955 CARBON MONOXIDE EXCRETION AS AN INDEX OF BILIRUBIN PRODUCTION IN NEWBORN INFANTS.

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The excretion rate of endogenously produced carbon monoxide (Ve_{CO}) was measured as an index of bilirubin production in human newborns. Using a simplified measurement technique, over 300 studies have been performed on infants of various gestational ages (GA) and risks for hyperbilirubinemia. Studies performed on 60 full term infants <5 days of age resulted in a mean value for Ve_{CO} of 18.0 ±4.1 (SD) µl/kg/hr. Infants of GA <33 weeks, 33-34 weeks, and 35-36 weeks had Ve_{CO} values of 17.7 ±5.2, 18.1 ±5.9, and 16.2 ±3.7 µl/kg/hr, respectively, over the first 10 days of life. No difference in Ve_{CO} was noted between Caucasian newborns and those of Spanish surname. In 14 infants with ABO or Rh hemolytic disease, Ve_{CO} ranged from 17.3 to 71.5 µl/kg/hr. Serial determination performed on 2 of these infants showed Ve_{CO} to be elevated for 30 days following birth. No infant with Ve_{CO} less than 50 µl/kg/hr required exchange transfusion. Eight infants of insulin-dependent diabetic mothers (IDM) were studied on 13 occasions and found to have a mean Ve_{CO} of 17.5 µl/kg/hr. However 2 premature newborns of this group who were also hypoglycemic exhibited increased Ve_{CO} levels of 28.7 and 29.2 µl/kg/hr. It has been shown that 1) measurement of Ve_{CO} by this method is a quick, non-invasive procedure; 2) Ve_{CO} seems independent of GA; 3) Ve provides valuable information concerning the rate of bilirubin production in isoimmune hemolytic disease; 4) non-hypoglycemic, full term IDM do not have elevated Ve_{CO} .

956 POSTNATAL DEVELOPMENT OF THE HYPOXIC VENTILATORY RESPONSE IN THE LAMB.

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The ventilatory response time of the fetal lamb to a hypoxic stimulus is relatively slow and appears to be centrally mediated (Woodrum, et al., J. App. Physiol., in press). To ascertain when the rapid peripheral chemoreceptor response appears postnatally, the hypoxic response was studied in unanesthesized newborn lambs before and after carotid body denervation. The response time was defined as the time from ↓ in aortic arch SaO_2 (fiber optic catheter) to a sustained increase in tidal volume or frequency. Twenty-three studies were done on 5 animals immediately following birth and 46 studies were done on 7 animals during the 2nd week of life. Prior to denervation the tidal volume response time decreased from 5.7 ± 4 sec. on day 1 to 1.8 ± .8 sec. during days 9-12 ($P < .025$). Following denervation the hypoxic response persisted (75% trials), occurring after a delay of 29 ± 32.5 sec. on day 1 and 12 ± 6 sec. in the older group. The frequency response was similar but more delayed than the volume response. The data indicate a maturational change in the hypoxic ventilatory response time of the newborn lamb over the first two weeks of life. There is a definite central hypoxic response in the newborn lamb up to 12 days of age. The mechanism of this response is unknown but may involve a specific central hypoxic receptor, or a CNS response to factors associated with hypoxemia (↓ cerebral blood flow, acidosis or altered arousal).

957 GASTROINTESTINAL MICROFLORA IN INFANTS WITH NECROTIZING ENTEROCOLITIS (NEC).

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Gastric and fecal microflora were studied in 3 groups of infants: I-27 infants with NEC; II-41 infants in the same neonatal intensive care unit; III-30 full-term neonates. There were no significant differences among the groups except for the gestational ages and birth weights in group III. Significantly greater ($p<0.05$) numbers of gram negative aerobic species were isolated from gastric aspirates of NEC patients than from infants and controls; for K. pneumoniae the difference between NEC infants and controls was significant at $p<0.001$. Fecal gram negative aerobic organisms were recovered from infants with NEC in a frequency similar to full-term infants but greater ($p<0.01$) than other sick neonates. Fecal anaerobes were recovered from infants with NEC and other sick neonates significantly less frequently ($p<0.005$) than from healthy infants.

	Frequency (%)			
Organism	Gp I	Gp II	Gp III	Remarks
E. coli	50.0	29.3	66.7	Gp II sig. lower at $p<0.05$
B. fragilis	11.5	9.8	43.3	Gp III sig. greater at $p<0.005$

Analysis of the gastric and fecal microflora of infants with NEC shows a characteristic pattern. This may, in part, account for the development of NEC in certain infants. It may also explain the benefits accrued from aminoglycoside therapy in NEC.

