† **931** INHIBITION OF HEMATOPOIESIS BY SUPRESSOR-T CELL DERIVED LYMPHOKINE IN PURE RED CELL APLASIA (PRCA) Rukmani Pennathur-Das, Elliot P. Vichinsky, Stefan E.G. Burdach, Bertram H. Lubin and Lee L. Levitt, Stanford University, Bruce Lyon Research Lab, Childrens Hospital, Oakland,CA.

T-cell derived lymphokines have been linked with the pathogenesis of bone marrow failure state in humans. We have investigated the mechanism of PRCA in a 10 year old boy with associated neutropenia (granulocytes 780/mm^3). Serum mediated effects on hematopoiesis were evaluated by cytotoxicity assays with and without complement, followed by in vitro cultures in methylcellulose with erythropoietin (Ep) alone or Ep plus Mo conditioned medium (containing erythroid burst-promoting activity, BPA). Regulation of hematopoiesis was evaluated after T-cell depletion by indirect immunoabsorption (panning) techniques with Leu 1 (pan-T) or Leu 2a (suppressor monoclonal antibodies. Following was the number of colonies/10^5 cells plated: BFU-E-45±13 (Ep), and 63±10 (Mo and Ep). CFU-GM 61±17 (Mo and Ep). Patient serum produced complement independent inhibition of autologous BFU-E (100%) and CFU-GM (63%). Heat inactivation of patient serum decreased the inhibition to 59% in BFU-E and 0% in CFU-GM. Removal of either marrow pan-T (44%) or suppressor-T (21%) cells resulted in a 2-3 fold increase over the expected BFU-E and a 1.5-fold increase over expected CFU-GM. Addition of 10% autologous suppressor T-cells to bone marrow T-free target cells produced a 43% inhibition of both BFU-E and CFU-GM. Taken together, these data strongly suggest that a suppressor T-cell derived lymphokine inhibited both erythroid and to a lesser extent, myeloid progenitor cell expression in PRCA.

932 MULTIMODAL TREATMENT OF CHILDHOOD NEUROGENIC SARCOMA (NGS). B. Raney, MD, L. Schnaufer, MD, M. Ziegler, MD, P. Littman, MD, and J. Chatten, MD. Children's Hospital Cancer Research Center (CHCRC),Philadelphia, PA 19104.

24 patients (pts) aged 3 mo.-16 yr.(median, 12 yr.) were treated for NGS at the CHCRC from 1958 through 1984. 16 pts (67%) had neurofibromatosis (NF). The tumors arose in an extremity or the trunk (14 pts), retroperitoneum-pelvis (6 pts), or other sites (4 pts). 13 pts underwent grossly complete excision of localized sarcoma; of them, 7 had no known residual tumor and 6 had microscopic residual. The other 11 pts had visible residual localized (10 pts) or metastatic sarcoma (1 pt). 8 pts were treated on a protocol with radiation therapy (4000-6000 rad) and VAC (vincristine, actinomycin D, cyclophosphamide) ± Adriamycin. The other 16 pts were treated variably. The proportion of pts continuously tumor-free and alive is:

Pt Status	Tumor Status	Protocol Rx	Non-Protocol	Total
NF Present	Excised	2/3	1/5	3/8
NF Present	Not Excised	0/2	0/6	0/8
NF Absent	Excised	2/2	3/3	5/5
NF Absent	Not Excised	1/1	0/2	1/3

Five of 8 protocol pts are tumor-free survivors (TFS), compared to 4 of 16 non-protocol pts. Surgical removal of all gross tumor is important: 8 of 13 pts with excision are TFS compared to 1 of 11 with gross residual sarcoma. Pts with NF fare poorly: only 3 of 16 are TFS compared to 6 of 8 without NF. We conclude that a more effective treatment program is needed for children with NGS, especially for those with NF.

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● **933** ALTERED SPECTRIN SELF-ASSOCIATION AND MEMBRANE FRAGILITY WITHOUT HEAT SENSITIVITY IN A CASE OF CONGENITAL HEMOLYTIC ANEMIA WITH MICROPOIKILOCYTOSIS. Yaddanapudi Ravindranath, Robert M. Johnson (Spon by Jeanne M. Lusher,M.D.) Departments of Pediatrics and Biochemistry, Wayne State University Medical School and Children's Hospital of Michigan, Detroit, Michigan.

In hereditary pyropoikilocytosis (HPP) and one type of hereditary elliptocytosis (HE) defective spectrin self-association has been described. Spectrin extracted from normal erythrocyte membranes at 0^o is nearly all tetrameric, while in HPP and HE (type I) a substantial amount of the extracted spectrin is dimeric. We here report the case of a family in which the child has moderately severe hemolysis with extreme microcytosis and poikilocytosis (Hg 7.6-8.8 gm/dL, retics 20-54%,MCV= 44-52). The spectrin extracted at 0^o is predominately dimer. Parents had levels of dimer intermediate between patient and controls:

	controls	patient	father	mother
% dimer	11 ± 6(7)	77(2)	27(2)	49(2)

The case is not HPP, since the temperature dependence is normal for (a) erythrocyte fragmentation; (b) spectrin extractability; and (c) circular dichroism of purified spectrin. It is not HE, since neither the patient nor the parents had elliptocytic red cells as judged from smears and scanning electron microscopy. It therefore appears to be a new type of hereditary hemolytic anemia characterized by defective spectrin self-association. In this family, the degree of mechanical stability of the erythrocyte membrane, as determined by ektacytometry,correlated with the amount of tetramer found in the membrane.

