

▲284

TRANSFER OF GASTROINTESTINALLY ADMINISTERED  $^{125}$ I-EPI-  
DERMAL GROWTH FACTOR INTO SUCKLING RAT BRAIN. Radha  
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Epidermal growth factor (EGF) and its receptors  
have been detected in developing rat brain (BR). In adult rat,  
intravenously administered  $^{125}$ I-EGF does not cross the blood  
barrier. We investigated the possibility of transfer of  $^{125}$ I-EGF  
into suckling rat (SUR) BR after gastrointestinal administration.  
 $^{125}$ I-EGF (80 ng) was first introduced orogastrically to SUR; 30  
min later animals were killed. Blood (BL) and BR were analyzed  
for total (TR) and immunoreactive (IR) radioactivity. TR detected  
in brain was  $0.09 \pm 0.016\%$  (mean  $\pm$  SEM) of radioactivity fed  
( $28.7 \pm 12.1\%$  of TR in BR was IR). A second experiment was per-  
formed in which  $^{125}$ I-EGF (16 ng) was introduced to isolated loops  
of jejunum (J) or ileum (I) of anesthetized SUR. After 60 min,  
animals were killed; the amount of TR in BR after introduction to  
I ( $0.49 \pm 0.11\%$  of total administered) was 7 times greater after  
I administration than that after introduction to J ( $0.07 \pm$   
 $0.006\%$ ). IR  $^{125}$ I-EGF in BR after administration into J was  $46.7 \pm$   
 $3.4\%$ , and into I was  $32.6 \pm 3.8\%$ , respectively.

**Conclusion:** Results suggest that  $^{125}$ I-EGF introduced to the gas-  
trointestinal tract is transferred in SUR to BR in IR form.  
Furthermore, regional difference in capacity to absorb EGF exists  
in SUR intestine.

285

FETAL HEMOGLOBIN LEVELS IN CORD BLOOD. Sudha Rao,  
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Cord blood electrophoresis normally reveals high  
levels of Hb F with smaller amounts of Hb A. At the  
University of Illinois Comprehensive Sickle cell Center, 9,832  
consecutive cord bloods were screened since October 1983 by both  
Cellulose acetate and Citrate agar electrophoreses. These included  
infants of all ethnic groups. Of the tested infants, 21 had Hb F  
as the sole detectable hemoglobin. These included 14 (66%) preterm  
infants. Cesarean section was performed for varying reasons in 6  
instances. Mothers of 2 infants had gestational diabetes as per  
glucose tolerance tests; 4 mothers were chronic asthmatics on  
long-term bronchodilator therapy during pregnancy; 4 were habitual  
drug abusers (heroin and marijuana) even during pregnancy; three  
mothers had chronic hypertension, one of these was preeclamptic;  
and one mother had chronic renal insufficiency requiring hemo-  
dialysis 3 times per week and frequent blood transfusions. Almost  
half the mothers smoked  $\frac{1}{2}$ -1 pack cigarettes/day. Multiple param-  
eters including expected date of delivery, gestational age of  
infant per physical exam, placental weight, birth weight, mother's  
gravida and para status were studied but found to be of no sig-  
nificance. High fetal hemoglobin in cord blood has been well de-  
scribed in infants of mothers with chronic anemia during preg-  
nancy as well as in infants of diabetic mothers. As 7 of the 21  
mother-infant cases studied in this group had no identifiable  
factors, we speculate that there might be yet other determinants  
influencing expression of hemoglobin patterns at birth.

●286

THE CIRCADIAN-GATED TIMING OF BIRTH IN RATS: DIS-  
RUPTION BY MATERNAL SCN LESIONS OR BY REMOVAL OF THE  
FETAL BRAIN. Steven M. Reppert, William J. Schwartz  
& David R. Weaver, Children's and Neurology  
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Medical School, Boston, MA.

In rats, the hour of birth is gated over a 36-hr temporal  
window by the phase of the daily light-dark cycle during  
pregnancy. We have previously shown that the suprachiasmatic  
nuclei (SCN), the site of a known circadian pacemaker, are  
oscillating in phase with the prevailing light-dark cycle in the  
fetus. Since the onset of parturition is governed by the fetal  
brain in some species, we have speculated that a possible role of  
a functioning and entrainable circadian clock during fetal life  
is that it might be involved in the circadian-gated initiation of  
parturition. First, we showed the circadian gating of birth in  
our animals by exposing different groups of dams to lighting  
cycles of opposite phase during pregnancy. Regardless of the  
phase of the prenatal lighting cycle, the time of birth was gated  
over a 36-hr temporal window so that most births occurred during  
the daytime hours. Next, we found that destruction of the  
maternal SCN (on day 7 of gestation) eliminated the circadian  
gating; births occurred in a single distribution that peaked in  
the middle of the 36-hr window. Finally, removal of all the  
fetal brains from each litter also disrupted the circadian gating  
of birth; dams of brain-aspirated fetuses no longer exhibited a  
daytime preference for births. These results show that the  
maternal SCN are necessary for the normal circadian gating of  
birth and are also consistent with a role for the fetal brain  
(and possibly the fetal SCN) in this process. Support by HD14427.

