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DIFFERENT LEVELS OF DOCOSAHEXAENOIC ACID (DHA) IN FORMULA AFFECT RED BLOOD CELL DHA LEVELS IN TERM INFANTS.

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DHA is an important component of the brain. Red blood cell (RBC) DHA levels are thought to be related to brain DHA content and to visual acuity in infancy. The DHA content of the RBC of infants is determined by the DHA content of the feeding. To assess the effects of different levels of formula DHA on RBC DHA levels of infants, we conducted a multi-center, double-blind, prospective study. Infants were randomized to one of two infant formulas: Formula Higher DHA with DHA at 0.32% of total fatty acids, similar to worldwide mean levels found in breast milk, and Formula Lower DHA with DHA at 0.15% of total fatty acids, similar to lower levels typically found in breast milk in the USA. Infants were fed study formula from 14 through 120 days of age. Fatty acids in blood lipid fractions were analyzed by capillary gas chromatography at 120 days of age. The table summarizes DHA levels in total-RBC lipids, RBC-phosphatidylcholine (RBC-PC), RBC-phosphatidylethanolamine (RBC-PE), and plasma phospholipids (Plasma-PL) at 120 days (% of total fatty acids, Mean ± SE).

	Higher DHA (n = 30)	Lower DHA (n = 26)	P-value
DHA, Total RBC	6.67 ± 0.13	4.74 ± 0.15	<0.001
DHA, RBC-PC	3.73 ± 0.09	2.39 ± 0.10	<0.001
DHA, RBC-PE	10.85 ± 0.21	7.65 ± 0.24	<0.001
DHA, Plasma PL	5.85 ± 0.13	4.01 ± 0.14	<0.001

Both formulas were well tolerated, and infants in both groups had similar growth. We conclude that infants fed formula containing higher levels of DHA have significantly higher circulating levels of DHA. We speculate that greater incorporation of DHA into brain and retinal tissues may result from higher circulating levels of RBC DHA.

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EGR-1 NULL MICE EXHIBIT IMPAIRED HEPATIC REGENERATION.

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The liver regenerates itself in response to a wide variety of injuries. The rodent partial hepatectomy model has been a useful tool with which to investigate the signals that regulate this regenerative response. These signals include activation of an immediate-early gene expression program during early liver regeneration which directs growth factor-dependent hepatocellular proliferation and leads to restoration of normal hepatic mass. The early growth response 1 transcription factor (EGR-1), whose expression is known to be regulated in a variety of models of cellular growth and differentiation, has been shown to be induced as part of the immediate early gene expression response during liver regeneration. In the studies reported here the functional significance of EGR-1 expression during liver regeneration was examined by characterizing the hepatic regenerative response to partial hepatectomy in EGR-1 null mice. The results of these studies showed that liver regeneration in EGR-1 null mice is impaired. Although the early signaling events leading up to the first wave of hepatocellular DNA synthesis occurred normally following partial hepatectomy in EGR-1 null mice, subsequent signaling events and cell cycle progression after the first round of DNA synthesis were deranged. This derangement was characterized by increased activation of the p38 mitogen activated protein kinase and inhibition of hepatocellular metaphase-to-anaphase mitotic progression. Together these observations suggest that Egr-1 is an important regulator of hepatocellular mitotic progression through the spindle-assembly checkpoint. In support of this, microarray-based gene expression analysis showed that induction of expression of the cell division cycle 20 gene (CDC20), a key regulator of the mitotic anaphase promoting complex, is significantly reduced in EGR-1 null mice. Taken together these data define a novel functional role for EGR-1 in regulating hepatocellular mitotic progression during liver regeneration.

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THREE-YEAR ASSESSMENT IS PREDICTIVE OF OUTCOME AT 8 YEARS OF AGE FOR ELBW SURVIVORS.

