● 794 α_2-MACROGLOBULIN AND ANTITHROMBIN III ARE EQUALLY IMPORTANT INHIBITORS OF THROMBIN IN NEONATAL PLASMA. Barbara Schmidt, Francoise Fernandez, Gaman Modi, Fred Ofosu, Maureen Andrew (Spon. by Ronald G. Davidson). McMaster University, Depts of Pediatrics and Pathology, Hamilton, Ontario, Canada.

Healthy newborn infants rarely suffer from thrombosis, despite their low plasma antithrombin III (ATIII) levels. In adults, ATIII is the main inhibitor of thrombin; α_2-macroglobulin (α_2M) and heparin-cofactor (HCII) are of lesser importance. In infants and children, plasma α_2M concentrations are higher than in adults and exceed ATIII activities by about 2-fold. Therefore we determined the contribution of all 3 antiproteases to the inhibition of ^{125}I-thrombin in defibrinated pooled adult and cord plasmas. Thrombin-inhibitor complexes were quantitated by SDS-PAGE. Thrombin was inhibited to a similar extent in both plasmas. The proportions of thrombin complexed to α_2M, ATIII and HCII are summarized below:

	α_2M	ATIII	HCII
Adult plasma	31%(5.8)	59%(6.4)	10%(3.5)
Cord plasma	48%(5.9)	44%(6.1)	8%(1.9)

Values are means (SD) of 18 determinations/pooled plasma. The observed differences in distributions are consistent with calculated velocities which favour the complex formation between α_2M and thrombin in neonatal plasma. Upon addition of heparin, ATIII became the most important inhibitor of thrombin in cord plasma. Conclusion: In the absence of heparin, α_2M and ATIII are equally important inhibitors of thrombin in neonatal plasma. Speculation: High α_2M plasma concentrations may protect healthy newborn infants and possibly also ATIII deficient children from thrombosis.

795 LONGITUDINAL STUDY OF GROWTH IN CHILDREN TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA. Elizabeth A. Schriock, Michael J. Schell, Judith J. Ochs, (Spon. by William M. Crist) U. of Tennessee, Dept. of Pediatrics and St. Jude Children's Research Hospital, Memphis, TN.

To evaluate growth retardation and obesity in relation to treatment of ALL children in initial remission (7.3 to 17.5 yrs), the heights (HTs) and weights (WTs) of 74 boys and 83 girls diagnosed prior to 1976 were analyzed. Patients were treated with chemotherapy and cranial or craniospinal irradiation (2400 rads) after diagnosis at 0.2 to 16.6 yrs of age (median 4.4). HT and WT are expressed as SD from the mean of the normal population by age and sex (NCHS standards). A decrease in HT SD occurred between diagnosis and last HT recorded for boys (mean ± 1 SD: 0.1±1.0 vs -0.9 ±1.2, p<0.001, Wilcoxon) and for girls (-0.1±1.1 vs -1.4±1.2, p<0.001). Boys lost -0.7±0.4 SD in HT during therapy; -0.1±0.6 SD from the end of therapy until age 11.6 yrs; and -0.3±0.7 SD thereafter. Girls lost -0.7±0.6 SD in HT during therapy; 0.0±0.6 SD from end of treatment until 2 yrs prior to menarche, and -0.7±0.9 SD thereafter. 35% of boys and 48% of girls lost ≥1.5 SD in HT during the study period. As an index of appropriateness of WT for HT, HT SD was subtracted from WT SD. For boys, last (WT-HT) SD was 1.3±1.3 compared to -0.2±0.9 at diagnosis; 76.2% had a final positive index of obesity. For girls, last (WT-HT) SD was 1.3±1.2 compared to - 0.2±0.8 SD at diagnosis: 85.7% had a final positive index. Last (WT-HT) SD inversely correlated to last HT SD among girls (r= -0.45, p<0.001) but not boys. Additional girls receiving 1800 rads (20) or no rads (23) were compared to girls receiving 2400 rads for change in HT during treatment and a difference was found (-0.4±0.6 vs -0.3±0.6 vs -0.7±0.6, respectively, p<0.02, ANOVA); no difference was found with similar groups of boys. In conclusion, many long-term survivors of ALL develop linear growth retardation and obesity. Much of the height loss occurs during therapy and may be related to radiation; an adequate "catch-up" phase of growth does not occur.

796 CLINICAL AND ULTRASTRUCTURAL OBSERVATIONS OF BENIGN NEUTROPENIA OF CHILDHOOD AND NEUTROPENIA ASSOCIATED WITH HYPOGAMMAGLOBULINEMIA. Ann O. Shigeoka, Theodore J. Pysher, Elizabeth H. Hammond. University of Utah School of Medicine, Primary Children's Medical Center, Pediatrics and Pathology, Salt Lake City.

Chronic neutropenia of childhood and neutropenia associated with hypogammaglobulinemia may have autoimmune etiologies. We observed 9 patients with isolated neutropenia and 5 boys with neutropenia associated with hypogammaglobulinemia. Both types of patients presented between 4 and 24 months of age with recurrent otitis media, skin infections caused by S. aureus, P. aeruginosa or candida and chronic diarrhea. Only the 5 patients with hypogammaglobulinemia developed invasive infections such as bacterial pneumonias and sepsis due to pseudomonas and clostridia. No patients developed an invasive infection while receiving gammaglobulin. No demargination was observed after epinephrine, and no sustained response occurred with steroid therapy. Anti-neutrophil antibodies were not detected in 10 of 12 patients. All patients with hypogammaglobulinemia had elevated percents of T4 lymphocytes. Marrow aspirates showed deficiency of granulocytes beyond the myelocyte or metamyelocyte stage. Ultrastructural studies showed reduction in secondary granules and increased lucency of primary granules. However, myeloperoxidase content was normal by electronmicroscopy. This morphologic appearance may represent accelerated neutrophil senescence. Analysis of both the clinical course and laboratory findings in patients with isolated neutropenia, or with neutropenia associated with hypogammaglobulinemia, thus revealed no distinguishing characteristics. Neutropenia may have a common pathogenesis in both groups of patients.

