

**217** PRECOCIOUS INDUCTION OF RAT JEJUNAL SUCRASE BY TRIIDO THYRONINE ( $T_3$ ): IN FETUSES BY ADMINISTRATION TO THE PREGNANT MOTHER AND IN SUCKLINGS BY ADMINISTRATION TO THE LACTATING MOTHER. Otakar Koldovsky, Jocelyn Jumawan, Paul Celano, Carolyn Horowitz, Ladislav Krulich and Herbert Lau (Spon. by Philip G. Holtzapfle). Children's Hospital of Philadelphia, Philadelphia, Pa.

Daily application of  $T_3$  (20  $\mu$ g/100 g body wt) to female rats in the last (third) week of pregnancy elicits a precocious appearance of sucrase activity in fetal jejunum. Similarly, administration of  $T_3$  in much higher doses (1.25 mg/100 g body wt) from day 11 to 15 postnatally evokes a precocious appearance of jejunal sucrase activity in sucklings.  $T_3$  administration to lactating mothers is followed by decrease of TSH and  $T_4$  levels in sera of sucklings and by an increase in the  $T_3$  levels in the sera and milk of lactating mothers as well as in sera of sucklings.

These experiments thus show: (a) sucrase activity is already inducible in fetuses, (b)  $T_3$  administration in very high doses to pregnant rats might be transferred to the fetus to the extent of still effective doses, (c) milk may function as an endocrine link between the mother's hormonal and metabolic systems and those of the sucklings.

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**218** LENGTH OF GESTATION IN MICE UNDER A 21-HOUR DAY. Jonathan T. Lanman, National Institute of Child Health and Human Development, Bethesda, MD.

Both pre- and postmaturity are hazardous to the offspring, therefore factors influencing the timing of parturition are important. Among the determinants of gestation length in some mammals is a fetal contribution related to both their maturation and size. Circadian rhythms are prominent in many physiologic processes, including growth. We were curious whether the length of pregnancy (normal for C57BL mice: mode 19, range: 18-21 days) was governed by the number of light-dark cycles or by an absolute length of time. C57BL mice were bred under conditions of a 21-hr. day (10 $\frac{1}{2}$  hr. light-10 $\frac{1}{2}$  hr. dark) and their offspring used for these experiments. They were bred first (Period A) under the 10 $\frac{1}{2}$ L-10 $\frac{1}{2}$ D 21-hr. cycle (21 pregnancies), then for a few weeks (Period B) under a 12L-12D cycle (10 pregnancies; this was their only exposure to a 24-hr. day), then again (Period C) under the 21-hr. cycle (9 pregnancies). Observed pregnancy lengths (mode and range in 24 hr. days) were A:20 (19-20); B:20 (20-21); C:21 (20-22). A trend of decreasing litter size occurred with each successive breeding period; in the last, with aging mice, breeding ceased after 9 litters. Entrainment to the 21 hr. cycle was demonstrated by measuring running activity. A gestation length of 20 "days" of 21 hours would shorten the normal length by 60 hours. Our results indicate that gestation length in mice is controlled by factors other than the number of light-dark cycles and remains approximately constant in terms of absolute time when mice are entrained to a shortened cycle.

**219** MATERNAL FETAL OSMOLAR HOMEOSTASIS: FETAL POSTERIOR PITUITARY AUTONOMY. Rosemary D. Leake, Richard E. Weitzman, & Delbert A. Fisher, Depts. of Pediatrics & Medicine, UCLA-Harbor General Hospital, Torrance, California.

The fetal pituitary contains arginine vasopressin (AVP) from the first trimester and releases AVP in response to osmolar stimuli during the last trimester. The fetal AVP response to maternal osmolar change has not been examined. We measured plasma AVP and sodium (Na) levels after maternal hypertonic saline injection (HS-225 mEq in a 23% solution) in 5 chronically catheterized sheep preparations between 112-135 days gestation. Average results collated for 10-20 minute intervals were:

Time in min. =	10-0	0-20	20-40	40-60
Maternal Na	143	153	150	149
Fetal Na	141	143	144	147
Maternal AVP	0.32	0.70	0.56	0.82
Fetal AVP	0.47	1.46	5.55	2.47

Maternal HS infusion evoked a prompt and significant rise in maternal Na which then fell slowly over the observation period. Fetal Na rose slowly approaching the maternal level by 60 min. Significant increments in maternal AVP correlated with the peak Na concentrations. Significant sustained peaks in fetal AVP levels occurred between 20 and 60 min. The fetal stimulus response ratio (SRR),  $\Delta \log AVP / \Delta Na$ , was greater than the maternal SRR and exceeded the fetal SRR to fetal HS suggesting that there was a rapid fetal to maternal flow of water after maternal HS and a combined volume-osmolar stimulus to the fetus.

**220** THIRD TRIMESTER DEVELOPMENT OF SMALL INTESTINAL ENTEROKINASE (EK) AND DISACCHARIDASE ACTIVITIES IN THE HUMAN FETUS. Emanuel Leberthal, Irena Antonowicz, Harvard Medical School, Children's Hospital Medical Center, Department of Pediatrics, Boston, Massachusetts.

