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C3d, A MARKER OF EARLY T-CELLS IN MAN? A. Shore*, E. W. Gelfand, H. M. Dosch*, Dept. Immunology, Res. Institute, Hospital for Sick Children, Toronto, Ont.

A small proportion (2-3%) of normal human peripheral blood lymphocytes (PBL) have receptors for both E (SRBC) and the third component of complement (C3). C3 complexes were formed with ox red cells (O), IgM rabbit anti-ox (u), and different sources of complement. Using OpC3 complexes and fluorescinated SRBC, co-rosetting cells were enumerated in normal tissues, T-cell lines, E-positive ALL (E⁺-ALL) blasts, and PBL from a patient with severe combined immunodeficiency disease (SCID). The detection of co-rosetting cells was optimized using mouse sera as the source of complement with prolonged incubation to insure generation of C3d. Cells from four T-cell lines, and six E⁺-ALL had a high proportion of co-rosetting cells (20-55%). A high proportion of bone marrow T-cells also demonstrated C3d receptors. C3d⁺/E⁺ T-cells in normal PBL were enriched in the low density precursor cell fractions after separation by albumin gradient centrifugation. These cells were induced to become C3d⁺/E⁺ following incubation with thymic humoral factors or modulators of cAMP. The patient with SCID demonstrated large numbers of C3d⁺/E⁺ cells early in his course following transplantation with cultured thymic epithelium. As this patient's E-rosettes increased from <1% to 30%, co-rosetting cells dramatically declined. These data suggest that a C3d⁺ T-cell occurs early in ontogeny and becomes C3d⁺ at a post-thymic epithelial stage of development. Furthermore, E⁺-ALL may represent a clonal expansion of T-lymphocytes at this stage of ontogeny.

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IMPLICATIONS CONCERNING THE COMPLEMENT SYSTEM IN A PATIENT WITH GLOMERULONEPHRITIS AND IMMUNOCHEMICAL FINDINGS OF HEREDITARY ANGIONEUROTIC EDEMA. Roger E. Spitzer, Ann E. Stitzel and Joan R. Urmson. State University of New York, Upstate Medical Center, Department of Pediatrics, Syracuse, NY

An 11-year-old white female with focal glomerulonephritis was found to have an absence of functional C1 esterase inhibitor, 5% of normal levels of serum C2 and C4, as well as evidence of circulating, active C1 esterase. C1 esterase inhibitor measured by immunochemical means, however, was only reduced by 25%. Several family members had similar findings. Neither the patient nor her family had clinical signs of hereditary angio-neurotic edema (HANE) despite continued and persistent complement consumption for at least 18 months. These data suggest that mechanisms controlled by C1 esterase inhibitor, other than those related to complement, might be responsible for the clinical features of HANE. In addition, evidence from immuno-fluorescent studies of the deposition of IgG and C3 on the kidney of this patient suggests the participation of an immune complex and terminal complement activity in the genesis of the glomerulonephritis. The prolonged and marked depression of C2 and C4, however, precludes any utilization of the classical pathway in that process. Further, it would appear that the hypocomplementemia antedated the onset of the nephritis and, therefore, may be a predisposing factor in the persistence of the immune complex and its presumed activity via the alternative pathway.

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CIRCULATING IMMUNE COMPLEXES IN CHRONIC MUCOCUTANEOUS CANDIDIASIS. Elizabeth M. Smithwick, Werner E. Brandeis, Savita G. Pahwa, Robert A. Good, Noorbibi K. Day

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Chronic mucocutaneous candidiasis (CMC) is characterized by clinical and immunologic variability. Reported findings in CMC have included high levels of candida antibody, free candida antigen and decreased total hemolytic complement (TCH50) which suggested the possibility of circulating immune complexes. Serial samples from 7 CMC patients have been tested for complexes by the radioimmune Raji cell assay which detects complement-fixed IgG immune complexes bound to the complement receptors of cultured lymphoblastoid Raji cells. Three patients had the severe granulomatous form of CMC while 4 had mild disease. Six of the 7 had circulating immune complexes; 16 of 22 sera from the 7 patients were positive with values ranging from 192-1552 µg/ml (normal <16 µg/ml). No correlation can be made with defects in cell-mediated immunity; 2 patients with immune complexes responded normally to candida stimulation (skin test, lymphocyte proliferation, lymphokine production). One patient with granulomatous disease has had high levels of immune complexes both in relapse and remission. The only patient without detectable complexes was tested at a time of minimal involvement. Complement studies (TCH50, C1q, C3) done on 6 of the positive samples were within normal limits. All patients have had positive agglutinins or precipitins for candida. Although the composition of the circulating immune complexes is unknown at this time, a positive Raji cell assay appears to be the most consistent immunologic aberration in the study patients.