287

MATURATIONAL CHANGES OF INSULIN BINDING TO FETAL  
HEPATOCTYES. Robert A. Richman, Mark R.  
Benedict, and Barbara A. Toly. SUNY Health  
Science Center, Department of Pediatrics, Syracuse.

To determine if the reported lack of direct  
insulin metabolic effects in fetal tissues is due to  
alterations in hormone binding and/or processing, we  
characterized the binding, internalization, and degradation of  
insulin by cultured hepatocytes from rat fetuses of 17, 19, and  
21 days gestation. When insulin (100 nM) was incubated with  
fetal hepatocytes, we observed substantial reductions (66%-100%)  
in immunoreactive insulin. This loss was greatest in cultures  
prepared from 19 day fetuses.  $^{125}$ I-Insulin binding at 37 C  
rapidly reached a peak at 30 min. Specific binding was greatest  
in 19 day cells; 460 fmole/mg protein compared to 150 and 190  
fmole/mg protein in 17 and 21 day fetal hepatocytes,  
respectively. Prior exposure to insulin (100 nM) induced an  
inhibition of subsequent binding, increasing with gestational  
age. Only minimal down-regulation was detectable in 17 day  
hepatocytes. Both internalization and intracellular degradation  
of  $^{125}$ I-insulin occurred rapidly, following a similar time  
course for all three ages. Despite the ability of 17 day fetal  
hepatocytes to bind, internalize, and degrade insulin, we were  
unable to demonstrate receptor down-regulation. The  
dissociation of these related processes raises the possibility  
that these cells have a more rapid rate of receptor turnover  
than those from 19 and 21 day fetuses.

●288

UPTAKE OF INTRAFETALLY ADMINISTERED  $^3$ H-1,25 DIHYDROX-  
VITAMIN D<sub>3</sub> (1,25) BY THE MATERNAL SMALL INTESTINE.  
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Pregnancy is associated with increased maternal  
calcium requirements that are met by enhanced intestinal calcium  
absorption. Maternal serum concentrations of total 1,25 are  
elevated, perhaps in response to a physiological hyperparathy-  
roidism. An alternative explanation is that 1,25 produced by the  
fetoplacental unit gains access to the maternal compartment and  
influences maternal 1,25 status and intestinal calcium absorp-  
tion. To test the hypothesis that fetal 1,25 gains access to the  
maternal intestine, we gave an intravenous injection of  $^{20}$ Ci of  
high specific activity (90 Ci/mmol)  $^3$ H-1,25 to a chronically  
catheterized fetal sheep at 138d of gestation (term=145d).  
Sequential samples of fetal and maternal plasma were obtained  
during the next 4 hours. Thereafter, samples of fetal and  
maternal small intestinal mucosa were obtained. Plasma and  
mucosal homogenates were lipid extracted and analyzed for  $^3$ H-1,25  
content. There was a rapid disappearance of  $^3$ H-1,25 from the  
fetal circulation and a progressive accumulation of  $^3$ H-1,25 in  
the maternal circulation. Plasma and intestinal mucosal content  
of  $^3$ H-1,25 at 4 hours were as follows:

	Fetal	Maternal
Plasma $^3$ H-1,25 (dpm/ml)	11590	620
% dose in plasma pool	6.21	4.23
Mucosal $^3$ H-1,25 (dpm/g)	8438	261

**Conclusion:** Intrafetal administered  $^3$ H-1,25 crosses the  
placenta and is taken up by the maternal small intestine.

289

DIURNAL RHYTHM OF  $\beta$  ENDORPHIN IN NEONATES.  
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In an attempt to demonstrate whether  $\beta$  endorphin (BED)  
diurnal rhythm existed in neonates, 17 infants with mean ( $\pm$ SD)  
gestational age of  $31.7 \pm 4.8$  weeks and birth weight of  $1790 \pm$   
 $898$  grams were studied at a mean postnatal age of  $3.3 \pm 0.5$   
days. Plasma samples were obtained from a pre-existing um-  
bilical arterial line at 9:00 a.m., noon and 3:00 p.m. Plasma  
BED was isolated using Sephadex column chromatography and  
radioimmuno assay. Sensitivity was between 5 and 500 pg/.1 ml  
of sample. Recovery was 84%. Mean plasma concentrations of  $\beta$   
endorphin were  $68.3 \pm 27.7$  pg/ml,  $54.5 \pm 13.7$  pg/ml and  $45.1 \pm$   
 $10.8$  pg/ml respectively. Highly significant ( $P=0.0002$ )  
variation of plasma  $\beta$  endorphin concentration was observed in  
these neonates using one way analysis of variance with  
repeated measures with 3 points in  
time suggesting the presence of  
a diurnal rhythm of  $\beta$  endorphin  
in neonates. It is important  
to specify the time of col-  
lection of blood samples for  
determination of opiates in  
neonates.

