33RD Annual

THOMAS F. BOAT DAY OF SCHOLARSHIP

April 26th, 2018

The Thomas F. Boat Day of Scholarship

"Since 1985, the intellectual highlight of the Department of Pediatrics has been its annual Evening of Scholarship. This was conceived by Dr. Boat as a festive evening in which pediatric residents and fellows could present the results of their scientific studies to their peers and faculty members. Although initially proposed as an Evening of Research, several members of the faculty suggested that Evening of Scholarship be substituted, since the term "research" often conjured up a limited image of wet bench research. Such a perception might have a negative effect on the main goal of the exercise, which was to encourage each of our pediatric house staff to engage in some sort of scholarly activity beyond their usual ward and clinic assignments. Such activities might range from a case report and review of the literature about some disease to a sophisticated laboratory or epidemiologic study. Since its inception the Evening of Scholarship has developed into a showcase event in the Department's spring calendar."

- Taken from "From Infancy to Maturity: The History of the Department of Pediatrics, The University of North Carolina at Chapel Hill, 1952-1995".

Awards Presented at the Day of Scholarship

The primary intent of the Thomas F. Boat Day of Scholarship is to acknowledge and honor residents and post-doctoral fellows in the Department of Pediatrics for their scholarly efforts during the academic year. While all the presentations offered at this event are meritorious, a committee has been appointed to identify presentations and posters of particular distinction. The committee is charged with evaluating these presentations and awarding the best basic science presentation, the best clinical science presentation, the best QI presentation, the best overall presentation, and the best presentation by a pediatric resident. In 2002, the decision was made to name the basic science award in honor of Dr. Jud Van Wyk and the clinical science award in memory of Dr. Walter Tunnessen. In 2009, a new prize was established, the Johnny L. Carson Award. This award is non-categorical and is given to the presenter showing significant scholarly contribution to the Day of Scholarship. The award is named in the spirit of Johnny L. Carson, a leader in promoting scholarship in the Department of Pediatrics. In 2010, the best Quality Improvement presentation was named after Gerald Fernald, MD, an advocate for resident education. Even in his retirement, Dr. Fernald was active in resident recruitment and the Day of Scholarship. In 2012, the Best Resident Award was named in honor of Alan Stiles, former Chair of the Department of Pediatrics. During Dr. Stiles' 11 year tenure as department chair, resident scholarship was emphasized and expanded, and always at the forefront of research initiatives. The recipients of these honors receive an individual plaque, a monetary award, and have their names added to a large plaque that is permanently displayed in the Curnen-Denny Conference Room. All monetary awards come from the generous gift of Dr. and Mrs. Jack Lynch that originally established the London-Lynch Learning Center. Dr. Lynch passed away November 16, 2010. The London-Lynch Learning Center has contributed to promoting the Evening of Scholarship and in funding these awards.

On behalf of the London-Lynch and the Resident Scholarship Support Committees, we congratulate all the participants in this year's event and welcome you to a lifetime of learning for 21st century pediatricians.

Schedule

8:00am **Oral Presentations**
Kirkland Auditorium (Dental School)

Anti-Human CD4 and CD8 Antibody Co-Therapy Induce T-Cell Egress from Inflammatory Tissues via the FOXO1 Pathway
Mark Henin, MD
Endocrinology Fellow
Mentor: Roland Tisch, PhD
Abstract available on page 13

Efficient, dried blood spot-based determination of hepatitis B seroprevalence from a national survey in the Democratic Republic of the Congo
Peyton Wilson, MD
Infectious Disease Fellow
Mentors: Ravi Jhaveri, MD and Steve Meshnick, MD, PhD
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Risk factors for chronic lung disease and asthma differ among children born extremely preterm
Wes Jackson, MD
Neonatal-Perinatal Medicine Fellow
Mentor: Matt Laughon, MD, MPH
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Decreasing length of stay and use of pharmacotherapy for neonates with NAS on an inpatient floor
Tom Blount, MD
Pediatrics Resident
Mentor: Ashley Sutton, MD
Abstract available on page 40

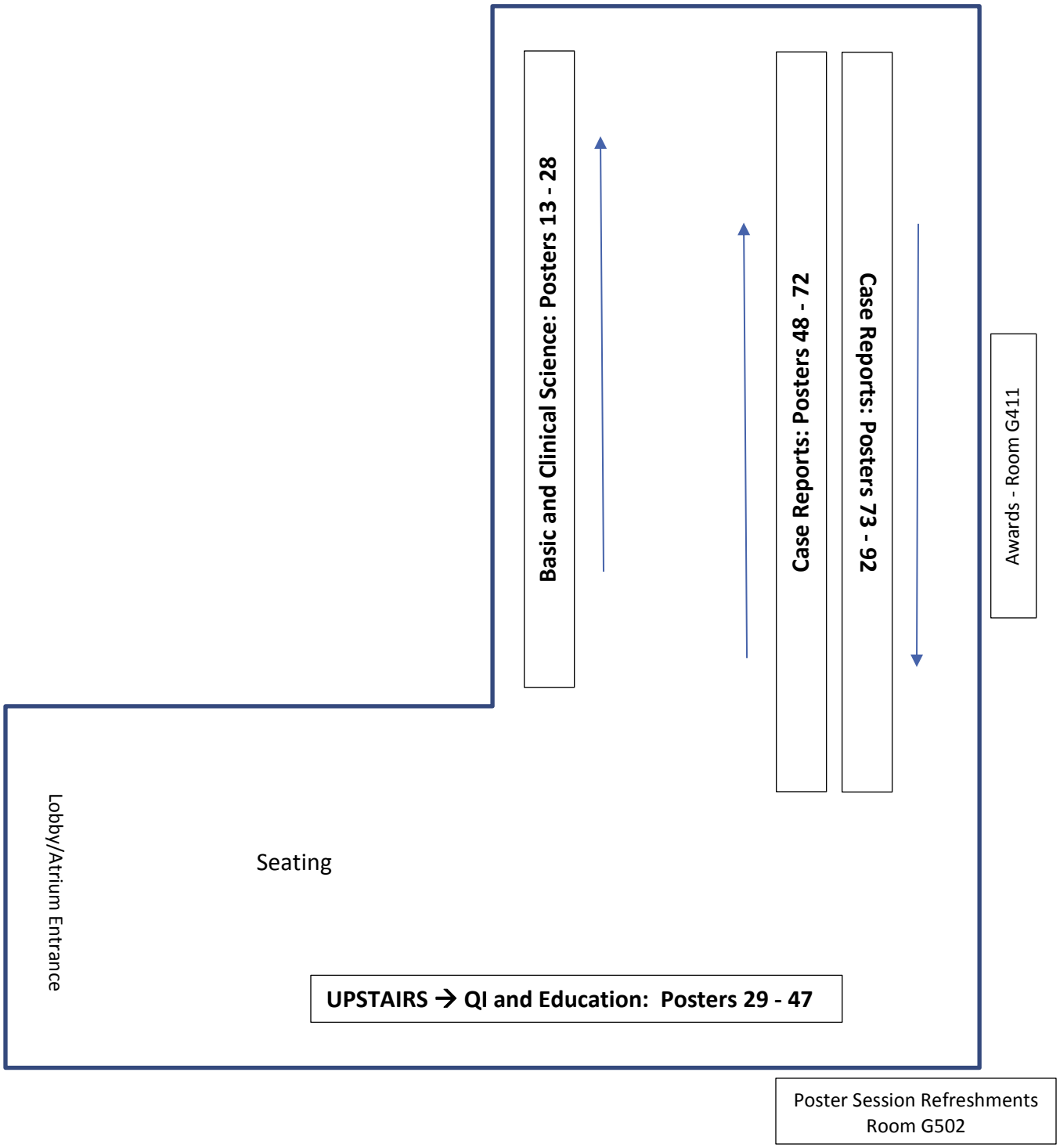
12:00pm **Noon Conference presented by Ian Davis, MD, PhD**
Curnen Denny Conference Room
Lunch Provided

3:50pm **Poster Session**
Dental School Lobby/Atrium Level
Refreshments Provided in Room G502

5:00pm **Award Ceremony**
Dental School - Room G411 (lobby level; near posters)

Lobby/Atrium Level - UNC School of Dentistry

***Booklet page numbers correspond with poster numbers.**



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Internal Medicine - Pediatrics Resident
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Anti-Human CD4 and CD8 Antibody Co-Therapy Induce T-Cell Egress from Inflammatory Tissues via the FOXO1 Pathway

Mark Henin, MD
Roland Tisch, PhD

Additional Authors; Division/Institution: Matthew Clark, Ph.D.; UNC Department of Microbiology and Immunology, Post-Doctoral Fellow

Background/Introduction:

NRG mice have a targeted mutation in the recombination activating 1 (Rag1) gene rendering them T and B-cell deficient. The severe immunodeficiency allows the mice to be "humanized" by engraftment of human T-cells. These humanized mice develop xenographic graft vs host disease causing systemic illness and death. Treatment of humanized NRG mice with anti-human CD4/CD8 antibodies suppress human T-cell activation, causing egress from inflamed hepatic and pancreatic tissues. The underlying mechanism is unknown but thought to be related to the FOXO1 family of transcription factors. These transcription factors are important for downregulation of CD69, an early T-cell activation factor, and upregulation of S1P, a membrane receptor signaling T-cell egress. T-cell activation leads to downstream phosphorylation of FOXO1, inhibiting its transcription. It is hypothesized that anti-CD4/CD8 antibodies block T-cell activation, allowing for upregulation of S1P and downregulation of CD69 via activation of the FOXO1 pathway.

Methods:

Whole blood was collected from five healthy human donors and peripheral blood monocytes (PBMCs) were extracted using Ficoll-Paque Plus. NRG were mice reconstituted with 1x107 PBMCs via intraperitoneal injection. Human reconstitution of mice was monitored via flow cytometry for human CD3+ T-cells in peripheral blood. Four to six weeks post-PBMC transfer, NRG mice were injected with 500µg of either control, anti-human CD4/CD8 antibody, control + S1P inhibitor, or antibody + S1P inhibitor. Mice were then sacrificed for flow cytometry analyses 72 hours post-treatment.

Results:

T-cells found in the pancreases of NRG mice treated with anti-human CD4/CD8 antibody showed increased frequency of expression of CD127 and CCR7, two FOXO1-regulated transcription factors. In addition, they showed decreased frequency of expression of CD69 compared to controls. There were significantly decreased numbers of T-cells seen in pancreases of mice treated with anti-human CD4/CD8 versus controls. Mice treated with anti-human CD4/CD8 + S1P inhibitor showed pancreatic T-cell numbers similar to control mice.

Conclusions:

These initial results suggest anti-human CD4/CD8 antibody treatment is involved in upregulating the FOXO1 pathway. This is demonstrated by the increased frequency of expression of two key FOXO1 regulated transcription factors as well as the decreased frequency of CD69 expression. Furthermore, inhibition of S1P, the end product of the FOXO1 pathway, prevents anti-human CD4/CD8 antibody mediated T-cell egress from inflamed pancreatic tissues. Currently, mRNA is being extracted and reverse transcribed to cDNA for RT-PCR studies to further examine expression of FOXO1 regulated genes in the control versus antibody treatment groups. While the results are suggestive, repeat studies with increased sample sizes are necessary prior to making any definitive conclusions.

COMPARING NASAL AND BRONCHIAL EPITHELIAL CELL RESPONSES TO CFTR ACTIVATION

Bruehl, M; Quinney, NL; Boyles SE; Cholon, DM; Esther Jr, CR; Gentzsch, M

Introduction

In cystic fibrosis (CF), drugs that can improve the function of mutant cystic fibrosis transmembrane conductance regulator (CFTR) proteins signal a new age of targeted therapies. The clinical impact of these drugs can be highly individual. Nasal epithelial cells are being studied as a method to assess individual responses to CFTR drugs, but the relationships between nasal and bronchial cell responses are not well understood.

Objective

To compare the responses to CFTR activation of nasal and bronchial epithelial cells using electrophysiological techniques.

Methods

Nasal cells were obtained from CF and non-CF subjects by brushing or scraping. CF and non-CF bronchial cells were obtained from explant lungs with additional non-CF cells obtained from bronchial brushes. All cells were cultured at an air-liquid interface until well-differentiated. Responses to CFTR activation with forskolin were analyzed in Ussing chambers by measuring changes in short-circuit current (Isc). The same measurements were taken from CF cells after treatment with lumacaftor plus ivacaftor.

Results

Responses to CFTR activation in CF nasal cells (n=6) and CF bronchial cells (n=4) were minimal at baseline, with similar mean increases in Isc of 0.43 ± 0.12 μA/cm2 and 0.30 ± 0.17 μA/cm2 respectively (p=0.54). However, mean Isc increases after treatment with lumacaftor-ivacaftor were significantly lower in CF nasal cells (1.2 ± 0.17 μA/cm2) relative to CF bronchial cells (8.6 ± 1.2 μA/cm2, $p<0.0001$). In non-CF cells, the mean increase in Isc in response to CFTR activation in nasal cells (19 ± 1.3 μA/cm2) (n=6), bronchial cells from explant lungs (32 ± 1.1 μA/cm2) (n=3), and bronchial cells from bronchial brushings (18 ± 6.8 μA/cm2) (n=3) showed a statistically significant difference between samples as determined by one-way ANOVA ($F(2,9) = 5.4$, $p=0.029$). Post hoc comparisons using the Tukey HSD test indicated that the mean increase in Isc of the nasal ($p=0.036$) and brushing ($p=0.049$) samples were each statistically significantly different than the explant sample. However, the nasal and brushing sample means did not show a statistically significant difference ($p=0.97$).

Conclusion

In nasal and bronchial epithelial cells there are clear differences in response to CFTR activation between CF and non-CF cells. In both CF nasal and bronchial cells, treatments with lumacaftor and ivacaftor increase Isc responses to forskolin. To account for subject-specific variability, additional identical studies are in progress using paired nasal and bronchial cells from the same subjects.

Gamma Tocopherol (γT) Supplementation Reduces Endotoxin-Induced Sputum Neutrophilia in Healthy Volunteers and Asthmatics Regardless of BMI or glutathione-S-transferase Mu1 (GSTM1) Genotype

A Sood1,2, AJ Burbank1,2, CG Duran1, K Enders3, H Zhou3, DB Peden1,2, ML Hernandez1,2

1Center for Environmental Medicine, Asthma, and Lung Biology, University of North Carolina, Chapel Hill, NC; 2Division of Allergy, Immunology and Rheumatology, Department of Pediatrics, University of North Carolina, Chapel Hill, NC; 3Department of Biostatistics, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC

Rationale: Through its unique antioxidant and anti-inflammatory properties, γT supplementation has shown benefit in reducing airway inflammation in preclinical and early-phase clinical studies. However, obesity increases systemic inflammation while the GSTM1 null genotype may alter host antioxidant defenses. This study, therefore, examines whether BMI and/or GSTM1 genotype modifies the response to inhaled endotoxin and/or the reduction of endotoxin-induced sputum neutrophilia following γT supplementation in healthy volunteers (HV) and asthmatics.

Methods: Thirteen HV and 15 asthmatics underwent γT treatment followed by inhaled endotoxin challenge in two double-blind, placebo-controlled, cross-over studies. γT supplementation reduced post-challenge sputum neutrophilia compared to placebo in HV (p=0.03) and asthmatics (p=0.04). The effect of BMI and GSTM1 genotype on response to inhaled endotoxin and the reduction in endotoxin-induced sputum neutrophilia following γT treatment in each study was assessed using linear regression models and Wilcoxon Rank Sum Tests, respectively.

Results: BMI and GSTM1 genotype had no effect on response to inhaled endotoxin, as measured by increase in sputum neutrophils, in HV (p=0.17 and p=0.90, respectively) or asthmatics (p=0.81 and p=0.52, respectively). GSTM1 genotype had no effect on the reduction in endotoxin-induced sputum neutrophilia following γT treatment in HV (p=0.42) or asthmatics (p=0.78). Higher BMI was associated with greater reduction in post-challenge sputum neutrophilia following γT treatment in HV (p=0.03) but not in asthmatics (p=0.14).

Conclusions: Response to inhaled endotoxin in HV and asthmatics is not affected by BMI or GSTM1 genotype. γT treatment reduces endotoxin-induced sputum neutrophilia regardless of BMI and GSTM1 genotype with enhanced responses seen in those with higher BMI.

EPIDEMIOLOGY OF PEDIATRIC ACUTE KIDNEY INJURY FROM A NATIONAL COHORT

Authors: Erica C. Bjornstad, MD MPH; Emily Gower, PhD; Amy Mottl, MD MPH

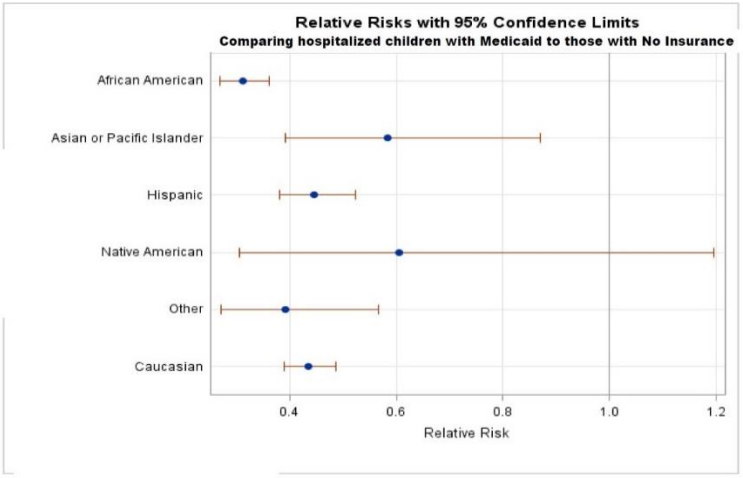
Affiliations: UNC Kidney Center, UNC Gillings School of Public Health

Background: Pediatric acute kidney injury (AKI) significantly increases morbidity and mortality for hospitalized children. However, few studies have evaluated the relationship between race/ethnicity and pediatric AKI. We proposed to evaluate the relationship of race/ethnicity on the outcome of AKI in a national pediatric cohort.

Methods: The Kids' Inpatient Database, developed by the AHRQ's Hospital Care and Utilization Program, is a nationally representative sample of pediatric discharges from >4100 community hospitals throughout the United States. We conducted a prospective cohort study from the most recent database (2012) to assess for racial disparities in the development of AKI and used weighted sampling methods to obtain national estimates. Logistic regression analyses were used to assess the relationship between race and AKI, adjusting for comorbidities.

Results: In 2012, approximately 1.2% of all pediatric hospitalizations had AKI, which is a national estimate of almost 30,000 children. Hispanic children were less likely to have an episode of AKI (adjusted RR 0.90, 95% CI 0.83-0.96) compared to Caucasian children after adjustment for comorbidities, while African American children were more likely (adjusted RR 1.11, 95% CI 1.04-1.17). When race was stratified by age, only older Hispanic children were less likely to have AKI episodes than same-age Caucasian children (RR 0.67, 95% CI 0.62-0.74). However, older African American children (11-20 years) were more likely to have AKI, yet younger African American children (1-10 years) were less likely to have AKI than same-age Caucasian children. Crude analyses also showed that children with insurance (regardless of payer) were significantly less likely to have AKI compared to those with no insurance. Insurance was protective regardless of race, but it seemed to be most protective in the adolescent population, where adolescents with Medicaid were almost two-thirds as less likely to have AKI compared to adolescents without insurance (RR 0.36, 95% CI 0.33-0.39). Overall, our data suggest that we could prevent one episode of AKI if 75 children currently uninsured were able to obtain Medicaid (absolute RD -0.013, 95% CI -0.015 to -0.012). The highest at-risk group of those without insurance (compared to Medicaid) were African American adolescents who were almost 3.5 times as likely to have an episode of AKI compared to same-age African Americans (RR 3.41, 95% CI 2.97-3.91).

Conclusion: Pediatric AKI seems to occur more frequently in older African American children compared to Caucasian children. However, the highest risk group prior to hospitalization are children without insurance, regardless of race/ethnicity.



PEDIATRIC LYMPHOMA PATIENTS IN MALAWI PRESENT WITH POOR HEALTH-RELATED QUALITY OF LIFE THAT IMPROVES THROUGHOUT TREATMENT AS MEASURED BY THE PROMIS-25 QUESTIONNAIRE

Kate Westmoreland, Alyssa Tilly, Amy Amuquandoh, Toon van der Gronde, Salama Itimu, Ande Salima, Olivia Manthalu, Paula Ward, Atupele Mpasa, Stella Wachepa, Idah Mtete, Mercy Butia, Peter Wasswa, Nader El-Mallawany Kim, Stephen Martin, Peter Kazembe, Bryce Reeve, Satish Gopal.

Introduction

The Patient-Reported Outcomes Measurement Information System 25-item (PROMIS-25) pediatric questionnaire has been translated and validated in Malawi. We describe health-related quality of life (HRQoL) for pediatric lymphoma patients at baseline and during treatment.

Methods

The PROMIS-25 questionnaire was administered to patients in Lilongwe. Participants reported on 6 HRQoL domains (mobility, anxiety, depression, fatigue, peer relationships, and pain interference) by answering four question items per domain using a 5-point Likert scale. A single-item pain intensity question was scored 0-10. Each domain was transformed to a T-score with a mean of 50 and standard deviation of 10 based on the original PROMIS reference sample.

Results

Of the 148 PROMISE-25 questionnaires, 85 were administered at diagnosis and 63 during active treatment (median days since diagnosis: 93, IQR: 65-136). Median age was 10 years (IQR: 7-12) and 117 (79%) male. At diagnosis, children reported poor HRQoL that improved during treatment. Very low levels of mobility (median: 33, IQR: 23-38) improved to average (median: 49, IQR: 43-57, $p<0.0001$). High anxiety (median: 62, IQR: 52-69) improved to average (median: 44, IQR: 38-55, $p<0.0001$). High depressive symptoms (median: 63, IQR: 55-67) improved to average (median: 50, 44-57, $p<0.0001$). High fatigue (median: 61, IQR: 54-67) improved to average (median 47, IQR: 43-52, $p<0.0001$). Average satisfaction with peer relationships (median: 52, IQR:47-55) remained stable (median: 49, IQR: 39-55, $p=0.29$). High pain interference (median: 57, IQR:49-66) improved to average (median: 53, IQR: 43-57, $p<0.0001$). The highest score for pain intensity of 10 was given by 47/85 (55%) of patients at diagnosis and 2/63 (3%) subsequently during treatment.

Conclusion

HRQoL for pediatric lymphoma patients at diagnosis in Malawi is poor across various domains, and improves during treatment. Validated methods to assess HRQoL over time among children with cancer are essential in low-resource settings, to comprehensively understand effects of cancer and treatment on children's lives.

Characteristics of Preschool-Aged Children Currently Enrolled in a Phase II Double Blind Placebo Controlled Study of Peanut Sublingual Immunotherapy

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RATIONALE:

A recent study of early peanut oral immunotherapy (OIT) in preschoolers demonstrated significant efficacy with higher rates of sustained unresponsiveness than has previously been seen in older cohorts. Sublingual immunotherapy (SLIT) for peanut has demonstrated moderate efficacy in school age cohorts, but has not been studied in this younger age group.

METHODS:

Children aged 12-48 months with peanut allergy or sensitization to peanut were enrolled in a multi-center phase II double blind placebo controlled study of peanut SLIT. We reviewed screening and entry challenge data of 40 subjects enrolled at a single site, between April 2015 and May 2017.

RESULTS:

The majority of participants were male (55%) and Caucasian (80%). Average subject age was 29.5 months (12.4-47.4 months). Median peanut-specific IgE at enrollment was 14.3 kU/L (mean = 26.7, 0.35-100 kU/L) and peanut 1:20 skin prick test (SPT) size was 10.5 mm (mean = 11.1 mm, 4-24 mm). Multiple atopic co-morbidities were reported (75% atopic dermatitis, 40% allergic rhinitis, 23% asthma or recurrent wheezing). No subjects reported diagnosed eosinophilic GI disease. All subjects underwent a 1000 mg double blind placebo controlled food challenge (DBPCFC) at enrollment and tolerated a median dose of 30 mg (mean = 64.7 mg, 0-300 mg).

CONCLUSIONS:

This cohort of preschool age children is representative of high-risk peanut allergy with SPT and IgE at the 95% predictive level and a low DBCPFC threshold providing an ideal opportunity to assess the effect of younger age on the overall efficacy of peanut SLIT.

ASSESSMENT OF ADOPTION OF THE 2013 INFECTION PREVENTION AND CONTROL GUIDELINE

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Introduction:

In 2013, the CF Foundation (CFF) published updates to the 2003 guideline for infection prevention and control (IP&C) based on new evidence concerning pathogen transmission. This study evaluated if CF centers adopted new recommendations from the 2013 guideline, and to determine center characteristics that predicted increased adoption of the recommendations.

Methods:

We requested written IP&C policies from all the CF Care centers in the U.S. Written materials regarding CF center IP&C policies, including formal IP&C policies, proposed IP&C policies, presentation material, and written communications were gathered. Surveys on implementation of additional IP&C practices were completed by CF center directors. Each policy and survey were de-identified and analyzed to determine whether an individual center adopted 9 selected new recommendations from the 2013 CFF IP&C guideline. Weighted scores (0-1) were calculated for each center using item response theory, as adopting a certain recommendation may enhance the likelihood for adopting other recommendations. Weighted scores were analyzed by linear regression to determine if center type (pediatric, adult, or affiliate), size, and geographic region (NE, S, W, MW) were associated with increased adoption of recommendations from the 2013 IP&C guideline.

Results:

We received responses from 144 centers (51% of all U.S. CF centers). Complete information (written IP&C policies; director survey, center characteristics) was available for 130 centers (46%). The total number of new recommendations adopted by each center ranged from 0 to 9; 2 centers (2%) adopted none of the new recommendations and 13 centers (10%) adopted all 9 recommendations. The mean number of new recommendations adopted was 6.5, and the median number was 7. Implementation of contact precautions for all CF patients in inpatient (n=117, 94% of centers with inpatient policies) and outpatient (n= 117, 94% of center with outpatient policies) settings was the most commonly adopted new recommendation. The '6 feet rule' in the inpatient setting (n=66, 53% of centers with inpatient policies) and audits of cleaning and disinfection of surfaces in the outpatient setting (n=66, 51% of centers with outpatient policies) were the least adopted recommendations from the 2013 IP&C guideline. No association was found between center characteristics including center size, geographic region, or type and weighted adoption score ($p>0.4$ for all characteristics).

Conclusions:

There was a wide range of adoption of new recommendations by CF centers from the 2013 IP&C guideline. Center characteristics were not associated with increased adoption of the new recommendations. These data suggest that other factors besides center characteristics determine a center's adoption of IP&C recommendations, and that efforts to improve adoption of IP&C recommendations should be determined on an individualized basis.

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Cost Effectiveness of Early Treatment in Pediatric Patients with Hepatitis C Virus Infection

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Background: Hepatitis C virus (HCV) has received significant attention in recent years due to dramatic increases in cases attributed to injection drug use and the availability of highly curative direct acting antiviral (DAA) therapy. Adolescents represent a population that is impacted by HCV but is not routinely considered for therapy.

Aim: The goal of this study was to evaluate the cost effectiveness of early treatment initiation in pediatric patients with chronic HCV infection compared to previous standard of care of deferring treatment until adulthood.

Methods: We constructed a Markov model to assess the cost effectiveness of treating a hypothetical cohort of pediatric patients with chronic HCV aged 12 years with recently approved DAA therapy compared to deferring treatment until adulthood from the societal perspective. HCV transition state probabilities, treatment costs, HCV medical care costs, and quality-adjusted life year utility estimates were derived from the literature. Discounted costs per person, total life years per person, total QALYs per person were quantified after 30 Markov cycles. Cost effectiveness was measured as the incremental change in total medical costs per average QALY gained. One-way sensitivity analyses were done by varying scenario parameters for treatment cost, cost of non-HCV related medical care, reinfection rate after treatment, treatment uptake in adults, disease progression in childhood, liver transplant survival, and treatment with recently approved pangenotypic DAAs.

