demonstrated downregulation of proinflammatory cytokines. IL12/23p40 showed a higher fold upregulation in the wound which transitioned into the healing phase. In contrast, IL17 was elevated in the wounds that remained recalcitrant.

CONCLUSIONS:

This study demonstrates that wound fluid cytokine profiles are useful for investigating the inflammatory milieu in wound healing. Upregulation of IL12p40 in the healing wound suggests that TH1 responses may play a crucial role in the proliferative phase of wound healing. Elevated IL-17 levels in the recalcitrant wound suggest Th17 responses may play a role in inflammation amplification, hindering the transition to healing.

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To Explore the Relationship between Affective disorders and Eating habits with Body Mass Index and Chronic Kidney Disease

AIM:

Obesity, defined as a BMI > 30, is an epidemic in the United States. Obesity is a known risk factor for many chronic medical conditions among which chronic kidney disease is included. In patients with end stage renal disease (ESRD) there is a relationship between ESRD and depression. The goal of this study is to explore the relationship of affective disorders and eating habits in obese individuals with chronic kidney disease.

METHODS:

With an IRB approved protocol and patient consent, patients in the Medical Faculty Associates clinic completed two surveys - 1) Beck's Depression Inventory and 2) Diet/Exercise Survey. Additional information was obtained from the patient's chart (demographics, number of medications, comorbidities, BMI, eGFR, zip code). The surveys were scored for degree of depression and diet/exercise. Statistical analyses were performed using T-test for discrete variables and analysis of variance for continuous variables. Statistical significant was defined as $p < 0.05$.

RESULTS:

Of the 177 participants recruited, there was no statistically significant correlation between eGFR versus depression score and BMI versus depression score. There was also no statistically significant correlation between eGFR versus diet score and BMI and diet score.

CONCLUSION:

Although there was no statistically significant correlation between eGFR, BMI and depression in this subset of the population, these findings are worth documenting. Nevertheless, patients should be screened for affective disorders, particularly depression.

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Checking In: A Physician-Delivered Intervention to Improve Parent-Adolescent Communication Regarding Blood Glucose Monitoring

OBJECTIVE:

There is a significant need to develop brief, low-cost interventions to improve adherence and glycemic control in adolescents with type 1 diabetes (T1D). This study evaluated a physician-delivered intervention designed to increase parent-adolescent communication about blood glucose (BG) monitoring.

METHOD:

Thirty adolescents (M age=13.7 years; 46.7% female) enrolled in Checking In, completed baseline psychosocial questionnaires, and received the physician-delivered intervention, consisting of print materials and encouraging parents and adolescents to schedule "3 minute meetings" (3MMs) 3 times/week to jointly review BG meter data. Participants received weekly text message boosters for 12 weeks after intervention delivery, and completed a satisfaction survey and follow-up psychosocial questionnaires at 12 weeks. HbA1c and glucometer data (30 days) were abstracted from medical charts.

RESULT:

Fifty-one percent of eligible families agreed to participate. Sixty-three percent of dyads completed follow-up questionnaires, and follow-up medical data were obtained for 93% of participants. Parent-reported diabetes-specific family conflict significantly decreased from baseline to follow-up ($p=.05$). While changes were in the expected direction for other T1D outcomes, there were not statistically significant changes from baseline to follow-up for BG monitoring frequency (4.07 checks/day vs. 4.52 checks/day), mean BG level (216.28 mg/dL vs. 209.77 mg/dL), or HbA1c (8.83% vs 8.61%). Subset analyses revealed non-significant clinical improvement in glycemic control for high-risk participants ($HbA1c \geq 9.0\%$; $n=10$), with HbA1c values decreasing from 10.52% to 10.05%. Further, families who reported holding 3MMs once a week or more ($n=15$) demonstrated a significant increase in BG monitoring frequency (4.29 checks/day vs. 4.82 checks/day; $p<.05$) and a trend for improved HbA1c (9.05% to 8.47%; $p=.08$).

Participants were generally satisfied with the program. All parents (100%) and most adolescents (74%) reported a desire to continue 3MMs, and 55% of parents and 63% of adolescents reported an improvement in T1D management due to Checking In. Physicians delivering this intervention were also satisfied with the program, stating that it was relevant for families and quick and easy to incorporate into a routine clinic visit.

CONCLUSION:

Results of this low-cost physician-delivered intervention targeting parent-adolescent communication demonstrate feasibility as well as a trend towards improvement in HbA1c values, BG monitoring frequency, and diabetes-related family conflict in adolescents with T1D. Frequent review of BG meter data can be a useful strategy to improve T1D-related health outcomes and parent-adolescent communication. This pilot should be conducted with a larger, potentially more selective (i.e. high-risk) sample to evaluate program impact and potential areas for improvement.

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Not just skin deep – a case of simulatenous presentation of pemphigus foliaceus and systemic lupus erythematosus.

CASE:

A 46 year-old man with a history of Stevens-Johnson Syndrome was admitted for fatigue and a rapidly developing non-photosensitive rash that started on his chest and progressed to his face and scalp. He had no family history of autoimmune disease and took no medications. Physical examination revealed a confluent, ulcerating, excoriated rash with honey-colored crusting on the scalp, chest, and face sparing the naso-labial folds without mucosal ulcers. Joints were benign. Complete blood count showed macrocytic anemia and leukopenia. Complete metabolic panel was normal. C-reactive protein and erythrocyte sedimentation rate were elevated at 11.1 and 44, respectively. Anti-nuclear antibody staining revealed a speckled pattern, positive at a dilution of >1:1280. Anti-double-stranded DNA antibody was positive, as were anti-ribonucleoprotein, -Smith, and -chromatin antibodies. Other ANA-associated antibodies were negative. Urinalysis was negative for protein, red blood cells or casts. Arm punch biopsy showed superficial dermal perivascular lymphocytic infiltrate without acantholysis. Direct immunofluorescence (DIF) revealed granular IgG interkeratinocyte and IgM dermal papillae staining typical of pemphigus and linear IgG and C3 staining the basement membrane, similar to the linear immune-complex dermal-epidermal junction deposition seen in systemic lupus erythematosus (SLE). Given the DIF staining patterns and lack of mucosal involvement, the patient was diagnosed with pemphigus erythematosus (PE). With review of all laboratory and clinical data, including repeat urinalysis positive for proteinuria, he was diagnosed with SLE in addition to PE.

DISCUSSION:

Pemphigus comprises a spectrum of rare autoimmune skin and mucosal disorders with a classic blistering rash cause by IgG autoantibodies against cell surface keratinocytes, specifically the adhesion protein desmoglein. The commonest subtype, pemphigus vulgaris, has both mucosal and skin involvement, with antibodies against desmoglein-1 and -3, and linear interkeratinocyte DIF staining pattern. Pemphigus Foliaceus (PF) has no mucosal involvement and autoantibodies are directed only against desmoglein-1. PE, a variant of PF, typically has basement membrane IgG deposition, the so-called "lupus band".

SLE and pemphigus are well-known to overlap or coexist with many other autoimmune/ connective tissue diseases, however SLE co-presenting with pemphigus, especially PE, is rare. Associated PE and SLE has been described, however a recent case review refutes this, clarifying that only one patient in the literature meets current American College of Rheumatology diagnostic SLE criteria.

This case underscores the importance of the rash's distribution and biopsy findings in differentiating between pemphigus subtypes. It reminds us that autoimmune diseases are inter-related and complete rheumatologic work-up in patients with pemphigus aids accurate diagnosis.

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Correlation of retroillumination photography analysis and clinical severity grading method in Fuchs Corneal Dystrophy

PURPOSE:

Fuchs Corneal Dystrophy (FCD) is a progressive, hereditary corneal disorder marked by central corneal edema and the presence of guttae, excrescences of Descemet membrane. Traditional grading of severity is based on slit-lamp biomicroscopy and subjective clinical assessment of the distribution of guttae and presence of corneal edema; however, we have previously shown that retroillumination photography analysis (RPA) can objectively and reliably assess progression of disease and distribution of guttae, which accelerate in their development over time. Here, we explore the correlation between two methods and implications for high levels of severity.

METHODS:

Retroillumination photography was conducted in 54 individuals affected with FCD; all subjects provided written informed consent. The number of guttae were summated manually. Exclusion criteria included history of intraocular surgery or inflammation. Clinical grading using the Krachmer scale measuring 1 to 5 was documented for each eye at the time of examination. Regression analyses were performed to identify the best-fit model between the two methods. Ranges of guttae were assessed at each stage of clinical grading.

RESULTS:

A total of 96 retroillumination photographs passed exclusion criteria and were analyzed. Krachmer score ranged in severity from 1 to 5, with mean score of 2.625. The mean number of guttae in corneas at each clinical level of severity (Krachmer grading in parentheses) were 289 (1+), 999 (2+), 2669 (3+), 5474 (4+), and 7133 (5+). Higher levels of clinical grading were associated with larger ranges of guttae ($p < 0.02$), with corneas identified as 5+ demonstrating 7227 guttae between the maximum and minimum affected. A power model resulted in a strong and greater fit between RPA and Krachmer score ($r^2 = 0.78$) than a linear model ($r^2 = 0.62$).

CONCLUSIONS:

In this largest study of RPA data and comparison with subjective clinical grading of FCD severity, RPA correlates well and demonstrates better resolution of severity at advanced stages of disease. This method provides objective levels of severity and may benefit clinicians and researchers who seek to track detailed rates of progression over time.

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Hyperglycemia management among inpatients in George Washington University Hospital

It is estimated that up to one third of hospitalized patients experience significant hyperglycemia and/or hypoglycemia, leading to adverse outcomes and prolonged hospital stay. The American Diabetes Association (ADA) has developed guidelines for optimal glucose control in hospitalized patients, and the use of sliding scale insulin alone has been shown to be significantly less effective than scheduled basal/bolus insulin in preventing hyperglycemia. Effective and safe inpatient diabetes management reduces complications and length of stay in the hospital.

This project addresses the need to enhance knowledge and awareness in treating hyperglycemia on the inpatient services by giving residents and the house staff management tools as reference guides.

Data for patients on the 4 South and 5 South floors at GWU Hospital was collected from June to July 2014 to determine the use of insulin sliding scale versus a basal-bolus regimen in the treatment of hyperglycemia. Following this collection of baseline data, the intervention included development and distribution of pocket guides for insulin management as well as an educational conference for housestaff held on July 28, 2014. Data was collected again from August to September 2014 to determine the use of insulin sliding scale versus a basal bolus regimen after introducing the intervention.

Results were analyzed and compared using Chi-square analysis, showing minimal change in hyperglycemia management before and after the intervention.

In conclusion, we find the need to pursue further approaches of pre-defined quality improvement cycles to better address hyperglycemia management on the inpatient wards at George Washington University Hospital. Such approaches could include introducing an easily accessible mobile phone app as a reference guide and posting signs for hyperglycemia management on the wards to increase awareness among patients and hospital staff.

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Wernicke's Encephalopathy as a Complication of Abdominal Surgery: A Systematic Review

OBJECTIVE:

To review the essential clinical features of Wernicke's encephalopathy (WE) as it relates to complications of abdominal surgeries.

Introduction: WE is syndrome caused by vitamin B1 deficiency and commonly presents as a triad of altered mental status, ataxia, and ophthalmic changes. However, most clinicians associate WE to alcoholism when in fact it has been linked to many other nutritional deficiency states including as a post-operative complication of abdominal surgery. Here we perform a systematic review of the literature to describe commonly reported findings seen in cases of post-operative WE.

METHODS:

We performed a review of US National Library of Medicine using the search terms "Wernicke's encephalopathy" and "post-operative" and now present 39 articles describing 43 cases (including our own case) published up to January 2015. Here we provide a review of this complication of abdominal surgery and assess the prevalence of specific signs and symptoms of the disease to improve clinicians' ability to make a diagnosis in non-alcoholics with recent history of abdominal surgery.

RESULTS:

The average age of patients was 40 years old and most commonly seen in females (67%). Post-operative WE was seen predominantly in bariatric-related surgeries (67%). Symptoms were reported 17.4 months after the surgery on average, however, dropped to 5.67 months after extreme outliers were excluded. 77% reported mental status change, 88% reported ocular changes, and 85% reported ataxia. Caine criteria was 3.36 out of 4 on average.

CONCLUSION:

WE after abdominal surgery is an important post-operative complication. Clinicians must be aware of atypical etiologies for the disease in order to prevent progression of the syndrome.

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Concentration Changes of MRS-Determined Brain Metabolites for Ornithine Transcarbamoylase Deficiency Patients

Ornithine transcarbamoylase (OTC) deficiency is a rare metabolic disease that affects the urea cycle, which can result in frequent brain damage due to hyperammonemia. OTC is an enzyme involved with urea synthesis from ammonia. When OTC is deficient the urea cycle cannot proceed, thus ammonia accumulates in the blood and, eventually, in the brain. When ammonia accumulates, there is a significant increase in glutamine in the brain and glutamine draws water into the astrocytes causing them to swell and alter the metabolites of the brain. In this study, the Magnetic Resonance Imaging (MRI) isolated the regions where the lesions occurred, while the functional MRI (fMRI) attempted to visualize the cognitive changes caused by the hyperammonemic episodes. The Magnetic Resonance Spectroscopy (MRS) quantified the metabolites in the brain, specifically; creatine, choline, N-acetyl aspartate, myoinositol, glutamine, and glutamate. Every week we had about two subjects with a total of forty-two by the end of the project. Each subject had a morning structural MRI and MRS taken and fMRI in the afternoon. There were 25 controls and 17 OTC deficient subjects. The raw data from the MRS was processed by a CSF correction MATLAB program. In the control subjects, there was no relationship between myoinositol and glutamine, however the population of OTC deficient subjects had an inverse relationship between the two metabolites. The OTC deficient subjects also exhibited a decrease in dexterity, visuospatial performance, and executive function/attention/cognitive control. Interestingly, these deficits were observed in patients even with normal global IQ. To conclude, OTC deficiency causes patient's brains to have an altered metabolite ratio, which correlate with decreases in different areas of cognitive function.

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Determine How Often MRI-Guided Biopsy, Which Demonstrates a Papillary lesion or Atypia are Upgraded to Cancer Upon Surgical Excision

The purpose of this study is to accurately determine how often MRI-guided biopsies that demonstrate a papillary or atypical lesion are upgraded to cancer upon surgical excision. A total of 318 MRI-guided biopsies performed between May 1, 2011 and May 31, 2014 were retrospectively reviewed. A 9-gauge MR compatible vacuum-assisted biopsy probe (Suros Surgical Systems-Hologic, Bedford, MA, USA) was used, with 6 to 12 samples obtained. Patients whose pathology demonstrated a papillary and/or atypical lesion, who subsequently underwent surgical excision were included in the study. Out of 318 samples obtained, 25 demonstrated papillary lesions and 23 demonstrated atypical lesions. Five papillary lesions and 2 atypical lesions that did not undergo surgical excision were excluded. The mean age was 52.6 (range 34-71). Three out of 20 (15.0%) excised papillary lesions were upgraded to cancer. Pathology demonstrated ductal carcinoma in-situ (DCIS) in 2 and invasive carcinoma with lobular features in 1. Two out of 3 (66.7%) patients reported having a previous diagnosis of breast cancer, and 1 out of 3 (33.3%) reported having a family history of breast cancer. Seven out of the 21 (33.3%) excised atypical lesions were upgraded to cancer. Pathology demonstrated DCIS in 3, invasive ductal carcinoma with DCIS in 3, and invasive lobular carcinoma in 1. Six out 7 (85.7%) patients reported having previous diagnosis of breast cancer, and 3 out of 7 (42.9%) reported having family history of breast cancer. The overall underestimation rate was 24.3%. We recommend that atypical and papillary lesions identified by MRI-guided biopsies should undergo surgical excision.

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Reproducibility of Retinal Nerve Fiber Layer Thickness Measures Using Eye Tracking in Children With Nonglaucomatous Optic Neuropathy

PURPOSE:

To determine the intra- and intervisit reproducibility of circumpapillary retinal nerve fiber layer (RNFL) thickness measures using eye tracking-assisted spectral-domain optical coherence tomography (SD OCT) in children with nonglaucomatous optic neuropathy.

DESIGN:

Prospective longitudinal study.

METHODS:

Circumpapillary RNFL thickness measures were acquired with SD OCT using the eye-tracking feature at 2 separate study visits. Children with normal and abnormal vision (visual acuity ± 0.2 logMAR above normal and/or visual field loss) who demonstrated clinical and radiographic stability were enrolled. Intra- and intervisit reproducibility was calculated for the global average and 9 anatomic sectors by calculating the coefficient of variation and intraclass correlation coefficient.

RESULTS:

Forty-two subjects (median age 8.6 years, range 3.9-18.2 years) met inclusion criteria and contributed 62 study eyes. Both the abnormal and normal vision cohort demonstrated the lowest intravisit coefficient of variation for the global RNFL thickness. Intervisit reproducibility remained good for those with normal and abnormal vision, although small but statistically significant increases in the coefficient of variation were observed for multiple anatomic sectors in both cohorts. The magnitude of visual acuity loss was significantly associated with the global (β [0.026, $P < .01$]) and temporal sector coefficient of variation (β [0.099, $P < .01$]).

CONCLUSION:

SD OCT with eye tracking demonstrates highly reproducible RNFL thickness measures. Subjects with vision loss demonstrate greater intra- and intervisit variability than those with normal vision.

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3-Dimensional High frequency Representation of Triplane Fractures Using CT Multi-planar Modeling

INTRODUCTION:

The triplane fracture of the distal tibia is a complex fracture in pediatric patients characterized by coronal, sagittal and axial fracture planes. This fracture is best categorized via CT due to its 3-dimensional configuration and presentation with multiple fracture lines. The proper assessment of triplane fracture subset and fracture pattern has implications for treatment and long-term management in a pediatric population. Successful treatment is critical for fractures involving an open physis to prevent subsequent complications. Delineating the most common location of triplane fracture lines could aid in optimizing treatment planning for these injuries.

METHODS:

CT images from 27 pediatric patients were segmented using ITK Snap (version 3.0.0) to create a 3-dimensional model of fracture lines for each patient. These models were then normalized to a common size, and a subsequent single 3-dimensional model generated. This model uses color to create a map on the surface of a model distal tibia to indicate frequency of fracture locations. We set our analysis to indicate fracture lines present in $\geq 75\%$ of patients.

RESULTS:

The following fracture lines were found to have a frequency map of $\geq 75\%$: 1) from the center of the physis, distally and anteriorly in the sagittal plane into the joint space; 2) laterally extending through the physis, stemming from the mid sagittal line of the tibia; 3) distally in a posterior to anterior fashion from the posterior metaphysis and into the physis; and 4) in the posteromedial portion of the physis.

CONCLUSION:

High incidences of certain fracture lines were mapped via analysis. The constructed frequency model shows the most high frequency fracture lines correspond quite well with the fracture patterns described in the traditional classification of this injury (2,3, or 4 part fracture classification). However, variability in the exact anatomic position for these fracture lines was found through frequency mapping. The described fracture lines could be found centered in a radius of potential fracture locations. Understanding the variation in the location of triplane fracture lines could help improve the surgical approach used to manage this physeal-based fracture.

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Laparoscopic Surgery for Patients with Severe Chronic Obstructive Lung Disease

INTRODUCTION:

Laparoscopy is a minimally invasive procedure that associated with decreased morbidity and hospital stays. There are over two million laparoscopic surgeries performed annually in the US. Several studies have shown that patients with mild (Stage I) to moderate (Stage II) Chronic Obstructive Pulmonary Disease (COPD) develop hypercapnia during laparoscopy procedures. However, hypercapnia in this population did not affect the rate of complication or prolonged hospital stay. We report a case of very severe (Stage IV) COPD, who developed an acute respiratory failure with an increase in hospital stay during a laparoscopic procedure. We write this to bring awareness to the use of alternative techniques to more optimally manage patients with severe COPD.

CASE REPORT:

A 56-year-old man with past medical history of HIV, TB, and Stage IV COPD, who presented for an outpatient bilateral hernia repair. His symptoms are well controlled as an outpatient with persistent hypercapnia with a PCO₂ of 50 mmHg. The patient underwent bilateral laparoscopic hernia repair with mesh placement without any complications. However, he was somnolent and confused after extubation and received 0.8 mg of naloxone with minimal response. An ABG revealed an acute respiratory acidosis with a PH of 7.25 and pCO₂ of 80 mmHg. We started him on BiPAP as well as albuterol and Atrovent nebulizers every four hours. The following day he was more oriented, and a repeat ABG showed a pH of 7.36 and pCO₂ of 60 mmHg. He was discharged home on budesonide and formoterol nebulizers and albuterol as needed.

DISCUSSION:

Laparoscopy has improved outcomes and decreased length of hospital stay as compared to open procedures for most patients. However, this may not be ideal for all patients. During a laparoscopic procedure, carbon dioxide (CO₂) is inflated the abdomen to improve visualization of intra-abdominal organ. CO₂ is absorbed into the body due to the difference in partial pressure of CO₂ in the abdomen and blood. For most patients, the rapid absorption of CO₂ can be offset by the adjustment of the anesthetic ventilator. This adjustment is not always possible for patients with severe lung pathology including COPD. The combination of increased CO₂ absorption, and decreased ability to efficiently expel CO₂, may lead to hypercapnic respiratory failure postoperatively as observed in the case discussed.

CONCLUSION:

Two approaches may be used to combat the accumulation of excess CO₂ in patients with severe COPD. Postoperative monitoring and treatment of hypercapnia or prevention of hypercapnia via alternative surgical procedures including an open technique with an aid of local blocks. Further studies should be conducted to assess the effectiveness of alternative surgical approaches in patient with stage III and IV.

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Detection Rate of Chromosomal Microarray: Our First Year of Experience at Children's National Health Systems

INTRODUCTION:

The Molecular Diagnostics Laboratory in the Division of Laboratory Medicine at Children's National Health Systems (CNHS) established chromosomal microarray (CMA) in the summer of 2013 to better support the Division of Genetics and Metabolism with over 7,000 patient encounters a year.

METHODS:

During the first 12 months of offering CMA, 603 samples were received, tested and resulted. Of the 603 patients tested, 181 patients had a positive finding on initial microarray, and 422 patients tested negative for genetic abnormality. The patients positive for a copy number variant (CNV) were further categorized based on the clinical prognostic value of the finding. Each negative patient report (normal CMA result) was also further assessed to trace documented subsequent genetic testing, and to determine the associated degree of clinical pathology.

RESULTS:

Of the positive results, 135 (22% of all tested) had a CNV detected, and 46 (7% of all tested) had significant area(s) of homozygosity (AOH). For those with a CNV, there were 49 duplications, 59 deletions and 20 complex rearrangements. Additionally, there were 6 times where aneuploidy was detected: Trisomy 21; Trisomy 18 (n=2); 47,XXY; 47,XYY (n=2), and one instance where a 46,XY female was identified. In regards to pathogenicity of the CNVs identified: 2 were benign; 9 were uncertain, likely benign; 48 were uncertain; 10 were uncertain, likely pathogenic and 66 were pathogenic. Of those with AOH, 34 (5% of all tested) were found to have AOH >2.5% of the autozygome suggestive of identity by descent and 12 (2% of all tested) were suggestive of uniparental disomy (UPD) or isodisomy. For the 422 with normal CMA results at the time of this review, 62 have undergone additional molecular genetic testing based on their phenotype. Of the 62 additional tests performed, 12 (20%) were positive with mutations identified. A variant of uncertain significance was identified 5 times (ATRX, CNTNAP2, NF1, PFKM and MLL2). A likely pathogenic mutation was identified twice (FRMD and COL3A1). A pathogenic mutation was identified 5 times in 4 genes (SBDS, L1CAM, PTEN (n=2), and TH).

CONCLUSION:

This study demonstrates the high detection rate of CMA, especially in the pediatric population that led initially for it to be recommended as a first-tier test by ACMG and more recently approval by the FDA for the detection of CNVs associated with developmental delay and/or intellectual disability (DD/ID), congenital anomalies, and/or dysmorphic features.

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Platelet Inhibition is Common Following Injury but is Not Associated with Hemorrhage

INTRODUCTION:

There are few studies evaluating platelet dysfunction following injury. Thrombelastography platelet mapping (TEG-PM) allows for measurement of degree of clot strength (MA) and inhibition of the adenosine diphosphonate (%inhADP) and arachidonic acid (%inhAA) receptors on the platelet. We hypothesize that platelet inhibition is common following injury but is not predictive of transfusion need.

METHODS:

After obtaining IRB approval, a retrospective study of adult trauma patients evaluated at a level I trauma center from August 2013-September 2014 was performed. A TEG-PM was obtained on all patients. Patients were divided into those with and without traumatic brain injury (TBI). Patients on anticoagulant and antiplatelet agents and those whose anticoagulation status was not known were excluded. Demographic variables, injury severity score (ISS), laboratory test results, and transfusion need were abstracted. Statistical significance was assessed using the student t-test.

RESULTS:

459 patients were enrolled, and 70% were male. Mechanism of injury was 90% blunt. Average age and ISS in the overall cohort were 43 ± 19 and 6.5 ± 6.5 , respectively. TBI patients ($n=102$) were significantly older (52 ± 21 v 40 ± 18 years, $p < 0.0001$) and more severely injured (ISS 12 ± 9 v 5 ± 5 , $p < 0.0001$). TEG-PM results and transfusion need are shown in Table 1. Average MA was normal in all groups but MA (AA) and MA (ADP) were reduced in both groups. There was no difference in MA (AA) and MA (ADP) between the TBI and non-TBI groups. There was no relationship between degree of inhibition and need for RBC or platelet transfusion in any group or in the overall cohort.

CONCLUSION:

Platelet inhibition is common following even minor injury but does not appear to be associated with risk of hemorrhage. Studies in more severely injured patients are needed to verify these results in an at-risk population.

Test	Overall Cohort (n=459) (average±SD)	TBI (n=102) (average±SD)	No TBI (n=357) (average±SD)
Platelet Count	230±65	215±67	234±64
MA	63±6	64±7	63±6
MA (AA)	47±16	46±15	47±16
MA (ADP)	32±17	32±16	32±17
%Inh AA	30±26	32±25	30±26
%inh ADP	58±27	59±27	58±27
Red Blood Transfusion	3.5±2.3 (n=31)	2.5±2.5 (n=6)	3.8±2.5 (n=25)
Platelet Transfusion	2.5±2.4 (n=28)	2.6±0.8 (n=18)	2.7±2.2 (n=10)

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A Rare Disease with a Rare Complication

Swyer James syndrome (SJS) is a rare disorder that may develop in children with recurrent respiratory infections. It has subtle symptoms and is often diagnosed in adulthood for this reason. We describe a case of SJS with a rare complication of treatment.

A 26 year-old female presented to pulmonary clinic for evaluation of dyspnea on exertion over two years. She denied chronic cough, chest pain, wheezing, or fatigue. Past medical history was notable for SJS and severe childhood meningitis, but no history of recurrent respiratory infections. A chest Xray showed left tracheal and mediastinal shift with cystic and fibrotic changes in the right middle lobe. Chest CT showed hyper-inflated right upper and middle lobes with emphysematous changes and diffuse cystic cavities. Over expansion of the lung is not a typical feature of SJS, but is a rare variant reported in the literature. A ventilation/perfusion scan showed significantly decreased right lung function. The patient was referred for a total right pneumonectomy. Post-operative course was uncomplicated. She did well over a year before again presenting with dyspnea on exertion. Repeat chest CT showed displacement of the heart and mediastinal structures into the right hemithorax and rightward midline shift of the left mainstem bronchus. These findings were consistent with post pneumonectomy syndrome (PPS). The patient subsequently had two saline implants placed to correct the displacement of structures. She did well after the second operation, eventually even completing a successful pregnancy.

SJS can develop in children who have recurrent respiratory infections. It has an incidence of 0.01%, characterized by a unilateral hyperlucent lung thought to be associated with post-infectious bronchiolitis obliterans. There is pulmonary parenchymal hypoperfusion secondary to underdevelopment of the pulmonary arteries, with chest Xray showing a hyperlucent, underdeveloped lung. Symptoms include cough, dyspnea, or hemoptysis, although patients can be asymptomatic.

PPS is an equally rare complication of pneumonectomy, reported in 73 adult cases over 28 years. It's caused by a dramatic shift in mediastinal structures and central airway obstruction. Presenting symptoms include shortness of breath or dsypnea on exertion, which can be misleading as pneumonectomy patients often have these symptoms post-operatively. Treatment involves saline implants to reposition the mediastinal structures. This case represents two rare conditions occurring in the same patient. It emphasizes the subtlety of symptoms that occur and stresses the importance for pulmonologists to recognize post-operative complications from thoracic surgery as patients often present to them first.

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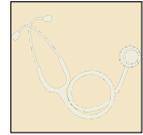
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The Optimization of Treatment Planning and Ablation Rate Improvements on Feasibility of Pediatric MR-HIFU Applications

BACKGROUND/INTRODUCTION:

Magnetic resonance-guided high intensity focused ultrasound (MR-HIFU) ablation provides a precise, non-invasive treatment for lesions in adults. In children, MR-HIFU's potential remains largely unexplored, though its non-invasive and non-ionizing nature holds promise. Yet, pediatric patients pose challenges affecting treatment: young children require general anesthesia, exhibit wide ranges of anatomy, and have varying lesion sizes and locations. These demonstrate a need for standardized treatment approaches and physical aids to optimize patient position, reduce time-intensive repositioning, and thus reduce overall treatment time. Further improvement of ablation rate and reduction of risk are also possible via improved monitoring of skin temperature during ablation and mild hyperthermia. Improvements in treatment planning and volumetric rate may save time and allow for treatment of larger lesions, increase patient throughput, and possibly increase efficacy and lower cost. This study aims to quantify and examine how such improvements could increase the time allocated for direct ablation and produce better outcomes.

METHODS:

Forty-one pediatric patients with various limb tumors at Children's National Medical Center from November 2005 to October 2013 were examined retrospectively as potential candidates for MR-HIFU ablation therapy. After identifying the tumor location, software (Avizo Standard Edition 8.0.0, Visualization Sciences Group, SAS, Berlin, Germany) was used to define its area through axial slices and create a 3D segmented model to measure its volume. As a reference, treatment time was estimated at a maximum (180 cc/hour) rate used in ablation of uterine fibroids (obtained from Phillips Healthcare, Vantaa, Finland). Four hours maximum anesthesia time was selected due to risks to children and restraints on surgeon time and focus, room and machine time, and cost. Tumor volume and ablation rate data was graphically combined to show effects of theoretical improvements.

RESULTS & CONCLUSIONS:

Increasing the time available for ablation can substantially increase treatable tumor volume. In the examined 41 patients, utilizing only 1 hour for ablation (at 180 cc/hour) leaves 13 patients (32%) untreated. With more time, all but 2 patients (5%) are treatable with 3 or 4 hours of ablation. Conversely, complete treatment of a lesion is directly related to ablation rate. At the current rate of (180 cc/hour), 2 (5%) are untreatable, yet with double the current rate (360 cc/hour), all 41 lesions can be treated. Improvements in planning guidelines and treatment rates could have substantial impacts on the effectiveness of MR-HIFU ablation and the size of treatable tumors and number of patients treated with this technique.

ACKNOWLEDGEMENTS:

This study was conducted at The Sheikh Zayed Institute at Children's National Medical Center and funded by the W.T. Gill, Jr. Summer Research Fellowship through the George Washington University School of Medicine.

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Anterior Cervical Fusion versus Minimally Invasive Posterior Keyhole Decompression Surgeries

BACKGROUND CONTEXT:

Treatment modalities for degenerative cervical spine disease are widely debated and refined as new surgical techniques are developed. The current case series compares two common cervical spine procedures, anterior cervical discectomy and fusion (ACDF) and minimally invasive posterior keyhole foraminotomy (MIPKF). The decision making process of the two surgical approaches is discussed, and the long term outcomes are presented.

PURPOSE:

To present a decision making paradigm in treating degenerative disc disease in the cervical spine.

STUDY DESIGN/SETTING:

Retrospective clinical analysis

PATIENT SAMPLE

Over 570 patient charts were identified and reviewed between 1994 to 2011. A total of 268 patients were identified in the ACDF group, and 112 patients were identified in the MIPKF group.

OUTCOME MEASURES:

Primary outcome measurement was the need for any reoperation, whether at the same level or adjacent levels due to recurrence of disease or adjacent level disease.

METHODS:

A retrospective chart review using current procedural terminology (CPT) codes identified surgical patients having either an ACDF or MIPKF performed. An extensive chart review was able to determine the follow-up time period and if-or-when patients required a reoperation. There was no funding utilized for this study and there are no conflicts of interested to disclose. This study was approved by our institutional review board under IRB Protocol # 100724.

RESULTS:

An average followup of 11.8 (+/- 3.0) years in the ACDF group and 6.4 (+/- 4.4) years in the MIPKF group was determined over a 17 years period. There was a reoperation rate of 2.6% in the ACDF group and 2.7% in the MIPKF group during the 17 year time period.

CONCLUSION:

ACDF has been demonstrated to be an effective surgical procedure in treating degenerative spine disease in patients with radiculopathy and/or myelopathy. However, in a population with isolated radiculopathy and radiological imaging confirming an anterolateral disc or osteophyte complex, the MIPKF can provide similar results without the associated risks that accompany an anterior cervical spine fusion.

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A rare case of non-cardiogenic pulmonary edema

INTRODUCTION:

Nephrotic syndrome is identified by a significant proteinuria more than 3.5 g/day, hypoalbuminemia less than 3 g/dl, and peripheral edema. It associated with risks of thrombosis, infection, and hyperlipidemia due to loss of plasma protein. Several studies have shown patients with nephrotic syndrome do not develop non-cardiogenic pulmonary edema. However, we report a case of nephrotic syndrome caused by diabetic nephropathy and presented with non-cardiogenic pulmonary edema.

CASE REPORT:

37-year old man with past medical history of diabetes mellitus, hypertension, dyslipidemia, Charcot foot, who presented with dyspnea, orthopnea, and non-productive cough for two days. He had been developing progressive abdominal distention and lower extremity (LE) swelling for three weeks before admission. He denies chest pain, fever, or chills. He appeared uncomfortable and hypoxic and had abdominal distension with bilateral LE edema. Initial laboratory test revealed BUN of 33, creatinine of 1.8, Bicarbonate of 34, and albumin of 2.1. Random urine protein-to-creatinine ratio was 8.36. He had a normal complement three and four levels. Hepatitis panel, HIV, anti-GBM Ab, ANCA, ANA, anti-dsDNA, and RA were negative. EKG showed sinus rhythm, and echocardiogram revealed normal systolic and diastolic function with ejection fraction of 55-60%. Chest X-ray was consistent with volume overload and pulmonary edema. Kidney ultrasound was unremarkable. However, his kidney biopsy confirmed diabetic nephropathy as a cause of his nephrotic syndrome. During this admission, he was diuresed with furosemide, metolazone, and acetazolamide with significant improvement of his volume status. Patient required oxygen supplementation to keep oxygen saturation above >91%. However, it was improved with diuresis and was slowly weaned off oxygen. He was discharged home off oxygen supplement.

DISCUSSION:

The causes of nephrotic syndrome divided into two groups primary and secondary causes. The most common secondary cause is diabetic nephropathy. Nephrotic syndrome usually manifest by LE edema, weight gain, fatigue, and dyspnea due to pleural effusion. Patients with nephrotic syndrome do not present with pulmonary congestion or infiltrate. However, there are two cases published in the medical literature presented with nephrotic syndrome and non-cardiogenic edema. First case is a patient that was diagnosed with nephrotic syndrome and pulmonary edema due to bilateral renal artery stenosis. Second case is a patient had non-cardiogenic pulmonary edema and nephrotic syndrome due to collapsing glomerulopathy.

CONCLUSION:

We report this case to raise the awareness of clinician that patients with nephrotic syndrome might present with non-cardiogenic pulmonary edema and hypoxia. This complication could be managed effectively with diuresis.

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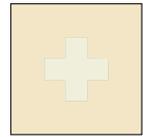
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Randomized Controlled Trial of Virtual Coaching to Enhance Medical Students' Clinical Reasoning During FCR Case Presentations

BACKGROUND:

Oral case presentations (OCP) are an opportunity for students to communicate their clinical reasoning. Deliberate practice is important to develop expertise in OCP skill. Could a blended learning curriculum providing additional practice and feedback beyond daily presentations during rounds will enhance OCP clinical reasoning and be perceived as effective by students and faculty?

OBJECTIVE:

To assess the effectiveness of 2 interventions, "VIRTUAL COACHING" (VC) vs small group case discussion (SG) in improving students' OCP over a 2 week period when combined with an eLearning module.

DESIGN/METHODS:

Students from 2 medical schools were randomly assigned to 3 groups during the 1st 2 weeks of the inpt pediatric clerkship. All students completed an eLearning module teaching use of illness scripts to promote clinical reasoning during OCP. In Group 1 (VC) students audio-recorded a "CLIPP" case 2x/wk, with on-line faculty feedback & student self-reflection using the OCP tool. In Group 2 (SG) faculty facilitated student discussion/feedback of an OCP using the same "CLIPP" cases 2x/wk. Group 3 completed "CLIPP cases" & weekly standard faculty feedback. Students were videotaped presenting 1/4 new cases pre and 1/4 different cases post intervention. Inter-rater reliability using the validated OCP tool was established between 2 reviewers. Reviewers rated videos blinded to assignment group and pre/post intervention.

RESULTS:

We analyzed 30 students' pre-post OCP scores using our validated tool. 16 students were in the VC group & 14 SG/control. Although clinical reasoning measured by student's data analysis improved for all, there was a significant group difference in pre-post on the Analysis sub scale (Wilks' Lambda=0.86, Hotelling's Trace=.016; p=0.04) for the VC group (pre M=2.27/post M=2.68) compared to SG/control. 83% of VC students & 100% of SG students rated the intervention as enjoyable/effective. Faculty had difficulty scheduling time to facilitate the SG when the clinical service was busy.

CONCLUSIONS:

A blended learning curriculum to enhance clinical reasoning during OCP using VC was effective in a randomized, controlled trial with blinded reviewers using a validated assessment tool. Students perceived VC as enjoyable and effective. Although SG teaching was preferred by students, faculty found it difficult to schedule teaching sessions.

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Stress and Fatigue Management in Physicians

Recognizing affected or at-risk health care providers with stress or fatigue problems that may lead to burnout can be very difficult. Wellness requires setting realistic work expectations, prioritizing and balancing non-work activities and attending to mental, physical and spiritual needs. Proper nutrition is of particular importance in decreasing the likelihood of "ego-depletion." In cases where the brain is low on glucose, executive functions are the first to suffer, resulting in poor decision-making. Regular exercise and sleep are also important in achieving overall wellness for the healthcare professional.

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Health Provider Trust in Washington, DC

Washington, DC is home to a diverse population. This paper explores the reasons behind why three of the major Medicaid populations, African Americans, Hispanic Americans, and Ethiopian Americans, do not seek similar amounts of healthcare as other Medicaid recipients. While the barriers include lack of information, fear, payment, and physical barriers such as transportation, they also include trust issues. Why do these populations trust their doctors less than other populations? Is it due to cultural or language differences, or does it stem from something larger? Through a literature review, this paper seeks to answer some of these questions. Using the PubMed and MEDLINE databases, searches were conducted using combinations of the following terms, for both the general population and specific ethnic groups: "mistrust," "trust," and "physician-patient relations."

