HEMATOLOGY & ONCOLOGY

PRODUCTION OF GRANULOCYTIC COLONIES IN-VITRO FROM THE PERIPHERAL BLOOD (PB) OF A CHILD WITH ADULT-TYPE CHRONIC GRANULOCYTIC LEUKEMIA (CGL). Arnold J. Altman and Robert L. Baehner. Indiana Univ., Dept. of Ped., Indianapolis.

PB from a 5 y.o. child with untreated adult-type (Ph^1 chromosome positive) CGL was studied for in-vitro leukocyte colony production. Both the number of colonies obtained and the morphologic nature of the cells in the colonies were assessed. Unfractionated buffy coat produced 21 ± 5 colonies/10^5 cells. When buffy coat was fractionated by centrifugation over ficoll-Hypaque, colony forming units (CFU-c) were found to be concentrated in the low density top layer containing myeloblasts, promyelocytes, and myelocytes (70 ± 5 colonies/10^5 cells were obtained from this layer). The bottom layers contained metamyelocytes, bands, and polymorphonuclear cells, but no CFU-c. When studied morphologically and histochemically the vast majority of colonies derived from both whole buffy coat and from the low density cell layer were found to be comprised of mature granulocytes, a result consistent with that described for adults with CGL. We have previously reported that colonies formed from the PB of children with so called juvenile-type (Ph^1 chromosome negative) CGL are exclusively monocytic in nature. It would thus appear that in children with Ph^1 chromosome positive CGL (like adults with the same condition), the leukemic process affects predominantly the granulocytic precursor cells whereas in children with Ph^1 chromosome negative CGL, the monocyte precursor is the cell most prominently involved.

NORMAL URBAN INCREASES IN RED CELL LEAD AND DEPRESSION OF RED CELL MEMBRANE Na/K ATPase. Carol R. Angle and Matilda S. McIntire. Univ. of Nebr. Col. of Med., Dept. of Ped., Omaha.

Na/K ATPase of the red cell membrane was investigated as evidence of a biochemical effect of moderate, "subtoxic" increases in blood lead.

Na/K ATPase averaged 62% (61.7 ± 10.4) of total red cell membrane ATPase in 49 urban and suburban boys, ages 10-18, with a whole blood lead (Pb-B) of 10-32 µg% and a mean red cell lead (Pb-Rbc) of 33 µg% (33.4 ± 12.2). Within this group it was unaffected by age, race or hematocrit. Mean Na/K ATPase in 10 adult controls with Pb-B of 9-26 µg% was 70% (69.7 ± 6.47%). In 10 lead workers with a Pb-B of 55-102 µg% and mean Pb-Rbc of 121 µg% (120.6 ± 16.4%) the mean Na/K ATPase was 32% (32.1 ± 6.8%).

The correlation coefficient of Pb-rbc with Na/K ATPase in the 49 students and the 10 lead workers was 0.75, with the regression equation of y (Na/K ATPase) = 71.9% = 0.316 Pb-rbc. The linear correlation of red cell lead with Na/K ATPase at normal urban levels of blood lead suggests a significant health effect based on the known association of decreased enzyme activity with increased red cell permeability and loss of intracellular potassium.

STUDIES ON THE PATHOGENESIS OF CONGENITAL NEUTROPENIA. D. Amato, E. F. Saunders, M. H. Freedman, E. W. Gelfand and W. D. Biggar. Univ. of Toronto, Hosp. for Sick Children, Depts. of Hematology and Immunology, Toronto, Canada.

Three children with severe congenital neutropenia, 2 Kostmann type and 1 associated with dysgammaglobulinemia, were studied. Marrow aspirates were normocellular but lacked granulocytic cells beyond the myelocyte stage. In a methylcellulose culture system the numbers of granulocytic colony-forming units (CFU-C) were 246, 135, and 153/10^5 nucleated marrow cells respectively. These values were in the highest 10th percentile of a group of 47 control children (geometric mean of controls: 48 colonies/10^5 cells). The numbers of CFU-C in peripheral blood of 2 patients were 2.7 and 9.6/10^5 nucleated cells after ficoll-Hypaque separation (normal range 3.6 to 19.2). Differentiation in culture proceeded through all stages of granulopoiesis. Colony-stimulating activity (CSA) prepared from peripheral leukocytes of 2 patients demonstrated 88 and 106% of the activity of a normal CSA standard, in stimulating colony growth of several normal marrows. Urinary CSA levels were normal to increased. Varying amounts of patients' sera failed to inhibit colony formation by their own or control marrows, with or without CSA.

