A symposium of this kind is very valuable in that it directs attention to problems arising from a wide range of studies and in providing a meeting ground for people of very diverse interests. The Washington symposium was successful in both ways and is likely to lead to some interesting new work in the region common to optics and microwaves. J. BROWN

THE MEANING AND REACTIONS OF COMPLEMENT

BY definition, complement is a hypothetical substance present in fresh serum that has the property of causing the escape of hæmoglobin from red blood cells that have combined with antibody. There are, however, also a number of other reactions for which complement or substances resembling complement are essential; these other reactions were the chief subjects discussed in the symposium on "Complement" at the first meeting of the newly formed British Society for Immunology during November 9–10.

As Prof. J. R. Marrack pointed out in his introduction to that symposium, the first and second components of complement can be separated in mid- and end-piece, and the third component can be obtained free from other components; but the fourth component has not been prepared free from other components and may well be an active group of the first and/or second component.

Bordet[1] wrote of 'fixation' of complement and the expression is established by long usage. But all that is observed when complement is 'fixed' by antigen–antibody complexes is that complement activity is lost. It seems that the only evidence that the active substance actually combines is found in experiments that Dean[2] published in 1912. He found that an antigen–antibody precipitate, formed in the presence of mid-piece in the cold, washed and resuspended, had mid-piece activity. Otherwise the only evidence that any component of complement is fixed are the facts, first shown by Heidelberger[3] in 1941, that a complement-fixing antigen–antibody system forms more precipitate in the presence of fresh serum than in inactivated serum; and that this difference is not found when the antigen–antibody system is one, such as pneumococcal polysaccharide and horse antiserum, that does not fix complement. Mr. R. G. S. Johns presented a diagram showing this increase in precipitate over a wide range of ratios of antigen (ovalbumin) to antibody in the presence of fresh human serum; in the presence of heat-inactivated serum the amounts of precipitate were almost identical with those of the saline controls. With horse serum as the source of complement the matter was less simple; for over a wide range of antigen/antibody ratios the amount of precipitate formed in the presence of heat-inactivated horse serum was less than that formed in saline. This recalls the demonstration by Maurer and Talmage[4], using antigen and antibody labelled with iodine-131, that the amounts of antigen and antibody precipitated differed in the absence or presence of complement.

Heidelberger has shown that most of the protein taken up from fresh serum by an antigen–antibody precipitate comes from the fraction containing the first component. Mr. Johns could find no evidence that the second and fourth components added anything to the precipitate; they may therefore be inactivated and not actually fixed. The extra protein derived from fresh serum is not merely entrapped when the antigen–antibody precipitate is formed, for Mr. Johns found that a pre-formed precipitate, resuspended with fresh serum, will eventually take up as much protein as would have been added if the precipitate had been formed in the presence of the fresh serum.

The work of Levine, Mayer and colleagues[5] has demonstrated three stages in the interaction of complement with sensitized red-blood cells. In the first stage, which requires calcium ions, the first and fourth components are involved; in the second, which requires magnesium ions but not calcium ions, the second component is involved; in the third stage, which is very slow at temperatures below 17°, the third component effects a change in the red cells, the result of which is the escape of hæmoglobin. The product (*a*) of the first stage and that (*b*) of the second stage are unstable; at 37° they are inactivated—that is, they undergo such a change that the further stages no longer take place on addition of the appropriate components. The inactivation of *b* is rapid, so that the eventual degree of lysis depends on a race between this inactivation and the action of the third component. Furthermore, Levine[6] has found that after treatment of *a* with *iso*propylfluorophosphate, which is regarded as a specific inhibitor of esterases, hæmolysis does not occur on addition of second and third components. Treatment of serum that contains complement—that is, treatment of complement that has not been fixed—does not inactivate the complement. Also, Becker[7] finds that product *b* (or its inactivated form) hydrolyses tosylarginine methyl ester, whereas neither the serum from which the complement is derived nor red blood cells without complement hydrolyse this substrate. We have, therefore, a method of demonstrating a change in complement after 'fixation', apart from the hæmolysis of red blood cells. It would be interesting to know whether an esterase is either formed or becomes activated when complement is fixed by simple antigen–antibody precipitates.