Results of our investigation found many common themes among these groups. Lack of trust in doctors and the health care system often stems from cultural differences, historical injustice, and differing expectations of the medical system. Both African-Americans and Latino immigrants report feeling unvalued, disrespected, and discriminated against. For African-Americans, these concerns stem from a long, brutal history of abuses and discrimination within the health care and medical research fields. Hispanic-Americans and Latino immigrants have experienced similar abuses. However, their concerns often stem more from concerns about legal status and comparisons of the American system to their home country's. There is common ground, too, between the experiences of Latinos and Ethiopian immigrants. In both groups, faith is often an integral, complementary component of treating disease and maintaining health. In addition, traditional medicines and self-treatment are cultural norms - if not integral components of local cultures - in the home countries of many immigrants. Immigrants to the United States may trust these familiar systems of care more than mainstream American medicine, resulting in decreased interfacing with the health care system.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Out and About in Medicine: GW Out for Health

The time is right to devise and implement a more coordinated approach to LGBT patient care and health professional training within the Washington, DC metropolitan area and beyond. The following George Washington University School of Medicine and Health Sciences (GWSMHS) and Hospital (GWUH) LGBT Health Initiative proposal highlights possible strategies for addressing this need through a more centralized fashion. The seven focus areas proposed for the GW LGBT Health Initiative include: 1) Climate/Visibility; 2) Health Education; 3) Policy/Advocacy; 4) Community Outreach; 5) Research; 6) Patient Care; and 7) HIV/AIDS. A key stakeholder that is helping to realize this vision of a comprehensive, coordinated GW LGBT Health Initiative is the student organization GW Out for Health (GWOFH). Led by an executive board of medical students and a faculty advisor, GWOFH has been working to improve the climate for LGBT and ally professional health students and visibility of LGBT health issues on campus through grass roots efforts. GWOFH has approached these goals by emulating aspects of successful student organizations, namely Student National Medical Association, as well as reaching out and building relationships with LGBT resources in the community. Altogether, members of the group will provide critical perspectives on the initial needs assessment and gap analysis of LGBT health at GWSMHS and GWUH necessary to developing a strategic plan for the GW LGBT Health Initiative. In the past year, GWOFH has achieved concrete steps towards improving the climate and visibility of LGBT health issues by building up their organizational infrastructure and membership, which is evidenced by the three-fold growth in membership and creation of a private campus Listserv. To provide social support for LGBT and ally medical students, GWOFH hosted a welcome potluck for GWSMHS students and a social mixer with the LGBT student organizations at Georgetown and Howard medical schools. To improve the visibility of LGBT health issues on campus, GWOFH launched a successful Lunchtime Lecture Series on current research and best practices for reducing LGBT health disparities. GWOFH's accomplishments have set a solid foundation for providing professional and social support for incoming LGBT and ally professional health students. Furthermore, GWOFH's reputable presence on campus will be leveraged to help support the proposed GW LGBT Health Initiative in the coming year by providing an advisory role on the development of an initial needs assessment and gap analysis, especially in the areas of climate and visibility, health education, political advocacy, and patient care.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Validity of a Novel Observational Tool to Assess Residents' Education of Patients

BACKGROUND:

Residents are expected to assume the role of educator with patients, colleagues and students. This expectation is highlighted in the ACGME milestones. However, the availability of observational assessment tools to measure the patient's perspective of the education provided by residents is lacking.

OBJECTIVE:

To develop and validate an observational assessment tool for use by faculty that mirrors patient's perceptions of the education that is provided by residents in clinical settings.

METHODS:

We adapted 15 questions that assess patients' experiences with their provider from the Agency of Healthcare Research and Quality's Community Assessment of Healthcare Providers and Systems (CAHPS) Clinician and Group Surveys. We selected items from the health literacy and communication domains that directly addressed the provider's ability to educate. The tool was beta-tested through an iterative process of feedback from medical educators, statisticians and clinical faculty, to determine face validity. Inter-rater reliability for the final tool was calculated (Fleiss' kappa = 0.61). Core faculty at two institutions participated in rater training and assessed the performance of residents educating patients. The patient also rated the provider using the adapted CAPHS questionnaire. The faculty and patient assessments were analyzed for predictive validity by looking for correlation between responses.

RESULTS:

Seven faculty observers and 14 patients recorded observations of 18 residents. The residents assessed were PGY1 (55%); PGY2 (28%) and PGY3 (17%). 56% were on an inpatient ward; 44% in clinic. The correlation between faculty and patients' assessments was 0.59 ($p = 0.026$).

CONCLUSIONS:

This study provides evidence of the validity of a tool to assess residents' skills in delivering patient education. A unique feature of the tool is the correlation of faculty's assessments to patient's perceptions of the education received from resident educators. The study was limited by the small numbers of participants. Future research will extend the sample size and explore the use of this assessment tool to measure residents' progress as educators over a longitudinal period of training.

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Differences in Protobacco Advertising and Smoking Imagery Online and on TV in a Changing Media Landscape

INTRODUCTION:

Exposure to protobacco advertising and smoking imagery have been shown to impact smoking behavior. With more youth watching TV shows and other videos online, and an ever-changing media landscape where distinctions between TV and online consumption are increasingly blurred, it is important to assess whether exposure to protobacco ads or smoking imagery is different based on video consumption medium (i.e., watching online vs. live TV on a traditional TV set) or content (i.e., watching original online content such as user-generated video or Netflix-original shows vs. watching traditional network or cable TV shows).

METHODS:

Legacy's cross-sectional Media Monitoring online questionnaire surveys 15-21 year olds weekly. This analysis includes data from the second half of 2014 (n=2410). Multivariate models examined the relationship between video consumption medium/content and self-reported protobacco advertising or smoking imagery exposure.

RESULTS:

Differences in video consumption medium and content by race/ethnicity are nuanced, with more Hispanic and Other Race individuals consuming video online (both medium and content), more Whites using a TV medium, and more Blacks consuming TV content. Additionally, those watching more hours of video more often consume video online (medium and content) and younger youth more often consume online content. Controlling for demographics, time spent watching video, and smoking status, young people who watch video largely via online medium are 1.24 times more likely to report protobacco ad exposure ($p=0.020$) and 1.21 times more likely to report smoking imagery exposure. Controlling for the same factors, young people who watch largely original online content are 0.63 times less likely to report protobacco ad exposure ($p=0.001$) but there is no statistically significant relationship between watching largely original online content and reporting smoking imagery exposure.

CONCLUSIONS:

Those watching largely via an online medium may be more exposed to tobacco advertising online, whereas tobacco advertising is prohibited on traditional TV programming. The difference in exposure to non-advertising smoking imagery may be driven by exposure to smoking imagery on social media or other sites. Alternatively, confounding factors related to video consumption patterns but not captured in the covariates used in this analysis may be driving these observed differences. Overall, these results highlight the importance of better understanding protobacco ad exposure across media channels and content, and whether differences in advertising restrictions and other regulations on cable/network TV versus online play a role.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

The Pedagogy of a Spiritual History

Spirituality can be defined as “the aspect of humanity that refers to the way individuals seek and express meaning and purpose, and the way they experience their connectedness to the moment, to self, to others, to nature and to the significant or sacred” (Puchalski). A spiritual history is a set of questions that engages patients in sharing their religious or spiritual beliefs. The current model of social history taking traditionally leaves out questions of purpose and meaning. Multiple studies have shown that engaging such questions create a positive impact on the doctor-patient relationship and the overall well being of the patient. The FICA tool is a modality developed by Dr. Christina Puchalski that facilitates conversations about spirituality, which can often be a difficult task for students and physicians alike. This project aimed to properly teach the FICA tool and the role of spirituality in health to first year medical students by adapting an online module generated by the George Washington Institute of Spirituality and Health.

The first goal was to develop an online teaching module for first year medical students to learn how to effectively use the FICA spiritual assessment tool and learn the role of spirituality in health care. The next goal was to develop an interactive simulated patient encounter to examine the students’ use of the FICA tool while taking a spiritual history. A standardized questionnaire or assessment was developed and used as a measuring tool to determine the ability of students to use the FICA tool and elicit a spiritual history as well as assess their attitudes and knowledge of spirituality within a health context. Finally, the effectiveness (through the above measuring tool) of the teaching module was assessed by conducting a randomized, controlled trial comparing students that have seen the teaching module, students that have seen the teaching module and participated in a simulated patient encounter where they conduct a live spiritual history, and students that have not had any educational intervention related to spirituality and health.

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The Impact of Instructional Design in a Case-Based, Computer-Assisted Instruction (CAI) Module on Learning Liver Pathology in a Medical School Pathology Course

The purpose of this quantitative experimental study was to test the impact of three learning interventions on student learning and satisfaction when the interventions were embedded in the instructional design of case-based, CAI modules for learning liver pathology in an in-class, self-study, laboratory exercise during a Year-2 medical school Pathology course. The hypothesis was that inclusion of the learning interventions would enhance student satisfaction in using the CAI and improve subsequent exam performance.

Three learning interventions were studied, including the use of virtual microscopic slides instead of static images, the use of interactive image annotations instead of still annotations, and the use of guiding questions before presenting new information. Students were randomly assigned to one of eight CAI learning modules configured to control for each of the three learning interventions. Effectiveness of the CAI for learning was assessed by student performance on CAI-directed exams in a pretest and on posttests immediately after the exercise, and at two weeks and two months. Survey was used to assess student satisfaction and perceived learning.

Results showed that the CAI learning interventions did not improve subsequent exam performance, although satisfaction and perceived learning was enhanced. Student class rank was evaluated to determine if the learning interventions might have a differential effect based on class rank, but there were no significant differences. Class rank at the time of the lab exercise was itself the strongest predictor of exam performance.

The findings suggest that addition of virtual slides, interactive annotations and guiding questions to self-study, case-based CAI for learning liver pathology in a medical class room setting are not likely to increase performance on subsequent MCQ-based exams, but may increase student satisfaction with use of the CAI, which could be an incentive for students to use similar CAI learning modules for future self-directed learning.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Medical Students in Microscopic Anatomy and Pathology Laboratories: Design of an E-Learning Histology and Histopathology Atlas

Computer-assisted learning, also known as e-learning, has been successfully implemented to educate students in anatomical knowledge as well as transferrable skills, such as critical analysis, teamwork, leadership and communication. E-learning allows students to self-teach material at their own paces and provides a platform for team-based laboratory approaches. Several institutions have already integrated histology and physiology in team based laboratory approaches, but integration of histology and pathology instruction has been done to a lesser extent. Our aim was to develop an e-learning atlas that integrates microanatomy and pathology laboratory for an interdisciplinary pre-clinical medical curriculum.

A multidisciplinary team of teaching faculty and students developed an online atlas (microanatomyatlas.com) that includes a library of histology and histopathology images. Traditional laboratory manual instructions and study objectives were added onto the digital interface and made interactive by linking it to specific labeled images to allow for self-testing. Online clinical case studies involving a disease entity in a specific organ system were incorporated, which allows students to toggle between the normal as well as the pathological slides involving the disease as they apply their clinical reasoning skills to arrive at the correct diagnosis. We are collecting data on the number and frequency of students using the atlas. We are also administering a detailed survey to assess student satisfaction and learning. To assess the impact of this new teaching tool, a comparative study of two years of student performance and course evaluations between students who used the online atlas and students who did not use the online atlas in the pre-clinical medical curriculum will be conducted.

Our preliminary data so far shows that student feedback has been positive and an e-learning atlas integrating microanatomy and pathology laboratory may be an essential tool that guides the studies and enhances the performance of students in an interdisciplinary pre-clinical medical curriculum.

DISCLOSURES/ACKNOWLEDGEMENTS:

American Educational Institute, University and Campus Management (AEIUCM) developed, designed, and maintains the online portal.

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Proficiency Based Robotics Training Curriculum: Simulation Based Standardized Training to Test Skill Acquisition and Retention

BACKGROUND:

Minimally invasive surgery (MIS) involves the use of a small laparoscopic camera that projects abdominal images onto a monitor and allows for surgery to be performed through tiny keyhole incisions. While many gynecology residency program directors believe the role of robotic surgery will increase and play a more essential role in gynecologic surgery there is still limited availability of effective resident training in robotics.

IMPORTANCE:

Simulation-based standardized clinical training is important in the teaching and maintenance of operative skills of physicians practicing robotic surgery. Therefore it is of primary importance to investigate how these skills can be acquired and maintained from the robotic simulation program.

STUDY OBJECTIVE:

To investigate the total training time to achieve proficiency (91%) and the recommended intervals between training sessions to maintain operative performance. These findings may help identify factors affecting improved operative performance to be incorporated in the robotics-training curriculum for gynecology residents at GW.

DESIGN:

Prospective cohort study

SETTING:

Large academic teaching hospital

PARTICIPANTS:

33 medical students lacking skills in robotic surgery

INTERVENTIONS:

Participants trained with the dVSS in 4 exercises until competent (defined as an overall score of at least 91%) or a maximum of 10 times each. Participants returned after a 1-, 3-, 5-, or 7-week interval to re-achieve competence or complete the same 4 exercises 10 times each during their follow-up. (Once a participant achieved 91% in an exercise - they did not have to complete it 10 times.)

MAIN OUTCOMES AND MEASURES:

Total training time (TTT), # of attempts per exercise, Total Follow-up Time (TFT), maximal score, mean score

CONCLUSIONS AND RELEVANCE:

Physicians in training can acquire robotic surgery competency. Participants who were able to develop skills more quickly on the selected activities on the robotic simulator also regained those skills more quickly after a training hiatus. During the follow up period (retraining) all participants were able to re-achieve similar scores when compared to their initial training. This information provides a benchmark for a simulator-training program.

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Perception of STEP 1 topics compared to average scores in the Introduction of Clinical Medicine course

Starting with the Class of 2018, the George Washington University School of Medicine and Health Sciences initiated a revised medical education curriculum stressing active learning outside of the classroom. In an effort to continue with the innovative education theme, we developed a set of review videos to assist the Class of 2017, the final traditional class, in its STEP 1 preparation. The initial video was a review of online resources available for exam preparation. To guide the development of further videos, we then surveyed the Class of 2017 and asked them to identify their weakest subjects. The results of this survey were not only used to determine topics for the remaining review videos, they were compared against the class average scores on the corresponding topics in the Introduction to Clinical Medicine Course to determine how student perception of mastery correlated with objective evidence of mastery.

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Diabetes Care Management Using Interprofessional Student Teams to Improve Care and Training in Patient-Centered Care Principles

INTRODUCTION:

It is critical for medical students to receive adequate training as members of an interprofessional team. Team-based care, specifically the patient-centered medical home (PCMH) model, provides patients more effective care, improves patient satisfaction, lowers healthcare costs and reduces health inequalities (Wong W, et al., 2012) (Stange K, et. al, 2010). Louisiana State University Health Sciences Center (LSUHSC) is designing an interprofessional practice of medicine program called the DIME Clinic (Diabetes Internal Medicine Clinic) to introduce PCMH principles to medical, nursing, pharmacy and social work students. Together students develop a team-based care management system for a high-risk population of uncontrolled diabetic patients.

OBJECTIVES:

Objectives for developing DIME Clinic training include: 1) Create a module for health coaching and patient action plan development including student trainings, reference materials and patient simulations; and 2) Develop a reflective exercise including guidelines and a checklist for students to practice evaluating one another and providing peer feedback. Course development included participation from LSUHSC and Xavier University School of Pharmacy.

RESULTS:

The developed DIME student training and reference materials include three components: 1) A simulation case for the students to practice walking through a patient encounter complete with electronic medical record (EMR) data; 2) A care plan template for the students to practice developing these plans with patients and then engage the patients in their health goals; and 3) Peer review training for the students to gain comfort observing each other, giving and receiving feedback on one another as well as on their care team. Educational measures being studied are knowledge of the PCMH model and disease management, teamwork skills, and teamwork attitude.

CONCLUSIONS:

Early results from the original course design indicated students improve their teamwork skills and knowledge of team-based care while contributing positively to patient outcomes. Patients reported successful lifestyle changes and a more positive perception of their care. The course design was recognized by the AAMC as a Clinical Care Innovation Challenge Winner. The next step is to assess student performance and patient outcomes on these same metrics with the further developed training materials. In addition to developing future healthcare professionals who are experienced in interprofessional team-based care, secondary outcomes being analyzed include improved access to care, improved clinical outcomes and lowered costs through enhancing coordination of care.

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STATUS

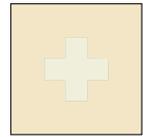
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Remote Access of Electronic Health Records by Physicians-In-Training: Perceived Benefits and Risks

INTRODUCTION:

Although many physicians agree that electronic health records (EHRs) have positive aspects such as the ability to access charts remotely, many report negative impacts on efficiency and quality of life⁽¹⁾. Previous studies suggest this is the prevailing attitude among those who have been in practice for many years; however, the attitudes of physicians-in-training are not well known. Thus, we investigated attitudes of residents toward remote EHR access.

METHODS:

Approval from the George Washington University institutional review board was obtained for a focus group and subsequent questionnaire. The focus group was used to generate questions on attitudes toward remote access, which were then incorporated into an online questionnaire. Participants were recruited by email from the internal medicine residency program (n=99) for both stages.

RESULTS:

The focus group (n=5) revealed a primary belief that remote access was beneficial and essential, despite consequently feeling bound by electronic tasks. The questionnaire received a response rate of 29% (n=29), distributed evenly across PGY levels. The majority of respondents (n=28) reported less than 5 hours per week of remote EHR access, although 1 individual reported 5-10 hours per week. The majority (n=27) do not routinely log remote EHR access as part of their duty hours. The most common reason for remote EHR access was checking tasks, as indicated by all respondents (n=29). The majority believed remote EHR access has a positive effect on work/life balance (n=24) and on training (n=18), although it was associated with the following obstacles: delays in checking tasks (n=21), technical difficulties (n=16), lack of immediate feedback/supervision (n=17), and hesitation in contacting patients from a personal phone (n=15). Given these issues, some respondents found it harder to provide follow-up care remotely (n=11), some were less efficient (n=9), and some felt they provided worse care (n=6).

CONCLUSION:

Ours is one of the first studies to focus on the attitudes of physicians-in-training towards remote EHR access. In striking contrast to perceptions of older physicians, residents seem to believe that the flexibility of remote EHR access enhances work-life balance. However, there were concerns about delays in patient care and difficulty providing follow-up care remotely. Although it is important to uphold physician preference and well-being, the impact of remote EHR access on patient safety and quality of care must be examined further.

1. McDonald CJ, Callaghan FM, Weissman A, Goodwin RM, Mundkur M, Kuhn T. Use of Internist's Free Time by Ambulatory Care Medical Record Systems. *JAMA Intern Med.* 2014; 174 (11): 1860-1863.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Preparing Health Care Professionals to Teach Overseas: An Overview of the Global Health Service Partnership 2014 Orientation

In 2012, the Peace Corps and Seed Global Health established the Global Health Service Partnership (GHSP) to help build health workforce capacity in developing countries by educating nursing and medical students who will become direct care providers, as well as potential future educators. Qualified American physicians and nurses volunteer to teach for one year alongside host-country faculty in Malawi, Tanzania and Uganda, providing classroom education as well as mentoring and supporting students in the clinical setting. In order to prepare volunteers to live and teach in resource-scarce settings, the volunteers attend an eight-day pre-departure orientation in Washington, D.C., followed by two to three weeks of further training upon arrival in their countries of service. The objectives of the July 2014 orientation in Washington, D.C. for the second cohort of volunteers were (1) to provide technical training on health conditions, (2) to prepare GHSP volunteers to be effective lecturers and clinical educators, (3) for volunteers to understand Peace Corps' approach to development and their role in Peace Corps, (4) for volunteers to understand their role in program evaluation, and (5) to build relationships between volunteers, Peace Corps staff, and Seed Global Health staff. Through anonymous surveys completed at the end of the July 2014 orientation, over 87% of the volunteers reported they had a better understanding of technical health topics, current approaches in medical and nursing education, GHSP and Peace Corps, and monitoring and evaluation of the program. However, 25% of volunteers did not feel better prepared to teach at the bedside. Volunteers will complete another survey at the end of their service to comment further on the utility of the orientation and areas for improvement.

STATUS

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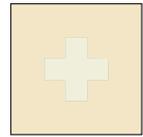
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Developing and Assessing an E-Learning Module Using Illness Scripts to Improve Students Diagnostic Reasoning Skills

BACKGROUND:

There is debate regarding how to effectively teach diagnostic reasoning to medical trainees. Our goal is to teach key elements of diagnostic reasoning during oral case presentations. Following data acquisition, the expert creates a "problem representation" to define the case, which then triggers recollection of "illness scripts." An illness script is medical knowledge stored with a predictable structure: predisposing conditions, pathophysiological insult, and clinical consequences. This allows related knowledge to become accessible for creating a reasonable differential and course of action. Third year medical students at Children's National are introduced to a framework "PBEAR" (Problem representation, Background Evidence, Analysis, Recommendation) for presenting oral case presentations (OCP) based on this theory.

OBJECTIVE:

Develop and assess the effectiveness of an eLearning module for medical trainees that

- 1) Provides an organized framework for clinical diagnostic reasoning
- 2) Models PBEAR format for OCP
- 3) Provides practice opportunities to assess case presentations using the OCP tool

DESIGN/METHODS:

A 20-minute interactive elearning module was developed focusing on illness scripts and problem representation statements. The module demonstrates effective strategies to study and store medical knowledge and opportunities to apply knowledge by analyzing cases and practicing creating problem representations statements. The module describes the OCP Tool, developed to provide feedback to students during bedside rounds. The module concludes with 3 videos, the 1st depicts a poor, the 2nd an average, and the 3rd an excellent presentation. The student is asked to rate each presentation using the OCP tool. We analyzed ratings assigned by 31 students to the cases, to determine if the students correctly rated the cases as poor, average, or excellent.

RESULTS:

68%, 78% and 95% of students correctly assigned each of the 3 cases an overall rating of poor, average and excellent respectively. 75% of students agreed with the statement "The module enhanced my diagnostic reasoning skills."

CONCLUSIONS:

After completing the module, the majority of students correctly scored the cases using the OCP tool, suggesting that the module conveyed the concepts of illness scripts and problem representation statements. Most medical students perceived the module enhanced their diagnostic reasoning skills.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Learn to Appropriately Call a Cath Attack in Acute ST Elevation MI: A Teaching Module for Fourth Year Medical Students

In the last 10 years, cardiovascular mortality has dropped by 30%. This results from various innovations in preventive cardiology, diagnostic testing, and a number of treatment modalities. None affects the outcome of myocardial infarction more than the 90-minute reperfusion strategy, the so-called “Door-to-Balloon time”. This approach has resulted in a 5% 30-day mortality for acute myocardial infarction.

To achieve this, everybody caring for patients with ST elevation myocardial infarction (STEMI) - medical students, residents, cardiology fellows, ER physicians, attendings, and first responders - must be proficient in ECG STEMI diagnosis. Accurate diagnosis leads to appropriate cardiac catheterization laboratory activation with improved outcomes for patients.

An extensive literature review was conducted to compile evidenced-based criteria to identify classic anterior, inferior, and lateral STEMI patterns. Criteria for myocardial infarctions that do not meet these classic patterns, known as STEMI-equivalents, were also identified. These include Hyperacute T-waves, STEMI with existing left bundle branch block (LBBB), and Wellens’ syndrome. Finally, criteria for non-ischemic conditions with ECG manifestations that can easily be confused with STEMIs, known as STEMI-mimics, were identified. These include known LBBB, pericarditis, ventricular aneurysm, pulmonary embolism, left ventricular hypertrophy, hyperkalemia, Brugada syndrome, early repolarization, and takotsubo cardiomyopathy.

This literature review informed a subsequent case review of cases seen at the GW Hospital that demonstrate the identified evidence-based ECG criteria. After review and selection by a panel of GW cardiologists, cases were selected for publication in a teaching module, which presents ECGs with pertinent clinical information, describes salient ECG criteria that make the diagnosis, and provides supporting imaging from studies undertaken during patient management, including cardiac catheterization, echocardiography, and CT imaging.

To validate the module, fourth-year medical students and interns will be enrolled in a prospective controlled education trial. Self-blinded with a pre- and post-test, the study includes cases from the review that exemplify characteristic features of STEMIs, STEMI-equivalents, and STEMI-mimics. Following the pre-test, a staff cardiologist will review the module cases with study participants in a didactic session. The participants will study the module prior to returning one week later for the post-test. The study is powered to demonstrate an increased diagnostic accuracy from 80% to 95% from pre- to post-test. A sample size of 38 achieves 90% power to detect this improvement with a significance level (α) of 0.05 using a two-sided one-sample t-test. Findings from the validation study will be submitted for publication in a peer-reviewed journal.

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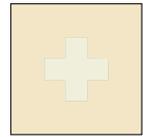
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Establishing Validity of PBEAR: An Oral Case Presentation Tool to Promote Clinical Reasoning

BACKGROUND:

Providing effective feedback on diagnostic reasoning to medical trainees during oral case presentations (OCP) is an important component of clinical clerkships. Few tools are available for faculty to provide structured feedback.

OBJECTIVE:

1) To design a new feedback tool assessing diagnostic reasoning and communication skills of medical trainees during OCP 2) To assess the tool's content and response validity, and internal structure

DESIGN/METHODS:

Our framework for OCP, "PBEAR," differs from traditional presentations. Learners start with a "Problem Representation" to share their mental model from the outset. In "Background Evidence" learners filter relevant data from the history. "Analysis" encourages comparing and contrasting patient's findings with known illness scripts. "Recommendation" is a problem-based plan. Students are also evaluated on communication skills. To assess content evidence for the tool, we requested feedback from > 100 hospitalists at pediatric national meetings. To assess response validity for the tool, 10 hospitalist educators rated an oral case presentation video and discussed their scoring rationale. Internal structure was analyzed from ratings of 53 audiorecorded case presentations. Three items were excluded (appropriately defers parts of the plan, uses notes minimally, makes appropriate eye contact) because they could not be assessed by audio recording. Sub-scales of the tool were also analyzed with Cronbach's alpha.

RESULTS:

Content evidence: After recommended changes to scoring rubric, the tool was piloted with 10 medical students, who endorsed the tool's usefulness. Response validity: Tool was further modified, based on hospitalist educators' feedback. Internal validity: Cronbach's alpha for overall scale was excellent ($\alpha=0.89$). Internal reliability of the 6 sub scales was good: Problem Representation Statement (0.88), Background Evidence Objective (0.62), Analysis (0.87), Recommendation (0.89), and Communication Skills (0.79). Internal reliability of Background Evidence -Subjective (0.57) was weaker.

CONCLUSIONS:

The PBEAR OCP Tool is a valid rating instrument for measuring students ability to effectively present a synthesized case while promoting clinical reasoning.

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SCHOOL OF NURSING

Accelerated Second-Degree BSN Graduates: Are They Ready for Professional Practice?

The accelerated second-degree Bachelor of Science in nursing (ABSN) program is a curricular innovation to enroll more students in nursing programs and to meet workforce needs. However, there is scant literature about the outcomes of these programs in terms of their effectiveness in preparing graduates for practice. What is known is that current literature indicates there is a very high attrition rate of new graduate RNs, which is a problem given the nursing workforce needs. The purpose of this study was to develop a broader understanding about the transition of the new graduate nurses from an ABSN program, 1-year after working as a professional nurse, to include the level of satisfaction with the ABSN program's effectiveness in preparing them. A phenomenological design was used to describe experiences as they were lived. It consisted of new graduate nurses from an ABSN program having worked as a professional nurse for approximately 1-year for participation in a focus-group interview. The focus-group questions were developed from the literature and were directed toward the nine participants. Three themes emerged from the focus groups analysis as impacting their transition to professional practice (1) environmental challenges within the hospital setting (2) lack of confidence in preparedness (3) understanding just what the role of the professional nurse truly means and how it feels. The results of the study indicate that there are implications for undergraduate programs in preparing students for the reality of professional practice. The information gained from this study of graduates 1 year after program completion provides evaluative data for our program and a beginning evidence base for others developing accelerated programs of study. Building from the themes, adjustments within the curriculum might be imposed to allow for a successful transition and to decrease the high attrition rate of new graduate nurses.

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Analysis of Demographic Health Survey Data to explore impacts of Household Air Pollution and WASH on ARI

OBJECTIVE:

Children in Nigeria and Haiti suffer from diarrhea and acute respiratory infection (ARI) frequently. The two health outcomes were thought to be water-borne and air-borne. However, we explored whether there exists shared risk factors for both conditions so that the diarrhea-related exposure makes the same population prone to ARI. We explored whether environmental factors, household air pollution and access to clean water or toilets and impact on ARI rates.

METHODS:

We used categorical data analysis of complex survey data from the Nigerian and Haitian Demographic and Health Surveys (DHS). The complex sample survey data were analyzed by the survey procedure in SAS 9.3. The survey analysis takes into account characteristics of the sample design, including stages of clustering, stratification, and unequal probabilities of selection. In addition, multi-way tables were produced by domain (subgroup) analysis.

RESULTS:

Children in Nigerian households where solid fuel is used were at higher risk of getting ARI than those households that utilize kerosene. After taking diarrhea-related factors into consideration, the association between fuel use and ARI was impacted. When a non-improved water source is used, the solid fuel users have a much higher risk of ARI than those using kerosene ($OR_{\text{improved}}: 2.95$ 95%CI=(1.84, 4.75); $OR_{\text{non-improved}}: 6.82$ 95%CI=(2.97, 15.63)). Using improved water and not sharing the toilet facility negate the odds difference of ARI risk comparing the solid fuel and kerosene groups ($OR: 0.52$ 95%CI=(0.23, 1.1)). Haitian children had no significant difference in odds of risk for ARI among cooking fuel groups. However, a significant association was present when the diarrhea-related factor was considered. When a non-improved toilet type is used, the kerosene group has a lower odds of ARI than the solid fuel group ($OR: 0.23$ 95%CI=(0.15, 0.38)).

CONCLUSION:

The burden of ARI and diarrhea among children living in households that primarily use solid fuels and non-improved water sources may be reduced by targeting interventions for shared risk factors related to household air pollution and water sanitation.

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Fast Food: a Source of Exposure to Phthalates and Bisphenol A in a Nationally Representative Sample

BACKGROUND:

Certain phthalates and bisphenol A (BPA) are industrial chemicals widely used in consumer products that can adversely impact human health. Diet is hypothesized to be a major source of exposure but little is known about the impact of specific food sources. This study aims to investigate the association between fast food consumption with human exposure to high-molecular weight phthalates (di(2-ethylhexyl) phthalate (DEHP) and diisononyl phthalate (DINP)) and BPA, in 8876 participants, aged 6 to 85 years old, from the National Health and Nutrition Examination Survey (NHANES), 2003-2010.

METHODOLOGY:

During the NHANES mobile exam, participants: 1) provided a spot urine sample which was measured for metabolites of DEHP, DINP, and BPA; and 2) completed a 24-hour dietary recall survey. We calculated kilocalorie intake of fast food from the dietary survey, and modeled fast food consumption in the prior 24-hours dichotomously and categorically as the percent of total daily calories (0%, <50%, ≥50%). We evaluated associations between fast food consumption and urinary chemical concentrations using linear regression. We also divided fast food into food groups (dairy, eggs, grains, meat, other) and examined the association between percent of total daily calories from each group and phthalate metabolites.

RESULTS:

The majority of study subjects had detectable levels of urinary phthalate and BPA metabolites in their urine. Those who had eaten fast food had significantly higher urinary metabolite levels of Σ DEHP [percent change (95%CI): 18.63% (10.38%, 27.50%)] and DINP [percent change (95%CI): 32.17% (20.04%, 45.52%)], but not BPA [percent change (95%CI): 2.36% (-2.59%, 7.56%)] compared to those who had not eaten fast food in adjusted models. For Σ DEHP and DINP, there was evidence of a positive dose-response effect (p for trend < 0.0001). Only meat consumption was associated with either Σ DEHP or DINP when adjusting for all food groups.

DISCUSSION:

Findings suggest that fast food consumption may be an important exposure source for DEHP and DINP, but not BPA, among the general population. Consistent with other studies that report high phthalate residues in high fat foods, our findings suggest that meat-centric meals may in part be responsible for this association. Further research should investigate which components of the fast food industry (production and storage, cooking process, packaging, etc.) contribute to this association.

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Bioethanol Cookstove Sustained Usage among Previous Kerosene Users in Ibadan, Nigeria: SUMs Evaluate Liquid Fuel Substitution

The promotion of clean cooking practices to reduce exposures to household air pollution (HAP) has been a recent focus of several health initiatives. These initiatives are inherently complex as they involve dissemination and adoption of cleaner cooking technology. Unbiased assessment of differences in cooking behaviors over the course of a cookstove intervention is necessary to reach the ultimate adoption phase of these health initiatives and quantifiably link cooking patterns to HAP exposures. This paper presents a new method of analyzing time integrated temperature data from Stove Use Monitors (SUMs) that is cost effective and sensitive to household level variations in ambient temperatures. The algorithm was applied to a randomized controlled intervention trial in the urban city of Ibadan, Nigeria. In the RCT, women that predominately use kerosene for cooking were randomized to a bioethanol stove intervention or the control group. The unbiased SUMs analysis revealed sustained use of the bioethanol “CleanCook” stove and a steady decline of traditional kerosene stove usage. Eighty four percent of women in the CleanCook intervention arm gave away their kerosene stove prior to the conclusion of the study, and 56% gave away their traditional stove within the first month of enrollment in the trial. In addition, CleanCook stove users cooked an average of 17 minutes less per day than those that used kerosene stoves. To the authors’ knowledge, the SUMs analytical methods utilized are the first to evaluate the substitution of one liquid based fuel for another liquid based fuel. Future analysis on individual level HAP exposures among our study population will allow for precise evaluation of the health impacts in an urban setting via introduction of a cleaner cookstove and reduction in daily cooking time on the cleaner cookstove.

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What Factors Are Associated with Compliance of Integrated Management of Childhood Illness Guidelines in Egypt?

BACKGROUND/OBJECTIVE:

6.6 million children under the age of five die annually from preventable diseases. The Integrated Management of Childhood Illness (IMCI) strategy was developed in 1992 to reduce mortality and morbidity largely due to preventable diseases. This study explores whether provider, facility, region, child, and caregiver characteristics are associated with compliance with IMCI clinical guidelines in Egypt to ultimately identify priority program and project area improvements.

METHODS:

The study uses child health service data from the 2004 Egypt Service Provision Assessment Survey (ESPA). The ESPA collects data about health facility service delivery, compliance with standards of care, and client and provider service delivery satisfaction. A nationally representative sample of 659 health facilities were surveyed, of which 479 provided child health services. The child health module consists of facility, provider, and caregiver surveys. The sample consists of 2,071 child observations (1,164 were male). Two multivariate regression models were developed to identify statistically significant predictors of observed care.

RESULTS:

Full IMCI compliance was low. About 70% of physicians checked for fever, 36.3% weighed the child, and 17.6% checked for anemia. In only 3% of child visits were caregivers asked about three key danger signs and three or more key symptoms as per IMCI guidelines. After controlling for the patient's and provider's demographics and background and facility characteristics, we found that providers with IMCI training had a significantly greater odds of asking two or more danger signs adjusted odds ratio (AOR)=6.7 (95%CI 3.8, 12.9) if the patient had diarrhea, AOR=6.2 (95%CI 3.5-10.9) for cough/respiratory, and AOR=6 (95%CI 3.7, 9.7) for fever. No evidence was found that compliance is associated with child sex, caregiver attributes (except in cases of diarrhea), or region. About half of health care facilities lacked handwashing equipment in the exam room, reliable electricity, and generators.

CONCLUSIONS:

IMCI is a promising strategy to improve quality of care and thereby reduce childhood morbidity and mortality, but compliance is low. This study recommends a new SPA to be carried out. Following the 2011 revolution, Egypt experienced a severe economic downturn. Anecdotal evidence points to the deterioration of quality of care in government facilities serving low-income populations. The findings illustrate the potential for further analysis of the factors that influence compliance. The small sample size for private facilities, however, limited analysis for comparison with government facilities.

FUNDING:

None

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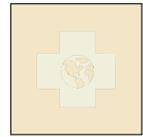
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Quantitative evaluation findings of a participatory video project aimed at reducing gender-based violence and harmful traditional practices in conflict-affected settings

BACKGROUND:

Gender-based violence (GBV) and harmful traditional practices (HTP) are prevalent in post-conflict settings. Although GBV-prevention interventions are in place in these settings, there is a lack of research evaluating GBV-prevention activities. The current study analyzed the association between exposure to “Through our Eyes” (TOE), a community participatory video project, and GBV-related knowledge, beliefs and behaviors.

METHODS:

This study analyzed quantitative evaluation data previously collected by the American Refugee Committee. The dataset comprised household surveys (n=576) from communities in Liberia, Rwanda, Southern Sudan, Uganda, and Thailand. The data were analyzed using STATA/IC 13.

RESULTS:

Statistically significant associations were seen amongst participants with increased exposure to TOE. For example, participants who had seen 2 or more TOE films had 16.6 ($p < .001$) times greater odds of disagreeing with the belief a woman who is raped should keep it to herself than those who had never heard of TOE. Of note, amongst males and females, differences were seen in various analyses. For example, for males, exposure to TOE was not associated with disagreeing with the belief; it is okay for a man to hit his wife if she won't have sex with him. Conversely, for females, exposure to TOE was associated with disagreeing with the belief (OR: 1.99; $p = .03$). Furthermore, for males, there was no association between having seen 2 or more TOE films and the intention; tell someone seen hitting a female to stop. However, females who had seen 2 or more TOE films had 3.17 ($p < .02$) times greater odds of reporting having agreed with the intention than those who had never heard of TOE.

DISCUSSION:

TOE had an overall positive influence on the knowledge, beliefs, and behaviors regarding GBV/HTP throughout the surveyed communities. Results revealed that males and females responded differently to exposure to TOE. These findings provide evidence that future GBV-prevention interventions should tailor messages and activities by gender.

KEYWORDS:

Gender, Violence, Communication, Refugees, Intervention

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Multidrug-resistant Tuberculosis in Cordoba, Argentina

Multidrug-resistant tuberculosis (MDR TB) is defined as a resistance to at least isoniazid and rifampin, two extremely potent first line drugs used in the treatment of patients with TB. World wide, there are an estimated 500,000 cases of MDR-TB. The largest number of MDR TB outbreaks are found in Spain and Argentina. Argentina is unique in that it provides free, universal health care coverage to all citizens. In addition, all citizens are vaccinated against TB. Still, MDR-TB remains prevalent. The purpose of this study is to identify social factors that also play a large role in TB infection and subsequent progression to MDR TB.

To investigate these causal social agents, I conducted four in-depth case studies of patients with MDR-TB, utilizing patient medical and social records. My results are as follows. Poverty was the primary social factor found in all the cases that predisposed each patient to different secondary conditions and led to the development of MDR TB. While poverty did not prevent access to health care, it did propagate a culture of nonchalance that prevented continued adherence to the treatment prescribed by the doctor. In addition, poverty increased the likelihood patients lived in unsanitary environments without proper ventilation or hygiene, increasing the likelihood of infection with TB. It also limited access to healthy food. In half of the patients that achieved successful remission of TB initially, malnutrition preceded development of MDR-TB with resistance to isoniazid. Half of patients also suffered from prior HIV infection. Both malnutrition and HIV create a state of immunosuppression that not only increases risk of infection but also prevents the body from mounting a healthy immune response against TB. Finally, in half of patients, poverty led to an unstable lifestyle centered on drug abuse and stealing as a means of earning a living. This prevented patients from adhering to and completing treatment regimens mandated by the doctor. This cultivates an environment within the body that is favorable to the proliferation of resistant strains of TB.

Thus, poverty was the primary social factor that predisposed patients to a host of secondary social factors including malnutrition, prior HIV infection, drug abuse and criminal activity that increased the likelihood of developing MDR-TB. This study provides insight on the deficits that exist even in a system of free, universal health care. This research can be utilized by legislators to create more effective public policy that minimizes these social deficits to successfully combat MDR-TB in Argentina.

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Reliability of Dried Blood Spots for HIV-1 Drug Resistance Testing and Surveillance in Resource Limited Settings

BACKGROUND:

In 2013, 64% of HIV-infected adults and 77% of HIV-infected children worldwide did not receive antiretroviral therapy. While access to therapy has significantly expanded in the past two decades, there are still an estimated 35 million people living with HIV worldwide. Efforts to diagnose and treat HIV must still be improved. Dried Blood Spotting (DBS) is a specimen sampling recommended by the WHO to diagnose HIV and assess for HIV drug resistance mutations (DRM). It is better suited for resource limited settings (RLS) due to its low cost, ease of administration, storage and shipment.

OBJECTIVE:

This study assesses DRM prevalence and subtype characterization from HIV-1 infected participants from Central American countries. The samples were collected from Mexico, Nicaragua, Honduras, Panama and Guatemala and sent to the only certified WHO center for HIV testing and drug resistance surveillance in Central America.

MATERIAL AND METHODS:

Whole blood was blotted onto circles on 903 filter paper cards upon arrival of samples from the participating countries. Two DBS circles were placed in lysis buffer for 10 minutes using a Qiagen extraction kit. Following WHO protocol, 106 HIV-1 pol sequences were amplified using specific primers and so far 53 samples have been sequenced in house. Paired plasma and DBS samples were analyzed. HIV-1 infecting variants were characterized using the Stanford subtyping tool.

