

**Department of Pediatrics Spring Research Day
Friday, April 8, 2011
Health Sciences Learning Center**



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Department of Pediatrics Spring Research Day Resident Abstracts

Creation of an Adolescent IBD Transition Clinic: A Baseline Survey of Patient and Parent Knowledge, Preferences, Challenges, and Behavioral Practices

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BACKGROUND: Approximately 25% of patients with inflammatory bowel disease (IBD) are diagnosed before the age of 16. These patients face unique challenges and, in general, have more complex disease. Adolescent IBD transition clinics have been proposed as a means of addressing the disease-related issues of this population and preparing patients for the eventual transition from pediatric to adult gastroenterology.

OBJECTIVE: To assess the baseline knowledge, preferences, challenges, and behavioral practices among patients eligible to participate in an IBD transition clinic and their parents.

METHODS: Established patients ages 11 to 21 with IBD at a midwestern pediatric hospital and their parents were invited to participate in a 24-item online survey. Item choice was based on the review of the literature. Content and face validity were established prior to the survey's launch. Categorical data was collected and analyzed.

RESULTS: Ninety-five patient and parent pairs were eligible to participate. Surveys were completed by 23 patients (24.2%) (16 with Crohn's disease and 7 with ulcerative colitis) and 11 parents (11.6%). 56.5% of patient respondents and 54.5% of parent respondents were male. The mean age \pm SD for patients was 15.56 ± 2.7 yrs. Regarding self-assessed baseline knowledge, 59.3% of patients and 36.4 % of parents reported having only limited knowledge of IBD. When questions regarding IBD arise, 65% of patients and 100% of parents reported they use the internet to obtain information, although 91.3% of patients reported approaching a parent first before searching the internet. Regarding preferences, most patients (69.6%) want a parent to be present for their entire doctor's visit while a minority (22.7 %) reported wanting a parent to be present for only part of the visit. Regarding disease-related challenges, 43.5% of patients reported needing to be reminded on a daily basis to take their medication, while an additional 13% reported needing to be reminded at least once a week. In fact, when asked about the disease-related issue they struggle with the most, 40.9% reported medication adherence. Social isolation also appeared to be a challenge with 60.9% of patients reporting that they do not know anyone else their age with IBD and 23.4% reporting that they never speak to their peers about their disease. Most (90.4%), however, expressed interest in using the internet to connect with others their age with IBD.

CONCLUSION: Our survey verified the need for greater disease-related education geared at adolescents with IBD and their parents. It also identified medication adherence and social isolation as the most prevalent challenges facing this population. Given the widespread use of the internet by our patients and their parents, web-based education and online social networking may be particularly effective for addressing these challenges. Such interventions are currently being piloted at our institution within our IBD Transition clinic.

MixL1 Expression Identifies Putative Hematopoietic Stem Cells in the Murine Allantois

Adam D Wolfe, MD/PhD¹ and Karen M Downs, PhD². ¹Department of Pediatrics, University of Wisconsin Hospital and Clinics, Madison, WI, United States and ²Department of Anatomy, University of Wisconsin, Madison, WI, United States.

BACKGROUND: MixL1, a homeodomain transcription factor, is implicated in pre-hematopoietic commitment of stem cells. In human lymphoma and leukemia lines, MixL1 is inappropriately expressed (Drakos et al., Human Pathol 2007:38:500). When over-expressed in mice, MixL1 is sufficient to induce acute myeloid leukemia (Glaser et al., PNAS 2006:103:16460). Thus, MixL1 may guide cells to remain poorly differentiated rather than proceeding to hematopoietic stem cell identity. The mouse allantois, which will form the umbilical cord, exhibits hematopoietic potential (Ziegler et al., Development 2006:133:4183). It has recently been demonstrated to contain a core of stem cells, the Allantoic Core Domain (ACD), where cells involved in placental hematopoiesis are thought to originate (Downs et al., Dev Dyn 2009:238:532).

OBJECTIVES: We set out to evaluate MixL1 expression in the allantois, and to establish its precise spatiotemporal whereabouts with respect to an early marker of hematopoiesis, Runx1 (Chen et al., Nature 2009:457:887).

DESIGN/METHODS: MixL1 expression was evaluated by immunohistochemistry. MixL1 coexpression with Runx1 was evaluated by immunostaining specimens from the LacZ/Runx1 reporter mouse (North et al., Development 1999:126:2563).

RESULTS: During early development, MixL1 is expressed in yolk sac blood islands and in a posterior embryonic domain that includes the ACD. Allantoic MixL1 expression temporally precedes that of Runx1. As development proceeds, MixL1 becomes prominent in nascent blood cells budding off from the vessel common to the allantois, yolk sac and dorsal aortae (DA), which we have called the "Vessel of Confluence" (VOC), and from which the umbilical artery (UA) arises. There are two additional domains of MixL1 expression in tailbud mesoderm adjacent to sites of vascular anastomosis: the site of joining of vitelline arteries of the yolk sac to form the omphalomesenteric artery (OMA) at the ventral midline; and surrounding the VOC at the site of origin of the UA.

CONCLUSION: We have shown that MixL1, which is implicated in leukemogenesis, is expressed within the allantois and nascent blood cells. MixL1 may identify one of the earliest hematopoietic precursor populations thus far known in mammals. Tailbud MixL1 expression is also temporally and spatially coincident with major arterial anastomoses, suggesting a role in vasculogenesis. These data provide additional evidence that the allantois is a promising and accessible model system for the study of definitive hematopoiesis.

SESSION DATE & TIME: Saturday, April 30, 2011, 10:30 am ? 12:30 pm

ROOM: Korbel 4F (Colorado Convention Center)

PRESENTATION TIME: 11:15 am

Extensive Dural Venous Hemorrhagic Stroke during Induction therapy in Acute Lymphoblastic Leukemia.

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POSTER PRESENTED BY: Jennifer Mosher, MD and Rachel Ershler, MD

We report the case of a 4 yr old girl with T-cell ALL who developed extensive dural venous thrombosis during induction cycle. She was initiated with four-drug induction chemotherapy regimen with vincristine, daunorubicin, prednisone and Peg-Asparaginase (ASP). On day 27 of induction, she presented with focal headaches and left-sided focal seizure activity. MRI with MRV scan of the brain showed a nearly occlusive thrombus of the superior sagittal sinus, distal straight sinus, torcular, right transverse sinus, right sigmoid sinus and proximal right internal jugular vein. Parenchymal hemorrhage

was visualized within the posterior right frontal lobe, right parietal lobe, and anterior right temporal lobe. She received intravenous heparin for anticoagulation for several weeks. She was later switched to subcutaneous injections of low molecular weight heparin. She developed left-sided hemiplegia from which she had a complete recovery. Her laboratory findings were significant for a low fibrinogen level. The risk of thrombotic events in children with acute lymphoblastic leukemia is not uncommon. However a vast thrombotic event in venous sinuses, as seen in our case, has not been reported. Although the etiology is multifactorial, ASP is one of the most likely culprit in this case. ASP is an essential drug for the treatment of ALL. The precise mechanism of ASP induced coagulopathy remains unclear. The postulated mechanisms include alteration of hemostasis system by reducing the synthesis of both coagulation factors and inhibitors, as a consequence of asparagine depletion.

Social Networking and the Female College Student: Privacy Setting Attitudes

Megan E. Lederer, Sarah A. Rastogi, Megan Moreno. University of Wisconsin Hospitals and Clinics, Madison, WI.

BACKGROUND: The use of FacebookT, the social networking site, is extremely prevalent among college students. Concerns about privacy and safety surrounding this method of communication have increasingly been raised in the media, among law enforcement, healthcare personnel, educators and parents. These concerns may be particularly salient for women given their increased risk of unwanted attention resulting from online disclosures.

OBJECTIVE: We conducted focus groups with college women to discuss privacy and safety concerns on FacebookT and to identify thoughts, behaviors and actions taken in response to these issues.

DESIGN/METHODS: A convenience sample of university women between 18 and 22 years of age were recruited from several campus organizations between September and October of 2009. Two trained facilitators asked subjects for their views about privacy and safety on FacebookT. All tape-recorded data was fully transcribed and then analyzed to identify common themes.

RESULTS: 39 female undergraduate students were divided into five focus groups. Each participant had an active FacebookT account and nearly all reported accessing it multiple times a day. Several themes emerged from our data: 1. Students consistently identified certain types of FacebookT information, such as addresses and phone numbers, as being too personal to share public; 2. Most students were interested in discussing, Learning about, and enhancing their privacy settings. Some students stated that they planned to increase their privacy settings as a result of the focus group discussion; 3. Students who reported having privacy settings enforced by their student organizations described significant efforts to subvert these enforcements.

CONCLUSIONS: In our study population, FacebookT is a very common method of communication and consumes a substantial amount of female student's time. These students were largely aware of privacy settings and had some concern about the safety of the information available about them on Facebook T, leading them to increase their privacy settings over time. While students were interested in learning about privacy settings from others, enforced settings were seen as punitive and a substantial amount of time was spent subverting these enforcements. This suggests that efforts towards education rather than enforcement may benefit this population.

SELF-PROMOTERS AND STALKERS: GENDER DIFFERENCES IN SNS USE AMONG OLDER ADOLESCENTS

Megan Moreno, Erika Mikulec, Rosalind Koff, Megan Lederer, Molly Carnes

INTRODUCTION: Early studies of adolescent internet use focused on time spent on the internet, and consistently found males to have higher use patterns. Currently, up to 98% of older adolescents are social networking site (SNS) users. Less is known about gender differences in SNS use; this information would contribute to developing conceptual models of adolescent internet use that could be used towards health intervention development. The purpose of this study was to evaluate older adolescent males' and females' SNS use.

METHODS: Gender-specific focus groups were recruited by convenience sample at a large Midwestern university. Focus groups were led by a trained same-gender facilitator. Facilitators used both open-ended and prompting questions to explore how participants used SNSs including frequency, motivations for use and experiences with SNSs. All focus groups were recorded and manually transcribed. Analysis was conducted by three investigators using an iterative process in which all investigators first reviewed transcripts individually and then discussed together to determine consensus on themes and representative quotations.

RESULTS: 12 focus groups were conducted including 28 males and 39 females between the ages of 18 and 23 years. All participants reported SNS use. The major theme derived from our data was that males tended to approach SNS use through an individualistic framework and females tended to approach SNS use through a communal framework. This theme was expressed in several ways. First, males often described their motivation to have a SNS profile as one of self-promotion: "It's a great way to get my name out to people." Females frequently discussed SNS use as a way to be connected to their community: "I use it to send messages to friends that I don't see all week." Second, males described logging onto their SNS profile with a goal-oriented approach. Many males described using only the applications needed for their intended task, and then logging off. In contrast, females often described logging onto their profile as part of a routine habit: "I talk to other people on there, or I check the home page for updates, or I check my friends' walls and stuff for new pictures." Third, males and females both stated that they used Facebook to communicate with friends. However, females reported pursuing in-depth profile investigations of people they did and did not know: "It makes stalking acceptable. Not actual stalking. But, offline you never look at someone's actual photo albums you don't know. But on Facebook...I look at them."

