PRIMARY MACROGLOBULINEMIA IN A CHILD. Robert W. Reid, Lester Weiss, Thomas Fraher, Elliott F. Osserman. Depts. of Medicine and Pediatrics, Henry Ford Hospital, Detroit/ Dept. of Medicine, College of Physicians & Surgeons, Columbia University, New York.

A four year old girl (consanginous parents) with primary macroglobulinemia was followed for 3 years. She presented with cogenital hypotonia, recurrent infections, splenomegally, eosinophilia and increasing serum IgM to 4 grams percent. The serum protein electrophorectic pattern revealed three distinct gamma spikes, two of which were seen in the concentrated urine. A high molecular weight IgM with both kappa and lambda determinants was isolated from the serum indicating at least a biclonal dyscrasia. More lambda than kappa light chains were associated with the IgM on immunoelectrophoresis. The abnormal IgM has euglobulin, cryoglobulin, absent isohemagglutinins, and high anti-IgG activities with low serum complement levels. The initially normal serum IgA fell to zero. Impaired IgG antibody responses were found. Progressive cell-mediated immune deficiency is suggested by an uncomplicated smallpox vaccination at one year followed by persistent mucocutanous candidiasis with a negative delayed skin test to candida and a impaired PHA response of the peripheral lymphocytes at 4 yrs.. This is the first described case of primary macroglobulinemia in a child. The abnormal serum IgM level progressively fell with chlorambucil therapy.

SUBACUTE SCLEROSING PANENCEPHALITIS AND MEASLES VACCINE, John L. Sever, Jonas H. Ellenberg, Helen M. Krebs, and J. T. Jabbour, Nat. Insti. of Neurological Diseases and Stroke, NIH, Bethesda, Maryland and Dept. of Neurology, Univ. of Tennessee, Memphis, Tennessee.

The mean interval between measles and onset of subacute sclerosing panencephalitis (SSPE) is approximately 6 years. Death usually occurs in 6 to 12 months thereafter. Measles virus may be recovered from brain tissues at time of biopsy and autopsy. High measles antibody titers are present in the serum and spinal fluid. The use of killed and live measles vaccines for young children has introduced the possibility that the vaccines may cause the disease or stimulate expression of a latent infection. A history of measles infection was documented in 114 of the 200 patients with SSPE. The mean incubation period between time of measles infection and onset of SSPE was 6 years + 2.5 years. The administration of measles vaccine following measles infection did not effect this interval. In this population there was no evidence that measles vaccine shortened the "incubation period" of SSPE.

ALTERATION OF HUMAN T-CELL FUNCTION AFTER THYMIC IRRADIATION. Christian H.L. Rieger, Sumner C. Kraft and Richard M. Rothberg University of Chicago Hospitals, Departments of Pediatrics and Medicine, Chicago, Illinois 60637.

Lymphocyte responses and delayed skin reactions were studied in 12 healthy adults given thymic x-irradiation in childhood and in a 7-year-old female (K.W.) whose mother received ^{131}I early in pregnancy. The adults' lymphocytes responded normally to PHA, Vaccinia and PPD, but poorly to Candida. The mean stimulation index to Candida of the 8 subjects who were irradiated at < 1 year of age was 2.2 (controls 10.4; $p < 0.01$). The skin responses of all 12 adults to Candida were poor with a mean induration of < 0.5 cm^2 (controls 3.1 cm^2; $p < 0.005$). The lymphocyte and skin responses correlated in 13 of 14 healthy controls, but only in 5 of 12 irradiated adults. Three of these 5 were anergic despite the presence of Candida precipitins in the serum of two. The child, K.W., was born athyrotic and had 13 nonbacterial pneumonias. She was vaccinated successfully at age 1, had normal serum immunoglobulins, and responded to streptococcal infections with an anti-Streptokinase titer of 1:640. Her lymphocytes responded to PHA but not to Vaccinia, PPD, Candida or Streptokinase/Streptodornase, and she was anergic to the latter 3 antigens on repeated skin testing. These data suggest that irradiation to the thymus early in life can induce T-cell lesions similar to those seen in certain disease states, e.g., chronic mucocutaneous candidiasis. However, except possibly in K.W., immune defense mechanisms appear unaltered after thymic irradiation.

DEPRESSED LEVELS OF ANTIBODY TO GROUP A STREPTOCOCCAL CARBOHYDRATE IN JUVENILE RHEUMATOID ARTHRITIS. Stanford T. Shulman and Elia M. Ayoub, Univ. of Fla. Dept. of Ped., Gainesville.

