ISOLATED WORKING HEARTS OF OFFSPRING OF DIABETIC RATS DEMONSTRATE PHYSIOLOGIC DIFFERENCES IN RESPONSE TO ISCHEMIA/REPERFUSION INJURY

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Infants of diabetic mothers are known to be at an increased risk of congenital heart disease and increased rates of asymmetric cardiac hypertrophy. Currently, it is unknown whether the intrauterine environment created by gestational diabetes may have lasting effects on cardiac function in hearts that are presumed “normal” from birth or have resolved hypertrophy. We hypothesized that being an offspring of a diabetic mother (ODM) would have negative long term sequelae on cardiovascular function. Pregnant rats were injected with either 50 mg/kg streptozotocin or buffer on day 12 of gestation (p0) to induce diabetes, and had their glucose levels controlled by twice daily insulin given on a sliding scale. All offspring were fostered by healthy dams. At 10 months of age, hearts were studied in an isolated, working heart preparation with a 30 minute ischemia and 2.5 hour reperfusion period. Rate pressure product (RPP) (left ventricular developed pressure x heart rate; bpm*mmHg), maximum generated pressure in change per time (max dp/dT; mmHg/s), systolic function, and minimum generated change in pressure per time (min dp/dT; mmHg/s) was measured. A statistically significant association was observed between ABCG2 (rs7699188) and protection against GI side effects (2-sided Fisher’s Exact Test p = 1.00E-05); the association remained significant (p = 0.023); the association remained significant (p = 0.023). Associations between genotype and outcome was performed using Chi-square analysis or Fisher’s exact test and, where applicable, logistic regression controlling for NSAID and TNF use. Outcomes measured included: the presence of active joints, GI toxicity, and LFT abnormality. Results: Forty-seven subjects with JIA were enrolled. Allele frequencies for all 15 genes validated were in Hardy Weinberg equilibrium. Genotype frequencies between MTX responders (no active joint involvement) and non-responders (1 or more active joints) were compared. A similar analysis was conducted for toxicity endpoints. The only significant association was between ABCG2 +5994 C>T (rs698188) and protection against GI side effects (2-sided Fisher’s Exact Test p = 0.023); the association remained significant (p = 0.041) after controlling for concurrent medication use (NSAID/TNF) with logistic regression. Due to the large number of comparisons, this result may only be significant due to chance. Conclusions: No allelic variation in any single folate pathway gene was associated with MTX efficacy and toxicity. Given that response to MTX (efficacy and toxicity) is a complex phenotype involving multiple gene products, we conclude that genotype analysis may be too far removed from the clinical phenotypes of interest. Therefore, future studies should be directed at characterizing interindividual variability at more proximal levels, including mRNA, enzyme activities and/or cellular MTX and folate concentrations to develop more useful biomarkers of MTX response.
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Objective: To determine the utility of antibiotic (abx) in the management of skin abscess following I&D. Methods: This is a double-blind, randomized controlled trial at an urban pediatric emergency department. Sample size (161) was based on a threshold equivalence of 7% (α = 0.05, power ≥ 80%). Inclusion criteria: non-toxic, immunocompetent, 3 months to 18 years old, English-speaking patients (pts) with clinical or ultrasound identified skin abscesses who were not on abx. Pts were block randomized to receive placebo or trimethoprim/sulfamethoxazole for 10 days following I&D. Follow-up was a call at 2–3 days & a repeat visit or call at 10–14 days. Treatment failure: persistent erythema, tenderness, and/or draining lesions. New lesion: primary resolution with development of an abscess at a different location. Compliance was evaluated by the return of the study medication or by pt report. Results: One hundred and sixty-one pts enrolled (12 lost to follow-up). Main pathogens: CA-MRSA (119, 80%) with 15% clindamycin resistance, methicillin-sensitive Staphylococcus aureus (13, 9%), Prostas mirabilis (6, 4%) & Group A streptococcus (2, 1%). Overall tx failure rate was 5% (7/149), 4/66 on placebo (5%) & 3/73 on abx (4%) (R R = 0.99, 95%CI 0.93, 1.06). New lesions occurred in 28 pts (19%) - 18 on placebo (25%) & 10 on abx (14%) (RR = 0.87, 95%CI 0.75, 1.04). Ninety-nine patients (66%) took < 50% of the medication - 54 on placebo & 45 on abx. In this compliant population, tx failure was 2/54 on placebo and 0/45 on abx (RR = 0.96, 95%CI 0.97, 1.03). New lesions occurred in 14 pts/12/54 on placebo and 2/45 on abx (RR = 0.81, 95%CI 0.74, 0.96). Conclusion: After I&D of skin abscesses in children, antibiotics do not appear to be helpful in resolving the primary lesion but may be beneficial in preventing the appearance of new lesions. Larger trials are needed to validate these results.

6
DIFFERENTIAL MECHANISMS FOR CD4+ AND CD8+ INFILTRATION IN THE DEVELOPMENT OF EXPERIMENTAL IDIOPATHIC PNEUMONIA SYNDROME

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Idiopathic pneumonia syndrome (IPS) is a frequently fatal complication following allogeneic bone marrow transplantation (allo-BMT). The pathophysiology of IPS is complex and involves both soluble and cellular effectors. We hypothesized that donor T cell-mediated injury during IPS involves the generation of cytotoxic T lymphocytes (T lymphocytes). We examined the role of CTL effector function in the development of IPS using well-established murine BMT models. In initial experiments, lethally irradiated B6D2F1 (F1) mice received BM from either allogeneic C57Bl/6 (B6) or syngeneic (F1) donors. Mice were subsequently analyzed for the expression of both perforin and FasL in allo-BMT mice at week 2 compared to controls. In order to ascertain the role of perforin and FasL in IPS, we examined the phenotype and activation status of naı¨ve CD4 T cells in this setting.

Results: Following TCR stimulation. Failure of costimulatory pathways likely contributes to the naı¨ve T cell homeostasis in HIV infection and impaired generation of memory/effector CD4 T cells from healthy donors. TCR-activated naı¨ve CD4 T cells from HIV+ persons increased surface expression of the co-receptors CD27 and CD28 significantly less than from healthy donors (p = 0.01). Induction of CD27 and CD28 was directly related to the induction of Ki67 (Spearmann’s r = 0.05, p = 0.015) among naive CD4+ T cells from healthy donors. In contrast, a significant correlation between these indices was not observed in naive CD4+ T cells from HIV-infected persons (r = 0.16, p = 0.50), unless CD31– cells were excluded from analysis. These differences likely stemmed from an inability of CD31– cells to express Ki67 after stimulation even though these cells could increase cell surface expression of CD27/CD28. Conclusions: Naı¨ve CD4+ T cells from HIV+ persons fail to upregulate co-receptors for T cell activation and CD27 and CD28 after TCR stimulation. Failure of costimulatory pathways likely contributes to the naive T cell expansion failure that characterizes HIV infection and may determine both failure of naive T cell homestasis in HIV infection and impaired generation of memory/effector CD4+ T cells after antigen recognition.

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ONCOSTATIN M, AN INFLAMMATORY CYTOKINE, PROMOTES CLONODYSTROPHIC MEIOPHILIC PROGENITORS IN UMBILICAL CORD BLOOD

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Background: Activated tissue neutrophils release cytokines that promote the attraction of circu-

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FAILURE OF CO-STIMULATORY PATHWAYS AND NAIVE CD4+ T CELL EXPANSION IN HIV DISEASE

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Background: Naive T cells require balanced signaling through T cell receptors and coreceptors for T cell activation to maintain homeostasis and to mature after antigen presentation. To characterize better the impairment in naive T cell expansion capacity in HIV infection, we examined the phenotype and activation status of naive CD4+ T cells after TCR engagement. Methods: PBMC obtained from 9 healthy controls and 20 HIV+ volunteers were depleted of CD8RO+ cells using magnetic microparticles, then stimulated with anti-CD3 anti-CD28 Ab. After 2 days of culture, cells were stained with antibodies to CD4, CD27, CD28, CCR7, and CD31 and Ki67 and examined using multi-color flow cytometry. Naive CD4 T cells were defined as CD45RO/CD4+ /CD27+/CD28+ /CCR7+ /CD31+ or CD31–. Results: Naive CD4+ T cells from HIV+ individuals displayed impaired entry into cell cycle as reflected in impaired induction of Ki67 expression after TCR stimulation (20.2% (±5.9 SEM) vs. 9.6% (±3.8 SEM, p = 0.034). In addition, TCR-activated naive CD4+ T cells from HIV+ persons increased surface expression of the co-receptors CD27 and CD28 significantly less than from healthy donors (p = 0.01). Induction of CD27 and CD28 was directly related to the induction of Ki67 (Spearmann’s r = 0.05, p = 0.015) among naive CD4+ T cells from healthy donors. In contrast, a significant correlation between these indices was not observed in naive CD4+ T cells from HIV-infected persons (r = 0.16, p = 0.50), unless CD31– cells were excluded from analysis. These differences likely stemmed from an inability of CD31– cells to express CD27 after stimulation even though these cells could increase cell surface expression of CD27/CD28. Conclusions: Naive CD4+ T cells in HIV+ persons fail to upregulate co-receptors for T cell activation and CD27 and CD28 after TCR stimulation. Failure of costimulatory pathways likely contributes to the naive T cell expansion failure that characterizes HIV infection and may determine both failure of naive T cell homestasis in HIV infection and impaired generation of memory/effector CD4+ T cells after antigen recognition.
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HYPERGLEUCYEMIA AS A RISK FACTOR FOR THE DEVELOPMENT OF RETINOPATHY OF PREMATUREITY

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Background: Retinopathy of prematurity (ROP) is a proliferative vascular disorder of the retina that can lead to vision impairment or complete vision loss in premature infants. Low birth weight infants or those that are born at a lower gestational age are particularly vulnerable to develop ROP.

There is currently evidence that hyperglycemia may be a risk factor for the development of ROP.

Objective: To analyze the effect of hyperglycemia as a risk factor for the development of moderate to severe ROP.

Design/Methods: A prospective cohort study of infants less than 32 weeks who were admitted to the NICU at the University of Iowa Children’s Hospital was performed. Initial univariate analysis was performed using Chi-square analysis and simple logistic regression to determine risk factors for ROP. A multiple logistic regression model was then created incorporating these factors to determine the effect of hyperglycemia on the development of moderate to severe ROP. SAAS v 9.1.3 was used for all analyses.

Results: There were 347 infants less than 32 weeks gestation available for study, with information available for 330. There were 184 males (55%) and 146 females (45%). 228 subjects had 0, 40 had stage I ROP, 35 had stage II ROP, and 27 had stage III ROP. No subject had stage IV or V ROP. Univariate analysis demonstrated that gestational age (p < 0.0001), presence of a patent ductus arteriosus (PDA) (p < 0.0002, OR 2.5, 95% CI 1.54 – 4.05), days on oxygen (p < 0.0001, OR 1.016 (CI 1.010 – 1.022)), and days of glucose greater than 150 (OR 1.161, CI (1.098 – 1.228)) were associated with the development of ROP.

Weight appropriate for gestational age, intraventricular hemorrhage, and gender were not significantly associated with the development of ROP. When gestational age, presence of a PDA, and days of glucose greater than 150 were incorporated into a multiple logistic regression model, days of glucose greater than 150 was significantly associated with the development of moderate to severe ROP (stage II – III) (p = 0.002). Significance of days of glucose greater than 150 was decreased when days on oxygen was included into the model (p = 0.09).

Conclusion: Our data suggests that hyperglycemia may play a role in the development of moderate to severe ROP. Further study on a larger patient population will be required to fully investigate the impact of hyperglycemia on the development of ROP.

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HUMAN P-GLYCOPROTEIN REDUCES BILIRUBIN-INDUCED CELL DEATH IN VITRO

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Background: Transporters play a critical role in protecting cells from xenobiotics and toxins. Evidence demonstrates multidrug resistance-associated protein 1 (MRP1) protects against bilirubin-induced cytotoxicity. The human multidrug resistance transporter P-glycoprotein (Pgp) may also provide cytoprotection against bilirubin-induced cell death. Objective: Characterize the unconjugated bilirubin (UCB) exposure conditions (concentration and duration) that lead to cytotoxicity in human HL-60 cells and assess the potential cytoprotective role of Pgp.

Design/Methods: Human HL-60 parent cells (express MRP1 but no Pgp) and HL-60/VCR cells (express Pgp but no MRP1) were studied in vitro under control conditions (no bilirubin) and during 24 and 48 hr exposure to 3 different UCB concentrations (0.5, 1 and 2 μM). UCB cytotoxicity was assessed using: 1) trypan blue staining (cell viability), 2) fluorescent microscopy of morphological changes of apoptosis (nuclear condensation and fragmentation) and necrosis using Hoechst 33342 and propidium iodide stains, and 3) flow cytometry analysis of cell viability. Results: Cell viability and proliferation were affected by UCB as they were decreased in HL-60 parent cells as contrasted with HL-60/VCR cells. Moreover, microscopy demonstrated UCB induced apoptosis and necrosis in HL-60 parent cells in a dose and time dependent manner with apoptosis greatest at low UCB - longer exposure durations, and necrosis predominating at high UCB regardless of exposure duration. In contrast, HL-60/VCR cells demonstrated UCB induced apoptosis and necrosis in HL-60 parent cells in a dose and time dependent manner with apoptosis greatest at low UCB - longer exposure durations, and necrosis predominating at high UCB regardless of exposure duration. In contrast, HL-60/VCR cells demonstrated minimal UCB cytotoxicity under the same conditions.

