hrs. Base deficits were significantly smaller for the first 3 hrs in the Group A and for the first 24 hrs for group C. The PaO_2 and $PaCO_2$ values were not significantly different between early and late Rx groups. The incidence of RDS between groups was similar. The degree of severity of RDS was significantly greater in the late treatment groups from 12–96 hrs of age. A higher mortality rate was observed in infants weighing between 1001–2250 gms with late Rx. This study suggests that early correction of neonatal acidemia favorably influences the course of RDS, and that it may reduce the mortality of infants between 1001 and 2250 gms.

DEVELOPMENTAL BIOLOGY

Cartilage ultrastructure in the chondrodystrophies. D. L. RIMOIN, R. SILBERBERG, R. L. KAUFMAN, and R. ROSENTHAL (Intr. by J. W. St. Geme). *Harbor Gen. Hosp., UCLA Sch. Med., Torrance, Calif., and Washington Univ. Sch. Med., St. Louis, Mo.*

The chondrodystrophies are a heterogeneous group of disorders which have been classified on the basis of clinical, radiographic and genetic criteria. Histopathological studies of costochondral junction and iliac crest biopsies have allowed for the further classification of these disorders on the basis of the type of derangement in endochondral ossification. Electron microscopic studies of resting cartilage from these biopsy specimens demonstrate that the chondrodystrophies may be further characterized on the basis of ultrastructural abnormalities in the chondrocytes or intercellular matrix.

For example in achondroplasia, a disease associated with normal endochondral ossification, no ultrastructural abnormalities are present in either the chondrocyte or the matrix. In the mucopolysaccharidoses, the matrix is ultrastructurally normal, but the chondrocytes are filled with large cytoplasmic vacuoles of possible lysosomal origin. These vacuoles are uniform in appearance in the Hurler syndrome whereas in the Sanfilippo syndrome, two distinct populations of vacuoles can be identified. These ultrastructural observations provide a further clue as to the specific pathogentic mechanisms operative in the bone dysplasias.

Subcellular studies of the abdominal musculature in the prune belly syndrome. D. T. MININBERG, K. OKADA, R. PERSUTTI, and F. MONTOYA (Intr. by M. Lending). *New York Med. Coll., N. Y., N. Y.*

Light microscopy and electron microscopy were used to study the abdominal musculature in two infants with the prune belly syndrome. The electron micrographs demonstrated derangement in the coherence of the Z lines and myofibrils. This evidence supports the theory of developmental arrest at a 10 week level. We believe this to be the first time these electron microscopic studies have been made.

"Skin age" as a predictor of gestational age. A study of within-litter and between-litter variability in fetal rabbits. MARY E. AVERY, WILLIAM L. TAEUSCH, and N. S. WANG. *McGill Univ., Montreal, Que., Canada*

Recent studies in fetal rabbits led to the hypothesis that organ systems may mature at different rates among littermates, and raised the question of which organs were coupled in maturation, and presumably responsive to the same regulators. The number of epiphyseal centers and body weight were closely correlated and could vary 100% between littermates. Lung distensibility and stability (lung age) was predicted by gestational age better than by body weight. (Kotas, Avery, Pediat. 47: 1971). "Skin age" was assessed by histologic criteria in 70 rabbits from 14 litters delivered between 22 days gestation and term (30 days). Significant morphologic changes were evident from 24 to 30 days. "Skin age" was remarkably constant between littermates regardless of their weight, and in this sense it resembled lung age. In rabbits, at least, the skin is a predictor of maturity.

Evaluation of human gestational age by albumin, IgG globulin, and alpha-1-fetoprotein measurements. M. A. HYVARINEN, P. ZELTZER, E. R. STIEHM, and W. OH. *UCLA Sch. of Med., Harbor Gen Hosp., Torrance, Calif.*

Serum albumin (Alb) and IgG globulin levels in the developing fetus increase with maturity because of an increasing placental passage from the maternal circulation to the fetus. In contrast, levels of alpha-1-fetoprotein (AFP) decrease with maturity from a maximum serum level at 20 weeks of gestation (mean level $>$ 140.0 mg%) to trace levels (mean 5 mg%) at 40 weeks gestation. These observations permit an estimation of gestational age by measuring levels of cord blood IgG, Alb, and AFP, and when paired maternal IgG and Alb levels are available, by calculating fetal/maternal IgG and Alb ratios. Cord sera (and the matched maternal sera) from 55 infants (23 preterm, 32 term) on whom gestational age had been estimated by maternal history and physical examination (Dubowitz criteria, J. Ped. 77:1, 1970) were studied. Gestational age was correlated ($p < .001$) directly with cord levels of IgG ($r = 0.81$) and Alb ($r = 0.76$) and inversely with AFP ($r = -0.79$). Birth weight was also correlated ($p < .001$) with cord IgG ($r = 0.79$), Alb ($r = 0.73$) and AFP ($r -0.76$). Using a fetal/maternal IgG and Alb ratio did not result in an improved correlation. Although AFP was detected in all cord sera, AFP was not detected in the maternal circulation, nor in 14 of 15 amniotic fluid samples. Cord IgG and albumin levels best reflect gestational duration while cord AFP levels reflect fetal maturity.