CONCLUSIONS: Our findings suggest differences in male and female older adolescents' motivations towards and use of SNSs. Males' approach to SNSs was more centered on individual goals and existing relationships; females approach was more centered on routine maintenance of their online community, as well as exploration within the Facebook site and larger online community. As health interventions using the internet are increasing, a clear understanding of gender differences in SNS use will be essential to create interventions that are effective and targeted.

Sources of support: The work described was supported by award K12HD055894 from NICHD.

Relationship of Weight References to Depression and Stress References on College Freshmen's Facebook Profiles

Emily Kolpa, MD and Megan Moreno, MD, MPH, MEd

PURPOSE: Overweight and obesity are significant health problems affecting adolescents. Some studies have found that depressed and stressed adolescents are at increased risk for the development and persistence of obesity. The social networking site Facebook is used by the vast majority of college students. This website may present an innovative venue to identify and reach out to students with weight concerns along with stress and depression. The purpose of this study was to determine whether student Facebook references to weight concerns are associated with higher likelihood of references to depression and stress.

METHODS: We examined 300 randomly selected public Facebook profiles of freshmen at a large state university. Profiles were analyzed by coding variables of demographics and references to weight concerns, depression, and stress. A 20% subsample was evaluated for interrater reliability; Cohen's kappa for categorization of weight references was 0.78, depression references was 0.79 and for stress 0.78. Qualitative analysis of text references to weight concerns was conducted through content analysis with two investigators assessing individual references and meeting to discuss concurrence on themes.

RESULTS: Of 300 profiles, 84% were female, and all were ages 18 and 19. Weight references were displayed on 6.4% of the profiles, and women were 3.5 times more likely to display weight concerns on Facebook (CI: 1-12, $p=0.05$, 95%). Those who displayed references to weight on Facebook were 4.6 times more likely to also display references to depression (CI: 1.7-12.8, $p=0.003$, 95%). Those who displayed references to weight on Facebook were also 3.9 times more likely to display references to stress on Facebook (CI: 1.4-11.8, $p=0.01$, 95%). Qualitatively, posted comments regarding weight were largely in reference to being overweight. Comments were overwhelmingly negative and self-depreciating, with major themes of calling oneself fat or describing overeating, for example "Jess is fatty. Jess is obese," "Eva is a fatass eating ice cream," and "Sara needs to not eat ALL the time!" There were rare comments on plans for exercise or healthy diet, with focus on self criticism and regret. The vast majority of weight references were made through status updates, with few bumper stickers (2/19 references).

CONCLUSIONS: References to weight concerns are highly associated with references to depression and stress concerns among college freshman Facebook users. This suggests that older adolescents, who are worried about their weight and publicly display these concerns, are more likely to also publicly display struggles with depression and stress. This represents an at risk population which may benefit from early outreach and intervention.

Examining the Refusal of Newborn Eye Prophylaxis and Vitamin K in Wisconsin

Benjamin R Hanisch, MD; Angela M Rohan, PhD; Beth C Becker, MD; Pamela J. Kling, MD; Murray L Katcher, MD, PhD

STATEMENT OF PROBLEM Routine newborn care includes eye prophylaxis to prevent ophthalmia neonatorum (ON) and Vitamin K supplementation to prevent hemorrhagic disease of the newborn (HDN). State statutes in Wisconsin mandate eye prophylaxis. Parenting websites give strategies to empower parental choice to opt out of these treatments. However, institutional protocols for these treatments vary, with little information on rates of and reasons for parental refusal.

OBJECTIVES AND RESEARCH: The objective of this study was to determine the extent of, and reasons for, parental refusal of eye prophylaxis and vitamin K administration in Wisconsin birthing hospitals and centers.

METHODS: Newborn nursery supervisors at Wisconsin birthing hospitals and centers (N=100, with 93 usable email addresses) were sent an online questionnaire related to parental refusal of eye and vitamin

K prophylaxis and asked to complete or forward the survey to the appropriate person. The response rate was 70 %, representing approximately 66% of newborns in Wisconsin.

RESULTS: The statewide refusal rates for eye and vitamin K prophylaxis are each less than 1%, with much higher refusal rates in some hospitals. Most have policies that require eye prophylaxis and vitamin K administration but also allow refusal of either or both interventions. The major reason reported for Parental refusal was the perception that the interventions were unnecessary, followed by religious reasons and concerns about disrupting maternal/infant bonding.

CONCLUSIONS: A low refusal rate of these prophylactic interventions occurs in most, but not all, Wisconsin nurseries. The parental belief that interventions are unnecessary may be due in part to the success of these interventions in making ON and HDN rare occurrences. An institution's reported refusal rate for eye prophylaxis and vitamin K were often similar, possibly indicating that a given parent may commonly refuse both. Physicians and hospital staff should be reminded about the Wisconsin law that eye prophylaxis be administered during the first 2 hours of life. Also, prenatal classes and physicians should inform parents-to-be about the importance of these interventions and the medical consequences of refusal.

Department of Pediatrics Spring Research Meetings

Accepted Abstracts

PAS/ASPR Poster Presentations

April 30 – May 3, 2011

Denver, Colorado

WAIST CIRCUMFERENCE PREDICTS MRI-MEASURED VISCERAL ADIPOSITY AND METABOLIC MARKERS BETTER THAN BMI AND CVF IN ADOLESCENT

Vanessa A Curtis, M.D.¹, Aaron L Carrel, M.D.¹, Jennifer L Rehm, M.D.¹, Brett P Sjöberg, B.A.¹, Jens C Eickhoff, Ph.D.¹ and David B Allen, M.D.¹. ¹University of Wisconsin, Madison

Background: Risk for metabolic syndrome is mediated by genetics as well as cardiovascular fitness (CVF) and obesity. Adipose tissue secretes cytokines that contribute to metabolic health, and the compartment in which adipose tissue accumulates influences its bioactivity. Genetically-determined distribution of adipose tissue into visceral (VAT) and subcutaneous (SCAT) compartments may influence risk for metabolic syndrome. BMI, DXA, air and water displacement fail to distinguish the more harmful VAT from SCAT. Accurate measurement of adipose tissue quantity and location would improve assessment of risk for metabolic syndrome.

Objective: Compare quantitative MRI to other measures (BMI, Waist Circumference (WC), CVF) in determining metabolic syndrome risk in overweight/obese children.

Design/Methods: This single cohort prospective study includes 18 healthy females (mean age 12.7y, 89% non-Caucasian). Local middle school students were recruited at enrollment for an after-school fitness club. Fasting blood was collected for lipid panel and insulin. Adiposity was evaluated with BMI, WC, and MRI performed on clinical 3T scanner. Analyses included VAT and SCAT area at the level of L4. CVF was measured with VO₂ max treadmill test.

Results: Mean BMI was 30.4 +/- 4.1. VAT at L4 correlated with fasting insulin ($r = 0.78$, $p = 0.0002$), waist circumference ($r = 0.73$, $p = 0.001$), triglycerides (TG) ($r = 0.62$, $p = 0.007$), and HDL ($r = -0.56$, $p = 0.02$) but not BMI or VO₂ max. In contrast, SCAT at L4 correlated with BMI ($r = 0.92$, $p < 0.0001$) and VO₂ max ($r = -0.61$, $p = 0.009$), but did not correlate with TG, HDL, or fasting insulin.

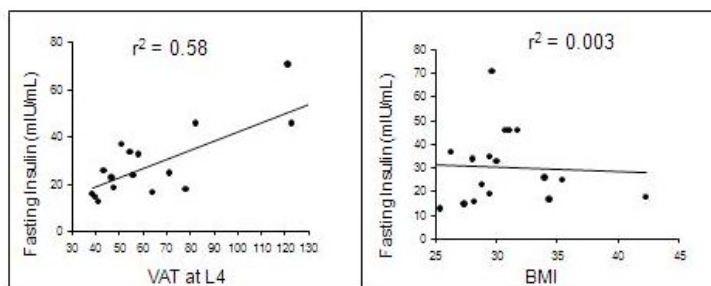


Fig. 1. VAT at L4 correlates well with Fasting Insulin.
BMI does not correlate with Fasting Insulin.

Conclusions: In an ethnically diverse group of middle school females, VAT predicts metabolic syndrome risk better than SCAT or BMI. MRI is a powerful tool for assessment of visceral adiposity. In clinical settings, WC appears to provide a reasonable approximation of visceral adiposity superior to BMI.

Acknowledgements: NIH T32 DK077586-01

SESSION DATE & TIME: Sunday, May 1, 2011, 4:15 pm - 7:30 pm

CELL LINES COMMONLY USED AS MODELS FOR INFLAMMATION CONTAIN GENETIC VARIATION IN TOLL-LIKE RECEPTOR GENES

Jessica A DeValk¹, Sara A Tokarz, PhD¹, Bikash Pattnaik, PhD¹ and De-Ann M Pillers, MD, PhD¹.

¹Pediatrics, University of Wisconsin, Madison, WI, United States.

Background: A549 is a pulmonary type II alveolar epithelial cell line obtained from a human lung carcinoma (ATCC, Rockville, MD). These cells are commonly used in studies to investigate inflammation pathways, including the up-regulation of interleukins and other inflammatory cytokines after exposure to pathogens. Toll-like receptors (TLRs) are a family of transmembrane receptor proteins present in many cell types including epithelial cells of the lung and serve as the first point of defense in the innate immune system. TLRs are essential in initiating the inflammatory cascade in response to infectious microorganisms. Single nucleotide polymorphisms (SNPs) in genes for TLRs 1, 2 and 4 occur in up to 20% of the population. TLR4 D299G, TLR4 T399I, TLR2 P631H, TLR2 R753Q and TLR1 N248S SNPs have been shown to be associated with a decrease in the innate immune response.

Objective: We sought to determine the presence of a subset of common TLR SNPs associated with inflammation in a cohort of cell lines that are used extensively for inflammation studies.

Design/Methods: DNA was isolated from the following cell lines: Human Umbilical Vein Endothelial Cells (HUVEC), Human Embryonic Kidney (HEK293), A549 lung epithelial, Human Retinal Pigment Epithelium (HRPE), HeLa, Jurkat lymphocyte cells, MCF-7 human breast adenocarcinoma, A431 human epithelial carcinoma, Y79 human retinoblastoma. Cell line TLR genotype was established using ABI TaqMan[®] SNP Genotyping Assays. The Step OnePlus[™] software was used to analyze the intensity of each fluorescent probe assigned to either the wild-type (WT) or natural variant (NV) allele and to produce an amplification plot of the data along with the C_t value.

Results: TLR4 D299G, TLR4 T399I and TLR2 P631H SNPs showed heterozygosity for the WT and NV alleles in HeLa cells while the other cell lines were homozygous for the WT alleles. HeLa and HEK293 lines were homozygous for the WT allele for the TLR1 N248S SNP and all other cells were homozygous for the NV allele. All cell lines were homozygous for the WT allele for TLR2 R753Q.

Conclusions: HeLa cells are used as a cell model for many inflammation studies, which may not be appropriate considering the heterozygosity of the TLRs in this cell line. The phenotypic effects of SNPs is a newly developing field and it is important for investigators to know that the pathway they are studying in a cell model is functioning properly before they conduct research

SESSION DATE & TIME: MONDAY, MAY 2, 2011 4:15 PM – 7:30 PM

ELBW Infants with Protein Added to Enteral feeds Show Enhanced Growth within Three Weeks of Supplementation

Ditzenberger GR, Wallen LD, Phelan LA, Collins SD, Binder ND

Nutritional support to promote optimal postnatal growth for extremely low birth weight (ELBW) infants <1000g at birth remains a significant challenge. Up to 45% of postnatal growth restriction reported for ELBW infants may be associated with inadequate protein and caloric intake during postnatal hospital course. The purpose of this study was to test the effect of protein supplement added to enteral feeds on postnatal growth of ELBW infants.

