The Art and Science of Pediatrics

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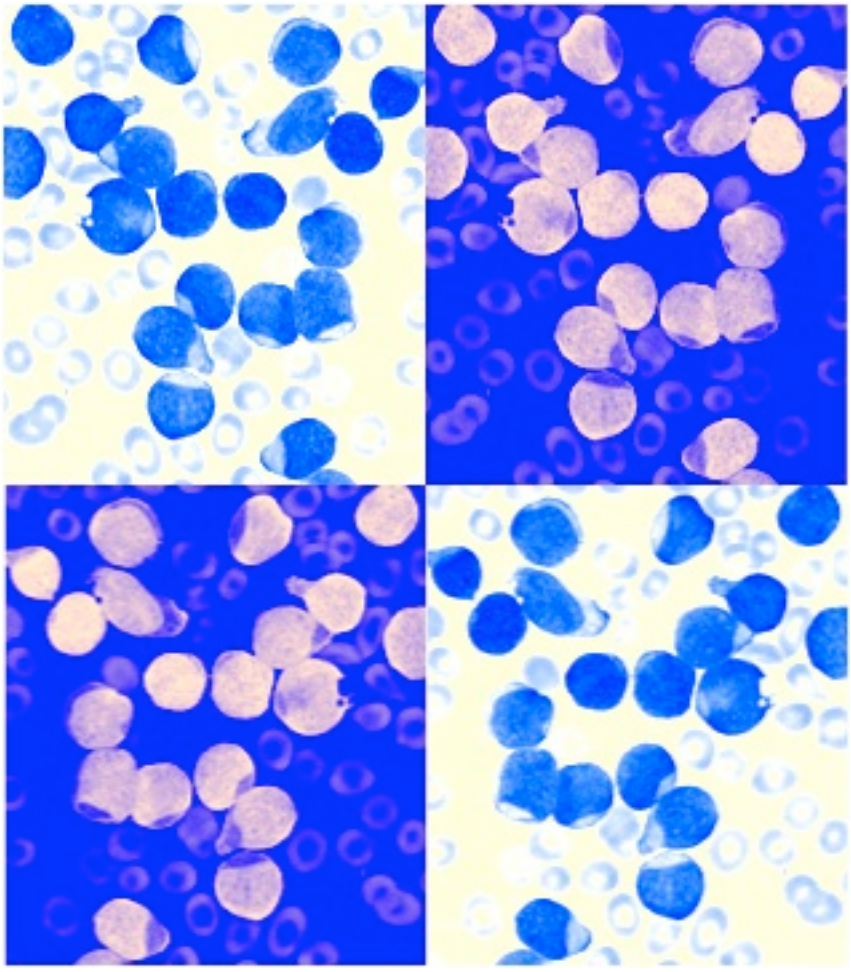

Pediatric Interest Group Weill Cornell Medical College

2011-2012

Weill Cornell Medical College

Dear Weill Cornell Medical Students and Faculty:

One measure of the quality and success of a special event lies in the support it generates in subsequent years. The reviews of all of previous Pediatric Medical Student Research Days have been overwhelmingly positive. The consensus of all in attendance at these events was that they were a tradition worth continuing.

On behalf of the Department of Pediatrics and the Pediatric Interest Group, it is a pleasure for me to welcome you to the Ninth Annual Pediatric Medical Student/Faculty Research Day. In the spirit of last year's Journal, this year's Journal, "The Art and Science of Pediatrics," contains original prose by students about their experiences in pediatrics and features on community service opportunities, as well as student, resident, fellow, and faculty research abstracts. The work presented in this journal and displayed at pediatric research day is the product of a wonderful collaboration between our medical students, residents, and faculty committed to developing the next generation of pediatric scientists. What makes this work even more special is that our students accomplished this work in spite of the tremendous demands placed on their time by medical school. We believe this exposure to research early in one's medical career is an essential first step in not only launching a successful career in investigation but also in establishing a foundation for lifelong learning for those who choose to pursue clinical medicine.

As Chairman of the Department of Pediatrics, I congratulate the students and their faculty mentors on the success of their research efforts and acknowledge the strong leadership of the Pediatric Interest Group, Alexandra M. Satty, Misha Pangasa, Sisi Zheng, and their advisors, Drs. Susanna Cunningham-Rundles and Thanakorn Jirasevijinda, on organizing and continuing this important pediatric program.

Sincerely,

Gerald M. Loughlin, M.D.
Nancy C. Paduano Professor and Chairman
Department of Pediatrics
Weill Cornell Medical College

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Cover Design by Corynn Kasap, MD/PhD Candidate
A Wright's stained bone marrow aspirate smear of patient with precursor B-cell acute lymphoblastic leukemia.
(Image source: http://en.wikipedia.org/wiki/File:Acute_leukemia-ALL.jpg)

Faculty Profiles

INTERVIEW WITH DR. THANAKORN JIRASEVIJINDA

Julia Rosenberg

Dr. Thanakorn Jirasevijinda, affectionately known as Dr. TJ, graciously took time out of his Thanksgiving break to chat with me about his roles at Cornell. As Director of Pediatric Undergraduate Medical Education at Weill Cornell, Dr. TJ interacts with most medical students early in their careers. This is no accident; Dr. TJ wears many hats at this medical institution, and many of his roles revolve around improving medical education. His primary areas of focus are clinical reasoning/evidence-based medicine, cultural competence, and service learning. Throughout our conversation, Dr. TJ made it clear that he welcomes medical students to participate in his research, clinical, and educational initiatives.

Clinical Work: Life as a Hospitalist & Burn Unit Physician

While Dr. TJ spends much of his time in administrative and teaching roles, about half of his time is devoted to being an attending. Dr. TJ works on the inpatient ward in a multidisciplinary team. He also works with the burn team to provide a comprehensive care to these patients and their families who endure many psychosocial stresses. Burn care integrates medical therapy with physical therapy, play therapy, music therapy, and Child Life, just to name a few. In addition, Dr. TJ works as a preceptor for the residents in the outpatient setting, where care is focused on health maintenance and prevention.

Many (Many!) Contributions to Medical Education

Dr. TJ clearly has a passion for medical education, as is evident from his dedication to his many roles in the medical education realm. These include both teaching and administrative responsibilities; Dr. TJ serves on the admission committee for the medical college and also sits on the clinical curriculum and global health committees.

Dr. TJ is the director of the third year pediatric rotation, and he helps coordinate subspeciality elective rotations. He serves as one of the academic advisors for students interesting in pursuing a residency in pediatrics. He is also faculty mentor for the pediatric interest group and for Camp Phoenix, a group that volunteers with and organizes a camp for pediatric burn patients.

In addition, Dr. TJ and Dr. Kevin Kelly (Department of Psychiatry), co-direct the Oates Communication Skill Curriculum. This program incorporates standardized patients and group feedback format to teach medical students to integrate clinical reasoning with communication skills: “It helps students become mature physicians who can seamlessly integrate communication skills, physician interaction, and problem-solving,” explains Dr. TJ. A similar philosophy extends to his work with the Clinical Skills Center, where students undergo the Objective Structured Clinical Examination (OSCE) throughout their four years of medical school. There, Dr. TJ helps to train standardized patients, grade student write-ups, and provide individualized feedback to students using their videotaped encounters.

This dedication to medical education expands into Dr. TJ’s research, and, in keeping with his commitment to education, he encourages interested students to contact him if they are interested in participating in the following research opportunities.

Research – a Focus on Medical Education & Health Services

Dr. TJ joined Cornell in 2007, but initially, “I went to Bronx Lebanon because I wanted a program with a focus on teaching and also a diverse and underserved population, which has always been my area of interest.” This experience, “opened [his] eyes to the health disparities as far as access, quality of care, and health outcomes.”

During this time, Dr. TJ realized that many residents, including those who have been trained or have practiced in other countries faced significant communication challenges based on culture, language, and value systems. In response to these gaps, he developed a program, called the Interactive Workshop on Communication and Cultural Sensitivity (IWOCCS), to train residents how to enhance their interactions with diverse and underserved patient populations.

Connected to cultural competence are the concepts of health literacy and shared decision-making. At Cornell, Dr. TJ has been working with fourth year medical student Brandon Greene and another faculty member in the Department of Pediatrics, Mary Jo Ward, to study these two concepts in the outpatient setting.

Global Health

Dr. TJ's commitment to underserved populations expands to work in resource poor settings worldwide. He has developed a relationship with several urban and rural hospitals and clinics in his native country of Thailand. He also has served on the global health committee here at Cornell for the past two years.

Dr. TJ spent elective time in Thailand as a medical student: "I gained a lot from that experience and I wanted to make sure that students and residents would also in some way benefit from that." Since then, he has given back to his home country by strengthening a relationship with medical schools there. When Dr. TJ visits Thailand yearly, he gives lectures and conducts workshops for faculty and students to enhance their skills in patient-physician interaction, interview preparation and scholarship projects. The sites with which he has on-going relationships include urban medical schools, affiliated hospitals in Bangkok, and a hospital in a rural/provincial town near the Northwest Thai-Burmese border serving border refugees.

"I'm happy that Cornell students have a chance to be exposed to those settings and bring back a lot of experience, knowledge, and enthusiasm to work with populations in resource poor settings."

As part of the global health committee, Dr. TJ works to foster student clinical skills in underserved settings while also ensuring that students abroad care for themselves as they cope with language issues, cultural barriers, limited resources, and potential burnout. Several second-year Weill Cornell students traveled to Thailand during the summer of 2011 under the mentorship of Dr. TJ: "He introduced me to working in the Thai healthcare system," says Edmund Chen. Caroline Miranda, adds that he, "stressed the importance of reflection and planning before, during and after involving oneself in the global health setting."

About 50% of Cornell Medical Students spend time overseas, and Dr. TJ has worked with the global health committee to ensure that the program is more rigorous, so that students have a meaningful experience abroad. There is an intimate relationship between service and scholarship, and with meaningful preparation, implementation, and reflection, the scope of students' time abroad can be expansive in terms of professional and personal growth, and future activities and research.

A Piece of Advice

Dr. TJ has quite a breadth of experience, so I asked him for advice for students who may be aspiring to follow a similar path. Much of his advice is reflected in his actions, and Dr. TJ clearly leads by example through his devotion to continuing medical education, commitment to improving care for underserved populations, and continual reflection in order to improve. He closed by advising, "Really take advantage of and try to be open-minded to every learning opportunity. The end is important, but the journey is just as valuable."

INTERVIEW WITH DR. SUJIT SHETH

Miheer Sane

Dr. Sujit Sheth, an associate attending pediatrician at New York Presbyterian Hospital, was recently appointed as the Division Chief of Pediatric Hematology/Oncology. Dr. Sheth's focus has been in hematology with particular expertise in iron metabolism, thalassemia, and sickle cell disease. Dr. Sheth was kind enough to talk with me about his path in medicine, interest in medical education, research in iron metabolism, and recent appointment.

"It was fascinating to think that one person could contribute so much to another person's well being and overall sense of wellness."

Dr Sujit Sheth had always wanted to be pediatrician, due in a large part to his interactions with his own pediatrician growing up. Dr. Sheth began his medical education at Seth G. S. Medical College in Bombay, India where he also went on to complete his residency in pediatrics. Reflecting on his education, he describes that it really was a different time. As a medical student in India 28 years ago, the infrastructure was not as well developed. He described how they had few journals and the ones they did have were six months to a year old, making access to new and current information difficult. Clinically, however, his education helped develop a holistic approach to looking at the entire child. "Learning and practicing medicine in a developing country, you saw so much related to nutritional status and infectious diseases… you had to address where the child lived, how they lived, etc." It also required him to really develop his clinical skills because he couldn't just rely on expensive tests, as they were not available. His advice for current students is to "use your clinical skills more; it makes you a more complete physician."

"Half of what I saw here, I had no way of even seeing there."

Dr. Sheth traveled to the US in 1992 to begin a fellowship in Pediatric Hematology/Oncology at Columbia University. For him, the transition was a complete culture shock. During his education in India they didn't have ICUs, so he didn't have the opportunity to care for critically ill children. "You could learn about these things, but didn't get to see them applied". Contrasting his experiences, he was also surprised by the overdependence on tests here, the underutilization of clinical skills, and the degree of defensive medicine. These findings still resonate with his practice of medicine today. Though the transition was a bit difficult, he found it to be a positive experience. He initially intended to return to India after completing his fellowship, but the research he began intrigued him, and so he stayed. He continued as an attending and researcher at Columbia for almost 15 years.

"I feel most satisfied when actually teaching people."

During his time at Columbia, Dr. Sheth was repeatedly nominated as attending of the year and received the honor in 1998 and 2010. When asked why students and residents enjoyed working with him as a teacher, he shared that he places importance on teaching people to develop a logical approach to clinical problems rather than facts to memorize, something many students would appreciate. Dr. Sheth is actively involved in education and finds it to be a highlight of his job.

"I'm a red cell and iron person… functionally, structurally, it really intrigued me."

Dr. Sheth's research has focused on determining how much iron is in a person's body, which is of concern for patients receiving blood transfusions or those with hereditary hemochromatosis. Currently this is best measured by liver biopsy, which is quite invasive. Dr. Sheth began his research under the mentorship of Dr. Gary Brittenham to develop noninvasive methods to measure tissue iron by magnetic susceptibility. He worked on the development, evaluation, and further development of newer generations of this technology. Recently he has also been studying

the effects of the age of red blood cell transfusions on iron physiology. The research is still underway, however preliminary results suggest that there is a difference in giving transfusions of fresh blood versus blood that can be up to 40 days old in terms of an inflammatory response and free radical generation. The study could have many implications for the clinical practice of transfusions.

"Its exciting- I bring a lot of energy to the job, [including] things that are very practical and useful to the department as a whole."

Regarding his recent appointment, Dr. Sheth explains that he really wasn't looking for a new position, but with no pun intended, Cornell was looking for "fresh blood". He looks forward to being able to take on more leadership and broaden his perspective. His short-term goals include making the clinical program more streamlined and efficient while in the long-term, he will be working to find what Cornell NYP does best and develop its niche within the field. It was a pleasure talking with Dr. Sheth and it will be great to see how the department of hematology/oncology will continue to develop and grow.

Student Writing

A SURPRISING PEDIATRIC EXPERIENCE ON THE OTHER CORNELL CAMPUS

Maricela Castillo

One of the unique features of the Primary Care clerkship at WCMC is that students have the opportunity to leave the Big Apple and experience community-based medicine in the small city of Ithaca. Nevertheless, when I first learned of the opportunity, I was admittedly a bit reluctant to sign up. Perhaps I had just grown accustomed to the conveniences of big city life, or maybe I envisioned Ithaca as being a bit too cold for my liking. Not being a Cornell undergrad alum myself, I failed to understand the enthusiasm that some of my friends had for their alma mater campus. Thankfully, before I dismissed the opportunity entirely, I had the chance to speak with friends who had recently completed a rotation in Ithaca. After hearing their praises, I decided to give Ithaca a chance, and thanks to Caryn Davi, I headed upstate for my Primary Care rotation.

During my six weeks in Ithaca, I had the opportunity to work in two very different practices: one at Gannett, the Cornell Student Health Clinic, and the other at Buttermilk Falls Pediatrics. While I imagine Cornell alums might view Gannett as being standard for a college health center, I was truly impressed by the facility, which far surpassed my own undergraduate experiences. One of the most striking features was the physicians' ability to obtain and apply laboratory testing immediately to clinical practice. For example, if fine crackles were heard on lung auscultation, doctors could quickly get X-rays to rule out pneumonia and discuss results with patients during the same visit. At Gannett, physicians could even perform lab tests themselves. In fact, before my Ithaca rotation, I had never seen a KOH prep for tinea. I was amazed when we collected the sample ourselves, put it on a slide, and observed it under a microscope. Although it seems ridiculous to me now, I had never before seen hyphae other than in books or slide presentations. Despite all of these great aspects of Gannett the one feature I found to be the most incredible was the mental health services available to students. Psychiatrists and counselors were available to see students on a weekly basis, and there was even a hotline students could call if they needed help in the middle of the night. Overall my time at Gannett was extremely valuable because it allowed me to see how medicine should be practiced at a student health center.

In contrast to the college student population of Gannett, Buttermilk Falls Pediatrics was the epitome of a small town pediatrics practice. I found that most appointments were well baby/child visits or sick visits for common bread-and-butter pediatric complaints such as viral respiratory infections. Often, families would bring in multiple children during a single visit so the whole family had a strong relationship with the pediatrician. Like Gannett, I was impressed with the hands-on approach to laboratory testing. For example, cultures for Group A Beta Hemolytic Strep were done in-house on Blood Agar plates and put in an incubator to be read the next day. This method was both time and cost-efficient for the practice, and gave me useful insight for the management of strep throat. In addition to working in the outpatient clinic, these doctors also managed the Pediatric Unit and Well Baby Nursery at the local hospital, Cayuga Medical Center. Every other week, we visited the hospital to examine new babies. This active involvement of private pediatricians in the hospital gave me a better appreciation for the spirit of community medicine. The health of the children in the community depended on a strong relationship with their pediatricians who played an integrated role in both outpatient and inpatient care.

As I am currently on my Pediatrics clerkship at NYPH, I am constantly finding similarities and differences between my experiences. While some differences might represent distinctions between inpatient medicine and primary care, others stem from the disparate resources between a large academic medical center and a small community hospital. My time in Ithaca has given me, a self-proclaimed city lover, a new outlook on what practicing medicine in a small town is really about and I'm quite impressed with the type of medicine I previously though was only available in a big city.

DISCOVERING HUMANISTIC MEDICINE OVERSEAS: MY EXPERIENCE AT SIRIRAJ HOSPITAL, BANGKOK, THAILAND

Edmund Chen

As far as daily commutes go, mine was fairly interesting and almost enjoyable this summer. I would leave my apartment in central Bangkok, join the mass of office workers on the streets below and grab a steamed pork bun from a street cart, the Bangkok equivalent of the ubiquitous bagel and coffee street carts that are seen everywhere on a NYC morning. From my apartment, it was a short walk to catch the Skytrain, the aboveground metro system that resembled our own 6 train above 96th street, if our 6 train was perfectly clean. After a couple of stops, I would transfer, but not onto a bus. Rather, I would jump onto a boat and head upstream to the hospital, the highlight of my commute.

Riding a boat to work was just one of the many unique aspects of my experience working at Siriraj Hospital in Bangkok, Thailand this past summer. Siriraj Hospital is the largest public hospital in Thailand, and with the help of Dr. Thanakorn Jirasevijinda, I had the opportunity to rotate through their Pediatrics department. It was an eye-opening experience; not only was this one of my first concentrated clinical experiences, but I was also observing cases that I have never seen and working in a hospital setting very different from ours. Some of my days at Siriraj began in their Pediatric Emergency Room. The pediatric emergency room only existed from 8 in the morning to 1 in the afternoon. The official, "adult" emergency room was often so crowded that from these hours, pediatric cases were shunted from the official ER to the temporary pediatric ER. This was a common theme throughout my time at Siriraj; how to deal with a constant influx of patients in the context of limited beds.

As to be expected, many of the patients in the ER had simple presentations of infection: fever for the past few days, rhinorrhea. The residents on staff would take the required culture swabs, but then rather sending the swabs down to a central lab, they would walk to the corner of the room and perform their own gram stain to identify the bacteria. I had just learned the technique of gram staining a week weeks prior in Host Defenses and had largely considered it more of a "classical" skill to learn; I could not imagine a content in a NYC hospital where I would be asked to perform by own stain. But now here I was, watching a resident drop crystal violet on a bacterial sample. Knowing the technique well, I was happy to volunteer to perform the stain.

Aside from the Emergency Room, I also worked in within the hospital wards and in their Developmental Clinic. I saw many of the cases that I had learned about in my first year; I watched an echocardiogram of a baby with Tetralogy of Fallot, comforted a young girl with acute lymphoblastic leukemia who missed her father, turned on the phototherapy lights for a baby with jaundice. At the Developmental Clinic, I evaluated a child for autism and saw the signs of Fragile X-syndrome. However, for all these cases that I recognized, there were many more that were new to me. On my very first day on the wards, I observed a 10-year boy presenting with high-grade fever for the last 40 days. His blood work was negative and his fever was unresponsive to steroids and other anti-pyretics. After exhausting all possible diagnoses, the residents settled on a diagnosis of Juvenile Idiopathic Arthritis. And of course, there were the multiple cases of children presenting with Dengue Hemorrhagic Fever. There were cases that I did not expect given my background working in a first-world healthcare system. I evaluated a spiky-haired, 5-year-old boy's developmental milestones in light of his deafness caused by his mother's Rubella infection during her pregnancy. Another child was brought in with the classic presentations of fetal alcohol syndrome. The mother felt very guilty; she was not aware of the dangers of drinking alcohol while pregnant.

Working in this environment, I learned a different side of medicine than the one that I was used to: medicine that included tropical diseases and strange parasites. Medicine that was practiced in a country without the strong public health program that we take for granted in the United States, a public health system that provides easy access to vaccines and disseminates information regarding teratogenic substances to expectant mothers. But in this context, I saw how doctors worked to overcome these challenges through their perseverance, creativity, and dedication to deliver the best healthcare they could. From medical students to fellows, everyone knew the signs and treatments for Dengue Fever immediately. The residents called upon a local organization to donate a hearing aid to the deaf, spiky-haired, friendly boy. The fellow working with the boy with fetal alcohol syndrome recommended the boy to a local speech therapist near the boy's hometown that could help the boy with his communication skills. It was extremely heartening and inspiring to see medicine practiced in this way: humanistically and personably. The experience is one that I will not easily forget.

THE MAChO LESSON

Dan Cook

It was an overcast morning, and I waited, as I had for many Saturday mornings before, at Settlement Health, a primary care institution in East Harlem devoted to providing health care to an underserved community. It was a bittersweet day: volunteers, children, and parents were gathering for the final Saturday session of Motivating Action through Community Health Outreach (MAChO). Over 30 weeks, I had seen the program exceed its own expectations, and had proudly been a part of the process. MAChO had begun just two years earlier, the endeavor of a handful of medical students at Weill Cornell to reach out to the local Harlem community, make an impact on the obesity epidemic, and limit the increases in cardiovascular disease and diabetes that has hardest hit low-income families. I began working with MAChO early in my first year of medical school. In one year, I had seen the program grow to include volunteers from Hunter College and Columbia University, reach out to more children than the year before, and begin to encourage parent participation. At a personal level, the program challenged me with a new leadership role: the opportunity and responsibility to shape the educational experience of my group of children. I was involved in developing the nutritional curriculum, teaching sessions, planning group exercise activities, and coordinating field trips. At times, it was an overwhelming amount of work. And, as the program neared its end, I began to wonder, “What have we accomplished?”

With this question in the back of my mind, we set out from Settlement Health to Cornell, leading children and parents downtown by subway. For the last session, the volunteers were holding an awards ceremony for participants at Cornell to recognize their achievement and dedication to the program. En route the children chatted and joked with each other and the volunteers. Despite the difference in ages and the schools they attended, the children, initially strangers, had become friends, looking forward to seeing each other every session. I marveled at our good fortune in the kids who joined the program, and realized that I was going to miss them. In the Cornell student lounge, we celebrated the last session with a motivational speaker who spoke about making healthy choices. I smiled to myself as the children excitedly and correctly called out answers to the questions posed to the group. While outwardly I hushed the rambunctious participants and told them to raise their hands, inwardly I was proud to witness their new understanding of nutrition and exercise and see their enthusiastic participation. After the talk, the children received certificates and gifts, and we had a healthy lunch of turkey subs on wheat rolls with water. It was satisfying to see the children's acceptance of lunch: no soda, no juice, and no chips. They understood and expected a healthy meal. After taking a few last pictures and allowing time for the kids to play with the new toys, we rounded them up to return to Settlement Health.

As we arrived back in East Harlem, the kids said goodbye to each other for the last time - for just a while, I hoped- as we had encouraged their future participation for the following year. Making sure they had each other's phone numbers, they promised to look each other up on Facebook. When the last child went home, I headed home too, reflecting on our accomplishments. In terms of our manifest goals, the program was a success. We had expanded outreach to more participants, welcomed parents, included volunteers from a variety of backgrounds and institutions. We had exposed a group of children to ideas and habits that could help them lead healthier lives. I realized, though, that the most important accomplishment of MAChO was the intangible one: we created a community, bringing together kids of different ages and schools to support each other in making good choices and striving to high achievement. I realized that the future success of MAChO, and indeed of all grassroots outreach programs like ours, would depend on the ability to cultivate this positive environment, building on and strengthening the relationships between children and volunteers to provide a strong foundation for the mission of the program. In the end, this lesson was the most unexpected and the most rewarding.

MALARIA, EDUCATION, AND NETWORK AGAINST MALARIA IN UGANDA

Margaret McGlynn (NETworkAgainstMalaria.org)

59 premature and low birth weight babies wrapped in cotton blankets are waiting to use the one functional incubator. An eight-year-old girl with a hemoglobin of 3g/dL lies listlessly on a bed. There is no blood in the hospital to give her, and her father cannot afford the USD $2.50 ride to a nearby hospital with blood. If they can't help her here, he will take her home to die. A seven-year-old girl lies unconscious, gasping for air as her lungs crack audibly from across the room. She is in a coma. After not eating for several days, her family tried to feed her. During the summer of 2011, I witnessed these cases at the pediatric acute care unit at Mulago Hospital, the largest public hospital in Uganda where treatments and diagnostics are limited due to poor funding and poverty. The only lab test I saw performed during my seven weeks was a blood smear, and that seemed to be all the physicians needed to diagnose the underlying cause of comas, anemia, and even low birth weight—malaria.

It is difficult to describe the burden that malaria places on Uganda. It accounts for 24-40% of all hospital visits, 15-20% hospital admissions. Half of hospital deaths in children are due to malaria. Parents miss days of work and income. These malaria infections result in between 4-10 million missed school days each year in Africa which means that malaria is responsible for 5-8% of all missed school days and 50% of preventable absenteeism.[1] In addition to being responsible for lost school days, malaria also impairs learning and cognition through anemia and cerebral malaria which impairs performance, and in the case of cerebral malaria causes irreversible cognitive deficits (in 16% of children who recover).[2,3,4]

One of the cases I most remember during my stay in Uganda is that of six-year-old Sarah. Her father carried her into the room, stiff and moaning, her arms clenched, eyes wide open, and her large pupils stared at nothing. What grade was she in? "P3," (third grade) her father answered. How long ago? "Three weeks." It was hard to imagine three weeks ago, this child attended third grade. Today, her Glasgow Coma Score is 3. Three weeks ago she was ok? "Yes, she was a little scared of animals, but she was okay."

"Her arms are clenched like that because of lesions in her brain." The doctor told her guilt-ridden father. They have already given her antimalarials at another hospital, so there is nothing that we can do but try to relieve her pain.

To portray Uganda through its healthcare system is not a fair representation of the country. Winston Churchill described it as the "Pearl of Africa", and after spending seven weeks where it was 85 degrees, sunny, and without humidity every day, I understand the inspiration behind Churchill's description. Uganda's recently discovered oil, as well as, "organic" produce is cause for foreign investment. Educated Ugandans are undertaking careers in finance and business. Nonetheless over 90 percent of Ugandans are "peasant farmers" and live on less than $2USD/day.

It is equally unfair to describe malaria through case reports and statistics. I first learned about the burden of malaria in Uganda when a Ugandan priest, Michael Mujule, moved to my town in Southern Illinois. Through the 70s-90s Michael built several schools prioritizing girl's educationin larger villages where boys already had access to education, and building co-ed schools in smaller villages where no schools previously existed. He was often met with resistance when he encouraged the people in rural areas to educate their girls. Truly a man a head of his time, Michel persisted despite threats because he believed girl's education is essential for Uganda's future.

When my four sisters and I met him in 2007 we asked what we could do to help with his schools. He answered, "Send malaria nets." His students miss around 60 days of school/year with malaria or perish from the illness. In 2007, my sisters and I began a nonprofit called NETwork Against Malaria. We continue to send insecticide treated nets to Uganda to protect these students.