RESULTS:

Of the 53 patients with available pol sequenced data, 28 patients (52.8%) harbored DRM to at least one drug class. One patient (1.8%) had one DRM (M46L) to Protease Inhibitors (PI). Twelve patients (22.6%) were infected with HIV-1 variants that had selected mutations to Nucleoside Reverse Transcriptase Inhibitors (NRTI) while 15 patients (24.5%) had mutations to Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI). Seven patients (15.1%) were infected with HIV-1 variants that selected DRM to at least two drug families, and ten patients (18.9%) demonstrated resistance to three or more drug families. The prevalence of drug resistance to each PI, NRTI and NNRTI is 1.8%, 22.6% and 24.5%, respectively. All infecting variants were B subtype.

CONCLUSION:

HIV drug resistance leads to treatment failure requiring more costly second line treatments and the potential spread of infection of drug resistant HIV. Expanding research in the uses of cost-effective diagnostic tools will enable better surveillance of HIV particularly in RLS. This has the potential to improve screening, which can ultimately reduce morbidity and mortality associated with HIV.

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Characteristics of HIV/AIDS and Hepatitis C Virus Knowledge in Egypt

BACKGROUND:

Good health knowledge is important because it leads to better behaviors, ultimately, protecting individuals from health risks and diseases. Historically, Egypt has had the highest Hepatitis C virus (HCV) prevalence in the world (14.7%). Although the overall HIV/AIDS prevalence is low (<0.1%), a concentrated HIV/AIDS epidemic among high risk groups has been documented. There have been many health education interventions in Egypt that focused on improving the population's knowledge of HIV/AIDS and HCV and few have been evaluated. We compare HIV/AIDS and HCV knowledge prevalence and sources among the general population.

METHODS:

Data was analyzed from the 2008 Egypt Demographic and Health Survey (DHS), a nationally representative sample of 16,527 ever-married women. Bivariate logistic regression analysis assessed preliminary associations between the outcome knowledge variables and demographic variables. Multivariate logistic regression was then conducted. Data were analyzed using Stata®, Version 12.

FINDINGS:

After controlling for important socioeconomic variables, older age, higher education, and being a female were significantly associated with a greater odds of receiving information about HIV/AIDS or HCV in the last six months. Urban areas had higher odds of receiving information about HIV/AIDS, whereas rural areas had higher odds of receiving HCV information. Overall, 94% reported having negative views toward people living with HIV/AIDS. 84% would not buy food from a vendor who had the virus, and 67% would want to keep family members' HIV/AIDS sickness a secret. 72% and 89% received information from the television about HIV/AIDS and HCV, respectively. 11% received HIV/AIDS information from health workers, whereas only 0.70% received HCV information from health workers.

DISCUSSION:

HIV/AIDS is highly stigmatized in Egypt particularly in rural areas, and rural populations report a lower knowledge of HIV/AIDS. Experts warn of a hidden epidemic in rural areas, especially given the high stigma and limited ongoing campaigns. The majority of people received HIV/AIDS and HCV information from television. The lack of data surrounding the quality of television messages, including its content given the high stigma prevalence warrants further investigation. Despite high HCV prevalence, very few respondents received information about it from health workers, suggesting a lack of education or training in the healthcare system.

CONCLUSION:

The research provides an overview of HIV/AIDS and HCV knowledge prevalence and sources, which are necessary to understand when developing effective strategies to combat these diseases and protect individuals from health risks.

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Use of Mobile Health Technology to Strengthen Health Systems Through the Six WHO Building Blocks

TITLE:

Is there evidence that the use of mobile information and communication technologies (mHealth) can improve health outcomes through strengthening the six WHO health systems building blocks of: health system delivery, health workforce, health information system, essential medical products and technologies, health financing, and leadership and governance?

BACKGROUND:

mHealth is the use of mobile information and communication technologies for improving health. It can be used for a wide range of purposes, including health promotion and illness prevention, health care delivery, training and supervision, electronic payments, and information systems. mHealth has the potential to shift the paradigm on when, where, how and by whom health services are provided and accessed. The effect of mHealth interventions can be magnified if used to strengthen health systems. WHO has outlined six building blocks as the main foundations of health system delivery, called the WHO Health System Framework which include: health system delivery, health workforce, health information system, essential medical products and technologies, health financing, and leadership and governance. In this literature review my goal is to evaluate the peer-reviewed literature on mHealth's effectiveness in strengthening health information systems.

METHODS:

Conducting a rigorous systematic evaluation of the literature published on mobile information and communication technologies aimed at improving health, while applying the WHO Health System Framework to highlight ways in which mHealth could further strengthen health systems. I searched for all mobile technology-based health interventions delivered to health care consumers using Scopus, MEDLINE, and CINAHL. 272 articles were retrieved, which will be assessed to fit our criteria for strengthening health systems through the use of the health information system WHO building block.

CONCLUSION AND RESULTS:

Our review is underway, but we anticipate that the results will highlight the significance of mobile-based technology in strengthening health systems.

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Omni Med Uganda: Community Empowerment in Health

Uganda is an East African country of 38.9 million people with 1 in 4 living in poverty. The average Ugandan has a life expectancy of 59 years and 1 in every 23 infants dies before their first birthday. In response to soaring mortality and morbidity rates among its rural populations lacking sustained access to formal health care, the Uganda Ministry of Health (MOH) in 2002 created the Village Health Team (VHT) program. In this program, locally elected individuals would be trained in preventive strategies directed at addressing the most pervasive causes of poor health among its citizens. These strategies included: infectious disease prevention and treatment (especially malaria and HIV/AIDS); basic sanitation initiatives such as the use of clean water and hand washing; increased rates of immunization; and more effective pre- and postnatal care. Following training, each VHT member would be responsible for imparting these techniques to 25 households in their local villages, and for making regular progress reports to the government and/or partnering agencies. In 2008, Omni Med, a Boston-based global health non-profit, partnered with the MOH to continue this mobilization of local empowerment in the Mukono region east of Kampala. To date, over 1,000 VHTs have been trained by Omni Med, resulting in over 25,000 households being directly influenced.

Together we participated in a week-long training that resulted in 35 newly-trained VHTs in the remote village of Kabalanga. While not working on the direct training of new VHTs, we conducted maintenance activities such as home visits for health inspections, hearings for concerns of active VHTs, and continuing education courses throughout the Mukono region.

In addition to our work on these health education activities with VHTs, each of us assumed responsibility for the initiation/advancement of a distinct project recently undertaken by Omni Med. These were:

1. Implementation of new health education curriculum in local schools, modeled on the VHT program but appropriately age-adjusted for elementary, middle, and high school levels and,
2. Construction of efficient, cleaner-burning cooking stoves out of local, renewable materials, and the development of quality control measures aimed at maximizing the quality of all stoves built in the Mukono region.

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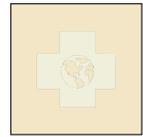
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Factors contributing to high pregnancy rates in Cordoba, Argentina

My summer research project investigated multiple factors, such as education, family history, and aspirations that lead to high pregnancy rates in Cordoba, Argentina. I surveyed nearly 100 women at the Maternal Provincial Hospital in Cordoba both in the Outpatient setting and in the Emergency Room setting. The purpose of my research started with exploring why teen pregnancy in Latin American countries, including Argentina, were among the highest in the world and more specifically why in Argentina the pregnancy rates continued to stay high despite the free education and health care.

I conducted a 5-10 minute 12 question survey that evaluated the following topics: education level, why she continued or stopped her education, aspirations and goals, health insurance status, sexual history, if the pregnancy was intended, and how she felt discussing her sexual practices with her partner. Considering prior research in the field, it has been shown that lower education and family history of teen pregnancy has an impact on pregnancy age. However, considering that education is free in Argentina, there seemed to be another component. Through my research, a repetitive theme that came up was that most women did not have aspirations, dreams, or goals. When asked the question: "What are your dreams? What is your hobby? If you could do anything, what would you do?" the woman would often stare blankly and be caught off guard. The majority could not come to any conclusion and if they did they would say they enjoy working at the house or cleaning. Many woman also said they do not have any dreams or hobbies. Through more discussion it seemed that many woman had never been asked the idea, not even in school. In contrast to the American dream where people are constantly being told that they can achieve anything with hard work, that same sentiment does not exist in Cordoba. Another contributing factor is that families are better off with government subsidies rather than having their own job. More research needs to be done in this field and should examine more specifically the education and themes prevalent in elementary, middle school, and high school. I spoke with local high schools to see how the hospitals and education system can collaborate to see what can be done in the education system to incorporate aspirations and goals more in the curriculum.

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Discrepancies Between Author Self-Disclosure and Pharmaceutical Company Reporting: An Analysis of ACC and AHA Guideline Authors

BACKGROUND:

Industry manufacturers are required by the Sunshine Act to disclose payments to physicians. These data recently became publicly available, but some manufacturers pre-released their data since 2009. We tested the hypothesis that there would be discrepancies between manufacturers' and physicians' disclosures.

METHODS:

The financial disclosures by authors of all 39 ACC and AHA guidelines between 2009-2012 were matched to the public disclosures of 15 pharmaceutical companies during that same period. Duplicate authors across guidelines were assessed independently. Per the guidelines, payments <\$10,000 are modest and ≥\$10,000 are significant. Agreement was determined using a kappa statistic; Fisher's exact and Mann-Whitney tests were used to detect statistical significance.

RESULTS:

The overall agreement between author and company disclosure was poor ($\kappa=0.238$). There was a significant difference in error rates of disclosure among companies and authors ($p=0.019$). Of disclosures by authors, companies failed to match them with an error rate of 71.6%. Of disclosures by companies, authors failed to match them with an error rate of 54.7%.

CONCLUSIONS:

Our analysis shows a concerning level of disagreement between guideline authors and pharmaceutical companies' disclosures. Without the ability for physicians to challenge reports, it is unclear whether these discrepancies reflect undisclosed relationships with industry or errors in reporting, and caution should be advised in interpretation of data from the Sunshine Act.

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Mandated Prescriber Education for Opioid Analgesics: A National Strategy to Address the Overdose Epidemic

America urgently needs prescribing reform. Adverse events associated with opioid prescribing are not isolated incidents that affect only a few Americans. In 2010, prescription opioids were involved in almost twice as many deaths as HIV/AIDS. Moreover, fraudulent diversion, non-fatal overdose, and prescription opioid addiction cost healthcare institutions, insurers, and taxpayers millions annually. Mandatory Continuing Medical Education (CME) has potential to rapidly retrain the existing physician workforce and other prescribers. The Obama Administration's prescription drug policy plan, Epidemic: Responding to America's Prescription Drug Abuse Crisis, included a proposal for mandatory CME legislation as one part of a broad policy solution intended to address the consequences of narcotic prescribing practices. This and other mandatory CME efforts have been met with resistance. In 2012, the Food and Drug Administration enacted a voluntary prescriber education initiative for extended-release and long-acting opioids. However, this focused, optional program is unlikely to address those most in need of remediation or those who limit their practice to use of short-acting opioids. We review the scope of the prescription opioid problem and assert that CME is the best approach to address the well-documented educational shortcomings in the physician workforce. We propose that an iterative CME development process and a mandatory education requirement is the most feasible route to prescribing reform, now and in the future.

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HEALTH POLICY



SCHOOL OF MEDICINE & HEALTH SCIENCES

The Role of Health Policy with the Centers of Disease Control

Within the Centers for Disease Control and Prevention there are several distinct departmental divisions designed with the intention to address unique concerns. Accordingly, the Office of the Associate Director for Policy (ADP) acts to coordinate policy activities for the CDC and to promote CDC's goal to utilize policy to effectively promote a healthier world. According to the World Health Organization (WHO), health policy is defined by the decisions, strategies, and actions that when taken collectively work together to attain particular health care goals within a society. During the course of this internship there were several objectives met by working hand-in-hand with policy analysts (i.e. representing the CDC at Congressional hearings, working one-on-one with Congressional staff members, and acting to promote the mission of the CDC). It was the objective of this internship to investigate the role of the CDC in health policy and the translation of health policy into clinical medicine. Oftentimes, policy, health care, health status, medical professionals, etc., are seen as distinct entities with little to no overlap; however, this experience has shed some light on the interconnected nature of health policy and the application of clinical medicine. The benefits gained from participation in this internship will be one of life long benefit, both in my role as a future physician and as a continuing public health professional. Participation in hearings, briefings, one-on-one interactions with Congressional members and staff, will prove to serve as both professional and personal development. Ultimately, it became evident that health policy by design is interwoven in clinical medicine and helps drive various changes (i.e. recommendation for mammography, access to women's health facilities, and much more).

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Patient Experiences With Family Planning in Community Health Centers

INTRODUCTION:

Federally Qualified Health Centers (FQHCs) are a main source of primary care and family planning services for women; however there is a limited understanding of the patient experience and priorities when accessing care. This study reports on patient focus groups at non-Title X funded community health centers designed to probe the provision of family planning services, patient satisfaction, perceived facilitators of care, and perceived barriers to accessing high quality, comprehensive, family planning services.

BACKGROUND:

Family planning services are delivered in a variety of ways, and there are recognized barriers to access. Guidance released by the Office of Population Affairs and the Centers for Disease Control and Prevention in 2014 outlined how to provide quality family planning services, including: contraceptive services, pregnancy testing and counseling, basic infertility services, preconception health services, and sexually transmitted disease services.

METHODS:

To supplement a patient experience survey, 12 focus groups were conducted in 6 US Census regions. Women participating in the focus groups were between 18-44 years of age and patients at a community health center at the time of the focus group. Transcripts from the focus groups were coded in NVivo for data analysis.

FINDINGS:

Participating health centers are organized differently and located in areas with diverse health care services, resulting in varying experiences among women at each location. Despite this, a few major themes emerged as a result of the data analysis. Across the focus groups, participants indicated that confidentiality, convenience, cost, and manageable wait times were facilitators of accessing family planning services. Barriers to care included: long wait times, inconsistent provider interaction, stigma, and lack of counseling on methods and services, and difficulty obtaining referrals.

DISCUSSION:

The patient focus groups indicate that additional work needs to be done to improve family planning services in non-Title X community health centers. Additional direct funds are needed to improve access to family planning in certain areas. Access to various methods of family planning, in addition to confidential services are required to improve patient experiences with family planning care. Finally, further guidance is needed from the Health Resource and Services Administration (HRSA) to match the delivery of family planning services to guidelines released by OPA and CDC.

STATUS

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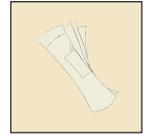
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Development & Implementation of Evidence-Based CPGs Decrease Mortality After Injury at an Urban, Academic Level 1 Trauma Center

OBJECTIVE:

Mortality rate is significantly lower when care is received in a designated trauma center, but the reasons for this remain unclear. Use of clinical practice guidelines (CPG) has been championed for decades, but compliance remains suboptimal. Mortality variability across centers with similar verification status suggests that other factors aside from minimal requirements to obtain verification have a bearing on outcome. We postulate that implementation of CPGs is associated with a decrease in mortality.

METHODS:

A retrospective study from 2010-2013 was performed at a single, urban hospital that transitioned from a non-verified to American College of Surgeons-verified level 1 trauma center. CPGs were developed starting in February 2012. An auditing strategy was implemented starting August 2013 to measure compliance with and reasons for deviation from each guideline. The primary outcome measure was in-hospital mortality stratified by injury severity score (ISS). Statistical significance was assessed using two-tailed, two-proportion z-test, student t-test, and chi-square test as appropriate, and was defined as p less than 0.05.

RESULTS:

The study includes 5051 patients. From 2010 to 2013, trauma activation volume increased from 608 to 1528 (151%) and trauma admission volume increased from 836 to 1664 (99%). Mean ISS was 7.9 +/- 7.53 and remained unchanged during the study period. There was no significant change in age, gender, or mechanism of injury. 15 CPG were implemented. Reorganization of the trauma center did not involve a significant change in physicians in that only 2 persons were added to the trauma surgeon cadre, and no one was removed. Mortality decreased significantly in patients with ISS greater than 24 (41% to 19%, p=0.004). Mortality decreased 40% in those with ISS less than 25, but this was not statistically significant. Much of the reduction in mortality occurred during the time that CPGs were being discussed and written, and preceded the time during which a formal auditing of the CPGs was implemented.

CONCLUSION:

The multidisciplinary approach to drafting and implementing CPGs resulted in standardization of care in the trauma center. This strategy demanded sustained teamwork and communication among care-providers. These less tangible quality measures appeared to have a positive impact on the delivery of quality trauma care as measured by in-hospital mortality.

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Portomesenteric Venous Thrombosis treated with Thrombolysis and Thrombectomy in a 68-year old Woman: A Case Report

Portal vein thrombosis (PVT) is a rare cause of abdominal pain and can be acute or chronic in presentation. Lifetime risk of developing PVT is only 1% in the general population, which places it lower on most clinicians' differential diagnosis for abdominal pain. The most common risk factors include malignancy and cirrhosis, followed by abdominal inflammatory foci such as diverticulitis or appendicitis. An overwhelming 10-30% of PVTs, however, are idiopathic and require an astute physician to properly diagnose. If missed, the outcomes can be fatal.

A 68-year-old African-American female with a history of hypertension and hyperlipidemia presented to the emergency department with two weeks of severe, worsening postprandial pain in her epigastrium which radiated toward the back. She denied any new exposures or change in diet. On exam, she had significant epigastric tenderness without peritoneal signs and labs were notable for mildly elevated transaminases and a leukocytosis of 22,000. CT imaging demonstrated a portal vein thrombosis that extended to the superior mesenteric and splenic veins along with associated stranding of small bowel mesenteric fat. Heparin drip was immediately initiated, and a repeat CT taken after 48 hours of anticoagulation showed stable thrombus. Interventional radiology was consulted who recommended thrombolysis given that the patient was unlikely to improve on anticoagulation alone. The concern was that she would almost certainly suffer from future gastrointestinal complications without full resolution of the thrombus given the extent of her clot burden. In addition, she was at risk for bleeding from varices that had developed as a result of the obstruction. Mechanical and pharmacological thrombectomy of the superior mesenteric and portal veins was performed without any complications, and subsequent venography showed improved patency of the superior mesenteric and portal veins. The patient was sent to the ICU for monitoring, and returned to the floor where her diet was advanced and abdominal pain improved before being discharged on therapeutic lovenox.

This case illustrates an atypical presentation of portal and mesenteric venous thrombosis considering that the patient did not have any risk factors for this rare condition. She did not have any known coagulopathy and denied a family or personal history of blood clots or fetal losses. Her cancer screening was up to date and she was not a cirrhotic. Additional research on thrombolysis as a treatment modality for portal vein thrombosis is needed since current literature is limited. Although the management aspect may be controversial, the diagnosis alone necessitates a thorough work-up that can be lifesaving.

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Risk Profiles of Youth Single, Dual, and Polytabacco Users

The concurrent use of more than one tobacco product among youth and the use of tobacco products other than cigarettes among US youth is on the rise. Much previous research on youth dual and poly tobacco use has been anchored on cigarette smoking. Given increased widespread availability of other tobacco products and increased uptake of non-cigarette tobacco among youth, a comprehensive exploration of the phenomenon of concurrent tobacco use is needed. Data from the 2012 National Youth Tobacco Survey (n=24,658), including US Middle and High School youth, ages 9 to 18 were analyzed to create mutually exclusive categories of single, dual, and poly tobacco use defined as use of only one, any two, and any three or more tobacco products in the last 30 days. Multinomial logistic regression was used to develop a risk profile for each type of use. Among youth who reported using tobacco in the past 30 days (n=4,001), the majority were single tobacco product users (41.5%), followed by poly (32.8%), and dual users (25.7%). 64% of dual users and 67% of poly users smoke cigarettes. As the number of tobacco products used increased, nicotine dependence and perceived tobacco use among peers increased, whereas quit intentions and harm perceptions decreased. These results illustrate the distinctive nature of dual and poly users: Compared to single and poly users, dual users expressed higher quit intentions and risk perceptions suggesting different motivations for this use pattern than for poly use, which may be driven by addiction. Roughly 1/3 of dual and poly users do not use cigarettes; studies that define dual and poly users as users of cigarettes plus any other tobacco product miss this distinct set of users.

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Further Expansion of Nested E-Modules to Address Anatomical Knowledge Retention in Medical Students entering the Obstetrics and Gynecology Clinical Rotation

Previous work has shown that a curriculum that included computer-based teaching modules (“e-modules”) improved retention of preclinical concepts of gross anatomy, as medical students transitioned to the third-year OBGYN clerkship. However, data showed that deficiencies still remained in areas not addressed by the curriculum. Two of these areas were microscopic anatomy and embryology, where retention scores were 4% and 38%, respectively (Jurjus et al., unpublished). Based on this research, an expanded series of e-modules will be created to target these anatomical topics that still require improvement, specifically in microscopic anatomy and embryology: 1) Ultrasound in Pregnancy using Embryological Knowledge 2) Pregnancy Timeline and the Embryo and 3) The Cervix in Health and Disease. The learning objectives correlate clinical medicine and anatomical categories. Once finalized, these e-modules will be live on the Himmelfarb Library website. By further expanding the number of e-modules available to students, we hope to improve retention of clinically relevant anatomical knowledge in adult learners.

FUNDING:

GW Office of the Vice Provost for Teaching and Learning, Spring 2013 Grants for High Impact Teaching and Learning Practices.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

A Structured Teaching Rotation for Senior Internal Medicine Residents

The current George Washington University Hospital (GWUH) inpatient medicine ward teams consist of a post-graduate year two (PGY-2) and post-graduate year three (PGY-3) resident with two first year internal medicine residents (interns) as well as medical students in their clinical years of training, all supervised by an attending hospitalist. The PGY-2 is the team leader and is expected to manage the interns and students and guide treatment of the team's patient panel. The PGY-3 role is to provide supplemental clinical guidance and dedicated teaching to medical students and interns. There have been anecdotal reports of poor utilization of PGY-3 time dedicated towards these academic goals.

To address these concerns, we created a work group as a part of the quality improvement curriculum. We developed a survey that was sent to internal medicine residents of all years and internal medicine faculty to evaluate their opinions of the current and ideal role for the PGY-3 resident.

Based on this data, we proposed an alternate curriculum for the PGY-3 on GWUH medicine ward teams to best utilize their skill sets, provide sufficient teaching experience for the PGY-3, and maximize the amount of elective time for research and sub-specialty training for the PGY-3. Our curriculum includes training in medical education techniques, expectation of presenting clinical topics to medical students, fellow residents and interns with feedback on these sessions from attending physicians and chief residents. PGY-3 residents will continue to be available to the team on admitting "Call" days to assist with the busier work load and on weekends to maintain continuity of care. Additionally, the PGY-3 teaching resident will provide medical student education through bedside teaching sessions and review of medical students' notes.

A pre-test and post-test survey will be utilized to ensure that this provides equal or improved experience in medical education for the PGY-3 and other members of the team. A secondary goal of this intervention is to liberalize PGY-3 scheduling for elective time while increasing the autonomous role of the PGY-2 as a medical team leader.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Rhabdomyosarcoma of the Head and Neck in Children: Review and Update

OBJECTIVE:

To review the clinical presentation, histology, staging, treatment modalities, and survival for pediatric head and neck rhabdomyosarcoma (non-orbital).

STUDY DESIGN:

Retrospective

SETTING:

Tertiary Pediatric Hospital

SUBJECTS:

Children treated over 18 years (1996 - 2014) for primary head and neck non-orbital rhabdomyosarcoma.

METHODS:

Medical charts were examined for clinical presentation, staging, histology, treatment modalities, recurrence and complications from treatment.

RESULTS:

Our cohort was 17 children (7 male, 10 female) with rhabdomyosarcoma with a median age of 6.3 years (range <1-19). The majority of tumors were parameningeal (13/17) with embryonal histology (11/17). Twenty-nine percent (5/17) demonstrated advanced metastatic disease at initial referral. Fifty three percent (9/17) had skull base erosion and/or cranial nerve deficits. PET CT scan was performed in 7 patients. The 5-year overall survival was 75%. Primary surgical excision was performed in all 4 patients with nonparameningeal tumors. All received chemotherapy and radiotherapy, as none had completely resectable disease on presentation.

CONCLUSION:

Pediatric non-orbital primary rhabdomyosarcoma of the head and neck usually presents with rapid onset and advanced disease. The first mode of surgical intervention should be directed toward biopsy in junction with a metastatic work-up. Primary excision with negative microscopic margins for nonparameningeal rhabdomyosarcoma is ideal to spare radiotherapy but was not achievable in our cohort. The benefits of second-look biopsy after chemotherapy and radiation are still unproven; however, it was beneficial in two patients in our review. Fluorodeoxy-D-glucose positron emission tomography (PET) to evaluate disease post treatment may further define the role for second look surgery.

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Anesthetic Management of a patient with placenta percreta for cesarean delivery.

Multiple cesareans sections increase the risk of abnormal placentation in the pregnant patient. Here we discuss a case of a 36 year old gravida eight, parity five (G8P5) with past obstetric history significant for four prior cesareans, including a placenta accreta during her most recent pregnancy, who on presentation was found to have a complete placenta previa with placenta percreta involving the lateral rectus muscle by magnetic resonance imaging. The anesthetic management of her cesarean delivery and literature review will be discussed in this presentation.

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Factors Associated with Social Cigar Smoking among Young Adults in the U.S.

Young adults have the highest prevalence of cigar use in the U.S. While data on this population indicate that cigars are often used socially, there is scant research on the characteristics of social cigar smokers and what factors influence social smoking of cigars. This study used data from Wave 1 (summer 2014) of Legacy's nationally representative truth® Longitudinal Cohort, focusing specifically on 18-21 year olds in the sample (n=7,591). Current cigar use was defined as cigar use on at least 1 day in the past 30 days. Social cigar smokers were defined as current cigar users who indicated that they only use cigars "when I'm out socializing with friends." Logistic regression was used to determine the factors associated with social cigar smoking. A total of 7.5% of young adults (n=850) were current users. Among them, 66.5% were social cigar smokers and 33.5% used cigars either alone or alone and with friends. Social cigar smokers were mostly male (70.7%), non-Hispanic White (82.0%) and high income (56.6%). On average, social cigar smokers began smoking cigars at 16.8 years old. Most social cigar smokers smoked on 1 (48.4%) or 2 (23.4%) of the past 30 days and smoked less than 1 cigar per day (66.5%). Those who smoked 16+ total cigars in their lifetime were 45% less likely to be social cigar smokers ($p < .01$) compared with those who had smoked fewer than 15 cigars in their lifetime. Non-Hispanic Whites were more likely (OR: 2.7, $p < .01$) to be social cigar smokers compared with non-Hispanic Blacks and those with the highest incomes were more likely to be social cigar smokers compared with those with lowest incomes (OR: 2.7, $p < .01$). Among current cigar users, social smoking is the most prevalent pattern of use. Results suggest that social cigar smokers tend to be less experienced cigar smokers. Future studies should monitor the smoking trajectory of social cigar smokers to understand how their patterns change over time.

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Ultrasound estimates of myosteatosis: reliability and comparison of Adobe Photoshop and ImageJ for grayscale analysis of muscle echogenicity

BACKGROUND:

Skeletal muscle tissue composition may be derived from ultrasound image echogenicity via grayscale analysis. Adobe Photoshop® and ImageJ, are two image processing programs with grayscale analysis capability. Comparative reliability of these image analysis programs has yet to be reported. The primary objective of this study was to determine the intrarater and interrater reliability of the above programs for grayscale analysis of ultrasound images of muscle tissue from older adults. The secondary objective was to compare the grayscale estimates calculated with the two image analysis programs.

METHODS:

The sample included healthy, older male Veterans ($n = 18$, age = 61.5 ± 9.8 years; BMI: 27.6 ± 4.9). Longitudinal B-mode ultrasound images of the right rectus femoris were obtained by a trained investigator using a 13-6 MHz linear array transducer. Two raters independently used the Rectangular Marquee Tool (RMT) and Quick Selection/Freehand Tool from Adobe® Photoshop® (version 6.0), and analogous tools from ImageJ (version 1.48) to select regions of interest (ROI) on images. Raters then quantified echogenicity within the ROIs via the mean values from grayscale histograms generated by the two programs. Each rater independently selected ROIs and completed grayscale analyses using each tool from each program on each image.

RESULTS:

Mean grayscale values obtained by Rater 1 were $27.47 \pm .66$, and $27.56 \pm .51$ for Rater 2, across all measurement techniques. The raters demonstrated strong intrarater reliability (ICC 3, $k = .993 - .995$, SEM = $.72 - 1.05$, $p < .001$) and interrater reliability (ICC 2, $k = .992 - .996$, $p < .001$) using both programs. The ROI selection methods used in Adobe Photoshop® and ImageJ exhibited a high degree of association across software platforms ($R^2 = .988 - .991$, $p < .001$). Grayscale analysis for muscle tissue echogenicity proved to be equally reliable using either program.

CONCLUSION:

Our findings indicate that Adobe Photoshop® and ImageJ are equally reliable programs for quantitatively assessing echogenicity in ultrasound images of the rectus femoris from older men. Both raters demonstrated a high degree of intrarater and interrater reliability performing grayscale analysis using both the RMT and Quick Selection/Freehand Tool methods of ROI selection. Grayscale values obtained from both programs were highly associated and selection techniques were equally reliable with either image processing program. (This study was funded by a Veterans Affairs VISN 5 Pilot Grant award - Station 688; VA OAA/RR&D (38 U.S.C 7406); NIH-CTSA awards: UL1TR000075 and UL1TR000101.)

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Transition Readiness Skills in Late Adolescents with Type 1 Diabetes

Transition from pediatric to adult medical care for youth with type 1 diabetes (T1D) is a critical component of T1D management and can lead to negative health outcomes if not successful. This study aimed to: 1) identify strengths and weaknesses in transition readiness tasks in late adolescents with T1D, and 2) evaluate relations among transition readiness, T1D self-efficacy, adherence, and T1D-related health indicators.

Participants included 74 high school seniors diagnosed with T1D (M age=18.1 yrs; 50.6% female) who completed the Transition Readiness Assessment Questionnaire (TRAQ); the Self-Efficacy for Diabetes Scale; and the Self-Care Inventory. A1c and glucometer data (30 days) were abstracted from medical charts.

Participants endorsed strong skills on TRAQ subscales of Talking with Providers and Managing Daily Activities, while rating skills as relatively lower on Tracking Health Issues, Appointment Keeping, and Managing Medications. Transition readiness was moderately correlated with adherence ($r=.30$, $p<.05$) but not correlated with T1D health outcome measures. Self-efficacy was associated with A1c ($r=-.23$) and mean BG level ($r=-.33$), $ps<.05$. Self-reported adherence was associated with A1c ($r=-.42$), BG monitoring frequency ($r=.35$), and mean BG level ($r=-.34$), $ps<.05$. Linear regression analyses found adherence to the T1D regimen was significantly associated with transition readiness skills, $F(1,71)=3.20$, $p<.05$, $\beta=.35$.

Results indicate several strengths in transition readiness skills, including managing daily activities and answering questions from doctors and nurses. Adolescents at risk for transition difficulties should not be solely identified by T1D health indicators such as A1c. Skills not as closely linked with daily T1D care, including making appointments, refilling prescriptions, and managing health insurance, could be targeted in interventions designed to best prepare youth for adult medical care. Future research should assess longitudinal outcomes post-transition to adult medical care to determine if and how transition readiness skills are associated with success in adult medical care.

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A microRNA Signature of Epithelial-Mesenchymal Transition in Progression of Chronic Renal Disease

OBJECTIVE:

The main objective of this study was to investigate the potential use of circulating and urinary microRNAs (miRNAs) as biomarkers for epithelial-mesenchymal transition (EMT) and the progression of renal fibrosis.

BACKGROUND:

Irrespective of the diverse initial causes, progression of chronic kidney disease is characterized by increasing tubulointerstitial fibrosis. EMT is a physiological program in which fully differentiated tubular epithelial cells give rise to mesenchymal cells such as fibroblasts and myofibroblasts in the fibrotic kidneys. There is a great need for accurate, noninvasive biomarkers for early detection of fibrosis in the kidney and the progression of kidney disease. Recent evidence suggests that miRNAs participate in the fibrotic process in the kidney. The aim of this study was to examine the urinary and circulatory miRNA expression profiles regulating the EMT and whether they are reflected by parallel changes in the pro-fibrotic factors and the progression of kidney disease.

METHODS:

Blood and urine samples were obtained from 28 patients with chronic kidney disease. Patients were divided into two groups according to their GFR: GFR < 30 (n=9) and GFR > 30 (n=19). Plasma and urinary levels of two biomarkers of fibrosis, namely collagens III (amino terminal peptide of procollagen III; PIIINP) and IV were measured. To analyze the involvement of miRNAs in kidney fibrosis, the plasma and urinary miRNA expression profiles of the patients were analyzed. Multiple regression analysis was applied to determine the predictive value of significantly dysregulated circulating and urinary miRNAs for the severity of renal disease. Real-time RT-PCR will be used to validate the miRNAs that are potentially targeting TGF- β 1/EMT, in the whole patient population.

RESULTS:

Urine and serum CIV and PIIINP levels were significantly increased in patients with GFR < 30 compared with those with GFR >30. To analyze the involvement of miRNAs, the miRNA expression profile of the patients was analyzed showing that 58 miRNAs were down-regulated and 60 up-regulated in urine of patients with GFR < 30 compared with those with GFR > 30, and 51 miRNAs were down-regulated and 61 miRNA were up-regulated in the plasma of the patients with GFR < 30 compared with those with GFR > 30. Most interesting, a panel of 4 urine miRNAs (miR-409-5p, miR-424, miR-206, and miR-30b) and 6 plasma miRNAs (miR-106b, miR-138-5p, miR-145-3p, miR-182-5p, miR-122-3p, and miR-30c) were identified which not only distinguished patients with GFR < 30 from those who had GFR > 30, but their altered expression have also been previously implicated with the phenotypic changes that occurs during EMT and the development of fibrosis.

CONCLUSIONS:

Plasma and urinary miRNAs are reliable, noninvasive, and inexpensive markers for CKD fibrosis and progression. These miRNA panels warrant study in larger cohorts since plasma- and urine-based assays could provide more feasible and safer screening compared to biopsy.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Forging American Medicine: Religion, the Frontier, and Medical Practice in Nineteenth-Century America

Strict adherence to evidence-based practice and ethical guidelines established by professional societies are hallmarks of the modern medical profession. But this is a relatively recent phenomenon, linked to the establishment of the American Medical Association in 1847. The Association gradually confronted a field of heterogeneous practitioners ranging from apprenticeship-educated physicians to naturalistic folk healers. This case study traces the career of Ephraim Menahem Epstein (1825-1913), a physician and preacher who spent his life trying to find a niche within the spectrum of healing arts. Epstein was, at various points in time, a Jew, a Christian, a Freemason, a missionary, a physician and surgeon, a teacher, and an editor of a medical journal. He was recruited by W.C. Abbott, the founder of what is today known as Abbott Laboratories, to translate medical literature for his periodical, *The American Journal of Clinical Medicine* (AJCM). The AJCM advocated for a type of medical practice called dosimetry, whose major tenets were marginal even in the permissive context of nineteenth-century medicine. This study uses primary sources, largely contemporary print materials preserved at the National Library of Medicine, in order to ascertain the nature of Epstein's medical and religious thinking and to evaluate how it was received. Epstein's Jewish knowledge informed his heterodox Christian beliefs, which were not appreciated at many Christian colleges where he taught. Importantly, his religious views informed his medical practice and contributed to his prestige at the AJCM. Epstein was not unique; many of his medical school classmates were recognized as preachers in the registry of graduates, indicating that medicine and religion were closely associated during this time period. This study aims not only to contextualize Epstein's religious, social, and professional views, but also to characterize the way in which unorthodox thinkers like Epstein were able to create places for themselves along the ideological (and geographical) periphery of society.

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Metformin Induced Lactic Acidosis

CASE:

A 41-year-old male with a history of diabetes was transferred from an outside hospital after presenting with two days of severe back pain, weakness and non-bloody emesis. On admission, he was in severe septic shock with a lactate of 23.5 Mmol/L. His blood pH was 6.8 and a pan CT scan was unrevealing. He was transferred to our institution for acute renal failure, persistent acidemia, and severe septic shock of unknown cause requiring three pressors. On arrival to our institution, he was aggressively fluid resuscitated and started empirically on broad spectrum antibiotics.

A complete history from the patient's partner and physician was obtained. His home medications included omeprazole, sitagliptin and metformin. We discovered through the patient's partner that he was a heavy alcohol user. The patient had been in Atlantic City the weekend prior to admission and consumed over 20 alcoholic beverages.

We suspected metformin-induced lactic acidosis and initiated Continuous Veno-Venous Hemofiltration, the only known treatment to improve lactic acidosis caused by metformin. His hospital course was complicated by myopericarditis, shock liver, and alcohol withdrawal. After a prolonged ICU stay, all organ functions returned to baseline. He was discharged home with instructions to stop his metformin.

DISCUSSION:

Lactic acidosis is a commonly discussed side effect of metformin, but the actual occurrence of this complication is quite rare without associated risk factors such as renal or hepatic dysfunction, alcohol consumption, or sepsis. Elucidating a detailed history from a patient, both in the outpatient setting prior to starting metformin and on presentation to the hospital, is important to avoid complications.

Metformin causes a shift from aerobic to anerobic metabolism leading to the production of lactate and a decrease in intracellular pH leading to a decrease in cellular utilization of lactate. In our patient, these processes were likely exacerbated in the setting of alcohol abuse and further in the setting of septic shock.

The key to diagnosing the etiology of this patient's severe lactic acidosis was in his history, including his heavy alcohol consumption and his medication use. In retrospect, given his heavy alcohol consumption, it would not have been prudent to prescribe this patient metformin. However, it is difficult to correctly assess for complications from medication treatments when a patient withholds vital information from the prescribing doctor. Thus, establishing a good therapeutic patient physician relationship that enables a patient's trust which is essential to optimize care and prevent severe complications.

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Calibrating and Validating the Motivation Assessment for Team Readiness, Integration, and Collaboration (MATRICx) Model and Instrument and its Applicability for Self-reflection and Intervention

OBJECTIVE:

To complete a pilot study in preparation for calibrating and validating the Motivation Assessment for Team Readiness, Integration, and Collaboration (MATRICx) model and instrument and relate findings from data collections and analysis to a strategies for self-reflection and educational interventions that enhance collaboration readiness in individuals.

METHODS:

A scoping review of the team science literature was used to compile a list of motivators and deterrents to collaboration that were aligned with a collaboration theory suggesting four levels of formal integration—cooperation, coordination, collaboration, and coadunation (Bailey & Koney, 2000; Gajda, 2004). This list informed the development of 55 indicators representing a hierarchical spectrum of collaboration (Bailey & Koney, 2000). Rasch analysis was used to investigate the rating scale structure, unidimensionality, and person-item fit of responses from 16 participants. Items were analyzed applying a 1-parameter Rasch model using Winsteps® 3.80.1 (Linacre, 2013).

RESULTS:

Preliminary Rasch analysis indicates that the rating scale is working as intended and steps proceed monotonically. Five items underfit the model; 11 overfit the model; these represent items for revision or deletion. Items calibrations reflect a hierarchical order from easiest to endorse items. “Easy items” reflect personal concerns for enjoyment and advancing own career; “challenging” items reflect fears and concerns related to loss of independence and promotion. Only 1 respondent misfit the model. Person reliability was .85 and person separation ratio 2.34. Principal component analysis indicates acceptable unidimensionality.

SUMMARY OF FINDINGS:

Preliminary results suggest that the MATRICx tool has promise for capturing readiness for collaboration in a way that usefully distinguishes both items and people. Refinement of misfitting items, deletion of redundant items, revising instructions so participants reflect about a particular collaboration, and further cognitive testing will be completed prior to a larger round of data collection and analysis.

IMPACT:

Once outcome indicators of high impact are identified, these can serves as means for self-reflection and ultimate learning interventions that target specific motivational barriers to achieving desired collaboration along the degree scale. Utilizing an attitude-social influence-self-efficacy model (De Vries and Backbier, 1994; De Vries, et al., 1986) the relationship between how individual motivations or intentions determine behaviors and action plans can be organized. This model allows for motivational factors to be grouped into attitudes and social norms (Fieshbein & Ajzen, 1975), social influences (Ajzen, 1991, Ajzen & Madden, 1986), and self-efficacy expectations (Bandura, 1986). This organization of the MATRICx output provides a means by which to develop interventions and training opportunities that specifically address the individual, social, and functional requirements associated with achieving various degrees of collaboration (Koney and Bailey, 2000) along the MATRICx model scale (Lotrecchiano et al., 2014).