Results: Compared to deferring treatment to adulthood, treatment of children for chronic HCV resulted in an average of 1.96 additional QALYs. The incremental cost effectiveness of early compared to deferred treatment was approximately $30,000 per QALY gained after 30 Markov cycles. Cost effectiveness estimates for early treatment initiation were sensitive to variations in DAA costs, reinfection rates in adults, and treatment uptake in adults. Hypothetical treatment initiation with currently available pangenotypic agents was estimated to be cost effective and within the generally accepted US willingness to pay threshold ranging from $6,300 to $21,000 per QALY gained.

Conclusions: Early treatment initiation in pediatric patients with chronic HCV infection results with currently available DAAs appears to be cost effective compared to deferred treatment. Future efforts to control the HCV epidemic should include increasing the number of children treated.

Blood culture results in term newborns of mothers with chorioamnionitis

Laura Parente, MD MPH; Lauren Bradford, MD; Jacob Lohr, MD

Objective: Current guidelines from the CDC and AAP recommend diagnostic evaluation and empiric antibiotic therapy for all newborns of mothers with chorioamnionitis. However, the broadness of this recommendation has been called into question recently, particularly for well-appearing newborns, since multiple studies have shown a substantial reduction in the rate of positive blood cultures in chorioamnionitis-exposed newborns. This study's objective was to determine the rate of positive blood cultures resulted from term newborns born to mothers with chorioamnionitis in our own newborn nursery population.

Methods: Retrospective chart review of 708 term newborns (gestational age greater than or equal to 37 weeks) born to mothers with chorioamnionitis during the years 2012-2016 at UNC Hospitals.

Results: Of the 708 term newborns exposed to chorioamnionitis, 635 (90%) were admitted to the newborn nursery with either a well-appearing or equivocal exam. In this newborn nursery population, there were zero true positive blood cultures. There were six positive blood cultures (1%) that were deemed to be contaminants. The remaining 73 newborns (10%) were ill-appearing and admitted to the NICU. In this NICU population, there were two true positive cord blood cultures (3%), with the remainder of blood cultures being negative. The demographics of our study population include a 50% Medicaid insurance rate, as well as a 34% rate of documented psychosocial risk factors (mental illness, alcohol or substance use, teen pregnancy, other social work consult) in the mothers.

Conclusions: Most term newborns of mothers with chorioamnionitis are admitted to the newborn nursery with a well-appearing or equivocal exam. The risk of true positive blood cultures among this newborn nursery population is low, and in fact there were none in our study population. However, there is a risk of false positive blood cultures. This data should further add to the discussion surrounding the current guidelines and empiric antibiotic usage in chorioamnionitis-exposed infants in an effort to limit over-evaluation and treatment. Our study population differs from that of other studies in that it is fairly high risk, with high levels of Medicaid insurance coverage and documented psychosocial risk factors. Further data analysis will identify rates of clinically relevant unintended sequela such as repeated lab work, increased length of stay, and refusal of hepatitis B vaccine.

Secondary impact on newborn hospitalization for infants at risk for hypoglycemia after an intervention to reduce NICU transfer

A. Painter, S. LeBlanc, J. Haushalter, A. Sutton

Background:
Neonatal hypoglycemia is a common problem with well-described risk factors. We completed a successful quality improvement initiative to reduce intensive care transfer in this population at our hospital including a new protocol emphasizing early skin-to-skin care (SSC) and feeding, initial blood glucose at 90 minutes of life and measurable supplementation for hypoglycemia. While reducing NICU transfer is important, it remained unclear what impact our intervention had on other aspects of care for infants at risk for hypoglycemia that are valued by families.

Objective:
To assess secondary impacts of an intervention aimed at reducing intensive care transfers for infants at risk for hypoglycemia, including: number of blood glucose checks required to "pass" the protocol, percent of infants exposed to intravenous (IV) dextrose, ability to breastfeed if desired and documentation of SSC and breastfeeding within one hour of life for infants at risk for hypoglycemia.

Methods:
We analyzed data on consecutive infants born at our institution with a risk factor for hypoglycemia over a two-year period around our prior intervention (n=628 pre-intervention, n=772 post-intervention). Infants were excluded for NICU admission for reason other than hypoglycemia, <35 weeks' gestation, or <2 kg. Data were obtained from a report in the EMR including number of blood glucose checks obtained in hospitalization, utilization of intravenous dextrose, and initiation of breastfeeding. Manual chart review was performed to assess for inclusion. Statistical analysis included two-tailed t-test and chi-squared tests where appropriate.

Results:
NICU transfer rate was reduced from 9% of newborns at risk for hypoglycemia pre-intervention to 3% post-intervention ($p<0.001$), with a similar reduction in IV dextrose ($p=0.01$). Post-intervention, the mean number of blood glucose checks decreased from 6 to 5 ($p<0.005$) with significantly more infants passing the protocol with the minimum number of 3 glucose checks ($p<0.001$). Documentation of SSC and breastfeeding in the first hour of life increased from 48% to 62% ($p<0.001$) and 40% to 48% ($p=0.010$), respectively. The number of mothers initiating breastfeeding on the first day of life increased from 83% to 88% ($p=0.002$). [Table 1]

Conclusion:
Secondary analysis of an intervention aimed at reducing NICU transfer for infants at risk for hypoglycemia resulted in lower rates of IV dextrose, fewer blood glucose checks and increased likelihood of breastfeeding initiation despite encouragement of measurable supplementation when hypoglycemia occurred.

Table 1: Group comparisons for pre/post protocol change

	Protocol			
	Pre (N=628)	Post (N=772)	p-value	95% CI for difference*
NICU admission	55 (9%)	27 (3%)	<0.001	-0.05 (-0.08, -0.03)
Skin-to-skin	300 (48%)	476 (62%)	<0.001	0.06 (0.02, 0.11)
Missing	271 (43%)	246 (32%)		
Breastfed - 1 hour	249 (40%)	367 (48%)	0.010	0.05 (-0.01, 0.1)
Missing	301 (48%)	317 (41%)		
IV dextrose	39 (6%)	24 (3%)	0.010	-0.03 (-0.05, -0.01)
Breastfed attempt	523 (83%)	680 (88%)	0.002	0.01 (-0.02, 0.04)
Missing	49 (8%)	27 (3%)		
# Glucose checks				
3	285 (45%)	422 (55%)	<0.001	-0.09 (-0.15, -0.04)
4 to 6	209 (33%)	230 (30%)	0.08	
7 to 9	60 (10%)	63 (8%)	0.3	
10 or more	74 (12%)	57 (7%)	0.009	

**proportion and mean differences based on complete data. Thus, reported percentages for pre/post subcohorts may not match computed differences.*

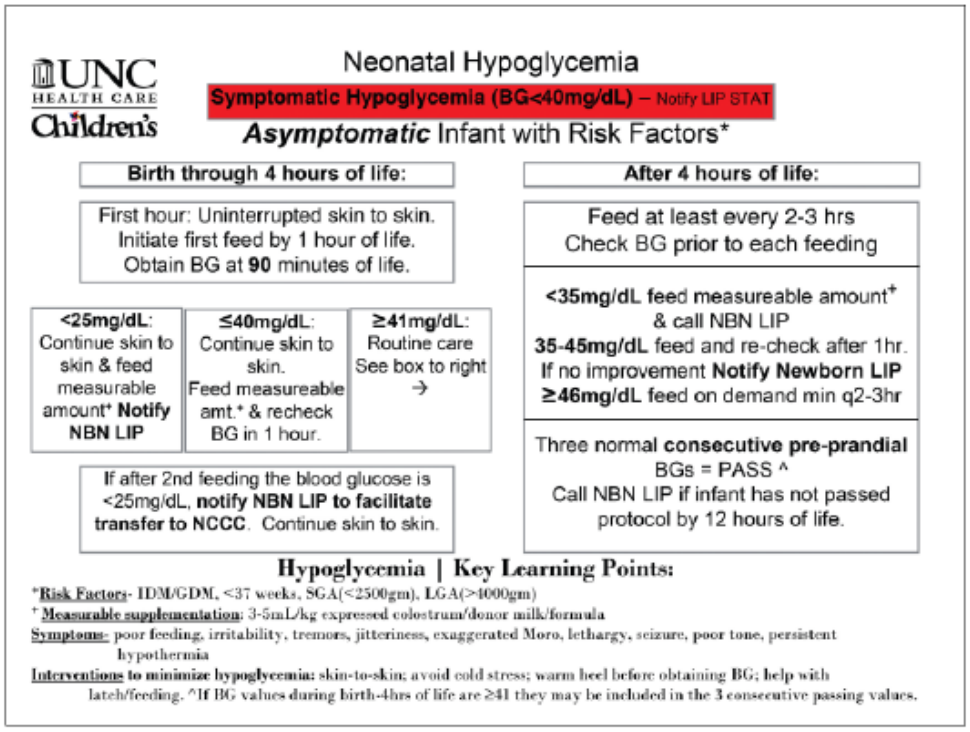

Figure 1. Updated protocol during quality improvement intervention for management of infants at-risk for hypoglycemia

Healthcare utilization among Latino children before and after executive actions on immigration

Rushina Cholera, MD, PhD, Julie Linton, MD, Shahar Shmuel, ScM, Anna Miller-Fitzwater, MD, MPH, Debra Best, MD, Shruti Simha, MD, Kori B. Flower, MD, MS, MPH

Background: Changes to immigration policy followed the 2016 US presidential election, including executive orders which expanded immigration enforcement and may influence healthcare utilization by Latino children.

Objective: To describe and analyze appointment status among Latino children in outpatient clinics across North Carolina in comparable time periods before and after executive immigration actions.

Methods: We included children seeking care at outpatient clinics associated with three health systems in North Carolina during pre (Oct 2015-March 2016) and post (Oct 2016-March 2017) time periods. We described changes in no-show and cancellation percentages and visit volume among Latino and non-Latino populations. We assessed spatial variation in healthcare utilization at the county level, dichotomizing counties as those with strict immigration enforcement policies and those without.

Results: Over 330,000 appointments by 108,726 children from three health systems were included. The percentage of total appointments scheduled for Latino children decreased from 18% to 16% in the pre and post time period, respectively. Visit completion percentages among Latino patients overall were approximately 70% in both time periods. There were no substantial changes in the overall no-show and cancellation percentages between the time periods or between counties with strict immigration enforcement policies. However, site-specific comparisons suggested differences in visit completion percentages in primary care versus referral settings and among particular populations. For example, cancellation percentages among Latino patients increased (15% to 18%), and visit completion percentages decreased (78% to 74%) in primary care settings at one site but these trends were not observed in the other health systems. Additionally, two systems saw fewer absolute numbers of Latino uninsured visits in the post-executive order time period while one system saw an increase in visits from this population.

Conclusions: Despite potential barriers to care, Latino patients served by the included facilities have high proportions of visit completion. However, visit completion and number of Latino patients served may have changed before and after immigration policy changes in ways that are specific to particular institutions, geographic localities, and practice settings.

Mental Health and Behavioral Screening in Pediatric Type 1 and Type 2 Diabetes Mellitus

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Katherine Cooper LCSW, Division of Pediatric Endocrinology
Robert Agans PhD, Department of Biostatistics
Nina Jain MD, Division of Pediatric Endocrinology

Objectives: To describe the findings of mental health and behavioral screening performed as part of routine pediatric type 1 and type 2 diabetes care.

Methods: A retrospective chart review focused on children aged 11 to 17 with type 1 and type 2 diabetes cared for in a multidisciplinary pediatric endocrinology practice. As part of routine diabetes care, the Strengths and Difficulties Questionnaire (SDQ) self-reported version was completed by patients as a behavioral and mental health screening tool. Scores from each of the 5 domains of the SDQ and the impact supplement were collected and compared to age-matched normative data from parent-reported SDQ.

Results: SDQ results were collected from 128 patients with type 1 diabetes. When considering only children aged 11 to 14, patients with type 1 diabetes had significant higher or more concerning scores in the following scales of the SDQ: total difficulties ($z = 2.38$, $p < 0.05$), emotional difficulties ($z = 3.79$, $p < 0.01$), and hyperactivity ($z = 2.08$, $p < 0.05$). Patients with type 2 diabetes had significant higher scores in only one domain, hyperactivity ($z = 2.17$, $p < 0.05$). In the 15 to 17-year-old group, patients with type 1 diabetes scored significantly higher in all scales except conduct problems: total difficulties ($z = 4.34$, $p < 0.01$), emotional problems ($z = 5.46$, $p < 0.01$), hyperactivity ($z = 2.44$, $p < 0.05$), peer problems ($z = 4.08$, $p < 0.01$), prosocial ($z = -4.66$, $p < 0.01$), and impact supplement ($z = 2.07$, $p < 0.05$). Patients with type 2 diabetes scored significantly higher in three scales: total difficulties ($z = 2.58$, $p < 0.01$), emotional problems ($z = 2.08$, $p < 0.05$), and hyperactivity ($z = 2.55$, $p < 0.05$).

Conclusions: This study suggests that patients with type 1 and type 2 diabetes, particularly older teenagers, have a higher burden of behavioral issues and emotional symptoms when compared to their peers without diabetes. Older teens scored higher in domains suggesting risk for psychologic disorders including anxiety and depression, in addition to difficulty interacting appropriately with peers. Furthermore, the significant elevation of the impact score indicates that these patients perceive that there has been some impairment of their daily function. These findings highlight the importance of routine behavioral and mental health screening in pediatric patients with diabetes, in addition to underscoring the need for a multidisciplinary management team including social work and psychology.

Making the Case for Universal Screening of Pregnant Women for Hepatitis C Virus: One State at a Time

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Background: New cases of Hepatitis C virus (HCV) infection are climbing in young adults and particularly in women of childbearing age. Despite this growing burden, a risk-based screening approach is still recommended when testing for HCV in pregnant women and young adults. Risk-based screening was abandoned for "Baby Boomer" adults in favor of universal screening due to concerns for insufficient capture of cases.

Objective: We analyzed public health department data for all 50 states to compare the published rates of HCV infection among young adults and Baby Boomers

Methods: Public health department websites for all 50 states were reviewed for the most recent information on HCV incidence and prevalence. Age-specific rates were recorded for young adults (ages 20-39) compared to Baby Boomers (ages 50-70). When specific rates were not available, data on year over year trends were noted for both age groups.

Results: Using their own published data, we identified 11 states where rates of HCV infection in young adults surpassed that of Baby Boomers, and 4 states where the rates of HCV were equal between the 2 age groups. These states alone make up 25% of the entire US population. When we include 6 additional highly populous states with reported HCV incidence on the rise in young adults, these 21 states account for more than half the US population. Only 4 states reported HCV rates in Baby Boomers to be higher than young adults and 25 states had no recent data to review. Of note, most of these states are direct neighbors to states in the first 2 categories with a higher burden of HCV.

Conclusions: Even using a risk-based screening strategy with lower case capture rate in young adults compared to universal screening in Baby Boomers, we identified that many states have HCV rates in young adults that is as high or higher than Baby Boomers. These results suggest that universal screening in this age group is warranted. Pregnant women represent an easy group to target given their frequent medical visits, frequent lab testing and that exposed infants would require follow up testing.

Efficient, dried blood spot-based determination of hepatitis B seroprevalence from a national survey in the Democratic Republic of the Congo

Authors: Peyton Wilson,[1] Jonathan B. Parr,[2] Vera Holzmayer,[3] Margaret Carrel,[4] Antoinette Tshefu,[5] Kashamuka Mwandagalirwa,[5] Jérémie Muwonga,[6] Franck Fwamba,[6] Mary Kuhns,[3] Ravi Jhaveri,[1] Steven R. Meshnick,[7] and Gavin Cloherty[3]

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Background and Aims: Hepatitis B virus (HBV) is endemic throughout sub-Saharan Africa, but the burden of this disease has yet to be fully elucidated in the Democratic Republic of the Congo (DRC). Dried blood spot (DBS) sampling is an efficient method to determine HBV prevalence in low-resource countries such as the DRC and has the potential to replace conventional venous blood sampling in large surveys.

Method: DBS collected from adults and children during the 2013-2014 DRC Demographic and Health Survey and selected at random from all provinces were tested using Abbott ARCHITECT Qualitative hepatitis B surface antigen (HBsAg) assay. Sequencing and phylogenetic analysis was attempted on all positive HBsAg samples. HBsAg-positive DBS samples were further tested for the presence of antibodies to hepatitis D virus (HDV) using the ARCHITECT research anti-HDV assay. The weighted country-wide and provincial prevalence of HBV were calculated, and the performance characteristics of the HBsAg assay were evaluated.

Results: We identified 39 HBsAg-positive cases among 980 samples tested. The overall weighted national prevalence of HBV was 3.3% (95% confidence interval [CI], 1.8-4.7%), with a prevalence of 3.7% (95% CI, 1.9-5.5%) among adults and 2.2% (95% CI, 0.3-4.1%) among children. HDV prevalence was 1.5% (95% CI, 0.9-2.1%) among adults, with no co-infections noted in children. The limit of detection (LOD) for HBsAg testing using DBS was 0.75 IU/mL, and its specificity was 99%. HBsAg results near the LOD were highly reproducible (coefficient of variation 5.8%). We successfully sequenced the S and reverse transcriptase regions of 10 of 39 HBsAg-positive DBS tested. Phylogenetic analysis revealed a predominance of genotype E (60%) and a unique cluster of genotype A isolates (30%) that were distinct from other subgenotypes.

Conclusion: HBV is highly prevalent in both adults and children living in the DRC, with rates approximating those in other sub-Saharan African countries. These findings support the need for public health interventions to address HBV and prevent its ongoing transmission. DBS-based testing using ARCHITECT HBsAg is a convenient method for the detection of HBV in large-scale surveys and can be easily used to monitor and map the burden of HBV in sub-Saharan Africa.

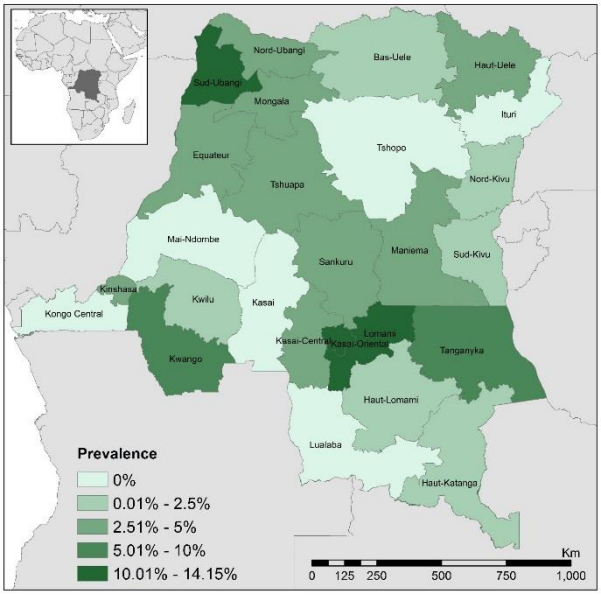

Figure 1: Province-level weighted distribution of HBV prevalence, measured by HBsAg

Risk factors for chronic lung disease and asthma differ among children born extremely preterm

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Objectives: To evaluate the hypothesis that chronic lung disease of prematurity (CLD) is a risk factor for asthma in children born extremely preterm, and the hypothesis that the risk factors for CLD are similar to those for asthma.

Study Design: A prospective cohort analysis was performed using data from 882 children born before the 28th week of gestation between 2002-2004 who returned for follow-up at ages 12 and 24 months and 10 years. We created time-oriented logistic regression models to compare risk factors for CLD, defined as need for supplemental oxygen at 36 weeks postmenstrual age, and parent-reported asthma at 10 years of age.

Results: CLD diagnosed during the neonatal period was associated with bronchodilator use at 12 months and 24 months ($p < 0.001$), but not with an asthma diagnosis at 10 years (Odds Ratio 1.3; 95% confidence interval 0.98-1.8). While risk factors for CLD include lower gestational age (OR 2.7; 1.5-4.7) and fetal growth restriction (OR 2.3; 1.4-3.7), risk factors for asthma include mother's eligibility for public insurance (Medicaid) (OR 1.8; 1.1-2.8), and higher weight gain velocity during the first year (OR 1.5; 1.02-2.2) and between the 2nd and 10th year (OR 1.7; 1.2-2.4).

Conclusions: Among children born extremely preterm, the diagnosis of CLD and its antecedents were associated with transient preschool wheezing, but not with asthma. Post-NICU factors, such as growth velocity and socioeconomic disadvantage, appear to have stronger associations with asthma than exposures during NICU admission.

INCREASING RESIDENT ENGAGEMENT THROUGH INTERACTIVE LEARNING AT MORNING REPORTS

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Background: Morning report is a commonly used venue to utilize clinical cases for teaching core pediatric topics. Given the competing demands of residency training, as the academic year progresses, active resident participation in morning report can be difficult to sustain. We hypothesized that interactive, competitive and team-based activities would increase resident engagement and participation in our morning conferences series.

Objective: Introduce interactive teaching modalities to improve resident engagement, participation, learning and satisfaction at morning report conferences. Methods: We developed interactive learning activities to integrate into the traditional format of our morning reports. Following a resident's presentation of a clinical case, the chief resident would lead a learning activity. Among others, these included "Pick 5", a detective style approach to diagnosis; "Matching" an image and fact matching activity highlighting high yield board review topics; and "Charades Race", a fast-paced race to identify pictures and buzz words. All activities were designed to be competitive with teams of mixed learner levels participating. Activities were followed by a brief didactic session with learning points from the case. A web-based survey was used to evaluate the efficacy this curriculum.

Results: Residents overall reacted very positively to the activities, with favorable evaluations at both three and six months interval. At six months, in comparison to traditional morning report format, 85% of residents surveyed report they participate more with the new activities; 85% report more engagement; 77% reported higher knowledge acquisition; and 77% report more satisfaction.

Conclusions: Team-based and competitive learning activities easily integrated into a traditional morning report format. These activities emphasized active learning and created opportunities for residents to teach in the small groups. Residents report improved satisfaction, engagement, participation and learning. These activities could be adapted for use at other residency programs that have clinical case based conferences.

Pediatric Residency Transgender Education Initiative

Elizabeth Sandberg, MD, Amalia Lee, BS, Steven Weinberg, MD, Zachary Smith, MD, Martha F. Perry, MD, Emily Vander Schaaf, MD, Sue Tolleson-Rinehart, PhD

Background/Introduction: Pediatricians are often the first healthcare providers informed of a transgender youth's gender-related questions or concerns. Prior to June 2017, our institution's pediatric residency did not have a formalized curriculum regarding the health care needs of transgender youth. To evaluate pediatric resident comfort and knowledge with care of transgender youth, we distributed a baseline survey which revealed 4 in 10 pediatric trainees were uncomfortable providing services to transgender youth, and only 1 in 4 reported feeling prepared to meet the needs of transgender youth. Our aims are to develop a pediatric residency curriculum to achieve 90% of pediatric residents reporting 1) comfort, 2) familiarity, and 3) feelings of preparedness to meet the clinical needs of transgender patients.

Methods: Six months into our initiative, we monitored our progress in achieving our three global aims by distributing a follow-up survey to assess residents' comfort, familiarity, and feelings of preparedness regarding the medical care of transgender patients. This was composed of selected components of the BASE All Staff Assessment Survey from The Fenway Institute. We distributed the survey via email to be completed voluntarily and anonymously. Chi-square tests were used to ascertain differences in the residents' response to the survey questions before and after the initiation of this initiative. We used STATA 15.1 (StateCorp, Inc., College Station, TX) for all analysis and $P<0.05$ was considered significant.

Results: 64 residents completed the baseline survey (96% response rate) and 29 residents completed the follow-up survey (48% response rate). Results are outlined below:

% Agreeing or Strongly Agreeing	Pre Survey Responses % (N)	Post Survey Responses % (N)	Chi-Square (χ^2)	p-value
Familiar with the unique health issues affecting transgender people	50 (32)	86 (25)	11.29	0.004
Prepared to meet the clinical needs of transgender patients	23 (15)	52 (15)	7.31	0.03
Comfortable providing services to transgender people	58 (35)	70 (19)	1.15	0.56

Conclusion: Six months into our quality improvement initiative, we have had statistically significant improvements in overall pediatric residents' reports of familiarity and preparedness to care for transgender patient, and a trend of improvement in overall pediatric residents' reports of comfort providing this care, through the development of a formal pediatric residency transgender curriculum. We continue to work to refine the content and structure of this curriculum to achieve our aims, focusing on increasing trainee firsthand experience caring for transgender patients in a variety of clinical settings.

Acknowledgements: A special thanks to the Improvement Scholars Program for funding in support of this project, and to The Fenway Institute for access to their BASE All Staff Assessment Survey.

A Update to the Quality Improvement Initiative to Design and Implement an Outpatient Education Pathway for Newly Diagnosed Insulin-Dependent Diabetes

Elizabeth Estrada, MD; Nina Jain, MD; Michelle Curl, BSN, RN, CDE; Christy Bogardus, MS, RD, CDE, LDN; Katie Cooper, LCSW, LCAS; UNC Pediatric Endocrinology, Christine Walsh-Kelly, MD; UNC Pediatric Emergency Medicine

Background/Introduction: The significant emotional stress associated with a new diagnosis of insulin-dependent diabetes (IDDM) may be exacerbated by the historic process of hospitalization after diagnosis. As of November 1, 2016, UNC Pediatric Endocrinology transitioned to an outpatient diabetes education model for patients with newly diagnosed IDDM. Given the chronic nature of IDDM, in which long-term outcomes are associated with a patient's diabetes self-management skills, self-management strategies are essential components of diabetes education provided at diagnosis. To optimize the outpatient diabetes education model, an improvement initiative has focused on redesigning the outpatient care processes, refining patient education content, and identifying ideal educational strategies. Our aims are to 1) achieve patient self-management, 2) reduce stress and 3) ensure patient/family and provider satisfaction with the outpatient pathway.

Methods: A multidisciplinary team collaborated as part of this improvement initiative. The 4-day outpatient diabetes education pathway includes criteria for eligibility, and the curriculum content and education program is approved by the American Diabetes Association. Using formal QI methods and tools, the initiative focused on redesigning the content and format of the pathway based on results from key measures and individual PDSA cycles. Patient and family input into content and format was integral to our PDSA cycles. Primary outcome measures include: self-efficacy, stress and satisfaction. Key process indicators include knowledge and presence of a school plan. School absences and unplanned readmissions and ED visits were monitored as balancing measures and investigated for opportunities to improve the pathway.

Results: This Quality Improvement initiative achieved our goal of patient/parent self-management skills, while maintaining high satisfaction for parents and providers throughout the implementation and refinement of an outpatient diabetes management pathway. Key pathway components include refined education content, interactive educational tools, and close collaboration with social work and dietary specialists. Despite multiple PDSA cycles and pathway modifications, including early involvement of a social worker, addition of nutrition resources earlier in education, and simplification of education resources, we have had difficulty modifying the stress experienced by caregivers of children with new IDDM. The majority of the stress reported relates to factors that are difficult to modify, specifically emotional burden and interpersonal distress, and is rarely attributed to regimen-related or physician-related distress. Overall, subjective response from families have been overwhelmingly positive in support of an outpatient management pathway for newly diagnosed IDDM.

Conclusion: We achieved our target self-management goals, and success is attributed to a standard management pathway with consistent and clear education being provided by a specialized team. Our aim of reducing reported stress for patients with newly diagnosed IDDM was not achieved.

Improving Newborn Care in Ethiopia: Evaluation of a Quality Improvement Workshop

Denise Jones, MD, Steven Weinberg, MD, Bogale Worku, MD, Michael Jones, MS, Carl Bose, MD, Jackie Patterson, MD, MPH

Introduction:

Almost 3 million newborns die annually, making up nearly 50% of under-5 child mortality, with 98% of these deaths occurring in low and lower-middle income countries (LMICs). With the goal of reducing neonatal mortality, the American Academy of Pediatrics (AAP) developed *Helping Babies Survive* (HBS), an educational program to teach evidence-based newborn practices in low-resource settings. While HBS has been widely disseminated in LMICs, barriers to implementation often challenge translation of this knowledge into practice. To address these barriers, the AAP and partners developed a simplified guide, *Improving Care of Mothers and Babies* (ICMB), to teach quality improvement (QI) methods to facility-based providers in LMICs. Its effectiveness remains un-tested.

