● 996 SUPPRESSIN, A PEPTIDE THAT INDUCES SUPPRESSOR T-CELLS: IDENTIFICATION, CHARACTERIZATION AND CLINICAL RESULTS.

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We report at this time the identification and characterization of suppressin, a novel peptide that induces suppressor T-cells. Following calf thymus homogenization the peptide is isolated by ultrafiltration, $(\text{NH}_4)_2\text{SO}_4$ precipitation, and ion exchange and hydrophobic chromatography. The isolated peptide has a MW of approximately 2000, consists of 16-18 residues and is distinct from other previously described thymic hormones. Incubation of human thymocytes in suppressin causes expression of (OK)T8 antigen and histamine H2 receptors, lymphocyte phenotypes associated with suppressor T-cells. Functionally, the induced suppressor cells can suppress, in vitro, autologous lymphocyte response to PHA as well as both specific and non-specific antibody production. When administered in vivo, suppressin causes significant suppression of delayed type hypersensitivity (DTH) response to both modified self-antigen and allo-antigen, improves the clinical course of experimental allergic encephalitis and adjuvant induced arthritis, and produces decreased antibody production in NZB/W mice. When suppressin was administered in a clinical trial to patients with suppressor T-cell deficiency, 11/13 demonstrated significant increase in suppressor T-cell number and function. This newly identified hormone will be useful in the understanding of thymic function and T-cell differentiation and offers the potential for therapeutic benefit in the treatment of autoimmune/hyperimmune diseases characterized by suppressor T-cell deficiency.

● 997 TRANSFER OF CELL MEDIATED IMMUNITY (CMI) TO THE FETUS

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Previous evidence of transfer of CMI to the fetus (Field & Caspary, Lancet 2: 337, 1971) was limited to in vitro demonstration of sensitivity in mononuclear cells (MC) of mother and newborn to purified protein derivative (PPD). If such transfer indeed occurs, it could theoretically reduce the efficacy of BCG immunization given often shortly after birth. We examined MC response from mothers and their infants, using PPD (Connaught), Candida extract (Hollister Stier) and/or streptokinase streptodornase (SKSD) (Lederle) as mitogens. The response was measured by tritiated thymidine incorporation on the 6th day in triplicate microcultures, containing 2×10^5 MC in 15% autologous or pooled AB serum and RPMI medium. The stimulation index (SI) (CPM of stimulated divided by CPM of unstimulated cultures) was used to determine positive (SI > 2.5) or negative responses.

Of 63 mothers with a positive response to PPD, 22 infants were positive. Of 46 mothers positive to Candida, 17 infants were positive to Candida. Of 27 mothers positive to SKSD, 9 infants were positive to SKSD. Mothers with negative responses to any of the antigens had infants negative to the same antigens. Positive responses in infants persisted for at least 3 weeks in all infants tested but eventually all were negative. Karyotyping of male newborns' MC stimulated with specific antigens revealed that the transformed cells were of XY karyotype. We conclude that specific CMI is indeed transferred from mother to fetus. This may be an important argument to postpone BCG immunization till after the newborn period.

● 998 ACTIVE JUVENILE DERMATOMYOSITIS (JDMS) IS ASSOCIATED WITH COMPLEMENT AND COAGULATION ACTIVATION, AND INCREASED TITERS TO ANTINUCLEAR (ANA) AND COXSACKIE B VIRAL (COX-B) ANTIGENS.

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Seven active JDMS children had increased complement activation products (C3d and C4d), endothelial cell perturbation (increased factor VIII related antigen), and intravascular thrombosis (generation of fibrinopeptide A), despite normal routine coagulation studies. When 12 JDMS sera obtained within 4 months of disease onset were tested for complement fixing antibody to Cox-B, 83% were positive to at least one antigen, compared to 25% of controls matched for age/sex/date of visit. In contrast, assays for antibody to 15 other possible viral antigens, including *Mycoplasma pneumoniae*, did not give greater than expected titers. When neutralizing antibody was measured, an increase in Cox-B2 (58%), B4 (58%), B5 (67%), was seen vs a maxima of 26% in control sera. Finally, when these sera were tested for ANA, 50% were positive. We conclude that newly diagnosed JDMS is associated with increased antibody to Cox-B and ANA; active disease perturbs the coagulation and complement systems. We speculate that these events may be related to the pathophysiology of this chronic illness. Supported in part by grants from Illinois Chapter Arthritis Foundation, Marlene Apfelbaum Memorial Foundation, and AM-21589.