Conclusion: We conclude that UCB impairs cell viability and induces apoptosis and necrosis in HL-60 parent cells in a dose and time dependent fashion whereas HL-60/VCR cells are relatively protected against UCB cytotoxicity. These findings suggest that human Pgp affords cytoprotection against UCB. Moreover, under the current study conditions, this Pgp cytoprotective effect appears to exceed that afforded by MRP1.

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EFFECT OF MORPHINE ON NEUROGENESIS IN THE DEVELOPING RAT HIPPOCAMPUS

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Background: Pain management is an important aspect of neonatal care. Chronic pain during a neonate’s stay in the NICU has been shown to have long lasting changes in pain tolerance, spinal cord level sensitization and altered pain-related behavior in later childhood. Opioids, such as morphine, form the mainstay of pain management in the preterm newborn infant. The adverse effects of morphine on the developing brain given in the days shortly after birth are not known. In adult rats, recurrent administration of morphine decreases the neurogenesis in the hippocampus. In humans and rats, the rapid phase of hippocampal development spans both pre- and postnatal periods. Morphine administration during the neonatal period may adversely impact hippocampal neurogenesis and result in cognitive impairments.

Objective: To evaluate the effect of recurrent morphine administration on neurogenesis in the granular cell layer of the dentate gyrus of the hippocampus in developing rats.

Design/Methods: Sprague Dawley rat pups were administered morphine (10 mg/kg, intraperitoneal) (i.p.) twice daily from postnatal day (P) 3–7 (neurodevelopmentally equivalent to 24–34 week human neonate). Littermate controls were given normal saline as a vehicle. Bromodeoxyuridine (BrdU) was injected (100 mg/kg, i.p.) on P7 to label newly dividing cells and brains were harvested on P8.

The BrdU positive cells in the granule cell layer of the hippocampus of morphine group and control group were counted and compared in 20 μm coronal brain sections using Image J program (N = 32 brain sections from 2 rats/group).

Results: Compared with the control group, the mean ± SD BrdU positive cells in the dentate gyrus were 50% lower in the morphine treated group (control group 220 ± 77 and morphine group 109 ± 48, p = 0.001).

Conclusions: Recurrent morphine exposure during the postnatal period is associated with decreased neurogenesis in the dentate gyrus of the hippocampus in developing rats. Altered hippocampal development may lead to cognitive deficits in human preterm infants exposed to recurrent opioid administration.

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GABAERIC NEURONS IN THE NUCLEUS TRACTUS SOLITARIS ARE NOT INVOLVED IN THE LARYNGEAL CHEMOREFLEX

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Activation of laryngeal mucosa causes apnea in neonates and newborn animals. This reflex apnea is mediated through, and can be activated by electrical stimulation of, the superior laryngeal nerve (SLN). Blocking GABA_A receptors was shown to prevent SLN stimulation induced apnea. It was suggested that second order neurons in the Nucleus Tractus Solitarius (NTS) activate GABAergic neurons within the NTS that inhibit inspiratory neurons and cause apnea during laryngeal stimulation. We aimed to identify if GABAergic neurons in the NTS are activated during SLN using c-Fos expression as non-specific marker of neuronal activation. Three week old rats pups, (n = 10), were initially anesthetized using urethane then ventilated through a tracheostomy and vagotomized. In five electrical stimulation of the SLN was performed for 15 seconds every 4 minutes for 30–60 minutes using currents that caused cessation of diaphragmatic activity. The other five rats underwent sham surgery without SLN stimulation. All animals were perfused using 4% paraformaldehyde 1–2 hours after the end of stimulation or comparable time in the control group. The brainstem was excised and immunohistochemistry double-staining for parvalbumin, a marker for GABAergic neurons, and c-Fos protein were employed to identify GABAergic neurons activated during SLN stimulation in medullary slices. We observed that there was increased c-Fos expression within the NTS in the stimulated animals relative to the control. While we observed parvalbumin positive cells in the NTS, there was no co-localization of parvalbumin with c-Fos in any of these neurons. From these preliminary studies we conclude that SLN stimulation activate non-GABAergic neurons within the NTS. We further conclude that GABAergic inhibition of respiration during laryngeal stimulation is localized outside the NTS. We speculated that SLN stimulation activates neurons in the NTS that stimulate GABAergic interneurons in the ventilatory medulla causing release of GABA at, and inhibition of, inspiratory neurons and subsequent apnea. Future experiments will try to identify the location of these activated GABAergic neurons.
13

A GAIN OF FUNCTION MUTATION CAUSING SKELETAL OVERGROWTH IN THE RAPUNZEL ZEBRAFISH MUTANT

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Background and Purpose of Study: Human skeletal disorders are prevalent in medicine yet the genetic and physiologic mechanisms that regulate skeletal growth, homeostasis, repair and regeneration are poorly understood. For example, of the 372 skeletal dysplasias, a genetic etiology exists for only 140 of them. Zebrafish are well suited for investigating skeletal biology. They possess a classic vertebrate skeleton including endochondral and membranous elements, they have the three signature skeletal cell types (osteoblasts, osteoclasts and chondrocytes) and they are amenable to forward genetic studies. Therefore, zebrafish mutants that alter skeletal morphology and physiology may provide insight into the fundamentals of human skeletal biology.

Methods and Summary of Results: An ENU-based forward mutagenesis screen identified the overgrowth mutant rapunzel (rpe). Adult rpe heterozygotes have defects in skeletogenesis, resulting in overgrowth of the axial and the appendicular skeleton. We mapped rpe to a 46 kb critical region on chromosome 16. This critical region contained four novel, paralogous genes. We then used a combination of genomic BAC sequencing in addition to 3’ and 5’ RACE to examine the coding sequences of the paralogs in the rpe critical region. One transcript, heretofore referred to as rpe, contained a missense mutation (T269A) that would result in a non-conserved amino acid substitution (Y90H). Using the rpe homologous embryonic phenotype as a surrogate, we show that knockdown of rpe completely rescues the homoezygous embryonic phenotype, but has no effect on wild type or heterozygous rpe embryos, suggesting that rpe is a gain of function allele. In silico data suggest that rpe is a transmembrane protein, a model supported by preliminary experiments both in transfected mammalian cells and in zebrafish cell lines using an antibody generated against the endogenous rpe protein. Finally, we used blastula transplantation to explore the cell/tissue autonomy of the rpe mutation. Analysis of rpe chimeras suggests both cell autonomous and non-cell autonomous mechanisms for skeletal overgrowth in rpe mutants.

Conclusions: Forward genetics identifies rpe, a skeletal overgrowth mutant caused by a gain of function lesion in the previously undescribed rpe gene. rpe encodes a novel, transmembrane protein. Progress in characterizing the rpe protein will be described.

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EARLY TREATMENT OF IDA DOES NOT REMEDIATE BEHAVIORAL DEFICITS IN RATS

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Background: Iron deficiency anemia (IDA) during development has been demonstrated to have long-lasting effects on cognition and behavior in humans. In rats, IDA during early development is associated with delayed motor development and poor performance in the spatial watermaze in adulthood with treatment by P21. In the P25 watermaze, the IS pups swam significantly faster than the ID pups (p < 0.05). In the 1-minute probe trial, ID rats show a lower percent path in the platform quadrant (p < 0.001) compared to IS pups. Assessing across all training days at P9, IS pups performed significantly better than ID pups (p < 0.0001). In the 1-minute probe trial, ID rats show a lower percent path in the platform quadrant (p < 0.05) and a trend for a higher thigmotaxis path (p = 0.07).

Conclusion: Despite iron treatment for ID by early lactation, previously ID pups demonstrated lags in motor development and poorer watermaze performance at P25 and in adulthood. This study suggests that ID during gestation can have long-lasting behavioral effects that are not remediated by iron treatment.

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BIOENGINEERING OF COAGULATION FACTOR VIII FOR EFFICIENT EXPRESSION: ELIMINATION OF A DISULFIDE LOOP IMPROVES SECRETION

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Coagulation factor VIII (FVIII), a glycoprotein cofactor, performs a critical function in the intrinsic blood coagulation pathway and a quantitative or qualitative deficiency of this protein results in Hemophilia A. The primary obstacle to producing low cost replacement therapy is the inherent limitation of commercial recombinant FVIII (rFVIII) production since its expression is 2 to 3 orders of magnitude lower than that of other comparably sized proteins. Inefficient mRNA expression, protein misfolding & chaperone mediated retention and the requirement for facilitated transport from the Endoplasmic Reticulum (ER) to Golgi have been identified as the major bottlenecks to efficient expression of rFVIII. Bioengineering strategies aimed at clearing each of these hurdles have resulted in the generation of several rFVIII variants with more efficient expression rates. Elimination of specific disulfide loops has previously been shown to confer a secretion advantage in certain proteins. In this strategy, the effect of each of FVIII’s eight disulfide bonds on FVIII secretion was determined. The disulfide bonds were eliminated by replacing the corresponding cysteine residues with glycine residues by a PCR-based site-directed mutagenesis protocol using mutagenic primers. The disulfide mutants were created both in the full length FVIII as well as a bioengineered rFVIII variant (226N66) with enhanced (5-10 fold) secretion efficiency. All the mutants were characterized by restriction enzyme digestion and DNA sequencing. The secretion capabilities of all the mutants were studied by transient transfection in Chinese Hamster Ovary (CHO) and COS-1 cells. FVIII activity was measured by one-stage and two-stage clotting assays and the antigen levels were quantified by anti-FVIII light chain sandwich enzyme-linked immunosorbent assay (ELISA). Elimination of the disulfide loop between cysteine residues at positions 1899 and 1903 resulted in a 1.5-2 fold increase in secretion of both wild-type FVIII and even the 226N66 variant as reflected in both the antigen levels and the activity of the protein. Disruption of each of the other seven disulfide bonds resulted in retention of the protein, intracellularly indicating that these were indispensable for the correct folding and secretion of FVIII. Such combined targeted bioengineering strategies may facilitate more efficient production of rFVIII toward lower cost replacement therapy.

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EFFECTS OF IRON DEFICIENCY AND ERYTHROPOIETIN ON TRANSFERRIN RECEPTOR EXPRESSION IN NEWBORN RAT

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Background: The availability of iron is critical in cell proliferation necessary for infant growth. Duodenal intestinal epithelium absorbs mild-borne iron, delivering it to enterohepatic circulation. Once inside, the epithelial cell exports iron-transferrin complexes via the transferrin receptor (TR) to be transported via the bloodstream to liver. Hepatic iron directly regulates intestinal iron absorption by negative feedback. Erythropoietin (Epo), found in human milk, stimulates erythropoiesis, but its role in iron absorption is unclear. Epo may upregulate TR expression in some cell types. Purpose: Our aim was to understand whether Epo increases duodenal iron transport in iron-deficient anemic (IDA) newborn rats. First, we hypothesized that duodenal TR expression would be higher in dam fed or IDA rats fed enteral Epo, compared to control. Methods: We studied newborn Sprague-Dawley rats from postnatal day 4-12, damfed or iron-deficient artificial milk via gastrostomy (IDA): Enteral Epo was administered as 425 U/kg/d (IDA + Epo, Enteral Epo). H&E and Prussian blue iron analysis was performed on duodenum and liver. Immunohistochemistry for TR was performed on duodenum, and color expression quantitated. Body or liver iron content was measured. Images were analyzed digitally by Spot and Metamorph Software. Results: Although body iron content was 30% lower in IDA group (p < 0.005), weights were similar. Duodenal weights were greater in IDA and IDA + Epo than either Dam or Dam + Epo (p < 0.05). Epo treatment did not alter weights. No Russian blue staining of duodenum was observed, supporting no hemosiderin/storage iron buildup in enterocytes. TR density was slightly higher in IDA, compared to DF (p < 0.05), but was the same for the other groups. Liver iron content (µg/g rat wt) was greater in IDA and IDA + Epo than Dam or Dam + Epo, p < 0.0005, but liver Russian blue staining for hemosiderin was markedly lower in IDA and IDA + Epo, compared to Dam or Dam + Epo (p < 0.0001). Liver weights were greater in IDA and IDA + Epo than either Dam or Dam + Epo (p < 0.05). Epo did not alter liver weights. Conclusions: We observed greater TR density with iron deficiency, but no appreciable effect with Epo. Because duodenal weights differed in iron sufficient vs. deficient rats, and Epo is known to increase villus surface area, we should examine TR expression more quantitatively by immunoblot. Because Russian blue hemosiderin does not account for the finding of greater liver iron in IDA, we will examine whether hemoglobin or ferritin iron is responsible for the greater total iron content.
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ASSESSMENT OF AIRWAY GROWTH IN-VIVO USING HIGH RESOLUTION COMPUTED TOMOGRAPHY IN INFANTS AND TODDLER


Background: Obstructive airways disease is a common respiratory problem early in life; however, our understanding of normal airway growth, as well as our ability to assess airway dimensions is relatively limited in this very young age group. High resolution computed tomography (HRCT) offers the potential to measure airway diameters in vivo and assess airway growth early in life. Hypothetical HRCT imaging can assess the growth of the conducting airways in infants and toddlers. Materials and Methods: Infants and toddlers scheduled to have a CT scan with sedation for non-respiratory problems were recruited. Infants were excluded for premature birth, cardio-respiratory anomalies or recurrent respiratory symptoms. Volumetric HRCT chest scans were obtained at an elevated lung volume (airway pressure of 20 cm H2O pressure). Lumen cross sectional area (CSA) was measured for the trachea and the first 4 generations (G1–4) into right (R) and left (L) lower lobes.