934 THE TWO-HOUR SICKLE CELL PREP (SCP) FOR RAPID DETERMINATION OF % SICKLE HEMOGLOBIN (HB S). A. Kim Ritchey, Edmund Sullivan, Yolanda Rooks (Spon. by H.A. Pearson). Dept. of Ped., Yale U. School of Medicine, New Haven, CT

A rapid and accurate means of determining the percentage of Hb S in blood would be of value in the management of sickle cell patients undergoing emergency exchange transfusions and on chronic transfusion programs. To determine the usefulness of the 2-hour SCP in predicting the % Hb S we compared the % of sickled cells in blood incubated for 2 hours in sodium metabisulfite to the % Hb S simultaneously determined by column chromatography (Sickle Cell Quik Column Method, Helena Laboratory.) Seventeen blood samples from 6 transfused patients with homozygous sickle cell disease were studied. Combined data from the 17 samples revealed a mean (±SEM) % of sickled cells determined by the 2-hour SCP of 30±6 and a mean % Hb S by column of 30±5. There was no significant difference between the two values as determined by the paired T-test (p=.96). Comparison of the two methods on individual samples revealed that 8 determinations by the 2-hour SCP were higher than those obtained by the column method, while 7 were lower. The discrepancy between the two methods on individual samples was usually less than 10 percentage points, although 6 samples had differences of 10-18 percentage points. We conclude that the 2-hour SCP is a simple, reliable, and accurate method of estimating the % Hb S and can be used as a guide in the management of sickle cell patients undergoing transfusion therapy.

935 **THYROID ABNORMALITIES IN LONG-TERM SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL).** Leslie L. Robison, Mark E. Nesbit, Harland N. Sather, Anna T. Meadows, Jorge A. Ortega, G. Denman Hammond. The Childrens Cancer Study Group (CCSG), Los Angeles, CA 90031

175 long-term survivors of childhood ALL were studied for thyroid function (thyroid stimulating hormone, triidothyronine resin uptake and thyroxine). Patients (pts) were diagnosed between 1972-1974 and treated on CCSG studies 101/143. Induction and maintenance chemotherapy was identical for all pts. Central nervous system therapy consisted of either 1800 or 2400 rad of cranial radiation (C-RT) or craniospinal (CS-RT). The 81 males and 94 females were first evaluated 7 yrs from the time of diagnosis and have been studied annually for an average of 2.1 yrs. Pts had a mean age of 5.3 yrs at diagnosis and all had discontinued therapy. 17/175 (10%) were identified to have thyroid function abnormalities. 5 pts (3%) had primary hypothyroidism of whom one developed thyroid carcinoma. Compensated hypothyroidism was found in 11 (6%) of whom 8 became euthyroid without replacement therapy while 3 pts remain compensated for 2,3 and 3 years. 1/175 pts was found to have transient hyperthyroxinemia. One pt with normal thyroid function studies developed a thyroid adenoma. The frequency of thyroid hypofunction was more common in females (12.8%) vs males (4.9%), p=0.07. No significant association was observed between thyroid hypofunction and radiation field (CS-RT vs C-RT), dose of radiation, duration of chemotherapy or age at radiation. This study found that 10% of pts had thyroid function abnormalities with compensated but temporary hypothyroidism being most common.

● **936** PROCOAGULANT (PC) AND PLASMINOGEN ACTIVATOR (PA) FUNCTION OF CHILDHOOD LEUKEMIC BLASTS. J. Paul Scott, Richard M. Emrich and Elaine R. Morgan. Northwestern U. Med. School, Dept. of Pediatrics, Children's Mem. Hosp., Chicago, IL. Spon. by James A. Stockman, III.

The incidence and etiology of coagulopathy in childhood acute leukemia (AL) have not been well characterized. We have studied 11 children with AL prospectively at the time of diagnosis or relapse. A DIC screen, fibrinopeptide A (FPA) assay and assays of blast cell procoagulant (PC) and plasminogen activator (PA) were performed. Patients were evaluated for clinical prognostic features, blast cell morphology and surface markers. Blast cells were separated on Ficoll-Hypaque and then used as a source of procoagulant material in normal plasma and factor VIII, X and VII deficient plasma. Fibrinolytic activity was measured using the substrate S-2251 with des-fibrin I. We found:

	Abnl DIC Screen	↑FPA	PC	PA
ALL	7/8	7/8	2/8	4/8
ANLL	3/3	1/3	1/3	1/3

Overt laboratory evidence of DIC was present at diagnosis and worsened after therapy in one patient with ALL. This patient's blasts produced the highest level of procoagulant material. From these preliminary data, we conclude: 1. Coagulation abnormalities are common in childhood AL. 2. FPA levels are frequently increased in childhood AL. 3. Some leukemic cells produce potent procoagulant activity which may be associated with overt DIC. 4. ALL cells also frequently produce a plasminogen activator. 5. Production of PC and/or PA by blast cells was not clearly related to morphologic or immunologic characteristics.