● 797 THE POTENTIAL OF TIN-PROTOPORPHYRIN AS AN ADJUVENT THERAPY FOR IRON OVERLOAD IN THALASSEMIA MAJOR. A. Solomon, R.W. Grady, H.H. Liem and U. Muller-Eberhard (Spon. by M.W. Hilgartner). Cornell University Medical Center, Division of Pediatric Hematology/Oncology, New York, New York.

Despite present therapies of hypertransfusion and chelation of iron with desferrioxamine (DFO), patients with thalassemia major continue to succumb in their early to mid twenties to fatal iron overload, especially of the heart. Our laboratory has been involved in investigations of the use of tin-protoporphyrin (Sn-PP) as an adjuvent therapy for these patients. Sn-PP an analogue of heme, blocks microsomal heme oxygenase, and thus heme metabolism, thereby causing an increased excretion of intact heme (and with it iron) into the bile. Initial experiments using hypertransfused iron overloaded rats showed that Sn-PP, while having no effect upon total iron stores, caused a redistribtuion of iron, with significant decreases (up to 50%) in the iron content of the heart, kidneys and liver with corresponding increases in that of the spleen. Similar experiments done with splenectomized animals also showed decreases in the iron content of the heart with increases in liver iron. We conclude that Sn-PP does not cause a decrease in total iron stores, but it may cause a significant diversion/redistribution of iron from the heart to liver and/or spleen. We are now conducting experiments to determine whether Sn-PP given together with DFO leads to enhanced iron excretion.

798 ISOLATION OF HIV FROM HEMOPHILIACS John L. Sullivan, Charla A. Andrews, Doreen B. Brettler, Ann D. Forsberg and Peter H. Levine. U. Mass. Med. School, Dept. of Pediatrics and Medicine, Worcester, MA.

As part of a prospective study of human immunodeficiency virus (HIV) infection in hemophiliacs, peripheral blood mononuclear cells from 72 individuals without AIDS or ARC were cultured for virus. HIV was isolated from 15 out of 66 (23%) of hemophiliacs who were seropositive for HIV, and 0 of 6 seronegative patients. Virus isolation-positive hemophiliacs had significantly (p<.05) reduced T-helper cell numbers, T-helper/T-suppressor ratios, pokeweed mitogen responsiveness and total platelet counts when compared to seropositive hemophiliacs who did not yield HIV upon cultivation. One virus-positive patient has developed AIDS during the study period but no other virus-positive or negative hemophiliac has yet developed ARC or AIDS. Virus isolation-positive hemophiliacs did not differ from virus isolation-negative hemophiliacs in their HIV neutralizing antibody titers. Five of six HIV isolation-positive hemophiliacs were again successfully cultured for virus at later dates ranging from 3-12 months. Nine virus negative individuals remained virus negative when re-cultured at later dates. These data suggest that a significant subgroup of HIV seropositive hemophiliacs persistently harbor live virus and that seropositivity is a valid indication of virus infection. The significant decrease in the number of T-helper cells and the presence of thrombocytopenia in the isolation-positive group may be a reflection of a heavier virus load, and might be an early marker of more significant disease.

● 799 A MORE ECONOMICAL AND EFFECTIVE BLOOD PRODUCT FOR CHRONIC TRANSFUSIONS. William Tilton, Carol Seaman, Vijayalaxmi Malavadi, and Sergio Piomelli. *Columbia University, College of Physicians & Surgeons, Division of Pediatric Hematology-Oncology, and the New York Blood Center, New York, N.Y.*

Frozen red blood cells *(RBCs)* are commonly used in chronic transfusion programs for patients with homozygous β-thalassemia, sickle cell anemia after stroke, etc., to avoid the severe transfusion reactions due to sensitization to WBCs. An alternative technique for removal of WBCs consists of filtration on cotton wool. We have used for transfusion RBCs first filtered on cotton wool filters (Imugard IG500, Terumo Corp., Tokyo, Japan) and then washed with a solution containing NaCl 0.8%, Dextrose 0.2%, buffered with phosphate to pH 7.4. These cells appear superior to frozen RBCs, as they are less expensive to prepare ($55 vs. $119), equally free of WBCs (200/ μl vs. 300/ μl), and yield an equal volume of RBCs per unit (180 vs. 170 ml). In seven splenectomized patients with homozygous β-thalassemia, we compared one year of filtered RBCs to the previous year of frozen RBCs. The transfusion interval remained unchanged (19.5 vs. 20.5 days) as did the transfusion requirement (118 vs. 125 ml/kg/yr). We noticed an improvement in p50 with the change to filtered RBCs. All of our patients with homozygous β-thalassemia have been switched to filtered RBCs: there has been no reaction in over 1500 transfusions. Filtered RBCs appear to be the product of choice for chronic transfusion programs, as they are cheaper and easier to prepare than frozen RBCs, using ordinary blood bank equipment, and probably also more effective in oxygen delivery. We recommend that all patients on chronic transfusion be switched to filtered RBCs.