806 IMMUNODEFICIENCY (ID) AS A SUSCEPTIBILITY FACTOR FOR MALIGNANCY IN ATAXIA-TELANGIECTASIA (A-T): REPORT FROM THE IMMUNODEFICIENCY-CANCER REGISTRY (ICR). Alexandra H. Filipovich, Beatrice D. Spector, (Spon. by John H. Kersey), U. MN Med. Sch., Depts. Peds. & Lab. Med./Path., Mpls.

A-T is an autosomal-recessive syndrome characterized by neurologic abnormalities, variable ID, and a 10% prevalence rate of cancer at a mean age of 12.5 yrs. A-T patients have excess proportions of lymphoid tumors and selected carcinomas compared to types in the general population. A-T lymphomas resemble nonlymphoblastic childhood forms and differ from the immunoblastic sarcomas prevalent in Wiskott-Aldrich syndrome and combined ID. To test the hypothesis that ID predisposes to cancer in A-T, particularly to lymphoma, we selected cases in which serum IgA, and/or mitogen assays and skin tests were measured prior to or at cancer dx. Immune function test results were available on 1/3 of ICR cases (36/108). Malignancies by type were lymphoma (44%), leukemias (22%), Hodgkin's disease (8%), and carcinomas (25%); these proportions were not different from that observed for the other 72 cases (X^2=.684; 1>P>.1). The prevalence of -/↓ IgA and/or ↓ cell-mediated immunity (CMI) among these 36 patients paralleled the immune function patterns abstracted from detailed literature reports for 57 A-T patients without cancer. A-T cases with both -/↓ IgA and ↓ CMI developed carcinoma and non-Hodgkin's lymphomas with similar frequency (29%, 36%, respectively). This retrospective analysis suggests that defects of humoral and/or CMI do not alone predict susceptibility to lymphoma or other cancer in A-T. Supported by USPHS CP-43384.

● **807** T-LYMPHOBLASTS WITH ERYTHROPOIETIC HELPER FUNCTION IN ACUTE 'T'-CELL LEUKEMIA. J.L. Finlay, D.J. Ganick, N.T. Shahidi, R. Hong, P. Sondel, Dept of Pediatrics, Univ. of WI., Madison, WI., and Stanford Univ., Stanford, CA.

Recent studies have uncovered lymphocyte factor(s) capable of enhancing erythropoiesis in vitro. The in vivo significance of this finding remains unknown. Recently a nine-year-old boy with ALL and replaced marrow (90% lymphoblasts) presented with a [Hgb.] of 11.9g/dl. Eighty-eight % of the patient's bone marrow cells reacted with antihuman T-cell monoclonal antibody (OKT3. pan). Sixty percent of the cells reacted with monoclonal antibody identifying helper cell function (OKT4, ind). 10^5 patient's T-lymphoblasts were co-cultured with 2 x 10^5 normal marrow cells in methylcellulose and erythroid colonies (CFU-E) were counted. The T-lymphoblasts exerted a marked helper effect (+130%) on normal colony growth. The patient's plasma exerted no effect. Conditioned media derived from the T-lymphoblasts similarly stimulated normal erythropoiesis (+150%). During remission the patient's [Hgb.] dropped to 7 g/dl and his peripheral blood mononuclear cells exerted no helper effect upon normal CFU-E. During relapse concomitant with a rise in the number of blasts in the patient's bone marrow, the [Hgb.] rose steadily and reached a level of 13.4 g/dl preterminally. Repeat studies using the patient's peripheral blood mononuclear cells (87% T-lymphoblasts) again stimulated normal marrow CFU-E (+54%) We conclude that in this patient with T-ALL, the T-lymphoblasts exerted a stimulatory effect on erythropoiesis helping to maintain the [Hgb.] within normal limits.

808 THE EVALUATION OF AUDITORY FUNCTION IN HOMOZYGOUS SICKLE CELL DISEASE (SCD). Bonnie Forman-Franco, Gungor Karayalcin, Debra Mandel, Allan Abramson, Philip Lanzkowsky. Sch. of Med., Health Sciences Ctr.,State Univ. of N.Y. at Stony Brook and Long Island Jewish-Hillside Medical Ctr., Department of Pediatrics, Division of Otolaryngology and Communicative Disorders, New Hyde Park, N.Y. 11042.

Vaso-occlusive crises in SCD may compromise the blood flow of the inner ear. For this reason the incidence of peripheral hearing loss in patients with SCD may be greater than in the normal population. Forty-five patients with SCD, aged from four to nineteen years, were evaluated for peripheral and central auditory function. Results were compared with an age and race matched control group.

Routine audiometry and electroacoustic measurements of middle ear impedance were performed on all patients. Katzs' Staggered Spondaic Word test was administered to patients ten years of age and older to assess central auditory function. Mean hearing and acoustic reflex levels were well within normal limits for both groups. Eight of 33 patients (24 percent) on whom central auditory function was assessed showed various degrees of dysfunction. Two of these 8 patients previously had a cerebro-vascular accident.

This study is the first to suggest a significant degree of central auditory impairment in patients with SCD. It also reveals, contrary to previous studies, no greater incidence of either conductive or sensorineural hearing loss in these patients. Frequent CNS involvement in SCD is the possible cause of central auditory dysfunction.