This summer I traveled on dirt paths to villages that cannot be found on maps to distribute insecticide treated nets (ITNs). I met girls in schools and families living in 10-foot huts who benefitted from our nets sent in years past. The region where we currently distribute nets is considered a region of "very high" endemicity by the CDC, and it is also extremely poor. Refugees from Kenya, Sudan, and DR Congo live among the Internally Displaced Population from the war that ended in Northern Uganda in 2008. Because aid for war-affected individuals withdrew from the area in 2008, all the people are now "peasant farmers," making less than 2USD/day. I spoke with girls and families who had received our nets. They all said the same thing—they aren't getting malaria anymore. It is "reduced to 0 percent", keeping girls in school, helping parents escape from poverty and provide food for their children, and most importantly, preventing avoidable deaths. Most families in Uganda have lost a child, sibling, or cousin to malaria.

In the process of distributing nets, people invited me into their homes and communities. Protecting families and children that I now know makes my ITN campaign more personal. In one village, a group of children gathered and sang for me for three hours. I sat on a tree stump while they danced, taught me to dance, and I learned their names ...Koskova, Margaret, Samuel… We are in the process of raising funds to buy bed nets for these children and the knowledge that they are likely getting malaria while we wait to distribute nets is hard to cope with. We are raising funds for these children and children in 58 schools in surrounding areas, 33,345 students total.

At times, I wonder if distributing nets is enough. Can schooling really help these children help themselves? Our efforts in Uganda are currently run by two young men, Francis Banura and Jawe Emmanuel. Francis currently oversees the 33,345 students at 58 schools where we will next distribute nets, and Emmanuel is in charge of the finances for a large international aid organization. Both are extremely successful and impressive, both are from Hoima, the area where Michael Mujule originally worked. After we distributed nets one day, Michael Mujule called me to see how smoothly our mission went. In the conversation he said, "Yes, I helped pay the school fees for both Francis and Emmanuel, so they could stay in school. Francis was one of 12, and Emmanuel's father passed away." Hopefully, the students who receive our nets can stay in school and become as accomplished as these two volunteers. Perhaps one day they will return to their village and give nets to the children trying to follow in their footsteps.

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A DAY IN THE LIFE, RESEARCHING ABOUT A DAY IN THE LIFE: A GLIMPSE INTO THE LIVES OF MOTHERS AND CHILDREN IN SANTA CRUZ LA LAGUNA, GUATEMALA

Julia Rosenberg

"Buenos días Elisa. Podemos hacer unos cuestionarios hoy?"

Alex and I had just arrived at the clinic in Santa Cruz, La Laguna, Guatemala. That was no small feat. Getting to the clinic—in our small indigenous town of a few thousand individuals nestled in the mountain—involved a 20-minute trek up seemingly endless rocks and steep slopes. We were rewarded for that walk every morning with a beautiful view of the volcanic lake and bright blue skies (the clouds of the rainy season would inevitably settle in a few hours later). We also were drenched in a refreshing layer of sweat and still very out of breath from the steep hike.

Elisa, a 19-year-old from this town who liked to wear the traditional black long skirts paired with a more modern magenta T-shirt, was our translator. She looked up from weighing an infant patient and gave us a big smile. By now, she was used to helping us go from house to house in the community, translating our broken Spanish into the indigenous *K'atchiquel* language of the local Mayan community.

"*Ahorita*," she replied, as she grappled with the child to put a thermometer under his armpit. *Ahorita* technically meant "right away," but Alex and I were used to Guatemala time by now, and took a seat to wait for her. A half hour later, *cuestionarios* in hand, we headed out into the town to talk. We left the clinic to wind up footpaths further into the town, passing stray dogs, houses painted from floor to roof with propaganda for the upcoming presidential elections, and laundry basking in the fleeting morning sun on the aluminum rooftops.

The aim of our interviews was to better understand some of the nutritional habits of the women in the town, especially during pregnancy and the first few years of life. The American doctor with whom we were working felt that, by waiting too long, often until age four or so to stop breastfeeding, mothers were unknowingly depriving their children of vital nutrients and calories during critical periods of growth and development.

Alex and I had set out to obtain data to support this hypothesis and also to learn more about other aspects of maternal and infant nutrition: what did a typical daily diet consist of? How many children did they have? Did they deliver at a hospital or at home? Were they with a midwife or a nurse? Some answers had been a bit predictable; to get to the nearest hospital, one needed a lot of strength, time, and money to hike down the mountain, pay for a boat across the lake, and then pay for a car to the hospital. So it made sense that home births were the norm.

Other answers were more surprising. We learned that most women consider it normal to feed their newborns coffee within a few weeks or months of birth. We also learned the hard way to explicitly ask women not only *what* they had eaten for breakfast, nor *if* they had eaten tortillas, but simply to ask, *how many* tortillas? Without that explicit question, all women somehow universally neglected to mention 10 tortillas that accompanied their breakfast of a single egg.

We rarely entered a home; Elisa would shout a greeting in *K'atchiquel* from outside the gate, and we would wait patiently for a woman to poke her head out from behind the door, usually with an infant slung from their back in a colorful blanket and another small child hugging her legs. After Elisa's brief explanation, nearly every mother would stop what she was doing to spend a half hour chatting with us. Most of our interviews were conducted under the bright burning morning sun right in the doorway to the house. Children would run barefoot past us, and we'd only get a brief glimpse into the houses beyond those doorways.

We have many stories from our time in Santa Cruz La Laguna—many experiences were rewarding, and others were frustrating, challenging, or even scary—but, quite literally, we barely got our foot in the door during our time there. In the 7-week glimpse we had, however, we learned so much from the graciousness of the women and community members who welcomed us into their community.

MTOTO, WE'RE NOT IN KANSAS ANYMORE

Kristopher Schwebler

As I walked along the rocky, red dirt road to the hospital, I had to continue reminding myself to walk on the left side to avoid being grazed by the oncoming, overcrowded minibuses and Land Rovers whizzing by on the right. The morning air was surprisingly cool for sub-Saharan Africa during my daily commute to the Kilimanjaro Christian Medical Centre, where I was completing a two-month-long medical school elective in pediatrics. Staying to the left side of the road in this ex-British colony was something I had never experienced before, something so different from what I was used to. At the time, I had not realized how many of these constant, daily reminders I would have to give myself throughout my stay in northeastern Tanzania.

The hospital, locally known as KCMC, was located on the outskirts of the mid-sized town of Moshi, at the foot of Mt. Kilimanjaro. It was one of the nation's four tertiary referral hospitals, each of which serves a quarter of the expansive country. I chose to spend a summer here to obtain firsthand experience of what it is like to practice medicine internationally in a resource-limited setting. As a medical student, I was ready to learn. As an optimistic, liberal twenty-something, I was ready to see capacity building in action. And as a lover of travel, I was ready to experience, explore, and connect. My expectations quickly changed.

Throughout my first day, my impression of the hospital oscillated. On one hand, I was impressed by the size and comprehensiveness of the fenced-in compound, which includes a university, a medical school, and many unexpected specialty departments. However, upon closer inspection, I saw the scarcity of resources that seemed to mark every aspect of the hospital, from the open-air building that appeared more like a war bunker than a hospital to the jammed hallways filled with upsettingly ill patients. Nonetheless, I had previous knowledge about the lack of resources plaguing sub-Saharan Africa, and I was careful to avoid the colonialist mentality of judgment and paternalism as well as imperialistic "othering."

I was assigned to a pediatrician, who during rounds, took particular interest in my background and seemed dedicated to teaching. He, like most of his colleagues, had received some portion of his training in the West, and he was very interested in contrasting care in our respective countries. The room in the pediatrics department had twelve beds, and one guardian could stay with each patient. The room was made of bare concrete and had glassless windows opening to the subtropical vegetation outside. Beds were rusty. Sheets were stained and torn. And IV bags were hung from nails in the wall. The physicians and students spoke in English to each other after brief interviews with the patient conducted in Swahili. It was unlike anything I had ever experienced.

The first child I saw was terminal—renal failure; we moved on. The second child was terminal—heart failure secondary to rheumatic fever. Here we stopped for about half an hour for the next few days to review rheumatic fever, infective endocarditis, congestive heart failure, etc. For a medical student who had just finished his first year and had received a cursory overview of these pathologies, this was fascinating. However, as days progressed, I began to realize things about this second patient. She needed a heart and lung transplant. She was not going to get it. She and her mother likely had no idea what the prognosis was. They were Maasai and relied on the fortunate happenstance that another Maasai patient was present and able to translate to and from Swahili. Even then, the physicians only spoke to each other about the child's condition in English. This patient gave me the first two realizations of which I had to remind myself constantly: First, the resources and level of care to which I am accustomed are simply not available here. Antibiotics years ago or surgery now may have been able to save this girl's life. I knew I would inevitably come to this realization, but watching a young girl die slowly and painfully

personifies this fact and demonstrates its reality. Second, the level of patient self-determination, involvement and education is different in Tanzania. While initially discomforted, I tried to remember that this could be cultural and by the patients' choice, so I did not judge but rather continued to observe.

While it was an initially dismal picture, I began to see the less severe and more common cases. Most times, symptoms were the same: fever, headache, coughing, and diarrhea. Consequently, pneumonia, meningitis, malaria, and gastroenteritis were always on the differential diagnosis. HIV was always tested for and considered, as approximately 50% of patients at the hospital were HIV positive. Due either to the inability to do cultures or blood smears or to their delayed results or unreliability, it seemed that every patient was perfunctorily put on the trinity: ampicillin, gentamicin, and quinine —with luck, killing any potential bacterial infection as well as malaria. Despite the relative rarity of malaria in the area and the more likely prevalence of viral infections, this requisite combination seemed odd to my untrained eye. I did see children getting better on this regiment, however, though perhaps this was just due to rest and rehydration. Nevertheless, they did indeed recover and were discharged. With this record and no alternative methods, I again observed and learned what seemed to work here.

Though the majority of patients did recover, I saw dying children on a daily basis, as I did on my first day. While this is an unfortunate sight in every hospital in the world, what is not globally ubiquitous, however, is the commonness of countless children suffering and dying from preventable diseases. I witnessed an infant gasping for his last breaths due to a lack of early treatment of his pneumonia. I saw a pre-pubescent eighteen-year-old diabetic who was not taking insulin and a stage-four AIDS patient suffering from oral and esophageal candidiasis, Kaposi's sarcoma, and tuberculosis. I spoke with an unvaccinated child suffering from measles in isolation. I saw an infant dying of tetralogy of Fallot, which could have been cured through simple screening and surgery. Knowing that these cases could have been prevented in my country was heartbreaking.

However, in addition to these blatant and depressing results of a lack of resources, I began to see deficits in care not related to scarcity of money or supplies. For example, the lack of patient involvement and autonomy I mentioned above, in my opinion, appeared to stem from a lack of regard in many cases. Patients' pain was rarely treated, even in terminal cases. They were prodded and moved without explanation or warning. They were talked over, and rarely informed. Paradoxically, patients and their parents appeared complacent, likely never experiencing any other type of care. When asked about this treatment of patients, two residents explained to me essentially that the lack of resources makes it too difficult to continue to invest in patients. One stated that when he knows how to treat patients' illnesses but instead does not have the necessary supplies and sees the patient deteriorate and die in his care, it becomes too arduous to remain caring and interested. In truth, however, I could do no better. I was unable to communicate with the majority of patients despite my earnest effort to learn Swahili, yet this was not as large of a barrier as was the color of my skin. Everywhere I went people shouted "*Mzungu!*" the Swahili word for white person. There always seemed to be a disconnect between the Tanzanians and me, which made being part of the care team essentially unviable.

In addition, there appeared to be a lack regulation or implementation of what we in the United States take for granted. For example, I only once saw a pediatrician wash his or her hands, perhaps due to the scarcity of soap throughout the hospital. However, moving between children with probable active tuberculosis and pediatric AIDS without proper hand hygiene seems unfathomable in the United States, but I witnessed this and similar occurrences nearly daily. From an administrative or public health perspective, it seems that small changes in care, such as in hand hygiene or patient placement, would likely save many lives in locations like this. Nonetheless, as an outsider looking in at those who are actually working in the trenches, it is far

too easy to critique. In reality, I have a great deal of respect for those who choose to save lives in this environment. This experience showed me just how difficult that feat is, and I hoped to have learned ways in which global medicine can change to best serve medically disadvantaged populations.

I know I have given a bleak and perhaps discouraging illustration of what my time was like learning in a Tanzanian hospital, but my goal was to provide an honest depiction of the struggles healthcare providers, especially pediatricians, face in resource poor settings and to contrast it with my experience at home. Despite being the most demanding time in my life, I can honestly say it was well worth it. I saw cases I would have never encountered at home, and I was challenged academically and personally. I was able to resuscitate a newborn, translate for tourists, and give many silly smiles to pediatric patients, hopefully making some sort of difference during my time. To do this sort of work, however, one must continually remember that it is vastly different from practicing medicine in the United States or similarly developed countries. Financial and cultural barriers will exist. One can only remind oneself to do what one feasibly can while continuing to build capacity in an experienced, sustainable, and non-condemnatory manner—not an easy task, one which I am only learning piecemeal. And lastly, always remember to keep left.

STOPPING TRAFFIC: A MEDICAL STUDENT'S EXPOSURE TO THE ISSUE OF STATELESSNESS, AND A TRANSFORMATIVE YEAR OF WORKING WITH AT-RISK CHILDREN TO PREVENT HUMAN TRAFFICKING IN NORTHERN THAILAND

Jessica Yee

As a recognized source, transit and destination country for human trafficking, Thailand is home to 2 to 3.5 million stateless individuals, though the exact figure is impossible to measure. Most of them belong to ethnic minority groups – or hill tribes – along the border areas in Northern Thailand. Statelessness does not simply refer to a person's lack of any citizenship. It means that the individual is not recognized by any government as a citizen of any country. That she/he has no legal status to receive legal protection from any government. That she/he has had little to no access to affordable education, medical care or other social services. That she/he is denied basic rights like the right to vote, legal employment or freedom to travel. Statelessness, in so many ways, is synonymous to a cycle of life-long poverty and lack of opportunities that propagates from one generation to the next. And it leaves behinds thousands of families at extreme risks for human trafficking.

As "the northernmost city in Thailand," Mae Sai is a town located directly on the Thai-Myanmar (Burmese) border, and that was where I learned on the ground about statelessness and witnessed the devastating challenges of being stateless on children and their families through my yearlong volunteership at DEPDC. In addition to a significant stateless population made up by more than 10 ethnic minorities, Mae Sai sees a daily influx of Burmese migrants from all over the border areas in Burma in search of better economic opportunities and freedom from the political and social oppression. Most arrived as undocumented migrants with no means to apply for eligibility and no social protection. Meanwhile, thousands of children are born each year in Thai hospitals to stateless ethnic minority and migrant parents, unwanted and unrecognized by any government. From birth, these children are denied rights to education, medical care or any other social welfare. Stand over at the border for ten minutes, and you are bound to see Burmese children as young as 5 years old climbing agilely over dangerously high fences and platforms to cross the border illegally, only to beg on the streets for food and change from the more affluent Thai and foreigners.

This is precisely this group of children from a mixture of ethnic minority and migrant backgrounds that are hit hardest by their statelessness, and are at the highest risk of falling into the hands of unscrupulous traffickers. Without intervention, there is a substantial chance that poverty and the denial of basic rights like education, healthcare or legal employment would one day send them to a brothel, or a sweatshop, or an illegal fishing boat.

That is why grassroots NGOs like the Development and Education Programme for Daughters and Communities (DEPDC), where I volunteered, play an extremely vital role in preventing those highly vulnerable populations – especially children and young women – from entering modern slavery through providing basic services like education, awareness raising and advocacy. Since its establishment by Ajarn Sompop[†] in 1989, DEPDC runs a free Half Day School that provides basic primary education to stateless and migrant children, a Community Learning Centre that is open to all members of community to learn basic literacy and computer skills, a variety of vocational training classes to arm young women and children marketable skill sets, a 24-hour Child Help Life to encourage reporting of families and children at imminent risks, among other programs. More importantly, as a grassroots NGO run by local community members, DEPDC is trusted to tackle with the more insidious and ingrained challenge of changing the local community's mindset on a long recognized but never unacknowledged taboo of human trafficking through holding community-wide awareness workshops and involving the next generation to join the fight through different youth empowerment programs. After all, who are in a better position to

talk about statelessness issues and human trafficking to at-risk children and youth than their fellow peers?

For the entire year at DEPDC, I learned about sustainable community engagement and development from a team of directors and administrators who have fought for the rights of the voiceless for over two decades. I worked closely with the local staff to develop capacity-building programming that would improve and update project management skills. I spent months learning about every detail of each of the DEPDC initiatives in order to target appropriate grants and channels for fundraising. I corresponded closely with the various international donors and partners of DEPDC to make new proposals and programming. I served as the visitor coordinator who introduced visitors near and far to the philosophy and work of DEPDC. I helped with event planning at the community and other special projects such as designing exhibitions on human trafficking. I even became a weekly DJ on the Child Voice Radio, a DEPDC initiative that broadcasts messages of human trafficking awareness and prevention along the Thai-Burmese border in seven languages and dialects. The learning curve was steep as I explored the different aspects of non-profit management; but the process was fun as I dusted off and exercised areas of my brain that had lain dormant in the previous three years.

Yet, every time when I felt like I had contributed something to the well-being of the children and the communities there, I was humbled instead by just how much more I received from each and everyone around me and how generously they taught me, this ignorant foreigner, about their work, their stories, their issues. From the directors of DEPDC, who freely shared with me their in-depth experience in community organization and development based on their decades-long combat against child exploitation. From the teachers at the Half Day School, who showed me what true dedication was when many times their work mandated tireless, long hours with little pay (not to mention the occasional threats they received from traffickers and corruptions by local authorities). From the youth leaders trained by DEPDC, who, even at their young age (late teens and early twenties), shouldered up the responsibility of organizing and educating their fellow peers in communities across borders on the dangers of sex trafficking and domestic violence. And, perhaps most importantly of all, from the stateless and migrant families and children served by DEPDC, whose resilience to the many hardships rendered by their lack of citizenship and government protection never ceased to humble me. Whose generosity in opening their homes and sharing their food as well as their life stories with me was all the more evident by the meanness of their circumstances.

The sobering fact is that, for every child that DEPDC has rescued or prevented from exploitation, dozens and hundreds more stateless children remain at high risk of abuse and trafficking, not only in Thailand but around the world. My time at DEPDC has allowed me to glance but at the tip of the iceberg that is statelessness. It is a global humanitarian issue, whether the group in question is the Rohingya refugees in Bangladesh, the Roma in Europe, the Dalit in Nepal, the Mauritanians or the Nubian Kenyans in Africa. Without more support of local NGOs like DEPDC, the advocacy of agencies and organizations from the international communities, and real, timely cooperation from the governments, those 15 million people without a nation to call their own will continue to have their most basic human rights denied, and continue to suffer from the thin disguises of human traffickers with false promises of a better livelihood that would never come for the children.

My time with DEPDC was an eye-opening journey of personal growth, a humbling experience that teaches me the most hands-on nature of community development work and grassroots non-profit operation. Interestingly enough, just when I was removed from the daily clinical context of medical studies to volunteer in the field, I was reminded everyday of the very reasons that first drew me to medicine – the desire to help, to be involved with my community, and to advocate

with the less privileged. I might not have my stethoscope with me at the time, but I was never surer of my choice of profession.

Last but not least, I hope to take this opportunity to encourage my fellow medical students to consider international volunteerism as an option for a leave of absence. I had always known since college that I wanted to volunteer overseas for a humanitarian cause, and I cannot express how grateful I feel to have finally experienced it in time before residency. Finally, for those of you who are interested to find out more about DEPDC, I encourage you to visit their homepage at www.depdc.org. Better yet, follow the many amazing activities and programs at their frequently updated blog at www.depdcblog.wordpress.com. Even a small donation will go a long way to supporting the programming at DEPDC that directly benefits hundreds of stateless children and youth. Or help us spread the messages, and lend your voice for those without one.

† A four-time Nobel Peace Prize nominee. “Ajarn” is the respectful form of address in Thai equivalent to “Professor.”

Acknowledge

I salute all the staff, youth leaders and volunteers at DEPDC, as well as humanitarian workers across the globe, for their tireless efforts and dedication to see to the welfare and the safety of those in dire need, sometimes at great personal risks and sacrifices. I also thank Dr. Thanakorn Jirasevajinda for his mentorship and guidance, as well as fellow volunteer Sarah McCormick for revision support of an earlier draft.

In a Burmese border village during a home visit of an ethnic minority child who attends school for free at DEPDC. Such visits are vital in establishing communication with the family and the community, and ensuring the safety of the children.

Medical Student Abstracts

A DESCRIPTIVE ANALYSIS OF THE SLEEP PATTERNS OF SCHOOLCHILDREN AND ADOLESCENTS IN QATAR

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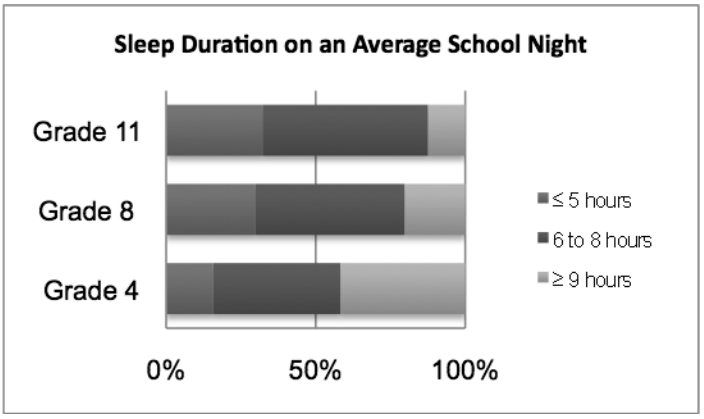
Background: Insufficient sleep is associated with a number of chronic illnesses such as diabetes, cardiovascular disease, obesity, and depression. Not getting enough sleep may also complicate the management and outcome of these diseases. Children between the ages of 5 and 10 years need 10 to 11 hours of sleep per night, whereas, adolescents need 8.5 to 9.5 hours. In 2010, a nationwide study done by the Centre of Disease Control and Prevention (CDC) reported that only 30.9% of high school students had 8 or more hours of sleep on an average school night. There is insufficient data regarding this topic in Qatar. Our objective is to describe the sleep patterns among schoolchildren and adolescents (9-18 years) in independent schools in Qatar.

Methodology: This cross sectional study was conducted in governmental (Independent) schools selected by the Supreme Council of Education in Qatar. Participants were sampled from schools managed by the Ministry of Education of Qatar using a multi-stage random selection with clusters being school type (primary, preparatory, secondary), grade, class section and gender of students. Validated questionnaires were used to gather information about sleeping hours as well as nutritional and physical activity behaviors and BMI.. Ethical boards approvals as well as Parental permission and student's assent were obtained.

Results: Data was collected from 19 schools (7 elementary, 6 middle and 6 high schools). A total of 480 children and 1,333 adolescents were enrolled. Our results show that on an average school night: a) among Grade 4, 15.7% sleep ≤5 hours, 42.6% sleep 6-8 hours and 41.7% sleep ≥9 hours, b) among Grade 8, 29.7% sleep ≤5 hours, 50.1% sleep 6-8 hours and 20.2% sleep ≥9 hours, c) among Grade 11, 32.2% sleep ≤5 hours, 55.4% sleep 6-8 hours and 12.4% sleep ≥9 hours.



Conclusion: Most of the schoolchildren and adolescents sleep between 6 and 8 hours on an average school night. Compared to Grade 4, a greater percentage of Grade 8 and Grade 11 students sleep less than or equal to 5 hours. Actually only 12.4% of high school adolescents sleep ≥ 9 hours. This pilot study highlights the need for a larger scale study to further evaluate the sleeping habits of schoolchildren and adolescents in Qatar and increase awareness in the community of the importance of healthy sleep habits.

Acknowledgement: QNRF and UREP fund

N-3 POLYUNSATURATED FATTY ACIDS INHIBIT INFLAMMATORY CYTOKINE RESPONSE TO LPS IN THP-1 DERIVED MACROPHAGES AND NEONATAL CORD BLOOD MONONUCLEAR CELLS

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Background: Emerging evidence indicates that n-3 polyunsaturated fatty acids (PUFAs) such as docosahexanoic acid (DHA) and eicosapentaenoic acid (EPA) are beneficial in chronic and acute disease states. In contrast to n-6 fatty acid arachidonic acid (AA), which gives rise to proinflammatory eicosanoids, when n-3 PUFAs are incorporated into inflammatory cell phospholipids instead of AA, inflammation is reduced. EPA and DHA inhibit AA metabolism, produce a different set of eicosanoids (e.g. PGE3)), with lower potency and lipid mediators called resolvins that have anti-inflammatory and inflammation resolving properties. Preterm and critically ill neonates are prone to serious morbidities such as bronchopulmonary dysplasia (BPD) and cerebral palsy (CP) in which inflammation from chorioamnionitis or other causes such as ventilator trauma or late onset sepsis plays a key pathogenetic role. The objective of this study is to examine the potential anti-inflammatory effect of n-3 fatty acids on neonatal immune cells.

Methods: Healthy term and pre-term (<36 wks gestational age) neonates delivered at the New York Presbyterian Hospital–Weill Cornell Medical Center, New York, NY eligible for the study were enrolled. Cord blood samples from 20 subjects were collected within 12 hours. Mononuclear cells were isolated by density gradient centrifugation, pre-treated with DHA and then stimulated with lipopolysaccharide LPS. Supernatants were collected/frozen until analysis. We also studied the effect of DHA treatment at 25 or 12.5μL after LPS stimulation for 20 minutes at 37ºC in 5% CO2. DHA and then followed by incubation with DHA for an additional 1 hour after which they were spun and supernatants frozen at -80ºC until analysis. Cytokine analysis was performed using the MSD Human Pro-inflammatory 7 multiplex assay to assess TNF-alpha, IL-1beta, IL-6, IL-8, IL-10, IL-12, and IFN-gamma using the Weill Cornell Clinical & Translational Sciences Center Core Laboratory. Analysis was preformed one-way ANOVA (GraphPad Prism).

Results: DHA Pretreatment: TNF-alpha, IL-1beta, IL-6, and IL-8 were produced in response to LPS. IL-8 response to LPS was reduced by the 25μM dose of DHA but not by12.5μM. Both DHA doses inhibited IL-6, TNF-alpha, and IL-1beta response. Post-treatment: When LPS was used to stimulate cells before DHA was added, significant inhibition of TNF-alpha, IL-1beta, IL-6, and IL-8 response was still evident. Dose dependent inhibition was observed and was greater with 25μM of DHA for all cytokines.

Conclusions: These experiments show that n-3 PUFA are potent inhibitors of cytokine response to LPS in neonatal cells. We observed dose dependent effects when DHA was given in advance of LPS. Therapeutic benefit would require treatment with DHA after encounter with LPS (endotoxin). We evaluated the effect of DHA after LPS pretreatment. This is the first study to demonstrate a protective anti-inflammatory effect of n-3 PUFA in neonatal immune cells.

A RADIOGRAPHIC STUDY OF THE OSSIFICATION OF THE POSTERIOR WALL OF THE ACETABULUM: IMPLICATIONS FOR THE CHARACTERIZATION AND TREATMENT OF FAI RIM LESIONS IN CHILDREN AND ADOLESCENTS

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Objectives: Both open and arthroscopic techniques for treatment of femoroacetabular impingement (FAI) have been described and current research has begun to validate their utility and safety in children and adolescents. Proximal and global acetabular retroversion has been largely implicated as a cause of femoroacetabular impingement (FAI). The ossification pattern of the posterior wall of the acetabulum (PWA) however is not well described. Several radiographic parameters (eg. crossover sign, posterior wall sign) are assessed in pelvic radiographs during evaluation for FAI, however without an understanding of the ossification of the posterior wall retroversion may not be adequately determined by plain x-ray or CT. The purpose of this study is to characterize the radiographic ossification pattern of the PWA, and determine when existing radiographic parameters may be assessed and treatment initiated.

Methods:180 MRI studies performed in patients 4 to 15 years old were evaluated. Studies were excluded if patients carried diagnoses that would affect physeal growth. MRI sequences (including physeal- specific sequences) and corresponding plain radiography were evaluated by an attending radiologist to characterize ossification of the PWA and triradiate cartilage (TRC).

