

697 CONGENITAL LEUKOCYTE MOVEMENT DISORDER AND RECURRENT INFECTIONS. Thomas H. Howard, Jerry A. Winkelstein, Min-Fu Tsan, William H. Zinkham. The Johns Hopkins

Hospital, Departments of Pediatrics and Medicine, Baltimore, Md. A 4½ month old black female with omphalitis at 4 days of age, recurrent infections of the skin, an acquired rectovaginal fistula, marked lymphadenopathy proximal to sites of infection and delayed wound healing had a peripheral WBC count of 70-100,000/mm³ with 70% PMN's and 10% monocytes. PMN's were absent in exudates of infected areas and a Rebuck skin window at 4, 8 and 12 hours. A chemotactic assay under agarose revealed absent directed movement and decreased non-directed movement of PMN's and monocytes. Zymosan activated serum from both patient and normal controls attracted normal cells to the same degree. No serum, plasma or cellular inhibitor to normal PMN movement was found. The patient's mean PMN velocity by direct observation was 2.4 μ/min. (control 11.9 μ/min.) and her mean monocyte velocity was 2.1 μ/min. (control 4.5 μ/min.). By light microscopy the patient's cells formed multiple, small lamellipodia without developing a single dominant lamellipodium; electron microscopy of the cells was normal. Associated findings included marked pancytopenia with an IgE of 2600-4300 ng/ml. Assays of the phagocytes' metabolic, phagocytic and bactericidal functions, T and B cell functions and complement system were normal. This black child with severe infections from birth, a markedly elevated IgE without allergic symptoms and defective movement of both PMN's and monocytes represents a congenital and possibly genetically determined abnormality of cell mobility.

698 HUMORAL AND CELLULAR IMMUNE RESPONSES TO PRP. Virgil M. Howie, John H. Ploussard, David H. Smith, Porter Anderson, John L. Sloyer, Jr., Univ. of Ala., Huntsville, Ala. and Children's Hospital, Boston, Mass.

Immune responses to Hemophilus influenzae, type b, polyribo-phosphate (PRP) were studied in 4 infants vaccinated at 6 months with 3 injections of PRP spaced 2 to 3 weeks apart. The injections totaled 1.6 μgm of PRP mixed with 0.2 μgm of cellular protein. Antibody to PRP was assayed by the Farr technique. Cellular responses were evaluated by incubating peripheral blood lymphocytes with several dilutions of pure PRP or PRP with protein and assaying for either protein or DNA synthesis. Generally significant increases in antibody to PRP were not seen as a result of this vaccination. No pre or post-vaccination lymphocyte cultures displayed increased DNA synthesis to the various dilutions and preparations of PRP tested. On the other hand, post-vaccination lymphocyte cultures from 2 infants displayed increased protein synthesis to pure PRP and one of these infants reacted similarly to PRP-protein. A third infant had significant pre-vaccination stimulation of protein synthesis and remained so following vaccination. The significance of cellular immune responses to PRP is unknown, however since antibody to PRP is not normally generated in the young infant, evaluation of both humoral and cellular immune responses may reveal additional mechanisms of immunity to infection with H. influenzae.

699 MIXED CONNECTIVE TISSUE DISEASE IN CHILDREN. Jack H. Hutto and Elia M. Ayoub, University of Florida College of Medicine, Dept. of Pediatrics, Gainesville.

Mixed connective tissue disease (MCTD) is a collagen-vascular disease with multiple organ system involvement. MCTD is characterized by clinical features of systemic lupus erythematosus, scleroderma, and dermatomyositis. Serological characteristics include absence of anti-DNA but presence of antibody to extractable nuclear antigen-(ENA) in titers >1:10,000 (Sharpe et al, Am. J. Med. 52:148, 1972). We are aware of reports on only two children with this disease. Six children with MCTD have been seen by us, four females and two males between 7 and 19 (mean=13) years of age. All six patients had symptoms or laboratory values suggestive of myositis indistinguishable from childhood dermatomyositis. All patients had Raynaud's phenomenon. Four patients were suspected of having nephritis based on hematuria and/or proteinuria; this was confirmed in two patients by percutaneous renal biopsy. One patient responded to salicylates. Four of 5 patients treated with daily prednisone, 2 mg/kg, had resolution of symptoms of arthritis, myositis, Raynaud's phenomenon and all evidence of nephritis. The fifth patient developed peripheral vasculitis while receiving prednisone. MCTD may be more common in children than previously recognized and may mimic a variety of collagen vascular disorders in its presentation. Anti-ENA is essential in the diagnosis of this disease. Therapy with salicylates should be initiated on patients without nephritis. Cases with nephritis and those recalcitrant to salicylates, should receive steroid therapy.

