ABSTRACTS

Meeting of The American Pediatric Society and The Society for Pediatric Research

Atlantic City, New Jersey, May 2, 1970

SPECIAL SESSIONS

- 1 *Anti-DNA Antibodies and Virus-like Structures in the Renal Disease of Systemic Lupus Erythematosus.* THEODORE PINCUS and JOSEPH A. BELLANTI, NIH, Bethesda, Md., and Georgetown Univ. Sch. of Med., Washington, DC.

Four patients, two males and two females, ages 12-16 years, with systemic lupus erythematosus (SLE) were found to have active renal disease. All had reduced serum complement (C') and high levels of antibodies to DNA, as measured by the radioactive DNA ammonium-sulfate precipitation method. With improvement in clinical condition and renal function, all four patients showed a significant rise in serum C' levels and reduction in antibodies to DNA. In three cases these changes occurred with the institution of corticosteroid therapy and in the fourth while this therapy was tapered. A renal biopsy from the most-recently-studied patient who had not received prior corticosteroid or immunosuppressive therapy was examined by electron microscopy. Myxovirus-like structures, similar to those described recently in SLE, were observed in capillary endothelial cells. These studies corroborate evidence for the possible role of immune complexes involving nucleic acids in the pathogenesis of SLE nephritis, and support the possibility for the presence of a viral agent in untreated disease.

- 2 *Clinical Correlates of Serum IgE in Asthmatic Children.* LATA KUMAR, RICHARD W. NEWCOMB, KIMISHIGE ISHIZAKA and ELLIOTT MIDDLETON, Jr., Children's Asthma Res. Inst. and Hosp., Denver, Colo. (introduced by David Pearlman).

Serum IgE levels were measured by radioimmunoassay in 116 asthmatic patients aged 6-16 years, and were compared to their clinical profiles. The IgE level was ≤ 700 ng/ml (normal) in 86 children and > 700 ng/ml (high) in 30. The incidence of positive skin tests was directly related to high IgE levels ($p < 0.01$). Of 94 children without eczema, 76 had normal values, whereas 12 of 22 children with eczema had high IgE concentrations ($p < 0.01$). Of 57 children receiving systemic corticosteroid therapy, only 5 had high IgE levels in comparison with 25 of 59 patients not on steroids ($p < 0.001$). History, skin sensitivity and bronchial challenge to allergens enabled us to classify 79

children into an 'extrinsic' or 'mixed' group (65) or an 'intrinsic' group (14). Of the 'extrinsic' or 'mixed' group, high IgE levels were found in 24, of whom only 3 were receiving steroids, whereas 21 of the 41 with normal IgE levels were on steroids ($p < 0.01$). All 14 'intrinsic' had normal levels; 10 of these were on steroids. No significant correlations were found with several other measured clinical attributes. Repeated measurements of serum IgE concentrations revealed consistent values over a 4-month period in most children, however significant variation occurred in some.

These data indicate a direct relationship of IgE level to incidence of positive skin tests and presence of eczema, but a reciprocal relationship to systemic corticosteroid therapy, even in so-called 'extrinsic' or 'mixed' asthma. (Supported by USPHS grants AI-08500, FR 5523 and a Hartford Foundation grant.)

- 3 *Ataxia-telangiectasia and Autoimmunity.* ARTHUR J. AMMANN and RICHARD HONG, Univ. of Wisconsin Med. Center, Dept. of Pediatrics, Madison, Wisc.

The ataxia-telangiectasia (A-T) syndrome consists of multiple abnormalities of the neurologic, vascular, endocrinologic and immunologic systems. Any postulate regarding the pathogenesis of the clinical syndrome must explain the multiple system involvement and account for the progressively more widespread and severe involvement with time. Some of the features of this syndrome might be explained if an autoimmune process were operative.

17 patients with A-T, ages 4 to 39 years, were studied for laboratory evidence of autoimmune phenomenon. The following investigations were performed: rheumatoid factor, anti-IgA antibodies, anti-deoxy-nucleoprotein antibodies, anti-thyroglobulin antibodies and fluorescent antibodies directed against the stomach, muscle, adrenal, pituitary, ovary, testis and thymus. 12 of 17 patients demonstrated 1 or more of the above antibodies. One patient was positive for rheumatoid factor, 6 patients without serum IgA had anti-IgA antibodies, 2 had antithyroid antibodies and 2 had anti-muscle antibodies. Especially striking was the finding of anti-IgA antibodies in 3 patients with

normal serum IgA levels. 30 age-matched controls were negative for all the above tests.

The fundamental defect in A-T is probably immunologic. An altered immunologic response could lead to multiple system disease as a direct result of autoantibody destruction. It is also possible that deficient immunity may permit an infectious agent to cause widespread tissue damage with secondary production of autoantibodies. (Supported by NIH AI-07726 and National Tuberculosis Foundation.)

- 4 *Nasal Immunization of Asthmatic Children With Killed Influenza Vaccine.* RICHARD W. NEWCOMB and JERRY ELLER, Children's Asthma Research Inst. and Hosp. and U.S. Army Med. Res. and Nutrition Lab. (introduced by David Pearlman).