Results: 15 subjects (6 males), mean age of 15.6 months (range: 3.9–23.2) were evaluated. Increasing lumen CSA correlated with increasing body length (Table). CSA decreased from trachea to more peripheral generations (G1 to G4) and the larger airways had higher R2 than the smaller airways. In addition, conducting airways in the R lung were larger than comparable generations in the L lung. Conclusions: HRCT can be used for in-vivo measurement of airway size in infants and toddlers and the conducting airways grow linearly with body size in this age range.

NIH grant HL054862.

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THE SIMPSON GOLABI BEHMEL GENE, GLYPICAN-3, MODULATES CORONARY VASCULAR DEVELOPMENT, AND LOSS OF FUNCTION RESULTS IN CORONARY ARTERY FISTULAS

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INCREASE OF B-TYPE NATRIURETIC PEPTIDE FROM BASELINE INCREASES THE RISK OF DEATH OR RE-TRANSPLANT IN PEDIATRIC CARDIAC TRANSPLANT PATIENTS

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The purpose of this study was to analyze longitudinal BNP data in pediatric cardiac transplant patients. Several studies have demonstrated the utility of BNP in the months following cardiac transplant. Our goal was to determine the utility of BNP in routine follow-up years after transplant and its relationship to the adverse event of death or re-transplant.

From October 2002 to July 2007, 53 pediatric cardiac transplant patients were treated in an unmatched case-control study. Along with routine studies, BNP values were drawn at regular intervals. 6 patients were excluded due to recent transplant, and 2 patients were excluded due to poor compliance. A baseline mean BNP was established for each subject utilizing all BNP values during year 2 post transplant, or the first year of measured BNP in those patients whose transplant preceded the study by more than 2 years. Another surrogate baseline value was used was the median BNP of all data points since transplant. Univariate logistic regression was used to evaluate various BNP summaries and possible covariates on cardiac death.

There were 1260 BNP data points spanning 174 patient years. 10 (22.2%) of the 45 subjects experienced an event. Patients who eventually experienced an adverse event had a significantly higher baseline BNP mean (397 ± 292, median 407 ± 347) when compared to patients without an event (mean 128 ± 78, median 121 ± 62; p = 0.0170; p = 0.0284 respectively). Patients who received pulsed steroids within the last 210 days were more likely to experience an event than patients who did not (OR 16.36, 95% CI 1.64 - 164; p = 0.0085). All subjects with adverse events attained a BNP value ≥250 during the 180 days preceding the event compared to only 37.1% of those who did not (OR: 21.19, 95% CI 3.04 – 0.30, p = 0.007). The log fold increase of the maximum BNP value in the last 180 days compared to the baseline median BNP is a risk for cardiac death (OR: 4.51, 95% CI 1.15-17.6, p = 0.0307).

Routine BNP measurements in the post-cardiac transplant pediatric patient allow for the determination of a median BNP which can be used as a baseline. Log fold increases from the median BNP as well as attaining a BNP value ≥250 increase the risk of death or need for re-transplant.

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EFFECT OF HEMODIALYSIS ON AORTIC STIFFNESS IN CHILDREN WITH END STAGE RENAL DISEASE

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Background: Children with end stage renal disease (ESRD) have significant cardiovascular morbidity and mortality. The pathogenesis of which may include altered aortic mechanics. Chronic volume overload may decrease the aortic distensibility (AD) and increase aortic stiffness (AS). We hypothesized that among children with ESRD, AD and AS would improve following HD. Methods: This was a prospective non-interventional study involving children (n = 12) with ESRD, who underwent echocardiograms immediately before starting HD, mid-way during HD, and within 1/2 hour of completion of HD. Aortic systolic and diastolic diameters (SD and DD) were measured by 2D guided M mode echocardiography. Systolic (SBP) and diastolic blood pressure (DBP) was measured and pulse pressure (PP) calculated. Measurements of AD and AS were derived as: Aortic strain (S) = (SD-DD)/(SD+DD) and AD = 2 X strain X PP. AS was calculated as: Pressure strain elastic modulus (Ep) = PP/Ep and Pressure strain normalized to DBP (EpDBP) = Ep/DBP. Results were expressed as mean ± SD. Comparisons of measured variables were tested by ANOVA; statistical significance was assumed at p < 0.05. Results: The mean ±SD fluid removed during HD was 1.7 ± 1.5L. The causes for ESRD varied. BP was not significantly different before, during or after HD. Both Aortic distensibility and Aortic Stiffness significantly worsened during hemodialysis and remained impaired at completion of HD. Change in AD and AS did not correlate with amount of volume removed, duration of HD, or duration of ESRD.

Conclusion: Aortic distensibility was impaired and the aortic stiffness increased significantly in children with ESRD following hemodialysis, irrespective of the underlying renal diagnosis and independent of a change in the blood pressure or volume removed. We speculate that the acute increase in aortic stiffness during hemodialysis may be secondary to endothelial dysfunction, which may impair the cardiovascular benefits of volume unloading.
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cD11b+ and CD11c+ Cells Are Increased in the CawS Mouse Model of Kawasaki Disease (KD) Suggesting a Role for Macrophages and Dendritic Cells (DCs) in the Pathogenesis of Coronary Artery and Aortic Atherosclerosis

Purpose: To identify the phenotype(s) involved in the coronary artery and aortic inflammation induced by Candida Albicans Water Soluble fraction (CAWS). In this model, a single immunization with CAWS causes coronary artery and aortic inflammation within three weeks. Methods: 6-12 week old C57Bl/6 (wt) mice were immunized once with CAWS intraperitoneally (IP). Mice were sacrificed on day 21-28 post immunization. Hearts were dissected and sectioned. Heart cells and spleen cells were analyzed by flow cytometry. Hearts were embedded in OCT. For H&E staining or for frozen sectioning. Summary: H&E staining showed that on average greater than 66% of immunized mice were affected. H&E showed aortic and coronary artery inflammation and appeared to contain neutrophils, macrophages and plasma cells. Subendothelial proliferation was prominent adjacent to the aorta. Coronary arteries was frequently accompanied by obstruction of artery lumens. Disruption of the elastic lamina was observed in some but not all specimens. Affected mice exhibited splenomegaly consistent with immune activation. Flow cytometry showed increased numbers of spleen cells that expressed CD11b+/c and the combination of CD11b and CD11c compared to mock immunized mice. Single color staining of cells isolated from cardiac lesions suggested the presence of cells that expressed CD11b and/or CD11c, and were virtually undetectable in non-immunized mice. Additional multicolor analysis of lesions including staining for MHC Class II are underway to further identify the CD11b+/c cells as DCs.

Conclusion: CAWS immunization induces mouse coronary arteries, aortas, splenomegaly, and alten immune composition in the spleen. CD11b+ cells have also been reported to be increased in another mouse model of atherosclerosis in which injury with gamma herpes virus leads to atherosclerotic artery phenotype, and in patients with atherosclerosis distinguished by auto-antibodies to anti-proinflammatory CD11b/c DCs have been reported in the coronary arteries of patients following KD. We hypothesize that in the CAWS model activated CD11b+/c macrophages and CD11c+ DCs produce chemokines which then recruit T-cells and macrophages into the coronary arteries and aorta thus perpetuating an initial inflammatory trigger. Our results suggest that the CAWS model may mimic features of KD and human atherosclerosis and thus may be useful in studying basic mechanisms of susceptibility and damage.

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PEDIATRIC DUODENAL CANCER AND BI-ALLELIC MISMATCH REPAIR GENE MUTATIONS

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Gastrointestinal (GI) malignancies are extremely rare in the pediatric population, and have been observed to associate with functional deficiencies of the mismatch repair (MMR) system causing a cancer predisposition syndrome. We report the case of a 16-year-old female with personal history of duodenal adenocarcinoma and medulloblastoma and family history of T-cell leukemia in her brother at age 5. The purpose of this study is to describe the phenotype of bi-allelic MMR mutations and to underscore the features of pediatric duodenal carcinoma. Methods: Duodenal tumor tissue was evaluated for microsatellite instability (MSI) and protein expression. Blood samples of the proband and her parents were tested for mutations in the MMR gene. Results: Duodenal carcinoma demonstrated high degree MSI and absence of MMR in tumor and normal tissue, with intact expression of MLH1, MSH2, and MSH6. Germline testing revealed a homozous truncating mutation of the PM2.1 mismatch repair gene (Q171X) in exon 9. The parents are first cousins, and each parent is heterozygous for PM2.1 Q171X. A comprehensive literature review highlights that mismatch repair deficiency syndrome (MMR-DS) resulting from germline biallelic MMR inactivation significantly differs from heterozygous germline mutation in MMR gene that causes Hereditary non-polyposis colorectal cancer (HNPCC). Omit of tumors in MMR-DS is as early as the first decade of life and most patients have cafe-au-lait macules. The tumor spectrum includes colorectal, brain, and hematological malignancies. Homozygous mutations in MMR, MLH1 and MSH6 account for the majority of the MMR-D cases. Conclusions: It is important for pediatricians and pediatric oncologists to be aware of the possibility of occurrence of GI malignancies arising on the basis of defective mismatch repair in children and young adults with GI cancer. The pattern of a GI malignancies arising in children and young adults with GI cancer depends on the presence of cafe-au-lait macules, should raise suspicion on the basis of defective mismatch repair in children and young adults with GI cancer. The pattern of a GI malignancies arising in children and young adults with GI cancer.
SCHOOL-BASED HEALTH PROMOTION: A POTENTIAL TOOL FOR MOSQUITO BITE AND MOSQUITO-BORNE DISEASE PREVENTION IN CHILDREN
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Purpose: Children are at high risk for mosquito-borne disease exposure because they spend large amounts of time outdoors and often do not wear protective clothing or mosquito repellent. Our objective was to assess whether a school-based educational intervention focused on mosquito bite prevention and mosquito-borne disease, particularly West Nile virus (WNV), was able to: 1) improve WNV-related knowledge, 2) change WNV-related attitudes, 3) maintain these improvements, and 4) promote personal protective behaviors (PPBs) among participants and their families. Methods: Multisite, group-randomized, controlled trial. Students were randomized by classroom to either Neato Mosquito (NM) or Tar Wars (TW). Pre- and post-intervention knowledge, attitudes, and practices (KAP) surveys were compared to assess immediate KAP changes. Follow-up surveys, administered after the summer break 5–6 months later, assessed long-term KAP changes. Follow-up surveys, administered 1 month apart) of children.

Methods: All children undergoing autonomic testing were enrolled in this IRB approved prospective study. EEG was recorded 10 minutes in supine position and during the upright portion of the tilt. EEG findings were correlated with autonomic diagnostic using Wolmers Rank Sum test. For the purpose of statistical analysis children were divided into two groups: 1) POTS and or vasodepressor syncope (VDS) 2) Non-POTS group include normal subjects and subjects with autonomic neuropathy. Results: 50 patients participated (20 females). Mean age 14 ± 3.5 years. 20 had POTS/VDS, 5 autonomic neuropathy, 5 were normal. 11 subjects with POTS replicated symptoms during upright portion of the tilt. When evaluating Channel 1 of EEG, subjects with POTS/VDS, but not those without POTS, showed a tendency for an increase in % arhythmia (p = 0.02) and a decrease in % normal gastric electrical activity (p = 0.02) as the upright position in relation to the supine position.

Conclusion: This exploratory study suggests that the electrical activity of the stomach during the upright position in children with POTS/VDS, but not in children without this diagnosis. These changes could reflect abnormal autonomic control of gastric electrical activity and bear some relationship to the chief complaint of pain which worsens in the upright position.

Further studies are needed to corroborate these findings.

Legend to Figures: Changes in % normal gastric electrical activity lying vs standing. (Stars: POTS subjects, dots: non-POTS subjects, p < 0.02).

EKG criteria

<table>
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<tr>
<th>AGE: 2–11 (specificity 80)</th>
<th>AGE: 12–18 (specificity 80)</th>
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<tr>
<td>Sensitivity</td>
<td>Cut off point</td>
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<td>SV1 (in mV/RV6s (mV)</td>
<td>30% (1/1)</td>
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<td>TMD (ms/MSLV)</td>
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<td>QRSV (ms)/QRS2 (ms)</td>
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SCHOOL-BASED HEALTH PROMOTION: A POTENTIAL TOOL FOR MOSQUITO BITE AND MOSQUITO-BORNE DISEASE PREVENTION IN CHILDREN

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Background: The electrocardiogram (EKG) is a simple and widely used tool to screen for left ventricular hypertrophy (LVH). Voltage criteria are typically used to define LVH in children. Other criteria such as QRS voltage, QRS duration, and heart rate variation have also been attempted. The objective was to assess whether the EKG could be used to define LVH in children. Methods: We performed a retrospective analysis of EKGs and echocardiograms performed <1 month apart of children (1-18 yrs) with four chamber cardiac anatomy presenting to our clinic/echocardiography lab. Patterns with open heart surgery, arrhythmias and bundle branch blocks were excluded. EKGs were evaluated for QRS duration (QRSd, ms), average time to maximal QRS deflection (TMD, ms), average 12-lead QRS voltage (12QSV, mV), average product of 12QSVand QRSd (12QSVxQRSd, ms mV), R wave in V6 (RV6), S wave in V3 (SV3), Sokolow-Lyon voltage (SLV, mV; S in V1+V2 + R in V5+V6), Cornell voltage (CV, mV; R in V1 + S in V3), SLV duration product (SLVd), CV duration product (CVd) and left ventricular mass (LVM) from EKG (LVMeKG). LVM was defined as LVM index >39.2 g/m2 height1.73 for males and 38.2 g/m2 height1.73 for females as derived from M-mode echocardiography by ASE formula. Sensitivity and specificity of each EKG criteria in detecting LVH was calculated. Results: Out of 179 children 66 children had LVH by echocardiography and 113 had no LVH. Conclusion: Standard EKG voltage criteria particularly RV6 is a poor indicator of LVH and LVH calculated by EKG is the most sensitive screening parameter for LVH in both age groups. We therefore propose that LVH calculated by EKG should be used to screen LVH in children and should be incorporated in current EKG machine software.

