degrees of linear growth failure due to undernutrition, which is compatible with the known effect of chronic undernutrition on cell size. In concluding therefore that changes in CNo were responsible for this observation, it is suggested that the lower regression for PIUGF was also due to a lower CNo. By testing patients with persistent growth failure after birth we apparently singled out cases with "hypoplastic" IUGF.

Experimental alteration of intrauterine growth pattern in rhesus monkeys. DONALD E. HILL, ALAN B. HOLT, and DONALD B. CHEEK. *Johns Hopkins Univ. Sch. of Med., Baltimore, Md.*

The purpose of these studies is to indicate the biochemical alterations in intrauterine growth produced by interference with placental circulation or the chemical ablation of the fetal pancreas. In a group of pregnant rhesus monkeys the injection of Streptozotocin (approximately 75 mg/Kg) directly into the fetus produced cytotoxic effects on the pancreatic B-cells. Five of nine surviving animals had significantly large adrenals and livers. Body weight was normal. Two animals were significantly small for gestational age and had normal adrenals and livers. The remaining endocrine organs were of normal size in all animals. The protein:DNA ratio in muscle was increased in four animals. The fetal insulin levels at term were normal as were the blood glucose values. Regions of pancreatic regeneration and B cell activity could be identified on histological section. In a second group of pregnant monkeys the interplacental fetal vessels were ligated at 100 days gestation producing a reduction in placental mass and a placental insufficiency. Nine of 16 surviving fetuses had significantly low birth weights (2 S.D. below the mean) for gestational age. The brain was least affected while the liver was most affected and the small animals had a high brain:liver ratio. Total DNA, RNA, and protein were significantly low in muscle and liver. The protein:DNA ratio and the number of nuclei (cell number) were significantly low in muscle. The percentage fat was reduced in the carcass as well as the total fat, protein and collagen.

Secretory function of isolated parotid acinar cells. JOHN A. MANGOS and N. R. MCSHERRY. *Univ. of Wisconsin Med. Sch., Madison, Wisc.*

Functionally and anatomically intact acinar cells were obtained from the parotid gland of the rat by enzymatic dispersion. After exsanguination of the animal, the duct system of the gland was filled with a solution of hyaluronidase and collagenase (0.1%) in Ca±Mg free Hank's salt medium. The parotid was removed, minced and the tissue was incubated in the same enzyme solution for 60 min at 37°C. Then, the suspension was filtered through nylon mesh, the clumps of cells were separated by centrifugation, were suspended in a solution of trypsin (0.1%) and reincubated for 20 min. Finally, the cells were dispersed by pipetting the suspension 10 times, washed and then suspended in balanced Hank's solution containing bovine serum albumin (2 gm/100 ml). Yield of cells was ~60% of the original gland tissue. The cells were anatomically intact and did not stain with 0.2% trypan blue for up to 8 hours. They showed normal respiration (O_2 uptake: 21.4 ± 2.7 μl/hour·mg protein) and responded to stimulants of secretory activity (epinephrine, isoproterenol, dibutyryl cyclic AMP, theophylline and NaF) by secreting amylase into the medium at rates approximately equal to those observed in the intact gland in situ.

This method permits the investigation of aspects of the secretory processes of exocrine glands which cannot be studied in the intact glands of experimental animals in situ or in gland slices. Furthermore, as preliminary experiments have shown, living acinar cells for similar secretory studies can be obtained from human salivary glands and pancreas immediately after death.

Regulation of cellular growth: Control of pyrimidine biosynthesis. RODNEY L. LEVINE, NICHOLAS J. HOOGENRAAD, and NORMAN KRETCHMER. *Stanford Univ. Med. Sch., Stanford, Calif.*

Dividing cells require adequate amounts of purine and pyrimidine nucleotides for nucleic acid synthesis. The *de novo* pathway of pyrimidine biosynthesis is regulated to meet these growth requirements. In mammalian tissues the first enzyme in the pathway, carbamoyl phosphate synthesis (CPS), is inhibited by the pyrimidine nucleotide UTP. This inhibition may effectively limit *de novo* pyrimidine synthesis since CPS activity is the limiting enzyme for the pathway.

A detailed study of the kinetics of UTP inhibition provides support for the hypothesis that regulation of CPS is the physiological mechanism for control of the *de novo* pathway. CPS gives a sigmoidal velocity curve when the substrate ATP is varied in the absence of UTP. The curve fits a 2/1 function which suggests that ATP stimulates activity by acting both as a homotropic substrate and as an allosteric effector. UTP inhibits by competition with ATP and increases the sigmoidality of the curve. The K_i for UTP is 35 μM. The kintetic constants (K_m for ATP = 3 mM) are such that CPS should be extremely sensitive to deviations from the normal cellular concentrations of ATP and UTP.

The purine nucleotide ATP stimulates CPS while the pyrimidine nucleotide UTP inhibits so that precursors of nucleic acid interact on the enzyme. Thus CPS may play a pivotal role in the regulation of cellular proliferation. These findings might explain the observation that uridine greatly reduces urinary excretion of orotic acid in children with hereditary orotic aciduria. This action further supports the concept that regulation of CPS is a physiologically important control mechanism.

The relation between DNA polymerase activity and DNA synthesis in specific regions of proliferating rat brain. JO ANNE BRASEL (Intr. by Myron Winick). *Cornell Univ. Med. Coll., N. Y., N. Y.*

In a previous report demonstrating that activity of DNA polymerase parallels the rate of DNA synthesis in rat brain, we theorized that activity of this enzyme might serve as an *ad hoc* index of proliferative cell growth in normal tissues. Since individual brain regions have different rates of cell division and different times when maximum rates are attained, regional patterns of DNA polymerase activity have been examined and the characteristics of the enzyme further delineated. The data demonstrate that the enzyme is replicative and not reparative, is stimulated by glycerol, is linear with concentration and time and has an almost absolute requirement for DNA primer. Activity is always higher in cerebellum where the rate of DNA synthesis is rapid than it is in forebrain where cell division is slower. Activity in forebrain peaks between 10 and 12 days precisely when the rate of DNA synthesis is maximal in this region. By contrast in cerebellum there are two peaks of DNA synthesis at 7 and 13 days. DNA polymerase activity is also biphasic with peaks just preceeding each of the synthesis peaks. These data reinforce the concept that activity of this enzyme parallels the rate of cell division during proliferative cell growth. As such it should provide a