Subjects: 28 ELBW infants were enrolled after parental consent & randomized into intervention (13) and control (15). There were no differences between intervention & control for demographic information, gender ($p < 0.1$), or birth weight ($807 \pm 111\text{g}$ vs $826 \pm 92\text{g}$; $p = 0.687$). There was a difference in birth gestational age (26 ± 1.1 weeks vs 27 ± 1.2 weeks; $p < 0.001$).

Method: NICU-standard parenteral 2gprotein/100 mL solution was initiated by 4 hours of admission, total parental nutrition by day of life (DOL) 2, & enteral feeds by DOL 3. Study protocol was started when infants reached 100mL/kg/d enteral intake. The control group received standard feeds of premature formula or fortified breast milk. Intervention group received whey based protein added to standard

feeds according to 3 weight groups: 1) < 1000g; 2) 1000– 1499g; and 3) 1500–2000g. Supplements were calculated to reach goal protein when enteral intake was 150mL/k/d. At study start, all infants were < 1000g; protein goal was 4.2g/k/d. Protein goal was decreased to 3.7g/k/d when infants reached \geq 1000g and to 3.3g/k/d when infants were >1499g. Supplementation was discontinued when infants reached 2000g or at discharge. Weight, length, and head circumference (HC) were measured for 8 weeks. There were no differences in parenteral nutrition, enteral fluid or caloric intake. There were significant differences of protein intake during study weeks 2 – 5. Peak protein intake occurred during study week 3 (4.4 ± 0.6 g/kg/d vs 3.5 ± 0.4 g/kg/d; $p < 0.0001$). When controlled for postmenstrual age, differences in study week 3 for weight (1332 ± 52 g vs 1149 ± 61 g; $p < 0.005$) & length (38 ± 0.7 cm vs 37 ± 0.8 cm, $p < 0.05$) were significant. Intervention HC was larger but not statistically significant (27 ± 0.8 cm vs 26 ± 1.0 cm; $p = 0.316$). This study demonstrates that early increased enteral protein may have a positive effect on ELBW postnatal growth.

SESSION DATE & TIME: Saturday, April 30, 2011, 1:00 pm – 4:00 pm

RELIGION AND SEX IN COLLEGE FRESHMAN: A LONGITUDINAL STUDY OF FACEBOOK

Gannon Kerry E, Moreno MA, Becker T.

The relationship between religious involvement and sexual behavior has been well studied in adolescents. However, the role of religion in decreasing sexual activity is less clear in college students. Freshmen year is an ideal time to monitor this relationship. Facebook is a social networking site used by the majority of college students to create personal profiles; it provides venue to evaluate their beliefs and behaviors over time.

PURPOSE: The purpose of this study was to conduct a longitudinal evaluation of references to religion and sexual behavior on Facebook profiles during freshman year of college.

METHODS: Public Facebook profiles of freshmen undergraduates age 18 to 19 from a large state university were examined at four time periods during freshman year. At Time 1, data was collected during high school until starting college. Time 2 occurred early in fall semester, Time 3 at the conclusion of fall semester and Time 4 at the end of freshman year. Content analysis included self-displayed demographic information, religious affiliation, references to religious behavior, and references to sexual behavior. A 20% subsample was evaluated for interrater reliability; Cohen's kappa for categorization of sex references was 0.71. Analyses included mixed-effects logistic regression, mixed-effects Poisson regression and nonparametric Kruskal-Wallis test.

RESULTS: Of 330 screened Facebook profiles, 150 profiles met inclusion criteria. 97% were 18 years old; 55% were female. At Time 1 52% of profiles displayed a religious affiliation; by Time 4 13% of profiles displayed a religious affiliation. At Time 1 51% of students displayed references to sexual behavior; at Time 4 23% of students displayed sexual references. Women were more likely than men to decrease sexual references (OR=4.7). References to religious behavior increased from 7% of profiles at Time 1 to 10% at Time 4. When compared across all time points, adolescents who displayed at least one reference to religious behavior had 65% fewer sexual references than those who did not display religious behavior ($p = 0.002$).

CONCLUSIONS: During freshman year, students use Facebook to publicly display religion and sexual behavior. College freshmen removed both religious affiliation and references to sexual behavior, demonstrating a decreased willingness to share this information with the public. Freshmen who displayed references to religious behavior were less likely to display references to sexual behavior. These findings suggest that the relationship between religious behavior and sexual behavior established by self-reported data in adolescents may persist into freshman year of college.

SESSION DATE & TIME: SATURDAY, May 1, 2011, 4:15 pm – 7:30 pm

ASSESSING THE NEED TO TRANSFORM A RESIDENCY CORE CURRICULUM

Gwen C McIntosh, MD, MPH¹, John G Frohna, MD, MPH¹ and Megan A Moreno, MD, MEd, MPH¹.

¹Department of Pediatrics, University of Wisconsin School of Medicine and Public Health

Background: The evolution of duty hour requirements in residency education creates new challenges for the teaching of a residency core curriculum. To accommodate duty hour restrictions, residency programs are implementing increases in shift work, increases in night rotations, and an overall decrease in direct patient care hours. With reduced in-house work hours, residents face conflicting demands on their time for direct patient care duties and for didactic educational sessions. Under these conditions, the traditional noon conference model of residency education may be suboptimal for the delivery of an effective core curriculum.

Objective: 1. To assess barriers to resident attendance at the traditional noon teaching conference 2. To assess faculty satisfaction with resident attendance at these conferences 3. To assess resident and faculty perception of the effect of attendance at noon teaching conference on direct patient care duties 4. To measure resident and faculty interest in an alternative format for delivery of the residency core curriculum

Methods: Email survey to all clinical faculty and residents at an academic pediatric residency program.

Results: 26 residents (72%) and 56 clinical faculty (53%) completed the survey. Residents identified the following barriers to noon conference attendance: inpatient clinical obligations (42%), outpatient clinical obligations (35%) and travel time between clinical sites (58%). Residents stated that daily noon conference attendance made it difficult to accomplish clinical duties (58%) and to comply with duty hour requirements (23%). Clinical faculty were unhappy or very unhappy with resident attendance at noon conference (30%). Many faculty agreed that daily noon conference attendance made it difficult for residents to accomplish clinical duties (45%) and to comply with duty hour requirements (29%). Residents expressed greater enthusiasm than faculty for pursuing an alternative format for delivery of the residency core curriculum (69% vs. 23%).

Conclusions: These data suggest that the traditional noon teaching conference is a suboptimal method of delivering a residency core curriculum given the challenges of providing clinical care under duty hour restrictions. Residents expressed significant interest in pursuing an alternative format for delivery of the residency.

SESSION DATE & TIME: Tuesday, May 3, 2011, 12:30 pm – 2:00 pm

PRECEPTORS PERCEPTIONS OF USE OF AN EVALUATION TOOL FOR MEDICAL STUDENTS IN ROUTINE CLINICAL ENCOUNTERS WITH REAL PATIENTS

Caroline R. Paul, MD; Craig L. Gjerde, PhD; Gwen C. McIntosh, MD, MPH; Lori Weber, MD

There is a need to establish more objective and rigorous measurable outcomes in learners' routine clinical settings with real patients. Our aim was to assess preceptor perceptions of use of an evaluation instrument in their encounters with medical students. A curriculum for pediatric otoscopy was implemented during the pediatric clerkship. A key outcome measure was use by the preceptor of a pre- and post-intervention checklist. The preceptors, faculty affiliated with a large teaching hospital, were assigned as the student's preceptors for 3 weeks. Preceptors were asked to complete the checklist during routine clinical encounters with real patients before and then following the curriculum intervention, during specific periods. The 12-item checklist adapted from ePROM focused on 5 domains of the pediatric ear exam: discussion with caregiver, equipment, distraction techniques, holding positions, and exam. Preceptors were not able to alter the checklist content. Eight core preceptors participated in this evaluation component. After participation in the study for 17 months, preceptors were asked to complete a web-based 12-item Likert-type survey. 100% of the preceptors completed the survey. 63% of preceptors liked using the checklist with their students and the majority reported the

checklist was easy to implement during clinic time (88%) and was of the appropriate length (100%). While 50% of preceptors reported that their method of performing otoscopy varied from that described in the checklist, use of the checklist did not interfere with their teaching style (100%) or with patient care (100%). 25% of preceptors reported checklist use interfered with their clinic flow and efficiency. Checklist use enhanced the teaching experience (50%) and encouraged greater preceptor observation of students (63%). 88% of preceptors recognized potential for similar checklist use for other clinical topics including the neurological exam and focused musculoskeletal exams. Preceptors perceived that use of an evaluation tool in students' routine clinical encounters with real patients enhanced their teaching experience and did not interfere with patient care. Similar efforts to systematize evaluation of medical student and resident performance in real clinical settings by their preceptors should be considered for other clinical areas.

SESSION DATE & TIME: Wednesday, May 11, 2011, 12:00 pm – 2:00 pm

EVALUATION OF A PEDIATRIC OTOSCOPY CURRICULUM

Caroline R. Paul, MD; Craig L. Gjerde, PhD; Gwen C. McIntosh, MD, MPH; Lori Weber, MD

Competency in pediatric otoscopy is critical to the diagnosis of acute otitis media. Acquiring this skill should begin in the clinical years. Our aim was to evaluate a curriculum in pediatric otoscopy for 3rd year medical students. A curriculum was implemented in a pediatric clerkship. Objectives focused on the approach to the ear exam and tympanic membrane findings. The instructional strategy was a 2 hour practical lab. After demonstrating a skill checklist (24 points), the lab instructor had students practice skills on themselves and on mannequins and gave facilitated feedback. Pre- and post-intervention written tests (25 points) assessed gains in knowledge and skill. The intervention was completed on 101 consecutive students. A subset of 41 students already assigned to clinic sites performed ear exams on their patients. Their preceptors assessed their skills as per the checklist before and after the lab. Students in the intervention group (IG) also completed a survey. A non-intervention group (NIG) (n=10) received the same pre- and post-intervention measures. Paired t-tests were used to compare pre- and post-intervention scores on both written tests and checklists. ANCOVA tests were used to compare differences between the IG and NIG. Pre-intervention written test scores were similar ($p=0.67$) for the IG and NIG. There were significant differences between the pre- and post- written test scores for both groups. (IG mean pre 12.9, mean post 22.6; $p<0.001$, NIG mean pre 12.9, mean post 14.4; $p=0.03$). Gain scores were significantly higher ($p<0.001$) in the IG than the NIG (mean gain 9.7 IG, mean gain 2.9 NIG). Pre-intervention checklist scores were similar ($p=0.07$) for the IG and NIG. There was a significant difference ($p<0.001$) between the pre- and post-scores on the checklist for the IG (mean pre 10.9, mean post 19.2; $p<0.001$) and no difference for the NIG (mean pre 8.2, mean post 11.3; $p=0.13$). Gain scores were significantly higher ($p=0.004$) in the IG than the NIG (mean gain of 8.3 for IG, 2.9 for NIG). 90% of the IG desired to have their clinic preceptors observe their otoscopic skills, following the lab. Students who received this curriculum demonstrated gains in knowledge and skill including skill observed with real patients. This curriculum can be adapted for other learner groups. Its instructional strategy and outcome measures involving real patients and clinical settings can be generalized to other topics.

