721 ANALYSIS OF "NATURAL CYTOTOXICITY" IN IMMUNODEFICIENCY PATIENTS. David L. Nelson and Bonita M. Bundy (Spon. by R.M. Blaese), Metabolism Branch, NCI, NIH Bethesda.

Cytotoxicity occurring in vitro mediated by lymphocytes from non-immunized donors is termed "natural cytotoxicity"(NC) and studies in experimental animals have suggested that NC is related to immune surveillance in vivo. Therefore, we have investigated the NC effector cell potential of peripheral blood lymphocytes from a variety of immunodeficiency patients. Cytotoxicity was assessed employing ^{51}Cr labelled allogeneic Chang targets. NC effector cell activity was normal in patients with hypogammaglobulinemia (hypo-γ) (N=25), selective IgA deficiency (7), Wiskott-Aldrich syndrome (5), ataxia-telangiectasia (2), and dysgammaglobulinemia (3). NC activity was present inspite of profound functional deficiencies in T-cells and B-cells as assessed both in vitro and in vivo. Cytotoxic activity was present in hypo-γ patients with and without sIg bearing B-lymphocytes. NC effector activity was present in one patient with severe combined immunodeficiency and absent in a second such patient. This finding suggests that assessment of NC effector activity may provide unique insights into lymphocyte differentiative defects in some human diseases. The finding of normal NC activity in most immunodeficiency patients demonstrates that certain non-specific cellular effector mechanisms are preserved in patients lacking specific immunologic responsiveness and suggest that the increased incidence of neoplasia observed in these patients may not be attributable to defective immunologic surveillance.

722 LONGITUDINAL STUDY OF CELL-MEDIATED IMMUNITY (CMI) IN INTRAUTERINE GROWTH RETARDED (IUGR) INFANTS. Charlotte G. Neumann, John Zahradnick, Carter F. Newton, Jean Carney, E. Richard Stiehm, James D. Cherry, Hans Weber and Nimrod Bwibo, UCLA Public Health and Pediatrics, Los Angeles.

A longitudinal study was carried out from birth on 149 IUGR Kenyan infants and 111 controls to see if intrauterine malnutrition adversely affects CMI. Three birth weight (BW) groups were studied: 76 infants $<$ 2500 gms; 73 infants between 2500-2800 gms; 111 control infants $>$ 2800 gms. T-cell function was assessed by % rosette forming cells (RFC) with sheep erythrocytes (mean ± SD). Simultaneous nutritional studies were obtained. Studies were done on cord blood, at 6 to 7 mos. and at 12 mos. of age with 58% of the original group available at 6 to 7 mos. and 48% of the original group available at 12 mos. for follow-up. At birth the %RFC was 51.8 ± 12.6% in infants $<$ 2500 gm; 53.0 ± 12.2% in the 2500-2800 gm infants; and 60.2 ± 11.9% in the controls. Both IUGR groups were significantly lower than controls, $p < .05$. At 6 to 7 mos. partial recovery took place with the $<$ 2500 gm BW infants with %RFC of 56.6 ± 7.0%; 2500-2800 gm BW infants 57.8 ± 7.2% and control infants 58.6 ± 7.3%. At 12 mos. %RFC in the $<$ 2500 gm BW infants was 55.6 ± 8.3%; in the 2500-2800 gm BW infants 57.8 ± 9.7% and in the controls 60.1 ± 6.0%. The $<$ 2500 gm BW infant group was still significantly lower ($p < .05$) than the control group. Thus, there is a significant depression of CMI in IUGR infants $<$ 2500 gm and between 2500-2800 gm at birth with partial recovery but still showing significant differences from normal in the $<$ 2500 gm BW group by 12 mos. of age.

723 STEM CELL DEFECTS IN SEVERE COMBINED IMMUNODEFICIENCY (SCID). R. Pahwa, S. Pahwa, R.J. O'Reilly and R.A. Good, Memorial Sloan-Kettering Cancer Center, New York, N.Y.

Fractionated bone marrow cells from normal volunteers can regularly be induced to bear the human T-lymphocyte antigen (HTLA) marker to form E-rosettes and respond to concanavalin A (Con A) following coculture with normal thymic epithelial monolayers (TEM) or supernatants (SUP). T-cell differentiation done in this way on marrow cells of 5 patients with SCID revealed the following results:

# Patients	HTLA		E-Rosettes		ConA Response	
	TEM	SUP	TEM	SUP	TEM	SUP
3	+	+	+	-	-	-
1	ND	ND	+	-	-	-
1	+	+	-	-	-	-

+ = induction; - = no induction; ND = not done

Previously, Touraine et al found no induction of HTLA marker in the marrow of a patient with SCID after incubation with thymic extract suggesting absence of stem cells but Incefy et al showed that some patients may have stem cells inducible to HTLA but not to E-rosettes or functional markers. We conclude that in variants of SCID precursor cells are present but are arrested at different steps along the T-cell line. In T-cell differentiation HTLA marker probably appears before E-rosettes, followed by a state of responsiveness to mitogens. (Supported by grants CA-17404, CA-19267 and Judith Harris Selig Foundation)

724 FAILURE TO GENERATE PLAQUE FORMING CELLS (PFC) IN X-LINKED AGAMMAGLOBULINEMIA. Savita Pahwa, Rajendra Pahwa, Elizabeth Smithwick and Robert A. Good, Memorial Sloan-Kettering Cancer Center, New York, N.Y.

