984 T LYMPHOCYTE SUBSETS AND NEUTROPHIL CHEMOTAXIS AND ADHERENCE IN HEMOPHILIA (H) AND ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS). J Lewis, JA Church, ED Gomperts, CA Nye and W Richards. USC Sch Med, Childrens Hospital of L.A., Dept Peds, Los Angeles, California.

AIDS, characterized by T-cell dysfunction, has been reported in H. However, many of the infections in AIDS may reflect neutrophil (PMN) dysfunction. 15 healthy adults (Gp 1), 18 adult H patients (Gp 2) and 5 adult AIDS patients (Gp 3) were studied. T-cells (Leu-1), helper T-cells (Leu-3) and suppressor T-cells (Leu-2) were determined. PMN chemotaxis (CTX) was measured with an agarose technique. PMN adherence (ADH) was measured with a nylon wool column assay. Results were expressed as means ± SEM percent of lymphocytes or migrating neutrophils.

	Leu-1	Leu-2	Leu-3	3/3	CTX	ADH
Group 1	69±3	26±3	42±3	1.8±.3	454±79	81±3
Group 2	57±2*	32±3	33±3*	1.2±.2*	237±59*	73±6
Group 3	48±4*	37±6	10±4*	0.3±.1*	388±41	75±9

* Indicates a significant difference from controls (Gp 1).

These results confirm similiar abnormal T-cell subsets in H and AIDS. PMN ADH in H patients and PMN ADH and CTX in AIDS patients were normal. However, CTX was impaired in 12 of 16 H patients studied. Incubating control cells with sera from H and AIDS patients did not affect CTX.

Although H and AIDS have similiar T-cell abnormalities, the normal PMN CTX in AIDS is in contrast to the decreased CTX in H patients. The immune dysfunction seen in H appears to have pathogenetic factors in addition to those that cause AIDS.

985 THE INDUCTION OF HUMAN IgG ANTI-HERPES SIMPLEX VIRUS TYPE 1 (HSV) ANTIBODIES AFTER IN VITRO STIMULATION WITH HSV. Lawrence G. Lum. (Spon. by Dr. Herbert Abelson). Fred Hutchinson Cancer Research Center and Department of Pediatrics, University of Washington, Seattle.

We previously reported that HSV can induce T-dependent in vitro immunoglobulin secretion in individuals sero "+" to HSV (Immunobiology 162:94, 1982). This study shows that 12-day culture supernatants from peripheral blood mononuclear cells or T and B cells cultured in RPMI 1640 with antibiotics and fetal calf serum stimulated with HSV produce IgG anti-HSV which can be detected using an ELISA (detects high titer anti-HSV serum at a dilution of 10^{-12}). Since an individual's immune status, precursor frequency of antigen specific T and B cells, antigen dose, and culture conditions can limit antigen-specific ab responses, culture supernatants were screened for specific ab from 15 sero "+" (titer $\geq 10^{-3}$ by ELISA) and 7 "-" individuals at varying cell concentrations, at varying doses of antigen and from different types of culture vessels. Our results show that net ab synthesis occurred: in lymphocytes from 10 of 15 sero "+" and none of 7 sero "-" individuals; at cell concentrations between 0.5-0.8 x 10^6 cells/well; in round bottom microtiter wells; at T:B ratios from 0.5:1 to 3:1; and optimally after washout of HSV after 4 days of culture. Replicate cultures were needed for detecting ab. These findings illustrate the immunobiology of in vitro specific ab synthesis in that high numbers of in vivo sensitized antigen-specific precursors T and B cells cultured in high density configurations after antigen washout to prevent suppression of ab synthesis were necessary for ab synthesis.

† **986** DEFECTIVE IMMUNOREGULATORY FUNCTIONS OF LYMPHOCYTES FROM PATIENTS WITH THE CHEDIAK-HIGASHI SYNDROME. Madhavan P.N. Nair, Stanley A.Schwartz, and Laurence A. Boxer. Univ. of Michigan, Department of Pediatrics.

Lymphocytes (PBL) from 2 Chediak-Higashi (CH) syndrome patients were examined for natural killer (NK) activity, antibody dependent cellular cytotoxicity (ADCC), target binding capacity (TBC), lectin dependent cellular cytotoxicity (LDCC), Con A induced suppressor cells, soluble suppressor factor (SSF), and responsiveness to interferon (IF) and interleukin-2 (IL-2). PBL from CH patients showed little NK or ADCC activity at various effector to target cell ratios. However, the TBC of patients' PBL was comparable with controls, indicating that the defect in cytotoxicity was not due to lack of target recognition. PBL from CH patients cultured with and without Con A failed to suppress the NK activity of fresh allogeneic effector cells in contrast to normal PBL, suggesting that defects in immunoregulatory lymphocytes may coexist with abnormal effector functions in CH patients. Although residual cytotoxicity of CH lymphocytes could be considerably enhanced with PHA in the LDCC system, enhancement was markedly less than that of normal control cells. Preincubating CH lymphocytes for 24 hr produced a slight increase in NK activity when IF was added to the cultures, whereas IL-2 did not enhance cytotoxicity in contrast when normal PBL were precultured with IF and IL-2. SSF from CH patients significantly inhibited the NK activity of normal PBL. The diminished cytotoxicity, defective immunoregulatory functions and reduced responsiveness to IF, IL-2 and LDCC of PBL from CH patients may contribute to their increased risk of infection and malignancies.

