43 MULTIVARIATE ANALYSIS OF FACTORS RELATED TO NON-HEMOLYTIC HYPERBILIRUBINEMIA OF FULL-TERM NEWBORN INFANTS.

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The relation between hyperbilirubinemia in the first 4 days of life and a number of perinatal variables was studied in 456 healthy full-term (GA≥37 weeks) singleton infants delivered consecutively between Jan and May 1987. All infants were free from malformations and/or any other disease requiring treatment, they were ABO and Rh compatible with their mothers and were not G6PD deficient. The serum bilirubin level was <137 μmol/L (<8 mg/dl) in 46% of the study subjects, between 137 and 255 μmol/L (8-14.9 mg/dl) in 39% and ≥256 μmol/L (≥15 mg/dl) in 15%. An association (P<0.05) with hyperbilirubinemia was found for male sex, low gestational age (GA), prolonged labour or rupture of membranes, instrumental vaginal delivery, excessive weight loss (in turn related to poor feeding), delayed meconium passage, high levels of alpha-fetoprotein (AFP) in cord blood and history of jaundice in a previous sibling born at term. It was not possible to compare breast vs formula-feeding since nearly all babies (94%) were exclusively breast-fed. After adjustment for confounders with a log-linear model, only high levels of AFP, excessive weight loss, jaundice in a previous sibling and low GA still showed an independent association with hyperbilirubinemia. These results suggest that in our population inherited and constitutional factors and feeding play the most important role in the genesis of non-hemolytic jaundice in healthy full-term infants.

44 DOPPLER PARAMETERS AND GESTATIONAL AGE.

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The cerebral circulation of 58 normal neonates(23 term infants and 35 preterm) was investigated between 24 and 72 hours of life with a 5 MHz transducer(Duplex Scanner). Blood flow velocity (V), area under the velocity curve (AUVC), resistance index (RI), rise and fall slopes were obtained in the anterior cerebral artery. An increase of V (r=0.57) and AUVC (r=0.58) was observed throughout gestation. To a lesser extent, V (r=0.47) and AUVC (r=0.39) increased with increasing systolic blood pressure. Between 26 and 40 weeks, V varies from 16.9 to 28.8 cm/sec and AUVC from 37 to 63 KHz x min. This data suggest maturational changes. By contrast, RI, rise and fall slopes were found to be not gestation dependent. This could imply that capillaries of the germinal layer in the preterm infant with their architectural and anatomical immaturity would be exposed to the same blood flow velocity acceleration, expressed by the rise slope, as compared to therm infant. Further studies are needed to draw inferences regarding Doppler patterns in relation to metabolic and circulatory disturbances - hypoxaemia, hypercapnia, acidosis, hypotension - and cerebral damage.

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45 LACK OF NEUROPATHOLOGICAL CHANGES AFTER BILIRUBIN (B) ENCEPHALOPATHY (BE) IN RATS.

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BE was induced in 6 weeks old male SPRD rats by a 3hr infusion of B, resulting in mean serum B levels of 133-183μmol/l. Controls were infused with B-free solvent. Two hours into the infusion period some rats were given sulfisoxazole 50mg/kg as a bolus dose, others were given carbamide 75mmol/kg as a bolus dose, and yet others breathed 20% CO_2 in air for the last hour of the infusion period. Three weeks later behavioral studies in an open-field apparatus demonstrated changes in the B-treated rats interpreted as indicative of changes in stimulus processing. After fixation in 4% formaldehyde, sections from the brains of 68 rats were stained with hematoxylin-eosin and studied with light-microscopy by a pathologist (BW) who was blinded to the preceding treatment of the rats. Evidence of neuronal loss or glial proliferation was not found in any of the brains, indicating that BE manifesting itself with changes in behavior may occur without discernible microscopic changes in the brain.

46 LACK OF REGIONAL DIFFERENCES IN ENTRY OF BILIRUBIN (B) INTO YOUNG RAT BRAINS DURING CONTROL, DISPLACER, HYPERCARBIC, AND HYPEROSMOLAR CONDITIONS.

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In kernicterus the concentration of B is higher in cerebellum and basal ganglia than in other parts of the brain. The mechanism for this is unknown. We have studied the entry of B during short-term (1hr) hyperbilirubinemia created by infusing ^{3}H-B into young,male SPRD rats. Some rats were given sulfisoxazole 50mg/kg to displace B from the binding to A, some rats were made hypercarbic (PCO_2 18-21kPa, pH 6.9), and some rats were made hyperosmolar (serum osmolality 400mosm/l).The brains were dissected into 7 regions: cerebral cortex, hippocampus, striatum, midbrain, hypothalamus, cerebellum, and medulla oblongata. After correcting for B remaining intravascularly, interregional differences in brain B were not significant under any of the conditions employed. Differences in B concentrations between brain regions in kernicterus may not be related to differences in B uptake.

47 HYPEROXIA (HO), HYPOXANTHINE (HX) AND XANTHINE OXIDASE (XO) DO NOT INCREASE THE ENTRY OF BILIRUBIN (B) OR ALBUMIN (A) INTO YOUNG RAT BRAIN.

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HO has been suggested as a risk factor for kernicterus. Free radicals may be involved in oxygen toxicity. HX 10mM was infused at 0.1ml/min for 30min into retrograde carotid catheters in awake,young,male SPRD rats. The infusion was then briefly interrupted to inject XO 1U/kg through the same catheter, and the HX infusion continued at half the initial rate for another 30min. In group I (controls) 0.9% NaCl was infused instead of HX/XO. Groups I and II breathed 21% O_2 at all times, while group III breathed 90% O_2 from the start of the experiment. After 60min all groups were given a bolus dose of ^{125}I-HSA through a peripheral venous catheter, followed by B 25mg/kg for 5min, then B 35mg/kg for 55min. Brain B was determined by chloroform extraction, and brain A by gamma counting. There were no significant differences between the groups as regards serum B, serum A, brain B, or brain A. HO, HX, and XO do not increase the entry of B or A into rat brain.

48 THE PARTICIPATION OF SELENIUM IN OXYGEN RADICAL PROTECTION OF THE HEART

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Selenium (Se) is an essential constituent of the peroxide metabolising enzyme glutathione peroxidase. Isolated perfused hearts from rats fed a Se-deficient diet were investigated. Glutathione peroxidase content in Se-deficient hearts was less than 5% of controls, and examination of ultrastructure revealed some areas with moderate cellular damage, mainly slight oedema of cells and mitochondrial changes. Se-deficient and control hearts were exposed for 11 min to a high and a low concentration of oxygen radicals generated by xanthine oxidase 0.0125 and 0.025 U/ml, and hypoxanthine 0.96 mM. With the low dose of oxygen radicals contractile function was gradually reduced, but in Se-deficient hearts the decrease was significantly more pronounced than in controls (32.7±6.5 vs 58.3±8.4% of initial values, mean±SEM). With the high dose of oxygen radicals contractility decreased abruptly in both groups, but a significantly lower tissue content of adenosine triphosphate was detected in the Se-deficient hearts. It is concluded that Se-deficiency reduces the tolerance of the heart to oxygen radicals.