14th Annual Pediatric Research Day
Department of Pediatrics

Program and Abstracts

Photo Courtesy of Leigh Goldstein: “Fast Food and Convenience Stores within One Block of East Harlem Schools” (Division of Preventive Medicine)

Thursday, April 5, 2012
Hatch Auditorium & Guggenheim Pavilion
8:00 a.m. – 1:00 p.m.
A Program of

The Jack and Lucy Clark
Department of Pediatrics

Pediatrics Research Day Steering Committee:

M. Cecilia Berin, PhD, Chair
  Dennis Chia, MD
  David Dunkin, MD
  Maida P. Galvez, MD
  Bruce Gelb, MD
  Jeff M. Saland, MD
  Lisa M. Satlin, MD
  Scott Sicherer, MD
  Annemarie Stroustrup, MD, MPH
  Nita Vangeepuram, MD, MPH

Administrator: Carla Monaco

Breakfast is courtesy of the
Dr. Howard Rappaport Memorial Lectureship Fund

Grand Rounds Special Guest Speaker:
Jean-Laurent Casanova, M.D., Ph.D.
Mount Sinai School of Medicine
Fourteenth Annual Pediatric Research Day
Thursday, April 5, 2012 – Hatch Auditorium
Schedule of Events

7:45-8:00 a.m.  
Coffee and Tea

8:00-8:05 a.m.  
Chair’s Welcome and Introduction  
Lisa M. Satlin, MD

8:05-9:00 a.m.  
Grand Rounds: The Dr. Howard Rappaport Memorial Lecture  
“Toward a Genetic Theory of Infectious Diseases”  
Jean-Laurent Casanova, MD, PhD  
Professor, The Rockefeller University  
Head, St. Giles Laboratory of Human Genetics of Infectious Diseases  
Senior Attending Physician, The Rockefeller University Hospital

9:00-9:05 a.m.  
Recognition of the Recipients of the Second Annual Rappaport Memorial Resident Research Award  
Presented by Annemarie Stroustrup, MD, MPH

9:05-9:30 a.m.  
Breakfast

9:30-11:30 a.m.  
Plenary Presentations – Hatch Auditorium  
Moderators: Dennis Chia, MD and Julie Wang, MD

9:30-9:45 a.m.  
Susceptibility to Measles Among Perinatally HIV-Infected Adolescents and Young Adults  
Lee Morris, Roberto Posada, Carole Hickman, Don Latner, Tricia Singh, Alyssa Rautenberg, Jennifer Jao, William Bellini, Rhoda Sperling

9:45-10:00 a.m.  
Discovery That Mutation of the Membrane Type-1 Metalloproteinase Gene (MT1-MMP) Causes Winchester Syndrome  
Rebecca Mosig, Brad Evans, Mollie Lobl, Chiara Martignetti, Catalina Camacho, Valerie Grum-Tokars, Marc Glucksman, John Martignetti

10:00-10:15 a.m.  
Early Enteral Feeding Doesn’t Prevent Hypoglycemia in SGA Neonates  
Jennifer J. Bragg, Robert Green, Ian R. Holzman

10:15-10:30 a.m.  
Abnormalities in Noonan Syndrome and Noonan/JMML hiPS-Derived Hematopoietic Cells  
Sonia Munero-Navarro, Ilan Riess, Ana Sevilla, Dung-Fang Lee, Sunita D’Souza, Christoph Schaniel, Ninette Cohen, Ihor Lemischka, Bruce D. Gelb

10:30-10:45 a.m.  
Dietary Therapy and Topical Corticosteroids Can Reverse Esophageal Fibrosis in Patients with Eosinophilic Esophagitis  
Jay Lieberman, Raffaella Morotti, Oksana Yershov, Mirna Chehade

10:45-11:00 a.m.  
Maternal ASHMI Therapy Reduces Offspring Asthma Susceptibility in a Murine Asthma Model  
Kamal D. Srivastava, Hugh Sampson, Xiu-Min Li

11:00-11:15 a.m.  
Going Beyond PALS: A Simulation-Based Curriculum to Improve Pediatric Care  
Thomas Connors, Adrienne Davis, Sheemon Zackai, Alexandar Hogan, Christopher Strother

11:15-11:30 a.m.  
The Effectiveness and Mechanism of a Traditional Chinese Herbal Formulation for Crohn’s Disease  
David Dunkin, Ying Song, Stephanie Dahan, Keith Benkov, Lloyd Mayer, Xiu-Min Li

11:45 a.m.-12:45 p.m.  
Poster Session and Lunch  
Annenberg West Lobby

12:45-1:00 p.m.  
Poster Presentation Awards Ceremony  
Presented by M. Cecilia Berin, PhD
Statement from the Chair

Welcome to the 14th Annual Pediatric Research Day at Mount Sinai! This event aims to highlight the outstanding research activities of students, housestaff, fellows, post-docs, research staff, social workers, nurses and junior faculty in the Department of Pediatrics at Mount Sinai and our affiliates. The basic, translational and clinical research, broadly related to the health and welfare of infants, children and adolescents, presented in today’s plenary and poster sessions, exemplifies the commitment to scientific discovery and scholarship central to our academic mission. The event provides a unique opportunity for our Department’s young investigators to share the results of their research with colleagues, and thereby discover new applications for their work or identify potential future areas for collaboration.

I thank you for attending and congratulate all the participants on their accomplishments!

Lisa M. Satlin, MD
Chair, Department of Pediatrics
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- **Predicting Timely HPV Vaccination Uptake in Vulnerable Youth** - Julie Nagpal, Lourdes O. Linares, Angela Diaz, and Anne T. Nucci-Sack

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The Contribution of Ambivalence, Partner Sabotage, Depression, and Risky Substance and Sexual Behavior to Adolescent Contraceptive Use

Author Name(s): Jenny Francis MD, Katherine Malbon MD, Linares Lourdes PhD, Christine Soghomonian MA

Department: Pediatrics

Division: Adolescent Medicine

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Despite the recent decline in unintended pregnancy by 10% for 15-17 year olds from 2001 to 2006, the overall rate remains highest among teens than any other age group. (56,65) Over half of pregnancies occur unintended despite a female’s use of birth control (56); thus supporting the need to identify psychosocial factors associated with poor contraceptive use. The literature suggests a complex set of interrelated influences including attitudes toward pregnancy, the role of the partner, psychological distress, and risky practices all which may ultimately affect contraceptive behavior. (29,53,58,69)

Hypothesis: 1. Ambivalence, partner sabotage, depressive symptoms, substance abuse and risky sexual history assessed at baseline will predict poor contraception use singly and in combination at 4-months follow-up.
2. Attitudes about ambivalence and partner sabotage change over time and influence contraceptive behavior.

Methods: This is a prospective, observational cohort study of 120 adolescent females conducted at a comprehensive, urban adolescent health center. Adolescents aged 15-19 year-old, who present to initiate a new method of contraception (pill, patch, ring, shot or IUD), will complete a self-administered baseline questionnaire about ambivalence towards pregnancy (20-21, 24,59) partner influence/sabotage (39-40,45-47), depressive symptoms (66-67,70), sexual and substance use (68-69). Participants will be contacted four months after baseline via a telephone questionnaire to gather birth control continuation and adherence data as well as reassessment of attitudes; electronic medical record will be checked for birth control use. Logistic regression analyses will be conducted to predict the odds of which variables are associated with discontinuation or poor adherence.

Results: This project will launch March 2012.

Conclusions: Ultimately, when teens start a new contraception, the identification of vulnerable characteristics related to discontinuation and non-adherence may provide a valuable tool for clinicians to use when counseling adolescents about susceptibility to poor contraceptive use and ultimately avoidance of unintended pregnancies.
Predicting Timely HPV Vaccination Uptake in Vulnerable Youth

Author Name(s): Julie Nagpal, Lourdes O. Linares, Angela Diaz, and Anne T. Nucci-Sack

Department: Pediatrics

Division: Adolescent Medicine

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Despite increased access to human papilloma virus (HPV) vaccines for adolescents, a number do not complete vaccination schedules on time. Recognizing that access to free vaccines is necessary but not sufficient step in vaccinating high-risk youth, we examined the psychosocial characteristics for 3-dose vaccine uptake in a sample of N = 447 adolescents between ages 14-19 recruited for participation in an HPV vaccination study.

Hypothesis: Higher HPV knowledge will be associated with timely completion of vaccination as per CDC recommended schedules.

Methods: Baseline data gathered included family characteristics, risky behavior (antisocial behavior, alcohol and drugs) and self-reported knowledge of HPV. The HPV measure consisted of a 32-item scale assessing prevention, transmission, consequences, and vaccine efficacy. Outcome measure was duration (months) for 3-dose HPV completion. Controlling variables included age, SES, and past 6-months number of sexual partners.

Results: We found that 85% completed all 3-doses (378/447) surpassing current rates for US adolescents. Among vaccine completers, duration to complete varied widely (Mean = 12.13 months; SD = 7.71) with 33% (269/401) youth not completing the 3-doses within 12-months. The multivariate regression equations model indicated after controlling for age, SES, and number of sexual partners, US born youth (p <.05), not attending school (p <.03), and reporting lower HPV knowledge (p <.000) showed longer duration in completing all 3-doses.

Conclusions: These findings suggest that background characteristics and informed HPV knowledge are associated with timely vaccine uptake. The identification of certain subgroups and the development of education programs to improve understanding of HPV may be important in obtaining better HPV adherence with schedules among highly vulnerable youth.
Chemically Modified Peanut Proteins Exhibit Lower Allergenic Potency in Mediator Release Assay

Author Name(s): Ramon Bencharitiwong¹, Hanneke P. van der Kleij², Stefan J. Koppelman², and Anna H. Nowak-Węgrzyn¹

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: ²HAL Allergy BV, Leiden, the Netherlands

Introduction: Modification of native peanut extracts could reduce side effects of peanut immunotherapy. We sought to compare purified native Ara h 2/6 and chemically modified extracts with in vitro mediator release assay based on the rat basophilic leukemia (RBL) cell line transfected with human Fcε receptor.

Hypothesis: Chemical modification of purified native Ara h 2/6 extracts reduces mediator release in an in vitro assay.

Methods: Sera obtained from 26 subjects (16 males and 10 females, median age 7 years, 25%-75% interquartile range (IQR), 5.5 – 10) with a history of peanut allergy were used for overnight passive sensitization of RBL cells. Stimulation was done with purified Ara h 2/6 extracts and with extracts modified by reduction and alkylation (RA), and with additional glutaraldehyde treatment (RAGA). Peanut allergen-induced β-N-acetylhexosaminidase release (NHR) in the supernatant was used as a marker of RBL degranulation and expressed as a percentage of total degranulation caused by Triton X.

Results: Median peanut-specific IgE was 76.6 kU/L (IQR, 49.4 - 307; UniCAP). Nineteen subjects were responders, NHR ≥ 10%; seven subjects were non-responders, NHR < 10% in the mediator release assay. In responders, modified Ara h 2/6 (RA and RAGA) extracts gave significantly lower NHR compared to native Ara h 2/6; median 1.2, 3.5, and 15.7, respectively; P = < .001 and < .001. Both modified Ara h 2/6 (RA and RAGA) extracts gave significantly lower NHR compared to native Ara h 2/6; median 4.4, 4.5, and 13.9, respectively; P=.026 and .041.

Conclusions: We demonstrated that chemically modified RA-Ara h 2/6 and RAGA-Ara h 2/6 gave reduced mediator release in an in vitro assay about a hundred fold, suggesting a significantly decreased allergenicity. This is in line with observations made for modified Ara h 2/6 using a solid phase IgE-binding assay. The confirmation of the decreased IgE-binding of chemically modified native peanut extracts is an important milestone for further development of this alternative candidate for safe and successful peanut allergy immunotherapy.
In Vitro Assessment of the Allergenicity of Novel MF59-Adjuvanted Pandemic H1N1 Influenza Vaccine Produced in Dog Kidney Cells in Subjects with Dog Allergy

Author Name(s): Ramon Bencharitiwong¹, Stephanie Leonard¹, Theordore Tsai², and Anna H. Nowak-Węgrzyn¹

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: ²Novartis Vaccines, Cambridge, MA

Introduction: A licensed inactivated MF59-adjuvanted seasonal influenza vaccine (Optaflu) produced in canine kidney cells (MDCK 33016-PF) contains no egg proteins and did not trigger degranulation in rat basophilic leukemia (RBL) cells passively sensitized with human anti-dog IgE, supporting its safe use in dog-allergic individuals. The cell-derived pandemic H1N1 vaccine, however, was adjuvanted with the emulsion adjuvant MF59, and support for its similar safe use was sought.

Hypothesis: The MF59-adjuvanted cell-derived pandemic H1N1 influenza vaccine does not trigger degranulation in RBL cells passively sensitized with human anti-dog IgE.

Methods: RBL-2H3 cells transfected with human Fce receptor-1 were sensitized with sera from adult dog-allergic subjects and stimulated with serial dilutions of pandemic H1N1 influenza vaccine and dog dander extract. β-N-hexosaminidase release (NHR) was used as a marker of RBL degranulation.

Results: The median dog dander-specific IgE in 30 dog-allergic subjects was 27.7 kU/L (range 10.1; >100); and in 5 dog non-allergic subjects was < 0.35 kU/L. Median (range) maximum NHR in dog-allergic subjects was: 1) H1N1 influenza vaccine- 1.1% (0; 4.4); 2) Dog dander-6.9% (0.7; 37.3), P< 0.001. Mean (SD) maximum NHR in dog non-allergic subjects was: 1) H1N1 influenza vaccine-2.1 (0.53); 2) Dog dander-2.3 (0.15), P= 0.6. There was no difference in peak mediator release upon stimulation with pandemic H1N1 influenza vaccine in dog-allergic [mean (SD): 1.6 (1.3)] versus dog non-allergic subjects; [mean (SD): 2.1 (0.5)], P= 0.43.

Conclusions: The MF59-adjuvanted pandemic H1N1 influenza vaccine produced in continuous canine kidney cells did not trigger degranulation in RBL cells passively sensitized with human anti-dog IgE, supporting its safe use in dog-allergic individuals.
Altered Frequency and Composition of Cultured Natural Killer Cells from Food Allergic Subjects

Author Name(s): Akshay Bhatt, MS, Lara Ford, MD, Madhan Masilamani, PhD, Hugh Sampson, MD

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: NK cells have been shown to differentiate into NK1 and NK2 cells and secrete Th1 and Th2 cytokines respectively. Patients with asthma have a significantly reduced percentage of CD56bright NK cells resulting in weak IFN-g production and tend to have high frequency of IL-4+ NK2 cells in circulation. We investigated the percentage of NK cells in PBMC cultures from food allergic individuals.

Hypothesis: The frequency of circulating NK cell subsets and their function will be altered in food allergic individuals.

Methods: PBMC from healthy controls (HC, n=9), cow’s milk allergic (CMA, n=15), and individuals with resolved milk allergy (RMA, n=9) were cultured with medium alone, casein and IL-2 for 7 days and analyzed by flow cytometry. The percentage of CD3-CD56+CD16+ NK cells and expression of c-kit, IL-2R, NKG2a, and IFN-g in these NK cells was determined.

Results: The percentage of NK cells in CD3- populations from CMA and RMA were significantly reduced after 7 days of culture with medium alone, compared to HC [mean = 0.92 (P<0.05), 1.14 (P<0.05) & 5.6 respectively]. PBMCs cultured with casein showed a trend toward lower percentage of NK cells in CMA compared to RMA and HC (mean = 4.6, 4.9 & 8.0 respectively). CD25 expression in NK cells was comparable in all groups. There is a trend toward higher NKG2a in NK cells of HC compared to CMA. C-Kit showed a higher expression in CMA compared to HC.

Conclusions: The percentage and composition of cultured NK cells are altered in food allergic individuals. The function of these NK cells needs further investigation.
Ovalbumin and Ovomucoid IgE/IgG\textsubscript{4} Epitopes in Patients Ingesting Baked Egg Products by Peptide Microarray Immunoassay

**Author Name(s):** Gustavo Gimenez, Jean Christoph Caubet, Stephanie Leonard, Jing Lin, Zhiyan Fu, Luda Bardina, Hugh Sampson, Ania Nowak-Wegrzyn

**Department:** Allergy and Immunology

**Division:** Pediatrics

**Institution Affiliation:** Mount Sinai School of Medicine

**Introduction:** We have previously demonstrated that the majority of egg allergic patients can tolerate baked egg (BE) products. Using peptide microarray immunoassay (MIA), we sought to identify IgE and IgG\textsubscript{4} epitopes of the egg white major allergens, ovomucoid (OVM) and ovalbumin (OVA) and to determine how peptide binding diversity differs between BE-reactive and tolerant patients.

**Methods:** Twenty-four BE-reactive and ten BE-tolerant subjects (median age, 6 and 5.9 yrs, median egg white-specific IgE, 26.2 and 13.7 kU/L, respectively) were selected from a larger study investigating the effects of ingesting BE. Clinical reactivity to BE was determined by oral food challenge. Serum samples were collected at baseline, and analyzed using MIA according to the previously published protocol.

**Results:** We identified several IgE and IgG\textsubscript{4} OVM and OVA sequential epitopes. The OVM regions were consistent with those previously established using SPOTS membranes. We found overall higher intensity and diversity of binding to IgE and IgG\textsubscript{4} epitopes of OVM and OVA in the BE-reactive group as compared to the BE-tolerant group, who demonstrated minimal binding to the same epitopes. These findings were consistent when OVA and OVM were evaluated separately.