Consistent with trends in other LMICs, newborn mortality in Ethiopia has not improved recently despite a dramatic decrease in under-5 child mortality. To improve newborn mortality in collaboration with the Ethiopia Pediatric Society, we recently completed HBS training in 169 primary and secondary hospitals using a train-the-trainer cascade. A subset of these hospitals was selected for further training using the ICMB guide. A central aim was to determine the gain in knowledge about QI methods resulting from this guide-directed training.

Methods:

In December 2017, participants from 18 hospitals in Addis Ababa attended a 2-day workshop to learn QI methods using the ICMB guide. Instructors presented key background information on the QI process outlined in the guide, and participants completed practice exercises in small groups. An 18-item multiple-choice questionnaire (MCQ) was given to participants before and after the workshop to assess knowledge acquisition.

Results:

We had 34 participants complete both pre- and post-workshop MCQs. One of the questions did not perform well, so was dropped from the questionnaire before final analysis of results. The percentage of correct answers on the 17-item MCQ significantly increased from 63 ± 15 % to 81 ± 14% ($p<0.001$) after training. Passing scores (≥80%) significantly increased from 15% pre-workshop to 65% post-workshop ($p<0.001$). Neither a greater level of practice experience nor any degree of QI background was statistically significantly associated with test scores.

Conclusion:

Following a workshop using the ICMB QI guide, participants demonstrated significant improvement in knowledge of QI methods. However, we are uncertain if the final knowledge base will be sufficient to conduct a QI project. Therefore, we are currently collecting data on the hospitals' progress with QI projects following the workshop.

Reducing time from hospital arrival to start of inpatient methotrexate chemotherapy

Elizabeth Finch MD, Jennifer Brondon MD, Ian Davis MD, PhD, Cassidy Faircloth PharmD, BCPS, BCOP, CPP, Jenna Kaplan PharmD, Cammie Presler RN, MSN, CPNP, CPON, Stephanie Risgaard, RN, Stephanie Schouten RN, MSN, CPNP, CPHON, Tara Sotak RN, Patrick Thompson MD, Pat Yee RN, MSN and John Hipps MD.

Introduction: Many pediatric oncology patients receive high dose methotrexate (1-12 g/m^2) as part of therapy. High-dose methotrexate is given inpatient and frequently hospitalizations can be prolonged by one full day if there are delays in starting the chemotherapy infusion. In order to administer the drug in the safest possible manner patients typically receive alkalinized IVF fluids until their pH urine is ≥ 7.0 because alkalinized urine improves excretion of methotrexate and its metabolites. Delays in achieving appropriate urine alkalization can delay the start of therapy. Our multidisciplinary team sought to reduce the time between clinic arrival and start of methotrexate infusion by 30% over a 12 month period by using home oral bicarbonate.

Hypothesis: The administration of home oral bicarbonate will decrease the time required to achieve appropriate urine alkalization and in turn decrease delays in drug administration.

Methods: In our first PDSA (plan, do, study, act) cycle, we started patients on oral sodium bicarbonate for 72 hours prior to admission to help increase urine pH more quickly. We examined two endpoints: 1) Time from clinic arrival to urine alkalization, and 2) Time from clinic arrival to start of methotrexate infusion.

Results: The mean time between clinic arrival and when urine parameters were adequate for treatment decreased from 10.1 hours in the group that did not receive bicarbonate at home to 5.3 hours in the group that took sodium bicarbonate at home (p=0.002). However, the time from clinic arrival to start of methotrexate was not significantly different in the not pretreated and the treated groups- 10.4 hours and 10.2 hours respectively (p=0.9).

Conclusion: Starting sodium bicarbonate at home prior to admission for high dose methotrexate decreased the time to meeting urine parameters to meet treatment but did not decrease the time to actually receiving the chemotherapy. Future PDSA cycles will need to focus on decreasing the time from meeting parameters to actually receiving the medication.

Pre-Departure Simulation Curriculum: Improving Learner Preparedness for Global Health Rotations

Alyssa E. Tilly, MD, Emily J. Ciccone, MD, MHS, Benny L. Joyner, Jr., MD, MPH, and Elizabeth C. Fitzgerald, MD.

Background: Residency programs and medical schools are offering more global clinical experiences. These rotations differ from domestic training, and many learners, while able to intellectualize global health, have little actual experience and are often not appropriately prepared. Few programs offer pre-departure training, and if offered, its content varies widely. Simulation allows learners to develop skills and knowledge via hands-on instruction. The goal of this curriculum is to use simulation to replicate Pediatric clinical scenarios in low-resource settings and objectively assess its effect on clinical competence.

Methods: Twenty-one learners participated in 2 sessions after completion of a pre-survey on past experience and a knowledge assessment based on WHO standards. Learners then completed a triage exercise and 3 simulated scenarios: cerebral malaria, respiratory distress, and shock with malnutrition. A didactic highlighting key points and procedures followed each case. Participants then repeated the simulation. Time to performance of critical actions was measured before and after the didactic during the second session. After the training, learners completed a post-survey and repeated the knowledge assessment.

Results: Twenty of the 21 participants completed both surveys. The proportion of learners who reported feeling somewhat or very confident in their clinical global health abilities increased from 35% to 95%. The median knowledge assessment score improved from 62.5% to 75%. Fifty-five percent of participants increased their score, 30% had the same score, and 15% decreased their score. The scores that decreased were primarily impacted by 2 of the 8 questions. Interestingly, for the other questions, the average score increased from 67% to 87%. On average, the time to each critical action improved by 116 seconds across all groups between repeated simulations.

Conclusion: This project demonstrates the value of simulation-based, pre-departure training for learners in improving comfort in, knowledge of, and competence with situations encountered when pursuing global health experiences.

Pediatric Kidney Transplant Post-operative Care Guidelines: A multi-disciplinary quality improvement project

Authors: Erica C. Bjornstad, MD MPH, Katherine Westreich, MD

Affiliations: UNC Kidney Center

Background: Approximately 800 pediatric kidney transplants (KT) occur annually in the United States. Patients in the immediate postoperative period require a multidisciplinary team comprised of surgeons, intensivists, nephrologists, nurses, and support staff to meet their complex medical needs. Coordination of multiple specialists can be fragmented and lead to confusion amongst front-line caregivers. Our goal was to assess if creation of a pediatric KT clinical practice guideline could help provide role clarity to front-line caregivers in the post-operative period.

Methods: Surveys conducted at NC Children's Hospital May to June 2017 assessed baseline understanding of roles and responsibilities in post-operative care of pediatric KT recipients among all residents, fellows, nurses, and support staff (pharmacy, care coordinators) providing care to new pediatric KT recipients. A clinical practice guideline was implemented. The same groups were again surveyed after implementation (June to August 2017). In the survey, we assessed team-member understanding of roles and responsibilities around key management areas of immunosuppression, intravenous fluids, blood pressure, and pain control.

Results: Data was collected from 42 respondents after the care of 7 pediatric KT recipients. Prior to guideline implementation, each key area had a range of 8-17% of respondents being "unsure" who was primarily responsible. The remainder of respondents were confident in their knowledge of the primary managing team for each area, but there was significant heterogeneity regarding which team was believed to be primary. In immunosuppressant management, 25% of respondents chose Nephrology as the responsible team, while 53% chose Transplant Surgery. After implementation of the guideline, 0% of respondents were "unsure" of roles for all four key management areas, and 3 of 4 key management areas had 100% agreement across respondents in which team was responsible.

Conclusion: Our multi-disciplinary approach shows that a unified clinical guideline can be created and used in the post-operative care of pediatric KT recipients. Implementation of such a guideline led to a significant improvement in the understanding of roles and responsibilities of front-line caregivers, clarifying the roles of multiple sub-specialists for these medically complex patients. Future directions will be to standardize orders and assess impacts on patient outcomes, such as length of stay and medical errors.

Use of Unfractionated Heparin Levels for Heparin Titration and Anticoagulation Management in Pediatric Extracorporeal Life Support

Melissa Crowder, MD; Katherine Clement, MD

Historically, anticoagulation for all extracorporeal life support (ECLS) patients at UNC Medical Center was monitored using the activated clotting time (ACT) anticoagulation test. The ACT has been the gold standard for anticoagulation monitoring for ECLS patients of all ages in all centers due to its historical use in cardio-pulmonary bypass surgeries [1]. Unfortunately over the last several years, ACT testing seems to have become a less reliable strategy for heparin titration [2]. Due to the clinical observation of ACT inaccuracies in our own unit, it has been difficult to standardize ACT driven anticoagulation using our existing standardized clinical pathway. Outcomes from several pediatric studies demonstrate better correlation using unfractionated heparin levels compared to the ACT [3-4]. We then initiated our own new standardized anticoagulation protocol using unfractionated heparin levels as a quality improvement project. Primary aims were to reduce bleeding and clotting events and ECLS circuit changes. Other objectives being investigated are total number of blood product transfusions, total heparin dose, time to steady state heparin dose, overall patient survival, lab test costs, and relationship of the ACT to heparin levels and other anticoagulation markers. Data was collected prospectively, and is compared to retrospective data from ECLS patients in our unit before the new protocol was initiated. We hypothesize that the new anticoagulation protocol will not increase, and could potentially decrease, bleeding and clotting events and circuit changes compared to the prior protocol.

Implementation of an Algorithm for Pediatric Obesity Prevention and Treatment

Elyse Barnett, MD; Elizabeth Darnell, MD; Alese Hunt, MD

Background/Introduction: Obesity is a growing epidemic in the US. More children suffer from obesity than other chronic diseases and 1/3 of all children are overweight or obese. Most of these obese children will continue to be obese adults and suffer the consequences of this disease.

Evidence demonstrates that BMI is not effectively communicated by physicians to patients.

Objective: The objectives of this QI project were to create a standardized approach to address obesity in the clinic setting and to improve the education of families.

Design/Methods: This QI project was designed using the Lean Six Sigma and A3 model. A root cause analysis guided the project. The site included the Tim and Carolynn Rice Center for Child and Adolescent Health in Greensboro, NC. Patients between the ages of 2---18 presenting for their WCC with a BMI greater or equal to the 85th percentile were included.

Interventions included the design and utilization of a standardized treatment algorithm and computerized smart set. Utilization of the algorithm and smart set by physicians was measured. The use of a color---coded BMI chart and healthy lifestyles questionnaire at each WCC and subsequent obesity follow up visits was measured for each participating provider.

Results: Post intervention, 83% of patients had some recommended screening labs done in comparison to 47% found on retrospective chart review. 9% of patients had BMI FU post intervention compared to 19% on chart review. Addressing BMI increased from 85% to 97% post intervention. Overall, 41% of patients with stable or decrease in BMI at FU visits increased to 61% post intervention.

Conclusions: Target state metrics were met except for BMI FU appointment scheduled, documentation of BMI being addressed at WCC and stable or decrease in patient BMI at subsequent visits. This was likely due to FU not being scheduled immediately, not enough appointment slots, already addressing BMI as well as not documenting and not enough time passing between visits to see change in weight.

Limitations to our project include small sample size, small group of providers and length of project (Oct---Feb). Future plans include color---coded BMI charts in each room, surveys at all WCCs and food security questions on questionnaires. This project has shown an algorithm and survey can help streamline the care of overweight and obese children and be beneficial to families.

It's never too early: Design and implementation of a novel "resident as teacher" program for interns
LeeAnne Flygt, MD, MA, Eric Zwemer, MD

Purpose:
While many residency programs have "Resident as Teacher" programs, such training is often geared towards senior residents, though interns are often working most closely with students. We designed, implemented, and evaluated an "Intern as Teacher" (IAT) curriculum to provide interns with educational tools and training early in their residency.

Methods:
The rising juniors (class of 2019, n=18) completed an end-of-year survey assessing confidence in teaching and knowledge of teaching methods and available resources. A novel IAT curriculum was developed based on review of this survey, educational literature, and expert consensus. The final curriculum was comprised of two one-hour sessions reviewing IAT expectations, the one-minute preceptor (OMP) model, resources available, chalk talks, and giving feedback. Incoming interns (class of 2020, n=20) attended these sessions in the first month of residency. Surveys were administered to interns pre- and post-intervention.

Results:
13 interns completed the curriculum and post-intervention survey. Within the intern class of 2020, completion of the IAT curriculum was associated with increases in overall confidence in teaching ($p=0.00004$) and confidence that teaching was effective ($p=0.00003$), engaging ($p=0.047$) and efficient ($p=0.00008$). More concretely, knowledge of (45% vs 100%) and confidence in using ($p=0.00002$) the OMP model increased, as did the number of residents with chalk talks prepared (0% vs 46%).

Compared to the rising junior class of 2019, post-intervention interns reported higher confidence in the effectiveness ($p=0.041$) and engagement ($p=0.009$) of their teaching, as well as confidence in using the OMP model ($p=0.00008$). No difference in overall confidence in teaching was seen ($p=0.07$).

Discussion:
Our novel, low-cost, and low-time burden IAT curriculum was associated with increased confidence in teaching and knowledge of educational resources. Class of 2020 interns will complete surveys at the end of their intern year for more direct comparison to the class of 2019. Medical student evaluations of residents will also be analyzed to see whether increased intern confidence translates into more and/or better teaching throughout the year.

Implementation of a risk calculator safely decreases empiric antibiotic use in term and late preterm newborns.

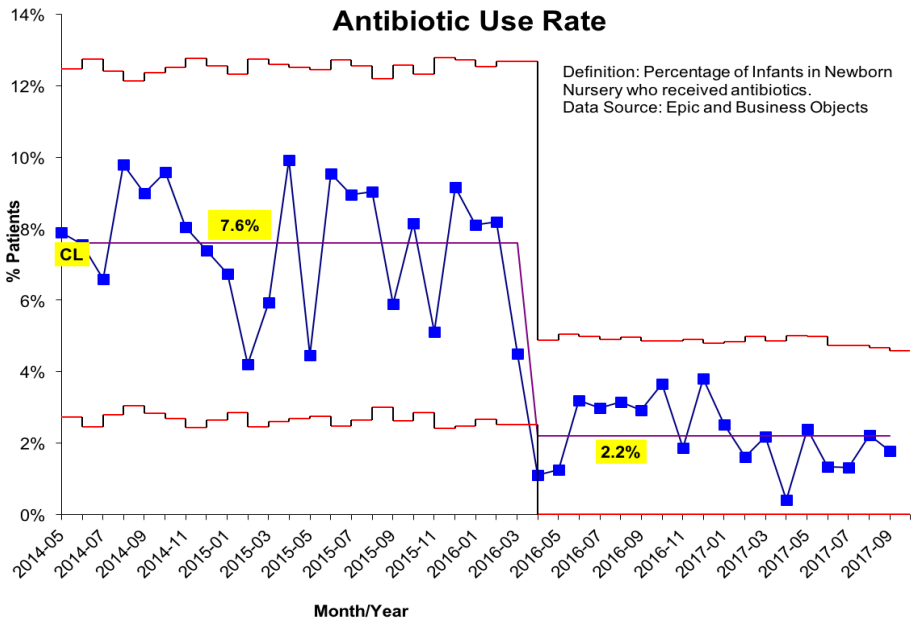
Mary Terrell MD, Ashley Wallace FNP-C, Narges Farahi MD, Matthew Zeitler MD, Laurel Slough DO, Carl Seashore MD

Birth is the most common reason for hospitalization in the United States. Among term and late preterm newborns in the newborn nursery, 15-20% are evaluated for early-onset sepsis (EOS) and 5-8% are treated with empiric antibiotics based on current guidelines. These guidelines were developed prior to widespread adoption of intrapartum antibiotic prophylaxis (IAP), when neonatal EOS incidence was 5- to 10-fold higher than it is at the present. This management, which leads to common interventions in the newborn nursery where infants are otherwise generally "healthy", contributes to increased cost, resource utilization, maternal-infant separation, parental anxiety and potential harm to the neonate's developing microbiome.

Emerging evidence suggests there is an opportunity for more individualized decision-making that could safely lead to improved antibiotic stewardship, less resource utilization and overall savings. The Kaiser EOS Calculator (KSC) is an online tool released in 2014 that provides clinical care algorithms based on a predictive model. Using objective maternal data combined with a clinical assessment of the newborn, the model calculates an individualized sepsis risk score (SRS) with recommendations for management.

As part of a quality improvement initiative, we sought to gradually introduce use of the KSC within our busy newborn nursery to allow for clinician comfort and buy in with the tool with the goal of safely reducing unnecessary evaluation, monitoring and empiric antibiotic use for neonatal EOS. In the pre-intervention period, our antibiotic use rate (AUR) was 7.6% with relatively wide variation month to month. Following widespread implementation of the calculator our AUR dropped to 2.1% with narrowing month-to-month variation (statistical significance?). No adverse events such as missed sepsis, death, or readmission were identified. The KSC can safely be used to decrease neonatal exposure to antibiotics, decrease the need for cultures, and provide recommendations for management in a newborn nursery. Implications for cost savings, antibiotic stewardship, and high value care are substantial.

Figure 1. Antibiotic Use Rate



Statistical Process Control Chart (p-chart) showing antibiotic use rate (AUR) in the pre- and post-implementation periods. Pre-intervention AUR averaged 8%, while post-intervention AUR averaged 2%. Also note the decreased variation in the post-implementation period.

Decreasing length of stay and use of pharmacotherapy for neonates with NAS on an inpatient floor

Thomas Blount, MD

Alana Painter, MD

Emily Freeman, MSN, CPNP

Ashley Sutton, MD

Background

Prior efforts focused on the newborn population of opioid-exposed newborns at UNC Hospitals have improved early management of neonatal abstinence syndrome (NAS) or opioid withdrawal in newborns. Yet, if NAS symptoms progress, requiring transfer to the inpatient floor, scheduled morphine is typically utilized and infants experience prolonged length of stay (LOS) due to strict medication weaning parameters tied to frequent reassessment using the modified Finnegan Neonatal Abstinence Scoring System (FNASS).

Objective

To reduce average LOS in infants with NAS transferred to the inpatient floor for symptom management. Secondary outcomes included reducing the percentage of infants at risk for NAS managed with pharmacotherapy and reducing the total morphine dose in infants who require morphine.

Methods

Using QI methodology, data for infants with NAS, identified by ICD-10 codes, FNASS recordings and transfer from the nursery, were obtained; these included LOS, number of morphine doses and cumulative morphine dose for the newborn hospitalization. Infants requiring NICU transfer for >12 hours for reasons other than NAS were excluded. Iterative PDSA cycles included implementation of a revised wean tool emphasizing as-needed morphine as initial pharmacotherapy, and replacement of FNASS scoring with the recently published “Eat, Sleep, Console” (ESC) tool for withdrawal assessment, which emphasizes non-pharmacologic management and a “common-sense” approach to escalating NAS therapy when necessary.

Results

LOS for infants with NAS transferred to the inpatient floor decreased from 257 to 117 hours [FIGURE 1]. Percent of all infants at risk for NAS treated with morphine decreased from a baseline of 33% (n=132) to 12% (n=33) ($p<0.001$) and all treated infants (n=4) in the improvement period received only one dose of morphine. Total morphine doses per infant transferred to the floor decreased from 39 to 0.2 [FIGURE 2] and total dose decreased from 1.34 mg/kg/infant to 0.02 mg/kg/infant. There were no adverse events.

Conclusion

Using QI methodology, adoption of the ESC tool has revolutionized the management of infants with NAS at our institution by almost eliminating the use of morphine pharmacotherapy to manage this population. Under the new protocol, infants with NAS transferred to the floor averaged a reduction in LOS of nearly 6 days and overall nearly 1300 fewer doses of morphine have been given to newborns during the 5 months since implementation.

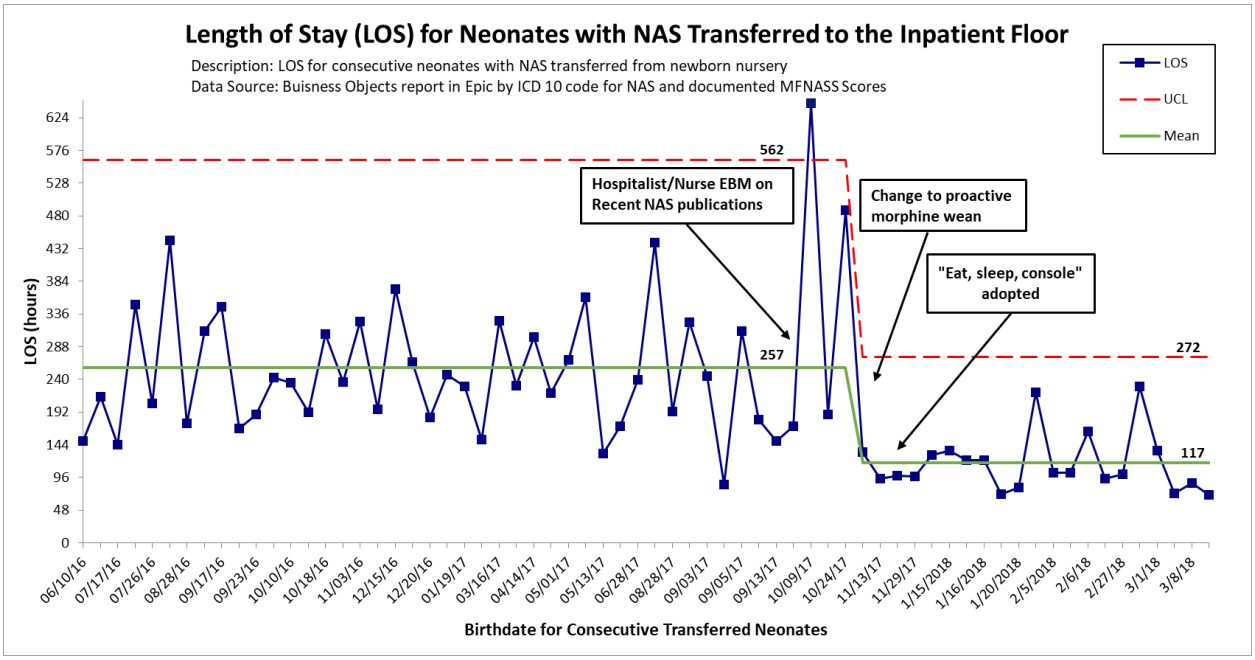


Figure 1. Length of stay for neonates with NAS transferred to the inpatient floor

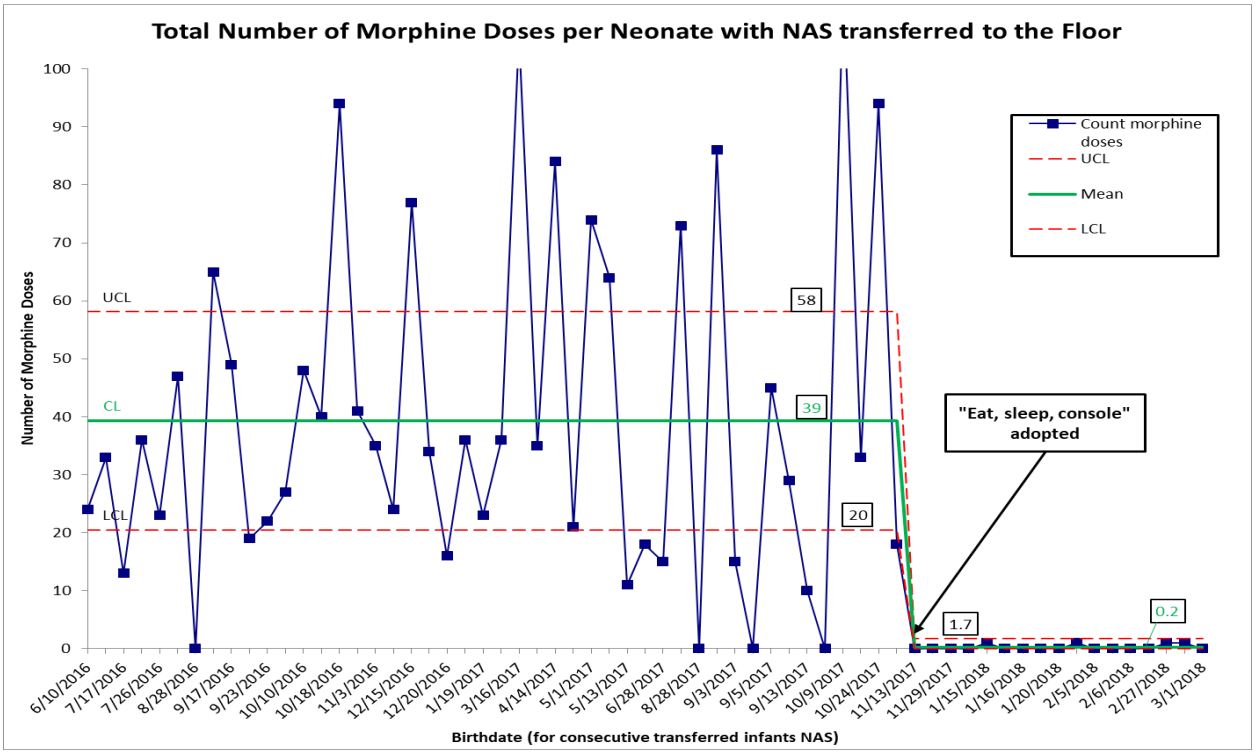


Figure 2. Total number of morphine doses per infant with NAS transferred to the inpatient floor

What's in a name? Improving inpatient team communication

Weinberg, Steven; Zwemer, Eric; Wynn, Maria; Slater, Robert; Gailin, Sheryl; Sutton, Ashley

Purpose: Interdisciplinary communication is critical to quality patient care and prevention of medical errors. Familiarity amongst team members is known to increase productivity and effectiveness, but is difficult in the hospital due to shift and rotation schedules resulting in intermittent contact. Pediatric residents at our institution anecdotally reported challenges in effectively communicating with nurses.

A team including nurses, residents, and hospitalists was formed to improve interdisciplinary communication and inpatient team dynamics, in part by increasing ability of nurses and residents to identify each other by face/name.

Design: A needs assessment survey was administered electronically to nurses (n=49) on an inpatient unit and to residents (n=28) at the completion of intern year. Questions assessed perceptions of multidisciplinary participation in rounds and adequacy of nurse-resident communication, including plan updates and responses to post-rounds queries. The survey also assessed ability to name 10 randomly selected photos of the other discipline by free response. Iterative PDSA cycles were conducted. A nurse and resident face sheet was created that included photos, names, hometowns, and personal fun facts. Multiple iterations of a rounding sheet for each team were created that included daily nursing assignments with photos to encourage nurse invitation by residents to rounds and document nurse updates on plan changes.

Follow-up surveys were completed by each group of residents after inpatient rotations and by nurses at the three-month mark of the project.

Results: Overall, 41 (84%) nurses and 22 (79%) interns completed the initial survey. 35 (71%) nurses and 24 (96%) residents completed the follow-up surveys to date. Three-quarters of residents reported use of daily nurse assignment sheets and 91% reported use of face sheets. Both intern ($p=0.04$) and nurse ($p=0.003$) ability to recognize more than 3 faces improved. On follow-up survey, 40% of nurses reported they felt both communication and team dynamics improved during the project period and 3% felt they had worsened. However, most nurses reported frequency of updates and involvement in rounds had not changed.

Conclusion: Preliminary data suggest cost-free tools to increase interdisciplinary familiarity and identification of care team members by face/name can improve perception of team communication and dynamics. Future efforts will quantify the benefit of these tools, including nurse involvement in rounds.