Statement of how the research advances the Science-of-Team-Science-field. The MATRICx model and assessment provide a means by which we can measure individual motivation and degrees of collaboration on a correlative and parallel scale. The generalizable team science literature that informs the compilation of factors associated with why individuals choose or don't choose to collaborate provides the foundation for research that can measure, analyze, and contribute to sector-specific calibrations of the most significant factors affecting collaboration success between scientific stakeholders. Once identified within a particular teaming population (in this case health and biomedicine), interventions and training opportunities can be designed that target these most significant sector-specific factors. In addition to this outcome, the method associated with this research is generalizable to other sectors and can be reoriented to provide a means for isolating key factors that affect those sector's collaborative requirements and challenges and therefore can also serve as a means for self reflection in those sectors with specific learning interventions in mind.

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Vitamin D and drug interactions: clinical relevance

The prevalence of drug-drug interactions mediated by CYPs (cytochrome p450 enzymes), is a critical clinical issue because the interactions could result in reduced drug efficacy or adverse drug overdosing in patients. In light of the fact that vitamin D and statin drugs are subjected to CYP-mediated metabolism, we have conducted a research of various biomedical literature data bases to assess vitamin D-statin interaction and its clinical relevance. Available information indicates that vitamin D is primarily metabolically inactivated by CYP3A4 and that several statins, namely, atorvastatin, simvastatin and lovastatin, are substrates of CYP3A4. Thus, patients on atorvastatin, simvastatin, or lovastatin may have elevated plasma vitamin D levels due to inhibition of CYP3A4 by the statins. Conversely, administration of high doses of vitamin D to some patients improved statin induced rhabdomyolysis. These findings are relevant for clinical practice, where the incidence of statin induced rhabdomyolysis is significantly elevated with concomitant use of macrolide antibiotics, antifungal azoles, and other CYP3A4 inhibitors or inducers. As vitamin D may prove to be an alternate form of treatment for patients with such adverse drug reactions and since daily intake of high doses of vitamin D supplement is almost a norm of life for individuals, it is essential to determine the interactive relationship between vitamin D and commonly utilized medications in the future.

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Predictors of Cigarette and Marijuana Use Among Adolescents: A Systematic Review

BACKGROUND:

Cigarette and marijuana use are increasingly prevalent among U.S. adolescents. In addition to the adverse health effects from each substance alone, dual use can create an even greater health concern and elevate future health risks. Understanding the predictors of adolescent substance use in the years immediately preceding and during adolescence is vital for future prevention efforts.

PURPOSE:

The purpose of this systematic review is to identify the evidence-based predictors of both cigarette and marijuana use in adolescence through a comprehensive search of the literature from 1990 to October 2014.

METHODS:

Four databases were searched (PubMed, PsychINFO, MEDLINE, PsychArticles) for terms related to cigarette and marijuana predictors among adolescents. In particular, longitudinal national studies including youth predictors from ages 6-11 years through adolescence were captured.

RESULTS:

Nine studies met inclusion criteria. Results of these studies highlight a variety of predictors of use, including social predictors, behavioral factors, mental health issues and family characteristics as categories of predictors.

CONCLUSION:

Deviant peer influence, aggression, risk-taking, lack of self-control, stressful life events, depression, larger family size, and negative family events were all identified as predictors of both cigarette and marijuana use among adolescents. Future research is needed to further understand the impact of these factors across the lifespan and to validate the findings of the included studies.

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Dual anti-GBM positive and c-ANCA positive necrotizing crescentic glomerulonephritis

BACKGROUND:

Necrotizing crescentic glomerulonephritis can be associated with anti-GBM antibodies, ANCA positive antibodies, or immune complexes. Anti-GBM disease on renal biopsy immunofluorescence (IF) typically shows a linear pattern of immunoglobulin deposition along the basement membrane, whereas ANCA-related disease usually shows unrevealing IF or only mild immune deposition¹. Few cases of patients with both anti-GBM positive and ANCA positive antibodies have been discussed in the literature. Prior studies determining the incidence of double anti-GBM antibody (Goodpasture syndrome) and ANCA positive disease found dual positive sera in 2% of patients with suspected rapidly progressive glomerulonephritis. Of these, most have anti-MPO (p-ANCA) antibodies with very few cases of anti-PR3 (c-ANCA) antibodies². Patients presenting with suspected pulmonary-renal syndrome should be tested for both anti-MPO and anti-PR3 ANCA-related disease and anti-GBM disease.

CASE:

We report a 63 year-old Caucasian male with dual-antibody positive Goodpasture disease. The patient presented to a community hospital complaining of shortness of breath, non-exertional chest pain and a recent history of hemoptysis. He had not been seen by a doctor in several years and has no known medical problems. He denied edema, weight gain, orthopnea or paroxysmal nocturnal dyspnea. Presenting serum chemistry and urinalysis showed a creatinine of 11 and proteinuria respectively. Initial cardiac evaluation due to chest pain ruled out acute coronary syndrome. Further work up with chest X-ray showed possible consolidation and follow-up CT revealed multiple pulmonary nodules and interlobular thickening and a negative lung biopsy. Renal biopsy demonstrated linear staining of IgG suspicious for Goodpasture syndrome and necrotizing crescentic glomerulonephritis with 70% interstitial fibrosis on immunofluorescence microscopy. The patient was treated with hemodialysis, plasmapheresis, rituximab and corticosteroids. The patient is doing well, still requiring hemodialysis. The patient was discharged to out-patient rheumatology and nephrology follow-up on oral prednisone, 10mg daily and with a permacath for further hemodialysis.

CONCLUSION:

Dual positive anti-GBM and ANCA antibodies are rare. This case illustrates the need to test for both ANCA-related and anti-GBM antibodies in patients with pulmonary-renal syndrome. Therapy should include immunosuppression with corticosteroids, plasmapheresis and rituximab. Morbidity and mortality are significant in this population, and close monitoring is required for the identification of relapse.

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Cross-sectional associations between exposure to persistent organic pollutants and leukocyte telomere length among US adults

Leukocyte telomere length (LTL) is considered a measure of cellular aging and is associated with chronic disease, including cancer. Exposure to environmental chemicals may influence LTL. For example, in vitro research suggests dioxins may elongate telomeres by binding to the aryl hydrocarbon receptor (AhR) and inducing telomerase activity (which regulates LTL). However, few epidemiologic studies have investigated associations between dioxins or polychlorinated biphenyls (PCBs) and LTL. In this analysis, we examined the association between exposure to 19 PCBs and 17 dioxins and LTL among 1,329 US adults from NHANES 2001-2002. LTL was measured using quantitative polymerase chain reaction relative to standard reference DNA (T/S ratio). We created 3 summary metrics from lipid-adjusted serum measurements of the PCBs and dioxins, grouped by affinity to the AhR (non-dioxin-like PCBs, non-ortho PCBs, and weighted toxic equivalency (TEQ)). We used linear regression models to test the association between each metric and LTL, adjusting for demographic factors, blood biochemistry, and another metric with different AhR affinity (e.g. the TEQ was adjusted for non-dioxin-like PCBs). Non-ortho PCBs and the TEQ were associated with longer LTL in adjusted models (β : 0.062, 95% CI: (0.033, 0.091), $p < 0.001$; and β : 0.080, 95% CI: (0.022, 0.14), $p < 0.01$, respectively). In contrast, non-dioxin-like PCBs were not associated with LTL (β : 0.0070, 95% CI: (-0.041, 0.055), $p = 0.76$). We stratified models by cancer diagnosis; effect estimates for non-ortho PCBs and the TEQ were larger among participants with cancer, but the interaction term was not significant. PCBs and dioxins that activate the AhR were associated with longer LTL in a population-based sample. Because some dioxin-associated cancers are also associated with longer LTL, these results suggest that telomere regulation may lie on the mechanistic pathway between dioxin exposure and cancer.

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Rhabdomyolysis with kidney injury in a patient with uncontrolled hypothyroidism

CASE:

A 40-year-old woman with post-ablative hypothyroidism from Graves Disease presented with 3 weeks of fatigue and myalgia. She reported severe constipation and worsening bilateral anterior thigh pain exacerbated by movement. Physical examination revealed a depressed, flat affect, bilateral exophthalmos, dry skin with pretibial edema, and hypoactive bowel sounds. Strength and reflexes were intact and symmetric, but there was tenderness to palpation of the proximal muscles of both upper and lower extremities. No visible bruising or injuries noted to suggest undisclosed recent trauma. Initial labs were significant for creatine kinase (CK) 4163 U/L (normal 35-200), creatinine 1.8 mg/dl (0.7-1.2), moderate blood with 2 RBC on urinalysis, serum myoglobin 175 ng/mL (25-58), thyroid stimulating hormone (TSH) 57.3 microU/ml (0.4-4.7), and free T4 0.1 ng/dL (0.7-1.8). She was subsequently admitted for suspected rhabdomyolysis with acute kidney injury from uncontrolled hypothyroidism. Rhabdomyolysis and kidney injury resolved with aggressive hydration. Within 6 months of adequate levothyroxine treatment, TSH normalized and constipation and weakness resolved.

DISCUSSION:

Rhabdomyolysis is commonly seen on the inpatient medicine wards. Though treatment with hydration and supportive care generally results in resolution of metabolic abnormalities and muscle pain, the condition may recur if an underlying cause is not identified and treated. Hypothyroid induced muscle disorders often cause mild CK elevation. However, in most cases described in the literature, the development of significant rhabdomyolysis in hypothyroidism was precipitated by another pathogenetic factor such as hypoxia, hypotension, medications, trauma, or exercise. Our patient had no such identifiable risk factors, suggesting that uncontrolled hypothyroidism alone can result in clinically significant rhabdomyolysis. The pathophysiology behind thyroid induced muscle injury is unclear but thyroid hormones are known to play an important role in regulating glycogenolysis, lipid metabolism, protein synthesis, and mitochondrial oxidative metabolism. Thyroxine deficiency may lead to changes in muscle fibers, deposition of glycosaminoglycans, poor contractility of actin-myosin units, low myosin ATPase activity, and low ATP turnover in skeletal muscle. These injuries could result in increased sarcoplasmic calcium and persistent muscle contraction, ultimately causing muscle fiber necrosis and leakage of muscle-cell contents including potassium, phosphates, myoglobin, CK, and uric acid into the extracellular space and bloodstream. In conclusion, hypothyroidism should be considered in patients presenting with rhabdomyolysis for whom an alternate etiology is not immediately clear. Identifying and treating this underlying disease could prevent recurrence of muscle breakdown in patients with hypothyroidism.

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Is There Pandemic Vitamin D Deficiency in the Black Population? A Review of Evidence

Although 1,25-dihydroxyvitamin D [1,25(OH)₂D] is the biologically active form of vitamin D, measurement of the total serum 25-hydroxyvitamin D [25(OH)D] level is the gold standard used to define vitamin D status. Currently, it is widely accepted that serum 25 (OH) D levels below 20 ng/ml defines vitamin D deficiency. According to this definition, there appears to be pandemic vitamin D deficiency in the Black population. However, there is no evidence of higher-than normal rates of common complications and symptomology of true vitamin D deficiency in the Black population. What is going on? We researched the MEDLINE databases to find studies, from 1967 to present, that directly compare between Blacks and Caucasians the following: serum vitamin D level, serum calcium level, serum parathyroid hormone level, bone mineral density and health, and non-skeletal risks associated with vitamin D deficiency. The available studies consistently show that Blacks tend to have serum 25(OH)D levels in the deficient range while their serum 1,25(OH)₂D level is similar to, if not even slightly higher than that of Caucasians, and that the serum Ca²⁺ level in Blacks is virtually identical to that in Caucasians. Therefore, it appears that the serum 25(OH)D level is not the best marker of vitamin D sufficiency or deficiency in Blacks. In the future, clinical evaluation of the vitamin D status in the Black population needs to consider other serum biomarkers such as 1,25(OH)₂D and/or bioavailable 25(OH)D.

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Characteristics associated with patients discharged from pain clinic

INTRODUCTION:

According to the CDC, the US is experiencing a “growing, deadly epidemic of prescription painkiller abuse.” Opioids are used to treat chronic pain and patients are closely monitored in pain clinics for compliance. We evaluated characteristics in patients dismissed from our pain clinic.

MATERIALS AND METHODS:

With IRB approval we reviewed charts of patients at the GW Spine and Pain Center from 03/01/13 through 03/01/14. We identified 39 subjects dismissed from clinic. We randomly selected 41 patients seen during this period as control. We looked at reasons for discharge, age, sex, race, employment status, BMI, co-morbidities, specialty of referring physicians, surgical history and medications prescribed. Univariate associations with discharge status were examined using chi-square or Fisher’s Exact test, or independent-groups t-tests. A multivariate model was tested using logistic regression, including all predictors with univariate $p < .20$.

RESULTS:

We reviewed 80 charts. Of the 39 patients discharged, 14 were discharged for illicit drug use with or without inconsistent urine drug screen, 3 for lack of prescribed drug in urine and 5 patients for presence of opioids not prescribed. Patients on disability or unemployed were more likely to be discharged ($p = .016$), smokers were 7 times more likely ($p < .0001$) and patients with low back pain were 4 times more likely ($p = .0017$) to be discharged.

CONCLUSIONS:

The most common reason for discharge in our pain clinic was illicit drug use. Unemployment, disability, smoking, and low back pain were significant characteristics in patients who were discharged.

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Time to Death Following Injury – A Contemporary Assessment of the Trimodal Distribution of Death

BACKGROUND:

The trimodal distribution of death following injury was first described by Trunkey in 1983. Subsequent studies have found that admission to a trauma center significantly decreases the probability of death following injury. However, there have not been any recent studies to determine the time to death following injury. Given advances in trauma care, we postulate that the time to death histogram has shifted to the right. This study seeks to determine the timing of trauma-associated mortality and to describe injury or combination of injuries that are associated with early or late death versus survival.

METHODS:

A retrospective analysis was conducted on the National Trauma Data Bank (version 7.2) from 2002 to 2006. Pediatric patients (age < 18) and burn victims were excluded. Early death was defined as dead on arrival or died within 24 hours of admission. Pearson's χ^2 was used to compare region of injury to mortality. Multivariate logistic regression was conducted to show the independent effect of region of injury on mortality while controlling for demographic factors and injury type.

RESULTS:

The cohort includes 989,982 patients. The mean injury severity score (ISS) was 10.54 ± 10.11 . Overall mortality rate was 5.14%. The majority of all deaths 2002-2006 occurred between day 0 and day 1 with 41% occurring on day 1. However, compared to Trunkey's report fewer deaths occurred early (56% v 82%) and more deaths occur in the first two weeks. Torso injuries were more prevalent among early deaths (7.78% v 5.43%, $p < 0.001$). Survivors were more likely to have a blunt mechanism of injury (89% v 11%, $p < 0.001$) These results did not change on multivariate regression modeling.

CONCLUSION:

Time to death following injury has shifted to the right since 1983. The long-standing trimodal distribution is now resembles an exponential decreasing curve suggesting modern advances have made a difference in trauma mortality. In addition to stressing injury prevention, ample opportunity remains to impact mortality in the first 24 hours following injury, particularly penetrating or torso injuries. Studies directed at early treatment of these injuries are needed.

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Creating Emergency Department Point-of-Care Testing Protocols: An Expert Panel and Delphi Process

BACKGROUND:

Point of care testing (POC) is commonly used in emergency departments (ED) to obtain rapid laboratory test results. The objective of this study was to develop protocols for the use of POC testing in adult patients early in the ED care process.

METHODS:

We convened a 16-provider expert panel consisting of ED nurses and physicians to create POC protocols. This was achieved through a pre-meeting survey to identify priorities for ED POC testing, a full day in-person meeting to discuss how best to use POC testing early in the ED care process, followed by a two round Delphi process to achieve consensus on the protocols that were developed.

RESULTS:

Through this process, the study team and the expert panel created two POC protocols: An early prioritization POC protocol with 12 chief-complaints that involved a parsimonious testing strategy to identify potential life-threats early in the ED care process and a rapid post-triage assessment protocol with 10 chief-complaints that involved a more extensive testing strategy intended to reduce length of stay by improving the time from arrival to laboratory results.

CONCLUSION:

Early prioritization and rapid post-triage assessment are potential uses for ED POC testing. They are two distinct concepts where separate protocols may be helpful in improving care quality and reducing length of stay.

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What Do People Want to Know About Their Doctors?

BACKGROUND:

There is a plethora of research that demonstrates what general characteristics patients value in their doctors, but little is available on what people would like for their doctors to disclose to them. Literature from doctors' financial disclosures suggests that transparency and voluntary disclosures by doctors can increase trust.

OBJECTIVE:

We aim to determine the type of information people are interested in knowing about their doctors.

METHODS:

This was a cross-sectional descriptive study. The study population was adult volunteers randomly selected at three types of settings in Washington, D.C.: metro stops, public parks, and sidewalks. Participants were asked questions in two categories: first, how they found a doctor; second, what information they would want to know about their doctors. Data were analyzed using grounded theory methodology.

RESULTS:

Of the 100 subjects interviewed, 48 were female and 52 were male, with an age range of 19-83 (mean = 48). The most common way people found their doctors is through recommendation of friends or family. Less than half have tried to look up information about their doctors online (44%), though 85% would look to online sources if they were available. The three most common types of information people wanted to know about their doctors were patient reviews (85%), educational background and medical expertise (85%) and their views on alternative medicine and preventive health (83%). Other factors included demographic information such as age (31%), gender (25%) and social habits such as smoking (23%).

CONCLUSION:

Using an innovative methodology, our "street study" finds that people are interested in having more information about their doctors. There is wide variation in the type of information people find useful. With the increased trend towards transparency, further studies can investigate doctors' willingness to voluntarily share information about themselves, and what impact this may have on the doctor-patient relationship.

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Analyzing toxic inhalation and developing incident management guidance for mass inhalation injuries

INTRODUCTION:

Inhalation of toxic gases can cause devastating injury that requires rapid, sophisticated emergency and critical care interventions to prevent death. Current emergency preparations exist for inhaled toxin situations, but many are not adequate for large-scale mass inhalation incidents. We developed and conducted an exercise using a simulated but realistic hazardous materials scenario, where patients' critical care needs exceeded available healthcare resources under normal standards of care. From this exercise, we developed modifications to current critical care services in order to save more lives.

METHODS:

We designed a simulation (train crash with tanker rupture) that presented an inhaled chlorine gas situation in Washington, DC, exposing a very large number of people. Many seriously injured victims then arrived at hospitals and other healthcare facilities, exceeding the usual capacity of personnel, equipment/supplies, and beds. Professionals from public health agencies, healthcare organizations, and other relevant sectors participated in the exercise and voiced their actions to save lives according to current response protocols. They then stated what they would do if these protocols were flexible. Realistic urgency was injected, allowing only five minutes for participant discussion before reporting to the collective groups. Recorders were dispersed throughout the audience and documented both formal and informal comments. We analyzed the discussion and comments to specifically investigate the health organization decisions and actions in scarce resources situations, as well as the response from DC and federal agencies. From these discussions, we constructed specific ideas for improvement in healthcare delivery for situations where critical patient needs exceed available healthcare resources.

RESULTS:

Participants confirmed that the usual medical care approaches would quickly exceed healthcare capacity. Strategies for modifying those practices were proposed and discussed. Physician/nurse extenders using non-credentialed staff under close supervision, prolonged bag-valve-mask ventilation using rotating volunteers, and even sharing of ventilators were among the many ideas developed to overcome resource constraints and save lives. Admitting above the licensed bed capacity, converting non-critical care patient areas into critical care units, and converting non-patient space, such as the cafeteria, into a stable patient ward were all discussed as possibilities that would require temporary modifications to a range of regulatory, licensure, and reimbursement constraints. For this to occur, methods for healthcare to request, and for relevant agencies to grant, temporary modifications to legal and financial constraints must be established. This process needs to be far more expeditiously conducted than current guidelines allow in order to meet the needs of a rapidly evolving emergency.

CONCLUSION:

The simulated mass inhalation exercise prompted the recognition of a wide range of current limitations to the provision of adequate healthcare in extreme, resource-constrained mass casualty situations. Participants endorsed the concept of modifying healthcare delivery, including nonstandard medical responses and regulatory requirements, so that critical patient needs can be met and contingency plans developed for extreme events.

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The Association of Perioperative Opioid Use With Hospital Readmissions: A Population-Level Analysis

INTRODUCTION:

Few studies have sought to identify economic outcomes associated with opioid use, despite evidence indicating a high rate of high-risk opioid use in veteran administration (VA) patient populations.¹ An important driver for increased costs to a healthcare system is hospital readmissions.² The objective of this study was to quantify the rates of hospital readmission associated with perioperative opioid use and important prognostic risk factors.

METHODS:

Data was obtained from the VA electronic medical records for all VA surgical patients who underwent inpatient surgery in FY2011. Patients were grouped based on type of perioperative opioid usage: 1) opioid-naïve, 2) taking tramadol only, 3) taking short-acting opioids only on an acute or intermittent basis (≤ 90 days), 4) taking short-acting opioids only on a chronic basis (> 90 days), or 5) taking any long-acting opioid. After calculating descriptive statistics, Cox regression models with a priori identified predictors (age, socio-demographic status, surgery type, etc.) were developed. SAS software, version 9.2 (SAS Institute Inc., Cary, NC) was used for the analysis with two-sided P-values. $P < 0.05$ was considered statistically significant.

RESULTS:

The sample ($N=64,391$) consisted primarily of older men (55-65 years [47.6%]), white (79.9%), urban, married, who underwent a diverse set of surgeries, and had significant comorbidity burden (Charlson score $2+=38.5\%$). Many patients had chronic pain (56.9%) and were on adjunctive pain pharmacotherapy (e.g., non-opioid analgesics; 49.7%) following discharge. Post-operative opioid use was associated with a lower risk of hospital readmission within the first 30 days post-operatively based on type of opioid use (see table below).

CONCLUSION:

Post-operative opioid usage is associated with delayed hospital readmission with varying risks based on of opioid prescription use. To help decrease risks of hospital readmission, particular attention may be necessary for adequate pain control postoperatively.

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Assessing the Effectiveness of “Partners in Quitting;” A Text Message-Based Smoking Cessation Program

The study aims to assess the effectiveness of a new GW Healing Clinic outreach program called Partners in Quitting, a free, six-week smoking cessation intervention via text message. The purpose of the intervention is to provide participants with an evidence-based, comprehensive smoking cessation program that eliminates common barriers to access. The text messages will be sent and received through a web-based platform called CareMessage. Student volunteers will be recruiting participants at Bread for the City, located in the Shaw neighborhood of Washington, DC. Participants will receive daily text messages, first preparing them for their Quit Date, and then helping them stay quit. The messages will provide participants with tools to recognize triggers, fight cravings, improve cessation skills, and find ways to substitute smoking for healthier activities. Some messages are interactive and prompt the client with a question. Participants will also have the opportunity to “Text Me” to receive personalized counseling. To assess the effectiveness of the intervention, we will be distributing a pre- and post- intervention survey, collecting participant response data, and holding a post-intervention focus group discussion.

Text message-based interventions for smoking cessation have shown to increase long-term quit rates. A recent study analyzed the text message smoking cessation program, Text2Quit, and found biochemically confirmed repeated point prevalence abstinence rates of 11.1% in the intervention group vs. 5.0% in the control group.

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Effect of Imputation of Missing Data in the State Inpatient Databases on Racial Disparities Research

RESEARCH OBJECTIVE:

Racial disparities (RD) in healthcare outcomes in the U.S. have been identified in recent decades for total joint arthroplasty, particularly total knee arthroplasty (TKA). We sought to study RD in TKA using the HCUP State Inpatients Databases (SID). However, as with any large scale data collection effort, the SID have a moderate amount of missing data (MD) in several patient-level variables. In particular, "patient race" has a high proportion of missingness. As a result, researchers often conduct inappropriate analysis leading to invalid inferences. This study aimed at identifying appropriate imputation methods for the SID.

STUDY DESIGN:

We compared five imputation methods for MD (mean imputation, random draw, hot deck, joint multiple imputation [MI], conditional MI) through a simulation constructed on real data from the SID so that the hierarchical data structures and MD patterns of the database were retained. We generated MD in a mixed types of variables including continuous (total charge), binary (sex), ordinal (household income), and unordered (race) variables. Additional predictive demographic information in patients' places of residence and hospital characteristics were obtained from outside sources (Census, American Hospital Association) and incorporated into the imputation. To assess the performance of these methods, we reported root-mean-square error (RMSE) and bias of the imputed values with respect to the true values for continuous variables; the correctly imputed proportion for categorical variables. In addition, we formulated regression models for interesting RD outcomes including length of hospitalization (< or >=4 days) and utilization of high-volume hospitals (low, medium, high) in patients undergoing TKA. This was to assess the accuracy of coefficient estimates using imputed data.

POPULATION STUDIED:

Hospital discharges from Colorado in the 2005 HCUP SID.

PRINCIPAL FINDINGS:

Conditional MI prediction was uniformly equivalent or superior to the best performing alternatives for all missing data structures while substantially outperforming each of the alternatives in various scenarios. Hot deck was particularly poor for binary prediction (23% correct), random draw was particularly poor for ordinal data prediction (26%), and mean imputation (5%) and joint MI (52%) did not perform well for unordered data. In addition, conditional MI had the lowest RMSEs and biases of the coefficient estimates associated with race in regression analyses, leading to the highest proportion of correct statistical significance. In contrast, mean imputation was particularly poor for assessing significance of race in utilization of high-volume hospitals (68% correct) and joint MI was particularly poor for race in length of hospitalization (32%).

CONCLUSIONS:

The use of conditional MI substantially improved statistical inferences and this method outperformed other popularly used methods for MD in Colorado SID.

FOUNDING RESOURCE:

This study was supported by the research grant (R01HS021734) funded by the Agency for Healthcare Research and Quality.

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Biomarkers in the reproductive tract of sexually active and inactive adolescent girls: Implications for HIV susceptibility

BACKGROUND:

15-24 year old women account for 22% of all new HIV infections globally. Little information is available on the immune conditions in the adolescent female reproductive tract (FRT), particularly comparing sexually active and inactive adolescent girls. This pilot study aims at determining the feasibility of recruiting subjects from this population and to explore the biomarker milieu relevant to HIV infection, in the adolescent FRT.

METHODS:

Subjects include 12-19 year old girls in Washington DC coming for IUD placements at Children's National Hospital or MedStar Health Center. This being a pilot study to judge feasibility and perform exploratory analyses on immune biomarkers, we plan to recruit 10 sexually active and 10 sexually inactive girls. So far, 5 sexually active and 4 sexually inactive girls have been recruited.

Cervico-vaginal lavage (CVL) samples were collected and tested for IL6, IL8, TNF α , Elafin, MIP3 α and HBD2. We compared biomarker levels in sexually active and inactive adolescents, with data from a cohort of sexually active premenopausal adult women (n=60) and sexually active post-menopausal women (n=20). In all cohorts, the immune biomarkers were tested in fresh CVL samples.

RESULTS:

Of the 11 eligible adolescents approached for the study, 9 consented. Comparing all groups, sexually inactive adolescents had the highest levels of IL-6 and MIP3 α . Sexually active adolescents and adult premenopausal women had similar levels of MIP3 α and HBD2; whereas IL-8 and Elafin was highest in the sexually active adolescents. TNF α , a pro-inflammatory cytokine, was similar among sexually active and inactive adolescents and significantly higher in the adolescent cohorts compared to the two adult cohorts. The post-menopausal cohort had consistently lower values for all biomarkers compared to all other groups tested.

CONCLUSION:

Our preliminary data shows feasibility of recruiting sexually active and inactive adolescents from the Washington DC area. Although we observed trends in alteration of biomarkers in FRT, statistically significant difference was found only in TNF-alpha possibly due to the small sample sizes. Interestingly, we observed that the biomarker milieu in adolescents differ based on sexual activity as well as from premenopausal and postmenopausal adults. Continuation of our studies and expanding into larger cohorts will enable us to delineate immune mechanisms in adolescent FRT relevant to HIV acquisition and transmission.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Modulation of HERV family expression after treatment with HDAC inhibitors

Human Endogenous Retroviruses (HERVs) comprise about 8% of the human genome. Some autoimmune diseases and cancers have been associated with the expression of HERV-K, which is the most recently integrated family of endogenous retroviruses. The production of HERV-K derived proteins in HIV infected cells provides a potential target for HIV eradication. Latently HIV infected remain as the major obstacle for HIV eradication. Use of histone deacetylase inhibitors (HDACis) to induce HIV expression in resting cells is a promising strategy for HIV latency reversal.

In this study we quantified the reactivation of five different families of HERVs by three non-selective HDACis (Vorinostat, Panobinostat and Romidepsin) in a latently HIV-1 T-cell model.

After a 5-hour pulse with each HDACis, Vorinostat (1000nM), Panobinostat (50nM) and Romidepsin (50nM), we detected a 23.8%, 32.1% and 58.9% reactivation of HIV-1, respectively by measuring intracellular KC57 expression by flow cytometry. We also detected an increase in the gene expression of tested HERV families (R, K, H and P), with panobinostat having the strongest ability to induce expression HERV-K. Further analysis within the HERV-K family, revealed that the pol gene was the most expressed gene compared to gag and env.

These data demonstrate the dynamic regulation of HERV expression after treatment with HDACis and future HIV-1 therapeutic strategies should consider the influence of the reactivation of endogenous retroviruses in infected cells.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Extrapulmonary Tuberculosis in an HIV Positive Patient: A Case Report

BACKGROUND:

Although extrapulmonary tuberculosis (EPTB) is rarely seen in the United States, more than 50% of HIV-positive patients with TB have extrapulmonary manifestations. This case illustrates the unique challenges and complications surrounding treatment of EPTB in HIV patients.

CASE DESCRIPTION:

A 36-year-old man from Congo with a history of poorly-controlled HIV due to non-compliance and EPTB presented with a two week history of back pain, anorexia, and drenching night sweats. He was previously treated with an 11-month regimen of ethambutol, isoniazid, rifampin, pyrazinamide, and streptomycin. On examination he was found to have diffuse lymphadenopathy and a sinus tract on his right chest. Imaging revealed progression of known necrotic adenopathy and multiple disseminated fluid collections of varying sizes in the pericardium, spleen, liver, and peritoneal cavity, as well as a new upper lobe cavitating lesion (See Fig. 1). Upon admission, he was treated for multi-drug resistant TB and restarted on antiretroviral therapy. Aspiration of 750 milliliters from an abdominal fluid collection revealed no growth on bacterial or fungal culture and was negative for acid-fast bacilli (AFB) smear. Bronchoalveolar lavage was AFB smear-negative but grew multi-drug resistant Klebsiella.

DISCUSSION:

This case is unique because such extensive EPTB is rarely seen in the United States. The patient's diffuse lymphadenopathy depicted all stages of disease progression--ranging from enlarged, mobile, firm nodes with reactive hyperplasia (early stage) to large nodes with necrotic centers that form abscesses or sinus tracts (late stage, collar stud abscesses). One focus originated in the pericardial space and compressed the right atrium, which could progress to acute pericarditis, chronic pericardial effusion, pericardial constriction, cardiac tamponade, or invasion into the atrium. A complicating factor was the inability to grow MTB in culture medium to evaluate for sensitivities, which highlights the importance of histopathologic diagnosis by PCR. This case also illustrates the importance of close follow-up after treatment of EPTB due to the possibility of resistance. Additionally, the growth of Klebsiella from his upper lobe cavitory lesion should serve as a reminder about the possibility of alternate diagnoses, as this was initially presumed to be tuberculosis.

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Figure 1:

- A. Pericardiac abscess with right upper lobe cavitory lesion.
- B. Multiple intraperitoneal abscesses.
- C. Multiple splenic abscesses





INSTITUTE FOR BIOMEDICAL SCIENCES

Lysine Residues at Positions 4 and 7 on Nef are Critical for Interaction with Calnexin that leads to impairment of ABCA1

HIV patients are at a greater risk of developing atherosclerosis than non-infected individuals, partly due to the impairment of the ATP-Binding Cassette A1 (ABCA1) cholesterol transporter by the HIV-1 viral protein Nef leading to accumulation of cholesterol inside the cell. While studying the possible mechanism of Nef-mediated disruption of cholesterol efflux, we found that ABCA1 interacts with Nef, but a direct interaction with Nef is dispensable for the inactivation of ABCA1. Using mass spectroscopy we identified calnexin as a protein that associates with both ABCA1 and Nef and provided evidence to show that in the presence of Nef, ABCA1-calnexin interaction is disrupted leading to ABCA1 retention in the ER, subsequent degradation and impairment of cholesterol efflux. However, the molecular interactions taking place remained unknown as Nef is not known to enter the ER lumen and the domain of calnexin involved in binding to substrate proteins is located within the ER lumen. We hypothesized that Nef interacts with the C-terminal cytoplasmic domain of calnexin and that inhibiting this interaction would rescue ABCA1 function and expression. Using calnexin mutants lacking a luminal or cytoplasmic domain, we identified that the C-terminal cytoplasmic domain is responsible for Nef interaction. Using structural models of Nef and calnexin, possible Nef-calnexin interaction models were built using docking servers. Interacting residues in Nef were identified by calculating intermolecular contacts in the resulting complexes. Identified residues were mutated to confirm loss of interaction and this loss of interaction was found to associate with rescue of ABCA1 expression and restoration of cholesterol efflux. In conclusion, lysine residues at positions 4 and 7 on Nef were found to be indispensable for interacting with calnexin and inactivation of ABCA1. As cardiovascular diseases like atherosclerosis have emerged as an important cause of morbidity and mortality in HIV- infected individuals, there is a great need for targeted therapeutic strategies. This study identifies important targets that can be manipulated to inhibit the pathogenic effect of HIV on cholesterol metabolism.

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An epidemiologic comparison of *Mycobacterium tuberculosis* strains isolated from HIV-co-infected individuals to those without HIV

Mycobacterium tuberculosis (Mtb), the etiologic agent that causes Tuberculosis (TB), is one of the most successful bacterial pathogens. Moreover, human immunodeficiency virus (HIV) infection is the most common risk factor for the development of active TB and there is a significant increase in mortality from TB among individuals co-infected with HIV. Mtb is one of few pathogens able to survive within the phagocytic lung cells that are an integral part of the host innate antimicrobial defense system. However, some Mtb strains are better able to survive in the presence of host immune mechanisms than others; providing enhanced fitness to these organisms. In addition to fitness, the ability of Mtb strains to survive is based on the immune response of the infected host. Considering that HIV affects the cellular immune response of the infected host, it is not surprising that Mtb infection is one of the major risk factors for individuals with HIV. Hence, it is plausible that individuals with compromised immunity, such as those infected with HIV, are more likely to be infected with less-fit Mtb strains compared to immunocompetent hosts. Therefore, the overall goal of this study was to determine if there are Mtb strain types (genotypes and lineages) that are more highly prevalent among HIV-co-infected individuals in the Baltimore, MD metro area compared to Mtb strains isolated from non-HIV infected individuals. In this study, epidemiologic data (e.g., age, ethnicity, gender, HIV status, zip code, strain genotype and strain lineage) was collected from all TB patients at the Department of Health and Mental Hygiene (DHMH) in Baltimore, MD between 2009 to present and statistically analyzed (univariate, bivariate and chi square) via SAS 9.3 to determine if certain Mtb genotypes are more highly prevalent among TB-HIV-co-infected individuals compared to TB patients without HIV. The increasing spread of antibiotic-resistant Mtb strains and the increased risk of TB among HIV-infected individuals emphasize the need to further understand the epidemiology and transmission patterns of the various Mtb strain-types being spread among the HIV patient population. Consequently, this study provides essential data regarding Mtb strain types that are infecting HIV and non-HIV infected individuals with the ultimate goal of providing information that may lead to the development and implementation of improved surveillance and strategies to control the spread of TB among the HIV-positive population.

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Innate iNKT cell sensing of HIV-1 infection in dendritic cells is an early immune detection system inhibited by Nef and Vpu.

Invariant natural killer T (iNKT) cells are innate-like T cells that respond rapidly with a broad range of effector functions upon recognition of glycolipid antigens presented by CD1d. HIV-1 carries Nef- and Vpu-dependent mechanisms to interfere with CD1d surface expression. This suggests a role for iNKT cells in control of HIV-1, and here we have investigated whether iNKT cell can directly detect this virus. Dendritic cells (DCs) responded to HIV-1 infection with increased expression of CD1d and elevated intracellular levels of the endogenous glucocylceramide antigen. This occurred in a TLR7-dependent manner and involved the modulation of enzymes in the sphingolipid pathway. iNKT cells were able to specifically detect and respond to rare productively infected DCs, and this response was inhibited by viral CD1d down-regulation. DCs expressing CD1d as well as iNKT cells resided in the endometrial and cervical female genital mucosa, and the DCs having higher levels of HIV-receptors were CD1d+ and therefore putative iNKT cell targets. These findings indicate that innate iNKT cell sensing of HIV-1 infection in DCs is an early immune detection mechanism which is independent of priming and adaptive recognition of viral antigen, and is actively targeted by viral immune evasion mechanisms.

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Decreased interferon signature in HIV-1 viremic controllers

BACKGROUND:

Several host-encoded interferon-inducible antiviral factors suppress HIV-1 replication in a cell-autonomous fashion in vitro. The relevance of these defences to the control of HIV-1 in vivo in humans remains to be elucidated. Recent data from Sandler et al. suggest that administration of interferon in monkeys, and hence the modulation of restriction factor expression at different stages of SIV infection dramatically determines disease outcome. We hypothesized that host restriction factors play a role in disease outcomes in chronically HIV-1-infected individuals.

METHODS:

A total of 99 chronic HIV-1-infected individuals were selected from the cohort at the National Institute of Respiratory Diseases in Mexico City and divided into 3 groups: 1) Low Viremic (VL < 2,000 copies and CD4 >250), 2) High Viremic (VL >10,000 copies and CD4 >250) and 3) Advanced Infection (VL >10,000 copies and CD4 < 250). 20 HIV-1-uninfected individuals from the same ethnic background were used as a control group. CD4+ T cells were enriched from whole PBMC and the expression of 42 established anti-HIV-1 genes was determined by quantitative real-time PCR.

RESULTS:

We consistently detected an overexpression of restriction factors and ISGs in individuals with advanced disease, followed by high viremic individuals ($p < 0.0001$, Krustal-Wallis Test). Low viremic individuals had the lowest expression, even compared to uninfected. The expression of IFITM1, RTF1, TRIM22, RSAD2/Viperin and SLFN11 significantly correlated with VL in individuals with advanced infection ($r > 0.43$, $p < 0.05$). Finally, we performed 4-digit HLA typing and found unconventional HLA-B haplotypes to be associated with either control (B*3902) or risk (B*3905) of HIV-1 disease and restriction factor expression profile.

CONCLUSIONS:

In conclusion, we show evidence for the existence of novel mechanisms associated with protection or risk of HIV disease progression in a previously uncharacterized population with unique immunogenetic characteristics.

