Acknowledgements

The seventh biennial Penn State Hershey Children's Hospital Research Day demonstrates the exciting research performed in the Department of Pediatrics. Penn State Hershey Children's Hospital has put a major emphasis on research in order to advance the quality of care we provide for children, enhance understanding of disease mechanisms, improve treatment outcomes, and prevent childhood illnesses. Research at the Children's Hospital has flourished, even in this time of shrinking NIH funding. Our research is supported by numerous scientific funding agencies and philanthropies, particularly the Children's Miracle Network and the Four Diamonds Fund, providing invaluable assistance allowing us to make significant advances. Major research areas in pediatrics include the Center for Host Defense, Inflammation, and Lung Disease Research (CHILD), the Four Diamonds Pediatric Cancer Research Program, the Neonatal Development Collaborative, the Penn State Hershey Pediatric Cardiovascular Research Center, and the Pediatric Clinical Research Office. The Four Diamonds Fund has been key to our involvement in leading pediatric cancer consortiums through which we offer state-of-the-art Phase I, II, and III clinical trials and foster nationally-recognized translational research into basic mechanisms. The energy that our faculty, nurses, residents, fellows, and medical students have for new investigation is demonstrated by the breadth and depth of the research presented here. Diverse research interests include basic science and clinical investigation in a wide spectrum of pediatric fields and involve important collaborations with the University Park campus. The presentations today demonstrate the significant research accomplishments that have been made at Penn State Hershey Children's Hospital in the last two years. This research is key to making the dream of reducing side effects and improving the outcomes of treatment a reality for many childhood diseases.

Barbara A. Miller, M.D.
Professor and Vice Chairman for Research, Department of Pediatrics
Christopher Millard Endowed Chair in Pediatric Oncology

Special thanks to the members of the Penn State Hershey Children’s Hospital Pediatric Research Day Planning Committee for organizing this event:

- Zissis Chronos, Ph.D.
- Mark S. Dias, M.D., FAAP, FAANS
- Sinisa Dovat, M.D., Ph.D.
- Brett Engbrecht, M.D., M.P.H.
- Gavin R. Graff, M.D.
- Barbara A. Miller, M.D.
- Barbara E. Ostrov, M.D.
- Ian M. Paul, M.D., M.Sc.
- David S. Phelps, Ph.D.
- Dorothy V. Rocourt, M.D.
- Lisabeth V. Scalzi, M.D., M.S.
- Deepa L. Sekhar, M.D.
- Adam Spanier, M.D., Ph.D., M.P.H.
- Denise Block
- Heather Stokes
Agenda

Hershey Lodge White Room | Convention Center Entrance

Noon–12:45 p.m.  Lunch and Poster Viewing

12:45–1:00 p.m.  Welcome
A. Craig Hillemeier, M.D.
Chair, Department of Pediatrics
Vice Dean for Clinical Affairs, Penn State College of Medicine
Medical Director, Penn State Hershey Children’s Hospital
Professor of Pediatrics

1:00–1:30 p.m.  Clinical Year in Review Highlighting Publications
Adam Spanier, M.D., Ph.D., M.P.H.

1:30–2:30 p.m.  Slide Presentations #1 - Clinical
Co-Chairs: Adam Spanier, M.D., Ph.D., M.P.H.; Deepa Sekhar, M.D., and Mark Dias, M.D., FAAP, FAANS

Ian M. Paul, M.D., M.Sc.
“Early Weight Loss Nomograms for Exclusively Breastfed Newborns By Method of Delivery”

Kristen M. Glass, M.D.
“Oral Care With Colostrum For Immune Stimulation In Very Low Birth Weight Infants”

Robert F. Tamburro, M.D., M.Sc.
“Respiratory Syncytial Virus (RSV) Infection in Pediatric Oncology and Hematopoietic Stem Cell Transplant (HSCT) Patients”

Terri A. Nicely / Rollyn M. Ornstein, M.D.
“Prevalence and Characteristics of the DSM-5 Avoidant/Restrictive Food Intake Disorder in a Cohort of Young Eating Disordered Patients in Day Treatment”

Clinical Young Investigator Award Presentation

2:30–2:50 p.m.  Clinical Manned Poster Session / Coffee Break

2:50–3:00 p.m.  Introduction of Keynote Lecturer
A. Craig Hillemeier, M.D.
Chair, Department of Pediatrics
3:00–4:00 p.m. Keynote Lecture:
“The Scope and Gravity of Childhood Maltreatment: Consequences for Children, Families, and Public Health”
Jennie G. Noll, Ph.D.
Professor, Human Development and Family Studies
Director of Research and Education,
Network on Child Protection and Well-being, Penn State

4:00–4:30 p.m. Basic Science Manned Poster Session / Coffee Break

4:30–5:00 p.m. Clinical Year in Review Highlighting Publications
Zissis Chroneos, Ph.D.

5:00–6:00 p.m. Slide Presentations #2 - Basic Science
Co-Chairs: Sinisa Dovat, M.D., Ph.D., and Zissis Chroneos, Ph.D.

Ying Liu, M.S. (Wang Lab, College of Medicine)
“Role of Bif-1/SH3GLB1 in obesity”

Patricia Silveyra, Ph.D. (Floros Lab, College of Medicine)
“Sequence polymorphisms at the 3' UTR of Human Surfactant Protein A gene variants differentially affect gene expression levels and miRNA regulation in vitro”

Sarah A Owusu, B.S. (Ross Lab, University Park)
“Ontogenic expression of retinoid homeostatic genes in principal vitamin A storage organs”

Chunhua Song, M.D., Ph.D. (Dovat Lab, College of Medicine)
“Epigenetic control of cell proliferation and cell cycle by Ikaros and HDAC1 in leukemia”

Basic Science Investigator Award Presentation

6:00 p.m. Closing Remarks
Ian M. Paul, M.D., M.Sc.
Research Groups and Support

CHILD

The Center for Host defense, Inflammation, and Lung Disease (CHILD) Research is a center in the Department of Pediatrics. Penn State CHILD Research is a collaborative alliance of basic science and clinical investigators who have united to focus on the study of mechanisms for maintaining optimal lung health. The center focuses on innovative and collaborative partnerships between members of the center, those throughout the entire Penn State system, and scientists and clinicians worldwide. Through these affiliations, investigators focus on conducting scientific research in the fields of host defense and inflammation, with the goal of bridging the broad expanse that presently exists between basic science discoveries and the implementation of these advances into clinical practice.

Another goal is the development and assessment of innovative approaches and technologies to study disease mechanisms and deliver care to patients of all ages. Penn State CHILD Research serves as a training ground for the basic science and clinical science investigators of tomorrow.

Joanna Floros, Ph.D., Evan Pugh Professor of Pediatrics and Obstetrics and Gynecology, is the director of the center.

The Four Diamonds Pediatric Cancer Research Program

The Division of Pediatric Hematology/Oncology faculty conduct cutting-edge basic, translational, and clinical cancer and hematology research aimed at understanding fundamental mechanisms that lead to cancer, and the development of novel treatment strategies for childhood malignancy. Research areas include the regulation of cell proliferation by intracellular signaling; tumor suppression in acute leukemia; the regulation of cellular senescence; accelerated drug discovery; cell death through autophagy and apoptosis; and Phase I to III therapeutic trials.

The Division of Pediatric Hematology/Oncology participates in state-of-the-art clinical trials through the Children's Oncology Group (COG) and offers novel approaches to refractory and relapsed disease through the Pediatric Oncology Experimental Therapeutics Investigators’ Consortium (POETIC) and the Neuroblastoma and Medulloblastoma Translational Research Consortium (NMTRC).

Research is supported by the National Institutes of Health, the Four Diamonds Fund, and other philanthropic organizations including the St. Baldrick's Foundation, and Hyundai Hope on Wheels.

The Four Diamonds Pediatric Cancer Research Center was established in 1999 and is supported by generous philanthropy, particularly endowments from the Four Diamonds Fund including the Penn State IFC/Panhellenic Dance Marathon Chair, the Christopher Millard Endowed Chair in Pediatric Oncology, the Experimental Therapeutics Program, and the Molecular Oncology Program.
Research Groups and Support

Penn State Hershey Center for Pediatric Cardiovascular Research

A multidisciplinary research team has been established over the past ten years at Penn State Hershey with the goal of improving the outcomes for children undergoing cardiac surgery with cardiopulmonary bypass and mechanical circulatory support. The Penn State Hershey Center for Pediatric Cardiovascular Research has been established with the collaboration of teams from multiple academic departments and representing multiple disciplines. This center combines basic science, engineering, and clinical applications under the unified mission of pediatric cardiovascular research. Scientists and clinicians in the center represent the departments of pediatrics, surgery, bioengineering, anesthesiology, comparative medicine, public health sciences, pharmacology, and obstetrics and gynecology.

Its major objective is the development of novel technologies and methodologies to be used in minimizing the adverse effects of cardiovascular operations and cardiopulmonary bypass in neonates, infants, and children. Particular attention is focused on reducing the associated morbidities of cerebral, myocardial, pulmonary, and renal injury.

Its long term goals are to:

1) establish The Penn State Hershey Center for Pediatric Cardiovascular Research as a leading center for further development of novel treatments and cutting edge devices for cardiovascular health in pediatric populations, both at Penn State Hershey Children's Hospital and other pediatric heart centers around the world;

2) educate more bioengineers, medical students, residents, postdoctoral fellows and junior faculty members in pediatric cardiovascular research; and

3) ensure that its international conference continues to be the leading conference for defining the problems of current mechanical circulatory support systems in pediatric patients and suggesting appropriate solutions for these pediatric cardiac patients.

The first annual meeting was held at The Hotel Hershey, Hershey, Pa.in May of 2005. Since then, nine international conferences have been held with more than 2,250 participants from 33 countries in attendance.

Based on full manuscripts, sixty-eight Young Investigator Awards were awarded during the past nine years. As a result of these events, more than 400 peer-reviewed articles have been generated for this underserved research area. These publications have become the largest resource for the investigators of pediatric mechanical cardiovascular research.

Akif Ündar, Ph.D. is the founder and director for the center.

For more information: www.pennstatehershey.org/web/pedscardiaresearch/home
Research Groups and Support

Penn State Public Health Sciences Graduate Program

Master of Science
Penn State College of Medicine's Master's Degree Program in Public Health Sciences includes graduate-level coursework in biostatistics, epidemiology, and health services research, and provides knowledge and insight required in health related research.

Master's degree or certificate completion in public health sciences can lead to careers in a wide variety of fields and settings, including:

- Academic health centers
- Health insurance industry
- Health Services Networks
- Local, state, and federal government agencies
- Pharmaceutical industry

For more information, visit www.med.psu.edu/phs.

Certificate in Clinical Research
The Certificate in Clinical Research is a one-year program requiring 15 course credits. Certificate candidates follow the same course schedule as master's candidates through the first three semesters.

Additional information about the program and application materials are available on the PHS Graduate Program Web site at www.med.psu.edu/phs.

Master of Public Health
The 47-credit M.P.H. program can be completed in two or more years on a full- or part-time basis. All courses are offered in the evenings to accommodate students who work during the day, and several required and elective courses can be completed at Penn State's University Park, Harrisburg, Great Valley, or World (online) campuses.

Students may choose to specialize in one of three areas of concentration:

1. Community and Behavioral Health
2. Epidemiology and Biostatistics
3. Health Services Organization and Policy

For more information, visit www.med.psu.edu/phs.
Research Groups and Support

Penn State Hershey PRO Wellness Center

Penn State Hershey PRO Wellness Center is the trusted resource for project management, educational programming, collaborative partnerships, and proven wellness interventions in schools and communities.

The center is committed to helping youth and families in the Commonwealth of Pennsylvania learn how to eat well, engage in regular physical activity, and incorporate healthy habits into their daily lives.

A joint collaborative between Penn State College of Medicine’s Department of Public Health Sciences and the Department of Pediatrics at Penn State Milton S. Hershey Medical Center, the center has led statewide efforts to promote healthy eating and active living for youth and families.

Historically focused on childhood obesity, it has helped Pennsylvania communities live healthier lives using evidence-based strategies for measurable and sustainable results.

Its approach of Prevention, Research and Outreach provides schools, communities, and organizations with:

- program development and implementation,
- assessment and evaluation services,
- capacity building,
- technical assistance,
- collaborative partnerships,
- access to proven wellness interventions, and
- assistance with obtaining grant funding to support wellness initiatives.

It has demonstrated proven success in areas including:

- active living,
- healthy eating,
- community health,
- school and community-based organization environments, and
- partnerships and collaborations.

To learn more about the center and its work or to connect research interests with those of like-minded partners, call 717-531-1440 or e-mail PROwellness@phs.psu.edu.
Shared Research Facilities

This section offers a complete catalog of shared core facilities and services, including institutional, departmental, and cross-campus facilities available to all.

- Completely Renovated Microscopy Imaging Facility on the first floor
- JEOL 2100 Cryo Electron Microscope (CryoEM)
- JEOL 1400 Transmission Electron Microscope (TEM)
- DeltaVision Elite Deconvolution Microscope
- Leica SP8 White Light Laser Confocal Microscope (Live Cell)
- Imaris 3D-4D Image Processing Software
- Fortessa 14 color Flow Cytometer
- 16-color FACSArray SORP high speed 4-way cell sorter
- SWATH Mass Spectrometry (general coverage label-free peptide quantitation)
- PUNCH-P measurement of proteins being actively synthesized on ribosomes
- Identification and quantitation of phosphorylated peptides
- Whole Genome Sequencing (Illumina HiSeq 2500, Illumina MySeq)
- Gene Expression Analysis through RNA-Seq analysis
- QuantStudio Quantitative Real-Time PCR
- Illumina BeadArray, Affymetrix, TaqMan assays for SNP analysis and mRNA abundance measurements
- DNA sequencing & SNPlex capacities
- TripleTOF 5600 and other Mass Spectrometers for high ID yield Proteomic, Lipidomic, and Metabolomic studies (up to 6500 proteins confidently identified from a single sample; Quantitation from up to eight samples at once (iTRAQ); 2D DIGE or Laemli gel spot quantitation and identification; separation and identification of co-immunoprecipitated proteins; identification of post-translational modifications)
- High-throughput quantitative cytokine and hormone assays
- Six additional Research and Clinical Flow Cytometry and High-speed Flow Sorting instruments, including 15-color LSRII Flow Cytometer.
- Leica SP2 and Olympus Spinning Disk Confocal microscopy
- Complete Histology services
- Laser Capture Microdissection for separation of histologically distinct tissue populations from slides
- Bioluminescence and MicroCT imaging of animals
- MRI and MRS imaging for whole animals as well as human subjects, including fMRI, with twinned human studies MRI instruments at HMC and University Park
- Animal Optical Imaging Core in the Penn State Hershey Cancer Institute
- DNA and peptide sequencing and synthesis services
- Organic Synthesis services
- Breeding of Transgenic and Knock-out research animals, and re-derivation services
- Wyatt Light Scattering determination of macromolecular aggregation state and size.
Research Groups and Support

- Tecan Evo robotics for high throughput sample handling
- Drug Development/Screening Core, with Biacore Surface Plasmon Resonance (SPR) biomolecular interaction affinity assays

“How-To” and SOPs on web pages (med.psu.edu/core) for common techniques.

Penn State Clinical Research Office (PCRO)

The mission of the Pediatric Clinical Research Office (PCRO) is to enhance, foster, and promote organized pediatric clinical research within Penn State Hershey Children’s Hospital. By stimulating clinical research, the PCRO helps Penn State Hershey Medical Center meet its goals of patient care, teaching, service, and research. The PCRO is currently and strives to continue to be active in Penn State investigator-initiated research through collaborations between faculty and PCRO and its research staff. The PCRO helps investigators initiate new studies and provides recruitment, consent writing, regulatory, budgetary, and data collection assistance where needed. This help may also include administrative, procedural, and case report documentation. Help is also provided to investigators with industry-sponsored clinical trials. The PCRO promotes investigator initiated research within central Pennsylvania, trains our staff to promote quality research within the Medical Center, and the adoption of “Good Clinical Practices.”

Please visit: http://www.pennstatehershey.org/web/childrens/research/programs/pediatric-clinical-research
Research Support

Children's Miracle Network (CMN) and The Four Diamonds Fund directly support Penn State Hershey Children's Hospital. Through the generous support of individual, corporate, and organization donors, CMN and Four Diamonds provide resources to the team of nurses, doctors, technicians, social workers, and child life specialists at Children's Hospital who are dedicated to the delivery of world-class care for kids. Both pediatric funds are committed to supporting research at Children's Hospital to develop technology and knowledge that will enhance the medical care provided to children.

The mission of The Four Diamonds Fund is to conquer childhood cancer by assisting children treated at Penn State Hershey Children's Hospital and their families through superior care, comprehensive support, and innovative research. Any family with a child being treated for pediatric cancer at Children's Hospital is automatically eligible for support. The fund has helped nearly 2,000 families since 1972, and approximately 100 new families receive support each year. The fund supports the medical team that cares for the children and funds pediatric cancer research through start-up grants and the Four Diamonds Pediatric Cancer Research Endowment. For more information on The Four Diamonds Fund, call 717 531-6086 or visit www.fourdiamonds.org.

Research projects that have been funded by Four Diamonds are denoted by a diamond reference in this program.

Penn State Hershey Children's Hospital is one of the 170 Children's Miracle Network affiliated hospitals across the United States and Canada. The founding philosophy of CMN is that the money stays in the community in which it was raised. Funds raised by CMN in central Pennsylvania stay local to support patient services, vital pieces of equipment, program services, and educational resources for various pediatric departments at Children's Hospital. In addition, a percentage of CMN funds are allocated annually to support pediatric research projects at Children's Hospital. Over the last 23 years, CMN has raised more than $50 million for Children's Hospital. For more information on CMN, call 717-531-6606 or visit www.pennstatehershey.org/cmn.

Research projects that have been funded by Children's Miracle Network are denoted by a location pin reference in this program.
<table>
<thead>
<tr>
<th>FIRST AUTHOR</th>
<th>ADVISOR</th>
<th>CLINICAL - ABSTRACT TITLE</th>
<th>FUNDING SOURCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelumi Adedayo, M.S.</td>
<td>Akif Ündar, Ph.D.</td>
<td>Impact of Pulsatile Flow Settings on Hemodynamic Energy Levels Using the Novel Diagonal Medos DP3 Pump in a Simulated Pediatric ECLS System</td>
<td>PSH-PCRC/Medos Medizintechnik AG, Stolberg, Germany/Novalung GmbH, Heibronn, Germany</td>
</tr>
<tr>
<td>Mehmet A. Ağirbaşlı</td>
<td>Akif Ündar, Ph.D.</td>
<td>Comparative Effects of Pulsatile and Nonpulsatile Flow on Plasma Fibrinolytic Balance in Pediatric Patients Undergoing Cardiopulmonary Bypass</td>
<td>PSH – PCRC, CMN</td>
</tr>
<tr>
<td>Dara Babinski, Ph.D.</td>
<td>James G. Waxmonsky, M.D.</td>
<td>Treating parents with Attention-Deficit/Hyperactivity Disorder: the effects of behavioral parent training and acute stimulant medication on parent-child interactions</td>
<td>Mark Diamond Research Foundation</td>
</tr>
<tr>
<td>Dara Babinski, Ph.D.</td>
<td>James G. Waxmonsky, M.D.</td>
<td>Observations of parents with Attention-Deficit/Hyperactivity Disorder (ADHD) in group behavioral parent training</td>
<td></td>
</tr>
<tr>
<td>Marina Boushra</td>
<td>Gail Rudnitsky, M.D.</td>
<td>Patient Satisfaction with Pain Management in Pediatric Intravenous Catheterizations</td>
<td>PSMSHMC - Emergency Medicine</td>
</tr>
<tr>
<td>Gina Bretsford, Ph.D.</td>
<td>Kristen Veneman, D.O.</td>
<td>Religious Coping and Family Relationships in the Neonatal Intensive Care Unit</td>
<td>PSU-Harrisburg</td>
</tr>
<tr>
<td>Larisa Buyantseva, M.D.</td>
<td>Tracy Fausnight, M.D.</td>
<td>Mosaic Monosomy 7 is Associated with an Abnormal Trec Screen</td>
<td></td>
</tr>
<tr>
<td>Andrew T. Catherine, B.S.</td>
<td>Robert P. Olympia, M.D.</td>
<td>EMS activations for school aged children from public buildings, places of recreation or sport, and healthcare facilities in Pennsylvania</td>
<td>Internal PSU start-up funds</td>
</tr>
<tr>
<td>Terri Cravener, M.S.</td>
<td>Kathleen L. Keller, Ph.D.</td>
<td>Feeding strategies derived from behavioral economics can increase vegetable intake in children as part of a home-based intervention</td>
<td></td>
</tr>
<tr>
<td>David G. Currie, B.A.</td>
<td>Linda Pauliks, M.D., M.P.H., FACC</td>
<td>Systolic to Diastolic Duration Ratio and Exercise Stress Response in 150 children with and without Heart Disease - a Tissue Doppler Stress Echocardiogram Study</td>
<td></td>
</tr>
<tr>
<td>Esther Dell, AMLS, AHIP</td>
<td>Kim Kopenhaver Doheny, Ph.D.</td>
<td>Custom Access to Library Resources: A Collaboration</td>
<td></td>
</tr>
<tr>
<td>S. Nicole Fearnbach</td>
<td>Kathleen L. Keller, Ph.D.</td>
<td>Music and Mother’s Voice as a Therapeutic Intervention for Convalescing Preterm Infants in the NICU</td>
<td>The Social Science Research Institute at PSU Level 2/USDA/AFRI</td>
</tr>
<tr>
<td>Sarah Findeis</td>
<td>Timothy Craig, D.O.</td>
<td>The Relationship between Insect Sting Allergy Treatment and Anxiety and Depression</td>
<td>Dr. Craig’s Fellowship Program Fund</td>
</tr>
<tr>
<td>V.J. Flaherman</td>
<td>Ian Paul, M.D., MSc</td>
<td>Relationship between newborn weight change, maternal anxiety, and breastfeeding outcomes</td>
<td></td>
</tr>
<tr>
<td>V.J. Flaherman</td>
<td>Ian Paul, M.D., MSc</td>
<td>Early Weight Loss Nomograms for Exclusively Breastfed Newborns By Method of Delivery</td>
<td></td>
</tr>
<tr>
<td>Kristen M. Glass, M.D.</td>
<td></td>
<td>Oral Care with Colostrum for Immune Stimulation in Very Low birth Weight Infants</td>
<td></td>
</tr>
<tr>
<td>Darcy Güngör, M.S.</td>
<td></td>
<td>5210 Healthy Military Children: A U.S. Military Initiative That Uses Primary Care And Other Community Sectors To Reduce Childhood Obesity And Improve Child Health</td>
<td>Nat’l Inst of Food and Agriculture/U.S. Dept of Agriculture/Office of Family Policy, Children and Youth/U.S. Dept of Defense</td>
</tr>
<tr>
<td>Author(s)</td>
<td>Title</td>
<td>Institution(s)</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Nicole M. Hackman, Ian Paul, M.D., MSc</td>
<td>Breastfeeding Outcome Comparison Between Experienced and Primiparous Women</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Jonathan Hilton, B.S.</td>
<td>Application of the Pediatric Emergency Care Applied Research Network (PECARN) head trauma prediction rules to pediatric trauma activations in central Pennsylvania</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Christine Jones, M.D.</td>
<td>Alicefield Methods: Is The Q-SORT Method Equivalent With 2D Photos And 3D Surface Imaging?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Krisoula Horiates, PharmD</td>
<td>Nephrotoxicity in pediatric patients receiving vancomycin alone or in combination with piperacillin-tazobactam</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jonathan Hilton, B.S.</td>
<td>Validation of a Screening Tool for Pediatric Abusive Head Trauma (AHT)</td>
<td>Private Family Found/Dartmouth-Hitchcock MC/Gerber Foundation</td>
<td></td>
</tr>
<tr>
<td>Sarah M.J. Iriana, M.D.</td>
<td>Effect of Electronic Health Record Implementation on Ambulatory Academic Practice Visit Volume</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Christine Jones, M.D.</td>
<td>Do Pharyngeal Flaps Restrict Midface Growth In Cleft Patients?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Christine Jones, M.D.</td>
<td>Structural Fat Grafting To Improve Reconstructive Outcomes In Cleft Lip</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kelly M Kalovcak,</td>
<td>Effects of Exercise Stability Balls on BMI and Blood Pressure in the Educational Settings</td>
<td>PSUCOM-Pediatrics</td>
<td></td>
</tr>
<tr>
<td>Neelu Kalra, M.D.</td>
<td>Treatment of Hereditary Angioedema at the time of prodromal symptoms: An international survey of physicians</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nancy Kashlak, DNP, CRNP, CPNP</td>
<td>The Acceptability of Imagery-Hypnosis for Management of Pain, Anxiety, and Distress Related to Needle Procedures in Pediatric Oncology-Hematology Patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alexander Kish, B.S.</td>
<td>Fixation of Type 2a Supracondylar Humerus Fractures in Children with a Single Pin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afif Kulaylat, M.D.</td>
<td>Transumbilical laparoscopic-assisted appendectomy is associated with lower costs compared to multiport laparoscopic appendectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afif Kulaylat, M.D.</td>
<td>Pleural Effusion Following Blunt Splenic Trauma in the Pediatric Trauma Population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afif Kulaylat, M.D.</td>
<td>The Impact of Children’s Hospital Designation on Outcomes in Children with Malrotation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afif Kulaylat, M.D.</td>
<td>A Comparison of Thoracoscopic and Open Approaches to Resection in Pediatric Congenital Lung Malformations: A Pediatric NSQIP Analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitin Kumar, B.S.</td>
<td>Noninvasive detection of coronary artery anomalies in complete transposition of the great arteries – does color Doppler improve diagnostic accuracy?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Susan Lane-Loney, M.D.</td>
<td>Treatment of Avoidant/Restrictive Food Intake Disorder in a Day Hospital Program for Young Patients With Eating Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Martha Peaslee Levine, M.D.</td>
<td>Putting Team-Based Learning in “The Cloud”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Samantha Lin, M.D.</td>
<td>Patient Ratings of Various Eosinophilic Esophagitis Treatment Options</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eric I Marks, MS4</td>
<td>Absolute Lymphocyte Count as a Predictor of Mortality in Pediatric ALL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ryan K. Mathis</td>
<td>Evaluation of Four Pediatric Cardiopulmonary Bypass Circuits in Terms of Perfusion Quality and Capturing Gaseous Microemboli</td>
<td>PSH – PCRC</td>
<td></td>
</tr>
<tr>
<td>Susan Dickerson Mayes, Ph.D.</td>
<td>Victims and Perpetrators of Bullying: Differences in Frequencies between Psychiatric Diagnoses</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Presenters</td>
<td>Title</td>
<td>Institution</td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>-------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>Susan Dickerson Mayes, Ph.D.</td>
<td>Mother, Father, and Teacher Agreement on Victimization and Bullying in Children with Psychiatric Disorders</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Susan Dickerson Mayes, Ph.D.</td>
<td>Suicide Ideation and Attempts are Associated with Comorbid Oppositional Defiant Disorder and Sadness in Children with ADHD</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Susan Dickerson Mayes, Ph.D.</td>
<td>Correlates of Suicide Ideation and Attempts in Children and Adolescents with Eating Disorders</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Susan Dickerson Mayes, Ph.D.</td>
<td>Suicide Behavior and Bullying in Children with Psychiatric Disorders and General Population Samples</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Christian S. McEvoy, M.Ph.</td>
<td>Marsha Novick, M.D.</td>
<td>Efficacy of Using Medical Students and a Flipping the Classroom Program in Nutrition Education for 4th Grade Students</td>
<td>Virginia Commonwealth University Presidential Research Incentive Program</td>
</tr>
<tr>
<td>Austin Mullay, Ph.D.</td>
<td>Effects of restricted diets on challenging behavior and symptomology in young children with autism spectrum disorders and chronic constipation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Athira Nair, M.D.</td>
<td>Linda B. Pauliks, M.D., MPH</td>
<td>Pulmonary arterial hypertension following dasatinib treatment in an adolescent with myelogenous leukemia – case report and review of the literature</td>
<td></td>
</tr>
<tr>
<td>Neel Nene, M.D.</td>
<td>Lidija Petrovic-Dovat, M.D.</td>
<td>Exposure therapy with a nonverbal child: A case report</td>
<td></td>
</tr>
<tr>
<td>Neel Nene, M.D.</td>
<td>Lidija Petrovic-Dovat, M.D.</td>
<td>Exposure therapy with a nonverbal child: A case report (2)</td>
<td></td>
</tr>
<tr>
<td>Terri A. Nicely</td>
<td>Rollyn M. Ornstein, M.D.</td>
<td>Prevalence and Characteristics of the DSM-5 Avoidant/Restrictive Food Intake Disorder in a Cohort of Young Eating Disordered Patients in Day Treatment</td>
<td></td>
</tr>
<tr>
<td>Anne Odom</td>
<td>Brandt Groh, M.D.</td>
<td>A Home-Based Survey on Diarrheal Knowledge Among Mothers in San Pablo</td>
<td></td>
</tr>
<tr>
<td>Christina Oji-Mmuo, M.D.</td>
<td>Charles Palmer, M.D.</td>
<td>Skin Conductance Provides Early Objective Identification of Neonatal Opiate Withdrawal</td>
<td></td>
</tr>
<tr>
<td>Robert Olympia, M.D.</td>
<td></td>
<td>Compliance of camps in the United States with guidelines for health and safety practices</td>
<td></td>
</tr>
<tr>
<td>Rollyn Ornstein, M.D.</td>
<td></td>
<td>Distribution of Eating Disorders in Children, Adolescents, and Young Adults Using the Proposed DSM-5 Criteria For Eating and Feeding Disorders</td>
<td></td>
</tr>
<tr>
<td>Rollyn Ornstein, M.D.</td>
<td></td>
<td>Food Acceptance and Fears in Young Patients with Anorexia Nervosa, Bulimia Nervosa, and Avoidant/Restrictive Food Intake Disorder</td>
<td></td>
</tr>
<tr>
<td>Barbara E.Ostrov, M.D.</td>
<td></td>
<td>Strategies for Assessment and Management of Severe Environmental Allergies at “Camp JRA”</td>
<td></td>
</tr>
<tr>
<td>Barbara E.Ostrov, M.D.</td>
<td></td>
<td>Patient Preferences and Satisfaction in a Multispecialty Infusion Center</td>
<td></td>
</tr>
<tr>
<td>Elyse K.Pagerly, MS4</td>
<td>Andrew Freiberg, M.D.</td>
<td>Low Incidence of Intracranial Hemorrhage in Acute Idiopathic Thrombocytopenic Purpura (ITP) in Children</td>
<td>Division of Newborn Medicine, PSUCOM</td>
</tr>
<tr>
<td>Rohit Passi, M.D., FAAP</td>
<td>Charles Palmer, M.D.</td>
<td>Electrical Grounding (EG) Improves Parasympathetic Tone in Preterm Infants in the NICU</td>
<td></td>
</tr>
<tr>
<td>Sunil Patel, M.D.</td>
<td>Howard Weber, M.D.</td>
<td>Transcatheter device closure of partial anomalous pulmonary venous return (PAPVR) with “intrapulmonary duplicating drainage” – A newly described entity and a single center experience.</td>
<td></td>
</tr>
<tr>
<td>Sunil Patel, M.D.</td>
<td>Howard Weber, M.D.</td>
<td>Transcarotid balloon valvuloplasty (TCBV) for critical aortic valve stenosis (AS) utilizing continuous transesophageal echocardiographic (cTEE) guidance: A 22 year single center experience from the cath lab to the bedside</td>
<td></td>
</tr>
<tr>
<td>Ian Paul, M.D., MSc</td>
<td></td>
<td>The Mercy TAPE: A New Device for Pediatric Weight Estimation</td>
<td></td>
</tr>
<tr>
<td>Title</td>
<td>Authors</td>
<td>Institution</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Allergic Diseases in Children with Anxiety Disorders</td>
<td>Lidija Petrovic-Dovat, M.D.</td>
<td>Department of Psychiatry - Department of Pediatrics Collaborative Study</td>
<td></td>
</tr>
<tr>
<td>The Factors Most Important for Quality of Life in Adolescents with Cerebral Palsy</td>
<td>Brian Piazza, William Henrikus, M.D.</td>
<td>CMN</td>
<td></td>
</tr>
<tr>
<td>Endobronchial Occlusion with One-way Endobronchial Valves: A Novel Technique for Persistent Air Leaks in Children</td>
<td>Abigail Podany, M.D., Robert E. Citlley, M.D.</td>
<td>PSU</td>
<td></td>
</tr>
<tr>
<td>Vancomycin Resistant Enterococcus Infections are Associated with a Higher Prevalence of Reported Penicillin Allergy</td>
<td>Vinitha Reddy, M.D., Faoud T. Ishmael, M.D.</td>
<td>PSU</td>
<td></td>
</tr>
<tr>
<td>Return to school in students after a sport-related concussion: the role of the school nurse</td>
<td>Jed Ritter, B.S., Robert P. Olympia, M.D.</td>
<td>PSU</td>
<td></td>
</tr>
<tr>
<td>Respiratory Syncytial Virus (RSV) Infection in Pediatric Oncology and Hematopoietic Stem Cell Transplant (HSCT) Patients</td>
<td>Mansi Sachdev, Robert Tamburro, M.D.</td>
<td>PSU</td>
<td></td>
</tr>
<tr>
<td>Right ventricular cardiac hemangioma in a competitive basketball player presenting with chest pain – a case report</td>
<td>Marie Shaner, M.S., Linda Pauliks, M.D., M.P.H., FACC</td>
<td>PSU</td>
<td></td>
</tr>
<tr>
<td>Identification of Micro RNA Biomarkers for Pediatric Bronchopulmonary Dysplasia</td>
<td>Patricia Silveyra, Ph.D., Neal Thomas, M.D.</td>
<td>PSU</td>
<td></td>
</tr>
<tr>
<td>The effect of well-controlled maternal diabetes on fetal heart function - a tissue Doppler study</td>
<td>Ashish Saini, M.D., Linda B. Pauliks, M.D., MPH</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Risk Factors for Adolescent Iron Deficiency vary by the Ferritin vs. the Body Iron Model</td>
<td>Deepa Sekhar, M.D., MSc, Ian Paul, M.D., MSc</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Risk Factors for Anemia Among United States Adolescent Females</td>
<td>Deepa Sekhar, M.D., MSc, Ian Paul, M.D., MSc</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Adolescent Anemia Screening During Ambulatory Pediatric Visits in the United States</td>
<td>Deepa Sekhar, M.D., MSc, Ian Paul, M.D., MSc</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Impact and Control of Contamination in Pediatric Research on Child Maltreatment</td>
<td>Chad Shenk, Ph.D.</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Triclosan and Paraben Exposure are Associated with Allergen Sensitization</td>
<td>Adam Spanier, M.D., Ph.D., MPH</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Chorioamnionitis is associated with low heart rate variability in preterm infants</td>
<td>Pratima Toom, M.D., Charles Palmer, M.D.</td>
<td>NIMH</td>
<td></td>
</tr>
<tr>
<td>Using a Secondary Reservoir for Pump Suckers to Avoid the Generation of Foam during CPB Procedures in Pediatric Patients</td>
<td>Akif Ündar, Ph.D.</td>
<td>PSH – PCRC</td>
<td></td>
</tr>
<tr>
<td>Active Parenting and Parental Role Attainment in Parents of Preterm Infants in the NICU</td>
<td>Kristin Veneman, D.O., Kim Doheny, Ph.D.</td>
<td>PSU Interdisciplinary Seed Grant</td>
<td></td>
</tr>
<tr>
<td>Comparison of Atopic Features between Children and Adults with Eosinophilic Esophagitis</td>
<td>Natalia Vernon, M.D.</td>
<td>NIMH</td>
<td></td>
</tr>
<tr>
<td>The effect of the autism insurance mandate on healthcare utilization and costs</td>
<td>Li Wang, Ph.D.</td>
<td>NIMH</td>
<td></td>
</tr>
<tr>
<td>Behavior Therapy in Conduct Problem Children with Callous-Unemotional Traits: A Pilot Test of Increasing Reward and Decreasing Punishment</td>
<td>Dan Waschbusch, Ph.D.</td>
<td>NIMN</td>
<td></td>
</tr>
<tr>
<td>“The Impact Of Extended Release Stimulant Medication On The Growth Trajectories Of Children With Attention Deficit Hyperactivity Disorder”</td>
<td>James Waxmonsky, M.D.</td>
<td>NIMH</td>
<td></td>
</tr>
</tbody>
</table>

