740 ANEMIA IN CHILDREN AND YOUNG ADULTS WITH HEMOPHILIA. G.R.Buchanan, C.A. Holtkamp, Dept. of Pediatrics, The University of Texas Health Science Center at Dallas, Southwestern Medical School, Dallas, Texas.

Mild reductions in WBC and platelet counts are extremely common in multi-transfused hemophiliacs. Little attention has previously been directed to parameters of erythropoiesis in hemophiliacs even though anemia might be expected as a result of internal and occult external hemorrhage and impaired iron reutilization. Therefore, we examined hemoglobin (Hgb) concentration and red blood cell indices in 94 patients at times of comprehensive clinic visits. Additional studies performed in many included free erythrocyte protoporphyrin (FEP) and serum transferrin saturation, ferritin and haptoglobin. Hgb and MCV values were recorded as age-related percentile values. Hemophiliacs of all ages and degrees of severity often had lower than average values for Hgb; 31% had Hgb less than the 3rd percentile, 46% below the 10th percentile, and 83% below the mean value. MCV was less than the 3rd percentile in 11% of cases. Reduced Hgb percentile value was unrelated to age, severity of disease, or human immunodeficiency virus antibody status. Only 5 patients had an obvious cause of anemia (thalassemia trait, blood loss, or iron deficiency). Serum ferritin, transferrin saturation, and FEP values were abnormal in just 6%, 4%, and 10% of patients respectively, indicating that iron deficiency or anemia of chronic disease was uncommon. Haptoglobin was low in 44% of patients, but reticulocyte count was > 2.5% in only 11%. In conclusion, Hgb values are commonly below the mean normal values for age in hemophiliacs. Frank anemia is present in 31% of patients, is usually mild, and is without obvious cause.

●741 ALUMINUM CONTAMINATION OF PLASMA CONCENTRATES. James Bussel and Nancy Alcock (Spon. by M.W. Hilgartner). Cornell University Medical Center-New York Hospital, Department of Pediatrics and Memorial Hospital Sloan Kettering-Cancer Center, Department of Clinical Chemistry. New York City, NY.

Aluminum (Al) toxicity causes bone disease and encephalopathy in patients on renal dialysis. No studies have been done of Al levels in plasma concentrates or in patients with normal renal function exposed to Al. We report here the Al levels in different lots (from different manufacturers) of intravenous gammaglobulin (IVGG), Factor VIII and IX concentrates (F.VIII, F. IX), and in sera of patients receiving these products. Specimens were collected in Al-free plastic syringes and vials and Al levels measured using a flameless atomic absorption spectrophotometer with a Zeeman graphite furnace. 2 lots of F.VIII, 1 of F.IX, 1 of FEIBA and 9 lots of IVGG had Al levels < 100 ug/l. However, high Al levels were seen in 5 lots of F.VIII ($\bar{x}$ = 500 ug/l, range 270-600), 1 of F.IX (965 ug/l), and 1 of IVGG (234 ug/l). At 40 u/kg twice weekly, F.VIII or F.IX infusions could lead to receiving > 1 mg/kg/yr of Al. IVGG at a 6 gm/kg total dose could lead to receiving a total of 27 ug/kg of Al. 1 patient tested after receiving "high Al" F. VIII and 1 tested after "high Al" F.IX, had Al levels of 19 and 10 ug/l (normal < 4 ug/l). Safe Al levels have never been defined: Al infused into hemophiliacs may contribute to bone disease or long term CNS changes. Further studies will include serial Al levels in additional patients, measurement of Al tissue levels,and study of mobilization in response to Desferal to investigate Al accumulation. If Al is shown to accumulate or to be toxic, low Al products should be used.

●742 SERIAL STUDY OF IMMUNE FUNCTION IN CHILDREN WITH HEMOPHILIA. James Bussel, Carl Welte, Pablo Rubinstein, and Margaret Hilgartner, Cornell Medical Center-New York Hospital, Department of Pediatrics. Memorial Sloan Kettering-Cancer Center, Department of Developmental Hematopoeisis. New York City, NY.

Since the development of AIDS in patients with hemophilia, studies have revealed decreases in T4/T8 ratios and other immunologic parameters. We report here serial studies over 5 years of lymphocyte proliferation (LP) using OKT3 and PHA as mitogens and of T cell numbers and subsets using OKT3, OKT4, and OKT8 including 31 observations in 14 children with hemophilia now < 15 years of age. 12 of 14 were anti- HIV+. LP-T3 increased in 10 of 14 patients. The mean LP-T3 per year from 1983 to 1986 was: 38,900 cpm (n=5), 38,100cpm (8), 52,100cpm (8), & 71,300cpm (9) respectively (p<0.05 for increase over time); controls were 66,000cpm. The other data were consistent with the serial decreases found by other studies. LP-PHA was decreased and did not change from '83 to '86. The T4/T8 ratios averaged 1.0 and were unchanged, and the absolute number of T4+ cells decreased but not significantly. There was an increase in %T3-(%T4+%T8) over time but it and changes in LP-PHA were unrelated to changes in LP-T3. Children with hemophilia exposed to HIV, as with our older patients, have had a dramatically increased responsiveness to OKT3 in 1985-1986 compared to 1983-1984 without change in other immune parameters. This may be the first sign of immune recovery from chronic HIV infection, perhaps because of the universal use of heat-treated factor VIII concentrate. Alternatively this may be a sign of the immunopathy of HIV reflecting the appearance of abnormal OKT3+ T4-T8-cells.

743 SEPTICEMIA IN CHILDREN WITH LEUKEMIA: A TEN-YEAR SURVEY. Josette Champagne and Yves A. DeClerck, University of Southern California, Childrens Hospital of Los Angeles, Department of Pediatrics, Division of Hematology-Oncology, Los Angeles.