Since exocrine antibodies are produced and secreted in the nose in response to local antigens, and may be important for local immunity, we investigated the effectiveness and safety of nasal vaccination with a killed influenza virus (monovalent 'Hong Kong' strain) in 12 children with asthma and 2 normal adults. Significant hemagglutination-inhibition (HAI) and neutralizing antibody activities occurred in serum and nasal fluids of all subjects whether given 2 doses of antigen nasally, or one subcutaneously, then one nasally. Serum and nasal fluid titers were highest, however, in unvaccinated, naturally infected children. No adverse reactions to the killed virus were found; specifically, no aggravation of asthma, no increased sensitivity to bronchoconstricting chemicals, and no sensitization to egg antigen were discovered. Fractionation of nasal fluids by gel filtration revealed that most HAI and neutralizing antibody activity accompanied exocrine γ A. Reduction and alkylation of these fractions sufficient to convert 11S exocrine γ A to 7S γ A decreased both antibody activities, but the activities of γ G-rich fractions were not thus decreased.

These data suggest that nasal immunization with killed influenza virus is both safe and effective in producing nasal antibody in asthmatic children, although no conclusions can be drawn regarding whether the antibody levels attained are protective, or how long they will persist. (Supported by USPHS grant AI-08500 and NIAID contract PH 43-62-477.)

- 5 *A Sensitive Microtiter Test for Detecting Rheumatoid Factor in Children.* JOHN KATTWINKEL and REBECCA H. BUCKLEY, Duke Univ. Sch. of Med., Durham, N.C.

Serologic tests helpful in confirming rheumatoid arthritis in adults are most often negative in juvenile rheumatoid arthritis (JRA). Since rheumatoid factors (RF) have been shown to have iso- as well as hetero-antigenic specificities, this study was designed to determine whether a test employing human gamma globulin with a number of isoantigenic determinants would permit more frequent detection of RF. Human O, Rh+RBC were sensitized with an incomplete anti-D antibody (Ri) known to be positive for a number of Gm isoantigens. Dilutions of sera (heated at 56°C for 30 min) were made in V-bottomed microtiter plates, 0.1% (Ri) cells added, the plates centrifuged and tilted 35° from the vertical for 20-30 min before reading. Sera from children with no disease, acute rheumatic fever (ARF) and JRA were tested with sensitized sheep cells (SSC), the Hyland latex slide test, and (Ri) cells. A titer of 1:32 was considered positive for the SSC and (Ri) tests.

Results

	No. of chil- dren	Average age	(Ri) Cells+	SSC+	Latex+
Controls	37	8.3 yr	4 (11%)	3 (8%)	0
ARF	10	8.9 yr	0	0	0
JRA	11	7.8 yr	5 (46%)	3 (27%)	2 (18%)

The findings confirm those of others showing a low but definite incidence of RF in normal children. The (Ri) test detected RF more frequently in JRA than the SSC and latex tests. The data suggest: (1) the (Ri) test may be helpful in the differential diagnosis between ARF and JRA, and (2) with the significantly ($p < 0.005$) higher percentage of (Ri) positive reactors in the JRA group that this test may be a more sensitive laboratory aid than those presently available for confirming JRA.

- 6 *An in vitro Test for Detection of Specific IgE-mediated Penicillin Reactions in Children.* ZACK H. HADDAD and JOEL KOROTZER, Los Angeles County-University of So. Calif. Med. Center, Dept. of Ped., Los Angeles, Calif. (introduced by John James).

The diagnosis of untoward immediate hypersensitivity reactions to penicillin(s), thus far had to be made presumptively on, at best, subjective clinical impression for lack of a simple, rapid, sensitive, reliable and reproducible *in vitro* immunological test. The objective of this work aims at fulfilling most of these criteria. Sera from 20 children clinically sensitive to penicillin and/or ampicillin, were incubated on a slide with a suspension of rat mast cells and various concentrations of penicillin, ampicillin, or penicilloyl-polylysine, under optimal conditions of pH and temperature. The cells were then examined microscopically for degranulation. A total number of 100 cells were counted over several randomly selected fields. The same model also was employed, using a monospecific goat antiserum to human myeloma IgE, instead of the specific drug. On incubation of equal volumes of cell suspension and serum from sensitive children, both the suspected drug and anti-IgE caused *specific* degranulation of the cells in a statistically significant fashion: average number of degranulated cells in presence of sensitive sera and drug or anti-IgE was 3-4 times the number of altered cells in the absence of drug or anti-IgE, or in the presence of equivalent concentrations of anti-IgG, IgA, and IgM. Control sera from nonsensitive matched children caused no significant degranulation. Our data indicate that: 1. This *in vitro* test can be used for rapid detection of penicillin-specific IgE antibodies. 2. Human IgE can sensitize rat cells *in vitro*, affording a test which may obviate skin testing for penicillin allergy in children.

- 7 *In vitro Transformation of Cord Blood Lymphocytes by Antigens.* SANFORD LEIKIN, Children's Hosp. of D.C., and Geo. Washington Univ. Sch. of Med., JACQUELINE WHANG-PENG, NCI, Bethesda, Md., and JOOST J. OPPENHEIM, NIDR, Bethesda, Md.

Newborn human lymphocytes respond vigorously to immunologically specific stimulation with homologous cells in mixed leukocyte cultures and to non-specific stimulants. Certain maternal infections can be transmitted to the human fetus and induce antibody produc-