XIV
<table>
<thead>
<tr>
<th>Title</th>
<th>Authors</th>
<th>Abstract</th>
<th>Sponsor</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Does Pharmacological Treatment of ADHD in Adults Enhance Parenting Performance?”</td>
<td>Shire Pharmaceuticals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The Impact of BUZZY® on Outpatient Venipuncture in Children</td>
<td>The Association of Faculty and Friends Grant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A Novel Group Based Therapy for School Aged Children with ADHD and Severe Mood Dysregulation</td>
<td>NIMH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pediatric Referrals to the Emergency Department from Urgent Care Centers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compliance of urgent care centers in the U.S. with pediatric care recommendations for emergency and disaster preparedness</td>
<td>Department of Health of Guangdong, China;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effects of Preterm Delivery and Early Intervention on Infants’ Mental Development: A Two-year Follow-up Study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A Case of Severe Malnutrition and Profound Anemia in a 4 Year Old Girl</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In vitro cytokine assay to identify the medications responsible for a drug eruption</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In Vitro Comparison of the Delivery of Gaseous Microemboli and Hemodynamic Energy for a Diagonal and a Roller Pump during Simulated Infantile CPB Procedure</td>
<td>PSH – PCRC Medos Medizintechnik AG, Stolberg, Germany Novalung GmbH, Heilbronn, Germany</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of a Novel Diagonal Pump in an In Vitro Neonatal Pulsatile Extracorporeal Life Support Circuit</td>
<td>PSH – PCRC Medos Medizintechnik AG, Stolberg, Germany Novalung GmbH, Heilbronn, Germany</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemodynamic Evaluation of Novel i-cor Pulsatile ECLS System during Various Cardiac Arrhythmias: In Vitro Study</td>
<td>PSH – PCRC Xenios AG, Heilbronn, Germany Medos Medizintechnik AG, Stolberg, Germany Novalung GmbH, Heilbronn, Germany</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handling Ability of Gaseous Microemboli of Two Pediatric Arterial Filters in a Simulated CPB Model</td>
<td>PSH-PCRC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impact of Pulsatile Flow Settings on Hemodynamic Energy Levels Using the Novel Diagonal Medos DP3 Pump in a Simulated Pediatric ECLS System</td>
<td>PSH – PCRC Medos Medizintechnik AG, Stolberg, Germany Novalung GmbH, Heilbronn, Germany</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evaluation of Conventional Non-pulsatile and Novel Pulsatile ECLS Systems in a Simulated Pediatric ECLS Model</td>
<td>PSH – PCRC Medos Medizintechnik AG, Stolberg, Germany Novalung GmbH, Heilbronn, Germany</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In Vitro Performance Analysis of a Novel Pulsatile Diagonal Pump in a Simulated Pediatric Mechanical Circulatory Support System</td>
<td>PSH – PCRC Medos Medizintechnik AG, Stolberg, Germany Novalung GmbH, Heilbronn, Germany</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIRST AUTHOR</td>
<td>ADVISOR</td>
<td>BASIC SCIENCES - ABSTRACT TITLE</td>
<td>FUNDING SOURCE</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>----------------------------------------</td>
<td>------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------</td>
</tr>
<tr>
<td>Marie Bulathsinghala, MS4</td>
<td>Sinisa Dovat, M.D., Ph.D.</td>
<td>Regulation of Drug Resistance in Leukemia</td>
<td>NIH/NHLBI/St. Baldrick’s Hyundai Hope on Wheels/ Four Diamonds</td>
</tr>
<tr>
<td>Shu-Jen Chen, Ph.D.</td>
<td>Sinisa Dovat, M.D., Ph.D.</td>
<td>Human Ion Channel TRPM2 Protects Cell Viability through Modulation of Mitochondrial Function</td>
<td>NIH/Hyundai Hope-on-Wheels/ Four Diamonds</td>
</tr>
<tr>
<td>Kim K Doheny, Ph.D.</td>
<td>Alberto Travagli</td>
<td>Low Vagal Tone is a Predictive Biomarker of Necrotizing Enterocolitis (NEC)</td>
<td>CMN, Johnson &amp; Johnson/NIH</td>
</tr>
<tr>
<td>Kenichiro Doi, M.D., Ph.D.</td>
<td>Hong-Gang Wang, Ph.D.</td>
<td>Characterization of Pyoluteorin Derivatives as Mcl-1 Antagonists</td>
<td>Lois High Berstler Endowment/PSUCOM</td>
</tr>
<tr>
<td>Christopher Dower</td>
<td>Hong-Gang Wang, Ph.D.</td>
<td>The Role of Hypoxia-Induced Autophagy in Tumor Progression</td>
<td>NIH</td>
</tr>
<tr>
<td>Kristen M. Glass, M.D.</td>
<td>Sinisa Dovat, M.D., Ph.D.</td>
<td>A Multi-Faceted Curriculum to Enhance Pediatric Resident Communication skills with End-of-Life Discussion</td>
<td>NIH</td>
</tr>
<tr>
<td>Chandrika Gowda, M.D.</td>
<td>Sinisa Dovat, M.D., Ph.D.</td>
<td>Regulation of Cell Cycle Progression by Casein Kinase II (CK2) via Ikaros and effects of CK2 Inhibitors in Leukemia</td>
<td>St. Baldrick’s/Hyundai Hope on Wheels/ Four Diamond</td>
</tr>
<tr>
<td>Qiang Liu, B.S.</td>
<td>Hong-Gang Wang, Ph.D.</td>
<td>Maritoclax Induces Apoptosis in Acute Myeloid Leukemia Cells with Elevated Mcl-1 Expression</td>
<td>Lois High Berstler Endowment/PSUCOM</td>
</tr>
<tr>
<td>Ying Liu</td>
<td>Hong-Gang Wang, Ph.D.</td>
<td>Role of Bif-1/SH3GLB1 in Obesity</td>
<td>NIH</td>
</tr>
<tr>
<td>Vikas Mishra</td>
<td>Joanna Floros, Ph.D.</td>
<td>Sex differences in the lung inflammatory microRNA profile in a mouse model of ozone-induced oxidative stress</td>
<td>BIRCWH</td>
</tr>
<tr>
<td>Sunil Muthusami, M.D.</td>
<td>Sinisa Dovat, M.D., Ph.D.</td>
<td>Novel Anti-Leukemia Therapy with an Isatin Derivative: Dual Inhibition of Tubulin Polymerization and AKT Pathway</td>
<td>Four Diamonds Fund</td>
</tr>
<tr>
<td>George Noutsios, Ph.D., MSc</td>
<td>Joanna Floros, Ph.D. and Evan Pugh</td>
<td>14-3-3 isoforms bind directly Exon B of the 5’UTR of human surfactant Protein A2 mRNA – correlation with SP-A2 protein expression</td>
<td>NIH</td>
</tr>
<tr>
<td>Sarah Owusu, B.S.</td>
<td>Catharine Ross, Ph.D.</td>
<td>Ontogenic Expression of Retinoid Homeostatic Genes in Principal Vitamin A Storage Organs</td>
<td>NIH/Alfred P. Sloan Scholarship</td>
</tr>
<tr>
<td>Xiaokang Pan</td>
<td>Sinisa Dovat, M.D., Ph.D.</td>
<td>Identification of Binding Site Enrichment of Ikaros in Leukemia</td>
<td>Four Diamonds</td>
</tr>
<tr>
<td>David S Phelps, Ph.D.</td>
<td>Sinisa Dovat, M.D., Ph.D.</td>
<td>Sex differences in the acute in vivo effects of different human SP-A variants on the mouse alveolar macrophage proteome</td>
<td>NIH/Natl Heart, Lung and Blood Institute/Natl Instit of Environmental Health Sciences</td>
</tr>
<tr>
<td>Mansi Sachdev, M.D.</td>
<td>Sinisa Dovat, M.D., Ph.D.</td>
<td>Selenium-containing histone deacetylase inhibitors (HDACi) - Novel therapeutic approach for leukemia treatment</td>
<td>Four Diamonds Fund</td>
</tr>
<tr>
<td>Patricia Silveyra, Ph.D.</td>
<td>Joanna Floros, Ph.D.</td>
<td>Sequence polymorphisms at the 3’UTR of human Surfactant Protein A gene variants differentially affect gene expression levels and miRNA regulation in vitro</td>
<td>CMN/Sigma Delta Epsilon-Graduate Women in Science Adele Lewis Grant Fellowship/NIH</td>
</tr>
<tr>
<td>Chunhua Song, M.D., Ph.D.</td>
<td>Sinisa Dovat, M.D., Ph.D.</td>
<td>Epigenetic control of cell cycle by Ikaros and HDAC1 in leukemia</td>
<td>NIH/Four Diamond Fund</td>
</tr>
<tr>
<td>Name</td>
<td>Affiliation</td>
<td>Title</td>
<td>Institution</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>----------------------</td>
<td>-------------------------------------------------------------------------------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Ashton Strother</td>
<td>Akif Ündar, Ph.D.</td>
<td>Handling Ability of Gaseous Microemboli of Two Pediatric Arterial Filters in a Simulated CPB Model</td>
<td>PSH-PCRC</td>
</tr>
<tr>
<td>Bi-Hua Tan, M.D., Ph.D.</td>
<td>Sinisa Dovat, M.D., Ph.D.</td>
<td>Reduced PIP2 Binding to KCNJ2 Channels is Linked to Type 1 Andersen-Tawil Syndrome</td>
<td>American Heart Association/Four Diamonds</td>
</tr>
<tr>
<td>Mala Telekar, M.D.</td>
<td>Wafik El-Deiry, M.D., Ph.D.</td>
<td>ONC201 (TIC10) Exerts Cytotoxicity in Preclinical Models of Pediatric Lymphoma: A Novel Approach</td>
<td></td>
</tr>
<tr>
<td>Nikolaos Tsotakos</td>
<td>Joanna Floros, Ph.D.</td>
<td>Regulation of translation by upstream translation initiation codons of surfactant protein A1 (SP-A1) splice variants</td>
<td>NIH</td>
</tr>
<tr>
<td>LinLin Yang, M.D., Ph.D.</td>
<td>Zissis Chroneos, Ph.D.</td>
<td>Targeting of the surfactant protein A receptor SP-R210L variant by influenza A virus in macrophages</td>
<td>CMN</td>
</tr>
<tr>
<td>Megan N Young</td>
<td>Hong-Gang Wang, Ph.D.</td>
<td>The interplay between mTOR signaling, autophagy, and sphingosine kinase 1: A Novel approach to induce autophagy-dependent cell death</td>
<td>NIH</td>
</tr>
<tr>
<td>FIRST AUTHOR</td>
<td>ADVISOR</td>
<td>ENGINEERING/CLINICAL - ABSTRACT TITLE</td>
<td>FUNDING SOURCE</td>
</tr>
<tr>
<td>--------------</td>
<td>---------</td>
<td>--------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Ranjodh, Dhami, M.S.</td>
<td>Akif Undar, Ph.D.</td>
<td>In Vitro Comparison of the Delivery of Gaseous Microemboli and Hemodynamic Energy for a Diagonal and a Roller Pump during Simulated Infantile CPB Procedure</td>
<td>PSH – PCRC Medos Medizintechnik AG, Stolberg, Germany Novalung GmbH, Heilbronn, Germany</td>
</tr>
<tr>
<td>Alissa Evenson</td>
<td>Akif Ündar, Ph.D.</td>
<td>Use of a Novel Diagonal Pump in an In Vitro Neonatal Pulsatile Extracorporeal Life Support Circuit</td>
<td>PSH – PCRC Medos Medizintechnik AG, Stolberg, Germany Novalung GmbH, Heilbronn, Germany</td>
</tr>
<tr>
<td>Sunil Patel</td>
<td>Akif Ündar, Ph.D.</td>
<td>Hemodynamic Evaluation of Novel i-cor Pulsatile ECLS System during Various Cardiac Arrhythmias: In Vitro Study</td>
<td>PSH – PCRC Medos Medizintechnik AG, Stolberg, Germany Novalung GmbH, Heilbronn, Germany</td>
</tr>
<tr>
<td>Ashton Strother</td>
<td>Akif Ündar, Ph.D.</td>
<td>Handling Ability of Gaseous Microemboli of Two Pediatric Arterial Filters in a Simulated CPB Model</td>
<td>PSH-PCRC</td>
</tr>
<tr>
<td>Akif Undar, Ph.D.</td>
<td>Akif Ündar, Ph.D.</td>
<td>Impact of Pulsatile Flow Settings on Hemodynamic Energy Levels Using the Novel Diagonal Medos DP3 Pump in a Simulated Pediatric ECLS System</td>
<td>PSH – PCRC Medos Medizintechnik AG, Stolberg, Germany Novalung GmbH, Heilbronn, Germany</td>
</tr>
<tr>
<td>Shigang Wang, M.D.</td>
<td>Akif Ündar, Ph.D.</td>
<td>In Vitro Performance Analysis of a Novel Pulsatile Diagonal Pump in a Simulated Pediatric Mechanical Circulatory Support System</td>
<td>PSH – PCRC Medos Medizintechnik AG, Stolberg, Germany Novalung GmbH, Heilbronn, Germany</td>
</tr>
</tbody>
</table>
Impact of Pulsatile Flow Settings on Hemodynamic Energy Levels Using the Novel Diagonal Medos DP3 Pump in a Simulated Pediatric ECLS System

Pelumi Adedayo, MS¹, Shigang Wang, MD¹, Allen R. Kunselman, MD², and Akif Ündar, PhD¹,³
Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics¹, Public Health and Sciences², Surgery and Bioengineering³. Penn State College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
The objective of this study was to evaluate the pump performance of the novel diagonal Medos Deltastream DP3 diagonal pump under non-pulsatile to pulsatile mode with varying differential speed values in a simulated pediatric Extracorporeal Life Support (ECLS) System.

Methods:
The experimental circuit consisted of a Medos Deltastream DP3 pump head and console, a Medos Hilite 2400 LT hollow fiber membrane oxygenator, a 14Fr Medtronic DLP arterial cannula and a 20Fr Terumo TenderFlow Pediatric venous return cannula. Trials were conducted at flow rates ranging from 500 ml/min to 2000 ml/min (500 ml/min increments) and pulsatile differential speed values ranging from 500 rpm to 2500 rpm (500 rpm increments) using human blood (Hematocrit 35%). The post-cannula pressure was maintained constantly at 60 mmHg. Real-time pressure and flow data were recorded using a custom-made data acquisition system and Labview software.

Results:
Under all experimental conditions, pulsatile flow generated significantly greater energy equivalent pressure (EEP), surplus hemodynamic energy (SHE) and total hemodynamic energy (THE) compared to non-pulsatile flow (Figure 1, 2). Under non-pulsatile flow, SHE was zero. Higher differential speed values generated greater EEP, SHE and THE values. There was little variation in the oxygenator pressure drop and the cannula pressure drop in pulsatile flow, compared to non-pulsatile flow.

Conclusions:
The novel Medos Deltastream DP3 diagonal pump is able to generate physiological quality of pulsatile flow, without backflow. With increased differential rpm, the pump generated greater EEP, SHE and THE. Compared to diminished quality of pulsatility, physiological quality of pulsatility may maintain better microcirculation and vital organ recovery because of greater EEP, SHE and THE.

Figure 1. Flow waveforms at pre-oxygenator site under non-pulsatile (NP) and pulsatile (P) mode.

Figure 2. SHE at 2000ml/min. * p<0.01, NP vs. P (P500, P1000, P1500, P2000, P2500) mode.
Autism and Vaccines: Are Siblings Affected?

Edeanya Agbese, MPH, Douglas L. Leslie, PhD
Department of Public Health Sciences,
Penn State College of Medicine, Hershey, Pennsylvania, USA

Purpose:
To compare the vaccination rates of the immediate younger siblings of children with autism spectrum disorders (ASDs) to those of younger siblings of children without ASDs. Research on autism conducted in 1998 showed a link between autism and the measles, mumps and rubella (MMR) vaccine and aroused parents’ concerns about inoculating their children. This led to a decrease in vaccination rates and an increase in measles, mumps, rubella and other vaccine preventable diseases. Although the 1998 study has been invalidated, the decrease in vaccination rates remains a national problem. While research exists regarding the relationship between ASDs and the MMR vaccine, there is a critical gap in ASD research with respect to how an ASD diagnosis affects younger siblings’ vaccination rates.

Methods:
The research design was a secondary data analysis of a large, national commercial base claims database, MarketScan®. Immediate younger siblings of children with ASD were identified, along with a matched control group of children without an older sibling with ASD. Controls matched on age, birth order and sex. The final dataset contained 15,770 participants. The proportions of children who received any vaccine or one of several vaccines were determined and compared across groups using t-tests. In addition, generalized estimating equations (GEE) regression was used to determine whether the effect of group remained after controlling for other patient characteristics.

Results:
Results showed that the vaccination rates for all studied vaccines among children with an older sibling with ASD were significantly lower than those of matched controls. In addition, birth order was significant for the influenza vaccine (OR=0.88; 0.84 – 0.93), the HepA/B vaccine (OR=0.91; 0.86-0.97) and any vaccine (OR=0.92; 0.87 – 0.97). Table 3 summarizes the results from the GEE regression.

Conclusions:
Vaccination rates of younger siblings may be influenced by the diagnosis of an ASD in an older sibling.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MMR (N=3,369)</th>
<th>Any Vaccine (N=9,762)</th>
<th>Influenza (N=4,990)</th>
<th>HepA/B (N=4,308)</th>
<th>Chicken Pox (N=3,607)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.32</td>
<td>0.27 - 0.39</td>
<td>4.78</td>
<td>4.14 - 5.53</td>
<td>0.92</td>
</tr>
<tr>
<td>Case</td>
<td>0.72</td>
<td>0.68 - 0.78</td>
<td>0.85</td>
<td>0.80 - 0.91</td>
<td>0.8</td>
</tr>
<tr>
<td>Age</td>
<td>0.96</td>
<td>0.94 - 0.99</td>
<td>0.78</td>
<td>0.77 - 0.80</td>
<td>0.91</td>
</tr>
<tr>
<td>Gender</td>
<td>1.07</td>
<td>0.98 - 1.16</td>
<td>1.03</td>
<td>0.97 - 1.11</td>
<td>1.01</td>
</tr>
<tr>
<td>Birth Order</td>
<td>1.02</td>
<td>0.96 - 1.09</td>
<td>0.92</td>
<td>0.87 - 0.97</td>
<td>0.88</td>
</tr>
</tbody>
</table>
Comparative Effects of Pulsatile and Nonpulsatile Flow on Plasma Fibrinolytic Balance in Pediatric Patients Undergoing Cardiopulmonary Bypass

Mehmet A. Ağırbaşlı¹, Jianxun Song², Fengyang Lei², Shigang Wang³, Allen R. Kunselman⁴, Joseph B. Clark³,⁵, John L. Myers³,⁵, and Akif Ündar³,⁵,⁶
¹Department of Cardiology, College of Medicine, Istanbul, Turkey; ²Department of Microbiology and Immunology; ³Pediatric Cardiovascular Research Center, Department of Pediatrics, ⁴Public Health Sciences, ⁵Surgery, and ⁶Bioengineering, Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
In the brain, the components of the fibrinolytic system, tissue plasminogen activator (tPA) and its endogenous inhibitor plasminogen activator inhibitor-1 (PAI-1), regulate various neurophysiological and pathological responses. Fibrinolytic balance depends on PAI-1 and tPA concentrations. The objective of this study is to compare the effects of pulsatile and nonpulsatile perfusion on fibrinolytic balance in children undergoing pediatric cardiopulmonary bypass (CPB).

Methods:
Plasma PAI-1 antigen and tPA antigen were measured in 40 children (n = 20 pulsatile and n = 20 nonpulsatile group). Plasma samples (1.5 mL) were collected (i) prior to incision, (ii) 1 h after CPB, and (iii) 24 h after CPB. PAI-1 and tPA levels were measured at each time point.

Results:
PAI-1 and tPA levels were significantly increased at 1 h after CPB, followed by a decrease at 24 h. Nonpulsatile but not pulsatile CPB lowered PAI-1 : tPA ratio significantly at 24 h (median PAI-1 : tPA ratio 4.63 ± 0.83:1.98 ± 0.48, P = 0.03, for the nonpulsatile group and 4.50 ± 0.92:3.56 ± 1.28, P = 0.2, for the pulsatile group).

Conclusions:
These results suggest that pulsatile flow maintains endogenous fibrinolytic balance after pediatric cardiopulmonary bypass. Further studies are needed to define the clinical significance of these differences.

Figure 1. PAI-1 : tPA molar ratio results. Nonpulsatile, but not pulsatile, CPB lowered PAI-1 : tPA ratio significantly. Nonpulsatile, but not pulsatile, flow lowered plasma PAI-1 : tPA ratio by increasing tPA levels at the end of 24 h; this effect remained significant for the nonpulsatile group. *P < 0.05 versus 24 h post-CPB within the same group.
Observations of parents with Attention-Deficit/Hyperactivity Disorder (ADHD) in group behavioral parent training

Dara E. Babinski, Ph.D. and James G. Waxmonsky, M.D.
Department of Psychiatry, Division of Child and Adolescent Psychiatry
Penn State College of Medicine, Hershey, Pennsylvania, USA

Purpose:
Several studies suggest that parental ADHD may impede behavioral parent training (BPT) outcomes (Johnston et al., 2012), although it is not clear why parents with ADHD are at-risk for less optimal BPT outcomes. One possible explanation may be that parental ADHD symptoms reduce parents’ ability to focus on information discussed in BPT, thereby reducing the likelihood of implementing and adhering to BPT. This study explored associations between ADHD symptoms and observations of parents with ADHD attending behavioral parent training (BPT) for their child with ADHD.

Methods:
Fifty-three parents of children with ADHD attending weekly group BPT were recruited. Parents completed ratings of their ADHD symptoms, and parents indicating a moderate level of ADHD symptomatology were administered a clinical interview for ADHD. Observations of parents’ behavior were also collected during BPT, using a coding scheme well-established in observational studies of children and adolescents with ADHD (Pelham et al., 2000). Parents’ attendance and tardiness to BPT sessions were also assessed.

Results:
A high prevalence of ADHD was reported in the sample (approximately 40% by self- and clinician-report). Self- and clinician-rated ADHD symptoms were significantly correlated. Self-ratings of ADHD symptoms were significantly related to higher rates of rule violations (i.e., inappropriate behavior) during the BPT session, while clinician ratings were associated with decreased attendance and increased tardiness to sessions. Additional analyses categorizing parents by self-reported diagnosis (i.e., ADHD vs. non-ADHD) showed notable observable behavioral differences (see Figure below).

Conclusions:
Our study, while exploratory in nature, suggests that the BPT setting may be an opportune setting to identify and engage adults with ADHD in treatment. Self-reported ADHD symptoms were visibly manifested during BPT session, suggesting that parents’ behaviors, particularly difficulty staying on task, may partially explain the relation between parental ADHD and impaired BPT outcomes.

NOTE: Results include the 36 (17ADHD, 19 Non-ADHD) parents who were observed. All behaviors presented were significantly different by diagnostic status at the p<.05 level.
Treating parents with Attention-Deficit/Hyperactivity Disorder: the effects of behavioral parent training and acute stimulant medication on parent-child interactions

Dara E. Babinski, PhD¹, James G. Waxmonskey, MD¹,², and William E. Pelham, Jr., PhD²
¹Division of Child and Adolescent Psychiatry, Department of Psychiatry, Penn State College of Medicine, Hershey, Pennsylvania, USA
²Center for Children and Families, Florida International University, Miami, Florida, USA

Purpose:
Parents with ADHD may not benefit from behavioral parent training (BPT), and additional enhancements may be necessary (Chronis et al., 2004). Parenting improvements have emerged for parents with ADHD treated with stimulant medication (Chronis-Tuscano & Stein, 2012), but it is not known whether there is additional benefit to receiving medication and BPT. This study evaluated the efficacy of BPT for parents with ADHD, and also explored the acute effects of medication and BPT on parent-child interactions.

Methods:
Twelve parents diagnosed with ADHD completed an open-label stimulant medication titration to optimal dose. Then, parents and their children (ages 6-12, also diagnosed with ADHD) completed two laboratory tasks, within two weeks, once on their optimally-dosed medication and once on a placebo to assess the effects of medication on parent-child behavior (Wells et al., 2006). Parents then completed BPT (Barkley, 1997), during which they were unmedicated, followed by two more parent-child tasks (medication vs. placebo) to assess the acute effects of medication after receiving BPT.

Results:
Ten parents completed the trial. As seen in the figure, moderate to large BPT effects emerged across all parent and some child behaviors (*=significant BPT effect). No medication or interaction effects emerged.

Conclusions:
BPT was associated with improvements in parent-child interactions. This contrasts previous studies suggesting that BPT is less effective for parents with ADHD (Chronis et al., 2004). While no medication or interaction effects emerged, parents in this study received medication only during the parent-child assessments, and it may be the case that medication effects emerge over a longer period of time, when administered during BPT. These results, although preliminary, suggest that at least some parents with ADHD benefit from BPT.
Patient Satisfaction with Pain Management in Pediatric Intravenous Catheterizations

Marina Boushra, Ming Wang, PhD, Gail Rudnitsky, MD
Department of Emergency Medicine, Penn State College of Medicine, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania, USA

Purpose:
To evaluate how well our providers are addressing pain during intravascular catheterization in the pediatric emergency department

Methods:
This quality improvement study utilizes a survey of 0-21 year old patients to compare patient satisfaction with the use of ELA-MAX topical cream and ethyl chloride numbing spray in the management of IV insertion pain as well to assess the effect of the presence of Child Life specialists on pain during IV insertions. Pain scores were based on a 1-10 scale. Patients over the age of 12 were asked to fill out their own surveys; parents filled out the surveys of younger patients. ANCOVA adjustment was used to account for the difference of ages in different treatment groups.

Results:
The pain management modality choice was left to the nurses, who overwhelmingly chose ethyl chloride over ELA-MAX because of rapidity of onset. Although clinical studies comparing the efficacy of ELA-MAX and ethyl chloride have shown ELA-MAX to be superior, this study showed no statistically significant difference in patient-reported pain scores in patients who received ethyl chloride versus ELA-MAX, with average pain scores of 2.62 and 2.82 out of 10, respectively. Patients were equally satisfied with the use of ELA-MAX and ethyl chloride spray, perhaps because they were tuned into the fact that we were paying attention to managing their pain. On the whole, 99% percent of patients and their parents were satisfied with how we addressed pain during IV insertion and comments regarding the quality of care were universally positive. The presence of Child Life did not cause a statistically significant reduction in pain scores, although it should be noted that patients who received Child Life care were more likely to leave comments regarding their satisfaction with their experience.

Table 1: Summary of study results

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Treatment</th>
<th>Number of Patients</th>
<th>Average Pain Score</th>
<th>% Satisfied with Amount of Pain Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Ethyl Chloride</td>
<td>54</td>
<td>2.66</td>
<td>98%</td>
</tr>
<tr>
<td>B</td>
<td>Ethyl Chloride and Child Life</td>
<td>40</td>
<td>2.58</td>
<td>95%</td>
</tr>
<tr>
<td>C</td>
<td>ELA-MAX</td>
<td>9</td>
<td>2.56</td>
<td>100%</td>
</tr>
<tr>
<td>D</td>
<td>ELA Max and Child Life</td>
<td>19</td>
<td>2.92</td>
<td>100%</td>
</tr>
<tr>
<td>A + B</td>
<td></td>
<td>94</td>
<td>2.62</td>
<td>97%</td>
</tr>
<tr>
<td>C+D</td>
<td></td>
<td>28</td>
<td>2.82</td>
<td>100%</td>
</tr>
<tr>
<td>A+ C</td>
<td></td>
<td>63</td>
<td>2.65</td>
<td>98%</td>
</tr>
<tr>
<td>B+D</td>
<td></td>
<td>60</td>
<td>2.65</td>
<td>97%</td>
</tr>
</tbody>
</table>

Conclusions:
Patients and parents are satisfied with pain management during IV insertions. These results suggest that there is no difference in pain scores between ELA-MAX and ethyl chloride. Furthermore, the presence of Child Life does not impact pain scores during IV insertions.
Religious Coping and Family Relationships in the Neonatal Intensive Care Unit

Gina M. Brelsford, Ph.D.¹, Kim Doheny, PhD², NNP-BC, Kristen Veneman, D.O.², & Joshua Ramirez, B.A.¹
Penn State Harrisburg, Middletown, Pennsylvania, USA¹, Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA²

PURPOSE:
Parents’ unfamiliarity with the NICU environment can result in high levels of stress and may have implications for family functioning. The use of effective coping strategies, including religious coping, may have important repercussions for family outcomes in the stressful NICU setting.

METHOD:
Feasibility data were collected from 52 parents seven to 10 days after entrance into the NICU at the Penn State Hershey Medical Center. Parents completed demographic questionnaires related to their extent of religiousness and spirituality, their use of coping strategies (Brief COPE; Carver, 1997 and the Brief RCOPE; Pargament, Koenig, & Perez, 2000) and their family relationships (FES-R; Moos & Moos, 1994) while in the NICU.

RESULTS:
Results revealed a significant inverse correlation between use of negative religious coping and family cohesion (r = -0.43, p < .001) and a correlation approaching significance between positive religious coping and family conflict (r = 0.26, p < .06). Results also revealed significant correlations between negative religious coping and instrumental support (r = 0.32, p < 0.05), and denial (r = 0.40, p < 0.01) for NICU parents. Finally, significant correlations were evidenced between family relationship qualities, behavioral disengagement, and denial. Further hierarchical regression analyses revealed religious coping added incremental validity to family cohesion above secular coping, behavioral disengagement and denial, respectively.

CONCLUSIONS:
Exploration of secular and religious coping strategies in the face of stressful family situations, such as the NICU, is necessary to further explore and can have implications post-discharge.

Funding: Supported by a Research Council Grant from Penn State Harrisburg.
Regulation of Drug Resistance in Leukemia

Marie Bulathisnghala, Chunhua Song, PhD, Bihua Tan, PhD, Mansi Sachdev, MD, Sunil Muthusami, MD, Haijun Wang, MD, Yali Ding, PhD, and Sinisa Dovat, MD PhD
Pediatric Cancer Research Center, Departments Pediatrics, Hematology Oncology, Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Ikaros, encoded by the gene *IKZF1*, is a sequence-specific DNA binding protein essential for normal hematopoiesis. Ikaros participates in a complex network of interactions to recruit chromatin-modifying machines to gene regulatory regions promoting their transcriptional activation or repression via chromatin remodeling. Studies in mice with a disruption in *IKZF1* have established Ikaros as a potent tumor suppressor in leukemia. Despite remarkable advancements in treatment, leukemia remains the leading cause of cancer-related mortality in children, primarily because there exists a subset of patients that have a high risk of relapse and a significantly worse outcome. Mutations and deletions in *IKZF1* have been identified as useful predictors of poor response to therapy in leukemia. This work aims to understand the mechanism by which the loss of Ikaros function is involved in the development of high-risk, drug resistant leukemia.

Methods:
Ikaros target genes were identified by anti-Ikaros Chromatin Immunoprecipitation (ChIP) followed by deep sequencing (ChIP-seq). Gene targets were confirmed with individual ChIP reactions followed by quantitative PCR (qPCR). Mechanisms of Ikaros gene regulation were tested using various methods such as luciferase assay, Ikaros over-expression, CK2 inhibition, and qPCR. Finally, cytotoxicity assays were performed on leukemia cell lines to test the effects of combination therapy with CK2 inhibitors.

Results:
We report Ikaros binds to upstream regulatory elements (UREs) and decreases the expression of several genes important in drug resistance in human leukemia. The target genes identified are intricately involved in the pathways responsible for folate metabolism and the breakdown of 6-Thioguanine (6TG) into its inactive metabolites. We found that inhibition of the pro-oncogenic protein Casein Kinase 2 (CK2), the protein responsible for decreasing Ikaros DNA-binding via phosphorylation, resulted in increased binding of Ikaros at the UREs of target genes and a subsequent reduction in target gene expression. Furthermore, we demonstrate combination therapy using CK2 inhibitors with Methotrexate (MTX) or 6-TG produce synergistic effects in cell cytotoxicity assays.

Conclusions:
In this study we have determined a mechanism by which Ikaros regulates drug resistance in leukemia. Results suggest Ikaros represses the expression of several genes that negatively influence the anti-tumor effects of common chemotherapy agents used in high-risk acute lymphoblastic leukemia (ALL) maintenance therapy. Furthermore, inhibition of CK2 restores Ikaros function resulting in increased Ikaros DNA binding and enhanced repression of genes. High-risk ALL is characterized by Ikaros haploinsufficiency, therefore this work provides support for combination therapy with CK2 inhibitors as a promising, novel treatment for ALL.

This work is supported by NIH/NHLBI R01 HL095120, Hyundai Hope on Wheels, and the Four Diamonds Fund.
MOSAIC MONOSOMY 7 IS ASSOCIATED WITH AN ABNORMAL TREC SCREEN

L. Buyantseva MD, MS, A. Horwitz MD, T. Fausnight, MD
Penn State Hershey Children’s Hospital, Penn State College of Medicine,
Hershey, Pennsylvania

INTRODUCTION:
Testing for T-cell receptor excision circles (TREC), a DNA biomarker of normal T-cell development. It is used to screen newborns for severe combined immunodeficiency (SCID) and syndromes associated with T cell lymphopenia (DiGeorge syndrome, ataxia-telangectasia, and Jacobsen syndrome). It has also identified other conditions with non-specific immune dysfunction, such as Trisomy 21. Monosomy 7 is a frequent precursor of myelodyplasia and AML in 30% of children. It occurs in 5% of de novo cases and associated with poor clinical outcomes. We present a case of an infant with an abnormal TREC screen, mosaic monosomy of chromosome 7 and multiple congenital anomalies.

CASE REPORT:
We describe a 3 month-old boy born at 27 weeks of gestation by C-section for a low biophysical profile and severe intra-uterine growth retardation. Amniocentesis showed 46 XY karyotype. He had multiple congenital abnormalities including ambiguous genitalia, congenital adrenal hypoplasia, an atrial septal defect, and spina bifida with associated ventriculomegaly. His NICU course was complicated by hypotension, hypoglycemia, persistent acidosis, electrolyte imbalances and pancytopenia. Newborn SCID screening at birth was inconclusive, but when repeated at 40 week adjusted age revealed undetectable TRECs. A microarray study performed after the second abnormal newborn screen revealed mosaic monosomy 7. Additional testing showed low but present T, B and NK cells. His IgG and IgM were low; IgA was normal. Based on poor prognosis, the family withdrew support and the patient died at 41 weeks of age.

CONCLUSIONS:
Population-based TREC screening is helpful in identifying cases of SCID and T-cell lymphopenia. As screening increases, other syndromes with variable degrees of lymphopenia are being diagnosed. The practitioner should consider microarray testing in a child with an abnormal TREC screen and multiple congenital abnormalities. This is the first published report of a patient with mosaic monosomy 7 and an abnormal TREC screen.
EMS activations for school aged children from public buildings, places of recreation or sport, and healthcare facilities in Pennsylvania

Andrew T. Catherine, BS, Robert P. Olympia, MD
Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
To determine the etiology of EMS activations in 2011 to public buildings, places of recreation or sport, and healthcare facilities involving children aged 5 to 18 years in Pennsylvania.

Methods:
A retrospective observational study was conducted on electronic records documenting 2011 EMS response calls as provided by the Pennsylvania Department of Health’s Bureau of EMS. Data from patients aged 5 to 18 years involved in an EMS response call originating from either a public building (school, child care facility, government building, shopping facility, etc.), a place of recreation or sport (gymnasium or sporting event, park or playground, camp, pool or aquatic facility, etc.), or healthcare facility (medical office or urgent care center, etc.) were included.

Results:
12,289 records were available for analysis. The most common primary impressions from public buildings were traumatic injury, behavioral/psychiatric problem, syncope/fainting, seizure, and poisoning. The most common primary impressions from places of recreation or sport were traumatic injury, syncope/fainting, altered level of consciousness, respiratory distress, and abdominal pain. The most common primary impressions from healthcare facilities were behavioral/psychiatric problem, traumatic injury, abdominal pain, respiratory distress, and syncope/fainting. When examining mechanism of injury for trauma related primary impressions, falls were the most common mechanism at all three locations. Of the 664 serious incident calls (5% of the total EMS activations), 76.7% were from public buildings, 7.7% from places of recreation or sport, and 15.6% from healthcare facilities.

Conclusions:
Traumatic injury secondary to falls, behavioral and psychiatric disorders, respiratory distress, and syncope/fainting accounted for many EMS activations. Although a small percentage of EMS activations were considered serious incident calls, these locations should be prepared to deal with life threatening illness and injury. Basic Life Support and CPR should be offered to staff members at these locations, and emergency medications/equipment should be readily available.
Human Ion Channel TRPM2 Protects Cell Viability through Modulation of Mitochondrial Function

Shu-jen Chen, PhD¹, Lei Bao MD, PhD¹, Kerry Keefer¹, Kathleen Conrad¹, Iwona Hirschler-Laszkiewicz, PhD¹, Nicholas E. Hoffman⁴, Jufang Wang⁵, Yuguang Shi PhD², Yoshinori Takahashi PhD¹, Michael Bayerl³, HG Wang PhD¹, Muniswamy Madesh PhD⁴, Joseph Y. Cheung MD, PhD⁵ and Barbara A. Miller, MD¹

¹Pediatric Hematology/Oncology Research Laboratory, Department of Pediatrics, ²Cellular and Molecular Physiology, and ³Pathology, Penn State College of Medicine, Hershey, Pennsylvania, USA, Department of ⁴Biochemistry and ⁵Medicine, Temple University School of Medicine, Philadelphia, Pennsylvania

Purpose:
The ion channel TRPM2 is highly expressed in a number of cancers. In neuroblastoma, full length TRPM2 (TRPM2-L) protects cells from oxidative stress whereas a dominant negative short isoform (TRPM2-S) enhances ROS, leading to decrease cell viability. Mitochondria are a key site of ROS production. The present study was undertaken to examine the role of TRPM2 isoforms in tumor growth, cell survival and mitochondrial function.

Methods:
To evaluate the effect of TRPM2 isoforms on tumor growth, a xenograft mouse model was established. Neuroblastoma cell lines stably expressing TRPM2-L,-S or both S and L were injected into athymic nude mice. Tumor growth was determined by tumor volume and weight measurements. Protein expression in tumors was examined by Western blotting. Mitochondrial ATP production in tumors was measured using Cell Titer-Glo luminescence. Mitochondrial function was determined by measurement of mitochondrial membrane potential and Ca²⁺ uptake. Oxygen consumption rate was measured by using the Seahorse. Structure of mitochondria was visualized using electron microscopy analysis. The response of TRPM2 isoforms-expressing cells to chemotherapeutic agent (doxorubicin) and TRPM2 inhibitor (clotrimazole) were measured by XTT assay.

Results:
Growth of tumors expressing TRPM2-S was significantly reduced compared to tumors expressing only TRPM2-L. Mitochondrial membrane potential, calcium uptake, oxygen consumption, and ATP production were significantly decreased in TRPM2-S expressing cells. Mitochondria in TRPM2-S expressing cells were swollen and dysmorphic compared to TRPM2-L expressing cells. Expression of HIF-1/2α was significantly reduced in TRPM2-S expressing cells, as was expression of mitochondrial proteins regulated by HIF-1/2α including those involved in mitochondrial oxygen consumption and ROS production (BNIP3 and NDUFA4L2) and mitochondrial electron transport chain activity (complex IV, cytochrome oxidase 4.2). Cells transfected to co-express TRPM2-S and TRPM2-L demonstrated tumor growth reduction, mitochondrial dysfunction, and protein expression similar to TRPM2-S expressing cells. Inhibition of TRPM2-L by expression of TRPM2-S or pretreatment with clotrimazole also increased sensitivity of cells to doxorubicin.

Conclusions:
TRPM2 activity is important for tumor growth and viability. Interference with TRPM2-L function may be a novel approach to reduce tumor growth through inhibition of mitochondria-derived bioenergetics.
Feeding strategies derived from behavioral economics can increase vegetable intake in children as part of a home-based intervention

Terri L. Cravener1, Katharine L. Loeb2, Cynthia Radnitz2, Marlene Schwartz3, Nancy Zucker4, Stacey Finklestein5, Y. Claire Wang6, Barbara J. Rolls1, Kathleen L. Keller1

1Nutritional Sci., Penn State University, University Park, PA, 2Psychology, Fairleigh Dickinson University, Teaneck, NJ, 3Yale University, New Haven, CT, 4Psychiatry & Behavioral Sci., Duke University School of Medicine, Durham, NC, 5Marketing, Baruch College, NY, NY, 6Health Policy & Management, Columbia University, NY, NY

Purpose:
We tested the effect of using behavioral economic strategies to increase children’s vegetable intake in the home. These strategies included pairing cartoons with vegetables to increase appeal and presenting vegetables as the optimal default.

Methods:
Children (n=24; 3-5 years-old) in both control and treatment groups received weekly supplies of plain packaged vegetables, presented as a free choice with an alternative snack (granola bar), during baseline (wk 1) and follow-up (wk 4). During wks 2-3, the control group continued to receive plain packages, but the treatment group received vegetables packaged with their favorite cartoons with sticker incentives, presented as the default choice at snacks/meals. Children were allowed to opt for the granola bar after an imposed wait time. Weekly nutrition lessons were delivered to both groups.

Results:
Repeated measures ANOVA revealed a time* treatment interaction on vegetable intake; during wks 2-3, the treatment group doubled vegetable intake from baseline, while the control showed no change (p<0.01). Increased vegetable intake during weeks 2-3 was correlated with decreased granola bar intake (r=-0.50; p=0.01).

Figure 1. Vegetable intake at baseline, treatment and follow-up (week 4).

Conclusions:
Behavioral economics has the potential to inform parental feeding practices and improve children’s food choices. Additional longer term studies are needed to determine the effectiveness of this strategy for obesity prevention.
Systolic to Diastolic Duration Ratio and Exercise Stress Response in 150 children with and without Heart Disease - a Tissue Doppler Stress Echocardiogram Study

David G. Currie, BA, Matt Dean, MS, Stephen Cyran, MD, Linda B. Pauliks, MD, MPH, Pediatric Cardiovascular Research Center, Department of Pediatrics Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Background:
In pediatric heart failure, systolic to diastolic duration ratio (SD ratio) may be an age-independent marker of disease. SD ratios are increased in cardiomyopathy and hypoplastic left heart syndrome. We analyzed SD ratio and exercise performance in children with and without heart disease.

Methods:
In this study, 56 children with structural heart disease and 94 age-matched controls (Table) underwent clinically indicated Bruce treadmill maximum exercise stress echocardiograms. All reached ≥85% of maximum predicted heart rate (HR). Baseline and peak SD ratios were calculated from color tissue Doppler velocity traces, defining systolic duration as time from onset of QRS complex on ECG to end of isovolumic relaxation wave.

Results:
SD ratio increased significantly with exercise stress in diseased hearts but not in controls (Table). Baseline SD ratio weakly correlated with exercise time for all patients (R -0.22; p<0.01) but not for controls alone. There was a strong correlation of HR and baseline SD ratio (R 0.78; p<0.001) but not for HR and peak SD ratio. Groups were otherwise comparable (Table).

Conclusions:
In this study, the presence of structural heart disease altered the normal exercise response of the systolic to diastolic duration ratio in children (despite normal baseline SD ratios and exercise times). Only diseased hearts showed an increase of the SD ratio with stress: In controls SD ratios were maintained. This marker appears to be highly sensitive for subclinical cardiac dysfunction.

Table 1: Effect of exercise stress on the systolic to diastolic duration ratio in 150 children

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Diseased (n=56)</th>
<th>Controls (n=94)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>13.0±3.5</td>
<td>13.2±3.2</td>
<td>NS</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>152.5±20.5</td>
<td>155.4±17.6</td>
<td>NS</td>
</tr>
<tr>
<td>HR pre (bpm)</td>
<td>90.6±16.8</td>
<td>88.9±15.1</td>
<td>NS</td>
</tr>
<tr>
<td>HR post (bpm)</td>
<td>194.4±8.7</td>
<td>196.8±9.5</td>
<td>NS</td>
</tr>
<tr>
<td>HR post (% predicted)</td>
<td>93.3±4.7</td>
<td>94.5±5.1</td>
<td>NS</td>
</tr>
<tr>
<td>Exercise time (min)</td>
<td>12.8±2.7</td>
<td>12.7±2.4</td>
<td>NS</td>
</tr>
<tr>
<td>Peak MET</td>
<td>14.9±3.3</td>
<td>14.7±2.9</td>
<td>NS</td>
</tr>
<tr>
<td>SD ratio pre stress</td>
<td>0.86±0.22</td>
<td>0.86±0.22</td>
<td>NS</td>
</tr>
<tr>
<td>SD ratio post stress</td>
<td><strong>0.94±0.24</strong></td>
<td><strong>0.85±0.17</strong></td>
<td>P&lt;0.01</td>
</tr>
</tbody>
</table>

Abbreviations: HR heart rate. SD systolic to diastolic.

