631 CONGENITAL DYSERYTHROPOIETIC ANEMIA (CDA) TYPE IV. Denis R. Miller, Anneliese L. Sitarz, Philip H. Lieberman, Esmail D. Zanjani and Stephen B. Shohet, New York Hospital-Cornell Medical Center, Babies Hospital, Memorial Hospital, Mt. Sinai Medical Center, New York, and University of Calif. Medical Center, San Francisco.

The heterogeneous disorder, CDA, is characterized by ineffective erythropoiesis and ultrastructural alterations of late erythroblasts. Three major types have been described: Type I with macrocytosis, Type II (HEMPAS) with abnormal RBC antigens, and Type III with gigantoblasts. Studies of RBC antigens, metabolism, lipids, ferrokinetics, in vitro erythroid colony formation, and globin-chain synthesis were performed in a 15 year old male with atypical CDA. Ferrokinetics showed ineffective erythropoiesis, chromium survival was shortened, bone marrow revealed 25-35% 2-3 lobed late normoblasts, and electron microscopy showed dyserythropoiesis but no "double membranes" or internuclear bridges. Acid hemolysis tests with 20 ABO compatible sera were negative and hemolysis by anti-I, anti-i, or hemolytic anti-B was not increased. Activity of i matched that of fetal cells. Increased membrane phosphatidyl choline (36%, normal 29%) and decreased sphingomyelin (19%, normal 27%) were noted. The ratio of α and β chain synthesized by peripheral blood and BM RBC was normal; glycolytic intermediates and enzymes were normal except for pyruvate kinase. Erythroid colony formation in vitro was normal; dyserythropoiesis was not observed. The findings are compatible with CDA Type IV, a rare disorder with morphologic features of Type II but lacking abnormal serology. Attempts to apply distinctive ultrastructural features to CDA may be misleading.

632 SPONTANEOUSLY ACQUIRED FACTOR IX INHIBITOR IN A NON-HEMOPHILIAC CHILD. Kenneth Miller, John E. Neely, William Krivit, J. Roger Edson. University of Minnesota Medical School, University of Minnesota Hospitals, Dept. of Pediatrics and Dept. of Laboratory Medicine and Pathology, Mpls.

A previously healthy 2-1/2 year old child was hospitalized for progressive swelling of the left leg and a falling hemoglobin (11.9-8.8 gm %). The partial thromboplastin time (PTT) was prolonged (88 secs.) while the prothrombin time (PT), platelet count and bleeding time were normal. The PTT did not shorten despite the administration of 225 ml of fresh frozen plasma. An ecchymotic right sided chest mass was noted. Upon arrival at the University of Minnesota Hospitals, the PTT was 79.2 sec. with a normal PT and thrombin time (TT). The Factor IX was 27% and 15% respectively on two specimens with an inhibitory curve. The remaining factor assays were within the normal range. In vitro inactivation of Factor IX in normal plasma by patient plasma was also demonstrated. Treatment consisted of a four volume exchange transfusion, cyclophosphamide 10 mg/kg for four days and prednisone 60 mg/m^2/day tapered gradually over one month. Following exchange transfusion, Factor IX levels remained normal. Within five days the swelling diminished and the ecchymotic mass resolved. Presently off all medications the Factor IX level is 124%. Numerous laboratory studies obtained prior to immunosuppressive therapy were normal except for a positive fluorescent nuclear antibody (FANA) in an indeterminant pattern. The patient has had no signs or symptoms consistent with a collagen vascular disease.

633 CELL ELASTIMETRY IN THE DETECTION OF IMMUNE NEUTROPENIA -- DEMONSTRATION OF A MEMBRANE PERTURBATION. Michael E. Miller and Laurence A. Boxer. UCLA and Indiana U. Schs. Med., Harbor Gen. Hosp. and J. W. Riley Hosp. for Children, Depts. of Peds., Torrance, Ca. & Indianapolis, Ind.

Anti-neutrophil antibodies (ANA) have been demonstrated in the serums of recipients of multiple transfusions, mothers of infants with transient neonatal neutropenia, and in some patients with idiopathic neutropenia. Ingestion of sensitized neutrophils by other phagocytic cells has been observed, but direct evidence of membrane alteration of polymorphonuclear leukocytes (PMNS) by ANA is limited. We have used cell elastimetry to explore the problem. This technique measures, under direct visualization, the negative pressure required to aspirate PMNS into small pored pipettes. We have previously shown that the assay primarily reflects rigidity or deformability of the cell membrane. When incubated with normal PMNS, eight of nine serums from patients with known ANA significantly decreased membrane deformability -- i.e. cells became more rigid. The mean negative pressure required to aspirate PMNS incubated in normal plasma was 11.4 $\pm$ 3.6 (2 S.D.) cm Hg. PMNS incubated in the various ANA positive serums ranged from 25.9 to >43 cm Hg negative pressure required for aspiration. To insure objectivity, the study was conducted in an entirely blind fashion. Randomly coded serums from patients and controls were studied for deformability by observers unaware of the code. We conclude: 1) Elastimetry is a reliable and sensitive probe for the detection of ANA; 2) A primary effect of ANA upon PMN membranes has been demonstrated.

