Table 1. Effect of environmental temperature (T_E) on rate of ^{3}H-NE turnover in rat hypothalamus. Rate constants (k) and half-time values ($T_{\frac{1}{2}}$) for ^{3}H-NE disappearance from hypothalamus and rest of brain were calculated (*10*) from data presented in Fig. 1. Values are given as mean ± standard error.

T_E (°C)	Hypothalamus		Rest of brain	
	k (hr^{-1})	$T_{\frac{1}{2}}$ (hr)	k (hr^{-1})	$T_{\frac{1}{2}}$ (hr)
9	0.120 ± .054	5.78	0.238 ± .045	2.91
24	.136 ± .062	5.09	.256 ± .049	2.72
32	.392 ± .060*	1.77	.318 ± .067	2.18

*$P < .01$ when compared with value at 24°C.

.005) at 9°C. The rate of disappearance of ^{3}H-NE from the rest of the brain was similar at all three temperatures.

Although there has been recent controversy (*11*) over whether the rate of disappearance of ^{3}H-NE from tissues can be used to calculate the turnover rate of endogenous NE, this technique can at least provide an index of the turnover of endogenous NE. Our results, therefore, suggest that there is an increased activity of NE-containing nerve terminals in the hypothalamus during heat exposure, but no change in the cold. The failure to detect any such change in the other brain regions studied indicates that generalized heat stress is not involved and that the hypothalamic changes probably reflect the activity of a part of the temperature-regulating mechanism. These findings are consistent with the theory of thermoregulation proposed by Feldberg and Myers (*2*) and provide the first evidence that hypothalamic NE may regulate heat loss under normal physiological conditions in the rat.

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12. Supported by a grant from the U.K. Science Research Council. M.A.S. is a Beit Memorial fellow.

5 September 1968

Complement-Immunoglobulin Relation: Deficiency of C'1q Associated with Impaired Immunoglobulin G Synthesis

Abstract. *Concentration of the complement protein C'1q was determined immunochemically in serums of individuals with a wide variety of immunoglobulin abnormalities. A significant correlation was observed between decreased concentration of C'1q and deficient synthesis of immunoglobulin G; C'1q was particularly diminished in subjects with congenital, sex-linked (Bruton) agammaglobulinemia. In contrast, two to five times the normal concentration of C'1q was found in the serum of three patients with heavy chain disease (subtype immunoglobulin G3). No significant relation was found between C'1q and concentrations of immunoglobulins A and M.*

The C'1q subunit of the first component of human complement (C'1) (*1*) is a glycoprotein with a molecular weight of 400,000 and the electrophoretic behavior of a very slowly migrating γ-globulin (*2*). It carries the site through which C'1 combines with γ-globulin or with specific antibody, and, as such, C'1q constitutes an anti-γ-globulin factor. It is endowed with differential specificity for the immunoglobulins, reacting readily with immunoglobulins G1, G3, and M (IgG1, IgG3, and IgM), but only slightly with IgG2 and little or not at all with IgG4 and IgA. Although it is possible that C'1 q may be related to the immunoglobulins, immunochemical analyses have failed to establish such a relation.

Initially, C'1q could be measured only in relative terms either by its hemolytic activity or its ability to precipitate soluble γ-globulin aggregates (*3, 4*). It was markedly diminished in serums from three patients with Bruton agammaglobulinemia (*3*). When monospecific antiserums to C'1q were produced, it became possible to detect and to quantitate C'1q in serum as an individual protein (*5, 6*). Recently, the classical C'1 hemolytic activity was found lacking in a 3-week-old infant with Swiss type agammaglobulinemia (*7*); serum from this patient was markedly deficient in C'1q (*6*). These observations prompted the present investigation, which is

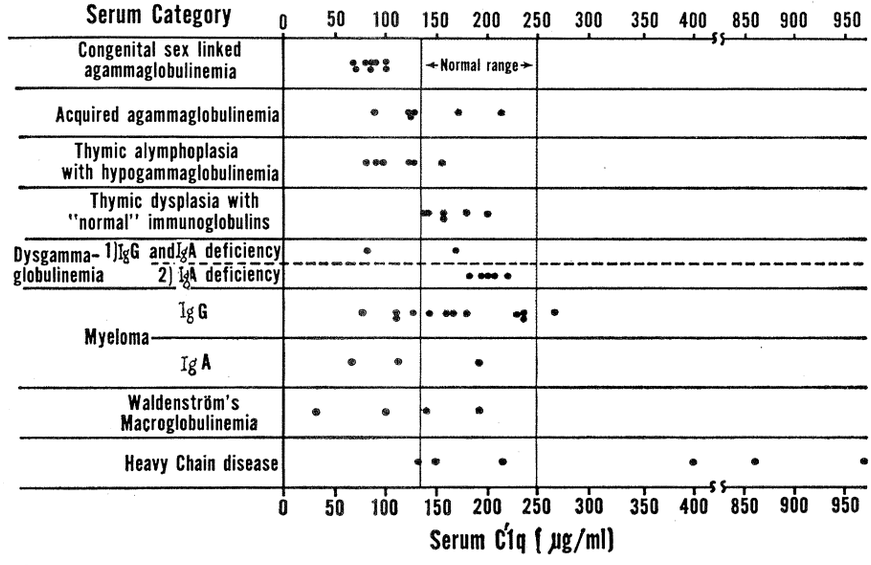

Fig. 1. Serum C'1q concentrations of 58 subjects with serum immunoglobulin abnormalities. The normal range of C'1q is between 134 and 246 μg/ml.