Results: Ossification of the PWA followed a specific and predictable pattern. At age 7, the central ossification center of the PWA begins to ossify, followed by a discrete posterior rim area of calcification noted on MRI and plain radiography peaking at age 12, followed by fusion of all posterior wall centers to the pelvis. Complete posterior fusion took place by age 13 in a vast majority of subjects, followed by closure of the TRC (Figure 1). On average, males' PWA fused 1- 1.5 years after females'.

THE PREVALENCE OF OBESITY AMONGST SCHOOL CHILDREN AND ADOLESCENTS IN QATAR

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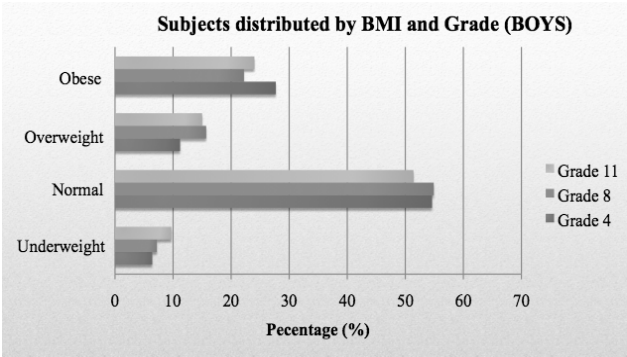
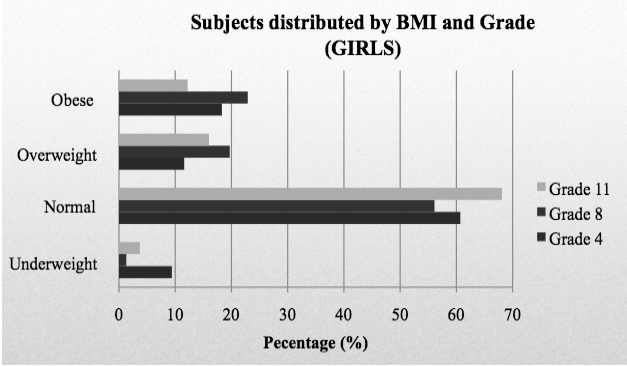
Undergraduate Research Experience Program (UREP) Grant.

Background: There has been a great increase in the worldwide prevalence of childhood and adolescent overweight, obesity and secondary diseases such as diabetes mellitus type II in recent years. Since childhood and adolescent obesity are risk factors for obesity in adulthood, an emphasis on raising awareness earlier in life is of upmost importance. However, there is insufficient data regarding this topic in Qatar and the gulf region. Our objective is to assess obesity prevalence among schoolchildren and adolescents (6-18 years) in independent schools in Qatar.

Methods: This cross sectional study was conducted in independent schools selected by the Supreme Education Council of Qatar. Participants were sampled using multi-stage random selection including school type (primary, preparatory, secondary), grade, class section and gender of students. Two validated questionnaires were adopted from the School Physical Activity and Nutrition (SPAN) project at University of Texas and translated to Arabic (one for grade 4 & one for grade 8 & 11). Height and weight were measured using a portable stadiometer using standard protocols.

Results: Data was collected from 19 schools (7 elementary, 6 middle and 6 high schools). A total of 480 children and 1,333 adolescents were enrolled. Height and weight were measured, and body mass index (BMI) was calculated using Center for Disease Control (CDC) guidelines. Overall prevalence of obesity among: a) Grade 4 was 23.3% (27.7% boys and 18.3% girls), b) Grade 8 was 22.4%, (22.2% boys and 22.9% girls), and c) Grade 11 was 17.5% (24% boys and 12.2% girls). Grade 4 and 11 boys were (1.7 and 2.6 times respectively) more likely to be obese than girls while in grade 8, no statistically significant difference among genders was found. The rates of obesity for grades 4 and 8 (23.3% and 22.4%, respectively) were higher than the American rate of 16.9% for children between the ages of 2 to 19 years by National Health and Nutrition Examination Survey (NHANES).





Conclusions: There is a high prevalence of obesity amongst Qatar schoolchildren and adolescent, boys more than girls. Overall, 1 in every 3 Qatari children is either obese or overweight. This pilot study highlights the need for a larger scale study to further evaluate obesity among children and adolescents and start concrete interventions including student and parental education.

PERCEIVED FRIEND AND PEER SMOKING, AND DIRECT AND INDIRECT REFUSAL SKILLS AS PREDICTORS OF CIGARETTE SMOKING IN US AND JAPANESE MIDDLE SCHOOL STUDENTS

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Background: Tobacco use is a leading cause of preventable morbidity and mortality worldwide. In Japan, the smoking rate in adult males (38%) is nearly double that of US men (22%). An understanding of the psychosocial factors that contribute to smoking risk within each culture is crucial to the development of effective prevention strategies. Furthermore, since most tobacco users begin smoking as teenagers, it is essential to develop prevention strategies that target youth. In prior US studies, high perceived friend and peer smoking prevalence, and poor smoking refusal skills have been identified as potential risk factors for youth tobacco use. The present study assessed the relationship between these factors and rates of tobacco use in US and Japanese middle school students.

Methods: US (n=539) and Japanese (n=644) 12-14 year olds completed surveys regarding tobacco use, perceptions of friend and peer smoking, and their own likelihood of using five smoking refusal skills. Prevalence of tobacco use was compared between groups using Fisher's exact test, while the relationship between risk factors and tobacco use was tested using logistic regression.

Results: US youth were more likely than Japanese youth to report lifetime or monthly tobacco use. Rates of weekly smoking were similar in the two populations. Japanese tobacco users (27.8%) were more likely than US users (6.9%) to smoke a pack of cigarettes (20) or more per week. US 12 and 13 year olds were more likely than same-age Japanese participants to report that any of their friends ($p<.05$) or peers ($p<.001$) use tobacco. High perceived friend and peer smoking prevalence significantly predicted smoking, especially among males: US OR=58.26 (7.55, 449.44), Japan OR=34.76 (4.26, 283.72). Older Japanese males tended to be less likely than younger Japanese males to report that they would use refusal skills, while the opposite trend was evident in US males. The use of direct refusal skills (e.g., "saying no") predicted less lifetime tobacco use, particularly in the Japanese sample, OR=22.00 (5.88, 82.37). The use of indirect refusal skills (e.g., "changing the subject") was not significantly associated with tobacco use.

Conclusions: Higher perceived prevalence of friend and peer smoking in US teenagers may contribute to the earlier onset of experimental smoking compared to Japanese teenagers. The use of direct refusal skills appears to be more protective than indirect refusal skills among both US and Japanese youth. In Japanese boys, higher rates of heavy smoking and decreased refusal skill use in older age groups may contribute to increased rates of smoking during adulthood.

MISSING THE MARK? CONSISTENCIES AND DISCREPANCIES BETWEEN PEDIATRIC PROVIDER AND PARENT PERCEPTIONS OF HEALTH LITERACY AND SHARED DECISION-MAKING

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Background: Low health literacy (HL) has been found to correlate with poor health outcomes. Ability of physicians to work effectively with patients requires understanding of HL, cultural competence (CC), and shared decision-making (SDM). To date, there is little literature on the discrepancy between perceptions of HL, CC, and SDM in pediatric providers and their patients.

Objective: (1) Measure HL in parents of children in an urban pediatric practice; (2) Assess parent perceptions of resident skills in HL/CC/SDM; (3) Evaluate differences between resident and parent perceptions in HL/CC/SDM.

Design/Methods: We administered an anonymous survey to a convenience sample of 200 caregivers in an urban pediatric practice at a tertiary care hospital. The survey, in English and Spanish, included Newest Vital Sign (NVS) to measure caregiver HL, and questions to assess parental perceptions of resident skills in HL, CC and SDM. Pediatric residents (n=30) completed the same survey online, from the perspective of the average patient in their practices. Analyses compared resident and caregiver responses.

Results:

Parent Report vs. Resident Estimate

Parameter	Parent	Resident
Education (years)	12.3±0.2 (range=3-doctoral)	11.9± 0.4 (range=5-15)
NVS Score	2.5±0.13 (range=0-6; mode=1)	2.2±0.3 (range=0-5; mode=2)
Used teachback	37%	89%
Used visual aids	26%	89%
Asked re CAM use	8%	39%
Used professional interpreter	61%	100%

Caregiver characteristics: age=30.6±0.6 years; education=12.3±0.2 years; 88% Medicaid eligible; 75% English-speaking; 98% child's biological parent. Residents accurately estimated the mean level of education achieved by the parents (11.9±0.4). They also accurately estimated their HL. The mean HL score as measured using the NVS tool was 2.5±0.13 (range=0-6); mean resident estimate was 2.2±0.3 (range=0-5). There was also a high concordance (>95%) between parent reported and resident self-perception of SDM: provider gave options for care, elicited concerns and fears, provided mutually acceptable solutions when conflicts arose. However, residents overestimated their use of HL/CC strategies: teachback—resident 89% vs. parent 37%; query about CAM use—resident 39% vs. parent 8%; use of visual aids—resident 89% vs. parent 26%; use of professional translator—resident 100% vs. parent 61%.

Conclusions: Residents accurately estimated their SDM skills, the education level of the average parent, as well as their HL, but underestimated the large range of NVS scores. Residents overestimated their use of standard HL/CC techniques such as teachback, use of visual aids, CAM, and use of professional interpreters.

NEED FOR EARLY INTERVENTION IN CHILDHOOD OBESITY: RESULTS FROM THE MOTIVATING ACTION THROUGH COMMUNITY HEALTH OUTREACH (MAChO) SUMMER PROGRAM

Pending

NEED FOR EARLY INTERVENTION IN CHILDHOOD OBESITY: RESULTS FROM THE MOTIVATING ACTION THROUGH COMMUNITY HEALTH OUTREACH (MAChO) SUMMER PROGRAM

Pending

INTERMITTENT OBSTRUCTIVE HYDROCEPHALUS SECONDARY TO THIRD VENTRICULAR CYSTS

J. Bryan Iorgulescu, Konstantinos Margetis, Joshua Marcus, Mark M. Souweidane

Introduction: Mass lesions within the 3rd ventricle have long been postulated to present a risk for intermittent CSF obstruction. This phenomenon, however, has seldom been documented with an imaging correlate. Further, no feature of these lesions that might predict this behavior has been previously defined.

Methods: The clinical features, radiographic evidence, treatments, & outcomes were reviewed for two patients with lesions in the third ventricle.

Results: Two patients presented with paroxysmal symptoms of raised intracranial pressure & imaging confirmation of varying ventriculomegaly. The patients, 9 year-old & 3 month-old males, both had a third ventricular cystic lesion - confirmed as a pineal & choroid plexus cyst, respectively. Both were treated by a primary endoscopic cyst fenestration & remain without symptoms at 3 & 0.5 months of follow-up. Neither patient required a secondary procedure or placement of an indwelling shunt.

Discussion: Intermittent occlusion has been theorized as being secondary to lesion mobilization at the 3rd ventricle's ependymal surface. The unifying characteristic in this limited series is the cystic nature of the mass lesion, a feature that may contribute to the pathological basis for this rare clinical syndrome. Our cases add toevidence that a normal-sized ventricular system cannot rule out the diagnosis of intermittent hydrocephalus in a symptomatic patient who has a lesion that can potentially obstruct CSF flow. Our findings suggest that patients with symptoms of raised intracranial pressure that have third ventricular cystic masses & normal sized ventricles, should be offered cyst decompression.

SINGLE AGENT CARBOPLATIN VERSUS CARBOPLATIN-VINCRISTINE IN PEDIATRIC LOW-GRADE GLIOMA PATIENTS

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[1]Weill Cornell Medical College, [2]Memorial Sloan-Kettering Cancer Center

Background: Combination therapy with carboplatin and vincristine is a regimen frequently used in the treatment of pediatric low-grade glioma (LGG) patients when surgery and/or radiotherapy are not possible or have failed. Carboplatin-vincristine therapy provides disease stabilization for long-term survival with moderate toxicity. Vincristine has a well described toxicity profile commonly causing neuropathic side effects. Symptoms may include poor gait, foot drop, ptosis and other cranial neuropathies, parasthesia of the extremities, and numbness. While not all children receiving vincristine develop adverse toxicities, those who do can frequently suffer long standing and functionally compromising disabilities. These patients must have the vincristine dose either reduced until the neuropathy is tolerated or completely discontinued in order to prevent long-term toxicity. Because of this response to vincristine, a carboplatin-only regimen would be desired and in some centers, including MSKCC, has often been implemented. The objective of this study is to address the possible efficacy of such a carboplatin-only treatment option. This study reports the results of a comparison of progression and survival rates in pediatric LGG patients who received the unaltered carboplatin-vincristine regimen to those who had vincristine dose reduction due to an adverse neurotoxic reaction.

Methods: Patient data was culled from the pediatric neuro-oncologic patient database of 259 patients. Eligible patients were diagnosed with pediatric low-grade gliomas – specific eligible diagnoses included juvenile pilocytic astrocytomas (WHO grade I), WHO grade II astrocytomas, optic pathway gliomas, oligodendrogliomas, and low grade ganglioglial tumors. Patients were followed at MSKCC by the pediatric neuro-oncology team and treated with carboplatin and vincristine on or as per the Children's Oncology Group protocol A9952. To eliminate the possibility of chemotherapy resistance complicating the results of this study, patients were censored if they had received any prior chemotherapy.

Documented patient data included start and end dates of the regimen, date of vincristine dose modification, total dosage of vincristine received, date of diagnosis, dates of other therapies, tumor response at the end of carboplatin-vincristine treatment, date of disease progression, and most recent follow-up appointment. Lengths of time were rounded to the nearest month.

Surgical procedures were divided into the following categories as reported by post-surgical CT or MRI: biopsy, tumor removal of less than 10%; gross total resection (GTR), no visible tumor left at the time of surgery; subtotal resection (STR), removal of 10% or greater of the tumor mass.

Standard tumor response criteria as per the COG A9952 protocol were followed. The length of progression-free survival for carboplatin-vincristine therapy was measured from the date of patient diagnosis to the date of progressive disease after the start of the COG A9952 regimen. Percent of vincristine received was determined by considering the expected amount of vincristine administration according to COG A9952 up until regimen discontinuation, completion, or present as the full complement and comparing this amount to the actual total dosage of vincristine received over treatment. Distributions of event-free survival were estimated using the technique of Kaplan and Meier.

Results: Patient data for 21 children with LGG on COG A9952 was collected. The median age at diagnosis was 35.7 months (range, 7-123 months). Five patients (24%) had physical

characteristics of NF-1, and 17 patients (81%) had juvenile pilocytic astrocytomas with the majority being optic pathway gliomas. Eleven patients (52%) had surgery prior to initiation of carboplatin-vincristine therapy with no children receiving prior chemotherapy or radiotherapy. Twelve patients had a SD, 1 patient had a MR, 5 patients had a PR, 1 patient had a CR, and 2 patients had PD on treatment. Objective responses (MR + PR + CR) were observed in 7 children (33%), and disease stabilization (SD + MR + PR + CR) occurred in 19 children (90%). In follow-up, 7 children (33%) have yet to have any progressive disease and 1 patient died (5%) following multiple therapies.

Nine children (43%) had their vincristine dose reduced or discontinued because of neurotoxic effects. The remaining twelve children (57%) received the full complement of vincristine or had the entire regimen halted early due to progressive disease, but never had vincristine administration altered prior. Toxicities most frequently observed in those having reduction or discontinuation of vincristine included foot drop in 4 children (19%), gait abnormalities in 5 children (24%), ptosis in 3 children (14%), and parasthesia/peripheral neuropathies in 3 children (14%). The mean percent of total vincristine dosage received in children who had dose reduction/discontinuation was 56%. Five of the 9 children (56%) with vincristine dose alteration received >50% of the total expected vincristine complement, and 4 children (44%) received <50% of the total complement.

The event-free survival rate at 5 years was 65 ± 7.6% for children with vincristine reduction/ discontinuation in comparison to 44 ± 6.3% for children without vincristine dose alteration (P=0.579). 7 children (4 with vincristine reduction/discontinuation and 3 without) are progression-free survivors a median of 21 mos. since completing treatment.

Chemotherapy administration was trackable in 19 of 21 children in the study (91%) with the 2 non-trackable having had received the full COG A9952 regimen at another center. Patients who had vincristine reduction/discontinuation had treatment held an average of 3.6 weeks during the entire 60 week COG A9952 regimen in comparison to patients without vincristine dose alteration having treatment held an average of 11.1 weeks.

Conclusions: The results in this retrospective chart study of 21 children with low-grade gliomas treated initially with carboplatin-vincristine demonstrate that a carboplatin-only regimen will provide at least the same efficacy in stabilizing the disease. Patients who had their vincristine reduced or discontinued during treatment had a greater 5 year event-free survival rate at 65% in comparison to those who had no vincristine modifications during therapy at 44%. As indicated, the high p=0.579 for the 5 year event-free survival show that these two survivals are relatively the same over a larger population. In such case, the removal of vincristine from therapy, especially in children with adverse toxicities, is warranted in that it has no statistical benefit towards the patient's survival.

The total length in which therapy was held (due to toxicities or myelosuppression) was determined in order to assure that the similar event-free survivals for the two groups was not due to decreased dose intensity. The results show less weeks of treatment held (3.6 weeks) in patients who had vincristine reduced/discontinued in comparison to those who had no vincristine modification (11.1 weeks). As such, the carboplatin dose intensity was even greater for those patients with vincristine reduced/discontinued. In the future, single-agent carboplatin therapy should be further investigated as a treatment option for pediatric LGGs.

POSTNATAL EFFECTS OF MATERNALLY-ADMINISTERED FETAL THERAPY FOR NEONATAL ALLOIMMUNE THROMBOCYTOPENIA (NAIT)

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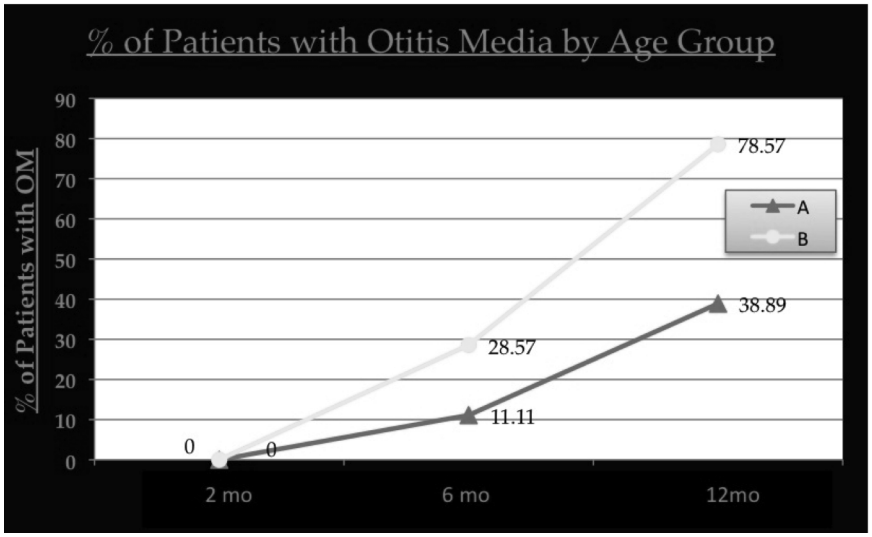
Background: AIT stems from maternal antibodies against paternally-derived fetal platelet antigens causing thrombocytopenia and, in 10-20% of cases, intracranial hemorrhage (ICH). Antenatal therapy often increases fetal platelet counts and prevents ICH.

Objective: To follow infants treated as fetuses from 0-12 months of age.

Design/Methods: The ongoing study randomized 96 maternal-fetal pairs to receive maternally-administered IV gammaglobulin (IVIG) 2g/kg/wk (Group A) OR IVIG 1g/kg/wk + prednisone 0.5 mg/kg/d (Group B) starting at 22.8 weeks of gestation on average. Pediatric follow-up questionnaires were sent to pediatricians.

Results: Thus far, results were obtained in 18/51 Group A and 14/45 Group B children. There were no significant differences in growth parameters and platelet counts at 2, 6 and 12 months between the groups. Mean height and weight were >25th-50th percentiles at 2, 6 and 12 months. Mean head circumference fell within the 10th-25th percentiles at 2 months and the 25th–75th percentiles at 6 and 12 months. Mean platelet counts were 458, 414, and 415 (Group A) and 476, 452, and 431 (Group B) at 2, 6 and 12 months, respectively. More cases of otitis media (OM) infections occurred in Group B (27 cases) than Group A (12 cases, p=0.02); most occurred at 6-12 months (Group B:20 cases, 78% affected; Group A:10 cases, 39% affected, p=0.008).



Group B had more cases of OM on average (1.93/y) than Group A (0.65/y). Group B tended to have a higher incidence of bronchiolitis (Group A:2 cases, Group B:6 cases; p=0.09), but a lower incidence of gastroenteritis (Group A:6 cases, 33%; Group B:1 case, 7%, p=0.08).

Conclusions: Preliminary results of this 1-year follow-up of antenatally-treated AIT patients demonstrate no differences in growth parameters (all normal) and platelet counts among either treatment arm. Group B (prednisone-treated) children had an increased incidence of otitis media and possibly bronchiolitis but not gastroenteritis. We anticipate at least doubling the data and obtaining IgG levels to amplify these results.

THE EFFECT OF ELTROMBOPAG ON PLATELET RESISTANCE TO APOPTOSIS: THE ROLE OF THE Bcl-xL PATHWAY

W. Beau Mitchell, Michele N Edison, Mariana P Pinheiro, Nayla Boulad, Bethan Psaila, Marissa Karpoff, David Kaplan, Benjamin T Kile, Michael J White, Emma C Josefsson, and James B. Bussel

INTRODUCTION: Immune thrombocytopenia (ITP) is typically characterized by increased platelet destruction and reduced platelet production. Eltrombopag and Romiplostim are thrombopoietin receptor (TPO-R) agonists that are known to increase platelet counts in patients with ITP by stimulating thrombopoiesis. Platelets also express TPO-R on their surface, but it is unknown whether the thrombopoietin mimetics (TPO-M) have a direct effect on the circulating platelets. Although controversial, in a very small number of ITP patients, TPO-M agents may increase platelet counts in 2-5 days, earlier than would be expected from de novo megakaryocytopoiesis. Platelet survival is hypothesized to be mediated by two molecular intermediates in an apoptotic pathway, Bcl-xL and Bak. Bcl-xL/Bak protein expression in megakaryocytes is regulated in part by TPO-mediated activation of Akt pathways through Jak2 and Stat5. We hypothesized that an increase in platelet count in the first week of treatment might be mediated by TPO-R signaling, resulting in decreased platelet apoptosis. This study explored whether Eltrombopag or Romiplostim treatment has anti-apoptotic effects on platelets of patients with ITP.

METHODS: Following a treatment wash out period, 75 mg of Eltrombopag once daily or 10 mcg/kg weekly of Romiplostim was initiated for 2 weeks. Blood counts were measured on days 1, 3, 5, 8, 10, 12, and 15. Platelet function and survival was assessed on days 1, 8, and 15 by: immature platelet fraction (IPF), glycocalicin index, Bcl-xL inhibitor (ABT-737) assay, measurement of Bcl-xL by western blot, measurement of several members of the Bcl-xL Akt mediated, apoptotic pathway by flow cytometry (FACS), bleeding score, measurement of thrombin-anti-thrombin complexes (TATs), and quantification of microparticles.

RESULTS: Eight of 10 patients responded to treatment with Eltrombopag with a platelet count ≥ 50,000/μL, and 6 of the 8 responders at least doubled their counts during the 2 weeks of treatment. All 3 patients treated with Romiplostim responded with platelet count ≥ 50,000/μL. In both treatment groups there was a significant increase in median platelet count ($p<0.001$), median large platelet count ($p<0.01$), and median absolute IPF (A-IPF, $p<0.01$), while there was no significant change in median % IPF. The dose of ABT-737 required to kill half of the platelets in the sample (IC50) in the Eltrombopag group was lower in patients at day 1 than in non-ITP controls, and there was an increase in resistance to apoptosis between days 1 and 8, but these changes did not reach statistical significance. Between days 8 and 15 the IC50 declined to pre-treatment levels. In the Romiplostim group there was no significant difference in IC50 between the control and the patients over the 2 weeks of study. There was no significant correlation between the platelet counts and the IC50 values. FACS analysis of members of the AKT signal transduction pathway revealed increased activation of each of the markers between days 1 and 8, followed by a decrease between days 8 and 15. The levels of Bcl-xL and phosphor-AKT(308) decreased from day 1 to day 15. The other lab tests are pending.

DISCUSSION: Because the A-IPF increased by less than the platelet increase and because the lifespan of the A-IPF is not known, it is unclear if the platelet count increase is solely a result of increased platelet production. Platelet lifespan may be enhanced by Eltrombopag treatment as there was a parallel albeit transient increase in AKT activation markers and platelet apoptosis resistance in the Eltrombopag group. Treatment with Romiplostim did not appear to affect apoptosis resistance although it did result in transient AKT activation. Our data suggest that platelets are more resistant to apoptosis when the levels of anti-apoptotic factors (eg. PTEN,

Phospho-GSK3β) involved in the AKT/Bcl-xL pathway are greatest despite a concomitant increase in pro-apoptotic factors (eg. Bak, Bax). Since both the increased AKT activation and apoptotic resistance returned to baseline at day 15, megakaryocytes and platelets already present at the start of treatment may respond differently than those generated de novo in the presence of TPO mimetics.

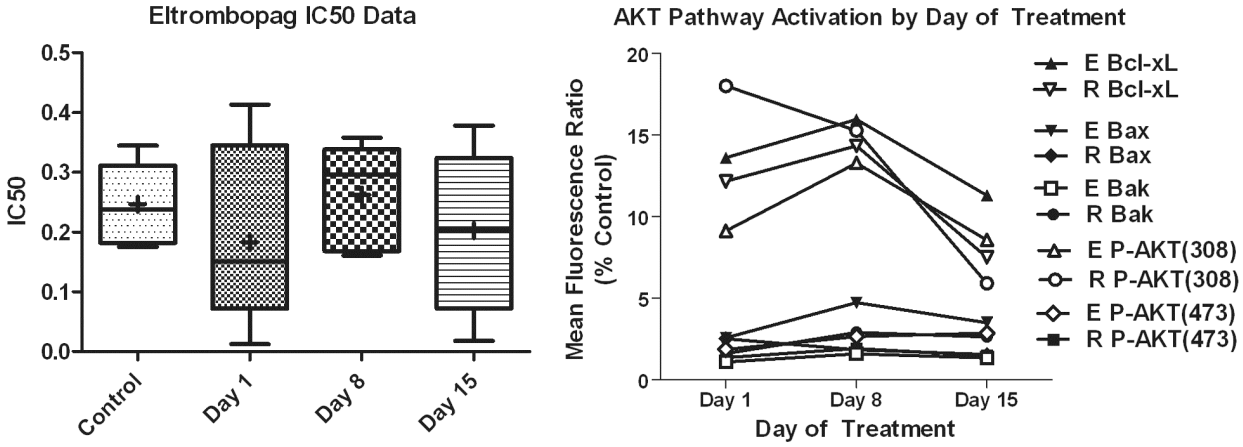


Fig. 1 *Left*: Resistance to apoptosis after treatment with Eltrombopag. *Right*: Protein levels after treatment with Eltrombopag (E) or Romiplostim (R).

THROMBOPOIETIC AGENTS IN THE TREATMENT OF CHILDHOOD IMMUNE THROMBOCYTOPENIA (ITP): CLINICAL TREATMENT AT 2 CENTERS

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Introduction: Thrombopoietic agents (TPO-A) are widely used in adults for difficult ITP. However only 1 study has been published describing the use of a TPO mimetic (Nplate) in 22 children with ITP. This study is a post hoc analysis of 32 children (<21yr) who received clinical treatment (off study) with either Nplate or Promacta.

