901 ACQUIRED VON WILLEBRAND'S DISEASE (vWD) SECONDARY TO SPLENIC HEMANGIOMA. D.M. DiMichele, M.J. Pushchak, W.E. Hathaway, M.J. Christian, C.F. Abildgaard, J.H. Githens, Dept. of Pediatrics, Univ. of Colo. School of Med., Denver, and Univ. of Calif. Davis, Sacramento.

Acquired vWD was found in a 2½ yr. old girl who presented with ecchymoses and conjunctival hemorrhages. Marked splenomegaly was present. Diffuse hemangiomatous transformation of the spleen suspected clinically, by CT scan and antiography, was confirmed at surgery. Coagulation studies were done at diagnosis, pre- and post-DDAVP infusion (0.3 mcg/kg) and 1 week post-splenectomy.

	BT (min)	Plt Ct ($x10^3$)	I (mg/dl)	VIII (u/ml)	vWF:Ag (u/ml)	vWF (u/ml)	VIII Multimers
Initial	>20	118	113	.55	.45	.31	-
Pre-DDAVP	>20	85	126	.67	.48	.40	NL
Post-DDAVP	>20	76	-	1.14	1.14	1.14	NL
Post-Splen	4½,5	1,020	268	1.24	1.10	1.20	NL

Initial factor VIII studies were consistent with Type I vWD. Fibrin monomer was positive and FSP's negative. Platelet function studies were suggestive of platelet exhaustion. Factor VIII components normalized with DDAVP but all coagulation and platelet defects were corrected only with splenectomy. No in vitro evidence of VIII-vWF:IgG immune complexes was found using Protein A Sepharose. The 140 gm spleen showed diffuse hemangiomatosis without thrombosis. A vWF:Ag-specific immunoperoxidase stain revealed intra-endothelial cell as well as diffuse perivascular staining. Acquired vWD has not been previously reported with visceral hemangiomata. We postulate tissue adsorption of the VIII complex in its pathogenisis.

902 SEVERE CEREBELLAR DEGENERATION AND DELAYED ONSET ATAXIA IN HISTIOCYTOSIS X., Ronald L. Dubowy, Maura J. Rossman, Michael D. Kanzer, Michael Oliphant, Charles J. Hodge Jr. Carl J. Crosley, SUNY-Upstate Medical Center, Syracuse, New York 13210 (Sponsored by M.J. Stuart).

A rare, and poorly understood syndrome of progressive cerebellar ataxia can be seen in pts. with Histiocytosis X. We report two patients who had bone involvement of the skull and orbit, and developed delayed onset (3 and 4 yrs from diagnosis) of progressive cerebellar ataxia, corticospinal tract abnormalities, and functional weakness. Pt. #1, diagnosed in 1969 at age 2, now wheelchair bound, has moderately severe cognitive deficits and a seizure disorder. Pt. #2, diagnosed in 1977 at age 4, now has progressive truncal ataxia and rt. hemiparesis. Brain CTs of both pts. show symmetric hypodense areas in the cerebellar hemispheres, including the dentate nuclei. The vermis, and cerebellar and perimesencephalic cisterns are normal. No pathologic calcifications, or supratentorial abnormalities are noted. Brain stem evoked potentials are abnormal in both.

A cerebellar biopsy was performed on pt. #2 at age 11. Histologic findings included a marked ↓ in Purkinje and granule cells and gliosis of the white matter and granular and Purkinje layers. A marked loss of myelin and axons in the white matter, and ↓ ramifications within, and width of, the molecular layer are also noted. Rare large mononuclear cells at the granular layer-white matter junction were observed. In our two patients with selective neurologic deterioration, clinical and histologic criteria fail to explain their symptoms as the direct consequent of their disease or its treatment. Early biopsy is essential to establish the pathologic basis of this syndrome prior to its treatment.

● **903** JUVENILE CHRONIC MYELOGENOUS LEUKEMIA (JCML): CHARACTERIZATION OF THE DISEASE AND PATHOGENESIS USING CELL CULTURES. Zeev Estrov, T. Grunberger, H.S.L. Chan, B. Zimmerman, & Melvin H. Freedman. Univ of Toronto, Hosp for Sick Children, Divs of Hematology & Allergy, Dept of Pediatrics, Toronto, Canada.

The pathogenesis of JCML was studied in 9 pts. Using cell cultures and chromosome markers, marrow and peripheral blood consistently showed 2 features: impaired expression of normal hematopoietic progenitors (CFU-E, BFU-E, CFU-GEMM), and excessive clonal proliferation of monocyte-macrophage elements whose growth was independent of added CSA or an adherent cell fraction. In contrast, 5 adult CML's (Ph^1+) showed normal hematopoiesis in vitro and CSA-dependent CFU-C growth similar to controls. Using monoclonal antibodies, cloned JCML cells were positive for surface antigens Ia, Mo_2, $LeuM_1$, $LeuM_3$, and OKM_1, thus confirming monocytic lineage. Characterization studies on cloned cell populations revealed a wide spectrum of features, some mature (latex ingestion, non-specific esterase positive, sensitivity to growth inhibition by PGE_2 and to gene-cloned interferon), and some primitive (negative for lysozyme, β-glucuronidase, procoagulant activity, and plasminogen activator). Functionally, JCML cells markedly impaired hematopoiesis in vitro from normal marrow; thus, co-cultures of normal marrow with JCML adherent cells, or fresh JCML marrow, or JCML plasma, resulted in suppressed normal colony formation. We conclude that JCML is a malignant clonal disorder of monocytic lineage, and that cell cultures provide a reliable and specific diagnostic test. The mechanism of hematopoietic failure in JCML is likely mediated by an inhibitory monokine secreted by JCML cells.