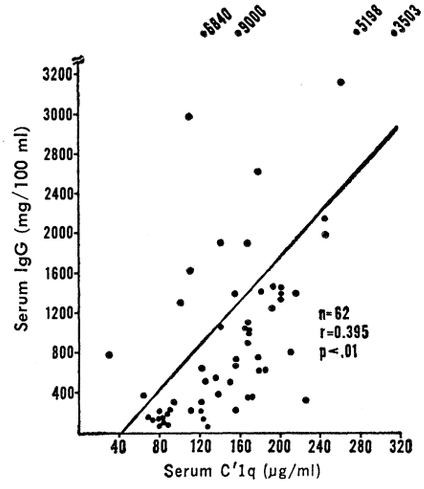

Fig. 2. Relation between serum IgG and C'1q concentrations for all subjects listed in Fig. 1, except for the six H-chain disease patients. Concentrations in an additional 10 serums are also included ($n = 62$). The correlation between concentrations of IgG and C'1q is highly significant ($r = 0.395$, $P < .01$).

concerned with the quantitative relation of C'1q and the three major classes of immunoglobulins (IgG, IgA, and IgM) in serums from individuals with a wide spectrum of immunoglobulin abnormalities.

Concentration of C'1q was determined by the quantitative radial immunodiffusion technique (*8*). In brief, a potent, monospecific rabbit antiserum to human C'1q (*9*) was incorporated in 1.5 percent agar in phosphate buffer, *p*H 8 (*10*); the final concentration of antiserum was 0.15 percent. Constant volumes of test serum and standard serum were placed in wells cut in the agar gel that contained antibody and were incubated at room temperature for 72 hours. The concentration of C'1q in test serums was determined by relating the resulting precipitin areas to those of the standards, which in turn had been calibrated with the use of known amounts of highly purified C'1q (*2*). In 35 healthy adults the concentration of C'1q in serum ranged from 134 to 246 µg/ml with a mean ± 1 standard deviation of 190 ± 28 µg/ml. The concentrations of IgG, IgA, and IgM were determined by a quantitative adaptation of the Oudin tube technique as described by Claman and Merrill (*11*).

Concentrations of C'1q and immunoglobulin were ascertained for serum samples of 68 individuals with a variety of immunoglobulin abnormalities or thymic deficiency states, or both. The C'1q concentrations observed in the selected serum categories are recorded in Fig. 1. All eight individuals with congenital sex-linked (Bruton) agammaglobulinemia had significantly reduced C'1q. Similarly decreased levels were present in infants with thymic alymphoplasia and agammaglobulinemia (Swiss type), while normal amounts of C'1q were present in the serum of patients with isolated thymic dysplasia and normal immunoglobulins (Nezeloff type) (*12*). Some patients with acquired hypogammaglobulinemia, either idiopathic or secondary to disease of the lymphoreticular system, had decreased C'1q as did 45 percent of the patients with IgG and IgA multiple myeloma and Waldenström's macroglobulinemia.

The serum of six patients with heavy chain (H-chain) disease was examined. While three serums contained normal amounts of C'1q, the other three showed two to five times the normal concentration of C'1q. The three serums with abnormally high concentrations of C'1q (Mat, 400 µg/ml; Re, 860 µg/ml; and Zu, 970 µg/ml) contained H-chain protein of subgroup IgG3; the other three (Cr, 132 µg/ml; Man, 212 µg/ml; Ha, 150 µg/ml) contained the IgG1 type of H-chain protein.

When a comparison was made between concentrations of C'1q and individual immunoglobulins, a direct relation with IgG, but not with IgA or IgM, was observed. This positive correlation was significant at the 1-percent level and is illustrated in Fig. 2.

These data strongly suggest a relation between serum levels of C'1q and IgG. They suggest further a dependence of the concentration of serum C'1q upon synthesis of IgG. Serums from individuals with deficient IgG synthesis, in particular those with Bruton and Swiss type agammaglobulinemia, showed abnormally low concentrations of C'1q. In contrast, a patient with intestinal lymphangiectasia (*13*) with markedly decreased IgG (90 mg/100 ml), but with normal IgG synthesis, had a normal concentration of serum C'1q. The findings of markedly elevated C'1q in the three H-chain disease serums of the IgG3 subclass compared to normal levels in three H-chain disease serums of the more common IgG1 subclass may be indicative of an association between C'1q and IgG of a particular H-chain subgroup (*14*).

Although the reduction of C'1q in patients with impaired synthesis of IgG was proportionally less than the corresponding reduction of IgG, the present observations raise the possibility of a link between these two proteins. Investigation of the metabolism of C'1q in normal and agammaglobulinemia subjects and studies of the cellular basis of C'1q synthesis are needed.

Note added in proof: Gewurz *et al.* have recently reported decreased C'1q concentrations of 27 percent of normal in three infants with Swiss type agammaglobulinemia and 75 percent of normal in nine children with other agammaglobulinemia syndromes (*15*).

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16. Supported by PHS grants 1 R01 HD 03381-01 and AI-07007, and by American Heart Association, Inc. grant 65-G-166. We are indebted to Miss Deborah Merrill and Dr. H. N. Claman for providing many of the serums and the data on immunoglobulin concentrations. The H-chain disease serums were provided by Drs. E. F. Osserman (Zu, Cr, Man), K. Bloch (Re, Ha), and Z. A. Zawadzki (Mat). We also thank Dr. V. Fulginiti for his gift of serums from patients with Bruton's and Swiss type agammaglobulinemia.

5 September 1968