**Conclusions:** Ingestion of BE products has been shown to be safe for most egg-allergic patients. The identified differences in recognition patterns of IgE and IgG\textsubscript{4} epitopes BE-reactive and tolerant groups may be helpful in the future for determining which egg-allergic patients may tolerate BE. Use of peptide MIA may provide an important tool in the proactive treatment and management of egg allergy.
Feeding Difficulties and Food Allergies

Author Name(s): Marion E Groetch, RD, Ann Tran, Julie Wang, MD

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Feeding difficulties are reported to affect up to 25%-45% of the pediatric population and there is perceived increase risk in children with food allergy. (1)

Hypothesis: Children with food allergies are at greater risk of feeding difficulties, which may increase their risk of poor growth.

Methods: A survey was completed by parents of children age 6-36 mo with food allergy (n=90, median age 20.4 mo, 41 female); anthropometrics were obtained. Sixteen children without food allergies were used as controls.

Results: Sixty eight percent of food allergic (FA) children had parental report of feeding difficulty. Children of parents who reported difficulty with feeding had significantly lower mean weight for age percentiles (33.4) than those not reporting difficulty (58.1) (P=0.027); this was significantly correlated with reports of the child requiring distraction to eat, child refusing food regularly (unrelated to taste, texture or temperature), and child considered a “picky eater”, but independent of type or number of food allergies. Mean weight for age percentile was 38.98 in the cow’s milk allergy (CMA) group vs 51.93 in the FA without CMA group (P=0.04). Mean length for age percentile was 36.63 in the CMA group vs 51.74 in the FA without CMA group (p=0.01). No differences were noted between the controls and other FA groups for weight, length, weight for length percentiles or stress in feeding.

Conclusions: Food allergic children with parental perceived feeding difficulties or cow’s milk allergy may be at risk for poor growth.
Home Care Use of Intravenous and Subcutaneous Immunoglobulin for Primary Immunodeficiency in the United States

Author Name(s): Faith Huang, MD, Charlotte Cunningham-Rundles, MD, PhD

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: We sought to characterize how immunoglobulin is used for primary immunodeficiency in the United States.

Hypothesis: While immunoglobulin is used for varying diseases, it is more frequently prescribed for appropriate diagnoses for which it has been indicated.

Method: Cross-sectional data on 4580 patients in the U.S receiving immunoglobulin (Ig) in 2011 was provided by a major home supplier of intravenous and subcutaneous and Ig. Demographics, routes and use patterns of patients with ICD-9 coded primary immunodeficiencies were analyzed.

Results: Of 4580 patients, 3187 had ICD-9 codes for primary immunodeficiencies; 1939 (60.8%) patients were female and 1248 (39.2%) were male. Age distribution ranged from birth to 95 years, with 36.5% in their 5th and 6th decade. 3187 patients were diagnosed with: common variable immunodeficiency (279.06; n=1764; 55.3%), hypogammaglobulinemia (279.00; n=635; 19.9%), unspecified immunity deficiency (279.3; n=286; 9%), other select Ig deficiency (279.03; n=171; 5.3%), agammaglobulinemia (279.04; n=127; 4%), and combined immunity deficiency (279.2; n=105; 3.3%). Of note, 18 (0.6%) patients were diagnosed with selective IgA immunodeficiency (279.01), and 9 (0.3%) with selective IgM deficiency (279.02). Fifty four percent of patients received Ig subcutaneously, and 45.5% intravenously, with a trend towards more subcutaneous use by older patients.

Conclusions: Treatment with home Ig in the U.S. for patients with immunodeficiency was mostly appropriate for the diagnoses for which it has been indicated. More females with immunodeficiency diagnoses received Ig compared to males. For this provider, the subcutaneous route, with a trend to more use by older patients, was used in the home more than the IV route.
Effect of a Reaction During Oral Food Challenges on Food-Specific Serum IgE Levels

Author Name(s): Yiqun Hui, Jay A Lieberman, Scott H Sicherer

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: Mount Sinai School of Medicine, Jaffe Food Allergy Institute

Introduction: Oral food challenge (OFC) is the definitive test to diagnose and follow up food allergy. There are limited data on the impact of allergen encounter during a positive OFC on sIgE.

Hypothesis: A positive OFC may not have a significant impact on sIgE.

Methods: Retrospective chart review of children undergoing outpatient OFCs for clinical purposes from 2008-10 with inclusion of those having sIgE measured (ImmunoCAP, kIU/L) to the challenged food within a year prior and at least once in the 36 months following OFC. Post-OFC sIgE was compared with pre-OFC by non parametric paired t-tests. Data from individual patients with multiple sIgE determinations were tested independently by time post-OFC, grouped as 0-12mo, 12-24mo, and 24-36mo.

Results: Of 142 positive OFCs (20% positive rate from 701 OFCs to 15 foods), 69 (49%) had qualifying tests performed (4 had 3 post-OFC sIgE; 29 had 2; and 36 had 1 test). Data pooled from all challenges showed that sIgE were elevated in the 1st year post-OFC (mean [median], post-OFC vs baseline): 5.86 [1.34] vs 2.91 [0.91]; p<0.01, n=51), approached pre-challenge level in the 2nd year (4.92 [1.00] vs 2.49 [1.07]; p=0.21, n=45), and continued to decline in the 3rd year (1.31 [0.58] vs 1.33 [0.85]; p=0.36, n=11).

Conclusions: Food-specific serum IgE levels were transiently elevated in the year following a positive OFC, but fell to baseline afterwards. Prospective study with controls is required to validate and quantify the impact of this observation.
Soybean Isoflavones Inhibit DC-SIGN Signaling: Implications for Allergenicity of DC-SIGN-Binding Food Allergens

Author Name(s): Mohanpriya Kamalakannan, MS, Madhan Masilamani, PhD, Galina Grishina, MS, Luda Bardina, MS, Hugh Sampson, MD

Department: Pediatrics
Division: Allergy and Immunology
Institution Affiliation: Mount Sinai School of Medicine

Introduction: DC-Specific Intercellular adhesion molecule-3-Grabbing Non-integrin (DC-SIGN) is a C-type lectin receptor involved in recognition of distinct carbohydrate structures of pathogens and allergens. It has been shown that Ara h1, the major peanut allergen binds to DC-SIGN and activates DCs to prime Th2 responses. Soybeans are rich in immune-modulatory compounds called isoflavones. We have recently shown that soybean isoflavones, genistein and daidzein regulate dendritic cell (DC) activation and suppress allergic reactions to peanut in a murine model.

Hypothesis: Isoflavones inhibit allergen induced DC-SIGN signaling in DCs, thereby suppressing food allergy. To address our hypothesis, we sought to identify and characterize DC-SIGN binding molecules from known allergenic foods and test if all DC-SIGN binding allergens can induce signaling and to test the effect of isoflavones in allergen induced DC-SIGN signaling.

Methods: Human monocyte-derived DCs (MDDC) were activated by cross-linking DC-SIGN with antibody in the presence of genistein and daidzein (100μM each) and tested for phosphorylation of Erk, Jnk and p38 MAP kinase by immuno-blotting. Western blots were performed with defatted protein extracts from the following potentially allergenic foods: peanut, soy, egg, milk, almond, Brazil nut, walnut, pecan, cashew, hazelnut, sunflower seed, mustard, sesame, shrimp, oyster, squid, clam, lobster, crab, Bengal gram, black gram, mung bean, millet, poppy and kiwi. The blots were probed with DC-SIGN-human Fc chimeric protein followed by detection with anti-human IgG-horse radish peroxidase and chemiluminescence.

Results: Soybean isoflavones inhibited DC-SIGN induced Erk phosphorylation in MDDCs. DC-SIGN-Fc immunoblots identified several DC-SIGN binding proteins from 19 out of 24 food extracts tested. We plan to characterize every DC-SIGN binding allergenic protein by proteomic techniques.

Conclusions: We propose that inhibition of DC-SIGN signaling by isoflavones could abrogate immune responses toward certain food proteins.
Casein-Specific Regulatory T Cells in Patients with Variable Milk Protein Tolerance

Author Name(s): Jacob Kattan, Anna Nowak-Węgrzyn, Madhan Masilamani, Akshay Bhatt, Hugh Sampson

Department: Pediatrics

Division: Allergy and Clinical Immunology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: About 75% of children with cow’s milk allergy tolerate baked milk (BM), and addition of BM to the diet appears to accelerate unheated milk tolerance. We sought to examine the contribution of casein-specific regulatory T (Treg) cells to milk tolerance among milk allergic children.

Hypothesis: Treg cells play a significant role in the development of milk tolerance.

Methods: We examined 99 subjects classified as BM-reactive (32), BM-tolerant (21 muffin-tolerant, 7 pizza-tolerant, 31 rice pudding-tolerant), or unheated milk-tolerant (8) based on oral food challenge (OFC). From blood obtained at the baseline, 6 and 12 month OFCs, PBMCs were cultured with purified caseins and controls for 7 days; proliferating Treg cells were identified by flow cytometry.

Results: There were no significant differences between the 5 clinical groups in the median Treg cell frequencies at baseline. At 1 year, there was a greater increase in the median Treg frequency from baseline in subjects able to incorporate milk into their diet (5%) compared to those who maintained strict avoidance (2.1%), and there was a greater increase in the median change in Treg values from baseline in subjects able to tolerate less heated forms of milk, though these changes were not significant.

Conclusions: Baseline Treg cell frequency is not a useful diagnostic marker for predicting clinical reactivity. There was a greater increase in the median Treg values from baseline at 1 year in subjects who were able to incorporate milk into their diet. There was also a greater increase in the frequency of casein-specific Treg cells in children who advanced at least 2 clinical groups. Further longitudinal studies examining the development of tolerance to less-baked products will elucidate the role of Treg cells in this process.
Role of Egg-White-Specific IgA and IgA2 Levels in Egg Allergy: A Longitudinal Cohort Stud

Author Name(s): Konstantinou G.N., Nowak-Węgrzyn A., Bardina L., Sicherer S.H., Sampson H.A.

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Serum food-specific IgA antibodies have been associated with allergic symptoms mainly in cross-sectional, case-control studies. We sought to prospectively determine and compare egg-white-(EW)-specific IgA and IgA2 levels between EW-allergic children and children tolerating egg.

Methods: Nine children (8.5±2.6 years old) allergic to egg and all egg-containing foods were followed prospectively until they became tolerant at least to foods containing baked-in egg. Serum samples from all patients were available at all follow-up time points. Four age-matched children (8.8±3.6 years old), with no previous history of egg allergy and with serum samples available from time points comparable to that of the study group, were used as controls. A specific, ultra-sensitive ELISA (range 0.391-50ng/ml) was developed and utilized for EW-specific IgA and EW-specific-IgA2 determinations.

Results: EW-specific IgA2 levels increased significantly over a mean±SD time of 2.6±0.9 years in allergic children that became tolerant [median(IQR): 23.9(18.9-44) ng/ml vs 30.6(22.8-45.3) ng/ml, P=0.038], but there was no significant change in EW-specific IgA [134.7(113-189.1) ng/ml vs 176.1(101.1-208.6) ng/ml, P=0.086]. EW-specific IgA and EW-specific IgA2 in control subjects did not change over 2.3±0.7 years [EW-specific IgA 125 (94-200.2 ng/ml vs 129.9 (96.5-161.3) ng/ml, P=0.465 and EW-specific IgA2 182.2 (114.6-314.6) ng/ml vs 180.2 (130.3-223) ng/ml, P=0.273]. In addition, EW-specific IgA and IgA2 levels were significantly lower in egg-allergic patients compared with control subjects, (P<0.01).

Conclusions: These results suggest a potential role for food-specific IgA, and in particular food-specific IgA2 antibodies, in the induction of food tolerance. Furthermore, this supports the potential role of immaturity or impairment of IgA production in the pathophysiology of food allergy.
Dietary Therapy and Topical Corticosteroids Can Reverse Esophageal Fibrosis in Patients with Eosinophilic Esophagitis

Author Name(s): Jay Lieberman¹, Raffaella Morotti², Oksana Yershov¹, Mirna Chehade¹

Department: Pediatrics, Pathology²

Division: Allergy and Immunology¹

Institution Affiliation: Mount Sinai School of Medicine

Rationale: Esophageal lamina propria (LP) fibrosis is a common histological finding in patients with eosinophilic esophagitis (EoE). While topical corticosteroids have been shown to reverse it, no sufficient data exist as to whether dietary therapy can reverse it. We sought to determine which therapy is more likely to be associated with fibrosis resolution, and to check for predictors of fibrosis resolution.

Methods: We performed a retrospective chart review of patients diagnosed with EoE at our center. Patients with esophageal fibrosis in pre-treatment biopsies and LP present in post-treatment biopsies were identified. H&E-stained biopsy sections were reviewed for intraepithelial and LP eosinophil counts (peak eosinophils/HPF), eosinophilic microabscesses, and epithelial desquamation. Additional sections were cut and evaluated for LP fibrosis using trichrome stain, and for eosinophilic degranulation using immunohistochemical staining for major basic protein.

Results: Twenty-six patients (mean age 10.8 years) were analyzed. Nine were treated with topical corticosteroids and 17 with dietary restriction. Topical corticosteroids were more effective in reducing peak intraepithelial eosinophils (median 50/HPF to 0/HPF, p=0.008) when compared to dietary therapy (median 60/HPF to 20/HPF, p=0.018), p=0.022. Resolution of fibrosis was seen in 5/9 (55.6%) of patients treated with corticosteroids and 3/17 (17.6%) of patients receiving dietary therapy, p=0.078. We found no clinical or histological predictors of fibrosis resolution except for LP eosinophils, lower in number in those whose fibrosis resolved (median 3/HPF versus 8/HPF, p=0.028)

Conclusion: Both dietary and corticosteroid therapies can resolve esophageal fibrosis. Corticosteroids may be more effective in this regard. Higher LP eosinophil counts are related to fibrosis persistence.
Role of IgM in Pulmonary Complications of Common Variable Immunodeficiency (CVID)

Author Name(s): Paul J. Maglione and Charlotte Cunningham-Rundles

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Children, particularly those under the age of 2 years, do not mount sufficient antibody responses against carbohydrate antigens. IgM is produced by young children and fixes complement on bacteria, but the contribution of this isotype is immunity is unclear. CVID patients offer a unique population to study the role of IgM in host defense as they have variable levels of this antibody isotype.

Hypothesis: Higher levels of IgM correlate with reduced pulmonary complications in CVID.

Methods: The electronic medical records of 33 patients with CVID and the absence of detectable IgM were compared with 21 patients with CVID and IgM levels greater than 25 mg/dl. The incidence of chronic lung disease was quantified in either group and defined as pulmonary pathology on CT scan, interstitial disease on chest xray, abnormal pulmonary function tests, or a diagnosis of bronchiectasis or chronic lung disease made upon clinical grounds.

Results: Patients with CVID and undetectable serum IgM had a significantly increased risk of chronic lung disease compared with CVID patients with serum IgM greater than 25 mg/dl (60.6% vs 28.6%, 95% CI 1.0222 - 4.4020, p < 0.05).)

Conclusions: The absence of IgM may correlate with the progression of pulmonary disease in CVID. Further efforts to determine the protective role of IgM in pulmonary disease in CVID patients are necessary.
Relationship of Asthma and Food Allergy in an Urban Pediatric Population

**Author Name(s):** H. Mehta, J. Wang

**Department:** Pediatrics

**Division:** Allergy and Immunology

**Institution Affiliation:** Mount Sinai School of Medicine

**Introduction:** Food allergy and asthma often co-exist and some studies demonstrate that having food allergy increases the risk for asthma morbidity.

**Hypothesis:** To determine whether children in an urban hospital-based clinic with asthma who also have a diagnosis of food allergy have increased asthma morbidity as compared to asthmatics without food allergy.

**Methods:** A retrospective chart review of 455 urban, predominately Hispanic and African American, pediatric patients from the Mount Sinai Allergy & Immunology clinic was performed to examine the association between food allergy and severity of asthma (defined by inhaled corticosteroid use and healthcare utilization).

**Results:** 38% of asthmatic children seen at the Mount Sinai Allergy & Immunology clinic had evidence of food allergy to at least one food (convincing reaction history and positive food specific IgE and/or skin prick test). There was no significant difference in inhaled corticosteroid use, hospitalizations, or PICU admissions between asthmatics who had food allergy as compared to asthmatics without co-morbid food allergy.

**Conclusions:** In this urban minority pediatric population, there is not significant association between food allergy and severity of asthma. Environmental allergens and irritants such as dust mite, cockroach, and smoke may be the predominating factors in asthma morbidity in these children.
Relative Severity and Treatment Response to Peanut and Tree Nut Allergic Reactions in a Self-Report Registry

Author Name(s): Manish Ramesh, MD, Hugh A. Sampson, MD, Scott H. Sicherer, MD

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: Mount Sinai School of Medicine

Rationale: There are few data on relative severity of reactions to peanut and tree nuts and predictors of treatment response.

Methods: We previously reported (JACI 2001;108:128-32) clinical and demographic characteristics of 5149 participants in a national self-report registry of peanut and tree nut allergy. Briefly, registrants were primarily children (89%), reporting isolated peanut allergy 3482 (68%), isolated tree nut 464 (9%), or allergy to both 1203 (23%). Here we analyzed the relative self-reported severity of reactions (coded by symptoms as mild, moderate, severe) to peanut and 8 tree nuts (walnut, pecan, cashew, pistachio, pine, hazelnut, Brazil, almond) and treatment response with epinephrine. Chi square analysis and ordinal logistic regression were used to compare groups.