999 B LYMPHOCYTE DYSFUNCTION IN HOMOSEXUAL MEN AND IN CHILDREN WITH THE ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

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Patients with AIDS are frequently hypergammaglobulinemic, but their capacity to make antibodies has been questioned. In the present study, severe abnormalities in in vitro differentiation of B lymphocytes into immunoglobulin- and antibody secreting cells in response to T-dependent and T-independent polyclonal stimuli (pokeweed mitogen, S.aureus Cowan 1, (SAC); Epstein Barr virus) & antigen SRBC were noted in homosexual (HS) men who were symptomatic (AS) or asymptomatic (S) but without the CDC criteria for AIDS, and in children (C) and adults (A) with established AIDS. Antibody responses were poorly amplified by the delayed addition of Concanavalin A to antigen-stimulated cultures. Polyclonal responses were more severely affected in symptomatic HS, but A and C with AIDS manifested the most profound abnormalities in antigen-specific antibody responses. In studies with separated B & T cells, intrinsic B and T helper cell functions were markedly deficient. Depressed proliferative responses of lymphocytes to B cell-mitogen SAC as well as increased spontaneous ISC were frequently noted. Clinical follow up was suggestive of a direct correlation between morbidity and mortality and severity of B cell dysfunction. These observations suggest that AIDS is a form of combined B & T cell immunodeficiency and that certain AS and S individuals in risk groups for AIDS may have demonstrable B & T cell abnormalities.

1000 LYMPHOCYTE SUBPOPULATIONS IN HIGH RISK INFANTS: POLYMORPHISM OF T4 ANTIGEN AND INFLUENCE OF BLOOD TRANSFUSIONS.

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T cell subsets analyzed with Ortho monoclonal antibodies (mo ab) on microsamples of blood obtained by heel puncture on 38 infants in a high-risk nursery revealed that after birth, the OKT8 subset gradually increases while the OKT4 subset and T4/T8 ratio decrease. Mean $\pm$ SEM values of lymphocyte subsets at different ages are shown below:

Age	(n)	%OKT3	%OKT4	%OKT8	T4/T8 Ratio
<1wk	(15)	67.3 $\pm$ 3.3	49.2 $\pm$ 2.7	18.1 $\pm$ 1.5	3.0 $\pm$ 0.2
1-4wk	(13)	67.5 $\pm$ 2.4	46.9 $\pm$ 3.2	19.6 $\pm$ 1.1	2.6 $\pm$ 0.3
5-12wk	(19)	63.0 $\pm$ 3.3	46.1 $\pm$ 1.7	22.4 $\pm$ 1.7	2.3 $\pm$ 0.2
3-7mo	(9)	59.0 $\pm$ 3.1	41.6 $\pm$ 2.5	23.7 $\pm$ 1.0	1.8 $\pm$ 0.1

In each group, lower T4/T8 ratios were noted in infants who had been given blood transfusions, and linear regression analysis in a restricted age group (2-12wk) revealed a significant reduction in T4/T8 ratio with increasing numbers of transfusions ($p < 0.05$).

A high frequency of genetic polymorphism of the OKT4 antigen was noted in blacks. Lymphocytes of 3/7 black infants failed to react with OKT4 mo ab but had normal reactivity with mo ab OKT4A. Incubation with thymic epithelial monolayers and thymosin fr. V failed to induce the T4 antigen on these lymphocytes which were otherwise functionally normal. Family studies suggest that transmission of this feature may either be autosomal dominant or recessive. Cautious interpretation of T cell subsets is advised in blacks and in infants given multiple transfusions.

1001 DEFECTIVE IMMUNOREGULATION IN CHILDREN WITH PERSISTENT MIDDLE EAR EFFUSION.

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Otitis media and middle ear effusions (MEE) are most common clinical problems in early childhood for which an estimated one million tympanostomies are performed each year in the US. Although many factors have been associated with MEE (age, sex, genetics, otitis media, socioeconomic status, feeding style, atopy or hypersensitivity, a certain bacteria and viruses), a defective immunoregulatory mechanism in the host may also contribute to the pathogenesis. During the past 2 years, we have evaluated immune function in 78 randomly selected children who underwent tympanostomy for persistent MEE. The T-cell subset ratio (OKT-4/OKT-8) was reduced (below 1.25) in 30%. In 8 children, generation of T-cell growth factor (IL-2) by peripheral blood lymphocytes (PBL) was evaluated and found to be decreased in all; below 50 units (normal 50-180 units). The mitogenic response to PHA stimulation was normal in most cases. The subsets of lymphocytes were examined in the tonsils from those patients who underwent tonsillectomy at the time of tympanostomy. The tonsillar lymphocytes had an increased ratio of T-4/T-8 and an increased proportion of B-cells as compared to the matched PBL. Imbalance of T-cell subsets and decreased production of IL-2 indicate a defective immunoregulatory function in some of these children, which may play a role in the pathogenesis of persistent MEE. (Supported in part by USPH grant DE-05505).