700 IMMUNOGLOBULIN PRODUCTION IN SEVERE COMBINED IMMUNODEFICIENCY DISEASE (SCID) AFTER THYMUS EPITHELIAL EXPLANT THERAPY. J.F. Jones, O.F. Sieber, J. Pinnas,

R. Hong, V.A. Fulginiti, University of Arizona, Tucson and University of Wisconsin, Madison. The development of immunoglobulin production in a child with autosomal recessive ADA+ SCID after therapy with cultured thymus epithelial cells is reported. The child is unique because she had not received gamma globulin or plasma prior to transplant while in laminar flow isolation. Transplacental IgG decreased to 2.7 mg/dl at 9 months of age, or 28 days post-transplant (PT). A steady increase of IgG began at 37 days PT, with IgA appearing at 70 days as determined by immunoelectrophoresis (IEP) and radial immunodiffusion (RID). IgM appeared 12 weeks PT on the surface of lymphocytes, 7 days prior to its detection in the serum. Five months after therapy IgG was 2030 mg/dl, IgM was 29 mg/dl, IgA was 55 mg/dl and IgA in lacrimal fluid was 3.2 mg/dl. Initial IEP patterns with polyvalent antisera to IgG had 3 distinct overlapping arcs, gamma chain had one arc, kappa had 2 arcs and lambda and alpha each had one arc. Kappa chains were in excess over lambda. Repeated IEP over 3 months continue to show multiple arcs but IgG arcs are now joined and IgM is present. The "reversed" order of appearance of IgG and IgM may be related to: a) the underlying defect; b) lack of antigenic stimulation during the first year of life; or c) this form of immune therapy. The joining of the multiple precipitin lines may represent normal development of immunoglobulin. This case stresses the necessity for thymus function in immunoglobulin production in SCID patients.

701 THYMOSIN RESPONSIVE NULL CELLS EXPRESS HUMAN T LYMPHOCYTE ANTIGENS. Joseph Kaplan, Wayne State

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Null cells, lymphocytes which are both E rosette negative and surface Ig negative, express either human T lymphocyte antigens (HTLA antigens) or human B lymphocyte antigens (HBLA antigens). To determine if one or both of these null cell subsets contain T cell precursors, 5 separate null cell enriched suspensions (each containing fewer than 10% E rosette positive or surface Ig positive cells) were first treated with anti-HBLA or anti-HTLA antisera and complement, and then incubated with or without thymosin for 2 hours and tested for % E rosettes.

Thymosin induced an increase in % E rosettes (13±4%) in null cell suspensions depleted of HBLA⁺ cells by anti-HBLA + C' but did not induce an increase in % E rosettes (1±1%) in null cell suspensions depleted of HTLA⁺ cells by anti-HTLA + C'. This strongly suggests that some, if not all, HTLA⁺ null cells are precursors of mature E rosette-positive T cells.

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702 COMPARISON OF E ROSETTE NEGATIVE AND E ROSETTE POSITIVE T CELL SUBSETS. Joseph Kaplan, Ricardo Bernales, Susumu Inoue and Mark Ottenbreit, Wayne State

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Like E rosette positive (E⁺) T cells, a subpopulation of null cells express human T lymphocyte antigens (HTLA antigens). To shed light on the relationship of E⁺HTLA⁺ and E⁻HTLA⁺ cells we compared their prevalence in newborns vs adults, their cell size distribution and their spontaneous ³H-thymidine uptake.

Compared to adults, newborns had lower proportions of E⁺HTLA⁺ (newborns 61±9% vs adults 73±11%, p < 0.05) and higher proportions of E⁻HTLA⁺ cells (newborns 15±12% vs adults 3±2%, p < 0.05).

By velocity sedimentation analysis, 52% of E⁻HTLA⁺ had sedimentation rates > 5mm/hr. By comparison, only 16% of E⁺HTLA⁺ lymphocytes had sedimentation rates > 5mm/hr.

Lymphocyte suspensions depleted of B cells by nylon fiber column filtration and containing both E⁺HTLA⁺ and E⁻HTLA⁺ cells had 18 hr spontaneous ³H-thymidine uptakes of 2417±1879 cpm/10⁵ cells. By contrast the ³H-thymidine of purified E⁺HTLA⁺ cells obtained by gradient separation of E rosetting cells was 836±359 cpm/10⁵ cells.

These findings indicate that the E⁻HTLA⁺ cell subset consists of large, dividing cells which are prevalent in the blood during the neonatal period. (Supported by USPHS NIH Grant CA 17534 and Contract 1-CP-33333. J. Kaplan is recipient of NIH Research Career Development Award CA 00188).