CORRECTION OF PLATELET DYSFUNCTION AND BLEEDING IN CYANOTIC CONGENITAL HEART DISEASE BY SIMPLE RED CELL VOLUME REDUCTION. *Harold M. Maurer, Carolyn M. McCue, Louise Robertson, Joyce C. Haggins, Department of Pediatrics, Medical College of Virginia, Richmond, Virginia.*

Red cell volume reduction corrected the platelet aggregation abnormality and bleeding tendency exhibited by 4 boys, ages 5 to 16, with severe cyanotic congenital heart disease and polycythemia (Hcts 68-75%). Red cell volume was lowered by replacing 15 to 20 ml/Kg of the patient's blood with plasma in 50 ml increments over a 1 to 2 hour period. Within 3 days, platelet aggregation was restored to normal, and previous bleeding symptoms disappeared. Platelet aggregation remained normal during 3 weeks of follow-up while hematocrits remained at palliative levels. The procedure was safe, simple, and produced beneficial effects not only on bleeding, but,also on other symptoms related to polycythemia and high blood viscosity.

The mechanism by which platelet function is corrected is not yet understood. In vitro studies showed no corrective effects of donor plasma on the abnormal platelets.

For polycythemic patients with cyanotic heart disease and platelet defects who require surgery, red cell volume reduction is recommended preoperatively to lessen the risk of serious bleeding during the early postoperative period. Palliation of severely cyanotic children who are inoperable is another indication for this procedure.

SPLENIC FUNCTION AND HEMATOLOGIC CHANGES DURING THE FIRST YEAR OF LIFE IN SICKLE CELL ANEMIA. Richard T. O'Brien, Sue McIntosh, Gregg T. Aspnes and Howard A. Pearson, Dept. of Pediatrics, Yale Univ. Sch. of Med., New Haven, Conn.

Seven infants with sickle cell anemia have been identified in routine screening of cord blood from 1500 neonates. These children have been followed serially for up to 2 years. Hemoglobin levels fell most rapidly during the first 3 months and then declined more slowly, stabilizing between 7 and 10 gm% by 10 months of age. The post natal decline of Hgb F was slower than normal but showed considerable variability. There was close correlation between the rate of fall of Hgb F and the development and severity of hemolysis. Clinical vasocclusive symptoms occurred as early as 4 months but were also variable. ^{99m}Tc colloid scans showed normal splenic activity in all infants before 6 months. The onset of functional asplenia was documented in four infants at 7,8,10 and 11 months. Thus, functional asplenia is an acquired defect in sickle cell anemia. Howell-Jolly bodies were noted prior to the abnormal scan. Functional asplenia occurred when Hgb F fell below 20%. Two infants retain normal splenic function at 12 and 20 months. These observations indicate variability in the development of hematologic and splenic abnormalities in children with homozygous Hgb S disease. The fact that splenic dysfunction, with resultant susceptibility to overwhelming sepsis may occur as early as 7 months of age in this disease, provides impetus for early diagnosis.

SUCCESSFUL MARROW RE-TRANSPLANTATION FOLLOWING FAILURE OF FIRST TRANSPLANT FOR APLASTIC ANEMIA, H.J. Meuwissen, E.C. Moore and H. Strauss, (Intr. by Ian H. Porter), New York State Dept. of Health, Birth Defects and Kidney Disease Institutes and Department of Pediatrics, Albany Medical College, Albany, New York.

An 11 year old girl with aplastic anemia of unknown etiology was transplanted with MLC and HLA identical sibling marrow following 4 doses of Cyclophosphamide (CY) 50 mg/kg. She had received multiple blood transfusions before transplantation (TP). Three weeks following TP the marrow was repopulating, but 4 weeks later the marrow was again aplastic. Immunosuppression with Procarbazine, anti-thymocyte globulin, and a repeat course of CY were given followed by a second TP from the same donor. A take of donor marrow cells now occurred and has persisted to the present (140 days after TP). No evidence of graft-versus-host disease was seen; PHA responsive peripheral blood lymphocytes have remained predominantly of host type. The patient has remained in excellent clinical health. Her B cell function is normalizing, but her T cell function is as yet depressed.

