

alkaline phosphatase activity and phosphoethanolamine excretion, eight heterozygotes were found in the family. In these heterozygotes phosphate reabsorption was normal, alkaline phosphatase activity was significantly decreased in the urine, but normal or elevated in the granulocytes. When their marker features were examined, the small number of the hypophosphatasia gene-bearing patients allowed no statistical analysis, but it was conspicuous that these persons were Rh negative, were nontasters for phenylthiocarbamide (PTC), and had an excess of ulnar loops in finger dermatoglyphics.

51. Control of erythropoiesis in the fetal and neonatal rat. Y. MATOHI and R. ZAIZOV. *Tel Aviv Univ. Med. Sch., Israel.*

Erythropoiesis in the fetal rat was studied by measuring the incorporation of Fe<sup>59</sup> into red cells of fetuses following injection of the isotope into their mothers on the 18th day of gestation. Two days later the amount of radioactivity present in the fetuses was determined by whole body counting. From this value and from the radioactivity found in fetal blood, the percentage incorporation of Fe<sup>59</sup> into red cells (PI) was calculated. About 60% of the injected dose was found in the fetuses. The PI in individual fetuses varied with fetal weight, showing a linear relationship. It was therefore concluded that the rate of fetal growth is an important determinant of the rate of erythropoiesis. When mothers were bled or subjected to hypoxia during the 3rd week of pregnancy, or given 75–100 units of erythropoietin, they showed, as expected, an increase in PI. The fetuses likewise showed a significant increase in PI, controlled for fetal weight. The PI was decreased in mothers made polycythemic or kept at 4 atm abs but not in their fetuses. It has therefore been shown that in the rat erythropoietin can pass through the placenta and that the fetus responds to erythropoietin, either endogenously produced or transferred from the mother. Newborn rats hypertransfused during the 1st and 2nd postnatal weeks showed a marked decrease in PI and a good response to exogenous erythropoietin. Since the rat is born relatively immature and follows a fetal pattern of erythropoiesis for the first 2 postnatal weeks, these observations provide further evidence that erythropoiesis in the fetus is regulated through the hypoxia-erythropoietin mechanism.

52. Erythropoietic inhibitors in plasma and urine. S. HALVORSEN, R. LINDEMANN, and P. SKJAEELAAEN. *Rikshospitalet, Oslo, Norway.*

The existence of specific inhibitors of erythropoiesis (EIF) has been suggested by several authors. The demonstration of this inhibitor, suggests that both activators (ESF) and inhibitors (EIF) participate in the normal regulation of erythropoiesis. In this study the presence of EIF in urine and neonatal plasma has been investigated.

Urine from normal healthy persons, from patients with aplastic anemia, and from patients with severe anemia due to chronic renal failure was investigated. The urines were passed through a Sephadex column, and the different fractions were tested for stimulatory and inhibitory effect of erythropoiesis. Plasma from normal newborn babies was withdrawn on the first 4–6 days of life. Plasma from newborns with hyperbilirubinemia but normal hemoglobin levels was also used for the plasma studies. Erythropoiesis in exhypoxic polycythemic mice was either stimulated by erythropoietin injections or by a second hypoxic period. Saline and test material were given simultaneously with erythropoietin or before and after the second hypoxic period. The effect was measured as <sup>59</sup>Fe uptake in red blood cells.

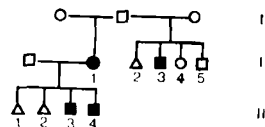
A marked inhibitory effect was found in the urine from normal healthy persons and from patients with aplastic anemia. In patients with chronic uremia a slight inhibitory effect and no active erythropoietin was found. The mice given neonatal plasma showed a marked reduction in iron uptake when the plasma was withdrawn between the 4th and 14th days of life.

The mode of action and the physiological role of EIF are unknown. EIF may be related to chalone. This is supported by the finding that EIF has the same molecular weight as reported for the chalone.

53. Dominant inheritance of congenital hypoplastic anemia. S. GARWICZ and N. W. SVENNINGSEN. *Univ. of Lund, Sweden.*

This paper is presenting the family history of a boy (III-4), who at the age of 2 months developed a typical picture of congenital hypoplastic anemia. His bone marrow showed 10.6% erythroblasts with predominance of young forms. Favorable response to corticosteroids was observed and at the age of 8 months the patient is doing well on small doses of prednisolone.

At the age of 2 months his older brother (III-3) showed a moderate anemia (lowest Hgb 7.9 g%), which subsided spontaneously at 7 months of age. Their mother (II-1) is herself the first case of Blackfan-Diamond anemia described in Europe 1939 by G. v. Sydow. She had been spenectomized at the age of 1½ year and later on showed a stationary course of the disease. During pregnancies her Hgb values were 7.8–8.7 g% without any blood transfusions. Her step-brother (II-3) developed a classical syndrome of congenital hypoplastic anemia at the age of 4 months. He was treated with blood transfusions and later on with corticosteroids. He died at the age of 12 and the autopsy showed generalized hemosiderosis. These step-siblings were described by Förare in 1963. According to available records the father of both step-siblings and his ancestors (mother, maternal uncle, and grandmother) had apparently had some kind of anemia. The family described indicates that dominant inheritance occurs in at least one type of hypoplastic anemia.



54. Binding capacity of human albumin for bilirubin. D. BRATLID, J. FOG, and S. O. LIE. *Rikshospitalet, Oslo, Norway.*

The binding between bilirubin and human serum albumin was studied spectrophotometrically and with Sephadex gel filtration. Spectral absorption curves of solutions of bilirubin in buffers containing decreasing amounts of albumin were registered. At a molar bilirubin to albumin ratio of 1:1 a change in these curves takes place, indicating that only one molecule of bilirubin is tightly bound to albumin. Sephadex gel filtration studies also showed that with solutions containing bilirubin and albumin in molar ratios above 1:1, bilirubin was retained on the column. A second molecule of bilirubin seemed, however, to be more loosely bound.

The toxic effect of bilirubin on human fibroblasts in tissue culture was also tested. When solutions containing bilirubin to albumin ratios above 1:1 were added to the growth medium, a toxic effect was seen on the fibroblast growth. With a bilirubin to albumin ratio of 2:1 rapid cell death was found with total bilirubin concentrations as low as 5 mg/100 ml. On the other hand, when the bilirubin to albumin ratio in the growth medium