● **987** BIOSYNTHESIS AND POSTSYNTHETIC ASSEMBLY OF HUMAN C REACTIVE PROTEIN (CRP). E. C. Mantzouranis, G. Goldberger, L. A. Potempa, A. S. Whitehead, H. Gewurz, H. R. Colten, Harvard Medical School, Boston, MA and Rush Medical College, Chicago, IL.

C reactive protein (CRP) increases up to 100 or 1000 fold during acute tissue injury, hence serum CRP measurements have been useful in clinical evaluation of inflammatory diseases. Since the molecular mechanisms that regulate the acute phase response are unknown, we undertook a study of the CRP gene and biosynthesis and postsynthetic processing of CRP protein. We have isolated a CRP specific human cDNA probe and used it to localize the gene to chromosome 1 (Science 221:69). CRP cDNA hybridized with poly A^+ mRNA (2.2 Kb) that directs cell free translation of monomeric preCRP (26,000 Mr). PreCRP expressed antigenic determinants not detectable in the native plasma protein. When mRNA is translated in the presence of microsomes or in Xenopus oocytes, the 18 amino acid signal peptide of preCRP was cleaved, the monomer assembled to the pentameric form, characteristic of native serum CRP, and lost the antigenic determinant associated with the cell free translation product. Induction with turpentine of a acute phase response in rabbits demonstrated a dose dependent specific rise in CRP mRNA detected by Northern blot analysis and an increase in cell free pre-CRP synthesis. These data provide a model of molecular control of the acute phase response and regulation of other plasma proteins.

988 ORALLY-ADMINISTERED BOVINE COLOSTRAL IMMUNOGLOBULINS (BCI) PROTECT LEUKOPENIC MICE AGAINST Ps.AERUGINOSA (Ps). Richard McClead, Susan Gozs, Chris Budde, (Spon. by Grant Morrow), Dept. Ped., Children's Hospital, OSU, Columbus.

We immunized pregnant cows with Ps Extract Vaccine (Wellcome, UK) to produce anti-Ps BCI. Anti-Ps BCI have agglutinating and opsonizing activity against Ps, but are not bacteriacidal or static. By adsorption with Ps, these activities can be removed from BCI. Bovine IgG1 can be identified on the surface of Ps adsorbed with anti-Ps BCI. We compared the protective effect of orally-fed anti-Ps BCI, control BCI from non-immunized (NI) cows, pooled human immune globulin (HIG), and D5W on the mortality of leukopenic mice orally-inoculated with Ps. Mice (18-22g) were made leukopenic with cyclophosphamide, fed globulins or D5W daily (days 1-6) per gavage, and orally-inoculated on day 4 with 10^6 Ps serotype 10. WBCs on day 4 were 2331 ± 696. Survival data were evaluated by the Kruskal-Wallis statistic and nonparametric log-rank test with adjustment for multiple comparisons.

			Accumulative % Mortality		
Group	n	Feeds	Day 5	Day 6	Day 7
Anti-Ps BCI	59	200 mg/d	0	15.3	33.9
NI-BCI	30	200 mg/d	3.3	30.0	50.0
HIG	30	165 mg/d	13.3	30.0	50.0
D5W	86	1 ml/d	7.0	47.7	61.6

Treatment group survival curves were not equal ($p<0.01$). Anti-Ps BCI-fed animals had less mortality than NI-BCI, HIG, or D5W-fed animals, but these differences reached statistical significance only for anti-Ps BCI vs D5W ($z=3.676$, $p<0.05$). Conclusion: Orally fed anti-Ps BCI may reduce the incidence and mortality of Ps sepsis in the transiently leukopenic host

989 SYNERGISTIC EFFECT OF POKEWEED MITOGEN AND S. AUREUS COWAN I IN VITRO BLOOD B CELL DIFFERENTIATION. K. Miller, W.B. Pittard, R.U. Sorensen, Depts. Peds. & Path. CWRU Cleveland Ohio

Neonatal B cells, unlike adult B cells, do not develop into immunoglobulin secreting plaque forming cells when cultured in the presence of pokeweed mitogen alone or killed S. aureus Cowan I alone. We found that simultaneous addition of these two B cell activators significantly increased the development of plaque forming cells in cord blood mononuclear cells. In 55 neonate cultures, pokeweed mitogen and S. aureus Cowan I together induced 7114(±10,077) plaque forming cells/10^6 cord blood mononuclear cells, compared to 875(±2527) with pokeweed mitogen alone or 672(±1590) with S. aureus Cowan I alone. This effect was not seen with adult cells. Additional experiments indicate that the synergistic effect of pokeweed mitogen and S. aureus Cowan I on cord blood mononuclear cells can best be explained by a two-phase model of B cell differentiation wherein the macrophage and its soluble product governs an early first phase, while the T helper and its soluble mediator governs the later second stage. We propose that in the neonate, S. aureus Cowan I acts on the macrophage to initiate the differentiation, and pokeweed mitogen acts on the T helper to complete the development into plaque forming cells.