LETTERS TO THE EDITORS

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Non-precipitating Protein Antigens

WHEN some protein antigens are heated with serologically unspecific proteins they cease to be precipitated by their antisera, and their behaviour *in vitro* approximates to that of non-precipitating haptens[1]. Evidence from different sources suggests that this change in behaviour is brought about by the antigens combining with the other protein during the early stages of heat denaturation to form complexes, which after combination with antibodies still remain soluble.

We have now studied such complexes *in vivo* and find that they differ from haptens in being active as producers of antibodies. The antigens we used were tomato bushy stunt virus and whole globulin from human serum. These were turned into non-precipitating complexes by heating them in the presence of rabbit serum albumin in physiological saline at *p*H 7·0. 0·1 per cent solutions of bushy stunt virus were heated for 10 minutes at 83° C. in the presence of 0·5 per cent rabbit albumin, and 0·1 per cent solutions of human globulin were heated for 5 minutes at 100° C. in the presence of 0·2 per cent rabbit albumin. None of the sera produced by injecting rabbits with solutions of these complexes precipitated the materials used for immunization. The serum produced against the virus-albumin complex, however, precipitated solutions of both unheated virus and virus heated in the absence of rabbit albumin; indeed, no differences have been detected between this serum and those produced by injecting rabbits with virus only. The serum produced against the globulin-albumin complex precipitated solutions of the globulin heated in the absence of the albumin. In other words, although the immunizing systems were active in producing precipitating antibodies, these could be demonstrated only when one component of the system free from the other was used as a test antigen.

It is possible that these complexes are split in the rabbit before acting immunologically, so that the antigenic component is liberated and acts alone in the production of antibodies. Whether this is so or not, it should be realized that failure to obtain a positive precipitin test between an antiserum and the material used for its preparation cannot be regarded as proof that no precipitating antibodies have been formed, for complexes behaving like those we have produced by heating may occur naturally.

Complement fixation provides a suitable test for the antigenicity of such non-precipitating complexes. With antisera prepared against either the virus or against the virus-albumin complex, solutions of the virus-albumin complex fix complement as strongly as solutions of the virus alone. Similarly, the globulin-albumin complex fixes complement with antisera to the unheated globulin and with those prepared against the complex itself. This fixation of complement equally by an antiserum with antigens with which precipitation does and does not occur is evidence for the independence of the two reactions, and strongly supports the view that complement is fixed by the union of antigen and antibody and not by the formation of a precipitate.

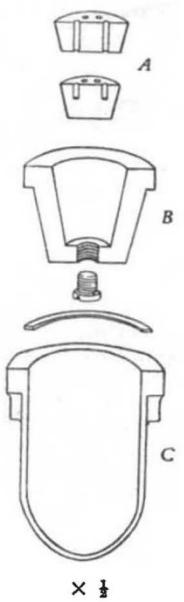
F. C. BAWDEN.
A. KLECZKOWSKI.
Rothamsted Experimental Station,
Harpenden, Herts.
Oct. 28.

[1] Bawden, F. C., and Kleczkowski, A., *Brit. J. Exp. Path.*, **22**, 208 (1941).

A New Capillary Cell for Measuring the Rate of Sedimentation of Virus Particles in a Centrifugal Field

ELFORD[1] has developed a method of particle size determination by centrifuging solutions in inverted capillaries. The sedimentation within the capillaries fulfils Stokes's law, that is, there is a uniform movement of the particles until the boundary approaches the lower open end of the capillary. At this point the boundary comes in contact with disturbing effects such as vibrations and heat convection currents in the outer fluid. These effects tend to reduce the true rate of sedimentation.

In order to eliminate these disturbing effects on the sedimentation in the capillaries I have constructed a new type of capillary cell as illustrated in the accompanying figure.



× ½

A is a cone made of M.V.C. alloy in which a series of capillaries are drilled in such a way that those of the upper section coincide accurately with those of the lower section, into which they extend a few millimetres. The two sections of the cone fit in a conical cup *B* made of the same metal. The cup is provided with a screw at the bottom which enables the cone to be forced out without disturbance after centrifugation. Four vertical grooves are cut into the inner surface of the cups. The cup, together with the conical cell, is supported by means of a rubber washer on the rim of the centrifuge cup.

The method of using this cell is as follows:

The surface between the two sections of the cone is smeared with a thin layer of a paste made of a mixture of beeswax and wool grease, and the two sections pushed together. Care should be taken to ensure that the capillaries of the two sections coincide accurately. Some of the fluid to be centrifuged is then placed in the cup, and the cone with

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