SESSION DATE & TIME: Wednesday, May 11, 2011, 12:00 pm – 2:00 pm

SOCIAL NETWORKING SITES AND GLOBAL HEALTH ELECTIVES: A RECIPE FOR DISASTER OR AN OPPORTUNITY FOR EDUCATION

Erin L Turner, MD¹ and Sabrina M Wagner, MD¹. ¹Pediatrics, University of Wisconsin

Background: During the same period of time that Web 2.0 use has been blossoming, interest in participating in global health electives by health professionals and trainees has grown. While institutions have increased the availability of global health experiences for learners, there is an urgent need to

create best practices for global health education and formalize preparatory training.

Objective: To characterize the perceptions and use of social networking sites among trainees participating in global health electives, determine whether these can be modified via a targeted educational intervention and describe how trainees' actual practices during global health field experiences differ from their previously stated plans.

Design/Methods: We surveyed medical and pharmacy students and residents planning global health electives about their knowledge, attitudes and behaviors related to social networking sites (Facebook, blogs, photo sites). We repeated the survey after an educational intervention discussing the implications of public postings while participating in global health work and again following completion of a global health field experience.

Results: Preliminary data of 63 participants suggests the use of Web 2.0 technology is widespread (91% use Facebook and post photos online and 87% are familiar with blogs). While about 50% of participants initially planned to communicate via Facebook postings, data collected after the educational intervention revealed significant ($p < 0.05$) differences in planned practices during upcoming trips, including being less likely to post photos online (18% down from 54%) and about half as likely to post updates to Facebook. This effect persisted; most participants chose to communicate via email or phone during their elective and no one reported using blogs.

Conclusions: With the advent of online social networking forums and the expanse of global health experiences at the professional school level, it is imperative we begin asking how these two intersect. It is inevitable that information shared via the internet is seen by a global community and that a single inappropriate post has the potential to undermine global partnerships and have devastating long-term consequences. Challenging trainees to critically examine their preconceived notions regarding ethics in global health work and initiating change in their behavior is vitally important and may be as simple as starting the discussion through education.

SESSION DATE & TIME: Tuesday, May 3, 2011, 10:00 am – 2:00 pm

PAS/ASPR Oral Presentations/Workshops
April 30 – May 3, 2011
Denver, Colorado

GH Treatment and Enhancement: Clinical and Historical Perspective

David B. Allen, MD
Sunday, May 1, 8:00 AM

Presidential Lecture: Lessons Learned from the hGH Era

David B. Allen, MD
Sunday, May 1, 1:20 PM

Are IRBs Seriously Outmoded? Yes. (Debate with Doug Diekema MD MPH)

Norman Fost MD MPH
Monday, May 2, 12:00-1:30pm, Korbel 4E

USE OF SYNTENY CONVERSION IN IDENTIFICATION OF CANDIDATE GENES FOR CONGENITAL MALFORMATIONS IN HUMANS

Philip Giampietro, MD PhD¹, Denis Larkin, PhD², Robert Blank, MD PhD¹, Cathy Raggio, MD³ and Haris Lewin, PhD². ¹University of Wisconsin, Madison, Wisconsin, United States; ²University of Illinois, Urbana-Champaign, United States and ³Hospital for Special Surgery, New York, New York, United States.

Background: The majority of information regarding genes contributing to vertebral development has been obtained from the study of non-human organisms. Applying this information to study genetic causes associated with vertebral development assumes that somitogenesis is conserved across species. One means of assessing the validity of this assumption is using synteny block analysis. This methodology compares the distribution of genes across species between homologous syteny blocks and breakpoint regions. Genes that are evolutionarily conserved tend to lie within synteny blocks. Genes which lie within breakpoint regions are associated with rapid evolution.

Objective: We hypothesized that vertebral developmental genes are conserved in amniotes and their location is within stable or "synteny conserved" regions of chromosomes.

Design/Methods: 78 patterning genes involved in FGF, Wnt and Notch signaling pathways were analyzed in order to determine their location within synteny blocks or evolutionary breakpoint regions in the genomes of several amniotic species including (human, chimp, macaque, mouse, rat, dog, pig, opossum and chicken). The human genome was divided into 1 Mbp intervals and a comparison was made to determine whether these genes were preferentially localized within homologous synteny blocks or breakpoint regions, which are associated with rapid evolution.

Results: The results indicate that genes associated with vertebral development in humans are preferably located away from the evolutionary breakpoint intervals, 0.017 genes in breakpoint intervals on genome average vs. 0.030 on average in other parts of the genome (t test P-value = 0.038). Examination of large blocks of 7 homologous synteny >16.3 Mbp in human coordinates) demonstrated 0.04 genes from the 78 genes studied are positioned on synteny blocks on genome average while 0.03 genes on average are situated on the rest of the genome.

Conclusions: The concentration of vertebral patterning genes in synteny blocks as opposed to evolutionary breakpoint intervals provides evidence that developmental pathways involved in vertebral morphogenesis are likely conserved across amniotes, which is consistent with their known function. These genes represent excellent candidates for the utilization of next generation sequence technologies to identify sequence variants contributing to the development of congenital vertebral malformations.

SESSION DATE & TIME: Monday, May 2, 2011, 3:30 pm – 5:30 pm

Obtaining High-Quality Pediatric Evidence for Use in Practice and Teaching

Leader: John G. Frohna, Co-Leaders: Jonathan E. Fliegel, Dawn Ebach

Target Audience: Students/residents/fellows and faculty interested in expanding their use of evidence in patient care and teaching.

Objectives:

- Describe the Evidence-Based Medicine information cycle and list strategies for integrating it into your teaching
- Identify high-quality information resources for acquiring evidence
- Appraise the quality of different sources of evidence for use at the point of care
- Describe resources available for teachers of EBM

Practicing evidence-based medicine (EBM) is essential for lifelong learning and critical thinking among pediatricians, both those in training and in practice. Despite the proliferation of evidence resources, being able to identify, evaluate, and apply that evidence at the point of care is not always straightforward. Participants will work in small groups to identify the most useful evidence sources to address common clinical scenarios in inpatient or outpatient settings. They will work together to evaluate the quality of the evidence and discuss ways in which this evidence could be applied in patient care at the point of care. The session will conclude with a participant-generated discussion of useful pearls for finding the best evidence for the practice and teaching of EBM in different settings, facilitated by presenters who use and teach EBM in multiple venues. Participants will receive EBM curricular materials and a list of resources that can foster the efficient use of evidence. Whether you are a novice or an expert, as a participant in this workshop you can expect to participate actively, gain additional resources, and leave with new ideas for using and applying evidence in practice.

SESSION DATE & TIME: WORKSHOP, Saturday, April 30, 2011 Room 502

TRENDS IN BLOOD LEAD LEVELS AMONG WISCONSIN CHILDREN: DEVELOPMENT OF A LEAD POISONING NOMOGRAM

Mateusz Karwowski, MD; Jeffrey Havlena, MS; Marjorie Coons, MS

Background: Wisconsin ranks 2nd among Midwestern states for lead poisoning (≥ 10 mcg/dL) in children up to age 6 years: 2.6% statewide, 6.1% in Milwaukee. Of those who undergo blood lead level (BLL) testing, the proportion with lead poisoning is greatest in 30- \leq 42 month-olds (m/o), yet 4 times as many 12- \leq 24 m/o are tested. Tests performed at an early age may be falsely reassuring, leading to less testing of high-risk older children.

Objectives: To describe lead poisoning among 30- \leq 71 m/o WI children, determine risk factors (RF), and construct a validated model to guide BLL testing in this age group. **Methods:** BLL data from 1996- \leq 2004 were compiled retrospectively from a comprehensive statewide surveillance database. Inclusion criteria were children aged 30- \leq 71 months who either had no previous BLL test or no BLL ≥ 10 mcg/dL, yielding data on 23,500 children. The dataset was randomly split: approximately 80% for model development and 20% for validation. With child as the unit of analysis, repeated measures multivariate analysis was performed.

Results: The proportion of 30- \leq 71 m/o children found to have lead poisoning was 1.8% statewide and 3.4% in Milwaukee. Those with at least one normal BLL before age 30 months were less likely to be poisoned than those with no testing history (odds ratio: 0.30; 95% confidence interval: 0.27- \leq 0.33). For children with no testing history, RF were: sibling history of poisoning (3.3; 2.8- \leq 3.9), race/ethnicity (1.6; 1.5- \leq 1.7), and mean Neighborhood BLL (1.5; 1.4- \leq 1.6). For children with a history of normal BLL, RF were: socioeconomic status (2.0; 1.4- \leq 2.9), sibling history of poisoning (1.6; 1.3- \leq 1.9), race/ethnicity (1.3; 1.2- \leq 1.4), mean neighborhood BLL (1.2; 1.2- \leq 1.3), and highest previous BLL (1.2; 1.15- \leq 1.21); number of previous tests was protective (0.59; 0.53- \leq 0.66). Age at first test and time since first test were not significant. Using the validation data, the predictive model has an area under

the receiver operating characteristic curve of 0.79-°@-0.8 statewide and 0.74-°@-0.76 for Milwaukee.

Conclusions: Lead poisoning remains a significant concern for 30-°@-71 m/o Wisconsin children. After accounting for known risk factors, children who have not had a normal BLL before age 30 months are more than 3 times as likely to be poisoned as those who have. These two groups have unique risk factors that guide model development. Using validated models, healthy 30-°@-71 m/o children at high risk for poisoning can be identified for targeted BLL testing.

SESSION DATE & TIME: Saturday, April 30, 2011, 8:00 am – 10:00 am

ROOM: 4C (Colorado Convention Center)

PRESENTATION TIME: 8:30 am

Maternal Obesity at Delivery: A Risk Factor for Newborn Iron Deficiency

ALYSSA PHILLIPS^{ab}; SHEILA ROY^a; BETH FISCHER^d; SHARON BLOHOWIAK^{ab}; CHRISTOPHER COE^c; PAMELA KLING^{ab}, ^aSchool of Medicine & Public Health, ^bDept of Pediatrics, ^cHarlow Ctr for Biological Psychology, ^dU of Wisconsin and ^dZane State University

Background: Obesity, a risk factor for poor iron status in non-gravid adults, impacts 50% of US women of childbearing age. Obesity-related inflammation impedes intestinal iron transport, increasing risk for iron deficiency anemia (IDA). In late pregnancy, iron needs increase 4-fold. The placenta uses the same iron transporters as intestine, but the effects of maternal obesity on fetal iron are unknown. **Objective:**

Because obesity may impair placental iron transport, we examined the effect of maternal obesity on newborn iron status. **Methods:** In a study of newborn IDA, cord zinc protoporphyrin/heme (ZnPP/H), reticulocyte-enriched (RE) and DZnPP/H were used as sensitive indices of iron. Cord C-reactive protein (CRP) indexed neonatal inflammation. Maternal body mass index (BMI) was calculated as weight (kg)/length² (m²). BMI ≥30kg/m² defined maternal obesity. **Results:** After informed consent, a total of 281 mothers/newborn pairs were studied. Higher RE ZnPP/H and DZnPP/H were seen with a pre-delivery BMI ≥30 vs. lower BMI (p<0.05). Pre-delivery BMI and RE ZnPP/H exhibited a weak direct linear relationship (R=0.14, p<0.05). Maternal IDA in pregnancy was similar with obesity vs. non, and RE ZnPP/H was not elevated by maternal IDA. No relationship was observed between pre-delivery BMI, washed cord ZnPP/H and cord CRP. Diabetes was more common with obesity (p<0.05), but subset analysis of obese women revealed RE ZnPP/H was not higher in those with diagnosed diabetes vs. not.

