the left. X-ray revealed absence of the tubular bones of the metacarpals and phalanges bilaterally. The feet showed similar abnormalities. There was micrognathia, glossoptosis, cleft soft palate and tracheomalacia. Eyes and fundi were normal. The baby expired after numerous apneic spells associated with cyanosis.

Baby boy D was born at term to a 29-year-old mother who was hospitalized for schizophrenia during the pregnancy; she showed intermittent glucosuria. The infant exhibited micrognathia, shortening of the right femur and bilateral club feet. X-rays showed the cortex of the femurs to be abnormally thick, and defects were noted in the vertebral bodies of the lower lumbar column. Ocular fundi were normal. The baby expired after a gastrostomy and repeated apneic episodes.

Cytogenetic studies on both patients were normal. Our two patients, together with the previously reported two cases [PASSARGE, *Lancet* *i*: 324, 1965; CENTA and ROVEL, *Pathologica* 57: 245, 1965] appear to represent a distinct syndrome.

- 27 *Development of Transsulfuration in the Human Fetus, Premature and Newborn: Clinical Implications.* GERALD GAULL, JOHN STURMAN and NIELS RAIHA, Dept. of Ped. Res., N.Y.S. Inst. Basic Res. Ment. Retard., Dept. Ped., Mt. Sinai Hosp. Sch. Med., New York, and Depts. Clin. Chem. and Obst. and Gyn., Univ. Helsinki (introduced by Horace Hodes).

In the human adult, 90% of ingested methionine is converted to cystine, a nonessential amino acid. The ability to make this conversion was investigated in the developing human. Enzymes on the pathway of conversion of methionine to cystine in the liver of 24 fetuses (2.5–20.5 cm crown rump length), three prematures and one full-term newborn were assayed. *Cystathionase* activity was undetectable, and administration of massive doses of vitamin B₆ to the mother had no effect on this activity in three fetuses. *Cystathionine*, the substrate of *cystathionase*, not normally present in measurable quantities in adult human liver (which has considerable activity of *cystathionase*) was present in large concentrations. Considerable activity of methionine-activating enzyme was present ($\frac{2}{3}$ of adult); *cystathioninesynthase* activity was also present ($\frac{1}{3}$ – $\frac{1}{2}$ of adult). A similar pattern of transsulfuration enzymes was seen in brain, but there are no antemortem adult controls for comparison. The concentration of *cystathionine* in whole brain was constant during this period and, in contrast to the adult, well below the concentration in liver. The placenta cannot subserve the transsulfuration function for the fetus, since the enzymatic mechanism was absent. Fetal rat liver, in contrast, is able to convert methionine to cystine. Thus, cystine may be an essential amino acid until sometime after birth, and the human fetus is entirely dependent upon the mother for its supply of cystine for protein synthesis. The implications for infant nutrition and metabolic screening will be discussed.

- 28 *Chloramphenicol Causes Ultrastructural and Biochemical Alterations in Developing Chick Liver.* J. B. WARSHAW, Harvard Med. Sch., Massachusetts Gen. Hosp., Children's Service and the Shriners Burns Institute, Boston.

Chloramphenicol (Ch) administration has been associated with the fetal 'gray baby syndrome' and depression of the hematopoietic system. Ch also causes alterations of mitochondrial morphology and inter-

feres with mitochondrial energy metabolism in a variety of species. We have investigated the effects of Ch on mitochondrial energy metabolism and structure in the developing chick liver. Ch and ¹⁴C-leucine were injected through shell windows into 12 to 17 day chick embryos. After 3 days of exposure to the drug the livers were fixed for electron microscopy and were also used for biochemical studies. Electron micrographs of the Ch treated livers showed major ultrastructural alterations characterized by profound mitochondrial swelling and distortions of mitochondrial structure. There was also a great abundance of free ribosomes. The cytochrome oxidase activity of the treated liver homogenates and the mitochondrial yields from Ch treated livers were approximately 40 to 50% of those of the controls. Mitochondrial profiles of Ch treated liver homogenates on sucrose density gradients were greatly diffused when compared with controls, presumably because of the ultrastructural abnormalities. ¹⁴C-leucine incorporation into the Ch treated liver mitochondria separated on a sucrose density gradient was significantly less than observed with controls. Those mitochondria which were isolated had some biochemical activities similar to the controls (isocitric dehydrogenase, malate dehydrogenase) but rates of oxidation with NADH limited substrates were less than control values. These data suggest that Ch may interfere with energy metabolism in rapidly proliferating tissues because of its effects on protein synthesis and mitochondrial structure and function.

- 29 *The Metabolism and Transplacental Passage of 3H-Vitamin D3 in the Pregnant Primate, Macaca mulatta.* HENRY RIKKERS, Univ. of Wisconsin Med. Sch., Dept. of Ped., Madison, Wisc. (introduced by C. C. Lobeck).

In animal systems excessive maternal ingestion of vitamin D during pregnancy has been shown to cause in the offspring most of the bony and arterial pathology seen in idiopathic hypercalcemia of infancy. This disease is felt by some to be due to altered responsiveness of the fetus and/or mother to vitamin D. Mammals, including man, convert vitamin D to 25-hydroxy vitamin D before the vitamin has its characteristic effects. A previous study demonstrated nonspecific antirachitic activity in cord serum of rabbits whose mothers had been given massive vitamin D doses during pregnancy. The current study demonstrates not only how much, but also, in what metabolic form the vitamin traverses the placenta.

C-sections were performed 6, 24, 48 and 100 h after IV administration of 3H-vitamin D3 in non-physiologic doses to pregnant rhesus monkeys. All tissues within the fetal compartment were studied for the amount and metabolic state of the vitamin present. Results show that the placenta acts as a barrier and storage organ from which the fetal serum somewhat selectively supplies fetal tissues with, mainly, 25-hydroxy vitamin D. Fetal tissues do not appear to convert vitamin D to 25-hydroxy vitamin D. The data suggest that at physiologic doses the fetal tissues would probably not be exposed to unaltered vitamin D. This suggests that the teratogenicity of vitamin D is due to undue exposure of fetal tissues to the unaltered vitamin.

- 30 *Early Mammalian Development: Nucleoside Transport and RNA Synthesis.* DONNA L. DAENTL and CHARLES J. EPSTEIN, Univ. of California, Dept. of Ped., San Francisco.