Results: In an analysis of all reactions to the 9 foods, the odds ratio (OR) of having a severe reaction was significantly lower to peanut, 0.70 (95% CI, 0.61-0.80; p< 0.001) and higher to cashew [OR 1.36 (95% CI 1.12-1.65; p=0.002). The remaining nuts were not significantly associated with a differential risk. Collectively, reactions to tree nuts were more likely to be treated with epinephrine compared to peanut (p < 0.001). The odds of using epinephrine on a subsequent exposure did not increase for those with an initial severe reaction compared to those with initial mild reactions.

Conclusions: The risk of a severe reaction following exposure was highest for cashew and lowest for peanut. Persons with tree nut allergy were more likely to use epinephrine for reactions compared to peanut. Counter-intuitively, prior reaction severity did not predict subsequent epinephrine use.
A Scoring System to Determine the Need for Immunoglobulin Therapy in Patients with Humoral Immune Defects

Author Name(s): Elena S. Resnick M.D., Sarah Taylor-Black M.D., Shradha Agarwal M.D., Charlotte Cunningham-Rundles M.D., PhD

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: Mount Sinai School of Medicine

Rationale: Patients with varying degrees of immune deficiency often present for evaluation of the necessity of immunoglobulin therapy (Ig). While Ig is the standard of care in Common Variable Immune Deficiency (CVID), a scoring system may be useful in the decision to treat patients with milder humoral immune defects such as IgG deficiency.

Methods: We previously developed a scoring system based on clinical and laboratory parameters to suggest whether or not a patient should be considered for Ig replacement (Agarwal, S. et al, submitted AAAAI abstract 2012). This system was applied here to 70 patients with humoral immune deficiency who did not meet criteria for CVID and presented for an opinion about the necessity of Ig replacement.

Results: Data for 29 males and 41 females (median age 51) were reviewed. Median immunoglobulin levels were IgG 562 mg/dL, IgM 62 mg/dL, and IgA 86 mg/dL. Patients had protective titers to a median of 5/14 pneumococcal serotypes; 2 were not immune to tetanus or diphtheria. Based on a composite of laboratory and clinical criteria, the median score was 13 for males (range 0-32) and 18 for females (range 7-36; p=0.0003). 30 patients with a median score of 19.5 (range 4-36) had been placed or were subsequently placed on Ig. For 40 others, Ig replacement was not recommended; this group had a median score of 13 (range 0-34) (p=0.0007).

Conclusions: A scoring system to suggest the necessity of Ig replacement in patients with variable degrees of humoral immune deficiency may be of value.
Maternal ASHMI Therapy Reduces Offspring Asthma Susceptibility in a Murine Asthma Model

Author Name(s): Srivastava KD, Sampson HA and Li, X-M

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Maternal asthma increases asthma risk in children and poor asthma control during pregnancy is associated with higher risk of childhood asthma. The anti-asthma herbal formula ASHMI has been found to effective in human and animal studies.

Hypothesis: We hypothesize that maternal ASHMI therapy will reduce offspring asthma susceptibility in a murine model.

Methods: Female Ovalbumin (OVA)-allergic balb/c mice with established asthma were treated daily for six weeks with either oral ASHMI, intraperitoneal dexamethasone (Dex) or oral water (Sham). Unsensitized and untreated mice served as naive mothers. After treatment all mice were mated with naïve males. Offspring were sub-optimally sensitized with 5 mcg OVA + 1mg alum when 14 days old. Intranasal OVA challenge was given on days 28, 29 and 30. Analysis of airway hyperreactivity using invasive measurement and assessment of pulmonary inflammation by bronchoalveolar lavage (BAL) cell count followed on day 31. Unsensitized offspring from each maternal group given PBS challenge served as naïve controls.

Results: Offspring of ASHMI-treated mothers (O-AM) and Dex-treated mothers (O-DM) showed decreased total cell numbers in BAL compared to offspring from Sham-treated mothers (O-SM) (P<0.05 for both vs. O-SM). Eosinophil counts were decreased in O-AM (52% reduction) but not O-DM. Reduction in neutrophil counts were more impressive in O-AM than O-DM (79% and 47% respectively) when compared to O-SM. Airway hyperreactivity was reduced in both O-AM and O-DM (26% and 33% respectively) when compared to O-SM.

Conclusions: Maternal ASHMI therapy reduced asthma susceptibility in offspring from asthmatic mice. Effect of maternal ASHMI therapy in humans merits investigation.
Impact of Diet on Allergen-Specific Stool IgA

Author Name(s): Lauren Steele, Sumintra Wood, Ivan Lopez-Exposito, Hugh Sampson, Anna Nowak-Wegrzyn, Cecilia Berin

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Intestinal immunoglobulins can facilitate (IgE, IgG) or inhibit (IgA) allergen uptake across the epithelium, but little is known about the role of food-specific gastrointestinal immunoglobulins as food allergy resolves. Inclusion of heated milk in the diet has been shown to facilitate tolerance in milk-allergic children.

Hypothesis: Inclusion of extensively heated milk (EHM) into the diet will promote tolerance through the induction of allergen-specific IgA.

Methods: Stool samples at baseline and 12 months were obtained from milk-allergic children enrolled in a trial to investigate the effects of ingesting EHM on development of milk tolerance. Casein-specific, wheat-specific (as control), and total IgA were measured in pre- and post-treatment stool extracts by ELISA.

Results: We previously found that in children avoiding milk at baseline (n = 78), stool allergen-specific IgA was not predictive of clinical reactivity, and stool allergen-specific IgE and IgG were undetectable. Samples at baseline and follow-up were available from 25 children. 19 were tolerant to some form of EHM at baseline and began daily ingestion of EHM, while 6 continued to avoid milk. Despite lack of milk in the diet, 21/25 (84%) had detectable casein-specific IgA at baseline. Inclusion of milk in the diet did not affect stool casein-specific IgA when normalized to stool total IgA (paired t-test, change from baseline=93%, 95%CI, -185.1 to 1101%). There was no difference in stool total IgA of patients avoiding milk compared to those ingesting milk (p=0.57).

Conclusions: Casein-specific IgA is detectable in stool samples of children with milk allergy before and after treatment with heated milk, but levels do not change with inclusion of milk in the diet.
Prevalence of Food Allergy in Urban Children

Author Name(s): Sarah Taylor-Black MD, Julie Wang MD

Department: Pediatrics

Division: Allergy and Immunology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Although it has been well documented that urban children have high rates of asthma and allergic rhinitis, little is known about food allergy in this population.

Hypothesis: Food allergy rates are higher than the reported prevalence in the general population.

Methods: A retrospective review of electronic medical records from July 1, 2008 to July 1, 2010 was performed of children from the Mount Sinai Pediatric clinic which serves East Harlem, NY. Charts for review were selected based on ICD-9 codes for food allergy and/or epinephrine auto injector prescriptions. The majority of the patients (89%) were insured with Medicaid/Medicaid managed care.

Results: Of 9314 children seen in this predominantly minority clinic (Hispanic 52%, Black 31%), 3.6% had physician-diagnosed food allergy, with 1.5% having peanut allergy. Among children with food allergy, the mean age was 8.5 years (range 14 mo to 21 yrs), and 59% were male. Three percent of Hispanic and 5.6% of Black children were diagnosed with food allergy. The most common food allergies were peanut (40.1%), shellfish (30.1%), egg (22.6%), tree nuts (18.4%) and milk (13.2%). Nine percent of food allergic children had a documented episode of anaphylaxis; triggers were most commonly peanut (15.2%), milk (13.6%) and shellfish (6%). Among food allergic children, asthma (48.8%), eczema (50.3%), and allergic rhinitis (47.6%) were common.

Conclusions: The prevalence of food allergy in this urban minority population is consistent with the reported prevalence in the general population. Peanut and shellfish food allergies were most common, and anaphylactic reactions most frequently affected children with peanut and milk allergies. Concomitant allergic disease was also prevalent.
Bullying of Food-Allergic Youth: Results from a Parent and Child Survey

Author Name(s): Michael A. Ambrose¹, B.A., Rachel A. Annunziato¹, Ph.D., Noga L. Ravid¹, B.A., Kelley Chuang¹, M.A., Chloe Mullarkey¹, H.S., Eyal Shemesh¹, M.D., Scott H. Sicherer², M.D.

Department: Pediatrics and Department of Psychology, Fordham University

Division: Behavioral and Developmental Health¹ and Allergy/Immunology²

Institution Affiliation: Mount Sinai School of Medicine, Fordham University

Introduction: Parents’ reports suggest that bullying of food-allergic (FA) youth is prevalent, but child reports are lacking.

Hypothesis: We hypothesized that children with FA are bullied more than a nationally representative sample of non food-allergic children.

Methods: Families with children ages 8 to 17 were surveyed for bullying, teasing and harassment (both generally and specific to FA), using a version of a validated questionnaire, during an allergy clinic visit.

Results: A planned interim analysis of 111 cases found that 28.8% of children said that they were “bullied, harassed or teased” due to FA, and 43.8% reported having had those experiences for any reason. Among respondents in the age range of 6th-10th graders, 32.6% reported having been bullied, harassed, or teased due to FA while 48.8% reported having had those experiences for any reason (compared with 17% of bullying in 6th-10th graders in a national survey). Parents did not know about 32% of the child-reported FA-related cases, and about 64% of the most severe cases. Offenses were most likely to occur at school.

Conclusions: Children with FA are vulnerable to bullying, harassment, and teasing. At least one third of the incidents do not come to parents’ attention. Practitioners should consider specifically asking about bullying in this vulnerable population and provide anticipatory guidance about it even if it is not initially disclosed.
Child Social Skills and Parenting Stress in Mothers of Children with Autism Spectrum Disorders, 2007 National Survey of Children’s Health (NSCH)

Author Name(s): Cristina E. Farrell, Ellen J. Silver, Ruth E.K. Stein

Department: Pediatrics

Division: Behavioral and Developmental Medicine

Institution Affiliation: Mount Sinai School of Medicine, Albert Einstein College of Medicine

Introduction: Parents of children with autism spectrum disorders (ASD) report more parenting stress (PS) than parents of children with typical development (controls). Few studies have investigated the connection between child social skills (CSS) and PS in ASD.

Hypothesis: Mean maternally-reported CSS is lower and PS higher in ASD compared to controls; inverse correlation exists between CSS and PS in both groups and is stronger in ASD.

Methods: 2007 NSCH was used to analyze children 6-17 with ASD vs. controls; higher scores reflect better CSS and more PS. We compared mean group CSS and PS scores and correlation coefficients, adjusting for complex sampling design and confounders.

Results: Compared to controls (n= 30,920), children with ASD (n=560) were more likely male, publically insured, with older, foreign-born mothers lacking emotional support, and less likely to have 2-parent families, excellent/very good maternal mental health, or medical homes. CSS was lower and PS higher in ASD. Correlations between CSS and PS were -0.37 (controls) and -0.28 (ASD), p<0.001. In both groups, poor maternal mental health and non-English primary maternal language predicted PS; CSS and medical home were protective.

Conclusions: CSS and PS were more strongly inversely correlated in controls, possibly due to lower ASD parent expectations regarding CSS. Medical home protected against and maternal mental health predicted PS in both groups. Children with ASD were less likely to have medical homes and more likely to have mothers reporting poor mental health. Interventions to decrease ASD-related PS should target medical home and maternal mental health.
“Girl Talk” Child Life Intervention: Preliminary Efficacy Data

Author Name(s): Sharon Granville, MS, CCLS, CTRS, NCC, Sarah Roffe, CCLS, Diane Rode MPS, CCLS, LCAT, Rachel A Annunziato PhD, Cristina Farrell, M.D., Carol Torchen, RN, MSN, CNA, Eyal Shemesh M.D.

Department: Pediatrics and Department of Psychology, Fordham University

Division: Division of Behavioral and Developmental Health and Child Life and Creative Arts Therapy Department

Institution Affiliation: Mount Sinai School of Medicine, Fordham University

Introduction: The Child Life and Creative Arts Therapy Department in collaboration with Art of Elysium, has devised a group “Girl Talk” for girls aged 10-17 who are suffering from chronic medical conditions. Girls attend weekly groups led by a volunteer artist and a child life specialist designed to decrease depression, increase positive body image and self-esteem and build skills to cope with teasing, bullying, shyness and social isolation.

Hypothesis: We hypothesized that participants will experience a significant reduction in depression scores after their participation, and that those reduced scores will be sustained over a period of 3 months of follow-up.

Methods: Consenting parents / assenting patients (girls, aged 10-17) were surveyed for depression symptoms before the intervention, immediately after that, and 3 months later using the Child Depression Inventory (CDI), a validated scale and the PedsQL, Pediatric Quality of Life, a validated scale.

Results: 7 participants consented to the study, and reported a significant reduction in CDI scores, from a mean of 2.6 pre-intervention to 0.8 and 0.7 immediately after the intervention and 3 months later, respectively repeated measures (ANOVA, , F=8.86, p=0.02)

Conclusions: The intervention was significantly associated with improved mood of participants who consented to this study; this improvement was sustained 3 months after termination of the group. The relatively low CDI score at baseline suggests that participating girls hail from the less-depressed spectrum of affected children.
Project PARIS: Parents and Residents in Session – Studying the Teaching of Person and Family-Centered Care in a Residency Program

Author Name(s): Christine Low, LCSW, Rachel A Annunziato, PhD, Melissa Rubes, BA, Eyal Shemesh, MD, Diane Rode, MPS, CCLS, LCAT, Joel Forman, MD

Department: Pediatrics and Department of Psychology, Fordham University

Division: Divisions of Behavioral and Developmental Health (CL, RAA, MR, ES) and Pediatric Medical Education (JF), and Department of Social Work Services (CL) and Department of Child Life and Creative Arts Therapy (DR).

Institution Affiliation: Mount Sinai School of Medicine, Fordham University

Introduction: Project PARIS, funded by the Picker-Gold Foundations, investigates an innovative method to teach person and family-centered care to pediatric residents at Mount Sinai Medical Center.

Hypothesis: Using family faculty to teach medical trainee’s tenets of family centered care would significantly improve the pediatric residents’ trainee knowledge and attitudes towards such care.

Methods: Family Faculty (parents of previously hospitalized children) volunteered to present specific tenets of family-centered care to pediatric residents. Parents use their own experiences to discuss person-centered care, for one hour, using a manualized approach. Residents’ acceptance of person-centered care is evaluated via a Likert-like scale with 6 questions, with a range of scores of 6-30.

Results: Mean scores on the Attitudes measure significantly improved after the session from 22.71 to 25.84. Knowledge scores also significantly improved from a mean of 1.86 to 3.14. 100% adherence to the protocol did require minor redirection from senior faculty. Descriptive statistics from the resident assessment of acceptability and usefulness further establish the success of the pilot project. Participant feedback resulted in the addition and refinement of discussion topics to the manualized training

Conclusions: The use of parents to teach residents leads to greater acceptance of the centrality of the patient and family in providing care.
Identification of a true allometric model for normalization of Left Atrial volume and utilization towards derivation of Z scores in Pediatric age group

Author Name(s): Puneet Bhatla, James C Nielsen, Helen Ko, Shubika Srivastava

Department: Pediatrics

Division: Cardiology

Institution Affiliation: Mount Sinai School of Medicine

Purpose: Increase in left atrial volume (LAV) is indicative of left ventricular diastolic dysfunction and is a known predictor of morbidity and mortality in adults. It has also been utilized as a surrogate marker of significant left to right shunts in children. Normalization of LAV has been traditionally performed by indexing to BSA and normative data has been published using this model in both children and adults. Indexed LAV thus derived does not account for the nonlinear relationship of physiologic variables to body surface area (BSA) and has not been tested for independence to body size. We sought to test the linear model for indexing LAV, identify a valid allometric model and use it to develop Z-scores for normal children.

Methods and Results: LAV was measured in 300 consecutive normal subjects by TTE using the Biplane area length method. The mean absolute LAV for the entire group was 24.8 ± 4.6 ml. There was a strong positive correlation observed between LAV and BSA (r= 0.96, P<0.0001). Indexed LAV using BSA was regressed against BSA to test for independence to body size. The indexed LAV using BSA had a significant residual relationship with BSA (r=0.52, p<0.0001), hence failed validation criteria. Using the least square regression analysis, the AE derived for the whole group was 1.27. But this allometric model also failed validation secondary to a negative residual relationship (r= -0.15, P=0.01). This was hypothesized to be due to the error in TTE derived AE, related to technical underestimation of LAV in larger subjects. To overcome this error, the entire cohort was divided into two groups with cut-off value of 1m² for BSA such that each group had a best fit allometric model. The allometric models identified for each group; AE of 1.48 for BSA <1 m² and 1.08 for BSA >1m² were tested to be valid and indexed LAV for each group were independent of body size, age and gender. For the group with BSA<1 m², the mean indexed LAV ± SD is 31.5± 5.5 ml for and 26± 4.2 ml for BSA>1 m². Subsequently, this data was used to develop normative Z-scores. Furthermore the hypothesis of underestimation in larger subjects was tested by comparing LAV measurements by TTE to those by cardiac MR (CMR) in 10 subjects. There was consistent underestimation of LAV measurement by 2DE when compared to CMR (mean difference of -26 ml with limits of agreement of -8 to -46 ml) for subjects with BSA>1 m². However Comparison of absolute LAV measurement between 2DE and CMR in 8 subjects with BSA <1 m² showed excellent agreement with a mean difference of 0.16 ml with limits of agreement (-4.1 to +4.2 ml).

