DNA SYNTHESIS FROM THE β-CARBON OF SERINE BY FETAL AND MATURE HUMAN LIVER. Gerald E. Gaull, John A. Sturman*, and Niels C. Raiha*. Dept. Res., N.Y. State Inst. Res. Ment. Retard., Staten Island, N.Y.; Dept. Ped., Mt. Sinai Sch. Med., N.Y., N.Y.; Depts. Obstet. & Med. Chem., Univ. Helsinki, Finland.

In human fetal liver we showed: that cystathionase is absent; methyltetrahydrofolate-homocysteine methyltransferase is higher than in mature human liver; and the alternative remethylation pathway, betaine-homocysteine methyltransferase, is lower. In fetal brain the same enzymatic pattern is found, and serine hydroxymethyltransferase, the enzyme which transfers the β-carbon of serine to tetrahydrofolate to form methylenetetrahydrofolate, is also higher than in mature brain. We predicted that the β-carbon of serine was being shunted into de novo synthesis of DNA, via methylene tetrahydrofolate, rather than serine accepting the sulfur of homocysteine to form cysteine.

We now show that incorporation of 3-^{14}C-L-serine into DNA is at least 2-fold higher in fetal human liver slices than in mature human liver slices; incorporation into RNA was 10-fold lower than into DNA. These incorporations were not limited by endogenous methionine. These results confirm our hypothesis directly and provide further evidence that in human fetal liver the sulfur of homocysteine is recycled to methionine at the expense of making cyst(e)ine essential, in order to facilitate the biosynthetic reactions (de novo DNA synthesis, polyamine synthesis, lecithin synthesis, protein synthesis) related to that cycle.

PERINATAL CHANGES IN THE ACTIVATION AND ESTERIFICATION OF FATTY ACIDS IN THE RAT INTESTINAL MUCOSA. Philip Holtzapple, Glen Smith and Otakar Koldovsky. Univ. of Penna., Children's Hosp. of Phila., Philadelphia, Pa. 19146

The high dietary triglyceride intake in the perinatal period of all mammals including man occurs when the lipolytic activity in the gastrointestinal tract is low. In previous experiments the activity of one of the enzymes of the re-esterification pathway, acyl-CoA:monoglyceride acyltransferase was found to be higher in microsomes prepared from suckling rat jejunal mucosa than in adults(Experientia 29, 405, 1973). To evaluate conclusively the esterification processes during the suckling period, the activity of the fatty acid: CoA ligase in jejunal microsomes and the in-vitro esterification of 1-^{14}C-oleic acid by jejunal segments was determined. The activity of the fatty acid:CoA ligase in newborn, 5, 12 and 90 day old rats was 239±15, 154±24, 149±10 and 195±21 nmoles/min/mg protein, respectively. The results of these enzymological studies were confirmed by the finding that the esterification rate of oleic acid occurs as rapidly in jejunal mucosa of suckling rats as in adults. Thus these studies indicate that, of the phases of fat absorption, the re-esterification processes are not a limiting factor. The apparent discrepancy of low lipolytic and high esterification activity during the suckling period remains to be explained.

THE ONTOGENY OF RECEPTORS AND RESPONSIVENESS TO INSULIN IN HUMAN CELL CULTURES. D. G. Handelsman, S. Nakagawa, and H. M. Nitowsky, Dept of Ped, Albert Einstein Coll Med and Bronx-Lebanon Hosp Center, Bronx, N.Y.

Fibroblast cultures from human fetuses (12-14 wk), neonates, amniotic fluid, and older children were examined for insulin-I^{125} binding. In addition, studies were made of fetal and neonatal cell cultures for growth rate and density at confluence. Synthesis of protein, DNA, and RNA and intracellular content of cAMP were measured in cell cultures under the following conditions: a) immediate refeeding of confluent cultures with medium containing 20% fetal calf serum (FCS) or serum-free medium containing 10^{-9}M or 10^{-6}M insulin; b) similar refeeding of log-phase cultures after 24 hr. maintenance in serum-free media. Fetal cells have less than 10% of the net insulin binding capacity and none of the high-affinity binding sites (10^{-10}, 10^{-9}M) observed with fibroblasts from neonates and older children. Metabolic response correlates with high-affinity binding sites. Fetal fibroblast cultures grow more rapidly and to greater densities than cultures from neonates. At confluence and after serum-deprivation, fetal cells are unresponsive to insulin, whereas cells from neonates respond to insulin in a dose-related manner. However, this response is insignificant when compared to that with medium containing FCS. The findings suggest that the appearance of insulin binding sites and metabolic response to insulin in vivo takes place sometime after 14 wks. gestation.