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Cocaine promotes initiation and elongation phase of HIV-1 transcription by NF- κ B and MSK1 activation

Cocaine accelerates human immunodeficiency virus (HIV-1) gene expression by altering specific cell-signaling and epigenetic pathways. In this study, we have elucidated the underlying molecular mechanisms through which cocaine exerts its effect in myeloid cells, a major target of HIV-1 in central nervous system (CNS). We demonstrate that a short-term (acute) cocaine treatment promotes HIV-1 transcription by activating both nuclear factor-kappa B (NF- κ B) and mitogen- and stress-activated kinase 1 (MSK1). However, during longer-term or chronic cocaine treatment, MSK1 is the main facilitator of HIV1 transcription. These activation events enhance the interaction of NF- κ B with histone acetyltransferases (HATs) and promote the recruitment of the positive transcription elongation factor b (P-TEFb) to the HIV-1 LTR, supporting the development of an open/relaxed chromatin configuration, and facilitating the initiation and elongation phases of HIV-1 transcription. Results are also confirmed in primary monocyte derived macrophages (MDM). Overall, our study provides detailed insights into cocaine-driven HIV-1 transcription and replication.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Unilateral Methotrexate Induced Lung Toxicity

62 yo Korean M with diet controlled type 2 diabetes and RA (controlled with Methotrexate and Etanercept) presented to the emergency department with a 3 week history of progressive nonproductive cough, fevers, congestion, dyspnea on exertion and malaise. After 2 weeks of symptoms, he visited his primary care physician and was prescribed a course of Azithromycin, followed by Levofloxacin. He then developed a severe drug rash due to Levofloxacin and was prescribed prednisone. He initially noted clinical improvement, but his symptoms soon progressed. A near syncopal episode prompted his visit to the emergency room. Physical examination on admission was notable for BP 108/65, HR 76, RR 20, Pulse Ox 87% on RA, up to 97% on 2L O₂ by NC, Temp 97.7F. He was pale and mucus membranes were dry. There was no cervical, axillary, or supraclavicular lymphadenopathy. Pulmonary examination was notable for right sided ronchi. CBC was notable for: WBC 15.01 (55% N, 22% L, 8% M, 3% E), Hgb 10.7, Hct 32.3, Plt 372. Chemistry was unremarkable. CT showed extensive alveolar infiltrate in right lung compatible with multifocal pneumonia.

Upon admission, the patient reported that he has had rheumatoid arthritis for the last 7 years, well controlled on Methotrexate and Etanercept for the last 5 years. His Methotrexate dose has been stable at 5 mg weekly. His pre-immunosuppression PPD was negative. He worked as an accountant but denied contact with pets, sick contacts, outdoor activities or housework. He did report travel to Russia for vacation about 3 months ago.

Due to progressive clinical deterioration, including interval development of high fevers and progressive hypoxia, a bronchoscopy with BAL was performed. BAL cell count showed: Nucleated cells 518, neutrophils 58%, lymphs 2%, macrophages 9%, Eosinophils 19%. Due to the eosinophilia, his antimicrobial regimen was expanded to include Voriconazole for antifungal coverage. The patient's hypoxia continued to progress and a repeat CT of the chest was performed, which demonstrated progression to bilateral infiltrates and new bilateral pleural effusions. PFTs were performed and demonstrated reduced volumes suggest of a restrictive pattern: FVC 1.94 (43%), FEV1 1.62 (48%), FEV1/FVC 84%. For the pleural effusions, a chest tube was placed and pleural fluid analysis was consistent with an exudative effusion, though all microbiology, including bacterial, fungal and mycobacterial cultures were negative. After all cultures and a quantiferon returned negative, methylprednisolone was initiated. The patient demonstrated rapid improvement in hypoxia, fevers and pulmonary infiltrates.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

DRESS Syndrome with Predominant Neurologic Symptoms after Initiation of Mycobacterium Avium Complex Osteomyelitis Treatment

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome is characterized by fever, rash, eosinophilia, and organ damage that develops two to six weeks after the initiation of a medication. The syndrome is potentially life threatening with a mortality rate of 10%. Diagnosis can be challenging, but early recognition and cessation of a culprit drug are critical to minimize morbidity and mortality.

We report a case of DRESS syndrome in a 79-year-old man that developed after the introduction of rifabutin, ethambutol, and clarithromycin used to treat Mycobacterium avium complex (MAC) vertebral osteomyelitis. The patient presented with fevers, a generalized rash, eosinophilia, and generalized weakness. Despite the cessation of the offending medications, the patient developed worsening mental status and signs of hepatic damage. Oral steroids were initiated, resulting in dramatic improvement of the patient's clinical status and laboratory findings. This presentation is unique in that it is the only case to our knowledge that developed after the initiation of extapulmonary MAC treatment. We discuss our multidisciplinary approach to diagnosis and treatment of this challenging case of DRESS syndrome requiring prolonged steroids in a patient with known MAC vertebral osteomyelitis.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Fighting a Losing Battle- A Case of Refractory Pyoderma Gangrenosum

CASE PRESENTATION:

A 57-year-old man with history of tobacco use, heart failure, and pyoderma gangrenosum (PG) presented for opioid withdrawal symptoms (nausea, vomiting), requesting early refills of his home morphine for chronic leg pain. Exam revealed severe bilateral pitting edema to the knees and multiple deep ulcers with granulation tissue, hyperpigmented borders, and malodorous serous drainage. About one year prior, he noticed a small lesion on his right leg after an possible insect bite which rapidly grew in size, progressing to multiple sites bilaterally. This progression was despite systemic steroids, Ustekinumab injections, Collagenase, Tacrolimus, and IVIG. His leg pain has been poorly controlled. He denied any fever, chills, new redness, increased discharge or change in smell. He was afebrile, with a normal white count, but was admitted for IV antibiotics for possible soft tissue infection.

DISCUSSION:

PG is an inflammatory disorder affecting 3-10 new people per million annually and is commonly associated with hematologic, arthritic, endocrine, malignant, and inflammatory bowel diseases. Pathogenesis of PG remains unclear; theories include neutrophilic dysfunction, immune dysregulation, and genetic susceptibility. There are four subtypes of PG: ulcerative (most common), bullous, pustular, and vegetative. Typical presentation is an inflammatory papule, pustule, vesicle, or nodule, which rapidly develops into an erosion or ulcer with a violaceous border. Pain is often greater than expected based on appearance. The lesions are often mistaken for an infectious etiology, but there is no benefit from antibiotic treatment.

There is little data on the efficacy of treatment options for PG. In addition to local wound care, initial treatment includes topical corticosteroids (clobetasol) or calcineurin inhibitors (tacrolimus). For extensive disease, treatment includes systemic corticosteroids or cyclosporine. Adjuvative options include TNF-alpha inhibitors (infliximab), immunosuppressants (mycophenolate or methotrexate), dapsone, and minocycline. Refractory disease options include IVIG and alkylating agents (cyclophosphamide and chlorambucil). Surgery or debridement is highly controversial due to pathergy and risk of seeding new ulcers. Other treatment options are topical (nitrogen mustard, timolol, or platelet derived growth factor), colchicine, interferon alpha, or plasmapheresis.

CONCLUSIONS:

There have been reported attempts but no clear efficacious treatment for PG, especially in refractory cases. A multidisciplinary approach is critical to enhancing patient experience in this disfiguring and painful disease. For our patient, his heart failure worsened his pain and his smoking impaired the wound healing process. Specialists invaluable to the patient's treatment team include dermatology, wound care, pain management, rheumatology, and smoking cessation.

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Intermingled *Klebsiella pneumoniae* populations between retail meats and human urinary tract infections

BACKGROUND:

Klebsiella pneumoniae is a common colonizer of the gastrointestinal tracts of humans, companion animals, and livestock. The objective of this study was to characterize a collection of *Klebsiella pneumoniae* isolates from retail meat and human urinary tract infections (UTIs) to assess their similarity in terms of antibiotic resistance, phylogenetics, and virulence.

METHODS:

Klebsiella pneumoniae isolates were collected from raw retail meats purchased from Flagstaff area grocery stores during 2012 and from positive, standard of care urine or blood cultures collected at Flagstaff Medical Center between November 2011 and June 2012. Isolates were screened for resistance to 14 antibiotics and subjected to whole genome sequencing (WGS). Relationships among isolates were assessed with multi-locus sequence typing (MLST) and WGS phylogenetic analyses. Finally, five closely related isolate pairs were tested in a mouse-lethality model to assess virulence.

RESULTS:

Meat-source isolates were significantly more likely to be resistant to tetracycline, gentamicin, and to be multidrug resistant, than were UTI isolates. MLST analysis identified four sequence types containing both meat-source and UTI isolates and WGS-based phylogenetic analyses revealed close relationships among meat-source and UTI isolates. Meat-source and UTI-source isolates showed similar virulence in the mouse lethality model.

CONCLUSIONS:

Meat-source *Klebsiella pneumoniae* isolates were more likely than UTI isolates to be antibiotic resistant, possibly resulting from selective pressures imposed by antibiotic use during food-animal production. The close phylogenetic relationships among isolates from these different sources, coupled with similarities in virulence, suggest that the barriers to transmission between these two sources are low. Taken together, our results indicate that retail meat is a potential vehicle for the transmission of antibiotic-resistant *K. pneumoniae*.

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Immune response induced by vaccination with non-replicative type I strain of *Toxoplasma gondii* (CPS-1) induces more tetramer specific CD8 T cells with central memory phenotype

Role of CD8 T cells in immunoprotection against *Toxoplasma gondii* infection is well established. However, in an encephalitis model, CD8 immunity is functionally impaired (immune exhaustion), leading to reactivation of latent infection. Studies from our laboratory have reported that functional defect during chronic infection is primarily exhibited by memory subset of CD8 T cells. Thus restoration of dysfunctional CD8 response may be critical for maintaining the chronicity and preventing the reactivation of latent infection. As a first step we evaluated and compared the antigen-specific CD8 T cell response induced by vaccination with the non-replicative type I strain of *Toxoplasma gondii* (which efficiently controls per-oral infection with type II strain) to the one induced during chronic infection. While type II strain induced a stronger SLEC (short lived effector CD8 cell) response as compared to vaccine strain in all the tissues tested, MPEC (memory precursor effector cell) response with both the strains was similar. However, interestingly the frequency of central memory cells subset (CD127+CD62Lhigh) in the vaccinated mice was significantly higher as compared to those receiving type II infection. These findings suggest that the development of inadequate central memory CD8 response may be an important defect responsible for reactivation of infection in mice susceptible to toxoplasmic encephalitis.

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Upregulation of innate immune response after oral microsporidia infection

Microsporidia are obligate intracellular parasites that infect a range of animals, including humans. In persons with normally functioning immune systems, these fungi seldom elicit a response with any clinical signs or symptoms. Because infection is usually asymptomatic in immunocompetent individuals, microsporidia were not recognized as more than pathogens of agricultural animals until the Acquired Immunodeficiency Syndrome (AIDS) pandemic. However, it has since then been publicized that severely immunocompromised hosts, such as those infected with human immunodeficiency virus (HIV) develop Microsporidiosis, which can have a debilitating effect. Moreover, an increasing number of cases have recently been recorded in individuals receiving immunosuppressant's due to a bone marrow or solid organ transplant, including cancer patients undergoing chemotherapy. Immunocompromised murine models show that protective immunity to *E. cuniculi* is primarily T cell dependent. It has been demonstrated that cytotoxic CD8 T cells play the most crucial role in fighting microsporidiosis, by secreting increased Granzyme B, IFN γ , and TNF α . However, the mice are still able to survive for 40 days in the absence of T cells, suggesting an important role for innate immune response early after infection. Natural Killer (NK) cells are one of the main components of the innate immunity and have been shown to play an important role against cancer and various infections. These effector cells can contribute to pathogen control and clearance during the acute phase of infection with mediated cytotoxicity against infected cells, making them the most likely candidate for investigation. This study describes the potential role of NK cells in fighting the infection caused by *E. cuniculi*. Using markers specific to activation and function, we analyze NK cells from the spleen and mesenteric lymph nodes (MLN). Our data show that NK cells in experimental microsporidia model are activated early after oral infection.

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Intestinal CD4 T cells are important for polyfunctional CD8 T cell response against *E.cuniculi* infection

Encephalitozoon cuniculi, a microsporidial pathogen capable of infecting humans, is an understudied spore-forming parasite that poses a serious problem for immunocompromised hosts, especially those suffering from AIDS. The infection is mostly contracted by the consumption of water or food contaminated with spores. Once inside the host, the pathogen in a unique manner infects the cell by extending the polar tube to inject its sporoplasm into the target cell. Host protection is pre-dominantly dependent on adaptive immune response, as mice lacking T cells are unable to control the infection. Amongst the T cell subsets, CD8 T cells are the primary effector cells responsible for host protection, especially when the pathogen is acquired via intra peritoneal route. However, during per-oral/natural route of infection CD4 and CD8 T cells apparently play a synergistic role as only combinatorial treatment with anti CD4 and anti CD8 antibody leads to the mortality of infected animals. As *E. cuniculi* is primarily acquired via oral route, GALT (gut associated lymphoid tissue) play an important role in restricting the dissemination of the pathogen. In this regard, intraepithelial lymphocytes (IELs) in the gut tissue act as a first line of defense against oral pathogens. The majority of IEL population is comprised of CD8 T cells but a minor subset expresses a CD4 phenotype. Previous studies from our laboratory have reported that CD8 $\alpha\beta$ IEL, which produce IFN γ and exhibit cytolytic effect against infected targets, act as a major effector population against *E.cuniculi* infection. Both of these functions are critical for keeping the pathogen under control. As CD4 T cells in the gut appear to have a synergistic effect in host protection we want to decipher their role during per-oral infection. Interestingly the number of CD4 T cells in the gut tissue raises in response to infection and their depletion compromises the functionality (IFN γ and cytotoxic response) of CD8 $\alpha\beta$ IELs. Our data show that CD4 T cells in the IEL compartment play an important role in the development of a polyfunctional CD8ab response.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Laser Speckle Contrast Imaging Characterizes Delayed Reperfusion After Transient Brachial Artery Occlusion in Patients with SCD

BACKGROUND:

The pathophysiology of sickle cell disease (SCD) involves vascular complications such as stroke and pulmonary hypertension. Elevated pulmonary artery pressure estimated by cardiac ultrasound or measured by invasive right heart catheterization is associated with early mortality among patients with SCD. Peripheral vascular dysfunction has also been observed in SCD and may be easier to assess than pulmonary vascular resistance and therefore more suitable for epidemiologic or interventional studies of SCD. Three previous studies found no difference in the maximal blood flow (or percentage increase) stimulated by occlusion and reperfusion of the brachial artery, a conduit vessel, when measured by Doppler ultrasound at periodic intervals. However, a study using continuous laser Doppler measurements of cutaneous microvascular blood flow found that patients with SCD had prolonged time to maximal blood flow and prolonged time to return to baseline compared to healthy controls. In our study, we used two-dimensional laser speckle contrast imaging (LSCI) to assess the cutaneous microvascular blood flow response in adults with SCD after five minutes of brachial artery occlusion.

METHODS:

Nine subjects with sickle cell disease were enrolled and compared against nine healthy African-American control subjects matched for age, sex, ethnicity, and body mass index. Cutaneous blood flow was directly measured using LSCI at baseline, during and after a standard brachial artery occlusion-reperfusion maneuver (inflation of an occlusive pneumatic cuff for five minutes). This stimulates a transient increase in blood flow to levels above baseline during the reperfusion phase. Blood flow data were averaged over a defined region of interest on the medial aspect of the forearm. Microvascular blood flow responsiveness was calculated as the time to maximum (time elapsed from 50% of maximum to maximum blood flow) and the time to return to baseline (time elapsed from maximum to 50% of maximum blood flow). We performed measurements on each individual on two separate days, and compared the microvascular blood flow responses between the groups using two-way ANOVA with repeated measures.

RESULTS:

We enrolled nine patients with sickle cell disease (age 35 ± 8.8 , BMI 23 ± 3.9 , 3 men / 6 women) and nine healthy controls (age 35 ± 10.7 years, BMI 25 ± 3.2 , 3 men / 6 women). Baseline microvascular blood flow measured in arbitrary units (AU) was greater in patients with sickle cell disease compared to healthy controls (53.1 ± 9.2 AU vs 37.2 ± 4.4 AU, $p < 0.0001$) but maximal microvascular blood flow was similar (121.3 ± 29.3 AU vs 124.7 ± 26.6 AU, $p = 0.58$). Analysis of the time from half-maximum to maximum blood flow revealed that patients with sickle cell disease take longer to reach maximum blood flow (19.1 ± 11.6 s vs 11.8 ± 1.0 s, $p = 0.03$) and longer to decrease from maximum to half-maximum blood flow during the recovery period (43.5 ± 13.0 s vs 28.6 ± 10.4 s, $p = 0.002$).

CONCLUSION:

Compared to healthy individuals, patients with SCD have greater baseline microvascular blood flow but similar maximal blood flow during reperfusion. However, patients with SCD differ significantly from healthy control subjects in the time required to reach maximal blood flow and the time required to return to baseline, both of which are prolonged in patients with SCD. This may reflect delayed or impaired endothelial responses to shear stress and/or greater viscosity of blood. Time to maximal blood flow might represent a useful physiological biomarker as a proxy for clinical severity of sickle cell anemia, and a potential surrogate marker in early phase clinical trials. This technique merits additional characterization and validation.

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Altered levels of soluble immune mediators in HIV-negative postmenopausal women: Implications for HIV acquisition in the elderly

PROBLEM:

The female reproductive tract (FRT) secretes immune mediators protective against sexually transmitted infections, including HIV. As multiple immune factors in FRT are hormone-responsive, the loss of sex hormones with aging may undermine these defense mechanisms. Women are disproportionately affected by the HIV/AIDS epidemic with heterosexual contact being the major source of new infections. Reports indicate older women are sexually active and often do not use protection as pregnancy is a non-issue. Therefore, investigating the effects of sex hormone-loss on FRT mucosal immune factors represents an important target to curtail HIV acquisition.

METHODS OF STUDY:

CVL samples were collected from 20 HIV-negative premenopausal and postmenopausal women. Whereas each postmenopausal woman provided only one sample, each premenopausal woman provided 3 samples, collected during proliferative, ovulatory, and secretory stages of menstrual cycle. Commercially available ELISA kits were used to assess the levels of IL-6, IL-8, TNF α , Elafin, HBD-2, MIP3 α /CCL20 and SLPI. Samples were analyzed for their anti-HIV activity against HIV-1 IIB and BaL strains via the TZM-bl assay.

RESULTS:

We observed significantly lower levels of critical immune mediators in CVL from postmenopausal women compared to those from premenopausal women: TNF α (11.59 versus 51.46 pg/mL), MIP3 α (1.00 versus 93.77 pg/mL), SLPI(39,598 versus 239,184 pg/mL) and HBD-2(626 versus 6821 pg/mL). Levels of IL-6 and IL-8 displayed a trend toward lower levels in postmenopausal samples whereas Elafin levels remained unchanged. Inhibition of HIV-1 infection was observed for X4/IIB and R5/BaL strains in both pre and postmenopausal samples with inhibition of BaL stronger in premenopausal samples (54.2 versus 37.6%).

CONCLUSIONS:

Our findings indicate that levels of critical mucosal immune factors and anti-HIV-1 activity in CVLs are affected by the hormonal status of healthy HIV-negative women. This suggests the need for specific therapeutic interventions to boost genital tract immunity against HIV in older women.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Identifying the essential region of a putative, regulatory small RNA in *Mycobacterium tuberculosis*

Toxic radicals, such as reactive oxygen species (ROS) and reactive nitrogen intermediates (RNI), are produced by macrophages to kill invading microorganisms. However, *Mycobacterium tuberculosis* (Mtb) is one of few bacteria able to survive within the harsh environment of the human alveolar macrophage. Bacteria utilize numerous mechanisms to adapt to environmental stress. To date, more than 90 sRNAs have been identified in *E. coli* that play a regulatory role in growth and survival. While several genes and gene products involved in Mtb stress regulation have been described, sRNAs have yet to be characterized. Our lab has evidence that a sRNA exists and affects Mtb growth. Specifically, we have identified a 30-nucleotide sequence, termed small anti-stress RNA (SasR), from Mtb that enhances the growth kinetics and survival of Mtb as well as recombinant *E. coli* and *Salmonella*. We previously demonstrated that recombinant *E. coli* containing SasR confers up to 5 logs greater survival to both *E. coli* and *Salmonella* in the presence of 1.5 mM hydrogen peroxide (H₂O₂, a form of ROS) compared to the same hosts containing the vector control. To determine if SasR functions in Mtb, an in-frame deletion of SasR was previously generated via homologous recombination and demonstrated altered growth characteristics. For example, wildtype Mtb colonies were significantly larger than a SasR mutant and at 22 days of incubation the null mutant demonstrated two logs less growth compared to wildtype Mtb and a complemented SasR mutant. The goal of the current study was to identify the functional region of SasR by generating mutations altering the SasR RNA secondary structure. The phenotypes were tested using recombinant *E. coli* H₂O₂ survival assays. Our results demonstrate that mutants vary in their ability to grow and survive. For example, a mutation (GT break) that adds a loop to the secondary structure is significantly ($p < 0.05$) less able to survive in the presence of 1.5 mM H₂O₂, suggesting that the RNA structure is critical for function. Although the mutations generated in this study had an effect on survival, none of the mutations abolished the survival phenotype. Hence, additional SasR mutations will be generated and tested for function in recombinant *E. coli*. Moreover, future studies will be carried out to further characterize SasR's regulatory mechanism in Mtb. In conclusion, these findings provide evidence of a putative, novel regulatory mechanism in Mtb and may contribute to the overall understanding of *M. tuberculosis* growth and persistence.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Jarisch-Herxheimer Reaction (JHR) in the setting of Syphilis and Human Immunodeficiency Virus (HIV)

LEARNING OBJECTIVE 1:

Recognize the clinical features of Jarisch-Herxheimer Reaction

LEARNING OBJECTIVE 2:

Prevention and management of Jarisch-Herxheimer Reaction

CASE:

A 47-year-old male with HIV presented with one week of blurry vision in the left eye. He denied fevers, chills, ocular pain, confusion, and neck stiffness. He was not on anti-retroviral therapy.

The patient was unable to read fine print within 1-foot length of the left eye. Ophthalmologic exam was significant for chorioretinitis of the left eye. Laboratory studies revealed a positive Serum FTA-ABS and RPR (titer 1:512). CD4+ count was 470 and HIV viral load was 39,172.

Lumbar puncture was performed with cerebrospinal fluid positive for VDRL. The patient was immediately started on IV penicillin G. Within three hours, the patient endorsed rigors, and chills. Vital signs showed fever, tachycardia, and mild hypotension. Given concern for Jarisch-Herxheimer Reaction (JHR), he was moved to a medical intensive care step-down unit for aggressive supportive care. Vital signs normalized within 24 hours and penicillin was continued for treatment of syphilis.

DISCUSSION:

Center for Disease Control (CDC) estimates there are approximately 55,000 new cases of syphilis in U.S. annually. In the current HIV pandemic, management of syphilis is crucial as syphilis may increase the rate of acquisition and transmission of HIV. JHR, a complication of syphilis treatment, has been reported at rates of 10-25% and may be as high as 50-75% in cases of primary and secondary syphilis. It is rare in latent and late syphilis. Rates are even higher in HIV patients. JHR is mostly self-limited, but consequences include discontinuation of treatment and rarely death.

Although the cause of JHR is unknown, it is proposed that release of cytokines after administration of anti-microbial agents is responsible. Commonly associated with underlying syphilis or louse-borne relapsing fever, it can also occur with non-spirochete disease including brucellosis and meningococcal septicemia. JHR occurs with numerous agents including penicillins, tetracyclines, macrolides, and sulfonamides.

JHR occurs within hours to one day of administering penicillin. Clinical features include fever, tachycardia, tachypnea, and hypotension. Patients may endorse chills, myalgias, and flushing. If a syphilitic rash is present, it may worsen.

Current treatment options are supportive only (anti-pyretics, fluids). Discontinuation of the treatment agent or transfer to ICU level care may be considered, although no studies exist that support these measures. Corticosteroids have been studied as pre-treatment measures for JHR and showed decreased incidence or duration of fever. However, none demonstrated a mortality benefit. United Kingdom guidelines recommend use of steroids in certain cases of neuro- and cardiac-syphilis while CDC guidelines do not endorse use of steroids. Given lack of evidence and consensus, steroids are not considered routine treatment of JHR. In patients with louse-borne relapsing fever, murine Anti-TNF- α antibodies have shown to reduce vital sign disturbances and levels of cytokines. These agents could be promising in prevention of JHR.

Syphilis is a common disease that has become more important in the setting of the HIV pandemic. JHR is a complication associated with the treatment of syphilis. Although usually self-limiting, it can lead to treatment failure and death. Therefore, it is essential to recognize JHR and understand current and future management options.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

When Lymphocytes Disappear

A 42 year old female with past medical history of seasonal allergies presented to allergy clinic with recurrent episodes of angioedema. She complained of angioedema of the lower lip and inner cheek after eating chicken, spinach, artichoke and a baked potato. She denied hives, pruritus, throat closing sensation, shortness of breath, wheezing, cough, chest tightness, nausea, vomiting, diarrhea, abdominal pain, or lightheadedness. The swelling gradually resolved within 24 hours, using Diphenhydramine 25mg orally immediately after onset of symptoms. On exam, lungs were clear and no evidence of a rash on skin exam. Skin prick tests were only positive for tree pollen, dust mite, weed pollen, and cat. She had slightly elevated allergen specific IgE to only spinach and artichoke. C4 levels were repeatedly normal as were C1 esterase inhibitor levels and C1 esterase functional levels, thus excluding C1 esterase inhibitor deficiency. She was found to have elevated anti-thyroid antibodies, and elevated thyroid stimulating hormone, consistent with the diagnosis of Hashimoto's Thyroiditis. Repeatedly low absolute CD4 counts (67-85) were noted, with negative studies for HIV-1 and HTLV 1/2 on multiple occasions. The consistently low CD4 levels with negative HIV meet the criteria for the diagnosis of idiopathic CD4 lymphocytopenia.

Idiopathic CD4 lymphocytopenia (ICL) is a rare disorder defined by the Centers for Disease Control as a documented absolute CD4 T lymphocyte count of less than 300 cells per cubic millimeter or less than 20% of total T cells on more than one occasion, and no evidence of HIV, any defined immunodeficiency or therapy associated with depressed levels of CD4 T cells. There have been multiple associations with this disorder including: opportunistic infections and autoimmune disease. This is a case of a woman presenting with facial angioedema, found to have ICL after thorough evaluation. Labs were consistent with Hashimoto's thyroiditis which studies have shown can correlate with increased T cell turnover. This case shows a rare presentation of ICL, with a woman presenting with angioedema secondary to food allergy found to have Hashimoto's thyroiditis and CD4 lymphocytopenia. It shows the importance of thorough investigation in a patient presenting with angioedema. Based on elevation in TSH, she was treated with low dose Levothyroxine with complete resolution of her angioedema, and some improvement in her absolute CD4 cell levels now ranging from 119 to 123. She no longer uses any antihistamines and has not developed any opportunistic infections.

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IMMUNOLOGY/INFECTIOUS DISEASES



SCHOOL OF MEDICINE & HEALTH SCIENCES

Demonstrating the Need for a Multimodal, Integrative Educational Curriculum for Graduate Medical Education in Vaccinology

BACKGROUND:

There are a growing number of individuals and groups who challenge healthcare providers (HCPs) by refusing to vaccinate their children. The success of immunization strategies and the reduction in the number of children on alternative vaccine schedules is dependent on effective interactions between primary care physicians and their patients. HCPs play a crucial role in communicating information and advice to the public on vaccine promotion yet several studies have found concerning results that HCPs do not possess adequate knowledge of vaccines. If HCPs are not adequately trained on all aspects of vaccines, from components, to manufacturing, to the licensing process, it will be difficult for physicians to regain public confidence in recommended vaccine schedules. In addition, several studies have made recommendations regarding the need to revise medical education curriculum with the growing importance in the role that HCPs have in vaccine promotion.

METHODS:

To assess current opportunities for vaccinology training available at institutions across the US, a 13 question survey was sent to all Pediatric Infectious Disease fellows and fellowship directors.

RESULTS:

64 people responded to the survey; 31 program directors and 33 current fellows. The survey found that some Pediatric Infectious Disease fellows do not receive any education and/or training about vaccine specific antigens (1), non-antigen components of vaccines (4), manufacturing of vaccines (12), and licensing and regulation of vaccines (10). When asked to assess the adequacy of their knowledge in each of these areas using a scale of 1-100, the results were 62.39, 50.53, 45.95, and 52.69, respectively. The most common way fellows receive training in these areas is informally through experience with specific cases or patients. Few fellows reported having access to online lectures/presentations on the topic, having access to powerpoints or other multimedia on the topic, or formal required reading materials. The most desired educational method among survey respondents was recorded lectures provided by experts. The majority of respondents felt 6-10 hours of time should be dedicated to formal education on vaccine specific topics.

CONCLUSION:

The results of this study demonstrate the need and desire for a more robust formal training curriculum in vaccinology for graduate medical education. The development and implementation of multimodal, integrative vaccinology training modules will address the gap in the education of pediatric infectious disease physicians. HCPs across the United States have a tremendous challenge to overcome regarding anti-vaccine movements, but with the proper tools and training, they may be able to tackle the problem in a timelier manner.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Chronic Fatigue Syndrome in US Service Members

BACKGROUND:

Military members returning from recent conflicts in Iraq and Afghanistan face a spectrum of health issues ranging from PTSD to physical trauma. Among these is Chronic Multisymptom Illness, which encompasses a number of ICD-9 CM diagnoses including Chronic Fatigue Syndrome. The etiology of the syndrome is not well understood. Therefore, treatment is limited to symptom relief. Understanding the etiology of Chronic Fatigue Syndrome will lead to improved treatment models for the syndrome, especially in troops returning from conflicts in the Middle East. Bartonella is a gram negative bacterium that causes chronic illness in patients with symptoms that can overlap with Chronic Fatigue Syndrome. In addition, Bartonella has been found in animals native to Afghanistan and Iraq.

THESIS:

This research seeks to demonstrate an association between positive Bartonella serology and Chronic Fatigue Syndrome in U.S. service members returning from Operations Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn.

METHODS:

Serum samples obtained from the DoD Serum Repository will be analyzed using an indirect immunofluorescent antibody test (IFA) in the CDC's Bartonella lab. Serum samples which are positive in screening assays will be titrated to end point against a variety of Bartonella antigens, which include but not limited to *B. henselae*, *B. quintana*, *B. koehlerae*, *B. clarridgeiae*, *B. tamiae*, *B. tribocorum*, *B. elizabethae*, and *B. vinsonii*. Serum will be classified as "Positive" with a titer of $\geq 1:256$ to one of the antigens in the assay and either "Identified Bartonella Species" (four-fold difference between titer level and next closest antigen titer) or "Probable Identified Bartonella Species" (two-fold difference between titer level and next closest antigen titer) and/or having "Strong Cross-Reactivity" (does not have at least a two-fold difference between titer level and next closest antigen titer). Subsets of serum samples will also be analyzed for presence of Bartonella DNA by PCR assays. Data will be analyzed using odds ratios and conditional multivariable logistics regressions examining a relationship between antibody levels to Bartonella and CFS. An identified subset of 1000 subjects and 1000 control subjects will be analyzed at a fixed power of 90% and p-value < 0.05 .

RESULTS:

Pending.

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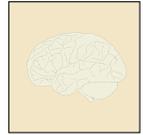
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Thymectomy is Safe for Myasthenia Gravis Patients: Analysis of the NSQIP Database

OBJECTIVES:

To determine thymectomy-associated morbidity and mortality outcomes among myasthenia gravis (MG) patients.

METHODS:

Patients undergoing thymectomy were identified from the American College of Surgeons National Surgical Quality Improvement Program Database from 2005 to 2012 using Current Procedural Terminology (CPT) codes. Patient demographics, clinical characteristics, and postoperative outcomes were stratified by MG diagnosis. Logistic regression was used to identify predictors for morbidity outcomes. Chi-square was used to examine the association between MG diagnosis and surgical approach; the outcome of each approach was stratified by MG diagnosis.

RESULTS:

1148 subjects, of whom 108 had MG, were identified. Patients with MG were younger, less likely to have hypertension or be on dialysis, had a lower mean serum creatinine level, had a more severe American Society of Anesthesiologists (ASA) physical classification, and frailty index scores than subjects without MG. Of the MG patients, 51.9% were using corticosteroids compared to 6.5% of non-MG patients. There were no deaths among MG patients. The rate of re-intubation was 6.5% among MG subjects compared to 1.1% of control subjects. The majority of MG patients were coded as transsternal thymectomy. There were no differences in the outcomes among the surgical approaches.

CONCLUSION:

Although patients with MG have a greater preoperative morbidity and a higher frequency of reintubation, thymectomy is overall a safe procedure for patients with MG. Despite the development of videoscopic procedures, the most commonly used procedure to perform thymectomy is the transternal approach.

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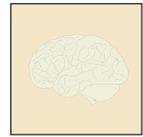
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Cerebral Perfusion and Brain Injury in the Very Preterm Infant

Prematurely born infants account for 12% of all the live birth in the USA. Medical advances in neonatal clinical care have dramatically increased the survival rate; however survivors of preterm birth are at higher risk of developing life-long disabilities. Brain injury [BI] is a common complication of preterm birth and it is associated with a high prevalence of long-term neurodevelopmental impairments. Hemodynamic instability and resulting alterations in cerebral perfusion is a key mechanism in brain development of the critically-ill preterm infant. However, the association between the severity of prematurity related brain injury and cerebral perfusion in this high-risk population is currently unknown. The objective of this study was to examine the relationship between brain injury severity and brain perfusion in very preterm infants at term-equivalent age [TEA] using non-invasive magnetic resonance perfusion imaging [MRI].

We prospectively enrolled very preterm infants (gestational age [GA] at birth \leq 32 weeks; birthweight < 1.5 kg). Infants underwent 3T brain MRI study under natural sleep at TEA. All MRI studies were reviewed by an experienced pediatric neuroradiologist, and categorized into four groups: (i)=normal; (ii)=minimal i.e., non-parenchymal injuries (grade I-II intraventricular hemorrhage); (iii)=mild supra/infratentorial parenchymal injuries (e.g., mild white matter injury, mild volume loss); or (iv)=moderate/severe BI (e.g., cystic periventricular leukomalacia, hydrocephalus). We quantified cerebral blood flow [CBF] using arterial spin labeling and neonatal specific parameters (units: mL/100g/min). Regions of interest included left/right: thalami, basal ganglia [BG], central sulci, and hippocampi. Mean global and regional CBF were compared between the four groups controlling for GA at MRI.

We studied 78 preterm infants who underwent a MRI at a mean age of 40.4 ± 1.4 weeks. Of these, 26(33%) had a normal MRI, 20(26%) had minimal-BI, 17(22%) exhibited mild-BI and 15(19%) demonstrated moderate/severe BI. Global and regional CBF was statistically different between the four groups (all $p < 0.04$). Pairwise comparisons revealed that CBF was significantly decreased in moderate/severe BI versus normal ($p < 0.05$): global CBF=18.6/21.9, thalami=33/43, BG=31/38, central sulci=26/33 and hippocampi=28/34. Cerebral perfusion was also significantly reduced in mild-BI versus normal for global CBF=18.9/21.9, thalami=37/43, BG=33/38, and hippocampi=27/34. In conclusion, our data suggest that both mild and moderate/severe parenchymal BI in preterm newborns at TEA is associated with reduced global and regional CBF. Improving our understanding of altered brain perfusion in the very preterm infant may provide important insights into resulting impairments in brain growth and development in this high-risk population.

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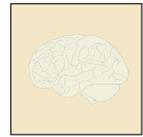
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Environmental Enrichment Promotes Generation of New Oligodendrocytes and Attenuates Hypoxia-Induced Perinatal White Matter Injury

Hypoxic damage to the developing brain is associated with permanent neurodevelopmental disabilities in preterm infants. This failure of oxygenation predisposes to white matter injury and is associated with many anatomical changes, the most distinctive of which is damage to the periventricular white matter. This diffuse white matter injury results in the loss of glial cells and causes a significant disruption in myelination, which leads to cognitive and behavioral impairments throughout childhood. The cellular and molecular mechanisms underlying diffuse white matter injury are poorly defined. Previous studies demonstrated that the environment affects both neural plasticity and functional recovery after brain injury. Furthermore, the level of maternal education and presence of a two-parent household have been shown to positively influence the long-term neurological outcome of preterm infants. Therefore, the environment plays a crucial role in promoting functional recovery in the CNS, and may play a role in the repair of the developing white matter. Here, we utilize enrichment of the environment in an established rodent model as a means to attenuate the effects of perinatal hypoxia on white matter development. Environmental enrichment (EE) is a noninvasive combination of social and physical enhancement of surroundings that provides mammals with an opportunity for more complex social interactions and voluntary physical activity. Combining the benefits of exercise and socialization in a stimulating environment, EE has been shown previously to normalize the neurochemical profile of inhibitory interneurons after hypoxia-induced developmental delay (Komitova et al., 2013), and to enhance the generation of oligodendrocyte (OL) progenitors after focal cortical ischemia (Komitova et al., 2006). By characterizing the effects of EE on hypoxia-induced cellular changes in developing mouse white matter, we hope to determine if a critical window of recovery exists. We show here that EE attenuates the effects of perinatal hypoxia and enhances OL regeneration after injury. Mice were exposed to hypoxia from P3 until P11, and to EE from P15 until P45. After two weeks of EE (P30), we observed an increase in the number of Olig2- (transcription factor expressed throughout the entire OL lineage), NG2- (marker of OL progenitors), and CC1- (marker of mature OLs) expressing oligodendroglial cells in the corpus callosum of mice exposed to hypoxia. EE also increased NG2 cell proliferation, and enhanced expression of myelin proteins. Importantly, we also observed a direct and significant positive effect of EE on the generation of new OLs in corpus callosum. Interestingly, EE only affected OL development after hypoxia, but appeared to have no effects in mice maintained under normal physiological conditions. While considerable progress has been made in identifying and modulating the cellular and molecular mechanisms involved in premature brain injury, developing new strategies aimed at decreasing the considerable long-term neurologic sequelae of preterm survivors—including EE—should be an important goal.

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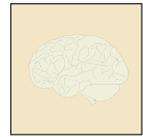
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Parcellation Scheme for a Spatio-Temporal Atlas of Fetal Brain Lobe Development In the Third Trimester

Fetal brain development is a complex and dynamic process. During the third trimester of pregnancy the brain's surface landscape changes from a smooth layer into a complex canopy with convolutions called gyri. The emergence of quantitative magnetic resonance imaging (MRI) has allowed for in vivo acquisition of high-resolution images of the fetal brain. Although a timeline for the emergence of important gyri exists; we currently lack an in vivo MRI model—or atlas—of the developing brain. Therefore, our objective was to develop a scheme to parcelate the third trimester in vivo fetal brain into lobes, and apply this scheme onto scans in healthy fetal MRI brains to create a spatiotemporal atlas.

Based on a previous parcellation scheme of the neonatal brain, and conventional anatomical landmarks for classic brain lobe divisions, we devised a scheme to parcellate the fetal brain between 29-37 weeks into five lobes: frontal, parietal, temporal, occipital, and insular. We used an atlas of T2 weighted MRI images from 80 fetuses without any known pathological conditions.

Fetal atlases at 31, 33, 35, and 37 gestational weeks were parcellated into five lobes. Gestational week 29, the youngest gestational age in our sample, could not be parcellated because the landmarks outlined in our parcelation scheme have not yet appeared in the brain at this gestational age.

Taken together, our results show that available conventional anatomical landmarks for the division of the third trimester brain into classic lobes are only reliably applicable down to gestational weeks 30-31. A parcellation scheme for the fetal brain younger than 30 weeks will require different anatomical parameters from higher resolution MR images. Nevertheless, the fetal brain lobe parcellations presented here can be used in their current form as a tool to identify regional, lobular brain growth disturbances in third trimester high-risk fetal populations.

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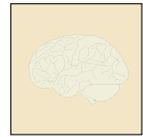
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Investigating the Role of Neuronal Activity During Target Selection by Retinal Ganglion Cells

Retinal Ganglion Cells (RGCs) are an integral part of the visual system, conveying all visual information to the brain. The importance of proper RGC development in humans is exemplified by a class of diseases categorized as optic retinal neuropathies, which are associated with many debilitating disorders. RGCs innervate several targets, including the thalamus, hypothalamus, and superior colliculus (SC). How particular sets of RGCs are guided to innervate selective nuclei remain unclear. In this project we aimed to test the hypothesis that neuronal activity plays a role in target selection by RGCs. Previously, we used a transgenic mouse line in which *Isl2*+ RGCs were marked with GFP (*Isl2*-GFP) to demonstrate that this subset of RGCs initially projects to the suprachiasmatic nucleus (SCN), medial tegmental nucleus (MTN), olivary pretectal nucleus (OPN), dorsal lateral geniculate nucleus (dLGN), and SC. However, by postnatal day 12 (P12) *Isl2*-GFP RGCs terminate only in the dLGN and SC. To determine if neuronal activity mediates refinement of *Isl2*-GFP projections, we injected the GABA agonist muscimol or saline intraocularly daily from P1 - P8 into both eyes. Immunostaining for the immediate early response gene *cFos* showed that muscimol effectively decreased RGC activity for an hour after injection. However the effects of muscimol on neuronal activity were negligible after 24 hours. Based on these data, we conclude that more frequent injections of muscimol are required to test our hypothesis.