SCHOOL-BASED HEALTH PROMOTION: A POTENTIAL TOOL FOR MOSQUITO BITE AND MOSQUITO-BORNE DISEASE PREVENTION IN CHILDREN

The school-based educational interventions can play a significant role in promoting mosquito-bite prevention and can serve as an effective tool to communicate public health information to children. Immediate and long-term improvements in WNV-related knowledge resulted from our intervention. We also reported more PPB use among their family members than those in the TW arm. The NM arm reported more PPB use than those in the TW arm; they were 5 times more likely to dump out standing water and 3 times more likely to wear pants or long sleeves. The NM arm also reported more PPB use among their family members than those in the TW arm.

Conclusions: Immediate and long-term improvements in WNV-related knowledge resulted from our intervention. Importantly, significant increases in PPBs were reported among NM participants and their families. Simple school-based educational interventions can play a significant role in promoting mosquito-bite prevention and can serve as an effective tool to communicate public health information to children.
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PROLонGED CAPILLARу REFILL TIME IS ASSOCIATED WITH CENTRAL VENOUS SATURATIONS > 70%  
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Background: Septic shock makes demonstrate that early goal-directed therapy targeting superior vena cava oxygen saturations (ScvO2) improves outcome. Most sick children present to community hospitals where expertise and equipment to place central venous catheters (CVC's) to obtain ScvO2 measurements may not be readily available. PALS recommends using capillary refill time (CRT) for shock assessment in children because it is non-invasive and easy to perform. The relationship between CRT and ScvO2 has not been determined.

Objectives: To test the hypothesis that prolonged CRT (CRT 2 seconds) is associated with ScvO2 > 70%.

Methods: Prospective cohort study at a 16-bed tertiary-care PICU. Any critically ill child with a CVC was eligible for study. Patients with hypoxia (arterial saturation 96%) were excluded. Whenever ScvO2 was obtained, central (catheter) and peripheral (finger or toe) CRT's were measured using a stopwatch.

Results: 39 paired CRT-ScvO2 data from 17 patients were recorded. ROC curve analyses revealed that CRT's ability to discriminate ScvO2 > 70% was good peripherally and excellent centrally (Figure). Optimal discrimination was found at CRT 2 seconds for both central (sensitivity 0.79, specificity 0.83) and peripheral (sensitivity 0.60, specificity 0.79).

Conclusions: CRT > 2 seconds is associated with ScvO2 > 70%. These data support PALS recommendations for goal-directed shock resuscitation targeting normalization of CRT (CRT=2 seconds), especially if CRT is assessed centrally. This endpoint remains particularly relevant in community hospitals where CVC access may be limited and ScvO2 data unavailable.

CRT A.U.C. (95% C.I.)

central 0.935 (0.856 – 1.014)

peripheral 0.774 (0.623 – 0.925)


39 paired CRT-ScvO2 data from 17 patients were recorded. ROC curve analyses revealed that CRT's ability to discriminate ScvO2 > 70% was good peripherally and excellent centrally (Figure). Optimal discrimination was found at CRT 2 seconds for both central (sensitivity 0.79, specificity 0.83) and peripheral (sensitivity 0.60, specificity 0.79).

Conclusions: CRT > 2 seconds is associated with ScvO2 > 70%. These data support PALS recommendations for goal-directed shock resuscitation targeting normalization of CRT (CRT=2 seconds), especially if CRT is assessed centrally. This endpoint remains particularly relevant in community hospitals where CVC access may be limited and ScvO2 data unavailable.

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INTRAVENTRICAL HEMORRHAGE IN PREDITERM INFANTS: A CHANGE IN TIMING  
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Introduction: The detection of intraventricular hemorrhage (IVH) in very low birth weight (VLBW) infants was timed to the first three days of life in reports from the 1980s. More current practices including the prenatal administration of steroids and the postnatal use of surfactant are among practices that could alter the timing of IVH. The purpose of this study is to determine the ability to detect IVH by ultrasound within the first 3 days as early and after three days as late. We excluded infants with incomplete records or those with ultrasound images that did not allow proper classification into early or late IVH.

Results: We evaluated data of 152 infants and included 88 infants with grades II-IV in the analysis. Late IVH was common and occurred in 32 (34%) while early IVH occurred in 56 (64%). Birth weight (mean, SD: 896 g vs 800 ± 256 g), gestational age (mean, SD: 26.2 ± 1.6 weeks vs 26.0 ± 1.9 weeks), birth outside a subspecialty center (31.2% vs 41.1%), male gender (43.8% vs 48.2%), treatment with surfactant (96.9% vs 96.4%), severe IVH (56% vs 57%) and death prior to discharge to home (37.5% vs 35.7%) were not statistically different between infants who had late versus early IVH. However, mothers of infants with late IVH were more frequently treated with steroids (75% vs 55%, p < 0.04). Within the group of infants who had late IVH, 12 (37.5%) had their IVH detected on or after DOL 10. Conclusions: Intraventricular hemorrhage was frequently detected in VLBW infants after the first three days of life. Prenatal treatment with steroids was associated with late IVH. We speculate that there is a change in the timing of IVH in VLBW infants associated with changes in perinatal practices introduced over the last few decades. Overall, this change is important when considering the timing of routine screening for IVH and when providing counseling to families.

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NOT HOOKED ON THE CLASSICS: AWARENESS OF KEY CASES IN NEONATAL ETHICS  
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Background: The implementation of the Born-Alive Infants Protection Act (BAIAP) in 2002 has made infant resuscitation a prominent issue. A handful of legal cases are fundamental to understanding important neonatal ethical considerations. This study aimed to determine the knowledge base regarding some cases considered “classic” by the legal/ethical community. Methods: Two lectures on legal/ethical issues at the Neonatology 2008 conference (Atlanta). Audience comprised of 152 ICU RNs, NNP’s, and neonatologists. Anonymous audience-response system polled awareness and opinions.

Results: Baby Doe - 1982 - infant with Down’s Syndrome and TEF allowed to die without surgery. Most were aware (69%) of the case and disagreed (69%) with the court.

Baby K - 1994 - court required a hospital to provide ventilation to an anencephalic infant. Most were unaware (63%) of the case and disagreed (73%) with the court.

Miller (Jury) - 1998 - Hospital sued for resuscitating a 23-week infant without consent and against parental request. Family awarded $65 million (later overturned). Most were unaware (62%) of the case and agreed (87%) with the jury.

Montalvo - 2002 - Hospital sued for resuscitating a 23-week infant without consent. The court found that the Baby Doe regulations prohibited the parents from withholding treatment because the child was not dying or comatose. Most were unaware (82%) of the case and disagreed (63%) with the court.

Sun Hudson - 2005 - Court allowed hospital to withdraw support on an infant with hypoxic encephalopathy due to hypotension over the objections of his mother. Most were unaware (84%) of the case & all agreed (100%) with the court.

Conclusion: Certain legal cases can fundamentally impact care in the NICU. This study is the first to look at awareness of these decisions in a group of NICU providers.

1. There are a large number of providers who are unaware of important legal cases.

2. There is generally no moral consensus among providers on the appropriateness of neonatal care for extremely ill newborns.

3. Efforts should be directed to educating providers on the “classic” cases in neonatal ethics.

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EFFECT OF INTERMITTENT HYPERCAPNIA ON RESPIRATORY CONTROL IN RAT PUPS  
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Premature infants are subject to fluctuations in blood gas status associated with immature respiratory control. Intermittent hypoxia during early postnatal life has been shown to increase chemoreceptor sensitivity and desaturate breathing pattern; however, intermittent hypcapnia remains poorly studied. Therefore, to test the hypothesis that intermittent hypcapnia results in altered respiratory control, we examined the effects of daily exposure to intermittent hypcapnia on the ventilatory response to subsequent hypoxic and hyperoxic exposure in neonatal rat pups. Exposure cycles consisted of five minutes of intermittent hypercapnia (5% CO2, 21% O2, balance N2) followed by ten minutes of normoxia. Rat pups were exposed to 18 exposure cycles each day for one week, from postnatal day 7 to 14. We analyzed EMG recordings of diaphragm from pups exposed to subsequent acute hyperoxic (5% CO2) and hypoxic (12% O2) challenges. In response to a subsequent hypoxic challenge there was no significant difference in the ventilatory response between control and intermittent hypcapnia-exposed groups. In contrast, intermittent hypcapnia-exposed rat pups showed an enhanced ventilatory response to hypoxic challenge with an increase in minute EMG to 118 ± 14% of baseline versus 107 ± 13% for control pups (p < 0.05). We speculate that prior hypcapnic exposure may increase peripheral chemoreceptor response to subsequent hypoxic exposures and result in perturbed neonatal respiratory control.
MATEMATICAL BIRTHWEIGHT: IMPACT ON TWIN PREGNANCY OUTCOME
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Background: It is known that increased maternal birthweight (MBW) is associated with increased gestational age in singleton births. Similarly, studies have demonstrated a positive association between MBW and infant birthweight (BW). One relatively small cohort study (N = 131) by Medley et al (2007) recently reported that MBW has an even stronger effect in twin pregnancies. Objective: To confirm the positive correlation of MBW with infant gestational age and BW in a large, multiethnic, geographically defined population. Method: We selected the birth records of 3536 mothers born in 1956–73, matched with the birth records of their twin infants delivered in 1989–91, from the Illinois Transgenerational Birth File (TGBF). We then analyzed the relationship of MBW to gestational age and combined BW of each twin pair. The effect of MBW was then determined separately for African American (AA) and White sub-populations. Results: The positive effect of MBW on gestational age and twin pair combined BW was confirmed in the large birth population from Illinois. The gestational age increased by 0.65 weeks (95% CI 0.41–0.89) per kg increase in MBW. There is a rise of 452 g (95% CI 376–528) in twin pair combined BW per kg increase in MBW. The relatively narrow confidence intervals derived from our population included the past estimates reported by the previous, much smaller study. Similar effects were demonstrated among African Americans and Whites, but the effect was stronger in African Americans, for whom the gestational age increase per kg MBW was 0.78 weeks, (CI 0.24 –1.32), compared with 0.65 weeks (95% CI 0.41–0.89) per kg increase in MBW. In our study, the increase in BW of each twin is similar for MBW increase per kg MBW. Conclusion: The positive effect of MBW on infant gestational age and BW is confirmed across all racial groups.

