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## COMPARISON OF MEASURED AND CALCULATED SERUM BILIRUBIN BINDING CAPACITY (BBC)-A DANGER EXPOSED.

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We devised a paper chromatoelectrophoresis technique to measure serum BBC which compares favorably with results from Sephadex G25 chromatography. We measured serum BBC and total protein (TP) concentration in 27 infants of various gestational ages who required no special care (normal) and 51 infants with various problems who received treatment beyond routine (abnormal). The mean  $\pm$  1 SD of the BBC/TP ratio is  $3.92 \pm 0.47$  (range 3.20-5.40) and  $3.59 \pm 0.74$  (range 1.50-5.29) respectively for the normal and abnormal infants ( $p < 0.05$ ). If normal and abnormal infants are grouped together, the mean of the ratio is 3.75, which is similar to the derived value of 3.7 presented in some textbooks of neonatology. Many use that value together with a patient's serum TP in grams/dl to calculate an artificial BBC which then becomes the serum bilirubin concentration in mg/dl used to determine the need for exchange transfusion. If that process were applied to our subjects, 27% of normal and 18% of abnormal infants would receive an unnecessary exchange transfusion and the risk of bilirubin encephalopathy would be increased in 22% of normal and 51% of abnormal infants because they would not have received an exchange transfusion before the primary protein binding sites for bilirubin were saturated. It is clear that measuring the BBC of each infant's serum is imperative for accurate and reliable information. A calculated value based on a fixed ratio such as 3.7 appears to be unsafe.

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## LARYNGEAL CHEMOREFLEX - NEWBORN APNEA AND SUDDEN INFANT DEATH SYNDROME (SIDS). Ilya Kovar, Urban Selstam, William Z. Catterton, Marilyn B. Escobedo,

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The coordinated interaction of breathing and swallowing which is developed by 32-34 weeks human gestation is reflex in nature. Chemosensitivity of the laryngeal area can be shown to influence this interaction. A relationship between disturbances of this coordination, newborn apnea and SIDS is postulated. A laryngeal reflex which is elicited by chemical stimulation has been studied in a standardized manner in 18 newborn lambs using acute and chronic preparations. Water, various concentrations of salts and foreign (e.g. formula) solutions, applied above a tracheostomy, cause reflex hypoventilation or apnea, rapid swallowing, hypertension and blood flow redistribution (increase in carotid artery flow, decreased flow in descending aorta), with variable bradycardia. Normal ventilation can be restored by application of 154meq/l saline. We have demonstrated that 1) the reflex is not all or none, but graded and dose-response in type with respect to all components: stimulus, response and recovery. 2) cardiovascular changes are an integral part of the reflex and not due to hypoxia 3) laryngeal sensitivity and the reflex can be altered by chemical modification of taste reception (by potassium gyemate and miraculin). It is concluded that: (1) Taste receptors present in the laryngeal area are also the likely receptor for mediation of the reflex; (2) this is a useful model to study newborn apnea and (3) the reflex may be involved in the etiology of SIDS.

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## INCREASE IN BILIRUBIN-ALBUMIN BINDING AFFINITY WITH CORRECTION OF NEONATAL ACIDOSIS. K. Kozuki, W.J. Cashore, J. Widness, and W. Oh. Brown University

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Hypothermia, hypoglycemia, hypoxemia, and acidosis may increase the risk of kernicterus at low serum bilirubin levels. When pH is lowered *in vitro*, no change in free bilirubin ( $U_B$ ) or in bilirubin binding affinity ( $K_a$ ) can be detected (Nelson *et al.* *Pediat. Res.* 8:963, 1974). In 11 newborns with respiratory distress and acidosis in whom body temperature, oxygenation, and blood glucose were normal, we measured  $U_B$  and  $K_a$  by peroxidase oxidation at a bilirubin:albumin molar ratio (B/A) of 0.8 before and after correction of acidosis with  $\text{NaHCO}_3$  and/or assisted ventilation. Serum albumin (3.3 vs. 3.1 gm%) and indirect bilirubin levels (2.3 vs. 2.8 mg%) were similar during acidosis and recovery. Results are as follows:

Age (hrs.)	pH	$U_B, \mu\text{g}\%$	$K_a \times 10^8 \text{ M}^{-1}$
$9.6 \pm 2.3^*$	$7.12 \pm 0.02$	$2.44 \pm 0.29$	$1.09 \pm 0.16$
$18.5 \pm 3.5$	$7.34 \pm 0.02$	$1.80 \pm 0.21$	$1.50 \pm 0.17$
$p^{**}$	<0.01	<0.05	<0.01

\*Mean  $\pm$  S.E.M. \*\* Paired "t" -test

$K_a$  of normal infants matched for gestational age is  $2.0 \pm 0.2 \times 10^8 \text{ M}^{-1}$  in our laboratory. The data indicate a significant decrease in  $K_a$  associated with neonatal acidosis; correction of acidosis results in improvement of  $K_a$  and reduction in free bilirubin.