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UTILIZATION OF PROPERDIN IN CHILDREN WITH VASCULITIS AND MILK ALLERGY. Roger E. Spitzer, Ann E. Stitzel, Joan R. Urmson and Mary Lou Farnett. State

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Patients with various types of vasculitis have serologic findings which indicate that properdin is consumed during disease activity. In all of 22 patients with documented Henoch Schönlein Purpura, the level of serum properdin was reduced more than 3 standard deviations below the mean in the first week of the disease. Patients with predominant signs of abdominal pain and glomerulonephritis had more pronounced reductions in serum properdin than did those patients with arthritis as a presenting symptom. Serum levels of properdin convertase were also reduced in 12 of the 22 patients. As the disease subsides, levels of properdin and properdin convertase return to normal. All other serum complement components and alternative pathway proteins were normal. Similarly, six patients with nonspecific vasculitis had isolated reductions in serum properdin which correlated well with disease activity. Of great interest is the fact that 3 patients with milk allergy also had isolated low levels of serum properdin. The level of properdin returned to normal on a milk-free diet and fell on challenge with milk. In addition, these latter patients demonstrate a functional inadequacy of the alternative pathway as judged by incomplete C3-C9 consumption on the addition of zymosan to their serum. These findings suggest that properdin and properdin convertase may be involved in those disorders effecting vascular inflammation.

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CANDIDACIDAL CAPACITY IN CHRONIC GRANULOMATOUS DISEASE. Elizabeth M. Smithwick, Savita G. Pahwa, Asha Kapadia, Robert A. Good, Memorial Sloan-Kettering

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Both neutrophils (PMN) and monocytes (MONO) from patients with chronic granulomatous disease (CGD) phagocytize normally but fail to kill catalase-positive intracellular organisms. While studying candidacidal mechanisms, Lehrer observed differential killing of Candida species by CGD cells. C. albicans was not killed by PMN or MONO but PMN showed a normal or relatively intact ability to kill 2 strains (C. parapsilosis, C. pseudotropicalis) which could not be killed by MONO. Our interest in these divergent candidacidal abilities was enhanced when C. parapsilosis was recovered from a CGD blood culture. Using the dye-exclusion assay of Lehrer and Cline, it was found that the patient's PMN failed to kill not only C. albicans but also C. pseudotropicalis and 2 strains of C. parapsilosis, including his own isolate. Studies of cells from 5 boys with X-linked CGD (Pt) and normals (NI) are summarized below. Results are expressed as mean % kill of ingested organisms in 1 hour; ()=number of tests.

	C. albicans	C. parapsilosis	C. pseudotropicalis
PMN--Pt	3.6 (7)	2.5 (6)	1.8 (3)
NI	34.4±7.4 (32)	23.9±6.6 (6)	43.7±12.5 (9)
MONO--Pt	3.6 (3)	0.1 (1)	0 (1)
NI	25.1±6.9 (15)	10.2 (1)	33.7 (3)

Thus in this series both CGD phagocytic cell types share the defective killing capacity for the catalase-positive Candida species tested.

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IDENTICAL TWIN GIRLS WITH RECURRENT SEVERE INFECTIONS ASSOCIATED WITH THE ABSENCE OF THE SECOND COMPONENT OF COMPLEMENT. Gregory L. Stidham, Anita Gewurz,

Henry Gewurz, and James V. Lustig. Dept. of Peds., Med. Coll. of Ohio at Toledo, and Dept. of Immunol., Rush Med. Coll., Chgo.
Deficiency of the second component of complement has frequently been reported but has only rarely been associated with severe infection. We now report identical twin girls with this defect who each have had four episodes of bacterial sepsis in the first 19 months of life; one episode was associated with meningitis in one patient. The twins have normal levels of circulating IgM, IgG, IgA, and IgE, and functional antibodies are present. There is no neutropenia or lymphopenia, and both girls have positive skin tests with more than 10 millimeters of induration to mumps and candida antigens as well as normal formazan slide tests. However, total hemolytic complement activity is undetectable, and attributable to selective and complete deficiency of C2 in each child; activity is restored with purified C2. Levels of C1q, C4, C3, C5, properdin and Factor B protein are each within normal limits, as is alternative pathway activity. These patients are similar to many others who lack C2 in that they have the Aw25, Aw33 and B18 antigens at the HL-A locus. There is no clinical evidence of a collagen disorder, but rheumatoid factor is present in a titer of 1:80 in both girls. There is a normal staphylococcal kill test but decreased ability to opsonize for phagocytosis of Candida albicans. These girls are unique in that they are identical twins with isolated C2 deficiency with a propensity to recurrent infections early in life.