Conclusions: This study is the first to observe a link between maternal obesity and impaired neonatal iron status, a vital finding due to the prevalence of obesity. Our results support a reduction in late pregnancy iron transfer when iron needs are highest. It is unlikely that maternal IDA accounted for the impaired fetal iron acquisition, as offspring of anemic mothers did not exhibit abnormal RE ZnPP/H, possibly due to prenatal iron supplementation. Fetoplacental inflammation was also not the likely mediator because cord blood CRP was not elevated with maternal obesity. Maternal inflammation could independently prevent the 4-fold increase of iron required to meet fetal needs, but maternal blood was unavailable. Although diabetes is known to interfere with fetal iron status, our findings suggest diabetes does not fully explain the poorer cord iron status in obesity. These relationships were previously unrecognized and further research is required to determine the full impact of maternal obesity on infant wellbeing.

SESSION DATE & TIME: Saturday, April 30, 2011, 10:30 am - 12:30 pm

ROOM: Korbel 4B (Colorado Convention Center)

PRESENTATION TIME: 12:15 pm

Also presenting posters at: WAPC and ERP in April

Fatty Liver Disease in Overweight Adolescent Girls Measured with Quantitative MRI and MR Spectroscopy

Jennifer L. Rehm, Ellen L. Connor, Scott B. Reeder, Vanessa A. Curtis¹, Aaron L. Carrel, Catherine DG Hines, David B. Allen

Background: The prevalence of non-alcoholic fatty liver disease (NAFLD) ranges from 28-38% in overweight children and is anticipated to become the leading cause of liver failure. Traditional NAFLD screening, (ultrasound or liver enzymes) misses early changes. For early diagnosis and intervention, a feasible, noninvasive method to detect the presence and severity of NAFLD is needed.

Objective: Assess prevalence and severity of NAFLD in overweight adolescent girls and demonstrate the accuracy and feasibility of novel, non-invasive quantitative MRI fat fraction (MR FF) compared to MR spectroscopy (MRS) for early diagnosis and quantitative grading of NAFLD.

Design/Methods: Cross-sectional study of 24 girls (mean BMI 30.9 ± 1.9 , mean age 13.5 ± 2 , 75% non-Caucasian). Fasting blood samples analyzed for glucose, insulin, lipids, ALT & AST. BMI, hip & waist circumference and BP were measured. MRI was performed on a clinical 3T scanner using an investigational water-fat separation method (3D-IDEAL-SPGR). Single voxel MRS and fat-water separation over the liver was analyzed.

Results: Prevalence of hepatic steatosis (MR FF $>5.6\%$) was 28%. Hepatic MRS and MR FF demonstrated excellent agreement ($r^2=0.98$). See Figure 1 for correlations.

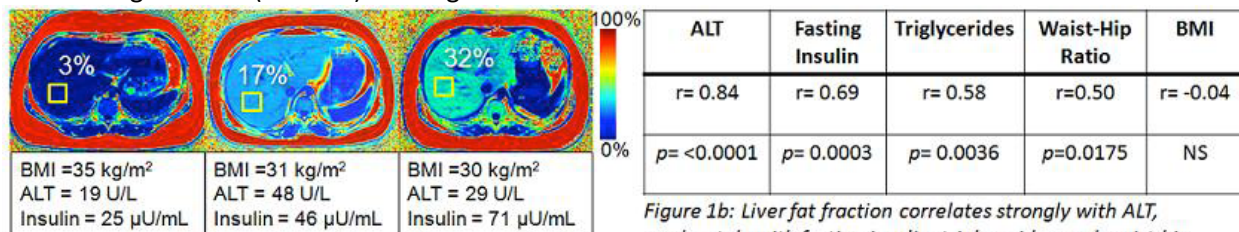


Figure 1a: Representative studies of low, moderate and high liver fat fraction and associated lab and anthropomorphic measures.

Figure 1b: Liver fat fraction correlates strongly with ALT, moderately with fasting insulin, triglycerides, and waist-hip ratio, but not with BMI.

Conclusions: NAFLD is common in overweight girls, and BMI alone does not predict risk. While ALT levels correlated strongly with fat fraction, they were in normal range in all but one patient and were not a sensitive indicator of early NAFLD. MR FF is a feasible and accurate measure of NAFLD in overweight adolescents and correlates with metabolic risk factors (insulin resistance, low HDL, and elevated triglycerides) and waist-hip ratio. This novel MRI technique is superior to traditional indicators of NAFLD and offers promise for evaluating treatments for NAFLD in obese adolescents.

Acknowledgements: NIH (R01 DK083380, R01 DK088925, RC1 EB010384 T32 DK077586-01), Genentech Center for Clinical Research, and the Endocrine Fellows Foundation

PRESENTATION TIME: PES Presidents Reception, Saturday, April 30, 3:45 Korbel Ball Room 4B

MixL1 Expression Identifies Putative Hematopoietic Stem Cells in the Murine Allantois

Adam D Wolfe, MD/PhD¹ and Karen M Downs, PhD².

Background: MixL1, a homeodomain transcription factor, is implicated in pre-hematopoietic commitment of stem cells. In human lymphoma and leukemia lines, MixL1 is inappropriately expressed (Drakos et al., Human Pathol 2007:38:500). When over-expressed in mice, MixL1 is sufficient to induce acute myeloid leukemia (Glaser et al., PNAS 2006:103:16460). Thus, MixL1 may guide cells to remain poorly differentiated rather than proceeding to hematopoietic stem cell identity. The mouse allantois, which will form the umbilical cord, exhibits hematopoietic potential (Ziegler et al., Development 2006:133:4183). It has recently been demonstrated to contain a core of stem cells, the Allantoic Core Domain (ACD), where cells involved in placental hematopoiesis are thought to originate (Downs et al., Dev Dyn 2009:238:532).

Objective: We set out to evaluate MixL1 expression in the allantois, and to establish its precise spatiotemporal whereabouts with respect to an early marker of hematopoiesis, Runx1 (Chen et al., Nature 2009:457:887).

Design/Methods: MixL1 expression was evaluated by immunohistochemistry. MixL1 coexpression with Runx1 was evaluated by immunostaining specimens from the LacZ/Runx1 reporter mouse (North et al., Development 1999:126:2563).

Results: During early development, MixL1 is expressed in yolk sac blood islands and in a posterior embryonic domain that includes the ACD. Allantoic MixL1 expression temporally precedes that of Runx1. As development proceeds, MixL1 becomes prominent in nascent blood cells budding off from the vessel common to the allantois, yolk sac and dorsal aortae (DA), which we have called the "Vessel of Confluence" (VOC), and from which the umbilical artery (UA) arises. There are two additional domains of MixL1 expression in tailbud mesoderm adjacent to sites of vascular anastomosis: the site of joining of vitelline arteries of the yolk sac to form the omphalomesenteric artery (OMA) at the ventral midline; and surrounding the VOC at the site of origin of the UA.

Conclusions: We have shown that MixL1, which is implicated in leukemogenesis, is expressed within the allantois and nascent blood cells. MixL1 may identify one of the earliest hematopoietic precursor populations thus far known in mammals. Tailbud MixL1 expression is also temporally and spatially coincident with major arterial anastomoses, suggesting a role in vasculogenesis. These data provide additional evidence that the allantois is a promising and accessible model system for the study of definitive hematopoiesis.

SESSION DATE & TIME: Saturday, April 30, 2011, 10:30 am - 12:30 pm

ROOM: Korbel 4F (Colorado Convention Center)

PRESENTATION TIME: 11:15 am

Presentations – Other Spring Meetings

Chest CT Scores of Severity Predict Future Lung Disease Progression in Children with CF

DB Sanders, Z Li, AS Brody, L Broderick, J Collins, PM Farrell

Rationale: The majority of children with cystic fibrosis (CF) have normal pulmonary function tests (PFTs) well into adolescence, although eventually lung disease progression invariably occurs. Chest CT has been shown to detect abnormalities even in children with CF with normal PFTs. Whether Brody chest CT scores of severity are associated with future lung disease progression in children with generally mild lung disease has not been previously assessed.

Methods: The Wisconsin Randomized Clinical Trial of CF Newborn Screening (WI RCT) is a prospective, longitudinal study of the effect of early diagnosis through newborn screening on children with CF. A chest CT was performed during a period of clinical stability on 82 children (mean age 11.5 years, range 6-17 years) enrolled in the WI RCT. Brody scores of severity were determined by two independent reviewers. Univariate linear regression was used to determine associations between Brody scores of severity and the most recent (i.e., age 21, or 6/30/2010, whichever was later) measures of CF lung disease: PFTs, RV/TLC, Wisconsin chest x-ray score (WCXR, range 0-100, a score > 5 indicates irreversible changes), Brasfield chest x-ray score (BCXR, range 4-25, scores < 21 indicate irreversible changes), and infection with *P. aeruginosa*. Data within 2 years of the chest CT was excluded.

Results: Study participant characteristics at the time of the chest CT included: 41% female, 57% homozygous F508del, 84% pancreatic insufficient, 24% history of meconium ileus, mean FEV₁ 91% predicted, mean WCXR 14.9, mean BCXR 18.8, and 48% with a respiratory culture positive for *P. aeruginosa* within the prior year. The median Brody chest CT score was 2.0 (range 0-12.8), indicating generally mild abnormalities. Follow up data was available for a mean of 5.6 years (range, 2-10 years). Mean age at follow up was 19.0 (SD 2.0) years. The table details the linear regression estimates of differences in the most recent lung disease measures associated with a unit change in Brody chest CT score. Chest CT score was more strongly predictive of measures of disease progression than FEV₁, RV/TLC, *P. aeruginosa*, BCXR, or WCXR obtained at the time of the chest CT.

Conclusions: Brody chest CT scores of severity are significantly associated with measures of progression of CF lung disease in children with mild lung disease at the time of the chest CT. Chest CT has added value in predicting which children with CF with mild lung disease may develop more progressive lung disease.

