●752 IMPROVED SURVIVAL IN BETA THALASSEMIA MAJOR. P.J. Giardina, K. Ehlers, M. Lesser, M. Connelly, D. Weinstein, E. Jew, and M.W. Hilgartner. Cornell Univ. Med Center-New York Hospital, Div. Ped. Hematology/Oncology, New York, N.Y.: North Shore Univ. Hosp. Div. Biostatistics, Great Neck, N.Y.

The natural history of transfusion (tx) dependent Beta thalassemia (thal) is changing owing to recent advances and progress in its clinical management. Historically, thal pts developed hemochromatosis and succumbed in the second decade of life with myocardial disease. Refinements in tx regimens including 1) maintaining pre-tx hemoglobin (Hg) levels greater than 11 gm/dl; 2) increased frequency of txs; 3) splenectomy for hypersplenism and 4) the regular use of iron chelation by prolonged subcutaneous infusions of desferrioxamine (s.c. DFO) have led to prolonged survival in the past decade. We reviewed thal survival using the product limit method and log rank test. Pts. were analyzed in two groups, those who since 1960 were maintained at pre-tx Hb levels of 8 gm and not chelated (51 deaths of 70 pts) and those since 1977 who were maintained at pre tx Hb levels of 11 gm and received 20 to 60 mg/kg s.c. DFO over 8 hr infusions more than 3 days per week (27 deaths of 89 pts). The undertransfused, nonchelated group had a median survival of 17.1 yrs in comparison to a 30 yr median survival in the hypertransfused chelated group. We demonstrate a significant ($p < .0001$) increased survival in tx dependent thals who are on a program to minimize iron loading and maximize iron excretion.

●753 THE COAGULOPATHY OF CHILDHOOD LEUKEMIA: DIC OR PRIMARY FIBRINOLYSIS? S.H. Gold, T.C. Abshire, B. Jamison, S.L. Clarke, M.J. Christian, T. Hays, J.S. Roloff, J.L. Ater, L.F. Odom (Spon. by W.E. Hathaway). Dept. of Ped., Univ. of Colo. School of Med. & The Children's Hosp., Denver, CO.

Recent information as well as our retrospective review of 50 patients (Group A) demonstrates that a coagulopathy is commonly seen at presentation in childhood leukemia. In order to determine whether the coagulopathy was primarily thrombin mediated (DIC) or plasmin mediated (primary fibrinolysis), a prospective evaluation of 30 untreated new onset acute leukemia patients (group B) was instituted. Studies were: PT, PTT, thrombin time (TT), fibrinogen (Fib), serum FDP, D-dimer (DD) and B-beta 1-42 peptide (BB). The DD is a measure of thrombin activation whereas the BB best defines primary fibrinolysis. The results to date are summarized below:

Group	PT(%+)	PTT(%+)	(TT(%+)	Fib(%+)	FDP(%+)	DD(%+)	BB(%+)
A(n=50)	52	16	10	8	39	--	--
B(n=30)	40	10	20	6.7	43.3	53	3.3

Only 32% (Group A) and 23% (Group B) had totally normal coagulation screens. Most notable is the high proportion of each group with elevated PT and/or positive FDP. In Group B, the DD was strikingly positive whereas the BB was essentially negative. These data indicate the mechanism of the coagulopathy of acute leukemia on presentation of disease is primarily thrombin activated coagulation. The incidence of increased PT lends support to a Tissue Factor/Factor VII complex causing activation of coagulation. Studies are underway to further elucidate the pathogenesis of the coagulopathy.

●754 ERYTHROCYTE ADHERENCE TO ENDOTHELIUM IS ASSOCIATED WITH LOSS OF SPLENIC FUNCTION. E.F. Grabowski, K. McKenney, and J. Sullivan (Spon. by M.W. Hilgartner). Cornell University Medical Center-New York Hospital, Division of Pediatric Hematology/Oncology, N.Y.,N.Y.

Previously we have shown that sickle (SS) erythrocytes adhere to endothelial cell monolayers (ECM's) under physiologic conditions of blood flow. To determine the role of splenic function in such adhesion, we collected bloods into heparin (4 U/ml FC) from children with sickle thalassemia (SThal) and hereditary spherocytosis both before (HS+) and after (HS-) splenectomy. Five percent of the packed RBC's from each of these bloods was incubated for one hr at 23°C with 0.9 mg/ml FC Na fluorescein, washed three times with buffer, and then combined with the corresponding unlabelled RBC's and platelet-poor plasma. The bloods were pumped through a flow chamber one wall of which was a bovine aortic ECM grown on a rectangular cover glass. RBC interaction with the ECM was assessed by epifluorescence videomicroscopy at a wall shear rate of 270 sec^{-1} after 6 min of blood flow:

RBC TYPE	# RUNS	# DONORS	(RBC's/cm^2 ECM) x 10^{-4} MEAN ± SE
AA	12	7	0.19 ± 0.086
STHAL	3	2	0.22, 0,0
SS	13	8	1.45 ± 0.23
HS+	4	3	0, 0, 0, 0
HS-	2	2	1.48, 1.04

RBC adhesion was increased in the presence of splenic autoinfarction (SS) or surgical asplenia (HS-). Erythrocyte adhesion to endothelium may therefore contribute to the removal of senescent RBC's in the eusplenic state.