Comment:
Custom Access to Library Resources: A Collaboration

Esther Y. Dell, AMLS, AHIP and Kathleen A. Zamietra, BA
Penn State College of Medicine, Hershey, Pennsylvania

Library resources have transitioned from print to electronic rapidly, especially in the last ten years. As a result, the George T. Harrell Library established a liaison program in 2008 and assigned librarians to individual departments to evaluate information needs and assist in optimizing the use of available resources. Leadership in the Department of Pediatrics appointed a faculty member to partner with the librarian, with the collaboration resulting in a resource guide that many are finding useful in their clinical practice, research and teaching endeavors.

This poster highlights the development of multiple platforms used to provide direct access to library resources to pediatricians and the ongoing collaboration to keep the tool relevant, current and easy to use.
In Vitro Comparison of the Delivery of Gaseous Microemboli and Hemodynamic Energy for a Diagonal and a Roller Pump during Simulated Infantile CPB Procedure

Ranjodh Dhami, MS¹, Shigang Wang, MD¹, Allen R. Kunselman, MD², and Akif Ündar, PhD¹,³
Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics¹, Public Health and Sciences², Surgery and Bioengineering³, Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Cardiopulmonary bypass (CPB) is used for a variety of procedures in pediatric patients. Flow settings of the CPB pump have dramatic effects on patient outcome, and gaseous microemboli delivery within the CPB circuit has been linked to neurological complications. To ensure the ongoing improvement of pediatric CPB, consistent evaluation and improvement of the equipment is necessary.

Methods:
In this study we analyze the Jostra HL-20 roller pump (Jostra USA, Austin, TX, USA) and a Medos Deltastream DP3 diagonal pump (MEDOS Medizintechnik AG, Stolberg, Germany) which has not yet received Food and Drug Administration approval. An infant CPB model with heparinized human blood is used to quantify the gaseous microemboli delivery (via an Emboli Detection and Classification Quantifier), as well as the hemodynamic energy delivered under flow rates of 400, 800, and 1200 mL/min.

Results:
Results show that at most flow settings the DP3 delivers fewer microemboli than the Jostra roller pump at the preoxygenator site, with an exception at 1200 mL/min under pulsatile mode. The total volume and the number of gaseous microemboli greater than 40 μm in diameter were lower in the DP3 group. The HL-20 exhibits less stolen blood flow (except at 1200 mL/min) and oxygenator pressure drops in both pulsatile and nonpulsatile mode. Additionally, under pulsatile flow the DP3 delivers greater surplus hemodynamic energy.

Conclusions:
Both pumps produce relatively few microemboli and deliver adequate hemodynamic energy to the pseudo-patient, with the DP3 performing slightly better under most flow settings.

Figure 1. The number of gaseous microemboli (GME) greater than 40 μm in diameter delivered at the preoxygenator site under pulsatile (P) and nonpulsatile (NP) mode. *P < 0.01, Medos DP3 versus Jostra HL-20.
Low Vagal Tone is a Predictive Biomarker of Necrotizing Enterocolitis (NEC)

Kim K. Doheny, PhD, Charles Palmer, MD, Rughi Bhagat, PhD, Kirsteen N. Browning, PhD, Puneet Jairath, MD and R. Alberto Travagli, PhD
Departments of Pediatrics and Neural Behavioral Science, Penn State College of Medicine and Penn State Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Necrotizing enterocolitis (NEC) is a prevalent and devastating bowel disease afflicting preterm infants. The high frequency (HF) component of heart rate variability (HRV) is a measure of vagal efferent activity which, among other functions, mediates the cholinergic anti-inflammatory reflex. The primary aim of this study was to test the hypothesis that HF-HRV may be used as a predictive biomarker for NEC-risk before the onset of clinical disease.

Methods:
70 stable preterm (28-35 week) infants had HRV power spectra analyzed from surface ECG waveforms taken postprandially on day 5-7 of life. Exclusion criteria were congenital anomalies or CNS lesions. Clinical outcomes were followed throughout hospitalization. Logistic regression was used to determine the utility of HF-HRV in predicting NEC. 20 Rat-pups separated from dams starting at 18 hours post-birth were exposed to cold stress, hypoxia and force fed with hypertonic formula to induce NEC. A subset of anesthetized pups underwent subdiaphragmatic vagotomy at P1. ECG measurement was done at P2 and analyzed using power spectra. Control animals were returned to dams and not handled after ECG measurement.

Results:
Nine/70 infants (13%) developed stage 2+ NEC confirmed by pneumatosis intestinalis median of 9 days after HRV measurement. HF-HRV power was 21.5±2.7 and 3.9±0.81 ms^2 in infants that remained healthy and those that later developed stage 2+NEC, respectively (P<0.001), Using logistic regression, the risk (odds ratio) of developing NEC was 10 per every one SD decrease in HF-HRV. In P2 rat pups, HF-HRV was significantly reduced in the highest NEC severity group vs controls (p < 0.05). Rat pups that underwent vagotomy and stress-induced NEC had the lowest HF-HRV. See Figures below for a summary of the preliminary (A-C human & D animal) results.

Conclusion:
These results suggest that vagal tone (HF-HRV) is a potential, non-invasive predictive biomarker of NEC.

Funding: Children’s Miracle Network (KKD), Johnson & Johnson Health Behaviors & Quality of Life (KKD), and National Institutes of Health-NIDDK 55530 (RAT).
Music and Mother’s Voice as a Therapeutic Intervention for Convalescing Preterm Infants in the NICU

Kim Kopenhaver Doheny, PhD, NNP-BC, Fumiyuki Chin, PhD, Janice Stouffer, MT-BC, Christina Myers, MMT, MT-BC, Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
To determine the effects of music and mother’s voice on the infant’s stress regulation system indexed by heart rate variability (HRV) and behavioral response characteristics.

Methods:
Convalescing, stable preterm infants (> 36 wks adjusted age) were enrolled in this pilot observational study. Infants with CNS lesions, anomaly, injury, or infection associated with potential hearing loss were excluded. The mother of each infant participant was recorded singing a lullaby to guitar accompaniment. Song selections were based on the infant’s development and parental preference. Recordings were adapted to reflect properties of sedative music. Each weekly 30-40 min MT intervention was done following standard afternoon care and was delivered by a board-certified music therapist using an MP3 player and portable speakers with attention to safety standards. A NIDCAP observer (inter-rater reliability > 85%) recorded physiologic and behavioral responses and sleep/awake states prior to, during, and after each MT intervention. HRV was obtained before and after the MT intervention each week.

Results:
Heart and respiratory rates were significantly lower during mother’s singing as compared to music alone. The percentage of sleep and non-nutritive sucking (NNS) during MT was lower for mother’s voice as compared to music alone. The percentage of wakening and moving toward the music source was highest during the mother’s voice recordings. HF-HRV averaged over 5 MT sessions increased post MT intervention (See Figure).

Conclusions:
Family-centered MT interventions resulted in positive effects on infants’ physiologic response systems and autonomic system balance, suggesting that MT enhances premature infants’ resiliency to stress. Mothers also reported positive perceptions regarding the MT intervention and their infants’ overall responses to MT.

Funding: Supported in part by a research grant from The Children’s Miracle Network and a private donation from SPD Music Productions
Characterization of Pyoluteorin Derivatives as Mcl-1 Antagonists

Kenichiro Doi, MD, PhD, Krishne Gowda, PhD, Qiang Liu, BS, Shen-Shu Sung, PhD, Jyh-Ming Lin, PhD, Shantu Amin, PhD, Hong-Gang Wang, PhD
Departments of Pediatrics and Pharmacology, Penn State College of Medicine, Hershey, Pennsylvania

Purpose:
The evasion of apoptosis is considered to be a hallmark of cancers and a cause of resistance to anti-cancer therapies. Consistently, aberrant overexpression of anti-apoptotic Bcl-2 family proteins such as Bcl-2, Bcl-xL and Mcl-1 is associated with tumorigenesis and increased chemo-resistance in multiple malignancies. Several small-molecule inhibitors that bind to BH3-binding pocket of the anti-apoptotic Bcl-2 family proteins have entered clinical trials. The most potent and selective agents are ABT-737 and its orally active analogs ABT-263 and ABT-199, which inhibit Bcl-XL and/or Bcl-2 but not Mcl-1. Consequently, cancers with elevated Mcl-1 do not respond to these drugs. We have recently identified and characterized the natural product marinopyrrole A (named as maritoclax) as a novel Mcl-1 inhibitor, which induces apoptosis by targeting Mcl-1 for proteasomal degradation without significant effect on mRNA levels. In this study, we aim to analyze the structure-activity-relationship and new derivatives of maritoclax

Methods:
Maritoclax has a N,C2-linked bispyrrole structure consisted of pyoluteorin motif as the key structure. In order to identify regions essential for inhibition of Mcl-1 and induction of apoptosis, we systematically altered or removed portions of the molecule in the pyoluteorin motif. To date, we have synthesized over 40 derivatives of maritoclax and evaluated their inhibitory actions toward Mcl-1 and cytotoxicity in human hematological malignant cell lines.

Results:
We have identified several pharmacophore sites in maritoclax that are required for biological activity and two pyoluteorin derivatives, KS04 and KS18, which bind to a similar site(s) in Mcl-1 as maritoclax, as determined by NMR titration experiments. Like maritoclax, KS04 or KS18 markedly reduced the half-life of Mcl-1 protein in U937 cells and induced apoptosis selectively in Mcl-1-dependent but not Bcl-2-dependent K562 cells. Also, these derivatives synergized with ABT-737 to enhance apoptosis in ABT-737-resistant HL60 cells. Similar to in vitro studies, the combination treatment of KS18 (10 mg/kg/d) and ABT-737 (20 mg/kg/d) significantly suppressed the growth of ABT-737-resistant HL60 xenografts in nude mice via the same mechanism (Figure).

Conclusions:
Our studies suggest that pyoluteorin derivatives have the potential to be developed as a novel class of Mcl-1 inhibitors for the treatment of hematological malignancies.
The Role of Hypoxia-Induced Autophagy in Tumor Progression

Christopher Dower, Yoshinori Takahashi and Hong-Gang Wang
Department of Pediatrics, Penn State College of Medicine, Hershey, Pennsylvania, USA

Purpose:
Autophagy is essential for tumor cell survival by responding to conditions of nutrient or oxygen deprivation, the hallmarks of the tumor microenvironment (TME). However, the relative contribution of autophagy within the TME to the pro-survival, metastasis-prone, and therapy-resistant phenotypes of tumor cells is essentially unknown. Therefore, there is opportunity to unravel the biology of how TME-induced autophagy plays a role in tumor progression. We hypothesize that hypoxia-induced autophagy within the TME contributes to tumor cell survival, tumor metastasis, and chemo resistance.

Method:
The effects of hypoxia-inducible inhibition of essential autophagy proteins (ULK1, BECN1, ATG5 and ATG7) on melanoma and breast cancer progression are being assessed both in vitro and in vivo. The use of a hypoxia-driven promoter to regulate expression of dominant negative autophagy genes in tumor cells will allow for physiological modulation of autophagic activity within the TME in a real-time manner. Currently, the DNA constructs allowing for hypoxia-inducible expression of a dominant negative ULK1 mutant (mULK1) has been developed. Preliminary in vitro studies were performed to verify hypoxia-induced expression of mULK1 results in inhibition of autophagy. The validated construct will subsequently be used to assess tumor growth and metastasis in mouse xenograft models.

Results:
The hypoxia-driven mutant ULK1 construct has been verified to yield hypoxia-dependent expression of mULK1 and down regulation of autophagy in the cancer cell lines B16F10 (mouse melanoma) and MDA-MB-231 (human breast cancer) (Figure). This construct has been stably transfected into B16F10 and MDA-MB-231 cell lines together with the luciferase reporter for noninvasive visualization of tumor growth and metastasis in vivo. These stable cell lines will subsequently be used to determine the importance of hypoxia-regulated autophagy in tumor growth and metastasis in xenograft mouse models.

Conclusions:
Hypoxia-driven mULK1 expression suppressed autophagy in cancer cells cultured under hypoxia but not normoxia conditions. The role of hypoxia-induced autophagy within the TME in tumor growth and metastasis is currently being determined.
Objective:
One approach with the potential to improve morbidity and mortality rates following extracorporeal life support (ECLS) is the use of pulsatile perfusion. Currently, no ECLS pumps used in the United States can produce pulsatile flow. The objective of this experiment is to evaluate a novel diagonal pump used in Europe to determine whether it provides physiological pulsatility in a neonatal model.

Methods:
The ECLS circuit consisted of a Medos Deltastream DP3 diagonal pump, a Hilite 800LT polymethylpentene diffusion membrane oxygenator, and arterial/venous tubing. A 300-mL pseudopatient was connected to the circuit using an 8Fr arterial cannula and a 10Fr venous cannula. A clamp maintained constant pressure entering the pseudopatient. Trials (64 totals) were conducted in nonpulsatile and pulsatile modes at flow rates of 200 mL/min to 800 mL/min. Flow and pressure data were collected using a custom-based data acquisition system.

Results:
The Deltastream DP3 pump was capable of producing adequate quality of pulsatility (Figure 1). Pulsatile flow produced increased mean arterial pressure, energy equivalent pressure (EEP), and surplus hemodynamic energy (SHE) at all flow rates compared to nonpulsatile flow (Figure 2). Pressure drop across the cannula accounted for the majority of pressure loss in the circuit. The greatest loss of SHE and total hemodynamic energy occurred across the arterial cannula due to its small diameter.

Conclusions:
The Deltastream DP3 pump produced physiological pulsatile flow without backflow while providing EEP and SHE to our neonatal pseudopatient. Further experiments are necessary to determine the impact of this pulsatile pump in an in vivo model prior to clinical use.
Child fitness and changes in energy intake in response to doubling portion size

S. Nicole Fearnbach¹, Laural K. English, MS¹, Lindsey M. O’Neill¹, Jennifer O. Fisher, PhD², Jennifer S. Savage, PhD³, Stephen J. Wilson, PhD⁴, Susan K. Lemieux, PhD⁵, Barbara J. Rolls, PhD¹, Kathleen L. Keller, PhD¹,6

¹Department of Nutritional Sciences, Penn State University, University Park, PA, USA
²Department of Public Health, Temple University, Philadelphia, PA, USA
³Center for Childhood Obesity Research, Penn State University, University Park, PA, USA
⁴Department of Psychology, Penn State University, University Park, PA, USA
⁵School of Science, Engineering, and Technology, Penn State University Harrisburg, Harrisburg, PA, USA
⁶Department of Food Science, Penn State University, University Park, PA, USA

Purpose:
Increasing portion size of common foods increases intake in both children and adults. This ongoing study examines possible mechanisms of portion size susceptibility in children. The purpose of this preliminary analysis is to explore the relationship between physical fitness and susceptibility to large portions.

Methods:
Children (n=10) ages 7-10 years-old and their parents reported to the laboratory for four ad libitum dinner test-meals of common foods varying in portion size completed across four weeks. Children were randomized to receive four portion size conditions that ranged in size from 100% (reference), 133%, 167%, and 200%. Intake was measured as the difference between pre- versus post-weights (grams) of foods consumed, which included: pasta, broccoli, garlic bread, tomatoes, grapes, and cake. Weight consumed was converted to energy intake (kilocalories) using nutrition labels. For this analysis, only condition 1 (100%) and condition 4 (200%) were analyzed to determine the percent increase in intake from smallest to largest portions, referred to as portion size susceptibility. Anthropometric measurements were also taken. On a fifth visit, children completed a shuttle run test. The time to complete this common field assessment was used as a marker of physical fitness. Analyses included descriptive statistics and Pearson correlations between intake, fitness, and anthropometrics.

Results:
There was a positive correlation (r = .69, p = .03) between children’s portion size susceptibility (mean ± SD = 55.5 ± 64.6%) and shuttle run time (14.4 ± 1.6 sec). There were no relationships between intake or fitness and child age, sex, body fat, or weight status.

Conclusions:
Children who had lower physical fitness, assessed by the shuttle run, were more susceptible to increasing food intake in response to doubling portion size in the laboratory. This relationship may be mediated by adiposity or weight status, but a larger sample is needed to examine this.
The Relationship between Insect Sting Allergy Treatment and Anxiety and Depression

Sarah Findeis, Andrew Fouche, Timothy Craig, DO
Penn State College of Medicine, Department of Allergy and Immunology, Hershey, Pennsylvania, USA

Purpose:
We sought to determine the depression and anxiety in three groups of individuals: patients with bee sting allergy without epinephrine, bee sting allergy with epinephrine and bee sting allergy receiving venom immunotherapy (VIT). Investigation will clarify differences between these group in regards to anxiety and depression differences and guide treatment recommendations.

Methods:
An initial list of 437 adult patients with documented Hymenoptera sting allergies previously treated at the Milton S. Hershey Medical Center was compiled. Ninety patients consented to phone interviews regarding their sting allergies, current therapies (without epinephrine, epinephrine injections, and/or VIT) and anxiety and depression (assessed through the Hamilton anxiety and depression indices). We compared the three groups using Wilcoxon Rank Sum test and statistical significance was evaluated using a p-value of 0.05. Additionally, a literature review using PubMed and OVID Medline was done using the terms ‘venom immunotherapy,’ ‘anxiety,’ ‘depression,’ ‘hymenoptera sting allergy,’ ‘bee sting allergy.’

Results:
Patients in the epinephrine group had higher mean anxiety and depression scores compared to the other treatment groups. The VIT group had the lowest mean and median scores for both anxiety and depression. The mean anaphylaxis score was highest for the VIT group and lowest for the group not carrying epinephrine.

Conclusions:
It appears that VIT not only decreases the risk of anaphylaxis and death, but also reduces anxiety and depression. These findings are in agreement with those from other countries and indicate that VIT has utility for both the biologic modulation of allergies as well as a psychologic impact in the areas of anxiety and depression. Future studies will include a larger study including the pediatric population.
Early Weight Loss Nomograms for Exclusively Breastfed Newborns By Method of Delivery

Flaherman VJ, Schaefer EW, Kuzniewicz MW, Li S, Walsh E, Paul IM
Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania

Background:
Hyperbilirubinemia and weight loss are common management challenges for exclusively breastfeeding newborns. For both, normal values vary profoundly by hour of age. The Bhutani nomogram delineates quantiles for bilirubin levels by hour of age and has been incorporated into guidelines and clinical practice for the management of hyperbilirubinemia. No hour-by-hour nomogram exists to delineate weight loss patterns for breastfed newborns during the first days after birth. Objective: To develop hour-by-hour nomograms for early weight loss among exclusively breastfed newborns by method of delivery. Methods: For 61,476 term singleton infants born ≥36 weeks at Northern California Kaiser Permanente hospitals in 2009-10 and weighing 2000-5000g, we extracted delivery method, race/ethnicity, feeding type, and weights from all inpatient electronic records. We included weights obtained between 6 and 48 hours for vaginally delivered infants and between 6 and 72 hours for Cesarean delivered infants. We excluded all weights measured subsequent to any non-breast-milk feeding. Quantile regression was used to estimate quantiles of weight loss as a function of time. Results: Of 34,406 infants who met all inclusion criteria, 26,487 were delivered vaginally and 7,919 were delivered by Cesarean. Differential weight loss by delivery method was evident as early as 6 hours and persisted over time [Figure]. Almost 5% of vaginally delivered newborns and almost 10% of those delivered by Cesarean had lost ≥10% of their birth weight by 48 hours age. By 72 hours of age, almost 25% of newborns delivered by Cesarean had lost ≥10% birth weight. Discussion: These newly developed newborn weight loss nomograms have the potential to aid clinicians and parents in their evaluation of healthy, breastfed newborns in a similar manner to nomograms commonly used for the evaluation of neonatal hyperbilirubinemia.

Currently at 95.8% of allowed characters.
**Relationship between newborn weight change, maternal anxiety, and breastfeeding outcomes**

Flaherman VJ, Beiler JS, Cabana MD, Paul IM
Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

**Background:**
Newborns who develop excess weight loss (EWL) ≥10% of birth weight are at increased risk of hypernatremia, hyperbilirubinemia and dehydration. EWL may cause anxiety for mothers, which might lead to increased formula supplementation.

**Objective:**
To examine the relationship between newborn weight loss, maternal anxiety and breastfeeding outcomes.

**Design/Methods:**
For a randomized controlled trial with mothers and “well” newborns ≥34 weeks gestation comparing two post-hospital discharge care models, mothers completed an in-person baseline interview during the postpartum stay and phone surveys at 2 weeks, 2 months, and 6 months to assess outcomes including those related to breastfeeding and anxiety. All participants intended to breastfeed, and daily newborn weights were recorded. From these daily weights, percent weight loss was calculated from the difference between birth weight and lowest recorded weight during the nursery stay. We measured maternal state anxiety using the State-Trait Anxiety Inventory (STAI), in which higher scores suggest greater anxiety and scores ≥40 considered as a positive anxiety screen. Analyses were conducted using chi-squared and Student’s t-tests as well as multivariate logistic regression.

**Results:**
Among 1174 newborns, mean weight loss during the birth hospitalization was 6.3 ± 2.5%, with 73 (6.2%) losing ≥10% birth weight. Mean maternal baseline STAI scores were 31.3 ± 8.6 and did not differ between newborns with ≥10% weight loss and those without. Mean STAI score at 2 weeks was 26.7±7.4. STAI scores at 2 weeks were higher for mothers of newborns who lost ≥10% of their birth weight (29.3±8.9) than for mothers whose newborns did not lose ≥10% of their birth weight (26.6±7.3) (p<0.005). Positive anxiety screen was more common among mothers of newborns who lost ≥10% of their birth weight (16.4%) than among mothers of newborns who did not (5.6%) (p<0.001). Higher STAI scores at 2 weeks predicted increased risk of formula use at 2 weeks, with an odds ratio for formula use of 1.27 (1.06, 1.51) for each 10-point increase in STAI score after adjusting for maternal parity, race/ethnicity, method of delivery and income.

**Conclusions:**
Maternal state anxiety is higher among mothers of newborns with EWL, and higher maternal anxiety scores were associated with a modest increase in formula use at 2 weeks. Preventing EWL might reduce maternal anxiety and improve rates of exclusive breastfeeding at 2 weeks.
A Multi-Faceted Curriculum to Enhance Pediatric Resident Communication Skills with End-of-Life Discussion

Kristen Glass, MD,1 Gary Ceneviva, MD,1 George Blackall, PsyD,1 Robert Shotto, LPN, BA,2 Melanie Comito, MD,1 and Robert Tamburro, MD1

1 Pediatrics, Penn State Hershey Children’s Hospital, Hershey, PA and 2 Medical Education, Penn State College of Medicine, Hershey, PA

Purpose:
Data suggest that most pediatric residents are not comfortable participating in end-of-life discussions with the current training they receive in palliative care medicine. Recent publications suggest that experiential, cased-based curricula are associated with enhanced resident confidence regarding end-of-life support decisions. Here we describe the development, implementation and early experiences of a curriculum to teach end-of-life care skills to pediatric residents.

Methods:
A multi-faceted curriculum was developed and implemented starting in January 2012 at Penn State Hershey Children’s Hospital. Participants included pediatric residents and fellows in critical care fields. Components of the course included: a computer-based tutorial, a multi-disciplinary workshop and a mentored, simulated patient care experience. Responses from pre and post course evaluations were analyzed to determine course efficacy.

Results:
Twenty paired responses were available for analysis. Three-quarters of the trainees reported they had not received strong training in end-of-life care during medical school. Following this course, the majority of trainees reported that they possessed a strong fund of knowledge in end-of-life care (70% of respondents) and felt comfortable in their ability to have meaningful end-of-life care discussions with families (75% of respondents). The format of the curriculum was also well-received with the mentored, simulated patient care scenario ranking highest of the three course components in usefulness (59% of respondents).

Conclusions:
This multi-faceted approach to teaching end-of-life care holds promise as a meaningful experience to improve trainee skill and comfort with end-of-life discussions as clinical opportunities may be sparse. Further implementation with continued and detailed trainee feedback is needed to assess its utility.
Oral Care With Colostrum For Immune Stimulation In Very Low Birth Weight Infants

Kristen M. Glass, MD¹; Kim K. Doheny, PhD¹; Coleen Greecher, MS, RD² & Robert Bonneau, PhD³
Division of Newborn Medicine, Departments of ¹Pediatrics, ²Surgery, ³Microbiology and Immunology
Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Colostrum, mothers’ early breast milk, contains factors that impact immune function in very low birth weight (VLBW) infants. Oral care with colostrum has been proposed as a means of administering this beneficial early milk in the first few days of life when illness often precludes enteral feeds. The purpose of this study was to determine the effect of oral care with colostrum on immune stimulation in VLBW infants, as measured by infant salivary secretory IgA (sIgA) levels. Additionally we set out to determine the effect of oral care with colostrum on rates of infection.

Methods:
In this randomized, placebo-controlled pilot study, 30 infants with birth weight < 1500 grams received oral care with either mother’s own colostrum or sterile water every 3 hours from day of life (DOL) 2 until DOL 7. Saliva collected at three time points (DOL 2, 7 and 14) was analyzed by quantitative enzyme-linked-immuno-sorbent-assay (ELISA) for sIgA. Due to skewness of the data on tests of normality, sIgA raw data were log transformed. Clinical outcomes were obtained by chart audit. Between group comparisons were made using independent samples t-tests for parametric data and Mann Whitney U for nonparametric data.

Results:
Sample characteristics between the colostrum group and sterile water group on key demographic variables showed no differences. Salivary sIgA levels were similar in both groups at DOL 2. At DOL 7, salivary sIgA was significantly higher in the colostrum vs sterile water group (p<0.05). However, this effect was not sustained at DOL 14. There also was no difference between groups in incidence of late-onset infection or necrotizing enterocolitis.

Conclusions: Our analysis shows oral care with colostrum increases salivary sIgA. A larger, multicenter study is needed to determine if increased salivary sIgA provides further immune benefits in VLBW infants.
Regulation of Cell Cycle Progression by Casein Kinase II (CK2) via Ikaros and effects of CK2 Inhibitors in Leukemia

Chandrika Gowda1, Chunhua Song1, Mansi Sachdev1, Xiaokang Pan1, Kimberly J. Payne2 and Sinisa Dovat1

1Pennsylvania State University, Hershey, PA; 2Loma Linda University, Loma Linda, CA

Purpose:
Molecular mechanism by which CK2, an oncogenic kinase exerts its function is largely unknown. CK2-mediated phosphorylation of Ikaros results in reduced DNA binding affinity, loss of pericentromeric localization and impaired Ikaros transcriptional repression. We hypothesize that the pro-oncogenic activity of CK2 in leukemia involves functional inactivation of transcription factor Ikaros, and that CK2 inhibition will result in restoration of the tumor suppressor function of Ikaros and have an anti-leukemia effect.

Methods:
1) quantitative Chromatin Immunoprecipitation (qChIP), 2) Luciferase reporter assay 3) Retroviral transduction 4) Cytotoxicity assay 5) Leukemia Xenograft mouse model

Results:
qChIP showed that Ikaros binds to the promoters of two genes that are essential for mitosis, ANAPC1 and ANAPC7, in leukemia cell lines and in primary leukemia cells. Increased expression of Ikaros via retroviral transduction was associated with increased binding of Ikaros to the promoters of ANAPC1 and ANAPC7 and their transcriptional repression. Luciferase reporter assay confirmed that Ikaros can directly repress transcription of both ANAPC1 and ANAPC7. These data suggest that Ikaros negatively regulates cell cycle progression during mitosis and that Ikaros function as a repressor of ANAPC1 and ANAPC7 is impaired in leukemia. To evaluate ability of CK2 inhibition to restore Ikaros repressor activity in leukemia, we treated pre-B acute lymphoblastic leukemia (B-ALL) cell line, Nalm6 with a specific CK2 inhibitor, both in vitro and in murine xenograft model of B-ALL. Treatment resulted in increased Ikaros binding to promoters of ANAPC1 and ANAPC7, along with transcriptional repression of both genes. This was associated with prolonged survival of B-ALL xenograft mice that were treated with CK2 inhibitors.

Conclusions:
These data suggest that CK2 inhibitors can regulate cell cycle progression in leukemia cells by restoring the transcriptional repressor function of Ikaros. Our results demonstrate efficacy of CK2 inhibitors as a novel treatment for leukemia.
5210 Healthy Military Children: A U.S. Military Initiative That Uses Primary Care And Other Community Sectors To Reduce Childhood Obesity And Improve Child Health

Darcy E. Güngör, MS, Jennifer M. DiNallo, PhD, Ryan P. Rosendale, PhD, Daniel F. Perkins, PhD
Resource Center for Obesity Prevention at the Penn State Clearinghouse for Military Family Readiness, University Park, Pennsylvania, USA

Purpose:
5210 Healthy Military Children was developed to provide consistent health-promoting messaging and strategies to Military communities in an effort to decrease the prevalence of childhood obesity. This program was designed to be implemented across multiple sectors of Military communities, including primary care.

Methods:
Based on the existing program, Let’s Go!, from the Kids CO-OP at the Barbara Bush Children’s Hospital at Maine Medical Center, 5210 Healthy Military Children aims to reach Military children and their families where they live, learn, work, and play with a consistent health message and supporting materials. The health message is the mnemonic “5210” which represents evidence-informed health behaviors children should strive for each day: 5 or more servings of fruits and vegetables, 2 or fewer hours of screen time, 1 or more hours of physical activity, and 0 sweetened beverages. 5210 Healthy Military Children makes the 5210 message accessible to Military communities by disseminating the message across Military sectors and providing sector-specific tips and tools to encourage 5210 behaviors in children.

Results:
5210 Healthy Military Children targets child development centers, family child care, elementary schools, middle and high schools, youth centers, after-school programs, Military dining facilities, on-installation eateries, commissaries, fitness centers, workplaces, healthcare professionals, leaders, and families. The materials for healthcare professionals equip pediatric primary care providers with tips and tools to reinforce the 5210 message from a clinical perspective. Materials and program assistance are available for free from the Resource Center for Obesity Prevention at the Penn State Clearinghouse for Military Family Readiness (www.militaryfamilies.psu.edu).

Conclusions:
5210 Healthy Military Children developed for the U.S. Military, targets primary care as one of several sectors within Military communities to disseminate a consistent health message, “5210”, and employ strategies to encourage and support healthy eating and active living in Military children.
Breastfeeding Outcome Comparison Between Experienced and Primiparous Women

Nicole M. Hackman, Eric W. Schaefer, Jessica S. Beiler, and Ian M. Paul
Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania

Background:
Little is known about how the breastfeeding experience differs between those who have previously nursed an infant and those who are primiparous.

Objective:
To contrast breastfeeding outcomes between primiparous women and those with previous experience spanning from the maternity-nursery hospital stay through 6 months postpartum.

Methods:
For a randomized controlled trial with mothers and “well” newborns ≥34 weeks gestation comparing two post-hospital discharge care models, mothers completed in-person interviews during the postpartum stay and phone surveys at 2 weeks, 2 months, and 6 months where questionnaires related to breastfeeding were completed including those adapted from the Infant Feeding Practices Study II. All participants intended to breastfeed.

Results:
Among 1099 mothers of singleton newborns eligible for this analysis, 542 (49%) were primiparous and 557 (51%) were multiparous and previously breastfed. Multiparous mothers had a longer intended breastfeeding duration (median 9 vs 6 mo; p<.001). Following delivery, primiparous mothers had a longer median time to first breastfeeding attempt (119 vs 96 min; p<.001) and fewer mean attempts in the first 24 hours (6.4 vs 7.0; p=.001). More primiparous women reported breastfeeding problems during the maternity stay (35% vs 20%; p<.001) and mixed feeding at hospital discharge (39% vs 23%; p<.001) despite having less breastfeeding associated pain during the first week (p=.04). Multiparous women were more likely to continue to breastfeed through 6 months (p<.001). [figure1]

In a multivariable Cox model for breastfeeding duration, an interaction existed between intended breastfeeding duration and parity (p=.006) such that multiparous mothers had increasingly lower hazards of breastfeeding cessation as planned intention increased.

Discussion:
Primiparous women have much different breastfeeding experiences than multiparous women who previously breastfed. Pre- and post-delivery breastfeeding support should differentially target primiparous women to improve breastfeeding outcomes.
Application of the Pediatric Emergency Care Applied Research Network (PECARN) head trauma prediction rules to pediatric trauma activations in central Pennsylvania

Jonathan Hilton, B.S., Christina Herting, M.D., Robert P. Olympia, M.D.,
Penn State College of Medicine, Penn State Hershey Children’s Hospital,
Hershey, Pennsylvania, USA

Purpose:
To determine whether the application of the PECARN prediction rules could identify children at low risk of clinically-important traumatic brain injury (ciTBI) and decrease the use of CT brain scans in children presenting as trauma activations to two trauma designated emergency departments in central Pennsylvania.

Methods:
A retrospective review of patients < 18 years, presenting as trauma activations within 24 hours of head trauma between 9/2009 and 6/2013, and with Glasgow Coma Scale scores of 14-15 was performed. Prediction rules were applied to these patients. Patients were considered to have a ciTBI if brain injury resulted in death, neurosurgical intervention required, intubation > 24 hours, or hospital admission > 2 nights.

Results:
819 charts were analyzed. Mean age was 10.2 years. 655 (80%) patients had a CT; 163 (25%) revealed a traumatic brain injury. 92 (14%) had a ciTBI (81 > 2 night admission, 7 neurosurgical intervention, 4 intubation > 24 hours, 0 deaths). Application of the prediction rules to all patients resulted in a sensitivity of 98.9% and negative predictive value of 99.5%; to all patients < 2 years, sensitivity of 94.7% and negative predictive value of 94.4%; to all patients ≥ 2 years, sensitivity and negative predictive value of 100%. Application of the prediction rules to all patients would have reduced the number of CT scans by 94 (7 patients < 2 years, 87 patients ≥ 2 years). One patient had a CT scan performed and a ciTBI despite the prediction rules recommending no CT. Of the 12 patients who did not have a CT performed despite recommendations by the prediction rules, none had an adverse outcome.

Conclusions:
Application of the PECARN prediction rules to pediatric trauma activations identified children at low risk for ciTBI for which a CT scan would have been avoided.
Nephrotoxicity in pediatric patients receiving vancomycin alone or in combination with piperacillin-tazobactam

Krisoula Horiates, PharmD, Kevin Mulieri, PharmD, Lindsay Trout, PharmD
Department of Pharmacy, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania, USA

Purpose:
Adult data supports an increased risk of nephrotoxicity when vancomycin is combined with piperacillin-tazobactam compared to other beta-lactam antibiotics. There is a lack of data confirming this increased risk in pediatric patients. The objective was to assess the incidence of nephrotoxicity in pediatric patients receiving vancomycin alone or in combination with piperacillin-tazobactam as well as vancomycin in combination with other antibiotics.

Methods:
A retrospective chart review was performed in patients aged 1 month to 17 years who received IV vancomycin for at least 42 hours at the Penn State Milton S. Hershey Medical Center. From January 2012 to September 2013, 188 patient profiles were screened with 103 patient profiles analyzed. Patients were excluded if there was not a baseline serum creatinine level and/or a serum creatinine level was not collected after vancomycin initiation. The primary outcome was to assess the incidence of nephrotoxicity, determined as serum creatinine increase of 0.5 mg/dL or 50% from baseline, in pediatric patients receiving vancomycin alone or in combination with piperacillin-tazobactam. Secondary outcomes include analysis of additional factors which may contribute to nephrotoxicity in these patients.

Results:
Overall, nephrotoxicity occurred in 12 out of 103 (11.7%) pediatric patients receiving vancomycin therapy. Nephrotoxicity was more common in patients receiving combination therapy with vancomycin and piperacillin-tazobactam (11/42 [26.2%]) than vancomycin without piperacillin-tazobactam (1/61 [1.6%]) (p=0.0002).

Conclusions:
These results suggest that the increased risk of nephrotoxicity seen in adult patients on vancomycin and piperacillin-tazobactam combination therapy may also be seen in pediatric patients. Further studies are warranted.
Validation of a Screening Tool for Pediatric Abusive Head Trauma (AHT)

Kent P. Hymel, MD, Department of Pediatrics, Center for the Protection of Children, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania, USA, for the Pediatric Brain Injury Research Network (PediBIRN) Investigators

Purpose:
A flawed decision to launch—or to forego—a child abuse evaluation can have serious adverse consequences. Unfortunately, physicians have demonstrated significant disparities in the evaluation and diagnosis of severe child maltreatment.

Focusing exclusively on the pediatric intensive care unit (PICU) setting, PediBIRN investigators derived two AHT clinical prediction rules—a 4-variable rule and a 5-variable rule—with screening sensitivities for AHT $>0.95$ and negative predictive values $>0.91$. More recently, they validated the screening performances of these two AHT clinical prediction rules in a new, equivalent, PICU patient population. Our objective was to compare and contrast the screening performances of these (4-variable and 5-variable) AHT clinical prediction rules using the data from our combined (derivation plus validation study) patient population of 500 acutely head-injured children under 3 years of age hospitalized for intensive care at one of our 18 participating PediBIRN sites.

Methods:
In this secondary analysis, we: (1) analyzed the data from our combined (derivation plus validation study) patient population; (2) applied each AHT clinical prediction rule to every child in our patient population; (3) categorized study patients who manifested any one or more of the (four or five) predictor variables included in a specific prediction rule as higher risk; (4) categorized all remaining patients as lower risk; (5) applied multiple (more inclusive and less inclusive) criteria to iteratively sort the patient population into novel comparison groups of abusive vs. other head trauma; (6) created multiple 2x2 contingency tables; (7) compared patient sorting based on each AHT clinical prediction rule (higher vs. lower risk) to patient sorting based on every unique criteria for defining AHT (abusive vs. other); and (8) serially re-calculated each AHT clinical prediction rule’s screening performance (sensitivity, specificity, predictive values, likelihood ratios).

Results:
No matter how we defined AHT, both AHT clinical prediction rules demonstrated screening sensitivities for AHT $\geq 0.96$ and negative predictive values $\geq 0.92$. Confidence intervals for specific, equivalent measures of screening performance overlapped considerably, suggesting that our 4-variable and 5-variable AHT clinical prediction rules would perform equally well as an AHT screening tool in the PICU setting—to help exclude AHT, when negative.

Conclusions:
Our analyses suggest that our 4- and 5-variable AHT clinical prediction rules would perform equally well as AHT screening tools in the PICU setting.
Background:
Many healthcare providers express concern about their ability to maintain patient visit volumes when transitioning from paper to electronic health records (EHR). Little is known about the actual impact of implementation on visit numbers or how long return to baseline productivity takes.

Objective:
To evaluate the impact of an EHR implementation on primary care pediatric practice visit volume.

Methods:
At an academic primary care practice, EHR (Powerchart, Cerner Corp.) was implemented in December, 2011. This included nursing intake, computerized physician order entry and physician visit documentation. Data on the number of visits for both the pre- and post-EHR implementation periods were obtained through the Powerchart scheduling system. As healthcare provider availability also changes month to month, physician clinical effort within the practice was determined by calculating the amount of “full time effort” (FTE) devoted to clinical care by the providers. Visit numbers per FTE were then calculated by month for ten months pre- and post-implementation of the EHR.

Results:
Upon transition to EHR in December, 2011, provider daily appointment availability was administratively reduced by 20% for two weeks followed by a 5% reduction for 6 months to grant providers a modest amount of extra time per visit to become familiar with the EHR. As such, initial visits/FTE declined compared with the prior year for the first 7 months post-EHR implementation. Alternatively, by months 8-9, provider visits /FTE had returned to those from the prior year. [figure]

Discussion:
EHR implementation was associated with a short-term modest reduction in provider visits, largely due to a self-imposed decrease in visit availability. While visits returned to baseline numbers during the traditionally slower summer months, whether this will occur during the busier winter months is unknown at this time, but return to previous levels of productivity appears to be possible within the first year post-EHR implementation.
Americleft Methods: Is The Q-SORT Method Equivalent With 2D Photos And 3D Surface Imaging?

Christine M. Jones, MD1; Donald R. Mackay, MD, DDS1; Thomas D. Samson, MD1; Ana M. Mercado, DMD, PhD2 ; Kathy A. Russell, DDS, MSc3; John Daskalogiannakis, DDS, MSc4; Ronald R. Hathaway, DDS, MS5; Ross E. Long, Jr., DMD, PhD6

1Penn State Hershey Medical Center, Hershey, PA, USA, 2Ohio State University, Columbus, OH, USA, 3Dalhousie University/IWK Health Centre, Halifax, NS, Canada, 4The Hospital for Sick Children, Toronto, ON, Canada, 5Peyton Manning Children’s Hospital at St. Vincent, Indianapolis, IN, USA, 6Lancaster Cleft Palate Clinic, Lancaster, PA, USA

Purpose:
To measure the relationship between photographic and 3D surface imaging ratings of patients with repaired complete unilateral cleft lip and palate (CUCLP). The ideal rating method would closely mimic a patient encounter, yet be practical and affordable for most centers to use.

