● **889** PNEUMOCOCCAL SEPTICEMIA DESPITE PENICILLIN PROPHYLAXIS IN CHILDREN WITH SICKLE CELL ANEMIA. George R. Buchanan and Susan J. Smith, Dept. of Pediatrics, Univ. of Texas Health Sci. Center, Dallas, TX.

Mortality due to S.pneumoniae septicemia in infants and young children with sickle cell anemia (SCA) remains unacceptably high. Pneumococcal vaccine and prophylactic penicillin (PRO PCN) have been used to prevent these infections. We have routinely used PRO PCN since 1978 for all patients with homozygous SCA between 6 mo and 5 yr of age: 125 mg b.i.d. for infants <2 yrs of age and 250 mg b.i.d. for those >2 yr old. Compliance is maximized by means of regular reminders. 71 patients have received PRO PCN for a total of 204 person yrs. During the past 6 1/2 yrs, 7 episodes of S. pneumoniae bacteremia occurred in 6 children (3.4 episodes/100 person yrs); 3 events were fatal. S.pneumoniae infections occurred in 4 clinical settings: (1) A 6 yr old girl died of sepsis 13 months after we electively terminated 4 yrs of prophylaxis. (2) A 14 month old girl died of sepsis 2 weeks after her PCN prescription ran out and her parents failed to refill it. (3) After missing only 1 or 2 doses, a 4 yr old girl died and another patient survived 2 episodes of sepsis. (4) Bacteremic pneumococcal pneumonia developed within 12 hours of the last PCN dose in a 9 month old girl who was reported not to have missed any recent doses. No examples of PCN insensitive or resistant S. pneumoniae were seen. In conclusion, PRO PCN may reduce the frequency of S. pneumoniae sepsis, but strict compliance is required. Prolonged administration may be advisable, with the understanding that absolute protection is not achieved.

● **890** MECHANISM OF INTRAVENOUS IMMUNOGLOBULIN TREATMENT IN CHILDHOOD ACUTE IDIOPATHIC THROMBOCYTOPENIC PURPURA. COMPARISON OF $F(ab)_2$ VERSUS pFc CONTAINING IgG. Stefan E.G. Burdach, Robert G. Geursen. Spon. by Stephen D. Smith. Children's Hospital of the City of Cologne, Department of Pediatrics, and Behringwerke Research Laboratories, D-5000 Koeln 60, FRG.

Treatment of idiopathic thrombocytopenic purpura (ITP) with high-dose intravenous immunoglobulins has been shown to be effective in several studies. It has not been demonstrated which part of the immunoglobulin molecule is decisive for the therapeutic effect. Based on a pilot study comparing 3.5 S, 5 S and 7 S-immunoglobulin (Ig) G which yielded treatment responses in each group, a prospective randomized study was conducted. This investigation compared a 7 S-IgG regimen to a 5 S-IgG regimen. The 7 S-IgG was prepared by limited sulfitolysis. The 5 S-$F(ab)_2$-preparation was produced by pepsin cleavage. Thrombocytopenic patients (platelet counts $< 30 \times 10^9/l$) were assigned to the treatment regimens randomly. Both groups were given 400 mg/kg body-weight Ig over 5 days. 9/10 patients in the 7 S treatment group responded to therapy compared to 3/10 patients in the 5 S treatment group ($p = 0.0099$ by Fisher's exact test). The mean platelet count 4 days after the last infusion was $209.5 \pm 136.7 \times 10^9/l$ ($\bar{x} \pm$S.E.M.) in the 7 S group compared to $79.7 \pm 75.0 \times 10^9/l$ in the 5 S group. The results of the study emphasize the necessity of the IgG molecule's pFc-part, which is contained in the 7 S preparation.

● **891** DETERMINATION OF GRANULOCYTE BONE MARROW STORAGE POOLS IN NEUTROPENIC PATIENTS WITH MATURATION STAGE SPECIFIC CHEMORECRUITINS. Stefan E.G. Burdach, Joseph H. Wissler. Spon. by Stephen D. Smith, Children's Hospital of the City of Cologne, Department of Pediatrics, and Max Planck-Institute of Physiology and Clinical Research, D-5000 Koeln 60, FRG.