We have further evidence of a change in complement on fixation in the conglutinin reaction. Bordet and Streng[8] found that bovine serum agglutinated sensitized red blood-cells and other antigen–antibody complexes that had fixed complement (particularly horse complement); they called this reaction conglutination and postulated a substance, conglutinin, in the bovine serum. Unfortunately, much confusion has been caused by the application of the name 'conglutination' to other reactions in which complement is not involved; but at this symposium the word was used in the correct sense. Streng[9] and Wartiovara[10] have shown that though normal rabbit serum contains little conglutinin, something very similar to it appears in the serum of rabbits after intravenous injection of antigen–antibody complexes that have fixed complement; this conglutinin-like substance, which appears to be an antibody against fixed complement, they called immunoconglutinin; it is permissible to suppose that the natural conglutinin is also an antibody against fixed complement. Wartiovara[10] and Coombs and Coombs[11] found that this conglutinin-like substance was also formed after bacteria alone, without antibody, were injected, and considered that this immunoconglutinin was antibody against the rabbit's own complement fixed on

the bacteria after these had combined with antibacterial antibody formed by the rabbit. Coombs and Coombs suggested that complement was so changed, when fixed, that it became a foreign protein and stimulated production of antibodies in the rabbit. Since first, second and fourth components are needed to render sensitized red blood cells agglutinable by conglutinin, and since the sensitized-red-cell–complement complex is agglutinable after incubation at 37°, it appears that conglutinin reacts with the complex in the inactivated *b*-stage.

In the symposium Drs. R. R. A. Coombs and J. Marks described an extensive investigation into the conglutinin levels in the sera of human beings. Normally the conglutinin titre is low; but in infectious diseases the titre rises and reaches a maximum at a time when antibodies against the infective agent should have appeared in the circulation. Among normal people the titres were lowest in those months in which infectious diseases are least common. It may be inferred that human beings also make antibody against their own complement which is fixed by an antigen–antibody complex. In the discussion it was suggested that the large amount of conglutinin in the sera of ruminants is due to the high bacterial content of the stomach.

Properdin was originally recognized by its ability to combine with zymosan to form a complex that inactivates the third component of complement at temperatures above 17°. The other components of complement and magnesium ions are required for the formation of this complex[12]. Purified properdin can be eluted from the complex and properdin-free serum can be prepared by adsorption with zymosan at 17°. It was later found that properdin is instrumental in killing certain bacteria. Dr. A. C. Wardlaw presented tables showing that the components of complement and magnesium ions are required for this bactericidal action as well. He also reported that the percentage of bacteria killed in a given time is independent of the number of bacteria. This may be interpreted as evidence that an enzyme action is involved; but, as pointed out in the discussion, it may be due to differences in resistance of the bacteria.

Dr. J. V. Dacie found that complement is necessary for firm combination of cold-agglutinin with red blood cells. It appears that cold-agglutinin is not a γ-globulin, as agglutination by a supposed anti-γ-globulin serum of cells that have combined with cold-agglutinin is not inhibited by γ-globulin; it may be an α- or β-globulin.

Reduction of complement in disease has been often reported; Dr. C. E. Kellett showed a number of cases of great reduction of complement, estimated by the method of 50 per cent lysis, in a variety of diseases, particularly acute nephritis. This reduction requires further investigation, particularly estimation of the different components.

Blood-coagulation and complement activity involve factors that have a superficial resemblance. Dr. A. A. Sharp reviewed investigations on the relationship between the two systems and could find no evidence that common factors are involved.

Pillemer and his colleagues have shown that the first component promotes the inactivation of the second and fourth components by plasmin[13]. In this reaction, as in the stages of the reaction with sensitized red blood cells, in the conglutinin reaction and in the properdin reactions, we find interactions of the components of complement with one another, set off by an antigen–antibody complex, by a zymosan–properdin complex or by an enzyme. This complicated system of interacting components is found in the serum of all mammals examined and something similar in the serum of birds. Complements have been divided into hæmolytic and non-hæmolytic. This distinction is artificial and due to the customary use, as a test system, of sheep red blood cells sensitized with rabbit or horse antibody; horse complement, which does not lyse this system, lyses rabbit red blood cells sensitized with sheep antibody[14]. The first components of mammals seem to be similar; the difference between guinea pig complement, which is hæmolytic (for sheep cells sensitized with horse or rabbit antibody) but not conglutinating, and horse complement, which is conglutinating, seems to lie in the fourth component[15]. The new methods of investigation, particularly the separation of the stages of interaction as done by Levine and Mayer and the study of enzyme activities, open up new possibilities in the study of these interactions and raise complement from the status of a mere diagnostic reagent.

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THE GIACOBINID METEOR STREAM

A PAPER on "The Giacobinid Meteor Stream", by J. G. Davies and A. C. B. Lovell (*Mon. Not. Roy. Astro. Soc.*, **115**, 1; 1955), gives an account of the radio-echo observations of the meteor shower associated with comet Giacobinid–Zinner during the unexpected return of the shower on October 9, 1952. The shower was first studied by radar in 1946, and the paper gives a description of the observations from 1947 to 1954, inclusive, and also discusses the unexpected return of the shower during daylight in 1952 as well as the significance of its absence in 1953. The equipment for observation has been described by A. Aspinall, J. A. Clegg and G. S. Hawkins (*Phil. Mag.*, **42**, 504; 1951), and, with the exception of the 1952 return, no activity beyond four or five meteors per hour—the background sporadic rate—was detected.

The records for October 9, 1952, are shown graphically, and from these it is obvious that the activity of the Giacobinid radiant became greater