Regression estimates of group mean differences in most recent lung disease measures associated with a unit change in Brody chest CT score

Lung disease measure	Parameter estimate	SE	P-value
FEV ₁ (% predicted)	-4.33	0.68	<0.001
FEF ₂₅₋₇₅ (% predicted)	-6.01	1.08	<0.001
RV/TLC	2.54	0.35	<0.001
<i>P. aeruginosa</i>	0.05	0.02	0.004
WCXR	3.38	0.47	<0.001
BCXR	-0.91	0.11	<0.001

Funding: ARRA

Oral Presentation - ATS

Endoplasmic reticulum stress regulates the transcription factor IRF3 and synergistically induces IFN- β during oxygen-glucose deprivation

Judith A. Smith¹, Austin Tian¹, Ling Zeng¹, Delia Gutman², Glen N. Barber², Yi-Ping Liu¹

Following hepatic ischemia, a gadolinium-sensitive phagocyte, most likely the Kupffer cell, plays a critical role in mediating inflammatory reperfusion injury. TLR4 induced Type I IFNs have also been implicated. We had previously shown that pharmacologic ER stress inducers and LPS synergistically induce IFN- β in macrophages and together increase IRF3 recruitment to the IFN- β promoter. In this study we found that RAW264.7 macrophages undergoing oxygen glucose deprivation produce greatly increase IFN- β mRNA in response to LPS compared to non-stressed cells. *In vivo*, 6h post-reperfusion, IFN- β was observed surrounding the hepatic central veins. IFN- β -/- mice were partially protected from ischemia reperfusion injury as determined by serum ALT. *In vitro*, treatment of murine embryonic fibroblasts with the ER stress inducers thapsigargin (Tpg), tunicamycin, and DTT, as well as oxygen-glucose deprivation resulted in IRF3 phosphorylation and nuclear translocation. Tpg treatment triggered the relocalization of TBK1 into a cluster with STING, and Tpg-induced IRF3 phosphorylation was dependent upon STING. Synergistic IFN- β induction by Tpg and LPS stimulation was markedly diminished in STING-/- MEFs and by STING RNAi in RAW 264.7 cells. Thus ER stress may activate IRF3 through TBK1 family kinases by mobilizing ER-resident infection sensing molecules such as STING. Together these data support the hypothesis that ischemia-induced ER stress contributes to reperfusion injury through activation of IRF3 and synergistic IFN- β induction.

Accepted: AAI/oral presentation and poster presentation

Bim is Responsible for the Inherent Sensitivity of the Developing Retinal Vasculature to Hyperoxia

Christine M. Sorenson^{1,2*}, Shoujian Wang³, SunYoung Park³, and Ping Fei³

Departments of ¹UW Eye Research Institute, ²Pediatrics and ³Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, Madison, WI 53792

Purpose: To determine the impact of bim deficiency on postnatal retinal vascularization, as well as retinal neovascularization during oxygen-induced ischemic retinopathy (OIR) and laser-induced choroidal neovascularization. **Methods:** We examined retinal vascularization during normal development, OIR and choroidal neovascularization using wholemount immunostaining. Apoptosis was monitored by TUNEL analysis. **Results:** Loss of bim expression was associated with increased retinal vascular density in mature animals. This was mainly attributed to increased numbers of pericytes and endothelial cells. However, the initial spread of the superficial layer of retinal vasculature and, the appearance and density of the tip cells were similar in bim +/+ and bim -/- mice. In addition, hyaloid vessel regression was attenuated in the absence of bim. Furthermore, in the absence of bim retinal vessel obliteration and neovascularization did not occur during OIR. Instead, normal inner retinal vascularization proceeded independent of changes in oxygen levels. In contrast, choroidal neovascularization occurred equally well in bim +/+ and bim -/- mice. **Conclusion:** Together our data suggest bim expression is responsible for the inherent sensitivity of the developing retinal vasculature to changes in oxygen levels, and promotes vessel obliteration in response to hyperoxia.

Poster Presentation at ARVO's 2011 Annual Meeting, Visionary Genomics, May 1-5, 2011, in Fort Lauderdale, Florida.

POSTER PRESENTATION

ABSTRACT TITLE: Gender Dependent Interplay of Iron and Lead in Newborns At-Risk for Iron Deficiency

FIRST AUTHOR: Patrick Halbach

SESSION DATE & TIME: Sunday, May 1, 2011, 4:15 pm - 7:30 pm

POSTER PRESENTATION

ABSTRACT TITLE: The Impact of Erythropoietin on Brain Growth and Development in Newborn Rats with Impaired Iron Status

FIRST AUTHOR: Karen Flores

SESSION DATE & TIME: Tuesday, May 3, 2011, 10:00 am - 2:00 pm

Human Kir7.1 Channel Mutation (R162W), Associated With Snowflake Vitreoretinal Degeneration (SVD), Renders Non-functional Channel due to a Dominant-Negative Effect.

De-Ann M. Pillers^{1A}, Sara Tokarz^{1A}, Matti Asuma^{1A}, Tyler Schroeder^{1A}, James Thoden^{1B}, Anil Sharma², Albert O. Edwards³, Bikash Pattnaik^{1A}.

^ADepartment of Pediatrics, ^BDepartment of Biochemistry, ¹University of Wisconsin-Madison, Madison, WI; ²Experimental Pathology, Mayo Clinic, Rochester, MN; ³Institute for Molecular Biology, University of Oregon, Eugene, OR.

Purpose: Mutations in the KCNJ13 gene impair the function of the Retinal Pigment Epithelial Kir7.1 channel and are associated with an autosomal dominant disorder SVD that causes degeneration of multiple ocular tissues. We previously showed that the mutation results in a non-functional channel. In this work we test our hypothesis that the mutant channel alters the function of wild-type protein through a dominant negative effect.

Methods: Fusion clones of wild-type (eGFP-hKir7.1, WT) and mutant (mCherry-hKir7.1M, M) were generated. K⁺ current due to WT, M or both transfected in CHO cells were studied by whole-cell patch-clamp electrophysiology. Protein localization in transfected cells were detected by live cell imaging. We used recently published molecular structure to determine alterations in M proteins. Total protein from transfected CHO cells was used for western blot analysis of Kir7.1 and β actin antibodies.

Results: Cells expressing WT channel had a membrane potential of -64 ± 2.4 mV (n=9) compared to -12 ± 2.1 mV (n=18) for the M and -34 ± 4.2 mV for WT+M expressing cells (p<0.005). Current-voltage curves for the WT was typical with a preference for Rb⁺ (WT: 9.2 ± 0.7 , M: 1.4 ± 0.4 , WT + M: 4 ± 1.5 fold increase). The WT localized to the membrane while the M was visible throughout the cell. Substitution of arginine to tryptophan results in a stiff C-linker domain in the protein structure. Mutant protein expression was less than the WT.

Conclusions: hKir7.1WT expression in CHO cells results in a highly selective current while the mutant did not exhibit any functional channels. The mutation alters the conserved C-linker domain and perhaps alters electrostatic interactions necessary for channel function and selectivity. The mutant channel makes the WT non-functional due to a dominant negative effect. All-in-all, the non-functional Kir7.1 channel may contribute to the classic phenotype of SVD, by distorting RPE transport function and altering RPE physiology.

Poster Presentation: ARVO, May 2011

Characterization of commercially available Human RPE Cell culture from LONZA®.

Bikash R. Pattnaik^{1A}, Fan Yang², Sara Tokarz^{1B}, Simran Brar^{1B}, Matti P. Asuma^{1B}, Marjorie Smithhisler², De-Ann M. Pillers^{1C}.

^APediatrics, Ophthal & Visual Sci, Eye Research Institute, ^BPediatrics, ^CPediatrics, Eye Research Institute, ¹Univ of Wisconsin, Madison, WI; ²LONZA Walkersville Inc., Walkersville, MD.

Purpose: Malfunction of retinal pigment epithelium (RPE) cells distorts the function of neurosensory retina and hence affects our vision. A viable approach to study disease mechanism and RPE physiology is to make available suitable RPE cells in culture which can also be used in gene and transplantation therapy. We have characterized the cryopreserved Clonetics® Human Retinal Pigment Epithelial (hRPE) cells (# 00194987) from LONZA Walkersville Inc.

Methods: Human RPE cells were isolated and cultured using optimized RtEGMTM growth medium BulletKit® (# 00195409). RPE cells were characterized by immunohistochemistry of pancytokeratin, Na+K+ATPase, ZO-1, CD31 and fibroblast marker for cell identity and purity. After the cells formed a tight monolayer with hexagonal morphology, they were enzymatically dispersed and used for electrophysiology analysis using standard whole cell patch-clamp method. RPE specific transcripts were detected by RT-PCR.

Results: Human RPE cells showed pigmented hexagonal monolayer after 4-6 days in culture. These cells expressed Kir7.1, bestrophin, pancytokeratin, Na+K+ATPase and ZO-1 but not endothelial and fibroblast markers. Unlike other RPE cells in culture, most of these cells showed inwardly rectifying K+-current. This current was significantly (4.5 ± 2.3 fold 12 of 12 cells) enhanced by application of Rb+ solution as this is a unique property of the RPE specific Kir7.1 channel. These cells tested positive for RPE specific transcripts.

Conclusions: This study demonstrated that commercially available Clonetics® human RPE cells from LONZA in RtEGMTM medium retain both molecular and electrophysiological phenotypes making them suitable for the study of disease mechanisms involving RPE. They can thus be used for the investigations of age-related macular degeneration, retinitis pigmentosa, determining gene expression profiles of RPE cells and potentially for subsequent transplantation studies.

Poster Presentation – ARVO, May 2011

Photoreceptor- and RPE-like cells derived from human pluripotent stem cells display characteristic responses to small molecule stimulation.

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Purpose: To examine the physiological responses of human pluripotent stem cell (hPSC)-derived retinal cell populations following exposure to selected small molecules.

Methods: Isolated optic vesicle(OV)-stage neurospheres derived from hPSCs were differentiated to photoreceptor(PR)- and/or RPE-like cells using an established protocol. Current responses of individual PR-like cells to applied voltage were recorded in the presence or absence of agonists and antagonists using standard whole-cell and perforated patch-clamp configurations. After recording, cells were backfilled with sulphorhodamine to facilitate identification. To monitor changes in intracellular calcium levels in response to ATP, hPSC-RPE cells were loaded with Fura2AM. Thereafter, fluorescence imaging was performed to obtain time-dependent, agonist-induced measurements of $[Ca^{2+}]_i$.

Results: Differentiating OV neurospheres expressed appropriate gene and/or protein markers, including those involved in phototransduction. PR-like cells demonstrated an outward current at depolarizing

voltages between -50 and +60 mV (holding potential = -70 mV) that was blocked by TEA. These PR-like cells possessed a resting membrane potential of -44 ± 4 mV and a current density of 34 ± 7.5 pA/pF at +40 mV. Upon treatment with membrane-permeable Br-cGMP, PR-like cells underwent depolarization. hPSC-RPE cells also responded to small molecule stimulation, consistently showing a transient increase in $[Ca^{2+}]_i$ after exposure to ATP.

Conclusions: hPSC-derived, PR- and RPE-like cells display important functional properties in vitro. Of particular interest, PR-like cells depolarized in the presence of the phototransduction second messenger cGMP, and RPE cells demonstrated an increase in $[Ca^{2+}]_i$ in response to exogenous ATP, a molecule postulated to govern the RPE light response. The capacity of hPSC-derived retinal progeny to respond to physiological stimuli in vitro extends their utility as tools for basic science and clinical research.