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MEDICAL HOME FOR NICU DISCHARGES AS TRANSITIONAL PRIMARY CARE-ELEVEN YEAR FOLLOW UP
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Background: Care after discharge from NICU is a complex task in inner city hospitals due to target populations 1) lack of insurance, 2) language barriers, 3) limited parental understanding of the child’s problems, 4) lack of family resources including transportation, and 5) literacy. Objective: 1) To establish developmentally-oriented, family-centered primary care model within developmental sub-specialist practice for all discharges from neonatal intensive care unit (NICU), 2) to address medical needs and provide care coordination for patients and families; 3) to facilitate transition of care to community providers; and 4) follow-up of patients with abnormal results of neonatal screen Design/Methods: First visit is provided irrespective of ability to pay or HMO authorization status. The neonatal course is reviewed with the family to improve their understanding of the child’s condition. The clinic social worker addresses the infant’s care and mother’s needs, and provides care coordination and access to governmental benefits. The child’s “risk” status is graded into three levels based on medical assessment and social worker’s assessment of environmental risk factors. Level-1 patients are provided with the opportunity to transition to community providers after initial visit; Level-2 infants (uncomplicated low birth weight infants) are cared for up to 1 year of age or longer based on parental preference; Level-3 infants with disabilities and complex medical needs are not discharged from the clinic. Results: A total of 400 newborn babies per year have been seen in the clinic for the past eleven years. Annual rate of transition to community care is 48%, 65% and 72% by age one, two and three respectively; attrition was minimal after four years of age - due to need of medicaid help or family’s desire to return for care. The number of neonates lost for follow up decreased from 50% to 10% in the last year due to addition of the nurse practitioner who co-ordinates care with primary care physicians. Conclusions: This model of outpatient care for high risk neonates by single provider team of social worker and nurse practitioner facilitates the successful and safe transition of patients from intensive care unit to health maintenance without interruption in continuity of care. Social worker is essential in ensuring continuity of care and family needs. Leaving it to the parent to decide when to transition out is not detrimental to clinical goal of seeing mostly neonates in their first year. Tracking all neonatal and hearing screens by a single provider improves compliance with follow up.
LYMPHANGIOGENESIS IN THE EMBRYONIC HEART

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The lymphatic network is essential for maintaining homeostasis within the internal environment, and the lymphatics of several adult organ systems, including the heart, have been described. However, the lymphatic vasculature of the developing heart has not been investigated in detail. There is clinical relevance to studying the cellular and molecular mechanisms of lymphatic vessel growth in the heart in order to treat or reduce edema due to congestive heart failure. This understanding may also be applicable to alleviating edema in other settings where it would be beneficial to initiate or enhance lymphangiogenesis. The transcription factor Prox-1 has frequently been used to label the lymphatics, and it is widely believed that Prox-1-positive lymphatic precursor cells have a venous origin. However, we propose that those of the embryonic heart may also arise from the proepicardial organ, which gives rise to the embryonic epicardium and cells comprising the coronary vessels. In our study, quail embryonic hearts were analyzed for Prox-1 immunofluorescence at developmental stages when vasculogenesis is active in the epicardium. For comparison, embryonic mouse hearts were also analyzed for expression of Prox-1 as well as two other lymphatic markers, lymphatic vessel endothelial hyaluronan receptor 1 (LYVE-1) and vascular endothelial growth factor receptor 3 (VEGFR-3). In the whole quail hearts, Prox-1 identified a widespread, branching network of lymphatic vessels that first appeared on the aorta and pulmonary trunk at HH Stage 26 (Embryonic Day 5) and then continued to extend over the base of the great vessels and a large portion of the ventricles. However, even at HH Stage 24 (Embryonic Day 4), Prox-1 was already present in atrial and ventricular cardiac myocytes, in the lining and mesenchyme of the endocardial cushions, and in a few epicardial cells. Thus, Prox-1 function in regulating valve development and cardiac myocyte differentiation, as well as lymphangiogenesis. In the mouse embryonic heart, Prox-1 staining was not colocalized with expression for Lyve-1, which was expressed in individual epicardial cells and vessels in the myocardium, until after Embryonic Day (E) 13.5. Furthermore, all three lymphatic markers were found in an in an adult rat epicardial cell line (AMEGOs) and an embryonic mouse epicardial cell line (EMEGOs), both of which also expressed a different form of Prox-1 in Western Blots compared to whole heart tissue samples composed primarily of cardiac myocytes. Our results suggest that the precursors of the cardiac lymphatics may migrate into the embryonic heart via the great vessels or originate from the epicardium.

THE EFFECTS OF BENZYL ALCOHOL AND PROPYLENE GLYCOL ON L1 MEDIATED ACTIVATION OF ERK1/2

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Intro/Background: Inactive ingredients in medications act as preservatives, preventing microbial growth, and stabilizing medications as liquids or creams. Typically these chemicals are used in small concentrations and their effects on patients are minimal if at all. Benzyl alcohol and propylene glycol are two chemicals that have had adverse effects in neonates including death, developmental delay, cerebral palsy, central nervous system depression, lactic acidosis, and seizures. Exposing premature neonates to these inactive ingredients could potentially affect their central nervous system growth and development. Objective: L1 is a transmembrane glycoprotein which promotes neurite outgrowth through an endocytic recycling pathway. ERK is a protein which is activated/phosphorylated through this pathway by L1. We hypothesize that by exposing neurons to benzyl alcohol and propylene glycol, activation of ERK decreases and subsequently L1 mediated neuronal growth will be affected. Design/Methods: We took cerebellar granule neurons from postnatal day 6 rat pups and plated them overnight on poly-L-lysine with DMEM/10% FBS on tissue culture plates. We then serum starved the cells for three hours prior to triggering. Benzyl alcohol, propylene glycol, and ethanol were added 1 hour prior to triggering. Ethanol was used as a negative control because it has already been shown to decrease activation of L1 and ERK. The amounts of benzyl alcohol and propylene glycol were equivalent to the chain lengths of those published for inhibition of L1 homophilic binding. Results: Benzyl alcohol and propylene glycol significantly inhibited activation of ERK. The relative densities of the protein bands compared to those not exposed to the chemicals were 34% and 62% respectively with a p value < 0.05. Conclusion: Benzyl alcohol and propylene glycol inhibit activation of ERK in a manner similar to ethanol and subsequently are likely to affect L1 mediated neurite outgrowth. It is still unclear, however, from just these experiments where in the endocytic recycling pathway benzyl alcohol and propylene glycol act.
**GHRELIN LEVELS IN CORD BLOOD FROM CONCORDANT AND DISCORDANT TWIN PAIRS: ASSOCIATION WITH BIRTH WEIGHT AND POST-NATAL CATCH UP GROWTH**


Ghrelin is a 28 amino acid octanoylated peptide, which has growth hormone releasing activity, and has been isolated from human gastric endocrine cells, pituitary, hypothalamus, placenta and gastrointestinal tumors. Ghrelin is actively synthesized by the placenta and has been detected in cord blood at 30wks gestational age indicating it may play a role in fetal growth and development. Previous research has found cord blood ghrelin concentrations of small for gestational age (SGA) infants to be greater than those of appropriate for gestational age (AGA) infants. SGA twins with high ghrelin concentrations may have a better chance for catch up growth after one year. In addition, differences in cord blood ghrelin levels within discordant twin pairs may correlate more strongly with catch up growth in the smaller twin. This is a prospective, observational study. After obtaining parental consent, a 1ml. venous cord blood sample was taken from 20 twin pairs; 13 concordant, 7 discordant. Blood samples were centrifuged and serum was immediately frozen. Plasma samples were sent to Millipore research lab for Ghrelin analysis. Ghrelin levels were then compared to infant size and growth progress at 2-months, 4-months and 6-months of age. Growth data is currently available for 20 infants up to 2 months of age. A negative correlation was observed in discordant twins between cord blood ghrelin levels and birth growth parameters, however none were significant. There appears to be a negative correlation between cord blood ghrelin levels and 2-month post-natal weight gain among all infants. However, this is not statistically significant. Lack of statistical significance may be a reflection of limited sample size as well as short-term follow-up data. Data collection and enrollment continues with goal sample size of 50 twin pairs upon study completion.

**HEMOLYTIC UREMIC SYNDROME—INCIDENCE AND ETIOLOGIES AT A REGIONAL CHILDREN’S HOSPITAL 2001–2006**

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Hemolytic uremic syndrome (HUS) is presenting itself as a serious health concern in children. HUS has primarily been linked to *E. coli* O157:H7 infections, however, non-O157 strains are increasingly gaining attention as potential causative agents. Progression of illness may or may not be preceded by diarrhea. However hemolytic anemia, thrombocytopenia, and acute renal failure are the defining characteristics of the syndrome. The objective of this study is to investigate the cases of HUS at a regional Children’s Hospital between 2001 and 2006 by retrospective chart review. A total of 44 cases were identified of which 57% were female and 43% were male with an age distribution of 13 months to 17 years. Data revealed 13 cases in 2006 compared to two cases in 2001 with 84% of all illnesses occurring in the summer and fall seasons. Fifty percent of all cases required dialysis for a mean of 5.9 days. Furthermore, stool cultures indicated *E. coli* O157:H7 as the predominant pathogen, however, 53% of the cases had no known etiology. Neurological complications occurred in 14% of patients and pancreatitis in 29% of the cases with a female predominance. This data may suggest a growing number of cases and an increased role of non-O157 serotypes as an etiology.

**FOLATE GENE POLYMORPHISM IN DOWN SYNDROME PATIENTS WITH ARTHRITIS**

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**Purpose:** Down syndrome (DS) patients have had well-described toxicity to high dose methotrexate (MTX) in the oncologic literature. It has been hypothesized that the increased sensitivity to MTX in DS may be due to immune and molecular pathways that are dysregulated in DS patients. We investigated polymorphisms in the *GSTM1* and *GSTP1* genes as potential contributors to toxicity. MTX is commonly used for arthopathy associated with DS. Genes for enzymes in the folate pathway have been investigated in rheumatoid arthritis to explain efficacy and toxicity with MTX. We investigated polymorphisms in the gene encoding soluble family member 19 (SLC19A1) which is responsible for transporting MTX into the cell and located on chromosome 21, was of interest.

**Objectives:** This study evaluated the role of polymorphisms in the folate pathway in DS with arthritis. We investigated the gene encoding SLC19A1 which is responsible for transporting MTX into the cell and located on chromosome 21. There are two common polymorphisms in this gene, one is a deletion, and the other is a SNP. The frequency of these polymorphisms was evaluated in our DS cohort and compared to a control group of age and sex-matched unaffected DS patients. Additionally, the clinical characteristics and outcomes of patients with these genotypes were also compared.

**Methods:** A total of 58 DS patients with arthritis were enrolled in the study. Selenocysteine and controls were matched for age and sex. DNA was extracted from peripheral blood. The gene encoding SLC19A1 was amplified in gene-specific PCR reactions. Subsequent genotyping of the PCR amplicons for SNPs in SLC19A1 was done by restriction fragment length polymorphisms. Results: All of the patients were heterozygous for SLC19A1 rs1051266 (80G>T). Fetal effects including nausea, emesis, and anxiety from methotrexate administration are significant in HUS. All patients required the addition of TNF inhibitors in addition to methotrexate for symptom control, and all had continued active arthritis at evaluation. Conclusion: Methotrexate is a folate analog that enters the cell via SLC19A1, which is encoded on chromosome 21. It is hypothesized that a gene dosage effect exists for SLC19A1 in DS. The third copy of the gene on chromosome 21 may lead to increased enzyme activity and thus enhanced transport of MTX into the cell, subsequently resulting in higher methylation demands which may lead to increased sensitivity to this medication in DS patients. However, all 3 patients required the addition of a TNF inhibitor and continued to have active arthritis, suggesting that at least in these patients, perhaps a third copy is inhibitory, and other factors beyond genotype are important contributors. Further analysis of the third allele via a copy number assay may elucidate allelic frequencies which may contribute to efficacy and toxicity in this population.

**EFFECTS OF A UTERINE RESTRICTION MODEL ON FETAL KIDNEY DEVELOPMENT IN SHEEP**

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**Background:** Fetal influences may alter the development of organs such as kidneys. A deficiency of kidney filtering units, nephrons, may ultimately result in hypertension as an adult. New nephrons develop until approximately 125 days gestation in sheep. A novel model of uterine size restriction and altered placental hemodynamics could be a tool to evaluate disturbances of fetal organ maturation.

**Purpose:** We set out to determine whether uterine restriction will decrease fetal weight and disturb kidney nephron development in the sheep fetus. Methods: Before pregnancy, a unilateral horn of the uterus was tied off in mixed-breed sheep (unilateral restriction) and compared to controls. The sheep were bred and pregnancy timed. Lambs were delivered at 120 or 130 days gestation (term 145). Results: Weights from 15 control fetuses (1.006 × NL) and 13 unilateral restriction fetuses (1.128 × NL) were equal and appropriately sized for gestation, based on published twin or triplet-specific normal values. p = 0.15. Crown-rump lengths were similar. As a measure of lean body mass, the ratio of weight (kg) to crown-rump lengths (cm) were not different (6.2 for controls and 7.1 for unilateral, p = 0.15). Fetal kidney weight/fetal weight was lower in unilateral lambs, p < 0.01. Histology showed disturbed nephron development and increased collagen staining. Conclusion: The unilateral fetuses were not smaller with Mean weight numerically greater, but not different than control. However, offspring kidney development was disturbed with smaller kidneys and tissue fibrosis after unilateral uterine restriction. More studies are necessary to examine potential mechanisms involved.
H. pylori has been recognized as an invasive microorganism causing gastric mucosal inflammatory and immune reaction. The gastric epithelium of H. pylori-infected individuals has been shown to have enhanced levels of several pro-inflammatory cytokines, including interleukin-1β, IL-6, IL-8, and TNF-α. Cytokine release is hypothesized to cause a substantial recruitment of inflammatory cells to the infected area, with subsequent release of reactive oxygen species (ROS). The ROS can cause the pathologic changes seen in the infected tissues. The increasing resistance to antimicrobials by H. pylori has resulted in the need for other agents to combat this bacterium. The antioxidant Optiberry®, which contains extracts of raspberry, strawberry, cranberry, elderberry, blueberry, and bilberry, was evaluated for its inhibitory effect on interleukin-6, IL-1β, and TNF-α production in vitro. In this study, human gastric adenocarcinoma cells of the MKN-45 cell line (HAC) were examined for the ethanol effect on ERK1/2 activation in a dose-dependent manner. Further research is needed to elucidate the underlying mechanism.

Results from this study indicate that MKN-45 cells infected with H. pylori reliably produced the cytokines IL-6, IL-1β, and TNF-α. In addition, Optiberry® was shown to reduce the levels of TNF-α production. However, Optiberry® had no statistically significant effect on IL-6 or IL-1β production by MKN-45 cells cocultured with H. pylori. It was concluded that there is a potential role for the antioxidant Optiberry® in therapeutic regimens for H. pylori infection.