Methods:
Twenty-seven consecutively treated patients with CUCLP who had complete 2D and 3D photographic documentation were included (mean age 6 yr 10mos). Frontal, profile, and 3D digital images were cropped similarly to show the nose and upper lip, and were coded. Nasolabial profile, nasolabial form, and vermillion border aesthetics were rated by 6 trained and calibrated raters (3 orthodontists, 2 surgeons, 1 prosthodontist) using the 5-point scale described by Asher-McDade and the modified Q-sort method. Cropped 3D images were available for viewing by each rater, allowing for complete rotational control to view the images from all aspects. 2D and 3D ratings were done separately and repeated the next day with the order reversed. Intrarater and interrater reliabilities were calculated using weighted kappa statistics. Correlation of 2D and 3D ratings was determined using Bland-Altman plots.

Results:
Intrarater reliability scores were good for 2D and fair to good for 3D imaging. Intrarater reliability was good to very good for 2D and moderate to good for 3D imaging. Bland-Altman analysis showed good agreement of 2D and 3D scores for nasolabial profile and nasolabial form, but there was more systematic error in the assessment of vermillion border.

Conclusion:
Although 3D images may be perceived as more representative of a direct clinical facial evaluation, their use for subjective rating of nasolabial esthetics was not more reliable than 2D images in this study. Conventional 2D images provide acceptable reliability while being readily accessible for most cleft palate centers.
Do Pharyngeal Flaps Restrict Midface Growth In Cleft Patients?

Christine M. Jones, MD; Donald R. Mackay, MD, DDS; Andrew F. J. Mackay, BS; Ross E. Long, Jr., DMD, PhD.

Department of Surgery, Division of Plastic Surgery, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA, and Lancaster Cleft Palate Clinic, Lancaster, Pennsylvania, USA

Purpose:
To investigate whether facial growth differs in children who undergo pharyngeal flap versus pharyngoplasty/palatal lengthening as compared to controls. Previous studies have yielded conflicting results, and none have shown comparison to palatal lengthening or pharyngoplasty.

Methods:
This retrospective cohort study included all patients with cleft palate who had undergone pharyngoplasty/palatal lengthening or pharyngeal flap for velopharyngeal insufficiency (VPI) and had adequate cephalometric data. Patients with craniofacial syndromes and those who underwent maxillary protraction were excluded. A control group consisted of patients who did not undergo surgery for VPI. The three groups were matched based on cleft type and ages at VPI surgery and cephalogram. Y-axis, SNA, SNB, ANB, effective maxillary length, effective mandibular length, maxillomandibular difference, A-NP, Pog-NP, gonial angle, anterior facial height, posterior facial height, and ratio of posterior to anterior facial height were evaluated on post-operative cephalograms using an ANOVA, with a Bonferroni adjustment for significant measures (alpha=0.05).

Results:
Seventy-two patients were included. Twelve of thirteen craniofacial measures were not significantly different among the three study groups; notably, this included maxillary height and projection. Only gonial angle was found to differ significantly (p<0.019), in that pharyngoplasty yielded a larger angle as compared to control. In other measures, there was a notable but statistically insignificant trend towards increased vertical facial height after all operations for VPI, but especially with pharyngeal flap.

Conclusion:
Surprisingly, maxillary growth was not altered as expected. The only significant difference was the increase in gonial angle, which reflects a more downwardly projecting mandible. Also, there was a tendency towards increased facial height. It is postulated that these changes in patients undergoing surgery for VPI result in narrowing of the airway at the level of palate. Children often become mouth breathers, and this open mouth posture causes the skeletal changes we see.
Structural Fat Grafting To Improve Reconstructive Outcomes In Cleft Lip

Christine M. Jones, MD; William B. Albright, MD; Brad T. Morrow, MD; Ross E. Long, Jr, DMD, PhD; Thomas D. Samson, MD; Donald R. Mackay, MD, DDS.

Department of Surgery, Division of Plastic Surgery, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA, and Lancaster Cleft Palate Clinic, Lancaster, Pennsylvania, USA

Purpose:
Patients with repaired cleft lip commonly develop soft tissue deficiencies, such as a tight, thin upper lip and paranasal areas. This study sought to describe the technique and results of structural fat grafting in cleft lip revision, including patient satisfaction and aesthetic outcome.

Methods:
All patients who underwent structural fat grafting between June 2006 and August 2010 for cleft lip revision with appropriate photographic follow up were included. Patients completed questionnaires assessing their satisfaction. Outcomes were evaluated using both the Pennsylvania Lip and Nose (PLAN) Assessment and the Asher-McDade nasolabial appearance rating scale. A Student’s t-test was used to test outcomes for significance (alpha=0.05).

Results:
Forty-two patients underwent fat grafting as an adjuvant to craniofacial reconstruction. Of these, 13 were for cleft lip. Eleven of these had sufficient data to be included: eight had unilateral cleft lip and three had bilateral cleft lip. The average age was nineteen (range: 9-43) with a male to female ratio of 3:8. The average length of follow up was 9.9 months. Aspirated fat was most commonly injected around the nostril base, philtral columns, and upper lip. Overall symmetry and aesthetics were improved based on both PLAN (p=0.04) and Asher-McDade (p=0.05) scales. No complications were recorded, and no patients required further lip revision. Patients were significantly happier with their appearance after fat grafting (p=0.008), and were uniformly positive when questioned about the ease of the surgery and rate of recovery. All patients reported they would choose this operation again.

Conclusion:
Structural fat grafting is a safe and effective way to improve symmetry and enhance facial proportions in patients with cleft lip. Given the high degree of patient satisfaction, few complications, and acceptable durability, fat grafting offers many advantages for its use in cleft lip revision.
Effects of Exercise Stability Balls on BMI and Blood Pressure in the Educational Setting

Kelly M. Kalovcak, MS-II, Dr. Marsha B. Novick, MD
Department of Pediatrics, Penn State College of Medicine,
Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Previous research shows that sitting on an exercise stability ball has a 4.1 kcal/hour greater energy expenditure compared to sitting in a chair. This study looked at whether the use of yoga stability balls in a fourth grade classroom improved students’ body mass index (BMI), blood pressure and pulse, and also determined the student satisfaction level with using the stability balls.

Methods:
45 students participated in this pilot study - 26 in Classroom A and 19 in Classroom B. At the beginning of the study, Classroom A incorporated the use of stability balls instead of chairs throughout the day. Meanwhile, Classroom B continued using chairs. Measurements (height, weight, blood pressure, pulse) were collected by the school nurse and recorded at the beginning and end of the study. At the conclusion of the project (3 month mark), the students in Classroom A completed a survey to determine their satisfaction level with using the stability balls.

Results:
No significant change was noted in BMI (p=0.194), systolic blood pressure (p=0.077), diastolic blood pressure (p=0.945) or pulse (p=0.977) between the classroom that used the stability balls (Classroom A) and the classroom that did not (Classroom B). Students in Classroom A, however, reported high satisfaction levels with the use of stability balls in the classroom (Figure 1).

Figure 1. Survey results indicating the high satisfaction level with the use of yoga stability balls instead of chairs.

Conclusions:
These results suggest that there was no change in BMI, blood pressure or pulse with children using yoga stability balls as chairs in the classroom setting. However, students enjoyed using the yoga stability balls, and felt that the balls improved their academic environment and increased their focus and ability to learn.
Rationale
Hereditary angioedema (HAE) is a rare life threatening disease characterized by painful and debilitating attacks of angioedema. In majority of patients HAE attacks are preceded by prodromal symptoms such as fatigue, rash and gastrointestinal symptoms. Treatment at the time of prodrome may prevent an attack and reduce morbidity and mortality associated with HAE. Physicians are hesitant to utilize this approach. The goal of this study is to understand barriers to this approach.

Methods
An internet based international survey was conducted of physicians with expertise in HAE. Information was collected regarding their experience with prodromal symptoms. A literature search (PubMed, Google) with term: HAE prodromal signs and symptoms was performed.

Results
A total of 65 physicians were contacted of which 43 participated. In our survey majority (70%) of physicians follow more than 15 HAE patients, consider prodromal symptoms to be sensitive in predicting HAE attacks and agree that treating prodomes will lead to rapid response, reduced disability and better quality of life. However, very few (12%) physicians use this approach due to lack of data about specificity of prodromal symptoms and difficulty identifying patients who would benefit from this approach. Literature suggests that prodromal symptoms are sensitive predictors of an impending attack, but specificity data are lacking.

Conclusion
Treating HAE at the time of prodrome in patients who are able to predict HAE attacks may lead to reduced morbidity and mortality and improve quality of life. Major barrier to using this approach is lack of data on specificity.
The Acceptability of Imagery-Hypnosis for Management of Pain, Anxiety, and Distress Related to Needle Procedures in Pediatric Oncology-Hematology Patients

Nancy L. Kashlak, DNP, CRNP, CPNP
Instructor, Pennsylvania State University College of Nursing, Hershey, Pennsylvania

Purpose:
The purpose of this study was to evaluate the acceptability and general effectiveness of imagery-hypnosis in the management of needle procedure-related pain, anxiety, and distress experienced by pediatric oncology-hematology patients.

Methods:
A repeated-measures, small n pilot trial elicited data from a convenience sample of 20 child-parent dyads accrued from the out-patient pediatric oncology-hematology clinics of two regional, university-based children's medical centers. Imagery-hypnosis was taught to each child. Visual Analogue Scales were used to assess the children's pain, anxiety, and distress and parental anxiety. Questionnaires elicited qualitative data from children, parents, and healthcare staff. Data were analyzed using descriptive and inferential statistical techniques. Content analysis was used for qualitative data.

Results:
Group mean scores for parental anxiety and children's distress and anxiety decreased over time. Children's group mean pain scores did not reveal an appreciable effect, but median scores showed a downward trend. Imagery-hypnosis was an enjoyable experience for children, and favorable perceptions were revealed by parents and healthcare staff.

Conclusions:
Imagery-hypnosis was found to be an acceptable and effective intervention for managing the pain, anxiety, and distress experienced by pediatric oncology-hematology patients during needle procedures. Dissemination of the use of imagery-hypnosis techniques in clinical practice for the management of pain, anxiety, and distress related to needle procedures is recommended.
Fixation of Type 2a Supracondylar Humerus Fractures in Children with a Single Pin

Alexander J. Kish, BS, William L. Hennrikus, MD, Department of Orthopaedics, Penn State College of Medicine, Hershey, Pennsylvania, USA

Purpose:
The AAOS guidelines recommend operative fixation of all type 2 supracondylar humerus fractures. Not all type 2 fractures are the same. Wilkins subdivided type 2 fractures into 2a: posterior hinge intact without rotation and 2b: posterior hinge not intact with rotation. The purpose of this paper is to report closed reduction and single pin fixations for Wilkins 2a fractures.

Methods:
Fifteen consecutive type 2a fractures treated with single pin fixation were prospectively evaluated. Procedure notes, age, gender, side involved, duration of immobilization, and complications were recorded. Radiographs were measured for the lateral humerocapitellar line and the humeral ulna angle. At final follow up the carrying angle, range of motion and the Flynn criteria were recorded.

Results:
The average age was five years. Three females and twelve males were studied. Eight right elbows and seven left elbows were injured. A 0.0625 K wire was used in two cases and a 2mm K wire was used in thirteen cases. On pre-op lateral radiographs, the anterior humeral line did not intersect the capitellum. On post-op radiographs, the anterior humeral line intersected the middle third of the capitellum. Following pinning, the elbow was immobilized in a long arm cast in pronation with elbow at 75 degrees of flexion. The cast and pin were removed at an average of twenty-seven days. One patient was lost to follow up. The remaining fourteen patients were followed for at least three months. At final follow up, the carrying angle was within two degrees of the opposite elbow and ROM was within three degrees of the opposite elbow in all cases. Final Flynn criteria were excellent in all fourteen patients. There were no complications.

Conclusion:
Treatment of supracondylar fractures has evolved from selective pinning of type 2 fractures to pinning all type 2 fractures. The results of the current study demonstrate the efficacy of using a single lateral entry pin for stabilization of type 2a fractures in children.
A Comparison of Thoracoscopic and Open Approaches to Resection in Pediatric Congenital Lung Malformations: A Pediatric NSQIP Analysis

Afif N. Kulaylat, MD, Brett W. Engbrecht, MD, MPH, Christopher S. Hollenbeak, PhD, Shawn D. Safford, MD, Peter W. Dillon, MD, MSc
Division of Pediatric Surgery, Departments of Surgery and Public Health Sciences, Penn State College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
Thoracoscopic pulmonary resection (VATS) has been increasingly utilized in treating pediatric congenital lung malformations (CLM). A multi-institutional study comparing VATS and open resection (OPR) has not been performed. We hypothesized that the minimally invasive nature of VATS would be associated with decreased morbidity and length of stay (LOS).

Methods:
There were 132 patients identified in pediatric NSQIP with a CLM and pulmonary resection in 2012. Patient characteristics, diagnoses, and operative details were abstracted. Primary outcomes included post-operative complications, 30-day readmission, and LOS. Comparisons of patient characteristics and outcomes between surgical approaches were made using standard univariate statistics. A multivariate analysis of outcomes was performed using logistic and generalized linear regression.

Results:
Fifty-six patients (42.4%) received VATS and 76 patients (57.6%) received OPR. Patients were similar in age, sex, race, and weight. Patients undergoing OPR were more likely to have a comorbidity/preoperative condition (55.3% vs. 25.0%, p=0.001). Both approaches were used in similar proportions across varying CLM, except in the management of congenital lobar emphysema (performed by OPR 10/12[83.3%], p=0.07). The extent of resection was a lobectomy in 71.4% of VATS and 85.5% of OPR patients (p=0.08). Mean operative time was similar between both groups (VATS-157±93.3 vs. OPR-153±66.1 minutes). On univariate analysis, VATS was associated with decreased post-operative complications (7.1% vs. 22.4%, p=0.03) and LOS (3 vs. 4 days, p<0.001). However, after adjusting for similar patient and operative characteristics, these differences were not found to be statistically significant.

Conclusions:
VATS and OPR provide comparable morbidity and LOS in the management of congenital lung malformations.
Pleural Effusion Following Blunt Splenic Trauma in the Pediatric Trauma Population

Afif N. Kulaylat, MD, Brett W. Engbrecht, MD, MPH, Carolina Pinzon-Guzman, MD, PhD, Vance L. Albaugh, MD, PhD, Susan E. Rzucidlo, RN, MSN, Jane R. Schubart, PhD, Robert E. Cilley, MD.
Division of Pediatric Surgery, Departments of Surgery and Public Health Sciences, Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Pleural effusion is a potential complication following blunt splenic injury. The incidence, risk factors, and clinical management are not well described in children.

Methods:
10-year retrospective review (January 2000-December 2010) of an institutional pediatric trauma registry identified 318 children with blunt splenic injury.

Results:
Of 274 evaluable non-operatively managed pediatric blunt splenic injuries, 12 patients (4.4%) developed left-sided pleural effusions. 7 of 12 patients (58%) required left-sided tube thoracostomy for worsening pleural effusion and respiratory insufficiency. Median time from injury to diagnosis of pleural effusion was 1.5 days. Median time from diagnosis to tube thoracostomy was 2 days. Median length of stay was 4 days for those without- and 7.5 days for those with pleural effusions (p<0.001) and 6 and 8 days for those pleural effusions managed medically or with tube thoracostomy (p=0.006), respectively. In multivariate analysis, high-grade splenic injury (IV-V) (OR 16.5, p=0.001) was associated with higher odds of developing a pleural effusion compared to low-grade splenic injury (I-III).

Conclusions:
Pleural effusion following pediatric blunt splenic injury has an incidence of 4.4% and is associated with high-grade splenic injuries and longer lengths of stay. While some symptomatic patients may be successfully managed medically, many require tube thoracostomy for progressive respiratory symptoms.
The Impact of Children’s Hospital Designation on Outcomes in Children with Malrotation

Afif N. Kulaylat, MD, Christopher S. Hollenbeak, PhD, Brett W. Engbrecht, MD, MPH, Peter W. Dillon, MD, MSc, Shawn D. Safford, MD
Division of Pediatric Surgery, Departments of Surgery and Public Health Sciences, Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
The importance of expedited treatment of malrotation with volvulus in children cannot be overstated. We hypothesized that outcomes would be optimized at designated Children’s Hospitals (CH) because of the availability of pediatric and pediatric surgery expertise.

Methods:
A total of 3,111 children were identified with malrotation and complete information from the Kids’ Inpatient Database (KID) during the years 2003, 2006, and 2009. Outcomes, including intestinal resection, mortality, in-hospital complications, length of stay (LOS), and costs, were compared between CH and Non-Children’s Hospitals (NCH). Logistic and linear regressions were used to model the effects of covariates on outcomes adjusting for potential confounders. Propensity score matching was used to balance covariates between CH and NCH.

Results:
There were 1,096 (35.2%) children with malrotation undergoing Ladd’s procedures treated at CH; 2,015 (64.8%) were treated at NCH. In multivariate analysis, CH were associated with a 37% lower odds of resection (p=0.002), with no differences observed for mortality, morbidity and LOS. Among all children with malrotation undergoing Ladd’s procedures, the risk difference for intestinal resection, between patients treated at CH relative to those who were not, was 3.3% (7.04% vs. 10.36%). Of this, the majority (97.7%) of the risk difference (3.2%) is attributable to treatment at CH. There were also higher costs of $12,739 attributable to treatment at CH.

Conclusions:
While most pediatric intestinal malrotation is managed at Non-Children’s Hospitals, Children’s Hospitals are less likely to perform intestinal resection during Ladd’s procedure with similar overall morbidity, mortality, and LOS, albeit with higher costs.
Transumbilical laparoscopic-assisted appendectomy is associated with lower costs compared to multiport laparoscopic appendectomy

Afif N. Kulaylat, MD, Abby B. Podany, MD, Christopher S. Hollenbeak, PhD, Mary C. Santos, MD, MSEd, Dorothy V. Rocourt, MD.
Division of Pediatric Surgery, Departments of Surgery and Public Health Sciences, Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Single-incision laparoscopic appendectomy has been associated with improved cosmetic benefits, and decreased postoperative pain. Less is known about costs and other outcomes. Our aim was to evaluate the costs and outcomes between transumbilical laparoscopic-assisted appendectomy (TULAA) and multiport laparoscopic appendectomy (MLA).

Methods:
IRB-approved retrospective review (September 2010-July 2013) of institutional medical records identified 372 pediatric patients undergoing laparoscopic appendectomy. Outcomes included costs, LOS and readmission. Costs were fully loaded operating costs from the hospital's cost accounting database. Generalized linear regression was used to assess costs of MLA and TULAA. A subgroup analysis was performed using only patients with non-acutely perforated appendicitis.

Results:
There were 132 patients (35.5%) that underwent TULAA while 240 patients (65.5%) underwent MLA. Compared to MLA, TULAA was associated with decreased operative time (0.6 vs. 1.0 hours, p<0.0001), used in comparable proportions of interval appendectomies, but was performed less often for acutely perforated appendicitis (9.8% vs. 22.9%, p=0.002). Readmission and postoperative complications were similar between both groups. In the setting of non-acutely perforated appendicitis, TULAA was associated with lower costs of $1,378 relative to MLA (p=0.009).

Conclusions:
In non-acutely perforated appendicitis, TULAA is associated with lower costs and comparable rates of readmission and postoperative complications.

Afif N. Kulaylat, MD, Audrey L. Stokes, MD, Brett W. Engbrecht, MD, MPH, J. Steele McIntyre, MD, Susan E. Rzucidlo, RN, MSN, Robert E. Cilley, MD
Division of Pediatric Surgery, Departments of Surgery and Public Health Sciences, Penn State College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
Selective non-operative management (NOM) of hemodynamically stable pediatric patients with blunt hepatic trauma is the standard of care. Traumatic bile leaks (TBL) are a potential complication following liver injury. The use of endoscopic retrograde cholangiopancreatography (ERCP) in the diagnosis and treatment of TBL is described in adults, but limited in the pediatric literature. We report our experience with a multidisciplinary and minimally invasive approach to the management of TBL.

Methods:
IRB approved 13-year retrospective review (January 1999-December 2012) of an institutional pediatric trauma registry. 294 patients (≤ 17 years old) sustained blunt hepatic injury; those with TBL were identified. Patient demographics, mechanism of injury, management strategy and outcomes were reviewed.

Results:
Eleven patients were identified with TBL. Hepatobiliary iminodiacetic scan (HIDA) was diagnostic. Combinations of peri-hepatic drain placement, ERCP with biliary stenting and/or sphincterotomy were performed with successful resolution of TBL in all cases. No child required surgical repair or reconstruction of the leak. Cholangitis developed in one child. There were no long-term complications.

Conclusions:
A multidisciplinary and minimally invasive approach employing peri-hepatic external drainage catheters and ERCP with sphincterotomy and stenting of the ampulla is a safe and effective management strategy for TBL in children.
Noninvasive detection of coronary artery anomalies in complete transposition of the great arteries – does color Doppler improve diagnostic accuracy?

Nitin Kumar, BS, J. Brian Clark, MD, John L. Myers, MD, Linda B Pauliks, MD, MPH, Pediatric Cardiovascular Research Center, Depts. of Pediatrics and CT surgery Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Background:
Complete transposition of the great arteries (TGA) is a cyanotic congenital heart defect requiring surgical repair in the newborn period. Literature reports show a frequent association with coronary anomalies. Many of these necessitate modification of the operation. Therefore, preoperative diagnosis of coronary anomalies is important in neonates with TGA.

Objective:
To assess the diagnostic accuracy of the preoperative echocardiogram to detect coronary artery anomalies before and after adding color flow Doppler interrogation of the coronary arteries to the imaging protocol in neonates with TGA.

Methods:
For this retrospective study, the surgical database at this institution was interrogated for infants undergoing the arterial switch operation in the years 2000-12. The preoperative coronary artery description on echocardiogram was correlated with the operative report. The cohort was divided in two eras, 2000-2007 and 2008-2012 since the routine imaging protocol only included color flow Doppler since 2008.

Results:
Among 70 infants with TGA, 16 (23%) had coronary abnormalities based on intra-operative findings. On echocardiography, the number of inconclusive studies declined from 18% to 10% in era 2. However, the sensitivity of the echocardiogram to detect coronary anomalies was modest in both eras (Table 1). Nonetheless, all 70 infants had successful arterial switch operations, suggesting that intraoperative diagnosis was sufficient for a good outcome in most cases.

Conclusions:
This study only showed a modest diagnostic accuracy for routine transthoracic echocardiography to detected coronary anomalies in newborns with complete transposition of the great arteries in our hands. The number of nondiagnostic studies decreased to 10% in era 2 but sensitivity remained unsatisfactory. Clinical routine lacks behind published reports when it comes to accurately delineating coronary anatomy.

Table 1: Diagnostic accuracy of transthoracic echocardiogram for anomalous coronary arteries

<table>
<thead>
<tr>
<th>Era</th>
<th>PPV</th>
<th>NPV</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-07 without Doppler</td>
<td>0.500</td>
<td>0.885</td>
<td>0.571</td>
<td>0.852</td>
</tr>
<tr>
<td>2008-12 with Doppler</td>
<td>0.600</td>
<td>0.762</td>
<td>0.375</td>
<td>0.889</td>
</tr>
<tr>
<td>All</td>
<td>0.538</td>
<td>0.830</td>
<td>0.467</td>
<td>0.867</td>
</tr>
</tbody>
</table>

Abbreviations: PPV positive predictive value. NPV negative predictive value.
Treatment of Avoidant/Restrictive Food Intake Disorder in a Day Hospital Program for Young Patients With Eating Disorders

Susan E. Lane-Loney, PhD, Terri A. Nicely, BS, Emily B. Masciulli, MSW, Rollyn M. Ornstein, MD
Department of Pediatrics, Penn State Hershey Children’s Hospital, Penn State College of Medicine, Hershey, Pennsylvania

Purpose:
To compare treatment outcomes of patients with Avoidant/Restrictive Food Intake Disorder (ARFID), a “new” diagnosis in the DSM-5, to those of patients with anorexia nervosa (AN), bulimia nervosa (BN), and Other Specified Feeding or Eating Disorder/Unspecified Feeding or Eating Disorder (OSFED/UFED) in a day program for young patients with EDs.

Methods:
A retrospective chart review of 177 (92% female) patients 7-16 (13.5 ± 2) yrs of age admitted to the program from 2008-2012 was performed. The program primarily uses an exposure-response prevention treatment paradigm, with extensive family involvement. All patients were classified using the proposed DSM-5 criteria. Both within and between groups analyses (ANOVA, repeated measures linear model) were performed on weight gain and psychometric tests.

Results:
Of the 173 included patients, 22.5% met criteria for ARFID, 53.8% for AN, 11.6% for BN, and 12.1% for OSFED/UFED. Children with ARFID spent fewer weeks in program than those with other EDs (7.4 vs. 11.0, p < 0.0001) and had a significant increase in % median body weight (from 87.1 to 97.3%, p<0.0001), which was similar to the other groups in which weight gain was recommended. Additionally, all patients were found to have significant improvements in their ED behaviors and psychopathology over the course of treatment, as measured by scores on the Children’s Eating Attitudes Test, Children’s Depression Inventory, and Revised Children’s Manifest Anxiety Scale (all p < 0.0001).

ChEAT Total Score Before and After Treatment

Conclusions:
This study demonstrates that patients with ARFID can be successfully treated in the same family-centered day program as patients with other EDs, with comparable improvements in weight and psychopathology in a shorter time period.
Putting Team-Based Learning in “The Cloud”

Martha Peaslee Levine, MD - Associate Professor of Pediatrics, Psychiatry and Humanities, Daniel R. George, PhD - Assistant Professor of Humanities
Penn State College of Medicine, Hershey, Pennsylvania

BACKGROUND:
Team-Based Learning (TBL) has been increasingly used in medical education. It enhances the quality of student learning and builds skills for collaboration in professional settings. While the method is dynamic, the majority of the activity is verbal and contained within the groups.

DESCRIPTION:
At Penn State College of Medicine, we previously integrated Google Docs, a free cloud-based word processor, into a lecture-based course. For this study, we incorporated Google Docs into a TBL session in the first year course, “Socio-Ecological Medicine”. The session required students to watch a “flipped” lecture about tobacco cessation strategies, and come to class prepared to think critically about how to address other leading health indicators from Health People 2020, a program of nationwide health-promotion and disease prevention goals set by the United State Department of health and Human Services.

During class, dual projection screens displayed a power point with the TBL prompts, and a laptop feed that displayed the Google Doc. Within the document, groups were provided space to include discussion and conclusions related to their health-indicators.

Students were given 5-10 minutes to discuss each prompt and transcribe the group’s answers into their section. Faculty leaders observed incoming text on the Google Doc and noted trends and patterns in student responses, which were referenced during the large-group discussion. Students then continued the discussion in their traditional small groups with the Google Doc available as a resource.

RESULTS:
The Google Doc generated a large amount of substantive text, which was utilized as a resource during discussions. Having a “cloud-based” document provided faculty insight into the thought process occurring in groups as formal responses were negotiated.

CONCLUSIONS:
Google Doc may be useful in understanding the learning process in TBL. It can help faculty understand the groups’ thought processes and discussions.
Patient Ratings of Various Eosinophilic Esophagitis Treatment Options

Samantha K. Lin, MD; Neelu Kalra, MD; Allen R. Kunselman, MS; and Gisoo Ghaffari, MD.
Departments of Medicine and Pediatrics, Section of Allergy, Asthma & Immunology, Penn State College of Medicine, Penn State Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Eosinophilic Esophagitis (EoE) is a chronic inflammatory disease of the esophagus. Diagnosis requires ≥15 eosinophils per high power field on esophageal biopsy following two months of adequate treatment with a proton pump inhibitor (PPI). Appropriate treatments include diet modification (Diet) and/or topical steroid therapy (TS). This study assessed which treatments patients were using, and determined patient/caregiver ratings of EoE symptoms, response to treatment, and tolerability of therapy.

Methods:
After IRB approval, patients with biopsy proven EoE followed in our allergy clinic were selected for a questionnaire based phone survey and chart review. We attempted to contact a total of 138 patients who met inclusion criteria. Survey data were obtained for 78 patients (ages 6-76 yrs, mean age 36 yrs ± 20). Patients rated the severity of their symptoms before and after treatment and their overall response to treatment on a scale from 0-5, with 0 being lowest. Treatment groups were compared using the non-parametric Wilcoxon Mann-Whitney test.

Results:
Dysphagia, food impaction, and regurgitation were the most common moderate or severe symptoms before treatment. Overall, moderate/severe symptoms decreased by 82%. The reported treatment regimens were PPI+TS (26%), PPI alone (22%), PPI+TS+Diet (15%), PPI+Diet (13%), TS alone (11%), Diet alone (10%), and TS+Diet (3%). Patients using combination therapy were on average 10 years younger than those using monotherapy, and patients using diet modification (alone or in combination) were on average 12 years younger than patients in the non-diet modification groups. The topical steroid containing treatment groups as a whole had a significantly higher average patient response rating than the non-steroid containing treatment groups (p=0.005). Only 3 patients on a TS reported side effects. Of those patients using diet modification, 15% rated the diet impossible/nearly impossible to follow at home, and 37% rated it impossible/nearly impossible to follow at a restaurant.

Figure 1 summarizes the changes in moderate/severe symptoms with treatment.

Conclusions:
EoE treatments decreased moderate to severe symptoms by 82% with few side effects, though many found diet modifications difficult to follow. Inclusion of a topical steroid in EoE treatment is associated with significantly higher patient response ratings.
Maritoclax Induces Apoptosis in Acute Myeloid Leukemia Cells with Elevated Mcl-1 Expression

Qiang Liu, BS, Kenichiro Doi, PhD, Krishne Gowda, PhD, Brian M Barth, PhD, David Claxton, MD, Shantu Amin, PhD, Hong-gang Wang, PhD
Departments of Pediatrics and Pharmacology, Penn State Hershey Cancer Institute, Penn State College of Medicine, Hershey PA

Purpose:
Acute myeloid leukemia (AML) is one of the deadliest leukemias for which there is an urgent and unmet need for the development of novel treatment strategies. Multiple drug resistance mechanisms mediate poor drug response and relapse in patients, and a selective Mcl-1 inhibitor has long been speculated to be a promising agent in the treatment of AML. Here, we describe that maritoclax, a small molecule Mcl-1 inhibitor, can kill Mcl-1-elevated AML cells through Mcl-1 down-regulation.

Methods:
In both AML cell lines and primary human AML cells, maritoclax-induced Mcl-1 proteasomal degradation and subsequent apoptosis were determined by immunoblotting and cell viability assays. We determined if maritoclax could overcome stroma-mediated drug resistance in leukemia cells by comparing the efficacy of maritoclax and daunorubicin in U937 cells cultured with HS-5 stroma cells. The toxicity of maritoclax compared to daunorubicin to HS-5 cells and primary mouse bone marrow was determined in cell viability and colony formation assays. We also tested the anti-tumor potency of maritoclax in against nude mice bearing U937 xenografts.

Results:
Maritoclax induced the proteasomal degradation of Mcl-1 without transcriptional repression. Maritoclax killed AML cell lines and primary cells with elevated Mcl-1 levels through selective Mcl-1 down-regulation, overcoming Mcl-1-mediated ABT-737 resistance. Maritoclax was more effective than daunorubicin at inducing cell death of leukemia cells co-cultured with stroma cells, while sparing more stroma cells, primary mouse bone marrow cells, as well as hematopoietic progenitor cells than daunorubicin. Moreover, maritoclax administration at 20 mg/kg/d (i.p.) caused significant U937 tumor shrinkage, as well as 36% tumors remission rate in athymic nude mice, without apparent toxicity to healthy tissue or circulating blood (Figure).

Conclusions:
Our studies suggest that maritoclax belongs to a novel class of Mcl-1 inhibitors that has the potential to be developed for the treatment of AML.
Role of Bif-1/SH3GLB1 in Obesity

Ying Liu, MS, Yoshinori Takahashi, PhD, Neelam Desai, MS, and Hong-Gang Wang, PhD
Departments of Pediatrics and Pharmacology,
Penn State College of Medicine, Hershey, Pennsylvania, USA

Purpose:
Bif-1 is a multifunctional membrane curvature-inducing protein involved in the regulation of apoptosis, mitochondrial morphology, endocytic tracking, and autophagy. The purpose of this study is to investigate the role of Bif-1 in the regulation of lipid metabolism and the pathogenesis of obesity and related comorbidities such as type 2 diabetes mellitus and cancers.

Methods:
Wild type and Bif-1 whole body knockout C57BL/6 mice were fed with either normal chow or high fat diet and monitored for body weights weekly over four months. Mice were then subjected to calorimetric clamps to measure their energy expenditure, food intake, and physical activities. Blood was collected to determine levels of adipose tissue-derived hormones, and adipose tissues were isolated for ex-vivo lipolysis, metabolism and immunoblot assays. Glucose tolerance and insulin sensitivity were compared in wild type and Bif-1 knockout mice.

Results:
Bif-1 knockout mice gained significantly more weight compared to the wild type in both genders and both diet types. The Bif-1 knockout mice also showed hyperinsulinemia and hyperleptinemia which are typical complications accompanying obesity. Mechanistically, loss of Bif-1 significantly decreased beta-adrenergic stimulated lipolysis in fresh white adipose tissues isolated from mice as well as in 3T3-L1 adipocytes.

Conclusions:
These results reveal a new role of Bif-1 in the regulation of lipolysis in white adipose tissue, and whole body energy and nutrient homeostasis. Its dysregulation could lead to the development of obesity and potentially metabolic disorders.
Absolute Lymphocyte Count as a Predictor of Mortality in Pediatric ALL

Eric I. Marks, MS4, Junjia Zhu, PhD, Andrew S. Freiberg, MD,
Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Therapy for children with acute lymphoblastic leukemia (ALL) is risk-stratified according to age and leukocyte count at diagnosis. Recently, absolute lymphocyte count (ALC) during induction has been examined as an independent risk factor for mortality and relapse. Prior studies examined single ALC measurements at specific points in time, typically between 15-29 days into treatment, with little investigation into effects outside that window. The goal of this study was to examine the relationship between ALC averaged across multiple spans of time and outcomes in cases of pediatric ALL.

Methods:
ALC measurements of 206 pediatric ALL patients were averaged over 10 day increments, extending from 10 days before diagnosis until day 40 of treatment. ALC as a continuous variable and dichotomized at <350/µL were tested for association with relapse, time until relapse, mortality, and time until death.

Results:
Mortality was significantly increased in patients with lower continuous ALC from day 21-30 of treatment. Patients with ALC<350/µL over the entire 50 days, treatment days 21-30, or treatment days 1-40 were at increased mortality risk. A nonsignificant trend towards increased mortality was observed with ALC<350/µL during treatment days 31-40. Risk of relapse was increased amongst patients with elevated continuous ALC averaged across day 1-10 of treatment, 1-23 of treatment, or the 50 day span of this study. There was no timeframe during which ALC<350/µL was associated with relapse. No relationship existed between continuous ALC or ALC <350/µL and time until relapse or death.

Conclusions:
Our study shows that average ALC<350/µL from day 21-30 of treatment is a risk factor for mortality in pediatric ALL. Although not statistically significant, average ALC<350/µL from day 31-40 may also be of some utility.
Evaluation of Four Pediatric Cardiopulmonary Bypass Circuits in Terms of Perfusion Quality and Capturing Gaseous Microemboli

Ryan K. Mathis, Judith Lin, Natalie M. Dogal, Feng Qiu, Allen R. Kunselman, Shigang Wang and Akif Ündar
Pediatric Cardiovascular Research Center, Departments of Pediatrics, Public Health and Sciences, Surgery and Bioengineering, Penn State College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
This study compared four pediatric cardiopulmonary bypass (CPB) circuits with four different hollow-fiber membrane oxygenators and their specific reservoirs, Capiox RX15, Quadrox-i pediatric, Quadrox-i pediatric with integrated arterial filter (IAF) and KIDS D101, in a simulated CPB circuit to test their ability to maintain hemodynamic properties, remove gaseous microemboli (GME), and to test the amount of blood “stolen” by the arterial filter purge line.

Methods:
The circuit was first primed with Ringer’s Lactate solution, then red blood cells were added and the hematocrit was maintained at 30%. A 5-cc bolus of air was injected just proximal to the venous reservoir over a thirty-second interval and GME were monitored using an Emboli Detection and Classification quantifier. Transducers were placed at pre-oxygenator, post-oxygenator and distal arterial line (post-filter) positions. Flow probes were also placed both pre and post filter. The injections were made at three flow rates, hypothermic and normothermic temperatures, and with the purge line in both the opened and closed positions. Six injections were done at each of the 12 experimental conditions.

Results:
Results demonstrated that GME in the arterial line increased with increasing temperature and flow rate. The Capiox RX15 had the least GME in the arterial line at all experimental conditions. The KIDS D101 had the largest pressure drop and the lowest retention of hemodynamic energy, while the Capiox had the lowest pressure drop (Figure 1). All of the oxygenators had a similar amount of “stolen” blood flow and it was consistently under 10% of the total flow reaching the patient.

Conclusions:
This study demonstrated that the Capiox RX15 circuit was the most efficient pediatric circuit tested in terms of removing GME from the CPB circuit. The pressure drop and THE of the Capiox, the Quadrox-i and the Quadrox-i with arterial filter were all similar.

Figure 1. Mean pressure drop across all four oxygenators at normothermic and hypothermic conditions. * p<0.001: KIDS D101 vs. other three oxygenators; # p<0.01: Quadrox-i with IAF vs. Capiox RX15 and Quadrox-i.
Correlates of Suicide Ideation and Attempts in Children and Adolescents with Eating Disorders

Susan Dickerson Mayes PhD, Julio Fernandez-Mendoza PhD, Raman Baweja MD, Susan Calhoun PhD, Fauzia Mahr MD, Richa Aggarwal MD, and Mariah Arnold MA
Department of Psychiatry, Division of Child Psychiatry, Penn State College of Medicine, Hershey, PA

Purpose:
Our study investigated the frequency of suicide ideation and attempts in children and adolescents with anorexia and bulimia and determined risk factors. Our study is unique from previous research in that our sample is younger than all other studies and uses a wide variety of sleep, psychological, and demographic variables to determine which of these factors are significantly related to suicide behavior.

Methods:
Mothers rated suicide ideation and attempts in 90 children with bulimia or anorexia ages 7-18. Predictor variables of suicide behavior were (1) demographic data (age, IQ, gender, race, and parent occupation), (2) eating disorder types and symptoms (BMI percentile and degree of restricting, self-induced vomiting, and binging), (3) comorbid diagnoses (depression, anxiety disorder, ADHD, and oppositional defiant disorder), (4) sexually or physically abused or bullied, and (5) maternal ratings of sleep disturbances, behavior problems (e.g., bullies other children, explosive, defiant, aggressive, and impulsive), anxiety, sadness, and somatic symptoms (e.g., lacks energy, headaches, and stomachaches).

Results:
Suicide ideation was more prevalent in bulimia (43%) than anorexia (20%). All children with bulimia who had ideation had attempts, whereas only 3% with anorexia had attempts. Predictors of suicide ideation were behavior problems and sleep disturbance. Predictors of attempts were bulimia, self-induced vomiting, nightmares, and physical or sexual abuse. The other variables did not contribute significantly more to the prediction of suicide behavior.

Conclusions:
Our data suggest that children and adolescents with eating disorders should not only be screened for suicide ideation and attempts, particularly those with bulimia, but also for sleep disturbances, behavior problems, and physical or sexual abuse, which increase the risk of suicide behavior. These symptoms should be targeted for treatment to reduce suicide behavior in patients with eating disorders.
Mother, Father, and Teacher Agreement on Victimization and Bullying in Children with Psychiatric Disorders

Susan Dickerson Mayes, PhD, Susan L. Calhoun, PhD, Farhat Siddiqui, MD, Raman Baweja, MD, Daniel A. Waschbusch, PhD, Richard E. Mattison, MD, and Dara E. Babinski, PhD
Department of Psychiatry, Division of Child Psychiatry, Penn State College of Medicine, Hershey, PA

Purpose:
This is the first study to investigate mother, father, and teacher agreement on bullying and victimization in a large psychiatric sample of young children and adolescents.

Methods:
Mothers, fathers, and teachers rated degree of bullying and victimization for 1,723 children 2-16 years of age with autism, intellectual disability, ADHD-Combined type, ADHD-Inattentive type, depression, anxiety disorders, eating disorders, and oppositional defiant disorder.

Results:
Mothers and fathers did not differ in rating their child as a bully, and mothers were only slightly more likely to consider their child a victim than fathers. Agreement between teachers and mothers and fathers was poor, particularly for victimization. Approximately half of mothers and fathers thought their child was a victim, which was nearly two times the percentage for teachers. Parents were 1.2 times more likely than teachers to perceive their child as a bully. The majority of parents reported that their child was involved in bullying behavior (as a victim or a bully), whereas the majority of teachers reported that the children were neither a victim nor a bully. For all informants, victim percentages were twice as high for our children as percentages reported by parents and teachers in general population studies, indicating that children with psychiatric disorders are at high risk for victimization. Informant discrepancies in our study were not moderated by age, IQ, gender, race, or socioeconomic status.