Conclusions: This study demonstrates the fallacy of using "per- BSA standards" for normalization of LAV in the Pediatric age group. Appropriate indexing methods to normalize for somatic growth and age are imperative. Although a simple linear regression model describes the relationship between LAV and BSA it cannot be used to derive normalized values in children. Indexing LAV to BSA for BSA <1 m² and to BSA for BSA >1 m² should be used to normalize LAV values in children and to develop z scores.
**Overexpression of PTPRM in a Mouse Model**

**Author Name(s):** Jonathan J. Edwards, Dhandapany S. Perundurai, Yong Zhao and Bruce D. Gelb

**Department:** Pediatrics

**Division:** Center for Molecular Cardiology

**Institution Affiliation:** Mount Sinai School of Medicine

**Introduction:** Congenital heart disease (CHD) continues to be the birth defects causing the most neonatal mortality. Recently, pathologic copy number variations (CNVs) have been implicated in CHD. We recently observed overlapping gain CNVs at chromosome 18p11.31-11.23 in two patients with hypoplastic left heart syndrome (HLHS). The common region contains only one gene, *PTPRM*, which is expressed in ventricular endocardium, aortic sac endothelium and dorsal aorta at E9.5 and in the aortic root endothelium at E14.5 during mouse embryonic development.

**Hypothesis:** We hypothesize that duplication of *PTPRM* causes HLHS.

**Methods:** To overexpress *Ptprm* in transgenic mice, we designed a BAC recombinengineering strategy to overexpress the *Ptprm* cDNA along with the β-galactosidase (*Lac-Z*) reporter gene driven by the *Ptprm* promoter.

**Results:** *Ptprm* comprises 31 exons spread over 700 kb so no BAC covered the regulatory and coding regions. To address this, we subcloned the *Ptprm* cDNA and *Lac-Z* reporter to create a bicistronic expression vector. Using galK-mediated recombinengineering, this cassette was targeted to the translational start site of exon 1 in a BAC also containing roughly 150 kb of *Ptprm*’s 5′ flanking region. F0 transgenic embryos are gestating and will be examined morphologically at E14.5. B-gal staining will reveal the expression pattern. *In situ* hybridization will be used to examine early genetic markers of left ventricular formation, myocardial cell proliferation and apoptosis.

**Conclusion:** We have identified *PTPRM* gain CNVs as a likely cause of HLHS. We are modeling this complex genomic lesion using mouse transgenesis. If successful, this model will provide a unique reagent for exploring the pathogenesis of HLHS.
The Role of Right Ventricular Function in Pediatric Idiopathic Dilated Cardiomyopathy

Author Name(s): Abraham Groner MD, Shubhika Srivastava MD

Department: Pediatrics

Division: Cardiology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Prevalence of right ventricular dysfunction in idiopathic dilated cardiomyopathy is incompletely studied in children. We attempted to evaluate the utility of recently published right ventricular function echocardiographic indices in identifying dysfunction in children with idiopathic dilated cardiomyopathy and to evaluate the impact of right ventricular dysfunction on need for transplant or death within a year of presentation.

Hypothesis: Children with idiopathic dilated cardiomyopathy have worse right ventricular function as compared to normals.

Methods: Retrospective database review of right ventricular function indices in thirty patients with idiopathic dilated cardiomyopathy were compared to sixty age and gender matched controls from January 2001 until December 2010. Right ventricular function was assessed by Doppler tissue peak systolic S’, early and late diastolic E’ and A’ waves and isovolumic acceleration at the tricuspid valve annulus; pulsed wave Doppler Tricuspid valve inflow E and A waves; right ventricle myocardial-performance-index; Tricuspid annular plane systolic excursion; right ventricle fractional-area-change.

Results: Right ventricular systolic and diastolic function in idiopathic dilated cardiomyopathy was significantly impaired. All measured indices except for isovolumic acceleration and fractional-area-change were significantly reduced with p<0.05. There was no right ventricular index predictive of death or transplantation. Patients with poor outcome were significantly more likely to need inotropic support (p = 0.018), be placed on a ventricular assist device (p = 0.005) and have a worse left ventricle ejection fraction z-score (p = 0.002).

Conclusion: Right ventricular systolic and diastolic dysfunction is under recognized in children presenting with idiopathic dilated cardiomyopathy. The need for major clinical circulatory support and left ventricle ejection fraction z-score < -8 were the main determinant of outcome independent of degree of derangement in right ventricular function.
Modeling Cardiac Defects in RASopathies Using Patient-Specific Induced Pluripotent Stem Cell-Derived Cardiomyocytes

**Author Name(s):** Rebecca Josowitz, Sonia Mulero-Navarro, Ilan Riess, Sherly Pardo, Sunita D’Souza, Xonia Carvajal-Vergara, Marco Tartaglia, Ihor Lemischka, Bruce D. Gelb

**Department:** Pediatrics

**Division:** Cardiology, Child Health & Development Institute

**Institution Affiliation:** Mount Sinai School of Medicine

**Introduction:** The “RASopathies” are a family of disorders due to mutations in genes involved in the RAS/MAPK pathway, and are comprised of LEOPARD (LS), cardio-facial-cutaneous (CFCS), and Costello (CS) syndrome. Hypertrophic cardiomyopathy (HCM) is observed in 50-90% of patients with these disorders. The precise molecular mechanisms underlying RASopathy-associated HCM are unclear and appear to differ in the limited available animal models of these disorders.

**Hypothesis:** We hypothesize that human induced pluripotent stem cell (hiPSC)-derived cardiomyocytes from patients with various RASopathy syndromes will recapitulate the cardiac phenotype observed clinically, and display signaling pathway dysregulation that varies among the disorders.

**Methods:** To further elucidate the molecular mechanisms of HCM and other prevalent cardiovascular manifestations in these disorders, we have generated hiPSC-derived cardiomyocytes as a representative model of these syndromes. Purification of the derived cardiomyocytes is achieved using a lentiviral selection cassette containing α-myosin heavy chain (αMHC) (gift from Mark Mercola) driving a puromycin resistance gene. We are exploring additional methods to purify cardiomyocytes, including purification of ventricular and atrial cardiomyocytes separately, to enable further investigation into chamber-specific cardiovascular abnormalities observed in RASopathies.

**Results:** Here we demonstrate the characterization and purification of hiPSC-derived cardiomyocytes from patients with a variety of mutations causal for RASopathies. These cardiomyocytes display a phenotype consistent with cellular hypertrophy. Additionally, we show these cardiomyocytes express calcium handling genes and functional calcium transients.

**Conclusions:** Using these lines, we will be able to compare pathogenesis across a variety of syndromes, which will help to illuminate the complex underlying mechanisms of HCM, and potentially lead to improved mutation-specific therapies.
Comparison Between Proximal Thoracic Vascular Measurements Obtained by CE-MRA & Transthoracic Echocardiography in Infants and Children with Congenital Heart Disease

Author Name(s): Nitin Madan, Jen Yau, Shubhika Srivastava, James Nielsen

Department: Pediatrics

Division: Cardiology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Accurate assessment of the thoracic vasculature in infants and children with congenital heart disease (CHD) is vital in deciding appropriate surgical or interventional procedure and predicting outcomes. When this information is unavailable by transthoracic echocardiography (TTE), Contrast enhanced MRA (CE-MRA) is frequently utilized. Lack of normative data prohibits calculation of Z-scores for measurements obtained by CE-MRA. Hypothesis: Reasonable agreement between the two modalities will allow use of TTE based Z-scores on measurements obtained from CE-MRA.

Methods: Infants and children < 3 years of age with CHD who underwent CE-MRA between August 2006 and May 2011 were identified (n=53). Subjects with unavailable TTE (n=12), infants with duration of >30 days (n=4) and children (1-3 years of age) with duration >60 days (n=2) between TTE & CE-MRA were excluded. Main and branch pulmonary arteries, ascending aorta, distal transverse arch and aortic isthmus were measured from CE-MRA and TTE in analogous imaging planes by two investigators blinded to each other.

Results: 35 patients were included, median age 129 days (0-1077); weight 4.1 Kg (2.16-17). Median time period between the two imaging modalities 9 days (0-60). Data analysis performed on 129/210 possible paired measurements. Range of vessel sizes 2.8-23.4mm. Excellent correlation between CE-MRA and TTE (r=0.94, p<0.001). Mean difference between the measurements -0.01mm ± 1.2mm with limits of agreement -2.5 mm to +2.3mm.

Conclusions: In this cohort, proximal thoracic vascular measurements obtained by CE-MRA and TTE have a strong correlation and adequate agreement. Until normative data for vessel size measurements obtained from CE-MRA is available, TTE based Z-scores can be applied to the measurements obtained by CE-MRA.
Abnormalities in Noonan Syndrome and Noonan/JMML hiPS-Derived Hematopoietic Cells

Author Name(s): Sonia Mulero-Navarro, Ilan Riess, Ana Sevilla, Dung-Fang Lee, Sunita D’Souza, Christoph Schaniel, Ninette Cohen, Ihor Lemischka, Bruce D. Gelb

Department: Pediatrics

Division: Cardiology, Child Health & Development Institute

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Noonan syndrome is a genetic disorder caused by deregulation of the RAS/MAPK pathway. Germ-line mutations in PTPN11 cause 50% of NS, while somatic mutations account for 35% of JMML. Children with NS and specific PTPN11 mutations are at increased risk for developing JMML.

Hypothesis: To elucidate pathway alterations in myeloid progenitors in NS and NS/JMML using hiPSC

Methods: We established hiPSC lines with germ-line PTPN11 mutations. We differentiated these into hematopoietic lineages using specific cytokines and determined cell types using FACS. Proliferation was determined with Ki67 staining. To check clonogenic capacity, cells were seeded on methylcellulose. We assessed clinical criteria for diagnosing JMML: hypersensitivity to GM-CSF and absence of BCR-ABL. We performed microarrays to characterize the gene expression profile from CD33+ Ctrl and NS/JMML, and in addition, RT-qPCR for miRNAs related to hematopoiesis from the same samples.

Results: Myeloid progenitors and monocytes were increased in NS/JMML compared to controls (45% vs. 15% and 18% vs. 8%, respectively). Clonogenic capacity was also increased in NS/JMML with more and larger colonies. The NS/JMML lines responded to GM-CSF 0.1 ng/ml while controls did not, evidence of GM-CSF hypersensitivity. BCR-ABL fusion was absent. Proliferation rate was increased approximately eight fold in NS/JMML myeloid cells. The expression levels of miR223 and miR15a were increased 20 and 6 fold, respectively, in the NS/JMML myeloid population. Further in silico analysis detected seven genes repressed in CD33+ NS/JMML that were targets for these miRNAs. Four of them (MTL5, SMAP1, DICER and NPM1) were analyzed in JMML patients and they appear repressed compare to healthy individuals.

Conclusions: This study provides the first model of leukemia using hematopoietic cells differentiated from hiPSCs. Moreover, it provides new insights about PTPN11-driven JMML, revealing up-regulation of miR223 and miR15a, suggesting these potential novel molecular regulators and their targets for treating JMML.
Left Ventricular Shortening Fraction Derived from Cross Sectional Area Change Demonstrates Excellent Agreement with Cardiac MRI Derived Ejection Fraction in Repaired Tetralogy of Fallot

Author Name(s): Ashley Siems MD; Helen Ko RDCS; Shubhika Srivastava, MBBS

Department: Pediatrics

Division: Cardiology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Left ventricular dysfunction is a risk factor for poor outcomes in repaired ToF patients. Altered LV geometry in this population invalidates all standard 2D echo function parameters. Cardiac MRI (CMR) is the reference standard to quantify LV function in these patients, but it is time consuming and expensive.

Objective: Assess reliability and correlation of non-traditional 2D echo and Doppler tissue imaging (DTI) derived parameters in identifying patients with decreased LV function, using CMR LV ejection fraction (EF) as the reference.

Methods: Retrospective review of 2D echo and CMR in patients with repaired ToF. The following DTI derived parameters from the lateral MV annulus were obtained; isovolumic contraction time, isovolumic relaxation time, ejection time, Tei Index, and peak systolic velocity. LV shortening fraction (SF) was derived from cross-sectional area change at the level just below the mitral valve by the formula SF=1-√(1-AC). SF and Z-scores of SF were compared to LV EF and LV EF Z scores from CMR. Abnormal LV function was defined as SF <28%, EF < 55%, SF or EF z-scores < -2, and Tei index > 0.44. Bland Altman analysis was performed.

Results: Sixty patients with repaired ToF were identified between 2005 and 2010 who underwent both CMR and 2D echo within 6 months of each other. 22% had LV EF <55% by CMR and 29% had LV SF< 28% by 2D echo derived SF 15% had Tei >0.44. Bland Altman curve showed strong agreement between LVEF z scores and Echo SF. CMR LVEF and Echo SF by Spearman's coefficient was 0.4 (p<0.003, 95% CI: 0.13 to 0.6). Tei Index and DTI indices had no correlation with LVEF.

Conclusion: LV SF is a reliable measure of LV function in repaired ToF and has good agreement with CMR derived LVEF. DTI derived indices and Tei index did not correlate. 2D echo derived SF using the CSA change method can be to follow patients with repaired ToF.
Arginine and Levo-Dopa Stimulation in Children: Timing of Peak Growth Hormone Response and Correlation with Body Mass Index

Author Name(s): Elizabeth Chacko, MD, Evan Graber, DO, Elizabeth Wallach, MD, Molly Regelmann, MD, Rachel Annunziato, PhD, Michelle Klein, MD, Dennis Chia MD, Robert Rapaport ,MD

Department: Pediatrics

Division: Endocrinology and Diabetes

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Growth hormone (GH) stimulation testing (ST) is part of the evaluation of growth failure in children. Studies to establish optimal times for measuring peak GH (PGH) levels are lacking for arginine and levo-dopa (ALD) ST. BMI has been reported to be negatively correlated with PGH in patients who had ST with various agents (n=15 received arginine and carbidopa/levo-dopa).

Hypothesis: To determine the time of PGH level during ALD ST and to assess a correlation between BMI and stimulated PGH.

Methods: Retrospective chart review of patients with growth failure who underwent ALD ST using a uniform and standard protocol. GH samples were obtained at baseline, 30, 60, 90, 120 and 180 minutes (min). Data collection included age, sex, height, weight, and BMI. GH levels were measured by Esoterix Lab (Calabasas Hills, CA). Statistical analyses included Pearson correlations.

Results: Data of 132 consecutively tested children (mean age of 10.5 ± 2.9 yr; BMI Z-score -0.176 ± 1.02) were reviewed. PGH level occurred at 120 min or earlier in all patients: at 30 min (56%), 60 min (16.7%), 90 min (10.6%) and 120 min (16.7%). BMI Z-score negatively correlated with PGH in all patients, subgroups Female (F), Prepubertal (P), and Prepubertal Female (PF) (see table).

<table>
<thead>
<tr>
<th>Correlation of Peak GH with BMI-Z Score</th>
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<tbody>
<tr>
<td>r-coefficient</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>All (n=132)</td>
</tr>
<tr>
<td>M (n=89)</td>
</tr>
<tr>
<td>F (n=43)</td>
</tr>
<tr>
<td>P (n=59)</td>
</tr>
<tr>
<td>PM (n=41)</td>
</tr>
<tr>
<td>PF (n=18)</td>
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<tr>
<td>PP (n=73)</td>
</tr>
<tr>
<td>PPM (n=48)</td>
</tr>
<tr>
<td>PPF (n=25)</td>
</tr>
</tbody>
</table>

M= Male P=Pubertal PM=Pubertal Male PF=Pubertal Female PPM=Prepubertal Male

Conclusions: All PGH levels occurred at ≤120 min suggesting that the standard 180 min sample can be omitted from ALD ST without compromising its diagnostic value. A negative correlation was found between BMI -Z score and PGH response to ST in all patients. Further analysis revealed the strongest negative correlation in PPF. The effect of BMI on PGH response to ALD should be considered when diagnosing GH deficiency in PPF. Other BMI constituents, including body composition and its effect in this group, need to be studied.
Arginine and Levo-Dopa Stimulation in Children: Association of Peak Growth Hormone Response with Homeostatic Model Assessment and Lipids

Author Name(s): Elizabeth Chacko, MD, Evan Graber, DO, Elizabeth Wallach, MD, Molly Regelmann, MD, Rachel Annunziato, PhD, Michelle Klein, MD, Dennis Chia, MD, Ahmed Khattab, MD, Gertrude Costin, MD, Robert Rapaport, MD

Department: Pediatrics

Division: Endocrinology and Diabetes

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Growth hormone (GH) stimulation testing (ST) is part of the evaluation of growth failure in children. Insulin resistance (IR) and lipid abnormalities have been reported in GH deficient (GHD) adults. In GHD children, positive and negative correlations between peak GH response (PGH) and IR have been found. We are not aware of studies relating PGH with IR and lipids in a population of unselected children.

Hypothesis: To correlate PGH levels in response to arginine and levo-dopa (ALD) ST with Homeostatic Model Assessment (HOMA-IR) and lipids.

Methods: Retrospective chart review of children with growth failure who underwent ALD ST. Data collection included age, sex, height, weight, pubertal status, HbA1c, fasting preserved glucose, insulin, c-peptide and lipid profile. GH levels were measured by Esoterix Lab (Calabasas Hills, CA). HOMA-IR was calculated by standard formula [HOMA-IR (mmol/L x μU/ml) = fasting glucose (mmol/L) x fasting insulin (μU/ml)/22.5]. Statistical analyses included Pearson correlations and t-tests.