755 EXTRAOCULAR RETINOBLASTOMA: SUSTAINED REMISSION IN 10 OF 12 CHILDREN TREATED WITH IRRADIATION AND COMBINATION CHEMOTHERAPY. Eric F. Grabowski, Robert E. Ellsworth, Beryl McCormick, Leticia Y. Du, Alice J. Lippner, and Margaret W. Hilgartner. Cornell University Medical Center-New York Hospital, Division of Pediatric Hematology/Oncology and the Opthalmic Oncology Center.

Of 170 children with retinoblastoma screened at our institution for metastatic disease since the fall of 1979, 20 (12%) had extraocular tumor. Twelve of these children, including 4 with bone marrow disease, were started on a modification of the former CCSG 962 protocol for extraocular retinoblastoma. This protocol utilized two years of systemic cyclophosphamide, adriamycin, and vincristine; intrathecal methotrexate, cytosine arabinoside, and hydrocortisone succinate; and cranial irradiation. Our modifications include: 1) omission (two cases) of cranial irradiation when bone marrow, but not cranial or cerebrospinal fluid (CSF), disease is present; 2) substitution (one case) of external beam irradiation to the calvarium when involvement of the calvarium, but not the cranium or CSF, is present; 3) scaling doses of intrathecal chemotherapy (all cases) to CSF volume; and 4) giving 2 mg/kg doses of adriamycin over 5 days instead of one. One child died of tumor progression, while another died of adriamycin-related cardiomyopathy. However, the remaining ten children are in bone marrow and CSF remission with a mean time from diagnosis of metastatic disease of 42 months (range 5 to 80 months). In contrast, all eight of the non-study children, treated palliatively or elsewhere, have expired.

756 ACUTE THROMBOCYTOSIS IN AMBULATORY PEDIATRIC PATIENTS. Harley W. Heath, Howard A. Pearson; Yale University School of Medicine, Department of Pediatrics, New Haven, Connecticut.

With the wide use of electronic blood counters which provide accurate platelet counts (PC), thrombocytosis is being observed frequently. We studied the frequency and the clinical and laboratory associations of high PC (>500k/mm^3) in ambulatory pediatric patients. All PC performed during 1985 on children seen in our ER and primary care center were retrieved from the Hospital's clinical laboratory computer. Patients with Hb SS and Kawasaki diseases were excluded from analysis. 108 of 824 (13.1%) P.C. were >500k/mm^3; 18 (2%) were >700k/mm^3. Clinical and laboratory data from the high PC group (>500k/mm^3) were compared with a randomly selected group of patients with normal PC (200-250k/mm^3). Compared to the normal PC group, the high PC group was more frequently diagnosed as having "infection"; had significantly higher white blood cell and absolute neutrophil counts and higher ESR ($p<0.001$). High PC was also significantly more frequently associated with age <2 years ($p<0.001$). This study indicates that thrombocytosis is frequent in pediatric ambulatory patients. The significant association of high PC with "infection" - both bacterial and viral - suggests that platelets are an acute phase reactant, especially in children <2 yrs.old. These high PC are transient. No adverse thrombotic consequences were recognized, even in children with PC <700k/mm^3, and so no treatment is indicated.

●757 IN VITRO ANALYSIS OF HEMATOPOIETIC PROGENITORS IN THE SYNDROME OF THROMBOCYTOPENIA WITH ABSENT RADIUS. Alan C. Homans, Janet L. Cohen, and Eric M. Mazur (Spon. by Edwin N. Forman). Brown University, Miriam and RI Hospitals, Depts. of Hematology and Pediatrics, Providence, RI.

The syndrome of thrombocytopenia with absent radius (TAR) is an autosomal recessive condition with poorly-understood hematologic abnormalities including a leukemoid reaction and hypomegakaryocytic thrombocytopenia. We studied bone marrow and serum from an infant with TAR using soft agar and plasma clot cultures of hematopoietic progenitor cells. Results with optimal growth stimulation are shown below:

Colony Type		# Colonies/10^5 cells TAR Pt.	Normals +/- SEM
myeloid	(CFU-GM)	479	80 +/- 24
erythroid	(CFU-E)	44	79 +/- 10
	(BFU-E)	75	23 +/- 7
megakaryocytic	(CFU-Meg)	5	47 +/- 4

Consistent with the near absence of CFU-Meg in this patient was the observation that the serum level of megakaryocyte colony stimulating activity (Meg-CSA) was markedly increased. TAR serum stimulated the growth of normal CFU-Meg from adult peripheral blood (82 colonies with TAR serum v. 0 colonies with normal AB serum). These in vitro data suggest that the hematologic defect in TAR is at the level of the megakaryocyte stem cell, and that normal humoral regulation of megakaryopoiesis is retained. Study of the patient's parents is in progress.