The early feeding of proteins and carbohydrates to premature babies necessitates knowledge of the developmental pattern of enzyme activities in the fetal gastrointestinal tract. The activities of EK and disaccharidases in small intestine obtained from 38 human fetuses between the ages of 21 and 40 weeks of gestation were investigated. EK was detected in fetal mucosa from the 26th week of gestation on, paralleling appearance of tryptic activity in meconium. The concomitant appearance of EK and trypsin activities in the human intestinal mucosa is indicative of the importance of EK as an activator of trypsinogen and therefore as the key enzyme in protein digestion. Between 26-30 weeks of gestation, the EK activity is only 6% and full term babies (40 weeks) 20% of that found in older children. In contrast lactase in 26-34 week fetuses was 30% and sucrase and maltase were 70% of the full term baby. In addition, the distributional pattern of EK differs from the disaccharidases, showing the highest activity in duodenum and the lowest in ileum, while disaccharidases are highest in jejunum with lower activity in duodenum and ileum. It is conceivable that the premature infant, between 26-30 weeks of gestation, is better equipped to deal with hydrolysis of  $\alpha$ -glucosides than lactose, and that the very low EK activity is a major contributing factor to the very low tryptic activity.

**221** POSTNATAL CHANGES IN OXYGEN TRANSPORT: RELATIONSHIP BETWEEN CARDIAC OUTPUT (CO), O<sub>2</sub> CONSUMPTION ( $\dot{V}O_2$ ), AND O<sub>2</sub> CARRYING CAPACITY (CAP). George Lister, Thomas K. Walter, Abraham M. Rudolph and Peter R. Dallman, University of California Medical Center, Department of Pediatrics, San Francisco

CAP falls rapidly after birth with a concurrent increase in P<sub>50</sub> (pO<sub>2</sub> at 50% Hgb saturation, pH 7.4, pCO<sub>2</sub> 40 torr, 39° C). However, it is not known whether there is also an increase in CO to maintain O<sub>2</sub> delivery to the tissues while CAP is low. To investigate this question we studied 7 lambs during the first 8 weeks after birth. Catheters were placed in the right atrium and carotid artery. We measured  $\dot{V}O_2$ , CAP, arterial and mixed venous O<sub>2</sub> content and blood gases, Hgb, P<sub>50</sub>, 2,3-DPG, and fetal and adult Hgb in quiet unsedated lambs. CO was calculated from the Fick equation. Means  $\pm$  SEM were:

	1-3 d	1 wk	2 wk	4 wk	8 wk
CO, ml/min/kg	368 $\pm$ 24	459 $\pm$ 54	457 $\pm$ 43	349 $\pm$ 30	281 $\pm$ 41
$\dot{V}O_2$ , ml/min/kg	14.1 $\pm$ 1.5	15.3 $\pm$ 1.8	14.5 $\pm$ 1.8	10.6 $\pm$ 1.5	8.7 $\pm$ 1.3
CAP, ml O <sub>2</sub> /dl	135 $\pm$ 12	118 $\pm$ 6	102 $\pm$ 11	89 $\pm$ 5	121 $\pm$ 11
AVDO <sub>2</sub> , ml/dl	4.0 $\pm$ 0.3	3.7 $\pm$ 0.4	3.3 $\pm$ 0.3	3.1 $\pm$ 0.2	4.0 $\pm$ 0.4
P <sub>50</sub> , torr	25.0 (n=2)	27.6 $\pm$ 3.3	26.6 $\pm$ 1.6	30.8 $\pm$ 2.4	33.1 (n=2)

There was an increase in CO/kg and  $\dot{V}O_2$ /kg in all lambs during the first 1 to 2 weeks followed by a steady, parallel decline to near adult values. Both peaked prior to the nadir of the anemia; thus CO/kg was decreasing when CAP was at a minimum. A rising P<sub>50</sub> contributed to maintaining relatively constant arteriovenous O<sub>2</sub> content differences (AVDO<sub>2</sub>) despite changes in CAP. We conclude that variations in CO are not a result of a decreased CAP, but occur primarily in response to changing metabolic needs after birth.

**222** THE RELATIONSHIP OF MEDICAL EVENTS TO DEVELOPMENT IN A GROUP OF PRETERM INFANTS. Bruce Littman and Arthur H. Parmelee, School of Medicine, University of California at Los Angeles, Department of Pediatrics.

It has long been known that the occurrence of perinatal complications shows an association with fetal and neonatal mortality. The infant who survives such events is presumed to be at risk for later development disability. Prior to this report no work had been done to show whether a quantitative relationship between the number of perinatal complications and outcome actually existed.

This study involved the use of a 41 item Obstetric Complications Scale (OCS) and a 10 item Postnatal Complications Scale (PCS) to see if such a correlation could be shown. 135 preterm infants with variable frequencies of prenatal, intrapartum and postnatal complications were enrolled. All had Gesell examinations at 9 and 24 months and a Bayley examination at 18 months. Ages were corrected for prematurity.

For the whole group there was no correlation between the OCS/PCS and the tests at 9, 18, 24 months. Infants with low developmental scores were not more inclined to have higher rates of perinatal complications. 5 who were found later to have cerebral palsy had very poor OCS/PCS scores but could not be distinguished in the newborn period from a larger group with equally low perinatal scores but normal later development.

This study shows the difficulties associated with trying to predict disability from data acquired solely in the perinatal period. The need to continue evaluation during infancy can not be stressed enough.