Results: Data of 132 (89 M) consecutively tested children (mean age 10.5 ± 2.9 yr; BMI Z-score -0.176 ± 1.02) were reviewed. Group 1 (n=62) had PGH<10 ng/mL and Group 2 (n=70) had PGH =/> 10 ng/mL. Results of statistical analyses are summarized in Tables 1 and 2. HOMA-IR and HbA1c were normal in all patients with no difference between the two groups. HOMA-IR was higher in group 1 in prepubertal females (PPF) and pubertal males (PM). No overall differences were seen in lipids between the two groups. In group 1, total cholesterol (TC) was higher in PM and lower in prepubertal (PP) children. LDL-C was lower in group 1 PPF. In all patients, PGH negatively correlated with HOMA-IR and in subgroups PPF. PGH negatively correlated with TC in all patients and especially so in pubertal females (PF). PGH negatively correlated with triglycerides (TG) in prepubertal males (PPM) and with LDL-C in pubertal females (PF) subjects.

Table 1. T-Test Analyses for Groups 1& 2

<table>
<thead>
<tr>
<th>GH Groups (1, 2)</th>
<th>N</th>
<th>Mean</th>
<th>p-value</th>
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<tbody>
<tr>
<td>IGF-1 (ALL)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;10 ng/mL</td>
<td>62</td>
<td>201.11</td>
<td>0.022</td>
</tr>
<tr>
<td>≥ 10 ng/mL</td>
<td>70</td>
<td>214.30</td>
<td></td>
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<tr>
<td>HOMA-IR (PM)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;10 ng/mL</td>
<td>15</td>
<td>0.574</td>
<td>0.007</td>
</tr>
<tr>
<td>≥ 10 ng/mL</td>
<td>18</td>
<td>0.3528</td>
<td></td>
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<tr>
<td>HOMA-IR (PPF)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;10 ng/mL</td>
<td>7</td>
<td>0.7171</td>
<td>0.022</td>
</tr>
<tr>
<td>≥ 10 ng/mL</td>
<td>10</td>
<td>0.2040</td>
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<tr>
<td>TC (PM)</td>
<td></td>
<td></td>
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<tr>
<td>&lt;10 ng/mL</td>
<td>15</td>
<td>171.80</td>
<td>0.034</td>
</tr>
<tr>
<td>≥ 10 ng/mL</td>
<td>9</td>
<td>164.67</td>
<td></td>
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<tr>
<td>TC (PP)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10 ng/mL</td>
<td>20</td>
<td>171.60</td>
<td>0.008</td>
</tr>
<tr>
<td>≥ 10 ng/mL</td>
<td>17</td>
<td>171.88</td>
<td></td>
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<tr>
<td>LDL-C (PPF)</td>
<td></td>
<td></td>
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<tr>
<td>&lt;10 ng/mL</td>
<td>5</td>
<td>102.20</td>
<td>0.040</td>
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<tr>
<td>≥ 10 ng/mL</td>
<td>8</td>
<td>110.38</td>
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</table>

ALL (All children), PM (Pubertal Male), PP (Prepubertal), PPM (Prepubertal Male), PPF (Prepubertal Female)
### Table 2. Correlation of Peak GH and Measure of Lipids and Insulin Resistance

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>All</th>
<th>M</th>
<th>P</th>
<th>PF</th>
<th>PP</th>
<th>PPM</th>
<th>PPF</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGH and HOMA-IR</td>
<td>All =92 PP=50 PPF=17</td>
<td>r: -0.224 p: 0.032</td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>PGH and TC</td>
<td>ALL= 70 M= 46 P= 33 PPF= 11</td>
<td>r: -0.289 p: 0.015</td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>r: -0.316 p: 0.032</td>
<td>r: -0.557 p: 0.001</td>
<td>r: -0.834 p: 0.001</td>
<td></td>
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<tr>
<td>PGH and TG</td>
<td>PP= 37 PPM= 24</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>r: -0.329 p: 0.047</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>PGH and LDL-C</td>
<td>P= 33 PPF= 11</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>r: -0.526 p: 0.002</td>
<td>r: -0.755 p: 0.007</td>
<td></td>
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<td></td>
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</tbody>
</table>

N= number of children in each group (All, M, P, PF, PP, PPM, PPF)  
M= Male  P=Pubertal  PF=Pubertal Female  PP= Prepubertal  PPM=Prepubertal Male  PPF=Prepubertal Female

**Conclusions:** In this group of non-obese, non insulin resistant children, HOMA-IR and lipids negatively correlated with PGH response to ALD ST. These findings suggest an effect of glucose, insulin, and lipids on growth hormone secretory dynamics.
Pituitary Volume Correlates with IGF-1 but not with Peak Growth Hormone Response to Stimulation

Author Name(s): Molly O. Regelmann, MD¹, Bradley Delman, MD², Elizabeth Chacko, MD¹, Evan Graber, DO¹, Elizabeth Wallach, MD¹, Dennis Chia, MD¹, Michelle Klein, MD¹, Rachel Annunziato, PhD³, Robert Rapaport, MD¹

Department: Pediatrics

Division: Endocrinology & Diabetes, Neuroradiology

Institution Affiliation: Mount Sinai School of Medicine
Psychology, Fordham University

Background: The evaluation of children with growth failure includes assessment of the growth hormone (GH)-insulin-like growth factor-1 (IGF-1) axis, GH stimulation testing (ST) and, when clinically indicated, magnetic resonance imaging (MRI) of the pituitary gland. Data on morphology of the pituitary gland and mean sagittal adenohypophysial height but not pituitary volume (PV), have been reported in children with GH deficiency (GHD). In a previous preliminary presentation, we have demonstrated, in a limited cohort (n=69), that IGF-1 correlates with MRI PV. Reports comparing pituitary volume (PV) and peak growth hormone (PGH) response to ST are lacking.

Objective: We hypothesized that PV correlates with PGH to ST, as well as with IGF-1.

Design/Methods: We performed a retrospective chart review of children followed for growth failure. Inclusion criteria for the study were MRI of the pituitary read by the same neuroradiologist (BD), GH ST, and GH and IGF-1 measured by the same laboratory (Esoterix Inc., Calabasas Hills, CA). PV was calculated using (4π/3)*(L*H*W). Pearson correlations compared PGH and IGF-1 SD as continuous variables with PV; t tests were used to compare PGH groups (<10ng/mL, □10ng/mL) with PV.

Results: A total of 161 patients (42 females, 119 males), with an average age of 11.4±2.5 years were reviewed. PV correlated with IGF-1 (r=0.376, p<0.01), IGF-1 SD (r=0.274, p <0.01), IGFBP-3 (r=0.300, p<0.01), bone age (r=0.475, p<0.01), height SDS (r=0.310, p<0.01) and BMI SDS (r=0.177, p=0.026). No significant correlations were found for PV and PGH as a continuous variable or in subgroup analyses, prepubertal males (PPM), prepubertal females (PPF), pubertal males (PM) and pubertal females (PF).

Conclusions: We confirm that IGF-1 correlates with PV. PGH did not correlate with PV. This finding may be consistent with hypothalamic, and not the pituitary, dysfunction being the cause of GHD in most patients. Additional analyses need to be performed to help elucidate the reported findings.
The Effectiveness and Mechanism of a Traditional Chinese Herbal Formulation for Crohn’s Disease

Author Name(s): David Dunkin, Ying Song, Stephanie Dahan, Keith Benkov, Lloyd Mayer, Xiu-Min Li

Department: Pediatrics

Division: Gastroenterology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: The prevalence of Crohn’s disease (CD) is increasing. Current therapies can have serious side effects. We developed an herbal formula, FAHF-2, which is based on a traditional Chinese herbal formula that has long been used in China to treat colitis.

Hypothesis: FAHF-2 will have anti-inflammatory effects on murine models of colitis, RAW264.7 macrophages, and peripheral blood mononuclear cells (PBMCs) from children with CD.

Methods: A CD45RBhi transfer model of colitis was utilized to assess the effectiveness of FAHF-2. The effects of FAHF-2 on TNF-α production were assessed in vitro and activation of NF-κB in LPS-stimulated RAW264.7 cells was determined by Western blot. PBMCs isolated from 26 CD children (8-19 yrs old) and 17 non-IBD children (4-18 yrs old) were cultured for 24 hours with or without FAHF-2 in the presence or absence of LPS. Cytokine and chemokine production in the culture supernatants were measured by multiplex bead immunoassay. The effect of FAHF-2 on TNF-α producing monocytes and T cells was determined by flow cytometry.

Results: FAHF-2 treatment in a murine model of colitis significantly decreased weight loss (11.3% vs. 19.2%, p<0.05) and caused less colitis (colitis score 3.7 vs. 6.3, p<0.001) than untreated controls over the course of 46 days. Pre-incubation of RAW267.4 cells with FAHF-2 decreased TNF-α production and caused decreased IκB-α phosphorylation, IκB-α degradation and AKT phosphorylation following LPS stimulation without inducing toxicity. A significant increase in TNF-α was detected in PBMC cultures stimulated with LPS from CD subjects as compared with PBMC cultures from non-IBD children. FAHF-2 treatment in vitro significantly reduced LPS-induced TNF-α, IL-12, IFN-γ, IL-2, IP-10, MIG, and MIP-1β production, and increased GM-CSF production by PBMCs from CD subjects (n=14), FAHF-2 also significantly reduced the percent of TNF-α⁺CD14⁺ monocytes in LPS-stimulated PBMCs from CD and the percent of TNF-α⁺CD3⁺ T cells in anti-CD3/CD28 mAb-stimulated PBMCs from CD (n=4).

Conclusions: FAHF-2 was effective in reducing weight loss and colitis in a murine model. It inhibited pro-inflammatory cytokine production and the number of TNF-α⁺CD14⁺ LPS stimulated monocytes and TNF-α⁺CD3⁺ CD3/CD28 stimulated T cells in PBMCs from CD children. FAHF-2 inhibition of LPS-stimulated TNF-α production may be due, at least partially, to blocking the NF-κB pathway. Further clinical investigation of FAHF-2 for the treatment of CD is warranted.
Going Beyond PALS: A Simulation-Based Curriculum to Improve Pediatric Care

Author Name(s): Thomas Connors, MD, Adrienne Davis, MD, Sheemon Zackai, MD, Alexandar Hogan, BA, Christopher Strother, MD

Department: Pediatrics

Division: Medical Education

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Pediatric cardiopulmonary arrests are rare and many pediatric residents have little exposure during training. Studies show pediatric residents do not feel comfortable or adequately trained to handle these events, despite BLS and PALS re-certification every two years. While residents perform well on standardized PALS tests, they perform poorly when evaluated for the technical skills necessary for actual pediatric arrests. Studies have shown that knowledge and skill retention in resuscitation training using high-fidelity simulation is superior to low-fidelity simulation and lecture-based learning. We developed a high-fidelity simulation-based curriculum with the aim of providing interval resuscitation training for our residents between PALS courses.

Hypothesis: Participation in a high-fidelity simulation curriculum will increase pediatric resident performance and comfort level managing simulated arrests compared to routine training.

Methods: Participants were Sinai pediatric residents. They underwent baseline assessment including a pre-test survey and videotaped evaluation managing two simulated scenarios: 1. Respiratory arrest and 2. Pulseless arrest/Asystole. Performance was scored using a validated scoring instrument designed to measure cognitive performance leading code scenarios. Participants were randomized into two groups: one receiving the curriculum (intervention) and those receiving routine training (control). The curriculum involved respiratory distress and pulseless arrest modules where residents took turns leading simulated arrests. Post-simulation debriefing was performed, after which participants repeated the scenarios. At 6 months time, all participants completed a post-test survey and underwent a second round of videotaped testing.

Results: 44 participants were enrolled; 43% were PGY-1s, 23% were PGY-2s and 34% were PGY-3s. 80% of participants had completed PALS certification <3 months prior to baseline testing. The intervention and control groups were not statistically different in number of interval ICU rotations (intervention: 0.95 +/- 0.805, control: 0.65 +/- 0.647, p = 0.178), number of PGY1s, 2s, and 3s, (p = 0.957), or time since last PALS certification (p = 0.254). At 6 months time, there was a statistically significant increase in comfort level managing patients with respiratory arrest in the intervention group compared to controls (mean [SD], 0.67 [0.73] vs. 0.09 [1.041], p = 0.04). There was also a statistically significant increase in comfort level managing patients in asystole in the intervention group compared to controls (mean [SD], 0.86 [0.854] vs. 0.00 [1.348], p = 0.017). [we are currently scoring our videos; performance data to come!]

Conclusions: Pediatric residents report increased comfort level managing patients with respiratory arrest and asystole after completing a high-fidelity simulator-based curriculum compared to those undergoing routine training. Limitations included small numbers which precluded comparing our curriculum to another intervention (computer-based, low fidelity or different frequency of sessions). Further research will further address skill and knowledge decay over time in order to inform the necessary frequency of curriculum sessions.
Pediatric Emergencies: A Simulation Curriculum for Medical Students

Author Name(s): Ilana Harwayne-Gidansky, MA, MD†, Alexandra Leader, MD†, Sheemon Zackai, MD,† Christopher Strother, MD

Department: Pediatrics

Division: Medical Education

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Pediatric crises are uniquely stressful and different than adult crises, and occur less often. Thus, students and residents have few exposures to these situations and are often ill prepared when they arise. Currently, there are no studies on medical student attitudes towards pediatric arrests or CRM. This makes CRM under simulation an even more important, yet under-studied area of training and research.

Hypothesis: We designed and tested a curriculum for third year medical students, incorporating exposure to a pediatric resuscitation using a high-fidelity simulator in order to practice both manual skills (effective bag valve mask ventilation), and communication skills (CRM). Our main objective was to assess students' baseline attitudes regarding pediatric resuscitation prior to the intervention, and improvement following intervention. Secondary was to objectively test improvement in BLS and communication skills using a previously validated tool (TRACS)

Methods: We designed a curriculum to train third-year medical students in CRM and basic components of resuscitation. A scenario is given to the students, followed by a brief didactic and practical teaching session. The scenario is then completed a second time. Students completed a pre-test prior to their simulation experience, and a post-test immediately following their simulation experience. Attitudes about CRM were assessed using a 5-point Likert scale (1= strongly agree, 5= strongly disagree).

Results: Fifty-four students have participated in our study thus far. Students showed subjective improvement in their comfort level in a pediatric resuscitation (p<0.001, 95% CI 1.14-1.78), their confidence in communicating during a pediatric resuscitation (p<0.001, 95% CI 1.30-2.13), and their confidence in knowing what their role is during a pediatric resuscitation (p<0.001, 95% CI 1.75-2.46).

Conclusions: Our study is unique, as we initially expect failure, give feedback, then watch success, or ‘do, teach, do’. These preliminary results suggest a subjective improvement in attitudes surrounding pediatric crises including comfort level, communication, and understanding of roles. A curriculum teaching crisis resource management to third-year medical students subjectively improves their attitudes and confidence level in a pediatric arrest. There is a need for more objective testing, which is a subject of future study (unpublished data).
Why Do Mothers Stop Breastfeeding in the US?

Author Name(s): Alma Natural, Lea Rivera-Todaro, Lawrence Noble

Department: Pediatrics

Division: General Pediatrics

Institution Affiliation: Elmhurst Hospital

Introduction: Many studies reveal that breastfeeding in the Latino community decreases with acculturation. The reason for this decline is not well understood.

Hypothesis: The purpose of this study was to understand the barriers to breastfeeding in the US as compared to Central and South America.

Methods: Using a community-based participatory approach, academic and community-based partners qualitatively assessed barriers to breastfeeding among Latina mothers in Queens, NY. Two focus groups were conducted in the community with a total of 20 mothers from South and Central America. Inclusion criteria were breastfeeding one baby for at least 6 months or more with weaning no more than 6 months prior. Interpreters assisted at sessions which were audio-taped, transcribed and translated. Using ATLAS.ti, coding was performed, categories were identified and emerging themes were agreed upon by consensus.

Results: Mothers agreed that breastfeeding support from healthcare professionals is greater in the US. However, breastfeeding is more difficult in the US secondary to lack of family presence, less societal acceptance of public breastfeeding and mother’s requirement to return to work. Family support is more evident in the countries of origin where cultural norms include that family provide physical and emotional support and whereby postpartum mothers stay home, breastfeed and rest. Most women have grown up observing family members and others in the community breastfeed, even in public. In the US, there is less family support, negative attitudes towards public breastfeeding and the need to return to work quickly.

Conclusions: Interventions to increase breastfeeding need to address the lack of family support, society's negative attitudes towards public breastfeeding and work issues.

Note: This study was supported by a grant from Mount Sinai Institutes of Clinical and Translational Sciences pilot project program.
Breastfeeding Support: It Takes A Village To Breastfeed A Child

Author Name(s): Princess Obieta, Lea Rivera-Todaro, Lawrence Noble

Department: Pediatrics

Division: General Pediatrics

Institution Affiliation: Elmhurst Hospital

Introduction: Recent breastfeeding statistics reveal 6 month rates of 43%, well short of the 2020 objective of 61%. New models for inner-city communities are needed. Community based participatory research assures that the models are culturally relevant and appropriate.

Hypothesis: The purpose of this study was to develop culturally appropriate interventions to increase breastfeeding duration.