634 ON THE HETEROGENEITY OF "BENIGN" NEUTROPENIA OF CHILDHOOD. Michael E. Miller & Jerry Z. Finklestein, UCLA School of Medicine, Harbor General Hospital, Department of Pediatrics, Torrance, Ca.

Chronic benign granulocytopenia of childhood (CBGC) is generally accepted as a homogeneous, self limited entity of variable duration, characterized by absolute peripheral blood polymorphonuclear leukocyte (PMN) counts <1500/mm^3, relative depletion of band and mature granulocytes in bone marrow and absent to mild infections. Our previous observations that some patients within this group have distinct functional aberration of PMNS -- e.g. "Lazy Leukocyte Syndrome" prompted the current study. Eleven children with CBGC were studied. Each had absolute PMN counts <1000/mm^3 with 6 <500/mm^3. Four functional PMN assays were performed: chemotaxis (Boyden chamber); capillary tube migration; phagocytosis (Baker's yeast ingestion), and; membrane deformability (cell elastimetry technique). The data showed marked heterogeneity in functional PMN profiles. One child had decreased capillary tube migration, one was deficient in all functions tested, six showed various combinations of functional abnormalities and only three children had normal PMN activities in each assay. We conclude: 1) CBGC is not a distinct clinical entity; 2) the spectrum of abnormal PMN functional profiles observed strongly suggests that abnormalities of a number of individual steps of normal PMN function may produce a common clinical phenotype; 3) of the assays employed, membrane deformability was most consistently abnormal; 4) the clinical course of these patients, when followed long term, may not always be benign.

635 GAMMA CISTERNOGRAPHY: DETERMINATION OF ADEQUACY OF INTRATHECAL THERAPY IN LEUKEMIC DISEASE. Merrill L. Miller, James A. Stockman III, James J. Campbell, Karen A. Smith and Edward G. Bell (Spon. by Frank A. Oski), Dept. of Peds., SUNY, Upstate Medical Center and Dept. of Nucl. Med., Crouse-Irving Memorial Hosp., Syracuse, N.Y.

The use of Central Nervous System (CNS) prophylaxis with intrathecal chemotherapy is now considered an important early measure in the treatment of acute lymphoblastic leukemia and lymphomas. It has been suggested that epidural or subdural extravasation at the time of lumbar puncture occurs frequently (NEJM 293:161, 1975). In order to determine the frequency of inadequately administered chemotherapy as well as its distribution within the CNS, Tc-99m labeled Inulin complex was admixed with chemotherapy and injected intrathecally during 75 procedures. Gamma cisternograms were performed within 2 hours of drug instillation, obtaining 4 position images of the head and an image of the injection site. In 59 studies (79%) the radiopharmaceutical was seen at the basal cisterns and over the cortical subarachnoid spaces with no extravasation at the injection site. In 13 studies (17%) there was slight extravasation with the bulk of the radiopharmaceutical normally distributed. In 3 studies there was epidural or subdural localization with no subarachnoid distribution, a 4% failure rate. In these 3 procedures, there was free flow of fluid prior to injection. Inadequacy of therapy would not have been realized without cisternography. These studies demonstrate that intrathecally administered chemotherapeutic agents distribute widely within the CNS and that gamma cisternography is a valuable means of monitoring the adequacy of administration.

636 REGRESSION OF OXYMETHOLONE INDUCED HEPATIC TUMORS FOLLOWING ALLOGENEIC BONE MARROW TRANSPLANTATION FOR IDIOPATHIC ACQUIRED APLASTIC ANEMIA (IAAA). Robert R. Montgomery*, Jonathan M. Ducore*, John H. Githens, Charles S. August, Univ. of Colo. Med. Ctr., Dept. of Ped., Denver, Colo.

Cessation of androgen therapy and successful allogeneic bone marrow transplantation in a boy with IAAA was followed by regression of his oxymetholone-induced hepatic tumors. This 13-year-old boy developed severe IAAA in 1972. He experienced a remission following therapy with oxymetholone and prednisone. After 34 months of oxymetholone he developed jaundice, an enlarged tender liver and elevated liver enzymes. Liver scans showed 3 intrahepatic filling defects. Because of thrombocytopenia, biopsy was not performed. A presumptive diagnosis of androgen-associated hepatoma was made and oxymetholone was discontinued. The patient's IAAA promptly relapsed and allogeneic bone marrow transplantation from his HLA-A, B, and D identical sister was performed following preparation with cyclophosphamide (200 mg/kg). Liver scans performed before and immediately after cyclophosphamide showed no change. The post-transplant course was benign and full hematologic reconstitution with donor cells occurred within 4 weeks. There were no signs of a graft-versus-host reaction. Follow-up liver scans have shown gradual disappearance of the filling defects and liver enzymes have dropped. The patient continues to do well 6 months after transplantation. This experience further supports the argument for early transplantation rather than androgen therapy whenever possible for patients with IAAA.