

846 INTRAVENOUS TREATMENT OF AUTOIMMUNE HEMOLYTIC ANEMIA WITH GAMMAGLOBULIN. James B. Bussel, Charlotte Cunningham-Rundles, and Margaret W. Hilgartner. NYH-CUMC Div. Ped. Hem/Onc. and Dept. of Immunology, Memorial Sloan Kettering Cancer Center, New York City.

Autoimmune hemolytic anemia of childhood (AIHA) is often refractory to 2 mg/kg of prednisone. We report 2 infants with AIHA treated with initial doses of 5 gm/kg IVGG followed by maintenance doses of 2 gm/kg/wk. Infant #1 had required greater than 20 mg of prednisone/day for more than 6 months and had previously received 2 gm/kg of IVGG without apparent effect. After 5 gm/kg IVGG treatment his hemoglobin rose slowly over 4 weeks from 7.7 to 10.9, despite tapering of prednisone, and remains stable. Infant #2 had his second relapse of immune hemolytic anemia with the hemoglobin decreasing to 7 gm/dl. Two weeks of IVGG treatment stabilized his hemoglobin; 1½ weeks after treatment was stopped his hemoglobin fell to 4.5 gm/dl. Reinduction with 5 gm/kg IVGG and continued maintenance reestablished his hemoglobin at 7. Both patients had IgG antibodies which failed to bind to r_h null cells after elution and abnormally decreased *in vitro* nonspecific antibody synthesis. Recent work by Salama et al demonstrates that a part of the RES Fc receptor blockade mediating an increased platelet count during IVGG treatment of ITP is due to low grade red cell immune hemolysis; therefore, they state that AIHA cannot be treated by IVGG. We demonstrate that AIHA can be treated by IVGG albeit at higher dosage than even in ITP (5 gm/kg vs 2 gm/kg). Other possible reasons for difficulty of treatment of AIHA by IVGG or steroids may include larger cell mass, lack of red cell Fc receptors or a more avid RES.

847 GOOD RESPONSE TO INTRAVENOUS GAMMAGLOBULIN OF PATIENTS WITH STEROID RESISTANT ACUTE ITP. James B. Bussel and Margaret W. Hilgartner. NYH-CUMC Div. Ped. Hem/Onc., New York City.

Eight patients with acute ITP steroid resistant (SR) to 2-4 mg/kg/day of prednisone for 1 to 6 weeks received 1 gm/kg/day IVGG up to 3 consecutive days depending on response. The table compares platelet count and IVGG treatments of the 8 SR patients with 10 previously untreated (U) acute ITP patients:

Group	Platelets/u1 x10 ⁻³			Followup		
	Initial	Peak	Last	Months	IVGG in gm/kg	Maintenance
(SR) 8	13	213	218	4.8	1.75	1.5
(U) 10	18	186	204	3.6	1.3	0.8

No SR patient still requires treatment: 5 are in remission and the 3 non-remission patients average 97,000/u1. The outcome of the U patients is 4 remission, 5 stable without therapy and 1 refractory (not different from the SR group). 4/10 U patients and 2/8 SR patients received only a single infusion total; 3/10 U patients and 1/8 SR patients received only 2 infusions. Sixteen patients were treated with Immuno IVGG, 2 with Sandoglobulin and no side effects were seen. Neither initial platelet count, platelet size, PAIgG, PAIgM, C₃, C₄, CH₅₀ nor serum immunoglobulin levels differentiated the SR vs U groups or predicted which patients would respond better to IVGG. In summary, IVGG effectively treated steroid resistant acute ITP patients (presumably the group at highest risk for intracranial hemorrhage) with rapid increases in the platelet count and excellent outcomes comparable to previously untreated patients. The only difference between the SR & U pts was the increased use of IVGG.

848 CHILDHOOD MONOSOMY 7 SYNDROME: A FAMILIAL DISORDER? William L. Carroll, Michael D. Amylon, Michael P. Link, Karen Backer and Bertil E. Glader, Stanford University School of Medicine, Children's Hospital at Stanford, Department of Pediatrics, Division of Hematology/Oncology, Stanford, CA

Preleukemic states are rare in children although monosomy 7 now is recognized as a genetic marker for a childhood myeloproliferative disorder which evolves into bone marrow (BM) failure or acute nonlymphocytic leukemia (ANLL). Recently we observed a Caucasian girl with this disorder. The salient features of her course included: (1) onset of pancytopenia at 9 months of age, (2) persistent granulocytopenia, thrombocytopenia and macrocytosis (MCV = 108) over a 6 year period, (3) evolution of marked dyserythropoiesis at 7 years of age, (4) presence of BM monosomy 7 in 100% of metaphases while PHA stimulated peripheral blood revealed a 46 XX karyotype, (5) conversion to ANLL at 7-1/2 years of age and (8) failure to achieve remission with currently effective ANLL chemotherapy. The patient's healthy 5 year old brother also manifested mild thrombocytopenia, macrocytosis (MCV = 98) and monosomy 7 in his BM karyotype. The observations described here now bring to 27 the total number of reported cases of childhood monosomy 7. Of particular interest, however, 8 of these cases represent 4 pairs of siblings. It thus appears that the frequency of familial involvement may approach 30%. For this reason, siblings of these patients should be serially evaluated for hematologic dysfunction and chromosomal changes. This is especially important since effective therapy for this condition may be bone marrow transplantation from a histocompatible sibling.