No intrinsic granulocytic stem cell defect was demonstrated in these patients. A deficiency of CSA or defect in CSA-producing cells is unlikely. No inhibitor directed against granulocytic precursors or CSA was found. Therefore, the defect appears to be an abnormal hemopoietic microenvironment in vivo.

BASOPHILIA IN JUVENILE RHEUMATOID ARTHRITIS. Balu H. Athreya, Children's Seashore House, Atlantic City (Intr. by W.W. Nichols)

Since mast cells may play a role in the pathogenesis of rheumatoid arthritis and since basophils and mast cells are similar in their structure and function, we decided to study circulating basophils in children with rheumatoid arthritis (JRA). Absolute number of basophils/c mm of peripheral blood and their percentage was estimated in 16 patients with juvenile rheumatoid arthritis and 20 normal controls using the method of James and Moore. Eight of the 16 patients had mono(pauci) articular arthritis and 8 had the polyarticular variety. Two patients were on steroid at the time of the study.

Mean absolute basophil count in normal children was 33/c mm (S.E.±3) compared to a mean value of 67/c mm (S.E.±7) for the entire group of children with rheumatoid arthritis ($P<0.005$) and a mean of 85/c mm (S.E.±5) for the subgroup of 6 children with active untreated polyarthritis. Children with polyarthritis in remission and children with mono(pauci)articular arthritis also had elevated mean basophil count but these were not statistically significant. The mean of basophil count expressed as percentage of total white cell count in controls was 0.45 (S.E.±0.005) compared to a mean of 0.85 (S.E.±0.25) in the JRA group ($P<0.005$).

It appears that the role of basophils in JRA deserves further exploration.

POSTNATAL SYNTHESIS OF FETAL HEMOGLOBIN (HbF) AND ADULT HEMOGLOBIN (HbA) IN NORMAL TERM NEWBORN INFANTS. H. Bard. Univ. of Montreal, Ste-Justine Hosp., Montreal, Canada.

In order to describe the complete switchover from HbF to HbA synthesis during pre and postnatal life, Hb synthesis was studied in normal term born infants during their first 5 postnatal months. The incorporation of ^{14}C leucine into newly synthesized hemoglobin provided a method of determining the proportions of HbF & HbA synthesis. 44 blood samples were incubated in an amino Acid mixture containing ^{14}C leucine. The cells were washed, lysed and the hemolysate purified by passage through a sephadex g-25 column. The hemoglobin solution was then subjected to ion exchange chromatography which provided a separation of the HbA & HbF fractions. Liquid scintillation counting was finally carried out on the separated HbA & HbF fractions. The results showed a progressive decrease in HbF synthesis from 59% ± SD 10% at birth to 7% ± SD 2% at 4 months of age. When this data is combined to that previously reported, the complete switchover from HbF to HbA synthesis can be described in terms of postconceptional age. It represents a sigmoid curve; the steep portion lies between the 30th and 52 nd postconceptional week, preceeded and followed by plateaus of 95% and 7% of HbF respectively.

PREGNANCY OUTCOME AND WEIGHT OF INFANTS BORN TO WOMEN WITH SICKLE CELL TRAIT. P. Blattner, H. Dar and H. M. Nitowsky, Depts Ped and Gen, Albert Einstein Coll Med, Bronx, N.Y.

A significant increase in perinatal mortality in association with anoxic stress has been reported among Nigerian women with sickle cell trait (AS). Moreover, a significantly lower mean birth weight was reported for infants born to American black AS mothers, although this retrospective survey provided no data concerning parity, or sex and gestational age of the newborn infants. A prospective study has been carried out on the outcome of pregnancy and distribution of birth weights of infants delivered by 73 AS women compared with a control group of AA women matched for race, age, parity and sex of their offspring. 67 (92%) of the pregnant AS women delivered infants at term (>37 weeks). The mean ± S.D. birth weights of term infants with uncomplicated gestation in relation to parity was: primipara, male 3.30 kg ± .42, female 2.77 kg ± .28; multipara, male 3.28 kg ± .54, female 3.25 kg ± .26. Eight (11%) of the infants were born at or before 37 weeks gestation or weighed less than 2.5 kg at birth. The distribution of birth weights and proportion of low birth weights does not differ significantly from the data from infants born to AA mothers. Five AS mothers had preeclampsia, and 4 had diabetes. There was no increased incidence of urinary tract infections or fetal wastage. These findings do not support the impression that there may be definable pathological correlates of childbearing in AS women.