Education on the flip side: Use of a newborn nursery iTunes U course for medical student flipped classroom learning

Nikkan Das MD, Emily Freeman NP, Jamie Haushalter NP, Ashley Wallace NP, Carl Seashore MD, Eric Zwemer MD

Background: Medical school curriculums are currently undergoing restructuring, and the flipped classroom (FC) model of education has begun to be incorporated into medical education. This model veers away from the traditional lecture-based educational system and encourages students to learn about a topic before class so that they can come to class prepared to discuss the material. There is limited data on the use of FC in the pediatric clinical setting, more specifically, in the newborn nursery. A recent study of the use of a FC model applied in an emergency medicine clerkship found that students found this model to be valuable and facilitators found students to be well-prepared and more engaged in clinical learning. Our aim was to assess third-year medical student use and perceptions of a newly designed and innovative Newborn Nursery iTunes U course created in line with the FC model.

Methods: We created an iTunes U course for the newborn nursery incorporating existing resources from the course website, review articles, UNC protocols, newly-developed quizzes on pertinent topics, and additional nursery resources. We introduced the course to third-year medical students at the start of their newborn nursery rotation, and a brief training on enrollment and use of the course was provided via email. After their rotation, students were surveyed about their experience using five-point Likert scales and free text comments.

Results: Nineteen students responded to the survey. Over half of the students had enrolled in the course (56%). Of those that enrolled, students reported use both at home (89%) and at the hospital (67%). The majority agreed that the course was easy to navigate (89%), educational (100%), engaging (67%), and positively impacted their clerkship experience (89%). Additionally, they felt that the course should continue to be used for students rotating through the newborn nursery (89%). Notably, only one student reported resident use of the course for student education (5%). Students commented that the course provided the most important materials, was helpful, well-organized, and effective in preparing them for the nursery rotation.

Conclusions: Medical students on their newborn nursery rotation who enrolled in the iTunes U course found it to be a valuable and educational part of their nursery education. The majority of students reviewed the course at home, in line with a FC model. Future directions include increasing enrollment in the course, as well as a focus on the course as an educational tool for residents to use for student education.

***Helping Babies Survive* in Ethiopia: Implementing Education via a Training Cascade**

Weinberg, Steven; Jones, Denise; Worku, Bogale; Kumera, Megerssa; McHugh, Kate; Bose, Carl; Patterson, Jackie

Background

Each year, 2.6 million babies die during the neonatal period; 98% of these deaths occur in developing countries. Recognizing that improving medical provider knowledge is necessary to reduce neonatal mortality, the American Academy of Pediatrics developed the *Helping Babies Survive* (HBS) educational suite. A train-the-trainer cascade is typically used to disseminate these programs. In 2016, the Ethiopian Pediatric Society disseminated HBS in Ethiopian hospitals using this method. They first trained 33 providers as HBS Master Trainers who then led regional workshops for 662 providers from 169 hospitals across Ethiopia. Regional workshop attendees were expected to return to their hospital and share what they learned.

Objective

To characterize the HBS train-the-trainer cascade in Ethiopia and understand the extent of dissemination.

Design

One year after the regional workshops, we administered a 13-question survey (in English) to one representative from each hospital to investigate hospital-based training activities. Scripted, qualitative interviews were then conducted (in Amharic) to further characterize training activities, enabling factors, and barriers. These were done in person or over the phone based on geographic accessibility.

Results

Of 130 hospitals interviewed thus far, hospital-based training after regional workshops occurred in 92 (71%); 37 (40%) of these hospitals trained all midwives at their facility. Of the 38 hospitals that reported no hospital-based training, 5 reported all of their midwives attended a regional workshop. Between regional workshops and subsequent hospital-based training, 1,208 providers at these 130 hospitals were trained. Hospital-based training ranged from informal, on-the-job overviews of HBS to formal classroom-style teaching of HBS at designated training sessions.

Minimal instruction in how to train others, lack of departmental support, and a lack of budget to support training were cited as barriers to training.

Conclusion

The train-the-trainer cascade reached 63% of midwives in the 130 hospitals interviewed thus far. Dissemination of HBS at the hospital-level may increase by providing specific instruction in how to train colleagues, encouraging departmental support, and allotting a small budget to support training. Future studies should explore effectiveness of knowledge and skill transfer with informal training, as well as improvement in processes of care and health outcomes following a train-the–trainer cascade.

The History of Joseph Merrick, "the Elephant Man:" From Freak Shows to Genomes

Erin Finn, MD; Stephanie Brown Clark, MD, PhD

Throughout history, ways in which people with genetic disorders have been viewed and treated by society has continuously evolved, in a way paralleling (and at times resulting from) knowledge of genetics and the human genome. Joseph Merrick was an English man who lived from 1862-1890 and had a mosaic genetic disorder called Proteus syndrome. PS is characterized by asymmetric, progressive overgrowth of tissues throughout the body. This causes severe orthopedic complications and can be dramatically disfiguring. Merrick was abandoned and put on exhibit in freak shows throughout London under the name "the Elephant Man."

In the 1800s, individuals with genetic disorders were hidden away or put on display as freaks in traveling shows. This view of these individuals as genetically defective or inferior was carried on into the eugenics movement in the United States, which peaked in the 1920s and 30s and championed beliefs that to improve the human race, those with "undesirable traits" should be prevented from procreating through sterilization. This movement lost momentum during the Holocaust, though elements persisted into the latter half of the 20th century. The Human Genome Project represented a concerted effort towards understanding genetics and disease through sequencing the DNA code. These efforts have continued into the 21st century, with plans to make genomic sequencing more affordable and common-place and to understand the complex ways in which our genome influences health and disease.

To understand the changes in societal perception of genetic disorders throughout the years, I compared firsthand accounts of journal articles and memoires by Merrick and his doctor and studied historical archives relating to freak shows and eugenics throughout the 20th century. I subsequently met with patients currently living with Proteus syndrome and discussed how their experiences have been growing up with this disorder. I also helped discover the cause of PS, which brought with it new advances and hope for treatments. Overall, it is clear that our scientific understanding of what causes genetic differences has progressed rapidly in the years since Joseph Merrick. While the treatment of individuals with genetic conditions has improved over the years, the age of genomics presents myriad new ethical questions that will no doubt be encountered. It is important to keep in mind the long and at times reprehensible history of society's interpretation of human genetics and the treatment of patients with genetic disorders to avoid falling into these patterns in the future.

Cognitive remediation in pediatric chronic kidney disease and end-stage kidney disease: rationale, candidate interventions, and applicability.

Karina Javalkar, Maria E. Ferris, Jessica Cuttance, Stephen R. Hooper

Introduction: The purpose of this paper is to address the potential use of cognitive remediation interventions for children and adolescents with chronic kidney disease (CKD) and end-stage kidney disease (ESKD). The prevalence and risk for neurocognitive dysfunction in children with this condition remains high, but, to date, interventions targeting these challenges have not been attempted either individually or as part of a larger treatment program. We aimed to identify candidate treatments in addressing the neurocognitive challenges observed in children and adolescents with CKD/ESKD.

Methods: We conducted a review of the literature documenting the neurocognitive deficits associated with pediatric-onset CKD/ESKD. This was followed by a review of candidate cognitive remediation programs that may be applicable to patients with this condition, and associated factors that could affect such treatment.

Results: Previous reviews of the literature have demonstrated a wide array of neurocognitive deficits and dysfunctions in children and adolescents with CKD. In general, studies have described problems with attention, memory, and various executive functions, with overall IQ being slightly lower during both the school-age and preschool developmental periods. There is a significant relationship between declining estimated glomerular filtration rate and decreasing cognitive function in children. Regardless of age, a longer duration of CKD has been associated with worse performance on tests of attention regulation and inhibitory control.

We identified and reviewed the following cognitive remediation programs that may be applicable to patients with CKD/ESKD: Captain's Log, Cognitive Medicine Working Memory Training, the CRP, AMAT-C, and Posit Science. These interventions have previously been used in children with chronic conditions such as Down syndrome, pediatric cancer survivors, and 22q11.2 deletion syndrome. Additionally, most have been tested and have been effective for children with ADHD, which may be present in at least 35% of patients with CKD/ESKD.

Conclusion: Neurocognitive deficits and dysfunction are now considered a serious comorbidity of CKD/ESKD that likely will not abate, even with renal replacement therapies. Therefore, intervention at the earliest possible signs of cognitive dysfunction may lead to benefits in long-term functioning, general health outcomes, and quality of life. The candidate cognitive remediation programs discussed in the present paper all hold promise for the pediatric CKD/ESKD population. Improving the cognitive functioning of these patients should be a key consideration in any treatment plan, and an empirical examination of the benefits of cognitive remediation training programs for this population could provide a new avenue of exploration for these children and adolescents.

Pediatric Complex Care and Diagnostic Interventions: A Systematic Review of Literature in English and Spanish

Blew, Kathryn, BS; deJong, Neal, MD, MPH; Steiner, Michael J., MD, MPH; Flower, Kori, MD, MS, MPH; Hart, Laura, MD; and Díaz-González de Ferris, Maria, MD, MPH, PhD

Introduction:
Children with medical complexity (CMC) and those with undiagnosed diseases account for a large amount of pediatric health services utilization, subspecialist consultations, and home- or facility-based care services. Complex care clinics or diagnostic referral clinics attempt to centralize services and improve care coordination to improve health and prevent unnecessary utilization. The aim of this study was to systematically review the published literature to summarize the characteristics of clinics that serve as pediatric complex care clinics or diagnostic referral clinics, and then also review outcomes from these clinic interventions.

Methods:
We completed a systematic review of the published literature in English and Spanish through PubMed, and supplemented that with a Spanish language review using Google Scholar and recommendations for articles from subject matter experts. Studies were selected for inclusion following title and abstract review by two authors and then study review. Results were summarized by one author then verified by a second.

Results:
We identified 1026 potential study titles and after review of abstracts, followed by published papers, 15 studies met inclusion criteria. Characteristics of interventions focused on these populations included outpatient care navigation, inpatient diagnostic and complex care admissions, and outpatient diagnostic clinic. We found that care coordination interventions for CMCs improved caregiver satisfaction and reduced healthcare utilization. Additionally, without care coordination many primary care providers report discomfort in co-managing CMCs. Outpatient diagnostic interventions were found to increase diagnostic rate for children with undiagnosed diseases, and multiple models for inpatient diagnostic care were detailed in included studies.

Conclusion:
Interventions focused on CMCs or children with undiagnosed diseases tend to be interdisciplinary in nature, and tend to improve caregiver satisfaction, decrease healthcare utilization, and improve diagnostic rate. Future research is needed to explore how to maintain continuity of care for patients in diagnostic or complex care panels while hospitalized.

Puff Laddy: A five-year-old-boy with forehead swelling

Laura Cannon, MD; John Stephens, MD

Case:

A previously healthy five-year-old boy presented with forehead swelling in the setting of a recent sinus infection. His initial symptoms were fever and nasal congestion for which he was prescribed a 10-day course of cefdinir, completed three days prior to admission. After finishing the antibiotic, he developed unsteady gait, photophobia, headache, vomiting, and progressive forehead swelling. He was afebrile. He was noted to have significant central forehead edema and tenderness without overlying erythema (Figure 1). There were no other neurological or ophthalmological deficits. MRI/MRV of the head demonstrated a 3.5 x 1.2 x 3.9 cm subgaleal abscess with communication to the frontal sinuses as well osteomyelitis of the frontal bone (Figure 1).

The patient was started on intravenous vancomycin and ceftriaxone. He underwent surgical drainage of the abscess with evacuation of purulent fluid (Figure 2). Culture from the procedure grew Streptococcus *anginosus*, and vancomycin was discontinued. He clinically improved following surgery and inflammatory markers normalized. He was transitioned to high dose amoxicillin/clavulanic acid and was discharged home to complete a 21-day total course of antibiotics.

Discussion:

The patient's history, examination, and imaging were consistent with Pott's Puffy Tumor, which is characterized by subperiosteal abscess of the frontal bone with associated osteomyelitis. It most commonly affects adolescents and typically follows frontal sinusitis or trauma. Younger children, as in our case, are less commonly affected, as frontal sinuses do not fully develop until middle or high school age.[1] Common pathogens associated with this entity include typical pathogens associated with bacterial sinusitis, such as streptococcus species, staphylococcus species, and *Haemophilus influenzae*.[1,2] There are a number of serious complications associated with Pott's Puffy Tumor including subdural empyema, brain abscess, epidural abscess and sinus venous thrombosis with potential for septic emboli. Pott's Puffy Tumor requires prompt diagnosis and management, including surgical debridement with ENT or neurosurgical consultation and intravenous antibiotics.

Conclusions:

Forehead swelling in a child with sinus symptoms should be presumed to be due to Pott’s Puffy Tumor until proved otherwise. Clinician knowledge of this condition is crucial in order to provide prompt treatment while avoiding serious complications.

References

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[2] Haider HR, Mayatepek E, Schaper J, Vogel M. Pott's puffy tumor: a forgotten differential diagnosis of frontal swelling of the forehead. J Pediatr Surg. 2012;47:1919-21.

Figure 1: Profile of the patient at presentation with significant swelling of the central forehead with imaging correlate of sagittal T1-weighted image demonstrating subgaleal abscess with communication to frontal sinuses.

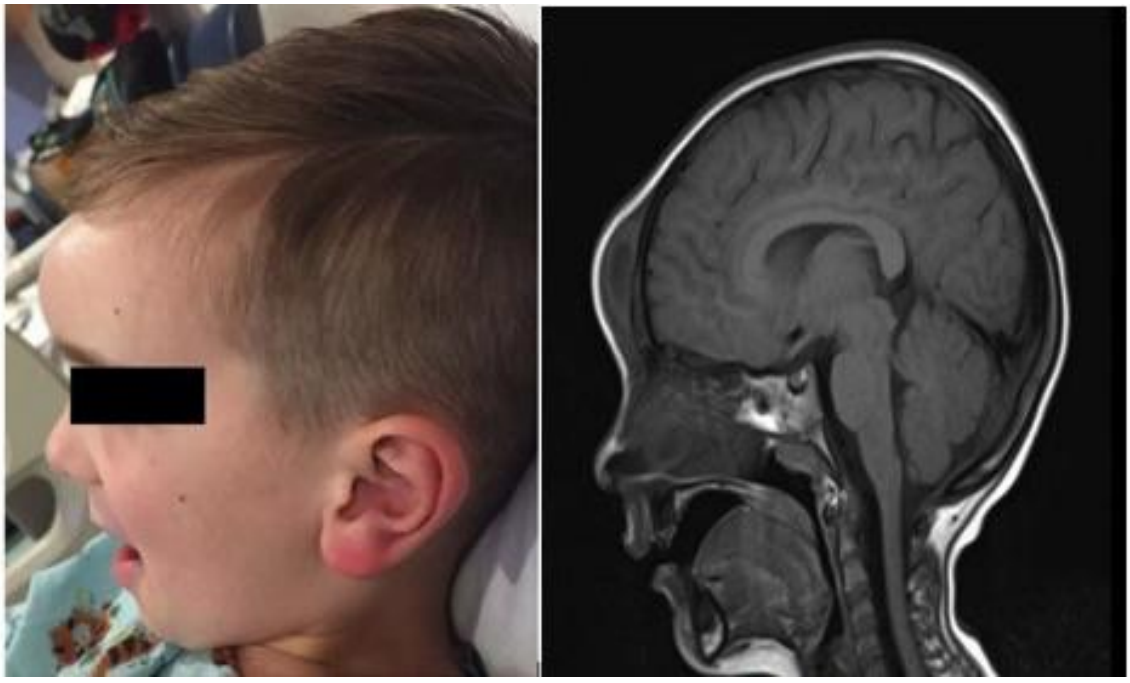
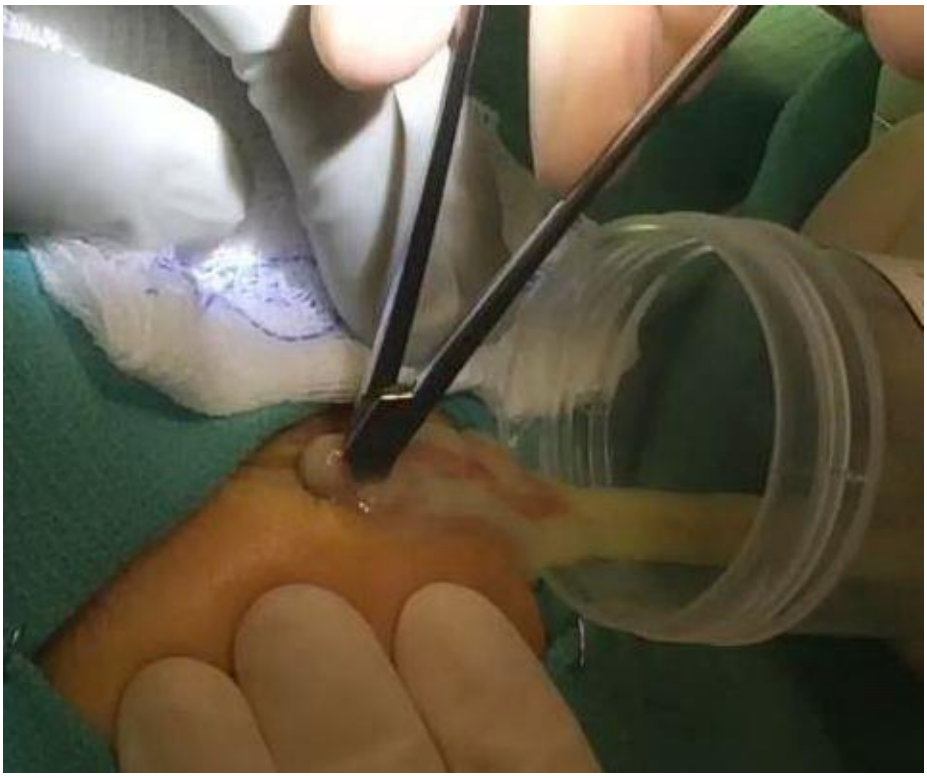


Figure 2: Purulent fluid expressed and sent for culture during excision and drainage in the operating room.



Ace The Case: A 14-year-old with Lower Extremity Weakness and Blurry Vision

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Case: A 14-year-old female presented with progressive upper and lower extremity weakness. Symptoms started five months prior with intermittent bilateral calf pain coincident with onset of lower extremity weakness. Initial evaluation revealed normal CBC, CMP, inflammatory markers, muscle enzymes, and MRI brain and spine with/without contrast. An EMG demonstrated an acute to subacute polyradiculitis affecting the upper and lower extremity.

She was admitted for expedited evaluation. Exam was significant for lower extremity weakness and absent reflexes. Lumbar puncture (LP) showed lymphocytic pleocytosis and markedly elevated protein. Thorough infectious, oncologic, and rheumatologic evaluations were all unremarkable. Most notable is CSF NMO IgG and paraneoplastic antibody panel were negative, and serum ACE was normal. She was started on IVIG for empiric treatment of chronic inflammatory demyelinating polyneuropathy (CIDP).

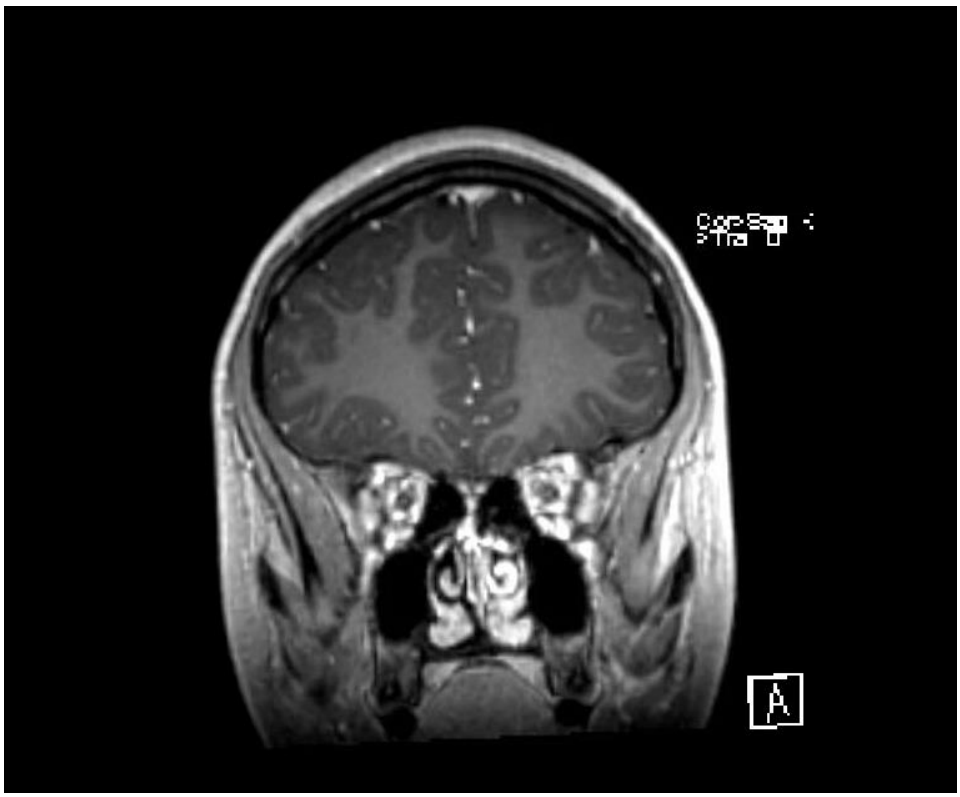
While hospitalized, she developed left eye blurred vision. Ophthalmologic exam demonstrated bilateral optic nerve edema. Repeat MRI brain showed enhancement of multiple cranial nerves. Initial MRI spine was re-interpreted as diffuse enhancement and mild thickening of the cauda equina and cervical nerve roots. Repeat LP had elevated opening pressure of >55 mmHg and IgG-index. She was started on intravenous methylprednisolone and acetazolamide with improvement. She was presumptively diagnosed with CIDP and discharged on a prednisone taper.

Symptoms were stable one week later. Her CSF ACE level returned elevated (3.1, reference <2.5 U/L). Given the clinical presentation, evidence of CNS inflammation by MRI and LP, and elevated CSF ACE level, she was diagnosed with possible neurosarcoidosis. She was continued on high dose corticosteroids with plans to start infliximab and methotrexate after completing evaluations for systemic disease.

Discussion: Sarcoidosis is a multisystem granulomatous inflammatory disease of unknown etiology. Neurosarcoidosis occurs in 5-10% of patients with systemic sarcoidosis. Isolated neurologic involvement at presentation is rare and presents a diagnostic challenge. Definite diagnosis requires demonstration of noncaseating granuloma on tissue biopsy, which is often unobtainable in patients with isolated neurosarcoidosis. Cranial neuropathies are the most common manifestation. Optic nerve involvement occurs in up to 38% of patients and typically presents with visual loss and papilledema. Elevated ICP at diagnosis has poorer long-term prognosis. The mainstay of treatment is corticosteroids, however additional immunomodulating therapy is often required in neurosarcoidosis.

Conclusion: Though rare, neurosarcoidosis is a differential diagnosis for a patient presenting with cranial neuropathy, elevated ICP, and/or optic neuritis. More study is needed to identify better diagnostic markers and clearer treatment guidelines.

Figure 1: T1-weighted MRI brain with MP RAGE sequence post-contrast demonstrating bilateral enhancement of the olfactory nerve.



A Hot Mess: The Mysterious Case of a Persistent Fever in a Young Man

Erin C Steinbach, MD PhD, Stephanie Mathews, MD, and Mildred Kwan, MD PhD

A previously healthy 21-year-old man presented with fevers, rash, lymphadenopathy, and anterior uveitis. Autoimmune, infectious, and malignancy evaluations were undiagnostic. Lymph node pathology showed Langerhans cell histiocytosis (LCH), a clonal expansion of Langerhans cells. LCH cells are immunophenotypically and genetically similar to myeloid dendritic cells and distinct from epidermal Langerhans cells1. It remains controversial whether LCH develops from malignant transformation or an inflammatory reaction2. There is an association between viral illnesses and LCH3; we wonder whether recent Coxsackie virus infection contributed. LCH occurs more frequently in patients younger than 10 years old. Adults often present with pulmonary lesions1. This patient had multi-organ involvement and significant inflammatory component; LCH should be considered in addition to autoinflammatory syndromes and HLH despite its rarity.

A previously healthy 21-year-old man presented with 2 weeks of daily fevers responsive to antipyretics, lymphadenopathy, rash, and anterior uveitis. His fevers typically returned 4-6 hours after antipyretic administration without periodicity. He had no infectious exposures, travel abroad, tick bites, or contributory family history. Initial labs showed leukocytosis with neutrophilia, lymphopenia, and eosinophilia, and transaminitis. Chest CT showed right hilar and mediastinal lymphadenopathy and pulmonary nodules. Infectious evaluation revealed only low-titer Coxsackie virus antibodies to serotypes B2-6 suggesting recent infection. Rheumatologic evaluation was non-specific, the exceptions being elevated CRP and positive ANA. Peripheral blood flow cytometry showed no aberrant lymphocyte immunophenotype; IgG, IgA, and IgM levels were normal. Imaging did not reveal additional lesions. Differential diagnosis included autoinflammatory condition, HLH, lymphoproliferative disorder, and malignancy. Per Eurofever Classification Criteria, he warranted testing for TRAPS although we had low suspicion for this; *TNFRSF1A* analysis revealed no mutation. Normal ferritin and the absence of peripheral blood cytopenias and splenomegaly made HLH less likely.

Lymph node tissue showed proliferation of mononuclear cells consistent with Langerhans cells. This with his clinical history was consistent with Langerhans cell histiocytosis. PET CT body scan showed FDG-avid mediastinal, hilar, axillary, and inguinal lymphadenopathy. He completed vinblastine and prednisolone induction therapy due to multi-organ involvement and is currently doing well. Next, he will undergo reassessment of his disease to determine whether further or alternative treatment is necessary.

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IgE-mediated anaphylaxis to Gadobenate Dimeglumine (Multihance®)

Jamie Waldron, MD, Onyinye I. Iweala, MD PhD, Simon Khagi, MD, Carlos A. Zamora, MD PhD, Edwin H. Kim, MD MS, Mildred Kwan, MD PhD
University of North Carolina at Chapel Hill, Chapel Hill, NC

Summary and Lessons Learned

A 26-year-old male with anaplastic astrocytoma status post gross total resection and chemoradiation developed pruritus, urticaria, and dysphagia immediately following intravenous gadolinium-based contrast agent (GBCA) administration during routine surveillance brain MRI despite premedication with corticosteroids and antihistamines. He tolerated gadobenate dimeglumine (Multihance®) during seven previous MRIs. Positive skin prick testing with gadobenate confirmed IgE-mediated hypersensitivity. GBCA avoidance was impractical as there were no alternative non-gadolinium contrast agents. Desensitization to GBCAs was unfeasible since this would compromise interpretation of brain imaging. Skin prick tests to two macrocyclic contrast agents gadoterate meglumine (Dotarem®) and gadobutrol (Gadavist®) were negative. The patient subsequently tolerated MRI brain with intravenous gadoterate.

Immediate hypersensitivity reactions to GBCAs are rare. Linear ionic GBCAs, especially gadobenate, are more frequently associated with anaphylaxis than macrocyclic GBCAs. In patients with recurrent hypersensitivity reactions to GBCAs who cannot avoid them, there may be negative predictive value in immediate hypersensitivity skin testing, improving chances of selecting safe alternative GBCAs for future imaging.

Patient Presentation and Testing

A 26-year-old male with an anaplastic frontal lobe astrocytoma status post resection and on maintenance chemotherapy presented with diffuse urticaria and oropharyngeal pruritus and throat tightness 30 seconds after intravenous gadobenate infusion during his ninth routine surveillance brain MRI, despite oral diphenhydramine and prednisone pretreatment. He required surveillance brain MRIs every 1 to 3 months and had tolerated seven previous MRIs with gadobenate. During his eighth MRI, he developed facial urticaria 20 minutes after contrast administration that resolved with oral diphenhydramine. His reaction during the ninth MRI was treated with intravenous steroids and antihistamines. He was discharged after symptoms resolved completely within 20 minutes. 12-18 hours after initial symptom resolution, he developed a biphasic protracted reaction with neck and arm erythema and diffuse pruritus requiring oral diphenhydramine every 6 hours until symptoms resolved 24 hours later.