Conclusions:
Our results and those of other researchers indicate that teachers underestimate bullying. Schools must implement procedures requiring all school personnel to report instances of bullying in all locations (playground, hallway, bus, and cafeteria) to fully appreciate the scope of the problem and determine intervention needs. This is critical because research shows that some intensive multi-component school wide anti-bullying programs are effective in reducing bullying behavior.
Suicide Ideation and Attempts are Associated with Comorbid Oppositional Defiant Disorder and Sadness in Children with ADHD

Susan Dickerson Mayes PhD, Susan L. Calhoun PhD, Raman Baweja MD, Lance Feldman MD, Ehsan Syed MD, Angela A. Gorman PhD, Jose Montaner MD, Jitendra Annapareddy MD, Nidhi Gupta MD, Ademola Bello MD, and Farhat Siddiqui MD
Department of Psychiatry, Division of Child Psychiatry, Penn State College of Medicine, Hershey, PA

Purpose:
Our study determined the relative importance of multiple demographic and psychological variables as risk factors for suicide ideation and attempts in a large sample of children with ADHD.

Methods:
Mothers rated suicide ideation and attempts on a 4-point scale (not at all, sometimes, often, and very often a problem) in 925 children with ADHD (3-16 years). Predictor variables were demographic data and maternal ratings of bullied by peers, bullies others, sad, anxious, oppositional, aggressive, angry/explosive, impulsive, social problems (e.g., difficulty making friends), eating and sleep disturbances, somatic complaints (e.g., headaches and stomachaches), and difficulty learning.

Results:
Suicide ideation and attempts were more than twice as common in ADHD-Combined type as in ADHD-Inattentive type. Ideation occurred in 19% of children with ADHD-C and in 7% with ADHD-I. Percentages for attempts were 7% and 3%. For children with comorbid sadness and oppositional defiant disorder (ODD), 46% had ideation and 21% had attempts (versus 6% and 2% for ADHD alone). For children with ideation, 78% had ODD or sadness. For children with attempts, 84% had ODD or sadness. The strongest predictors of suicide behavior were maternal ratings of angry/explosive, sad, and aggressive. The 16 other demographic variables (age, gender, IQ, and race) and psychological variables did not contribute significantly more to prediction in regression analysis.

Conclusions:
All children with ADHD should be screened for suicide ideation and attempts at every appointment with their primary care physician or mental health professional. This is especially critical for children who have ODD symptoms or sadness. These symptoms are common in ADHD, particularly in ADHD-C. These risk factors should be targeted for intervention in order to reduce and prevent suicide behavior. Effective pharmacological, behavioral, and cognitive-behavior interventions are available for children that decrease behavior problems and depression, thereby decreasing the risk of suicide.
SUICIDE BEHAVIOR AND BULLYING IN CHILDREN WITH PSYCHIATRIC DISORDERS AND GENERAL POPULATION SAMPLES

Susan Dickerson Mayes, Ph.D., Raman Baweja, M.D. Susan L. Calhoun, Ph.D., Ehsan Syed, M.D., Fauzia Mahr, M.D., Farhat Siddiqui, M.D. Department of Psychiatry, Penn State Hershey Medical Center, Hershey, PA 17033

Purpose:
Bullying is of huge national and international concern, and massive efforts are underway to reduce bullying and its consequences. Across studies, the median percentage of children and adolescents who are neither a bully nor victim is 62%, whereas 17% are victims only, 13% are bullies only, and 6% are bully/victims. Studies of the relationship between bullying and suicide behavior yield mixed results. This is the first study to compare frequencies of suicide behavior in four bullying groups (bully, victim, bully/victim, and neither) in two large psychiatric and community samples of young children.

Methods:
Maternal ratings of bullying and suicide ideation and attempts were analyzed in 1,291 children with psychiatric disorders and 658 children in the general population 6 to 18 years of age. Children in the psychiatric sample included those with ADHD, autism, oppositional defiant disorder, anxiety, depression, and eating disorders.

Results:
For both the psychiatric and community samples, suicide ideation and attempt scores for bully/victims were significantly higher than for victims only and for neither bullies nor victims. Differences between victims only and neither victims nor bullies were nonsignificant. Controlling for conduct problems and sadness, suicide behavior did not differ between the four bullying groups. All children with suicide attempts had a comorbid psychiatric disorder, as did all but two children with suicide ideation.

Table 1. Bullying Group and Percent of Children with Suicide Ideation and Attempts

<table>
<thead>
<tr>
<th>Group</th>
<th>% psychiatric sample</th>
<th>% general population sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ideation</td>
<td>Attempts</td>
</tr>
<tr>
<td>Bully and victim (288/48)</td>
<td>32.6</td>
<td>11.5</td>
</tr>
<tr>
<td>Bully only (100/47)</td>
<td>25.0</td>
<td>9.0</td>
</tr>
<tr>
<td>Victim only (479/134)</td>
<td>15.0</td>
<td>5.6</td>
</tr>
<tr>
<td>Neither (424/429)</td>
<td>9.0</td>
<td>3.8</td>
</tr>
</tbody>
</table>

At least sometimes.

Conclusions:
Although the contribution of bullying per se to suicide behavior independent of sadness and conduct problems is small, bullying has obvious negative psychological consequences, which make intervention imperative. Interventions need to focus on the psychopathology associated with being a victim and/or perpetrator of bullying in order to reduce suicide behavior.
Victims and Perpetrators of Bullying: Differences in Frequencies between Psychiatric Diagnoses

Susan Dickerson Mayes, PhD, Susan L. Calhoun, PhD, Raman Baweja, MD, Jose Montaner, MD, and Fauzia Mahr, MD
Department of Psychiatry, Division of Child Psychiatry, Penn State College of Medicine, Hershey, PA

Purpose:
This is the first study comparing the frequency of bullying behavior in a large sample of children with specific psychiatric disorders or typical development controlling for comorbidity across groups. Such analyses are important in order to identify psychiatric diagnoses that place children at risk for bullying behavior and to understand the psychological problems that may both underlie and result from bullying behavior.

Methods:
Mothers rated the degree to which their child was a bully and a victim for 1,707 children 6-18 years of age.

Results:
Children with autism, intellectual disability, and ADHD-Combined type had significantly higher victim and bully scores than children with ADHD-Inattentive type, depression, anxiety, eating disorders, and typical development. Children with ADHD-I, anxiety, and depression had higher victim scores than children with eating disorders and typical development, but these five groups did not differ from each other as bullies. The eating disorders and typical groups were the only groups in which the majority of children were not involved in bullying behavior as a victim or bully. Comorbid oppositional defiant disorder explained the higher bully scores for ADHD-C, autism, and intellectual disability. In contrast, victimization was not linked with any single psychological condition.

Conclusions:
Most psychiatric disorder place children at risk for victimization. The relationship may be bi-directional in that children who have psychiatric disorders may be targets because of their symptoms, differences, and vulnerability, and they may experience mental health problems as a result of victimization. Because of the significant connection between bullying and psychiatric disorders, intervention must continue to focus on treating the psychopathology underlying bullying, as well as the psychological problems resulting from bullying. Children should routinely be screened and monitored for bullying and victimization in school, primary care, community, and clinical settings in order to identify those in need of mental health treatment.
Efficacy of Using Medical Students and a Flipping the Classroom Program in Nutrition Education for 4\textsuperscript{th} Grade Students

Christian S. McEvoy, MPH, Kathryn M. Cantore, BA, LeAnn N. Denlinger, BS, Nicole M. Stevens, BS, Steven C. Swavely, BS, Anne A. Odom, BA, Marsha B. Novick, MD
Department of Pediatrics, Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
To evaluate the effectiveness of a flipped classroom program, designed and implemented by medical students, in communicating nutrition education to fourth grade students and to characterize teachers' assessments of the program, which was designed to minimize burden on teachers.

Methods:
A flipped classroom model is one in which students watch a video that introduces core learning objectives prior to a classroom session in which concepts are solidified through interactive activities. The healthSLAM (hS) program includes a web-based video that delivers nutrition education didactics, and it includes a classroom portion in which medical students guide exercises to reinforce nutrition concepts discussed in the video. A pre-test and post-test were given to students and teachers completed a survey to determine the effectiveness of the curriculum.

Results:
Significant improvements in nutrition knowledge in both median and mean test scores were found ($p<0.001$), and the raw pre-test and post-test score distributions were found to be homogeneous across the different classrooms studied. The hS curriculum was most effective at improving student scores regarding protein (27.1%; $p<0.001$), the purpose of protein (25.9% $p<0.001$), and fruits and vegetables (18.1%; $p=0.621$). Teachers reported the hS curriculum to be effective and grade-appropriate material.

Figure 1 summarizes the percentage of students answering incorrectly on pre-test and correctly on post-test, per topic of question.

Conclusions:
HealthSLAM, rooted in “flipping” pedagogy by using a video didactic lecture and medical student volunteers to solidify concepts, effectively communicates healthy nutrition information to elementary school students and is endorsed by educators.
Sex differences in the lung inflammatory microRNA profile in a mouse model of ozone-induced oxidative stress

Vikas Mishra¹; Susan L. DiAngelo¹; Joanna Floros¹; Patricia Silveyra¹
¹Department of Pediatrics, Penn State College of Medicine, Hershey, PA-17033. USA.

Purpose:
Ambient Ozone (O₃) affects lung function and immunity. Women and children are more susceptible to O₃-related damaging effects. The mechanisms behind sex differences in susceptibility of pulmonary disease are currently poorly understood. We investigated the effect of O₃-induced oxidative stress in the pulmonary expression of miRNAs associated with inflammation. We also investigated potential target genes, miRNA-gene networks and gender differences.

Methods:
Adult male and female mice were exposed to O₃ (2ppm) or filtered air for 3hs (n=4/group). Lung tissue was collected 4 hours post-exposure, and an array of 84 miRNAs, previously implicated with immunity and inflammation were assayed. Software mirPath was used to predict miRNAs-gene target interactions.

Results:
Differential expression of miRNAs was found between O₃-exposed vs. control mice, and between O₃-exposed females vs. males. O₃-exposure exhibited a signature of miRNAs with known association in lung cancer. O₃-exposed males resulted in up- and down-regulation of 20 and 11 miRNAs respectively; while in females, up-regulation of 17, and down-regulation of 17 miRNAs was found. Comparison of O₃-exposed males and females revealed up-regulation of 15 and down-regulation of 15 miRNAs. O₃-treated males and females exhibited divergent miRNA profiles with only mir-130 and mir-29b up-regulated in both groups, but only significant in males. Among down-regulated miRNAs, only mir-568 was found in both groups. Functional characterization of miRNAs indicated possible interference in regulation of O₃-associated inflammatory events, immune response and epithelial damage with overall agreement in pathways of cell-cycle deregulation and angiogenesis. Statistically significant down-regulation of miR-106a-5p (p<0.001) and miR-568 (p=0.04) and up-regulation of miR-15a-5p (p<0.01) and miR-30b-5p (p=0.03) in female mice lungs with known regulatory effects in progesterone-mediated oocyte maturation was observed.

Conclusions:
Sex differences exist in the lung inflammatory miRNA expression profile in response to O₃. Divergent pool of miRNAs indicated mechanistic differences in O₃-associated inflammatory processes between males and females.
Effects of restricted diets on challenging behavior and symptomology in young children with autism spectrum disorders and chronic constipation

Austin Mulloy, PhD, Penn State College of Education, University Park, PA; Pasquale Accardo, MD, Donald Oswald, PhD, Virginia Commonwealth University, School of Medicine, Richmond, VA; Irina Cain, Virginia Commonwealth University, School of Education, Richmond, VA

Purpose:
Survey research and parent testimonials suggest restricted diets are often used in treatment of autism spectrum disorders (ASD). However, the scope and rigor of research on diets’ effects is greatly limited. Consequently, parents and service providers lack science-based guidance for diet-related decisions. The purpose of this study was to document effects of a popular diet on challenging behaviors, core ASD symptoms, and gastrointestinal functioning in children with ASD and gastrointestinal dysfunction.

Methods:
The restricted diet involved combined protocols of the Specific Carbohydrate Diet and Low Oxalate Diet, and elimination of cow milk to protect against confounds (e.g., lactose maldigestion). Single-case ABAB withdrawal designs were used to examine relations between diet conditions (i.e., baseline and restricted diet) and levels of target behaviors during structured play sessions with a parent. Target behaviors were operationally defined, measured with frequency counts, and included child (a) verbalizations, (b) gestures, (c) vocal stereotypes, (d) echolalia, (e) non-sequiter comments, (f) responses to parent’s bids for attention, (g) initiated bids for parent’s attention, (h) elopement, (i) defiance, and (j) tantrums. Additionally, parents’ anecdotal reports on children’s behaviors and gastrointestinal functioning (e.g., stool counts) were recorded. Two children with ASD and chronic constipation, who hadn’t previously followed a therapeutic diet, participated in the study.

Results:
Behavioral measures and parent reports suggest consumption of the restricted diet was related to reductions in challenging behavior and increases in stool frequency. No systematic differences were observed between diet conditions on communication, joint attention, or stereotypical behaviors. Figure 1 presents data on challenging behavior in one participant.

Conclusions:
Results justify further research on the restricted diet and gastrointestinal functioning as an effect mediator. The small sample limits confidence in conclusions, however, the restricted diet appears to hold promise as treatment for challenging behavior and constipation, yet not for core ASD symptoms.
Novel Anti-Leukemia Therapy with an Isatin Derivative: Dual Inhibition of Tubulin Polymerization and AKT Pathway

Sunil Muthusami, M.D., Mansi Sachdev, M.D., Krishnegowda Gowdahalli, PhD., Chunhua Song M.D., PhD., Shantu Amin Ph.D., Sinisa Dovat M.D., Ph.D. Departments of Pediatric Hematology/Oncology, and Pharmacology, Penn State College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
The antitumor drugs, vinca alkaloids and taxanes, inhibit mitosis by targeting microtubules. Their major drawback is limited efficacy as single agents, prompting the quest for additional targets/agents with enhanced therapeutic potency, decreased side effects and drug resistance. Recent studies demonstrated the superiority of dibromo-isatin over other isatins in microtubule inhibition on U937 (leukemic monocyte lymphoma) cell lines.

Isatin-11, a novel dibromo-isatin has a thiocyanate conjugation, which augments the microtubule inhibition with Akt inhibitory activity. In solid tumor cell lines, Isatin-11 demonstrated greater inhibition of tubulin polymerization compared with vinblastine, and significant AKT inhibition. The PI3K/AKT/mTOR pathway is often abnormally activated in childhood leukemia due to constitutive activation of AKT, providing a rationale for targeted therapy. AKT inhibition results in apoptosis with decreased resistance to chemotherapy.

By inhibiting microtubules and the AKT pathway, Isatin-11 has anti-leukemia potential. We aimed to determine the potency of Isatin-11 and its mechanism of action on a panel of human leukemia and lymphoma cell lines.

Methods:
We performed cytotoxicity assays to quantify the therapeutic effect of Isatin-11 on acute lymphoblastic leukemia, acute myeloid leukemia, T-cell ALL and lymphoma cell lines. Annexin V/7-AAD staining was done at 24 and 48 hours post treatment. Caspase 3/7 assays were done at 24 hours post treatment.

Results:
Isatin-11 treated leukemia cell lines demonstrated significant dose-dependent cytotoxicity with IC50 values: 0.2 μM for Nalm-6 (B-ALL), CEM (T-cell ALL), HL-60, NB4 (APML) and Ramos (Burkitt's lymphoma) cell lines; 0.5 μM for MOLT-4 (T-cell ALL) ; 1 μM for U937 (AML). The Annexin V/7-AAD staining demonstrated significant apoptosis in all cell lines at 24 and 48 hours. Caspase 3/7 activity was increased 24 hours post treatment.

Conclusions:
Isatin-11 is effective against leukemia cell lines and potent at low micromolar concentrations showing promise for further testing in leukemia. Additional studies to elaborate its mechanism of action are underway.
Pulmonary arterial hypertension following dasatinib treatment in an adolescent with myelogenous leukemia – case report and review of the literature

Athira Nair, MD, Vincent Aluquin, MD, MS, Melanie Comito, MD, Linda B Pauliks, MD, MPH, Department of Pediatrics, Division of Cardiology and Division of Hematology-Oncology Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Background:
Dasatinib, a kinase inhibitor, is used as treatment for chronic myelogenous leukemia (CML). Pulmonary arterial hypertension (PAH) has been reported as potential side effect of this therapy in adults but not in children.

Case presentation:
A 19 year old Caucasian female was admitted with syncope and exertional dyspnea. She had a 1-year history of CML, originally presenting in blast crisis. She received dasatinib for 4 months which was discontinued prior to proceeding to allogeneic stem cell transplant. She remained in remission and was 6 months from her transplant when she presented with syncope. Cardiac workup showed PAH at 87% of systemic level by catheterization and echocardiogram (Figure 1). Patient’s symptoms didn’t resolve with sildenafil but improved after adding intravenous prostaglandins.

Discussion:
Kinase inhibitor therapy is considered one of the most promising innovations in oncology but may have significant side-effects. Review of the adult literature showed 18 prior cases reported of PAH after dasatinib in CML. The delayed onset of PAH in this teenage patient was different from prior case reports. Differential diagnosis included Idiopathic PAH, pulmonary veno-occlusive disease, and PAH secondary to myeloproliferative disorders. However, the patient had documented normal pulmonary artery pressures prior to the current illness and no evidence of the other two. Pediatric oncologists and cardiologists should be aware of this rare (<1%) but significant side effect of dasatinib.

Figure 1: Serial echocardiographic estimates of pulmonary artery pressure in a teenage patient with CML
Exposure Therapy with a Nonverbal Child: A Case Report

Neel Nene, MD, MBA, MS, Farhat Siddiqui, MD, Diane Jasmin, DO, Timothy Zeiger, PsyD, Lidija Petrovic-Dovat, MD
Child Psychiatry, Department of Psychiatry, Penn State College of Medicine, Hershey, Pennsylvania, USA

Purpose:
To develop and implement an exposure based intervention for a non-verbal child with CHARGE syndrome who developed anxious symptoms and behaviors (e.g.-hair touching, vocal sounds) after a stressful medical hospitalization.

Methods:
Baseline frequencies of the anxious symptoms and behaviors were collected during the intake psychotherapy session. The hair touching and vocal sounds occurred 4-5 times per minute without mention of the hospitalization. When the hospitalization was mentioned the hair touching and vocal sounds increased to 5-10 times per minute. During a preferred activity (e.g.-coloring) the behaviors occurred 0 times per minute. An exposure session was planned with the mother and child during the intake psychotherapy session. The exposure session was hospital based. Relaxation strategies (e.g.- playing with a service dog in the hospital lobby) were introduced before taking the child and family to the medical floor on which she had been hospitalized. There were no anxious behaviors prior to entering the medical floor by visual observation. The child and family interfaced with a nurse’s aide. The child’s hair touching and vocal sounds re-emerged (5-10 times per minute). Relaxation strategies were introduced (e.g.-verbal reassurance). The behaviors decreased in frequency to (0-5 times per minute). As the child attained a state of relaxation and was observably more comfortable in the environment the behaviors occurred 0 times per minute. Developed with the child and family were replacement behaviors (e.g.- alternative hand gestures) and transitional objects (e.g.-hand written message from the nurse to the child, pictures drawn by the child and nurse together, and photographs and videos taken during the visit).

Results:
Post exposure, the child with accuracy (80%) was able to use with and without verbal prompting from adults the replacement behaviors. The child was able to request through a communication devise or hand gestures her desire to see the transitional objects created during the intervention. The results were maintained for months following intervention.

Conclusions:
The child’s anxious symptoms and behaviors improved from baseline observation and frequency data collected prior to the exposure based intervention.
Prevalence and Characteristics of the DSM-5 Avoidant/Restrictive Food Intake Disorder in a Cohort of Young Eating Disordered Patients in Day Treatment

Terri A. Nicely, Susan E. Lane-Loney, PhD, Emily B. Masciulli, LCSW, Christopher S. Hollenbeak, PhD, Rollyn M. Ornstein, MD
Departments of Pediatrics, Surgery, and Public Health Sciences, Penn State Milton S. Hershey Medical Center, Penn State College of Medicine, Hershey, Pennsylvania

Purpose:
To compare the prevalence and clinical presentation in a cohort of patients with the new DSM-5 diagnosis Avoidant/Restrictive Food Intake Disorder (ARFID) to that of patients with anorexia nervosa (AN), bulimia nervosa (BN) and Other Specified Feeding or Eating Disorder/Unspecified Feeding or Eating Disorder (OSFED/UFED). ARFID includes children who present with restricted nutrition leading to low body weight, but without body image distortion and fear of weight gain.

Methods:
A retrospective chart review of 177 (93% female) patients 7-16 (13.5 ± 2) yrs old admitted to an eating disorders (ED) day program from 2008-2012 was performed. Patients were classified using the proposed DSM-5 criteria. Descriptive and between-groups analyses (Chi-square, ANOVA) were performed on demographic and physical characteristics, clinical features, psychological comorbidities, and psychometric tests.

Results:
Of the 173 included patients, 22.5% met criteria for ARFID, 53.8% for AN, 11.6% for BN, and 12.1% for OSFED/UFED. The ARFID group was younger than the non-ARFID group (11.1 vs 14.2 yrs, \( p < 0.0001 \)) and had a greater proportion of males (20.5 vs 4.5%, \( p = 0.001 \)). Similar degrees of weight loss and malnutrition were found between groups. Patients with ARFID reported greater fears of vomiting and/or choking (43.6%) and food texture issues (25.6%) than those with other EDs (<1%, \( p < 0.0001 \)), as well as greater dependency on nutritional supplements at intake (46.2 vs 14.2%, \( p < 0.0001 \)). Children’s Eating Attitudes Test scores were lower for children with than without ARFID (\( p < 0.0001 \)). A higher comorbidity of anxiety disorders (\( p < 0.0001 \)), pervasive developmental disorder (\( p=0.001 \)), and learning disorders (\( p< 0.0001 \)) and a lower comorbidity of depression (\( p < 0.0001 \)) were found in those with ARFID.

Conclusions:
This is the first study to describe and compare children and adolescents with the newly articulated diagnosis of ARFID to those with other EDs undergoing day treatment. This study demonstrates that there are significant demographic and clinical characteristics that differentiate children with ARFID from those with other EDs, and helps substantiate the recognition of ARFID as a distinct ED diagnosis in the DSM-5.
14-3-3 isoforms bind directly Exon B of the 5'UTR of human surfactant Protein A2 mRNA – correlation with SP-A2 protein expression

Georgios T. Noutsios¹, Paul Ghattas¹, Stephanie Bennett¹, and Joanna Floros¹,²
¹Center for Host Defense, Inflammation, and Lung Disease (CHILD) Research Department of Pediatrics and ²Department of Obstetrics and Gynecology, College of Medicine, The Pennsylvania State University, Hershey, Pennsylvania, USA

Purpose:
Human surfactant protein A, an innate immunity molecule is encoded by two genes SFTPA1 (SP-A1) and SFTPA2 (SP-A2). The 5' untranslated (5'UTR) splice variant of SP-A2 (ABD), but not of SP-A1 (AD), contains exon B (eB). eB is an enhancer for transcription and translation, and contains cis regulatory elements. Specific trans-acting factors including 14-3-3, bind eB. The 14-3-3 protein family contains 7 isoforms (ζ/δ, β/α, τ/θ, ε, γ, η, σ) some of which were found by mass spectroscopy to be present in eB electromobility assays (REMSA) (AJPLMP 304:L722, 2013). Here we sought to investigate whether 14-3-3 isoforms bind directly or indirectly to SP-A2 5'UTR.

Methods:
We employed three different approaches: i) REMSAs were performed, where either NCI-H441 cell extracts or purified 14-3-3 isoforms (β, η, τ, ζ) expressed in E. coli were incubated with wild type eB-, and random- RNAs. Formed complexes were analyzed with mass spectroscopy, ii) Surface Plasmon Resonance analysis (Biacore), and iii) eB RNA pull down assays in tandem with mass spec. We also used siRNAs to knock-down isoforms of 14-3-3 in NCI-H441 cells and determine the effect on SP-A2 expression.

Results:
We found by REMSA that 14-3-3 isoforms β, τ, and η (but not ζ) bind directly eB; these do not bind SP-A1 (AD) that does not contain eB. Moreover, when isoforms 14-3-3 β, τ, and η were tested with Biacore and pull down assays, a direct binding to eB RNA was observed as with REMSA. Isoform 14-3-3 ζ was not found to bind eB directly with REMSA, Biacore, and pull down assays. Knock-down of 14-3-3 isoforms β/α, η and σ was correlated with down-regulation of SP-A2 expression. Knock-down of 14-3-3 ζ isoform that did not bind eB directly had no effect on the expression levels of SP-A1 or SP-A2 proteins.

Conclusions:
These results suggest that isoforms of 14-3-3 protein family affect the differential regulation of SP-A1 and SP-A2 by binding directly to eB of the SP-A2 5'UTR.

Supported by NIH HL34788
A Home-Based Survey on Diarrheal Knowledge Among Mothers in San Pablo

Anne Odom, B.A.; Christian McEvoy, MPH; Diana Filtz, B.S.; Brandt Groh, M.D.
The Pennsylvania State University College of Medicine, Department of Pediatrics, Penn State Hershey Children’s Hospital, Hershey, PA, USA

Purpose:
To assess the prevailing knowledge regarding diarrhea and the most common forms of treatment in a rural, coastal Ecuadorian town.

Methods:
An interviewer verbally administered a survey assessing diarrheal knowledge to women in San Pablo, Ecuador. Survey data were analyzed to assess knowledge of diarrheal disease and treatments in this study population with respect to ages of children living in each participant’s home.

Results:
Characteristics of diarrheal disease were identified correctly by 31% of all women. The characteristics of diarrhea was correctly identified by 41% of the women with children under 18 years of age, and 59% reported using oral rehydration therapy. Of the women with children over 18 years of age, 46% correctly defined the characteristics of diarrhea, and 23% reported no previous knowledge of an oral rehydration therapy. In the population of women using ORT, only 65 women used ORT only without antibiotics, antidiarrheals, or other incorrect methods. Within the group of 65 using ORT, 0 created the correct formulation set forth by the WHO, while 16 utilized prepared solutions, Pedialyte or Suero Oral. Additionally, within the group of women using exclusively ORT, only 7 women could correctly define and provide correctly prepared solutions to treat diarrheal disease. Thus, of the entire sampled population of 212 women, only 10.8% could correctly define diarrhea and correctly treat with an appropriately prepared oral rehydration therapy.

Conclusions:
One of the greatest barriers to curtailing diarrheal disease is an adequate knowledge of the disease and its transmission. Prevention of the sequelae of pediatric diarrhea hinges on two steps taken by mothers in San Pablo. First, mothers must recognize the symptoms of diarrhea, and second mothers must treat diarrhea appropriately. Of the women we interviewed, only 10.8% could complete those two steps. In order to further decrease the burden of pediatric diarrheal disease in San Pablo, it is imperative to educate mothers in how to identify and treat diarrhea in their children.
Skin Conductance Provides Early Objective Identification of Neonatal Opiate Withdrawal

Christiana Oji-Mmuo, MD, Kim Doheny, PhD, Eric Michael, MD, Charles Palmer, MD
Division of Newborn Medicine, Department of Pediatrics. Penn State College of Medicine,
Penn State Hershey Children’s Hospital, Hershey, PA

Purpose:
To determine if SC measures correlate with the Modified Finnegan scores (MFS) and to
determine which infants will require treatment.
Neonatal Abstinence Syndrome (NAS) is a growing public health problem leading to lengthy
hospital stays. In NAS, autonomic dysregulation occurs with norepinephrine levels elevated
above baseline. There is a need for validation of tools for objectively assessing NAS symptoms in
afflicted neonates. Skin conductance (SC) measures the sympathetic system directly through skin
surface electrode changes mean of peak response (MP) and electrodermal responses/sec
(EDR/s)] induced by palmar and plantar sweating.

Methods:
In this prospective study, we enrolled 13 opiate-exposed term infants without anomalies or
exposure to magnesium at the time of delivery. SC and MFS were obtained for all infants at 24-
48 hours of life prior to pharmacological intervention. Trained nurses with established inter-rater
agreement >85% and blinded to SC measures performed the MFS within 2 hours of SC
measurement. Infants’ SC and behavioral responses were observed and video recorded before,
during, and after heel lance for routine newborn metabolic screening.

Results:
There was a significant positive correlation between SC (MP) and the Modified Finnegan Score
(Rs = 0.66; P = 0.02) at baseline. In a 2-group comparison of infants by need for later
pharmacological treatment, there was a significantly higher baseline SC (MP) in infants who went
on to require morphine for NAS symptoms.

Conclusions:
Baseline SC levels were elevated prior to the need for pharmacological therapy and were
positively correlated with MFS. Therefore, SC provides early, objective identification of NAS
which may be used as a predictive tool.
Compliance of camps in the United States with guidelines for health and safety practices

Robert P. Olympia, M.D., Kaylee Hollern, B.S., Caitlin Armstrong, B.S., Pelumi Adedayo, B.S., Jennifer Dunnick, MPH, Jessica Hartley, B.S.
Penn State Hershey Children’s Hospital, Penn State College of Medicine, Hershey, Pennsylvania, USA

Purpose:
In 2011 the American Academy of Pediatrics (AAP) published recommendations focusing on the health appraisal of children before attending camp and guiding health and safety practices for children while in camp. The objective of this study is to determine the compliance of camps in the U.S. with guidelines for health and safety practices as set forth by the AAP.

Methods:
A cross-sectional questionnaire based study was conducted during the summer of 2012. An electronic questionnaire, developed by the authors to reflect guidelines as set forth by the AAP, was distributed to camp administrators as identified by three on-line databases.

Results:
Analysis was performed on 433 completed questionnaires. 14% of camps were considered medically related. 93% of camps have established relationships with community EMS, 34% with local orthodontists, and 37% with local mental health professionals. Camps reported the immediate availability of the following: automated external defibrillators (75%), respiratory rescue inhalers (44%), epinephrine autoinjectors (64%), cervical spine collars (62%), backboard with restraints (76%). Camps reported the presence of the following written health policies: dehydration (91%), asthma and anaphylaxis (88%), head injuries (90%), seizures (78%), cardiac arrest (76%), drowning (73%). While 93% of camps have a disaster response plan, 15% never practice the plan. 68% of camps are familiar with community evacuation plans and 67% have access to vehicles for transport. Camps reported the presence of the following written disaster policies: fire (96%), tornadoes (68%), arrival of suspicious individuals (84%), hostage situations (18%).

Conclusions:
Areas for improvement in the compliance of U.S. camps with specific recommendations for health and safety practices were identified, such as medically preparing campers prior to their attendance, developing relationships with community health providers, increasing the immediate availability of several emergency medications and equipment, and developing policies and protocols for medical and disaster emergencies.
Distribution of Eating Disorders in Children, Adolescents, and Young Adults Using the Proposed DSM-5 Criteria For Eating and Feeding Disorders

Rollyn M. Ornstein MD\textsuperscript{a}, David S. Rosen MD\textsuperscript{b}, Kathleen M. Mammel MD\textsuperscript{c}, S. Todd Callahan MD\textsuperscript{d}, Sara Forman MD\textsuperscript{e}, Susan Jay MD\textsuperscript{f}, Martin Fisher MD\textsuperscript{g}, Ellen Rome MD\textsuperscript{h}, B. Timothy Walsh, MD\textsuperscript{i}.
\textsuperscript{a}Penn State Hershey Children’s Hospital, \textsuperscript{b}University of Michigan Medical School, \textsuperscript{c}Oakland University William Beaumont School of Medicine, \textsuperscript{d}Monroe Carell, Jr. Children’s Hospital at Vanderbilt, \textsuperscript{e}Boston Children’s Hospital, \textsuperscript{f}Children’s Hospital of Wisconsin, \textsuperscript{g}Cohen Children’s Hospital of the North Shore-LIJ Health System, \textsuperscript{h}Cleveland Clinic Children’s Hospital, \textsuperscript{i}New York State Psychiatric Institute at Columbia University School of Medicine

Purpose:
To determine the distribution of eating and feeding disorders in older children, adolescents, and young adults comparing the DSM-IV to the proposed DSM-5 criteria, with a particular emphasis on whether the proposed DSM-5 criteria led to a reduction in the use of Eating Disorder Not Otherwise Specified (EDNOS).

Methods:
The study population consisted of 220 consecutively enrolled new patients with an eating disorder (mean age 15.4 ± 3.3 years, 88.6% female) presenting for initial evaluation to adolescent medicine physicians from six institutions. Patients were evaluated according to the current clinical standard of care. Eating disorder diagnoses were assigned using the current DSM-IV criteria. Concurrently, the proposed DSM-5 criteria were employed to determine the presumptive DSM-5 diagnosis using a structured algorithm.

Results:
Diagnoses of anorexia nervosa (AN) and bulimia nervosa (BN) both increased by utilizing the proposed DSM 5 criteria (from 30.0% to 40.0% and from 7.3% to 11.8%, respectively, p<.001 for both). Approximately 14% of patients would receive the presumptive DSM-5 diagnosis of avoidant restrictive food intake disorder (ARFID). The DSM diagnosis of EDNOS decreased from 61.8% to 32.7% (p<.001). Of the 71 cases of EDNOS, preliminary analysis suggests that many would be classified as having a condition tentatively termed Atypical AN.

Conclusions: This study demonstrates that the proposed DSM-5 criteria would substantially decrease the frequency of EDNOS diagnoses, and modestly increase the number of cases of both AN and BN, in a population of children, adolescents, and young adults presenting for treatment of an eating disorder. Additionally, ARFID appears to be important as a new diagnosis.
Food Acceptance and Fears in Young Patients with Anorexia Nervosa, Bulimia Nervosa, and Avoidant/Restrictive Food Intake Disorder

Rollyn M. Ornstein, MD, Brandie LaSala, MD, Carissa Strohecker, Emily B. Masciulli, LCSW, Susan E. Lane-Loney, PhD
Division of Adolescent Medicine and Eating Disorders, Penn State Hershey Children’s Hospital
Hershey, Pennsylvania

Purpose:
To determine whether the Food Acceptance and Fears Survey (FAFS), an 88-item self-designed survey querying foods eaten, never eaten, and feared utilized in our family-centered ED day program for young patients distinguishes between different groups of eating disorder patients, especially those with Avoidant/Restrictive Food Intake Disorder (ARFID) and Anorexia Nervosa (AN). We also postulated that the FAFS would correlate with the Children’s Eating Attitudes Test (ChEAT).

Methods:
A retrospective chart review of 87 patients (95% female, 13.6 ± 2 yrs) admitted to the program from 9/2010-6/2012 was performed. Patients were administered the FAFS and ChEAT at admission [a] and discharge [d]. Changes over treatment were analyzed using paired t-tests. Pearson correlations were used to determine the relationship between the FAFS and the ChEAT. ANOVA and post-hoc analysis were used to compare between-groups effects for patients with ARFID, AN, and Bulimia Nervosa (BN).

Results:
At intake, patients with ARFID reported eating more foods than patients with AN (p<0.0001) or BN (p=0.008) and fearing fewer foods than those with AN (p=0.002) or BN (p=0.003). Overall, patients showed improvements in both the number of foods eaten (38.6 vs 62.6) and feared (34.4 vs 10.8) (both p<0.0001) from [a] to [d]. There were no significant group differences for the number of foods never eaten, nor for the number of foods eaten or feared at [d]. The ChEAT scores correlated with the number of foods eaten on the FAFS at both [a] (r=-.68) and [d] (r=-.73) (p<0.0001).

Conclusions:
Young ED patients showed significant improvements in the numbers of foods eaten and feared on the FAFS during day treatment and outcomes correlated well with the ChEAT. While ARFID patients reported eating more and fearing fewer foods initially, the number of foods they had never eaten was unexpectedly no greater than their counterparts. The FAFS appears to be a useful tool in assessing treatment progress in young ED patients.
Patient Preferences and Satisfaction in a Multispecialty Infusion Center

Barbara Ostrov, Kristine Reynolds, Lisabeth V. Scalzi

Department of Pediatrics and Medicine; Department of Nursing, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania

Purpose:
Direct feedback from patients about preferred modes of medication administration has been increasingly sought to develop care programs that best match patient goals. We assessed patient satisfaction as well as nursing and physician perceptions of patient preference with our multi-specialty Infusion Center to determine whether a separate unit should be recommended when designing our new Cancer Institute Infusion Center.

Methods:
A 7-question Likert scale Survey for patients and a separate survey to assess nurses’ and physicians’ perception of patient satisfaction was developed. The survey was administered to non-HO patients receiving infusions, doctors prescribing infusions, and nurses who administered infusions. Results of the survey were compared between groups to assess response differences.

Results:
Responses were received from 52 non-HO patients, 18 physicians, and 13 nurses. Patients had greater satisfaction with the multispecialty Infusion Center than had been realized by both physicians and nurses on all items. Analysis demonstrated that patients were satisfied with care in a multi-specialty (HO and non-HO) infusion unit and were in favor of continuing their care in this combined center. Total scores of patient surveys were significantly different (p<0.001) than physicians and nurses, who had assumed patients would prefer to have their care in a non-HO infusion setting. Responses between patients and providers/ nurses were significantly different for every question. The majority of nurse and provider responses were no different from one another.

Conclusions:
Understanding patient preferences is an important step in deciding the structure of infusion centers. Based on these survey conclusions, a combined multi-specialty infusion center has been continued at our institution.
Strategies for Assessment and Management of Severe Environmental Allergies at “Camp JRA”

Barbara E. Ostrov, MD, Lisa M Robbins, BSN, Tracy Fausnight, MD.
Department of Pediatrics, Division of Pediatric Rheumatology (1) and Division of Pediatric Allergy/Immunology (2)
Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
To share our strategy in addressing the growing concern about environmental sensitivities in a residential week long camp for children with rheumatic diseases.

Methods:
The emergence of the multiple allergies issues was a barrier to providing a confidently safe camp environment. New management approaches were developed and implemented.
1. We developed a new allergy history questionnaire that triggered progression to further detailed information about the sensitivities.
2. We consulted with our Pediatric Allergist to develop an algorithm for assessment of symptoms (attached to poster).
3. We developed an Allergy Action Plan specific to each camper with allergy issues, approved in advance by parent and signed.
4. We developed a system for Epi-pen storage: over the door holder with multiple clear pockets, with the Epi-pen, the child’s photo, the signed Allergy Action Plan.

Results:
We oriented all medical staff who worked in the Med-Shed to the new system. When implemented at Camp JRA in July 2013, we experienced no allergy response problems. Increasing allergy sensitivities in patients requires a proactive plan for residential camps. We have developed a model for assessing allergies and reaction preparedness. This plan has improved our confidence that we can provide safe rheumatologic AND allergy response care.

Conclusions:
The development of increasing allergy sensitivities and concerns by families and patients requires a proactive plan for residential camps of children with rheumatic disease. We have developed a model for assessing allergies and reaction preparedness.
Ontogenic Expression of Retinoid Homeostatic Genes in Principal Vitamin A Storage Organs

Sarah A Owusu, BS, A. Catharine Ross, PhD
Department of Nutritional Sciences, Intercollege Graduate Degree Program in Physiology
The Pennsylvania State University, University Park, Pennsylvania, USA

Purpose:
To advance the understanding of neonatal VA metabolism and catabolism in principal VA storage organs. We have previously shown that the combination of VA and 10% all-trans retinoic acid (VARA) works synergistically to increase retinol uptake and total retinyl ester storage in neonatal rat lung. In this study, we determined the developmental trajectory of VA metabolism in placebo-treated VA-marginal rats, and the response of plasma, liver, lung, and kidney to supplementation with VARA from birth to adulthood.

Methods:
Rat dams and their post-weaning offspring were fed VA-marginal diet, while pups received an oral dose of oil (placebo) or VARA on post-natal (P) day P0/1, P4, P7, P10, and as adult (2 months); tissues were collected 6 h after dosing. Gene expression was determined by qRT-PCR in liver, lung, and kidney.

Results:
During ontogeny, LRAT, RBP4, RALDH-1 and RALDH-3 mRNA levels did not differ in neonates, but were higher in adults, while CYP26A1/B1, STRA6, megalin, and RALDH-1 did not differ from the perinatal to adulthood stages. VARA significantly upregulated plasma and tissue retinol levels and expression of LRAT, megalin, Cyp26A1/B1, and STRA6, which are important for VA storage, VA recycling, RA terminal oxidation, and retinol uptake, respectively. However, VARA decreased expression of RBP4, responsible for VA trafficking, and RALDH -1 and RALDH-2, but not RALDH-3, which function in RA production.

