920 EFFECTS OF STEROID HORMONES ON IMMUNOGLOBULIN PRODUCTION IN ADULT AND CORD BLOOD LYMPHOCYTES. Jane Grayson, Nancy J. Dooley, Irma R. Koski, and R. Michael Blaese, National Institutes of Health, Bethesda, Maryland

The effect of steroid compounds on the in vitro production of immunoglobulins was evaluated in cultures of peripheral blood mononuclear cells (PBMC). In a reverse hemolytic plaque assay the addition of 10^{-5} to 10^{-8} M hydrocortisone to adult PBMC's in the absence of other stimulants or mitogens resulted in the dramatic induction of immunoglobulin secreting cells (IgSC). This response ranged from a 2-70 fold increase, comparable to or greater than that produced by pokeweed mitogen. Stimulation of IgSC by steroids was first seen after 48 hrs in culture and peaked at 8-10 days. IgG, IgA, and IgM production were all enhanced. All glucocorticoids evaluated, but not androgens, estrogens or steroids not binding to the glucocorticoid receptor, were capable of mediating this effect. The induction of IgSC was dependent on both T cells and monocytes. Glucocorticoids did not stimulate a detectable proliferative response in the cultures. In contrast to the above findings with adult cells, no enhancement of IgSC production could be demonstrated by cord blood lymphocytes at any time during culture or at any dose of steroid compound evaluated. Cord blood could produce IgSC when stimulated with Epstein-Barr virus. The capacity of glucocorticoids to stimulate functional maturation of adult B cells to become IgSC in the absence of cellular proliferation, while being unable to stimulate cord blood B cells, suggests that glucocorticoids may be functioning as maturation agents for memory B cells.

921 IMPROVED LYMPHOCYTE STIMULATION AFTER KETOCONAZOLE TREATMENT FOR CHRONIC MUCOCUTANEOUS CANDIDIASIS (CMC) Randall M. Goldblum, Jon T. Mader, James A. Reinarz. The University of Texas Medical Branch. Galveston, Texas.

The role of infection in the immunodeficiencies of CMC was investigated by monitoring immune function during treatment with the new antimycotic ketoconazole. Cellular and humoral immunity was evaluated before, during, and after 6 months of therapy in 5 patients (age 3-9 yrs). Prior to therapy, 5 patients had diminished lymphocyte stimulation to antigen, 4 had serum inhibitors of lymphocyte stimulation, 2 had low IgA class antibodies to candida and other antigens, and 1 was IgA deficient.

All responded to treatment with rapid clearing of mucosal and skin lesions. There were no consistent changes in serum immunoglobulins or class specific antibodies to candida or E.coli O antigens or in blood lymphocyte subpopulations. However, mitogen response increased ($\bar{x}$=1.8 fold pre-treatment) and serum inhibition of this response decreased during treatment. Stimulation indices increased in cultures with candida ($\bar{x}$=11 fold) and SK-SD ($\bar{x}$=6.2 fold) but the patient's sera continued to inhibit these responses. When treatment was discontinued in 3 patients during or after 6 months of therapy, candidal stomatitis recurred.

Since treatment of CMC patients with ketoconazole improved the responsiveness of lymphocytes to antigenic stimulation without removing the serum inhibitory capacity, these 2 mechanisms may be dissociated. Infection-independent and infection-dependent mechanisms appear to be involved; however, a direct role of ketoconazole on the immune system cannot be excluded.

922 TREATMENT OF MURINE AND HUMAN BONE MARROW WITH MONOCLONAL ANTIBODIES TO T LYMPHOCYTES TO PREVENT GRAFT VERSUS HOST DISEASE (GVHD). Brian Hamilton, Jeffrey M. Lipton, and Robertson Parkman, Division of Pediatric Oncology, Sidney Farber Cancer Institute and Divisions of Hematology and Immunology, Children's Hospital Medical Center, Boston, Massachusetts, 02115.

GVHD is the major limitation to human allogeneic bone marrow transplantation (BMT). A murine model of BMT was developed to study acute and chronic GVHD due to non-major histocompatibility region (MHR) antigens. Lethally irradiated C57Bl/6 mice were transplanted with bone marrow and spleen cells from LP mice. When recipients were transplanted with 1-10 X 10^6 spleen cells in addition to 10 X 10^6 bone marrow cells, 31 of 91 animals developed acute GVHD, 19 chronic GVHD, and 41 no GVHD. The in vitro removal of mature T lymphocytes by treatment with a monoclonal antibody to murine T lymphocytes and complement eliminated GVHD in all of 50 recipients. Recipient mice developed normal hematocrits, adult hemoglobin electrophoretic patterns, and normal T cell function by three months. Human bone marrow cells treated with a monoclonal antibody to mature T lymphocytes (OKT-3) and complement had no residual detectable T cells as determined by E-rosette formation (16% pretreatment; 0%, post-treatment) or by indirect immunofluorescence(17% pre; 0% post). The total number of nucleated cells was reduced by 50% during treatment with no decrease in the frequency of hematopoietic precursors (BFU-E colonies). The use of monoclonal antibodies to remove mature T lymphocytes from human bone marrow may be an effective method to prevent human GVHD.

