

● **801** ABSENCE OF COMMON ALL ANTIGEN ON NORMAL PLURIPOTENTIAL MYELOID, ERYTHROID AND GRANULOCYTE PROGENITORS. Luis Clavell, Robert Bast, Jeffrey Lipton, Stephen Sallan, John Pesando, and Jerome Ritz. (Spon. by David G. Nathan) Harvard Medical School, Children's Hospital Medical Center, and Sidney Farber Cancer Institute, Boston, MA.

The common ALL antigen (CALLA) is a unique cell surface glycoprotein detected on the lymphoblasts of most cases of childhood ALL and some B cell tumors to which Ritz et al (Nature 283: 583, 1980) have generated a cytolytic monoclonal antibody (J-5). To determine whether J-5 is distributed on the surfaces of hematopoietic progenitors and with the ultimate purpose of developing a useful approach to autotransplantation, we thrice exposed normal marrow and blood mononuclear cells to J-5 and complement after having determined that such treatment is sufficient to eradicate >99% J-5⁺ lymphoblasts. The cells were then cultured in both plasma clot and methylcellulose systems to which were added appropriate inducers. Erythroid, granuloid and mixed erythroid/granuloid colony growth was unaffected both with respect to number, size, and morphology. The normal colonies were preserved even in experiments in which J-5⁺ leukemic cells were added to the normal marrows and lysed during antibody exposure. These results suggest that CALLA is absent from the surface of committed marrow and peripheral blood myeloid progenitors. The antibody is a powerful potential tool for elimination of CALLA⁺ lymphoblasts from marrow prior to autologous bone marrow transplantation.

● **802** VARIANT VON WILLEBRAND'S DISEASE (vWD): ABNORMALITY IN MULTIMERIC ASSEMBLY OF FACTOR VIII RELATED ANTIGEN (VIIIIRAG). Herbert A. Cooper, Mary A. Lamb, and Robert H. Wagner. Univ. of N. Carolina, Ctr. for Thromb. and Hemostasis and Dept. of Pathology, Chapel Hill. Factor VIII in normal plasma is a complex of at least two molecules, VIIIIRAG and VIIIIC, each having distinct functional and antigenic properties. VIIIIRAG normally assembles as a series of multimeric forms ranging from 1 to >20x10⁶ daltons. We show, using a new crossed immunoelectrophoresis procedure, the importance of identifying alterations in the distribution of these multimeric forms. A normal distribution for at least 5 distinct forms of VIIIIRAG was established using both pooled and individual plasmas. The slowest migrating form contained the most of the antigen while the four faster forms had progressively decreasing concentrations. Two patients presented as possible vWD variants because of prolonged bleeding times and low ristocetin cofactor activity despite normal to elevated levels of VIIIIRAG. Both plasmas showed essentially complete absence of the larger multimers and an absolute increase in the concentration of the anodal forms that corresponded to the faster migrating forms in normal plasma. An additional faster migrating form was found in one of the plasmas. Patterns of cryo-supernatant and commercial FVIII preparations were similar to the variant patterns; cryoprecipitate resembled more closely the normal plasma pattern. Results suggest that some types of vWD can result from an abnormality in the ability of VIIIIRAG to assemble into the larger multimeric forms and supports the hypothesis that the largest forms of VIIIIRAG are necessary for normal hemostasis through participation in platelet-vessel wall interactions.

● **803** EFFECT OF VITAMIN E ON CHRONIC HEMOLYSIS DUE TO INCREASED SENSITIVITY TO OXIDANT STRESS. L. Corash, J.G. Bieri, M. Sheetz, B. Shafer, and J.D. Schulman. NIH, Bethesda, MD and Univ. Conn., Farmington, CT.

Chronic hemolysis and increased susceptibility to oxidant stress occur in two hereditary disorders associated with defective production of reduced glutathione: glutathione synthetase deficiency (GSD) and chronic hemolytic glucose 6-phosphate dehydrogenase deficiency (CHG6PD). High doses of d1, α-tocopheryl acetate (T), ester of the antioxidant vitamin E, improved red cell survival in a patient with each condition (Ann. Int. Med. 90:53, 1979). Additional patients, 2 with GSD and 7 with CHG6PD from 3 kindreds, have now ingested 1000 I.U./day of T for at least 6 months. One GSD patient was treated from birth; red cell half life (RBCT50) at age one yr. was 24.6d (normal = 25-28d), hemoglobin (Hgb) was 13.6g/dl and reticulocyte count (RC%) was 0.92-2.3%. An unrelated adult male GSD subject without oxoprolinuria had pretreatment RBCT50=8.5d increasing to 14.1d after T; Hgb rose from 13.3g/dl to 14.5g/dl as RC% fell from 10.2 to 3.8. Before T, the CHG6PD subjects had marked hemolysis: mean Hgb=12.7g/dl±.3SEM, RC%=14.1%±1.4, and RBCT50=6.6d±.7. Baseline mean plasma (870±116) and red cell (307±21) α-tocopherol levels (μg/dl) were normal before T and rose to 1793±398 and 563±108 respectively. These 7 CHG6PD subjects showed no improvement in any hematologic parameter after T, and their high molecular weight erythrocyte membrane protein aggregates were also unchanged. While T consistently ameliorates hemolysis in GSD, most CHG6PD patients do not respond.