Methods: All children described are from 2 centers: Weill Cornell in New York (n=22, 9 on Nplate, 13 on Promacta) and Childrens Hospital Orange County (10, all on Nplate). All patients in this abstract were treated off study although some had previously participated in the AMGEN195 (Pediatric) followed by AMGEN 213 (long term maintenance) studies. Responses (taken from the published study) were defined as platelet count (plt ct) > 50k on 2 consecutive weeks, plt increase ≥ 20k on 2 consecutive weeks, and the percent of weeks at > 50k independent of rescue therapy. Rescue therapy e.g. IVIG, steroids, plt transfusion, resulted in counts being considered "non-responder" for 2 full weeks after initiation of treatment. Bone marrows were evaluated for reticulin fibrosis (RF) using consensus grades 0-3. Several patients had more than one marrow during treatment; in these cases, the most recent on-therapy marrow was used.

Results: The median age of patients on Nplate was 10 years of age (2-19) while for those on Promacta it was 16 years (5-19). Of the 32 patients treated with TPO-A, 24 responded with a plt ct ≥ 50k twice; 19/32 received Nplate and 15/19 responded; 13/32 received Promacta and 9/13 responded. Plt increases ≥ 20k were seen in 23 of 32 patients. The number of patients whose platelet count was ≥ 50k for at least 50 percent of visits was 20/32. The mean number of previous treatments for responders to Nplate was 3.2 while for Nplate non-responders it was 2.25. For Promacta, the mean for responders was 2.9 treatments and for non-responders 3 treatments. Younger patients did not seem to respond as well to treatment with either TPO-A (see table). Nplate patients received treatment for a mean of 19.2 weeks; for patients treated with Promacta it was 13.7 weeks. Baseline bone marrows were available in 17 patients of whom 6 had grade 1 reticulin fibrosis (RF). There were 10 children with marrows performed after the start of TPO-A: 2 with RF score=0, 7 with score=1+, and 1 with score=2+ Adverse events (AEs) other than bone marrow fibrosis and bleeding (lack of efficacy) were all 1-2+ and not related to TPO-A. In particular, no thrombosis or development of malignancy was seen.

	Age of non-responders	Plt count > 50k x2	Plt ct>20k increase over baseline	Plt ct >50k for >50% of therapy	Mean time to plt > 50K (weeks)
N-Plate	4 of 5 youngest (2,5,5,6)	15/19	14/19	11/19	2.9
Promacta	4 of 6 youngest (3,10,14,15)	9/13	9/13	9/13	1.3

In conclusion, TPO-A were an effective treatment of chronic ITP in the 32 consecutive children retrospectively analyzed here from 2 centers. Younger children in this study seemed not to respond as well as older children, in contrast to small numbers of young children in published data who responded very well. No major changes were seen in the bone marrows but a formal baseline and on therapy study in children is needed to assess this issue. AEs were infrequent and tolerable. Additional studies with both Nplate and Promacta, either planned or in progress, are needed to clarify the response rates, AEs eg bone marrow fibrosis, and effects in subgroups of children.

CALORIC INFORMATION, BODY MASS INDEX AND OBESITY PREVENTION IN CHILDREN

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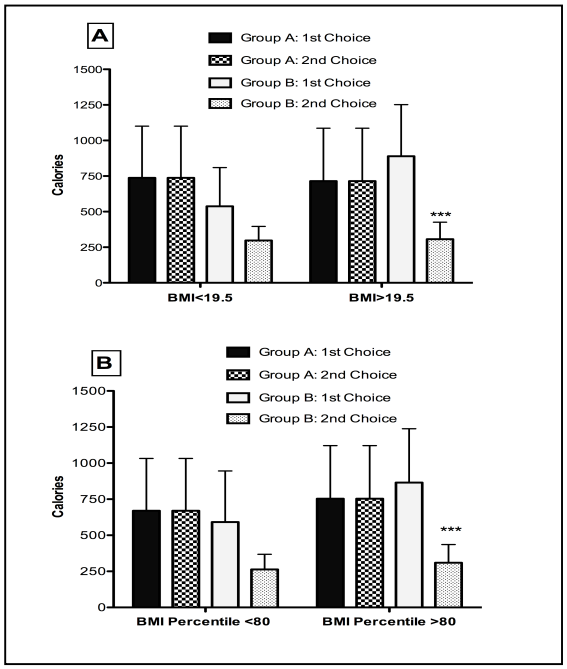
Background: Many factors influence the development of obesity. The main ones include high intake of sugars, sweetened beverages, increased fast food intake, and distorted perception of portion size. Children are widely exposed to pictorial information in televised food ads. Television viewing at 5 years of age is associated with later increase in BMI at 30 years of age. Adults given caloric information learn about food values and 1 in 6 will then choose lower calorie items. This study explored whether providing children with caloric information affected choices from a fast-food photo menu (PM).

Methods: In a randomized controlled study, 130 children, ages 5-19 years, were given questionnaires with typical fast-foods photos (PM) to select a meal option. Group 1 (n=44) received a PM without caloric values; Group 2 (n=41) got a PM with caloric values; Group 3 (n=42) initially got a PM without caloric values but after initial selection, got a PM with caloric values and asked if they wanted to reconsider their initial selection.



Results: Baseline calorie selections, Body Mass Index (BMI), and BMI percentile were the same across all groups. In Group 3, half of the subjects changed their menu; average calories from the second PM were lower (Δ173.8 ± 373.2) (p=0.006). There was a significant correlation between the calories of the first selection and the reconsidered one (p<0.01). Furthermore BMI greater than 19.5 and BMI percentile greater than 80 were strongly linked to reduced calorie selection after reconsideration in the subgroup who changed their selection by 2 way ANOVA and Bonferroni posttest (p<0.001).

Conclusions: While caloric information alone did not alter choices from a PM, children with low, or normal to high BMI did use calorie information to change their choices after reconsideration This is the first study to demonstrate that BMI and BMI percentile are factors in children's menu selection. The study indicates that the potential for enhancing caloric awareness leading to altered choices with the objective of obesity prevention in the pediatric outpatient setting.

STREP THROAT…TROPISM? A UNIQUE PHENOTYPE FOR *STREPTOCOCCUS PYOGENES* ON PALATINE TONSIL-DERIVED EPITHELIUM

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Background: Pharyngitis secondary to oropharyngeal infection with *Streptococcus pyogenes* is most commonly treated by using penicillin-derived antibiotics.While treatment failure in the 1950's was reported in 4-8% of children, more recent studies have alarmingly found antibiotic failure as high as 20-40%. Such recurring infections still remain a common indication for eventual tonsillectomy. Avoiding such an invasive intervention provides sufficient impetus to revisit preventative strategies. Neighboring mucosa in the oropharynx is classically unaffected during "Strep Throat" suggesting pathogen specificity for palatine tonsil epithelium. While recent studies are advancing the premise of pathogen-host microenvironment effects on streptococcal virulence, the specific interaction between *S. pyogenes* and the human tonsillar surface relative to neighboring tissues remains insufficiently understood.

Methods: An *in vitro* assay system was employed to assess streptococcal virulence when co-cultured with clinically-derived nasopharygneal (Detroit- 62) and palatine tonsil (UT-SCC-60B) epithelium, respectively. In brief, human epithelial monolayers were inoculated with a *S . pyogenes* strain SF370 (M1 serotype) cell suspension, respectively. Virulence parameters measured included the pathogen's: (1) efficiency at adhering to epithelial monolayer surfaces; (2) propencity towards invasiveness / becoming internalized by the epithelial cells; and (3) duration of intracellular viability following epithelial invasion.

Results: After being co-cultured at a multiplicity of infection (MOI) of 100 CFU's per individual epithelial cell for 2 hours, *S. pyogenes* adhered to UT-SCC-60B tonsil epithelium with greater efficiency than to nasopharyngeal cells as a percentage of inoculum. A greater percentage of the inoculum also tended to become internalized by tonsil epithelium than by nasopharyngeal cells. The percentage of initially adherent bacteria that subsequently became internalized also tended to be greater in tonsil versus nasopharyngeal epithelium, although this trend did not reach statistical significance across experiments. Once intracellular, *S. pyogenes* tend to remain viable and may continue multiplying at least during the initial hours following invasion. The tendency to continue growing while intracellular was most markedly observed within tonsil epithelial cells.

Discussion: Our experiments have demonstrated an apparent (albeit preliminary) phenotypic difference in pathogenicity when *S. pyogenes* was incubated with a nasopharyngeal epithelial cell line (Detroit 562) versus palatine tonsil-derived epithelial cells (UT-SCC-60B). This is the first time an *in vitro* assay system has shown a difference in pathogenicity or "preference" by *S. pyogenes* following co-culture with two anatomically neighboring epithelial cell types of the human pharynx.

ANTENATAL MANAGEMENT IN FETAL ALLOIMMUNE THROMBOCYTOPENIA: A RANDOMIZED CONTROLLED STUDY

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Fetal alloimmune thrombocytopenia (AIT) is an important cause of fetal and neonatal thrombocytopenia and intracranial hemorrhage (ICH). This study further explored treatment of subsequent affected pregnancies in mothers who had had an older sibling affected with AIT; pregnancies in which the previous fetus had suffered an ICH were excluded. Eligible mothers were randomized between 20 and 30 weeks to initiate treatment with IVIG 1 g/kg twice a week versus IVIG 1 g/kg once a week and prednisone 0.5 mg/kg po daily. At 32 weeks women underwent fetal blood sampling (FBS); those with fetal platelet counts (FPC) $\leq$ 30,000or who could not or would not be sampled intensified therapy to IVIG x 2 + Pred until delivery. 95 women and fetuses were entered in the study. 48 pregnancies were randomized to group A (IVIG x 2) and 46 to group B (IVIG + Pred).

Results: 1) the only ICHs that occurred were 3 grade 1 ICHs—this is similar to what would be expected in normal and the lowest birth platelet count was 49,000. 2) Both IVIG x 2 and IVIG + Pred were essentially equally effective although there were small differences between the 2 arms: higher mean FPC on the IVIG x 2 arm but slightly more failures (5 vs 10). 3) Only 1 of 95 fetuses who followed the protocol ie intensified therapy at 32 weeks for at least 3 weeks for a low FPC, had a low birth platelet count; no ICH occurred.

Conclusions: Future studies could avoid fetal blood sampling altogether in these standard risk AIT patients (no sibling ICH) by intensifying therapy at 30-32 weeks in all patients and delivering at 37-38 weeks. IVIG and prednisone would be simpler and less costly (only 1 IVIG per week) and could be the starting regimen in those without an absolute or relative contraindication to steroids.

CD99 AS A NOVEL THERAPEUTIC TARGET IN TREATING ACUTE MYELOID LEUKEMIA

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Background: Acute myeloid leukemia (AML) affects over 250,000 new patients each year globally. The majority of patients are destined to relapse, with a subsequent 5-year survival of less than 10%. AML is thought to be initiated and maintained by a small subpopulation of self-renewing leukemic stem cells (LSCs). This cell population is thought to be resistant to conventional therapies, providing the likely reservoir of minimal residual disease that leads to relapse. Surface markers that are preferentially expressed on LSCs, but not on normal hematopoietic stem cells (HSCs), provide an attractive antibody-based therapeutic target towards fully eradicating the disease while minimizing toxicity. In a preliminary analysis comparing the transcriptomes of LSCs and HSCs, we identified CD99 as a surface antigen expressed at high levels on a high frequency of AML LSCs (>70%). As it had not been previously described in myeloid malignancies, we chose to study it further, with a view towards potential therapeutic targeting.

Methods: We confirmed the expression of CD99 in 15 AML cell lines and 26 primary AML cells obtained through an IRB approved tissue acquisition protocol with Dr. Martin Carroll at the University of Pennsylvania. As CD99 was found to be consistently up-regulated on AML blasts and LSCs, we assessed its suitability as a therapeutic target by incubating the AML cell lines and primary samples with a monoclonal antibody against CD99 (12E7), with subsequent assessment of cell number. Controls included no Ab treatment, treatment with matched-isotype (mouse IgG1k), and treatment with vehicle control (NaN_3).

Results: Incubation of 15 AML cell lines with CD99 Ab (12E7, 10 μg/ml) for 48 hours leads to a significant decrease in cell number in 13 of 15 cell lines. Additionally, incubation of primary AML blasts with CD99 Ab (12E7, 20 μg/ml) for 48 hours leads to a 36-fold ($p<0.001$) and 50-fold ($p<0.01$) decrease in cell number, respectively. Using flow cytometry analysis, 13 out of the 15 AML cell lines express high surface levels of CD99. Of the two samples with lowest CD99 expression (K562, KSM51) and the two samples with highest c-Kit expression (KU812, SEL2), there is a reduced cytotoxic effect from CD99 ligation (12E7, 10 μg/ml). 30 min pre-treatment of AML cell lines with antibodies against c-kit (SR-1, 10 ug/ml), followed by 48 hr incubation with CD99 (12E7, 5 or 10 ug/ml) leads to more cytotoxicity than SR-1 or 12E7 treatment alone.

Conclusions: Ligation of CD99 leads to marked cytotoxicity in both AML cell lines and primary patient samples, with a relatively modest effect on normal CB HSC. Thus, therapeutic targeting of CD99 may be effective against AML with relative sparing of normal hematopoiesis. In addition, AML cell lines with higher expression of CD99 demonstrated greater susceptibility to CD99 ligation while cells with a higher expression of c-Kit demonstrated greater resistance. This suggests that CD99 expression is necessary for cytotoxicity and high c-Kit expression is associated with resistance to CD99 ligation.

THE OUTCOME OF TERM INFANTS WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY EVALUATED FOR HYPOTHERMIA THERAPY

Dara Zyburo, Gautam Shrivastava, Hannaise Cruz MD, Elena Wachtel MD, MPH, FAAP

Background: Hypoxic ischemic encephalopathy (HIE) is a neurological disorder in full-term infants characterized by muscle tone/reflex abnormalities, alterations in consciousness, and seizures in the early days of life. HIE affects 3/1000 US births; mortality rates are as high as 20% and up to 25% experience permanent neurological disabilities. Treatment has previously been limited to administration of anti-seizure medications with supportive care. Selective head cooling (cool cap therapy) is a new therapy that aims to reduce HIE-related morbidity and mortality by lessening metabolic demand, decreasing excitotoxic neurotransmitter release, and suppressing the inflammatory response by lowering the temperature of deep brain structures to 32-34*C.

Objectives:
1) To determine the degree of encephalopathy on initial evaluation and need for hypothermia therapy for all newborns diagnosed with HIE.
2) To determine short and long-term outcomes for cooled and non-cooled infants.
3) To assess clinical complications and management of infants during cooling and compare data with another cooling center.

Methods: This is a retrospective study of a prospective cohort of all newborns at NYULMC diagnosed with HIE between October 2008 and June 2011. Newborns were divided into two groups of differing HIE severity: stage 1 - HIE not severe enough to require cooling and stage 2 or 3 - severe enough to require cooling. Data was also obtained from Cornell Medical Center for comparison of patient demographics, clinical complications, and management.

Data:
Of the 45 patients diagnosed with HIE, 21 did not qualify for cooling. All of these newborns survived with normal MRIs. Of the 24 newborns that qualified for cooling, results indicate that pregnancy/labor complications, Cesarean section, intubation, CPR, and gestational age and birth weight are poor predictors of the necessity of selective head cooling in babies with HIE. Measures of first postnatal pHs, 10 minute APGAR scores, base deficits, and lactate levels were worse for babies requiring cooling than for those that did not qualify for cooling ($p < 0.05$ for each). Additionally, 63% of all cooled infants had severely abnormal background activity on aEEG and cooled infants had a mortality rate of 20.8%. Of the surviving cooled infants, 20% recovered normal aEEG activity by the end of cooling, 25% had a normal MRI, and 60% of those seen in follow-up had neuro-developmental disabilities.

The mean time to cool cap initiation was 4.5 hours for Cornell and 5.0 hours for NYU. NYULMC cooled patients experienced more severe encephalopathy (63%) compared to Cornell patients (22%) and had more critical lab values. Cornell was also found to treat seizures with a greater number of antiepileptic drugs, with 70% of all cooled infants receiving phenobarbital, Versed, and phosphenytoin.

Conclusions: The initial clinical presentation of cooled infants did not accurately correlate with the degree of encephalopathy as determined by aEEG, whereas the initial evaluation of infants who did not qualify for cooling is an accurate predictor of their short term outcomes. Therefore, it is important to streamline the evaluation process so the time to cooling will be shorter for patients who qualify. Most cooled infants at NYULMC have developed disabilities during their follow-up, highlighting the need for more research on longterm outcomes for patients who were evaluated for cooling.

Resident/Post-Doctoral Fellow/Faculty Abstracts

A CLINICAL PREDICTION RULE TO IDENTIFY PATIENTS AT HIGH-RISK FOR COMMUNITY-ACQUIRED MRSA CUTANEOUS ABSCESSES

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Background: Community-acquired MRSA (CA-MRSA) is the most common cause of skin and soft-tissue infections in many regions of the US. Empiric broad-spectrum antibiotic use may lead to greater bacterial resistance patterns; therefore, judicious use is critical. The objective of this study was to derive a clinical prediction rule to identify patients at high risk for CA-MRSA cutaneous abscesses**.**

Methods: A retrospective chart review of subjects under age 21 years treated in the pediatric emergency department of an urban tertiary care center between 1/2008 and 12/2011 was performed. Inclusion criterion: diagnosis of cutaneous abscess or incision and drainage of abscess. Exclusion criteria: (1) no wound culture (2) other skin infection. Potential predictors of CA-MRSA infection included historical, physical examination, and demographic data.

Results: To date, 192 of 400 subjects have been reviewed. The prevalence of CA-MRSA was 48%. Parameters were analyzed for association using odds ratios. No clinical parameter yielded a significant risk. Two demographic factors were associated with increased risk of CA-MRSA: Latino ethnicity (OR = 2.5, p<.05) and Medicaid insurance (OR = 1.4, p=.05).

Demographic and Clinical Factors	MRSA-negative culture (n=99)	MRSA-positive culture (n=93)
Gender	48% male	47% male
Geography (NYC)	34% outer boroughs	45% outer boroughs
Ethnicity (p<.05)	27% Latino	43% Latino
Insurance (p<.05)	51% Medicaid	65% Medicaid
Location of abscess	23% groin	29% groin
Season	39% summer	39% summer
Age (years)	9.6 ± 0.7	9.3 ± 0.7
Duration of abscess (days)	6.3 ± 1.2	4.8 ± 0.5
Size of abscess (cm)	3.6 ± 0.3	3.9 ± 0.3
Fever	27%	32%
Positive hx skin infection	27%	31%
Recent antibiotic use	34%	32%
Multiple abscesses	87%	82%
WBC	14,060 ± 1,128	14,850 ± 871

Conclusions: In this study sample the clinical parameters that are typically suggestive of CA-MRSA were not found to be associated with positive cultures. Certain demographic factors suggested increased risk for CA-MRSA. Limitations include reduced statistical power due to small sample size and incomplete data.

Future directions for this investigation include prospective data collection with a larger sample size and multivariate analysis to derive a clinical prediction rule identifying patients at risk for CA-MRSA infection. Defining which patients benefit from broad-spectrum antibiotics may help tailor medical therapies, while lessening risk for increased antibiotic resistance.

HYPOXIA-ISCHEMIA INCREASES ANNEXIN-2 EXPRESSION IN NEONATAL RAT BRAIN

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Background: Hypoxic-ischemic encephalopathy (HIE) occurs in over 1-2 per 1000 live term births and most of the survivors have lifelong neuro-developmental sequelae such as cerebral palsy, epilepsy, and cognitive disabilities. Appropriate treatment of HIE requires an understanding of the age-specific responses to the insult. Tissue plasminogen activator (tPA) is a serine protease that plays an important role in the hemostatic system by catalyzing the conversion of plasminogen to plasmin, the main mediator of fibrinolysis. tPA has been employed in the treatment of adult ischemic stroke, but may exacerbate HI-induced brain damage in neonatal and adult brain.

Annexin 2 belongs to a 113-member annexin family that binds acidic phospholipids in a Ca-dependent reaction. Annexin 2 is a cofactor in plasminogen activation on the membrane surface, where it works with tPA to increase conversion of plasminogen to plasmin. Thus, annexin 2 is thought to play a key role in cell surface fibrinolysis in the periphery. Little is known about annexin 2 in brain. While recombinant annexin 2 has been shown to be protective in an adult stroke model, it has not been studied in the neonatal brain. Recently, annexin 2 was shown to be upregulated by hypoxia (H) directly through HIF-1alpha signaling in retinal endothelial cells. The purpose of the present study was to investigate the expression of annexin 2 in neonatal rat brain, and to test the hypothesis that annexin 2 expression is increased following hypoxia-ischemia (HI).

Methods: Unilateral cerebral HI was induced in P10 (term equivalent) Wistar rats, according to our standard protocol of carotid ligation with 75 minutes of 8% O2/bal N2 . Rats were sacrificed at 1 and 20 hrs following HI. Brains were removed and ipsilateral (HI) and contralateral (H) cortices were analyzed for annexin 2 by Western blot. Age-matched, sham-operated rats served as controls.

Results: Annexin 2 was detected at a very low level in control brain and was slightly up-regulated 1 hour following H and HI. By 24 hrs there was a 5-fold increase in annexin 2 in HI brain and a 2-fold increase in the contralateral (H) brain, compared to control brains.

Conclusions: To our knowledge this is the first demonstration of annexin 2 expression in immature brain, and the first report of upregulation of annexin 2 in HIE. Whether annexin 2 mediates tPA-dependent effects in the post-hypoxic brain has yet to be elucidated. Annexin 2 could offer a potential therapeutic target in neonatal hypoxic ischemia.

THE ANTI−TUMOR EFFECTS OF POTENTIAL IRON CHELATORS FROM VACCINIUM MACROCARPON (CRANBERRIES) IN B16−F10 MELANOMA AND HUMAN LEUKEMIA CELLS IN VITRO

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Background: Many of the reported health benefits of cranberries, including anti−tumor activity and prevention of urinary tract infections, are associated with a unique class of proanthocyanidins known as A−type PACs, which consist of monomeric epicatechin units attached by a carbon−carbon bond (C4−C8) and an ether bond (C2−O−C7). Preliminary studies of the biological effects of A−type PACs, especially dimers and trimers, indicate these activities may be associated with their ability to chelate iron. Iron is crucial to normal cell metabolism and important for the rapid cell growth of tumor cells. Studies indicate that iron chelators have anti−proliferative and anti−tumor effects on several tumor cell lines. However, how they affect tumor progression is unknown and effort to develop and study iron chelators, especially from dietary sources, for treatment and prevention of cancer or for use as adjunctive therapies have been limited. In this study the effects of A−type PACs and markers associated with iron status were assessed *in vitro* with B16−F10 melanoma cell lines. The anti-tumor effects of A-type PACs with HL60 leukemia cells were also assessed.

Methods: B16−F10 melanoma cell lines were treated with a cranberry extract fraction consisting mostly of A−type PAC dimers/trimers (A−D/T), A−type procyanidin dimer (A2), and other iron chelators: deferoxamine (DFO) and Baicalin. By using the WST−1 assay, the antiproliferative activities of A−D/T were evaluated with and without iron added as ferric ammonium citrate (FAC). A2 was also assessed with or without the iron chelator DFO. HL60 leukemia cells lines treated with A-type PACs (A-D/T and Cysticran) were tested for cell viability using Annexin V/7-AAD. A-D/T by flow cytometry (FACS) and other iron chelators were similarly studied for effects on the transferrin receptor (CD71), reactive oxygen species (ROS) and apoptosis (annexin V) at 3 hrs, 18 hrs or both.

Results: DFO alone had little or no effect on cell proliferation. A2 and Baicalin inhibited proliferation and induced complete cell death of B16−F10 melanoma cells but A−D/T from cranberries was the most effective. A2 was a more effective at inhibitor of cell proliferation with DFO than without. Iron supplementation with A−D/T abolished inhibition of cell proliferation. FACS analysis indicated that A2 up−regulated the transferrin receptor up to 18 hrs whereas A−D/T down−regulated the transferrin receptor at 3 hrs but up−regulated by 18 hrs, suggesting in both cases that cells were starving for iron. Interestingly, over time we observed a different pattern of ROS inhibition or synthesis, although in both cases at 18 hrs cell death was associated with elevated ROS formation.

Conclusions: Results of this study suggest the anti−tumor activity of A−type PACs with B16−F10 cells are not exclusively associated with iron chelation but also involve production of toxic ROS. Our studies indicate that the biological activity of these compounds in relation to up−regulation of the transferrin receptor and ROS production is different than more common chelators. The data also suggest that A2 is more effective at inhibiting B16−F10 proliferation when used with other chelators. Future studies will analyze effects of A−type PACs in combination with iron chelators and i*n vivo* by using a mouse model we are developing. Using this model we will determine if these compounds alone or when co−administered with other therapeutic compounds will inhibit tumor progression, anemia, inflammation or have other effects associated with iron metabolism.

POTENTIAL THERAPEUTIC APPLICATIONS OF JAK2 INHIBITORS IN BETA-THALASSEMIA AND SICKLE CELL DISEASE

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Background: ß-thalassemia and sickle cell disease (SCD) are the most common genetic red cell blood (RBC) disorders characterized respectively by limited synthesis or production of aberrant ß-globin chains. In both cases, chronic transfusions and iron chelation are required to prevent the anemia and/or formation of abnormal RBC. In ß-thalassemia, anemia stimulates erythropoietin (Epo) synthesis, which in turn leads to increased erythropoiesis and development of hepatosplenomegaly, often resulting in the need for splenectomy. Recently we demonstrated that erythroid cells from ß-thalassemic mice have a hyper-activation of Jak2, a kinase that mediates the signaling triggered by the binding of Epo to the Epo receptor. This led us to hypothesize that Jak2 inhibitors could be utilized to minimize erythroid expansion in this disorder, limiting splenomegaly.

Methods and Results: A Jak2 inhibitor (Tg101209 or Tg) was first tested in mice affected by ß-thalassemia intermedia (*th3/*+). Two doses of Tg (150 and 100mg/Kg/day) were given orally for 10 days. Tg administration to *th3*/+ mice induced a mild decrease of hemoglobin levels (8.8±0.22, 8±0.2 and 7.8±0.2g/dL for placebo, Tg-100mg/Kg and Tg-150mg/Kg treated mice, respectively. $p<0.05$) and in the number of reticulocytes (approximately 75% of the levels seen in controls, $p<0.05$). Splenomegaly was also reduced in Tg-treated mice (up to 60%; $p<0.05$), the extent of this effect correlating with the dosage used. Reduction of splenomegaly was associated with a decrease in the number of erythroid progenitors in this organ ($p<0.05$) and amelioration of the splenic architecture. These data support our hypothesis that, in ß-thalassemia, splenomegaly is associated with increased erythroid proliferation and it can be alleviated by administration of Jak2 inhibitors, with a mild effect on anemia.

We further tested the effect of Tg in other anemias associated with extramedulary hematopoiesis (EMH) and splenomegaly, including SCD. Administration of the drug to mice affected by SCD led to a significant worsening of anemia (more pronounced than that seen in *th3*/+ mice) and a proportional reduction of splenomegaly and EMH. Then, we evaluated the outcome of combining Tg with blood transfusion, a common therapy in b-thalassemia and SCD. In β-thalassemia massively enlarged spleens are believed to sequester a significant proportion of circulating RBC, thereby limiting their lifespan and the efficacy of transfusion regiments. We hypothesize that decreasing splenomegaly by administration of Jak2 inhibitors could increase the efficacy of transfusion. This was first tested in *th3*/+ animals. In this case, transfusion alone was sufficient to increase the hemoglobin (Hb) levels approximately 3g/dL and reduce the spleen size to 65% of that seen in non-transfused controls. In this model, the combined effect of transfusion and administration of Tg was more effective in reducing splenomegaly (50% of non-transfused controls, $p<0.05$).

We further tested this approach in mice affected by ß-thalassemia-major (*th3/th3*), for which transfusion is required for survival and massive splenomegaly develops rapidly. Administration of Tg together with transfusion led to a greater increase in Hb levels compared to controls (9.3±0.4 vs 7.3±0.5g/dL, $p<0.05$). This was likely a consequence of reduced splenomegaly and decreased sequestration of RBCs in Tg/transfused mice.