923 HETEROGENEITY OF ALLELIC EXCLUSION IN WISKOTT-ALDRICH SYNDROME CARRIERS. John B. Harley, W. James Gealy, and John M. Dwyer. Yale Univ. School of Medicine, Dept. of Internal Medicine, New Haven. (Spon. by Michael R. Blaese)

Further studies on the carriers of the Wiskott-Aldrich Syndrome were performed. Three carriers (mothers) of this X-linked disorder were found who were heterozygous for the A and B isoenzymes of glucose-6-phosphate dehydrogenase (G6PD). Major cell types of their peripheral blood were purified; then the presence of the G6PD isoenzymes A and B was determined by an electrophoretic assay and compared to similarly prepared cells from normal control G6PD heterozygotes.

Carrier	#1	#2	#3	all controls
erythrocytes	AB	B	A	AB
granulocytes	AB	A⁻B	AB	AB
monocytes	AB	A⁻B	--	AB
T lymphocytes	B	B	A	AB
non T lymphocytes	AB	A⁻B	AB	AB
platelets	B	B	A	AB

There are two different patterns of allelic exclusion in the carriers studied. The pattern in carrier #1 shows allelic exclusion in platelets and T lymphocytes, whereas carriers #2 and #3 in addition show exclusion in erythrocytes. This finding is consistent with one of two conclusions: either there is variable phenotypic expression of the Wiskott-Aldrich defect among carriers or, alternatively, more than one genetic defect can cause the Wiskott-Aldrich Syndrome.

924 DIMINISHED T-LYMPHOCYTE COLONY FORMING CAPACITY OF HUMAN CORD BLOOD CELLS. Henry G. Herrod and William R. Valenski. (Spon. by Fred F. Barrett). University of Tennessee Center for Health Sciences, Department of Pediatrics, Memphis, TN, 38163.

Some aspects of cell-mediated immunity in newborns are normal while others are reported to be altered. We have evaluated cord blood mononuclear cells (MC) for their capacity to form T-lymphocyte colonies when stimulated with PHA. Compared to values obtained from blood MC from 15 normal adults, cord blood MC from 25 subjects demonstrated decreased colony formation (1351 ± 644 versus 592 ± 501, $p < 0.05$). This diminished colony forming capacity was not associated with impaired responsivenss to PHA nor to excessive suppressor cell activity. Depletion of adherent cells reduced cord blood MC colony formation by 39% (411 ± 186 versus 251 ± 196) while not affecting lymphocyte proliferation in liquid culture (233,294 cpm versus 279,171 cpm). Irradiation of cord blood cells with 125 R reduced colony formation by 78% (279 ± 139 versus 56 ± 67). Lymphocyte proliferation again was not affected. In contrast, the colony forming capacity of adult MC was not altered by either adherent cell depletion or irradiation. These results indicate that the progenitor cells of T-lymphocyte colonies in cord blood have distinct biologic characteristics when compared to colony progenitors present in normal adult blood. This assay may prove to be useful in our efforts to understand the differentiation of T-cell function in man.

925 PLASMAPHERESIS IN ADOLESCENT MIXED CONNECTIVE TISSUE DISEASE(MCTD). Alex Hertzman, Gilberto E. Rodriguez, David E. Sharp and Charles L. Cooke (Spon. by Harold M. Maurer) Medical College of Virginia/Virginia Commonwealth/ University, Department of Pediatrics, Richmond, VA

MCTD is more severe in children than in adults. Since children are more susceptible to long term corticosteroid side effects, we treated a 12 y/o white female with biweekly plasmapheresis, and induced remission of her MCTD. She presented with Raynaud's phenomenon of 5 months duration plus diffuse swelling of distal extremities. Three months later tender 1 cm. red nodules appeared in the anterior aspects of her legs. This was followed by anorexia, weight loss, and increasing weakness. Her fingertips were cyanotic, but did not have ulcers. There was moderate weakness of the proximal muscles without synovitis or limitation of motion. She had leukopenia, hypergammaglobulinemia, and elevated sedrate. SGOT was 155, and LDH 588 units. ANA was (+) at 1/6400 with a speckled pattern. ENA was (+) at 1/10,240, but only to RPN fraction. C_1Q of 2.4% was normal, but Raji cell assay was strongly (+). Anti$_{ds}$ DNA studies were negative. EMG revealed inflammatory findings became normal. On plasmapheresis q3w she has remained asymptomatic with normal lab titers. Her favorable responses suggest a wider use for this novel treatment in MCTD and other immune complex diseases of children.