904 E-Rosette Positive (ER+), T Antigen Positive (T cell) Acute Lymphocytic Leukemia (ALL)-Patterns of Relapse. Falletta JM, Pullen DJ, Shuster JJ and Borowitz MJ for the Pediatric Oncology Group.

ER+ T cell ALL is characterized by widespread extramedullary disease and early relapse when standard forms of therapy are used (ER+ defined as >40% bone marrow blasts forming rosettes with sheep erythrocytes at 4°C). One hundred forty-five children with ER+ T cell ALL received either of two intensive multiagent sequential therapy protocols ± multimodal CNS prophylaxis. Overall outcome was equal to or superior to reported results from other large series of similar patients. However, patterns of extramedullary relapse differed by treatment group (1=modified LSA_2L_2; 2=1 plus multimodal CNS therapy; 3 included multimodal CNS therapy but utilized limited asparaginase and no BCNU or Hydroxyurea):

	1	2	3
Total Patients	48	64	33
Males	35	41	22
Relapse (Expected)	29 (28.6)	27 (24.7)	17 (19.7)
Marrow	17 (18.1)	20 (14.4)	8 (12.4)
CNS	10 (5.4)	3 (4.9)	1 (3.8)
Testicular	1 (3.3)	2 (2.3)	5 (2.4)

The logrank comparison (three-way) for relapse at any site was p=.74 and for marrow relapse was p=.15. The comparison (two-way) for CNS relapse between treatment 1 vs. 2+3 (two-sided) was p=.006, and in males for testicular relapse between 1+2 vs. 3 was p=.048. The marrow remains the major site of relapse for these patients.

905 *ASSOCIATION OF A PLATELET AGGREGATION DEFECT WITH HEPATOCELLULAR CARCINOMA.* *James H. Garvin, Jr., John Owen, and Charles J.H. Stolar (Spon. by Sergio Piomelli). College of Physicians and Surgeons, Columbia University, Depts. of Medicine, Pediatrics, and Surgery, NY.*

Hepatocellular carcinoma has been associated with various coagulation abnormalities, including dysfibrinogenemia and production of a biochemically-abnormal prothrombin. A 10 year old girl presented with recent onset of severe epistaxis and was found to have hepatocellular carcinoma. The bleeding time (Ivy method) was prolonged (20 min.) and factor VIII-related antigen was electrophoretically abnormal, while factor VIII-procoagulant activity protein was normal. Platelet aggregation studies demonstrated abnormal and delayed agglutination in the presence of ristocetin (0.8-1.0 mg/ml), with essentially normal agglutination with collagen, ADP, and epinephrine. A major hepatic resection (trisegmentectomy) was performed, and the tumor was completely removed. Substantial bleeding was encountered at operation despite pre-treatment with cryoprecipitate and platelet infusions, but following surgery there were no further bleeding symptoms and the bleeding time and platelet aggregation tests returned to normal. The tumor was established in long-term culture to seek evidence for a postulated tumor-derived anticoagulant in this patient, possibly acting by interference with von Willebrand's factor. The case demonstrates that the occurrence of severe bleeding in a previously healthy child may be a manifestation of underlying hepatic malignancy.

† **906** A FAMILY WITH AN INHERITED PLATELET STORAGE POOL DEFECT ASSOCIATED WITH A HIGH INCIDENCE OF MYELOPROLIFERATIVE DISORDERS: Jonathan M. Gerrard, Agnes J. Bishop, Esther D. Israels, Marlis L. Schroeder, Lyonel G. Israels Dept. of Pediatrics and Internal Medicine, University of Manitoba

A boy, age 5, presented with easy bleeding since birth and was found to have a long bleeding time, thrombocytopenia and abnormal platelet function (absent second wave aggregation with epinephrine, decreased aggregation to collagen but a normal first wave response to ADP and normal aggregation to arachidonic acid). His bone marrow was normal. At age 6½ years this boy developed progressive anemia, thrombocytopenia and splenomegaly, and was diagnosed as having juvenile chronic myelogenous leukemia. This child's father, grandfather and two of the grandfather's sisters were found to have a similar bleeding defect with a long bleeding time, mild thrombocytopenia, abnormal aggregation pattern similar to the propositus, and deficiency of platelet ADP, serotonin and dense bodies. Thrombin-induced arachidonic acid release, conversion of arachidonic acid to thromboxane B_2 and phosphorylation of platelet proteins were normal. One of the grandfather's sisters with a lifelong bleeding tendency and a platelet storage pool deficiency documented at age 38, developed myelomonocytic leukemia at age 41. Another sister and a brother of the grandfather, bleeding history uncertain, died at ages 8 and 23 of leukemia. The great grandmother and her sister both with lifelong bleeding histories had died of leukemia. The findings suggest this family has an inherited platelet storage pool deficiency associated with an increased susceptibility to the development of a myeloproliferative disorder.