Latex-IgE was negative. Immediate hypersensitivity skin prick testing to linear gadobenate produced an 8mm wheal. Skin prick and intradermal tests with sterile water control and macrocyclic compounds gadoterate and gadobutrol were negative.

Diagnosis, Treatment, and Patient Outcomes

Skin-prick testing confirmed IgE-mediated hypersensitivity to gadobenate. Desensitization to gadobenate would hinder MRI interpretation, but surveillance MRIs were still required. For subsequent brain MRIs, the patient was premedicated with corticosteroids and antihistamines and tolerated intravenous gadoterate.

Near Fatal Asthma Provoked by Inhalational Injury

Katie Clouthier, DO; Allison Cummings, MS4; Rebecca Smith, MD; Katherine Clement, MD

Severe asthma exacerbations are a common cause for admission to the pediatric intensive care unit (PICU). We present a case of a 13 year old female with moderate persistent asthma who progressed to near fatal asthma requiring ECMO (extracorporeal membrane oxygenation). She had been treated in an Emergency Department for an asthma exacerbation 3 days prior to admission, but had an acute worsening that required PICU admission. Her respiratory distress progressed to respiratory failure despite maximal medical therapy with continuous albuterol, terbutaline, BiPAP, and heliox. She was intubated by Anesthesia with sevoflurane and ultimately cannulated for VV ECMO. Her course was complicated by *Pseudomonas aeruginosa* pneumonia. On her second day of ECMO her mother revealed the patient was observed inserting pieces of lipstick into a balloon, blowing it up and allowing it to deflate into her mouth. Bronchoscopy did not reveal any particulate matter, however, inhalational injury remained a concern. Ultimately, she was treated with a course of antimicrobials, was decannulated from ECMO on hospital day 10, and discharged on hospital day 21.

Pseudomonas is an aerobic gram-negative bacterium that grows in moist environments, infecting patients with immunologic abnormalities and/or those patients submitted to invasive therapeutic procedures. There is insufficient literature existing on inhalational injury associated with cosmetics, however the potential for pulmonary pathology resulting from exposure has been documented in multiple case reports. Pseudomonas has been implicated in cosmetic contamination, and has been isolated from both used and unused lipstick products. Zinc oxide nanoparticles are used in cosmetics for ultraviolet A and B protection, however can induce acute pathologic lung injury. Given our patient's significant respiratory decline in the setting of resolving asthma exacerbation, it remains possible that her respiratory failure was exacerbated by her inhalation event. Teenagers use inhalants as means of mental escape and social tool. To better serve patients in the primary care setting, it remains crucial physicians understand reasons for adolescent inhalant use and should council on the significant effects.

Seminal Fluid Hypersensitivity

Luanna Yang, MD[1], Onyinye I. Iweala, MD PhD[1], Amika Sood, MD[1], Aaron K. Kobernick, MD MPH[2], Edwin H. Kim, MD MS[1], Kevin J. Kelly, MD[1], Maya R. Jerath, MD PhD[1]

Institutional Affiliations:

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2. University of Utah Health, Salt Lake City, UT

Summary and Lessons Learned:

A 37-year old woman presented with vaginal irritation, burning, and itching following unprotected sexual intercourse with her husband. Condom use or coitus interruptus prevented symptoms. Cutaneous skin prick testing using her husband's semen produced a 7mm wheal, confirming IgE-mediated seminal fluid hypersensitivity. Allergen avoidance through abstinence, coitus interruptus, or condom use was unfeasible, as she wanted to conceive. Prophylactic oral antihistamine provided no perceivable benefit. 6% cromolyn applied intravaginally prior to sexual intercourse successfully prevented symptoms, allowing the patient to engage in asymptomatic unprotected coitus.

Symptoms of seminal fluid hypersensitivity caused by IgE-mediated sensitization to seminal plasma proteins range from post-coital vaginal pruritus to anaphylaxis. This condition makes conception challenging and causes significant stress. Allergen avoidance is the mainstay of treatment. In this case, we demonstrate that in patients with localized symptoms for whom abstinence or condom use is impractical, prophylactic topical cromolyn can prevent vaginal edema and pruritus.

Patient Presentation and Testing:

A 37-year-old G0P0 woman with sickle cell anemia, allergic rhinoconjunctivitis, and mild, persistent asthma presented to Allergy/Immunology clinic reporting vaginal irritation, and burning after sexual intercourse with her husband. Symptoms started 30 seconds after ejaculation. She denied systemic cutaneous rash, hives, nausea, vomiting, diarrhea, or dizziness. On two occasions, she developed cough post-coitus relieved with inhaled albuterol. Condom use or coitus interruptus prevented symptoms. Vaginal irritation improved with unprotected intercourse every-other-day, but rebounded with abstinence of one week or longer. She denied food, medication, or latex allergies. She and her husband had no histories of STIs. As the couple desired pregnancy, condom use and coitus interruptus during sexual intercourse was undesirable.

Her husband provided a fresh semen sample that was allowed to liquefy for at least 30 minutes at room temperature. The upper layer of sample, containing the seminal plasma proteins, was used for skin prick testing, producing a 7mm wheal. Histamine and saline controls produced 8mm and 3mm wheals, respectively.

Diagnosis, Treatment, and Patient Outcomes:

Skin prick testing confirmed seminal fluid hypersensitivity. Given the patient's desire to conceive, allergen avoidance was impractical. Cetirizine 10mg prior to intercourse did not prevent symptoms. Pretreatment with 6% cromolyn in VersaBase® applied intravaginally before intercourse successfully prevented symptoms with unprotected coitus. She and her husband are actively pursuing pregnancy.

Bile Acid Synthesis Defect and Hyperinsulinism: A Case Report

Michael Rogers DO, Francisco Sylvester MD, Steven Lichtman MD

Division of Pediatric Gastroenterology, University of North Carolina Children's Hospital, Chapel Hill, NC

Congenital defects of bile acid synthesis are rare disorders that cause progressive liver dysfunction. Prolonged Neonatal Hyperinsulism (PNH) is a separate entity that leads to persistent hypoglycemia secondary to stress. We present a case of a 4 month old infant who presented with liver failure secondary to a bile acid synthesis defect. The patient's liver failure resolved with oral cholic acid therapy. This patient also developed PNH which slowly resolved over time. This case illustrates a possible relationship between cholestatic liver failure and PNH. This relationship may help to define what specific stressors increase the likelihood of developing PNH.

Got some spleenin' to do: Isolated splenomegaly? Think Neimann-Pick C

Pete Leahy, MD; Laurie Smith, MD, PhD

Neimann-Pick C (NPC) is an autosomal recessive disorder of impaired intracellular cholesterol transport caused by altered function of *NPC1* or *NPC2*. It can present at any time, from infancy to adulthood. NPC is typically diagnosed in the adolescent or adult due to the gradual development of ataxia followed by vertical supranuclear gaze palsy and dementia. Other manifestations include seizures and psychiatric symptoms. Hepatomegaly or splenomegaly are often present at the time of diagnosis. We present a case of isolated spenomegaly in a 9 year old male lacking typical neurologic features diagnosed with NPC based on molecular and biochemical grounds. Prior hematology-oncology evaluation, including a bone marrow biopsy, was unremarkable. His fraternal twin brother also has splenomegaly and his work-up is in progress. This case exemplifies the various manifestations of NPC which are reviewed as are diagnostic and therapeutic approaches.

Fatal *Clostridium difficile* Infection in a 4-month old: Straying from the norm of asymptomatic carriage?

Peyton Wilson[1], Kara Levinson[2], Melissa Miller[2], Vincent J Moylan[3], Renee L Betancourt[3], Leigh B Thorne[3], Thomas Belhorn[1]

[1]Department of Pediatrics, Division of Infectious Diseases and; [2]Department of Microbiology and Immunology and; [3]Department of Pathology and Laboratory Medicine, University of North Carolina, Chapel Hill

Case: A 4-month-old full term male with a history of chromosome 13q deletion and Tetralogy of Fallot (TOF) with pulmonary atresia status post repair was hospitalized for feeding intolerance several weeks after an extensive repair of his cardiac defects. Two days prior to admission, the patient completed a 10-day course of metronidazole for presumed *Clostridium difficile* infection, diagnosed clinically due to fever, leukocytosis, antibiotic exposure and bloody, malodorous stools. Initial laboratory values were significant for hyponatremia (129 mmol/L) and leukocytosis to 28.3 x 10^9/L with neutrophil predominance. A stool pathogen panel was unrevealing (Luminex, Austin, TX). His dehydration, electrolyte abnormalities and persistent emesis were managed with administration of IV fluids and nil per os (NPO) status. He did not receive antibiotics during this course. He developed progressive abdominal distension, and abdominal imaging revealed ascites with developing ileus versus obstruction. He died on day nine of hospitalization from respiratory failure and metabolic acidosis. Autopsy revealed diffuse, severe pseudomembranous pancolitis and a Gram stain of formalin-fixed gastrointestinal tissue showed innumerable long Gram-positive rods with rare terminal spores. Retrospective review of suppressed results from the stool pathogen panel identified positive results for *C difficile* toxins A and B DNA.

Discussion: The American Academy of Pediatrics (AAP) recommends against testing of stool samples for *C difficile* in children under the age of two because of difficulty distinguishing between colonization versus true *C difficile* infection (CDI) in this age group. We present a case of pathologically- and microbiologically-confirmed CDI in a 4-month-old patient with a complicated medical history who did not receive adequate, potentially life-saving treatment. This should prompt further discussion of the possibility of CDI in select infants at high risk of infection, such as those with prolonged hospitalizations, exposure to broad-spectrum antibiotics and clinical signs/symptoms consistent with CDI.

Conclusion: While we agree with the AAP guidelines that *C difficile* testing should not be routinely performed for children younger than two, we highlight a case of confirmed CDI in a high-risk, medically complicated infant, which should spur pediatric infectious disease providers to consider *C difficile* in special circumstances involving infants at high risk for CDI.

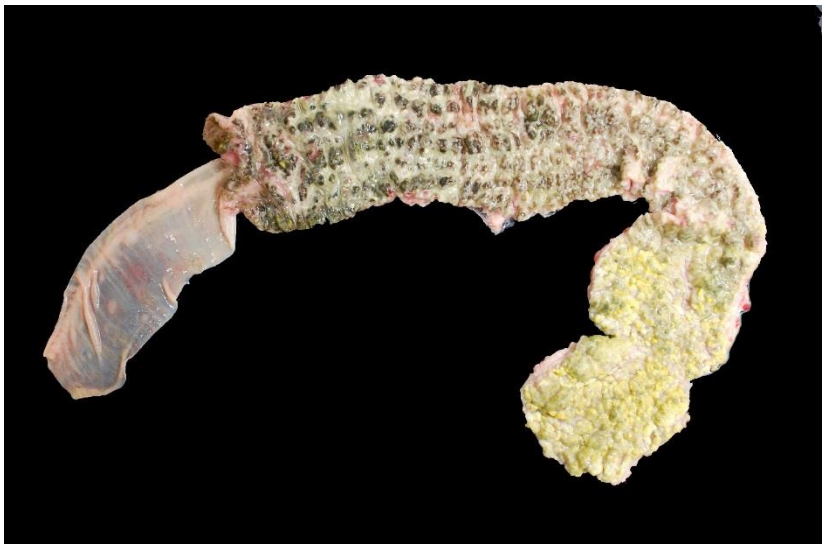

Figure 1: Terminal ileum and colon demonstrating diffuse pseudomembranous pancolitis.

Photo Credit: Vincent Moylan

An adolescent boy with cyclic hematuria, scrotal swelling and gynecomastia.

Winchester RJ*, Fellow in Pediatric Endocrinology;* Sutherland RW*, Division of Pediatric Urology;* and Calikoglu AS*, Division of Pediatric Endocrinology, UNC-CH*

A 13-year-old male presented with hematuria started four months ago and recurred every month since that time. Hematuria lasted 3-4 days and disappeared without intervention. He also had slowly growing breasts for over 6 months. Two months ago, he noticed bilateral scrotal swellings, which became bigger and painful at the time of hematuria episodes.

He was initially born with ambiguous genitalia (well-formed, but small phallus, perineal opening of urogenital sinus and unilaterally palpable gonad). The karyotype was 46,XX. Initially, congenital adrenal hyperplasia (CAH) was considered. However, laboratory analysis showed normal 17-hydroxyprogesterone, but high testosterone (555 ng/ml) and anti-mullerian hormone (AMH, 69 ng/ml). Pelvic US on showed presence of a uterus and an intra-abdominal gonad (most likely testis). Laparoscopic evaluation revealed a uterus, a vagina, a left fallopian tube, a right intra-abdominal gonad, a right epididymis, a right vas deferens, and a right fallopian tube. The gonadal biopsy demonstrated testicular tissue. While there was not a histopathological confirmation of both testicular and ovarian tissues in the same individual, ovotesticular DSD (disorder of sex differentiation) was the most likely diagnosis. After thorough discussion, parents decided to raise the baby as a boy. He received testosterone treatment to assess phallic response, and then underwent hypospadias repair and scrotoplasty. Further penile reconstruction occurred at 22 months with bilateral orchidopexy, uterine division, and urethroplasty.

He was then lost to follow up with us until the age of 13 years.

We felt strongly his cyclic hematuria was menstruation, which, together with breast enlargement indicates he has functioning ovary(ies) and uterus. While incomplete, in utero virilization of external genitalia, initially high testosterone levels, high AMH and histopathology confirm the presence of testis tissue at some point. We therefore feel the diagnosis of ovotesticular DSD is almost certain.

Scrotal swellings were cystic structures in US and a surgical removal was performed. The biopsy revealed “multicystic structures, tubular structures, and inguinal cord structures.”

Ovotesticular DSD is very rare, but presents a wide-spectrum clinical phenotype depending on the functionality of gonads, and introduces multiple challenges in different ages in the management of a child with DSD including diagnosis, gender assignment, surgical reconstruction, pubertal induction, malignancy risk, and fertility preservation. We will discuss all of these aspects of the case.

Severe Invasive GBS and Necrotizing Enterocolitis in an infant born to a GBS negative Mother via Water Birth

Shannon A. Solt DO, Rebecca Smith MD, Afsaneh Pirzadeh MD

Invasive infection secondary to group B Streptococcus (GBS) is a significant cause of morbidity and mortality in neonates[1,2]. Universal third trimester screening and intrapartum antibiotics have reduced the incidence of early onset invasive GBS disease, but has not impacted late onset disease[3]. Necrotizing Enterocolitis (NEC) typically affects pre-term infants, but 13% of reported cases occur in term infants[4]. We will describe a case of an exclusively breastfed full term infant, born via water birth, to a GBS negative woman, who presents with severe late onset GBS meningitis/septic shock and subsequently develops NEC.

The patient presented at eight days of life with periods of apnea and tachycardia to the 200's. He was intubated and started on broad-spectrum antibiotics. On laboratory evaluation, he was neutropenic, thrombocytopenic, and with CSF pleocytosis. Both blood and cerebrospinal fluid cultures grew GBS. As the mother had mastitis, her breastmilk was also tested and was positive for GBS. Patient's course was complicated by intractable seizures and sodium dysregulation secondary to liquefactive encephalomalacia with striking loss of brain tissue. On hospital day 16, he developed an acute abdomen with portal venous gas noted on abdominal XRay. He underwent surgical resection of 117 cm of necrotic bowel, but the extent of necrotic bowel on visualization two days later was thought to be incompatible with life and patient was terminally extubated.

Studies have shown no increase in the incidence of neonatal GBS colonization with water births despite more colonization of GBS in the water[5]. However, whether the mothers are more colonized with GBS has not been studied. Also, Berardi et. al, describes multiple cases of late onset GBS infection, with 6% secondary to breastmilk transmission of mothers with GBS mastitis[6]. It is therefore possible, that the patient's mother became inoculated with GBS during water birth, developed mastitis and then transmitted the disease via breastmilk to the infant leading to significant invasive GBS infection.

The pathogenesis of NEC is also not completely understood. One known risk factor is sepsis associated with many organisms[7], but GBS infection is not well described as one of those. Stafford, *et al.* describes a more than five-fold increase in the odds of developing NEC in newborns of GBS positive mothers[4] and there is one case report of early onset GBS sepsis associated with NEC in a full term infant[8]. This is the first report in the literature of late onset GBS infection resulting in NEC.

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New Onset Acute Neurologic Deficits in a Patient with Autoimmune Disease

M Shah, MD, E Brassfield, E Wu, MD, Y Shiloh-Malawsky, MD, S Hunter, MD, PhD, B Joyner, Jr., MD, MPH

An 18-year-old male with juvenile idiopathic arthritis, focal segmental glomerulosclerosis, and hypopituitarism presented to the pediatric emergency department with headache, confusion, and lethargy. He was admitted for his symptoms. Workup revealed a normal head Computed Tomography (CT), negative drug screen, normal electrolytes, and other than the symptoms listed had a nonfocal neurologic exam. He was given sumatriptan for his headaches and experienced some relief of symptoms and was diagnosed with complex migraines. Given his improvement and negative workup, consultants were not engaged and he was discharged home. He presented 2 days later with acute onset of severe headache, dysarthria, and left-sided weakness. He quickly progressed to respiratory failure and quadriplegia. Repeat head CT demonstrated hypoattenuation and swelling of the brainstem, concerning for brainstem edema. Magnetic Resonance Imaging (MRI) confirmed large midbrain infarction. Differential included stroke, central nervous system vasculitis, mass, encephalitis, infection, acute disseminated encephalomyelitis (ADEM) or posterior reversible encephalopathy syndrome (PRES).

Complete blood count (CBC), complete metabolic panel, Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), ammonia and infectious workup including blood, urine, respiratory, and CSF studies were unremarkable. Serial neurologic assessments demonstrated pinpoint pupils, autonomic instability, no response to painful stimuli, no purposeful movements, and an intermittent cough reflex. His therapies included broad spectrum antibiotics, high dose methylprednisone, plasma exchange therapy, and IVIG. Repeat MRI demonstrated extensive cranial nerve enhancement and lesions consistent with progression of hemorrhagic variant of ADEM. Death by neurologic exam was confirmed days later.

Review of the literature suggests pediatric patients with an autoimmune history are at a higher risk than the general pediatric population for developing ADEM and CNS vasculitis. Many forms of autoimmune encephalitis are treatable and early diagnosis will lead to quicker time-sensitive interventions (Armangue). This case reinforces that patients with autoimmune disease presenting with neurologic deficits warrant a thorough workup including early subspecialty consultation, thorough imaging including MRI even in the setting of a normal CT, infectious laboratory workup and a broad differential must be considered (Van Mater). With a heightened suspicion we will hopefully catch these cases early and minimize disease sequelae.

Not All That Wheezes is Asthma (or Foreign Bodies!)

William Stoudemire MD

Marianne Muhlebach MD

The University of North Carolina at Chapel Hill

Introduction: While asthma is common in children, other disorders may mimic asthma, and delayed recognition of alternative diagnoses may lead to significant morbidity. Here we describe the case of a young girl initially diagnosed with asthma found to have a tracheal mass causing airway obstruction.

Case Description: BH is a 4 year old girl admitted for respiratory distress. She was diagnosed with asthma six months ago due to intermittent cough and difficulty breathing. Two months ago, she was admitted for progressive respiratory distress requiring mechanical ventilation. She tested positive for parainfluenza virus, and was treated with albuterol and steroids for a presumed asthma exacerbation. She improved over several days, and was then discharged. She had intermittent cough and wheeze over the past two months with minimal response to albuterol.

BH was most recently admitted following acute onset of difficulty breathing. Her symptoms started four days prior to admission with rhinorrhea, cough, wheezing, as well as intermittent stridor. She then developed progressive respiratory distress refractory to maximum asthma therapy, and ultimately required intubation.

Following intubation, she continued to have poor oxygenation. Given her rapid decompensation, recent intubation, and intermittent stridor, CT scans of the neck and chest were obtained, which revealed opacity of the right mainstem bronchus suspicious for a mucus plug. A flexible bronchoscopy was performed which revealed a large pedunculated mass located on the distal anterior trachea superior to the carina. The mass was subsequently resected by otolaryngology. The patient was extubated immediately after surgery, and was discharged three days later. Pathology of the mass revealed a juvenile xanthogranuloma. Following resection, she had no further respiratory symptoms. A repeat endoscopy six months later revealed no evidence of residual tumor or regrowth.

Significance: Our patient was found to a juvenile xanthogranuloma of the trachea, an extremely rare location of a lesion typically found on the skin of young children. Juvenile xanthogranulomas are benign tumors caused by proliferation of dermal dendrocyte histiocytic cells. While they are the most common form of non-Langerhans cell histiocytosis, they typically occur as solitary granulomas in the skin during the first year of life. Juvenile xanthogranulomas of the airway are extremely rare, with only a handful of reported cases. While uncommon, lesions causing upper airway obstruction may be misdiagnosed as asthma in children, as in this case. Understanding of alternative diagnoses mimicking asthma, including airway masses, is important for accurate diagnosis and management in order to avoid harm to patients.

Endobronchial Histoplasmosis in a Pediatric Patient

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Introduction:

Histoplasmosis is a common endemic mycosis in the Mississippi and Ohio River valleys caused by the dimorphic fungus *Histoplasma capsulatum*. The clinical presentation of histoplasmosis varies ranging from asymptomatic infection to severe disseminated disease. Here we report a unique case of histoplasmosis presenting in a pediatric patient with endobronchial lesions.

Case Report:

A 3 – year – old male with a travel history significant for recent travel to Alabama and a past medical history significant for prematurity, mild subglottic stenosis, recurrent croup and protracted bacterial bronchitis on chronic azithromycin underwent scheduled bronchoscopy to evaluate his airway anatomy and obtain lower airway cultures. His bronchoscopy revealed improved subglottic narrowing, as well as unanticipated obstructive endobronchial lesions in the right bronchus intermedius and the right middle lobe orifice that were not present on airway evaluation the year prior. Biopsies of these lesions revealed small caliber fungal yeast forms consistent with *Histoplasma*. Repeat bronchoscopy one week after initial evaluation again showed endobronchial lesions. Bronchoalveolar lavage (BAL) cultures were significant only for oropharyngeal flora growth, with negative fungal stains and cultures. Laboratory evaluation demonstrated leukocytosis, positive serum titers for *Histoplasma* (1:128), and positive *Histoplasma* serum antigen, though BAL antigen was negative. Additional laboratory studies were negative for *Blastomyces*, *Aspergillus*, and *Coccidiodes,* and a basic immune profile was normal. Based on the above findings, he was diagnosed with endobronchial *Histoplasma* infection and started on voriconazole. Follow up five weeks after initiation of voriconazole showed a mild decrease in *Histoplasma* antigen, so treatment was continued with change to itraconazole.

Discussion:

Histoplasma capsulatum infection presents with a wide range of clinical manifestations with disease severity dependent on exposure and host immunity. While the majority of acute infections are asymptomatic, others may present as acute pulmonary histoplasmosis, subacute pulmonary histoplasmosis, chronic pulmonary histoplasmosis, mediastinal granuloma and progressive disseminated histoplasmosis. Histoplasmosis is diagnosed by histopathology and culture, cytology, complement fixation and immunodiffusion serology, or *Histoplasma* antigen detection, though demonstration of the fungi on histopathology or culture remains the gold standard. Treatment varies dependent on disease severity. When treatment is indicated, recommended antifungal agents include itraconazole and amphotericin B.

This case report identifies a rare presentation of endobronchial histoplasmosis without clear evidence of immunosuppression, and illustrates the challenges associated with diagnosis and treatment.

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Seeing Spots in the Newborn Nursery: A Newborn Female with a Giant Congenital Melanocytic Nevus

A Cline MD. C Orr MD

Case presentation:

A term infant female was born at 40w1d via vaginal delivery to a healthy 27 yo G4P4 female. Maternal labs and GBS were negative. Prenatal course and ultrasounds were normal. In the delivery room, newborn nursery (NBN) staff was called to examine infant immediately after birth due to concern for "spots on the back". On arrival, patient's dermatologic exam was notable for large, hyperpigmented, fleshy plaques encircling the back and lower flanks, extending laterally to the torso with multiple satellite lesions, and hypertrichosis, consistent with a diagnosis of giant congenital melanocytic nevus (GCMN). Dermatology team was consulted who recommended MRI brain/spine to rule out underlying CNS involvement, which was done, and was normal.

Discussion:

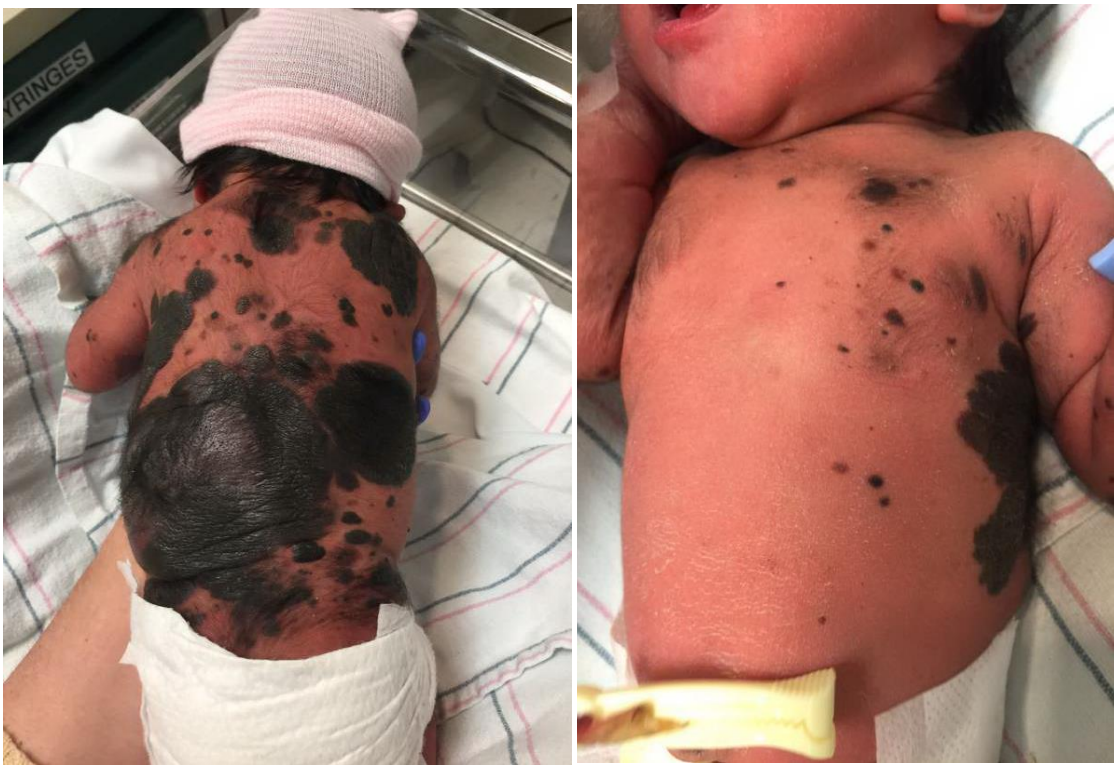
GCMN is a rare disorder with an incidence <1:20,000 newborns, defined as a congenital melanocytic lesion present at birth or that develops during the first years of life, and reaches a diameter of $\geq$20cm over time. It is hypothesized to occur in the first 24 weeks of gestation due to a neuroectodermal error that leads to the unchecked growth of melanocyte precursors that deposit and grow in the deep layers of the skin and subcutaneous tissue. The chest, limbs, and head are most commonly affected.

Patients with GCMN are at increased risk of lipomatosis, atrophy and/or hypertrophy of bones and soft tissue, vascular malformations, urinary abnormalities, and CNS abnormalities. Neurocutaneous melanosis (NCM) is the most serious CNS complication, defined as presence of benign or malignant melanocytic deposits in the leptomeninges of the brain/spinal cord. Thus, a full initial neurologic exam in the nursery is critical. The risk of melanoma in GCMN is controversial, but patients' estimated lifetime risk of malignancy is 5-10%. Most melanoma will present in childhood before puberty and often have a poor outcome, likely due to late presentation at time of diagnosis. Patients whose lesions involve the back, neck, and head have a higher risk of progression to malignancy. Surgical removal for cosmesis can be considered over time, dependent location and patient/family preference.