DIETARY ADAPTATION OF PANCREATIC AMYLASE AND CHYMOTRYPSINOGEN. Abiodun Johnson, Ruth Hurwitz, and Norman Kretchmer. Stanford Univ. Med. Ctr., Dept. Pediatrics, Stanford, Calif. 94305

There has been intensive investigation of the ability of the pancreas to enzymically adapt to various dietary regimes. The data indicate that when a high-carbohydrate diet is fed amylase is preferentially synthesized; but with a high-protein/low-CHO diet there is depression of synthesis of amylase and acceleration of manufacture of proteolytic enzymes. The methods used in the present study are specific and involve purification of amylase with immunologic techniques, and isolation of pure chymotrypsinogen (activated) with affinity column chromatography. Concentration and synthesis of both enzymes can be determined accurately. On a 66% sucrose diet (20% casein) there is a 2- to 3-fold increase in synthesis of amylase; with a 20% sucrose diet (66% casein) there is a significant increase in chymotrypsinogen. If poor-quality protein is used (gelatin, gluten, and zein), there is no change in synthesis of amylase regardless of the amount of carbohydrate. Gluten is the only poor protein effective in stimulating synthesis of chymotrypsinogen. Amylase synthesis in hypophysectomized animals is considerably depressed and unresponsive to increased carbohydrate. This effect can be partially relieved with hydrocortisone, corticosterone, or thyroxin, but not with growth hormone. There is little effect of hypophysectomy on synthesis of content of chymotrypsinogen. The ability for the pancreas to respond enzymically to diet is an important adjunct to digestion and utilization of foods.

EFFECT OF STARVATION ON FATTY ACID METABOLISM OF BROWN AND WHITE ADIPOSE TISSUES IN THE NEWBORN RABBIT

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Non-esterified fatty acid /NEFA/ turnover rate in serum /m_s/ and flow rates /m_{SF}/ of NEFA into the triglyceride- and phospholipid fatty acid and NEFA of brown /BAT/ and white /WAT/ adipose tissues were studied C^{14}-palmitate at an ambient temperature of 35 °C in 7 days old fed rabbits /Group I/ and in animals fasting 48 hrs at 20 °C /Group II/ or for 72 hrs at 35 °C /Group III/. A digital computer program of a two compartmental model was used for analysis.

The initial serum NEFA pool /M_s/, and it's absolute turnover rate /m_s/, were significantly reduced in both starving groups. There was no significant difference between half times /$t_{1/2}$/, turnover times /t_t/ and fractional turnover rates /λ/.

BAT of Group II received a considerably larger fraction of m_s than that of Group I, in Group III m_{SF} to BAT was consistently reduced.

The incorporation rate of serum NEFA into BAT lipids is not dependent solely on the pool size but appears to be also regulated by other mechanisms operating during starvation.

IS FETAL FIBRINOGEN UNIQUE? Sanford J. Kempin, Harold L. James, Carl W. Jackson, and Joseph V. Simone. Hematology Laboratory, St. Jude Children's Res. Hosp., Memphis, TN.

Fetal fibrin has been reported to be more resistant to streptokinase (SK) induced fibrinolysis than adult fibrin, and it has been suggested that this property may play a pathogenetic role in disorders of the newborn (*e.g.*, hyaline membrane disease). Whether fetal fibrinogen (FF) differs structurally is not known. To explore structural differences, highly purified FF from cord blood of normal newborns and adult fibrinogen (AF) were subjected to stepwise plasmin degradation and examined by means of polyacrylamide gel electrophoresis. The kinetics of peptide release during plasmin lysis were followed by pH Stat and spectrophotometric analysis. Cross-linked and non cross-linked reduced adult and fetal fibrin were also examined by gel electrophoresis.

AF and FF gel patterns showed identical alpha chain heterogeneity and migration of beta and gamma chains. Peptide release kinetics and stepwise plasmin degradation patterns were identical. Gel patterns for fibrin cross-linked by Factor XIII and for non cross-linked fibrin were the same for adult and fetal forms. The fibrinogenolytic pattern of degradation and the extent of fibrin cross-linking of FF and AF were the same.

These methods show no structural differences between FF and AF. The resistance of fetal fibrin to SK-induced lysis is more likely due to the diminished fibrinolytic potential of fetal blood.