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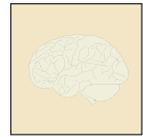
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NEUROSCIENCE



SCHOOL OF MEDICINE & HEALTH SCIENCES

Isolation and generation of oligodendrocytes from the subventricular zone and cortical gray matter of neonatal piglets

OBJECTIVES:

CHD is the most common major birth defect, affecting almost 8 in every 1000 infants born each year. It has been increasingly recognized that many children with severe/complex CHD suffer developmental delay, neurological impairment or behavioral problems. Recent MRI studies have demonstrated a high incidence of WM injury (25-55%) in the neonate and infant with CHD. However, cellular events secondary to CHD-induced hypoxia and the impact of cardiac surgery on these events in developing WM remain largely unexplored. Hence there is currently no perinatal treatment strategy for the brain damage that has been widely observed in MRI studies of patients with CHD. The objective of the study was to purify oligodendrocyte progenitors from neonatal piglets in order to transplant and track the migration, cell fate, and capacity to differentiate and myelinate within the host; the therapeutic application is to replace loss of oligodendrocytes in the white matter of injured brains caused by congenital heart disease.

METHODS:

Female Yorkshire piglets were used in this study. Previous attempts by others to study WM injury using rodent models have been limited by structural differences with the human brain. In the human brain, WM occupies approximately 50% of the total brain volume, while in rodents only 15%. In contrast the piglet brain is a powerful tool to study human brain development as it displays a highly evolved, gyrencephalic neocortex absent in many other mammals. Cortices were dissected from donor piglets at 2 days of age. The SVZ tissue was dissociated using a Papain Dissociate System kit. Mixed cells were plated in flasks. Once OPCs were visible atop an astrocyte monolayer, cultures were shaken. Suspended OPCs were re-plated and allowed to expand and then were incubated with SPIOs and suspended for transplantation.

CONCLUSIONS:

This novel culture system will allow us to better understand the normal course of WM development in a species whose brain is extremely similar to humans. This method allows us to longitudinally track the cells during brain development in living animals with MRI. These cells have the potential to replace lost oligodendrocytes and myelin, while aiding the normal endogenous repair capacity of the brain. This may have a wide array of therapeutic uses in diseases that affect neurological development.

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Highly Precise Quantification of Multiple Human Herpesviruses in Glioblastoma Samples by Droplet Digital PCR

BACKGROUND:

Glioblastoma (WHO grade IV astrocytoma) is a fatal CNS malignancy, representing 80% of primary adult brain tumors, with approximately 12-18 months survival time after initial diagnosis. Recently, the human herpesvirus cytomegalovirus (CMV) has been suggested to have an oncogenic role, yet this association remains controversial. In addition, the human herpesvirus 6 (HHV-6) has also been associated with low-grade gliomas, but few studies have examined HHV-6 in glioblastomas. Droplet digital PCR (ddPCR) is a validated, highly precise viral diagnostics tool that enables the absolute quantification of multiple viral target regions.

OBJECTIVE:

To quantitate CMV, HHV-6A, and HHV-6B viral DNA in glioblastoma tissue by ddPCR technology.

DESIGN/METHOD:

A total of 14 formalin fixed paraffin embedded (FFPE) and 10 optimal cutting temperature compound embedded (OCT) glioblastoma blocks were obtained from the George Washington University Hospital and the National Institutes of Health, respectively. All glioblastoma tissue samples were de-identified and pathologically confirmed. Each tissue block was sectioned for DNA extraction and two regions of the CMV UL55 gene, the U57 gene of both HHV-6A and HHV-6B and a cellular housekeeping gene, were amplified by ddPCR.

RESULTS:

Neither CMV nor HHV-6A were detected in any of the glioblastoma samples, however, HHV-6B was detected in a subset of both the FFPE- (5/14, 36%) and OCT-preserved (3/10, 30%) glioblastoma samples. The HHV6B viral load ranged from 92 to 13,389 copies/10⁶ cells.

CONCLUSION:

The absence of CMV in any of the glioblastoma samples does not support a CMV and glioblastoma association. However, the detection of HHV-6B in these tissues needs to be further investigated in different types of primary brain tumors. To this end, we are expanding the sample cohort, glioblastoma and low-grade glioma, to examine the correlation between pathological or clinical manifestations and HHV-6B viral burden.

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Aggression or mating: regulation of innate behaviors by embryonically defined medial amygdala cell populations

BACKGROUND:

The mammalian medial amygdala (MeA) is part of the limbic system circuitry implicated in the regulation of innate behaviors such as aggression, mating, and predator avoidance. As these innate behaviors are inborn, it seems likely that there are hard-wired embryonic mechanisms that specify the circuitry regulating these behaviors. Understanding these embryonic mechanisms under normal conditions will be the basis needed prior to unraveling disparities that might occur in disorders with a strong amygdala component, such as autism.

OBJECTIVE:

To define two distinct MeA cell populations by their differential expression of two embryonic transcription factors: Dbx1 and Foxp2 -the latter being encoded by an autism susceptibility gene-. Differentiate these populations by their molecular, electrophysiological and behavioral properties.

METHODS:

We used a Dbx1-Cre mouse model crossed with a YFP reporter to visualize Dbx1-derived cells in the adult MeA. We performed immunohistochemistry analysis for several cellular markers to look at the molecular profile of both the Dbx1-derived and Foxp2+ cell populations. In addition, we used c-fos, an immediate early gene that serves as a marker for neuronal activity, to observe changes in neuronal activation during innate behaviors, which included predator avoidance, mating, and aggression. Finally, we used patch clamp recordings to distinguish the electrophysiological profile of both cell populations.

RESULTS:

We found that this two progenitor populations migrate to generate two distinct output neuronal populations of the MeA as shown by their differential expression of molecular markers and intrinsic electrophysiological properties. Furthermore, we observed that Dbx1-derived and Foxp2+ cells in the adult MeA are activated by distinct innate behaviors.

CONCLUSIONS:

Hence, parcellation of MeA progenitor pools by embryonic transcription factor expression, predicts differences in electrophysiological, molecular and behavioral properties. Furthermore, as Foxp2 is a validated autism susceptibility gene, this work will help to better elucidate the amygdala neuronal specific pathologies associated with autism.

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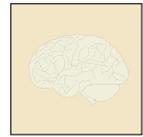
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COLUMBIAN COLLEGE OF ARTS & SCIENCES

Resistance to a model of Parkinson's Disease in Learning Mutants of *Drosophila Melanogaster*

Approximately one million people throughout the world are diagnosed with Parkinson's disease. One suspected mechanism for modeling Parkinson's concerns the Proteasome System, a protease involved in protein degradation. If the proteasome does not function properly, malformed proteins tagged for degradation build up and cause protein aggregation, leading to cell death in the nervous system. In the lab, we wanted to support previous research that the inhibition of the proteasome in *Drosophila Melanogaster* by the protein MG-132 models Parkinson's. We hypothesized that unlike normal *Drosophila*, the learning mutants *Dunce* and *Rutabaga* *Drosophila* are more resistant to neurodegeneration because of their impaired synaptic strengthening and resistance to excitotoxicity. To measure neurodegeneration, we tested the locomotion of *Drosophila* in plastic vials using a negative geotaxis assay. The vials were divided into three heights: <2 cm, > 2cm, and >6 cm. Thirty minutes after leaving the incubator, the number of *Drosophila* in each region was counted. Cell viability was measured using an MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) absorbance assay. Mortality was measured daily, and a Kaplan Meier statistical analysis was done. The results showed that the normal *Drosophila* were not resistant to neurodegeneration, and had a strong mortality rate over the course of eight days. The negative geotaxis assay results showed an impaired locomotive ability in treated normal *Drosophila*. In both tests the learning mutants resisted the effects of MG-132. The MTT absorbance assay values were not significant. It was concluded that MG-132 models Parkinson's in *Drosophila*, and that the learning mutants are resistant to neurodegeneration.

STATUS

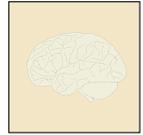
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Micro-RNA profile of myasthenia gravis thymus indicates anti-apoptotic mechanisms support maintenance of autoimmunity

OBJECTIVE:

To assess the miRNA profile of thymus of patients with myasthenia gravis (MG).

BACKGROUND:

A characteristic pathology of patients with MG is thymic hyperplasia with ectopic germinal centers (GC) that are absent in normal individuals. However, mechanisms that trigger and maintain thymic hyperplasia are poorly characterized. Micro-RNAs (miRNA) are small, non-coding RNAs that regulate gene expression and are increasingly appreciated to be involved in the pathology of several autoimmune diseases.

METHODS:

We utilized 20 samples from thymic specimens collected during the course of the NIH-supported study of thymectomy (MGTX, U01 NS4268). Cryopreserved specimens were used for sectioning and histological analysis to grade the degree of thymic hyperplasia. The samples were graded as 0 when no obvious GC was located and 1 through 4 depending on the number of GCs identified. The immediately adjacent specimen was used to extract total RNA using mirVana miRNA isolation kit (Ambion, Life Technologies). The RNA was labeled and hybridized on to GeneChip® miRNA 4.0 Array and analyzed by Expression Console and Transcript Analysis Console 2.0 (Affymetrix). Two independent programs, Partek Genomic Suite 6.6 and Transcript Analysis Console 2.0 were applied to identify miRNAs that were differentially expressed in grade 0 versus grades 1 to 4. ANOVA p-value <0.05 and FDR<0.05 was determined as significant. The miRNAs that showed greater than 1.5 fold difference as recognized by both the programs were selected for further validation by qRT-PCR. Ingenuity Pathway Analysis (IPA) Target filter (QIAGEN) was used to identify the putative targets and IPA Core Analysis was used to identify pathways involved.

RESULTS:

Total of 53 non-coding RNAs showed greater than 1.5 fold differences between grade 0 and grades 1 to 4. Out of which, 31 were upregulated and 22 were downregulated. Cluster analysis demonstrated separation of samples by grade. Thirty-four mature miRNA were identified. qRT-PCR of 19 miRNA transcripts were consistent with the array analysis. IPA identified cancer and apoptosis pathways as targets of the miRNAs identified. MiR-150-5p was elevated in grade 1-4, consistent with another report which demonstrated its increase in sera of MG patients.

CONCLUSIONS:

The miRNA profile of thymus from patients with MG indicates that maintenance of autoimmunity is supported by regulatory pathways known to be involved in neoplasia.

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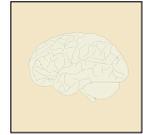
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COLUMBIAN COLLEGE OF ARTS AND SCIENCES

Periconception Iron Supplementation and Prevention of Neural Tube Defects

Neural tube defects (NTDs) are among the most common congenital defects observed in humans, affecting 1 in 1000 live births. Periconception folic acid supplementation can prevent many but not all NTDs. Data from the Zohn laboratory suggests that iron supplementation may prevent additional NTDs. In this project, the ability of iron supplementation to prevent NTDs and interaction with folic acid will be determined in various mouse models. The *Fpn1^{ffe}* line, which carries a hypomorphic mutation in *Fpn1*, an iron transporter required for iron delivery from mother to embryo, will be used for these studies. *Fpn1^{ffe}* mutants show NTDs along with telencephalon truncations. To study the ability of combined iron and folic acid supplementation to prevent NTDs in this mouse strain, female *Fpn1^{ffe}* mice were placed on one of four diets at weaning: (1) normal folic acid, normal iron, (2) high folic acid, normal iron, (3) normal folic acid, high iron, or (4) high folic acid, high iron. After three weeks on the diet, matings were established, litters dissected and NTDs scored by visual inspection. Maternal blood and embryos were collected for determination of folate and iron levels. Effect of supplementation on telencephalon defects will be determined by in situ hybridization and morphometric measurements. Supplementation with the high iron and high iron/high folic acid diet decreased NTD penetrance by 50% in *Fpn1^{ffe}* mutants. In contrast, folic acid supplementation did not prevent NTDs. Interestingly, iron supplementation resulted in lower maternal folate levels, suggesting some competition between absorption of these two nutrients. Analysis of ferritin levels in maternal serum demonstrated that iron supplementation increased iron status of mothers but folate supplementation had no effect on iron absorption. Future experiments will determine embryonic folate and iron levels and if iron supplementation rescues telencephalic defects. In addition, the ability of combined iron and folate supplementation to prevent NTDs in additional mouse lines (*Lrp2* and *Noggin*) with similar neural tube and telencephalic defects will be investigated.

STATUS

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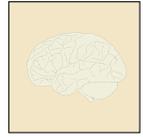
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SCHOOL OF MEDICINE & HEALTH SCIENCES

Identifying the effect of expression of FoxD4 in mouse embryos to implicate FoxD4 in acquisition of neural stem cell identity

A growing body of literature suggests the presence of stem-like cells in diffusely infiltrative astrocytic tumors resistant to treatment. Resistance to treatment of these stem-like cells may contribute to subsequent tumor progression and recurrence. While past research has focused primarily on isolating these neuronal precursor cells, I have focused on identifying molecular mechanisms that may define progenitors of neural stem cell lineages. The forkhead transcription factor FoxD4 has emerged as a candidate for mediating the initial transition to neural stem cells. FoxD4 expression triggers the expression of multiple cell markers such as Nanog, Oct4, and Sox2, which are characteristic of neuronal precursor cells. The expression of FoxD4 is thought to occur transiently in mice embryos at the E9.5 stage when neuro-ectodermal transition begins. Therefore, it is likely that the expression of FoxD4 is detectable in cell populations that have taken the first step towards becoming neural, such as those in the olfactory epithelium of mice at age E9.5. With this in mind, E9.5 mouse embryos, as well as neural differentiating embryoid bodies were immunostained for FoxD4 to confirm FoxD4 expression at the nucleus. FoxD4 was localized to the nucleus and perinuclear area of embryoid bodies, confirming its expression as a nuclear transcription factor. We have found that diminished expression of FoxD4 prevents, and over-expression of FoxD4 promotes neural stem cell identity and neuronal differentiation in embryonic stem cell (ESC) cultures in neural differentiation conditions. To understand the effect of FoxD4 activity on the differentiation of ectodermal stem cells into neurons in vivo, the ectodermal rudiment that gives rise to the olfactory neuroepithelium of the nose was transfected via electroporation in E9.5 mouse embryos to express a FoxD4 siRNA “knockdown” variant, an overexpression variant, or a control variant. A larger proportion of the cells overexpressing FoxD4 progressed to neuronal differentiation than either the knockdown or control variant. Apparently, FoxD4 influences ectodermal stem cell progression to neurogenic stem cells, as is the case for ESCs. Future studies may work to further understand the effect of the loss and gain of function of FoxD4 in cells that are confirmed to express FoxD4 at critical points in their neural differentiation.

STATUS

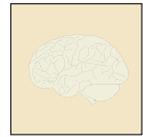
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SCHOOL OF MEDICINE & HEALTH SCIENCES

A Review of Patient Safety and Unique Considerations in the Epilepsy Monitoring Unit

Epilepsy, a chronic seizure disorder is a commonly recognized neurologic condition affecting an estimated 2.5 million Americans. Contrary to its prevalence, epilepsy has often been poorly understood, misdiagnosed, and improperly treated. Patients with a history of seizures that are refractory to pharmacotherapy are admitted to the epilepsy monitoring unit (EMU) for continuous video and electroencephalogram (EEG) monitoring in order to better characterize their seizure disorder or to localize a seizure focus for management of their epilepsy. The inpatient video-EEG is highly dependent on the recording of seizures and as a result, it has become standard practice to induce these symptoms (seizures) during an admission to an EMU using activation modalities such as reduction of antiepileptic medications, sleep deprivation, hyperventilation, and photic stimulation. These unique aspects of an EMU drive the importance of patient safety and in improving quality of care in order to avoid potential harms. Research and data involving patient safety, safety outcomes, and the development of quality indicators in EMUs are sparse; thus, there is a need to identify safety considerations in EMUs in order to develop standardized patient safety protocols to improve the utility of EMUs. This review aims to consolidate and examine safety outcomes and proposed safety considerations unique to epilepsy monitoring units. Literature search was performed through PubMed and MEDLINE databases, limited to the past twenty years. Further searches utilized MeSH databases using keywords: epilepsy monitoring unit, EMU, safety outcomes, patient safety, epilepsy, seizures. Manual reviews of articles collected were made, examining unique safety outcomes measured in those articles with regards to future safety considerations. Upon review of the literature, common quality indicators that were identified and used to determine safety outcomes in the EMU included the incidence of status epilepticus, seizure-related falls and injuries, postictal complications, medication related events, psychiatric complications, cardiac events and/or respiratory complications. Recurrent recommendations for future considerations concerning patient safety in EMUs included standardization of logistical procedures, adequate team support and leadership with focus on patient safety, mechanisms to process and identify adverse events, and providing indicators for measuring safety outcomes consistently. A standardized patient safety protocol for EMUs has yet to be developed. As a result, varying standards of care and practice guidelines exist between institutions. This brief review demonstrates the deficiency in research concerning validated safety indicators and safety outcomes data for improving the quality of care in EMUs. Several common quality indicators and mentioned recommendations for patient safety are highlighted with hopes that future research and data concerning EMUs will allow for the development of a universally recognized safety protocol, and ultimately improved patient care.

STATUS

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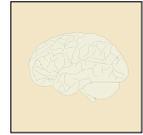
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SCHOOL OF MEDICINE & HEALTH SCIENCES

GR gene polymorphisms are associated with inter-subject variability in response to glucocorticoid used in patients with MG

INTRODUCTION:

Glucocorticoids (GCs) are currently the mainstay of the immune-directed treatment for patients with myasthenia gravis (MG). However, the response to GCs for MG patients is characterized by wide interindividual variability. We analyzed whether single nucleotide polymorphisms (SNPs) in glucocorticoid receptor (GR) gene are associated with inter-subject variability in response to GCs used in MG patients.

METHODS:

A cohort of 257 MG patients treated with GCs were evaluated for correlation between SNPs and the clinical response to GCs therapy.

RESULTS:

After 3 months of GCs therapy, the change of quantitative MG score (QMGS) ranged from -2 to 18 (mean 5.64 ± 3.72). We grouped the MG patients by response to GCs. Improvement to or more than 3 units of QMGS change or QMGS after treatment becoming zero was judged as being sensitive to GCs. The rs9324921*A allele was significantly more frequent in GCs insensitive group when compared to GCs sensitive group (24.13% vs 38.10%, $p = 0.046$, OR = 1.94, 95% CI = 1.00-3.74). The rs17209237*G allele was found to be less frequent in GCs insensitive MG patients than GCs sensitive subjects (2% vs 17%, $p = 0.013$, OR = 0.119, 95% CI = 0.016-0.877). The rs9324921 A/C + A/A genotypes were significantly more frequent in GCs insensitive group when compared to GCs sensitive group (66.7% versus 43%), indicating association with GCs insensitivity (dominant model: $p = 0.037$, Log-additive model: $p = 0.048$). The rs17209237 G/A + G/G genotype were significantly less frequent in GCs insensitive group when compared to GCs sensitive group (4.8% versus 31.9%), indicating association with GCs sensitivity (dominant model: $p = 0.009$, Log-additive model: $p = 0.013$). We found that there was association of GCs insensitivity with beginning of GCs usage after 6 months duration ($p = 0.027$, OR = 2.72, 95% CI 1.12-6.58). No associations were found between GCs insensitivity with age of onset, gender, absence or presence of thymoma, AChR antibody, involved muscles at disease onset or clinical type during follow-up ($p = 0.819, 0.780, 0.417, 0.686, 0.584$ and 0.245 , respectively). Results from multivariate logistic regression analysis showed that rs9324921 polymorphism was significantly associated with the response to GCs in the MG subgroup with disease duration more than 6 months before GCs treatment ($p = 0.032$), however, rs17208237 polymorphism was significantly associated with the response to GCs in the MG subgroup with disease duration within 6 months before GCs treatment ($p = 0.011$). According to Haploview, the significant association findings are restricted to the block (rs17339455, rs4912905, rs9324921 and rs41423247). One risk haplotype (TGAG) were identified (OR = 1.95, 95% CI = 1.01-3.78, $p = 0.043$) in GCs insensitive MG group compared with GCs sensitive MG group (38.1% versus 23.9%). The risk haplotype TGAG contained the risk allele (rs9324921*A). Finally, we established the correlation of QMGS changes in MG patients who were treated using GCs and different genotypes carried by them. The mean change in QMGS during 3 months of GCs treatment was significantly higher in MG patients carrying the rs17209237 AG or GG genotypes (6.44 ± 3.74) compared with subjects with rs17209237 AA genotype (5.30 ± 3.69 , $p = 0.027$).

DISCUSSION:

A SNP in the 3' near gene (rs17209237) was associated with sensitive GCs treatment and a intronic SNP (rs9324921) was associated with insensitive GCs treatment. Rs17209237 polymorphism may influence the response to GCs in MG patients.

KEY WORDS:

myasthenia gravis; glucocorticoid receptor; single nucleotide polymorphisms; efficacy of therapy; gene

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Associations of Liver Biopsy Glycogenated Nuclei with Diabetes Mellitus (DM) and Steatosis in Morbid Obesity (MO)

Hepatocyte Glycogenated Nuclei (GN) are glycogen-filled nuclei occurring most commonly in association with clinical DM and Non-Alcoholic Fatty Liver Disease (NAFLD). This study explores associations of GN with steatosis, clinical DM, and Non-Alcoholic Steatohepatitis (NASH) in patients with MO.

METHODS:

Wedge liver biopsies from 143 patients with MO were studied (mean age 38.7 years, 131 Female) to determine mean GN per HPF (average of 10 HPFs) and to correlate GN with steatosis (fat graded 0-3), presence of NASH and clinical DM.

RESULTS:

Clinical DM was present in 28 (19.5%), steatosis was present in 78 biopsies (54.5%), NAFLD in 82 (57.3%) and NASH in 26 (18.8%). GN were significantly associated with grade 3 steatosis, ($p=.001$) and with DM, mean GN per HPF was $6.49 \pm SE 1.04$ vs non-DM, mean $3.28 \pm SE 0.49$, $p=.02$. AUROC curve analysis showed GN number to be a relatively good indicator of clinical DM (area, 0.728) and steatosis (area, 0.737). GN were not significantly associated with NASH ($p=.159$).

DISCUSSION/CONCLUSIONS:

GN in liver biopsies from patients with MO were significantly associated with steatosis and clinical DM. but the association with DM had a relatively low Likelihood ratio of 2.6 (PPV 38%, Sensitivity 60%, Specificity 77%). The specificity of biopsy GN for DM was improved at mean $^3 8$ GN per HPF (Specificity 90%), but Sensitivity (30%), PPV (44%) and Likelihood ratio of 3.0 were not much improved. The predictive value of biopsy GN in MO is not as strong as that reported in a non-MO population, suggesting that increased steatosis and NAFLD in MO may weaken the predictive value of GN for DM. The pathogenesis of hepatic GN is not known, but the findings of this study support the idea that GN result from dysregulation of glucose and lipid metabolism.

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Does obesity affect kidney transplant outcomes? A single center retrospective analysis

BACKGROUND:

The number of overweight and obese patients undergoing kidney transplantation has increased dramatically over the past two decades, reflecting an increase in the obese US population. Obesity is associated with factors that increase post-transplant complications and may reduce kidney graft survival.

OBJECTIVES:

The purpose of this study was to examine the effect of obesity on transplant outcomes, including hospital readmissions, length of stay, and post-transplant infections.

METHODS:

Retrospective chart review was conducted using data from a single kidney transplant center. The specific outcomes that were reviewed included: early readmissions, infection rate and length of stay along with BMI of each kidney transplant patient. The subjects were patients transplanted during the time period of January 1, 2010 thru June 1, 2013, limited to kidney transplant only. The sample was divided into four cohorts: Body Mass Index (BMI) under 24.9 kg/m², 25-29.9 kg/m², 30-34.9 kg/m² and over 45 kg/m². The data analysis was performed using Microsoft Excel and SPSS software. The data analysis focused on the relationship that BMI has on length of stay, readmission to the hospital within 30 days of discharge and infection rate. Body Mass Index (BMI) was subdivided into four categories and coded in a single numerical value.

RESULTS:

The sample size was 110 subjects, the mean age of the subjects was 50.6 years and the mean BMI was 27.78. The results are showed that the BMI category with the longest length of stay was the BMI 25-29.9kg/m², which represents the overweight group. There was not a statistically significance between groups for readmission as determined by one-way ANOVA (F_{3,106})=0.760, p=0.550). A LSD post-hoc test revealed no statistically significant difference between the groups. There was not a statistically significant difference between groups as determined by one-way ANOVA (F_{3,106})=2.118, p=.102). A LSD post-hoc test revealed that the infection rate between BMI group 1 (<24.9 kg/m²) was statistically significant (p=0.021) with respect to BMI group 4 (<35kg/m²), however there was no statistical difference among the other two groups: group 2 (p=0.621) and group 3(p=0.463).

CONCLUSIONS:

In this single center retrospective study, it was revealed that obesity did not impact length of stay or readmissions for patients with kidney transplantation.

KEYWORDS:

kidney transplant, BMI, readmission, kidney transplant outcomes

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Obesity Derived Adipocyte Exosomes Alter TGF β Signaling and EMT Gene Expression in Lung Epithelium

RATIONALE:

Childhood asthma and obesity are growing epidemics that appear connected as obesity is associated with increased asthma severity and poor response to therapy. Obesity has been described as a systemic disorder with marked increase in circulating TGF β . Aberrant signaling of this cytokine is central to asthma pathobiology and repair processes. We have previously shown that obese (vs. lean) visceral adipocytes shed exosomes containing miRNA that augment TGF β /WNT signaling. In this study, we investigate the impact of obese vs. lean visceral adipocyte exosomes on TGF β -stimulated (increased systemically in obesity) A549 lung epithelial cells. We hypothesize that obese visceral adipocyte exosomes alter expression of TGF β signaling pathway genes in lung epithelium.

METHODS:

Previously characterized adipocyte exosome donors (n=3 obese, n=3 lean subjects) were used for this study. Immunofluorescence analysis for cellular uptake was performed by co-incubating PKH26-labeled exosomes [(2.0 ug/mL)] and A549 lung epithelial cells for 24 hours. Gene expression studies were performed after growing cells to 70-80% confluence and stimulating with TGF β [5ng/ml] or vehicle control for 48 hours. Cells were then co-cultured with obese or lean exosomes [2.8ug/ml] for the last 24 hrs. Cell lysates were evaluated for global mRNA expression using Illumina BeadChip microarrays. Stimulated obese vs. lean exosome exposed mRNA expression was analyzed using a paired, 2-tail t-test ($p < 0.05$, fold change ≥ 1.2). Bioinformatic analysis was performed using Ingenuity Pathways AnalysisTM and Partek. MiRTarVis, a visual analytics tool for integrated analysis of miRNA and mRNA expression profiles with miRNA target prediction algorithms, was used to analyze exosomal miRNA-lung epithelial mRNA interactions.

RESULTS:

Immunofluorescence analysis demonstrated PKH26-labeled exosomal uptake into A549 cells at 24 hours. Of the 55 miRNAs previously identified as differentially expressed in obese vs. lean adipocyte exosomes, 18 miRNAs targeted 1,157 gene transcripts that were differentially expressed in obese vs. lean exosome co-cultured A549 cells after TGF β exposure. Two of the top significant canonical pathways included TGF β signaling ($p = 2.01 \times 10^{-4}$) and regulation of Epithelial Mesenchymal Transition (EMT) signaling ($p = 0.017$). Four genes were identified in both TGF β signaling and EMT regulation pathways: MAP2K1, MAP2K6, and KRAS are known targets of miR-374b, and SMURF1, a known target of miR-10b.

CONCLUSION:

Our data suggest obese visceral adipocyte exosomal miRNA contribute to abnormal regulation of TGF β signaling and EMT in lung epithelial cells. Applying these methods to asthma will help elucidate one possible mechanism by which obesity promotes abnormal TGF β mediated regulation of epithelial-mesenchymal transition in asthmatic lung epithelium through adipocyte-derived exosomes.

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Type 2 diabetes associated beta-adrenergic receptor polymorphisms are independently associated with BMI and physical activity in college-age populations

Of the many genes associated with insulin resistance (IR), three belong to the adrenergic-receptor β family (ADRB): ADR β 1, ADR β 2, and ADR β 3. Each of these genes presents with single nucleotide polymorphisms (SNPs) that have been associated with IR, obesity, and/or T2D. ADR β 1 rs1801252 (S49G) and rs1801253 (R389G); ADR β 2 rs1042711 (5' UTR), rs1042713 (G16R), and rs1042714 (Q27E); and ADR β 3 rs4994 (W64R). The goal of our study is to determine if these SNPs are associated with other known T2D risk factors in a healthy, college-age population.

These SNPs were investigated in two cohorts of healthy, college-aged subjects: the Assessing Inherited Markers of Metabolic Syndrome in the Young cohort (AIMMY) with 566 subjects, and the Muscle and Bone cohort (MB) with 116 subjects. Anthropometric measures, body fat percentage, and physical activity questionnaires were collected. Weekly energy expenditure was calculated based upon the estimated metabolic equivalents (METs) attributed to specific activities. Genotyping was performed using DNA isolated from blood samples. Each SNP was evaluated for association with phenotypes using ANCOVA models testing for differences in mean outcomes between genotypes with age as a covariate. Phenotypes tested included BMI, percent body fat, and physical activity (MET minutes/week).

Four significant associations were identified. African American women in the AIMMY cohort homozygous for the serine variant of rs1801252 (AA), Caucasian men in the AIMMY cohort homozygous for the glutamine variant of rs1042714 (CC), and Caucasian men in the MB cohort homozygous for the T allele variant of rs1042711 (TT) reported higher levels of physical activity. Caucasian women in the AIMMY cohort possessing the G allele of rs4994 (AG/GG) were more likely to have a higher BMI.

In conclusion, our study found that not only are some T2D associated polymorphisms associated with BMI and physical activity in certain demographics, but also that they are present in young, healthy populations.

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Review of Current Physician Attitudes and Practices in Obesity Counseling and Potential Resources Relevant to the Primary Care Setting

OBJECTIVE:

To examine current attitudes and practices of primary care practitioners in obesity diagnosis, evaluation, and counseling, so as to identify resources and tools to improve these interactions.

METHODS:

Findings were obtained through a search of PubMed, Scopus, and Google Scholar for adult studies. Search terms included: obesity treatment in primary care, obesity diagnosis, barriers to obesity treatment, obesity bias in primary care, obesity discussion tools, motivational interviewing techniques, and physician training in obesity. We also reviewed relevant white papers for additional studies and resources.

RESULTS:

Our review led to three major conclusions regarding obesity treatment in primary care. First, most providers do not diagnose overweight or obesity in their patients, and even when they do, the resulting conversations are not sufficiently instructive thereby limiting the ability to engage patients in weight control efforts. Second, physicians who are motivated to discuss weight with their patients currently often lack the necessary language and expertise to treat patients with overweight and obesity. Improvised and uninformed discussions could further stigmatize or shame patients, leading to poor obesity treatment and even adverse patient outcomes. Finally, some tools and resources exist to provide assistance to primary care physicians treating obesity.

CONCLUSION:

Guidelines, professional societies, payers, and policy makers all recommend that primary care physicians address obesity management as a path to health improvement. Physicians are ill-equipped to meet this challenge. Future endeavors to provide successful obesity treatment should seek to educate patients through informed conversations, remove barriers to obesity treatment, and provide more effective physician-patient communication.

KEYWORDS:

obesity, obesity counseling, obesity treatment, primary care, weight bias, obesity diagnosis, barriers to obesity treatment, physician training in obesity, motivational interviewing techniques, obesity discussion tools

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Sucralose Promotes Fat Accumulation in Human Adipose Tissue Derived Mesenchymal Stem Cells

BACKGROUND:

Artificial sweeteners are extensively used as alternatives for caloric sugars. Given their sweet taste profile and lack of calories, diet sodas and other foods and beverages containing artificial sweeteners are often promoted as replacements for high sugar items for weight loss and/or maintenance. However, recent studies demonstrate that saccharin and acesulfame potassium may actually increase adipogenesis¹. Here we aimed to determine whether sucralose also promotes adipogenesis in human mesenchymal stem cells (MSCs). MSCs are multipotent cells which differentiate to adipocytes, myoblasts, osteoblasts or chondroblasts.

METHODS:

We cultured MSCs in Normal Glucose DMEM medium (5.5mM glucose) or in adipogenic medium (Lonza Inc., 5.5mM) with or without sucralose (0, 0.45mM or 4.5mM) for 6 days. At the end of day 6, cells were stained with Oil Red O stain (lipogenesis). Cells were lysed post staining and absorbance of the assimilated dye was measured using a plate reader (520 nm). Non-stained cells from each medium and each sucralose concentration were also lysed as control and RNA was collected for RT-PCR to measure oxidation, inflammation and adipogenesis related gene expression. Results: Before lysing the cells for absorbance readings, cells were observed under the microscope for phase contrast image. With increasing sucralose concentrations, more fat droplets were observed within cultured MSCs. Moreover, absorbance measurements showed that adipogenesis increased by 1.8 fold with increasing sucralose concentration (0 to 0.45mM) and further increased by 2.85 fold with increasing sucralose concentration in cells cultured in both Normal Glucose and Adipogenic Media.

We also conducted a 12 day experiment, where MSCs were cultured in Adipogenic Media for 12 days. In this experiment cytotoxic effects of Sucralose were noted, at 4.5 mM concentration along with increased intracellular fat droplet accumulation noted by microscopy. RT-PCR showed gene expression increases with increasing sucralose concentration from 0 to 0.45mM concentration, PPARG (2.28 fold), C/EBPb (1.14), C/EBPa (1.42), ADIPOQ (2.16) and Leptin (1.55 fold) We also noted increased Superoxide Dismutase (SOD) 1 and 2 gene expression by 1.59 folds and 1.39 folds respectively with increase in TNF alpha expression (1.36 folds).

In summary, sucralose appears to promote fat accumulation by Oil Red O stain quantification. It also appears to upregulate adipogenesis gene expression and also expression of inflammatory genes (TNF α) and anti-oxidant genes (SODs). Increase in SOD expression is possibly a cellular adaptive response to increased intracellular super-oxide. Conclusion: Our studies indicate that sucralose may promote intracellular fat accumulation with upregulation of key adipogenesis and inflammatory genes. This finding has public health implications and warrants further cellular and animal model studies.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Serial Users Do Not Explain Emergency Department Surge in Psychiatric Complaints

BACKGROUND:

In three years, we have observed a 300% surge in psychiatric visits at a single-center ED, an urban tertiary care center with approximately 75,000 annual visits. Many of our patients are high utilizers who have been treated multiple times for psychiatric complaints. The surge in psychiatric complaints was believed to be due to repeat visits by patients with psychiatric complaints.

OBJECTIVE:

To determine if the surge in psychiatric complaints could be explained by an increase in new complaints or repeat utilization.

METHODS:

We examined demographic and administrative data for all patients with psychiatric complaints a single tertiary-care academic Emergency Department. Patients were identified by existence of Behavioral Health documentation which is completed on all patients that receive a psychiatric evaluation in the ED. Records were reviewed for three years (1/2011-10/2014.) All statistical analyses were performed in the R environment. To compare trends in visits by patients who were treated once versus those who were treated multiple times, we performed a regression analysis with an F-statistic to determine significance.

RESULTS:

There was a 300% increase in all ED visits for psychiatric complaints from 2011 to 2014. A similar increase was observed in patients who presented for initial complaint. The overall increase in visits was statistically different from the increase accounted for by repeat patients ($P = 4.5 \times 10^{-13}$), suggesting that the increased number of repeat patients did not account for the majority of the overall increase. However, the increase in one-time patients did not fully account for the overall increase in visits ($P = 1.3 \times 10^{-12}$), suggesting that multiple factors likely underlie the increase.

CONCLUSION:

An increase in new patients with psychiatric complaints has contributed significantly to the psychiatric surge. Serial users could not explain the surge in psychiatric complaints. Future efforts need to address why psychiatric visits are increasing in addition to providing continuity of care for people who have already been identified.

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On the varying models of depression among people of different cultures.

While clinical depression is recognized as a widespread disease and a leading cause of disability worldwide, there has been little exploration into understanding the interplay between the medical diagnosis of depression within its wider cultural context. It is hoped that a better understanding of depression within its cultural context can illuminate the relationship between depression the disease and the depressed person. To that effect, it is first necessary to collect the current literature that attempts to define the relationship between depression and culture. Therefore, a survey of the current literature on the various modalities of understanding depression within its broader context was performed in PubMed, Medline, and Science Direct, with a focus on a cultural interpretation of depression. The parameters were from 1950-2014 in the English language. Three major groups of thought emerged from the literature. The oldest focus explores the relationship between depression and psychosomatic pain, where one is more likely to encounter depression as a physical complaint than a mental one. The second focus looks at the influence of stigma on the cultural perception of depression. This explains that the stigma, both external - from the surrounding culture - and internal, from the patient himself, have a negative impact on both patient willingness to seek medical care for depression as well as self perception. The most recent focus is the "explanatory model," which takes into account both cultural and scientific understanding. Split into two broad categories, there is the "situational model," where psychological distress is considered in the context of social and interpersonal situations. The above two interpretations can be grouped within this larger context. The latter category is the "biopsychiatric" model, which focuses on anatomy, hereditary, and disease process. It is hoped that with a better understanding of the broader cultural context in which depression resides healthcare providers will not potentially miss a diagnosis of depression due to it being portrayed psychosomatically, while patients would have a better understanding of the medical biopsychiatric model, and perceive less of an attached stigma. Ultimately, this will enable healthcare providers to be better able to provide for the many ethnic and immigrant populations that are currently underrepresented and undertreated for depression.

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Depression and Chronic Health Conditions among Hispanics and non-Hispanic Whites, United States BRFSS 2011

INTRODUCTION:

Depression is a prevalent, common and costly disorder often comorbid with many chronic health conditions. Hispanics are the fastest growing minority and the prevalence and association between those conditions varies among ethnic groups with equivocal prior data.

OBJECTIVES:

To explore current depression trends and treatment in Hispanics and assess the relationship between depression and chronic health conditions and related factors.

METHODS:

The study utilized an epidemiological design for a secondary data analyses of the data from the 2011 Behavioral Risk Factor Surveillance System (BRFSS) survey collected by the CDC. The sample comprised of Hispanic and non-Hispanic White adult respondents (N=14,384). Major variables included current depression symptoms measured by PHQ-8, lifetime depression diagnosis, chronic health conditions, current treatment and socio-demographic variables. Data analysis was performed with SPSS.

RESULTS:

Hispanics reported higher current depressive symptoms than non-Hispanic Whites, 13.3% vs. 9.8%, $p < 0.001$, while lifetime depression was equally highly prevalent at 21.2%. Logistic regression models indicated that in Hispanics arthritis (OR = 2.97, 95%CI = 2.24, 3.93), stroke (OR = 2.58, 95%CI = 1.44, 4.62) and COPD (OR = 2.31, 95%CI = 1.54, 3.47) were highly predictive of current depression symptoms. After controlling for socio-demographic variables angina and cancer were not significantly associated with current depressive symptoms.

CONCLUSION:

The prevalence of current depressive symptoms and the sequence of chronic health conditions as predictors differed between Hispanics and comparison group. This study underscores the need to design culturally sensitive collaborative depression and chronic disease management interventions tailored to meet the Hispanic population needs.

KEYWORDS:

Hispanics, depression, chronic health conditions, BRFSS

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Mindfulness Based Stress Reduction: Reasons for Participating

Mindfulness-based stress reduction is a course of 8 weeks that involves incorporating modalities such as yoga and mindfulness meditation in order to help the program participant to focus on awareness. Some studies suggest that MBSR may be beneficial for patients experiencing symptoms such as stress and chronic psychological symptoms. In addition, there have been indications that MBSR may help with adjusting coping mechanisms.

In light of the research that shows the effectiveness of MBSR, the aims of the current research project is to identify the groups that underutilize the program but have potential to benefit from it. The purpose is to understand who utilizes the MBSR program and for what reasons, as reasons for joining a class may expand beyond the scope of the classic symptoms of depression and anxiety. In addition, the results from the study may help health care providers target particular audiences for MBSR interventions. To address these questions, researchers distributed surveys to participants prior to enrollment.