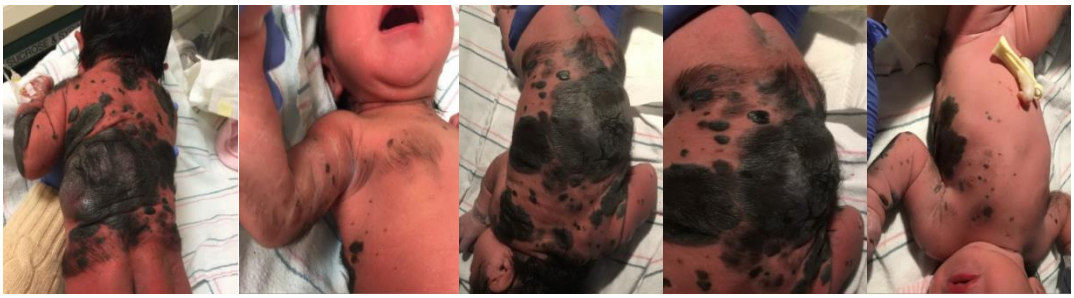
Conclusion:

While CGMN is rare, its surprising presentation in the NBN can be distressing for families; thus pediatricians should be versed on newborn nursery management. A baseline skin exam should be documented thoroughly as lesions can change over time. A baseline neurologic exam determines the necessity of MRI brain/spine with contrast in the newborn period vs in the first 6 months of life. Routine follow up with PCP to follow neurologic exam to assess for NCM as well as referral at discharge to dermatology for routine skin exams are paramount.

Figures 1,2 : Patient's dermatologic examination on admission revealing a giant congenital melanocytic nevus on the back (a), extending laterally to the anterior torso, with satellite lesions and hypertrichosis (b).



Additional Clinical Images:



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A REAL HEAD SCRATCHER: FUO AND SPLENIC MICROABSCESSES IN A TEENAGE GIRL WITH ECZEMA

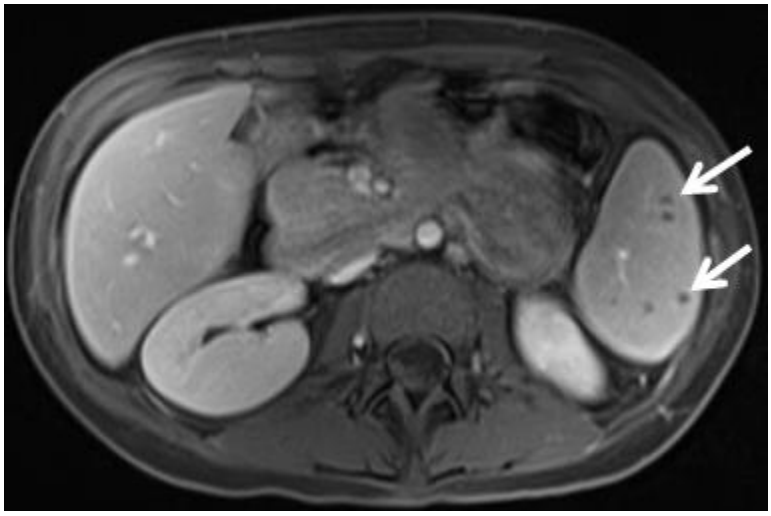
A Cline. C Liu. L Cannon. AG Sutton. J Galeotti. A Hartsell.

A 13 yo F with severe eczema treated with mycophenolate presented with two weeks of fever, vomiting, diarrhea, abdominal pain, and a 20 lb weight loss. Her PMH and SHx were notable for a hx of eating disorder, sexual activity with males and females, exposure to cats and rabbits, and a fondness for drinking kombucha tea with live cultures. Exam revealed cachexia. ESR and CRP were elevated. Extensive negative testing included: pan-cultures, serologic testing for HIV, CMV, and EBV, bartonella, tularemia, and brucella; PPD and quantiferon gold; and GI panel. Echocardiogram was normal. MRI demonstrated microabscesses of the liver and spleen. Zosyn was started empirically, but patient continued to spike daily fevers and developed severe bony pain. Repeat MRI showed new osseous lesions in the femur and sacrum and large axillary adenopathy. PET scan revealed multiple new bone lesions. Bone marrow biopsy was negative. Sternal and LN biopsies showed necrotizing granulomas. In the setting of continued fever 5 weeks into admission, repeat serologic testing was done and positive for *Bartonella henselae* (Bh), confirming a diagnosis of disseminated Bh. She was treated with doxycycline with marked improvement.

Bh is a fastidious organism that causes zoonotic disease in humans[1], commonly after a cat bite/scratch[2]. Infection causes a wide spectrum of disorders dependent on immune status[3,4], including regional adenopathy, fever of unknown origin (FUO), bacillary angiomatosis, oculoglandular syndrome, hepatic and splenic peliosis and/or microabscesses, encephalitis, culture negative osteomyelitis, and vascular lesions[1,5].Our patient's course was perplexing due iatrogenic immunosuppression, prolonged fever, new bone pain, negative serologic testing, and multiple culture negative biopsies, notable only for granulomatous inflammation, which is occasionally seen in disseminated Bh[2,4], and prompted repeat serologic testing for Bh. In retrospect, her symptoms of FUO, weight loss, fatigue, and organomegaly were hallmarks of disseminated Bh[3]. Identification of Bh can be difficult, as serologic testing has variable sensitivity[3,5] and can cross react with other organisms[3,5]. Thus, diagnostic testing with PCR[3] can be helpful. Doxycycline, azithromycin, and erythromycin [1,3,6] are the drugs of choice for disseminated Bh.

Bh infection can range from mild to severe, dependent on immune status, and should be suspected in an immunocompromised patient who presents with FUO, bony lesions, lymphadenopathy, microabscesses, or hepatosplenomegaly, in the setting of prior cat exposure. Treatment improves outcome in immunocompromised hosts with disseminated disease. Serologic testing can be unreliable; thus, PCR should be used in the setting of negative serology but high clinical suspicion.

Figure 1: Multiple splenic microabscesses seen on axial T1 weighted MRI, in a patient with disseminated bartonella



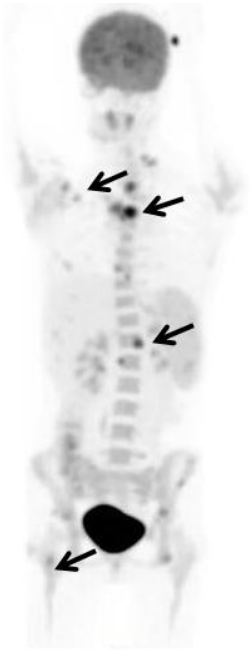
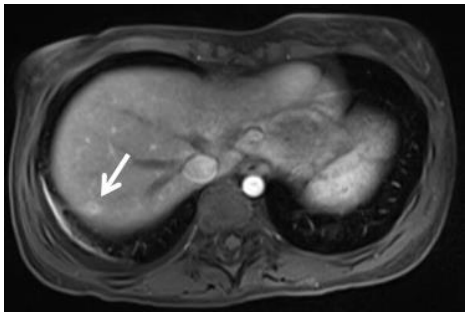
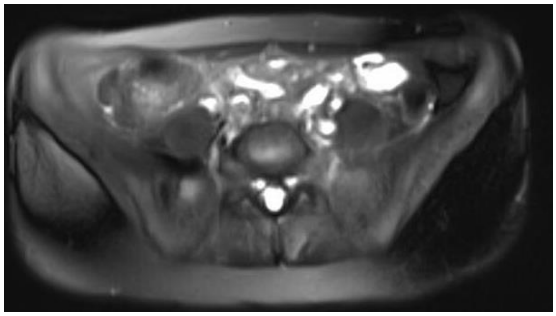


Figure 2: Whole body PET maximum intensity projection (MIP) image demonstrates numerous lesions including the manubrial, splenic, right femoral, and spinal lesions as well as splenomegaly and right axillary adenopathy in a patient with disseminated bartonella.

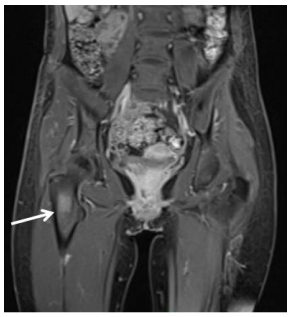
Additional Supporting Clinical Images:



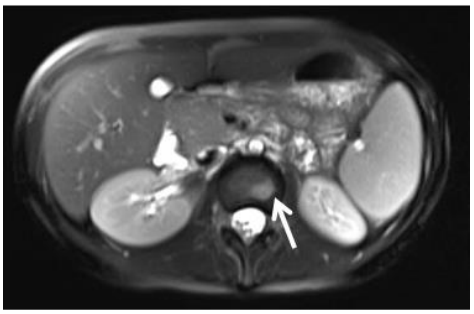
Rim enhancing lesion consistent with abscess in hepatic segment 7, axial T1 weighted MRI



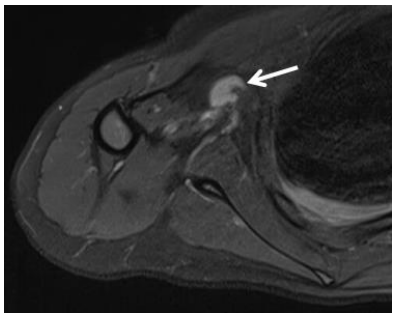
Abnormal high T2 signal in the superior right sacral ala, axial T2 weighted MRI



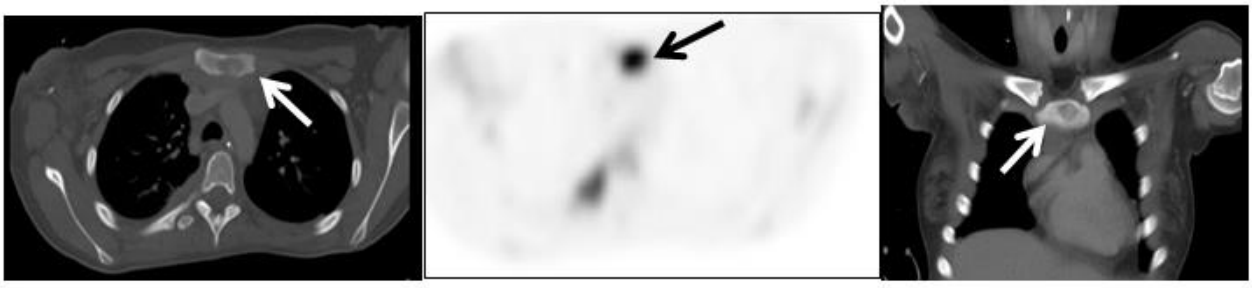
Coronal T1 weighted MRI demonstrates contrast enhancement in a R femur lesion



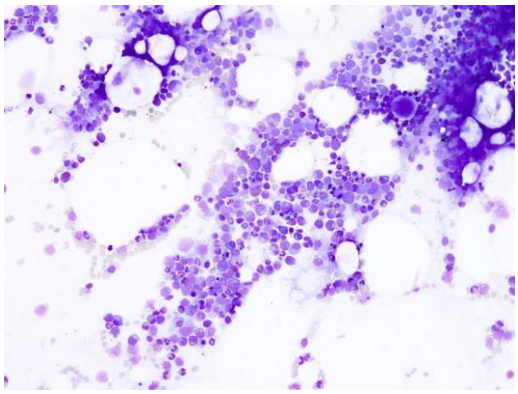
Axial T2 MRI demonstrates T2 hyper-intense lesion in the lumbar spine



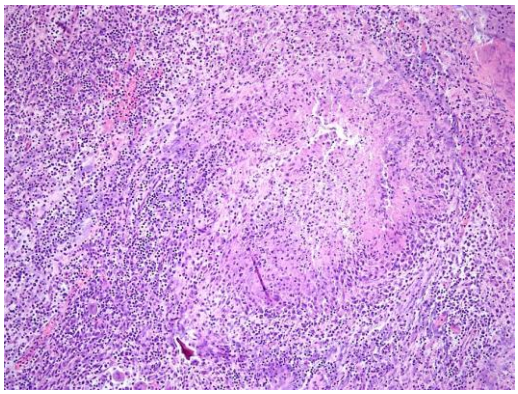
Right axillary lymphadenopathy on axial T2 weighted MRI



Axial CT and PET images, and coronal CT reformatted image demonstrate soft tissue attenuation lesion in the manubrium which is FDG avid.



Patient's Bone marrow biopsy which showed mildly hypocellular bone marrow with tri-lineage hematopoiesis and mild polytypic plasmacytosis in the setting of disseminated bartonella



Patient's sternal biopsy with necrotizing granuloma formation in the setting of disseminated bartonella.

A SCN-tillating diagnosis: An infant with recurrent thrush and new perineal lesions

A. Cline[1], L. Parente[1], A. Carroll[1], K. Westmoreland[2]

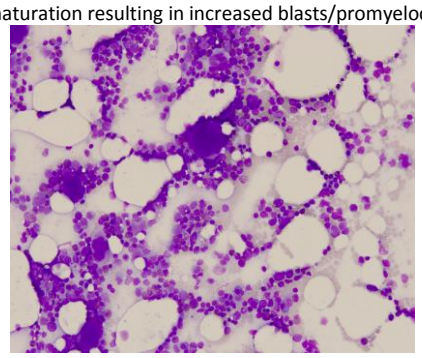
CASE PRESENTATION: A 7-mo F with a history of recurrent thrush and folliculitis presented with fever and new onset perineal lesions. Exam showed a fussy infant with multiple ulcerated labial and perianal lesions. Labs were notable for severe neutropenia with absolute neutrophil count (ANC) of 0.1x10*9/L. She was started on broad spectrum antibiotics and antifungals for neutropenic fever. Wound cultures and skin biopsy confirmed a *Pseudomonas* infection. Bone marrow biopsy showed left shifted granulopoiesis with an early arrest of myeloid maturation. Genetic testing for congenital neutropenia showed a heterozygous mutation in the ELANE gene, consistent with a diagnosis of severe congenital neutropenia (SCN). Other immunologic and infectious evaluation was normal. She was treated with high dose granulocyte-colony stimulating factor (G-CSF) resulting in resolution of neutropenia, IV antibiotics, and wound care with marked improvement in perineal lesions. Currently, she continues on daily G-CSF and is preparing for a matched sibling hematopoietic stem cell transplant (HSCT).

DISCUSSION: SCNs are a rare group of inherited primary immunodeficiencies characterized by maturation arrest of neutrophil granulocyte precursors at the level of the promyelocyte in the bone marrow. This results in severe chronic neutropenia, defined as ANC <0.5x10*9, leaving patients vulnerable to lifelong infections. SCN typically presents in early infancy with recurrent and/or life threatening infections. Diagnosis is made by bone marrow biopsy and genetic testing. Mutations in numerous genes have been linked to SCN, including the most common ELANE gene, which encodes neutrophil elastase, and is associated with the most severe infectious complications. Patients are also at increased risk of developing secondary malignancies such as myelodysplastic syndrome or acute myeloid leukemia. Treatment of choice is G-CSF, which increases ANC, reduces the risk for infections, and has improved overall survival to >80%. HSCT is the only curative therapy for SCN and is recommended for patients who do not respond to G-CSF, have a high risk genetic mutation, or who have a matched sibling donor.

CONCLUSION: SCN is characterized by impaired maturation of neutrophil granulocytes leading to severe chronic neutropenia and risk for life-threatening infections. While rare, clinical suspicion of SCN should be high in infants who present with recurrent and/or severe infections early in infancy. While treatment with daily G-CSF has led to decreased morbidity and mortality, it is essential that children with SCN presenting with fever or infection receive prompt evaluation and treatment. Providers should also be aware of the risk of more atypical infections as well as the risk of secondary malignancy over time.

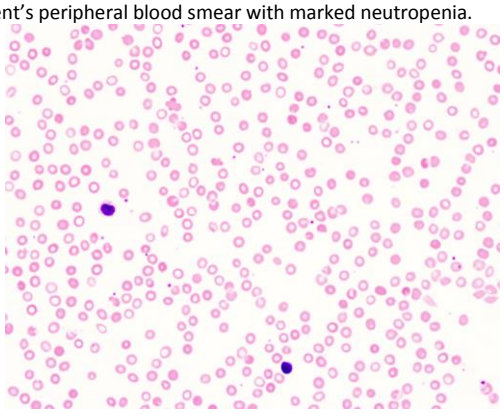
Figure 1: Patient's *Pseudomonas* perineal lesions on day of admission (A) and 15 days after presentation after treatment with IV antibiotics, G-CSF to increase ANC, and wound care (B).

Figure 2: Patient's bone marrow aspirate demonstrating classic findings for SCN: Cellular bone marrow with trilineage hematopoiesis with markedly left-shifted granulopoiesis with an apparent relative arrest of maturation resulting in increased blasts/promyelocytes.

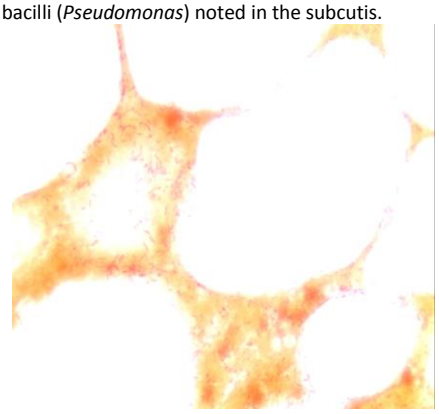


Supporting clinical evidence:

A): Patient's peripheral blood smear with marked neutropenia.



B) Patient's wound biopsy which highlights the presence of gram-negative bacilli (*Pseudomonas*) noted in the subcutis.



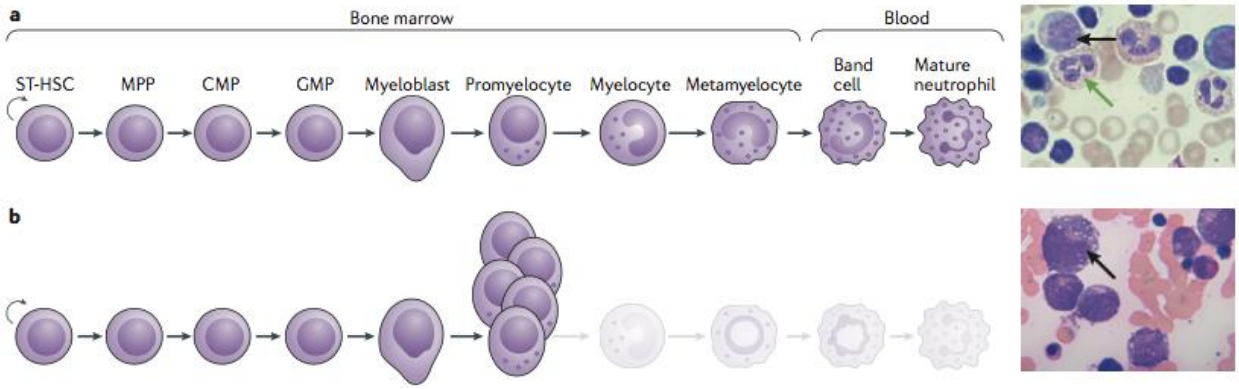
C) Patient's genetic screening results demonstrating heterozygous mutation in the ELANE gene.

Genes of Interest: *AP3B1, C16orf57, CSF3R, CXCR4, ELANE(ELA2), G6PC3, GATA1, GATA2, GFI1, HAX1, LAMTOR2(ROBLD3), LYST, RAB27A, RAC2, SBDS, SLC37A4, TAZ, VPS13B, VPS45, WAS, WIPF1*

***ELANE* Allele 1:** c.640G>A(p.Gly214Arg)
Allele 2: No Mutation Identified

RESULT: Affected; mutation in *ELANE* gene

D) Diagram showing A) normal maturation of neutrophils compared to B) arrested maturation at the level of promyelocyte in a patient with SCN[1].



A "BENIGN" PRESENTATION? A CASE OF FEVER, EMESIS, AND ABDOMINAL PAIN

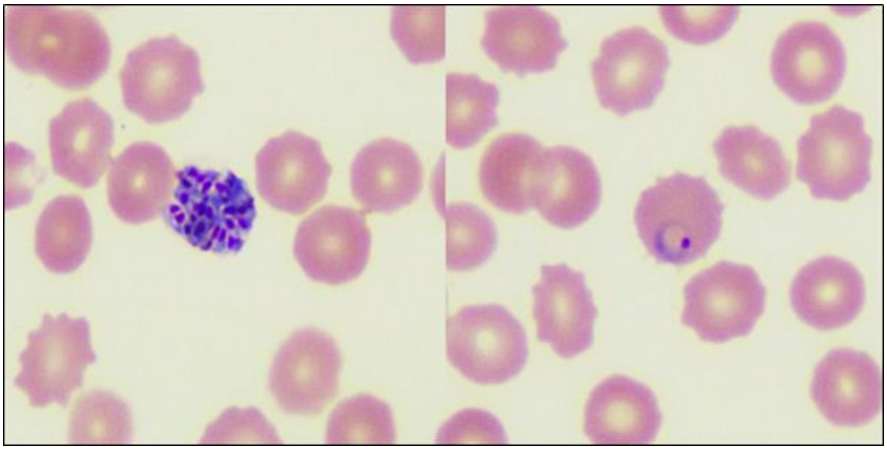
A Cline. J Guidici. Z Willis. ST Adams. L Chase. J Juliano.

A 24 mo F presented with two days of fever, emesis, and abdominal pain. Patient was from Uganda with history of malaria diagnosed at 4 months old, and treated with a 5 day course of artemether/lumefantrine. Patient immigrated to the US shortly after, without travel outside the US in the 16 months prior to presentation. In the ED, she was febrile (40.7 C), tachycardic (184 bpm), and lethargic. Exam was otherwise normal without rash, lymphadenopathy, or hepatosplenomegaly. Labs were remarkable for pancytopenia with WBC 2.4/mcL, Hgb 11.1 g/dL, and platelets 79/mcL. CMP was notable for bicarbonate of 9 mmol/L, glucose of 34 mg/dL, and elevated bilirubin. LDH and uric acid were elevated. Peripheral smear revealed parasitemia (<1%) with schizonts and trophozoites, consistent with *Plasmodium vivax* (Pv) malaria. Significant hypoglycemia and acidosis classified her by WHO and CDC criteria as "severe" malaria, a diagnosis typically associated with *Plasmodium falciparum* (Pf) species[1,2,9].She was transferred to the Pediatric ICU for initiation of IV quinidine, fluids, and antibiotics. She later was transitioned to oral atovaquone/proguanil, followed by primaquine, and did well.

Malaria is a protozoal infection transmitted via *Anopheles* sp. mosquito. Historically thought to cause milder disease due to lower parasitemia and lower rates of complications than in Pf malaria[3], recent studies show that severe manifestations of Pv malaria are increasingly prevalent[1]. *Plasmodium vivax* is one of two species of malaria that may cause relapse due to dormant liver stages called hypnozoites[4]. The periodicity of relapse can range from weeks to years[4]. Clearance of the hypnozoites requires terminal prophylaxis with primaquine[5]. Positive malarial screening tests do not always differentiate between species or identify co-infection. In Uganda, reports indicate very low rates of Pv species[6], likely due to a low population prevalence of Duffy antigen on erythrocytes, required for Pv infection[3]. As Pv malaria is much less common than Pf, our patient was treated for Pf without terminal prophylaxis, presumably due to the much greater prevalence of Pf than Pv in Uganda.

While commonly referred to as "benign tertian malaria", severe manifestations of Pv do occur, particularly in children[7]. This case was additionally unusual, as our patient's relapse occurred 20 months after her primary infection, which is atypical. Thus, as international travel and immigration become more prevalent, pediatricians should consider Pv malaria in the differential diagnosis of a child from an endemic area with anemia and systemic symptoms[8], even if travel history is temporally remote.

Figure 1: Patient's peripheral blood smear demonstrating *P. vivax* in both Schizonts (A) and ring form Trophozoites (B)



Turning yellow – as if puberty wasn't awkward enough

Katherine A. Despotes, MD, Eric Zwemer, MD, and Jennifer Law, MD

CASE PRESENTATION

A 9-year-old boy with history of constipation presented with left lower quadrant (LLQ) pain for 1 day. His last bowel movement was 4 days ago. X-ray revealed moderate stool burden. He did not tolerate Miralax orally due to emesis and was admitted for cleanout.

Admission vital signs were notable for sinus bradycardia to the 50s while asleep. Exam showed marked yellowing of skin, LLQ tenderness, and anicteric sclera. Neck was supple without masses. Laboratory studies revealed normal total and direct bilirubin but elevated AST of 109 U/L, ALT of 72 U/L, and creatinine of 1.7 mg/dL. Renal ultrasound showed left-sided hydronephrosis, and CT scan subsequently demonstrated left-sided renal stone and small pericardial effusion. Despite fluids and stone passage, creatinine remained elevated. Further labs revealed elevated CK at 1074, total cholesterol of 240 mg/dL, and LDL of 171 mg/dL. Repeat examination noted Tanner stage 2 testicular enlargement.

The family denied other changes of puberty except for dark pubic hairs. The patient also endorsed fatigue and cold intolerance. TSH was >1000 U/L with undetectable free T4. He was diagnosed with hypothyroidism and Van Wyk Grubach syndrome (VWGS) driving his precocious puberty. Levothyroxine was initiated and his skin discoloration, renal injury, other abnormal laboratory values, and precocious puberty resolved.

DISCUSSION

Constipation is a common presentation of hypothyroidism. This patient's yellow skin led to evaluation of his liver function and biliary system. His many lab abnormalities were initially confusing, but ultimately did fit with hypothyroidism. Carotene is the precursor of vitamin A, and excess levels cause yellow skin discoloration. In carotenemia, urine and stools are normal in color and sclera are anicteric, differentiating it from hyperbilirubinemia. Hypothyroidism leads to increased B lipoproteins that carry carotene in the blood, causing decreased carotene conversion to vitamin A.

This diagnosis of hypothyroidism was made during evaluation for precocious puberty. Van Wyk and Grumbach coined the constellation of hypothyroidism and precocious puberty in 1960. Hypothyroidism more frequently causes delayed puberty. Precocious puberty, however, can result from excess TSH cross reacting with FSH receptors in the gonads, leading to macroorchidism in males.

CONCLUSION

While constipation is frequently seen in hypothyroidism, the diverse clinical and laboratory findings of hypothyroidism can distract practitioners. In particular, carotenemia should be considered in patients with yellow skin discoloration without hyperbilirubinemia. Other less classic but associated findings of hypothyroidism include precocious puberty (VWGS), hyperlipidemia, steatohepatitis, muscle breakdown, elevated creatinine, and pericardial effusion.

Can't Keep a Straight Face: A 16-month-old with fever and facial droop

Alexandra Turek, MD, Sara Sanders, MD, and Eric Zwemer, MD

CASE: A 16-month-old presented with 1 week of daily fevers, 1 day of right-sided facial palsy, and left-sided purulent otorrhea. Exam showed both tympanic membranes obstructed by purulent material and right-sided palsy sparing the forehead. She had no pain with manipulation of the ears or palpation of the non-erythematous, non-edematous mastoid areas. White blood cell count was 24K/uL, CRP was <10mg/L, and CSF studies were unremarkable (4 WBC). IV ceftriaxone and Ciprodex drops were started for presumed bilateral perforated acute otitis media (AOM) with possible otitis externa. Due to persistent facial nerve palsy on HD3, she underwent bilateral myringotomies and tympanostomy tube placement, and started steroids. By HD 6, she had no improvement of palsy. MRI revealed bilateral mastoiditis and a 0.6 x 0.4 x 1.0 cm rim-enhancing fluid collection in the right mastoid. Her facial nerve palsy began improving on IV ceftriaxone by HD13 and she was discharged on cefdinir.