One hundred ninety episodes of septicemia were surveyed from 1973 to 1983 in childrens treated for leukemia at Childrens Hospital of Los Angeles. The mean number of episodes documented each year was 18 ± 5 (range 10-29) and significant changes in the type of organisms involved were observed, with an increased incidence of candida (from 0 to 9%) and gram positive septicemia over the last 5 years. Gram positive sepsis had a low mortality rate (8%) compared with gram negative sepsis (54%) or septicemia caused by multiple organisms (72%). Factors of risk included (1) absolute granulocyte count less than 500 (78%), (2) presence of relapse (62%), and (3) prolonged previous administration of broad spectrum antibiotics (35%). Over the last 3 years an increased incidence of gram positive septicemia in non-neutropenic patient was observed. 9 staphylococcus epidermidis septicemia were seen in the last 2 years compared to none in the 8 previous years. 3 of those 9 patients had a central venous line. These data have provided helpful informations in our therapeutic approach of febrile episodes in neutropenic patients.

▲744 HUMAN NEUTROPHIL (PMN) INTERACTIONS WITH HUMAN IMMUNE COMPLEXES (IC). Harvey J. Cohen, Kazuhiko Takahashi, John C. Whitin and Margaret E. Chovaniec. University of Rochester Medical Center, Strong Memorial Hospital, Department of Pediatrics, Rochester, NY.

PMN have Fc Receptors (FcR) for IgG when part of an IC. We employed homologous IC (tetanus toxin and human anti-tetanus toxin IgG) as a stimulus for human PMN responsiveness. IC, at equivalence, stimulated PMN to produce superoxide (O_2^-) in a dose-dependent manner. Neither antigen nor antibody alone had PMN stimulatory activity. The lag time for activation was 40-50 seconds and was dose-dependent. The addition of IC to PMN resulted in apparent membrane potential depolarization within 20 seconds (prior to the onset of superoxide production). IC-stimulated PMN increased their intracellular calcium, aggregated and degranulated. The addition of fresh human serum to IC resulted in enhanced O_2^- production and degranulation at less than saturating amounts of IC. Human monomeric IgG (3 mg/ml) did not inhibit IC mediated PMN O_2^- production. The FAB fragment of a monoclonal antibody (IV3) specific for a 40 kD FcR on human PMN selectively inhibited IC-mediated O_2^- generation by approximately 75%. The same observations were obtained when another monoclonal antibody (3G8) FAB fragment, specific for a 51-75 kC FcR on human PMN was used. Complete inhibition of IC-mediated PMN O_2^- production was achieved only when FAB fragments of both antibodies were utilized. These results show that human IC can stimulate human PMN, that these interactions can be enhanced, by the presence of complement components and that monoclonal antibodies directed against both FcR are necessary to completely inhibit functional activity induced by human IC.

●745 2,3-DPG LEVELS IN FETAL ERYTHROCYTES: EARLY DECREASES WITH ACIDOSIS. Elizabeth H. Danish,Linda P.Slater, Cynthia R.Moore(spon. by Satish C.Kalhan) CWRU School of Medicine,Cleveland Metropolitan General Hospital,Department of Pediatrics,Cleveland, Ohio.

To define the kinetics of decreases in DPG due to low pH, fetal erythrocytes (FE) of 10 nl term newborns (cord blood) and erythrocytes of 7 healthy adults (AE)were suspended in PBS, 1% BSA, 10 mM glucose, pH 7.40, 7.20 or 7.00 at 37°C. The following were determined at 0, 1, or 2, and 4 hrs: pH_e, pH_i, DPG, P_{50}(pH 7.40), P_{50}(in vivo),and methemoglobin. No hemolysis, crenation or significant changes in methb occurred. Mean FE Hb F=68%; FE P_{50}'s were accordingly lower than AE P_{50}'s.

pH_e		7.40			7.00		
TIME(HRS)		0	1-2	4	0	1-2	4
pH_i	FE	7.00(7)	6.94(7)	6.86(4)	6.82(8)	6.75(8)	6.71(6)
	AE	7.05(7)	6.95(7)	6.89(5)	6.82(5)	6.79(5)	6.72(4)
DPG(μm/ mL rbc)	FE	5.80(7)	5.76(9)	5.59(6)	4.98(8)	3.41(9)	1.85(6)
	AE	5.47(7)	5.20(7)	4.68(5)	5.11(6)	4.16(6)	2.35(4)
P_{50} (7.40)	FE	22.1(7)	25.3(6)	25.5(5)	21.1(8)	23.8(8)	21.9(6)
	AE	28.8(7)	32.2(7)	32.7(3)	26.9(6)	28.8(6)	27.9(4)
P_{50} (in vivo)	FE	22.8(6)	26.0(5)	26.7(2)	33.7(8)	36.7(8)	34.1(6)
	AE	30.4(7)	32.0(7)	33.3(5)	42.7(6)	43.4(6)	42.7(4)

At pH 7.00, DPG fell by 1 to 2 hrs,with similar rates of decline for both AE and FE. By 1-2 hrs (pH 7.00), P_{50}'s were higher than those at time 0, reflecting primarily the Bohr effect. By 4 hrs, P_{50}'s had decreased due to further drops in DPG's. Studies of 2 AE and FE samples at pH 7.20 had intermediate results. We conclude that exposure to 1 to 2 hrs of acidosis is associated with significant decreases in DPG levels. Although DPG regulates oxygen affinity of hb A and does not bind well to hb F, the effect on hb A (even though not the predominant hb) is sufficient to limit the Bohr induced increase in P_{50} due to acidosis. In addition, the early drop in DPG with acidosis means that DPG's may be a marker for acidosis occurring in utero or during labor and delivery.