The current study focused on two separate cohorts, based on the time of enrollment. Prior to enrollment, the participants were asked to self-report age, weight, height, reasons for wanting to learn MBSR, and current symptoms experienced, amongst other lifestyle-based questions. Analysis of the 52 participants from the first cohort showed that 40% of the participants were within the 31-40 age group. A majority of our participants were within the normal Body Mass Index range of 18.5-24.9. An analysis of the self-reported symptoms experienced by participants prior to the study showed that a majority of participants experienced symptoms of anxiety. Many patients also reported depressive symptoms, cognitive symptoms, sleep-related symptoms, as well as issues in interpersonal relationships. The second cohort consisted of 23 participants; 40% of the participants were within the 31-40 age group. The majority of the second cohort also was within the BMI range of 18.5-24.9. Analysis of self-reported symptoms experienced by the participants showed anxiety, depression, and musculoskeletal symptoms as most frequent.

The study suggests that prior to enrollment in a MBSR course, participants often times experience a significant amount of symptoms that impact quality of life, and that reasons for participating in a course may not be limited to only depression or anxiety. Future studies should examine whether there is symptom reduction in any of these other domains.

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Characterization of Greater Washington's Emerging Adult Jewish Community: The Role of Stress, Connectedness on Stress Outcomes

BACKGROUND:

Young adults face a numerous stressors that may contribute to psychological distress, anxiety, and depression. The Transactional Model of Stress Appraisal suggests that individuals seek social support as coping resources to reduce negative psychological impacts of stressors. This study examines the role of connectedness to the Jewish community as a buffer of stressful life events and daily hassles on perceived stress, symptoms of anxiety and depression among Jewish young adults aged 18-35 in the Washington, DC metropolitan area.

METHODS:

In July 2014, a convenience sample of n=221 young adults in the Washington, DC area responded to an online questionnaire (response rate =54%). The questionnaire included the Perceived Stress Scale and the Hopkins Symptoms Checklists for Anxiety and Depression, as well as adaptations of the Social Readjustment Scale and the Recent Life Experiences Survey. It also included a newly created scale to measure "Connectedness to the Jewish community." That scale and each of its five subscales (formal affiliation, network composition, strength of identification, informal engagement, and levels of ritual and personal observance) were found to be internally consistent. Logistic regression was used to examine relationships between stressors, psychological outcomes, and Connectedness.

RESULTS:

Stressor types were consistent with literature on emerging adults. Hassles were significant predictors of all stress outcomes and Life events were significant in predicting anxiety and depression symptoms. Connectedness was statistically significant in determining perceived stress and depression symptoms and in buffering the relationship between Life events and depression.

CONCLUSION:

Organizations serving this population should increase connectedness, as higher connectedness is associated with lower levels of stressful outcomes.

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Assessing for barriers to accessing clinical appointments

Patient non-compliance with doctor appointments is a major barrier to quality health care. Providers have tried to tackle this problem, however, there have been few studies to investigate the causes. To address this issue, on May 1 2014, the GW Medical Faculty Associates instituted a fee for missing appointments.

The aim of this study is to assess potential barriers that are contributing to patients missing their appointments and if the monetary penalty has improved compliance with appointments.

A patient questionnaire has been developed to assess this issue. This questionnaire is a three question survey which consists of the following: 1) Are you aware of the new MFA policy where they reserve the right to charge you for missing an appointment? 2) If you've ever been late to an appointment at the MFA, what was the reason? 3) If you have ever missed an appointment at the MFA, what was the reason? This survey will be administered at the internal medicine clinic from patients over a one month period. The data can then be used to address specific issues that arise when missing appointments.

The IT department will run a database search providing the no-show rates for November 2013 and November 2014. This data will be useful in determining if the monetary penalty has helped improve MFA internal medicine show rates

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Improving medical supplies stocking and organization in the outpatient internal medicine clinics

BACKGROUND:

The exam room can “make or break” the provider-patient relationship. An ideal room is organized and fully stocked with everything one needs to conduct a full history and physical examination efficiently and comfortably. A poorly organized room can lead to lost time, decreased provider and patient comfort, and increased frustration.

OBJECTIVE/PURPOSE:

The objective of this project was to improve the supply and stocking of internal medicine exam rooms at the Medical Faculty Associates (MFA,) by organizing and stocking the supplies regularly tailored to physician satisfaction.

METHODS:

We administered a pre- and post-intervention baseline survey to the internal medicine department providers regarding exam rooms’ supply to assess satisfaction. Following the Model for Improvement methodology and working together with a team of nurses and managers, we set to achieve a supply of at least 90% in the exam rooms over a period of 4 months, which should be measured after implementing par levels. The exam rooms’ supplies were organized and standardized using labelled bins. As a process measure, we also implemented a sign-in sheet in each exam room, with a goal of stocking the room and signing the sheet in at least 90% of exam rooms weekly.

RESULTS:

The project ran for 19 weeks. The baseline survey showed that 81% and 54% of the physicians in clinic 4A and 4B, respectively, were dissatisfied with the medical supply restocking and organization. A 5-week baseline median of the process measure yielded 42.8%, 17.65% and 0% from clinic 4A, 4B and ground clinic, respectively. Using a standard plan-do-study-act (PDSA) methodology, clinic 4A achieved the goal at week 8 and again at week 16 after which it was maintained. Clinic 4B achieved and maintained the goal at week 14. Ground clinic achieved the goal at week 7 and again at week 13 after which it was maintained. Outcome measures were calculated starting at week 14 through 19, and the 5 week median for clinic 4A, 4B and ground clinic were 96%, 94.67% and 97.67%, respectively.

CONCLUSION:

Using the Model for Improvement and interdisciplinary teamwork, we were able to achieve higher rates of exam room stocking and organization, tailored to physician satisfaction. The process measure of using sign-in sheets was highly effective at achieving the outcomes of stocked rooms and satisfaction in a relatively short period of time. We believe that this can be translated across departments and organizations to improve efficacy and work-flow.

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A grounded theory qualitative approach to quality improvement in debriefings after emergency department resuscitation

BACKGROUND:

American Heart Association guidelines recommend team debriefings after emergency department (ED) resuscitations to improve future performance. It is unknown whether the conversations that occur during post-resuscitation debriefing (PRD) sessions include the identification of opportunities to improve the quality of ED care delivery.

OBJECTIVE:

To use a grounded theory approach to describe the common themes in ED PRDs related to quality improvement (QI) and the facilitative methods used by PRD participants to generate discussions about QI.

DESIGN/METHODS:

One year ago in our ED, we initiated a structured, multi-disciplinary, participant-facilitated, PRD program. Team debriefing sessions are video-recorded and reviewed for quality improvement and research purposes (IRB approved). Between March and November 2014, we reached the recommend minimum of 20 separate observations for adequate thematic saturation (n=21). Research assistants transcribed the recorded PRD content into Nvivo qualitative software; for inter-transcriber reliability, three transcribers reviewed all audio and recorded transcripts. To enhance validity, triangulation of data will be performed using existing data from: 1) PRD forms completed by PRD participants at the time of debriefing, and 2) objective quantitative checklists of resuscitation activity and quality metrics. Using a grounded theory approach, data are being analyzed by content experts using the following methodology: 1) immersion of data, 2) iterative coding of data, 3) clustering of codes to generate themes, 4) inductive generation of hypotheses from themes.

RESULTS/DISCUSSION:

Analysis is expected to be complete by March 2015. Grounded theory qualitative analysis will describe the common Quality Improvement themes that can be generated by a structured, multi-disciplinary, participant-facilitated ED-based PRD program. Theories for how to facilitate the emergence of these themes will be generated and can be prospectively tested to determine if the quality of future debriefing conversations can be improved. These findings would have application in the ED and potentially other acute care settings.

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Hepatitis C Virus Infection Screening Test Compliance at Primary Care Clinic

INTRODUCTION:

Hepatitis C Virus (HCV) is the most common cause of liver cirrhosis and hepatocellular carcinoma, and it is the leading cause for requiring liver transplant in the US. About 3.2 million individuals are chronically infected with HCV. Most of those are unaware of their infection because they are asymptomatic. Approximately three-fourths of them were born between 1945-1965. Therefore, the U.S. Preventive Services Task Force recently recommends a one-time screening test for HCV for those individuals. It seems that the rate of HCV screening is low among medical residents in internal medicine clinic because the recommendation is new.

Furthermore, with the advances in HCV treatment, it is imperative to identify chronically infected individuals in order to avert the long-term, costly, sequelae of the virus. This study sets out to first assess a baseline current rate of HCV screening among a selected group of residents, and subsequently, assess changes in practice behavior after various educational sessions.

METHODS:

The patient panels being taken care of by the 20 resident physicians comprising Cohort will be evenly divided among the four research residents. The included patients will be those who have undergone a complete Health Maintenance Exam visit by the residents in Cohort. Each research resident will review the electronic charts of the patients to determine if the patient has Hepatitis C screening. Those patient's being those who were born between 1945 and 1965. All retrospective data will be coalesced into a baseline rate of adherence to this guideline. Short educational sessions will be performed to outlining the Hepatitis C screening age guideline. Additionally, a text-page and an email will be sent stating the importance of adhering to the guideline. Over a subsequent one month period, all of the HME visits will be assessed for adherence to Hepatitis C screening age guideline. At the end of one month, prospective data will be compiled, and the rate of adherence will be assessed and compared to the baseline.

RESULTS:

The results are in progress.

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Use of Technology and Patient Portal Interest Among A Low-Income Population

BACKGROUND:

In an effort to improve quality of care, healthcare providers are required to demonstrate "Meaningful Use" of Electronic Health Records (EHRs). One such requirement mandates increased patient engagement and communication through use of electronic patient portals, which merits special consideration for patients whose access to internet is not well understood or who have low literacy or English proficiency. A needs assessment was conducted at a network of three safety-net clinics for the uninsured to better understand how to meet the needs of this patient population.

METHODS:

150 surveys were collected at the clinic sites over a month-long period. The survey contained questions about patient use of technology and interest in using those technologies to communicate with their healthcare providers and was available in English or Spanish. In addition, a provider survey was conducted to identify potential provider barriers and facilitators and administered via an online survey to all physicians, nurse practitioners and physician assistants at the clinic sites.

RESULTS:

The patient survey findings indicated that the majority of patients had access to the internet, primarily through their smartphones, and were interested in using text messaging, patient portals and smartphone applications to communicate with their healthcare providers. While text messaging ranked as the most preferred method of communication (78%), over half of patients were interested in using a patient portal (59%), with most interested in scheduling appointments online, securing messaging with their providers and viewing lab results.

When examining the characteristics of patients who were interested in the patient portal, most had access to the internet (84.3%) and nearly two-thirds used the internet either several times per week or daily (64%). Interestingly, patient interest in using the portal was equal among age and language groups. Also of note, among those interested in the portal, 20% were patients whose highest education level was elementary or middle school, compared to 30% who were high school graduates and 42% who had some college experience or a college degree. Providers were asked to identify characteristics of patients who may have difficulty using a patient portal and older age and limited English proficiency ranked highest.

IMPLICATIONS:

Given these findings, it is important to develop appropriate promotional and patient education materials, including both video and written instructions. Portals should also be tailored to a variety of platforms, with a special emphasis on smartphones. It may also be worthwhile to have a computer kiosk in waiting areas with a staff navigator to guide patients through the sign-up process. Secure text messaging may also prove to be an easy way to communicate with patients. As a whole, electronic forms of communication have the potential to increase patient satisfaction and improve quality of care.

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Improving 30-day discharge summary completion rates at George Washington University Hospital

BACKGROUND:

The Joint Commission requires that no more than 50% of a facility's average monthly discharge records are over 30 days old. Current data shows that at George Washington University Hospital, the 2014 average monthly 30-day discharge record delinquency rate is 25-30%. While this percentage meets the 50% requirement, it still accounts for thousands of discharge summaries that are not completed in a timely manner. Discharge summaries are important for patient care continuity as the patient transitions from an inpatient hospital stay to medical management by the primary care provider. Delinquent discharge summary completion negatively impacts this continuity and likely contributes to an increased readmission rate, which has costly impacts to both the hospital and the patient. However, several barriers prevent residents from completing them in a timely manner.

METHODS:

We will obtain data regarding discharge summaries that were not completed within 30 days for patients admitted to an inpatient medicine service at GWUH from the Division of Health Information Management. In October 2014, a warning email was sent informing residents that if they had delinquent discharge summaries, electronic medical record (EMR) access would be deactivated. We will compare the data from before and after the email was sent to see if the intervention had an effect.

The second part of the project will assess what the current barriers to timely discharge summary completion are for residents. Current internal medicine residents will complete a survey about barriers to discharge summary completion. We will establish a protocol to target these barriers and establish a protocol for discharge summary completion. Survey results will be analyzed using descriptive statistics. No further statistical analysis is anticipated.

ANTICIPATED OUTCOMES:

This project will aim to identify barriers and evaluate interventions, such as e-mail reminders and the warning of losing EMR access, in efforts to improve timeliness of discharge summary completion. By conducting this study, we will be able to better understand the exact barriers that exist in preventing residents from completing discharge summaries in a timely manner. We then can target these barriers and create protocols that improve the discharge summary completion process and improve transitions of care by facilitating delivery of discharge summaries to the primary care provider. We also aim to share these best practices so that other institutions might implement them as well.

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Streamlining Scheduling: Improvement in Patient Continuity in a Resident-Run Primary Care Clinic

BACKGROUND:

Continuity of patient care has been shown to increase both quality of care as well as both patient and provider satisfaction. We sought to increase the patient continuity at a resident-run primary care clinic by improving the paper form used to schedule future appointments.

METHODS:

The authors, all resident clinic providers, had a focus group and edited the previously available paper checkout form to increase ease of scheduling future appointments. Patient visits were reviewed for approximately 1/3 of the residents. Residents within the primary care track were excluded from the study. For each resident included, we evaluated five days of clinic visits with the previous checkout form and five days of clinic visits after introduction of the new form. Microsoft Excel was used to create a database that included whether or not the patient was seen by his or her own resident provider, attending provider and provider team. A two-tailed Fisher's Exact Test was used with significance set at $p < 0.05$. Our study was exempted by the university IRB board as it was not human subjects research.

RESULTS:

A total of 786 visits were reviewed. After our new checkout form was implemented, there was a statistically significant increase in the percent of patients seen by their attending provider (37.6% vs 29.6%, $p=0.0216$) as well as the percent of patients seen within their provider team (87.0% vs 80.1%, $p=0.0283$). There was also a statistically significant drop in the number of patients that had visits where they were not seen by their resident provider, attending provider or within their provider team (9.9% vs 16.7%, $p=0.0217$). Finally, there was a trend toward an increase in the percentage of patients seen by their own resident provider although this was not statistically significant (52.9% vs 50.0%, $p=0.4721$).

DISCUSSION:

With simple changes to a paper form, we were able to increase patient continuity with attending providers and within provider care teams as well as decrease visits where patients had no continuity with the attending, resident or care team. As above, increasing continuity of patient care has many benefits; both patients and providers have higher satisfaction with improved continuity and quality of care increases as well. Particularly in resident-run clinics where continuity can be challenging, attention to detail in forms and systems used to engage patients is critical, as even minor decreases in barriers to continuity can have a profound effect.

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Geographic Healthcare Spending Variation

Large geographic variations in healthcare and healthcare spending have been demonstrated for Medicare fee-for-service patients through the Dartmouth Atlas of Healthcare. These variations are generally not associated with patient or physician satisfaction with care, or patient survival. Cumulatively, these findings have led policy analysts to conclude that as much as 30% of healthcare provided contributes little to patient welfare. The specific sources of this inefficiency, however, have yet to be identified. We selected 8 "supply sensitive" conditions and procedures based on a combination of frequency, cost, and degree of clinical discretion. From there I conducted extensive literature reviews of practice guidelines, any previous studies of geographic variation in the field, and any recent studies that have used administrative data to define the population of interest using ICD-9 coding. The next step will be to compile a practice profile of each condition population using Blue Cross Blue Shield insurance data at the hospital level. We will compare these guidelines to the current clinical practices at each hospital. We hope to begin a dialogue about the differences in practice and to define areas where physicians can become more efficient and effective in their practice.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Improving timeliness and ease of scheduling of hospital discharge appointments for internal medicine patients

OBJECTIVE:

To increase the ease of scheduling appointments after hospital discharge and increase the proportion of patients scheduled for follow-up within 2 weeks of discharge.

BACKGROUND:

Follow-up appointments after a patient is discharged from the hospital are known to improve patient outcomes, increase medication adherence, and reduce readmission rates. The current system for patients discharged from the internal medicine inpatient service at GWUH requires that providers schedule appointments for their patients, which is time-consuming. Additionally, appointments with a patient's PCP are frequently not available within 2 weeks of discharge. Our goal is to create a system that allows for timely follow up for patients as well as ease of scheduling for providers.

METHODS:

A "Discharge Clinic" was established at the Medical Faculty Associates (MFA) Ambulatory Care Center, held one half-day per week, during which patients with a primary care physician (PCP) at the MFA could be seen for post-discharge follow up, starting December 2014. Patients with PCPs outside of the MFA or no PCP were excluded from this discharge clinic. The discharge clinic was advertised to Internal Medicine providers through email and in-person announcements. To schedule a patient for this clinic, residents sent a message to the attending in charge of the clinic, who would send that information to the MFA scheduling team.

Prior to implementation of the discharge clinic, a voluntary, anonymous survey was distributed to residents to gauge time spent scheduling discharge appointments for patients and resident satisfaction with the process. This same survey was repeated after the discharge clinic was established.

With assistance from GWUH Medical Records and IT departments, a list of patients discharged from Internal Medicine wards teams during November 2014 and February 2015 was compiled. For each patient, the category of primary care provider (None, MFA, or non-MFA) was recorded. For all patients with MFA providers, we recorded whether a follow up appointment had been made prior to discharge, and the length of time from discharge to that appointment.

RESULTS:

Results of our data are currently pending. All results will be available prior to GW Research Day, for which this abstract is being submitted. Once available, the results of the database and surveys will be compiled to form a conclusion about the efficacy of the discharge clinic in improving patient follow up and ease of scheduling. We anticipate that this data can be used to further identify areas of improvement for post-discharge follow up.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Impact of condition specific camps on resiliency and adaptive behavior in children with heart conditions

Resilience is the ability to adapt in stressful situations and overcome adversity through the use of effective coping strategies. Previous studies have demonstrated that condition-specific camps designed for children with epilepsy can increase adaptive coping skills including social interactions, cooperation, initiative, and communication in participants over a three-year period [1,2]. Additionally, research indicates that as a group, individuals who live with chronic health disorders exhibit less hope and have worse health outcomes when compared to their normative peers. The aim of this study was to determine the impact of condition-specific camps on children with heart conditions. 39 of 75 youths, diagnosed with heart conditions, attended Brainy Camps and participated in this study between 2012-2014. Participants included 5 females and 11 males in the 8-11 year old range and 10 females and 13 males in the 12-17 year old range. The Price-Emory Resiliency Scales, Herth Hope Index, and the Loneliness Scales were completed pre and post camp. A T-score range was used to determine if children with heart conditions differed from normative data in terms of resiliency. Resiliency was evaluated among the campers using the subscales of mastery, relatedness, and emotional reactivity. Averages for the pre- and post- camp scores were taken for both single year and consecutive year participants and compared to average scores in the normative data. The 39 children who attended camp demonstrated positive changes in resiliency including emotional reactivity, and hope, by the end of their first year. However, decreased scores in mastery and relatedness and increases in loneliness were also noted. For the 13 children who participated for 2 consecutive years and 3 children who participated for 3 consecutive years, increases in hope and decreases in loneliness were improved with each additional year of attendance. These findings demonstrate a positive shift in hope, loneliness and resiliency in children with heart conditions who attended camp consistently over several years. These findings highlight the potential impact that hope and perceived social support can be influential factors on resilience. Some limitations of this study included small numbers of participants, having data collection pre camp in the child's home versus post camp at the campsite, and loss to follow up across years. Further research is needed to understand additional factors may influence resiliency in children with heart conditions. For children with chronic illnesses to successfully manage their healthcare, interventions tailored to encourage a sense of hope and social support may prove beneficial.

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3. Prince-Embury, S. (2007). Resiliency Scales and Profiles: T Score Ranges. *Resiliency Scales For Children & Adolescents: A Profile of Personal Strengths*. Pages 25-26.

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Improving Clinical Practice and Treatment Guidelines: Utilizing Electronic Health Records to Implement a Concussion Decision Rule

BACKGROUND:

Traumatic brain injuries (TBI) and concussions have rapidly ascended to the forefront of our public health agenda as a health concern that is both poorly recognized and inadequately managed in the Emergency Department (ED). While immediate recognition and active treatment in acute situations is necessary for a safe recovery, the diagnostic criteria established are poorly structured and our clinical tools are often inadequately utilized in the ED. As a result, patients have poor recorded follow-up and the utilization of diagnostic testing has become wasteful and dangerous.

PURPOSE OF STUDY:

The objective of this study was to determine the feasibility of Electronic Health Record (EHR) workflow integrated implementation of the ACE-ED and ACE-ED DI tools as a way to improve concussion recognition and management in the ED at Children's National Medical Center (CNMC).

HYPOTHESIS:

Integrating of ACE-ED and ACE-ED DI into the EHR will allow for a diagnosis and treatment of concussions in the ED in an effective and prompt manner.

METHODS USED:

We have integrated the ACE ED and ACE ED DI into our EHR to aid in provider workflow for the diagnosis and management of concussions and TBI in the ED. A team of nurses, physicians, subject matter experts, and IT analysts collaborated to embed the tools into the existing EHR at CNMC. Two icons were created for easy access on the homepage of the EHR - a brain, which was used for concussion evaluation, and a skull, which was used as a CT reduction tool. The healthcare providers were trained on use of the tools and implementation when concussion or TBI was suspected.

SUMMARY OF RESULTS:

Employment of the ACE ED and ACE ED DI tool into the EHR workflow was successful for the ED at CNMC. The emergency care providers were able to utilize the tools to manage concussion and TBI while increasing patient follow-up after discharge.

NEXT STEPS:

Based on the success of the ACE-ED and ACE-ED DI at CNMC, the goal is to implement the tool into the EHRs at the neighboring hospitals in Washington, DC in order to evaluate the effectiveness of this tool at alternative sites. Using the model that we have created to improve clinical approach of concussions and TBI, we hope to identify other areas of medicine that are ineffectively being managed and improve nationwide standards of practice.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

We're on the Same Page: Maintaining mutual understanding of currently prescribed medications between patient and provider

Medication reconciliation is crucial to preventing medication errors and is a National Patient Safety Goal recommended by the Joint Commission. Gathering a complete medication history is an essential first step in the medication reconciliation process but is often challenging and time-consuming because of outdated lists in electronic records, improper documentation by providers and uncertainty among patients about their medications. Several common barriers to implementing medication reconciliation exist, including lack of use of personal medication lists by patients and lack of established best practices. The primary objective of this study was to increase the percentage of completed medicine reconciliations during ambulatory visits in resident clinic. The secondary objective was to describe the challenges of medication reconciliation among medical residents and their attitudes toward the process. The goal of the study is to identify barriers in our practice and then to study specific interventions to address these barriers and increase provider satisfaction with medicine reconciliation. Improving medicine reconciliation rates may improve patient outcomes, and reduce costs by reducing medication errors. Systems that improve reconciliation will also allow physicians to spend their time on the patient rather than contacting family members or pharmacies for collateral information.

In this study, residents were asked if they were able to reconcile medications with each individual patient seen in that clinic session using a short questionnaire. This was done to perform a baseline measure of the prevalence of medication discrepancies. Residents also completed a survey on their beliefs and attitudes surrounding medication reconciliation in clinic. Subsequently, several interventions were implemented aiming to improve ease of medication reconciliation such as asking all residents to remind their patients to bring medications/medication list to their next appointment, sending a mass e-mail to all patients enrolled in MyHealth e-mails from the Department of Internal Medicine, asking staff at the outpatient-processing pod to verbally remind patients to bring in their medications at the next appointment, and placing posters in patient exam rooms encouraging them to bring in their home medications/medication lists to their next appointment.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Care Team Face Sheets: An intervention to improve communication, understanding, and satisfaction among hospitalized patients at The George Washington University Hospital

Patients in the hospital often have a large number of physicians caring for them including hospitalist and consultant teams. Further, in a teaching hospital, interns, residents and fellows can quickly multiply the number of providers a patient sees often leading to significant confusion for the patient. This is in addition to the many nurses, therapists, and other allied-health providers working with the patient during their hospitalization.

Our objective is to study whether the distribution of a Face Sheet including physician names, photographs, and roles, will improve hospitalized patients' ability to identify at least one of their hospital physicians by name. Further, we will assess if that is associated with improvements in important patient measures including physician communication, patient plan-of-care understanding, and satisfaction. We hypothesize that patients in the intervention group will have a better relationship with the physicians in their treatment team, which will lead to better communication, understanding, and satisfaction scores than a control group.

Our study will include hospitalized adults on the academic hospitalist service for whom English is a preferred language. Prior to the intervention, research volunteers will screen patients and enroll those meeting inclusion criteria. If the patient elects to participate, they will be asked a short series of research questions including demographic data. Data from subjects will be reviewed until approximately 100 participants have been included in the control group. The process above will be repeated with the next 100 patients as Face Sheet intervention group. In addition, patients in the intervention group will be asked if they received a physician face sheet. We will use an intention to treat analysis to compare a post-intervention sample to pre-intervention controls. Data is currently being collected with results to follow. There will also be potential for serial intervention groups to assess adherence among medical teams and it's association with above measured variables.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Improving Resident Confidence in Central Line Placement Using Simulation-Based Education

As part of board certification, the American Board of Internal Medicine requires competency in understanding the indication and management of central venous lines (CVL). An internal medicine resident (IMR) must perform 5 CVL placements throughout their training to demonstrate competency. When surveyed, George Washington University Medical Center (GWUMC) IMRs ranked CVL placement highest among procedures they wished to practice. CVL associated infections are preventable with proper sterile technique and infection rates are therefore tracked avidly by the hospital as a performance measure. The question remains on how to best train our residents to perform this procedure in a safe and sterile environment to avoid complications of CVL placement. Currently, IMRs only receive 1 CVL placement practice session prior to starting work at the hospital. The purpose of this quality improvement project was to increase resident confidence in CVL placement by offering an additional simulation in CVL placement under guided conditions, in hopes that this would translate to decreased CVL placement complications. Thirty residents were asked to participate, of which 12 IMRs volunteered. Participants then underwent a hands-on training session on the placement of a CVL on a mannequin. Residents were surveyed on baseline CVL placement experience and were also asked to rate their confidence in CVL placement on a 5-point scale both pre- and post-simulation. Final results are pending, but verbal feedback from project participants suggested improvement in resident confidence in CVL placement. This project will provide useful information on best practices for training residents in CVL placement, and may also decrease CVL placement complications.

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SCHOOL OF NURSING

Impact of Implementing the Geriatric Resource Nurse Model on Fall and Hospital Acquired Pressure Ulcer Rates, and Length of Stay

BACKGROUND:

Older adults are at high risk for adverse care outcomes, such as injuries from falls, hospital acquired pressure ulcers (HAPUs), and prolonged length of stay (LOS). Available evidence suggests outcomes may improve when older adults are cared for by healthcare providers with competence in geriatrics. To improve outcomes, an acute care not-for-profit teaching hospital in Washington DC area implemented a Geriatric Resource Nurse (GRN) model that prepares registered nurses (RNs) as clinical experts on core geriatric principles on four general care wards (three medical-surgical and one cardiac).

OBJECTIVES:

To examine the effects of GRN model implementation on fall and HAPU rates, and LOS in older adults in medical-surgical and cardiac units in an acute care hospital.

METHODS:

A retrospective chart review was conducted to measure fall and HAPU rates, and LOS before and after implementation of the GRN model. Data from 1176 charts (609 in before and 567 in after intervention group) was reviewed. Data analysis was performed in SPSS 22.

RESULTS:

Total number of falls was 24 (2.0%) with 13 (2.1%) before and 11 (1.9%) after intervention group. Total number of HAPUs was 26 (2.2%) including 18 (3.0%) before and 8 (1.4%) after intervention group. LOS ranged from 1-71 days. LOS mean for total population was 5.14 (SD=5.10), with a mean of 4.88 (SD=4.71) before and a mean of 5.41 (SD=5.49) after intervention. There were no statistically significant differences in fall ($\chi^2=0.06$, $p=0.81$) and HAPU ($\chi^2=3.24$, $p=0.07$) rates or LOS ($t=-1.78$, $p=0.07$) before and after the intervention.

CONCLUSIONS:

Our findings did not identify significant differences in fall and HAPU rates, and LOS before and after the intervention. These findings may be a result of inconsistencies in the institutional application of a systematic approach to geriatric care.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Improving Zostavax Vaccination Rates in Appropriate Patient Populations at the MFA

We would like to improve the rates of Zostavax vaccinations in the eligible resident MFA clinic population by 20% over the course of 3 months. Residents lack awareness of Zostavax indications and the ordering process for vaccine, which requires a "pre-authorization" process. These factors likely result in fewer eligible patients receiving the vaccine. In order to improve the knowledge level for Zostavax vaccination, there will be initial chart review for one cohort of medicine residents' rates of Zostavax vaccinations in appropriate patients (age greater than 60, not in current immunocompromised state). During one Wednesday didactics session, we will present a short 5 minute PowerPoint presentation on how to pre-certify vaccinations along with a reminder of which patients qualify for Zostavax to increase resident education of indications for Zostavax. We will also place flyers in the resident work room to remind them how to properly order the vaccination. In 3 months, there will be a chart review of patients in previously studied cohort group to see if the 5 minute didactic intervention and flyers in resident work room showed any improvement in vaccination rates for the applicable population.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Radio-frequency Identification Tags and Real-Time Interventions to Improve Health Outcomes

INTRODUCTION:

Preventable medical errors are the third leading cause of death in the United States, behind cardiovascular and cancer related deaths. According to the Journal of Public Safety, between 210,000 and 440,000 patients that seek help in the hospitals of our nation suffer from a "preventable harm that contributes to their death." We are working on creating a dynamic algorithm that senses object use through radio-frequency identification (RFID) tags, while identifying potential mistakes in the field and notifying the clinician in real-time. This technology could have the potential to eliminate preventable harms and change the face of medicine as we know it.

METHODS:

There are multiple cameras and views of the trauma bays in the ER at CNMC that automatically record sound and footage when movement is sensed in the rooms.

We tried various sizes of RFID tags before installing them on all objects in the trauma bays, including both permanent objects (like shears) and one time use objects (like cervical spine stabilizers).

We obtained Informed Consent from every patient and their family before looking at the recorded footage of the trauma resuscitation encounter.

I coded a total of 26 trauma resuscitations, which we then compared to the RFID data.

RESULTS:

I was able to set up a system with RFID readers, which pick up signals from a variety of objects throughout the trauma bays. I was also able to set up a system, which streamlined the coding process for various activities and objects, as expected with trauma resuscitation.

CONCLUSIONS:

We will use the data and systems I helped establish to build the next stage of our project to design an algorithm that synthesizes the live streaming data and compares it to the expected tasks and any prior negative outcomes. It will then project onto a TV screen in the trauma bay to alert the clinicians of avoidable negative outcomes.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Improving advanced care planning in primary care clinic

More than 90 million Americans live with at least one chronic illness, and seven out of ten will die from chronic disease. About one fourth of Medicare spending is currently utilized in the last year of life. A significant proportion of this is spent on intensive inpatient care that has not been shown to improve survival or quality of life. An increasing number of people are now dying in hospitals despite multiple studies that have shown that people would prefer to spend their last days at home. One important aspect of this seen in the SUPPORT trial is that physicians rarely discuss end of life preferences with patients and less than half of physicians knew when their patients would prefer to avoid CPR. Though we have made significant efforts towards having advanced directive discussions in the inpatient setting, a similar push has not been seen in the outpatient setting. Starting the discussion early in the diagnosis of chronic illnesses may help patients to stay out of the hospital and avoid having advanced care discussions in the last year of life when these decisions may feel forced or rushed to patients. Thus our quality improvement project aims to find ways to increase the rates of advanced care discussions and documentation at our internal medicine resident clinic in all patients aged 50 and above, especially those with a chronic illness.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Exploring the difference in Hemoglobin A1C measurement using In-Lab vs. Point-of-Care analysis

BACKGROUND:

Serum hemoglobin A1C level is often used as a surrogate marker for the average serum glucose of an individual over the previous two to three months. It provides valuable information to clinicians in the diagnosis and management of diabetes mellitus. At George Washington Medical Faculty Associates (MFA), Hemoglobin A1C can be measured either by sending venous blood for in-lab analysis or by fingerprick analysis using the point-of-care (POC) instruments in the office. Some clinicians use POC values alone in glucose monitoring while others prefer to confirm the value with the additional in-lab test.

OBJECTIVE:

To compare A1C measurements obtained by in-lab vs POC analysis.

METHODS:

Using MFA electronic medical record system, paired A1C measurements were obtained from patients' medical records, one from in-lab analysis and one from POC, done on the same day between August 2013 and August 2014. The differences between the two A1C values were analyzed and the average difference, r , r square value, and frequency plot were calculated. All hemoglobin A1C measurements were recorded as percentage of glycosylated hemoglobin.

RESULTS:

115 patients were identified with paired A1C measurements on the same day, one value from in-lab analysis and one from POC. Graphs comparing the in-lab analysis to POC values generated a mean linear regression slope of 1.06 with r of 0.97 and r square of 0.94. In addition, 94 measurements (84%) had in-lab measurements greater than POC. The differences between the two measurements ranged from 0 to 3.2 with an average difference of 0.2. 78% of the POC measurements fell within a difference of 0.5 from those of in-lab analysis.

CONCLUSION:

Our findings suggest that the A1C values obtained via POC instruments demonstrate acceptable levels of precision compared to those obtained via in-lab analysis. The average difference of 0.2 in A1C measurement is arguably insignificant in making clinical decisions during routine outpatient management of diabetes. Clinicians can be confident in making clinical decisions based on POC values without the need to confirm the result via in-lab analysis, unless there is a greater than 0.5 difference compared to patient's previous in-lab measurements. This can improve healthcare quality by reducing unnecessary blood draws and allocating healthcare spending more appropriately.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Discharge Checklist

The discharge process is often the most complex part of a hospitalization. Lots of logistics are involved in this process and it's important to have a comprehensive plan for discharge in order to safely send a patient home and to decrease re-admission rates. Many obstacles exist on a daily basis in order to send patients out and it is vital to each hospital to recognize and improve these factors.

Our study for improving the discharge process in the internal medicine wards was split in two parts. The first part involved identifying the obstacles related to discharge planning specific to the George Washington University Hospital. This has been done primarily through discussions with the various teams involved in patient care, including the residents, nursing staff, social workers, case managers, and attendings. We also used the hospital consumer assessment of healthcare providers and systems (HCAHPS) scores specific to the hospital to determine what factors were highlighted by patient surveys. We found that communication with doctors and communication about medications often fell below 70%. As a result, we designed a discharge planning session that teams should have with patients close to their discharge. The session includes the various team members meeting with the patient and his/her family as a group and specifically detailing the patient's principal diagnosis, changes in medications and why the changes were made, and imaging studies completed with discussion of results. The team then asks patients to teach back what they understood and then answer relevant questions. The second phase of this project will be to implement these sessions on a regular basis by the internal medicine teams. Ultimately, we will study the impact of these sessions through individual patients' HCAHPS scores.

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SCHOOL OF NURSING

Psychometric Evaluation of the Elopement Risk Assessment Tool

BACKGROUND:

Patient elopements from healthcare organizations can result in patient harm and civil actions against organizations. Elopement with harm is a sentinel event and identification of elopement risk and prevention of elopement occurrences is a priority safety goal. During the time frame of July 1, 2011 through April 30, 2014, an urban 926 licensed bed acute care hospital experienced 19 elopements. The majority of these elopements were associated with patients having co-existing or secondary psychiatric disorders. A literature review revealed minimal evidence on elopement within the acute care setting; the focus was on long-term care and inpatient psychiatric units. Articles supporting feasible assessment and prevention strategies were used to create an Elopement Risk Assessment Tool.

OBJECTIVES:

The purpose of this study is to estimate the inter-rater reliability and the predictive validity of the Elopement Risk Assessment Tool in an acute care setting.

METHOD:

A retrospective chart review of 19 eloped patients matched with 38 non-eloped patients was conducted to score each patient's risk for elopement using the Elopement Risk Assessment Tool. The Principal Investigator (PI) and trained co-investigator independently performed the retrospective chart reviews and scoring. The eloped patients were matched with the non-eloped patients by psychiatric diagnosis if existing, month and year, unit, age range, gender and ethnic origin.

RESULTS:

This study had a total of 57 participants (19 eloped and 38 non-eloped). The matching process produced two groups that were relatively equal on psychiatric diagnosis, age range and gender. Ethnicity was not matched there were no cases of Caucasian and other races in the eloped group. The participants were 51% male and 49% female. The average Kappa statistic for the 20 items within the Elopement Risk Assessment Tool was 0.73 with an average Pearson's r of 0.76 and average p value of 0.228. The findings support a substantial Kappa agreement and an acceptable Pearson's r .

CONCLUSION:

The findings support the Elopement Risk Assessment Tool is a valid and reliable tool for healthcare providers to assess and identify patients at risk for elopement within the acute care setting. Further research is recommended to apply the Elopement Risk Assessment Tool in other acute care settings to advance the estimation of reliability and validity of this tool.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Improving the GW Hospital Internal Medicine Inpatient Discharge Planning Process By the Implementation of Social Work Rounds

The George Washington University Hospital Internal Medicine Department is currently comprised of five resident-lead general medicine inpatient ward teams, a physician assistant service and three subspecialty inpatient services. After a patient is medical treated and ready for discharge many times they need outpatient services including rehabilitation placement, long-term care placement and home nursing services. The discharge planning process is lead by a team of social workers and nurse case managers who work with physicians to help ensure that patients have a smooth transition into the outpatient setting. Unfortunately, there are instances where there are delays in the patient discharge process prolonging hospital stay. Some of these delays are due to preventable causes. Improving the discharge planning process is important because prolonged hospital stay can increase the risk of healthcare-related infections, increase healthcare costs and overall result in poorer health outcomes. The aim of this quality improvement project is to decrease the number of days that patients on the GW internal medicine ward services remain admitted to the hospital after they have been medically cleared for discharge by 25% in three months. The intervention is the implementation of a standardized meeting with the social work team and the medicine ward teams three times a week to discuss patients' expected discharge needs. The project measures include staff satisfaction, patients' total length of stay and patients' length of stay after becoming medical ready for discharge. Staff was sent a pre-intervention and a one-month post-intervention satisfaction survey. 47% of 36 resident physicians who completed the pre-intervention survey were unhappy with the current level of communication between the social work team and the physician ward teams. 58% of those surveyed believed that creating a standardized meeting time between social work team and the ward teams would help improve discharge planning and patient care. Increasing communication between key parties in the discharge planning process is expected to eliminate some of the barriers that often result in a delay in patient discharge.

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SCHOOL OF MEDICINE & HEALTH SCIENCES

Improving Resident Hand-offs using HIPAA-Compliant Voice Recording

Physician hand-offs are a burgeoning area of research and debate. Resident hand-offs, in particular, are of particular interest due to duty-hour restrictions and the resultant increase in hand-offs. With the aim of increasing the quality of patient care by improving provider hand-offs, we instituted a new protocol for recording provider hand-offs for the nightfloat residents to utilize. On weekends at George Washington University Hospital, there are often two handoffs in one day, allowing for possible loss of information. Utilizing TigerText, a HIPAA-compliant text and audio message system, our residents and interns were required to record their patient handoff, in addition to completing the handoff in person. This allowed for the second resident to listen to the primary team's handoff, while also receiving the traditional in-person handoff from the covering resident. A pre-intervention survey was completed examining the quality of weekend handoffs, in particular. These data were compared with a post-intervention study. 4 weekends' worth of data were analyzed using qualitative and quantitative methods from the de-identified participating interns. The goal was improvement in comfort level, quantity, and quality of information conveyed to the night float team from the primary team. The results will be used to structure handoffs for residents within the Department of Internal Medicine, and perhaps with wider benefit throughout the Hospital.