DISCUSSION: Mastoiditis is a known complication of AOM. Facial nerve palsy is rarely a presenting sign of AOM or mastoiditis, occurring in approximately 0.005% of AOM cases and 1.3% of mastoiditis cases. Due to the extensive intracranial course of the facial nerve, its palsy in AOM is likely multifactorial. In our patient, palsy was most likely due to direct extension of infection into the fallopian canal. Facial nerve palsies are relatively common in children; most are non-progressive and self-resolving. Facial nerve palsy secondary to mastoiditis, however, requires urgent treatment to prevent permanent nerve Injury. Our patient notably had mastoiditis with abscess, but did not have the classic auricular protrusion, postauricular tenderness, or pain upon ear manipulation. Occult mastoiditis cannot be detected clinically, so imaging should be strongly considered when AOM with facial nerve palsy is not improving on treatment as expected. Treatments often include myringotomies +/- tympanostomy tubes, antibiotics, and steroids. Mastoidectomy is an important intervention for larger abscesses. Some data suggests prolonged IV antibiotics and steroids can provide satisfactory recovery without surgical intervention, especially in patients with less severe palsy or smaller abscesses.

CONCLUSIONS: Facial nerve palsy is a rare complication of AOM and mastoiditis. In patients with facial nerve palsy, clinicians should consider AOM/mastoiditis in the presence of fever or prolonged palsy, even in the absence of classic findings of mastoiditis. Given risk of permanent neurological sequelae, clinicians should have a low threshold to image the mastoids in these patients.

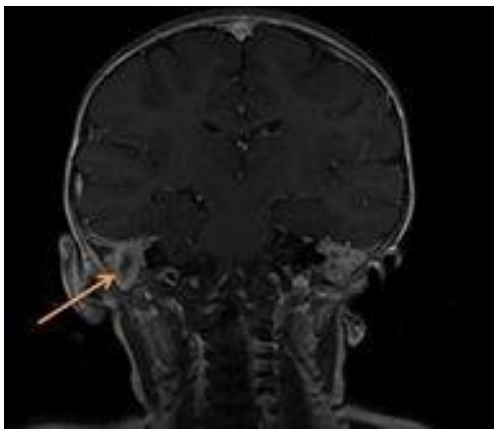


Fig. 1 Post-contrast T1 coronal MRI (series 4, image 21) with 0.6 x 0.4 x 1.0 cm rim-enhancing, centrally non-enhancing fluid collection in right mastoid bone (arrow) and bilateral enhancement of the mastoids consistent with mastoiditis.

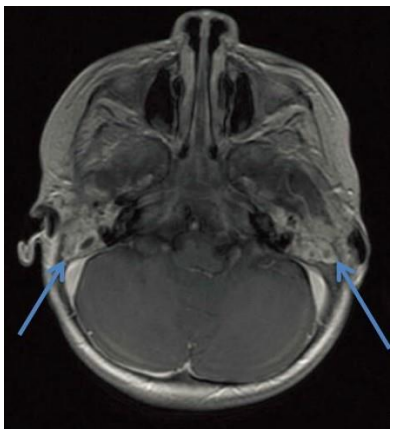


Fig. 2 Post-contrast axial MRI (series 3, image 15) with debris in the bilateral mastoid air spaces leading to loss of pneumatization (arrows), consistent with mastoiditis.

IT TAKES A DORF: A 17-YEAR-OLD WITH KNEE PAIN AND LYTIC BONE LESIONS

Joe Zakhar, MD, Alison R. Carroll, MD, Eveline Wu, MD, MSCR & Andrew Smitherman, MD, MSc

CASE PRESENTATION: A 17 y.o. African American male presented with 3-years of left knee pain and swelling refractory to NSAIDs. His pain progressed, leading to difficulty walking and sleeping. A left femur x-ray revealed lytic lesions and associated soft tissue mass prompting hospital admission. Exam showed tenderness and mild swelling of the left distal femur and proximal tibia. The left proximal humerus was also tender. He was unable to bear weight but tolerated passive range of motion. Initial evaluation showed anemia, elevated inflammatory markers, and myositis with rhabdomyolysis. Bilateral femur MRIs demonstrated expansile lesions in both medullary canals, cortical erosion, and breakthrough with soft tissue expansion in the distal left femur. PET-CT revealed hypermetabolic bony lesions with sclerotic and lytic features in the femurs, tibias, left humerus, and bilateral iliac bones. Circumferential aortic inflammation and multiple hypermetabolic chest and neck lymph nodes were also seen. Differential diagnoses included infectious, malignant, histiocytic, and rheumatologic etiologies. Left femur biopsy demonstrated S100+, CD68+, and CD1a– histiocytic proliferation with emperipolesis most consistent with Rosai-Dorfman Disease (RDD). No BRAF-V600E mutation was identified. He was first treated with prednisone 1.5mg/kg/day with subsequent addition of 6-mercaptopurine and methotrexate to allow prednisone taper. Pain resolved and he resumed normal activity.

DISCUSSION: Histiocytic disorders can be classified as dendritic cell disorders (Langerhans cell histiocytosis and Erdheim-Chester disease (ECD)) and macrophage cell disorders (RDD and hemophagocytic lymphohistiocytosis). While para-aortitis and retroperitoneal fibrosis/adenopathy are seen with ECD, the patient's age and histiocyte immunophenotype were more suggestive of extranodal RDD. Mixed phenotypes with concurrent ECD and RDD have been described. RDD is a rare, non-malignant, non-Langerhans cell histiocytosis. It typically affects individuals under 20 years old and is more common in males and African Americans. Most patients present with fever, massive cervical lymphadenopathy, and elevated inflammatory markers. Extranodal presentation is not uncommon, but bony RDD occurs in <10% of cases. Definitive diagnosis often requires tissue biopsy. Asymptomatic disease does not need treatment. Surgery can be curative for localized disease. Systemic RDD often requires treatment with steroids and chemotherapy, but no clear standard of care exists.

CONCLUSIONS: Bony pain refractory to typical treatment should prompt imaging. A high index of suspicion is needed to diagnose RDD as the differential is quite broad. Histiocytic disorders exist on a spectrum; as in this case, patients may have a mixed phenotype with features of both RDD and ECD. Extensive extranodal disease is often difficult to treat, and the optimal treatment regimen is unknown.

FIGURE 1. Expansile medullary bone lesions in left femur on x-ray (on the left) and in bilateral femur and tibia on MRI (on the right)

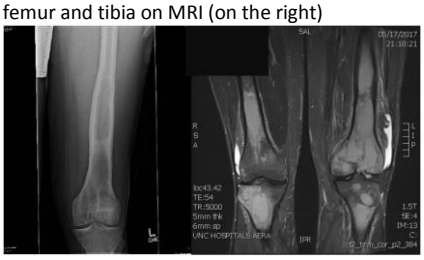


FIGURE 2. Circumferential inflammation of the thoracic and descending aorta on chest CT

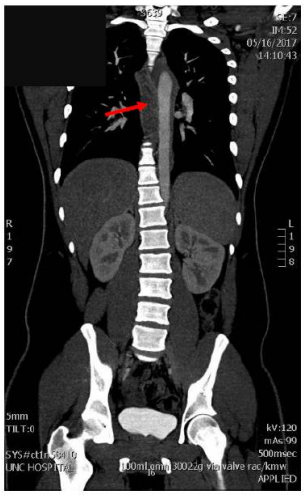
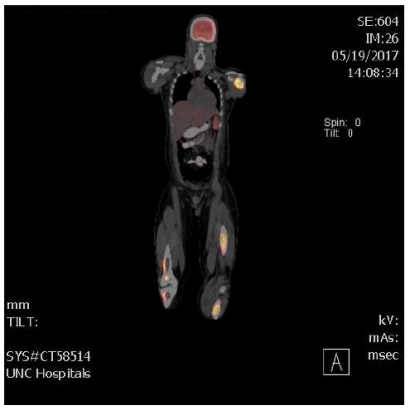


FIGURE 3. PET-CT scan showing multiple hypermetabolic bone lesions (yellow areas) in the humerus, bilateral femurs, and bilateral tibias.



GO WITH YOUR GUT: A SCHOOL-AGED CHILD WITH EDEMA AND VOMITING

Alison R. Carroll, MD, Tiffany St. Clair, MD, Kevin G. Greene, MD, Zachary Willis, MD, Francisco Sylvester, MD, & Alison Sweeney, MD

CASE PRESENTATION: A 12-year-old white female was admitted with 2-days of generalized edema in the setting of a 2-week history of abdominal pain and daily emesis, fatigue, and decreased intake. Two weeks prior to presentation, she was diagnosed with streptococcal pharyngitis and completed a course of amoxicillin. Review of systems was negative for fever, headache, dyspnea, night sweats, rashes, dysuria or hematuria. Vital signs were BP 78/42, HR 94, RR 20, T 37.2°C. Exam was significant for a fatigued and edematous child. Generalized pitting edema was noted. Abdomen was distended, tympanic and mildly tender to palpation diffusely. Differential diagnosis included heart failure, primary renal disease, liver failure, malignancy, and protein losing enteropathy. Laboratory tests were significant for a serum albumin of 1.5 g/dL, total protein of 2.9 g/dL, trace protein on U/A, normal creatinine and coagulation factors, and an elevated stool alpha-1 antitrypsin consistent with enteric protein loss. Abdominal ultrasound revealed ascites and splenomegaly. She had a normal EKG, echocardiogram, and chest x-ray. CT abdomen/pelvis demonstrated prominent gastric folds consistent with Ménétrier disease (MD). Upper endoscopy confirmed the diagnosis. Immunostaining for CMV from gastric biopsies was negative, but quantitative CMV PCR in blood was positive. Patient received supportive care with IV fluids, an H2-receptor blocker and a high protein diet but did not receive treatment for CMV. She had clinical improvement within 48 hours and was discharged. At a 1-month follow-up, patient had complete resolution of symptoms and albumin had normalized.

DISCUSSION: MD or protein-losing hypertrophic gastropathy is an uncommon pediatric disease, characterized by nonspecific GI complaints, generalized edema, hypertrophy of gastric rugae, and hypoalbuminemia due to protein loss through the gastric mucosa. While MD is often a progressive and chronic condition in adults, pediatric MD tends to be self-limited with resolution of symptoms in 4-6 weeks. Diagnosis is based on imaging studies showing prominent gastric folds and confirmed by endoscopy. Potential triggers for MD include cytomegalovirus (CMV) infection, *Helicobacter pylori*, nonspecific allergens, and medications (prostaglandin E1). Treatment is typically supportive with IV fluids, H2-receptor blockers or proton pump inhibitors. Antiviral treatment is typically not required.

CONCLUSIONS: While renal etiologies are more likely in a pediatric patient with generalized edema and hypoalbuminemia, a urinalysis without proteinuria in the setting of low serum albumin should prompt pediatricians to consider protein loss through the GI tract as seen in MD. Positive lab tests such as an elevated stool alpha-1 antitrypsin level and imaging results demonstrating prominent gastric folds should raise the suspicion for MD.

FIGURE 1. Axial and sagittal computed tomography of abdomen and pelvis demonstrating prominent gastric folds in the stomach (red arrows) and moderate volume ascites throughout the abdomen and pelvis (blue arrow) which is highly suggestive of Ménétrier disease.

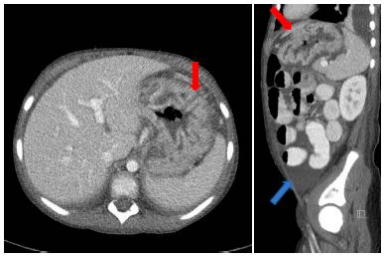


FIGURE 2. Diffuse prominent gastric folds in the gastric body found on endoscopy consistent with Ménétrier disease.

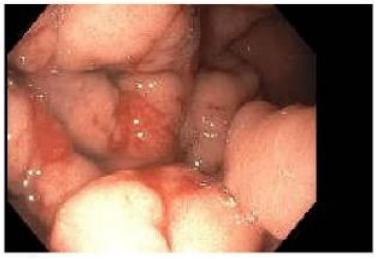
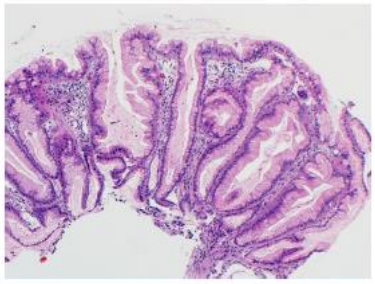


FIGURE 3. Microscopic examination of mucosal biopsies taken from the gastric body shows superficial fragments of gastric mucosa with prominent foveolar hyperplasia and lamina propria edema. Oxyntic-type glands appear diminished in number. There is no significant increase in mucosal inflammatory cells.



Fulminant viral myocarditis due to Parainfluenza 1 in a teenage girl: A case report.

Bobby Slater, MD. Erin Finn, MD. Sunita Ferns, MD.

Fulminant myocarditis is a rare disorder characterized by heart failure, rapid deterioration, and hemodynamic collapse with approximately 50% survival rate. Despite this poor prognosis, if a patient survives, there is often complete recovery of heart function. Fulminant myocarditis has an identified viral cause in 25-53% of cases with the majority attributed to enteroviruses, but recently viruses causing upper respiratory infections have been identified as a rare cause. Here we present the case of a 14-year-old girl who was admitted with syncope and rapidly deteriorated to the point of requiring ECMO. She subsequently recovered with normalization of her cardiac function. The only identifiable cause in her case was a nasal swab positive for Parainfluenza 1. Previous studies have identified superior sensitivity of viral PCR to identify causes of myocarditis in swabs compared to endomyocardial biopsies. A further look into the literature revealed few other cases of fulminant myocarditis related to Parainfluenza infection. Here we look at the underlying mechanism, etiology, and theoretical treatment methods to address this rare, but serious disease.

All I want for trismus is Ativan

Erin Finn, MD; Katie Jordan, MD

Case Presentation

A 3-year-old healthy girl presented with intermittent spells of difficulty opening her mouth, talking, and swallowing.

Episodes began 3 weeks prior without inciting incident. Initially occurring weekly, episodes were brief and self-resolving, but had begun increasing in frequency. Symptoms were typically worse later in the day. The presenting episode started thirty-six hours earlier. The child was eating when her jaw unexpectedly clenched tightly, preventing her from chewing, swallowing, or opening her mouth. She had no other neurologic symptoms. No new exposures or trauma. No systemic symptoms. Her father had severe blepharospasms in youth that resolved without treatment.

Her mouth was pursed and jaw tightly clenched. She was drooling and appeared unable to swallow secretions or speak, though was whining and appeared frustrated. TMJ was nontender with symmetric jaw musculature. She had fasciculations over her chin. Remainder of exam was unremarkable.

Neck xrays and CT were normal. MRI brain, EEG and CSF analysis were unremarkable. No autoimmune, infectious, or paraneoplastic etiology was identified. The patient was treated with diphenhydramine without improvement. She received lorazepam with rapid resolution of symptoms. Symptoms returned 24 hours later, and she again got lorazepam with resolution. She was diagnosed with oromandibular dystonia and discharged on clobazam with no episodes after discharge. Clobazam was tapered after 6 months. She continues to do well.

Discussion

The general pediatrician should recognize dystonia, which is characterized by sustained or intermittent muscle contractions resulting in abnormal movements and postures. Oromandibular dystonia is a specific form with involuntary contraction of the masticatory, lingual, and pharyngeal muscles. Although typically occurring in middle-aged adults, it can be diagnosed in children. It is typically idiopathic but can be associated with medications, autoimmune disease, or intracranial process (Yoshida 2017). Often initially misdiagnosed, diagnosis is made based on the characteristic clinical presentation with symptoms often absent in the morning and triggered by speaking or chewing (Jinnah 2015).

There is no standard treatment, but recognized treatments include botulinum toxin injection, benzodiazepines, anticholinergic or dopaminergic drugs, and muscle relaxants (Gautam et al 2016). The etiology of dystonia is not well-understood, but is hypothesized to involve dopamine transmission and the basal ganglia. There are known genetic causes, and a genetic cause is more often identified in early-onset dystonia (Jinnah 2015).

Conclusion

This case teaches pediatricians to recognize the presentation of oromandibular dystonia, a disorder more common in middle-aged adults. It reviews the effective treatments of this disorder.

Toxic Shock that Didn't Fit the Mould

Erin Finn MD, Bianca Allison MD, Rebecca Smith MD, Michelle Gombas MD, Jeremy Nel MD

Case Presentation:

A 17-yo girl was admitted for 3 days of vomiting, diarrhea, blurry vision, and dyspnea. She was found to have presumed Staphylococcal toxic shock syndrome from prolonged tampon use with resultant shock requiring CRRT and ECMO. Her course was complicated by left-sided BKA due to impaired perfusion and compartment syndrome. She improved and was decannulated and extubated by day 12. She was reintubated 3 days later due to new left exudative pleural effusion requiring chest tube drainage. She also required increasing pressors and steroids for worsening hypotension. Extensive infectious workup was negative and amputation site appeared clean, though she developed severe sacral pressure ulcers that required debridement. She was treated with broad-spectrum antimicrobials.

She developed abdominal distention and a CT on day 27 showed new infarcts throughout her abdominal cavity, including spleen, kidney, liver, and stomach wall. Laparotomy revealed extensive necrosis throughout her abdomen requiring debridement of multiple internal organs. Pathology was consistent with mucormycosis and intra-operative specimens cultured *Rhizopus species*. Family elected to withdraw care given the poor prognosis. Autopsy showed disseminated mucormycosis with multi-organ infarction.

Discussion:

Mucormycosis is a rare fungal infection caused one of the fungi from the Mucorales genera; it has a predisposition to angioinvasion, leading to extensive vessel thrombosis and tissue infarction. It is rarely reported in the pediatric population or immunocompetent patients. It commonly affects patients with immune compromise (eg uncontrolled diabetes, neutropenia, solid organ or bone marrow transplants, hematologic malignancy) or in patients undergoing iron chelation. The clinical presentation of mucormycosis is varied, requiring providers to have a high index of suspicion. Any organ can be infected, though the most common sites are rhino-cerebral, pulmonary and cutaneous. Our patient’s diagnosis was delayed due to her nonspecific symptoms and lack of typical risk factors. There are several possible explanations for her infection: she was on prolonged steroid treatment, had open sacral wounds as well as prolonged IV catheter use and surgery. These have been recognized as portals of entry in immunocompetent patients who developed disseminated mucormycosis. Successful treatment involves a combination of surgical debridement and antifungal therapy. Even with appropriate treatment, mortality is high in disseminated disease.

Conclusion:

Mucormycosis is a rare infection typically seen in immunocompromised patients. The incidence in immunocompetent patients is increasing, specifically in ICU patients. Efforts to develop more rapid PCR-based diagnostic testing and heightened awareness among providers will be essential to improving survival rates in these patients.

Slipping through the cracks: A case of tuberculosis in an adolescent

Hillary Spangler, MD; Peyton Wilson, MD; Thomas Belhorn, MD, PhD

Case report:

A 16-year-old Honduran female presented to an outpatient orthopedics clinic with a several month history of diffuse arthralgias. She also reported night sweats, cough and a 30 pound weight loss, so a chest x-ray was obtained and was concerning for a reactivated tuberculosis (TB) infection. The patient and her family were treated for latent TB 1.5 years prior and she admitted to poor compliance due to a lack of understanding of its importance. With an equivocal PPD and a history of incomplete latent TB treatment, she was started on empiric TB treatment. AFB sputum smears were positive and culture grew pan-susceptible *Mycobacterium tuberculosis.* The teen's 7-month-old brother was also admitted for active TB. Family members visited the ward without prior screening, concerning for inpatient exposures. However, all others screened negative for TB, so the teen was likely the source case. At 1-month follow-up, both patients were doing well; however, the teen was nervous to return to school due to stigmatization.

Discussion:

Despite a low incidence of TB in the United States, it is important for pediatricians to consider TB in the appropriate clinical setting, especially among foreign-born patients. A TB infection in a child represents a sentinel event, indicating other potentially infectious individuals; therefore, it is important that adult contacts be screened for TB. Patients and families need to be educated that TB is contagious but spread can be controlled with enforcement of infection control practices. Furthermore, communication between community and tertiary care providers needs to be in place for optimal exposure control and case finding. Teens with TB warrant special attention in order to ensure compliance with therapy and to avoid the negative effects of stigmatization.

Conclusion:

This case highlights the role of the pediatrician in both community and hospital-settings in the tracking and prevention of TB and in advocating for teen medication adherence and minimization of stigmatization. Future quality improvement work should focus on hospital-based exposure control programs and enhanced care for adolescents with TB.

Hypotonic Infant with Rhinovirus

Jeffrey Okonye, MD; Meg Kihlstrom, MD; Senyene Hunter, MD, PhD

Introduction

Spinal Muscular Atrophy type 1 (SMA1) is a rapidly progressive neurologic disorder causing diffuse muscle weakness by degeneration of anterior horn cells in the spinal cord. It presents in infancy and can lead to mechanical ventilation dependence or death by age 2 years. Early recognition guides treatment and disease outcomes. This case highlights a neonatal diagnosis and a new promising therapy.

Case

A term male infant was born by spontaneous vaginal delivery to a mother with history of HSV on suppression therapy. At birth, he had a weak cry, sluggish Moro and diminished grasp reflex. On subsequent exam, he moved all extremities, could mimic facial expressions, and demonstrated a good suck. His extremity reflexes were normal but he had slightly reduced tone globally. On day of life 3, he was discharged with slightly improved tone and planned follow up with Neurology. At home he was feeding well with adequate weight gain but had an unchanged neurological exam at his primary care physician's office. On day of life 12, he presented to the emergency department with 1 day of congestion, increased work of breathing, decreased tone, and delayed cap refill. Chest X-ray was concerning for right upper lobe pneumonia. Upon admission, he was started on antibiotics and placed on blow by oxygen. He later progressed to tachycardia, retractions, and diminished breath sounds with presumed left tension pneumothorax on chest x-ray. Needle decompression was performed followed by intubation due to concern for cardiorespiratory collapse. Head ultrasound showed no intracranial hemorrhage or hydrocephalus. A respiratory viral panel was positive for Rhinovirus. Initial blood and urine cultures were negative. An attempt was made to extubate, but he required re-intubation immediately secondary to weakness. Pediatric Neurology assessed him and discovered absent reflexes, diffusely reduced tone, and preserved cranial nerve function. Electromyography revealed severe axonal neuropathy. Genetic testing revealed 0 copies of SMN1 and 2 copies of SMN2 genes, confirming the SMA1 diagnosis. Treatment with Spinraza (nusinerson) was initiated.

Discussion

This infant was diagnosed early secondary to a rhinovirus infection. SMA1 is caused by the loss of functional SMN1 protein. In 2016, Spinraza became the only FDA approved treatment for SMA1. Spinraza modulates alternative splicing of SMN2 to allow creation of more SMN1 proteins. Although this drug does not fully reverse symptoms, it can both improve and prevent further loss of motor function.

Crossing the Mountains: A 5-year-old Girl with Altered Mental Status and Recent Travel

Chi An Liu, MD, MS, Joanna M. Hales, MD, and Katherine A. Jordan, MD

Case Presentation:

A 5-year-old girl presented with 1 day of confusion in the setting of 5 preceding days of headache, fever, and emesis. She woke up several times the night prior to presentation, and did not know where she was. She had no rashes, URI symptoms, diarrhea, ingestions, trauma, visual changes, or sick contacts. Travel history was notable for a trip to the Tennessee mountains 1 week prior. On presentation, she was tachycardic and febrile. Exam showed an ill-appearing and somnolent girl with meningismus and difficulty answering questions. Labs were notable for WBC count of 17.3 and CSF pleocytosis (295 nucleated cells, 8 RBCs, protein 51, glucose 52). She received ceftriaxone and doxycycline, and was admitted. MRI revealed left frontoparietal cortical inflammation with restricted diffusion, concerning for meningoencephalitis. Blood and CSF cultures, CSF enterovirus and HSV PCRs were all negative, as were serologic studies for Rocky Mountain Spotted Fever and Ehrlichia. Antibiotics were discontinued, and CSF and serum Arbovirus studies were sent. She initially had encephalopathy and aphasia, then slowly improved with return to baseline. She was discharged on hospital day 6. Shortly after discharge, her arbovirus panel returned positive for La Crosse IgM of the CSF and blood. She has been followed as an outpatient with no neurological sequelae.

Discussion:

The general pediatrician should recognize cases of La Crosse neuroinvasive disease, which is a rare cause of encephalitis in children transmitted by the *Aedes triseriatus* mosquito. Pediatricians should have a high index of suspicion when a child presents with classic symptoms of encephalitis in the setting of travel to higher risk areas including the Appalachian Mountains. Typical symptoms of illness include fever, headache, vomiting and fatigue although more severe illness can progress to encephalopathy, seizures, and coma. Notably, La Crosse encephalitis is often more severe than typical viral encephalitis. In pediatric patients at several centers in the Appalachian Mountains, data suggests risk for complications including hyponatremia (6-21%), seizures (13-46%), need for intensive care (26-57%) and rarely death (<1%-2%). Approximately 20% of patients may experience some level of neurological sequelae.

Conclusion:

La Crosse encephalitis typically presents with fever, headache, vomiting, and altered mental status in patients with a history of travel to the Southeastern or upper Midwestern states during the late spring through early fall. Pediatricians should consider La Crosse virus in these patients as it typically has more severe presenting symptoms and complications compared to other forms of viral encephalitis.

The hyperactive thyroid in the hyperactive child: When bad behavior isn't ADHD

Laura Parente, MD, MPH; Maggie Hall, MD

CASE PRESENTATION:

An 8-year-old female presented with hypertension and tachycardia. She had a history of ADHD and ODD and was started on methylphenidate six months prior to presentation. She had documented hypertension with systolics of 130s for the past month, and methylphenidate was discontinued the day prior to presentation due to elevated heart rate to 160s and blood pressure to 153/93. Vitals on admission were BP 179/111 and HR 160. She was in no distress with normal neurologic exam, but was restless with upper extremity tremors. She was admitted for hypertensive urgency and managed acutely with IV labetalol. Labs were notable for TSH of 0.061 and T4 of 5.59, consistent with a diagnosis of hyperthyroidism. Anti-thyroglobulin and anti-thyroperoxidase antibodies were elevated and thyroid ultrasound demonstrated a diffusely enlarged and hypervascular thyroid without nodules, further supporting Graves' disease. She was started on methimazole. She ultimately required two antihypertensives, atenolol and clonidine, before blood pressures were stable enough for discharge several days later.

DISCUSSION:

Hyperthyroidism is a rare but potentially serious disease in children that can present with a wide range of clinical manifestations including tachycardia, tremor, weight loss, and sleep and behavior disturbances. Diagnosis is based on history, physical exam, and results from thyroid function tests showing suppressed TSH and elevated T4 and T3. Additional workup such as thyroid antibody levels and radionucleotide uptake scans help differentiate the cause of hyperthyroidism. Graves' disease, caused by autoantibody stimulation of the thyrotropin receptor, is the most common etiology in children and results in overproduction of thyroid hormone and diffuse growth of the thyroid gland. Treatment includes antithyroid medication as well as more definitive therapy such as radioactive iodine and thyroidectomy, and symptom management is typically with beta-blockers.

CONCLUSION:

Signs and symptoms of hyperthyroidism may be subtle initially and often overlap with many other conditions, leading to a delay in diagnosis that can result in increased severity of disease. Behavioral disturbances are a frequent presenting complaint in children and are often initially attributed to other causes such as ADHD. This was demonstrated by our patient, whose worsening behavior was attributed to ADHD and ODD while her hypertension and tachycardia were thought to be secondary to stimulant medication. Pediatricians should be aware that cardiac manifestations and behavioral disturbances are among the most common presenting complaints for pediatric patients with hyperthyroidism, and clinical suspicion should be especially high when a patient presents with both. In particular, hyperthyroidism should be considered when a patient is admitted with persistent tachycardia or hypertension.

Figure 1: Patient's thyroid ultrasound images (A, isthmus; B, left; and C, right) with doppler flow demonstrating diffuse enlargement and hypervascularity.