Poster Presentation – ARVO May 2011

UNDERSTANDING BEST'S DISEASE DUE TO BESTROPHIN GENE MUTATIONS

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Background: Age-related macular degenerative diseases (AMDs) are a major cause of blindness around the world. In the retina pigment epithelium (RPE), a Ca^{2+} -activated Cl^- channel was identified and mutations in the gene product known as bestrophin was shown to be the cause of an inherited eye disease named Best's disease (Best's Vitelliform Macular Degeneration). Anions like Cl^- regulate various important cellular events for both excitable and non excitable cells. Although many mutations of the bestrophin ion-channel have been studied so far for their functional alterations leading to disease mechanism, we are interested in studying a recently reported novel mutation in one of the cytoplasmic amino acid.

Objective: The purpose of this project is to create bestrophin mutants and study the structural and functional consequences by ectopic expression in HEK-293 (human embryonic kidney) cells.

Methods: The hBest1 gene in pRK5 mammalian expression vector containing a PIREs and GFP was provided to us by Dr. Jeremy Nathans, Johns Hopkins University. We introduced the required hBest1 gene mutations (N296H and N296S) into this vector through site-directed mutagenesis approach. Both wild-type and mutant bestrophin vectors were prepared, purified, and transiently transfected to HEK293 cells using TransIT-2020.

Results: Amplification of the hBest1 constructs containing N296H and N296S mutations were successful through PCR. The N296H mutation generated a feasible image from transfection into HEK-293 cells displaying PIREs-GFP and expected electrophysiology.

Conclusions: We have successfully generated hBest1 mutants for our further study to determine their role in disease mechanisms.

Poster Presentation – ARVO, May 2011

NON-ALCOHOLIC FATTY LIVER DISEASE IN AN ADOLESCENT WITH POLYCYSTIC OVARY SYNDROME

Jennifer L. Rehm, MD¹, Ellen L. Connor, MD¹, Scott B. Reeder, MD, PhD²

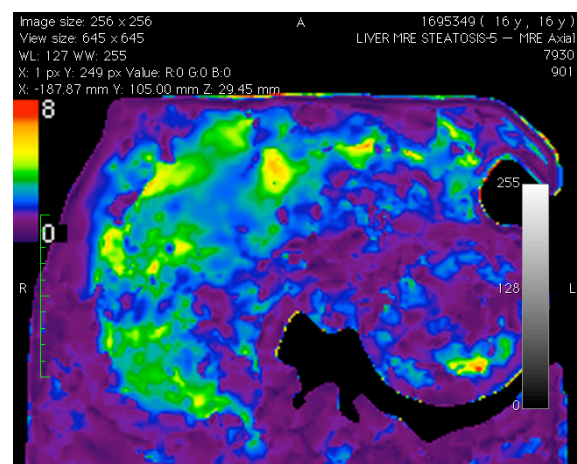
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BACKGROUND: NAFLD (nonalcoholic fatty liver disease) is anticipated to be the leading cause of liver failure in the future. Young women with polycystic ovary syndrome (PCOS), are at an increased risk for NAFLD as a complication of obesity which often accompanies PCOS. This abstract will review a case of NAFLD in an adolescent with PCOS and demonstrate the value of a non-invasive quantitative quick magnetic resonance imaging (MRI) technique for early diagnosis and quantitative grading of hepatic steatosis which may be of benefit to both pediatric and reproductive-aged female patients.

CASE: The patient is a 16-year-old young woman who presented to a multidisciplinary PCOS clinic. Initial history included irregular menses, acne, and hirsutism. Additional history included childhood obesity with significant weight gain at puberty to greater than the 99th percentile, and chronic elevation of hepatic transaminases. Physical exam was notable for a BMI of 44.6, BP 142/69, hirsutism, and acanthosis nigricans. Initial labs demonstrated hyperandrogenism, insulin resistance, and elevated transaminases. A diagnosis of PCOS was made according to the Androgen Excess Society criteria on the basis of oligomenorrhea and clinical and biochemical evidence of hyperandrogenism. The patient was prescribed drospirenone/ethinyl estradiol one tab daily and metformin with a goal dose of 1000 mg twice daily. Liver enzymes were repeated 3 months later and were further elevated with an ALT of 210 u/L and AST of 115 u/L. The following MRI scans were obtained to assess hepatic triglyceride fraction and hepatic elasticity:



IDEAL MR liver fat fraction image shows significant steatosis, estimated at 33% (normal less than 5%)



MR elastography shows mildly increased stiffness of the liver measuring 3.0-3.4 kPa (normal 2.9), suggestive of inflammation or mild fibrosis.

The patient was diagnosed with NAFLD and started on Vitamin E (400 IU BID) in addition to metformin to reduce hepatic insulin resistance and inflammation.

COMMENTS: The prevalence of NAFLD in children ranges from 1.2 to 9.6% worldwide and 28% to 38% in overweight children [1-3]. However, little is known about NAFLD in adolescents with PCOS [4-8]. Insulin resistance (IR) is strongly associated with NAFLD in children [3, 9, 10] and IR is seen in 50-65% of women with PCOS [11-14]. Increased androgen bioavailability in women with PCOS is associated with increased IR [15] as well as an increased prevalence and possible progression of hepatic steatosis [16]. In fact, the prevalence of NAFLD in PCOS has been reported to be between 15-30% versus about 10% in the general population [16-21]. While early NAFLD on imaging may be a reversible condition, there is evidence that

women with PCOS may be more likely to progress to more advanced disease or have more severe disease at diagnosis [18, 22, 23]. A novel MRI technique, which is now commercially available, holds promise as a method of identifying and following the effectiveness of interventions for NAFLD. Quantitative MRI hepatic fat concentration has equivalent accuracy to MR spectroscopy ($r^2=0.99$) but has high spatial resolution over the entire liver [24-26] and provides accurate measures of fat-fraction over a dynamic range of 0-100% [27]. This allows both clinicians and researchers access to liver images that not only provide quantitative information about total hepatic steatosis, but also measure liver elasticity, providing a means of assessing liver fibrosis and progression to NASH or cirrhosis [26].

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CASE Study NASPAG - 4/15/2011

FATTY LIVER DISEASE IN OVERWEIGHT ADOLESCENT GIRLS MEASURED WITH QUANTITATIVE MRI AND MR SPECTROSCOPY

Jennifer L. Rehm, MD¹, Ellen L. Connor, MD¹, Scott B. Reeder, MD, PhD²

Me, V, Cathy, Ellen, Aaron, Dave, Scott

Introduction: The prevalence of non-alcoholic fatty liver disease (NAFLD) in children ranges from 1-10% worldwide and 28% to 38% in overweight children.¹ In fact, NAFLD is anticipated to be the leading cause of liver cirrhosis, failure, and transplant in the future - surpassing alcoholic liver disease, viral hepatitis and liver cancer.² Therefore, early identification of NAFLD is important for intervention and prevention of progression. Unfortunately, traditional methods of detecting fatty liver, such as ultrasound or liver enzyme blood screening, miss early changes. A rapid, clinically relevant, non-invasive method for early detection and staging of NAFLD is urgently needed.^{3,4} In this work, we conducted a feasibility study in overweight, ethnically diverse adolescent girls comparing traditional serum and anthropometric biomarkers of metabolic risk to a non-invasive quantitative method for early diagnosis and quantitative grading of fatty liver disease, using magnetic resonance imaging (MRI).

Methods:

Subjects: This is a cross-sectional study involving 24 overweight/obese, pubertal girls with a mean age of 13.5 years \pm 1.956, 75% non-Caucasian. Subjects were recruited through a local middle-school and pediatric endocrinology clinics.

Anthropometric and Laboratory Measures: Blood was collected on the same day as imaging, for assays of glucose, insulin, lipids (total cholesterol, HDL, LDL, and triglycerides), ALT and AST after an overnight fast. All labs were performed in the same laboratory. Anthropometric measurements included height, weight, hip and waist circumference and blood pressure.

Imaging: Imaging was performed on a clinical 3T scanner (MR750, GE Healthcare, Waukesha, WI) using an investigational version of a chemical shift based water-fat separation method (3D-IDEAL-SPGR) and a 32-channel phased array body coil. Single voxel STEAM spectroscopy and fat-water separation over the liver were acquired. First, single voxel STEAM without water suppression was acquired in the posterior right lobe using the following parameters: TE = 10, 15, 20, 25, 30 ms acquired in a single TR of 3800ms, 2x2x2cm voxel, 1 signal average, 2048 points, and a spectral width of 5000, all acquired in a breath-hold of 23 seconds. Next, an investigational version of a quantitative chemical shift based MRI method (IDEAL) was acquired over the liver using the following parameters: FOV = 44x40cm, first TE/TR = 1.2/8.6ms, echo spacing = 2.0ms, echo train length = 6 (2 shots of 3 echoes), BW = \pm 111kHz, flip = 3° to minimize T1 bias, 8mm slices, 28 slices, and 256x160 matrix. 2D parallel imaging (ARC) with R=2.86 was used to reduce total imaging time to a 23 second breath-hold. An on-line reconstruction algorithm was used to perform T2* correction, spectral modeling and eddy current correction to create quantitative proton density fat-fraction maps over the entire liver. Fat-fraction measurements were made from PDF maps using a 2x2cm² voxel co-localized to the MRS voxel.

Statistics: Associations between fat fraction and other outcomes was examined using Spearman's correlation analysis and linear regression analysis. A two-sided p-value of <0.05 was regarded as significant.

Results: Figure 1 demonstrates excellent agreement between hepatic MR spectroscopy and quantitative MRI hepatic fat concentration. Liver fat fraction correlated strongly with ALT ($r=0.84$, $p<0.0001$), and moderately with fasting insulin ($r=0.69$, $p=0.0003$), triglycerides ($r=0.58$, $p=0.0036$), and waist-hip ratio ($r=0.50$, $p=0.0175$). Mean BMI was elevated at $30.9 \text{ kg/m}^2 \pm 4.162$. However, BMI did not correlate significantly with liver fat fraction. Figure 2 illustrates these correlations in patients with low, moderate, and high liver fat fractions. Prevalence of hepatic steatosis (defined as fat fraction greater than 5.56%) is 28% (7/24) in the girls studied.

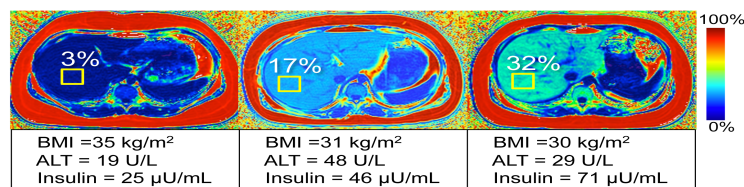
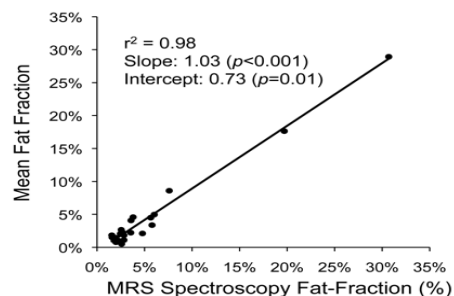


Figure 1: Quantitative MRI methods are equivalent **Figure 2:** Representative studies of low, moderate and high liver fat fraction. Liver fat

Discussion: Quantitative MRI is a feasible and accurate measure of NAFLD in overweight adolescents and correlates with metabolic risk factors including insulin resistance, HDL, triglycerides and waist-hip ratio. In contrast, BMI a common pediatric screening tool, does not offer predictive value of NAFLD risk. While ALT correlates strongly with liver fat fraction, only one of the subjects with NAFLD had an abnormally high ALT. Thus ALT is not a sensitive screening tool for early NAFLD. This novel MRI fat fraction technique offers a strong advantage over traditional measures in identifying NAFLD risk and following the effectiveness of interventions for NAFLD in obese adolescents. Future work will include the use of quantitative MRI to measure change in liver fat in prospective intervention studies

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Poster Presentation at ISMRM, May 2011

ALCOHOL ON UNDERGRADUATE MALES' FACEBOOK PROFILES

Egan KG, Moreno MA

Purpose: Over 90% of college students report alcohol consumption in the past year, and male students are more likely to suffer morbidity and mortality from their alcohol use. Perceived peer alcohol use is a predictor of consumption in college males; frequent references to alcohol on Facebook may encourage alcohol consumption. The purpose of this study was to perform a content analysis of male undergraduates' Facebook profiles for references to alcohol use.