Early fetal expression of genes for lysosomal enzymes. C. RONALD SCOTT, SANDRA H. CLARK, and JOHN S. O'BRIEN. *Univ. of Wash., Seattle, and Univ. of Calif., San Diego, Calif.* (Intr. by R. J. Wedgwood.)

Deficiency of specific lysosomal enzymes have been increasingly implicated in childhood storage diseases and the activity of these enzymes in cultured amniotic fluid cells has been used as an indicator of fetal genotype. To establish the time of expression of the genes for lysosomal enzymes during early human development, the activity and electrophoretic mobility of selected lysosomal enzymes were determined in fetal liver between 40 and 156 days' gestation and compared to infant and adult values. Only fetal liver obtained from therapeutic abortions performed by hysterotomy and dated by crown-rump measurements was selected. β-Glucosidase, β-glucuronidase, N-acetyl-glucosaminidase, α-glucosidase and β-galactosidase were assayed using their respective p-nitrophenol substrates. Activity of each enzyme was present in the earliest specimens and the specific activity remained constant between the 5th and 22nd week of gestation and were similar to those measured in infant and adult livers. Starch-gel electrophoresis was performed on those two enzymes, β-galactosidase and N-acetyl-glucosaminidase, known to have more than a single molecular form; there was no difference in their electrophoretic patterns during development.

This study establishes that for the five lysosomal enzymes

measured the genes controlling their expression were functioning as early as 40 days' gestation. Detection of hereditary disorders related to these enzymes could theoretically be accomplished as early as five weeks.

Human placental barrier to glucagon-I-125 early in gestation. P. ADAM, K. KING, R. SCHWARTZ, and K. TERAMO. *Case Western Reserve Univ. Sch. Med. at Cleveland Metro. Gen. Hosp., and Univ. Helsinki, Central Hospital, Helsinki, Finland.*

Studies of hormonal transfer have shown that the human placenta is impervious to 2 labeled polypeptide hormones-insulin and human growth hormone; but the transfer of glucagon, a polypeptide hormone of lower molecular weight, has not been evaluated previously in pregnant human subjects. Although its placental transfer has been demonstrated in other species, the results are confusing because of the non-specific methodology used. In order to determine whether the human placenta permits maternofetal transfer of glucagon, nine pregnant women at 15 to 17 wks of gestation were evaluated during legal therapeutic abortions by abdominal hysterotomy. The plasma concentration of glucagon-I-125 was maintained until delivery of the fetus by continuous intravenous infusion of the labeled hormone at the following rates: 20 μc/hr for 3–4 hrs in 4 women; and 60 μc/hr for 1 to 1.5 hrs in the other 5. The plasma concentration of the labeled glucagon was measured by a *specific* immunoprecipitation. Even with maternal plasma concentrations of radioactive glucagon between 599 and 1289 cpm/ml, no glucagon-I-125 was detected either in the umbilical venous or arterial plasma, or in the amniotic fluid. Early in gestation, therefore, the human placenta is an effective barrier to the rapid maternofetal transfer of glucagon-I-125. Based on this concept, regulation of the fetal plasma glucagon levels would depend on its secretion by the fetal rather than the maternal pancreas.

The placental calcium pump. INGEBORG C. RADDE, YEHEZKEL SHAMI, and DAVID K. PARKINSON. *Univ. of Toronto and Hosp. for Sick Children, Toronto, Ont., Canada* (Intr. by Andrew Sass-Kortsak).