Toluene inhibits L1 cell adhesion molecule signaling

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Background: Toluene is a commonly used organic solvent and an increasingly popular drug of abuse. Toluene abuse during pregnancy can result in a constellation of effects similar to fetal alcohol syndrome (FAS). Our previous studies have shown that inhibition of L1 cell adhesion molecule (L1) by ethanol has been implicated in the pathogenesis of FAS. We have shown that ethanol inhibits L1-mediated neurite outgrowth of cerebellar granule neurons (CGN). L1 activation of extracellular signal related kinases 1/2 (ERK1/2), and dephosphorylation of tyrosine Y177 of the cytoplasmic domain of L1. Due to the similarities between FAS and toluene embryopathy, we hypothesize that toluene and ethanol share similar mechanisms of toxicity. Objective: In this study, we examine the effects of pharmacological concentrations of tolune on the L1 mediated activation of ERK1/2 and dephosphorylation of tyrosine Y177 of L1 in rat postnatal day 6 cerebellar granule neurons (CGN). Design/Methods: CGN are plated on poly L-lysine and incubated overnight. Toluene dissolved in a vehicle of Alkamuls EL-620 (V) is added to the media for a final concentration of 10 mM, a concentration found in the blood of toluene abusers. Following a 1 h incubation, a monoclonal antibody to L1 crosslinked with mouse anti-IgG (ASCS4) is added to activate L1, and cells are harvested at 10 min. Cell lysates were immunoblotted for phospho-ERK1/2, total ERK, Y1176-L1 and total L1. Results: Toluene reduces L1 activation of ERK1/2 (P < 0.05) and dephosphorylation of tyrosine Y1176 of L1 (P < 0.05). Conclusion: L1 may be a target for toluene developmental neurotoxicity.

Choline and GM1 ganglioside supplementation abolish the ethanol inhibition of L1 cell adhesion molecule activation of extracellular signal-related kinases 1/2 (ERK1/2)

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Introduction: L1 cell adhesion molecule (L1) is critical for the development of the central nervous system. The neuropathologies of children with L1 mutations are similar to those with fetal alcohol syndrome implicating L1 as a target for ethanol toxicity. We have previously shown that ethanol inhibits L1 mediated neurite outgrowth and ERK1/2 activation of cerebellar granule neurons. Pharmacologic inhibition of ERK1/2 activation reduces neurite outgrowth of cerebellar granule neurons. Choline and GM1 ganglioside have been demonstrated to be protective against ethanol toxicity in recent studies. Objective: We sought to determine if choline and GM1 ganglioside can abolish the inhibition of ERK1/2 by ethanol and what is the most effective combination. Design/Methods: Cerebellar granule neurons, grown overnight in serum-free media containing various concentrations of choline and GM1 ganglioside were treated with 25 mM ethanol for 1 h, and then activated with L1 clustering (ASCs4) and cells are harvested at 10 min. Cell lysates were immunoblotted for phospho-ERK1/2, total ERK, and GM1 ganglioside were treated with 25 mM ethanol for 1 h, and then activated with L1 clustering (ASCs4) and cells are harvested at 10 min. Cell lysates were immunoblotted for phospho-ERK1/2, total ERK, Y1176-L1 and total L1. Results: Without GM1 ganglioside and choline (C/GM1) supplementation, ethanol can significantly inhibit the ERK1/2 activation by ACSS4 (P < 0.05). In addition, OptiBerry® was shown to reduce the levels of TNF-α production. However, OptiBerry® had no statistically significant effect on IL-6 or IL-1β production by MKN-45 cells cocultured with H. pylori. It was concluded that there is a potential role for the antioxidant OptiBerry® in therapeutic regimens for H. pylori infection.

Siglec-9 is expressed on CD44+ cells from umbilical cord blood and its expression increases during neutrophilic differentiation

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Background: Siglec-9 is a cell surface lectin shown to induce caspase-independent cell death in inflammatory adult neutrophils. Recently, surface expression of Siglec-9 was detected on a subset of acute myeloid leukemia (CD34-positive) cells, but was absent from normal adult bone marrow CD34-positive cells (Biedermann, 2006). Based on our recent observation of higher surface expression of Siglec-9 in neonatal neutrophils compared with those of adults, we hypothesized that Siglec-9 might also be expressed in umbilical cord blood (UCB) CD34 cells and that its expression might vary with maturation stage. Objective: To evaluate surface expression of Siglec-9 on CD34+ cells from umbilical cord blood and on HL-60 cells during neutrophilic differentiation. Design/Methods: CD34+ cells were isolated from UCB by density centrifugation and immunomagnetic enrichment of mononuclear cells. Cells were stained with fluorochrome-labeled Mab to assess co-expression of Siglec-9 and CD34 and analyzed by multi-color flow cytometry. In parallel studies, HL-60 cells were differentiated towards the granulocytic lineage with 1.5% DMSO for 6 days. On progressive days of culture, aliquots of differentiating cells were stained for expression of CD34 and Siglec-9, and then analyzed by multi-color flow cytometry. Results: In 6 separate studies, we observed that 39 ± 12% of UCB CD34+ cells expressed surface Siglec-9; of these, 31.5% were CD34+Siglec-9+ and 68.4% were CD34+Siglec-9-. During differentiation, HL-60 cells expressed generally increasing levels of Siglec-9, while expression of CD34 remained unchanged over a 6-day course. Conclusion: We observed a prominent surface expression of Siglec-9 on UCB CD34+ cells, which was reported absent from CD34+ cells in adult bone marrow. In addition, we determined that surface Siglec-9 expression increased during terminal neutrophilic differentiation. These and our previous studies suggest that Siglec-9 expression is dependent on the developmental stage of the host in hematopoietic cells, and that it may have a unique contribution to myeloid function in neonates.
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EARLY EXTUBATION AND HIGH FLOW NASAL CANNULA AFTER SURFACANT TREATMENT FOR RESPIRATORY DISTRESS AMONG PRETERM INFANTS
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Objective: 1) To retrospectively review the outcome and success rate of early extubation and humidified high-flow nasal cannula after surfactant treatment for RDS among preterm infants 24 to 35 weeks gestation. 2) To determine at which gestational age it would reasonable to attempt early extubation.

Methods: Charts of infants admitted to Loyola University Medical Center Neonatal Intensive Care Unit (LUMC NICU) between January to December 2006 with gestational age 24 to 35 weeks completed were reviewed. Those treated with intratracheal Curarospin® within two hours of birth, extubated within 48 hours of life, and survived until the time of discharge were included in the study. The study group was divided based on gestational age, 24–25 weeks, 26–27 weeks, 28–29 weeks, 30–31 weeks, 32–33 weeks, and 34–35 weeks. Exclusion criteria include major congenital anomalies and a 5 minute Apgar score <5. The four variables specifically analyzed as predictors of early extubation were, 1) gestational age (GA), 2) number of surfactant doses, 3) doses of antenatal steroids (Betamethasone), and 4) Apagar score at 5 minutes of life. This retrospective observational study was analyzed using logistic regression.

Results: A total of 88 infants fulfilled the criteria of the study; 24–25 weeks (n=7), 26–27 weeks (n=21), 28–29 weeks (n=16), 30–31 weeks (n=17), 32–33 weeks (n=12), and 34–35 weeks (n=15). Of the four variables analyzed, GA the most statistically significant with a P value <0.05. Successful extubation (defined as not requiring reintubation up to the time of discharge) at 24–25 weeks was (1/7) 14%, at 26–27 weeks (14/21) 67%, 28–29 weeks (12/12) 100%, 30–31 weeks (15/15) 100%. Conclusion: GA remains the most statistically significant among the predictors of early extubation. The earliest attempt of early extubation with a success rate of 66% in this study was between 24–25 weeks. At 28–29 weeks, the success rate of early extubation is 94%.

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ORAL FEEDING DIFFICULTY AT NICU DISMISSAL: A MARKER OF LATER DISABILITY IN PRETERMS?
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Purpose: This preliminary study investigates whether preterm infants with oral feeding difficulty (OFD) at intensive care nursery (NICU) dismissal manifest developmental delay by early childhood.

Methods: OFD was retrospectively defined by use of feeding tube, and/or feeding more often than every three hours, and/or use of formula concentration exceeding 24 kcal/ounce at NICU dismissal. Participants were chosen from a clinic database of 228 infants, born at <32 weeks gestation who were dismissed from NICU between 2002 and 2004. 71 patients with OFD were identified (22%) of which 35 were at birth weight (BW) and gestational age (GA) to 71 controls. These families were contacted in follow-up; responders included subjects with (n = 29) and without (n = 31) OFD, age between 43 and 81 months (mean 59.5). Families were interviewed by phone using the Vineland Adaptive Behavior Scales, Second Edition (VABS-II) plus a short questionnaire. Standard scores were calculated, and group comparisons were analyzed by chi-square and univariate analysis of variance with significance indicated by P < .05. Results: There were no group differences between OFD and control in BW (1044±379g vs.1052±310g), GA (28.1±1.2wk vs. 27.4±1.9wk), grade III/IV intraventricular hemorrhage, retinopathy of prematurity requiring surgery, or supplemental oxygen at 36 weeks GA. OFD subjects were more likely receiving occupational therapy at early childhood (P = .01). However, there were no differences in VABS-II domain scores of Communication (92±17 vs. 93±12), Daily Living Skills (65±15 vs. 89±15), Social (61±10 vs. 82±12), Motor (85±16 vs. 86±18), or any subdomain scores. Most OFD subjects (22/29) left NICU with feeding tube; VABS-II scores of these 22 subjects were also no different than controls. 5/29 OFD subjects (17%) still used feeding tube by early childhood, and VABS-II scores for these five children were significantly lower in all VABS-II domains except for socialization (P = .07). Conclusion: OFD is prevalent in preterm at NICU dismissal. However, OFD subjects did not differ from controls in adaptive behavior scores by early childhood. In this small sample, 1% of those discharged from the NICU with a gastrostomy tube still required device support for nutrition, and this subgroup of patients differed markedly in adaptive behavior scores compared to controls.

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EPIDEMIOLOGY AND OUTCOME OF PNEUMOCOCCAL MENINGITIS IN THE ERA OF PCV7
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Background and Study Purpose: Pneumococcal meningitis (PM) remains the most common cause of pediatric meningitis despite the advent of PCV7. Hearing loss remains the most common sequelae. An increased risk has been noted in children who have a short interval between first vancomycin (VAN) after ceftriaxone (CTRX) dosing. A single center retrospective observational study was undertaken to investigate the epidemiology of PM and evaluate the association between VAN and CTRX dosing and hearing loss.

Methods: Medical records of all children were reviewed from our urban tertiary care center with ICD-9 codes for PM from 1995-2007. Chart review included demographics, underlying disease, antibiotic susceptibility, neurologic presentation, and outcome including death, hearing loss, or other deficit. Dosing interval was recorded as ≤ 120 min or > 120 min for VAN after CTRX. Results: 59 cases of PM occurred in the study period; 4 died (6.8%). Hearing evaluations were available for 54/55 (98%). Overall, 15 (27%) had hearing loss, 9 profound, 14/15 had dosing interval data available. Dosing intervals among those with hearing loss were ≤ 120 min in 6 (43%) and > 120 min in 8 (57%). Odds ratio for hearing loss with short dosing interval was 1.08 (CI 0.31–3.72). Odds ratio for presence of underlying disease was 2.37 (CI, 0.76–7.39) for 2003–2007. Odds ratios for young age (≤30 mos) was 4.07 (CI 1.29–12.92) for 1995–2002. Discussion: Annual rates of PM in the PCV7 era have not decreased. PM is occurring in older children who more likely have an underlying disease. No correlation between timing interval between first VAN and CTRX with hearing loss was noted. Overall, morbidity and mortality rates are unchanged. Better strategies for prevention and treatment of PM are needed.

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ASSOCIATIONS BETWEEN VITAMIN D STATUS AND ASTHMA SEVERITY
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Background: Asthma prevalence has increased dramatically over recent decades, demonstrating that environmental factors may play a critical role. Previous studies have assessed the influence of diet and nutrition on the risk of acquiring childhood asthma, on asthma severity and on pulmonary function. Notably, positive associations have been found between some vitamins (e.g., ascorbic acid, α-tocopherol, and β-carotene) and pulmonary function in adults and adolescents. Vitamin D (Vit D) status may also have a role in the etiology of asthma. In experimental models, calcitriol has been shown to decrease pro-inflammatory cytokine production and promote anti-inflammatory pathways. Prior analysis of the National Health and Nutrition Examination Survey (NHANES) III found a strong positive association between Vit D status and pulmonary function in adults. However, similar analyses in children and adolescents have not been performed. Methods: This study evaluated associations between Vit D status, determined by serum levels of 25(OH) Vit D, and the prevalence and severity of asthma. We selected respondents between 6 and 20 with current asthma symptoms from the 2001–2004 NHANES III dataset. An asthma severity score (mild vs. moderate/severe) was developed using variables of recent asthma exacerbation, wheezing episodes, medical doctor and Emergency Department visits. Asthma (n = 614) and non-asthma cohorts (n = 5,606) were compared on serum levels of 25(OH) Vit D using survey-weighted chi-square tests and multivariable logistic regression models that included BMI and racial demographics.