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## ASSOCIATION OF MESENTERIC THROMBOEMBOLISM AND ORAL FEEDINGS WITH NEONATAL NECROTIZING ENTEROCOLITIS

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Splanchnic ischemia is believed to be a major factor in the development of neonatal necrotizing enterocolitis (NEC). The role of vascular occlusion in the pathogenesis of NEC was studied in 30 autopsies. Multiple histologic sections of the mesentery were examined for the presence of thrombotic phenomena. Evidence of systemic thrombosis was also sought. 16 infants had a postmortem diagnosis of NEC (Group A) and 14 infants had intestinal hemorrhage or congestion (Group B). The clinical course of each patient was reviewed. 15/16 in Group A received oral feedings and 5/14 in Group B ( $P < .001$ ).

In Group A 12/15 had thromboemboli in mesenteric muscular arteries (TMA). 10/16 had evidence of multiple thromboemboli in other organs: kidney 7, adrenal 4, lung 4, and liver 2. 11/13 had mural thrombi of the abdominal aorta and iliac arteries. 15 had umbilical artery catheters (UAC) and 8 had umbilical venous catheters (UVC).

In Group B 2/13 had TMA ( $P < .001$ ). 11/14 had multiple thromboemboli in other organs: kidney 4, adrenal 3, lung 7, liver 2, and spleen 5. 9/12 had mural thrombi of the abdominal aorta and iliac arteries. 11 had UAC and 7 had UVC.

There is an apparent association of NEC with mesenteric thromboembolism and oral feedings in this study.

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## BINDING OF BILIRUBIN IN NEONATAL SERUM STUDIED BY FLUORESCENCE QUENCHING. Rodney L. Levine

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The technique of fluorescence quenching was utilized to study the binding of bilirubin to serum albumin in certain jaundiced infants; e.g., babies with prematurity, possible kernicterus, isoimmunization, and biliary atresia. Free bilirubin, bilirubin binding capacity, and binding affinity ( $K_a$ ) for bilirubin were determined from a 25- $\mu\text{l}$  serum sample.

An infant with biliary atresia and mixed hyperbilirubinemia was studied to determine whether conjugated bilirubin affects binding of unconjugated bilirubin. While only unconjugated bilirubin is thought to be toxic to cells, both forms bind to albumin; therefore, conjugated bilirubin would be effectively toxic if its binding decreased the binding capacity or affinity of albumin for unconjugated bilirubin. Total serum bilirubin was 700  $\mu\text{M}$ , with 410  $\mu\text{M}$  direct and 290  $\mu\text{M}$  indirect. By fluorescence quenching the capacity was 0.93 moles unconjugated bilirubin/mole albumin, very close to the maximal capacity of 1.00. Binding affinity was  $5.2 \times 10^8 \text{ M}^{-1}$ , slightly greater than the average neonatal value. Hence, even a marked elevation of conjugated bilirubin did not affect the ability of albumin to detoxify unconjugated bilirubin.

A 600-gram, 28-week newborn was studied to determine binding properties of serum albumin in a premature infant. They were similar to those found in term infants; this baby's ability to detoxify bilirubin was therefore limited by her lower serum albumin concentration.

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## ARE APNEA MONITORS WORTHWHILE? Jerold F. Lucey, University of Vermont College of Medicine, Department of Pediatrics,

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Apnea monitors have been used in intensive care nurseries since 1969, but there are no studies to show that they have any effect on morbidity, mortality, or intact survival. There are studies which document that 1) these devices report artifacts such as false alarms, movement, heart beat or vibrations from nearby equipment. They may fail to alarm when breathing stops; 2) they do not detect obstruction of the airway; 3) they are incapable of detecting such common occurrences as "broken apnea" or disorganized, "ineffective" breathing; 4) the indicators of respiratory rate are unreliable, inaccurate and rarely used; 5) they are very susceptible to improper use and thus fail to detect about 40% of apneic episodes. A study by The Emergency Care Research Inst. found them "generally unreliable." 6) They do not detect hypoxia, the most important effect of apnea; 7) their use may result in sleep deprivation, and thus could theoretically interfere with the normal maturation of respiratory control; 8) they contribute to noise pollution. Should we not seriously question the continued uncritical use of these expensive, ineffective devices?