There have been recent suggestions in the literature that in x-linked agammaglobulinemia, precursor B-cells may be present in the marrow and, further, that the peripheral blood lymphocytes (PBL) can be stimulated to produce IgM under appropriate conditions. Utilizing a recently described hemolytic plaque assay (Fauci and Pratt, PNAS 73:3676, 1976) we studied the PBL of 7 patients and marrow of 1 patient for ability to generate PFC following polyclonal stimulation with pokeweed mitogen in a wide dose range (1:20 - 1:1000 final dilution/culture) for 6 days. No PFC were generated in either blood or marrow whereas PBL from normal donors studied simultaneously gave from 107-426 plaques/million cultured cells. No PFC were generated in the PBL (or marrow in 1 patient) even after addition of irradiated normal PBL (1200 R) which regularly provided help to normal autologous or allogeneic cells. In 2 patients, PBL demonstrated suppressor activity; adequate helper activity was seen in the single marrow sample and in the PBL of 4/5 patients after irradiation. These observations confirm the findings of several other investigators that x-linked agammaglobulinemia is indeed a primary defect of the B-cell line in which suppressor cells may or may not be present. (Supported by grants CA-08748, CA-17404, CA-19267, AI-11843, Berman Estate and Judith Harris Selig Foundation funds)

725 SUCCESSFUL CORRECTION OF A BONE MARROW STEM CELL DEFECT (WISKOTT-ALDRICH SYNDROME) BY ALLOGENEIC MARROW TRANSPLANTATION. Robertson Parkman, Joel Rappeport, Raif Geha, James Belli, Robert Cassady, Raphael Levey, and Fred S. Rosen. Division of Immunology, Department of Medicine, Children's Hospital Medical Center and Joint Center for Radiation, Boston, MA 02115.

Two patients with Wiskott-Aldrich syndrome have had the establishment of both normal immune and hemopoietic function following allogeneic bone marrow transplantation from HLA-A, -B, and -D identical sibling donors. Previous attempts by others had achieved only partial engraftment. The patients were successfully transplanted only after preparation with rabbit anti-human thymocyte serum (ATS) and total body irradiation (TBI). One patient was initially transplanted after preparation with high dose cytosine arabinoside (150 mg/m^2 x 7 days) and cyclophosphamide (50 mg/kg x 4 days). Only a T lymphocyte graft was achieved and the patient recovered his own hematopoietic function. After 6 months the recipient's T lymphocytes returned. The patient was successfully re-transplanted after ATS and TBI (880R) preparation. A second patient was successfully transplanted after initial ATS and TBI (850R) preparation. Both patients have normal platelet counts and function. The immune systems of both patients are of donor origin. Neither patient has had any acute nor chronic graft versus host disease. The successful treatment of the Wiskott-Aldrich syndrome may be a model for the treatment of other genetically determined bone marrow disorders. (Supported by NIH grants RR-128, AI-05877 and Ca-13472.)

726 CONTROL OF HUMAN MONOCYTE FUNCTION BY Fc FRAGMENTS OF IgG. Justen H. Passwell, Zvi Marom, Fred S. Rosen, and Ezio Merler. Spon. by Harvey R. Colten. Harvard Medical School, Children's Hospital Medical Center, Division of Immunology, Boston.

Fc receptors on human monocytes have an important role in the phagocytosis of sensitized red cells and antibody dependent cytotoxicity. Effects of human IgG fragments on monocyte function were compared with those of known "activators" of monocytes. Monocyte monolayers treated with Fc fragments exhibited a 10-100 fold increase in prostaglandin E release. On the other hand Fc fragments brought about a significant reduction in synthesis and/or secretion of the second component of complement (C2), lysozyme and acid phosphatase by the same monocytes. In contrast to these effects of Fc fragments on monocyte monolayers, latex particles caused a marked increase in C2 synthesis and lysozomal enzyme synthesis, but only a modest (<10-fold) stimulation of prostaglandin E release. The effects of supernatants of unfractionated mononuclear cells (lymphocytes and monocytes) stimulated with pokeweed mitogen or tetanus toxoid were different in that they enhanced C2 synthesis, but decreased lysozomal enzyme synthesis. Thus activation of monocytes results in different effects depending on the "stimulating" agent. Human monocytes are stimulated in an unique way by Fc fragments of IgG.

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