● **809** DETECTION AND CHARACTERIZATION OF ERYTHROPOIETIC INHIBITORS IN ANEMIA OF CHRONIC RENAL FAILURE Melvin H. Freedman, Tom Grunberger, E. Fred Saunders, H. Michael Dosch, Daniel C. Cattran and Eli Z. Rabin, Univ of Toronto, Hosp for Sick Children, Div of Hematology, Toronto, Canada.

The mechanism of anemia in pts with end-stage renal disease was studied by assessing erythroid colony growth in methylcellulose cultures. Peripheral blood BFU-E from 10 anemic pts were normal when cultured in control serum (mean 22 BFU-E/10^5, range 14-41 vs control mean 18±10/10^5), but declined a mean of 67% when autologous uremic serum was substituted. Sera from 53 of 60 pts cultured with control marrow produced a mean decrease in BFU-E of 74% and in CFU-E of 79%. The serum inhibition was confirmed by reproducing the effect on control marrow colony growth with specific fractions of pts' serum separated by sephacryl gel chromatography. Neither peritoneal dialysis nor hemodialysis reduced the inhibitory activity, but it disappeared with successful renal transplantation. Analysis of uremic serum revealed a striking increase in a ribonuclease of M.W. 33,000 in all pts (9,500-40,000u/ml vs control mean 1,047±247u/ml) that was not eliminated by therapeutic dialysis. Purified ribonuclease produced dose-dependent inhibition of control marrow CFU-E but had unpredictable effects on BFU-E. We conclude that in anemic uremic pts: erythroid progenitors are adequate; the serum contains erythropoietic inhibitors; a ribonuclease is increased and appears to have a role in the erythropoietic suppression.

810 TUMOR AND URINARY CATECHOLAMINES (CATS) IN CHILDREN WITH NEUROBLASTOMA (NB): CORRELATIONS WITH PATHOLOGY (PATH), STAGING, AND PROGNOSIS. John Graham-Pole, Aaron Anton, Toivi Salmi, and Carlos Abramovsky (Spons. by Milo Hilty). Case Western Reserve University Medical School, Rainbow Babies & Childrens Hospital, Department of Pediatrics, Cleveland.

Enzyme pathways in CATS metabolism are thought to influence the clinical expression of NB and its prognosis. We examined the diagnostic urinary CATS of 40 children with NB and the tumor CATS of 18 of these. Dopa (DA), dopamine (DM), epinephrine (Epi), norepinephrine (NE), normetanephrine (NM), vanylmandelic acid (VMA), and homovanillic acid (HVA) were routinely measured. We correlated the absolute and relative amounts with the child's age, site of tumor, stage, degree of path differentiation and prognosis. Results: 1. Tumor and urinary CATS correlated unpredictably, indicating that urinary CATS do not reliably reflect tumor CAT patterns. 2. Ratios of urinary NM and VMA to DA and DM provided most consistent information. 3. Relative increases in DA and DM were seen in advanced stages with poor outcome, but this did not correlate with path appearances. 4. Relative increases in NM and VMA were seen in infants less than 12 months, particularly with stage IVS NB, also not correlated with path appearances. Conclusions: CAT metabolism in NB has important biologic significance in terms of the tumor's clinical expression and prognosis. More sophisticated methodology is needed (eg, electron microscopy) to establish whether the degree of path differentiation correlates with tumor catecholamine patterns.

811 HIGH-DOSE MELPHALAN (HD L-PAM) THERAPY PLUS AUTOLOGOUS BONE MARROW REINFUSION TO TREAT REFRACTORY NEUROBLASTOMA (NB). John Graham-Pole, Samuel Gross, and Roger Herzig (Spons. by Milo Hilty). Case Western Reserve University Medical School, Rainbow Babies & Childrens Hospital, Department of Pediatrics, Cleveland.

New treatments are urgently needed for stage IV NB, which becomes resistant to chemotherapy (CT) in 75% of cases. We have treated 6 children (ch) with refractory NB with HD L-PAM, either 120 mg/m^2 (4 ch) or 180 mg/m^2 (2 ch), in 3 divided doses, followed by reinfusion of bone marrow (BM) previously frozen in liquid N_2 during BM remission. The ch were isolated during the neutropenic phase and supported with red cells and platelets, and hyperalimentation via Broviac catheters. Toxicity: all 6 recovered hemopoietic function, in median periods of 28 days (neutrophils 500), 34 days (retics 1%), and 35 days (platelets 50,000). Gastrointestinal side effects were severe but short-lived. 1 ch developed hepatic venocclusive disease, which regressed completely with supportive measures. 3 ch developed sepsis while neutropenic. 1 ch died after 3 mo complete response (CR) from complications of prior abdominal surgery and had no tumor at autopsy. Responses: 120 mg/m^2 (4 ch)--1 CR (6 mo), 1 PR (1 mo), 2 NR. 180 mg/m^2 (2 ch)--2 CR (3 mo and 4+ mo). Conclusions: 1. HD L-PAM is clearly active against NB. 2. Autologous BM reinfusions protect against severe myelosuppression. 3. BM autografting may uncover other dose-limiting toxicities of L-PAM. 4. L-PAM should be combined with other agents in further phase II and III studies.