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Background: Extremely low birth weight infants are at increased risk for neurodevelopmental disabilities. It would be useful to determine if preschool screening could predict which children will be normal at school age so follow-up resources could be directed to those at greatest risk. **Objective**: To determine if neurodevelopmental assessment at 3 yrs of age is predictive of outcome findings at 8 yrs of age for children who were <801 g BW. **Methods**: All surviving infants 450 to 800 g BW cared for at hospitals associated with UMKC School of Medicine were enrolled in a multidisciplinary follow-up clinic. Children were evaluated with a standard battery of cognitive, motor, and language tests. At 3 and 8 yrs, outcomes of children were categorized by composite results as having major disability, mild disability, or normal, according to pre-established criteria (Kilbride, Daily, *J Perinatol* 1998;18:102). The relationship between the neurodevelopmental category at 3 yrs and outcome measures at 8 yrs was assessed by ordinal logistic regression analysis, controlling for confounding variables (GA, BW, SES, and IVH). **Results**: 149 children were evaluated. Mean BW (range) was 702±80 g (490–800) and GA, 25.8±1.5 weeks (23–31). There was no significant relationship between BW or GA and outcome at 8 yrs. Infants without IVH were statistically more likely to be categorized as normal (51% vs 31%, grade I–II and 27%, grade III–IV, $P=.04$), and had higher IQ scores (89±15 vs 82±19, grade I-II and 82±17, grade III-IV). IQ scores were also related to SES (high SES, 90±15 and low SES, 82±19, $P=.05$). Independent of these variables, neurodevelopmental categorization at 3 yrs was highly correlated with 8-yr outcome findings ($P<.000$). At 3 yrs of age, 20% (43/149) were considered normal, 54% (80/149) mildly disabled, and 19% (26/149) had major disability. For those with a normal assessment at 3 yrs, 84% were considered normal and 16% mildly disabled at 8 yrs. None of these children had major disability. For those with mild disability at 3 yrs, 31% were normal and 10% had major disability at 8 yrs. 81% of those with major disabilities at 3 yrs remained in that category at 8 yrs; the other 19% were categorized as having mild disability. Overall, between 3 and 8 yrs, outcome status improved for 20% and declined for 10% of children. **Conclusion**: No child identified as normal at 3 yrs was found to have a major disability at 8 yrs of age. An evaluation at 3 yrs of age using composite categorization of cognitive, motor, and neurosensory assessments may accurately predict functional outcome at school age.

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INVOLVEMENT OF ENDOTHELIN RECEPTORS IN NEONATAL MORPHINE WITHDRAWAL.

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Purpose: Management of neonatal opioid tolerance and withdrawal symptoms remains a major clinical challenge in NICUs. Numerous neuromodulators are involved in tolerance and withdrawal mechanisms. We have previously shown that central endothelin (ET) receptors are involved in morphine tolerance. The purpose of this study is to investigate the involvement of central ET receptors in morphine withdrawal in neonatal rats. **Methods:** Pregnant rats were divided into two groups and rendered tolerant to placebo and morphine pellets, respectively, over a 7-day period. On day 8, both placebo and morphine pellets were removed and rats were allowed to undergo withdrawal for 24 hours. Rat pups were delivered by c-section. Neonatal rat brains were dissected and used for analysis. Changes in G-protein stimulation were determined by using [(35)S]-guanosine-5′-o-(3-thio)triphosphate ([^{35}S]GTPγS) binding assay in the brain of neonatal rats undergoing placebo and morphine withdrawal. **Results:** Morphine produced significantly higher ($P<0.05$) maximal stimulation in neonatal rats undergoing morphine withdrawal (83.60%) when compared to placebo (66.81%). EC_{50} values in morphine withdrawal group (6.825nM) were significantly lower ($P<0.05$) as compared to placebo (72.917nM). A significant increase in maximal G-protein stimulation was observed with ET-1 in the morphine withdrawal group (87.16%, $P<0.05$) as compared to placebo (74.88%). EC_{50} values for ET-1 in neonatal rats undergoing morphine withdrawal (93.75nM) were significantly higher ($P<0.05$) than placebo (62.5nM). ET_A receptor antagonist, BMS182874, did not stimulate GTP binding in placebo brains (EC_{50}1000nM), but significantly increased ($P<0.05$) maximal stimulation of G-proteins in morphine withdrawal group (86.07%, EC_{50}=31.25nM). ET_B agonist, IRL1620-induced stimulation of G-proteins was similar in placebo (73.43%, EC_{50}=13.26nM) and morphine withdrawal (75.08%, EC_{50}=11.70nM), respectively. **Conclusion:** Morphine-induced G-protein activation is increased while ET-1 induced G-protein activation is decreased in neonates undergoing morphine withdrawal. ET_A antagonist increases activation of G-proteins during withdrawal in neonates. In conclusion we provide evidence for the first time that central ET_A and not ET_B receptors are involved in morphine withdrawal.

