steadily during the first 3 to 4 months, and by 5 months of age approximates 2 to 3, which is similar to the ratio of the Hb-F from normal adults. These observations suggest that the switch from γ chain to β (and δ) chain production after birth apparently involves an unequal repression of the multiple γ structural genes at the time the β and δ structural genes are activated.

- 124 *Hemoglobin-Oxygen Affinity and Erythrocyte 2,3-Diphosphoglycerate (DPG) Content in Hyaline Membrane Disease (HMD) and Cardiac Malformations (CM).* GABRIEL V. DUC and KNUD ENGEL, Dept. of Ped., Coll. of Physicians and Surgeons, Columbia Univ., New York (introduced by John C. Sinclair).

The effect of DPG on the affinity of hemoglobin for oxygen, expressed as P^{50} (the PO_2 at which Hb is 50% saturated with O_2), is well known. In the present investigation whole blood from newborns with hyaline membrane disease (HMD) and cardiac malformations (CM) revealed a statistically significant difference between the two groups in both P^{50} and DPG content (HMD: P^{50} 24.6 mm Hg $\pm$ 3.5 S.D., DPG 0.78 mol/mol Hb $\pm$ 0.16; CM: P^{50} 29.1 mm Hg $\pm$ 3.4, DPG 1.31 mol/mol Hb $\pm$ 0.30). Patients with CM were more mature with higher birth weights and had lower arterial PO_2 and O_2 content (10.2 vol% O_2 $\pm$ 4.0 vs. 16.7 $\pm$ 4.9). BE, pH, PCO_2 , Hb and HbF were comparable. The effect of the observed difference in P^{50} between babies with HMD and CM can possibly explain the greater tolerance to hypoxemia of infants with CM since blood with P^{50} of 29.1 mm Hg can unload 15% more O_2 to the tissues than blood with P^{50} of 24.1 assuming the same PvO_2 , CaO_2 and cardiac output. Such differences in P^{50} have almost no effect on the amount of O_2 loaded in the lungs. Further observations showed that DPG concentration varied directly with pH in normoxemic patients (>90% saturation, >15 vol% O_2). Low pH could cause a decrease in DPG by inhibition of enzymes responsible for the synthesis, but also low DPG could produce a decrease in pH by impairment of unloading of O_2 to the tissues. The hypoxemic patients showed a higher DPG concentration than predicted from their Hb, again suggesting that hypoxemia causes an increase in DPG concentration.

- 125 *Molecular Interactions of Normal and Abnormal Hemoglobin in Cell-free Systems.* JAMES G. WHITE and BEATRICE HEAGAN, Univ. of Minnesota Sch. of Med., Minneapolis.

Increased viscosity, fragility and distortion of erythrocytes from patients with inherited defects of hemoglobin (Hb) have been related to sol-gel and sol-crystal transformation. A method has been developed in this laboratory which permits definition of the nature of molecular assembly underlying abnormal hemoglobin interactions. Cell free solutions of HbAA, HbAS, HbSS, HbSC, HbCC, and HbF combined with phosphate buffer, or phosphate buffer containing sodium metabisulfite, formed solid gels, crystals or amorphous precipitates. Gels of reduced HbSS, HbAS and HbSC consisted of masses of 170 Å rods identical to those observed in intact sickled erythrocytes. Gels of oxy HbSS, HbAS, HbAA and reduced HbAA contained 240 Å hollow tubular polymers similar to microtubules. Fresh samples of oxy HbSC and HbCC rapidly formed crystals, but a gel stage could be demonstrated by stirring solutions during transformation. Solutions of oxy and reduced HbF developed amorphous precipi-

tates, but did not gel or form crystals. Inability of HbF to form polymers may relate to its inhibitory effect on the assembly of HbS into rods. The capacity of oxy or reduced HbAA to transform into microtubules, on the other hand, reflects its ability to combine with HbS in rod-like polymers which distort cells containing HbAS. Molecular interactions of HbC favor crystallization, but as in all other examples, the gel state appears to precede crystallization. These findings indicate that hemoglobin molecules in intact normal and abnormal erythrocytes are in a high degree of molecular association or pre-gel state. Slight alterations in hemoglobin molecular structure can produce rapid and profound changes in the organization of hemoglobin into gels or crystals.

- 126 *Chronic Myelogenous Leukemia: Cyclic Leukocytosis and Identical Twin Discordance.* RICHARD A. GATTI, AMOS S. DEINARD, MARK E. NESBIT, WILLIAM A. ROBINSON and ROBERT A. GOOD, Univ. of Minnesota, Dept. of Ped., Minneapolis; Univ. of Colorado, Dept. of Med., Denver.

A cyclic leukocytosis with cycles of approximately 72 days and counts ranging from 4,000 to 145,000 cells/mm³ has been followed for 15 months with no treatment, in a 13-year-old white female with chronic myelogenous leukemia (Ph¹ positive). An identical twin has no clinical, morphologic or cytogenetic evidence of leukemia. Differential counts of per. bl. and marrow remain unchanged during the patient's cycles although marrow cellularity is increased during peaks. Studies which were normal include: Rebut skin windows, phagocytic and bactericidal functions of neutrophils, glutathione peroxidase levels, fetal hemoglobin and immunologic responses. Epinephrine stimulation produced a total release of marginal pool cells at the high point with only partial release of cells at a low point. Endotoxin and steroid stimulation studies indicate that mechanisms for delivery of cells from marrow are intact and of similar magnitude at both high and low points. Ph¹ positive cells were seen in 81% of mitoses from per. bl. cells taken at a peak while in per. bl. specimens taken at a low point such Ph¹ positive cells were absent. At both high and low points over 90% of mitoses of bone marrow cells were Ph¹ positive. Mixed leukocyte cultures showed a non-reciprocal response of the patient's leukocytes to cells of her identical twin, suggesting partial loss of transplantation antigens in some of the patient's cells. Leukokinetics with DFP³²-labeled cells, alkaline phosphatase and granulopoietin levels and marrow proliferation studies with H₃T were measured at high and low points. These studies would be compatible with the view that controls of leukocyte production and release as well as in immunogenetic characteristics of cells are involved in this leukemic process.

- 127 *An Unusual Neutrophil Cycle in Down's Syndrome and Acute Leukemia.* RENATO MASTRANGELO, DOUGLAS E. COX, WOLF W. ZUELZER and JAMIL KHEDEH, Child Res. Center of Mich. and Dept. of Ped., Wayne State Univ. Sch. of Med., Detroit, and Plymouth State Home and Tr. Sch., Northville, MI.

A short-term cyclic fluctuation (14 to 24 days) of the neutrophil count in normal adults was shown by MORLEY [Lancet ii: 1220, 1966]. In contrast, a longer duration cyclic fluctuation (30 to 120 days) was seen by MORLEY, BAIKIE and GALTON in 4 patients with