Methods: Facebook profiles of male undergraduate students at a large Midwestern university were identified through a search of public profiles (n=225). Profiles were included if they reported age of 18-22 years old and were currently enrolled undergraduates. Content analysis of Facebook profiles included references to alcohol from the date the profile was formed until date of June 1, 2009. Prevalence was identified and compared by grade and age. The time that each reference occurred was recorded. ANOVA was used to compare means between groups.

Results: Profiles of 225 undergraduate males were evaluated. The average age was 19.9 years, and 68% of profiles belonged to students who were under the legal drinking age of 21 years. Alcohol references were present on 85.3% of profiles; the prevalence of alcohol was similar across each undergraduate grade. The average number of alcohol references per profile was 8.5, but increased with undergraduate year ($p=.003$; CI:1.5-7.5). Students who were of legal drinking age referenced alcohol an average of 4.5 times more than underage students. The majority of profiles displayed references to alcohol only during college (77%), and a large increase in displayed references coincided with beginning college.

Conclusion: Our data showed similar prevalence of alcohol use to existing survey data; alcohol references on Facebook may reflect offline alcohol experiences by college students. The average number of references to alcohol per profile increased with age. This may be due to the upper grades having more students of legal drinking age, or an accumulation of references over time. Facebook alcohol references have a large potential to influence drinking behaviors because of the ubiquitous use of Facebook in the college population. Future research is needed to evaluate the motivation for displaying alcohol references on Facebook.

Sources of Support: This project was supported by an Undergraduate Research Grant from the University of Wisconsin School of Medicine and Public Health and by Award Number K12HD055894 from Eunice Kennedy Shriver National Institute of Child Health and Human Development.
Poster Presentation: SAHM, March 2011

INTERNET SAFETY EDUCATION

Egan KG, Moreno MA

Purpose: The Internet is used by 93% of teens 12-17 years old. The majority of teens have their own computer and maintain a Social Networking Site profile, and one third search for information about health and fitness online. Few resources are available for teaching Internet safety awareness to children and adolescents, and it is unclear who is responsible for this education. Over half of parents report having filtering software on their computers or checking in on their teen online. The purpose of this study was to survey teachers and healthcare providers about current Internet safety education practices and beliefs about Internet safety education.

Methods: Surveys were distributed to teachers and adolescent providers (pediatricians, family practitioners, nurse practitioners) regarding Internet safety education using two venues: a teachers' in-service conference and a regional pediatric conference. Survey questions were tailored for each audience and included questions such as "Do you currently teach students/patients about online safety?" "What age do you feel online safety should be taught?" and "What three topics would be most important to provide information to children or teens about online safety?".

Results: Teachers (n=77) and pediatric clinicians (n=111) completed the survey, 95% response rate. The mean years teaching or in practice was 14.6. There was overall an overwhelming consensus that parents should teach Internet safety (97%). Just under half (46%) of teachers and clinicians report currently advising teens about Internet safety, and 7% plan to begin doing so in the near future. Experience discussing online safety with teens was not related to years of experience as a teacher or clinician. The mean suggested age at which teaching online safety should begin was 7 years; the top three items to include in curriculum were protection of personal information, protection against predators, and evaluation of websites. One third of teachers and clinicians had heard of a student or patient who had either been a victim of cyberbullying or received unwanted online attention from a stranger.

Conclusions: The majority of teachers and clinicians are not teaching adolescents about Internet safety, and most believe this is the responsibility of the parents. It is common for adolescents to discuss negative experiences on the Internet with trusted adults such as teachers and clinicians. Age appropriate programs and resources should be developed to assist parents with educating their children about Internet safety. Further research should investigate parents' beliefs regarding Internet Safety Education.

Sources of Support: This project was supported by Award Number K12HD055894 from Eunice Kennedy Shriver National Institute of Child Health and Human Development

Poster Presentation: SAHM, March 2011

PLEASE 'DRINK RESPONSIBLY': OLDER ADOLESCENTS' RECOLLECTION OF ALCOHOL HEALTH MARKETING MESSAGES

Koff Rosalind, Swanson MJ, Moreno MA.

Purpose: Alcohol advertisements are frequently seen by adolescents and can be influential towards alcohol use. Females are traditionally more influenced by certain types of advertisements, and despite prevention efforts college females continue to be affected by the consequences of dangerous alcohol use. Alcohol health marketing messages (HMM) aim to promote reduced alcohol consumption or abstinence, however it is challenging to create messages which specifically targeting college females that are both memorable and influential. The purpose of this study was to evaluate female college students' recall of alcohol HMM in order to enhance future development of HMM.

Methods: A convenience sample of female undergraduate college students were recruited for focus groups at a large Midwestern university from February to July of 2010. A trained female facilitator asked participants to recall alcohol HMM they had seen and to elaborate on their views of those messages. All tape-recorded data was fully transcribed. Analysis was conducted by three investigators using an iterative process in which all investigators first reviewed transcripts individually and then discussed together to determine consensus on themes.

Results: A total of 43 students participated in 10 focus groups. Two main messages were recalled. First, the majority of groups reported recollection of televised drunk driving HMM which they recalled in detail. Example quotes include: "where the guy gets pulled over and opens up his door and a bunch of wine or something comes pouring out" and "the guy that puts down his window and the olives and vodka spill out." Though memorable, participants in each group mentioned this HMM had little influence on their views of alcohol use, and stated drunk driving messages were more compelling when learned through other sources such as parents or schools. The second message discussed in most groups was not created primarily as an HMM, but a tagline to alcohol commercials stating, "drink responsibly." The use of this line at the conclusion of alcohol commercials was considered humorous and ironic by participants. This message also had little perceived impact, as participants stated, "I notice it, but it doesn't change how I drink."

Conclusion: Current HMM campaigns are memorable but not influential, and the messages embedded within alcohol advertisements were viewed by students as irrelevant. As these visual ads were well-remembered among this at-risk population, future research could aim to understand why these campaigns are memorable yet non-influential. HMM campaigns may consider focusing on topics less targeted by current efforts that are relevant to this population, such as negative social consequences related to excessive drinking.

Poster Presentation: SAHM, March 2011

'Girls' Night Out!': Older Adolescents' "Favorite" Alcohol Advertisements

Koff, Rosalind, Moreno MA

Alcohol advertisements are frequently seen by adolescents and can be influential towards alcohol use. This study investigated female college students' preferences and evaluations of alcohol advertisements. 46 female college students were asked to select and discuss her "favorite" advertisement from a selection of 13 advertisements, and to elaborate their views of these messages during 10 focus groups, which were age-specific. Both freshman and upperclassman groups identified similar favorite advertisements. However, upperclassmen selected dramatically different advertisements when asked to choose the ads that they felt would have been their favorites as freshmen. This study reflects conflicting views of perceived experience and stages of development.

Poster Presentation: URS

Fitness on Facebook: Advertisements Generated in Response to Profile Content

Hope Villiard; Megan Moreno, MD, MPH, MEd

Obesity affects half of college students and only 30% of students obtain adequate physical activity for health benefits. Over 94% of college students currently maintain a Facebook profile; advertisements on Facebook are tailored to the displayed content. The purpose of this project was to determine if fitness key-words generate fitness-related advertisements. Individual profiles were examined to determine types of displayed fitness references; Facebook was explored to observe advertisements generated in response to fitness references. 71.9% of profiles evaluated referenced fitness behaviors; 70.2% referenced physical activity, 12.3% poor diet. Most advertisements were for fad diets or charity runs. Thus, students reference both healthy and unhealthy fitness behaviors on their Facebook profiles, and these trigger fitness-related advertisements of which few are healthy.

Poster Presentation: SAHM, March 2011

DRINKING TO MAKE FRIENDS: A MIXED METHODS APPROACH TO EXPLORING THE LINKS BETWEEN ALCOHOL USE AND SOCIAL MOTIVES IN COLLEGE FRESHMEN

Grant Allison M, Brown, B, Kacvinsky, L, Moreno, M.

Purpose: Freshman year in college is a high-risk time for binge drinking. Freshmen often report social motives for drinking, but it is unclear whether alcohol use actually facilitates new friendships. This study aimed to explore alcohol use patterns in relation to both friendship creation strategies (FCS) and number of new friends among college freshmen.

Methods: Data were collected from college freshmen at a large state university via an interview assessing (1) 28-day alcohol use via the Time Line Follow Back (TLFB) method, (2) strategies of friendship creation via an open-ended question asking how participants made friends on campus, and (3) self-reported number of new *casual* and *close* friends on campus. All tape-recorded data were fully transcribed. Analysis was conducted by three trained investigators using an iterative process in which all investigators first reviewed transcripts individually and then discussed together to determine consensus on strategies of friendship creation. Using TLFB data, we developed three alcohol use *categories*: abstainers, social drinkers (no binge drinking in previous 28 days) and binge drinkers (at least one binge

drinking episode). We used ANOVAs to determine if alcohol use category was associated with FCS or average number of casual and close friends.

Results: Overall, 60 freshmen participated (68.9% response rate), and 60% were female. Alcohol use categories included 7 (12%) abstainers, 15 (25%) social drinkers and 38 (63%) binge drinkers. The most commonly reported FCS were through “dorms” (15 nominations), “drinking” (14 nominations) and “classes” (12 nominations). Alcohol use categories were significantly related to “drinking” as an FCS ($F=3.748$, $p=.03$). Notably, binge drinkers made up 13 of the 14 nominations for this FCS. The average number of casual and close friends was 20.9 ($SD=14.9$) and 6.6 ($SD=3.5$), respectively. Alcohol use categories were significantly related to the number of casual friendships participants reported ($F=4.63$, $p=0.014$). Social drinkers reported the highest number of casual friends (mean= 26.3, 95% CI = 18.3- 34.3), followed by binge drinkers (mean= 21.4, 95% CI = 16.5- 26.3), and then abstainers (mean= 6.9, 95% CI = .9- 12.96). No significant differences were found in the number of close friendships across alcohol use categories.

Conclusion: Binge drinkers were more likely to report using alcohol as a means to make friends, however social drinkers reported similar numbers of casual friends. Additionally, there were no differences in close friendships across alcohol use categories. Future binge drinking prevention campaigns could consider addressing social motives (e.g. drinking to make friends) for alcohol use in college freshmen. Specifically, freshmen can be taught that binge drinking is not a necessary means for friendship creation.

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Poster Presentation: SAHM, March 2011