

703

**PROGRESSIVE SYSTEMIC SCLEROSIS (PSS)-LIKE SYNDROME FOLLOWING BONE MARROW TRANSPLANTATION.** Philip Herzog, Nigel K. Roberts, Philip J. Clements, Daniel E. Furst

and Stephen A. Feig. UCLA Center for Health Sciences, Dept. of Pediatrics and Medicine, Los Angeles, CA 90024.

A 15 year old boy developed skin changes compatible with chronic graft versus host reaction (CGVHR) following bone marrow transplantation. His skin was thin, dry, inelastic, and telangiectatic. Biopsy revealed basal vacuolization, loss of rete pegs, atrophy of sweat glands, perivascular lymphocyte cuffing, and dense dermal collagenization. Because of the dermatologic similarity to PSS, we compared this patient to 38 PSS patients for evidence of systemic involvement. He had significant restrictive lung disease (VC and TLC 50% of predicted), cardiac conduction abnormalities (first degree heart block, right bundle branch block), and a pericardial effusion. Each of these abnormalities was found in 30-40% of the PSS group. Arteriolar intimal proliferation was seen in the heart and kidneys of our patient at autopsy. This finding has been noted in approximately 25% of PSS patients. Our patient had Raynaud's phenomenon as did 95% of the PSS group. He had a striking polyclonal elevation in serum IgG (4 gms/dl), an uncommon finding in PSS. 84% of the PSS patients showed esophageal dysmotility, but our patient did not have this abnormality. The clinical and pathologic similarities between this patient and PSS patients suggest that CGVHR and PSS may have a common pathogenesis. The use of animal models of graft versus host reaction may lead to an understanding of mechanisms responsible for both disease processes.

706

**TRANSFER FACTOR THERAPY IN HYPERIMMUNOGLOBULINEMIA E.** Hemant H. Kesarwala, Ziad A. Alqusus, Rayasam VSK Prasad, Photini S. Papageorgiou. CMDNJ, Rutgers

Medical School, Department of Pediatrics, Piscataway, N.J. Two children, 21 months and 11 years, with extensive intractable atopic dermatitis for life, recurrent pyogenic skin infections, hyperimmunoglobulinemia E, defective neutrophil chemotaxis and depressed cell-mediated immunity *in vivo* and *in vitro* were treated with transfer factor. Transfer Factor was prepared by the method of Lawrence from healthy donors with strong delayed type hypersensitivity to a battery of skin test antigens. Each patient received two courses of TF. A course was defined as  $1 \times 10^9$  cells per week for 4 consecutive weeks. No clinical side-effects were noted. Following the first course of TF, significant clinical improvement was noted in both patients with disappearance of skin infections and pruritus. No new lesions have occurred 7 months after the completion of therapy in the first patient and 2 months after the completion of therapy in the second patient despite the discontinuation of steroids and antibiotics. Immunologic evaluation showed no consistent improvement *in vitro*. However, post TF in both patients delayed type cutaneous reactivity converted to positive and serum IgE levels increased significantly. These findings suggest that TF may be beneficial in hyper-IgE syndrome although the significance of rising IgE remains to be determined.

704

**CORRECTION OF NEUTROPHIL (PMN) DYSFUNCTION IN CHRONIC GRANULOMATOUS DISEASE (CGD) WITH AN IgG-OXIDASE CONJUGATE.** James R. Humbert, William R. Weston, and

Patricia A. DeArme, State University of New York at Buffalo, The Children's Hospital of Buffalo, Department of Pediatrics, Buffalo, and University of Colorado Medical Center, Departments of Pediatrics and Dermatology, Denver.

The bactericidal defect of CGD PMNs has been partially corrected in previous studies relying on the co-phagocytosis of bacteria and of either glucose oxidase (GO)-coated latex particles or GO-containing liposomes. We investigated the effect of opsonization of bacteria with an IgG-GO conjugate upon the bactericidal activity of CGD PMNs and monocytes (MC). Anti-staphylococcal rabbit IgG was prepared and conjugated to GO by diethylmalonimidation. The conjugate (final concentration of IgG: 2.0 mg/ml) was used to opsonize bacteria which were then ingested by PMNs or MCs of female CGD carriers. In control preparations IgG alone was used as opsonin. After 120 minutes of incubation with CGD PMNs, the number of surviving intracellular bacteria decreased from a mean of 42.3% (opsonin: IgG) to 17.7% (opsonin: IgG-GO conjugate). In MCs of CGD carriers the number of intracellular bacteria decreased by 45%. In PMN-free preparation the IgG-GO conjugate displayed negligible bactericidal activity. The bactericidal defect of CGD phagocytic cells can be successfully corrected by the intracellular introduction of an IgG-GO conjugate. Furthermore, such restoration of bactericidal activity may be enhanced by the close proximity between the bacteria and the hydrogen peroxide-generating opsonin.