Methods: Using a community-based participatory approach, academic and community-based partners qualitatively assessed interventions to increase breastfeeding in the predominately Hispanic, inner-city community in Queens, NY. Two focus groups were conducted in the community with a total of 20 mothers from South and Central America. Inclusion criteria were breastfeeding one baby for at least 6 months or more with weaning no more than 6 months prior. Interpreters assisted at sessions which were audio-taped, transcribed and translated. Using ATLAS.ti, coding was performed, categories were identified and emerging themes were agreed upon by consensus.

Results: Women expressed that, while health professionals provide technical support for breastfeeding, long term success requires family support, as mothers’ attitudes are most strongly influenced by relatives. The desire to breastfeed is promoted with societal acceptance and visual exposure to women breastfeeding. They identified several messages that mothers need to hear: breastfeeding is good, healthy, easy, natural, and helps bonding; mothers need to be patient as breastfeeding gets easier.

Conclusions: The paradigm of our approach to breastfeeding support needs to shift, as breastfeeding education starts with the family. The role of the healthcare professional is to assist their guidance. As many immigrants lack family supports, community health centers need to create a space where breastfeeding mothers can develop a sense of community.

Note: This study was supported by a grant from Mount Sinai Institutes of Clinical and Translational Sciences pilot project program.
Adolescent Contraceptive Adherence in Central Harlem and the South Bronx: A Follow-Up of the Authoritative-Directive Counseling Implementation

Author Name(s): Rebecca Voaklander, Lisa Handwerker MD

Department: Pediatrics

Division: CMCA & the Children's Aid Society

Institution Affiliation: Mount Sinai School of Medicine

Introduction: The Children’s Aid Society recently initiated a more assertive approach for prescribing reliable methods of contraception to sexually active adolescent patients of their medical centers. This initiative increased the number of patients receiving new contraceptives at the time of visit. At follow up, however, the centers found that a significant proportion of these patients are not adherent with their new contraceptive method. Given that poor health outcomes are associated with teen pregnancy and nearly half of adolescent female health center appointments address birth control methods, it is important to determine ways to increase patient contraceptive adherence.

Hypothesis: There is no hypothesis as this was a pilot study used to gather data to inform the hypothesis of a future study.

Methods: This study explored possible facilitators of and barriers to patient contraceptive adherence by conducting semi-structured interviews with patients receiving new contraceptives at the time of appointment and patients that received new contraceptives from the clinic at least 3 months ago. The patients that received new contraceptives at least 3 months ago were interviewed by phone and divided into groups based on their current use contraception.

Results: Fifty-seven patients with an average age of 18.3 years were interviewed. Older adolescent patients were more likely to discontinue a new contraceptive method within the first 3 months. Younger adolescent patients that started a new form of contraception were less likely to have cited birth control as the primary reason for their visit. Patients that discontinued their new contraceptive method did so an average of 29 days after starting. The most cited reason for not adhering to a new contraceptive method was side effects.

Conclusions: Clinicians should offer contraception to all female patients, regardless of reason for visit. Future studies should investigate the effect of structured follow-up conversations with adolescents that start a new form of birth control. Future studies should also investigate the effect of phone calls to remind adolescents to pick up refills of their contraceptive.
Discovery That Mutation of the Membrane Type-1 Metalloproteinase Gene (MT1-MMP) Causes Winchester Syndrome

Author Name(s): Rebecca Mosig1*, Brad Evans1*, Mollie Lobl1, Chiara Martignetti1, Catalina Camacho1, Valerie Grum-Tokars2, Marc Glucksman2, & John Martignetti1,3

Department: Pediatrics and Biochemistry and Molecular Biology

Divisions: Genetics and Genomic Sciences

Institution Affiliation: Mount Sinai School of Medicine, New York, NY and Rosalind Franklin University, Chicago, IL

Introduction: The “vanishing bone” syndromes represent a group of rare skeletal disorders characterized by osteolysis and joint destruction. The Winchester syndrome, described nearly 50 years ago in two sisters with a severe crippling osteolysis, was one of the first recognized autosomal recessive, multicentric forms of the disorder (Figure). The disease was initially described as a “new acid mucopolysaccharidosis” with skeletal deformities that simulated rheumatoid arthritis.

Hypothesis: Inactivation of the MT1-MMP gene in mice results in a similar phenotype: dwarfism, generalized osteopenia, and arthritis. We hypothesized that mutation of MT1-MMP, also an upstream activator of MMP-2, which is inactivated in a less severe “vanishing bone” syndrome, results in Winchester syndrome.

Methods: Cultured fibroblasts of the original proband were obtained. MMP-2 biochemical activity was measured by zymography. RNA and DNA were extracted and the MT1-MMP gene sequenced. *In silico* and *in vitro* analysis, including immunoblotting, cell fractionation, proteasome inhibition, and half-life analysis, were used to model the functional consequences of the mutation.

Results: Patient-derived fibroblasts demonstrated normal expression of MMP2 proenzyme but lacked active MMP2 and MT1-MMP. Sequencing MT1-MMP revealed homozygous mutations in the signal peptide domain. The mutation resulted in decreased protein half-life and impaired membrane targeting. Structural modeling demonstrated that the MT1-MMP mutation disrupts the ability of the nascent protein to interact with the signal recognition particle (SRP; Figure).
**Conclusions:** This identification will provide diagnostic clarity for this group of disorders and may provide insight into the pathogenesis of the more common, sporadic forms of osteoporosis, osteolysis and arthritis.
Chronic Granulomatous Disease Diagnosed in an Infant Whose Sibling Died of Serratia Sepsis and Hemophagocytic Lymphohistiocytosis

Author Name(s): Orly Klein, Lauren Marcewicz, Ilana Harwayne-Gidansky, Sarah Taylor-Black, James Yang, Charlotte Cunningham-Rundles, Edwin Forman

Department: Pediatrics / Medicine

Division: Hematology Oncology / Clinical Immunology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: We present case reports of two brothers with chronic granulomatous disease (CGD), one of whom died with hemophagocytic lymphohistiocytosis (HLH).

Cases: A full-term male presented at 3 months with lethargy, diarrhea and failure to thrive. History was significant for 2 previous admissions for fever and pneumonia. The patient was found to have Serratia sepsis, from which he ultimately expired. Hospital course was significant for a clinical and histological diagnosis of HLH. Postmortem tissue analysis revealed none of the known mutations for HLH; widespread necrotizing granulomas were noted on autopsy. A male infant was born 6 months later to the same parents. This second patient presented at 4 months with fevers, cervical lymphadenopathy and respiratory distress. History was significant for 2 episodes of pneumonia and 3 episodes of pustular skin rash. Given the family history, HLH was a concern, but this second patient never met criteria for diagnosis. Evaluation included testing for immunodeficiencies. A dihydroreductase assay was consistent with CGD; maternal assay was consistent with a carrier status.

Discussion: HLH is an infrequent diagnosis in pediatrics that may be due to inherited mutations. Other diagnoses, such as primary immunodeficiencies, may also lead to HLH, and should be considered in the differential diagnosis. CGD is not currently linked to HLH. However, CGD predisposes to an inefficient immune response and possible hypercytokinemia, common features in HLH. We recommend that patients who meet the criteria for HLH without a known underlying cause, particularly males with recurrent or severe infections, be evaluated for CGD.
Exogenous Mannose Supplementation Rescues Mpi-Deficient Zebrafish in a Model of Congenital Disorder of Glycosylation

Author Name(s): Jaime Chu\textsuperscript{1,2}, Alexander Mir\textsuperscript{2}, Ningguo Gao\textsuperscript{3}, Mark Lehrman\textsuperscript{3}, and Kirsten C. Sadler\textsuperscript{2}

Department: \textsuperscript{1}Pediatrics / \textsuperscript{2}Medicine / \textsuperscript{3}Developmental and Regenerative Biology / \textsuperscript{3}Pharmacology (UTSW)

Division: \textsuperscript{1}Hepatology

Institution Affiliation: Mount Sinai School of Medicine
University of Texas Southwestern Medical Center, Dallas, TX

Introduction: Patients with congenital disorders of glycosylation (CDG) have a recessive mutation of one of many genes needed for protein N-glycosylation. Lipid-linked oligosaccharide (LLO) synthesis is necessary for glycan transfer to asparagine residues of nascent polypeptides and requires conversion of fructose-6-phosphate to mannose-6-phosphate via phosphomannose isomerase (MPI; also called PMI). MPI-CDG patients can be treated with oral mannose supplements to restore mannose-6-phosphate through a minor complementary metabolic pathway, enabling LLO synthesis, and augmenting protein glycosylation. MPI-CDG is the only CDG subtype that can be treated. Patients receiving mannose therapy are largely devoid of symptoms.

Hypothesis: A zebrafish model of MPI-CDG will exhibit phenotypic abnormalities that can be rescued with mannose supplementation.

Methods: To study the cellular and genetic pathways that contribute to the multi-systemic disease of CDG patients, we aim to establish a zebrafish model of MPI-CDG using morpholino knockdown of Mpi in zebrafish embryos.

Results: mpi morphants have 12% residual Mpi enzyme activity at 4 days post-fertilization and show decreased levels of LLO by fluorophore-assisted carbohydrate electrophoresis analysis. These deficiencies result in 40% embryonic lethality with 70% of surviving embryos displaying several morphological phenotypes including small eyes, dysmorphic jaws, pericardial edema, and curled tails. Importantly, these morphological phenotypes are rescued by mannose supplementation. With mannose, less than 20% of mpi morphants are affected and those that are affected present a milder phenotype.

Conclusions: These findings not only validate zebrafish as a means to study MPI deficiency but also establish zebrafish as a useful tool to study other glycosylation disorders.
Serum Transaminase Elevation as a Marker for Disseminated Neonatal Herpes Simplex Virus Infection

Authors: Matthew Harris, M.D., Michael Tosi, M.D.

Department: Pediatrics

Division: Infectious Diseases

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Disseminated neonatal herpes simplex virus infection (DnHSV) is a rare but devastating illness. Mortality exceeds 80% if untreated. Early treatment with acyclovir reduces mortality by nearly half. Difficulty in clinically distinguishing DnHSV from sepsis in the first 14 days of life may delay effective treatment.

Hypothesis: A review of clinical and laboratory data in reported cases of DnHSV in the first 14 days of life might reveal a marker that permits earlier recognition and treatment of this illness.


Results: 71 cases of DnHSV were identified. 70/71 infants presented between days 2-12 of life (mean 5.8d). Presenting features were usually non-specific and typical of neonatal sepsis: fever (48%), lethargy (54.3%), poor feeding (50%), respiratory distress (47.8%), hemodynamic instability (23.5%), jaundice (20%), seizures (11.7%), vomiting (10.6%) and temperature instability (9.8%). Only 20% had cutaneous vesicles suggestive of HSV. 43 infants with DnHSV had serum transaminase levels tested at presentation. 42 (97%) had elevations in AST (mean = 5303 U/L), ALT (mean 1453 U/L), or both. Thrombocytopenia was documented in 13/26 (50%) infants, and was the second most common lab abnormality. Timing of initiation of acyclovir relative to presentation was reported for 51 infants. Early (<24hr), delayed (mean 4.8d), or no treatment occurred in 31.3%, 47.1%, and 21.6% respectively. Related mortality was 56%, 83.3% and 90.1% respectively.

Conclusions: Documentation of elevated serum transaminase levels at presentation was observed in 97% of tested infants with DnHSV in our review. This routine and inexpensive test may permit early recognition and treatment of this infection in infants who present with a sepsis-like illness in the first 14 days of life.
Susceptibility to Measles Among Perinatally HIV-Infected Adolescents and Young Adults

Authors: Lee Morris, Roberto Posada, Carole Hickman, Don Latner, Tricia Singh, Alyssa Rautenberg, Jennifer Jao, William Bellini, Rhoda Sperling

Department: Pediatric

Division: Infectious Diseases

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Many youth with perinatally-acquired HIV (PAH) exhibit poor immune responses to vaccinations, including measles, mumps and rubella (MMR). This has worldwide public health implications, particularly in areas where HIV and measles are prevalent. The objective of this pilot study was to determine the prevalence of measles immunity among individuals with PAH and prior MMR vaccination.

Hypothesis: There will be low rates of measles-immune individuals with PAH.

Methods: Individuals with PAH >13 years old, at Mount Sinai Hospital (MSH) with prior MMR vaccination were enrolled. Measles IgG titers were determined at MSH via commercially available ELISA and the Centers for Disease Control and Prevention by plaque reduction neutralization (PRN) assay. Measles immunity was defined as PRN assay IgG titers >120mIU. Medical records were reviewed for demographics and pertinent clinical data. P-values were calculated using Wilcoxon test, Chi-square or Fisher's exact test as appropriate.

Results: Only 6/34 (17.6%) subjects were measles-immune. Measles-immune subjects were younger [median age 14.5 vs. 19 years (p=0.01)]. Differences in gender and race/ethnicity were not statistically significant between immune and non-immune groups. One measles-immune subject had a history of opportunistic infections compared to 18 (62%) non-immune subjects (p=0.07). Median CD4 count at enrollment and nadir CD4 count were 682 cells/mm3 and 299 cells/mm3 in measles-immune subjects vs. 263 cells/mm3 (p=0.054) and 143 cells/mm3 (p=0.175) in non-immune subjects, respectively. Additionally, 83% immune subjects received antiretroviral therapy at vaccination compared to 30% non-immune subjects (p=0.025).

Conclusions: Most youth with PAH lacked protective PRN titers to measles despite prior vaccination. Further studies to understand the durability of measles immunity in this population are needed.
A comparison of High-Risk Behaviors in HIV-Infected, HIV-Uninfected and HIV Status Unknown Youth in Cameroon

Author Name(s): Lee Morris, Francine Kouya, Rene Kwalar, Mariecel Pilapil, Kohta Saito, Nancy Palmer, Roberto Posada, Tih Muffih, Thomas Welty, Jennifer Jao

Department: Pediatrics

Division: Infectious Diseases

Institution Affiliation: Mount Sinai School of Medicine, Cameroon Baptist Convention Health Services (CBCHS)

Introduction: Worldwide, HIV is spreading most quickly among adolescents and young adults. HIV prevention programs need strengthening as many youth lack the knowledge to avoid HIV exposure.

Hypothesis: There will be a high prevalence of sexual risk behaviors among youth in Cameroon, with higher rates of risk behavior among HIV-infected youth compared to HIV-uninfected and status unknown peers.

Methods: We conducted a cross-sectional survey in Northwest Cameroon to evaluate risk behaviors and substance use among youth ages 12-26 in 15 randomly selected schools, 2 churches and 3 HIV clinics. Randomly selected youth consented and completed the anonymous questionnaire.

Results: Overall, 534 surveys were completed (114 HIV-infected, 210 -uninfected, 210 unknown). HIV-infected youth surveyed were largely female (p< 0.001) and older than HIV-uninfected and unknown youth (mean age = 22.9 vs. 17.9 and 16.5 years, respectively, p< 0.001). HIV-infected participants had a higher mean age at first intercourse, (17.2 vs. 14.3 and 13.3 years, p< 0.001), were more likely to have first intercourse with someone older (p< 0.001) and reported being forced/pushed or needed/received money/gift as a reason for first intercourse (p=0.003). HIV-infected individuals had more lifetime partners (p=0.034) and reported the lowest rates of both condom use at last intercourse [55% vs. 71.2% and 59.5% (p=0.148)] and consistent condom use (p< 0.001).

Conclusions: Despite current HIV prevention efforts in Cameroon, this study demonstrates continued high-risk behaviors among youth. These results may help inform HIV prevention policy and curriculum for youth in Cameroon.
Gestational Diabetes in HIV-Infected Pregnant Women in Cameroon

Author Name(s): Margee Louisias MD, Marcia Wong MD, Christopher Sellers MD, Dennis Palmer DO, Emmanuel Nshom MPH, Jennifer Jao, MD, MPH

Department: Pediatrics

Division: Infectious Diseases

Institution Affiliation: Mount Sinai School of Medicine

Intro: Gestational diabetes mellitus (GDM) poses risks to the mother and child. HIV-infected pregnant women, particularly those on combination antiretroviral therapy (cART) may be at increased risk of GDM. Few studies to date have evaluated rates of GDM in HIV-infected and uninfected pregnant women in Africa.

Hypothesis: HIV-infected pregnant women, in particular those on cART have a higher prevalence of GDM.

Methods: We prospectively enrolled HIV-infected and HIV-uninfected pregnant women <36 weeks gestation at the Cameroon Baptist Convention Health Board from February 2011 to January 2012. Those with reported pre-existing diabetes were excluded. Data regarding risk factors for GDM, HIV clinical status, and ART was collected. GDM were measured using oral glucose tolerance test and were classified as having GDM according to WHO standards. P values were calculated using Wilcoxon, Chi-square or Fisher’s exact test as appropriate.

Results: 114 HIV-infected and 97 HIV-uninfected pregnant women have been enrolled to date. Overall, the rate of GDM was low (6/211) at 2.8%. Though not statistically significant, the difference in rates of GDM between groups was 3.5% (4/114) and 2% (2/97) respectively (p=0.69). In a sub-analysis of HIV-infected women, those on cART had a higher prevalence of GDM than HIV-infected women who were either not on ART or only taking zidovudine (5% vs 0%, p=0.005).