● **804** PLATELET ASSOCIATED IMMUNOGLOBULIN, PLATELET SIZE AND THE EFFECT OF SPLENECTOMY IN THE WISKOTT-ALDRICH SYNDROME. Laurence Corash, Brenda Shafer, Wendell Rosse, and R. Michael Blaese, National Institutes of Health, Bethesda, Maryland.

Severe thrombocytopenia, characterized by small platelets, is a major cause of morbidity and mortality in the Wiskott-Aldrich Syndrome (WAS). This microthrombocytopenia was assumed to reflect a primary defect in platelet production until the recent demonstration that splenectomy (Spx) frequently normalizes the platelet count. We have measured platelet mean volume (MPV) and platelet associated immunoglobulin (PAIgG) in WAS patients before and after Spx. WAS patients (n=14) average MPV pre-Spx was 3.2 μ³ ± .2 s.e.m. compared to normal controls' MPV of 6.6 μ³ ± .6, p<.001. 7 WAS patients underwent Spx, in each case a normal platelet count was achieved and the group MPV rose to 5.8 μ³ ± .3, within the normal range. PAIgG per platelet in the WAS subjects (n=10) pre-Spx ranged from 18.1 fg to 267.3 fg mean 78.9 fg ± 23.3, significantly greater than normal (<4 fg/platelet) and aplastic controls, p<.001. In 5 WAS subjects studied post-Spx, PAIgG mean declined to normal, ranging from 1.6 fg to 8.7 fg, with a mean 4.0 fg ± 1.25. Increase in MPV and decrease in PAIgG usually occurred within two weeks of Spx. Based upon the changes in MPV and PAIgG, we speculate that immune mediated platelet destruction occurs in WAS subjects, that this process requires an intact spleen and a complex interaction between the WAS IgG-coated platelet and splenic macrophages resulting in piecemeal loss of platelet membrane giving rise to the small WAS platelet.

● **805** AMIKACIN (AM) AND TICARCILLIN (TI) AS EMPIRIC THERAPY IN FEBRILE NEUTROPENIC CHILDREN WITH CANCER. G. Deshpande, H. Faden, M. Grossi, and A.I. Freeman (Spon. by J.R. Humbert). State Univ. of New York, Children's Hospital, Roswell Park Mem. Inst., Dept. of Pediatrics, Buffalo.

Efficacy and toxicity of Am (600 mg/M²/d IV) and Ti (12 gm/M²/d IV) as empiric therapy were evaluated in 46 febrile neutropenic (<1000 PMNs/mm³) children with cancer. Documented infection (DI), clinically apparent infection (CA), possible infection (PI) and doubtful infections (DoI) were evaluated as follows:

	DI (15)	CA (13)	PI (9)	DoI (9)
PMNs/mm ³ (x̄ ± SEM)	131±181	259±291	112±194	290±280
Improved (79%)	6	10	7	0
Temp. Improved (7%)	2	0	0	0
Failed (14%)	0	2	2	0
Not evaluable	7	1	0	9

Bacterial pathogens identified were *E. coli*-5, *P. aeruginosa*-2, *Klebsiella sp.*-2, *Serratia sp.*-1, *Staph. sp.*-5 and *Strep. sp.*-1. The 4 non-responders did not have documented infections. Blood urea nitrogen, creatinine, creatinine clearance, potassium and urine analysis obtained before and after antibiotic therapy showed no significant differences. Comparisons of mean peak/trough serum levels of Am obtained on day 2 (23.9/< 2μg/ml) and day 5 (24.2/< 2μg/ml) showed no accumulation. Two of 23 paired audiograms obtained early in the course of and after Am therapy showed transient mild high frequency hearing loss. Am and Ti have low toxicity, are well tolerated and are adequate empiric therapy for the febrile neutropenic child.

● **805A** PROGNOSIS AFTER 3-YEAR SURVIVAL IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL). N.L. Dunn, E.C. Russell, N.B. McWilliams, H.M. Maurer. Medical College of Virginia, Department of Pediatrics, Richmond, Virginia.

The appropriate duration of therapy for childhood ALL remains controversial.

82 children (M:F, 47:35) with ALL were diagnosed between 1965-1975. Forty (49%) children, including 18 males, remained in complete continuous remission (CCR) at 3 years. Between the third and fifth years of therapy, 3 males and 3 females relapsed. The sites of initial relapse were the CNS in 5 (4 had received CNS prophylaxis) and a simultaneous marrow and testicular relapse in the sixth. Five were initially high risk patients by age (<2 or >8 years) or white count (>30,000/mm³) criterion. One additional child died, in remission, of varicella complications.

33 patients (40%) remained in CCR at least 5 years. They had received chemotherapy for a median of 61 mos. Followup times off therapy ranged from 6-178 mos (median 36+ mos). One boy in this group subsequently relapsed in the marrow 16 months after therapy ended.

We conclude that the relapse rate of 17.5% (7/40) after 3 years of CCR is comparable to the 20% relapse rate reported by St. Jude Children's Research Hospital (NEJM 300:269, 1979), although our patients received therapy for an additional 2+ years. Continuing therapy beyond 3 years would therefore seem to subject patients to continued potential morbidity without improving ultimate prognosis.