THE MECHANISM OF 2,3-DIPHOSPHOGLYCERATE (DPG) INSTABILITY IN THE RED CELLS OF THE NEWBORN INFANT. **Frank A. Oski. State University of New York, Upstate Medical Center, Syracuse, New York.**

In the red cells from newborn infants, 2,3-DPG declines more rapidly upon incubation than it does in the cells from normal adults. The red cells from 10 cord blood samples and 10 adults were incubated for 4 hours in the presence or absence of glucose (10 mM), with fluoride (10 mM), or iodoacetate (0.5 mM), to determine if impaired 2,3-DPG synthesis or accelerated breakdown was responsible for the 2,3-DPG instability. Assays of DPG mutase, the enzyme responsible for DPG synthesis, were also performed on hemolysates. In the absence of glucose or in the presence of IAA, an inhibitor that acts proximal to the point of DPG synthesis, DPG levels declined more rapidly in the cells of the newborn (0.82 µmoles/ml/hr vs 0.50). The net synthetic rates appeared similar, averaging 0.37 µmoles/ml/hr in the infant and 0.42 in the adult. Fluoride, an agent that blocks glycolysis distal to the site of 2,3-DPG synthesis, produced a rise in 2,3-DPG in the cells of adults (0.25 µmoles/ml/hr), while DPG levels declined in the newborn. DPG mutase activity was similar in both infants and adults. These findings suggest that the DPG instability observed in the cells of the infant is a result of accelerated DPG breakdown and not a consequence of an impairment of glycolysis.

DECREASED MEMBRANE DEFORMABILITY OF NEONATAL LEUKOCYTES AND ITS RELATIONSHIP TO NEUTROPHIL MOVEMENT. Michael E. Miller and Kenneth Myers, Drew School, Dept. of Peds., Los Angeles, CA

In previous studies we have demonstrated two separate mechanisms by which human neutrophils (PMNS) move:1)chemotaxis,or directed migration,and;2)random, or non-directed migration.We have also shown that neonatal PMNS are deficient in chemotaxis but have normal random migration.In order to further characterize the nature of neonatal PMN movement,we have employed the study of membrane deformability.Using a micromanipulator,individual PMNS were directed to the orifice of 3-5u internal diameter hollow glass pipettes.The "deformability" of the membrane was measured by the amount of negative pressure required to draw the cell into the pipette.The assay is precise and highly reproducible.Neonatal PMNS showed markedly decreased membrane deformability over control PMNS-i.e.,were much more rigid cells.The finding of a functional abnormality of the neonatal PMN membrane is unique and has major significance:1)Since neonatal PMNS are deficient in chemotaxis but normal in random mobility, membrane deformability may play a role in chemotaxis.This is supported by the observation that iodoacetate,NaF and deoxyglucose,agents which decrease membrane deformability also selectively inhibit chemotaxis;2)PMN membrane deformability is an active process.The deformability defect here may,therefore,reflect metabolic immaturity of the neonatal PMN.

RED CELL TRIOKINASE DEFICIENCY - ANOTHER BIOCHEMICAL CHARACTERISTIC OF THE FETAL ERYTHROCYTE. Frank A. Oski, Joan R. Urmson and Patricia L. O'Neal. State University of New York, Upstate Medical Center, Syracuse, New York.

The erythrocytes of normal adults have the capacity to incorporate and metabolize dihydroxyacetone (DHA). This substrate has been found to be useful for the maintenance of 2,3-diphosphoglycerate (DPG) in stored red cells. The metabolism of DHA by cord blood erythrocytes was examined in an attempt to find a substrate for DPG synthesis that bypassed the early steps in red cell glycolysis. When the cells from adults and infants were incubated in the presence of DHA (10 mM), pyruvate (10 mM), and inorganic phosphate (10 mM), the DPG level increased by 2.34 µmoles/ml RBC's in the adult samples but only increased by 0.1 µmoles/ml in the cells of infants during a period of 2 hours. DHA consumption averaged 3.76 µmoles/ml RBC's/hr in the cells from adults but was only 1.16 µmoles/ml RBC's/hr in the erythrocytes of the newborn. Assays of triokinase, the enzyme responsible for the phosphorylation of DHA, were performed in the hemolysates from newborn and adult erythrocytes. Triokinase activity averaged 4.56 $\pm$ 0.69 units/100 ml RBC's in adults and was only 2.97 $\pm$ 0.54 units in the cells from newborns ($p < .01$). Relative triokinase deficiency appears to be another biochemical characteristic of the red cells of the newborn infant.