Conclusion: The overall rate of GDM in Cameroon is low. HIV-infected pregnant women on cART in Cameroon have a higher prevalence of GDM compared to those who are not on ART or only taking zidovudine.
Mechanoregulation of BK Channel Activity in the Distal Nephron: Role of the MAP-Kinase (MAPK) Pathway

Author Name(s): Cindy Else, Beth Zavilowitz, Dan Flores, Wen Liu, Lisa M. Satlin, Rajeev Rohatgi

Department: Pediatrics

Division: Nephrology

Introduction: An increase in tubular flow rate, associated with an increase in fluid shear stress (FSS), in the cortical collecting duct, a distal nephron segment, stimulates the rate of net K secretion (JK) mediated by the apical stretch/Ca⁺-activated BK channel. FSS stimulates the MAPK pathway in endothelial cells. Patch clamp experiments in rodent CCD reveal that suppression of ERK and p38 MAPK augments basal BK channel activity in the cell, therein, suggesting that basal BK channel activity is tonically suppressed by ERK and p38.

Hypothesis: FSS regulates MAPK signaling in CCD cells which, in turn, modulates BK channel-dependent K secretion in this segment.

Methods: Monolayers of an immortalized murine CCD cell line (mpkCCD) were grown to confluence on glass slides for 4-5 days and subjected to no or physiological FSS (0.4 dynes/cm²) for up to 60 min. Western Blot analysis was performed on cell lysates to quantitate phosphorylated p38 and ERK. To test the effects of p38 inhibition on JK, CCDs isolated from NZW rabbits were microperfused and net Na (JNa) absorption and JK (pmol/min.mm) measured in the absence and presence of SB203580, a p38 inhibitor.

Results: mpkCCD cells exposed to FSS for 10, 30 and 60 min expressed greater abundance of phospho-ERK and phospho-p38 than non-sheared cells at the same time points. Based on the patch clamp studies above, activation of the MAPK pathway should inhibit BK channel-mediated JK. However, JK (-8.6±1.3 vs. -8.7±2.1) and JNa (14.1±1.5 vs. 14.8±3.7) in CCDs perfused at 1 nl/min.mm showed no change after exposure to SB203580.

Conclusions: FSS induces phosphorylation of p38 and ERK. However, p38 inhibition does not affect basal JNa and JK. We speculate that MAPK suppresses basal channel activity, but does not affect transepithelial Na or K transport.
Flow Induced Prostaglandin E2 Release Regulates Na and K Transport in the Collecting Duct

Author Name(s): Daniel Flores BA1, Yu Liu MD PhD1, Wen Liu MD PhD2, Lisa M. Satlin2 MD, Rajeev Rohatgi MD1,2

Department: 1Medicine, 2Pediatrics

Division: 1, 2Nephrology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Fluid shear stress (FSS) is a critical regulator of cation transport in the collecting duct (CD). High dietary sodium (Na) consumption increases urine flow, Na excretion, and prostaglandin E2 (PGE2) excretion.

Hypothesis: We hypothesize that increases in FSS elicited by increasing tubular flow rate induce release of PGE2 from renal epithelial cells into the extracellular compartment and regulates ion transport.

Methods: To test this hypothesis, immortalized inner medullary CD (IMCD) cells were exposed to FSS and PGE2 measured in the conditioned media. Transepithelial Na and K transport were measured in microperfused rabbit CDs under slow and high flow rates, before and after indomethacin treatment; in order evaluate the role of PGE2 on cation transport.

Results: Media retrieved from CD cells exposed to FSS reveals several fold higher concentration of PGE2 compared to controls. Treatment of CD cells with either cyclooxygenase-1 (COX-1) or COX-2 inhibitors during exposure to FSS limited the increase in PGE2 concentration. Cytosolic phospholipase A2 (cPLA2), the enzyme which generates the COX substrate, is regulated by mitogen activated protein (MAP)-kinases and intracellular Ca2+ concentration ([Ca2+]i). MAP-kinase inhibition and chelation of [Ca2+]i limited the FSS mediated increase in PGE2 concentration. Sheared cells expressed greater phospho-cPLA2 protein abundance than static cells; however, COX-1/2 protein expression was equal in both groups. In microperfused CDs, COX inhibition enhanced flow stimulated Na reabsorption and abolished flow stimulated potassium (K) secretion, but did not affect ion transport at a slow flow rate.

Conclusions: In conclusion, FSS activates cPLA2 to generate PGE2 which regulates Na and K transport in the native CD.
Outcomes During Transfer to Adult Services for Pediatric Nephrology Patients

Author Name(s): Kathryn Kapoor, Robyn Matloff, Vinay Nair, Rachel Annunziato, Jeffrey Saland

Department: Pediatrics (KK, RM, RA, & JS) & Medicine (VN)

Division: Nephrology (KK, RM, VN, & JS) & Behavioral and Developmental Health (RA)

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Previously, a retrospective chart review was conducted of pediatric liver transplant recipients who transferred to adult-oriented services at MSSM revealing increased medication non-adherence and mortality. These findings lead to promising quality of care improvements (Annunziato et al., 2011). The Pediatric Nephrology/ Kidney Transplant team aims to examine if transfer is a problem point for their service so that organizational changes can be implemented if necessary. Therefore, a comprehensive chart review will be conducted of 30 recently transferred pediatric nephrology patients.

Hypothesis: The present study hypothesizes that transfer will be associated with deterioration in adherence. A novel aspect of this study is that we will examine different types of patients hypothesizing that there will be differences by patient type.

Methods: Variables to be studied for the time period one year prior to transfer and one year after include adherence (to medications and appointments) and corresponding medical outcomes. The specific variables are: type of patient (i.e. chronic kidney disease, transplant, or dialysis), number of missed appointments, number of inpatient admissions, creatinine level (a measure of kidney function), blood pressure, Kt/V, URR, yes/no anemia, infections, yes/no fistula use, yes/no listed for a transplant, tacrolimus values (proxy for adherence), yes/no history of missing tacrolimus doses) cyclosporine levels (another immunosuppressant), yes/no rejection and yes/no graft loss. Patient age at transfer, transfer date, and reason for transfer will be recorded.

Results & Conclusions: Based on our results, data-driven programmatic steps can be taken to improve the transfer process and implement safeguards for patients.
Moyamoya Syndrome Treated with Encephaloduroarteriosynangiosis Followed by Hematopoietic Cell Transplantation in Patients with Sickle Cell Disease: a Case Series

Author Name(s): Orly Klein M.D.\textsuperscript{1}, Mark Walters M.D.\textsuperscript{2}, Diane George M.D.\textsuperscript{3}, Roland Chu M.D.\textsuperscript{4}, James T Goodrich M.D., Ph.D., D.Sc.\textsuperscript{5}, Elizabeth Roman M.D.\textsuperscript{6}, Romaine Schubert M.D.\textsuperscript{7}, Gustavo Del Toro M.D.\textsuperscript{8}

\textsuperscript{1}Department of Pediatrics; \textsuperscript{2}Pediatric Hematology Oncology, Children's Hospital, Oakland; \textsuperscript{3}Pediatric Blood and Marrow Transplantation, Columbia University; \textsuperscript{4}Pediatric Hematology Oncology, Children's Hospital of Michigan; \textsuperscript{5}Pediatric Neurosurgery, Children's Hospital at Montefiore; \textsuperscript{6}Pediatric Hematology Oncology, NYU; \textsuperscript{7}Pediatric Neurology, NY Methodist Hospital; and \textsuperscript{8}Department of Pediatrics, Wyckoff Heights Medical Center.

Abstract: Patients with sickle cell disease (SCD) have a high risk of intracranial vasculopathy, leading to a proliferation of microvasculature at the base of the brain known as moyamoya syndrome. This confers a high risk of intraventricular hemorrhage. Moyamoya syndrome can be treated surgically with a revascularization procedure called encephaloduroarteriosynangiosis (EDAS), which has been shown to decrease but not eliminate the risk of stroke. Hematopoietic cell transplantation (HCT) from a compatible sibling is the most effective way of preventing central nervous system (CNS) complications in SCD patients at risk for CNS events. We report six pediatric cases of patients with SCD who developed moyamoya syndrome, all of whom successfully underwent EDAS followed by HCT. These are the first reported cases of EDAS successfully followed by HCT in patients with SCD and moyamoya syndrome. Patients with moyamoya syndrome and SCD who have a CNS event are significantly more likely to experience a recurrent CNS complication even while on chronic transfusions. Transplant-eligible SCD patients who develop moyamoya syndrome may benefit from EDAS prior to undergoing HCT in order to minimize CNS complications. Further investigation by way of an international, multicenter prospective study is needed to determine the long-term outcome and potential benefits of this therapeutic combination.
Prostaglandin E2 Mediates Proliferation and Chloride Secretion in ADPKD Cystic Renal Epithelia

Author Name(s): Yu Liu¹, Madhumitha Rajagopal², Kim Lee¹, Lorenzo Battini¹, Daniel Flores¹, G. Luca Gusella¹, Alan C. Pao² and Rajeev Rohatgi¹

Department:¹,²Medicine - Pediatrics

Division:¹,²Nephrology

Institution Affiliation:²Stanford University

Introduction: Studies indicate that prostaglandin E2 (PGE2) contributes to cystogenesis in genetically non-orthologous rodent models of autosomal dominant polycystic kidney disease (ADPKD). However, it remains unclear whether PGE2 induces the classic proliferative and secretory features of ADPKD cystic epithelia in a genetically orthologous model of ADPKD.

Hypothesis: We hypothesized that, in ADPKD tubular epithelia, PGE2 induces proliferation and chloride (Cl-) secretion, two archetypal phenotypic features of ADPKD.

Methods: To test this hypothesis, proliferation and Cl- secretion were measured in renal epithelial cells deficient in polycystin-1 (PC-1).

Results: PC-1 deficient cells increased in cell number (proliferated) faster than PC-1 replete control cells and this proliferative advantage was abrogated by cyclooxygenase inhibition, suggesting that PGE2 signaling is aberrant in PC-1 deficient cells. The administration of exogenous PGE2 increased the proliferation of PC-1 deficient cells by 38.8±5.2% (n=6, p<0.05) but inhibited the growth of PC-1 replete control cells by 49.4±1.9% (n=6, p<0.05). The growth advantage of PC-1 deficient cells was reverted by antagonizing PGE2-activated EP2- and EP4 receptors which reduced proliferation by 25.2±2.8% (n=6, p<0.05) and 36.5±4.0% (n=6, p<0.05), respectively. Next, PGE2 induced short circuit current (Isc) was measured in the PC-1 deficient and replete cells. PGE2 induced a five-fold higher increase in Isc in PC-1 deficient compared to replete cells. This PGE2 mediated Isc in PC-1 deficient cells was blocked by CFTR-172 and niflumic acid, indicating that PGE2 activates both CFTR and calcium activated chloride channels (CaCCs).

Conclusions: Exogenous and endogenous PGE2 activates aberrant signaling pathways in PC-1 deficient epithelia which may contribute to the proliferative and secretory phenotype characteristic of ADPKD and suggest a therapeutic role for PGE2 and EP receptor antagonism.
Urinary Exosomes To Study Renalase And Renal Development

Author Name(s): Robyn Matloff, Jeffrey Saland, Lisa Satlin

Department: Pediatrics

Division: Nephrology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Exosomes are microvesicles of 30-100 nm size secreted by various cell lines, carrying proteins and RNA representative of those cells. Thus, the composition and contents of urinary exosomes represent physiologic processes within the renal tubule. We were interested in the potential of urinary exosomes to uniquely address two areas of study: 1) developmental renal physiology because homeostatic demands on the kidney during development differ that of adults, and 2) expression of renalase. Renalase is synthesized by the kidneys and involved in the catabolism of catecholamines. Renalase levels are low in adults with CKD and may contribute to the hypertension commonly seen in these patients.

Hypothesis: Protein or RNA measures of renalase, channels, and transporters in urinary exosomes sampled from infants and children will demonstrate developmental differences in renal physiology compared to adults and establish methodology for clinical research of the role of renalase in children with CKD.

Methods: Urine from healthy volunteers ranging in age from 6 to 45 years was centrifuged to remove cellular debris and Tamm-Horsfall protein. Urinary exosomes were isolated via sequential ultracentrifugation of the remaining supernatant. RNA was harvested and amplified by qPCR using primers for renalase, actin, uromodulin and aquaporin. Renal biopsy tissue served as a control.

Results: Actin, uromodulin and aquaporin RNA was routinely detected in urinary exosomes. Abundance of mRNA was inversely associated with age. Renalase RNA was not consistently detected.

Conclusions: Urinary exosomes can provide a valuable non-invasive tool (“liquid biopsy”) for characterizing the developmental regulation of selected cell surface proteins, RNA and channels along the nephron. Renalase is not amenable to study by our current technique.
Isolation of Urinary Exosomes in Neonates to Determine Presence of Renal Ion Transporters

Author Name(s): Scarlett McKinsey MD, Ian Holzman MD, Lisa Satlin MD

Department: Pediatrics

Division: Newborn Medicine; Nephrology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Urinary exosomes, which can be isolated from urine collected from premature newborns, are small membrane vesicles that contain apical membrane and intracellular cytosol and are secreted into the urine from all nephron segments. Evidence from animal studies and postmortem human data suggests that premature newborns lose Na in their urine because of (1) limited expression of renal Na reabsorptive proteins, including the Na-K-2Cl and Na-Cl cotransporters in the TALH and DCT, respectively, and the epithelial Na channel ENaC in the distal nephron and (2) end-organ unresponsiveness of the distal nephron to hormones that regulate activity of these proteins.

Hypothesis: We hypothesize that Na-K-2Cl, Na-Cl and ENaC mRNA and protein expression in urinary exosomes will be low at birth in our cohort of premature newborns, will increase with advancing postnatal age, and will correlate with the ability of the infant to reabsorb Na.

Methods: Urine will be collected at birth and then weekly from newborns born at < 28 weeks gestation. Exosomes will be isolated using the ultracentrifugation technique previously described by Pisitkun et al. (2004) Exosome RNA will be quantified using RT-PCR.

Results: We expect to find limited expression of ion transporter RNA at birth with increasing expression correlating with increasing gestational age.

Conclusions: This study will help elucidate whether the newborn’s limited ability to handle Na is due to fewer transporters and whether these transporters increase in number over the first weeks of life. These data will be interpreted in the context of our assessment of the infant’s response to diuretics to determine whether the drugs are affecting their presumed target.
The Role of the BK Channel in the Renal Adaptation to Chronic Metabolic Acidosis (CMA)

Author Name(s): Carlos MN Schreck, Beth Zavilowitz, Lisa M. Satlin

Department: Pediatrics

Division: Nephrology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Basal K secretion into the urinary fluid in the cortical collecting duct (CCD) is mediated by the apical SK channel, present solely in principal cells, whereas flow-induced K secretion is mediated by the BK channel, predominant in intercalated cells (ICs) and inhibitable by iberiotoxin (IBX). Low basolateral (BL) Na/K ATPase activity in ICs does not support a significant role for K secretion. H secretion by the apical H/K-ATPase in ICs is inhibitable by luminal Ba (K channel inhibitor) and enhanced during CMA. It is possible that the BK channel recycles luminal K for the H/K-ATPase during CMA.

Hypothesis: Apical H/K-ATPase activity in H-secreting α-ICs during CMA is dependent on the BK channel.

Methods: H/K-ATPase activity was assayed in individual α-ICs in microperfused CCDs isolated from NZW rabbits subject to 5-7 d NH₄Cl-induced CMA, loaded with the pH-sensitive dye BCECF, and then subjected to an acute intracellular acid load (NH₄Cl prepulse technique). On BL NH₄Cl washout, the initial rate of cell pH (pHᵢ) recovery (pH U/min) was measured (1) in the absence of luminal and BL Na and K (H-ATPase), and then after sequential (2) BL K (BL H/K-ATPase) (3) luminal K (luminal H/K-ATPase) (4) BL Na (BL Na/H exchanger) replacement. The studies were performed ± luminal IBX.

Preliminary Results:

<table>
<thead>
<tr>
<th></th>
<th># (cells)</th>
<th>H-ATPase</th>
<th>BL H/K-ATPase</th>
<th>Luminal H/K-ATPase</th>
<th>BL Na/H exchanger</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>13</td>
<td>0.082±0.024</td>
<td>0.019±0.006</td>
<td>0.055±0.013</td>
<td>0.038±0.034</td>
</tr>
<tr>
<td>IBX</td>
<td>5</td>
<td>0.058±0.018</td>
<td>0.162±0.058</td>
<td>0.013±0.016 Δ</td>
<td>0.476±0.111</td>
</tr>
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</table>

* p=0.001
Δ 0.05 < p < 0.1

Conclusions: We speculate that reducing luminal K recycling (IBX) enhances BL K recycling which favors BL H/K-ATPase activity. Studies are in progress to test whether IBX inhibits luminal H/K-ATPase activity in CMA.
Early Enteral Feeding Doesn’t Prevent Hypoglycemia in SGA Neonates

Author Name(s): Jennifer J. Bragg, MD, Robert Green, MD and Ian R. Holzman, MD

Department: Pediatrics

Division: Newborn Medicine

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Prevention of neonatal hypoglycemia in at risk neonates isn’t well-defined. New guidelines recommend initiating enteral feeding within the first hour of life. The impact of early feeding to prevent hypoglycemia in small for gestational age (SGA) neonates in the first hours of life remains unclear.

Hypothesis: Early feeding does not affect the incidence of hypoglycemia in SGA neonates.