In patients with neutropenia, granulocytic reserve pools in the bone marrow are of diagnostic and prognostic relevance. This presentation describes a novel approach to the clinical assessment of neutropenia and reserve pool granulocytes. Based on previous studies in animals two different, highly purified polypeptide effectors were tested to mediate chemorecruitment of granulocytes from bone marrow: serum derived leukorecruitin (SLR, 8500 dalton) and monocyto-metamyelorecruitin (MMR, 6500 dalton) (Burdach et al. Fed. Proceed 1984, in press). SLR mainly recruited mature, segmented granulocytes, thus causing a leukocytosis without a prominent left shift. MMR mainly caused recruitment of immature granulocytes in concurrence with sequestration of mature cells and, thus, resulted in a left shift and leukopenia. One trial with SLR in 1 healthy volunteer and 8 trials in 6 patients with disordered granulopoiesis were performed. The response in the control as well as in infantile agranulocytosis and constitutional aplastic anemia correlated with the cellular content of the bone marrow. However, in patients with preleukemia and hypersplenic pancytopenia, no correlation was observed; suggesting defective granulocyte kinetics. Two trials with MMR in 2 patients with infantile agranulocytosis and osteopetrosis resulted in a storage pool dependent release of immature granulocytes.

892 INTRAVENOUS GAMMAGLOBULIN VERSUS SPLENECTOMY IN CHRONIC ITP: AN ANALYSIS OF BENEFITS AND COSTS. James B. Bussel, John J. Ferry, Jr., Karen F. Fifer, and Margaret W. Hilgartner, Dept. of Peds. Cornell Med. Coll., New York Hospital, N.Y., N.Y.

IVGG has been used as an alternative to splenectomy (SPL) in children < 14 years with ITP for > 6 months (J Peds 10/83). Decision analysis was used to compare the benefits and costs of IVGG vs. SPL in the initial management of chronic ITP. Published reports and a survey of 11 pediatric hematology centers provided data for the analysis. For IVGG, the experience of the first 25 patients treated at Cornell was used: (1) THERAPY/COSTS: induction IVGG dose of 73 grams/pt (2 gms/kg) at $40/gm=$3,000, avg maintenance IVGG dose in a subsequent 6 month period of 117 gms/pt $5,000, office visits & CBC's=$780. (2) OUTCOME/MANAGEMENT: 5 remissions, 6 stable without IVGG, 4 infrequent (<q2months) maintenance IVGG, 5 frequent maintenance IVGG, 5 refractory (with subsequent response to SPL not impaired). 60% pts remission, partial response: $1,000 for IVGG past 12 months, 40% pts failing IVGG get SPL. For SPLENECTOMY: (1) COSTS: Surgery=$7000, admissions (two) for high fever=$3,000, office visit and CBC's $220 (2) OUTCOME/MANAGEMENT: 80% remission/partial response, pts failing SPL get IVGG for 6 months ($8,780). The base case comparison yields costs of $12,868 for IVGG and $11,976 for SPL, nearly equal costs for the two strategies. The major determinant variables were the initial cost of surgery and the maintenance costs of continuing IVGG. As the cost of IVGG is a function of weight, the benefit cost ratio shifts in favor of IVGG for younger children for whom SPL is less desirable in any event.

Withdrawn

† **894** AUTOIMMUNE NEUTROPENIA: ASSOCIATION WITH LOW IgG_2 AND DECREASED NATURAL KILLER ACTIVITY. James B. Bussel, and Margaret W. Hilgartner, Cornell Med Coll. New York Hosp., Dept. Ped., NY, NY. Parviz Lalezari, Albert Einstein Coll. Med., Montefiore Hosp., Dept. Med., NY, NY. Senih M. Fikrig, State Sch Med., Dept. Ped, Downstate Med Center, NY. Patricia A. Fitzerald, Memorial Hosp., Dept Immunol., NY, NY.

Autoimmune neutropenia of infancy (ANI) is a common, usually benign disease; certain patients however have repeated and/or serious infections suggesting that other immunologic abnormalities could be present. We investigated 5 recurrently ill pts. with absolute neutrophil counts (ANC) < 200, and high level antineutrophil antibodies. Prior to treatment all patients had <50% of the nl IgG_2 level and <80% of the nl IgG_3 levels despite nl total IgG levels. 3 of 5 had decreased natural killer activity to K562 although 4 of 5 had normal lymphocyte responses to PHA. All 5 patients responded to Intravenous Gammaglobulin (IVGG) at a dose of 2 to 5 gm/kg (avg. 3 gm/kg) with ANC >1000 within 5 days and clinical improvement. Neutrophil function was nl in 2/2 pts tested after the ANC increased. After an average of 10 mos. 4 pts. were in remission and the fifth had an ANC of 600. Natural killer activity was nl in 4/4 patients in remission but IgG_2 levels remained low in 2/2 patients. ANI may be associated with IgG_2 and/or IgG_3 subclass deficiencies and decreased natural killer activity which could explain why these pts. were particularly ill. The NK abormalities resolved when the neutrophil antibodies disappeared but IgG_2 deficiency persisted. IVGG appeared to have a longer lasting clinical effect than the elevation of the ANC (2 weeks).