Reports of increased β-N-acetylglucosaminidase (β-NAGase) activity, the enzyme responsible for degradation of streptococcal A carbohydrate (A-CHO), in patients with collagen disease prompted study of the antibody response to A-CHO in 41 patients with juvenile rheumatoid arthritis (JRA). Antibody titers to two streptococcal protein antigens, streptolysin O (ASO) and desoxyribonuclease B (anti-DNAse B), as well as antibody levels to A-CHO (A-antibody) were assayed on JRA sera obtained prior to anti-inflammatory therapy and on matched controls. While no significant difference in ASO and anti-DNAse B response was found, A-antibody levels were significantly lower among JRA patients (mean antibody levels: 0.25 vs. 0.43, $p < 0.01$). Comparison of those JRA patients and controls with high ASO and/or anti-DNAse B titers revealed elevated A-antibody in 12/15 (80%) of controls and in only 3/10 (30%) of JRA patients ($p = 0.01$). Studies on 21 patients with other collagen vascular diseases (excluding rheumatic fever) failed to show similar differences. Isohemagglutinin levels performed to date on six JRA patients were normal, suggesting that JRA patients do not have a generalized inability to respond to carbohydrate antigens. The depressed A-antibody levels in JRA patients may be due to increased β-NAGase activity and prompt degradation of A-CHO following infection.

IMMUNEDEFICIENCY IN FEMALE SIBLINGS. Martin L. Schulkind, Jaime Frias, and Elia M. Ayoub. Dept. of Ped., Univ. of Fla. Col. of Med., Gainesville, Fla. 32610.

Although the familial occurrence of primary immunedeficiencies is not uncommon, the occurrence of immunedeficiencies among female family members is unusual. Most cases of familial immunedeficiencies occur in male siblings and usually obey an x-linked recessive mode of determination.

Data are presented on two sisters with identical primary immunedeficiencies. One sister presented with recurrent otitis, pyoderma, and H. influenzae ventriculitis. The second sister presented with what appeared to be pauciarticular rheumatoid arthritis. Both sisters had identical findings of decreased concentrations of IgG and IgA, normal concentrations of IgM, deficient antibody production, and absent lymphoid follicles and germinal centers in their lymph nodes, in the presence of normal cell-mediated immunity. These data are consistent with the diagnosis of primary immunedeficiency with hyper-IgM (dysgammaglobulinemia, type I) appearing for the first time in sisters. Chromosomal analysis revealed both sisters to have normal female karyotypes and study of the family pedigree failed to reveal consanguinity. This immunedeficiency probably represents a previously undescribed autosomal recessive form of primary immunedeficiency with hyper-IgM.

SPONTANEOUS EVOLUTION OF IMMUNE COMPETENCE IN DIGEORGE SYNDROME Otto F. Sieber, Jr., Brian G. Durie, Brack G. Hattler, Sydney E. Salmon, Vincent A. Fulginiti. Univ. of Az., Coll. Med., Univ. Hosp., Depts. of Ped., Med., and Thorac. Surg., Tucson.

Thymic hypofunction and increased susceptibility to infection in the DiGeorge Syndrome have been associated with reduced humoral and cellular immunity. As a result, thymic transplantation has been utilized to modify immune responses, with improved lymphocyte responsiveness to mitogens and antigens being attributed to the effects of therapy.

Over the past year we have studied a male infant with the DiGeorge syndrome as documented by 1) characteristic facies, 2) neonatal hypocalcemic tetany, 3) absent thymic shadow, 4) quintallogy of Fallot, 5) antibody deficiency and 6) cellular immune dysfunction. During observation in reverse isolation, serial studies showed spontaneous acquisition of normal levels of serum immunoglobulins and cell mediated immunity as measured in vitro with phytohemagglutinin, concanavalin A, pokeweed and staphylococcal antigens. Macrophage inhibitory factor and interferon were produced. Sheep RBC - lymphocyte "T-rosettes" have remained decreased. At one year of age parathormone levels and growth are normal. Only recurrent otitis media and one episode of pneumonia have occurred.

Significantly, we have documented progressive spontaneous improvement in immuno-responsiveness without immunotherapy or transplantation. Thus, spontaneous recovery may occur in selected patients with DiGeorge syndrome, and careful observation of such infants may avoid unnecessary transplantation.