Lastly, we tested the combination therapy in a mouse model of SCD. Mice treated with Tg and transfusion exhibited slightly lower levels of Hb than transfused-controls (Hb=9.7±0.2g/dL versus

Hb=10.9±0.2g/dL). However, compared to transfused-control animals, mice receiving the combination therapy exhibited a larger amount of donor RBC, whereas the endogenous erythropoiesis was markedly suppressed along with the production of sickle RBC ($1.3\pm0.3x10^6$ RBC/ul compared to transfused-controls exhibiting $2.7\pm0.3x10^6$ RBC/ul).

Conclusions: In summary, administration of Jak2 inhibitors might reduce the production of pathological cells that, together with preservation of the spleen, could minimize the propensity of patients for thrombotic events. Furthermore, suppression of the endogenous erythropoiesis and reduction of the transfusion regimen might also reduce iron accumulation, making it easier to prevent its toxic effects through chelation therapy**.**

ACCURACY OF PRENATAL ECHOCARDIOGRAMS IN PREDICTING COARCTATION OF THE AORTA

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Background: Prenatal diagnosis of isolated coarctation of the aorta is fraught with a high false positive rate. False positive results cause undue stress on families, but a missed diagnosis of coarctation can have catastrophic consequences. For these cases, data on specificity and sensitivity of echocardiographic measurements in diagnosing prenatal coarctation of the aorta are limited. The objective of our investigation was to assess the accuracy of fetal echocardiograms in diagnosis of coarctation of the aorta.

Methods: A retrospective chart review was conducted of subjects with a prenatal echocardiogram from April 2007 to July 2009. Indication for echo, gestational age and finding of each prenatal echo, and postnatal diagnosis based on echo were recorded. Classification of 3 grades of prenatal diagnosis was made, as outlined in the table below.

Results: 1415 charts were reviewed yielding 46 qualifying subjects with documented suspicion of isolated coarctation of the aorta in the echo report. Subjects lost to clinical follow-up (n=4) were excluded. Five pregnancies were terminated and there was 1 fetal and 1 neonatal demise. 35 subjects received postnatal diagnoses. Subjects classified as Grade 1 and 2 based on echo reports were significantly less likely (30 of 31 cases: 97%) to have coarctation of the aorta compared to those in the Grade 3 category (2 of 4: 50%).

	Postnatal Outcome	
Prenatal category	No Coarctation (n=32)	Coarctation (n=3)
Grade 1 (n = 22) Very low suspicion	22	0
Grade 2 (n=9) Moderate suspicion	8	1
Grade 3 (n = 4) High suspicion	2	2

The specificity and negative predictive value of prenatal echo classification were high: 97% and 97%, respectively. The sensitivity and positive predictive value were lower: 67% and 50%, respectively, given the low number of postnatal cases. Outcomes in this study showed no correlation with gestational age of first prenatal echo.

Conclusions: Prenatal echo findings consistent with a classification of Grade 1 (low-risk) are accurate predictors of no coarctation of the aorta. Conversely, echocardiograms consistent with Grade 3 classifications are significantly associated with a postnatal diagnosis of coarctation of the aorta. These data suggest that echocardiographic measurements and methodology currently used in the prenatal identification of coarctation are relatively effective in predicting postnatal diagnosis of coarctation. Additional research should identify the specificity and sensitivity of specific echocardiographic parameters in correctly diagnosing prenatally coarctation of the aorta as a path towards improving sensitivity of diagnosis.

INVESTIGATING THE ROLE OF CYTOKINES AND HEPCIDIN IN ANEMIA OF INFLAMMATION

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Background: Anemia of inflammation (AI) is a widespread multi-factorial form of anemia characterized by hepcidin-induced iron restricted erythropoiesis as well as direct cytokine effects on the bone marrow, blunted erythropoietin production and efficacy, and shortened red blood cell (RBC) lifespan. Our aim is to perform an in depth study of AI, identifying the components and mechanisms associated with its pathophysiology.

Methods: We generated a mouse model of AI using a single intraperitoneal injection of heat-killed *Brucella abortus* (HKBA). In this model we explored the role played by interleukin-6 and hepcidin in the onset of anemia. We utilized wild-type (WT), interleukin-6 knockout (*IL-6* KO) and hepcidin knockout (*Hamp* KO) mice (n ≥ 6/group) injected with HKBA, and conducted weekly CBC's for 7 weeks to follow the progression and resolution of anemia.

Results: Anemia started developing one week after HKBA administration and reached a nadir after 2 weeks in all mice. Hemoglobin values from WT mice were lowest 2 weeks after injection (6.4 ± 1.2 g/dl) but slowly recovered over 7 weeks. Initially, *IL-6* KO mice were equally affected with similar hemoglobin values at 2 weeks (6.9 ± 1.3 g/dl). However, these mice recovered after 3 weeks. *Hamp* KO mice were less anemic throughout the course of the study, with hemoglobin values of 10.3 ± 0. 9 g/dl at 2 weeks and resolution after 4 weeks. The data demonstrate that while both IL-6 and hepcidin contribute to AI, lack of either molecule alone is not sufficient to prevent AI. Therefore, additional factors likely play an important role in the etiology of AI.

In order to rule out the effect of iron overload on the reduced severity of anemia observed in *Hamp* KO mice injected with HKBA, 1 week-old mice were fed an iron-deficient diet to first deplete their iron stores, and then returned to normal diet before HKBA injection. We saw that iron-depleted *Hamp* KO mice were still less sensitive to HKBA, suggesting that this effect was independent of iron overload and dependent on the intrinsic lack of hepcidin expression.

We further investigated the erythropoiesis in WT, *IL-6* KO, and *Hamp* KO mice one week after HKBA injection. We performed FACS analyses of BM and spleen using CD44 and Ter119 antibodies. Both the mature RBCs ($CD44^-/Ter119^+$) and erythroid progenitor cells ($CD44^+/Ter119^+$) were dramatically reduced in the BM of HKBA-treated WT mice compared to controls ($CD44^+/Ter119^+$ cells diminished from 35.5 ± 0.2% to 2.8 ± 0.8%; $CD44^-/Ter119^+$ cells from 17.2 ± 0.2% to 8.2 ± 0.8%). The reduction of erythroid cells was attenuated in HKBA-treated *IL-6* KO mice ($CD44^+/Ter119^+$ cells diminished from 32.8 ± 0.1% to 7.5 ± 6.0%; $CD44^-/Ter119^+$ cells from 22.1 ± 0.5% to 10.4 ± 3.8%). *Hamp* KO mice, on the other hand, showed a dramatic reduction of the $CD44^+/Ter119^+$ population in their BM (from 24.1 ± 2.5% to 1.8 ± 0.3%), while mature $CD44^-/Ter119^+$ cells were less affected (from 15.4 ± 2.3% to 14.1 ± 2.6%).

Erythropoiesis was altered in the spleen as well. However, while the $CD44^+/Ter119^+$ cells were reduced in all the mice strains, the $CD44^-/Ter119^+$ population was increased one week after HKBA injection. This profile was more similar to ineffective erythropoiesis than iron-restricted erythropoiesis. Splenomegaly was also observed in all HKBA-treated mice. In addition, we measured increased apoptosis and production of reactive oxygen species (ROS) in the reticulocytes and orthochromatic erythroblasts of the spleen and BM of all mice.

Conclusions: Overall, these data suggest that, in addition to iron restricted-erythropoiesis, an acute inflammatory effect on erythropoiesis is occurring in the HKBA model of AI, affecting erythroid cell survival and/or proliferation. Further analyses aimed at determining the RBC life span and survival in these mice are in progress. Moreover, we are analyzing iron-related gene expression in all groups of mice, along with measurement of their serum iron levels, iron stores, and serum cytokine levels, at different time points. Preliminary data indicate that numerous cytokine mRNAs (including IL-1α, IL-1β, TNF-α, INF-γ) are elevated in the spleen of WT mice 6 hours after HKBA injection. We are investigating the role that these cytokines might have on erythropoiesis, and the anemia observed in *IL-6* KO and *Hamp* KO mice after injection of HKBA.

ADDRESSING THE NEW MENTAL HEALTH COMPETENCIES

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Background: As stated in recent AAP policy statements, pediatricians need to play a larger role in identifying and managing pediatric mental health (MH) issues; MH competencies were proposed by the AAP in a follow up statement. Data from resident focus groups presented last year demonstrated resident discomfort with handling MH issues and a need for increased training to achieve these competencies.

Objective: To perform a needs assessment of pediatric program directors (PD) about MH training for residents.

Design/Methods: Program characteristics, PD opinions on their residents' competencies in MH, and likelihood to implement curricular activities in MH were assessed via web-based survey sent to all PDs. Linear and logistic regression models predicted the curricular activities and awareness of the AAP MH competencies. $P < 0.05$ considered significant.

Results: Of the 99 PDs (60%) who completed the survey, 55% were not aware of the AAP MH competencies; PD of large programs were 15 times more likely to be aware of the competencies ($p=0.035$) compared to small programs. PD opinions of their resident MH competencies are highlighted in the attached graphs . Larger programs were less likely to implement more curricular activities compared to small programs ($p=0.02$).

Conclusions: PDs rate their resident competencies with MH issues as average at best. This is in agreement with our resident focus group data. Size of program correlate with PDs willingness to implement educational modalities. Curricular reform is needed to address gaps in knowledge and skill. Curricula needs to be flexible and modular to meet the needs of all programs.

STEROID VERSUS NON-STEROID BASED IMMUNOSUPPRESSION IN PEDIATRIC RENAL TRANSPLANT: COMPARISON OF OUTCOMES

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Background: Corticosteroids have been the mainstay of immunosuppression in pediatric renal transplant despite many side effects especially growth suppression in children. Since 2005 our center has been using steroids only as a premedication for thymoglobulin in the initial peri-operative and immediate post transplant period. Prior to that we used a steroid based protocol. Our induction protocol consists of 5 doses of Thymoglobulin and Methylprednisone. Mycophenolate Mofetil is given on day # 0 and Prograf is started on day # 1. Patients are maintained on Prograf and MMF long term.

Objective: To compare outcomes between patients on steroid (S) versus non-steroid (NS) based protocols**.**

Methods: Data on demographic, anthropometric, biochemical variables and medications were obtained from patient records. Comparisons between the S and NS groups were made for the following outcomes: graft survival, acute rejection, estimated GFR, height z scores, BMI, number of anti-hypertensives used and use of erythrocyte stimulating agents (ESA). Longitudinal data (at 3 time points up to 2 years) were available on acute rejection, height z scores and BMI so these data were analyzed by generalized estimating equations accounting for within person correlation, while other cross-sectional data were analyzed by standard linear or logistic regression. In all regression analyses, potential confounders such as age, donor source and time trend were controlled**.**

Results: There were 49 subjects, 20 in the S and 29 in the NS group. Height z scores were significantly higher (p=0.02) and acute rejection rate (p=0.01) and the number of anti-hypertensives used (p=0.02) were significantly lower in the NS group. The differences in graft survival, eGFR, BMI, and use of ESA's were not significant, likely due to insufficient statistical power. There were some limitations to our study: small sample size, retrospective chart review, historic controls.

Conclusions: Steroid free immunosuppression provides comparable outcomes in terms of graft survival and graft function but possibly better outcomes for linear growth and incidence of acute rejection in children.

PREVALENCE AND RISK FACTORS FOR 25 HYDROXY VITAMIN D DEFICIENCY IN PEDIATRIC CHRONIC KIDNEY DISEASE

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Background: Vitamin D deficiency is highly prevalent in adults with chronic kidney disease. Pediatric data are scarce. Children with chronic kidney disease are at higher risk of vitamin D deficiency.

Objectives:: Assess the prevalence and determinants of insufficient 25 hydroxyvitamin D (25 OHD) levels in children with chronic kidney disease (CKD).

Methods: Cross sectional analysis of 25 OHD levels in 114 pediatric patients with CKD stages 1 to 5 at two centers in the US. Levels < 30 ng/ml were considered insufficient.

Results: 25 OHD levels were < 30 ng/ml in 79% of the subjects. All racial groups had high prevalence of inadequate levels but the proportion was higher in nonwhite (86 % vs. 74%). Age and gender were not predictive of inadequate levels. Obesity was associated with lower levels (93% in obese vs. 75% non-obese, $p<0.01$). Those who were non-white ($p <0.05$) with higher BMI ($p<0.01$) and higher urine protein creatinine ratios ($p<0.01$) were more likely to have inadequate 25 OHD levels.

PTH levels were available pre and post ergocalciferol supplementation in 26 subjects. There was a trend towards lower PTH levels after increase in 25 OHD levels in the early stages of CKD (1 to 3).

Conclusions: Inadequate 25 OHD levels are highly prevalent in pediatric CKD and are associated with non- white race, higher BMI and proteinuria. These groups may need higher doses of supplementation and more frequent monitoring of levels. Normalization of 25 OHD levels is desirable even in early CKD to decrease PTH levels.

RITUXIMAB IN PEDIATRIC RECURRENT FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS)

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Background: FSGS recurs in 35-50% of allografts. Plasmapheresis (TPE) has been one of the mainstays of treatment but results are variable. Rituximab (RTX), a monoclonal antibody to CD20 is being used for treatment of recurrent FSGS but pediatric experience is very limited.

Objectives: To illustrate the benefits and possible adverse effects of Rituximab in 8 pediatric transplant patients with recurrent FSGS.

Results: See Table [1] for details. 8 children, age range 7 to 17 years had immediate post-transplant recurrence of FSGS. All were on TPE for a range of 7 days to 5 years with persistent nephrotic range proteinuria. They received 1 to 4 doses of RTX. Complete response (urine protein creatinine ratio less than 0.2) was seen in 2/8 patients. Partial response defined as 50% decrease in proteinuria was seen in 4 of the 8 patients. 2 patients had no response. 5/6 patients had a decrease in proteinuria within a month of starting Rituximab. One patient showed a response 7 months later with reduction in U p/c ratio from 9 to 0.35 mg/mg. One patient recurred thrice and responded with complete remission after single dose of RTX each time. No correlation was found between CD 19% levels and proteinuria.

Complications:
Some severe adverse effects were noted. The study results are unclear as to whether they can be attributed to RTX alone.

Severe respiratory failure leading to death 4 weeks post RTX was observed. No infectious agent identified on bronchoscopy. Autopsy suggested thrombotic microangiopathy in multiple organs, CNS malignancy 2 years post RTX, and Acute tubular necrosis post infusion.

Table 1

	Case1	Case2	Case3	Case4	Case5	Case6	Case 7	Case 8
Age at transplant (years)	15	12	8	16	17	14	7	15
Sex	m	m	m	m	f	f	m	m
Race	White	White	Black	Black	White	White	White	White
Donor	LRD	DD	LURD	LURD	DD	LRD	LRD	LRD
Pre TPE (Yes/No)	y	y	n	y	n	n	y	y
Native nephrectomy	no	no	no	no	one	no	yes, b/l	yes, b/l
Duration to RTX post-transplant (months)	2	47	36	0.5	17			
Duration of follow up post RTX (months)	18	8	9	1	6	NA	3	33
CD 19% pre RTX	23	17	11	67	12	na	1.2	1
CD 19% 4 weeks post RTX	0	0	0	0	1	0	0.5	0
S. creatinine pre RTX	1.2	1.25	0.74	4.22	2.2	1.8	1	1.2
S. Cr 4 weeks post RTX	0.9	1.13	1.24	1.57	2.8	1.7	0.8	1.0
S. creatinine last	1.23	1.13	1.02	1.57	2.9	1.8	0.79	1.3
Up/c pre RTX	2.3	8.1	4.4	5	10	25	23	4.19
Up/c 4 weeks post RTX	1.2	3.3	6.5	2.2	8	21	0.1	0.14
Up/c latest	0.72	2.2	0.35	1.9	7.7	11	0.14	0.12

Conclusions: Rituximab can be used as a treatment for recurrent FSGS. Major conclusions are that efficacy is variable with none to complete response. Factors that are predictive of response are unclear. Therefore adequately powered, long term, clinical trials are needed to:

1. Elucidate factors that may predict a favorable response
2. Prove its sustained efficacy in those who respond
3. Monitor for potentially serious adverse effects

PREVALENCE OF TOXIC CAMPHOR USE IN CHILDREN UNDER 6 YEARS OF AGE

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Background: Camphor is a well-established neurotoxin and causes many pediatric emergencies annually. It is found in health products, products for religious practices, unregulated imported products, and pest control products. Ingestion, inhalation, and topical use have been linked to seizures, respiratory problems, coma, and death in children. Camphor is sold legally in concentrations < 11% and is sold illegally in concentration > 11%.. The objective of this study was to evaluate the prevalence and methods of camphor use in homes with children under 6 years old.

Methods: A convenience sample was surveyed anonymously in ambulatory clinics affiliated with an urban community hospital over a six month period. The survey was available in English and Spanish. Caregivers of children < 6 years old were read aloud questions about purpose and frequency of product use and method of use in children.

Results: Ninety-five caregivers were surveyed: 97% were biological parents; mean age was 28 9 years; 50% had at least a high school degree; 96% identified as Hispanic. Mean child age was 3.1 1.9 years. 83 of 95 respondents (87%) reported use of camphor products in the home. Oil, liniment, and cubes/tablets were the most commonly used products, with prevalences of 22%, 82%, and 44%, respectively. Table 1 presents prevalence for specific uses of the 3 products.

Camphor oil and tablets, which contain high levels of camphor, were used with notable frequency in our survey. Oil and liniment were used for skin application by the vast majority of subjects. Although consumption of camphor is toxic, a small portion of caregivers endorse its ingestion.

Table 1: Use of Camphor Products in Homes with Young Children

Product	Prevalence of use (among n=83 who endorsed use)	Medicinal Use	Use more often when child sick	Use in children < 2 y/o	Use by ingestion	Use by inhalation	Use by application to skin
Oil/Tincture	22%	12%	10%	7%	1%	1%	99%
Rub/Liniment	82%	74%	31%	16%	4%	8%	93%
Cubes/Tablet	44%	4%	5%	4%	1%	4%	28%

Conclusions: These data suggest that camphor is widely used in homes with children. The very high rate of illegally imported and unregulated camphor product use reported here is of enormous concern, given the neurotoxicity of camphor. Topical, inhalational, and ingestion uses, especially in children less than 2 years old, is extremely dangerous. The results of this study create awareness of the hazardous uses of camphor products in children. Pediatricians are urged to proactively warn parents about the dangers of camphor products and to discourage their use.

CHARACTERIZATION OF HYPOXIA-ISCHEMIA INDUCED SEIZURES IN P7 NEONATAL RAT PUPS

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Background: Late preterm infants, 34-36 weeks, make up 71% of preterm births and 8.8% of all births. The perinatal course may be complicated by hypoxia-ischemia (HI), with resultant encephalopathy including seizures (Sz). Sz are more likely to be subclinical due to immaturity of the brain making diagnosis more difficult. Subclinical Sz, if untreated, may contribute to ongoing brain injury.

Objective: To characterize the occurrence & timing of clinical and subclinical Sz during & following HI in the postnatal day (P) 7 rat and resultant brain damage.

Design/Methods: P7 Wistar rats (brain development approximating a 32-36 wk gestation human) were used. EEG headmounts (HM) were placed on P7. P8 pups underwent unilateral right carotid artery ligation, were connected to video electroencephalogram (VEEG) & subjected to HI (8% O2/balance N) for 75 min at 36.5°C (n=11) or hypoxia (H) alone (n=4). Littermates underwent HI, no HM (n=11). Pups were monitored for 60 min post-HI during normoxic recovery. EEG Sz was defined as repetitive, rhythmic patterns with increased amplitude, lasting at least 10 sec. Sz were classified as clinical or subclinical by correlating with behavioral activity. Brains were removed at 48 hours post HI and stained with triphenyltetrazolium chloride (TTC) to assess damage.

Results: Subclinical Sz occurred in all 11 HI pups. 7/11 pups exhibited clinical Sz. Time to first Sz during HI was 43-75 min, median 65 min (subclinical) and 42-67 min, median 61 min (clinical). Total number of Sz per animal during HI ranged from 1-4 and 1-5 for subclinical and clinical Sz, respectively, with 68% of all Sz observed being subclinical. Sz continued into the recovery period in 9/11 pups; 84% subclinical. Brain damage was severe, greater than 50% of ipsilateral hemisphere damaged, in 10/11 rats with HI and HM and in 9/11 HI without HM. H only pups had no Sz and no damage.

Conclusions: Time to first Sz was longer during HI in these younger rats than we previously reported for P12, term equivalent, pups, and the total number of Sz were fewer. There was no exacerbation of injury due to the headmount itself. Also in contrast to older pups, the majority of Sz in the younger animals were subclinical. These subclinical Sz continued into the recovery period for most animals. This latter observation is important because it may provide opportunity to explore interventions i.e. anticonvulsants that could minimize or prevent ongoing injury following HI.

DISORDERED MINERAL METABOLISM IN THE CKID CHILDREN: ROLE OF FGF23

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Background: FGF23 is an important regulator of phosphorus (Pi) and vitamin D metabolism. However, little is known about the prevalence and determinants of FGF23 excess across the spectrum of CKD in children.

Methods: We measured plasma C-terminal FGF23 (Immutopics 2nd gen) in 426 children, ages 1-16 yrs, with CKD stages 2-4 enrolled in the observational Chronic Kidney Disease in Children (CKiD) study. GFR was measured by plasma clearance of iohexol (n=286) or estimated using the CKiD estimating equation.

Results: Mean age of subjects was 11.5 4.3 (SD) yrs. CKD was due to glomerular disease in 21% and non-glomerular disease in 79%. Mean GFR was 46 18 ml/min/1.73 m2; 18% of subjects had CKD stage 2, 59% stage 3, and 21% stage 4. Overall, median serum Pi and PTH levels were within the normal range, but median FGF23 was 132 RU/ml (IQR: 88-223), 2.3-fold higher than that in healthy children. 66% of subjects met criterion for FGF23 excess (>100 RU/ml), but only 12% had hyperphosphatemia. FGF23 was strongly associated with GFR (r=-0.44), age-adjusted Pi (r=0.30), and PTH (r=0.36) ($P<0.001$ for each). In stage 2 CKD, mean age-adjusted Pi was below the normal mean ($P<0.01$), PTH was >65 pg/ml in only 15%, whereas FGF23 was >100 RU/ml in 44% of subjects. As GFR declined further, the prevalence of FGF23 excess increased (stage 3, 66%; stage 4, 91%). FGF23 was higher in children with glomerular than with non-glomerular disease ($P<0.001$), after adjusting for age, GFR, and Pi.

Conclusions: Plasma FGF23 concentrations are increased early in the course of CKD in children, before increases in serum Pi or PTH. Thus, increased FGF23 may be an early biomarker of disordered Pi homeostasis and an initiating mechanism of abnormal mineral metabolism in children with progressive CKD.

HYPERTHERMIA, NOT HYPEROXIA, EXACERBATES HYPOXIC-ISCHEMIC BRAIN INJURY IN THE TERM-EQUIVALENT NEONATAL RAT

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Background: Hypoxic-ischemic (HI) brain injury in the newborn is an important cause of short and long-term morbidity and mortality. Clinical and experimental data suggest that variations in both oxygen and temperature may modulate the extent of brain injury during the immediate reperfusion period. The impact of concurrent hyperthermia and hyperoxia on the extent of brain injury during reperfusion is unclear. The study objective was to determine the effect of hyperthermia and hyperoxia, alone and in combination, on brain injury following HI in the term-equivalent rat pup.

Methods: Postnatal day (P) 10-11 Wistar rat pups underwent unilateral common carotid artery ligation plus hypoxia (8% O_2/ balance N_2) for 60 minutes. Following HI, rat pups were exposed to normoxia/normothermia (21% O_2/36.5^oC, n = 35), hyperoxia/normothermia (95% O_2/36.5^oC, n = 10), normoxia/hyperthermia (21% O_2/38.5^oC, n = 10), or hyperoxia/hyperthermia (95% O_2/38.5^oC, n = 17) for 2 hours. After 72 hours, the animals were sacrificed; brains were removed and frozen in isopentane (-30^oC). 18 µm coronal cryosections were stained with H&E. Extent of damage of the ipsilateral hemisphere was measured using ImageJ, NIH software; infarct area % was calculated after correction for edema. Data was analyzed using ANOVA and Wilcoxon rank-sum tests.

Results:
Rats recovered in a hyperthermic, or hyperthermic-hyperoxic, environment had similar mean infarct area that was larger than those recovered in normoxia-normothermia (P = 0.02). Rats recovered in a hyperoxic environment showed no difference in infarct area % vs. the normothermic-normoxic recovered rats. Additionally, 2 hyperoxic hyperthermic rats died during the recovery period.

Recovery group	n	Average infarct area (%) ± SEM	Deaths during recovery
Normoxia-normothermia	35	61.0±2.9	0
Hyperoxia	10	59.4±6.7	0
Hyperthermia	10	73.2±3.1*	0
Hyperoxia-hyperthermia	17	72.7±2.8**	2

*P = 0.03; **P = 0.02 versus control group

Conclusions: Elevated temperature during the recovery following hypoxia-ischemia caused a significant increase in infarct size, independent of inspired oxygen concentration. Hyperoxia alone had no effect on infarct size. Hyperthermia should clearly be avoided during resuscitation/post-resuscitation care of asphyxiated newborns. The precise role of supplemental oxygen during this period requires further study.

Pediatric Activities
Groups and Field Programs

BIG BUDDIES PROGRAM

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The Big Buddies Program is a student-run program that matches individual Weill Cornell medical students with a child or teenager from New York City Community. While the children may have ongoing medical needs, the focus of the program is for the medical student to serve as role model and mentor. The interactions give program participants an opportunity to see the students without their white coats and stethoscopes and the medical students the chance to see their Little Buddies as individuals rather than patients. Big Buddies have the opportunity to spend one-on-one time with their Little Buddies or participate in group events.
The activities are guided by the Big Buddy/Little Buddy pair, and are meant to meet their unique interests. The relationship of the pair develops over the year, as they meet up about once a month, as well as keep in touch via phone calls and email. Examples of past activities are trips to sporting events or the zoo, picnics, skating in Central Park, and trips to the movies. Group events have included Halloween and Thanksgiving parties.

From both pair activities and group events, the pairs come away with more than just a good time: The Little Buddies benefit from having a caring adult to look up to and confide in, as well as someone to share their love (or loathing) of the Yankees, their passion for Pokemon, or their dislike of algebra. Much of medicine is taught through a mentor/mentee system, with those who have less experience learning from those with more, the Big Buddies program provides a fun opportunity for students to practice being a mentor, to learn to listen carefully, and be a sounding board for a young person's ideas, while also providing guidance and support. It is a chance to put down the textbooks and connect with others, establishing relationship that can leave a lasting impression on all involved.

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CAMP PHOENIX

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Every year, almost one million American children are burned. Fortunately, advancements in trauma and resuscitative care have improved the treatment and survival of these young patients. Despite the medical and surgical advances, the psychosocial care of pediatric burn victims continues long after discharge. These children often return home with scars as permanent reminders of their trauma, and the aftermath of surviving a serious burn usually includes considerable stress, diminished self-esteem, and difficulty creating positive social relationships. Camp Phoenix, the first burn camp in the United States run by medical students, was founded in 2000 by Paul Mullan, a 2004 Graduate of Weill Cornell Medical College. Since then, Camp Phoenix has provided a safe environment for pediatric burn survivors and their siblings to interact with their peers and share their experiences.

Camp Phoenix sponsors three one-day events and one overnight camping trip each year. Past events have been held at Sony Wonder Technology Lab, Chelsea Piers, New York Knicks games, the Museum of Natural History, NYC Firehouses, Public School 242 in West Harlem, Riverbank State Park, Lenox Hill Neighborhood House, Camp Kinder Ring in upstate New York, YMCA Camp Fairview Lake and YMCA Camp Bernie in New Jersey. We have worked with over 200 children at these events, with an average of 35 campers and 20 volunteer counselors at each event. Camp Phoenix activities are designed to build confidence, emphasize teamwork, initiate friendship, and maximize fun.