Figure 1 summarizes the results of retinoid homeostatic gene expression through ontogeny and after VARA supplementation.

Conclusions:
These results define changes in retinoid homeostasis between the neonatal and adult periods and show that VARA promotes retinoid storage and alters retinoid homeostatic gene expression in both neonates and adults.
Low Incidence of Intracranial Hemorrhage in Acute Idiopathic Thrombocytopenic Purpura (ITP) in Children

Elyse K. Pagerly, MS4, Andrew S. Freiberg, MD,
Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Idiopathic Thrombocytopenic Purpura (ITP) is a common bleeding disorder in children. The disease is usually self-limiting with spontaneous recovery within a few months of onset. The most common manifestations include cutaneous and mucosal bleeding; the much more serious complication of intracranial hemorrhage (ICH) is much more rare, but accounts for the vast majority of the mortality. Identifying possible associations and risk factors for ICH in acute ITP as well as the value of treatment in decreasing its incidence has proven extremely difficult. This has made treatment of ITP controversial as it is unclear whether the best route is watchful waiting or pharmacologic intervention.

The goals of this study were to determine the incidence of ICH in our patient population and to determine whether there was a difference in risk of ICH for children with ITP who received treatment compared to those who were observed. In addition, we looked at whether there was a tendency in our institution to treat our pediatric patients with ITP or observe them.

Methods:
We reviewed all charts of children age 0 to 21 presenting with acute ITP between 1990 and 2010. Demographic factors were recorded as well as whether the child received active treatment for the ITP.

Results:
378 children presented to our institution with acute ITP during the study period. 69.6% received treatment while 30.4% did not. As expected, observed patients had higher platelet counts at diagnosis than those treated. Regardless of treatment ICH was rare with only three cases identified (0.79%). Two of these patients presented with ICH and the other received treatment and bled subsequently.

Conclusions:
Though the number of cases in our study is limited, we found no evidence that treatment prevents intracranial bleeding.
Identification of Binding Site Enrichment of Ikaros in Leukemia

Xiaokang Pan, Chunhua Song, Yali Ding, Sadie Steffens and Sinisa Dovat
Departments of Pediatrics, Penn State College of Medicine, Hershey, Pennsylvania, USA

Purpose:
IKZF1 (Ikaros) is a gene regulator and important tumor suppressor in leukemia. It, in complex with histone deacetylase 1 (HDAC1), binds DNA with unique forms. The Ikaros-HDAC1 complex also regulates gene expression and epigenetic changes via chromatin remodeling. In this study, we identify binding patterns of Ikaros and associated genetic and epigenetic factors, and then find the relationship between Ikaros and associated factors in gene expression and regulation in order to understand the mechanisms of Ikaros tumor suppression in leukemia.

Methods:
We have conducted microarray, RNA-Seq and ChIP-Seq experiments to study regulation effects of Ikaros and HDAC1 transcription binding and histone modification on gene expression in various leukemia cell lines in human and mouse. We then developed a data analysis pipeline to perform global genomic and epigenomic analyses for such datasets. After binding peak detection and gene expression analysis, we integrated the binding peaks with gene expression data. We then calculated binding site distribution of the transcription factors and histone modification marks in different gene regulatory regions. Based on the annotation of binding peaks and gene expression data, we studied the relationships among gene expression, binding sites and factors by performing the correlation analysis and permutation test and by constructing regulation networks. We also explored the binding site enrichment in peri-heterochromatin via graphical visualization and statistical test.

Results:
In human B-ALL cells (Nalm6 cell line), we have identified binding enrichment of Ikaros and HDAC1 transcription factors and five histone modification marks in the range around the TSS of highly expressed genes and in pericentromeric regions. We have also found that HDAC1, H3K4me3, H3K27me3, H3K36me3, H3K9me3 and H3K9ac histone modifications are highly correlated to Ikaros binding. Furthermore, we constructed an Ikaros regulation network to explicit the mechanisms of Ikaros in leukemia control.

Conclusions:
These results show how Ikaros regulates gene expression and histone modification to regress leukemia disease and provide scientific evidences to help people understand the mechanisms of Ikaros tumor suppression in leukemia.
Electrical Grounding (EG) Improves Parasympathetic Tone in Preterm Infants in the Neonatal Intensive Care Unit

Rohit Passi MD, Charles Palmer MD, Kim Doheny PhD,
Penn State Hershey Children’s Hospital, Hershey, Pennsylvania

Background:
Preterm infants cared for in NICU are exposed to electromagnetic fields (EMFs) from incubators and other electrical equipment. These fields create a measurable charge on infant’s skin (floating skin voltage). In adults, electrical grounding (EG) reduces this charge and improves parasympathetic tone, suggesting reduction in stress. No studies have examined the effects of EG on preterm infants.

Aims/Objectives:
1) To determine if EG lowers floating skin voltage. 2) To measure the effect of EG on heart rate variability (HRV). We hypothesized that EG would improve parasympathetic tone measured by high frequency spectral analysis of HRV (HF-HRV).

Inclusion/Exclusion Criteria:
NICU infants 28-36 weeks PMA, 5-60 days of age, clinically stable and off mechanical ventilation. We excluded infants with rhythm abnormalities.

Methods:
A voltmeter was used to measure skin voltage, as potential difference between infant’s skin and ground using a wire and standard electrode. EG was then achieved by connecting infant to grounding outlet using an additional electrode and wire. To measure HRV, the analog EKG from infant’s monitor was digitally captured for 20-40 minutes while standardizing for time of day, environmental stimuli and post-feeding behavioral state. HRV was calculated by averaging results of repeated 2 min epochs representing time before, during and after EG. For each epoch of sampling, HRV spectral analysis was used to determine HF power (0.3-1.3 Hz).

Results:
The skin voltage prior to EG was 39 to 1660 mvolts. It decreased over 93% upon grounding. HF-HRV increased during EG by 66.9% (See fig. for details) RM-ANOVA (p =0.001).

Conclusions:
EG raises parasympathetic tone within minutes. Parasympathetic tone is critically important for autonomic system balance and stress regulation.
Hemodynamic Evaluation of Novel i-cor Pulsatile ECLS System during Various Cardiac Arrhythmias: In Vitro Study

Sunil Patel, Dennis Chang, Shigang Wang, Allen R. Kunselman, and Akif Undar

Pediatric Cardiovascular Research Center, Pediatric Cardiology Division, Department of Pediatrics, Public Health Sciences, Surgery, Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Hershey, PA; and Bioengineering, College of Engineering, Pennsylvania State University, University Park, PA, USA

Background:
Surplus hemodynamic energy (SHE) can be generated under pulsatile extracorporeal life support (ECLS) system and higher SHE correlates with improved microcirculation and reduced inflammatory response. The latest i-cor ECLS system can generate pulsatile flow synchronized with patient’s intrinsic heart rhythm which may have a clinical benefit. Operational feasibility and clinical benefits of this novel i-cor ECLS system are not known in the setting of various life threatening cardiac arrhythmias along with acute hemodynamic derangements.

Objective: To evaluate the hemodynamic energy and suitable synchronization mode of novel i-cor diagonal pump during various arrhythmias in simulated adult ECLS system using fresh human blood.

Methods:
The ECLS circuit consisted of i-cor diagonal pump and console (Xenios AG, Heilbronn, Germany), iLA membrane ventilator (Xenios AG), 3/8-in of arterial and venous tubing. The circuit was primed with Lactated Ringer’s solution followed by fresh whole blood (hematocrit > 35%). A Phantom 320 ECG simulator (Muller & Sebastiani, Ottobrunn, Germany) was used to trigger pulsatile flow and generate various cardiac arrhythmias. Different flow rates (2.5L/min, 3L/min, 3.5L/min and 4L/min) were tested with three different ECG synchronization modes (1:1, 1:2 and 1:3 R-wave synchronization) under three different arrhythmia settings (ventricular fibrillation at 193 bpm, ventricular tachycardia at 177 bpm and atrio-ventricular sequential pacing at 75 bpm) at room temperature. A circuit pressure of 150 mmHg was maintained with a Hoffman clamp throughout all the conditions. Flow and pressure data were collected using a custom-based data acquisition system from which surplus hemodynamic energy (SHE) and total hemodynamic energy (THE) were derived.

Results:
Pulsatile flow with synchronization mode of 1:2 (one pump pulse for every 2 detected R waves on the ECG) generated significantly higher SHE (Figure 1) and better pulsatile flow waveforms (Figure 2) during ventricular fibrillation, ventricular tachycardia and atrio-ventricular sequential pacing. This finding was observed at all different flow rates but absolute values were lower at progressively higher flow rates. 1:2 synchronization mode appeared to the most superior followed by 1:3 and 1:1. During Atrio-ventricular sequential pacing at 75 bpm 1:1 synchronization appeared to be extremely insensitive for generation of pulsatile flow (Figure 2). Despite significantly higher SHE values, THE values were only minimally improved at a synchronization mode of 1:2 compared to 1:3 and 1:1 modes.

Conclusions:
The ECG synchronized i-cor diagonal pump can generate adequate pulsatile flow under various life threatening cardiac arrhythmias. Of the 3 synchronization modes tested (1:1, 1:2, 1:3), a mode of 1:2 delivered a substantially higher SHE under all simulated arrhythmia conditions (ventricular fibrillation, ventricular tachycardia and AV sequential pacing). A higher SHE has been show to account for better microcirculation and reduced inflammatory response. The benefits may be specifically important during acute hemodynamic compromise secondary to such cardiac dysrhythmias. In vivo studies are being performed to consolidate these findings. Bedside health care personnel using these novel ECLS system need to be aware of such potential benefit of changing adequate assist ratios during life threatening cardiac rhythm disturbances.
Transcarotid balloon valvuloplasty (TCBV) for critical aortic valve stenosis (AS) utilizing continuous transesophageal echocardiographic (cTEE) guidance: A 22 year single center experience from the cath lab to the bedside.

1Sunil Patel, MD, 1Ashish P. Saini, MD, 1Athira Nair, MD and 1Howard Weber, MD
1Pediatric Cardiology Division, Department of Pediatrics,
Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania

Background: cTEE guidance during the procedure allows real time hemodynamic assessment which might influence early and late outcomes.

Methods: From 1992 to date, 30 consecutive critical AS pts with adequate left ventricular size underwent TCBV with cTEE guidance. Critical AS was defined as neonates presenting with ductal dependent systemic circulation, LV systolic dysfunction or systolic gradient ≥100mmHg with hypoperfusion.

Results: The median age at intervention was 4 days (range 1-54 days). 19 (63%) patients required PGE1, 8 (27%) had reduced shortening fraction and 3 (10%) had a gradient ≥100 mmHg. Initial 15 patients (50%) were performed in the cath lab (fluoro time: 10±8 min) and subsequent 15 patients were performed at the bedside without fluoroscopy and all with cTEE guidance. The mean aortic valve Z score was -1.2±1.3. The peak systolic gradient decreased from 70±31 to 24±16mmHg (p<0.001). Five patients (17%) developed ≥ moderate aortic insufficiency. There were 4 (13%) early deaths likely secondary to associated cardiac anomalies including severe mitral stenosis (n=3), coarctation of aorta (n=2), severe mitral regurgitation (n=2). One patient developed severe aortic insufficiency immediately post intervention. During a mean follow-up of 10±7 yrs (range: 3-17yrs), there were 15 additional aortic valve interventions (50%). Seven (23%) patients had a Ross procedure, 4 (13%) patients had a primary aortic valve repair, 2 (7%) patients had aortic valve replacement and 2 (7%) had repeat balloon aortic valvuloplasty. All surviving patients underwent duplex vascular imaging of the right carotid artery (RCA) at 6.4±4.9 yrs. (range: 1-11yrs.). Five patients (17%) developed occlusion/stenosis of RCA without clinical consequences. Freedom from aortic valve reintervention and actuarial survival rate curves of this cohort is delineated in the Figure 1.

Conclusion: TCBV with cTEE guidance at the bedside is effective palliation in neonates with critical AS, allowing continuous hemodynamic assessment and avoiding exposure to ionizing radiation. Our results appear comparable to surgical aortic valvotomy.

Figure 1. Freedom from reintervention vs. survival analysis in patient with transcarotid balloon aortic valvuloplasty for critical aortic stenosis.(N=30)
Transcatheter device closure of partial anomalous pulmonary venous return (PAPVR) with “intrapulmonary duplicating drainage” – A newly described entity and a single center experience.

1Sunil Patel, MD, 1Ashish P. Saini, MD and 1Howard Weber, MD
1Pediatric Cardiology Division, Department of Pediatrics. Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Background:
Transcatheter closure of extra pulmonary PAPVR, either ‘scimitar vein’ or ‘vertical vein’ type, has been reported (Figure 1A). We describe our experience of non-surgical closure of “intrapulmonary duplicating pulmonary venous return” (Figure 1B).

Method:
Hemodynamics and selective pulmonary angiography were performed with and without temporary balloon occlusion of the anomalous pulmonary veins. Balloon occlusion reverse wedge pulmonary vein angiography was also performed if a single pulmonary vein was considered not to have dual supply from the affected lung segment. Device closure of the anomalous vein(s) was undertaken only when dual supply was present.

Results:
From 2004 -2013, 4 patients underwent cardiac catheterization and embolization therapy for PAPVR. Table 1 shows the clinical and intervention summary. The diagnosis remained undetected via MRI but was delineated in the catheterization lab using various angiographic techniques and successfully treated by device embolization.

Table 1. Clinical and interventional summary

<table>
<thead>
<tr>
<th>No.</th>
<th>Age at Cath (yr)</th>
<th>Type of PAPVR</th>
<th>Qp/Qs</th>
<th>Follow up (months)</th>
<th>Devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37</td>
<td>RUPV to SVC. RMPV and RLPV veins have dual pulmonary venous drainage</td>
<td>2.46 1.25 2</td>
<td>8 and 14mm AVP-II</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>Left VV with dual pulmonary venous drainage</td>
<td>1.73 1 6</td>
<td>12 mm AVP-Ii</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>Left VV with dual pulmonary venous drainage</td>
<td>1.27 1 37</td>
<td>8mm AVP</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>RUPV to SVC. RLPV vein has dual pulmonary venous drainage</td>
<td>1.52 1 96</td>
<td>6, 8, 10 and 12 mm AVP</td>
<td></td>
</tr>
</tbody>
</table>

AVP, Amplatzer Vascular Plug; VV, Vertical vein.

Conclusion:
PAPVR with intrapulmonary (duplicating) pulmonary venous drainage is a newer entity which is probably underappreciated on cardiac MRI. Cardiac catheterization with selective pulmonary artery and pulmonary vein angiography can effectively delineate this unique physiology. Transcatheter closure of such PAPVR with duplicating pulmonary venous drainage can be considered a safe non-surgical option in select patients.
The Mercy TAPE: A New Device for Pediatric Weight Estimation

Ian M. Paul, MD; Laura James, MD; Andrew Lewandowski, Ph.D.; Susan Abdel-Rahman, Pharm.D.
Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania

Introduction:
An accurate weight is critical for medical and pharmacologic interventions in children yet scales are not available or practical to use in some settings. The Mercy Method (MM) is a recently validated pediatric weight estimation strategy, based on humeral length (HL) and mid-upper arm circumference (MUAC), that is superior to other contemporary methods.

Objectives:
We sought to determine the predictive performance of two inexpensive devices based on the MM (2D- and 3D-TAPE, figure) in a prospective, multi-center, observational, blinded study.

Methods:
Eligible children (2 mo-16 yr) were stratified into 1-yr age blocks with the goal of enrolling 35-40 children/block. Qualified raters measured the height, weight, HL and MUAC for each child using calibrated scales and measures. Raters also made measurements using blinded versions of both the 2D- and 3D-TAPEs. TAPE generated weights were unblinded at study completion and evaluated against actual weight. Statistics such as mean error (ME) and mean percentage error (MPE) were used to assess the predictive performance of the TAPEs. Equivalence testing was used to compare the devices, the MM-estimated weight and the actual scale-derived weight.

Results:
664 participants were enrolled; 625 had evaluable datasets. Participants averaged 8.5 ± 4.9 yr, 127.8 ± 31.9 cm and 34.8 ± 23.1 kg. Children spanned the range of BMI% (0-99.9%.) The correlation ($r^2$) between predicted and actual weight ranged from 0.97-0.98 for all methods. Average error and percent error across all participants was 0.4 kg (1.8%), 0.3 kg (1.6%) and 0.2 kg (1.8%) for the MM, 2D-TAPE and 3D-TAPE, respectively. The proportion of children in whom the methods and devices predicted weight within 20% of actual ranged from 93-98%.

Conclusion:
The 2D- and 3D-TAPEs were statistically equivalent to the MM in approximating pediatric weights with acceptable variability from the true weight. The 2D- and 3D TAPEs can be utilized to optimize weight-based treatments for children when calibrated scales are inaccessible or impractical.
Allergic Diseases in Children with Anxiety Disorders:
Department of Psychiatry - Department of Pediatrics Collaborative Study

Lidija Petrovic-Dovat, MD, Tracy Fausnight, MD, Timothy Zeiger, PsyD, Diane Jasmin, DO, Amanda M. White, BS, Edward O. Bixler, PhD
Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
The purpose of this pilot study is to examine the association of anxiety with food allergies and allergic diseases in children. With an estimated lifetime prevalence of 31.9%, anxiety disorders are the most common mental health diagnoses in children and adolescents. A review of literature indicates a consistent association between anxiety disorders and allergic diseases in children. Functioning of the child may be negatively affected by comorbid diagnoses.

Methods:
This is an IRB approved prospective cohort study. Pediatric patients are recruited from allergy and anxiety clinics at our institution. Caregivers and patients at both clinics are given standardized screens including the SCARED (Screen for Child Anxiety Related Emotional Disorders) and questionnaires designed by our investigators to collect data related to food allergies, food sensitivity, asthma, and anxiety symptoms.

Results:
In the pilot phase of this study we analyzed data from 26 subjects: 12 pediatric allergy patients and 14 pediatric anxiety patients. In the anxiety clinic, 5/14 subjects reported a history of food allergies or sensitivity and 7/14 reported a history of asthma, eczema or both. Children with higher SCARED scores reported more allergies when compared to children with lower SCARED scores. All subjects who reported food allergies, food sensitivity or asthma reported a history of allergies in a parent or sibling. 9/14 subjects with a diagnosis of anxiety reported having a sibling, parent or both with allergies.

Conclusions:
Preliminary data suggest that subjects in the anxiety clinic are reporting higher rates of asthma and allergic diseases compared to historical data in a general pediatric population. Ongoing patient accrual and additional studies will be performed in order to confirm these results and determine if children with food allergies should be routinely screened for anxiety and referred as well as treated accordingly.
Sex differences in the acute in vivo effects of different human SP-A variants on the mouse alveolar macrophage proteome

David S. Phelps, PhD¹, Todd M. Umstead, BS¹, and Joanna Floros, PhD¹,²
¹The Center for Host defense, Inflammation, and Lung Disease (CHILD) Research, Department of Pediatrics, The Pennsylvania State University College of Medicine, Hershey, PA, USA and ²Department of Obstetrics and Gynecology, The Pennsylvania State University College of Medicine, Hershey, PA, USA.

Purpose:
To examine the in vivo effects of an acute, single dose of specific SP-A variants or combinations of variants purified from transfected cell lines, on the AM proteome from mice lacking endogenous SP-A (SP-A knockout, KO).

Methods:
KO mice received an intrapharyngeal bolus of either SP-A1 (10 µg/mouse), SP-A2 (10 µg/mouse), or combinations of SP-A1 and SP-A2 (5 µg or 10 µg each). AM were harvested by bronchoalveolar lavage 18 hours after SP-A treatment and their intracellular proteomes examined with 2-dimensional difference gel electrophoresis.

Results:
We identified 90 proteins and categorized them as being in groups related to actin/cytoskeleton, oxidative stress response, protease balance/chaperones, regulation of inflammation, and regulatory/developmental processes. SP-A1 and SP-A2 had very different effects on the AM proteome and these effects differed between males and females. In males, although there were similar numbers of overall significant changes (n=8 for SP-A1; n=11 for SP-A2), more changes were seen in the oxidative stress, protease/chaperones, and inflammation groups with SP-A2 treatment than with SP-A1. However, in females there were 13 significant changes in response to SP-A1, but only 4 with SP-A2. Most of the SP-A1-induced changes in the females were in the actin/cytoskeletal and oxidative stress groups. We speculate that the high number of changes in these groups may relate to better survival in females after infection and their more vigorous response to oxidative stress. However, the small number of changes in the protease/chaperone group in the females could indicate less effective systems for repair of cellular damage.

Conclusions:
After acute SP-A exposures with different SP-A gene products, significant differences were observed in the AM proteomes from KO mice and these responses differed between males and females. These observations not only demonstrate the therapeutic potential of exogenous SP-A variants, but also illustrate sex differences in their responses.
The Factors Most Important for Quality of Life in Adolescents with Cerebral Palsy

Brian Piazza, William Hennrikus MD, Ryan Schell, Douglas Armstrong MD, Kristine Fortuna MD.
Penn State College of Medicine, Hershey, Pennsylvania 17033.

Purpose:
The purpose of this study is to determine how adolescent patients with cerebral palsy (CP) rate various quality of life measures, in terms of importance. In addition, we aim to compare their parent’s perception of quality of life measures for their child with CP.

Methods:
The study was approved by the Penn State College of Medicine IRB. Thirty-one adolescent patients with CP were consented and administered a fifty-item questionnaire. The parents completed an identical questionnaire about their child. Statistical analysis was performed using the Wilcoxon rank-sum test.

Results:
The top five quality of life measures as rated by the patients were: (1) eating and drinking independently, (2) attending school, (3) walking, (4) using a computer, (5) forming relationships with their peers. The top five quality of life measures as rated by the parents were: (1) eating and drinking independently, (2) attending school, (3) using the toilet independently, (4) access to therapy, (5) access to health care.

Comparing the quality of life ratings of patients with CP to parents, five measures were statistically significant. Patients thought that playing video games (p=0.039), using the TV (p=0.004) and how their physical disability affects their appearance in comparison to their peers (p=0.018) were more important than their parents did. Parents thought their child’s future financial independence (p=0.017) and access to healthcare (p=0.008) were more important than their adolescent children did.

Conclusions:
Parents can accurately predict a few of the quality of life measures important to their child; however, disparities in many psychosocial domains do exist. A better understanding of the importance of quality of life themes for patients with CP will allow for more focused care by physicians and can be used to strengthen patient-doctor communication through common interest.
Endobronchial Occlusion with One-way Endobronchial Valves: A Novel Technique for Persistent Air Leaks in Children

Abigail B. Podany, MD, Michael F. Reed, MD, Dorothy V. Rocourt, MD, Christopher R. Gilbert, DO, Mary C. Santos, MD, Robert E. Cilley, MD, Peter W. Dillon, MD, Jennifer W. Toth, MD. Pennsylvania State Milton S. Hershey Medical Center, Hershey, PA, USA.

PURPOSE:
In the pediatric population, persistent air leaks can result from pulmonary infection or barotrauma. Management strategies include surgical intervention, prolonged pleural drainage, ventilator manipulation, and even ECMO. We hypothesized that endobronchial valve placement would be an effective minimally invasive intervention for prolonged air leaks in children.

METHODS:
Endobronchial valve placement was approved by the Institutional Review Board (IRB) under a Humanitarian Device Exemption, and review of children undergoing the procedure was also approved by the IRB. Children with prolonged air leaks refractory to conventional management strategies were evaluated by a multidisciplinary team (pediatric surgery, interventional pulmonology, and thoracic surgery) for endobronchial valve placement. Airway management and bronchoscopic techniques were adapted to accommodate the pediatric population. Flexible bronchoscopy was performed under general anesthesia. Airways leading to the air leaks were isolated with balloon occlusion. Retrievable one-way endobronchial valves were deployed via catheter (figure).

RESULTS:
Four children (16 months to 16 years) had prolonged air leaks following necrotizing pneumonia (2), lobectomy (1), and pneumatocele (1). All had pleural drains. The number of valves placed per patient ranged from 1-4. Average time to air leak resolution was 12 days (range 0-39). Average duration to chest tube removal was 25 days (range 7-39). All four children had complete resolution of their air leaks. All were discharged from the hospital. Three of four have had uneventful valve removal. None required additional surgical interventions.

CONCLUSION:
Endobronchial valve placement for prolonged air leaks due to a variety of etiologies is safe and effective in children for resolving fistulae, achieving early pleural drain removal and shortening length of stay. This novel technique has particular utility in the pediatric population to avoid the morbidity of thoracotomy and preserve lung volume and function.
Vancomycin Resistant Enterococcus Infections are Associated with a Higher Prevalence of Reported Penicillin Allergy

Vinitha Reddy, MD, Faoud T. Ishmael, MD PhD
Section of Allergy and Immunology, Penn State College of Medicine, Penn State Medical Center, Hershey, Pennsylvania, USA

Purpose:
Penicillin allergy has a reported high prevalence and occurs in approximately 10% of the population. It is estimated that 90% of these patients are not truly allergic, but patients labeled as allergic are treated with alternative antibiotics, which may be less efficacious or have more side effects. Penicillin-allergic patients may be more likely to receive vancomycin as an alternative antibiotic. In this study we investigated reported penicillin allergy prevalence in both the general hospital population as well as in patients with Vancomycin Resistant Enterococcus (VRE) infections.

Methods:
After IRB approval, lists of hospitalized patients with VRE infections were compiled from our institution. Retrospective review of electronic records was performed from hospitalized patients of all ages from January 2009 to December 2011 to obtain antibiotic allergy information. Differences between rates of drug allergy were analyzed by chi-squared tested, with a significance set at p<0.05.

Results:
Over a 36 month period there was a statistically significant increase in prevalence of penicillin allergy in patients with VRE (24%; 100/426; p<0.001) compared to the general hospital population (6%; 20249/369721). The prevalence of other antibiotic drug allergies not including penicillin was also higher in the VRE group (33.6%; 143/426) compared to the general hospital population (7%; 25589/369721; p<0.001).

Conclusions:
There is an increased prevalence of penicillin and other antibiotic allergies in patients with VRE infections compared to the general hospitalized population. Future studies are needed to determine whether inpatient penicillin allergy testing can improve antibiotic utilization and prevent these resistant infections.
Return to school in students after a sport-related concussion: the role of the school nurse

Jed Ritter, B.S., Robert P. Olympia, M.D., Jodi Brady, M.D., Harry Bramley, D.O.
Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
To determine the compliance of school nurses with recommendations as delineated by the National Association of School Nurses’ (NASN) position statement on the role of the school nurse in the post-concussion student.

Methods:
A prospective, electronic questionnaire-based study was conducted during the 2012-2013 academic school year. The questionnaire, distributed to members of NASN working at the high school level, focused on the responsibilities of the school nurse in post-concussion care and the presence of guidelines or protocols to assist the student’s return to school following a concussion.

Results:
Data analysis was performed on 1030 questionnaires. 66% of nurses have had special training in recognizing or managing students with a concussion. School nurses are involved in the following roles in regards to the care of the post-concussion student: identifying suspected concussions (80%), providing advocacy for the prevention of concussions (66%), guiding the student's post-concussion graduated academic and activity re-entry process (58%), providing daily medical evaluations (27%), communicating with the athletic trainer regarding progress or setbacks (50%), and providing emotional support for recovering students dealing with concussion related depression (59%). 46% of nurses work in districts that have an established policy that help students recovering from a concussion succeed when they return to school. 53% of nurses work in schools that have guidelines to assist students when returning to school following a concussion. These guidelines include excused absence from class (67%), rest periods during the school day (67%), extension of assignment deadlines (69%), postponement or staggering of tests (60%), accommodation for light or noise sensitivity (51%), use of a note taker or scribe (27%), temporary use of a tutor (25%).

Conclusions:
Guiding the student’s post-concussion graduated academic and activity re-entry process and establishing specific guidelines to assist students when returning to school are identified areas for improvement.
Respiratory Syncytial Virus (RSV) Infection in Pediatric Oncology and Hematopoietic Stem Cell Transplant (HSCT) Patients

Mansi Sachdev, Melanie Comito, Robert Greiner, Lisa McGregor, Teresa Shapiro, George McSherry, Kevin Mulieri, Lindsay Trout, Brooke Soulier, Jane Black, Tammy Angeletti, Wallace Greene, and Robert Tamburro

Departments of Pediatrics, Respiratory Care, Nursing, and Pharmacy, Penn State Milton S. Hershey Medical Center/ Penn State Hershey Children’s Hospital, Hershey, Pennsylvania

Purpose:
RSV is a major source of morbidity and mortality among pediatric cancer and HSCT patients. Therapies exist for prevention and treatment of severe RSV infections, but are expensive, labor intensive, and not without risks. Currently, there are no established guidelines for their use in this high risk population. To assess recent guidelines established by a multidisciplinary working group for treatment of RSV infections in pediatric oncology and HSCT patients.

Methods:
All RSV cases in this patient population from 05/2006-present were reviewed. Data collected included demographics, oncologic diagnosis, HSCT status, chest radiographic findings and use of RSV specific treatment. Criteria were developed to categorize patients as high or low risk and as upper or lower respiratory tract disease. Treatment guidelines were outlined for each of four patient groups: high risk/upper tract, high risk/lower tract, low risk/upper tract, low risk/lower tract. RSV specific treatment consisted of ribavirin (oral and/or aerosolized) and palivizumab.

Cases diagnosed before 09/2012 were assessed retrospectively, while cases diagnosed after that were assessed prospectively. Outcome variables included need for PICU admission and survival. Odds ratios were determined to assess association between adherence to guidelines and survival.

Results:
34 patients with RSV infection were identified; mean age was 90.9 +/- 12.2 months. Treatment consistent with guidelines occurred in 27 patients (79%). 23 (68%) patients were classified as high risk and 21 (62%) had lower respiratory tract disease. Four patients (12%) required PICU transfer. There were 2 deaths; both classified as high risk/lower tract disease. In neither case was treatment in accordance with suggested guidelines. Odds ratio for survival if guidelines were followed was 25(95%CI: 1.1, 596.0, p=0.04).

Conclusions:
Results of this single center study suggest that RSV treatment consistent with proposed guidelines may improve outcomes in pediatric cancer and HSCT patients. These data have provided the rationale for an ongoing multicenter analysis of these guidelines.
Selenium-containing histone deacetylase inhibitors (HDACi) - Novel therapeutic approach for leukemia treatment

Mansi Sachdev, MD\textsuperscript{1}, Dhimant Desai, PhD\textsuperscript{2}, Sunil Muthusami, MD\textsuperscript{1}, Chandrika Gowda, MD\textsuperscript{1}, Yali Ding, Ph.D., Chunhua Song, M.D., Ph.D\textsuperscript{1}, Shantu G. Amin, Ph.D\textsuperscript{2} and Sinisa Dovat, M.D., Ph.D\textsuperscript{1}

\textsuperscript{1} Department of Pediatrics, \textsuperscript{2} Department of Pharmacology
Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Epigenetic therapy with various types of HDACi, have demonstrated therapeutic efficacy in a range of malignancies, often with minimal side effects. Potent, novel, selenium-containing HDAC inhibitors (SelSA-1 and 2), have shown efficacy against Hodgkin’s lymphoma, lung cancer and melanoma cell lines. Here we expand efficacy studies of selenium-containing HDACi to include a broad range of hematopoietic malignancies and address the drug effects on cellular functions.

Methods:
Cell proliferation assay was done with WST-1 assay kit, cell cycle analysis and apoptosis was carried out with PI staining and Annexin-V/7AAD staining, respectively, by flow cytometry. Caspase-3/7 activity was measured with Apo-ONE Homogenous caspase 3/7 assay kit.

Results:
Cell proliferation assays demonstrated sharp dose-dependent cytotoxic effects in all the above cell lines at 96-hours post-treatment. Quantitative analysis showed that SelSa-1 and SelSa-2 have distinct effects in different types of hematopoietic malignancies. In non-Hodgkin’s lymphoma and in T-cell ALL, both SelSA-1 and 2 have similar therapeutic activity with IC50 of 1-2uM and 1uM, respectively. SelSA-1 has superior therapeutic activity compared to SelSA2 in B-cell ALL with IC50 = 0.2uM vs. 1.25uM, respectively. In acute promyelocytic leukemia (APML) without t(15;17) translocation, SelSA-1 was found to be superior to SelSA-2 with an IC50 of 0.25uM and 1uM, respectively, whereas APML with t(15;17) translocation showed similar sensitivity to both the compounds (IC50 = 1-2uM). Cell cycle analysis (via flow cytometry) revealed that these compounds induce G1-cell cycle arrest, induce apoptosis and increase Casp3/7 activity. Preliminary data suggests that both these selenium-containing HDACi have a synergistic effect when combined with other standard chemotherapeutic agents that induce DNA-damage.

Conclusions:
This preliminary data demonstrates the effectiveness of these selenium-containing analogs of SAHA, SelSA-1 and 2, on multiple leukemia cell lines. Additional studies to identify detailed mechanistic pathways of these drugs on cellular function are currently underway.
The effect of well-controlled maternal diabetes on fetal heart function - a tissue Doppler study

Ashish P. Saini¹, MD, Serdar Ural², MD, Linda B. Pauliks¹, MD, MPH
¹Pediatric Cardiology, ²Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Penn State College of Medicine, Hershey, Pennsylvania

Background:
Previous studies on fetal heart function in infants of diabetic mothers have shown altered diastolic myocardial velocities on tissue Doppler imaging (TDI) and an abnormal myocardial performance index (MPI) in affected fetuses even without hypertrophy. It is unclear whether better maternal glycemic control may prevent these fetal changes. This study therefore compared color TDI velocities and MPI in fetuses of mothers with well-controlled diabetes and normal controls.

Methods:
The study included 42 fetuses as 21 matched pairs of infants of diabetic mothers (DM) and controls. Color TDI cine loops of apical 4-chamber views were acquired as digital echocardiographic raw data. During off-line analysis, systolic (S') and diastolic (E', A') velocities and fetal MPI were measured at the tricuspid, septal and lateral mitral ring as average of 3 beats.

Results:
Fetal pairs were matched for maternal and gestational age (32.0±5.4 vs. 31.7± 5.4 weeks; NS). Among DM mothers, 14 were on insulin while 10/21 had gestational DM only. Fetal TDI velocities correlated with gestational age. All fetuses had similar S', E' and A' wave velocities (Table). Moreover, fetal MPI was also comparable: RV MPI in controls was 0.32±0.07 vs. 0.31±0.07 in DM (NS) and LV MPI was 0.34±0.07 vs. 0.33±0.07 in DM (NS).

Conclusions:
In this study, well-controlled maternal diabetes did not affect fetal MPI or color TDI myocardial velocities. These findings suggest that optimal maternal glycemic control may prevent injury to the fetal heart.

Table 1: Color Tissue Doppler Myocardial Velocities in 42 Fetuses with and without Diabetic Mothers

<table>
<thead>
<tr>
<th>Sample site</th>
<th>Control(N=21)</th>
<th>DM(N=21)</th>
<th>P value</th>
<th>Control(N=21)</th>
<th>DM(N=21)</th>
<th>P value</th>
<th>Control(N=21)</th>
<th>DM(N=21)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricuspid ring</td>
<td>S' velocity (cm/s)</td>
<td>7.0 ± 2.1</td>
<td>6.9 ± 2.5</td>
<td>0.855</td>
<td>-5.5 ±2.1</td>
<td>-5.7 ±2.5</td>
<td>0.763</td>
<td>-5.7 ±2.0</td>
<td>-5.9 ±2.4</td>
</tr>
<tr>
<td>Septal mitral ring</td>
<td>E' velocity (cm/s)</td>
<td>4.3 ± 1.3</td>
<td>4.7 ± 1.5</td>
<td>0.369</td>
<td>-3.8 ±1.2</td>
<td>-3.7 ±1.4</td>
<td>0.766</td>
<td>-3.8 ±1.2</td>
<td>-3.7 ±1.5</td>
</tr>
<tr>
<td>Lateral mitral ring</td>
<td>A' velocity (cm/s)</td>
<td>5.8 ± 2.2</td>
<td>5.0 ± 1.8</td>
<td>0.323</td>
<td>-4.6 ±1.9</td>
<td>-4.2 ±1.7</td>
<td>0.516</td>
<td>-4.7 ±2.0</td>
<td>-4.3 ±1.8</td>
</tr>
</tbody>
</table>

Abbreviations: S' peak systolic velocity, E' peak early diastolic velocity, A' atrial contraction velocity. DM fetuses of diabetic mothers.
Adolescent Anemia Screening During Ambulatory Pediatric Visits in the United States

Deepa L Sekhar, MD, MSc\textsuperscript{1}, Laura E Murray-Kolb, PhD\textsuperscript{2}, Luojun Wang, BS\textsuperscript{3}, Allen R Kunselman, MA\textsuperscript{3} and Ian M Paul, MD, MSc\textsuperscript{1,3}.

\textsuperscript{1}Department of Pediatrics, Penn State College of Medicine, Hershey, PA; \textsuperscript{2}Nutritional Sciences, The Pennsylvania State University, University Park, PA and \textsuperscript{3}Public Health Sciences, Penn State College of Medicine, Hershey, Pennsylvania

Purpose:
The Centers for Disease Control and Prevention recommend anemia screening for reproductive age women every 5-10 years and annually for those with risk factors. No data support this recommendation for younger women. The purpose of this study was to characterize current anemia screening patterns among adolescents by pediatric providers.

Methods:
We analyzed data from a nationally representative sample of ambulatory visits by using the National Ambulatory Medical Care Survey. In the subset of preventive care visits involving patients ages 12 to 21 years we estimated the frequency of screening for anemia with a hemoglobin/hematocrit or a complete blood count by patient sex. We used multivariable logistic regression to identify patient-, provider and practice-level factors associated with screening.

Results:
Anemia screening was ordered in 12.3\% of female and 16.2\% of male preventive care visits. An interaction term emerged between patient age and sex with older adolescent females screened in significantly smaller numbers compared with males. Additional significant factors associated with screening included patient’s race, patient’s tobacco use or exposure, pediatric training of the physician, patient visit length, geographic location of the practice, availability of laboratory testing at the physician’s office, practice size, and acceptance of managed care and Medicare.

Conclusions:
Significant heterogeneity exists in adolescent anemia screening based on patient-, provider- and practice-level variables. The interaction between sex and age suggests that in following current guidelines, pediatric providers may focus screening on younger adolescent females and may not routinely consider repeat testing for older adolescents.
Risk Factors for Adolescent Iron Deficiency vary by the Ferritin vs. the Body Iron Model

Deepta L Sekhar, MD, MSc¹, Laura E Murray-Kolb, PhD², Allen R Kunselman, MA³ and Ian M Paul, MD, MSc¹,³
¹Pediatrics, Penn State College of Medicine, Hershey, PA; ²Nutritional Sciences, The Pennsylvania State University, University Park, PA and ³Public Health Sciences, Penn State College of Medicine, Hershey, Pennsylvania

Background:
It is estimated that 9-11% of US adolescent girls and women of childbearing age are iron deficient. Iron deficiency has well-documented morbidity, but is easily correctable. A single, inexpensive test for iron deficiency is lacking, so pediatricians have traditionally used hemoglobin to screen adolescent girls in the office setting. However, this method misses a large number of non-anemic, iron deficient adolescents. A risk factor assessment for iron deficiency with lab testing of only “high-risk” adolescents may be preferable. The body iron model has been proposed as an alternative to the traditional ferritin model for diagnosis of iron deficiency, yet no studies have examined if the two models are associated with similar risk factors among adolescent females.

Objective:
To examine risk factors for iron deficiency by the ferritin versus the body iron model for females 12-<22 years-old using data from the National Health and Nutrition Examination Survey (NHANES) 2003-2006.

Design/Methods:
Iron deficiency by the ferritin model is defined as 2 of 3 laboratory values (transferrin saturation, ferritin, erythrocyte protoporphyrin) out of range. The body iron model involves a formula which requires laboratory values for transferrin receptor and ferritin. Bivariate analysis of questionnaire responses and laboratory data identified risk factors for adolescent iron deficiency.

Results:
Approximately 30 million adolescent females were represented over the 4-year period. 13% were iron deficient by the ferritin model and 9% by the body iron model. Only 4% were anemic.

Conclusions:
Risk factors for adolescent iron deficiency vary by the model used complicating screening of high-risk individuals. Consensus on the definition of iron deficiency with emphasis on overlapping risks will be a key part of developing screening tools for adolescent iron deficiency.
Risk Factors for Anemia Among United States Adolescent Females

Deepa L Sekhar, MD, MSc¹, Laura E Murray-Kolb, PhD², Allen R Kunselman, MA³ and Ian M Paul, MD, MSc¹,³.
¹Department of Pediatrics, Penn State College of Medicine, Hershey, PA; ²Nutritional Sciences, The Pennsylvania State University, University Park, PA and ³Public Health Sciences, Penn State College of Medicine, Hershey, PA.