During fetal life an uphill gradient for calcium ions exists between maternal and fetal circulations (maternal Ca^{2+} 1.95 mEq/l, fetal Ca^{2+} 2.45 mEq/l). We postulate that this gradient is maintained by an active transport system for calcium ions, similar to the calcium pump in renal tubular and intestinal mucosal plasma membranes. To characterize the enzyme, placental plasma membranes from guinea pigs were prepared according to the method of Post and Sen (Methods Enzymol. 10: 762, 1967). Samples were incubated for 30 min at 37 C in solutions containing 70 mM Na^+, 20 mM Tris (pH 7.6), Ca^{2+} or Mg^{2+} or both, in concentrations varying from 0.025 mM to 20 mM, and 5 mM Na_2ATP. P_i and protein were determined and results expressed as umole P_i released per mg protein in 30 min. Ca^{2+} in the absence of Mg^{2+} stimulated P_i production. Mg^{2+} in the absence of Ca^{2+} also stimulated the enzyme but to a lesser degree. 5 mM Ca^{2+} produced maximal stimulation (15–25 μmole P_i/mg protein in 30 min). Mn^{2+}, but not Sr^{2+}, stimulated P_i production, as with other Ca^{2+} ATPases (renal, intestinal mucosal). The pH optimum was 8.2; at 7.2 and 9.5 the enzyme activity was 50% of the maximum. Ouabain (1 mM) was not inhibitory, but addition of increasing amounts of EDTA led to progressive loss of activity; total inhibition occurring at 5 mM EDTA. Further fractionation of samples with sucrose-gradient centrifugation doubled the specific activity of the enzyme in the plasma membrane fraction. We believe that this enzyme of the placental plasma membranes activates a calcium pump which maintains the gradient of calcium ions between maternal and fetal circulations and ensures normal calcification in the fetus.

Fetal malnutrition. T. YOSHIDA, A. BERNAL, J. METCOFF, A. ROSADO, P. YOSHIDA, J. URRUSTI, L. VELASCO, and S. FRENK. *Univ. Oklahoma Med. Ctr., Okla. City, Okla., and Centro Medico Nacional, IMSS, Mexico City, D. F., Mexico*

Many instances of intrauterine growth retardation may represent fetal intrauterine malnutrition (IUM) rather than "placental insufficiency". Clinical, physiologic, and biochemical features simulate those of protein-calorie malnutrition (PCM) of infants. Cell size (protein/DNA) often is increased in IUM, but its relation to energy functions of the cell is uncertain. The present studies explored whether patterns of cell energy metabolism in IUM resembled those found in PCM, and if these patterns were similar in fetal and placental cells. Energy charge (EC) = (ATP + ADP/AMP + ADP + ATP), pyruvic (PK) and adenylic kinase (AK) and energy capacity (EC_a) = AK (ATP + ½ ADP) of leukocytes isolated from cord blood and of placentas were related to cell size (protein/DNA). For 13 IUM infants, leukocyte cell size was increased. PK and AK activities were reduced, compared to 28 low weight but appropriately nourished premies (P) or 33 full term (FT) infants. Most, but not all, of the differences were statistically significant. EC of the IUM leukocytes was not decreased; ATP and EC_a were. For placentas, while total DNA and RNA were reduced in 20 IUM's, cell size and ribosomal mass (RNA/DNA) were increased compared to 17 FT and 10 P. AMP was the only nucleotide significantly decreased in IUM's. Placental AK and PK were increased and correlated with cell size and birth weight in IUM babies. While EC was slightly decreased in IUM placentas, EC_a was increased. Thus, energy metabolism of IUM leukocytes is like infants with PCM, and metabolic changes in placental cells differ from those found in the infant's leukocytes.

Oxygen (O_2) consumption as measure of cell number in intrauterine growth failure (IUGF). INGEBORG KRIEGER and P. V. WOOLLEY, JR. *Wayne State Univ. Sch. of Med., Detroit, Mich.*

O_2-cons. in the basal state is a measure of the metabolically active tissue mass and, as such, may reflect cell number rather than cell mass. This was tested by comparing conditions which have a different ratio between cell number and cell mass (CNo). 24 patients with IUGF and persistent linear growth failure after birth (PIUGF) were assumed to have a low CNo. 31 patients with growth failure of postnatal onset due to undernutrition, group A, were assumed to have a higher CNo than PIUGF because undernutrition in not rapidly multiplying tissues decreases cell size. 24 patients with growth failure of postnatal onset and congenital anomalies were placed in group B, with unknown relative CNo. Ages were 4/12–10 years and height ages <3 years. 37 normal controls were <3 years old.

O_2-cons. for age and height age was significantly lower in PIUGF than all other groups. O_2-cons. of groups A and B was not different, i.e. significantly lower than the normal for age and similar to the normal for height age. O_2-cons. per body weight was normal in PIUGF and elevated in groups A and B. O_2-cons. per weight predicted from height was negatively related to height in per cent of the normal height for age. The regression for PIUGF was significantly lower than in groups A and B. A good correlation was evident only in group A ($r = .723$). This suggests an increase in metabolically active tissue with increasing