Last June, a group of almost 80 campers and volunteer counselors spent an incredible three days at Camp Taconic in the Berkshire Mountains of Western Massachusetts. The overnight camping trip is always especially memorable. Campers are introduced to new activities such as rope courses, archery, canoeing, and hiking. For many of our campers, this is their first time away from home and outside of an urban setting. Campers are divided into cabins, where they work together and quickly develop their sense of community and camaraderie. They create cabin names and cheers and group enthusiasm is rewarded as the cabins participate in one of Camp Phoenix's favorite traditions, the Messy Olympics. Campers compete for cabin pride in games such as the "Human Ice Cream Sundae," and "Spaghetti Speed Race."

In addition to helping the campers and their families, Camp Phoenix offers a unique educational experience for the medical students involved. Our volunteers serve as mentors for children with a range of medical and psychosocial issues, allowing them to hone their skills as leaders, role models, and caretakers. Positive experiences at the day events and overnight camp weekend have inspired many volunteers to develop interest in Pediatrics and Burn Surgery.

Camp Phoenix aims to give future physicians opportunities outside of the classroom to better appreciate the art of compassionate and empathetic care for complex patients. New this year is a shadowing program, which will allow medical students to spend time with the pediatric team in the burn unit. Students will learn about the inpatient experience of our campers, various treatments, and relevant psychosocial issues. We also developing a 3-part discussion series covering the three phases of burn care: burn shock, wound care/surgery, and rehabilitation as well as reconstruction. These expereinces are meant to educate all interested students about what our campers went through during the rehabilitation phase of their burn care and to have any questions and concerns fully addressed by experts.

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THE HEADS UP! PEDIATRIC LITERACY PROGRAM

A Project of the Weill Cornell Medical College Department of Pediatrics, Division of Child Development
Directed by Mary Jo Ward, PhD

By M Cheffers, B Oseroff, and C Prifti
Heads Up! Program Coordinators

Economic disadvantage and limited parental education mean that children born into poverty are susceptible to delays in language development. These children routinely lag behind their peers before pre-school or kindergarten even begin.[1] In most cases, this gap continues to widen in elementary and middle school as children with poorer educational foundations fall further below school standards. Weakness in language and reading skills can lead to poorer educational and health outcomes, such as school failure, low self-esteem, troubled behavior, and substance abuse.[2] In contrast, recent studies have shown that reading aloud to children from early on in life has positive effects on children's language and pre-literacy skills.[3]

In an effort to improve early literacy, the Heads Up! Pediatric Literacy program has initiated a mild intervention mediated by pediatric primary care physicians. Doctors are the professional constituent with the most access to children and parents before school begins. By having physicians alert parents to the need to read to their young children—and by giving an age-appropriate book as part of the physical exam—we make the promotion of early language and literacy development a standard part of primary pediatric care.

Beyond encouraging language development and school readiness, books can also be used for assessment in the exam room. Books can help physciains see whether a four month-old reaches for objects or if a child who moves to accept a book has a normal gait. At some sites, including WCMC, trained volunteers help children select more books and conduct parent outreach in the waiting room.

Heads Up! targets pediatric clinics that serve needy populations. At all of our 12 clinic sites—pediatric outpatient clinics affiliated with WCMC, Lincoln Hospital, St. Barnabas Hospital, Methodist Hospital, and New York Hospital Queens—at least 85% of patients qualify for Medicaid. In 2010-2011, Heads Up! distributed 40,391 brand-new books and corresponding literacy guidance to nearly 20,000 children.

Books are purchased using funding from two sources. Every year Heads Up! renews a grant with Reading Is Fundamental (RIF), in which RIF promises to pay over 75% of our book purchases provided Heads Up! spends the stated budget. In 2011-2012 the RIF book-purchasing budget is $129,938. Of this, Heads Up! is required to provide only $28,050 in "matching" funds, most of which is obtained through private donations, corporate gifts, or hospital auxiliary funds. The program also receives support from Reach Out and Read, which helps us secure additional books.

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HEALTH FOR LIFE

Health for Life is a program run by the NYPH Department of Pediatrics that works with overweight children. A team of pediatricians, physical therapists, social workers, nutritionists, and medical student volunteers help children and teens ages ~9 - 18 learn about how to lead a healthier life. The 10 week program has 2 major components: exercise and nutrition. During the exercise sessions, participants discover fun new ways to incorporate physical activity into their lives. As part of this, all participants receive pedometers that they carry around for the duration of the program. The nutrition sessions focus on learning about which foods are healthy and which ones should be eaten only rarely, and how to changes dishes you like.

Each medical student volunteer is paired with a program participant. In addition to attending the weekly nutrition sessions, mentors help their mentees stay on track with the program by offering encouragement and advice through weekly phone conversations between sessions. In return, volunteers get to be role models and make an impact on a child's life, and have a great time!

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KIDS IN CANCER SUPPORT (KICS)

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KICS is a student run program with the New York Presbyterian department of pediatric hematology/oncology that creates one on one matches between Weill Cornell medical students and children or adolescents currently receiving therapy. The focus of the program is to provide support for the children and their families; it gives the kids an opportunity to form a close, consistent relationship with someone outside of their treatment team. The pediatric oncology team interviews medical students and personally matches them with patients interested in having a buddy. Once a patient is matched, the student will make the initial contact with the patient during a clinic visit. After this, matches can spend time together whenever it is best for both, this can be during hospital visits or outside of the hospital. The relationship really develops on their own terms.

For the kids, the hospital can be an intimidating place associated with pain, sickness, and not to mention the terrible effects of chemotherapy. Medical students can help make it just a little better by having fun with the kids. Knowing they get to meet up with their match, play a game of Connect Four, or paint with watercolors might just make the hospital a little friendlier. Especially in pediatrics, the diagnosis of cancer can have a major impact not only on the patient but also on the patient's family. For parents, KICS can take just a little of pressure off of the situation and give them a needed break. For the medical students, the opportunity gives them insight into what it is like to be a child with a severe chronic illness.

The program is currently being restarted and is slowly but surely rebuilding to its previous state. Past members of the program have had positive experiences and spoke highly:

> "At first I thought, he's on chemo, I'm going to feel bad for him. But although his illness was always in the background that wasn't all there was to him, and you can lose sight of that when you're a doctor. You can forget the humanistic side, putting a person in the context of their life."
>
> "It's nice for the kids to have someone who's relatively young not their parent or a sibling, just somebody who wants to hang out with them. It distracts them from their treatment. We're medical students, but we're not there for any medical purpose... We just want to talk to them and have a little fun."
>
> "In the first two years you spend so much time learning basic sciences, it can be a real drag. Being able to take yourself out of that, to put a face to what you're doing, really motivates you."

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KOMANSKY CENTER INITIATIVES
FAMILY ADVISORY COUNCIL

The Komansky Center Family Advisory Council (FAC) is a group of dedicated parents and family members of pediatric patients who are committed to working with Komansky Center hospital staff and administration to provide family-centered care to all patients. Our vision is to achieve a level of care where patient and family involvement is expected and welcomed by all. Among the Council's many current initiatives are:

Family Education and Orientation Workgroup
The goal of the Workgroup is to improve care while at the hospital by helping patients' families and Hospital staff communicate more effectively. The *Family Education and Orientation Workgroup* tries to identify ways to 1) Orient family members to the Hospital with written and verbal communication tools; 2) Enhance communication skills of new and current Hospital staff members; 3) Improve communication between Hospital staff and families and, d) Revise preoperative procedures for outpatient surgeries.

Family Experience Workgroup
A child's stay in the hospital is often very stressful for his or her family. *The Family Experience Workgroup* is committed to creating a pleasant environment for patients and their families. Workgroup members identify different ways to improve and expand the infrastructure and recreational services currently offered at the Hospital. Recent activities have included distribution of gifts during the holidays, participation in the Thanksgiving festivities hosted by Child Life, and engaging local school children to create holiday cards for hospitalized children.

Family Support Workgroup
By sharing experiences, families can help each other through a tumultuous and traumatic time. The *Family Support Workgroup* is committed to identifying ways to provide support to families and to managing that support systematically. *Family Support* is focused on three areas: 1) The development of a resource center for families; 2) the creation of a parent-to-parent directory; and 3) the development of a mentoring program so that current families can seek advice from families who have "graduated" from the hospital**.**

Family Faculty Program
The *Family Faculty Program* works with hospital staff and administration to incorporate FAC parents in orienting and educating new residents on the topic of family-centered care. FAC parents help residents learn by sharing their own stories within the healthcare system. The *Family Faculty Program* hopes to expand their activities to student education**.**

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MOTIVATING ACTION THROUGH COMMUNITY HEALTH OUTREACH (MAChO)

Nil Koney, Diana Mosquera

Overview: Motivating Action through Community Health Outreach (MAChO) is a Weill Cornell Medical College student-led, community-centered response to the alarmingly increasing rate of childhood obesity, particularly within minority and socioeconomically disadvantaged communities. We target East Harlem children ages 7 to 13 with the goal of establishing healthy nutritional, fitness, and personal habits early in life to encourage children to achieve their fullest potential.

Mission: The goal of MAChO is to empower youth with the knowledge and practical tools to take control of their health and their lives through proper nutrition, fitness and personal development. We aim to accomplish this goal by:

> *Motivating Action* by *building a community of empowered youth* through dissemination of information that inspires the adoption of healthy living habits,
>
> *Motivating Action* by *pursuing a holistic, adaptive, and individualized approach* towards addressing poor nutrition and sedentary lifestyles, and
>
> *Motivating Action* by *partnering with community organizations to build a supportive network* of empowered individuals and families.

History: MAChO was established in the fall of 2009 by a handful of Weill Cornell Medical College students who recognized the desperate need for education and resources to fight the obesity epidemic. By pairing with Settlement Health, a nonprofit community health center in East Harlem, MAChO initiated a pilot-phase program to teach kids how to make healthy nutrition and fitness choices within their community. The pilot program met once a week for ten weeks. In 2010-2011, the program was expanded to a full-year curriculum that met once a week during the school year and every day in the summer. The scope of MAChO was broadened to include a pilot mentoring program, educational field trips, and assessments to track knowledge and fitness progress. The lessons from the first two years have served as a foundation for the revamped organization and new initiatives for the 2011-2012 year.

Program: The structure of the curriculum consists of biweekly after-school sessions coupled with a weekend mentoring and personal development component. For the after-school program, our volunteer graduate and undergraduate teachers lead the nutrition, physiology and exercise classes with the help of teaching assistants, who include high school students and former program participants. The Mentor program includes our personal development curriculum, where we use a multi-generational group-mentoring model: mentor teams are composed of college students who mentor high school students, who then serve as mentors to our middle school and elementary school participants. The mentor teams work on group projects to be presented at the end of each semester based on a specific theme surrounding health

Day 1			Day 2			Day 3		
Snack + HW	Exercise	Nutrition	Snack + HW	Exercise	Physiology	Exercise	Group Project	P.D. Curriculum

For the 2011-2012 year, we run sessions at the Boys' Club of New York in East Harlem and the Silberman School of Social Work at Hunter College. We have 40 participants, ages 7 to 13. We are currently tracking BMI, fitness test measures, and knowledge and behavior questionnaire scores to monitor the progress of the children and to continue to improve the program.

Members: MAChO volunteers include students from WCMC, Cornell University, Columbia University, Hunter College, high school students from Cristo Rey High School in East Harlem, and young professionals. We are overseen by faculty advisors from New York-Presbyterian Hospital Pediatrics department, WCMC, Hunter College, and Hunter School of Public Health and Social Work. Our community health outreach partners include the Boys' Club of New York, Settlement Health, Harlem Center for Healthy Living, and Choosing Healthy and Active Lifestyle for Kids (CHALK)

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WEILL CORNELL GLOBAL HEALTH CURRICULUM
FOCUS ON PEDIATRICS

Amita Kulkarni, Carrie Bronsther

Launched in the 2009-2010 academic year, the Global Health Curriculum prepares Weill Cornell medical students to be future leaders in global health through a longitudinal program featuring didactic course work, experiential learning, and a mentored pathway for engaging with resource-poor communities, internationally and domestically.

The curriculum consists of three courses, one Global Health Preceptorship with underserved or immigrant populations in New York City, two applied (service learning) experiences, and monthly Global Health Grand Rounds lectures. The three courses are Introduction to Global Health: A Case-Based Approach (Fall, Year 1), Foundations in Global Service (Spring, Year 1), and Global Health: Clinical Skills for Resource-poor Environments (Spring, Year 4).

The topics of pediatrics and maternal and child health are incorporated into every aspect of the curriculum, including lectures and hands-on components. The Introduction to Global Health course includes a foundational lecture on Maternal and Child Health, focusing on the leading causes of morbidity and mortality among mothers and children in the developing world. Additionally, the Food and Nutrition foundational lecture emphasizes child malnutrition, a leading cause of child deaths worldwide. The fourth-year elective, Global Health: Clinical Skills for Resource-Poor Environment, devotes one entire day to issues related to pediatrics in developing countries. In addition, several students shadow pediatricians who serve immigrant and/or underserved populations in New York City through our Global Health Preceptorship program. Other students choose to engage in pediatric-related research projects or clinical electives in resource-poor settings as part of their applied (service learning) experiences. Lastly, one to two Global Health Grand Rounds speakers each year focus on topics related to maternal child health topics. This past November, for example, Law Professor Jacqueline Bhabha of Harvard University spoke on the Health and Human Rights of Non-Citizens including Undocumented Migrants, Unaccompanied Children, and Refugees.

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Field(s) of Interest: Pediatric hospitalist and outpatient medicine, health services research, healthcare safety and quality research

Research Title: Health services research, healthcare safety and quality research

Project Description: Medication Safety
I am working on several studies looking at improving outpatient medication safety. One involves studying the impact of electronic prescribing on medication safety among community providers in New York State. Another involves improving patient safety for patients transitioning from the inpatient to the outpatient setting.

Students' Role in the Projects:
Students will learn how to consent patients, perform structured interviews in the hospital, and perform follow-up phone calls using surveys to detect whether a patient has experienced harmed from a medication.
Students would have the opportunity to participate in research team meetings where we discuss study design, data collection, analysis and manuscript writing.

Preferred Experience: None required

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Field(s) of Interest: Mineralization, matrix formation, bone development and repair.

Research Title: Mineral analysis in bones of animals with developmental abnormalities

Project Description: The goals of one of the major project in this laboratory is the determination of how matrix proteins regulate biomineralization. As such we study the effects of these proteins in solution, in culture, and when they are ablated or over expressed in transgenic animals. The project would be based on one of the models currently under investigation, where the student would do the histology, and work on the infra red imaging analysis of the bones of animals of different ages.

Students' Role in the Project: Infrared and microCT analyses of bones and teeth of a specific KO or TG animal. Student will learn about the ablated protein and perform IR Imaging and microCT

Preferred Background/ Experience: Student should have computer skills

References:

Mochida Y, Parisuthiman D, Pornprasertsuk-Damrongsri S, et al. Decorin modulates collagen matrix assembly and mineralization. Matrix Biol. Nov 18 2008.

Boskey AL, Roy R. Cell culture systems for studies of bone and tooth mineralization. Chem Rev. Nov 2008;108(11):4716-4733.

Verdelis K, Ling Y, Sreenath T, et al. DSPP effects on in vivo bone mineralization. Bone. Aug 16 2008.

Boskey AL, Spevak L, Weinstein RS. Spectroscopic markers of bone quality in alendronate-treated postmenopausal women. Osteoporos Int. Sep 4 2008.

Gourion-Arsiquaud S, West PA, Boskey AL. Fourier transform-infrared microspectroscopy and microscopic imaging. Methods Mol Biol. 2008;455:293-303.

Ward DF, Jr., Williams WA, Schapiro NE, et al. Focal adhesion kinase signaling controls cyclic tensile strain enhanced collagen I-induced osteogenic differentiation of human mesenchymal stem cells. Mol Cell Biomech. Dec 2007;4(4):177-188.

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Field(s) of Interest: Hematology/ Oncology

- *Antenatal Management of Fetal Alloimmune Thrombocytopenia*
- *Experimental treatments of Refractory ITP*

Project Description: Diagnosis, counseling, and entry into a multi-center randomized clinical trial. We design and coordinate this study, which is intended to prevent intracranial hemorrhage from immune thrombocytopenia in fetuses and neonates by administering treatment to mothers while they are who have a platelet antigen incompatibility with their husbands**.**

Children and adults with difficult to treat ITP are enrolled on treatment protocols of various agents including thrombopoietic agents, anti-CD20 including standard and augmented versions, anti-D, IV gammaglobulin, and inhbitors of syk and other novel agents. All of the studies have various research components (collaborative laboratory studies) connected with them.

Students' Role in the Project:
A) Helping to collect data. This entails contacting other centers to ensure that the various components of the trial are sent to us: consents and IRB paperwork; infusion related data, lab work (maternal data and fetal sonos), and follow up information on the neonates and infants. B) Helping to analyze the data that has been collected. C). Design and contribute to special projects related to AIT study.

1. Monitor the individual ITP patients to ensure that their visits and studies occur as per protocol and that the appropriate information is collected.

2. Help to develop new studies connected with individual protocol agents and/or help to develop novel studies of new agents .
3. Ongoing analysis of data to determine progress with protocols.
4. Facilitate laboratory studies by pulling freezer specimens to be batched and sent off

Preferred Background/ Experience: None requested

References:

Bussel Kuter et al AMG531 Treatment of ITP NEJM, 10/20/2006

Bussel JB, Cheng G, Saleh MN, et al. Eltrombopag for the treatment of chronic idiopathic thrombocytopenic purpura. N Engl J Med. Nov 29 2007;357(22):2237-2247.

Scaradavou A, Cunningham-Rundles S, Ho JL, Folman C, Doo H, Bussel JB. Superior effect of intravenous anti-D compared with IV gammaglobulin in the treatment of HIV-thrombocytopenia: results of a small, randomized prospective comparison. Am J Hematol. 2007;82(5):335-341

Psaila B, Bussel JB. Fc receptors in immune thrombocytopenias: a target for immunomodulation? J Clin Invest. Aug 2008;118(8):2677-2681.

Kuter DJ, Bussel JB, Lyons RM, et al. Efficacy of romiplostim in patients with chronic immune thrombocytopenic purpura: a double-blind randomised controlled trial. Lancet. Feb 2 2008;371(9610):395-403.

Bussel JB, Kuter DJ, Pullarkat V, Lyons RM, Guo M, Nichol JL. Safety and efficacy of long-term treatment with romiplostim in thrombocytopenic patients with chronic ITP. Blood. March, 2009

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Field(s) of Interest: Developmental cognitive neuroscience

Research Title: Research in Developmental Psychobiology

Project Description:

Work on developmental brain imaging studies using functional magnetic resonance imaging and fiber tracking with diffusion tensor imaging to examine limbic forebrain regions implicated in addiction and impulsivity.

Work on attention and reading training interventions and how they impact behavior and neural systems testing pre and post-training effects with functional magnetic resonance imaging and diffusion tensor imaging. This work is relevant for the disorders of ADHD and reading disorders.

Work on developmental brain imaging studies using functional magnetic resonance imaging and fiber tracking with diffusion tensor imaging to examine limbic forebrain regions implicated in addiction and impulsivity.

Work on attention and reading training interventions and how they impact behavior and neural systems testing pre and post-training effects with functional magnetic resonance imaging and diffusion tensor imaging. This work is relevant for the disorders of ADHD and reading disorders.

Students' Role in the Project: Students would be provided with background reading, IRB and HIPAA training, image analysis, behavioral testing, programming and scientific discussions. Typically students are exposed to every aspect of the study and depending on contributions in the lab can be a co-author on a paper or conference presentation and as such get writing experience too. The student is jointly mentored by a team of investigators including pre and post-doctoral fellows and a faculty PI.

Preferred Background/Experience: Yes, some general computer experience would be very helpful.

References:

Casey BJ, Getz S, Galvan A. The adolescent brain. Dev Rev. 2008;28(1):62-77.

Hare TA, Tottenham N, Galvan A, Voss HU, Glover GH, Casey BJ. Biological substrates of emotional reactivityand regulation in adolescence during an emotional go-nogo task. Biol Psychiatry. May 15 2008;63(10):927-934.

Casey BJ, Jones RM, Hare TA. The adolescent brain. Ann N Y Acad Sci. Mar 2008;1124:111-126.

Casey BJ, Nigg JT, Durston S. New potential leads in the biology and treatment of attention deficit-hyperactivity disorder. Curr Opin Neurol. Apr 2007;20(2):119-124

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Field(s) of Interest: Autoimmune Disease; Immunoregulation

Research Title: Regulation of the Immune Response in Autoimmune Disease

Project Description: The laboratory studies the human immune system in healthy individuals and patients with systemic lupus erythematosus to better understand the triggers and mediators of autoimmunity and inflammation in that disease. Students are welcome to participate in ongoing laboratory projects, or initiate their own projects, that use cell culture, flow cytometry, real-time PCR, cell transfection, protein analysis, and other approaches to study mechanisms of autoimmunity.

Preferred Background/ Experience: None, although laboratory experience helps.

References:
Crow MK. Collaboration, genetic associations, and lupus erythematosus. N Engl J Med. Feb 28 2008;358(9):956-961.

Crow MK. Anticyclic citrullinated peptide antibody-negative rheumatoid arthritis: clues to disease pathogenesis. Curr Rheumatol Rep. Jul 2008;10(3):165-167.

Niewold TB, Adler JE, Glenn SB, Lehman TJ, Harley JB, Crow MK. Age- and sex-related patterns of serum interferon-alpha activity in lupus families. Arthritis Rheum. Jul 2008;58(7):2113-2119.7.

Kariuki SN, Crow MK, Niewold TB. The PTPN22 C1858T polymorphism is associated with skewing of cytokine profiles toward high interferon-alpha activity and low tumor necrosis factor alpha levels in patients with lupus. Arthritis Rheum. Sep 2008;58(9):2818-2823

Aringer M, Crow MK. A bridge between interferon-alpha and tumor necrosis factor in lupus. J Rheumatol. Aug 2008;35(8):1473-1476

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Field of Interest: Cellular Immunology, host response to pathogens, development of immune response, cytokine regulation

Research Titles:

1. Role of beta glucans in immune response and hematopoiesis
2. Development of Neonatal Immune Response:

Project Descriptions:

Role of beta glucans in immune response and hematopoiesis: The overall objective of our studies in collaboration with the MSKCC Research Center for Botanical Immunomodulators (NIH P50) is to identify botanicals with potential bioactivity for enhancement of immune function and reconstitution of hematopoietic and immune function after cancer chemotherapy, and to investigate botanicals that have adjuvant activity for cancer immunotherapy.

Development of neonatal immune response: The increased susceptibility of neonates to infections stems from the immaturity of the immune system at birth. Hematopoiesis and host defense in the neonate are developmentally immature. Studies focus on the role of microbes both commensals and potential pathogens on neonatal immune response in the regulation of proinflammatory response.

Students' Role in the Project: Student will participate in all aspects of the studies including experimental design and hypothesis testing and will learn relevant technology.

Preferred Background/Experience: Knowledge of basic laboratory skills and sterile technique.

References:
Lin, H., Cassileth, B.,She, Yu-Hing, Sirotnak, F., and Cunningham-Rundles, Ph.D. 2004 Maitake beta-glucan MD- fraction enhances bone marrow colony formation and reduces doxorubicin toxicity in vitro International Immunopharmacology 4: 91-99.

Lin. H., Cheung, S.W.Y., Nesin, M., Cassileth, B.R., and Cunningham-Rundles, S. 2007 Enhancement of umbilical cord blood cell hematopoiesis by Maitake beta glucan is mediated by G-CSF production. Clinical and Vaccine Immunology 14: 21-27

Mohamed MA, Cunningham-Rundles S, Dean CR, Hammad TA, Nesin M. Levels of pro-inflammatory cytokines produced from cord blood in-vitro are pathogen dependent and increased in comparison to adult controls. Cytokine 2007 39(3): 171-177.

Tatad, A.M. F., Nesin, M, Peoples, JD, Cheung, S W-Y, Lin, H., Sison, C, Perlman J.M, and S. Cunningham-Rundles Cytokine expression in response to bacterial antigens in preterm and term infant cord blood monocytes (adv e pub12.19.2007) and Neonatology 2008; 94:8-15

Peoples, JD, Cheung, S W-Y, Nesin, M, Tatad, AMF, Lin, H, Hoang, D, Perlman, J, Cunningham-Rundles, S. 2008 Neonatal cord blood subsets and cytokine response to bacterial antigens Am J Perinatology 9: 647-57

Lin, H , De Stanchina, E, Zhou, XK, She, Y-H, Hoang, D 4, Cheung, S W-Y, Cassileth, B R., Cunningham-Rundles, S 2008 Maitake Beta-Glucan enhances umbilical cord blood stem cell transplantation in the NOD/SCID mouse Exp Biol Med 234:342–353 PMCID: 19144872

Lin, H, De Stanchina, E, Zhou, XK, Hong, F, Seidman, A, Fornier, M, Xiao, WL, Kennelly, E J. Wesa, K, Cassileth, B R, Cunningham-Rundles, S. 2010 Maitake beta-glucan promotes recovery of leukocytes and myeloid cell function in peripheral blood from paclitaxel hematotoxicity Cancer Immunology Immunotherapy Epub. Feb 6. PMC: 20140432

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Field (s) of Interest: Medical Genetics

Research Title: Student can work on one of two projects, these include study mage in adolescent patients with Marfan syndrome and or parental attitudes re: newborn screening.

Project Description: Both studies will involve the use of questionnaires. We are in the process of developing a questionnaire for IRB approval re: Newborn screening. The aim is to determine what information pregnant women and their partners have about newborn screening and the NYS Screening program in order to determine their needs as well as to develop an educational program about this subject in face of the expanded test panel. The educational program will be aimed at patients but will include a professional component. We plan to develop a questionnaire for adolescents with Marfan syndrome to learn more about their views on their asthenia appearance and life activities.

Students' Role in Project: Students can help develop and modify the questionnaires. Student will learn interview techniques.

Preferred background/Experience: None

References:
Offit K, Kohut K, Clagett B, Wadsworth EA, Lafaro KJ, Cummings S, White M, Sagi M, Bernstein D, Davis JG.: Cancer genetic testing and assisted reproduction. Oct 10; 24(29): 4775-82. 2007.

Carter EM, Davis JG, Raggio CL.: Advances in understanding etiology of achondroplasia and review of management. Current Opinion in Pediatrics. Feb; 19(1): 32-7. 2007.

Sills ES, Burns MJ, Parker LD, Carroll LP, Kephart LL, Dyer CS, Papenhausen PR, Davis JG. Further phenotypic delineation of subtelomeric (terminal) 4q deletion with emphasis on intracranial and reproductive anatomy. Feb 12;2:9. 2007.

Giampietro, P.F., Raggio, C., Davis, J.G.: Marfan Syndrome: orthopedic and genetic review. Current Opinion in Pediatrics 14(1): 35-41, 2002.

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Field(s) of Interest: Hematology, disorders of iron metabolism, anemia of inflammation, beta-thalassemia.

Research Title**:** Investigating the role of cytokines and hepcidin in a mouse model of anemia of inflammation

Project Description**:** Anemia of inflammation (AI) is the second most common form of anemia, affecting patients with chronic illnesses, such as infections, autoimmune diseases, or cancer. The aim of the project is to better characterize the complex pattern of inflammatory cytokines that is responsible for AI, with the purpose of identifying new therapeutic targets for this condition. It has already been shown that interleukin-6 is increased in AI, activating the production of the iron regulatory hormone hepcidin in the liver. Through hepcidin, IL-6 ultimately affects iron metabolism reducing the availability of iron for erythropoiesis, and thus generating the anemia. However, together with IL-6, other cytokines (e.g. IFN-g, TNF-a) have been shown to alter iron metabolism and erythropoieis, with mechanisms that still need to be fully elucidated.