Purpose:
Iron deficiency anemia affects 3.3 million US women, has well-documented morbidity, but is easily correctable. Published risk factors for anemia include race, poverty, obesity, a low-iron diet, heavy menses, and a prior diagnosis of iron deficiency anemia. Pediatric providers screen adolescent females for anemia, but screening recommendations are based on risk factors for all reproductive age women, typically defined as 12-49 years. Our objective was to examine anemia risk factors among adolescent females 12-21 years-old using data from the National Health and Nutrition Examination Survey (NHANES) 2001-2010.

Methods:
Anemia was defined by hemoglobin, a standard laboratory measure collected on NHANES participants. The sex, age and race cutoffs for hemoglobin as specified by the Centers for Disease Control and Prevention and International Nutritional Anemia Consultative Group were used. Questionnaire responses between anemic and non-anemic adolescent females were compared to identify risk factors for anemia.

Results:
Among 4,750 adolescent female participants, 3.8% were anemic. In the bivariate analysis anemia was associated with age, race, general health, family poverty income ratio, country of birth and treatment for anemia in the past 3 months. Multivariable modeling revealed only general health and treatment for anemia in the past 3 months as significant. In the presence of general health and treatment for anemia, age and years since menarche were not significantly associated with anemia.

Conclusions:
While NHANES cannot fully account for all variables historically associated with anemia, these data suggest that anemia risk factors among adolescent females differ from those cited for women across the entire reproductive age continuum.
Right ventricular cardiac hemangioma in a competitive basketball player presenting with chest pain – a case report

Marie Shaner, MS, John L. Myers, MD, Michele Monaco, MD, Don Leach, BS, Linda B Pauliks, MD, MPH, Pediatric Cardiovascular Research Center, Depts. of Pediatrics and CT surgery Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Background:
Less than 5% of chest pain in children is cardiac in origin, yet this complaint still represents one of the top referral reasons for cardiology consult. We present a unique case where a screening echocardiogram identified a significant problem.

Case presentation:
A 15 year old competitive basketball player presented with a 6 months history of sharp, brief and nondebilitating retrosternal chest pain. Past medical history was noncontributory. On physical exam, no murmurs were appreciated. Electrocardiogram showed prominent left ventricular forces and was otherwise normal. An echocardiogram was obtained at the same visit. It showed a 3 x 2 cm diameter homogeneous pedunculated mass attached to infundibular septum of the right ventricle (Figure 1A). It bounced back and forth in the right ventricular outflow tract but appeared to permit sufficient forward blood at rest. A cardiac MRI was confirmatory (Figure 1B). During open heart surgery, it was possible to remove the tumor via an incision into the main pulmonary artery, thus avoiding a ventriculotomy. Two additional smaller tumors measuring 6 to 7 mm were also resected. Patient recovered quickly and had a normal exercise stress test 3 months following his original presentation.

Discussion:
Cardiac hemangiomas are among the rarest of cardiac tumors in children. They have benign growth characteristics and may even regress spontaneously. Still, this case shows that they can cause problems due to location and impairment of cardiac blood flow and possibly myocardial blood supply. It is unclear whether the patient’s chest pain was ultimately caused by the mass although he was pain-free on follow up. This case illustrates the diagnostic dilemma of chest pain in children. The screening echocardiogram is usually negative but when it is abnormal, it may have life-changing consequences.

Figure 1: Right heart hemangioma on echocardiogram (A) and cardiac MRI (B).
Impact and Control of Contamination in Pediatric Research on Child Maltreatment

Chad Shenk, Ph.D.1,2,3, Jennie Noll, Ph.D.1,3, James Peugh, Ph.D.4, & Amanda Griffin, B.S.1
1 = Department of Human Development and Family Studies, Penn State University; 2 = Division of Child Abuse Pediatrics, Penn State Hershey Medical Center; 3 = Network on Child Protection and Well-being, Penn State University; 4 = Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children’s Hospital.

Purpose:
Variation in the significance and magnitude of effect size estimates has weakened conclusions about the long-term effects of child maltreatment on pediatric health. Contamination, or the presence of child maltreatment in a comparison condition, may explain this variation as it can weaken the magnitude of effect size estimates and increase the probability of Type II errors. This study tested multiple methods for assessing and controlling the impact of contamination in pediatric research on child maltreatment.

Methods:
The Female Adolescent Development Study (N=512; Age range: 14-17) is a multi-wave, prospective cohort study examining the long-term effects of substantiated child maltreatment, as determined by Child Protective Services (CPS), on female adolescent health. Maltreated (n=273) and demographically-matched comparison participants (n=239) completed annual study visits tracking severity and change in key, female health outcomes: teenage births, obesity, major depression and past month cigarette use. Contamination was measured prior to study enrollment and during longitudinal follow-up. Comparison participants experiencing child maltreatment, as assessed by adolescent self-report (n=90), CPS records (n=43), and a combined method that used both self-report and CPS records (n=109), were removed from statistical analyses, respectively, to control the impact of contamination on effect size estimates.

Results:
Adjusted relative risks (RRs) demonstrated that the combined method was the only method to significantly predict clinical health status for each outcome at the final study visit, RRs = 1.47-2.97, 95% CIs: 1.03-7.18, yielding the strongest effect size estimates across all methods (Table 1) and enhancing the representativeness of the comparison condition in relation to national prevalence estimates (Figure 1).

Conclusions:
A combined method for assessing child maltreatment provides optimal control of contamination, yields stronger, more generalizable risk estimates, and strengthens conclusions about the long-term effects of child maltreatment on important female health outcomes during the transition to young adulthood.
Identification of microRNA Biomarkers for Pediatric Bronchopulmonary Dysplasia

Patricia Silveyra, PhD; Christiana Oji-Mmuo, MD; Susan DiAngelo, BS; Judie Ann Howrylak, MD, PhD; Spear Debra, RN, CCRN; Faoud Ishmael, MD, PhD; and Neal Thomas, MD
Center for Host Defense, Inflammation, and Lung Disease (CHILD) Research, and Departments of Pediatrics, Biochemistry and Molecular Biology, Medicine, and Public Health Sciences.
Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Bronchopulmonary Dysplasia (BPD) is the most common and serious chronic lung disease of premature infants. Early detection of BPD is important to prevent disease progression and chronic lung remodeling that can increase the risk to develop pulmonary complications and disease later in life. There are currently no good biomarkers for identification of infants at risk of BPD. The goal of this study was to identify microRNA (miRNA) signatures in tracheal aspirates (TAs) of infants receiving mechanical ventilation that can serve as biomarkers for BPD diagnosis.

Methods:
We measured expression of miRNAs in TAs (discarded material obtained during routine care) from infants receiving mechanical ventilation at the Penn State Children’s hospital NICU and PICU. Patients had a confirmed clinical diagnosis of BPD (cases, n=13). Controls were age-matched with no evidence or history of lung disease (n=3). The miRNA fraction was purified with the serum and plasma miRNA Purification Kit (Norgen), and miRNA quality was confirmed by Bioanalyzer. The expression of 1,066 human miRNAs was quantified with the miScript miRNA PCR Array Human miRNome kit (QIAGEN). Data was analyzed with the manufacturer’s online software.

Results:
We found expression of >800 miRNAs in TAs from patients with BPD, and >480 miRNAs in controls. Of these, 266 and 72 miRNAs showed high expression (Ct<30) in BPD and control samples, respectively. Ten miRNAs (hsa-mir-21, -223, -574-3p, -720, -1207-5p, -1260, -1260b, -1280, -1281, and -4286) showed very high expression (Ct<25) BPD samples, and 7 miRNAs (let-7i, hsa-mir-21, -200c, -548d-3p, -720, -1260, -1280) in controls. Statistical analyses revealed differential expression of >30 miRNAs between BPD and control samples (p<0.05).

Conclusions:
We show for the first time that miRNAs are expressed in TAs of pediatric patients receiving mechanical ventilation. Our results indicate that differential expression of miRNAs can be used as potential molecular diagnostic markers for BPD.
Sequence polymorphisms at the 3’UTR of human Surfactant Protein A gene variants differentially affect gene expression levels and miRNA regulation in vitro

Patricia Silveyra, PhD; Susan L DiAngelo, BS; Joanna Floros, PhD.
Center for Host Defense, Inflammation, and Lung Disease (CHILD) Research, Department of Pediatrics; Department of Biochemistry and Molecular Biology, and Department of Obstetrics and Gynecology. Penn State College of Medicine, Hershey, Pennsylvania, USA

Purpose:
Surfactant protein A (SP-A), plays a vital role in maintaining normal lung function, and in host defense. Two genes encode SP-A in humans: SFTPA1, and SFTPA2, and several gene variants have been identified and associated with pediatric lung disease. We have previously shown that specific sequence elements of SP-A regulatory regions (3’UTRs) differentially affect translation efficiency in vitro. The goal of this study was to evaluate whether polymorphisms at the 3’UTRs of SFTPA1 and SFTPA2 variants can affect binding of miRNAs, a new class of small non-coding RNAs that regulate gene expression.

Methods:
We generated 3’UTR luciferase reporter constructs of the SP-A variants most frequently found in the population (4 SFTPA1 variants, and 6 SFTPA2 variants). We also generated mutants of a previously described 11-nt sequence element (refSNP rs368700152) present at the 3’UTR of SP-A variants, to study its role on miRNA-mediated regulation of expression. Reporter constructs were transfected in the lung adenocarcinoma cell line NCI-H441 in the presence or absence of miRNA mimics predicted in silico to differentially bind SP-A 3’UTRs (hsa-mir-183, -449, -612, -762, -767, -3940, -4417, and -4507). Luciferase activity was analyzed 48h post-transfection.

Results:
We found a differential impact of miRNA mimics on the expression of SP-A variants. The human miRNA mir-767 negatively affected reporter expression of constructs containing both SFTPA1 and SFTPA2 variants, whereas mir-4507 affected only constructs with 3’UTRs of SFTPA1 variants without the 11-nt element. Three miRNAs (mir-183, mir-449b, and mir-612) inhibited expression of SFTPA2 variants, and the SFTPA1 variant 6A2, all containing the 11-nt element.

Conclusions:
Our results indicate that sequence variability at the 3’UTR of SFTPA1 and SFTPA2 variants differentially affect regulation of gene expression by miRNAs. The differential impact of the miRNA-mediated regulation on SP-A levels may contribute to individual susceptibility to lung disease.
Epigenetic control of cell cycle by Ikaros and HDAC1 in leukemia

Chunhua Song, M.D., Ph.D1, Xiaokang Pan, Ph.D., Chandrika S. Gowda, MD3, Yali Ding, Ph.D. Kimberly J Payne, PhD2, Sinisa Dovat1

1Pediatric Hematology/Oncology, Pennsylvania State University Medical College, Hershey, PA; 2Anatomy, Loma Linda University, Loma Linda, CA; 3Department of Pediatrics, Pennsylvania State University Medical College, Hershey, PA

Purpose:
Ikaros acts as a tumor suppressor in leukemia. The molecular mechanisms through which Ikaros exerts its tumor suppressor function remain unknown. Here we present the evidence that Ikaros represses the genes that promote cell cycle progression and cell proliferation via chromatin remodeling.

Methods:
We used ChIP-SEQ to identify Ikaros binding genes in human B cell leukemia (B-ALL), the qChIP assay to confirm Ikaros binding to its targets, the luciferase reporter assay to observe the direct effect of Ikaros on transcription suppression of its targets. We also generate the Ikaros-expressed leukemia cells (the retroviral gene delivery system) and Ikaros knockdown cells to observe the effect of Ikaros on gene expression of Ikaros targets by qPCR and the effect of Ikaros on cell proliferation using the colorimetric cell proliferation assay.

Results:
We identified Ikaros target genes in human B cell leukemia (B-ALL). ChIP-SEQ revealed that Ikaros binds to the promoter regions of the large group of genes that are essential for the cell cycle progression and proliferation. Ikaros suppress the gene expression of its targets. Increased binding of Ikaros to the target genes was associated with recruitment of histone deacetylase HDAC1 to some, but not all of the target genes. Quantitative chromatin immunoprecipitation (qChIP) revealed that binding of Ikaros-HDAC1 complex is associated with increased H3K27me3 and decreased H3K9ac marks at the promoter of Ikaros target genes. In contrast, binding of Ikaros without HDAC1 resulted in formation of heterochromatin, characterized by presence of H3K9me3.

Conclusions:
Ikaros represses transcription of the genes on cell cycle progress and cell proliferation via chromatin remodeling by two distinct manners: HDAC1-dependence (recruiting H3M27me3) and HDAC1-independence (formation of H3K9me3 heterochromatin). Presented data revealed the role of Ikaros, HDAC1 and chromatin remodeling in regulation of the cell cycle and cell proliferation in leukemia.
Triclosan and Paraben Exposure are Associated with Allergen Sensitization

Adam J. Spanier, MD, PhD, MPH, Tracy Fausnight, MD, Fabian Camacho, MA, Joe Braun, MSPH, PhD, RN
Department of Pediatrics, Penn State University, Hershey, PA; Department of Public Health Sciences, Penn State University, Hershey, PA; Departments of Epidemiology, Brown School of Public Health, Providence, RI

Background:
Triclosan and parabens are chemicals used in many personal care and medical products as microbicides and preservatives. They have been noted to have an association with sensitization and immune modulation. These associations have not been evaluated with consideration of other atopic states like eczema.

Methods:
We performed a cross-sectional analysis of a subsample of US children age 6-19 years who participated in the National Health and Nutrition Examination Survey (years 2005-2006). We quantified triclosan and paraben exposure using urinary concentrations. We assessed associations of triclosan and parabens with allergic sensitization and asthma using logistic regression.

Results:
Sensitization and exposure data was available for 837 children. Aeroallergen sensitization (43%), food sensitization (19%), reported asthma diagnosis (14%), reported wheeze (11%), and reported eczema diagnosis (12%) was prevalent. After adjustment for potential confounders, increasing triclosan, and methyl and propyl paraben concentrations were associated with increased odds of aeroallergen sensitization. Children were 1.34 times more likely to have reported (95% CI 1.00, 1.81) atopic asthma for each quartile of increased triclosan exposure. Eczema did not significantly modify the association of triclosan or parabens levels with aeroallergen sensitization, asthma, or wheeze. There was a significant interaction of eczema and triclosan in relation to food sensitization (p=0.04). Children with eczema and triclosan exposure had 2.3 times the odds of food sensitization for each quartile increase in exposure (95% CI 1.14, 4.44), but this association was not significant among children without eczema (OR 1.25, 95% CI 0.93, 1.68).

Conclusions:
Triclosan and paraben exposures were associated with aeroallergen sensitization, and eczema status modified associations of triclosan with food sensitization. Prospective studies with repeated biomarkers of triclosan and paraben exposure and child allergen sensitization are necessary to confirm these findings and determine if these chemicals pose a risk to children’s health.
Handling Ability of Gaseous Microemboli of Two Pediatric Arterial Filters in a Simulated CPB Model

Ashton Strother1,2, Shigang Wang, MD2, Allen R. Kunselman, MA3, Akif Ündar, PhD2,4

1 Huron High School, Ann Arbor Public Schools, Ann Arbor, MI, USA; Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics2, Public Health and Sciences3, Surgery, and Bioengineering4. Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children’s Hospital, Hershey, PA, USA

Background:
The purpose of this experiment was to compare the Sorin KIDS D131 and Terumo Capiox AF02 pediatric arterial filters, in a simulated CPB procedure, to determine which filter is the best for clinical use.

Methods:
The experimental circuit was primed with 800 ml combination of lactated ringer’s solution and human blood (HCT 30%). The two filters were tested under flow rates of 500, 1000, and 1500 ml/min, at room temperature, and their purge lines open and closed, as 5cc of air was injected into the circuit.

Results:
As the flow rates increased the number of GME being returned to the pseudo patient increased for both of the pediatric arterial filters. Having an open purge line increased the number of GME removed from the CPB circuit, caused less of a pressure drop, than when closed, and increased the total hemodynamic energy loss, than when closed. Both of the filters performed and reacted similarly in decreasing GME, hemodynamic energy loss, and pressure drop. The only minor difference was that the Capiox AF02 had slightly less stolen blood flow (109.5 ± 1.7 ml/min at 500 ml/min, 114.7 ± 1.1 ml/min at 1000 ml/min and 105.8 ± 4.2 ml/min at 1500 ml/min) from the open purge line than the kids d131 (119.5 ± 2.5 ml/min at 500 ml/min, 128.3 ± 1.0 ml/min at 1000 ml/min and 126.3 ± 3.1 ml/min at 1500 ml/min).

Table 1. Total emboli counts at the inlet and outlet of Terumo and Sorin pediatric arterial filters at different flow rates

<table>
<thead>
<tr>
<th>Flow rate</th>
<th>Purge line</th>
<th>Terumo Capiox AF02</th>
<th>Sorin KIDS D131</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Inlet</td>
<td>Outlet</td>
<td>Trap (%)</td>
</tr>
<tr>
<td>500 ml/min</td>
<td>Closed</td>
<td>4.2±3.8</td>
<td>1.8±2.4</td>
</tr>
<tr>
<td></td>
<td>Open</td>
<td>5.0±6.7</td>
<td>1.8±3.3</td>
</tr>
<tr>
<td>1000 ml/min</td>
<td>Closed</td>
<td>222.8±50.1</td>
<td>123.0±24.8</td>
</tr>
<tr>
<td></td>
<td>Open</td>
<td>141.5±29.0</td>
<td>71.8±23.1</td>
</tr>
<tr>
<td>1500 ml/min</td>
<td>Closed</td>
<td>2960.7±792.4</td>
<td>1966.8±504.3 *</td>
</tr>
<tr>
<td></td>
<td>Open</td>
<td>2196.0±228.9</td>
<td>1402.3±163.6</td>
</tr>
</tbody>
</table>

* P <0.01, the arterial filter purge line: Closed vs. Open.

Conclusions:
Our study confirmed that both the Sorin KIDS D131 and the Terumo Capiox AF02 were equivalent in their ability to remove significant number of GME, the amount of pressure drop and total hemodynamic energy loss across the arterial filters, at the various flow rates. An arterial filter is not an option, but a necessity for removing microemboli delivering to the patient.
ONC201 (TIC10) Exerts Cytotoxicity in Preclinical Models of Pediatric Lymphoma: A Novel Approach

Mala K. Talekar, MD, Wafik El-Deiry, MD, PhD, FACP, Penn State Hershey Cancer Institute, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Outcome for pediatric NHLs using conventional treatment standards remains unsatisfactory, particularly in advanced stage/relapsed disease. TRAIL, an endogenous protein, induces apoptosis selectively in cancer cells by binding to death receptors. Previous TRAIL-targeting strategies have demonstrated unfavorable properties—poor biodistribution and pharmacokinetics, which hamper efficacy. ONC201 (TIC10), a novel compound (JE Allen et al), induces p53-independent TRAIL gene transcription and cell death in tumor cells (sparking normal cells) through dual inactivation of prosurvival kinases Akt and ERK. ONC201 has long half-life, stimulates TRAIL and death receptor expression, has lower production cost, ability to cross intact blood-brain barrier, is orally active and has potent anti-tumor efficacy in preclinical animal cancer models.

Objective:
Derive preclinical rationale for ONC201 as novel targeted therapy for pediatric lymphoma.

Methods:
Diverse sub-type panel of seven human lymphoma cell lines used to assess lymphoma sensitivity to ONC201. Luminescent cell viability assay to generate inhibition curves post-treatment (T/t) with ONC201 yielding IC50’s. Caspase-based Apoptosis assay to quantify sub-G1 DNA content. Surface TRAIL and surface DR5 expression via FACS. Inhibition of ONC201-induced apoptosis using Pan-caspase inhibitor (Z-VAD-FMK) at 72H post-T/t. Western blot analysis of representative cell lines at 48H post-T/t with ONC201 to validate mechanism of apoptosis induction.

Results:
Sharp dose-response curves at 72H post-T/t yielded IC50’s ranging from 1.3 - 5.0 micromolar. Significant levels of apoptosis noted in dose-dependent manner with increase in sub-G1 content ranging 1.8-fold - 4.15-fold. Increase in surface DR5 and surface TRAIL expression (correlating with increase in sub-G1 DNA content) noted in dose-dependent manner. ONC201-induced apoptosis demonstrably inhibited using Pan-caspase inhibitor. Western blot analysis of ONC201-treated cell lines suggests ERK inhibition and Foxo3a recruitment as potential mechanism of apoptosis induction.

Conclusions:
ONC201 is promising as monoagent in preclinical models of pediatric lymphoma and may be enhanced by combination with approved therapies to improve the standard of care for pediatric NHL.
Reduced PIP2 Binding to KCNJ2 Channels is Linked to Type 1 Andersen-Tawil Syndrome

Bi-Hua Tan, MD, PhD; Sinisa Dovat, MD, PhD; Blaise Peterson, PhD; Chunhua Song, MD, PhD
Department of Pediatrics and Cellular & Molecular Physiology, Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
Kir2.x subfamily members mediate the cardiac inward rectifier potassium current (I_{K1}). KCNJ2 encodes Kir2.1, the pore-forming alpha subunit responsible for cardiac I_{K1}, and the mutations in this gene are associated with type 1 Andersen-Tawil Syndrome (ATS1). A Kir2.1 missense mutation, M307I, has been identified in a Korean family with ATS1. We found that the ATS1-associated M307I mutation is a loss-of-function mutation in KCNJ2 that mediates a dominant-negative effect on wild-type (WT) channels. M307I is located in the intracellular C-terminal domain in a region known to be associated with putative phosphatidylinositol 4,5-bisphosphate (PIP2) binding and channel trafficking. Here we explored the mechanisms underlying the dominant-negative effect of the mutation.

Methods:
Human Kir2.1 was subcloned into IRES2-EGFP or pFlag-CMV vector and Kir2.1-M307I was generated by site-direct mutagenesis. The IRES2-EGFP-Kir2.1-WT and IRES2-EGFP-M307I mutant were expressed in HEK293 cells for electrophysiological study and confocal imaging experiments. The Flag-Kir2.1-WT and Flag-Kir2.1-M307I were expressed in HEK293 cells and affinity purified. PIP2-binding was assessed using a Lipid-bead-protein pull-down assay with cell lysate and Protein-lipid overlay assay with purified proteins.

Results:
The electrophysiological data showed that the M307I mutant channel significantly reduces whole cell current densities when co-expressed with Kir2.1-WT channels. Immunofluorescence (IF) staining assays reveal that M307I channels exhibit normal membrane trafficking. PIP2 binding assays show that Flag-Kir2.1-M307I channels exhibit dramatically decreased binding to PIP2 compared to WT channels.

Conclusions:
M307I is an ATS1-associated, loss-of-function missense mutation in KCNJ2 that mediates a dominant-negative effect on WT channels by reducing PIP2 binding to the channel.
Chorioamnionitis is associated with low heart rate variability in preterm infants

Pratima Toom, MD, Charles Palmer, MB, ChB, and Kim K. Doheny, PhD, Penn State Hershey Children’s Hospital, and Penn State College of Medicine, Hershey, Pennsylvania, USA

Purpose: Chorioamnionitis (CA) is responsible for 50% of the preterm births in the NICU. CA induces pro-inflammatory cytokines in 25-40% of preterm births and has been associated with morbidities such as necrotizing enterocolitis. Circulating cytokines in fetal circulation influence heart rate variability (HRV) through sympathetic and parasympathetic pathways. The vagus nerve (parasympathetic nervous system) regulates cytokine production during inflammation and HRV. By measuring these variations in HRV using the high frequency component of frequency domain analysis (HF-HRV), vagal tone of newborns can be estimated. Our primary aim is to determine if chorioamnionitis is associated with low vagal tone (HF-HRV).

Methods: Seventy LBW preterm (28-35 wk PMA) infants born at PSHMC and admitted to our NICU from Jan 2007 - July 2012 were included. Infants meeting exclusion criteria were excluded. HRV was measured between 5 and 8 postnatal days of life and analyzed using fast Fourier Transform. Data extraction included: maternal and fetal demographics, maternal h/o of clinical and histological CA, perinatal/postnatal history, and clinical outcomes.

Results: Of the 70 enrolled subjects, placental histology was available for 62 subjects (88.5%). Clinical chorioamnionitis was seen in 11% and histological chorioamnionitis in 19% of subjects. Fetal involvement was identified in 7 out of 12 (58%) subjects with histological chorioamnionitis. By independent samples t test, there was significantly lower HF-HRV power in infants identified to have chorioamnionitis with fetal involvement (See Figure).

Conclusions: Chorioamnionitis with either clinical or histological signs of fetal involvement is associated with low vagal tone measured at day 5-7 days of life in premature infants.
Regulation of translation by upstream translation initiation codons of surfactant protein A1 (SP-A1) splice variants

Nikolaos Tsotakos¹, Patricia Silveyra¹, Zhenwu Lin², Neal Thomas¹,³, Mudit Vaid¹, and Joanna Floros¹,⁴

¹Center for Host Defense, Inflammation and Lung Disease (CHILD) Research, Department of Pediatrics, ²Department of Cellular and Molecular Physiology, ³Department of Public Health Sciences and ⁴Department of Obstetrics and Gynecology. The Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA

Purpose:
Surfactant Protein A (SP-A), a molecule with roles in lung innate immunity and surfactant-related functions, is encoded by two genes in humans: SFTPA1 (SP-A1) and SFTPA2 (SP-A2). The mRNAs from these genes differ in their 5' untranslated regions (5'UTR) due to differential splicing. The 5'UTR variant ACD' is exclusively found in transcripts of SP-A1, but not of SP-A2. Its unique exon C contains two upstream AUG codons (uAUGs) that may affect SP-A1 translation efficiency. The purpose of the present study is to understand the role of upstream AUG elements in SP-A1 expression.

Methods:
We employed RT-qPCR to determine the presence of exon C-containing SP-A1 transcripts in human RNA samples. We also used a number of in vitro techniques including mutagenesis, reporter assays, and toeprinting analysis, as well as in silico analysis to determine the role of uAUGs.

Results:
We found that exon C-containing mRNA is present in approximately 75% of human lung tissue samples and its expression can, under certain conditions, be regulated by external factors such as dexamethasone or endotoxin. Luciferase reporter assays revealed a negative regulatory role for uAUGs, but the mature protein size was not affected by their existence, as shown by a combination of toeprint and in silico analysis for Kozak sequence, secondary structure, and signal peptide.

Conclusions:
These results indicate that alternative splicing may introduce uAUGs in SP-A1 transcripts, which in turn negatively affect SP-A1 translation, and possibly affect the SP-A1/SP-A2 ratio, with potential for clinical implications.

Supported by NIH HL34788
Using a Secondary Reservoir for Pump Suckers to Avoid the Generation of Foam during CPB Procedures in Pediatric Patients

Akif Ündar, PhD¹,², David Palanzo, CCP¹,³, Robert Wise, CCP¹,³, Larry Baer, CCP¹,³ and Shigang Wang, MD¹
Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics¹, Surgery and Bioengineering², Perfusion Department, Penn State Heart and Vascular Institute³, Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Translational research is a must when evaluating different oxygenators, pumps, cannulae, etc. for the safety of pediatric as well as adult cardiopulmonary bypass (CPB) patients. The primary goal of “translational research” is to take research from the “bench-to-bedside”.

Recently, a few pediatric centers found the incidents of foam breaking through from the cardiotomy reservoir in the venous reservoir when using certain types of pediatric oxygenators, when extreme sucker and vent return was required. We would suggest an approach that may eliminate this particular problem for neonatal and infantile patients, not just for these particular oxygenators, but for all other oxygenators with similar mismatches of flow rate between the oxygenator and the cardiotomy reservoir. We would suggest incorporating a secondary cardiotomy reservoir for pump suckers to avoid the foam from entering the venous reservoir. There will be a very small additional cost ($100) for a second reservoir, but this may be necessary for the safety of the patient. If the patient weight is below 12 kg, we use a secondary reservoir for pump suckers as a routine practice at Penn State Hershey (Figure 1). We started using this secondary reservoir over nine years ago when we noticed the same problem with a different oxygenator. Since then, we have always used a secondary reservoir, in particular for neonates and infants, although we have also changed the oxygenator. We have never seen these types of events after adding the secondary reservoir for pump suckers. We believe that the secondary reservoir is a necessity for minimizing not only microemboli counts, but also systemic inflammation during CPB for neonates and infants.

In summary, it is impossible to eliminate microemboli generation during pediatric and adult CPB, but translational research may significantly help to reduce the microemboli. We strongly recommend using a secondary reservoir, solely for pump suckers, to avoid the generation of foam during CPB procedures.

Figure 1. Penn State Hershey clinical CPB circuitry, including secondary cardiotomy reservoir for pump suckers.
Active Parenting and Parental Role Attainment in Parents of Preterm Infants in the NICU

Kristin Veneman, DO, Kim Doheny, PhD, and Gina Brelsford, PhD
Neonatal Perinatal Medicine, Penn State Hershey Children's Hospital/ Milton S. Hershey Medical Center, Hershey, Pennsylvania

Background:
Preterm birth causes stress for parents due to uncertainty and disruption of the parent-infant relationship. The infant’s hospitalization is also stressful for the infant. Parents can serve as buffers to this stress and enhance bonding and infant development. However, there are many barriers in the NICU that affect a parent’s ability to take on an active role as parent.

Objectives:
The primary aim of this study was to explore parents' views on involvement and advocacy and to identify barriers to active parenting. The secondary aim was to explore mothers’ sensitivity, interaction, and competence with their infants at the time of hospital discharge.

Methods:
20 preterm infants and their adult parents participated in this prospective, observational study. Maternal/infant risk factors and infant outcome measures were obtained by chart audit. Near discharge, parents completed a 35-item investigator generated Parenting in the NICU Questionnaire. Also, a naturalistic observation of mothers caring for their preterm infant was made using the Boston City Hospital Assessment of Parental Sensitivity (BCHAPS).

Results/Conclusion:
Data analysis revealed mothers as highly sensitive and competent in caring for their infants at the time of discharge by direct observation. In addition, mothers and fathers expressed that they had adequate support from staff and family in the parenting role, felt competent as parents at discharge, and celebrated milestones during their infant’s hospitalization in NICU. However, parents identified barriers to active parenting which included family involvement, communication, and advocacy. In addition, parents did not frequently engage in activities known to support language development (reading, singing, and talking to their infant) nor in pain-relief for their infant.
Comparison of Atopic Features between Children and Adults with Eosinophilic Esophagitis

Natalia Vernon MD¹, Shenil Shah MD², Sapna Shah MD³, Erik Lehman MS⁴ and Gisoo Ghaffari MD¹

¹Penn State University Hershey Medical Center, Division of Allergy and Immunology
²Penn State University Hershey Medical Center, Department of Medicine
³Penn State University Hershey Medical Center, Department of Pediatrics
⁴Penn State University Hershey Medical Center, Department of Public Health Sciences

Purpose:
Eosinophilic esophagitis (EoE) is a chronic inflammatory process characterized by esophageal dysfunction and eosinophilic infiltration. Evidence suggests that EoE may represent a combination of a Th1 and Th2 driven inflammatory disease. Allergic diseases and atopic predispositions are very common in patients with EoE. EoE presenting symptoms vary between the pediatric and adult population. We sought to investigate if atopic features vary between children and adults with EoE.

Methods:
After IRB approval, we conducted a retrospective chart review of 50 children (2-18 yrs) and 50 adults who were diagnosed with EoE by endoscopic biopsy. Variables of interest included: (1) history of asthma, allergic rhinitis, food allergy and atopic dermatitis; (2) immediate hypersensitivity reactions to foods and aeroallergens determined by skin tests and/or serum specific IgE testing; and (3) delayed hypersensitivity reactions to foods measured by patch testing. Chi-square and Fisher exact tests were used to determine the significance of the differences between adults and children.

Results:
Compared to adults, a higher percentage of children had asthma (52% vs 24%, p <0.05). There was no significant difference between children and adults regarding history of allergic rhinitis, atopic dermatitis and food allergy. There was no significant difference between adults and children regarding immediate type sensitization to foods and aeroallergens. Compared to adults, a higher percentage of children had a positive patch test to foods (62% vs 31%, p<0.05).

Conclusions:
In our patient population with EoE, children were more likely to have asthma and more likely to have a positive patch test to foods. There was no statistically significant difference between children and adults for the other atopic features analyzed in this study.
In Vitro Performance Analysis of a Novel Pulsatile Diagonal Pump in a Simulated Pediatric Mechanical Circulatory Support System

Shigang Wang, MD1, Allen R. Kunselman, MD2, and Akif Ündar, PhD1,3
Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics1, Public Health and Sciences2, Surgery and Bioengineering3. Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
The objective of this study was to evaluate the pump performance of the third-generation Medos diagonal pump, the Deltastream DP3, on hemodynamic profile and pulsatility in a simulated pediatric mechanical circulatory support (MCS) system.

Methods:
The experimental circuit consisted of a Medos Deltastream DP3 pump head and console (MEDOS Medizintechnik AG, Stolberg, Germany), a 14-Fr Terumo TenderFlow Pediatric arterial cannula and a 20-Fr Terumo TenderFlow Pediatric venous return cannula (Terumo Corporation, Tokyo, Japan), and 3 ft of tubing with an internal diameter of ¼ in. for both arterial and venous lines. Trials were conducted at flow rates ranging from 250 mL/min to 1000 mL/min (250-mL/min increments) and rotational speeds ranging from 1000 to 4000 rpm (1000-rpm increments) using human blood (hematocrit 40%). The post-cannula pressure was maintained at 60 mm Hg by a Hoffman clamp. Real-time pressure and flow data were recorded using a Labview based acquisition system.

Results:
The pump provided adequate nonpulsatile and pulsatile flow, created more hemodynamic energy under pulsatile mode, and generated higher positive and negative pressures when the inlet and outlet of the pump head, respectively, were clamped (Table 1). After the conversion from nonpulsatile to pulsatile mode, the flow rates and the rotational speeds increased.

Conclusions:
The novel Medos Deltastream DP3 diagonal pump is able to supply the required flow rate for pediatric MCS, generate adequate quality of pulsatility, and provide surplus hemodynamic energy output in a simulated pediatric MCS system.

Table 1. Mean pressures (MP) and energy equivalent pressures (EEP) with pulsatile and non-pulsatile modes.

<table>
<thead>
<tr>
<th>Flow rate</th>
<th>Mode</th>
<th>Post-pump site</th>
<th>Post-cannula site</th>
<th>Pre-pump site</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>MP</td>
<td>EEP</td>
<td>MP</td>
</tr>
<tr>
<td>250</td>
<td>NP</td>
<td>69.2±0.1</td>
<td>69.2±0.1</td>
<td>61.0±0.1</td>
</tr>
<tr>
<td></td>
<td>P500</td>
<td>70.6±0.2*</td>
<td>75.3±0.2*</td>
<td>62.4±0.2*</td>
</tr>
<tr>
<td></td>
<td>P1500</td>
<td>69.3±0.3</td>
<td>75.6±0.2*</td>
<td>60.7±0.3</td>
</tr>
<tr>
<td></td>
<td>P2500</td>
<td>69.9±1.0*</td>
<td>76.0±0.6*</td>
<td>61.5±0.8</td>
</tr>
<tr>
<td>500</td>
<td>NP</td>
<td>77.4±0.0</td>
<td>77.4±0.0</td>
<td>59.9±0.0</td>
</tr>
<tr>
<td></td>
<td>P500</td>
<td>78.9±1.1*</td>
<td>81.5±1.1*</td>
<td>61.5±1.1*</td>
</tr>
<tr>
<td></td>
<td>P1500</td>
<td>80.3±1.1*</td>
<td>84.9±1.1*</td>
<td>62.6±1.1*</td>
</tr>
<tr>
<td></td>
<td>P2500</td>
<td>78.7±2.0*</td>
<td>83.2±3.0*</td>
<td>61.2±2.0*</td>
</tr>
<tr>
<td>750</td>
<td>NP</td>
<td>88.5±0.0</td>
<td>88.5±0.0</td>
<td>60.5±0.1</td>
</tr>
<tr>
<td></td>
<td>P500</td>
<td>89.8±1.1*</td>
<td>91.8±1.1*</td>
<td>61.2±1.1*</td>
</tr>
<tr>
<td></td>
<td>P1500</td>
<td>90.9±0.3*</td>
<td>95.3±0.3*</td>
<td>62.1±0.2*</td>
</tr>
<tr>
<td></td>
<td>P2500</td>
<td>92.4±2.0*</td>
<td>96.9±2.0*</td>
<td>63.2±1.1*</td>
</tr>
<tr>
<td>1000</td>
<td>NP</td>
<td>103.4±1.0</td>
<td>103.4±1.0</td>
<td>60.7±0.0</td>
</tr>
<tr>
<td></td>
<td>P500</td>
<td>104.5±2.0*</td>
<td>106.1±2.0*</td>
<td>61.7±1.0*</td>
</tr>
<tr>
<td></td>
<td>P1500</td>
<td>107.2±0.3*</td>
<td>112.0±0.2*</td>
<td>63.7±0.2*</td>
</tr>
</tbody>
</table>

*Significant difference compared to non-pulsatile mode.
Evaluation of Conventional Non-pulsatile and Novel Pulsatile ECLS Systems in a Simulated Pediatric ECLS Model

Shigang Wang, MD1, Alissa Evenson, BA1, Brian J Chin1, Allen R. Kunselman, MD2 and Akif Ündar, PhD1,3
Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics1, Public Health and Sciences2, Surgery and Bioengineering3. Penn State College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
The objective of this study is to evaluate two extracorporeal life support (ECLS) circuits and determine the effect of pulsatile flow on pressure drop, flow/pressure waveforms, and hemodynamic energy levels in a pediatric pseudo-patient.

Methods:
One ECLS circuit consisted of a Medos Delastream DP3 diagonal pump and Hilite 2400 LT oxygenator with arterial/venous tubing. The second circuit consisted of a Maquet Rotaflow centrifugal pump and Quadrox-iD Pediatric oxygenator with arterial/venous tubing. A 14Fr Medtronic Bio-Medicus one-piece pediatric arterial cannulae (Medtronic, Inc., Minneapolis, MN, USA) was used for both circuits. All trials were conducted at flow rates ranging from 500-2800 ml/min using pulsatile or non-pulsatile flow. The post-cannula pressure was maintained at 50 mmHg. Blood temperature was maintained at 36 °C. Real-time pressure and flow data were recorded using a custom-based data acquisition system.

Results:
The results showed the Delastream DP3 circuit produced surplus hemodynamic energy (SHE) in pulsatile mode at all flow rates, with greater SHE delivery at lower flow rates. Neither circuit produced SHE in non-pulsatile mode (Figure 1, 2). The Delastream DP3 pump also demonstrated consistently higher total hemodynamic energy at the pre-oxygenator site in pulsatile mode and less pressure drop across the oxygenator.

Conclusions:
The Delastream DP3 pump generated physiological pulsatility without backflow and provided increased hemodynamic energy. This novel ECLS circuit demonstrated suitable in vitro performance and adaptability to a wide range of pediatric patients.

Figure 1. Flow waveforms at pre-oxygenator site (DP3 vs. Rotaflow).

Figure 2. SHE at different flow rates and sites in pulsatile (P) and non-pulsatile (NP) mode.
The effect of the autism insurance mandate on healthcare utilization and costs

Li Wang, PhD, Douglas Leslie, PhD,
Department of Public Health Sciences, Penn State College of Medicine, Hershey, PA

Purpose:
There is no study in the literature on the actual effects (though many projections exist) of the new autism insurance mandate, which requires that private insurers cover autism spectrum disorders (ASD). This study will fill this gap.

Methods:
Actual insurance claims data were obtained from the largest private insurer in Pennsylvania, whose mandate was among the earliest enacted and has been an example for other states.

Results:
Since the PA autism mandate went into effect in mid-2009, full change was seen in 2010. From 2008 to 2010, the treated prevalence of ASD increased by more than 20%. Overall costs per patient increased from $2916 in 2008 to $6343 in 2010. The biggest cost increase was from outpatient cost, which rose from $853 and $1381 to $4138 per patient from 2008 to 2010, and stabilized afterwards. The inpatient and prescription drug costs did not change much after the mandate.

PA’s autism mandate applies to large employers and excludes small employers. By insurance type, the overall costs in 2010 (in 2008) were $9337 ($2973), $5166 ($2738), $3498 ($2938), $1980 ($1750), $1562 ($1248) for large employer, self-insured, small employer, the state children’s health insurance program (CHIP) and individual groups respectively. The differential cost increase was largely due to the newly covered community-based wrap-around services, which alone increased the costs from 2008 to 2010 by $6057 and $1770 for large employer and self-insured groups, respectively.