Results: Asthma rates were highest in the children age 6–9 and 9–12 years with 25(OH) Vit D levels < 10 ng/dl (33.2% and 22.8%, respectively), however the numbers of subjects in these groups were small and associations did not reach statistical significance (P=0.35 and 0.24, respectively). The prevalence of asthma in the mild category, however still not significant (P=0.001). There is a trend between low Vit D status and increased asthma risk and asthma severity, but the small number of young asthma subjects in the 2001–2004 NHANES III dataset limits statistical analysis. Further studies utilizing different sampling methods are needed to further evaluate this relationship.
RESPIRATORY SYSTEM COMPLIANCE IN PREMATURE INFANTS IN RELATION TO ANTENATAL STEROIDS AND AS A GUIDE TO EXTUBATION
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Background: Premature infants with respiratory distress syndrome (RDS) are known to have poor respiratory compliance. Antenatal Steroids (ANS), administered in 2 doses, 24 hours apart have been shown to reduce the incidence of RDS. Whether this effect is primarily due to improvement in pulmonary mechanics is unclear. Our objectives were to examine the effect of varying timing of ANS exposure on respiratory compliance of premature infants and to evaluate measures of pulmonary mechanics in the prediction of successful extubation. Methods: Respiratory compliance (Crss) was measured in preterm infants (n = 60) born prematurely (<32 weeks) gestation and requiring ventilator support, within the first 6 hours of life prior to surfactant administration. Infants were divided in three groups based upon the dose and timing of ANS exposure: Group 1 (0 to 1 dose), Group 2 (2/3 doses 24 hours to 14 days prior to delivery) and Group 3 (2/3 doses > 14 days prior to delivery). Multiple measures of pulmonary mechanics were done within 6 hours prior to elective extubation before 3 weeks of age to predict success of extubation. Results: The mean birth weight and gestational age were higher in Group 3 compared to groups 1 and 2, 1239 gm (334) vs. 987 gm (419) and 915 gm (385) weeks of age to predict success of extubation.

Compliance soon after birth was significantly improved among premature infants whose mothers underwent PD A ligation. Demographic data, details of pre and post-operative clinical course and outcomes were abstracted. Statistical analysis (SPSS software) included chi-square test for nominal variables and t test for categorical variables. Results: Our cohort (n = 82) had a median (range) gestational age of 25.5 (23–28) weeks and birth weight 765 (485–1150) grams; 51 (62.2%) were males. The median (range) age at diagnosis and ligation of PDA was 6 (2–23) days and 215(±8) days. Primary ligation was performed in 28 (34.1%) infants. At 48 hours following ligation, an increase in FiO2 was needed in 49 (60%) infants and in the ventilatory support in 35 (43%) infants. Pressures were administered in 15 (17.9%) cases. An increase in respiratory or pressor support was required in 53 (64.6%) infants. Pneumothorax developed in 18 (22%) cases while X-ray findings worsened in 36 (44%) infants. The median (range) duration to return to baseline FiO2 was 3(1–30) days, to extubation was 16 (1–98) days and to start feeds was 3 (1–17) days. Post-operative outcomes did not differ significantly between the primary ligation and medically treated groups. Nine (11%) infants died, 35 (42.4%) had or severe bronchopulmonary dysplasia, 30 (37%) had severe intraventricular hemorrhage (Grade 3–4) and 16 (20%) developed necrotizing enterocolitis. Conclusion: PDA ligation in extremely preterm infants is associated with an increase in cardio-respiratory support in the immediate post-operative period in the majority. Whether the setback is temporary or adversely affects long-term outcomes remains to be determined.

SYMPTOMATIC SPONTANEOUS PNEUMOTHORAX IN TERM NEWBORN INFANTS: ALWAYS A BENIGN ENTITY?
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Background: Spontaneous pneumothoraces in newborns who have never been exposed to positive pressure ventilation and were without obvious pulmonary pathology often present soon after birth with varying degrees of respiratory distress. Not much however is known, as to how they should be managed and their outcomes. The purpose of this observational study was to characterize the clinical course and the outcome of the term newborn infants with spontaneous pneumothoraces. Methods: Retrospective review of term newborn infants with symptomatic pneumothoraces born between January 2002 and December 2006.

Results: Two hundred thirty-seven full-term and near-term infants were identified with symptomatic pneumothoraces: Sixty-two (26%) infants had spontaneous pneumothoraces, and the remaining 175 infants had obvious pulmonary pathology e.g. congenital diaphragmatic hernia, meconium aspiration syndrome etc., and/or were exposed to or receiving mechanical ventilation at the diagnosis of pneumothoraces. Forty-one (61%) of the 62 infants with spontaneous pneumothoraces could be managed conservatively while 21 required surgical interventions in the form of thoracostomy or thoracostomy drainage. Resolution of symptoms occurred in 1 day (median, range 1–2 days) in infants managed conservatively and 2 days (median, range 1–12 days) in infants requiring surgical intervention. Indications for surgical interventions in these 21 infants were: development of persistent pulmonary hypertension (PPHN) during conservative treatment in 9, imminent transport prompting elective evacuation of air at the referring hospital in 7, progressive deterioration in respiratory status with underlying pneumonia in 3 and without pneumonia in 2 infants including 1 infant who had tension pneumothorax. Thirteen of these 21 infants requiring surgical intervention needed mechanical ventilation and 3 infants subsequently required ECMO. Conclusions: Majority of term and near-term infants with spontaneous pneumothorax has a benign course with good outcome, and can be managed conservatively. Presence of PPHN or underlying pneumonia in newborns diagnosed to have spontaneous pneumothorax should prompt referrals to tertiary level neonatal units in anticipation of the need for surgical interventions and mechanical ventilation.

OUTCOMES IN INFANTS WITH CARDIAC DYSFUNCTION ASSOCIATED WITH BRONCHIOLITIS
C Stickney, K Mason. Department of Pediatrics, Rainbow Babies and Children’s Hospital, Cleveland, OH.

Background: Although bronchiolitis is a common cause of Pediatric Intensive Care Unit (PICU) admission in infants, associated cardiovascular dysfunction has only infrequently been reported in the literature. These isolated reports, the largest of which is a case series of eight patients with complete atral tachycardias, describe cardiac abnormalities in patients with acute bronchiolitis including dysrhythmia and myocardial dysfunction. Because of the rarely described occurrence of acquired heart disease in this patient population, little can be stated regarding the implications for morbidity, mortality, or recurrence of cardiac dysfunction in these patients. Our purpose is to examine the presentation, hospital course, status at discharge, and, when available, long-term outcomes of infants with bronchiolitis and evidence of cardiac dysfunction admitted to the PICU at Rainbow Babies and Children’s Hospital. Methods: We undertook a single-institution retrospective chart review of infants admitted to the PICU from January 1, 1998 to March 1, 2008 with a diagnosis of bronchiolitis who developed cardiovascular dysfunction as manifested by 1) hypotension requiring any combination of inotropes, vasopressors or extracorporeal membrane oxygenation (ECMO) support; 2) echocardiographic evidence of myocardial dysfunction or morphologic changes; or 3) cardiac arrhythmias. Results: Five infants were identified from the ten-year period reviewed. Two infants presented with supraventricular tachycardia requiring anti-arrhythmics and/or cardioversion. One infant had documented right ventricular hypertrophy which had resolved on follow-up echocardiogram three months following discharge. Two infants developed hypotension requiring inotropic support. Two infants had complete resolution of dysfunction at the time of hospital discharge. Two other infants were discharged on cardiac medications; one was subsequently lost to follow-up while the other was ultimately diagnosed with Wolff-Parkinson-White syndrome. There were no case fatalities in our cohort. Conclusions: During the past decade, cases of bronchiolitis-associated cardiac dysfunction at Rainbow Babies & Children’s have been rare. It of note, this series includes the first description of an infant presenting with reversible changes in cardiac morphology in the setting of RSV bronchiolitis. Additionally, we describe the first presentation of an infant with previously unknown WPW and onset of SVT precipitated by bronchiolitis. This single-institution case series of five patients contributes further data to the body of extant literature describing bronchiolitis-associated cardiovascular dysfunction.
DESCRIPTION OF A NEWLY INSTITUTED ANTIMICROBIAL STEWARDSHIP PROGRAM
J Newland, L Stach, MA Jackson. Children’s Mercy Hospital (CMH), Kansas City, MO.

Background: The Infectious Diseases Society of America established guidelines for antimicrobial stewardship programs (ASP). The guidelines request research on ASP strategies in pediatrics. Methods: A prospective study was begun to evaluate the ASP at CMH. On 3/3/08 a prospective audit ASP was implemented. The antibiotics (abs) audited: 3rd gen cephalosporins, cefepime, β-lactam/β-lactamase, van, lincosides, metronidazole, amikacin, tobramycin, aztreonam & fluoroquinolones. Data is collected on patients (pts) that receive a monitored ab for 2 days. Results: 860 pts and 988 monitored abs were reviewed from 3/3 to 5/31/08. The ab most frequently reviewed was ceftiraxone/cefotaxime 487. Services most often ordering a monitored ab were general peds 170, heme/onc 144, & hospitalist 144. The indications were made on 237 (28%) pts. Compliance occurred in 94% of pts.

Conclusions: A prospective audit with feedback ASP has been successfully implemented and accepted in a children’s hospital. Discontinuing therapy, shortening duration, and narrowing therapy were the most frequent recommendations and likely will affect cost savings and ab resistance.

Type of Recommendation N (311) % Recommended
Stop 105 34
Shorten duration 22 7
Narrow empirically 30 9.6
Narrow bic of culture & susceptibility (C&S) 42 13.5
IV to PO 22 7
↑ dose and ↓ dose 24 7.7
Redundant Rx & Reduce Frequency 13 4.2
ID consult 21 7

ANTEONATAL-NEONATAL RISK FACTORS IN LENTICULOGRAPHY
S Szkola, E Malone, A Kuder, R Mittendorf, JKM Uraskas. Loyola University, Maywood, Illinois.

Background: Lenticulostriate vasculopathy is a mineralizing vasculopathy confined to the blood vessels of the thalamus and basal ganglia of newborns. The incidence is 1-3% with no known etiology. LSV must often be an incidental finding on routine cranial ultrasounds of preterm newborns. Neuronal developmental sequences appear to be minor. Grey matter lesions are atypical in preterm newborns compared to the vulnerable periventricular white matter. Study Design: Over a 10 year period (1997-2007), we retrospectively identified 28 preterm newborns with the diagnosis of LSV on routine cranial ultrasounds prior to discharge from the NICU (Group 1). In this same period, we identified 40 preterm newborns without LSV as controls (Group 2). We examined the general characteristics of gestational age and birthweight, as well as antenatal variables of multiple gestation, antenatal steroid use, magnesium tocolysis, chorioamnionitis, and early respiratory alkalosis in preterm newborns.

Results:

Group 1 Group 2 p value
Antenatal Steroids 12(28.6%) 13(32.5%) 0.66
MgSO4 exposure 13(26.6%) 9(40.2%) 0.06
Chorioamnionitis 11(28.6%) 7(40.2%) 0.05
pH > 7.4 19(28.6%) 8(38.1%) 0.001
PaCO2 > 30 17(26.9%) 8(40.2%) 0.001

Conclusions: Our findings suggest that LSV is associated with decreased antenatal steroid use, increased magnesium sulfate tocolysis, chorioamnionitis, and early respiratory alkalosis in preterm newborns.

PREDICTING SURVIVAL IN CONGENITAL DIAPHRAGMATIC HERNIA
P. Muaw, F. Morris, J. Klein. University of Iowa Children’s Hospital, Iowa City, IA.

Background: Congenital diaphragmatic hernia (CDH) persists as a clinical challenge. A recent large single reported survival at 69%. Surgical timing and stomach location in left CDH are thought to impact CDH survival. Better predictive and explanatory survival models could enhance understanding of this disease. Objective: Establish factors that predict survival for patients with CDH. Design/Methods: Chart review of CDH cases with respiratory distress at birth from 1992-2007 at the UI NICU. Survival probability was calculated using a published model. A mean oxygenation index (OI) was calculated for the first 12 hours of life and again at surgery. Variables recorded included survival, stomach location, surgical timing, post-operative pulmonary hypertension (PHNT), multiple congenital anomalies (MCA), antenatal diagnosis, delivery location, birth year, and sex. Univariate and multivariate associations were performed to build predictive and explanatory logistic regression models. Results: 80 total cases. Antenatal diagnosis: 45/80 (56%). Outborn: 37/80 (46%). MCA: 18/80 (23%). Right CDH: 22/80 (28%). Left thoracic stomach: 32/80 (40%). Left-Lower abdominal: 36/80 (45%). Left-Lower abdominal and liver: 24/80 (30%). Conclusion: A prospective and explanatory survival model could enhance understanding of this disease.


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COST BENEFIT ANALYSIS OF UNIVERSAL NEWBORN SCREENING FOR MATERNAL ALCOHOL USE DURING PREGNANCY

A Gifford, KF Farkas, LW Jackson, CF BEarmer. Rainbow Babies & Children’s Hospital, Case Western Reserve University, Cleveland, OH.

The objective of this research is to estimate the cost-benefit ratio of universal meconium screening for maternal drinking. Fetal alcohol spectrum disorder (FASD) and its subset fetal alcohol syndrome (FAS) are preventable and remain a public health tragedy. The incidence of FAS and FASD have been conservatively estimated to be 0.07% per 1000 births. Fetal alcohol screening tests have demonstrated a promising at-birth method of detecting drinking during pregnancy. Design/Methods: The current costs of FAS and FASD, alcohol treatment programs, and meconium screening were estimated by literature review. Monetary values were converted roughly to equal dollars in 2006. Cost of meconium analysis as an additional part of the current newborn screening program and treatment for the identified mothers were estimated and compared to the potential averted costs that may result from identification and prevention for mothers. These potential maternal treatment strategies, residential, pharmacologic, and brief telephone interview, are analyzed. Results: Depending on the treatment type, the savings may range from $5 to $115 for every $1 spent on screening and treatment. Conclusion: We suggest that a universal meconium screening at birth to identify high-risk women and prevent the future costs of FASD be considered. Future research should be directed at improving detection and interventions as well as considering the ethical issues involved in such a screening program.