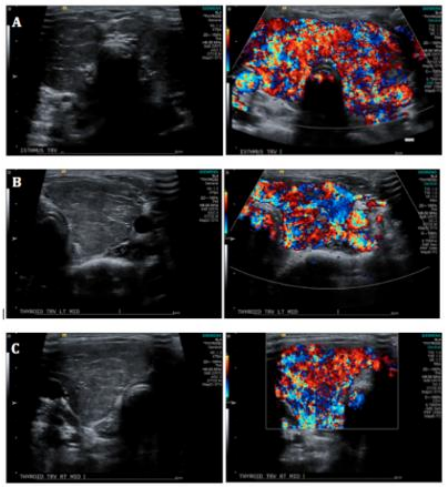


Figure 2: Table of commonly reported symptoms in children with Graves' disease, with cardiac and behavioral symptoms highlighted Sims, 2012.

Common Reported Symptoms in Children With Graves Disease

Symptom	No. of Patients (% of Total)
Palpitations/rapid heart rate	37 (48.7)
Temperature intolerance	36 (47.4)
Increased appetite	30 (39.5)
Weight loss or poor weight gain	30 (39.5)
Neck enlargement/goiter	27 (35.5)
Hyperactivity	24 (31.6)
Difficulty concentrating	21 (27.6)
Increased stool frequency	20 (26.3)
Sleep disturbance	20 (26.3)
Fatigue	19 (25.0)
Eye changes	17 (22.4)
Anxiety	15 (19.7)
Headache	14 (18.4)
Increased thirst	14 (18.4)
Jittery or restless	14 (18.4
Neck, throat pain, or difficulty swallowing	13 (17.1)
Increased urination	12 (15.8)
Mood changes	12 (15.8)
Excessive sweating	10 (13.2)
Nausea/vomiting	10 (13.2)
Respiratory symptoms	9 (11.8)
Abdominal pain	8 (10.5)
Abnormal menses	8 (10.5)

Why I now x-ray all babies…: A 4-day-old infant with increased work of breathing

Zachary Smith, MD, LeeAnne Flygt, MD, Eric Zwemer, MD

Case Presentation

A 4-day-old term male infant presented with increased work of breathing. He was born via NSVD to a healthy 31-year-old G5P2 with normal prenatal labs and 18-week anatomy scan. On day of life (DOL) 1 in the nursery he had increased work of breathing and tachypnea with normal oxygen saturation and reassuring pulmonary exam. Tachypnea resolved and he was discharged on DOL2. After discharge, parents noted continued tachypnea, increased work of breathing, and intermittent cyanosis of the hands, prompting presentation to the ED on DOL4. There his heart rate was 170, respiratory rate was 68 and oxygen saturation was 50% on room air. Exam was notable for nasal flaring, retractions, and cyanosis of the extremities. There was initial concern for ductal dependent cardiac lesion given timing of presentation. ECHO showed 4-chambered heart contracting normally in the right hemithorax. Chest x-ray showed bowel loops in the left hemithorax. NG tube was placed and the infant was admitted to the PICU. Surgical repair was performed thoracoscopically on DOL7, correcting a diaphragmatic defect of 2 cm. Large and small bowel within the chest were easily reduced into the abdomen. After diaphragm closure, the left lung was fully visualized with two well-formed lobes. The infant was discharged home on DOL13. No chronic pulmonary, gastrointestinal, or developmental concerns were noted at his 4-month well-child check.

Discussion

Respiratory distress and tachypnea in the newborn period are commonly encountered by pediatricians. Many common causes occur at or shortly after birth. Respiratory distress beginning after the initial newborn period, however, is a distinct clinical entity. While most infants have benign or easily recognizable causes, the differential diagnosis includes several life-threatening etiologies such as cyanotic congenital heart disease with ductus arteriosus closure, compensatory respiratory alkalosis in the setting of a metabolic disorder, and congenital diaphragmatic hernia (CDH).

While the majority of CDH cases are detected antenatally, CDH may occur with normal prenatal ultrasounds and a normal initial newborn course. As the infant feeds and the intestines expand, compression of the lung from thoracic intestines may lead to respiratory distress. Patients who are well-appearing at birth often have more favorable outcomes due to a lesser degree of pulmonary hypoplasia. Misdiagnosis or delayed diagnosis of CDH, however, is associated with significant morbidity and mortality.

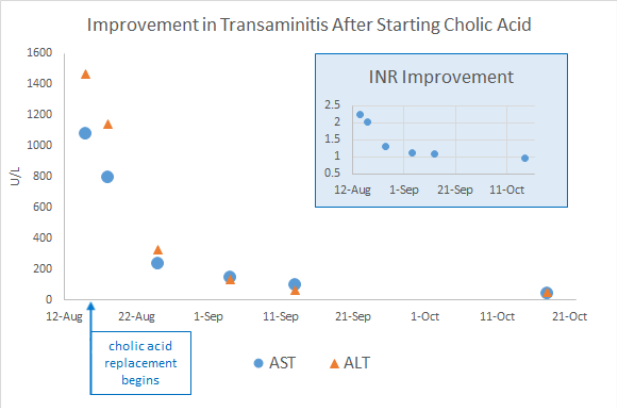
If it's Yellow, Don't Let it Mellow: An uncommon cause of jaundice and direct hyperbilirubinemia in an infant.

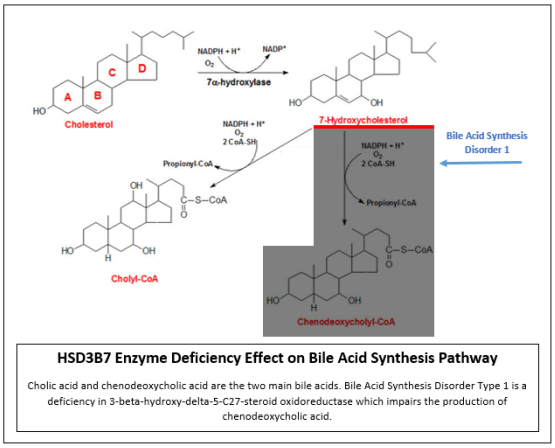
Elizabeth Willis, DO; Ali Carroll, MD; Michael Rogers, DO

Case Presentation A 4-month-old late preterm infant presented with jaundice, NBNB emesis, refusal to feed and lethargy with evidence of liver failure and direct hyperbilirubinemia on labs. Vital signs were BP 120/68 HR 129 Temp 36.9 °C RR 34. On exam patient had scleral icterus and full body jaundice. Abdomen was mildly distended but no hepatosplenomegaly. Labs were significant for markedly elevated transaminases (AST 1,079 U/L, ALT 1,465 U/L), direct hyperbilirubinemia (total bilirubin 11.4 mg/dL, direct bilirubin 6.8 mg/dL), prolonged prothrombin time, and hypoalbuminemia but normal gamma glutamyl transferase. Differential diagnosis included infectious, autoimmune, metabolic, malignant etiologies and cholestatic disorders. A liver ultrasound was unremarkable but a liver biopsy showed giant cell hepatitic pattern with marked hepatocanalicular cholestasis and ductular reaction with fibroedematous expansion of portal areas. In combination with the lab findings, liver biopsy was concerning for a bile acid enzyme defect. Patient was started on cholic acid (bile acid replacement therapy). Diagnosis was confirmed with urine organic acid spectroscopy and genetic testing showing an HSD3B7 gene mutation seen in congenital bile acid synthesis defect type 1. Infectious work-up was negative. Over the course of several weeks on cholic acid replacement the patient's transaminitis, synthetic liver function, and jaundice improved.

Discussion: Bile acid synthesis disorders are a rare and are estimated to account for only 1-2% of cholestatic disorders in childhood. Interruption in the bile acid synthesis pathway causes accumulation of hepatotoxic metabolites which can be detected on urine organic acid spectroscopy. Genetic testing will confirm the diagnosis but often takes days to return; therefore, immediate laboratory interpretation is important for initiating prompt treatment. Initial lab evaluation should rule out infectious causes of hepatitis. Presence of a normal gamma glutamyl transferase makes biliary atresia and other obstructive processes less likely and a liver ultrasound and biopsy can confirm this. Replacing cholic acid suppresses the toxin production in a bile acid synthesis disorder and allows the liver to repair. Improvement in transaminitis and hepatic function should be evident after starting cholic acid replacement.

Conclusion: Consider rare genetic causes of direct hyperbilirubinemia when obstructive lab patterns aren't present. Given the ease of cholic acid replacement and its importance in avoiding liver damage, it is imperative that identification of bile acid synthesis disorders and subsequent treatment begin quickly.





Epidural Blood Patches for Our Pediatric Patients: To Patch or Not, that is the Question

Marley Lawrence, MD, Gregory Maves, MD, Ashley King CPNP, Kimberly Blasius, MD

Introduction

Pediatric epidural blood patches (EBPs) come up as a question in clinical practice. The incidence of post-dural puncture headache (PDPH) from lumbar punctures (LPs) ranges from 2% to 15%, and is significantly less in children <10 years old.1 Severe PDPH occurs in only a small portion of PDPHs.2 PDPHs may require an EBP, but conservative treatment is usually effective.3 Families and health care providers often have a limited or skewed understanding of the indications, risks and benefits of this procedure.

Case Description

A 4-year-old male with a history of prematurity was admitted for persistent headache (HA) refractory to ibuprofen. The patient had presented to the emergency department (ED) with HA, fever and neck stiffness; a LP was performed and was negative for infection. He returned to the ED 3 days later with a persistent positional HA and concern for PDPH. Following admission, anesthesia's pediatric acute pain service was consulted. Prior to the anesthesia team's assessment, he was made NPO and the family was "waiting on anesthesia for a blood patch." After a long discussion with the family, including the risks of a required anesthetic for placement and explanation of EBP infection risk in a patient with a fever of unknown origin, anesthesia did not offer an EBP. Instead, conservative treatment with ketorolac and acetaminophen was utilized. Patient responded to treatment and was discharged home the following day.

Discussion

Determining whether a pediatric patient needs an EBP is not an uncommon scenario. The risks and benefits of an EBP should be weighed for each patient. EBPs are not well studied in pediatric patients and there is a paucity of information to guide clinical decision-making. Additionally, in the pediatric population, assessment of HA severity and characteristics can by itself be difficult, making the diagnosis of PDPH challenging. In this case, the clinical picture was further complicated with the presence of a HA even prior to the LP.

Conclusions

As illustrated by this case, an EBP is sometimes not the correct treatment choice for persistent HA status post-LP. Part of the challenge in this case was the expectation of the family. The family felt strongly that a blood patch would be an easy fix for the child's HA, and this idea was propagated by the ED providers and primary team. Education directed towards ED and inpatient providers about the risks, benefits and appropriateness of EBP in pediatric patients would be helpful.

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Measured fetal and neonatal exposure to Lumacaftor and Ivacaftor during pregnancy and while breastfeeding

Trimble AT, McKinzie C, Terrell M, Stringer EM, Esther CR Jr

With the growing class of CFTR modulator therapy available to more patients and with increasing pregnancies in individuals with CF, there is a growing need to understand the effects of these agents during pregnancy. There are few reports of their continued use in the literature, although it is likely that this is not an uncommon occurrence. We report the uncomplicated and successful pregnancy of a woman treated with lumacaftor/ivacaftor, as well as the clinical course of the infant during the first 9 months of life. We also report drug levels in plasma from the mother, cord blood, breast milk, and infant to estimate fetal and infant drug exposure.

Walking the plank: An adolescent with refusal to bear weight

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Case Presentation:

A 17-year-old boy with autism spectrum disorder presented with right leg pain, swelling and refusal to bear weight. The patient developed a petechial rash on his bilateral lower extremities six days prior and was treated with doxycycline for possible RMSF. He was afebrile and appeared well. Exam was notable for prominent gingiva, rough papules on posterior aspects of bilateral arms, petechiae on lower extremities and abdomen and tenderness to palpation with edema of bilateral lower extremities. Normal testing included: CBC, PT/INR, chemistry panel and lower extremity doppler ultrasound. ESR was mildly elevated. Lower extremity radiographs revealed a 7mm lucency over the medial distal metaphysis of the femur, consistent with a cortical bone cyst. Broad differential was considered. Further history revealed that patient was a selective eater with extremely limited dietary intake. He ultimately was diagnosed with vitamin C deficiency. He was treated with oral vitamin C with improvement in symptoms several days later.

Discussion:

Vitamin C plays many important roles in the body as a cofactor for collagen, prostaglandin and catecholamine synthesis. Vitamin C deficiency, or scurvy, is relatively rare in the general population. Individuals at risk for scurvy include those with developmental delay, iron overload secondary to frequent blood transfusions and patients with inflammatory bowel disease. Case reports identify children with autism spectrum disorder as being at a higher risk for nutrient deficiencies due to food selectivity. Symptoms of vitamin C deficiency typically become apparent after 1-3 months of inadequate intake. Related defects in collagen synthesis may manifest with dermatologic findings including petechiae, ecchymosis, follicular hyperkeratosis, coiled hair and gingivitis. The most common presentation of severe scurvy is lower extremity pain with refusal to walk. Symptoms can be caused by hemorrhage into muscle or periosteum, or by skeletal changes. Fasting vitamin C level < 0.2mg/dL is diagnostic but an insensitive test. Diagnosis can also be made after clinical improvement with treatment.

Conclusion:

This case emphasizes the importance of obtaining a dietary history for all patients and specifically for those with developmental delay. Scurvy should also be considered on the differential for refusal to bear weight or leg pain. Patients presenting with refusal to bear weight and possible vasculitis often get extensive work-ups and many consultations prior to a diagnosis being established. Clinical suspicion for scurvy may prevent unnecessary testing, imaging or procedures.

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THE 2AM WAKE UP CALL

Edgar Miles C. Leviste, MD and Katelyn Ammons, MD

Case Presentation:

13 month-old healthy boy admitted for two weeks of ataxia and difficulty bearing weight on his lower extremities following recent otitis media and respiratory illness. Parents were concerned for episodes of significant fussiness occurring at 0200 every morning for a two-week period. Prior to the onset of symptoms, the patient had reached all developmental milestones. Upon admission, the patient was well-appearing but displayed difficulty bearing weight on bilateral lower extremities without support and 2+ deep tendon reflexes in his patella and achilles tendon. On his first night of admission he awoke from his sleep, screaming in pain, similar to the episodes seen at home. A CT head without contrast was normal. MRI brain and lumbosacral spine revealed enhancement of the nerve roots descending from the lower thoracic levels and involving the cauda equina. A lumbar puncture revealed a CSF protein level of 324 with normal white blood cell count. This diagnostic work up was consistent with Guillain-Barre Syndrome. The patient was treated with a course of intravenous immunoglobulin (IVIG). His pain began to improve within 4 days of treatment, and he was ambulating within 4 weeks.

Discussion:

Guillain-Barre Syndrome is an acquired polyradiculoneuropathy, usually presenting as an ascending paralysis marked by weakness in the legs that spreads to the upper limbs and face along with complete loss of deep tendon reflexes. However, this patient presented with bilateral extremity pain, which can be seen in GBS. Other complications include autonomic instability, cardiac dysrhythmias, orthostatic hypotension, hypertension, paralytic ileus, transient bladder dysfunction, and weakness of the muscles of respiration. Typical CSF findings show an albuminocytologic dissociation, elevated protein level with normal cell count. The protein concentration is usually normal the first few days of illness and rises by the end of the first week.

Conclusion:

GBS has an annual worldwide incidence of 0.34 to 1.34 cases per 100,000 persons aged 18 years or less. Although studies mention that GBS in children under the age of 2 years old is rare, it can occur in younger populations, as seen in our report. It is possible that GBS may be under diagnosed in this age group. Therefore, we believe it to be important that GBS remain on the differential in kids under 2 years old who presents with bilateral lower extremity pain.

Wolf-Hirschhorn Syndrome & Hematologic Malignancies...is there a connection?

Nikkan Das MD, Tarshree Sawyer MD MPH, Thomas Alexander MD MPH

Case:

A 12 year-old male with Wolf-Hirschhorn Syndrome (WHS) presented with nausea, dehydration, weight loss, and pancytopenia. On exam, he had typical WHS features of growth delay, hypertelorism, flat nasal bridge, and frontal bossing, but was well-appearing with normal vital signs. Labs were significant for WBC 18.4 with 25% neutrophils, Hgb 6.8, Plt 85, MCV 115. Peripheral smear showed 45% blasts and many nucleated RBCs. Flow cytometry of peripheral blood was consistent with AML, confirmed on bone marrow biopsy. He was started on chemotherapy per study AAML1031. He tolerated three rounds of induction chemotherapy and subsequent hematopoietic stem cell transplant (HSCT) from a matched sibling donor. He is now doing well four months post-HSCT.

Discussion:

Wolf-Hirschhorn syndrome is a rare disorder related to deletion of the short arm of chromosome 4, including the *NSD2* (formerly known as WHSC1). Clinical features associated with WHS include typical craniofacial features, growth delay, cognitive disability, multiple congenital anomalies and seizure disorder. Since its first description in 1961, there has been significant progress in our understanding of clinical associations with this deletion. Recent malignancies have been described in these patients including, hematologic abnormalities, hepatic adenomas, hepatoblastoma, and neuroblastoma. Here, we present a case of acute myeloid leukemia (AML) in a patient with WHS. In our review of the literature, there have been 3 reported cases of hematologic abnormalities in patients with WHS. The cases included 2 children with myelodysplastic syndrome (MDS) of which one developed acute lymphoblastic leukemia (ALL), and 1 adult with cutaneous T-cell lymphoma. Activating *NSD2* mutations, associated with increased histone-3-lysine-36 dimethylation, have been implicated in the pathogenesis of ALL, raising the possibility that loss of 1 germline copy of *NSD2* in WHS, with somatic activating mutation in the retained *NSD2* gene, could contribute to the pathogenesis of hematologic malignancy.

Conclusion:

WHS is disorder of multiple congenital abnormalities that has been associated with malignancies. While there have been a few case reports of hematopoietic dysfunction in patients with WHS, to our knowledge, this is the first case of AML reported in a child with WHS. With this case and rare previous reports of association with ALL or MDS, further research into a correlation between WHS and hematologic malignancy is indicated, with particular attention to the potential predisposition caused by loss of *NSD2*

Having a Change of Heart: A 14-year-old female with syncope

Reshma Reddy, Eric Zwemer

Patient information:

A 14-year-old female presented with syncope and hypotension. She reported 4 preceding days of fatigue, URI symptoms, and headache. On the day of admission, she experienced mid-sternal chest pain, diffuse abdominal pain, emesis, dizziness, and syncope for 30 seconds. In ER, vitals were T 37.0, HR 89, BP 97/52, RR 20, and SpO2 99% on room air. Exam showed clear lungs and normal cardiac exam.

Labs were notable for mild anemia (Hgb 11.8), leukopenia (WBC 4.8), normal lactate (1.6), mildly elevated troponin (0.09), and mildly elevated BNP (80). EKG had mild ST elevations with question of early repolarization. CXR and pelvic US were normal, and CT abdomen/pelvis demonstrated pericardial effusion, mild ascites, and splenomegaly. She began to have hypotension with SBPs in the 60s and received 3 L of NS. She was admitted for undifferentiated shock with differential including hypovolemic, septic, and anaphylactic etiologies. Cardiogenic shock was considered though felt to be less likely given response to 3 L of NS, no tachycardia, and no pulmonary edema.

On admission, the patient was normotensive (BP 101/68). ECHO showed small pericardial effusion with no evidence of tamponade and normal LV systolic function. Repeat troponin remained mildly elevated (0.077). Within 12 hours of her initial echo, the patient decompensated due to tamponade physiology and required pericardial window. Troponin rose to 0.641. IVIg and IV steroids were started for empiric treatment of myopericarditis, but she progressed to fulminant heart failure requiring ECMO initiation. LV systolic function decreased to 20%, and transplant evaluation was initiated. On day 5 of ECMO, however, LV function significantly improved. She was decannulated and weaned off pressors with normal ventricular function on ECHO on HD13. Cardiomyopathy genetic testing was normal. She was discharged on HD25 with a diagnosis of fulminant lymphocytic myocarditis.

Discussion:

Myopericarditis has a broad clinical presentation ranging from malaise to fulminant heart failure and death. It should be high on the differential in pediatric patients presenting with chest pain and elevated troponin. Troponin has reported 100% sensitivity and 85% specificity in pediatric patients with suspected myocarditis. Only 50% of patients with myocarditis have abnormal CXR with pulmonary edema or cardiomegaly. Although cardiogenic shock and myocarditis are classically thought to worsen with aggressive fluid resuscitation, patients early in the disease course or patients with hypovolemia (and decreased preload) may improve with fluid administration.

Conclusion:

Myopericarditis should be considered in any patient presenting with syncope, particularly in the setting of recent illness. Troponin is a sensitive marker of myocarditis. Early in the clinical course of myopericarditis, hypotension may occur that is responsive to aggressive fluid resuscitation, with progression to true systolic failure as the disease progresses.

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Mandibular Chronic Recurrent Multifocal Osteomyelitis as Initial Presentation of Chronic Granulomatous Disease

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Case Presentation

A 4-year-old girl presented with right sided jaw swelling and dental pain for 2 months. She had seen several specialists and had been treated with antibiotics and steroids for presumed lymphadenitis with temporary improvement. She then presented with worsening daily pain and night sweats for 1 week. She denied fever, rashes, abdominal pain, vomiting, joint pain and swelling, recent travel, and exposure to tuberculosis. Physical exam was notable for marked facial asymmetry with tender right mandibular swelling and shotty cervical lymphadenopathy. Initial labs demonstrated normal blood counts and metabolic panel, CRP 11. 5 (normal <10), and indeterminate QuantiFERON®-TB test. CT showed lamellar new bone formation around the right mandible, consistent with chronic sclerosing osteomyelitis.

Biopsy of the right mandible demonstrated benign-appearing lamellar bone with osteoblastic rimming, fibrous medullary stroma with foci of neutrophils and plasma cells, without necrotic bone. Aerobic, anaerobic, fungal, and AFB cultures on the sample were negative.
She had two separate respiratory burst tests that were consistent with chronic granulomatous disease. Genetic testing revealed homozygosity for a known pathogenic mutation in NCF1. She is now on prophylactic sulfamethoxazole/trimethoprim and itraconazole.

Discussion

Chronic granulomatous disease (CGD) is a primary immunodeficiency that inhibits the ability of the respiratory burst in neutrophils through defects in one of any five subunits of the NADPH oxidase complex. CGD is inherited through CYBB on the X chromosome in approximately two thirds of cases and autosomal recessive mutations in NCF1 in ~20% of cases. The autosomal recessive inheritance pattern is associated with less severe disease and older age of presentation, consistent with this patient's disease course. Infections of the lung, skin, lymph nodes, and liver are the most common first manifestations of CGD. Although impaired primary immunity is the most commonly identified phenotype of CGD, it is also associated with a hyperinflammatory state in the gastrointestinal and genitourinary tracts. A recent case report described chronic recurrent multifocal osteomyelitis (CRMO) as a presenting illness for CGD that involved the long bones in an 11 year old male. However, no cases of CGD have been described with CRMO of the mandible as the initial presentation.

Conclusions

CRMO is a notoriously difficult diagnosis, requiring a confluence of tissue and diagnostic markers with clinical symptoms. As our laboratory initially attributed the patient's partial oxidative burst to collection error, these patients may benefit from further genetic exploration of CGD as an underlying cause of CRMO.

Just the Joints? A Teenage Boy with Migratory Arthritis

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Sara Sanders, UNC Pediatrics, PGY-2
Sara Duffus, UNC Pediatrics, PGY-3
Angie Hartsell, Moses Cone Pediatrics

CASE

A 14-year-old boy presented with a 1 month history of migratory arthralgias, arthritis, and fatigue. He was hospitalized with similar symptoms two weeks prior and was diagnosed with reactive arthritis after improvement with NSAIDs. In the interim, he developed symptoms including weight loss and headaches.

Physical exam revealed a fatigued appearing boy. His left elbow and right ankle were swollen, tender and erythematous with an effusion. He also had pain in the bilateral knees and shoulders without swelling. During the remainder of the admission, he had migrating erythema and swelling of multiple large joints.

Initial labs were notable for mild anemia (Hgb 12, downtrended to 10), while WBC and platelet count were normal. Initial inflammatory markers were elevated (ESR 136, CRP 21, ferritin 467) and progressively increased. Uric acid was normal (2.7), while LDH was elevated (350, increased to 1200). He had an unremarkable infectious and rheumatologic work-up including unremarkable synovial fluid cell counts and normal ANA, dsDNA, EBV, CMV, HIV, and parvovirus. Bone marrow biopsy revealed 64% blasts consistent with B-cell ALL. He was started on chemotherapy with good clinical response.

DISCUSSION

Initial work-up for joint pain and swelling in the absence of fever is often directed towards rheumatologic disease. However, malignancy should remain high on the differential in patients presenting with persistent joint pain. Thirty percent of children with leukemia present with bone or joint pain due to infiltration of malignant cells in the bone marrow.

This patient lacked the classic oncologic signs (fever, hepatosplenomegaly, lymphadenopathy, and derangement of multiple cell lines) that are often seen with hematologic malignancy. Leukemic patients who present with joint involvement often exhibit fewer classic signs, leading to diagnostic delay. In one case series, 6.4% of children with acute lymphoblastic leukemia (ALL) had an initial presentation that mimicked juvenile rheumatoid arthritis (JRA). In leukemic patients who were initially misdiagnosed as JRA, the degree of anemia was less significant than other ALL patients and almost one-third had normal cell counts at presentation. Leukemia was eventually suspected in the patients with joint pain based on atypical features, such as pain that awoke patients from sleep and nonresponse to NSAIDs.

CONCLUSION

Arthritis is a less common presentation of leukemia. Clinicians should maintain a high-index of suspicion for malignancy even in the face of a normal CBC. It is important to consider a bone marrow biopsy prior to initiating steroids if a rheumatologic diagnosis is uncertain.

Pneumococcal Endocarditis: An Infectious Melody

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Case: JW is a 12-year-old fully vaccinated male with a history of pulmonary atresia with multiple surgical repairs including transcatheter pulmonary (Melody^{TM}) valve implantation six months prior. He complained of fever, headache, and abdominal pain. Initial results included positive MonoSpot test, negative blood culture, and hepatosplenomegaly. Given persistent high fevers and negative confirmatory EBV testing, repeat blood cultures were obtained and grew *Streptococcus pneumoniae*. Broad-spectrum antibiotics were initiated. Initial echocardiogram showed no obvious vegetation. Cardiac MRI was unremarkable but limited by artifact from prosthetic valve. CXR showed left lower lobe consolidation. CT sinus showed extensive sinusitis. MRI brain was unremarkable. He remained febrile despite clearance of blood cultures. Repeat echocardiogram five days later demonstrated severely elevated right ventricular systolic pressure and flow gradient across the pulmonary valve with intraluminal shadowing concerning for vegetation. Pulmonary valve was explanted with large pseudoaneurysm and abscess noted in the pulmonary artery. He received a six week course of penicillin and recovered well.

Discussion: Infective endocarditis (IE) is relatively uncommon in children. Patients with congenital heart disease are known to be at increased risk, particularly those with surgically implanted intracardiac materials. The Duke criteria are often used to reach a confirmed clinical diagnosis; however there are circumstances where these criteria can be difficult to assess. For instance, *S. pneumoniae* is not commonly associated with IE, even in patients with prosthetic valves, and has not previously been reported to cause Melody valve endocarditis. In this case, initial cardiac imaging did not reveal a vegetation due to difficulty obtaining adequate views of the Melody valve. He rapidly developed an obstructive valvular lesion and progressed to heart failure despite broad-spectrum antibiotics, demonstrating the significant potential for morbidity and mortality. Given the imaging challenges, it is important to always have a high suspicion for IE in a febrile patient with a prosthetic valve and not be led astray by alternative diagnoses, such as mononucleosis in this case. Serial large-volume blood cultures are critical in the diagnosis, as evidenced by this patient with an initial negative culture.

Conclusion: Endocarditis must be strongly suspected in any child with a prosthetic valve and fever without a source. The critical diagnostic step is serial large-volume blood cultures before antibiotic administration if possible. Because of the difficulties obtaining adequate cardiac imaging and the significant potential for morbidity and mortality, endocarditis must be strongly suspected in patients with prosthetic valves even with unclear imaging and uncommon pathogens.