Conclusions:
The effects of the autism mandate were multi-folds. The treated prevalence of ASD increased. The post-mandate insurance cost increased greatly. Children with ASD did not benefit from the mandate equally, such as those in exempted small employer groups showing little service use increase. Further research is needed to explore why the PA CHIP program which the mandate applies to experienced little cost and service increase.
Behavior Therapy in Conduct Problem Children with Callous-Unemotional Traits: A Pilot Test of Increasing Reward and Decreasing Punishment

Daniel A. Waschbusch, Ph.D.
ADHD and Disruptive Behavior Program, Department of Psychiatry,
Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania, USA

Purpose:
Among children with significant conduct problems (CP), those who have low levels of guilty and empathy – referred to as callous-unemotional (CU) traits – display pernicious antisocial behaviors that are recalcitrant to treatment. Because children with CPCU overfocus on reward and underfocus on punishment in controlled lab tasks, it has been hypothesized that treatments that emphasize reward and de-emphasize punishment may more effective for these children. This study was a first test of this hypothesis.

Methods:
Participants were 11 children, ages 7 to 11 years, including 10 males and 1 female. All children met diagnostic criteria for oppositional defiant disorder or conduct disorder and had elevated levels of CU traits. Children participated in an 8 week summer treatment program. Behavioral treatment (BT) was delivered during naturalistic activities and was manipulated weekly to increase reward, decrease punishment, both, or neither. Effects were measured using observations and ratings of behavior.

Results:
First, decreasing the role of punishment was the most effective treatment condition overall. Second, there was significant variability in treatment response both within and across children, with about 1/3 of children showing a positive response to treatment, 1/3 showing a poor response to treatment, and 1/3 showing a mixed response to treatment.

Conclusions:
Children with CPCU may respond best to behavior therapy that de-emphasizes punishment. However, behavior therapy alone appears to be insufficient for children with CPCU and may need to be combined with treatments that target empathy and emotional processing skills. This project was funded by a grant from the National Institute of Mental Health (7R34MH085796) awarded to Daniel Waschbusch, Ph.D.
A Novel Group Based Therapy for School Aged Children with ADHD and Severe Mood Dysregulation

Waxmonsky J, Belin P, Babocsai L, Waschbusch D, Humphery H, Pettit J, Robb J & Pelham W. (Drs. Waxmonsky and Waschbusch are affiliated with the Penn State College of Medicine. All other authors are affiliated with the Center for Children and Families at Florida International University).

Purpose:
The NIMH created the diagnostic label of Severe Mood Dysregulation (SMD) to describe children with persistent irritability who overreact to minor stressors but lack discrete mood cycles. A similar construct, Disruptive Mood Dysregulation Disorder (DMDD) has been included in DSM-V. Despite the high reported prevalence of SMD, little is known about its treatment. Most children with SMD meet criteria for ODD and ADHD while SMD predicts the development of depression. Therefore, we integrated existing psychosocial treatments for these disorders to create a novel group therapy for SMD.

Methods:
56 children with ADHD and SMD were randomly assigned to the experimental 11 session therapy or community psychosocial treatment. All participants were first stabilized on stimulant medication. Therapy consisted of eleven 90-minute sessions with concurrent parent and child groups.

Results:
Families attended a mean of 9.7 sessions. Therapy lead to greater reductions in mood symptoms (p<.05) as measured by an aggregate score derived from the Children’s Depression Rating Scale and Young Mania Rating Scale. The therapy group experienced a larger decline in ODD symptoms (p=.095). Therapy parents were more likely to employ positive parenting techniques (p<.01) and less likely to use corporal punishments than control families (p=.05). Parents and children reported high levels of satisfaction with the therapy program, reporting it to be no more demanding than medication visits.

Conclusion:
The novel therapy program was feasible, well received and led to significant improvements in mood symptoms compared to community treatment.
Does Pharmacological Treatment of ADHD in Adults Enhance Parenting Performance?

J Waxmonsky M.D., D Waschbusch Ph.D., D Babinski Ph.D., H Humphrey M.D. A Alfonso M.A., K Crum M.A., M Bernstein M.A., J Slavec M.A.,* J Augustus B.A., W Pelham Ph.D. (Drs. Waxmonsky, Washbsuch and Babinski are affiliated with the Penn State College of Medicine. All other authors are affiliated with the Center for Children and Families at Florida International University.)

Purpose:
Attention Deficit Hyperactivity Disorder (ADHD) often persists into adulthood [1], with 25% of clinic-referred children with ADHD having a parent with ADHD. Emerging evidence has found that ADHD symptoms impair parenting performance. However, few studies have examined treatments for parental ADHD to determine if improving ADHD symptoms translates into improved parent-child interactions. This study explores the impact of lisdexamfetamine (LDX) in treating parents with ADHD.

Methods:
All 38 participants met full DSM IV criteria for ADHD and had a child between the ages of 5-15 with ADHD. Parents first had their LDX dose titrated to optimally control ADHD symptoms over 3 weeks. Then, in Phase I, parent-child dyads completed two laboratory interactions, once with the adult on blinded optimal dose of LDX and once on placebo, while the child was unmedicated for both assessments. In Phase II, parents were randomly assigned to continue blinded treatment or placebo for an additional month followed by a final parent-child interaction task.

Results:
Few changes in parenting behaviors were seen in phase I while significant reductions in child negative behaviors during the homework task were observed. In Phase II, parents continuously treated with LDX used significantly more praise (ES=1.6), and were more verbally responsive (ES=.48) while reducing their amount of total verbalizations (ES=-.58) and commands (ES=-0.75). Children whose parents were treated continuously with LDX exhibited significantly less negative behaviors (ES=-.71).

Conclusion:
Treatment of parental ADHD with LDX was associated with improved parenting performance and child behavior in the lab setting that emerged over time. These results suggest the potential benefits of pharmacologically treating parental ADHD for both parents and their children. (Research fully supported by an investigator initiated grant from Shire Pharmaceuticals.)
The Impact Of Extended Release Stimulant Medication On The Growth Trajectories Of Children With Attention Deficit Hyperactivity Disorder

(Dr. Waxmonsky is affiliated with the Penn State College of Medicine. All other authors are affiliated with the Center for Children and Families at Florida International University)

Purpose:
To examine the impact of extended release (ER) CNS stimulants on the growth of children with Attention Deficit Hyperactivity Disorder (ADHD). One of the most commonly reported side effects of stimulants is anorexia and weight loss, leading to concerns over the potential for stimulant induced growth suppression (SIGS). The NIMH’s Multimodal Treatment Study of ADHD (MTA) and other studies observed growth suppression with the use of short acting CNS stimulants (e.g. Ritalin®). However, most children are now treated with ER stimulants. None of the prior studies were primarily designed to assess growth and therefore had significant methodological limitations for assessing SIGS.

Methods:
Medically healthy children ages 5-12 with ADHD who had never taken CNS stimulants were randomly assigned to treatment with ER CNS stimulants (78%- primarily OROS Methylphenidate) or behavior treatment (22%) for 30 months. Height, weight and medication usage were measured every 2-4 weeks using standardized procedures with all medication provided through the study. After 6 months of treatment, children evidencing a decline in BMI z-score of >.5 units were randomly assigned to one of the weight recovery treatments (caloric supplementation, drug holiday or monitoring)

Results:
This report focuses on the growth rates during the first year of treatment (study is ongoing). The mean daily MPH dose was 24.5mg. Despite efforts to minimize weight loss, participants taking medication continuously (N=86) experienced significantly reduced height (.94cm) and weight (.83kgs) gain compared to those not taking medication (N=39) during the first year of treatment. Height suppression was comparable to that seen with studies of short acting stimulants (MTA). The degree of weight suppression was less than half that seen with short acting stimulants, possibly due to the effect of weight recovery treatments.

Conclusion:
Treatment with extended release stimulants is associated with reductions is expected height and weight gain over the first year of use in children with ADHD.
THE IMPACT OF BUZZY® ON OUTPATIENT VENIPUNCTURE IN CHILDREN

Hilary M Whelan, BS¹, Allen R Kunselman, MS¹,4, Neal J Thomas, MD, MSc¹,2,4, Jeffrey Moore³ and Robert Tamburro, MD, MSc¹,2,4.

¹Pennsylvania State University College of Medicine; ²Pediatrics, Penn State Hershey Children's Hospital; ³Pathology, Hershey Medical Center; ⁴Public Health Sciences, Pennsylvania State University College of Medicine

Background:
Venipuncture is a common procedure in children that may be the source of significant distress. Various techniques have been offered to minimize venipuncture pain, but all have limitations. Many complicate or delay successful completion of the procedure. Recently, the use of continuous mechanoreceptor stimulation, Buzzy®, has been offered as a therapy for venipuncture pain in children; to date, its use has not been assessed for pediatric outpatient venipunctures.

Objective:
To assess 1) the impact of Buzzy® on pediatric venipuncture pain; and 2) the phlebotomists’ perception of its effect on the procedure.

Design/Methods:
Survey data from 64 children ages 4-18 years undergoing outpatient phlebotomy was prospectively collected. Initial data was collected on 29 children prior to the implementation of Buzzy®. Subsequently, 35 children were surveyed after Buzzy® implementation. Procedural pain was reported using a 0-5 pain scale. Additional data collected included the patient age, their number of previous venipunctures, their desire for a pain reduction intervention (pre-Buzzy® cohort) and the effect of Buzzy® (post-Buzzy® cohort). Phlebotomists (n = 7) were surveyed regarding the impact of Buzzy® on the procedure.

Results:
Prior to Buzzy®, 17 (59%) children indicated that they wished something had been performed to decrease venipuncture pain. Twenty-three (79%) children prior to Buzzy® reported a 0 or 1 pain score. Similarly, 25 (71%) children that used Buzzy® reported a 0 or 1 pain score (p=0.92). Twenty-nine children (83%) reported that Buzzy® helped to alleviate pain; 80% indicated that they would like the use of Buzzy® for future venipunctures. Phlebotomists reported that Buzzy® made the procedure easier in 81% of the cases, had no effect in 19%, and did not complicate any of the venipunctures.

Conclusions:
These results suggest that Buzzy® may be useful to decrease the perception of pain in children undergoing venipuncture and to facilitate procedure completion.
Pediatric Referrals to the Emergency Department from Urgent Care Centers

Robert Wilkinson, D.O. 1, Jennifer Dunnick 2, Brendan J. Dougherty R.N.1, Robert P. Olympia, M.D. 1
1Penn State Hershey Children’s Hospital, 2 Penn State College of Medicine, Hershey, PA

Background:
Although minor emergencies and trauma in children are traditionally evaluated and treated in primary care offices and emergency departments (ED), limited office hours and long wait times have fueled the economy for urgent care centers.

Objectives:
To describe pediatric referrals from urgent care centers to the Penn State Hershey Medical Center ED over a one year time period, beginning April 2013.

Methods:
A prospective observational study was performed on patients less than 21 years of age referred to the ED directly from an urgent care center. Demographics and ED visit data were analyzed.

Results:
Preliminary data analysis was performed on 102 patients enrolled over the first five months of collection. 59% of patients were male with a mean age was 8.9 years. 95% arrived to the ED via private vehicle and 5% via ambulance. The top 10 ED chief complaints were abdominal pain, limb injury, facial injury, nausea/vomiting/diarrhea, respiratory distress, fall, foreign body, laceration of lip, ear pain, and headache. 61% of patients received ED diagnostic imaging (58% x-ray, 21% CT scan, 17% ultrasound, 16% MRI). 30% of the patients had diagnostic serum testing and 21% had urine testing performed in the ED. 36% of patients had a procedure performed in the ED, including IV placement (84%); fracture casting/reduction (24%); laceration repair, procedural sedation, and EKG (11% each); foreign body removal (5%); lumbar puncture or incision and drainage (3% each). 56% of patients received medications in the ED, including analgesia (40% intravenous, 25% oral), intravenous fluids (54%), antibiotics (18% intravenous, 5% oral), oxygen (4%), and respiratory beta-agonists (5%). 45% of patients required consultation from a subspecialist, the most common being surgical (85%).

The majority of patients (77%) were discharged home, while 14% were hospitalized and 9% had emergent surgical intervention. The most common discharge diagnoses were abdominal pain not otherwise specified, acute constipation, gastroenteritis, acute appendicitis, concussion, closed ankle fracture, facial injury, foreign body, viral syndrome, and ruptured tympanic membrane.

Conclusions:
Our preliminary data shows that many referrals to the ED from urgent care centers did not require emergent diagnostic or therapeutic interventions.
Compliance of urgent care centers in the U.S. with pediatric care recommendations for emergency and disaster preparedness

Robert Wilkinson, M.D. 1, Jennifer Dunnick 2, Robert P. Olympia, M.D. 1, Jodi Brady, M.D.1

1Penn State Hershey Children’s Hospital, 2Penn State College of Medicine, Hershey, PA

Background:
The American Academy of Pediatrics recently published a policy statement providing recommendations for ensuring appropriate stabilization in pediatric emergency situations and timely and appropriate transfer to a hospital for definitive care.

Objectives:
To describe the compliance of urgent care centers in the U.S. with pediatric care recommendations for emergency and disaster preparedness.

Methods:
An electronic questionnaire, based on pediatric care recommendations for preparedness, was distributed to urgent care centers as identified by the American Academy of Urgent Care Medicine directory.

Results:
Preliminary data analysis was performed on 81 questionnaires. In the past year, 71% of centers have contacted community EMS to transport a critically ill or injured child to the emergency department. Basic life support certification is required in 96% of centers for physicians, 72% for mid-level practitioners, and 78% for nurses. Pediatric advanced life support certification is required in 100% of centers for physicians, 59% for mid-level practitioners, and 59% for nurses. Protocols have been established in 48% of centers with their local hospital and 57% of centers with their community EMS to ensure prompt transport of critically ill or injured children. 44% of centers conduct formal reviews of emergent or difficult cases requiring stabilization and/or transport in a quality improvement format. Centers reported the availability of the following essential medications and equipment: oxygen source (87%), nebulized/inhaled beta-agonist (97%), IV epinephrine (67%), length-based resuscitation tape (38%), suctioning device (58%), bag-valve-mask resuscitator (78%), and automated external defibrillator (80%). Although 74% of centers have an office disaster plan, only half practice the plan at least once a year. 22% of centers have taken part in local community and hospital disaster planning, exercises, and drills.

Conclusions:
Areas for improvement in urgent care center preparedness were identified, such as establishing transfer and transport agreements with local hospitals and community EMS, ensuring a structured quality improvement program, increasing the availability of essential medications and equipment, and participating in community disaster plans.
Effects of Preterm Delivery and Early Intervention on Infants’ Mental Development: A Two-year Follow-up Study

Chengwu Yang, MD, MS, PhD\textsuperscript{1, a}; Lifang Liao, MD\textsuperscript{2, a}; Ruiyun Huang, RN\textsuperscript{2}

\textsuperscript{1}Department of Public Health Sciences, Penn State College of Medicine, Hershey, PA, USA
\textsuperscript{2}Department of Pediatrics, the First People’s Hospital of Shunde, Guangdong, China
\textsuperscript{a}These two authors contributed equally to this work.

Purpose:
To investigate effects of preterm delivery and early intervention on infants’ mental development during their first two years of life, and specifically, to explore if there is any effect of ‘artificially preterm delivery’ on infants’ mental development.

Methods:
Three groups of infants (54 naturally preterm, 39 artificially preterm, and 33 full term, 126 in total) with matched gender, socioeconomic status, marital status and age of mother, gestation age averaged at 35.3, 35.9, 40.0 weeks, respectively, were assigned randomly into intervention or control group. Only intervention group received early intellectual interventions since neonatal period. All parents participated regular routine children health courses in both examination and guidance at out-patient clinic. Apart from pediatric follow-up, a full neurologic assessment and the Chinese version of the Gesell Infant Development Scales were implemented at the corrected age of 24 months, and the mental development quotient (DQ) included 5 criteria for gross motor, fine motor, cognitive abilities, language skills, and social ability. Multivariate analysis of variance (MANOVA) was applied to assess the effects of early interventions and preterm delivery on these 5 criteria.

Results:
Among all six baseline factors of infants (gestational age, birth-weight, age of mother, gestational complications, type of delivery, neonatal disorders), only gestational age had influence on their intellectual development (p<0.01). After adjusting for gestational age, preterm delivery lowered gross motor (p<0.01) and cognitive status only (p<0.05), while early intervention improved all five mental criteria substantially (p<0.01). Artificial preterm delivery infants have lower gross motor score than nature preterm delivery infants (p<0.01), and have lower cognitive ability score than full term infants (p<0.05). MANOVA table listed below (partial).

\begin{tabular}{|c|c|c|c|c|c|}
\hline
Source & Development Quotient (DQ) & SS & df & MS & F & P-value \\
\hline
Preterm & Gross Motor & 45.70 & 2 & 22.85 & 8.36 & 0.00 \\
Fine Motor & 3.96 & 2 & 1.98 & 0.74 & 0.48 \\
Cognitive Ability & 21.56 & 2 & 10.78 & 3.97 & 0.02 \\
Language Skill & 15.02 & 2 & 6.51 & 1.16 & 0.32 \\
Social Ability & 5.27 & 2 & 2.64 & 0.79 & 0.46 \\
\hline
Intervention & Gross Motor & 157.69 & 1 & 157.69 & 57.69 & 0.00 \\
Fine Motor & 223.17 & 1 & 223.17 & 83.75 & 0.00 \\
Cognitive Ability & 208.74 & 1 & 208.74 & 76.89 & 0.00 \\
Language Skill & 199.58 & 1 & 199.58 & 35.45 & 0.00 \\
Social Ability & 206.92 & 1 & 206.92 & 62.24 & 0.00 \\
\hline
Preterm*Intervention & Gross Motor & 4.14 & 2 & 2.07 & 0.76 & 0.47 \\
Fine Motor & 12.92 & 2 & 6.46 & 2.42 & 0.09 \\
Cognitive Ability & 2.53 & 2 & 1.26 & 0.47 & 0.63 \\
Language Skill & 6.42 & 2 & 3.21 & 0.57 & 0.57 \\
Social Ability & 0.51 & 2 & 0.26 & 0.08 & 0.93 \\
\hline
\end{tabular}

Conclusions:
Although preterm delivery can lower infants’ Cognitive Ability and Gross Motor, early intervention can promote each of the five mental development quotients for infants during their first two years of life. Artificial preterm delivery has negative impact on infants’ gross motor and cognitive ability.

Corresponding:
Chengwu Yang, MD MS PhD, Assistant Professor of Biostatistics, The Pennsylvania State University College of Medicine. Email: yangc@psu.edu
Targeting of the surfactant protein A receptor SP-R210L variant by influenza A virus in macrophages

Linlin Yang, MD, PhD, Sanmei Hu, MS, Zissis Chroneos, PhD
Departments of Pediatrics, Penn State College of Medicine, Hershey, Pennsylvania, USA

Purpose:
Alveolar macrophages (AMs) are critical for controlling influenza A virus (IAV) infection by limiting virus release and initiating innate immunity. Surfactant Protein A (SP-A) and D (SP-D) are a primary line of defense against IAV, but the mechanism is still unclear. Here we aimed to study the role of SP-A receptor SP-R210 L form (SP-R210L) in IAV infection in macrophages (MΦ).

Methods:
SP-R210L deficient (DN) cell lines (300 & 350) were constructed by dominant negative disruption of SP-R210 in Raw264.7 MΦ. Transgenic mice with conditional disruption of SP-R210 L in MΦ were constructed by CRE-mediated inversion of SP-R210 exon 1. IAV infection in vitro was conducted by incubating virus with cells at 37°C. IAV infection in vivo was achieved intranasally. Flow cytometry and immunofluorescence microscopic were conducted to detect virus protein in cells. ELISA and flow cytometry were performed to detect cytokine production. Western blot was used for measure protein expression.

Results:
1. Disruption of SP-R210, in vitro blocked infection of MΦ with both H3N2 and H1N1 IAV strains;
2. Lack of SP-R210 blocks the endocytic trafficking of virus NP to the nucleus;
3. SP-R210L-mediated IAV infection of MΦ is coupled to production of TNFα;
4. SP-R210L-deficient MΦ and AMs are hyper-responsive to the TLR7 ligands ssRNA40 and imiquimod;
5. IAV infection results in inhibition of SP-R210L expression and activation of autophagy;
6. SP-R210L-deficient mice are significantly more susceptible to IAV infection as indicated by increased morbidity, decreased survival, and severe lung histopathology compared to littermate controls;
7. Disruption of SP-R210 in AMs delays replication of IAV in vivo.

Conclusions:
Taken together, these findings support the model that by co-opting SP-R210L, IAV causes a functional 'knock-down', reducing the beneficial function of SP-R210L in innate resistance to IAV infection, and leading to enhanced inflammation in vivo.
The interplay between mTOR signaling, autophagy, and sphingosine kinase 1: A novel approach to induce autophagy-dependent cell death

Megan M Young¹, Todd E Fox¹, Yoshinori Takahashi¹,², Mark Kester³, Hong-Gang Wang¹,²
¹ Department of Pharmacology, Penn State College of Medicine, Hershey, Pennsylvania, USA
² Department of Pediatrics, Penn State College of Medicine, Hershey, Pennsylvania, USA
³ Department of Pharmacology, University of Virginia, Charlottesville, Virginia, USA

Purpose:
To understand how sphingosine kinase 1 regulates cell fate and can be targeted for cancer therapy. Sphingosine kinase 1 (Sphk1) and its pro-proliferative product, sphingosine-1-phosphate (S1P), are upregulated in many, if not most, tumors and cancer cell lines. Despite being an attractive chemotherapeutic target, the effectiveness of Sphk1 inhibitors for cancer therapy remains unclear. We aim to understand why some Sphk1 inhibitors (e.g. SK1-i) are effective in inducing cell death while others do not alter cell growth or proliferation despite eliciting a decrease in S1P and increase in pro-apoptotic precursors, sphingosine and ceramide (e.g. PF-543).

Methods:
Mouse embryonic fibroblasts were treated with Sphk1-selective inhibitors, SK1-i or PF-543. Phase contrast microscopy, fluorescence microscopy, immunostaining, and western blotting techniques were used to analyze the effects of each drug. MS/MS lipidomic analysis was used to quantify sphingolipid levels in response to drug treatment.

Results:
Our results suggest that SK1-i alters local sphingolipid metabolism at the lysosome to enlarge the lysosome compartment, inactivate mTOR, induce autophagy, and promote lysosome membrane permeabilization. Interestingly, loss of autophagy sensitizes cells to SK1-i by prolonging lysosomal stress and preventing mTOR reactivation for lysosome reformation. In contrast, the small molecule inhibitor, PF-543, does not alter cellular morphology, enlarge the lysosomal compartment, or suppress cell proliferation.

Conclusions:
We propose that combinational treatment targeting the mTORC1 and lysosomal sphingolipid metabolism can switch cytoprotective autophagy to cell death by preventing lysosome regeneration and accumulating autophagosomal membranes for the assembly of intracellular death-inducing signaling complexes (iDISC) for the induction of autophagy-dependent apoptosis. As apoptosis-resistant cancer cells present a challenge for traditional chemotherapy, the induction of an alternative cell death pathway (e.g. autophagy-dependent apoptosis) can provide a novel approach to enhance the chemotherapeutic efficacy.
A Case of Severe Malnutrition and Profound Anemia in a 4 Year-Old Girl

Sarah Zader and Jamie Librizzi, MD
George Washington School of Medicine, Children’s National Medical Center, Washington, D.C.

Purpose:
To describe a challenging diagnosis of inflammatory bowel disease (IBD) in a young girl presenting with severe malnutrition and profound anemia.

Clinical Course:
H.M. is a 4 year-old vegan, non-immunized female presenting with crampy abdominal pain, intermittent bloody diarrhea, occasional nightly fever, decreased appetite for several weeks, and a 10lb weight loss over a 4-month period. She had no recent travel or sick contacts.

Physical exam was notable for a cachectic, tired, tachycardic (HR 135), female with diffuse, dry scaly dark patches most prominent on her extensor surfaces of her lower extremities bilaterally and a perianal skin tag. Her weight was 11.4 kg (<1st percentile).

In the ED, initial labs revealed severe anemia with Hgb 2.9, elevated CRP/ESR, hypoalbuminemia (1.0 gm/dL) and mild electrolyte derangements.

She was initially admitted to the PICU, received multiple blood transfusions in small aliquots, and then was transferred to the hospitalist service for further management of her anemia, severe malnutrition, and re-feeding.

Initial potential etiologies for her malnutrition were malabsorption (Crohn’s Disease, Ulcerative Colitis, Cystic Fibrosis, Celiac Disease), infection (Norovirus, Rotavirus, Clostridium Difficle, Parasites), cancer, or neglect.

Using a multidisciplinary approach, an extensive work-up was initiated. Stools were hemoccult positive indicating a potential source of her anemia. Stool studies revealed an elevated Calprotectin (>2000 mcg/g), indicating inflammation of the GI tract and an elevated Alpha-1-Antitrypsin (1.09 mg/g) suggesting a possible protein-losing enteropathy. Fecal fat was normal, demonstrating adequate fat absorption. Serum IgA was elevated (249 mg/dL) denoting a heightened immune response. Infectious etiology was ruled out with negative stool cultures and O&P. Nutritional work-up identified normal B12, RBC Folate, Copper, Vitamin B1 and low Zinc.

Due to high risk of refeeding syndrome, she required slow introduction of enteral feeds in addition to TPN with close monitoring of electrolytes. Once she met nutritional goals, she demonstrated a 4.3kg weight gain, down-trending Calprotectin, and improvement with her nutritional status evidenced by normalization of her albumin (1.9 gm/dL) allowing her to undergo an endoscopy/colonoscopy that revealed diffuse patchy ulceration consistent with Crohn’s disease.

Discussion:
H.M.’s case uniquely depicted Crohn’s Disease due to severe malnutrition and profound anemia. Research has not revealed a clear association of vegan diet and its effects on presentation of IBD. Possibly, H.M.’s vegan diet, holistic remedies, unvaccinated status, or a combination affected the severity of her disease presentation.

The mainstay of treatment includes suppression of the inflammatory process in active IBD, however research has identified that IBD associated anemia will have slow hematologic recovery unless anemia is directly addressed.
In vitro cytokine assay to identify the medications responsible for a drug eruption

Jose R. Zaragoza MD, Gisoo Ghaffari MD, Faoud T. Ishmael MD, PhD.
Division of Allergy and Immunology, Penn State College of Medicine
Hershey, Pennsylvania, USA

Purpose:
There is a lack of diagnostic assays available to characterize drug hypersensitivity reactions. We have developed an in vitro assay to profile cytokine expression in peripheral blood mononuclear cells (PBMCs) after exposure to suspected drugs as a means to characterize T-cell mediated hypersensitivity reactions. We report a case of a patient with a photosensitive rash that occurred while being treated with sertraline and lamotrigine, the use of an assay to characterize the cytokine responses to these medications.

Methods:
Blood was obtained from the patient and a negative control subject, PBMCs were isolated by Ficoll preparation and incubated with each medication. A gene expression array was used to quantify cytokine expression by real time polymerase chain reaction (PCR).

Results:
Case Report: A 15 year old female patient with a history of depression and mood disorder treated with Sertraline for 4 months was started on lamotrigine one month prior to developing a severe rash. She presented with malaise, a confluent erythematous maculo-papular rash over sun-exposed areas, and generalized pruritus one day after being exposed to sun light. A shave-biopsy report was consistent with a drug-induced photosensitive rash. Since the patient was on two medications at the same time, it was not clear which induced the reaction. The in vitro cytokine gene expression assay employed showed a greater than 5-fold increase in expression of the following cytokines in the patient’s cells but not the negative control subject: sertraline: IL-2, IL-4, IL-5, IL-6, IL-17A, GM-CSF, TNF-a, IFN-g; lamotrigine: IL-5, IL-17A, GM-CSF, TNF-a. Given the increase in cytokine response with both medications, we hypothesized that both medications acted in concert to produce the rash, possibly triggered by sun exposure. The rash improved after holding the medications. Sertraline was restarted and was subsequently tolerated.

Conclusion:
This case highlights the use of in vitro cytokine gene expression assay as a tool to evaluate suspected T cell mediated drug reactions, and raises the question of whether some drug reactions may be due to immunologic reactions to more than one medication.


18. Chronenos Z, PhD, Associate Professor Pediatrics: 32nd Symposium in Molecular Biology, “Sensing and Signaling Across the Mucosa: From Homeostasis to Pathogenesis”, Penn State University Park, June 4-6, 2013 The title of my talk was “Pulmonary Surfactant Regulation of Mucosal Immunity”


33. Halstead, ES, Carcillo JA, Schilling B, Greiner RJ, Whiteside TL. Reduced frequency of CD56dim CD16pos natural killer (NK) cells in pediatric systemic inflammatory response syndrome (SIRS)/sepsis patients. Pediatric Research. 2013 Jul


51. Lin C, Rountree CB, Methratta S, LaRusso S, Kunselman AR, Spanier AJ. Secondhand Tobacco Exposure is Associated with Nonalcoholic Fatty Liver Disease in Children. Accepted to Environmental Research April 2014.


106. Ündar A. Welcome to the 9th International Conference on Pediatric Mechanical Circulatory Support Systems & Pediatric Cardiopulmonary Perfusion. Artificial Organs 2013 (4); 354-356.


ABSTRACT INDEX

A
Abdel-Rahman, Susan 81
Accardo, Pasquale 61
Adedayo, Pelumi 1, 69
Agbese, Edeanya 2
Agirbasli, Mehmet A 3
Aggaral, Richa 54
Albaugh, Vance L 42
Albright, William B 36
Alfonso, A 113
Aluquin, Vincent 63
Amin, Shantu 18, 50, 62, 89
Angeletti, Tammy 88
Annappareddy, Jitendra 56
Armstrong, Caitlin 69
Armstrong, Douglas 84
Arnold, Mariah 54
Augustus, J 113

B
Baer, Larry 105
Babinski, Dara E 4, 5, 55, 113
Babocsai, L 112, 114
Bao, Lei 11
Bartha, Brian M 50
Baweja, Raman 54, 55, 56, 57, 58
Bayerl, Michale
Beiler, Jessica S 24, 29
Belin, P 112
Bello, Ademola 56
Bennett, Stephanie 66
Bernstein, M 113
Bhagat, Rughi 16
Bixler, Edward O 82
Black, Jane 88
Blackall, George 25
Bonneau, Robert 26
Boushra, Marina 6
Brady, Jodi 87, 117
Bramley, Harry 87
Braun, Joe 99
Brelsford, Gina M 7, 106
Brelsford, Gina M
Brownning, Kirsteen N 16
Bulathisnighala, Marie 8
Buyantseva, L 8

C
Cabana, MD 24
Calhoun, Susan L 54, 55, 56, 57, 58
Callahan, S. Todd 70
Camacho, Fabian 99
Campa, A
Cantore, Kathryn M 59
Catherine, Andrew T 10
Ceneviva, Gary 25
Chang, Dennis 78
Chen, Shu-jen 11
Cheung, Joseph Y 11
Chin, Brian J 109
Chin, Fumiyuki 17
Chroneos, Zissis 119
Cilley, Robert E 42, 45, 85
Clark, J Brian 46
Clark, Joseph B 3
Claxton, David 50
Comito, Melanie 25, 63, 88
Conrad, Kathleen 11
Craig, Timothy 22, 38
Cravener, Terri L 12
Crum, K 113
Currie, David G 13
Cyran, Stephen 13

D
Daskalogiannakis, John 34
Dean, Matt 13
Dell, Esther Y 14
Denlinger, LeAnn N 59
Desai, Dhiman 89
Desai, Neelam 51
Dhami, Ranjodh 15
DiAngelo, Susan L 60, 98, 97
Dillon, Peter W 41, 43, 85
DiNallo, Jennifer M 28
Ding, Yali 8, 89, 98
Dogal, Natalie M 53
Doheny, Kim 7, 16, 17, 26, 68, 77, 103, 106
DOI, Kenichiro 18, 50
Dougherty, Brendan J 116
Dovat, Sinisa 8, 27, 62, 89, 98, 102
Dower, Christopher 19
Dunnick, Jennifer 59, 116, 117
ABSTRACT INDEX

E
El-Deiry, Wafik 101
Engbrecht Brett W 41, 42, 43, 45
English, Laural K 21
Evenson, Alissa 20, 109

F
Fausnight, Tracy 9, 73, 82, 99
Fearnich, S. Nicole 21
Feldman, Lance 56
Fernandez-Mendoza, Julio 54
Filtz, Diana 67
Findeis, Sarah 22
Finklestein, Stacey 12
Fisher, Jennifer O 21
Fisher, Martina 70
Flaherman, VJ 23, 24
Floros, Joanna 70
Forman, Sara 84
Fortuna, Kristine 22
Fox, Todd E 120
Freiberg, Andrew S 52, 75

G
George, Daniel R 48
Ghaffari, Gisoo 49, 107, 122
Ghattas, Paul 66
Gilbert, Christopher R 85
Glass, Kristen M 25, 26
Gorman, Angela A 56
Gowda, Chandrika 27, 89, 98
Gowda, Krishna 18, 50
Gowdahalli, Krishna 62
Greecher, Coleen 26
Green, Wallace 88
Greiner, Robert 88
Giffin, Amanda 95
Groh, Brandt 67
Güngor, Darcy E 28
Gupta, Nidhi 56

H
Hackman, Nicole M 29
Hartley, Jessica 69
Hathaway, Ronald R 34
Hennrikus, William L 40, 84
Herting, Christina 30
Hilton, Jonathan 70
Hirschler-Laszkiewicz, Iwona 11
Hoffman, Nicholas E 11
Hollenbeak, Christopher S 41, 43, 44, 65
Hollern, Kaylee 69
Horiates, Krisoua 31
Horwitz, Alexandra 9
Howrylak, Judie Ann 96
Hu, Sanmei 119
Huang, Ruuyan 118
Humphrey, H 112, 113, 114
Hymel, Kent P 32

I
Iriana, Sarah MJ 33
Ishmael, Faoud T 86, 96, 122

J
Jairath, Puneet 16
James, Laura 81
Jasmin, Diane 64, 82
Jay, Susan 70
Jones, Christine M 34, 35, 36

K
Kalovcak, Kelly M 37
Kalra, Neelu 38, 49
Kashlak, Nancy L 39
Keefer, Kerry 11
Keller, Kathleen L 12, 21
Kester, Mark 120
Kish, Alexander J 40
Kulaylat, Aff N 41, 42, 43, 44, 45
Kumar, Nitin 46
Kunselman, Allen R 1, 3, 15, 20, 49, 53, 78, 91
Kunselman, Allen R 92, 93, 100, 108, 109, 115
Kuzniewicz, MW 23
**ABSTRACT INDEX**

**L**
Lane-Loney, Susan E 47, 65, 71
Lasala, Brandie 71
Leach, Don 94
Lehman, Erik 107
Lei, Fengyang 3
Lemieux, Susan K 21
Levine, Martha Peaslee 48
Lewandowski, Andrew 51
Li, S 23
Li, Tan 114
Librizzi, Jamie 121
Lin, Judith 53
Lin, Jyh-Ming 18
Lin, Samantha K 49
Lin, Zhenwu 51
Liu, Qiang 18, 50
Loeb, Katharine L 12
Long Jr., Ross E 34, 35, 36

**M**
MacKay, Andrew F 35
MacKay, Donald R 34, 35, 36
Madesh, Muniswamy 11
Mehr, Fauzia 54, 57, 68
Mammel, Kathleen M 70
Marks, Eric I 52
Marshall, R 114
Masciulli, Emily B 47, 65, 71
Mathis, Ryan K 53
Mattison, Richard E 55
Mayes, Susan Dickerson 54, 55, 56, 57, 58
McEvoy, Christian S 59, 67
McGregor, Lisa 88
McSherry, George 88
McIntyre, J Steele 45
Mercado, Ana M 34
Michael, Eric 68
Miller, Barbara A 11
Mishra, Vikas 60
Monaco, Michele 94
Monroy, K 114
Montaner, Jose 56, 58
Moore, Jeffrey 115
Morrow, Brad T 36
Mulieri, Kevin 31, 88
Mulloy, Austin 61
Murray-Kolb, Laura E 91, 92, 93
Muthusami, Sunil 8, 62, 89
Myers, Christina 17
Myers, John L 3, 46, 94

**N**
Nair, Athira 63, 79
Nene, Neel 64
Nicely, Terri A 47, 65
Noll, Jennie 96
Noutsos, Georgios T 66
Novick, Marsha B 37, 59

**O**
Odom, Anne A 59, 67
Oji-Mmuo, Christiana 68, 96
Olympia, Robert P 10, 30, 69, 87, 116, 117
O'Neill, Lindsey M 21
Ornstein, Rollyn M 47, 65, 70, 71
Ostrov, Barbara E 72, 73
Oswald, Donald 61
Owusu, Sarah A 74

**P**
Pagerly, Elyse K 75
Palanzo, David 105
Palmer, Charles 16, 68, 77, 103
Pan, Xiaokang 27, 76, 98
Passi, Rohit 78, 79, 80
Patel, Sunil 74
Paul, Ian M 23, 24, 29, 33, 81, 91, 92, 93
Paulikis, Linda B 13, 46, 63, 90, 94
Payne, Kimberly J 27, 98
Pelham Jr, William E 5, 112, 113, 114
Perkins, Daniel F 28
Peterson, Blaise 102
Petrovoc-Dovat, Lidija 64, 82
Pettit, J 112
Pew, James 95
Phelps, David S 83
Piazza, Brian 64
Pinzon-Guzman, Carolina 42
P
Podany, Abigail B 44, 85

Q
Qiu, Feng 53

R
Radnitz, Cynthia 12
Ramirez, Joshua 7
Reddy, Vinitha 96
Reed, Michael F 85
Reynolds, Kristine 72
Ritter, Jed 87
Robb, J 112
Robbins, Lisa M 73
Rocourt, Dorothy V 44, 85
Rolls, Barbara J 12, 21
Rome, Ellen 70
Rosen, David S. 70
Rosendale, Ryan P 28
Ross, A. Catharine 74
Rudnitsky, Gail 6
Russell, Kathy A 34
Rzucidlo, Susan E 42, 45

S
Sachdev, Mansi 8, 27, 62, 88, 89
Safford, Shawn D 41, 43
Saini, Ashish P 79, 80, 90
Samson, Thomas D 34, 36
Santos, Mary C 44, 85
Savage, Jennifer S 21
Scalzi, Lisabeth V 72
Schaefer, Eric W 23, 29
Schell, Ryan 84
Schubart, Jane R 42
Schwartz, Marlene 12
Sekhar, Deepa L 107
Shah, Sapna 107
Shah, Shenil 94
Shaner, Marie 88
Shapiro, Teresa 95
Shen, Chad 95
Shi, Yuguang
Shotto, Robert 25
Siddiqui, Farhat 55, 56, 57, 64
Silveyra, Patricia 60, 96, 97, 104
Slavec, J 113
Song, Chunhua 8, 27, 62, 76, 89, 98, 102
Song, Jianxun 3
Souther, Janice
Soulier, Brooke 88
Spanier, Adam J 99
Spear, Debra 96
Steffens, Sadie
Stevens, Nicole M 59
Stokes, Audrey L 45
Stouffer, Janice 17
Strohecker, Carissa 71
Strother, Ashton 100
Sung, Shen-Shu 18
Swavelly, Steven C 59
Syed, Ehsan 56, 57

T
Takahashi, Yoshinori 19, 51, 120
Talekar, Mala K 101
Tamburro, Robert F 25, 88, 115
Tan, Bi-Hue 8, 102
Thomas, Neal J 96, 104, 115
Toom, Pratima 103
Toth, Jennifer W 85
Travagl, Alberto 16
Trout, Lindsay 31, 88
Tsotakos, Nikolaos 104

U
Umstead, Todd M 83
Undar, Akif 1, 3, 15, 20, 53, 78
Undar, Akif 100, 105, 108, 109
Ural, Serdar 90

V
Vaid, Mudit 104
Veneman, Kristen 7, 106
Vernon, Natalia 107
PEDIATRIC RESEARCH DAY, May 22, 2014

ABSTRACT INDEX

W
Walsh, E 23
Walsh, B. Timothy 70
Wang, Y. Claire 12
Wang, Hong-Gang 11, 18, 19, 50, 51, 120
Wang, Haijun 8
Wang, Jufang
Wang, Li 110
Wang, Luojun 91
Wang, Ming 8
Wang, Shigang 1, 3, 15, 20, 53, 78,
Wang, Shigang 100, 105, 108, 109
Waschbusch, Daniel A 55, 111, 112, 113
Waxmonsky, James G 4, 5, 112, 113, 114
Weber, Howard 79, 80
Whelan, Hilary M 115
White, Amanda M 82
Wilkinson, Robert 116, 117
Williams, OD 114
Wilson, Stephen J 21
Wise, Robert 105

X

Y
Yang, Chengwu 118
Yang, Linlin 119
Young, Megan M 120

Z
Zadar, Sarah 121
Zamietra, Kathleen A 14
Zaragoza, Jose R 122
Zeiger, Timothy S 64, 82
Zhu Junjia 52
Zieger, Timothy
Zucker, Nancy 12