COMBINED POSTER SESSION

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EPIDEMIOLOGY OF PERSISTENT COAGULASE NEGATIVE STAPHYLOCOCCAL BACTEREMIA IN NEWBORN INTENSIVE CARE INFANTS.

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BACKGROUND: Coagulase-negative staphylococcal (CONS) bacteremia is the most common nosocomial infection in most newborn intensive care units (NBICU). Infected infants have increased mortality, and morbidity compared to uninfected peers. At the University of Utah NBICU increasing numbers of infants have developed persistent (cultures positive for >48 hours after initiation of antibiotics to which organisms are susceptible *in vitro*) and prolonged persistent (positive for > 96 hours) CONS bacteremia. **OBJECTIVE:** To determine rates of persistent CONS bacteremia in NBICU infants in 2002–2003 and to compare risk factors for prolonged persistent vs. persistent CONS bacteremia. **DESIGN/METHODS:** A computerized microbiology database identified positive NBICU blood cultures from 1999–2003. Chart review of infants with CONS bacteremia documented possible risk factors for persistent and prolonged persistent infection in 2002–2003. Discrete variables were analyzed by chi-square for trend. Analysis for normally distributed continuous variables was by t-test, for non-normally distributed continuous variables by Mann-Whitney test. **RESULTS:** From 2001–2003, the frequency of bacteremia due to all bacteria has remained stable (0.03/1000 patient days, $p= 0.9$). From 1999–2003, CONS bacteremia increased (0.3–0.8–0.7–0.9/1000 admissions, $p<0.01$). Persistent CONS bacteremia (culture positive for >48 hours despite appropriate antibiotics) also increased (0.0–0.2–0.3–0.4–0.5/1000 admissions, $p<0.01$). Analysis of 51 infants was performed to determine risk factors for prolonged persistent CONS. Sixteen had CONS infection for 48–96 hours vs. 35 for >96 hours. Significant differences were found in days of antibiotics prior to onset ($p=0.03$), feeding intolerance at onset ($p=0.03$), and ventilator days associated with CONS ($p<0.001$). No difference in gestational age, day of life (DOL) of bacteremia onset, DOL to full enteral feeds, birth weight, or association with central vascular catheter < 72 hours prior to first positive culture was found. **CONCLUSIONS:** Persistent CONS has increased in our NBICU from 1999–2003. Significant differences were found between bacteremia < or > 96 hours with respect to prior days of antibiotic exposure, feeding intolerance, and CONS associated ventilator days. Differences were not found in gestational age, DOL onset, birth weight, indwelling central line in the 72 hours prior to CONS onset or time to full enteral feeds.

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INCIDENCE OF CATHETER RELATED BLOODSTREAM INFECTIONS AFTER THE REMOVAL OF PERCUTANEOUS INTRAVENOUS CATHETERS IN PRETERM INFANTS.

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The use of PICC lines in preterm infants increases the risk for systemic bacterial infections. The overall incidence of Catheter Related Bloodstream Infection (CRBSI) after PICC line removal is not well known. A single dose of antibiotics is sometimes used to try to decrease the incidence of CRBSI. Antibiotic prophylaxis to prevent CRBSI on removal of a PICC and increased use of antibiotics may increase resistant strains of bacteria. A retrospective review of medical records of infants with gestational age less than 29 completed weeks was designed. Patients were hospitalized between January 2003 and December 2003. Infants were excluded if there was death prior to PICC removal. Data for collection were prospectively identified and included total days of PICC life, days of antibiotics through PICC, days of TPN through PICC, BSI within 48 hours of PICC removal, gestational age of infants and their birthweight, method and location of PICC placement, infections noted during PICC life, sepsis evaluations within 48 hours of PICC removal, and catheter tip culture results. About 80% of babies less than 29 weeks had a PICC placed during their hospital course. 3 infants out of 72 had a CRBSI associated with a PICC. No bloodstream infections were detected within 48 hours after the removal of a PICC. No infants with a PICC had a sepsis evaluation within 48 hours of PICC removal. All infants with a PICC received total parenteral nutrition through the line. Antibiotic administration was generally remote to PICC removal, but some received antibiotics up to the removal of the PICC. Catheter tips were rarely cultured after PICC removal. PICC removal is a safe procedure without antibiotic prophylaxis, even in the face of a PICC life greater than 20 days. There is not evidence to support the administration of antibacterial prophylaxis for removal of PICC.