958 HIGH-FREQUENCY MECHANICAL VENTILATION OF LOW-BIRTH-WEIGHT INFANTS WITH RESPIRATORY FAILURE FROM HYALINE MEMBRANE DISEASE: 92% SURVIVAL.

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Infants with hyaline membrane disease (HMD) breathe rapidly with low tidal volumes. Mechanical ventilation of small preterm infants with HMD often induces crippling or lethal complications. In 3 months we treated 24 infants in respiratory failure -- birth weight 750-1750 g -- with a new method of ventilation intended to simulate the breathing pattern of infants with HMD. Our approach included (1) initial paralysis with pancuronium bromide, 0.04-0.08 mg/kg, (2) rapid respiratory frequencies (60-110/min, sometimes with brief hand-ventilation at rates up to 180/min), (3) peak-inflation pressures of less than 35 cmH_2O, (4) end-expiratory pressures of 4-9 cmH_2O, and (5) weaning from mechanical ventilation by reducing tidal volume until peak-inflation pressures reached 20-25 cmH_2O, whereupon we decreased respiratory frequency. We kept $PaCO_2$ at 30-40 torr, Pa_{O_2} at 60-80 torr. All babies were born at outside hospitals; their average weight was 1244 ± 301 g ($7 < 1000$ g) and their average gestation was 30 ± 2 weeks ($6 < 28$ weeks); 14/24 were male. 22/24 (92%) survived, and complications included: pneumothorax 2, intracranial hemorrhage 2, pulmonary hemorrhage 3, chronic lung disease 4, and patent ductus arteriosus 10, of which 3 required surgical ligation. We conclude that mechanical ventilation with rapid respiratory frequencies and low end-tidal pressures may be effective for treating small preterm infants with severe HMD and merits controlled evaluation.

959 CRITERIA FOR ANALYZING MORTALITY OF NECROTIZING ENTEROCOLITIS (NEC).

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The mortality of 37 cases of NEC, between 1973 and 1976, were analyzed with reference to: Birth weight ≤2000 gm (Group 1) ≥2001 gm (Group 2); time of onset ≤7 days or ≥8 days; medical or surgical management; relationship to X-change transfusion (Group 3); site of bowel involvement, small and large (S,L) or large (L) bowel only.

Mortality is not significantly related to birth weight, age of onset or treatment modality.

Group	#	Site	#	Deaths
1 + 2	32	S,L	16	13
		L	16	4
3	5	S,L	2	1
		L	3	0

There is a trend for reduced mortality in Group 3 compared to Groups 1 and 2. There is a significant ($p<.01$) decreased mortality if large bowel only is involved compared to small and large bowel involvement.

960 MECHANISMS FOR FETAL EXCRETION OF HEPATOTOXIC MONOHYDROXY BILE ACIDS.

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Non-polar monohydroxy bile acids (MBA) either synthesized by the fetus as 3β Δ5 cholenoic acid (3β-OL) or transplacentally acquired as lithocholic acid(LC)are potentially hepatotoxic to the fetus. In order to establish whether MBA conjugates are secreted into bile by the fetus,bile acids in meconium from 15 fullterm infants were identified(before and after solvolysis)by thin layer chromatography and then by gas liquid chromatography-mass spectroscopy. 80-90% of the LC and all of the fetally synthesized 3β-OL were present as sulfated conjugates,suggesting that the fetus may detoxify MBA by sulfation and then concentrate the excreted bile acids in the intestine. Studies of sheep meconium demonstrated the presence of MBA including 3β-OL as the sulfate. Accordingly, the metabolism and biotransformation of ^{14}C-LC or Taurolithocholic acid(TLC)was studied in 10 fetal sheep near term.Both bile acids were cleared rapidly by the fetus($t_{½}$=11.0±5.4 min,AVG±SD); 23±4.6% of the dose was excreted transplacentally and recovered in maternal bile. The remainder was taken up by the fetal liver and secreted into the fetal bile. LC was conjugated 78.5±9.4% as TLC and 9.0±3.6% as glycolithocholate(GLC); 10% of the TLC and 40% of the GLC were sulfated without further metabolism. No hydroxylation of LC sulfate occurred. Conclusion: 1)the fetal liver can take up, conjugate and secrete LC into the fetal intestine,2) GLC is preferentially sulfated, and 3) two major mechanisms for MBA detoxification exist in the fetus: transplacental excretion and sulfation of conjugated derivatives.