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TO PREDICT DEVELOPMENT OF PERSISTENT PULMONARY HYPERTENSION OF NEWBORN IN CASES OF MECONIUM ASPIRATION SYNDROME (MAS)

K Jin, R Dudaq, M Khilleh, T F Yeh and S Pyati (Sponsored by Suma Pyati). Department of Pediatrics Division of Neonatology, John H Stroger Jr Hospital of Cook County, Chicago, IL.

Background: Persistent pulmonary hypertension of the newborn (PPHN) remains one of the major causes of death in infants with meconium aspiration syndrome (MAS). At present there is no tool to predict development of PPHN in MAS. Objective: To predict development of Persistent Pulmonary Hypertension (PPHN) in Meconium Aspiration Syndrome (MAS) and to explore the possible Pathogenesis. Design/Methods: We retrospectively analyzed 114 infants who were admitted to our NICU because of MAS between Jan 2002-Oct 07. MAS was diagnosed based on 1) Meconium staining of amniotic fluid 2) Respiratory distress and 3) Positive chest radiographs. PPHN was diagnosed by pediatric cardiologist based on Echo evidences of pulmonary hypertension and with right to left shunt through Foramen Ovale and/or ductus-arteriosus without other anatomic abnormalities. All infants followed a respiratory protocol in NICU. Results: Of the 114 newborns with MAS, 23 had PPHN (20.2%). Time of onset of PPHN: 6(26%) at 24 hrs, 12(52%) at 12-24 hrs and 5(22%) at > 24 hrs of postnatal age. All 23 infants required NO therapy, 3 required HFOV and 4 required ECMO. When compared infants with and without PPHN, the risk factor for PPHN include: outborn neonatal transfer (14/23 vs 32/91 p = 0.023), low initial pH (mean ± SD 7.19 ± 0.16 vs 7.29 ± 0.15 p = 0.001) lower PaO2( 64 ± 25 vs 113 ± 55mm Hg p < 0.05), high PCO2 (51 ± 12 vs 43 ± 14 mmHg p < 0.05), and higher proportion of hypocalcemia (< 6.5 mg %) (6/23 vs 7/68 p = 0.01) admission to NICU. There is tendency for higher incidence of maternal fever and fetoal distress in infants with PPHN. Conclusions: Mortality can be reduced in MAS cases by managing all MAS cases with the initial lower PaO2, pH, and Calcium in high dependency unit Considering, positive co-relation between these factors with MAS and development of PPHN.

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WOULD PROPHYLACTIC PDA TREATMENT DECREASE HOSPITAL RESOURCES UTILIZATION?

MA Amag, V Bhatt-Mehta, S Heibert, RE Schumacher. University of Michigan, Ann Arbor, MI.

Introduction: Patent ductus arteriosus (PDA) and its treatment are associated with multiple serious complications in very low birth weight (VLBW) infants. Methods: We evaluated the effect of prophylactic PDA treatment on the utilization of hospital resources in a regional neonatal intensive care unit (NICU). We retrospectively analyzed data including hospital length of stay (LOS) from medical record. We also compared observed LOS to predicted LOS (calculated and reported by the Vermont Oxford Network (VON) using a multivariate analysis, accounts for many variables contributing to variability in LOS). Prophylactic treatment within the first 24 hours of life with Indomethacin was used between September 2006 and April 2007. Infants born between January 1, 2005 and April 30, 2007 with gestational ages less than 28 weeks, survived for more than two days were included in the analysis. Results: Seventy nine patients met the study criteria, 20 received Indomethacin prophylactic treatment and 59 received no prophylactic treatment. Infants treated prophylactically had similar gestational age (median, IC range), 26(24–27) vs 26(23–27) weeks but higher birth weights (mean, SD), 890(219) vs 838, (198 p = 0.047 compared to untreated infants. The two groups had similar rates of prenatal treatment with steroids, treatment with surfactant, male gender, mortality and being born at a tertiary center. The two groups also had similar duration of support with mechanical ventilation. Treated and untreated infants died before hospital discharge had similar NICU LOS (mean, SD), 19 (25) vs 20 (15) days. Prophylactically treated infants needed rescue PDA pharmacologic treatment less frequently (20% vs 65%, p = 0.02) but had similar rates of surgical ligation (85% vs 29%) compared to untreated infants. Prophylactically treated infants also had significantly higher rates of intestinal perforation (30% vs 7%, p = 0.04) and abdominal surgeries (30% vs 8%, p = 0.03) and had a higher rate of necrotizing enterocolitis (20% vs 14%, p = 0.49) that was not statistically significant compared to untreated infants. Infants survived to discharge to home (17 treated and 45 untreated) had a similar total observed LOS (mean, SD), 89(29) vs 96 (32). However, infants prophylactically treated with indomethacin had a clinically important larger difference between observed and predicted LOS (mean observed-predicted, SD) 10 (17) vs 45 (45) than untreated infants, but that difference was not statistically significant, p = 0.14. Conclusions: Prophylactic PDA treatment with Indomethacin was associated with more abdominal surgeries. The independent effect of prophylactic PDA treatment on LOS should be included in assessing the efficiency of such a treatment.

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DIFFERENCES IN BELIEF AMONG PEDIATRIC SPECIALISTS REGARDING GASTROESOPHAGEAL REFUX DISEASE (GERD) IN PREMATURE INFANTS IN A NEONATAL INTENSIVE CARE UNIT SETTING: CLINICAL VIEWS AND IMPRESSIONS OF THE MEDICAL LITERATURE

C Golds1,2, F Rome1,2, R Martinez1,2, M Frank3,4,5, S Woreley1, Z Sun1 and AM Hibbs2,3, 1Cleveland Clinic Lerner College of Medicine of Case Western Reserve University (CWRU), 2CWRU School of Medicine, 3Dept. of Epidemiology and Biostatistics, CWRU, 4Dept. of General Pediatrics and Adolescent Medicine, Cleveland Clinic Children’s Hospital, 5Dept. of Pediatrics, Rainbow Babies and Children’s Hospital, 6Dept. of Family Medicine; 7Dept. of Quantitative Health Sciences, Cleveland Clinic; 8Cleveland, OH.

Background: There is wide variation in the treatment of suspected GERD in premature infants; it is unknown to what degree diagnostic and treatment choices are impacted by the treating physician’s medical specialty or impression of the medical literature. Methods: We conducted an online survey of board-certified neonatologists, pediatric pulmonologists, and pediatric gastroenterologists about their beliefs regarding the symptoms, diagnosis and treatment of GERD in premature infants in the NICU, based on both clinical impression and assessment of the literature. Results: 1013 neonatologists, 232 pediatric pulmonologists, and 222 pediatric gastroenterologists participated in the study (47.5% response). There was disagreement among specialties in nearly all aspects of the survey. Pulmonologists were most likely to report that respiratory symptoms are caused by GERD (p < 0.001). Neonatologists were least likely to report that a therapeutic trial of pharmacologic agents would be useful for diagnosing GERD (p < 0.001) or that lansoprazole, ranitidine, or cimetidine are safe or effective (p < 0.001). No pharmacologic therapy had >50% of respondents supporting its effectiveness. There was only moderate correlation between physician belief based on the medical literature and belief based on clinical impression (Spearman Rank Correlation 0.47–0.75). For therapies supported by multiple randomized controlled trials (RCT’s) in infants vs. therapies with fewer RCT’s in infants, physicians rated the evidence for effectiveness similarly. Conclusion: There is wide variation within and between pediatric specialties with regard to attitudes and beliefs about suspected GERD in premature infants, as well as about the weight of evidence in the medical literature for this patient population. Furthermore, there is no agreed-upon standard of care. Greater understanding is needed about the way in which physicians process evidence from the medical literature.
EVALUATION OF RESIDENT SURVEILLANCE OF PEDIATRIC PATIENT DEVELOPMENTAL STATUS AT THE TWO-MONTH PREVENTIVE CARE VISIT


Purpose: Assessment of the impact of performance-related feedback (based upon video-recorded observation) coupled with an educational module on resident demonstration of competency regarding the physical & developmental examinations component of developmental surveillance of infants at the two-month preventive care visit. Methods: Using a multiple baseline across subjects design, three residents were observed & video recorded while performing two-month preventive care visits. The visits were reviewed for the presence or absence of resident assessment of five specific criteria to establish baseline. Following baseline, individual feedback & a standardized educational module (lecture based with video components demonstrating milestones expected of two-month-old infants) were provided for the resident (intervention). Upon each resident’s completion of the intervention, the resident was again observed & video recorded while performing two-month preventive care visits. Results: As of today’s date, two residents have completed the study & one other resident is near completion. One completed resident was observed three times prior to receiving the intervention & demonstrated assessment of 2, 2, & 1 of the five criteria during those observations, respectively. Post-intervention, the resident demonstrated assessment of 4 of the 5 criteria during each of the 3 post-intervention visits. The second completed resident was observed 4 times prior to receiving the intervention and demonstrated assessment of 4, 2, 3, & 5 of the five criteria respectively. Post-intervention, the resident demonstrated assessment of 4 of the 5 criteria during each of the 3 post-intervention visits. The remaining resident was viewed during 5 post-intervention visits & demonstrated assessment of 2, 2, 3, 5, & 3 of the 5 criteria respectively. Post-intervention, the resident is pending to complete the study. Conclusion: Individual performance-related feedback coupled with a standardized educational module containing video components demonstrating milestones is an effective method of increasing resident demonstration of competency regarding the physical & developmental examinations component of developmental surveillance at the two-month preventive care visit.

Birth Injuries in Postterm Infants Born to Obese Women

DR Hallock1, K Bugler2, C O’Neil1, AB Caughhey3. 1Saint Louis University, St Louis, MO 2University of California, San Francisco, CA.

Purpose: Maternal obesity and postterm gestation are independently associated with increased perinatal complications including birth injuries. The purpose of the study was to determine the risk of birth injury in postterm versus term infants across maternal weight categories. Methods: This is a population-based cohort study utilizing information from birth certificates linked to hospital discharge data for all live, singletons born to Missouri residents between 1993 and 1999, excluding infants born by cesarean section or born to study utilizing information from birth certificates linked to hospital discharge data for all live, singleton infants postterm versus term infants across maternal weight categories.

Conclusions: We observed a statistically significant increase in birth injury rates at 40 weeks gestation, despite the current ACOG recommendation to induce labor beginning at 42 weeks to minimize complications. The rate of birth injuries was significantly higher among obese and overweight women but there was no multiplicative effect in postterm infants. Obstetricians should continue to counsel women about the risk of birth injuries associated with obesity and late gestation.

<table>
<thead>
<tr>
<th>Gestation (Weeks)</th>
<th>Normal Weight</th>
<th>Overweight</th>
<th>Obese</th>
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<tr>
<td>Rate/1000</td>
<td>aOR (95% CI)</td>
<td>Rate/1000</td>
<td>aOR (95% CI)</td>
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<td>39</td>
<td>31</td>
<td>referent</td>
<td>32</td>
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<tr>
<td>40</td>
<td>36</td>
<td>1.12 (1.05,1.20)</td>
<td>38</td>
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<tr>
<td>41</td>
<td>38</td>
<td>1.12 (1.03,1.22)</td>
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<td>42</td>
<td>42</td>
<td>1.28 (1.07,1.53)</td>
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Social Worker’s Role in Medical Home for NICU Graduates


Background: Post discharge from NICU (Neonatal Intensive Care Unit) is a difficult task in inner city hospitals due to target population’s lack of resources including transportation, literacy, language barriers, and lack of understanding or confusion regarding complex medical needs as well as not having a care provider in clinic settings to help them understand and navigate through medical needs, government agencies, and provide psychological support. Such patients and families consume a lot of physician’s time on non-medical issues. Often times, medical staff does not have the expertise to navigate the community and government systems that help families receive benefits needed for optimal care. Failure to address non-medical issues often results in lack of compliance; some patients were lost for follow-up for such reasons. Objective: To establish a model of care that addresses non-medical issues to avoid delays in care and improve communication with families and improve compliance with medical visits. Design/Methods: A dedicated bilingual social worker with experience with NICU graduates was employed by a grant-funded position for the last 3 years to manage non-medical issues. During the first year of the grant, issues were studied and a design was developed to serve efficiently. The child’s “risk” status is graded into three levels based on medical/social worker’s assessment of environmental risk factor; all patients were followed in the clinic until a safe transition or discharge could be arranged. Results: During the last year, 570 patients were served by the social worker (2007–2008). The number of non-medical issues after initial intake was in the range of 1–7 per visit per case; 50% time was spent on care coordination and remaining hours were spent on supportive counseling, education, and improving communication with medical providers. Most families were in need of case management, supportive counseling, and information on resources to improve care and guidance to manage their lives. Conclusions: Care coordination and tracking by dedicated social worker improves parents’ understanding of child’s health status and compliance with care.