849 LONGITUDINAL STUDY OF NEUTROPHIL FUNCTION IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL). AR Chauvenet, SK Dowell, JS Abramson, Bowman Gray School of Medicine, Winston-Salem, NC (sponsor: JL Simon).

Longitudinal studies of polymorphonuclear leukocyte (PMNL) function were done in 45 children with ALL (37 "null" cell, 7 T cell and 1 B cell). The oxidative burst of PMNLs was studied by measuring chemiluminescence (CL) with soluble and particulate stimuli. The capacity of PMNLs to become bipolar in shape in response to the chemoattractant formyl-methionyl-leucyl-phenylalanine (FMLP) was examined. Results from 84 of 90 CL assays were normal. Results were normal regardless of time since initial remission or end of therapy. Too few patients in relapse were studied for statistical analysis. Abnormal results occurred in 6 patients on a single occasion; there were no common features with regard to time from diagnosis, treatment or state of disease. 3 of these 6 had later measurements which were normal. Results from 14 of 89 assays measuring bipolar shape change were abnormal. 11 patients had increased numbers of bipolar shaped cells prior to FMLP stimulation and 3 patients had abnormally low numbers of bipolar PMNLs after FMLP stimulation. Abnormalities were found in 3 of 7 T cell and 10 of 37 "null" cell patients. No patients were infected at the time of these studies. Controls included children and adults not having cancer. These data suggest (1) children with ALL have normal PMNL oxidative metabolism in initial remission and during subsequent chemotherapy (2) 13/45 patients had abnormalities in the bipolar shape change assay suggesting that chemotactic activity may be adversely altered. Studies of chemotaxis are underway.

850 USE OF MONOCLONAL ANTIBODIES SPECIFIC FOR NEUROBLASTOMA (NB) IN THE DETECTION AND COMPLEMENT MEDIATED LYSIS OF MICROSCOPIC DISEASE. Nai-Kong V. Cheung, Ulla Saarinen, Duffy Donovan, Bonnie Landmeier, Peter F. Coccia, Case Western Reserve University, Rainbow Babies and Childrens Hospital, Department of Pediatrics, Cleveland, Ohio 44106.

Three murine hybridomas [3A7(IgM), 3G6(IgM), 3F8(IgG₂)] against human NB cell surface antigens were established using standard hybridization techniques. Both by ELISA and immunofluorescence, these monoclonal antibodies do not bind to normal bone marrow (BM) or peripheral blood cells. They all bind intensely to human NB and NB cell lines (except SKNSH and SKNSC). The cross reactivity patterns with other sarcomas and their relative degree of binding suggest that the three monoclonal antibodies have different specificities and are not reacting with common neuro-ectodermal antigens. Using immunofluorescence these antibodies can detect reproducibly $\leq 0.1\%$ of tumor cells seeded in BM samples. Patients with widespread NB even though negative in their BM aspirate and biopsy by standard light microscopy are often positive by immunofluorescence in their BM aspirates with all 3 monoclonals. Less than 250 ng of 3A7 or 3G6 can kill 100% of 3x10⁵ NB cells in the presence of 1:8 dilution of guinea pig complement, while not affecting normal blood or BM cells. In summary (1) these antibodies appear to be useful in detecting and monitoring residual NB in BM samples, (2) they are potent cytotoxic antibodies and may be suitable for complete and specific removal of residual NB cells before autologous BM transplantation.

851 PSEUDOMONAS AERUGINOSA SEPSIS IN THE NEUTROPENIC HOST: IN VIVO SYNERGY BETWEEN N-FORMIMIDOYL THIENAMYCIN AND AMIKACIN. Ellen G. Chadwick, Ram Yogeve, Stanford T. Shulman. Northwestern University Medical School, Children's Memorial Hospital, Department of Pediatrics, Chicago.

We developed a new animal model to study antibiotic synergy in neutropenia. Infant rats were rendered neutropenic by 3 intraperitoneal (IP) 50 mg/kg doses of cytarabine over 36 hrs. Mean absolute neutrophil counts were <math>< 300/mm^3</math> on post-treatment days 3-8 and normalized on days 9-10, with <math>< 1\%</math> mortality. Pseudomonas aeruginosa (PA) with MIC/MBC of Amikacin (A) = 8/16 µg/ml and N-formimidoyl thienamycin (T) = 4/8 µg/ml was studied; no synergy between A and T was demonstrated by the killing curve method. Neutropenic rats, inoculated IP with 2-6x10⁶ CFU of PA (~200 LD₅₀), were treated IP 4 hrs later with: saline (S); A 10 mg/kg; T 6.25 mg/kg; A + T (same doses); or A/2 + T/2, each every 6 hrs for 48 hrs. Peak serum levels of each antibiotic were less than the MIC/MBC for PA. Six hrs after the last dose, survival (# alive/#treated) was as shown:

Group	Survival(%)
S	0/15 (0)
A	0/25 (0)
T	7/23 (30)
A + T	19/23 (83)
A/2 + T/2	17/23 (74)

In vivo, both half-dose and full-dose combination therapy produced significantly greater survival than either agent alone. A + T was superior to T (p<0.005) and to A (p<0.001), and A/2 + T/2 was superior to T (p<0.01) and to A (p<0.001) by χ² analysis. This new, reproducible infant rat model of neutropenia enabled us to demonstrate "synergism" between A + T in Pseudomonas aeruginosa sepsis when *in vitro* synergy for this organism was not evident.