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Antibody Responses to a T Cell Dependent Antigen in C4 Deficiency FREE

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of zymosan-induced inactivation of C3. The corresponding increases for 50% inhibition of B inactivation were 70% in C3bINA and 43% in β1H. The 50% inhibitory effect of the combined additions of C3bINA and β1H was completely reversed by increasing either C3 by 60% or B by 50% above endogenous concentrations. Since a 1:7 dilution of C2-deficient serum in the presence of 1×10^8 E^r resulted in 50% lysis after 28 ± 1.2 minutes, the 30 minute time point in this system was chosen to determine the increment of control protein necessary to inhibit 50% of lysis. Under these conditions, a 40% increase of C3bINA and a 22% increase of β1H over endogenous concentrations were sufficient for 50% suppression of lysis. When these amounts of the control proteins were added simultaneously there was complete inhibition at 30 minutes. This effect was fully reversed and lysis even increased to 90% when the B concentration was augmented by 50%.

These experiments suggest that the component proteins C3 and B, because of the normal presence of $\bar{D}$ in serum, form an activation system that is equilibrated with the control proteins C3bINA and β1H. This equilibrium is sensitive to modest alterations in the concentrations of individual components. The increments in component and regulatory proteins utilized in these experiments are well within the ranges observed in patients with infections and other inflammatory conditions.

Studies of the Alternative Complement Pathway (AP) in Normal Children. Michael E. Norman, Arlene Taylor, Paul Green, Larry Laster, and Ulf R. Nilsson, University of Pennsylvania School of Dental Medicine, Phila., Pa.

Increasing evidence suggests that activation of complement by AP contributes an important protective mechanism in early defense against bacterial invasion, before effective antibody levels are established. Since this is particularly important in children, we undertook a survey of AP in 83 normal children, ages 3 days to 15 years ($\bar{x}$ = 54 months). There were approximately equal numbers of males and females, blacks and whites, and all children were free of fever and intercurrent infection. C3, Factor B, properdin,[1] and β_1H were quantitated by radial immunodiffusion with monospecific antisera; hemolytic function of AP was monitored by lysis of glutathione-treated human erythrocytes with inulin activated serum (N. Engl. J. Med. 286:180, 1973). Data were compared to normal adults:

	C3 (mg/dl)	Factor B (mg/dl)	Properdin (%)[a]	β_1H (mg/dl)	AP Lysis (%)[a]
Children	124 ± 24[b] (72–183)	19 ± 7 (6–39)	80 ± 30 (28–170)	129 ± 44 (30–248)	72 ± 33 (0–121)
Adults	119 ± 17 (73–145)	18 (12–30)	95 (67–190)	171 ± 23 (148–234)	91 ± 14 (64–109)

[a] Percentage of normal reference serum pool; [b] mean values ± 1 S.D.

There was a wide range of values when compared to adults except for C3. An intercorrelation matrix revealed that each parameter of AP in normal children was highly related to every other parameter ($p < .001$) and to age, as we had previously reported for C4 and C5 (J. Pediat. 87:912, 1975). Data were further analyzed statistically by a principal factor analysis in order to examine the underlying relationships among the variables. Results of these studies will be presented.

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[1] Anti-properdin antiserum was the generous gift of Dr. Roger Spitzer.

Antibody Responses to a T Cell Dependent Antigen in C4 Deficiency. Hans D. Ochs, Charles G. Jackson, Michael M. Frank, Stephen W. Hosea, Ralph J. Wedgwood. Department of Pediatrics RD 20, University of Washington School of Medicine, Seattle, Washington 98195 and the Clinical Immunology Section, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland.

Complete absence of the fourth component of complement has been described in man and in guinea pigs. Recently, a close linkage between the gene(s) controlling synthesis of C4 and the major histocompatibility complex has been demonstrated in man as well as in the guinea pig.

Because of a possible relationship between immune responses and the complement system, we have studied antibody responses to a T cell dependent antigen in a patient and in guinea pigs with C4 deficiency. Bacteriophage $\Phi\chi$ 174, given intravenously, was cleared within one week after primary injection, similar to normal controls. The primary antibody response was markedly suppressed and shortened: in normal controls, antibody titers (mean Kv > 8) persisted for over 4 weeks; in C4 deficiency, antibody (peak titer < 1) disappeared 2–3 weeks following immunization. In the normal control population, a second injection of antigen resulted in a rapid rise of antibody (Kv > 100) and transition from IgM to IgG. In contrast, both the C4-deficient patient and the C4-deficient guinea pigs lacked amplification of antibody production (Kv < 1) and failed to switch from IgM to IgG antibody. Again, the antibody in the C4-deficient population disappeared rapidly. Bacteriophage $\Phi\chi$ 174, mixed in complete Freund's adjuvant and injected into the footpad resulted in a continuous antibody rise for over 7 weeks in the normal guinea pigs (peak Kv > 1000). The antibody response in the C4-deficient guinea pigs was again depressed (mean Kv = 120) although the titer was much higher than in the nonadjuvant treated guinea pigs.

These experiments suggest that C4 may play an important role in antibody production and that a functioning classical complement pathway may be necessary for antigen trapping and processing.

The C2 Polymorphism: Its Genetics and Presentation of Typing Technique Modifications. B. Olaisen, P. Teisberg, E. Thorsby, and T. Gedde-Dahl Jr., Institute of Forensic Medicine, Rikshospitalet, Oslo; Medical Department 7, Ullevaal Hospital, Oslo; Tissue Typing Laboratory, Rikshospitalet, Oslo; Genetics Laboratory, Radiumhospitalet, Oslo.

The originally described C2 typing technique has been modified to allow typing on ordinary electrofocusing equipment, without the use of specific C2-deficient serum. The modifications include prolonged electrofocusing time, iodine treatment of gels after focusing, and the use of low concentration normal human complement as "C2-lacking complement."

In a Norwegian population sample C2 gene frequencies were: $C2^1$: = 0.97, $C2^2$: = 0.03, these frequencies fit well with those reported in other Caucasian populations.

C2-linkage relations and haplotype associations have been examined in an extensive Norwegian family material. No recombinations were found in 22 informative *C2/HLA-B* meioses and the rare $C2^2$ allele was accompanied by the *HLA-Bw15* allele in 6 out of 7 instances. Our data therefore confirm the linkage of *C2* to the HLA region loci, and we conclude that *C2* is situated in close proximity to the *HLA-B* locus.