Students' Role in the Project: Student(s) will participate in all aspect of the above-described research, learning numerous techniques. These include: tissue samples collection, tissue iron analysis, flow-cytometry, ELISA, RNA extraction and analysis, quantitative PCR. Students will gain experience in many of the following experimental approaches:

1. Use of mouse models lacking the expression of hepcidin (Hamp KO) or specific cytokines (IL-6 KO, IFN- g KO, and TNF-a KO), and generation of double knockout (e.g. IL-6/Hamp KO).
2. Induction of AI by injection of heat-killed *Brucella abortus* antigen (HKBA).
3. Study of iron metabolism by expression profile analysis of iron-related genes, and comparison of results to tissue and serum iron levels in HKBA-treated and control mice.
4. Study of erythropoiesis with the goal of elucidating the mechanisms responsible for anemia in mice.
5. Inactivation of specific cytokines by treatment with cytokine inhibitors to selectively analyze the effect of the numerous cytokines involved in AI.

Preferred Background/Experience: Basic knowledge of molecular biology and laboratory

techniques. Literature review skills. Interest and motivation are required**.**

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Field(s) of Interest: Developmental and Evolutionary Biology

Research Title: Evolutionary conservation of notochord gene expression in the ascidian, *Ciona intestinalis*.

Project Description: Our lab is interested in identifying the components of the gene regulatory networks underlying notochord development and evolution. This particular project consists in determining whether genes that are expressed in the vertebrate notochord are also expressed in the notochord of larvae of the sea squirt, Ciona. The ultimate goal of these experiments is to establish how many of the genes found in the vertebrate notochord are also present in the Ciona notochord, the most primitive notochord experimentally available. A better understanding of the nature and characteristics of the minimum complement of genes necessary to build a functional notochord is crucial for understanding how the vertebrate notochord develops and, in turn, controls proper development of floor plate, liver, pancreas, and, ultimately, the correct formation of the vertebral column.

Students' Role in the Project: The student would be synthesizing RNA probes to be used for whole-mount *in situ* hybridization experiments on *in vitro* fertilized *Ciona* embryos.

Preferred background/Experience: Good will and some basic knowledge of developmental and molecular biology

References:
Capellini, T.D.*, Dunn, M.P.*, Passamaneck, Y.J., Selleri, L. and Di Gregorio, A.: Conservation of notochord gene expression across chordates: insights from the Leprecan gene family. Genesis Special Issue on Chordate Origins and Evolution.2008. In press. (*equal contribution)

Kugler, J.E., Passamaneck, Y.J., Feldman, T.G., Beh, J., Regnier, T.W. and Di Gregorio, A. Evolutionary conservation of vertebrate notochord genes in the ascidian Ciona intestinalis. Genesis - Special Issue on Chordate Origins and Evolution. 2008. In press.

Capellini, T.D., Zewdu, R., Di Giacomo, G., Asciutti, S., Kugler, J.E., Di Gregorio, A. and Selleri, L.: - Pbx1/Pbx2 govern axial skeletal development by controlling Polycomb and Hox in mesoderm and Pax1/Pax9 in sclerotome. Dev. Biol. 2008. In press.

Passamaneck, Y.J., Hadjantonakis, A.-K., and Di Gregorio, A.: Dynamic and polarized muscle cell behaviors accompany tail morphogenesis in the ascidian Ciona intestinalis. PLoS ONE 2007 Aug 8;2:e714.

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Field(s) of Interest: Uretal obstruction- renal histopathology and function

Field(s) of Interest: Uretal obstruction- renal histopathology and function

Project Descriptions:

Renal Dysfunction models: Hydronephrosis and polycystic kidney disease: In children, the most commonly detected prenatal anomaly is hydronephrosis, the dilation of the renal collecting system. Our laboratory has had a long-standing interest in the molecular mechanisms of damage to the kidney after obstruction, especially the fibrotic response, in which there is a pathologic accumulation of extracellular matrix proteins, which damage the kidney and reduce its function. One of the first events in the obstructed kidney is the build-up of pressure, which results from obstruction of the ureter. We have previously found that pressure activates important signaling pathways in the generation of Nitric Oxide, a cytokine with an important role in renal. Currently, we are investigating how pressure activates the fibrotic process in various cells in the kidney. These studies will use gene array, proteomic and metabolomic approaches to identify appropriate candidates. These studies will be important to determine if there are pathways which might be amenable to therapeutic intervention to halt or reverse renal damage in obstruction. We are also investigating an in vitro model of polycystic kidney disease. Using embryonic kidneys, we are studying different signaling pathways and examining their role in cAMP-mediated cyst formation.

Design of a Synthetic Bladder Augment Patch: Bladder dysfunction related to small, fibrotic bladders is a significant problem in children, resulting in high bladder storage pressures and low bladder volume. The high pressures that build up impact upon bladder function by inducing fibrosis and on quality of life because of incontinence; if left untreated, high bladder pressure can lead to renal failure and a lifetime of dialysis, or renal transplantation. The conventional surgical approach to increase bladder size is bladder augmentation [ileocystoplasty], which is associated with significant morbidity. In our laboratory, we are interested in designing a synthetic bladder augmentation patch to increase the bladder storage capacity. This approach would reduce much of the current surgical morbidity, and would also eliminate the metabolic complications of ileocystoplasty. Studies are underway to determine the biocompatibility of the synthetic patch to determine its suitability for use in vivo.

Effect of Androgens on Development of Genitourinary Tissue **:** Congenital Adrenal Hyperplasia is an inherited deficiency of certain enzymes involved in the production of male hormones [such as androgens]. The most common deficiency is 21-hydroxylase, the enzyme involved in cortisol production. The deficiency of 21-hydroxylase not only decreases cortisol, but also stimulates adrenocorticotropic hormone, leading to excess male hormones. In females, the result of this enzyme deficiency is virilization [the appearance of secondary male characters in the female], which begin in utero; these girls are born with genital ambiguity and an enlarged clitoris. The molecular mechanisms controlling androgen's action in the clitoris are unknown. Therefore, we are studying the in vitro expression of androgen and estrogen receptors in surgical waste tissue obtained from CAH patients. These preliminary studies will allow us to understand how

androgens act on female genitalia, so that we may be able to design strategies to prevent female genitals from the negative effects of androgen excess in CAH.

Wound Healing: The healing of acute cutaneous wounds requires interactions among cytokines, immune cells, parenchymal cells, and components of the extracellular matrix. This process is dynamic and results in scar formation, which restores functional continuity in the affected area. Compromise of the wound-healing process contributes to significant morbidity and even death. Our laboratory has developed a model in which to study wound healing in full thickness human skin. This model was originally developed using pediatric foreskin and was used in several studies by our laboratory. We have recently expanded the model to use adult tissue and to study aspects of the immunology of wound healing in both adult and pediatric skin. We have further adapted this model for use in studies on squamous cell carcinoma.

Students' Role in the Project: Students will learn basic biochemical and molecular biology techniques including immunostaining, PCR, and western blot analysis. They will use these skills in experiments evaluating the effects of pressure on cells in the urinary tract.

Preferred Background/ Experience: Willingness to learn and work hard and committed interest are pre-requisites.

References:

Veerappan A, Reid AC,O'Connor N, Mora R, Brazin JA, Estephan R, Kameue T, Chen J, Felsen D, Seshan SV, Poppas DP, Maack T, Silver RB. Mast Cells are Required for the Development of Renal Fibrosis in the Rodent Unilateral Ureteral Obstruction Model. American Journal of Physiology Renal, in press, 2012. doi:10.1152/ ajprenal.00562.2010

Carlsen I, Donohue KE, Jensen AM, Selzer AR, Chen J, Poppas DP, Felsen D, Frøkiær J and Nørregaard R. Increased cyclooxygenase-2 expression and prostaglandin E2 production in pressurized renal medullary interstitial cells. Am. J. Physiol. Reg. 299: R823 - R831, 2010. PMID: 20610829 PMC2944419

Broadbelt NV, Chen J, Silver RB, Poppas DP and Felsen D. Pressure activates epidermal growth factor receptor (EGFR) leading to the induction of iNOS via NFκB and STAT3 in human proximal tubule cells (HKC-8). American J Physiol Renal 297: F114-F124, 2009. PMID: 19403642 PMC2711717

Mizuguchi Y, Chen J, Seshan SV, Poppas DP, Szeto HH and Felsen D. A novel cell permeable antioxidant peptide decreases renal tubular apoptosis and damage in unilateral ureteral obstruction. Am J Physiol, Renal 295: F1545-F1553, 2008. PMID: 18784263 PMC2584902

Petratos PB, Chen J, Soslow RA, Bleustein CB, Poppas DP, Felsen D. Full-Thickness Human Foreskin Transplantation onto Nude Rats as an In Vivo Model of Acute Human Wound Healing. Plast Reconstr Surg 111:1988-97, 2003. PMID: 12711961

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Field(s) of Interest: Obesity

Research Title: Effect of weight management program on weight/BMI, eating and physical activity behaviors, and quality of life.

Project Description: Data entry and management, study recruitment, medical student mentoring program, IRB proposal development.

Students' Role in the Project: Student will learn the basics of research project development, recruitment for research projects, formulation of an abstract.

Preferred Background/ Experience: Knowledge of Excel helpful, student wiil learn EndNote

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Field(s) of interest: Access to care, Pediatric mental health, Maternal literacy, Maternal depression, Medical Education.

Current Project Title: Addressing the Not-So-New Morbidity within Pediatric Medical Education

Principal Investigators: Dr. Susan Bostwick and Dr. Cori Green

Project Description: We are conducting a needs assessment of pediatric residents and program directors to assess their current training in pediatric mental health issues. A survey is being conducted of all Pediatric Program Directors and focus groups of residents are being run. This project will conclude with the creation of an educational intervention to better train pediatric residents to address mental health issues within the primary care setting. This intervention will be tested in further projects.

Students' Role in the Projects:
Students will learn how to create and help implement educational interventions. Students will be involved in creation of assessment tools, recruitment of resident subjects, analysis of data, and abstract writing.

Preferred Experience: None required

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Field(s) of Interest: Pediatric Orthopedic Surgery and Scoliosis

Research Title: Selected clinical projects in pediatric orthopedic surgery

Project Description: Previous projects include: DDH, congenital muscular torticollis, discoid meniscus, scoliosis and kyphosis.

Students' Role in the Project: Literature review, radiograph review, data analysis

Preferred Background/ Experience: None requested

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Research Title: Alterations in Brain Development following Prenatal Exposure to Cocaine

Project Description: We have a multidisciplinary basic research program in mice to study molecular, neuroanatomic, and behavioral alterations induced in mouse brain development following prenatal exposure to cocaine.

Students' role in the project: Basic Research Skills, including molecular biology, neuroanatomy, and behavioral analyses.

Preferred Background/ Experience: Bench lab experience preferred (especially molecular biology or neuroanatomy).

References:

Tropea TF, Guerriero RM, Willuhn I, Unterwald EM, Ehrlich ME, Steiner H, Kosofsky BE. Augmented D1 dopamine receptor signaling and immediate-early gene induction in adult striatum after prenatal cocaine. *Biol Psych*. 2008;63(11):1066-74.

Tropea TF, Kosofsky BE, Rajadhyaksha AM. Enhanced CREB and DARPP-32 phosphorylation in the nucleus accumbens and CREB, ERK and GluR1 phosphorylation in the dorsal hippocampus is associated with cocaine conditioned place preference behavior. *J Neurochem*. 2008;106(4):1780-90.

Malanga CJ, Ren JQ, Guerriero RM, Kosofsky BE. Augmentation of cocaine-sensitized dopamine release in the nucleus accumbens of adult mice following prenatal cocaine exposure. Dev Neurosci. 2009;31(1-2):76-89.

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Research Title: Neonatal Lung Function

Preferred Background/ Experience: None requested

References:

Ballabh, P. ; J. Kumari,; A.N. Krauss, MD; J. Shin, ; A. K. Jain; P.A.M. Auld, and S. Cunningham-Rundles 2003 Soluble E-selectin, Soluble L-selectin and Soluble ICAM-1 in Bronchopulmonary Dysplasia and Changes with Dexamethasone. Pediatrics 111(3):461-8

Ballabh, P.; M. Simm; J. Kumari, C. Califano, Z. Aghai, Laborada, G., C. Sison, and S. Cunningham-Rundles. 2003 Respiratory burst activity in bronchopulmonary dysplasia and changes with dexamethasone Pediatric Pulmonol 35(5): 392-9

Ballabh, P.; M. Simm; J. Kumari, A.N. Krauss; A. Jain, PAM Auld, and S. Cunningham-Rundles. 2003 Lymphocyte Phenotypes in Bronchopulmonary Dysplasia. Am J. Perinatol 8:465-475

Ballabh, P.; M. Simm; J. Kumari, ; A.N. Krauss; A. Jain, C. Califano, M.L. Lesser, and S. Cunningham-Rundles 2004 Neutrophil and Monocyte Adhesion Molecules in Bronchopulmonary Dysplasia, and Effects of Corticosteroids Arch Dis. Child 89: 76-83

Dermendjian, M., Varma, S., Krauss, A.N., Auld, P.A.M.: Functional residual capacity (FRC) does not predict response to surfactant in preterm infants. Am. J. Perinatology, 2002;19:155-162.

Aghai, Z., Arevalo, R., Lumicao, L., Lesser, M., Shi, Q., Jain, J., Krauss, A.N., Auld, P.A.M., Hanauske-Abel, H.M.: Basement membrane biomarkers in very low birth weight premature infants. Biology of the Neonate, 2002;81:16-22

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Field(s) of Interest: Sickle Cell Disease, Anemia, Coagulation and Bleeding Disorders, Myeloproliferative disorders, Leukemia, Bone Marrow Failure/Abnormal Hematopoiesis

Potential Research Topics: I do not have currently established projects for students, however I have some ideas for survey-based projects that could be of interest to students whom I will mentor

1. Pediatrician assessment of menorrhagia – screening if and how pediatricians assess their female adolescent patients for menorrhagia, and their referral practices, with possible educational intervention after
2. Pediatric care providers and pain management – assessing boundaries in our institution to providing pain management for pediatric patients; possibly working with anesthesia to develop educational interventions
3. Thrombosis in Pediatric Inpatients – we are currently submitting an IRB for a retrospective chart review to look at incidence of thrombosis in our pediatric inpatients and to identify the most common risk factors in our population and possibly identify new risk factors for thrombosis in hospitalized children

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Field(s) of Interest: Pediatric renal disease, vitamin D, cardiovascular outcomes of chronic kidney disease, kidney transport, • Focal segmental glomerulosclerosis

Research Projects:

1. Vitamin D in children with chronic kidney disease (CKD): prevalence of deficiency and clinical correlates: This is a NIH funded ancillary study to the ongoing multicenter, prospective cohort study of children with CKD (CKiD). My study aims to define the prevalence and correlates of vitamin D deficiency. It will also prospectively evaluate the role of Vitamin D deficiency in growth failure, progression of CKD and cardiovascular outcomes.
2. Vitamin D supplementation in children with chronic kidney disease: Current guidelines for vitamin D supplementation in children with CKD are not evidence based and are extrapolated from adults. This study aims to evaluate the adequacy of the current KDOQI recommendations for treating vitamin D deficiency in these children.
3. Kidney transplant outcomes: This proposal aims to evaluate the effects of using a steroid free immunosuppression protocol on outcomes such as growth, allograft rejection and cardiovascular profile.
4. Focal segmental glomerulosclerosis (FSGS): FSGS is a devastating glomerulopathy that leads to end stage renal disease. It also tends to recur in 30-50% of patients after kidney transplantation, eventually leading to allograft loss. We have used Rituximab as a rescue therapy in our patients with recurrent FSGS with partial remission of proteinuria. We are collaborating with other centers in the US to evaluate the practice patterns for Rituximab use in recurrent FSGS.

References:

1. Sharief S, Jariwala S, Kumar J, Muntner P, Melamed ML. Vitamin D levels and food and environmental allergies in the United States: Results from NHANES 2005-2006. J Allergy Clin Immunol. 2011 May; 127(5):1195-202. Epub 2011 Feb 16. PMID: 21329969
2. Skversky Amy, Kumar Juhi, Abramowitz Matthew, Kaskel Frederick, Melamed Michal. Association of Glucocorticoid use and low 25-hydroxyvitamin D levels: results from the National Health and Nutrition Examination Survey (NHANES): 2001-2006. J Clin Endocrinol Metab. 2011 Sep 28. [Epub ahead of print] PMID: 21956424
3. Kumar Juhi, Furth Susan, Warady Bradley. The Pediatric Patient with Chronic Kidney Disease-Mineral Bone Disorder. Accepted for publication in the Clinical Reviews in Bone and Mineral Metabolism. Anticipated Publication date 12/2011
4. Melamed ML, Kumar J. Low levels of 25-hydroxyvitamin D in the pediatric populations: prevalence and clinical outcomes. Pediatric Health, February 2010, Vol. 4, No. 1, Pages 89-97.

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Field(s) of Interest: Pediatric rheumatic diseases

Project Description: Students have been involved in a variety of clinical research projects over the past years.

Students' Role in the Project: Chart review, data tabulation. We also teach basic aspects of clinical pediatric rheumatology/history.

Preferred Background/ Experience: None requested

References:

Lehmann HW, Lutterbuse N, Plentz A, et al. Association of parvovirus B19 infection and Hashimoto's thyroiditis in children. Viral Immunol. Sep 2008;21(3):379-383.

Kieseier BC, Meyer Zu Horste G, Lehmann HC, Gold R, Hartung HP. Intravenous immunoglobulins in the treatment of immune neuropathies. Curr Opin Neurol. Oct 2008;21(5):555-562.

Kuerten S, Javeri S, Tary-Lehmann M, Lehmann PV, Angelov DN. Fundamental differences in the dynamics of CNS lesion development and composition in MP4- and MOG peptide 35-55-induced experimental autoimmune encephalomyelitis. Clin Immunol. Nov 2008;129(2):256-267.

Lehmann HC, Hartung HP. Complementing the therapeutic armamentarium for Miller Fisher Syndrome and related immune neuropathies. Brain. May 2008;131(Pt 5):1168-1170.

Lehmann GM, Garcia-Bates TM, Smith TJ, Feldon SE, Phipps RP. Regulation of Lymphocyte Function by PPARgamma: Relevance to Thyroid Eye Disease-Related Inflammation. PPAR Res. 2008;2008:895901.

Lehman HK, Ballow M. Immune deficiency disorders with autoimmunity and abnormalities in immune regulation-monogenic autoimmune diseases. Clin Rev Allergy Immunol. Apr 2008;34(2):141-145.

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Field(s) of Interest: Angiogenesis

Research Title: The role of bone marrow precursors in tumor angiogenesis and regeneration.

Project Description: Determine the role of VEGFR1 myeloid and VEGFR2 endothelial stem and progenitor cells in the formation of new vessels in tumor and Metastatic models and in wound healing studies such as burns and myocardial infarction.

Students' Role in the Project: The student will be responsible for leading one of several aspects in the study of neoangiogenesis.

Preferred Background/ Experience: None requested

References:

Kaplan RN, Lyden D. Metastases: setting up shop. Nature Reviews Cancer 2006 6 (1): 3.

Kaplan RN, Lyden D. Envoys of metastasis. Nature Medicine 2006 12 (1): 18.Jin DK, Kopp H, Petit I, Shido K, Young LM, Kanhai G, Amano H, Acevilla S, Heissig B, Hattori K, Zhang F, Hicklin DJ, Dunn A, Salari H, Werb Z, Hackett NR, Crystal RG, Lyden D, Rafii S.

Cytokine-mediated Deployment of SDF-1 revascularization through recruitment of CXCR4+ hemangiocytes. Nature Medicine 2006 12 (5):557-567.

Rafii S. and Lyden D. S100 chemokines mediate bookmarking of pre-metastatic niches. Nature Cell Biology. 2006 8:1321-1323.

Gilheeney SW, Lyden DC, Sgouros S, Antunes N, Gerald W, Kramer K, Lis E, Meyers P, Rosen N, Thaler HT, Trippett T, Wexler L, Dunkel IJ. A phase II trial of thalidomide and cyclophosphamide in patients with recurrent or refractory pediatric malignancies. Pediatr Blood Cancer 2007 49(3):261-265.

Rafii S and Lyden D. Cancer; A few to flip the angiogenic switch. Science 2008 319:163-164.

Podolanczuk A, Kaplan RN, Psaila B, Rafii S, Lyden D. ?Targeting the Steps in Metastatic Progression? in Bone and Cancer. (In Press, February 2008).

Shmelkov SV, Butler J, Hooper AT, Hormigo A, Kushner J, Milde T, St. Clair R, Murphy AJ, Valenzuela DM, Gale NW, Thurston G, Yancopoulos GD, Lyden D (corresponding author), Rafii S. CD133 identifies luminal differentiated epithelium and both CD133+ and CD133- cells initiate metastatic epithelial carcinomas. Journal of Clinical Investigation, Under 2nd Revision

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Field(s) of Interest: Benign Hematology, Thrombosis, Coagulation, Thrombocytopenia

Research Title**:** Quality Improvement/ Outcomes in Pediatric Hematology Population

Description of Project(s): To be decided in conjunction with research team. Prospective survey or retrospective chart review format. Ideas include looking at sickle cell pain management pathway, anti-coagulation adherence, etc.

Students' Role in the Project: Flexible. Would be developed as project expanded

Preferred Background/ Experience: None requested Enthusiasm is important.

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Fields of Interest: Clinical and laboratory aspects of bleeding, clotting, and platelet biology

Research Project 1: Bleeding complications in patients with connective tissue disorders.

Description of Project: We have seen a series of patients with connective tissue disorders who present with bleeding. This project will be a retrospective chart review to compile and analyze the bleeding characteristics of this population. Given the large sample size this project should provide unique information about bleeding in connective tissue disorders.

Students' Role in the Project: Chart review. Assistance with IRB process, scientific writing.

Preferred Background/ Experience: None

Research Project 2: A novel mutation resulting in an unusual type 2A von Willebrand Disease

Description of Project: We have identified a family with a novel mutation causing severe type 2A VWD. The mutation completely eliminates some aspects of von Willebrand factor function, but leaves others intact. Review of these patients' laboratory and clinical findings in concert with what is known of the VWF structure will likely reveal novel information about VWF structure and function.

Students' Role in the Project: Chart review. Assist with IRB submission. Review of literature. Scientific writing. Work with 3D structure imaging software.

Preferred Background/ Experience: None, although it would help if adept at computers.

Research Project 3: Morphology of platelets during thrombopoiesis

Description of Project: We are producing platelets from stem cells derived from umbilical cord blood cells. One critical question is whether the produced platelets are "normal". To determine this we are analyzing the platelets in several different ways. One of these ways is by morphology. We use both light and fluorescence microscopy to study the platelets as they are being produced in culture. This project will establish a baseline morphology by which to judge the effects of changes in the production techniques.

Students' Role in the Project: This will be primarily a visual cataloguing of microscopy images. The student will learn to use our imaging software and microscopes.

Preferred Background/ Experience: None, but will have to take the NYBC volunteer orientation.

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Matteo Porotto, PhD

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Field(s) of Interest: Infectious diseases – Virology (specifically respiratory viruses and viral agents of bioterrorism).

Research Title: Molecular pathogenesis of human paramyxoviruses: parainfluenza virus type 3, and Hendra virus.

Project Description(s) The laboratory's research centers on molecular pathogenesis of human paramyxoviruses: parainfluenza virus type 3, and recently also the emerging pathogen Hendra virus. Parainfluenza virus is an important cause of lower respiratory tract infections in children, including croup and bronchiolitis, and there are currently no vaccines or antiviral agents for these diseases. Hendra virus is a highly fatal paramyxovirus is a potential agent of bioterrorism. We are interested in how viruses enter cells by fusing with the cells' envelope, and in how we might interfere with entry.

Molecular basis for human parainfluenza virus 3 infection. This laboratory has identified the role of the parainfluenza virus receptor-binding protein hemagglutinin-neuraminidase (HN) in the virus-induced fusion process whereby all paramyxoviruses enter host cells. HN's receptor binding is the critical first step towards HN's role in fusion promotion, and leads to activating or "triggering" of the fusion protein (F) to mediate fusion. Our parainfluenza projects focus on the molecular mechanisms for HN in the viral life cycle and in lung pathogenesis. Ongoing studies have led to novel antiviral strategies that are being tested, and to understanding mechanisms of resistance to antivirals.

Role of human parainfluenza virus 3 hemagglutinin-neuraminidase in immunopathogenesis of lung disease. The role of HN in pathogenesis of lung disease in vivo is being studied in a cotton rat model. Our group showed that mutations in HN that alter HN-receptor interaction (but do not affect replication) lead to dramatic differences in the disease in the cotton rat lung. We are determining whether HN's receptor affinity, its receptor-cleaving, or its F-triggering activities determine its virulence in the lung. We also are interested in identifying which immune response is altered by HN mutations that lead to enhanced disease.

Triggering of fusion by Hendra virus F protein: the role of G: In the Hendra virus projects, we apply our strategies for the study of paramyxovirus entry and fusion to an emerging and potentially fatal paramyxovirus that is viewed as a potential bioterrorism agent. For Hendra virus, the receptor binding protein (G) is required in order for the F protein to mediate fusion. Hendra G binding to receptor, like parainfluenza virus HN binding to sialic acid, "triggers" F protein to mediate fusion. The study of the mechanism of triggering/activation of F protein in Hendra virus should lead to strategies for interfering with this key step in viral entry.

Triggering Hendra F to fuse: peptides to interfere with fusion: Taking advantage of our finding that peptides that correspond to regions of HPIV3 F are superior to those derived from Hendra F at inhibiting Hendra fusion, we will determine whether inhibitory F-peptides bind to Hendra F, as would be predicted if the peptides are preventing the formation of the 6-helix bundle (6HB) believed to be required for fusion, or if inhibitory F-peptides bind to G and interfere with G triggering of F.

Innovative approaches to developing therapeutic and diagnostic reagents for Hendra virus. Insertion of F into the target cell membrane leads to fusion of the viral envelope with the plasma membrane and release of the nucleocapsid into the cytoplasm. Efficiency of F-triggering by G influences the extent of fusion, and provides a range of strategies for preventing viral entry. Based upon our studies of the paramyxovirus F-triggering process, peptides corresponding to heptad repeat regions of F can be used to prevent F from reaching its fusion-active state. It may also be possible to induce F to trigger "prematurely", thus becoming incapacitated before it reaches its target. Finally, molecules that inhibit receptor binding may prevent receptor interaction and all downstream events. Targeting several stages of the entry process simultaneously may provide synergism.

Students' Role in the Project:
Virology, molecular biology, biochemistry, structural analysis, immunology

Preferred Background/Experience.
Some lab experience preferred but not required. Interest and motivation are required.

References:

DeLaMora P and Moscona A. A daring treatment and a successful outcome: The need for targeted therapies for pediatric respiratory viruses. Pediatric Transplan. 11(2): 121-123, 2007.

Moscona A, McKimm-Breschkin J. News about influenza B drug resistance that cannot be ignored. Journal of the American Medical Association (JAMA) 2007 Apr 4;297(13):1492-3.

Palermo LM, Porotto M, Greengard O, and Moscona A. Fusion promotion by a paramyxovirus HN: modulation of receptor avidity of binding sites I and II by pH, J. Virol. 81 (17), 9152-9161, 2007

Porotto, M., Carta, P, Deng, Y, Kellogg, GE, Whitt, M, Lu, M, Mungall, BA, Moscona, A. Molecular determinants of antiviral potency of paramyxovirus entry inhibitors. Journal of Virology 81 (19): 10567-74, 2007.

Moscona, A. CSI Microbiology: Emerging pathogens and a staged strategy for detection and discovery. Journal of Infectious Diseases 196: 1727-8, 2007.

Aljofan M, Porotto M, Moscona A, Mungall BA. Development and validation of a chemiluminescent immunodetection assay amenable to high throughput screening of antiviral drugs for Nipah and Hendra virus. J Virol Methods. 2008 Apr;149(1):12-9.