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Evaluation of Referral Processes and Coordination of Care between a Community-Based Primary Care Clinic and Subspecialty Clinic

INTRODUCTION:

Effective coordination between primary and subspecialty care is important for providing high quality comprehensive healthcare to a patient. Structural, procedural, and social determinants may create barriers that inhibit care coordination. This study identified barriers against effective patient care coordination between Bread for the City (BFTC), a local FQHC-look alike working with underserved populations and their referrals to specialty care at Medical Faculty Associates (MFA).

METHODS:

Semi-structured, anonymous, key informant consultations with organization leaders, medical staff, administrative staff, and patients were conducted at both BFTC and MFA. Tracking forms were used to collect information about various time points in the referral process including dates of referral requested, referral scheduled, subspecialist appointment, follow-up primary care appointment, and transfer of records from MFA to BFTC.

RESULTS:

Consultations revealed a number of barriers to effective care coordination including difficulty with reaching administrative staff for immediate scheduling of specialist appointments, transfer of records from primary care to specialists and vice versa before and after appointments, inappropriate requests for release of information forms, and characterization of urgency for specialist appointments. These barriers are the result of a de-centralized system with non-standardized work-flow processes, as well as lack of accurate information to facilitate medical record transfers.

DISCUSSION:

High quality patient care linking primary to specialist providers at differing health institutions requires strong coordination across systems and effective communication. Addressing administrative barriers and implementing processes to ensure smooth appointment scheduling and appropriate transfer of records is critical to ensure that health needs are effectively addressed and to foster collaboration between primary care physicians and specialists in patient care. At community clinics like BFTC exploring opportunities to expand coordinated patient care, it is important to manage patient care with support from specialists to ensure that plans are appropriately implemented, non-overlapping, and non-interfering to support optimal patient care.

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Vancomycin Trough Quality Improvement

BACKGROUND:

Vancomycin is one of the most widely used intravenous antibiotics in the United States for the treatment of severe gram-positive infections, specifically methicillin-resistant *Staphylococcus aureus*. Under-dosing of this medication (trough <10 mcg/mL) may result in ineffective treatment and an increased risk of vancomycin resistance. Over-dosing (trough >20 mcg/mL) may increase the risk of side-effects such as nephrotoxicity. Troughs are used to guide dosing of vancomycin in order to maintain a therapeutic concentration (between 15 and 20 mcg/mL) that achieves a steady-state before the administration of the fourth dose. Therefore, a vancomycin trough must be timed just prior to the fourth dose to ensure that a therapeutic steady-state has been achieved. It is important for any medical facility to implement a system to determine whether medications are within their therapeutic window to reduce the risk of such complications.

OBJECTIVE:

To improve quality of care by increasing the percentage of appropriately timed vancomycin troughs through nursing education and the institution of a vancomycin order-set.

METHODS:

Data was collected through retrospective chart review of patients admitted to George Washington University Hospital who received greater than 4 doses of vancomycin before a trough was reported. Patients who received oral vancomycin, were dosed in the emergency department, received less than four doses, and those with an estimated GFR < 40 were excluded. Afterwards, the percentage of properly timed troughs was calculated. The interventions we plan to implement include: 1. Nursing education regarding the necessity of proper timing in obtaining vancomycin troughs and 2. An EMR order-set for ordering vancomycin along with an appropriately timed trough. Data collection and analysis will be repeated after each intervention.

RESULTS:

Data collection reveals that in the month of October 2014, 1550 doses of vancomycin were administered to 270 patients in the GWUH. Of these, 106 patients met inclusion criteria. Only 36 out of these 106 patients (34%) were identified to have appropriately timed vancomycin troughs.

CONCLUSIONS:

The initial analysis of this study has revealed that only 34% of vancomycin troughs were timed properly. This confirms that there is much need for improvement in vancomycin level monitoring at GWUH to reduce the risks of the aforementioned complications. With interventions such as nursing education and order-set implementation, we hope to improve the efficacy of antibiotic therapy at GWUH.

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Point of Care Testing in the Emergency Department

Numerous studies examine the utility and effectiveness of point of care testing (POCT) in the Emergency Department. Typical hurdles in the emergency care setting include delays of treatment, risk stratification, poor outcomes, longer lengths of stay, and crowding. All of these hurdles contribute to poor performance measures, which means there are implications for quality of care as well as overall hospital metrics. In many cases, the determining factor in plan of care and decision-making are laboratory results. Thus, the utility of tools like POCT, which offers real time results at the patient's bedside, needs to be evaluated more thoroughly. There are currently over 110 such tests available on the market and this number continues to increase. Studies have shown that accuracy of POCT results are comparable to send-down labs. The potential gains in cost, patient satisfaction, and overall quality of care warrant more robust studies of outcome measures within the ER and studies of implementation across multiple centers. Additionally, we believe that development of a use model or protocol driven approach would facilitate incorporation of POCT to limit variability and gain maximal benefits.

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Improving Utilization of CRISP (the Chesapeake Regional Information System for Patients) Among Internal Medicine Residents

BACKGROUND:

CRISP is a regional health information exchange (HIE) serving Maryland and the District of Columbia. It is a not-for-profit organization advised by a wide range of stakeholders who are responsible for healthcare throughout the region¹. Since its launch in late 2010, the number of participating organizations and users has grown significantly involving multiple health care facilities across Maryland and DC. However, CRISP might still be underutilized for various reasons. Our aim is to understand the obstacles of enrolling into CRISP and improve its utilization among George Washington University Internal Medicine residents.

METHODS:

In the period between February - May 2015, An initial introductory email which includes a simplified stepwise approach to the CRIPS enrollment process and its requirement was sent to all George Washington University Hospital (GWUH) Internal Medicine residents. The email also include a baseline brief survey that included, but not limited to, questions about whether the residents were aware of CRISP, if they signed up for it or previously used it and if it has improved their management of patients. In late May a follow up survey similar to the initial one will be sent again and the results will be compared to the initial assessment.

RESULTS:

To be determined

CONCLUSION:

To be determined

REFERENCES:

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What Do People Want From Their Healthcare? A Qualitative Study

BACKGROUND:

Existing research on the patient experience has focused on patients in the hospital and other medical settings. We seek investigate the perceptions of people who may not self-identify as being patients. This innovative approach of the "street study" aims to understand what people want from healthcare.

METHODS:

This was a cross-sectional descriptive study. The study population was adult volunteers randomly selected at four types of settings in Washington, D.C.: coffee shops, metro stops, senior centers, and community centers. Participants were asked two questions: first, to recall a positive and negative experience with healthcare and to explain the factors that made it such, and second, what can be done to most improve healthcare in the US. Data were analyzed using grounded theory methodology.

RESULTS:

Of the 51 subjects interviewed, 28 were female and 23 were male, with an age range of 20-89. To both questions, all respondents cited examples from an interaction with a doctor; 47% added information about interacting with other healthcare professionals. Of the twelve themes identified, the three most cited as being critical to their healthcare experiences are having a doctor who listens to them, who is caring and compassionate, and who explains well.

CONCLUSIONS:

Using an innovative methodology, our "street study" finds that when people are asked about their healthcare experiences, they speak about the interaction between them and their doctors. The doctor-patient relationship remains at the heart of people's perceptions of healthcare.

IMPLICATIONS:

Innovations that aim for patient-centeredness should aim to strengthen the doctor-patient relationship.

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REHABILITATION AND RECOVERY



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Level of Sedation in Outpatient Ketamine Infusions

Ketamine, an NMDA receptor antagonist, helps reduce severe debilitating neuropathic pain in patients unresponsive to conventional treatment [3,6]. Potential ketamine side effects include sedation, hallucinations, hypertension and tachycardia [2]. Bispectral Index (BIS) measures depth of anesthesia or level of sedation using information from processed EEG and computing scores ranging from 0 to 99. Scores below 60 typically correlate with general anesthesia and scores above 80 are clinically unreliable. We report the BIS values in forty-five patients undergoing ketamine infusions at subanesthetic doses in an outpatient setting. Patients underwent infusions for intractable chronic neuropathic pain or generalized pain such as fibromyalgia. Each patient underwent a 4 hour infusion on 3 consecutive days with increasing doses. BIS scores were recorded every 5 minutes and correlated significantly with nurse's sedation scores. A gender difference was observed in women having an average score of -5 then men. Average scores did not fall below 80 at any point and no serious side effects were observed demonstrating the safety of this procedure for outpatient therapy. The BIS scores did not differ significantly with dose of ketamine, the day of infusion, or the age.

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REHABILITATION AND RECOVERY



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The Coma-Near Coma Scale: An Examination of the Psychometric Properties using Rasch Analysis

BACKGROUND/OBJECTIVES:

The Coma-Near Coma (CNC) scale is a clinical observation tool that evaluates level of consciousness in patients with seriously impaired consciousness (SIC). A clinician administers the sensory stimuli to the patient and observes and then scores the quality of the patient response. The objective of this study was to examine the construct validity and reliability of the CNC in patients receiving post-acute rehabilitation.

METHODS:

Ten items, each scored with a unique 3-point rating scale, were examined in 20 patients SIC who were evaluated during the course of post-acute rehabilitation. Each patient was evaluated four times - a total of 80 data points. Rasch analysis was used to evaluate the psychometric properties of the rating scale and items.

RESULTS:

Initial analysis indicated that the rating scale fit the Rasch model and there were no misfitting items. Principal component analysis indicated that there are two dimensions with an eigenvalue of 12.5. Examination of the factor loadings suggests one dimension related to visual system and the other related to tactile system. Person separation was 2.14 and reliability 0.82 indicating that the measure is adequate but not optimal for use in patient measurement. However, 45% of person responses misfit the measurement model.

CONCLUSIONS:

The CNC is a brief, observational tool that provides a rapid assessment of SIC. Future recommendations include further examination of the dimensionality of the items and the development of a Keyform tool that will aid in clinical practice.

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REHABILITATION AND RECOVERY



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Is Ankle Dorsiflexion In Healthy Subjects Improved With Closed Chain Joint Mobilization Using A Novel Device? A Pilot Study

BACKGROUND:

Ankle dorsiflexion is necessary for a multitude of functional activities, such as squatting, walking and stair navigation. The current study assessed the reliability of a trigonometric dorsiflexion measurement method between raters with varying levels of clinical experience as well as how a new ankle dorsiflexion stretching device, the "Dorsiglider", compared to self-stretching, to increase ankle dorsiflexion (DF) ROM in healthy subjects.

METHODS:

A pre-test, post-test randomized cross over design included 26 healthy subjects (M=8, F=18, 23-34 years). The protocol included a rest period, warm up, pre-test measurement, intervention and posttest measurement. Four raters (one with 16 years of physical therapy experience and three physical therapy students) measured DF of each subject in standing using a trigonometric measurement pre and post intervention. Interventions included self-stretching alone, and static and active self-mobilization using the "Dorsiglider". One-week later subjects returned and the protocol was repeated with the alternate intervention.

RESULTS:

Intra-rater and Inter-rater reliability of measurement of fibular length and angular measurement of DF were calculated using interclass correlation coefficients (ICC) (2,1). Intra-rater calculations for fibular length were: rater 1 = 0.939, rater 2 = 0.911, rater 3 = 0.915, and rater 4 = 0.865. Inter-rater calculations for session one were 0.947 and session two, 0.936. Intra-rater calculations for angular measurement of DF were: rater 1 = 0.759, rater 2 = 0.632, rater 3 = 0.563, and rater 4 = 0.623. Inter-rater calculations for session one were 0.887 and session two, 0.857. Test retest average for all raters for angular measurement DF was reported as ICC (2,k) 0.816 with the MDC = 3.32 degrees.

A paired t-test was used to calculate the mean difference in DF between the two interventions. A mean difference of 0.446 degrees in favor of the Dorsiglider with a 95% CI of (-0.244193,1.135154); p-value = 0.1954.

CONCLUSION:

Practice and standardization of measurement may have resulted in observed excellent test re-test reliability of fibular length. Fibular length was one component of the angular measurement of DF using a trigonometric measurement. The second component of the angular measurement was performed by measuring the distance from the head of the fibula to a perpendicular rod bisecting the lateral malleolus of the same ankle. Although the measurement was standardized we believe increased practice would result in improved outcomes; angular measurements of DF showed moderate test-retest reliability between a clinician with 16 years of experience and 3 physical therapy students.

There was no significant difference observed between the two interventions in young healthy subjects. The Dorsiglider proved to have no negative or harmful effects in 26 healthy subjects. Future studies should examine the effects of the Dorsiglider on participants with pathological DF ROM limitations.

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Quit4baby: Results from a pilot test of a mobile smoking cessation program for pregnant women

BACKGROUND:

Text messaging programs have been shown to be effective in helping adult smokers quit smoking. This study describes the results of a pilot test of Quit4baby, a smoking cessation text messaging program for pregnant smokers that was adapted from Text2quit.

OBJECTIVE:

The study aimed to demonstrate the feasibility and acceptability of Quit4baby for women currently enrolled in Text4baby, a perinatal health text messaging program.

METHODS:

Pregnant women enrolled in Text4baby and who were current smokers or had quit within the last 4 weeks (N=20) were enrolled in Quit4baby. Those under age 18, not pregnant, not current smokers, those using nicotine replacement therapy and those not interested in participating were ineligible. Participants were surveyed at baseline and at 2 and 4 weeks post-enrollment.

RESULTS:

Most participants responded to the program favorably. Highly rated aspects included the content of the program, skills taught within the program, and encouragement and social support provided by the program. Participants reported that the program was helpful in quitting, that the program gave good ideas on quitting, and that they would recommend the program to a friend. Suggestions for improvement included increasing the message dose and making the quitpal more interactive.

CONCLUSIONS:

The pilot test provides support for the feasibility and acceptability of Quit4baby. Future studies are needed to assess whether Quit4baby is effective for pregnancy smoking cessation.

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Effects of maturation on cerebral carbon dioxide vasoreactivity in very low birth weight infants

BACKGROUND:

Changes in carbon dioxide (CO₂) are known to change cerebral blood flow. Data are limited for the influence of maturation on cerebral CO₂ vasoreactivity (CVR-CO₂) in premature infants.

OBJECTIVE:

To characterize the role of maturation on CVR-CO₂ using simultaneous transcutaneous continuous CO₂ (tcCO₂) monitoring and cerebral near infra-red spectroscopy (NIRS).

METHOD:

Very low birth infants (<1500 grams and ≤ 34 weeks gestational age [GA]) without major congenital anomalies, admitted to the George Washington University Hospital neonatal intensive care unit, were enrolled in a prospective observational study. Simultaneous tcCO₂ and NIRS recordings were made over 12 hours at three time points (i) 1st week of life; (ii) 2nd week of life; and (iii) pre-discharge. CVR-CO₂ is quantified as the coherence between tcCO₂ and cerebral HbT (HbO₂ + Hb, i.e. oxygenated + deoxygenated hemoglobin). Data were partitioned into 2 hours epochs with a sliding window of 30 minutes to allow quantification of slow changes. In each epoch, spectral coherence (degree of concordance) was calculated between tcCO₂ and HbT signals. When coherence exceeded a predefined statistical threshold, spectral gain (DHbT/mmHgD tcCO₂) was calculated.

RESULTS:

We studied 72 patients with GA = 28.1±2.4 (mean±SD) weeks, and birth weight 1035 ± 291 g. Less than half of these patients needed invasive respiratory support (33 received conventional ventilation and 12 also received high frequency oscillation). IVH/PVL were diagnosed by cranial US in 16 patients (22.2%) and 2 patients died. All but 3 subjects showed at least one epoch with significant coherence. When epochs with significant coherence were studied, there was positive correlation between postmenstrual age (PMA) and spectral gain ($r= 0.19$, $p= 0.004$). This correlation continued to be significant after controlling for GA.

CONCLUSION:

In very low birth weight infants, CVR-CO₂ increases with advancing PMA. The role of reduced CVR-CO₂ reactivity in those brain lesions commonly occurring in the smallest VLBI warrants further study.

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Relation between EEG spectral power and cerebral tissue oxygenation in very low birth weight infants

BACKGROUND:

Spectral analysis is a standard technique used for quantifying EEG at different frequency bands. The development of EEG spectral power in preterm infants has been described. However there are limited data on the relation of changes in spectral power with changes in cerebral oxygenation.

OBJECTIVE:

To examine the relation between spectral power of EEG and cerebral tissue oxygen saturation (SctO₂) measured by near infra-red spectroscopy (NIRS).

METHODS:

A prospective study was conducted on VLBW infants (<1500 grams and ≤ 34 weeks gestation), admitted to the George Washington University Hospital NICU. Simultaneous continuous 2-channel EEG and NIRS were applied for 12 hours in first week of life, at 2 weeks and before discharge. C3-C4 EEG channel was used for analysis and periods of artifacts were visually identified and removed from further analysis. Sum of the spectral power of the following bands: delta (0.5-3.5Hz), theta (4-7.5Hz), alpha (8-13.5Hz), beta (14-30Hz) and total (0.5-40Hz), and relative power for each band have been calculated; average SctO₂ from corresponding NIRS has been calculated and was examined against changes in relative spectral power of different EEG bands.

RESULTS:

We examined 70 simultaneous EEG and NIRS collected from forty eight patients (gestational age (GA) = 28.3 ± 2.3 weeks, and birth weight (BW) = 1083 ± 287 g, median postmenstrual age 33.3 ± 3 weeks; 25 (52.1%) males and 25 (52.1%) black). They stayed in the NICU for 85 ± 92 days, all survived, but 11 had a degree of IVH. At time of recording 50% of patients were in room air and only one was on invasive ventilation. When EEG total power and relative powers were compared to changes in SctO₂, only relative power of delta band showed significant negative correlation with SctO₂ (r = -0.244 p = 0.048).

CONCLUSION:

Changes in EEG spectral power is associated with changes in cerebral oxygenation in very low birth weight infants. Further studies are needed to evaluate this association in presence of evidence of brain injury.

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Caretakers' Perspectives on Return Emergency Department Visits

BACKGROUND:

Approximately 5% of pediatric patients return to the Emergency Department (ED) within 72 hours of initial evaluation. Several studies have reported the reasons for returns based on chart reviews, but few have evaluated returns from a family-centered perspective.

OBJECTIVE:

The goal of this study was to quantify reasons for return visits from the caretaker perspective.

DESIGN/METHODS:

Based on themes identified in two caretaker focus groups, we designed a survey to quantify reasons for return visits from a larger cohort. Surveys were administered June-August 2013 to a convenience sample (when research staff was available). Caretakers were excluded from participation if the return visit was unrelated to the initial visit or the child was asked to return.

RESULTS:

Of the 305 caretakers eligible, 92 (30%) were approached, of whom 83 (90%) participated. Children were a median age of 3.3 years (range 6 weeks to 18 years). The most common diagnosis categories were respiratory diseases (n=15, 18%), systemic states (n=14, 17%), trauma (n=14, 17%), gastrointestinal diseases (n=10, 12%), and ENT, dental, and mouth diseases (n=10, 12%). Caretakers returned because their child was still sick (n=76, 92%), they didn't understand their child's illness (n=48, 59%), they were unable to see their child's pediatrician (n=37, 45%), and/or they were dissatisfied with medical care at the first visit (n=25, 31%). In reference to the initial visit, caretakers felt too little testing was performed (n=45, 55%), too few medications were prescribed (n=32, 41%), physicians spent too little time with their child (n=32, 39%), and too little information was provided (n=23, 28%). Of the 76 (93%) caretakers who read the discharge paperwork, 55 (72%) found it helpful and 8 (11%) found it confusing or hard to understand. A total of 16 (19%) children were seen by their pediatrician between ED visits. Of the 36 (45%) children who were prescribed a medication at the initial visit, 28 (78%) were taking the medication at the return visit.

CONCLUSION:

From the caretaker's perspective, the most common reasons for return ED visits include failures in health literacy, inability to follow-up, and dissatisfaction with the initial visit. Several of these are within the locus of control of the ED and several could be addressed by improving regional healthcare coordination. These data will be used to prioritize strategies to address the perceived need for return visits.

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Vulvar Vestibulectomy for Provoked Vestibulodynia: A Retrospective Case-Control Study

INTRODUCTION:

Since its first description by Woodruff in 1981, a vulvar vestibulectomy has been the surgical method of treatment for women with provoked vestibulodynia (PVD), formerly known as vulvar vestibulitis. Over 40 peer-reviewed papers have assessed the efficacy of the surgery, with the vast majority demonstrating a success rate of at least 80%. Despite this, several studies have suggested remission of PVD over time in the absence of surgery.^{1,2}

AIMS:

The goal of this research was to determine if patients who underwent vulvar vestibulectomy for treatment of neuroproliferative vestibulodynia (NPPVD) experienced less vulvar pain, dyspareunia and sexual dysfunction over time than women with NPPVD who opted out of surgical treatment.

METHODS:

Using a patient database from a center specializing in vulvovaginal disorders, 227 women with NPPVD who were diagnosed over a year prior and who had failed conservative nonsurgical treatment, were identified. A diagnostic algorithm designed by the authors was used to diagnose women with NPPVD. Patients with NPPVD were then given the option to undergo vulvar vestibulectomy. Of the 227 patients, 101 women elected surgical treatment while 126 opted for conservation therapies or declined all treatment. All 227 women were emailed a link to an electronic survey which posed questions pertaining to their treatment decision-making, current symptoms and sexual satisfaction. In addition, if they previously declined to have surgery, they were prompted to answer questions about the efficacy of treatments, if any, that they have undergone since diagnosis.

RESULTS:

Ninety-three of the 227 NPPVD patients contacted completed the survey. Of these 93 women, 42 women had undergone surgery, while 51 did not. Women who did not have surgery were more likely to report persistent vulvar burning (69%, $Z = -3.42$, $p = 0.001$), vulvar rawness (52%, $Z = -2.05$, $p = 0.04$), and vulvar cutting (29%, $Z = -2.33$, $p = 0.019$) as compared to women who underwent vestibulectomy (32.7%, 30.6%, 10.2% respectively). Only 2 of the 42 women (4.76%) who did not have surgery reported a remission of their vulvar pain. In contrast, 77% of women who had a vulvar vestibulectomy reported at least a 75% reduction of their pain. Women who did not have the vestibulectomy had more sexual dysfunction as measured by the FSFI ($M = 28.60$, $SD = 16.50$, $p = 0.02$) as compared to women who underwent vestibulectomy ($M = 19.67$, $SD = 16.96$, $p = 0.02$). Women who did not have the vestibulectomy reported fewer average episodes of intercourse each month ($M = 3.92$, $SD = 4.50$) as compared to women who had the vestibulectomy ($M = 10.3$, $SD = 5.93$) $p < 0.001$. Seventy-eight percent of the women who had the surgery were retrospectively pleased with their decision, 10% were unhappy with their decision, and 12% were unsure. In contrast, only 30% of the women who opted not to have surgery were happy with their decision, 58% were ambivalent about their decision not to have surgery, and 12% were unhappy that they had not chosen to have surgery.

CONCLUSIONS:

Despite inherent limitations of retrospective case-controlled studies such as reporting bias and the relatively small sample size, this study provides support that women diagnosed with NPVVD who undergo vulvar vestibulectomy report a reduction in pain and sexual dysfunction as compared to women with NPPVD who do not undergo surgery. These findings support the recommendation to offer surgery for the treatment of NPPVD, as outlined in the published diagnostic algorithm.³

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Risk factors for cesarean delivery among teenagers and non-teenagers

OBJECTIVE:

The objective of this study is to investigate if risk factors for cesarean delivery differ between teenagers and non-teenagers.

STUDY DESIGN:

We analyzed all term singleton births to primiparous women aged greater than 13 with a known mode of delivery in the 2013 CDC Natality data file. The sample was stratified by teen (age 13-19) and non-teen (age greater than 19). Univariate analysis was conducted to determine risk factors for cesarean delivery for both groups. We studied potential predictors of cesarean delivery in four domains: demographic characteristics, utilization of prenatal care, maternal medical risk factors, and fetal and labor characteristics. Chi-squared testing was used to identify risk factors that were significantly associated with cesarean delivery rate. Odds ratios were calculated for variables found to have a significant association with cesarean delivery.

RESULTS:

Among the 1,129,124 births in the sample, there were 182,461 births to women aged 13-19 and 946,663 births to women older than 19. The cesarean delivery rate was significantly lower for teens than non-teens (20.0% vs 30.5%, $p < 0.001$). Among demographic risk factors, race, maternal education, residency status, and payment status were all significantly associated with cesarean delivery rate for both teens and non-teens ($p < 0.001$). Marital status was not significantly associated with mode of delivery. On measures of prenatal care utilization, month of initiation of prenatal care was significantly associated with cesarean delivery rate for both teens and non-teens ($p < 0.001$), however the length of time between the last prenatal visit and delivery was a significant risk factor only for non-teens (teens: $p = 0.428$, non-teens: $p < 0.001$). Maternal medical risk factors including pre-pregnancy BMI, weight gain during pregnancy, pre-gestational hypertension, gestational hypertension, eclampsia, and diabetes were all significantly associated with a higher cesarean delivery rate for both groups ($p < 0.001$). Maternal pre-pregnancy smoking was associated with increased risk for cesarean delivery among both teens and non-teens (teens: $p = 0.002$, non-teens: $p < 0.001$), while smoking during pregnancy was a significant risk factor only for teens (teens: $p = 0.005$, non-teens: $p < 0.126$). Labor and fetal characteristics associated with mode of delivery included gestational age, induction and augmentation of labor, chorioamnionitis, fetal position, and birth weight.

CONCLUSIONS:

There are multiple risk factors for cesarean delivery. These risk factors appear similar between teens and non-teens. These findings may be useful in patient counseling and targeting interventions to reduce cesarean delivery rates.

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Body Mass Index, Gestational Weight Gain and Angiogenic Biomarker Profiles as a Proxy for Preeclampsia Risk

BACKGROUND:

Studies have independently demonstrated adipose tissue stimulation of angiogenesis and the association between lower pro-angiogenic biomarkers and increasing preeclampsia risk.

OBJECTIVE:

We evaluated whether overweight/obese (OW-OB) women compared to underweight/normal-weight women (UW-NW), and women with excessive gestational weight gain (EG) compared to women with inadequate/appropriate gestational weight gain (I-AG), would have altered angiogenic biomarker profiles.

DESIGN/METHODS:

This was a secondary analysis of a prospective study investigating angiogenic biomarkers and preeclampsia risk. Subjects with multiple gestations or hypertensive disease of pregnancy were excluded due to known significant aberrations in angiogenic biomarker profiles. Body mass index (BMI) measurements were used to categorize subjects into OW-OB (BMI \geq 25) and UW-NW (BMI < 25) categories. Gestational weight gain adherence categories (EG, I-AG) were based upon the 2009 Institute of Medicine (IOM) recommendations for underweight, normal weight, overweight and obese pregnant women to gain 28-40, 25-35, 15-25 and 11-20 pounds, respectively. Soluble fms-like tyrosine kinase-1 (sFlt1), soluble endoglin (sEng), placental growth factor (PlGF) and ratio of angiogenic activity ([sFlt1+sEng]/PlGF) were measured by ELISA. Comparisons between BMI groups at each gestational age window (window 1 = 22-26 weeks, window 2 = 27-30 weeks, window 3 = 31-37 weeks) were then calculated on log-transformed biomarker variables with Wilcoxon rank sum tests. These comparisons were repeated for gestational weight gain adherence categories.

RESULTS/DISCUSSION:

The analysis included 397 subjects. There was no significant difference between UW-NW versus OW-OB nor EG versus I-AG on gestational age at delivery, smoking and preeclampsia history. But there were significant differences in race, chronic hypertension, diabetes and having no living children. Analyzing the angiogenic biomarker profiles, the pro-angiogenic marker PlGF showed the most significant differences. It was significantly lower in OW-OB versus UW-NW in all three windows ($p < 0.05$). In EG versus I-AG, PlGF was significantly higher in window 2 ($p=0.002$). The anti-angiogenic markers (sFlt1, sEng) had only one significant difference each; sFlt1 in window 2 with EG being lower ($p=0.04$) and sEng in window 3 with OW-OB being higher ($p=0.03$). The ratio of angiogenic activity showed less pro-angiogenic activity in OW-OB versus UW-NW and more pro-angiogenic activity in EG versus I-AG. These results suggest that when assessing preeclampsia risk in women with a single gestation and no hypertensive disease of pregnancy, high BMI may be more predictive than the 2009 IOM gestational weight gain recommendations.

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Comparison of methods of morcellation: Manual versus power

OBJECTIVE:

To compare surgical outcomes of manual versus power morcellation.

MATERIAL AND METHODS:

Retrospective chart review of 274 patients who underwent a minimally invasive (laparoscopic or robotic) myomectomy or hysterectomy, between August 1, 2011 and June 30, 2014, requiring morcellation for tissue extraction. All procedures were performed by one of three minimally invasive gynecologic surgeons at a single urban teaching hospital. Surgical outcomes were compared between the 3 following approaches: power morcellation (167/274, 60.9%), manual morcellation through ancillary port enlargement (minilap) (75/274, 27.3%) and manual morcellation through the vagina (32/274, 11.6%). Primary outcome variable was operative time. Secondary outcomes were estimated intra-operative blood loss, length of hospital stay, change in peri-operative hemoglobin and peri-operative complications. Multiple linear regression models were used to control for surgeon, patient demographics (age, BMI, and parity), type of surgery (robotic vs. traditional laparoscopy), fibroid burden, uterine weight and hysterectomy type (total vs. subtotal).

RESULTS:

Indications for surgery, history of prior abdominal surgery, history of endometriosis and intraoperative findings in the 3 arms were comparable. No differences were noted between the 3 groups in terms of change in pre- and post-operative hematocrit, EBL and rate of intra-operative complications. Manual mini-laparotomy morcellation when compared to power morcellation, was associated with decreased length of stay after myomectomy (0.24 days [95% CI -0.09, 0.57] versus 0.88 days [95% CI 0.67, 1.09]; $p=0.0025$) and faster operative time during hysterectomy, (131.8 min [95% CI 110.6, 152.9] versus 179.9 min [95% CI 164.2, 195.7]; $p=0.0016$). On the other hand, a higher rate of post-operative complications was noted in the vaginal compared to the power morcellation group (RR = 5.35 [95% CI: 1.03, 27.78]; $p=0.0458$) with the majority of these complications related to vaginal cuff and pelvic infections. Further stratification by type of hysterectomy showed that the rate of post-operative infections among only total hysterectomy cases was not greater in the vaginal morcellation group compared to MMM group (RR = 1.35 [95% CI: 0.15, 11.91]; $p=0.7842$).

CONCLUSION:

Manual morcellation via mini-laparotomy compared to power morcellation is associated with shorter operative time during hysterectomies and shorter hospital stay after myomectomies. Vaginal morcellation might be associated with a higher incidence of cuff and pelvic infections when compared to power morcellation.

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2012 Consensus Pap Test Guideline: Women's Perceptions and Expectations

INTRODUCTION:

The 2012 consensus cervical cancer screening guidelines recommend longer intervals between Papanicolaou (pap) testing. We sought to evaluate the knowledge and attitudes of women regarding the purpose and frequency of pap test screening.

METHODS:

A 13-question anonymous survey was available to patients 18 years and older who presented for obstetrical or gynecological care. Survey topics included familiarity with the 2012 consensus screening guidelines, knowledge of cervical cancer, and attitudes towards screening frequency.

RESULTS:

Data from 149 patients was included for analysis, with a response rate of 41%. Participants were primarily age 20-29 (45%) or 30-39 (38%), Caucasian (52%) or African American (27%), and had completed at least a Bachelor's degree (80%). More than 89% of participants identified pap tests as a screening test for cervical cancer and 83% named Human Papillomavirus as the cause of cervical cancer. The correct screening intervals for patients age 21-29 were selected by 20% of respondents, and 9% selected the appropriate screening interval for patients age 30 and above. Overall, 43% were uncomfortable with lengthening screening intervals and 41% would prefer a yearly pap test. However, 70% believed that additional education would increase their comfort with less frequent pap tests.

CONCLUSIONS:

Our population was knowledgeable about the purpose of pap test screening and the cause of cervical cancer. Most women were unaware of the appropriate frequency for pap tests and many felt uncomfortable with increased screening intervals. Further education regarding timing of pap tests is necessary to improve women's comfort with the consensus guidelines.

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A Systematic Observation of Health Promotion Communication within the National Park Service

PURPOSE:

As domestic morbidity and mortality rates soar, public health practitioners and policy makers must look to new and more effective strategies to promote health and prevent disease. Nature contact provides a wealth of physiological, psychological and social health benefits. The National Park Service (NPS) has recognized its critical role in promoting health within the park system through its Healthy Parks, Healthy People (HPHP) initiative. It is important to monitor the progress of HPHP plan implementation in the short term so as to avoid missing an opportunity to reach millions of visitors over the next several years in the midst of unpredictable funding streams and budget constraints. This study measures whether basic steps are being taken to communicate a health promotion message to an NPS visitor population in the state of Virginia in keeping with the HPHP initiative. The parks, a beloved American institution, provide space for physical activity, community, ecological preservation, spiritual restoration, and healing.

METHODS:

Using a secret shopper approach, a systematic observation of 20 out of a total of 34 national park units in Virginia, was conducted between the months of August and November 2014. Data collection occurred on site and in person. Variables included park ranger awareness of HPHP and health promotion messaging in park brochures, introductory videos, and exhibits.

RESULTS:

Quantitative findings revealed statistically significant relationships between 1) park size and visitor spending levels and 2) presence of walking or hiking trails and ranger awareness of HPHP. Qualitative results showed compelling health promotion methods at Booker T. Washington National Monument and Shenandoah National Park.

CONCLUSION:

The American public cannot be described as healthy. New and more effective health promotion strategies and supports are essential to reverse disease trends and restore health, healing and well-being to women, children and families. Each year millions of visitors enjoy trips to national parks, signifying an opportunity to remind them, directly or indirectly, of the inherent health benefits of outdoor recreation. A systematic observation of a sample of national park units in Virginia has revealed gaps in health communication and HPHP program diffusion, suggesting channels to more effectively advance health promotion goals within the national park system.

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High prevalence of urinary tract infections among women in rural Malawi

BACKGROUND:

Nearly 250 million people worldwide have schistosomiasis, a neglected tropical infection caused by parasites of the *Schistosoma* genus. In women, *Schistosoma* eggs lead to inflammation, granuloma formation, ulceration and bleeding in the sites where they are deposited in the bladder, urethra and throughout the genital tract. Blockages and impeded urine flow from urinary schistosomiasis granulomas could make schistosomiasis-infected women more likely to develop bacterial urinary tract infections (UTIs), compared to women who do not have schistosomiasis. This study aims to establish the prevalences of, and correlation between, urinary schistosomiasis and bacterial UTIs in the Bwenzi La Thanzi ('Healthy Friend') study, a convenience sample of 200 women presenting for care at a rural health clinic in central Malawi.

METHODS:

Eligible women are those 18-50, non-pregnant or currently menstruating, Chichewa speaking, Lilongwe district residents who were seeking care for any of a broad range of genitourinary symptoms. Urinary schistosomiasis was diagnosed by urine microscopy. Genital schistosomiasis was assessed through colposcopic examination. UTIs were diagnosed by macroscopic urinalysis and urine culture.

RESULTS:

Recruitment began in January 2015 and to date 44 participants have enrolled. Recruitment will continue until 200 patients have enrolled. Participants' median age is 36 years (interquartile range (IQR): 30-39 years). Overall, 59% of women were using a modern method of contraception. Most participants (86%) are married and women reported a median of 4 children (IQR: 3-5 children). After urinating most participants (84%) cleanse and dry using only their petticoats. To date, 3 women (7%) have been diagnosed with genital schistosomiasis via colposcopy, although no woman has been positive for *Schistosoma haematobium* on urine microscopy. UTIs are very common: 50% of participants had urine cultures positive for at least one pathogenic bacterial species, including *Escherichia coli*, Group D streptococcus, *Staphylococcus saprophyticus*, *Citrobacter freundii*, Coagulase-negative staphylococcus, and *Proteus mirabilis*. Of the 3 women with genital schistosomiasis, one also had a UTI diagnosed by culture but not by dipstick, one was UTI negative, and urine culture results from the third are pending. We also identified multiple other infections among participants, including 7% who were HIV-positive, 10% with trichomoniasis, 7% with gonorrhea, and 37% with seroprevalent herpes simplex virus type 2.

CONCLUSIONS:

UTIs appear to be highly-prevalent in this sample of care-seeking women in rural Malawi. Whether an association exists between genital schistosomiasis and increased UTI prevalence will be assessed when the full study sample has been enrolled.

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Umbilical Cord Care and Related Cultural Beliefs in Haiti: A Mixed Method Study of Haitian Maternity Care Providers

Current research shows that delayed cord clamping is associated with an increase of 30% to 50% of additional blood volume in term and preterm babies respectively. Waiting to clamp the cord can increase newborn hemoglobin levels, and reduce infant anemia at four to six months in term infants; as well as decrease the incidence of intraventricular hemorrhage, need for transfusion and incidence of necrotizing enterocolitis in preterm infants. Three studies from India, Mexico and Peru have shown a pronounced benefit to delayed cord clamping (DCC) when the mother herself is anemic. In Haiti, over 60% of women are anemic. Of infants between 6 and 11 months, 63% are anemic with 44% having moderate or serious anemia. Anemia this soon after birth is a critical issue because infant brain formation is still occurring and iron stores are crucial to this process. The maternity care system in Haiti is complex. Skilled attendants are at 15% of rural births and 47% of urban births while only 36% of births in Haiti occur in an institution. A wide variety of care providers assist at births including traditional birth attendants (matrons), nurses (infirmière), direct entry midwives (auxiliaire sage femme), nurse-midwives (infirmière-sage femme), and a few physicians. Little is known about umbilical cord care in Haiti. One recent qualitative study by Walsh, Norr, Sankar and Simpsa (2015) focused on receptivity to using the World Health Organization's recommendation of dry cord care and chlorhexidine to prevent infections. Current practices and cultural beliefs demonstrated several at risk behaviors for infant infections, but willingness to change. This presentation reports on a mixed method, descriptive study of Haitian maternity care providers and their umbilical cord care practices as well as cultural beliefs related to the cord. A convenience sample of fifty matrons, nurses, infirmières, auxiliaire sage femmes, infirmière-sage femmes, and physicians were interviewed in January 2015. With respect to the potential of delayed cord clamping to prevent infant anemia, the questionnaire focused on timing of clamping of the cord as well as practitioner and parental care of the cord. Delayed cord clamping was a known practice to many of the care providers. This was significantly related to where they were trained. Beliefs varied from thinking that the baby would "bleed out" back into the mother if the cord was not cut immediately to a traditional knowing to wait to cut the cord because the baby needed the blood passed down through generations.

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The Impact of Chylothorax on Nutrition and Growth in Neonates Following Congenital Diaphragmatic Hernia Repair

Congenital diaphragmatic hernia (CDH) is a developmental abnormality characterized by lung and vascular hypoplasia that causes respiratory distress and pulmonary hypertension. Management of these infants involves respiratory stabilization, often in concert with extracorporeal membrane oxygenation (ECMO), followed by surgical repair of the diaphragmatic defect. Even with improvements in diagnosis and management, mortality with CDH remains high and survivors demonstrate striking growth deficits that are associated with early perioperative issues during the neonatal hospitalization. Research has shown high levels of metabolic distress characterized by increased whole-body protein catabolism in critically ill newborns on ECMO support, which was more marked in infants with CDH. This early nutritional insult may result in loss of lean body mass, prolonged respiratory failure, and failure to thrive. A known but uncommon post-operative complication of CDH repair is chylothorax identified by the presence of chyle in the pleural space secondary to rupture of the thoracic duct or one of its tributaries. Chylothoraces cause respiratory complications in these patients already at high risk for respiratory morbidity as a result of pulmonary hypoplasia. This study aimed to differentiate whether infants with post-operative chylothorax have worse growth and nutritional outcomes than infants with CDH without a chylothorax. An existing database of 165 newborns with CDH admitted to UCSF Benioff Children's Hospital Intensive Care Nursery from 2000-2013 was reviewed. Serial growth parameters of weight, length, and head circumference were compared between 17 infants with a chylothorax and 148 infants without this complication. Statistical methods were used to account for gestational age, birth weight, and markers of disease severity including non-primary repair of the diaphragm, history of ECMO support, and herniation of liver into the chest. Data is currently under analysis and review. These findings could ultimately impact the level and type of nutritional support provided for these critically ill newborns.

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