Methods: A retrospective medical record review to evaluate the association of hypoglycemia and early enteral feeding. Eligible patients were born term (37-42 weeks) between 1/1/2008-7/1/2011 and classified as SGA (birth weight < 10th percentile). We collected the first three point of care (POC) blood glucose values, time to initiation of enteral feeding and type of feeding. Primary outcome was incidence of hypoglycemia, defined as POC glucose values ≤35 mg/dL

Results: 460 records were reviewed. 203 were included in the analysis. 94 patients were fed after the initial glucose measurement; 109 were not. The incidence of hypoglycemia in the early enteral feeding group was 13% while the incidence in the group that didn’t was 4% (p=0.02). Neonates breastfed were less likely to become hypoglycemic (6%) than those fed formula (23%). Multivariate regression showed the initial POC value and if the neonate was fed to be significant predictors of the 2nd POC value (p<0.001).

Conclusions: This study suggests early enteral feeding does not prevent hypoglycemia in SGA neonates and in our cohort, it increased the incidence of hypoglycemia. Early enteral feeds of formula were more likely to precede hypoglycemia. Neonates with lower initial POC values merit closer monitoring as they are at higher risk for lower subsequent POC values, regardless of interventions.
Using Lung Ultrasound in the Diagnosis of TTN and HMD

Author Name(s): Claudia Cadet, MD, James Tsung, MD and Ian Holzman, MD

Department: Pediatrics

Division: Newborn Medicine

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Hyaline Membrane Disease (HMD) and Transient Tachypnea of the Newborn (TTN) are common neonatal respiratory disorders with overlapping clinical presentations, gestational ages, and radiographic pictures. Ultrasonographic findings may distinguish these disorders; however, data comparing diagnoses and disease severity by lung ultrasound with those by chest radiograph and clinical impression are lacking. This study aims to determine if ultrasound (1) can predict severity of clinical course and (2) is diagnostically consistent with chest radiograph and clinical impression.

Methods: We conducted a prospective study of infants ≥ 30 weeks gestation admitted from 10/15/11 to 2/15/12 with respiratory distress. A group of similar but well patients were enrolled as controls. Demographic data, duration of respiratory support (DRS), surfactant administration, radiographic diagnosis, and clinical diagnosis were collected. An expert blinded to clinical data determined ultrasonic diagnoses and percentage B-line confluence (PBC). Primary outcome was to correlate ultrasound PBC with DRS. Secondary outcomes were comparisons of ultrasound diagnoses with those by radiograph and clinical impression.

Results: 15 neonates (1040–4430 gm; 30-40 weeks) were enrolled. 8 had clinical diagnosis of TTN; 3, HMD; and 4, normal. DRS ranged from 0-8 days. Linear regression gave significant correlation of DRS with PBC (R=0.734, p=0.002), improved by gestational age in a multivariable model (R=0.844, p=0.001) but not by birthweight, age at ultrasound, maternal steroids, and mode of delivery. Surfactant administration was borderline (p=0.116). Chi square analysis of diagnoses show difference between ultrasound and clinical impression (p=0.006) and poor agreement with radiograph (p=.077).

Conclusions: Although this limited data do not allow us to determine whether ultrasound can distinguish HMD from TTN, this pilot study suggests that PBC on lung ultrasound is predictive of duration of respiratory support.
Ovulation Induction is Associated with Small for Gestational Age Neonates

Author Name(s): Loren M. DeLuca DO, Nathan Fox MD, Robert Green MD, Annemarie Stroustrup MD, Matthew Harris MD, Kathleen Gibbs MD

Department: Pediatrics

Division: Newborn Medicine

Institution Affiliation: Mount Sinai School of Medicine

Introduction: In the United States, 30 per 1000 livebirths are twins; 2/3 of these are a product of infertility treatments. Both in vitro fertilization (IVF) and ovulation induction (OI) are associated with twin gestation and adverse outcomes including an increased incidence of small for gestational age (SGA) infants.

Hypothesis: Ovulation Induction is associated with an increase incidence in SGA infants in twin gestations.

Methods: A retrospective cohort study was conducted. Modes of conception considered were spontaneous conception (SC), OI or IVF. Subjects were delivered by a high-risk obstetric practice between 2005-2011 at Mount Sinai Hospital. Maternal and neonatal data were recorded. Our primary outcome was the incidence of SGA from the three modes of conception. SGA was defined as birth weight <10th percentile. Chi square, ANOVA, and logistic regression were used in the analysis.

Results: Records of 772 infants from 394 mothers of twin pregnancies were reviewed. In univariate analysis, twins conceived by OI had an increased incidence of SGA (28%) when compared to both SC (16.4%) and IVF (16.3%) groups, (p=0.02). In multivariable modeling adjusting for gestational age, gender, and maternal age, SGA was more common in the OI group (odds ratio (OR) 2.16 95% CI 1.16-4.00, p=0.015) compared to SC group and compared to IVF group (OR 1.77 95% CI 1.04-3.01, p =0.34).

Conclusions: When adjusted for gestational age, gender, chorionicity, and maternal age neonates conceived by OI had a greater incidence of SGA. However, IVF was not associated with an increased risk of SGA as previously suggested in other studies.
Protective Effect of Methylxanthines in an In Vitro Model of Neuronal Injury

**Author Name(s):** John Ladino, MD, Javier Pacheco-Quinto, PhD, Ben Lee, MD, Hui Peng, PhD, Elizabeth Eckman, PhD, Christopher Eckman, PhD

**Department:** Pediatrics

**Division:** Neonatology

**Institution Affiliation:** Morristown Medical Center, Atlantic Health System, Morristown, NJ, United States

**Introduction:** Neonatal brain injury secondary to hypoxia-ischemia (HIE) is a frequent cause of neurodevelopmental disability. Recent studies have suggested that the methylxanthines may have anti-inflammatory and neuroprotective properties in the premature and therefore, may have a potential therapeutic benefit for HIE.

**Objective:** To investigate the effects of methylxanthines in an *in vitro* model of neuronal injury

**Methods:** Neuron-glial cells were isolated from Sprague-Dawley rats brain cortex at P2 and then grown in poly-D-lysine coated plates. On day 7, cells were treated with 10 μM of either caffeine (CAF), pentoxyfilline (PEN) or 1,7-Dimethylxanthine(DYM). At day 8, each treatment group was subjected to 1.5 hour of oxygen-glucose deprivation (OGD). Cell damage was assessed by measuring LDH release using an enzymatic colorimetric assay after a 20 hour recovery period. A group not subjected to OGD was used as control (C).

**Results:** Oxygen-glucose deprivation for 1.5 h produced a significant increase on LDH release after 20 hours in the non-treated cells. Exposure to caffeine, pentoxyfilline and 1,7-Dimethylxanthine significantly decreased the release of LDH after 20 h of oxygen glucose deprivation (p<0.0001) in each treated group.

**Conclusions:** All the methylxantines tested protected neuron-glial cells against OGD-induced injury. Further studies on animal models of neonatal brain injury are warranted. The methylxanthines may have neuro-protective effects after HIE in the newborn
Epidemiology of Periventricular Echodensities in Very Low Birth Weight Infants

Author Name(s): Richa Lakhotia, Lauren M. Priolo, Benjamin Rosenfeld, Ben H. Lee

Department: Pediatrics

Division: Neonatology

Institution Affiliation: Morristown Memorial Hospital, New Jersey

Introduction: Periventricular echodensities (PVE) are a common finding on cranial ultrasounds (CUS) of very low birth weight (VLBW) infants. Whereas outcomes associated with intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL) are well described, descriptions of those associated with PVE have been limited.

Hypothesis: PVE is associated with PVL and consequently, delayed NDO.

Methods: Infants born ≤1500g and ≤32.0 weeks gestational age (GA) admitted to NICU between 1/1/05 to 12/31/10 were included. Clinical data and neuroimaging results (CUS, MRI) were abstracted. Infants who died prior to 28 weeks corrected GA or in the first week of life were excluded. IRB approval was obtained.

Results: 568 infants met the entry criteria. PVL occurred in 3%. PVE was diagnosed in 7%, detected at a median age of 7 days of life (IQR 4-9 days). PVL was associated with PVE with an odds ratio (OR) of 2.6 (95% CI 1.6-3.7). PVL was more likely to occur when PVE was detected in the first week of life (PR 9.8, 95% CI 1.04-92.70). When PVE was documented to have disappeared, it did so after a median of at least 14 days (IQR 7-18); however, there was no association between PVE duration and PVL. Although PVE was detected bilaterally in 60%, right only in 32%, and left only in 8%, there was no association of unilateral PVE with PVL (OR 3.2, 95% CI 0.6-16.0).

Conclusion: PVE was commonly diagnosed in VLBW infants born under 32 weeks GA, typically detected within the first 2 weeks of life and associated with PVL, particularly when occurring in the first week of life. Association of PVE with NDO is ongoing.
Impact of Physician Awareness on Diagnosis of Fetomaternal Hemorrhage

Author Name(s): Callie Plafkin, BA, Annemarie Stroustrup, MD, MPH

Department: Pediatrics

Division: Newborn Medicine

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Fetomaternal hemorrhage (FMH) is a poorly understood condition where the placenta transfers fetal whole blood to the mother. FMH causes fetal anemia which can result in fetal distress, neonatal critical illness, death, or lifelong disability. This study evaluated diagnosis of FMH at MSSM in eight time epochs, seven before and one after an intervention to increase awareness of FMH by MSSM physicians.

Hypothesis: Diagnosis of FMH increases with physician awareness of the disease.

Methods: This is a retrospective cohort study of all neonates cared for at MSSM between 1988 and 2010. Neonates with congenital anemia compared to gestational age-adjusted normal hematocrit values were identified from a diagnosis database of all neonates admitted to our institution’s newborn medicine service. Medical records of anemic neonates were reviewed for diagnosis accuracy and any identified etiology of anemia. Comparisons were made by Student’s t-test, ANOVA, and $\chi^2$ test.

Results: Of 124,738 newborn admissions, 572 (0.5%) neonates with congenital anemia were identified. For the majority, the cause of anemia was unknown. Twenty-four cases of FMH demonstrated by positive Kleihauer-Betke testing (KB) occurred in our cohort. The mean incidence of diagnosed FMH among anemic neonates in the first seven epochs was 2.5% (0%-5.4%). In the epoch following increased physician awareness of FMH, the incidence of diagnosis was 18.2% ($p<0.001$). There were no significant differences in patient population, obstetric practice, or laboratory testing between epochs.

Conclusions: Diagnosis of FMH is highly dependent on physician awareness. If physicians do not order definitive testing for FMH in response to congenital anemia, the condition will go undetected. This has significant impact on management of the affected neonate and family planning for future pregnancies.
Introduction: Despite the debunking of the vaccine-autism link, parental concern regarding childhood vaccines (CV) persist. General pediatricians (GPs) are increasingly challenged by time needed to counsel parents and ensuring vaccination compliance. The newborn nursery may provide a key intervention point to improve parental knowledge and attitudes (PKA) regarding CVs.

Hypothesis: PKA in the newborn nursery towards vaccine safety, effectiveness, and immunization schedules are incongruous with factual information.

Methods: Parents of healthy neonates born 12/1/10- 5/1/11 at a single hospital were passively surveyed by an anonymous questionnaire distributed in the standard information packet. Surveys were collected via dropbox. IRB approval was obtained.

Results: 1424 mothers delivered infants admitted to the newborn nursery; 122 completed surveys were returned. Among respondents, 43% were first time parents, 65% were white, 11% were hispanic, 8% were black, and 87% were college graduates. 86% strongly agreed that vaccines help to keep children healthy but 8% denied that vaccine preventable deaths occurred in the US. Lack of knowledge existed for diarrheal (80%), meningococcal (33%), whooping cough (16%), and mumps (8%) vaccines; 96% knew of the measles vaccine. 40% expressed concerns regarding vaccines for their child; 75% strongly agreed that vaccines were safe for their own child. 31% believed vaccines cause autism and 23% strongly felt that simultaneous vaccinations could overwhelm the immune system. 44% strongly felt that the immunization schedule should be flexible; 25% strongly agreed that their GP should customize their infant’s schedule; only 20% strongly agreed that prolonging the schedule would increase the risk for childhood diseases.

Conclusions: In this educated population, PKA was poor and anxiety regarding vaccine safety remained high with a significant demand for customized, prolonged immunization schedules.
Unsafe Routes to School? Using GIS to Examine the Local Food Environment Around Schools in an Inner City Minority Community

Author Name(s): Leigh Goldstein, MS¹, Maida Galvez, MD, MPH²,³, Catherine Knuff², Kathleen McGovern, MPH², Susan Teitelbaum, PhD² and Barbara Brenner, DrPH²

Department: Pediatrics

Division: Preventive Medicine

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Geographic Information Systems (GIS) provide a unique methodology for examining children’s local food environment.

Hypothesis: To describe the food environment children encounter traveling from home to school and associations with body size.

Methods: Cross-sectional data from 304 children were included. Fast food and convenience stores data in East Harlem, NY were collected via a walking survey. Shortest paths between home and school were determined with GIS and number of establishments along the path was calculated for each child. Age and gender specific BMI percentile for children who did not pass any fast food or convenience stores was compared to those passing one or more using t-tests.

Results: Children traveled on average 447m (6 city blocks) on the shortest path from home to school (range 17-2336m). Mean fast food stores passed was 4 (range 0-19); mean convenience stores passed was 4 (range 0-23) and mean fast food and convenience stores combined was 8 (range 0-36). 6% (n=18) did not pass any of these food sources along this path. BMI percentile was significantly greater for those children passing 1 or more convenience stores on the shortest path to school compared to those passing zero (p=0.05) while there was no significant difference for those passing 1 or more fast food stores compared to those passing zero.

Conclusions: Inner city, minority children have many opportunities to purchase food from fast food and convenience stores en route from home to school. These data suggest interventions targeting the local food environment around schools may be warranted.
Evaluation OF PET/CT Imaging in Patients with Post-Transplant Lymphoproliferative Disorders After Solid Organ Transplantation in Pediatric and Adult Populations

Author Name(s): Mona Elmacken

Department: Pediatrics

Division: Radiology

Institution Affiliation: Elmhurst Hospital

Introduction: Post-transplant lymphoproliferative disorders (PTLD) are serious complications of solid organ transplantations. Early diagnosis of PTLD is difficult in the absence of an accurate and reproducible diagnostic modality and clinicians initially rely on clinical judgment and rising EBV viral DNA load. Accurate staging and early initiation of therapy is key in the management of patients with PTLD.

Hypothesis: PET imaging with Fluoro-2-Deoxy-D-Glucose (FDG) has been found to be effective in staging and therapy evaluation in malignant lymphoma. Recent studies have shown FDG PET to be useful in staging, follow up, and therapy evaluation in patients with PTLD.

Methods:
DESIGN: Retrospective observational study using FDG PET/CT imaging to stage and follow up PTLD patients following solid organ transplantation in pediatric and adult population.

OBJECTIVES:
To evaluate PET imaging as an independent modality for diagnosis in post-transplant patients with clinical suspicion of PTLD.
To determine accuracy of staging of patients diagnosed with PTLD.
To determine accuracy of restaging of patients with history of recurrent PTLD.
Evaluation of treatment response after initiation of therapy.
To evaluate FDG PET as an independent predictor of progression free survival in PTLD patients.

RESULTS: We recruited 39 patients, compared serial FDG PET/CT with biopsy results and clinical follow up, and the EBV viral load. We evaluated whether the patients were on medication or not and evaluated the response after initiation of therapy.

Conclusions: Still pending statistical results.
Sonographic Evaluation of Pediatric Skeletal Lesions: Is it Worthwhile?

Author Name(s): Amish Patel, Neil Lester, Henrietta Kotlus Rosenberg

Department: Pediatrics

Division: Radiology

Institution Affiliation: Mount Sinai School of Medicine

Introduction: Ultrasound (US) is a readily available, cost-effective, non-invasive, non-ionizing imaging modality but often underutilized in evaluation of pediatric skeletal abnormalities.

Hypothesis: Used properly, ultrasound is extremely practical in evaluation of pediatric skeletal abnormalities.

Methods: We reviewed clinical and imaging findings in 31 patients seen during the past 2 years where US demonstrated abnormalities related to the skeletal system.

Results: US proved useful in the following situations: evaluation hard superficial immobile mass (osteoma shin) (1), absent medial end clavicle on X-ray (US showed ABC medial end clavicle)(1), determination if soft tissue mass involves adjacent bone nodular fasciitis surrounding clavicular head) 1), for diagnosis and follow-up fracture in infants (4), diagnosis osteomyelitis in patients with cellulitis (4), question of fracture underlying cephalohematoma / subgaleal hematoma (4), rib mass (osteochondroma)(1)or mass costochondral junctions (contour deformities costochondral cartilage)(6), firm posterior knee mass (Baker’s cyst)(1), firm anterior knee mass (septated cystic mass suprapatella region from rheumatoid disease) (1),immobile hard scalp mass from epidermoid cranial vault(1), painful mass occipital bone with soft tissue components extending through skull externally and internally from Langerhan’s histiocytosis (1), indeterminate mass clavicle clinically thought to be post-traumatic sequelae, resolved on follow-up (1), assessment craniosynostosis (3), differentiation of pathological entity from normal anatomic structure (lump on back of slender baby proven to be normal posterior spinous process)(1).

Conclusions: US is worthwhile for evaluation of pediatric skeletal abnormalities and helps determine if a lesion is one that is “touch” or “don’t touch”. The imager should have thorough knowledge of clinical history, physical findings, laboratory and other imaging findings. In equivocal cases, in patients in whom field of view is insufficient for complete visualization of obvious lesion, or if malignancy is suspected, US triages patients in whom further imaging is necessary.