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Field(s) of Interest: Pediatric infectious disease

Research project 1: Serologic Response To High Dose Hepatitis B (HBV) Vaccine In HIV Infected Children

Project Description: The project is divided in 2 parts. Part 1) Is a retrospective chart review of all children/adolescents followed at our HIV Clinic to evaluate the response to the initial HBV

vaccine. For each patient the following information will be collected: date of birth, age, gender, CDC clinical stage, nadir CD4 count, age at different doses of HBV and CD4 count at time of each dose if available, antiretroviral treatment history and in particular if on highly active antiretroviral therapy (HAART) at time of vaccination. Part 2) Is a prospective evaluation of antibody response after re-vaccination with a high dose of HBV vaccine. All subjects will have the HBV titers checked at baseline (week 0); if identified as "non-immune" the subject will receive a new series of HBV vaccine. Again CD4 count and percentage, CD19 count and percentage and viral load will be recorded and antiretroviral regimen will be reviewed.
At Week 24 from the vaccine booster the HBV titers and/or "immune"/"non-immune" status will again be rechecked in all subjects receiving the new dose to evaluate immune response.
The purpose of the study is to identify the possible risk factors that predispose HIV positive children to have a reduced immune response to HBV vaccine and to evaluate if administering a higher dose would improve the immune response

Students' Role in the Project: Learn to review and collect the most important data from a medical history. Help creating a database, analyzing the data and eventually submitting an abstract to a national meeting.

Preferred Background/ Experience: None in particular. A lot of enthusiasm and willingness to spend some time looking into the charts and possibly interacting with a particular group of children with special needs.

Research project 2: Infectious Complications After Spine Surgery in Children

Project Description: Retrospective chart review. The medical records of pediatric patients who required from 2000 to 2010 a surgical spine fusion will retrospectively be reviewed. The medical records of pediatric patients who developed infections and required irrigation and debridement (I&D) will retrospectively be reviewed in detail. Among the data that will be collected are: underlying disease, the time of diagnosis of the infection from the surgery, antibiotics at time of surgery, organisms isolated, antibiotic therapy and length of therapy, outcome. The purpose of the study is to identify possible risks factors and most frequent microorganisms involved so to recommend the most appropriate prophylactic antibiotic regimen at time of the surgery.

Students' Role in the Project: Learn to review and collect the most important data from a medical history. Help creating a database, analyzing the data and eventually submitting an abstract to a national meeting.

Preferred Background/ Experience: None in particular. A lot of enthusiasm and willing to spend some time looking into the charts

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Field(s) of Interest: Obesity and Medical Communication skills

Title of Research Project: Medical Communication Skills and Exploratory cancer project

Project Descriptions: The project includes goals for empirical evaluation of the family-centered care program. There are two projects on Medical Communication Skills. A Third project is focused on the natural history of pre-malignancy and the metastatic niche.

The first project will assess parent satisfaction with patient care before and after the introduction of Family-Centered Rounds. Parent perceptions of clinical care will be assessed among all families of hospitalized pediatric service patients upon admission. Time series analyses will be used to evaluate changes in patient satisfaction in response to the new strategy for bedside rounds.

The second project is a study to evaluate the impact of Family Centered Rounds on medical commun-ications skills among pediatric residents. The study was designed with the directors of pediatric resident training at KCCH to introduce standardized scales to assess resident communication skills by parents, nurses, and supervising physicians. I will use the existing data from education files without identifiers from two time periods to assess the utility of a new clinical program of family-centered rounds. I am also working on developing communication curriculum for pediatric residents.

The third project is collaborative with Dr. David Lyden. This is an investigation of profiles of angiogenic and metastatic parameters in children with and without cancer. Emerging evidence suggests that bone marrow-derived , hematopoietic stem progenitor cells (HPC's) and endothelial progenitor cells (EPC's) contribute to tissue vascularization during both embryonic and postnatal physiological processes. Identification of cellular mediators and tissue-specific chemokines, which facilitate selective recruitment of bone marrow-derived stem and progenitor cells to specific organs, may provide insight into the mechanisms by which the pre-metastatic niche develops in patients with pediatrics malignancies. In this study, we seek to compare peripheral levels of circulating chemokines and progenitor cells in healthy pediatric controls to those of age-matched patients with pediatric malignancies. My role in this project involves recruiting and profiling blood samples from children who do not have cancer. Obtaining this information will be crucial in defining norms for the measures to be gathered among cancer patients. We will analyze blood samples gathered as "extra" blood when children already are undergoing blood testing. From these samples, we will measure plasma levels of growth factor and chemokine profile. This profile includes VGEF (vascular endotheiial growth factor), PIGF (Placental derived growth factor), FGF (fibroblast derived growth factor), and SDF-1 (stromal derived growth factor). We have obtained IRB approval for this project, which also is approved by the WCMC CTSC.

I am also expanding my research to study angiogenesis and vasculogenesis among children who are overweight, as it is well known that the population of obese pediatric patients faces a future that includes elevated risk for cancers and cardiovascular problems. Research in adults has demonstrated that angiogenic factors are elevated in overweight and obese individuals. Furthermore, previous research demonstrated that coupling of adipogenesis and angiogenesis is essential for differentiation of adypocytes in obesity and that vascular growth factor (VGEF) is a key mediator. We will explore what genetic variants are responsible for this effect and possible predict which subtypes of obesity are more prone to cancer. This research can be enhanced by studying other family members with obesity and malignancies to determine the genetic factors involved in the pre-metastatic setting.

Students' Role in the Project: 1. Medical Communication skills and patient satisfaction projects will provide the student with opportunities to learn how to develop questionnaire as an assessment tool, IRB process, how to analyze data. The third project is now centering on obesity-data collection, data entry, data analysis in collaboration with Dr. Lyden's lab.

Preferred Background/ Experience: None

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Field(s) of Interest: Neonatology, Brain development, Resuscitation

Title of Research Project: Evaluation of the Ergonomics of Chest Compressions in a Neonatal Manikin Model

Project Description: Evaluate the influence of compression rates on the depth of compressions including decay over time as well as the potential influence of surface location and gender.
Students' Role in the Project: Assist in the evaluations of data following a session and help to develop strategies to enhance CPR in the neonatal period

Preferred Background/ Experience: None

References:

Christman C, Hemway RJ, Wyckoff MW, Perlman JM The Two Thumb is Superior to the Two Finger Method for Administering Chest Compressions in Newly Born Infants. *Arch Dis Child Fetal Neonatal Ed 2011;96:F99-F101*

Hemway RJ , Huynh T, Perlman JM Chest Compressions in a Neonatal Manikin Model Vary in Depth and are Modulated by Duration, Height and Gender: Potential Implications for Asphyxial Arrest When Ventilation is Minimized. AHA Sessions 2011 Orlando Florida 2011

Huynh T, Hemway RJ, Perlman JM . The Two Thumb rather than the Two Finger (TF) Technique Using an Elevated Surface Rather than the Floor Should be the Preferred Method of Teaching Infant CPR Anytime™ PAS meeting. Denver 2011

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Project Description: Pediatric, clinical and lab research. Spine Osteogenesis Imperfecta, Skeletal Dysplasia

Students' Role in the Project: Patient interaction, dissection, x-ray review, computer work

Preferred Background/ Experience: Good work ethic and enthusiasm

References:

Giampietro PF, Peterson MG, Schneider R, et al. Bone Mineral Density Determinations by DualEnergy x-ray Absorptiometry in the Management of Patients with Marfan Syndrome-Some Factors Which Affect the Measurement. Hss J. Feb 2007;3(1):89-92.

Carter EM, Davis JG, Raggio CL. Advances in understanding etiology of achondroplasia and review of management. Curr Opin Pediatr. Feb 2007;19(1):32-37.

Raggio CL. Sexual dimorphism in adolescent idiopathic scoliosis. Orthop Clin North Am. Oct 2006;37(4):555-558.

Giampietro PF, Raggio CL, Reynolds C, et al. DLL3 as a candidate gene for vertebral malformations. Am J Med Genet A. Nov 15 2006;140(22):2447-2453.

Ghebranious N, Burmester JK, Glurich I, et al. Evaluation of SLC35A3 as a candidate gene for human vertebral malformations. Am J Med Genet A. Jun 15 2006;140(12):1346-1348.

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Research Title:
1) Development of new strategies to cure beta-thalassemia
2) The role of iron in cancer and anemia of inflammation

Project(s) Description:

Gene therapy of beta-thalassemia

Abnormal erythropoiesis and iron metabolism in beta-thalassemia

The role of iron metabolism in cancer and anemia of inflammation

The projects include:

- Design and generation of retro or lentiviral vector harboring genes involved in abnormal hematopoiesis and iron disorders
- Design and generation of retro or lentiviral vector with genomic elements to regulate gene expression
- Test of the system *in vitro*
- Test of the system *in vivo* (infection of hematopoietic stem cells, embryonic stem cells, bone marrow transplantation and/or generation of transgenic animals)
- Generation of new tumor models and their correlation with inflammation, anemia and tumor progression

Students' Role in the Project:
Microbiology: bacteria transformation, plasmid DNA preparation
Molecular Biology: generation of recombinant DNA vectors, Southern blot analysis

Tissue Culture: maintenance and expansion of primary and secondary tissue culture cell lines; retroviral production, viral transduction
Mouse handling: analysis of hematopoietic parameters (CBC), facs, iron, gene and protein analyses, gene transfer in the bone marrow and liver, tumor induction and analysis

Preferred Background/ Experience: Basic and good knowledge of molecular biology and laboratory techniques; good skills in reviewing and summarizing scientific literature. The subjects that the
candidate will review include: retrovirus, RNA interference, tetracycline controlled gene expression system, mouse embryonic stem cells. Good organization skills; computer literate.

References:

Breda L. and Rivella S. "Gene Therapy in Thalassemia and Hemoglobinopathies". Invited review: *Mediterranean Journal of Hematology and Infectious Diseases.* Epub 2009 Nov

Rivella S. and Rachmilewitz E "Alternative therapies for thalassemia". *Expert Review of Hematology.* Epub 2009 Oct

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Research Title: Vascular Endothelium – A Life Line During Development And In The Adult

Development of a functional circulatory system in the vertebrate embryo is crucial for delivery of nutrients and oxygen to the embryo. Defects in the development of blood vessels result in death before birth or in congenital cardiovascular abnormalities. During physiological angiogenesis in the adult organism such as wound healing and during pregnancy, endothelial cells are stimulated to form new vessels, a process termed neo-angiogenesis. Similarly, during pathological processes such as ischemia, myocardial infarct, repair of injured tissue and tumor growth, endothelial cells become activated to sprout, migrate, and undergo remodeling. Thus, endothelial cells constitute a dynamic system that changes in response to environmental stimuli. Research in my laboratory focuses on understanding the molecular mechanisms that orchestrate these processes, using the mouse as a model system.

In a genetic screen for early developmental genes, we identified two novel genes that play important roles in vascular development and homeostasis. One of these, Vascular endothelial zinc finger 1 (Vezf1) encodes an endothelial transcription factor that plays essential, dosage-dependent roles in vascular system development. Vezf1KO embryos die at midgestation due to vascular remodeling defects and hemorrhaging. Unexpectedly, we found that heterozygous embryos display lymphatic vessel abnormalities that are reminiscent of the human congenital malformation syndrome, nuchal edema. We are presently collaborating with clinicians in the Fetal-Maternal Medicine Division at New York Presbyterian/Weill Cornell Medical College to investigate if human fetuses with nuchal edemas carry mutations in the VEZF1 gene.

A second gene identified in our screen, EGF-like domain 7 (Egfl7), is an early embryonic marker for endothelial cells and their progenitors. EGFL7 is a unique angiogenic factor: it is secreted

specifically by endothelial cells, acts as a chemoattractant, and binds to the extracellular matrix. Importantly, we showed that EGFL7 interacts with and antagonizes endothelial Notch, a key vascular signaling pathway component. Overexpression or knockdown of Egfl7 in mouse embryonic stem cells, primary endothelial cells, mouse embryos and the post-natal retina results in defects in vascular sprouting, proliferation, and migration. Our ongoing studies indicate that Egfl7 expression is induced by hypoxia and Vascular endothelial growth factor, VEGF, and that it may play important roles in physiological angiogenesis during pregnancy. Specifically, we are examining its possible role in implantation and placentation, and how it may be involved in the development of preeclampsia

Students' Role in the Project:
The student would get "hands-on" lab experience. Initially, the student would work together with a research scientist in the lab to learn and master the required techniques, and later work more independently. The laboratory techniques could involve: Extraction of protein from tissue sample; protein gel electrophoresis; Western blot analysis Extraction of DNA from tissue samples; PCR amplification, DNA gel electrophoresis, preparation of sample for DNA sequence analysis Dissection of mouse embryos; embedding and sectioning, immunostaining/immunofluorescence analysis

Preferred Background/ Experience: Basic lab skills, knowledge in molecular and developmental biology, strong interest in research

References:

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Field(s) of Interest: Pediatric Infectious Diseases

Research Title 1: *Clostridium difficile* colonization in infants and young children

Project Description: *Clostridium difficile* can cause diarrhea and severe illness in children and adults. *C. difficile* infection is likely under-recognized in the young pediatric population. Infants and young children are often not evaluated for *C. difficile* infection because it is thought to colonize their gut. However, it is unknown how commonly it colonizes the stool of young children. The rates published are extremely wide ranging and reported as being anywhere from 10-100% during the first year of life. The objective of this study is to describe the prevalence of *C. difficile* colonization in infants and young children and to assess possible risk factors.

Students' Role in the Project: The student's role will be the recruitment of study subjects in the inpatient and outpatient settings. This would involve learning how to consent and enroll patients with one of the co-investigator's and then eventually doing this independently. Part of the student's role will also be entry of the information into the database.

Preferred Background/ Experience: Interest in participating in clinical research.

Chani Traube, MD
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Field(s) of Interest: Pediatric Critical Care Medicine; pediatric neuro-intensive care

Research Title: Detection of Pediatric Delirium: Validation of a Rapid, Observational Assessment Tool

Project Description: Delirium in critically ill children represents acute brain dysfunction, with short- and long-term health implications. There is an emerging literature suggesting that this is a common, serious, and under-diagnosed problem in seriously ill children. Evidence-based assessments of outcomes and interventions for pediatric delirium are lacking, largely due to the absence of a simple and reliable screening tool.

My research partners and I have developed a novel screening tool for the detection of delirium in this population, and have completed a pilot study confirming its feasibility, and suggesting a prevalence of >25% in our subjects. Once validated, this tool will allow for rapid and accurate identification of delirious children, facilitate appropriate interventions, and may improve long-term functional outcomes.

Students' Role in the Project: Students will have the opportunity to join a multidisciplinary team engaged in several projects regarding pediatric critical illness and its implications on brain function. They will participate in research study design, data collection, and manuscript writing. Students will learn how to obtain informed consent, conduct chart reviews, analyze data, and perform follow-up phone calls using surveys to detect whether a patient has experienced long-term effects from delirium.

Preferred Background/ Experience: None required. Interested students should be friendly, comfortable interacting with children and their families, and demonstrate organizational skills and attention to detail. Research is ongoing, with active clinical trials in progress, others pending IRB approval, and others in planning stage.

Susan J. Vannucci, PhD
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Field(s) of Interest: Developmental Brain Injury/Hypoxic Ischemic Encephalopathy/Hypoglycemia/Neonatal Seizures

Research Title: Hypoxia-Ischemia in the Immature Brain

Project Description: Hypoxic-Ischemic (HI) brain damage resulting from asphyxia in the neonatal period is a major cause of death of premature and term infants and responsible for permanent neurologic handicap in the survivors. We have developed an animal model to study this injury in the newborn rat and utilize this model in both preterm and term-equivalent rodents. HIE is a major cause of seizures yet there is continued debate as to whether these seizures contribute to or merely reflect the severity of brain damage. We have recently extended our HIE model to include the detection of behavioral and electrographic seizures to test several of these relevant questions. A second project using this model will continue to look at the role of mast cells in promoting inflammation and cell death following HI in the immature brain.

Students' Role in the Project: The student can assist in performing the surgeries to induce the hypoxia-ischemia, as well as in the recording of the video EEG. It is important that the student is comfortable working with animals and in survival surgeries as well as in euthanasia of the animals to study the effects on brain development and injury. In addition, the student could participate in the study of the role of mast cells in mediating the inflammatory cascade as well as potentially contributing to the tissue repair.

Maria Vogiatzi, MD
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Research Topics:

Studies of osteoporosis in thalassemia: Thalassemia is a congenital hemolytic anemia that is associated with high rates of osteoporosis. The etiology of osteoporosis in this disease is poorly understood. Our project examines the etiology of bone disease in thalassemia, by doing both clinical and animal studies. We use a mouse of model of thalassemia to determine the effect of certain medical interventions (such as PTH and bisphosphonates). The methodology that is used

includes imaging, such as micro-CT, histology for assessment of bone remodeling and other basic science techniques.

Effect of erythropoiesis on mesenchymal differentiation: In this project, we use the thalassemia mouse as of model to study the effect of hematopoiesis on bone remodeling. Our results so far support the hypothesis that hematopoietic progenitors affect mesenchymal differentiation leading to decreased osteogenesis. In addition, we have identified that this process involves erythropoietin (EPO). Cell cultures and co cultures, other basic science techniques and other mice models are used to examine the interactions of EPO and autocrine/paracrine factors on bone remodeling.

The role of iron in the development of osteoporosis: This project involves studies in iron overloaded mice, and the effect of iron overload on bone remodeling. The methodology that is used includes imaging, such as micro-CT, and histology for assessment of bone remodeling. Cell cultures and other basic science techniques are used to determine the role of iron on mineralization and the osteoclast.

Inflammatory response to iron excess: Iron excess has been thought to lead to increased oxidative stress. Our animal data support the presence of ROS and an inflammatory response. Our lab is in the processing of delineating the molecular mechanism by which iron excess triggers an inflammatory cascade. This is done by performing animal experiments using techniques such as flow cytometry.

Studies of diabetes in iron overload and thalassemia: Iron excess is associated with a number of endocrinopathies including diabetes. This project determines the development of insulin resistance and diabetes in our murine diabetes model as well the role of oxidative stress and inflammation in this process. In addition, we are conducting clinical studies that examine glucose abnormalities in iron overloaded patients with thalassemia by using continuous glucose monitoring by glucose sensors.

Studies of vitamin D supplementation on calcium excretion in thalassemia. This project studies the effect of various vitamin D doses on serum vitamin D concentrations and calcium excretion in regularly transfused patients with thalassemia. The study is supported by Cooley's Anemia Foundation grant.

Students' Role in the Projects: The student can be exposed to imaging techniques such as microCT, bone histology and dynamic histomorphometry for assessment of bone remodeling and basic science techniques including cell cultures and flow cytometry. The student will also have the opportunity to participate in clinical research in the area of diabetes and osteoporosis.

Preferred Background/ Experience: The student must be familiar with basic laboratory procedures. Biology majors preferred

References:

M.G. Vogiatzi, E.A. Maclin, E.B. Fung, E. Vichinsky, N. Oliveri, J. Kwiatkowski, A. Cohen, E. Neufield and P.J. Giardina for the Thalassemia Clinical Research Network. Prevalence of fractures among the thalassemia syndromes in North America. Bone, 2006; 38: 571-575.

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J. Tsay, C. Pomeranz, A. Hassoun, S. O. Zandieh, J. Rutledge, M.G. Vogiatzi, S.E. Oberfield, R. Motaghedi, Screening Markers of Impaired Glucose Tolerance in the Obese Pediatric Population. Hormone Research. 2010; 73 (2): 102 – 107

J. Tsay, C. Pomeranz, A. Hassoun, S. O. Zandieh, J. Rutledge, M.G. Vogiatzi, S.E. Oberfield, R. Motaghedi, Screening Markers of Impaired Glucose Tolerance in the Obese Pediatric Population. Hormone Research. 2010; 73 (2): 102 – 107

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Field(s) of Interest: Development: infants, children, mother-child interaction

Research Title: Infant feeding skills, parental feeding practices, and growth disorders

Project Description: We will evaluate the effectiveness of an intervention delivered to the parents of infants from birth to 6 months of age. The study will include 75 families in a standard care group and 75 in an intervention group. The first group (standard care group) will receive routine well-child care on the schedule recommended by the American Academy of Pediatrics. The second (intervention group) will receive routine well-child care plus an intervention focused on teaching parents about age-appropriate infant nutrition and infant feeding skills. Group assignment will be made on the basis of historical cohort membership: the standard care group will be enrolled first and the intervention group enrolled approximately 3 months later. Subjects in both groups will be followed for 6 months. Outcome measures include parent feeding practices, infant diet, infant feeding skills, and infant overweight. Measures will address cultural and familial biases in favor of overweight children.

The following hypotheses will be tested:

- Compared to parents in the standard care group, more parents in the intervention group will report feeding only single-grain infant cereal and Stage 1 fruits and vegetables to their 6 month-olds. In contrast, more parents in the standard care group will report feeding Stage 2 and 3 foods, snacks, juice, and table foods.
- At 6 months, the rate of infant weight for length above the 75th percentile will be higher in the standard care versus intervention group.
- Parents in the intervention group will be more likely to report receiving accurate information about infant feeding and nutrition from their pediatricians than parents in the standard care group.

- More infants in the intervention than standard care group will use a cup for drinking and fewer will have been fed solid food in a baby bottle.

Student's role in the project: Students will be trained to conduct standardized interviews, to gather anthropometric data on adults and children, and to monitor delivery of the intervention, according to the research protocol.

Preferred Background/ Experience: Skills in interacting with adults from varied cultural backgrounds, interest in infant growth and development and primary care intervention models.

References:

Gray, J.D., Punsoni, M.,Tabori, N.E.,Melton, J.T., Fanslow, V., Ward, M.J., Zupan, B., Menzer, D., Rice, J., Drake, C.T., Romeo, R.D., Brake, W.D., Torres-Reveron, A., Milner, T.A. (2007). Methylphenidate administration to juvenile rats alters brain areas involved in cognition, motivated behaviors, appetite, and stress. The Journal of Neuroscience, 27, 7196-7207.

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Field(s) of Interest: Cystic fibrosis / host defense in lung / gene therapy

Research Titles:
Lung antigen presenting cells in cystic fibrosis
Respiratory syncytial virus vaccine using capsid-modified adenovirus vectors

Project Descriptions:

1. Cystic fibrosis lung disease is characterized by exaggerated inflammation and increased susceptibility to infections. Although the CFTR protein is primarily thought to be expressed by epithelial cells we and others have studied the expression of CFTR in non-epithelial cells, in particular antigen presenting cells in the lung. This project studies the abnormalities of lung dendritic cells derived from CF knock-out mice. Our data so far indicates that abnormal CFTR expression lung macrophages and dendritic cells is related to abnormalities in innate immune responses. These findings are important in understanding lung disease in CF and also to identify new targets for therapy of this severe disease.

2. Infections with RSV are one of the major causes for viral lower respiratory tract illness, especially in young children. Our laboratory has been working on the development of genetic vaccines for pulmonary pathogens. This project aims to analyze the immunological properties of a novel anti-RSV vaccine using a capsid-modified adenovirus vector. Protection against RSV could be achieved with an efficient vaccination strategy inducing neutralizing humoral immunity as well as a Th1-dominant cellular response. Adenovirus gene transfer vectors can be used to evoke robust systemic and mucosal immunity against an immunogen expressed as a transgene and Ad functions as a potent adjuvants. The Ad modifications include the addition of a RGD motif to the fiber knob, a modification known to enhance infection of antigen presenting cells and to

increase Th1-type immune response, as well as the addition of RSV epitopes into the Ad capsid. These modified vectors will be assessed to induce immunity and protection against RSV in adult and neonatal mouse models. The study will evaluate if a modified Ad vector expressing the RSV F protein engineered to increase activation and infectivity of antigen presenting cells could be useful as a RSV vaccine.

Students' Role in the Project: Design of new and continuation of the present experiments. Student will be involved in cell culture studies and flow cytometry analysis of lung dendritic cells (project 1) and adenovirus vector construction and immunological analyses (project 2).

References:

Worgall S, Heguy A, Luettich K, Harvey BG, Quadri LE, Crystal RG. Similarity of Patterns in Gene Expression of Human Alveolar Macrophages Evoked by *Pseudomonas aeruginosa* and *Burkholderia cepacia*. Infect Immun 2005; 73: 5262-8

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Xu Y, Tertilt C, Krause A, Quadri LN, Crystal RG, Worgall, S. Influence of the cystic fibrosis transmembrane conductance regulator on expression of lipid metabolism-related genes in dendritic cells. Resp Res 2009, 10:26

Tertilt C, Joh J, Krause A, Chou P, Schneeweiss K, Crystal RG, Worgall S. Expression of B cell activating factor enhances protective immunity of a vaccine against *P. aeruginosa*. Infect Immun 2009; 77:3045-3055

Krause A, Xu Y, Joh J, Hubner R, Gess A, Ilic T, Worgall S. Overexpression of sonic hedgehog in the lung mimics the effect of lung injury and compensatory lung growth on pulmonary Sca-1 and CD34 positive cells. Mol Ther 2010; 18: 404-412

CLASS OF 2011 PEDIATRIC RESIDENCY MATCHES

Name	Program	Institution	City, State
Ahrens-Nicklas, Rebecca	Pediatrics - Medical Genetics	Childrens Hospital	Philadelphia, PA
Alex, Byron	Pediatrics	NYP - Weill Cornell	New York, NY
Copenhaver, Danis	Pediatrics	NYP - Columbia	New York, NY
Delfiner, Leslie	Pediatrics	Mt. Sinai Hospital	New York, NY
	Child Neurology	Albert Einstein	Bronx, NY
Eastman, Dawnnica	Pediatrics	NYP - Weill Cornell	New York, NY
Epstein, Alexandra	Pediatrics	Massachusetts Gen Hospital	Boston, MA
Farkhondeh, Mina	Pediatrics	University of Connecticut Health Ctr	Farmington, CT
Loeven, Michael	Family Medicine	Lancaster Gen Hosp	Lancaster, PA
Maddox, Gregory	Family Medicine	Swedish Medical Center	Seattle, WA
McCarthy, Matthew	Pediatrics	NYP - Weill Cornell	New York, NY
	Child Neurology	NYP - Weill Cornell	New York, NY
McClellan, Erin	Family Medicine	Sutter Health Program	Sacramento, CA
Miller, Erica	Medicine-Pediatrics	University of Rochester/Strong Mem	Rochester, NY
Wang, Jessica	Pediatrics	NYP - Weill Cornell	New York, NY

DEPARTMENT OF PEDIATRICS
GRADUATE MEDICAL EDUCATION
CLASS OF 2011

Natasha Afonso	Pediatric Critical Care Fellowship, Texas Children's
Elaine Barfield	Pediatric Gastroenterology, NYPH-Cornell
Catherine Chang	Neonatology, NYPH-Cornell
Lauren Cochran	General Pediatrics, St. Barnabas Hospital
Gina Coscia	Pediatric Pulmonology Fellowship, NYPH-Columbia
Michael Gillman	Pediatric Emergency Medicine, St. Christopher's
Lindsey Greene	2011 – Pediatric Chief Resident, NYPH-Cornell
	2012 – Pediatric Hematology/Oncology, CHOP
Sue Hong	Pediatric Critical Care, NYPH-Columbia
Esther Knapp	2011 – Hospitalist, Morgan Stanley
	2012 – Pediatric Hematology/Oncology, Montefiore
Nga Lau	Masters of Arts, Developmental Psychology, Columbia University
	Child Development Fellowship, University of Toronto
Jaspreet Loyal	2011 – Pediatric Chief Resident, NYPH-Cornell
Archana Mehta	Allergy/Immunology Fellowship, Thomas Jefferson-Dupont
Shannon O'Malley	Pediatric Emergency Medicine Fellowship, North Shore-LIJ
Brittany Pardue	Pediatric Emergency Medicine Fellowship, Mt. Sinai
Eunice Rhee	Neonatology Fellowship, UCSF
Beth Rosenberg	General Pediatrics – Private Practice, Tribeca Pediatrics
Janelle Sher	2011 – Pediatrics Chief Resident, Memorial Sloan Kettering
	2012 – Allergy/Immunology Fellowship, Winthrop
Elliot Stieglitz	Hematology-Oncology Fellowship, UCSF
Heather Walters	Rheumatology Fellowship, Hospital for Special Surgery
Suleka Neelagaru	

Chief Residents 2010-11

Daniel Kelly	Pediatric Critical Care Fellowship, Boston Children's
Cory Kercher	General Pediatrics – Private Practice, Weill Cornell