707

**ABNORMAL NEUTROPHIL (PMNS) CHEMOTAXIS AND ELEVATED IgE IN CHILDHOOD ASTHMA.** Abdul J. Khan, Hugh E. Evans

Yong H. Shin, Melanie Agbavani, Laura Inselman, and Parvin Khan. Dept. of Ped., Jewish Hosp. & Med. Ctr. of Brooklyn NY

PMNS chemotactic indices (CI) and random migration (RM) were determined for 12 asymptomatic asthmatic children (mean age 7.5 years) who were receiving no medication and for an equal number of age-matched controls by a modified Boyden's technique, in which PMNs, deposited on a  $3 \mu$  micropore filter, were placed in the upper chamber and endotoxin-activated AB serum (EAS) or endotoxin-activated patients' serum (EPS) in the lower chamber. For RM determinations, EAS was replaced by the Hank's balanced salt solution (HBS). EPS was also tested against patients' cells (PC) and control cells (CC). Mean ( $\pm$ 1SD) CIs and RMs are presented in the table. Patients' CIs and RMs were lower than

PC/EAS	PC/EPS	CC/EAS	CC/EPS	PC/HBS	CC/HBS
129 (59)	157 (51)	300 (69)	370 (55)	54 (17)	87 (27)

those of controls ( $P < 0.002$ ). EPS generated more chemotaxis for CC ( $P < 0.01$ ) than did EAS. In addition, serum IgE levels were determined on 6 of the asthmatic patients selected at random. The mean value of 733 units (range 473-1232) was about 2 1/2 times the normal value described for this age group. Defective CIs and RMs may be at least partly responsible for increased susceptibility to infection in asthmatics. Increased chemotaxis by EPS may be due to unknown cytotoxic factor (s). The mechanism of the PMN defects is unclear and may be related to increased IgE levels and/or deactivation of receptors by pre-existing cytotoxic factor (s).

705

**KILLER (K) CELLS RESPONSIBLE FOR ANTIBODY-DEPENDENT CELL MEDIATED CYTOTOXICITY EXPRESS HUMAN T LYMPHOCYTE ANTIGENS.** Joseph Kaplan. Wayne State University

School of Medicine, Children's Hospital of Michigan, Department of Pediatrics, Detroit.

The designation of K cells, effector cells of antibody-dependent cell mediated cytotoxicity (ADCC), as T, B, or null cells has been controversial. Using reciprocally absorbed rabbit antisera to autologous T and B lymphoblast cell lines HSB and SB which detect human T and B lymphocyte antigens (HTLA and HBLA) (Blood 49:371, 1977; Clin. Immunol. Immunopath. 8:530, 1977) we now demonstrate that K cells are HTLA-positive/HBLA-negative. Peripheral lymphocytes purified by nylon column filtration were incubated with anti-HTLA, anti-HBLA or normal rabbit serum plus complement. Viable cells remaining were then tested in a  $^{51}$ Cr-release assay for cytotoxicity against antibody coated Chang liver cells. Treatment with anti-HTLA + C but not anti-HBLA + C abrogated ADCC. This was due to lysis of K cells rather than antigen-antibody complex inhibition since no effect was seen with heat-inactivated complement. These findings support the concept that K cells belong to the T cell lineage.

(Supported by NIH Grant CA17534. J.K is recipient of NIH RCDA CA00188).

708

**RESISTANCE OF BLOOD LYMPHOCYTES IN ASTHMA TO THE ENHANCING EFFECT OF ISOPROTERENOL ON ROSETTE FORMATION WITH EAC1423 (EAC3).** Barry A. Kohn, Raif S. Geha,

(Spon. by Fred S. Rosen), Harvard Medical School, Children's Hospital Medical Center, Department of Pediatrics, Boston.

The effect of isoproterenol hydrochloride (I) on peripheral blood lymphocytes (PBL) rosette formation with sheep red blood cells (E) coated with C3 (EAC3) was studied. PBL from 25 allergic asthmatics, 25 normal subjects and 10 subjects with allergic rhinitis were separated over density gradients and incubated in RPMI medium and fetal calf serum (FCS) at 37°C overnight. From each subject  $0.8 \times 10^6$  PBL were incubated with phosphate buffered saline or I for one hour at 37°C, washed 3 times in Hanks' medium with FCS and rosetted with both E and EAC3 reagent.

E rosette formation was similar for all groups and unaffected by I. Baseline EAC3 rosette number was similar for all groups (normals:12%; rhinitis:13%; asthma:13%). Incubation with I of PBL from normal subjects and patients with rhinitis resulted in statistically significant increases in the number of EAC3 rosette forming cells (normals-base:12%, I:19%,  $p < .001$ ; rhinitis-base:13% I:20%,  $p < .001$ ). Incubation with I of PBL from asthmatics resulted in no increase in the number of EAC3 rosette forming cells (asthma-base:13%, I:13%). Similar results were obtained with theophylline (Th) in 15 pairs of normals and asthmatics. Bronchodilator therapy did not affect the results in either normals (3) or asthmatics. The resistance of PBL from asthmatics to the enhancing effect of I and Th on EAC3 rosette formation may be used to study the biochemical defect in asthma and may provide an *in vitro* test for the detection of the latent asthmatic.