

Inasmuch as animals can not be killed by the pure toxin, it is impossible to demonstrate antitoxic effect in the serum of animals that have received repeated doses of the toxin. The Bordet-Gengou fixation reaction failed to demonstrate the presence of antibodies in the sera of animals so treated.

The simplest prophylactic measure against *Rhus* poisoning is to wash well with soap and hot water as soon after exposure as possible. The protection of the skin by anointing with cottonseed oil before exposure and washing this off within a few hours with soap and water, renders prophylaxis fairly certain. The following remedies have therapeutic value: hot water, ichthyol collodion, permanganate of potassium, magnesium sulfate, and tincture of iodine.

45 (741)

**The failure of union between antigen and precipitin
when present in the same serum.**

By HANS ZINSSER and STEWART YOUNG.

[*Stanford University.*]

It has been frequently observed that the serum of rabbits, immunized with foreign protein, may, at certain times, contain not only precipitin, but also unaltered antigen remnants. Such sera not only precipitate the antigen, but also give precipitates when mixed with other antisera prepared with the same antigen (Linosier et Lemoine, Eisenberg, Michaelis, and Fleischmann, Ascoli, Von Dungern). They have been recently studied by Gay and Rusk. It has been difficult to explain why such sera do not spontaneously precipitate since both reacting factors are present.

In the cases of two sera recently studied by us the phenomena observed were as follows: Sera "3" and "4," obtained by injecting two rabbits with horse serum on three successive days and bleeding eight days after the last injection, were perfectly clear and showed no spontaneous precipitation on standing several days. Serum "3" precipitated horse serum in dilutions of 1 to 1,000, and serum "4" in dilutions of 1 to 500. When mixed with equal quantities of an antihorse serum precipitin, which contained no antigen, both sera were precipitated, "3" more strongly than "4." Neither of

these sera fixed complement. When "3" and "4" were mixed, slow and slight, but distinct precipitates occurred, unmistakable after 12 hours in the ice chest.

On standing for one month in the ice chest sera "3" and "4" were found to have spontaneously precipitated. The precipitate showed slight complement fixation and the supernatant fluid was found on titration to have lost about one half of its precipitating power.

Such spontaneous precipitation of precipitin sera has been repeatedly observed after prolonged conservation.

Von Dungern who has done much work on this question has assumed a multiplicity of antigens and precipitins to account for this failure of union between antibody and antigen in such sera. He says "Neben dem gebildeten Praecipitin bleibt aber ein anderer Theil der Praecipitablen Substanz der keine Affinitaet zu dem gebildeten Praecipitin besitzt, bestehen, solange bis ein anderes Partial Praecipitin von den Kaninchen geliefert wird, welches sich mit Gruppen der in Loesung gebliebenen Eiweisskoerper vereinigen kann."

We do not believe that this explanation is tenable in our cases since eventual precipitation, therefore union, took place after prolonged standing.

Another explanation (Eisenberg) accounts for the phenomenon by assuming that antigen and precipitin unite according to the laws of mass action, establishing an equilibrium, in which un-united portions of each of the reacting factors are therefore found. This explanation seems incompatible with the observation that the two sera did not bind complement, pointing to the absence of united antigen and precipitin in the sera.

We believe that the failure of union of the two elements may be regarded as closely analogous to phenomena occurring under the influence of protective colloids.

This is compatible with the original failure of the two substances to unite; with their precipitation by other sera in which there is present one or the other of the reacting bodies; and with their final spontaneous precipitation on prolonged standing.

It is more difficult to account, on this basis, for the mutual precipitation of these sera which occurs when they are mixed.

For this we have sought analogy. Fresh dog serum precipitates colloidal trisulphide of arsenic. Heated dog serum precipitates the arsenic only when small quantities of the serum are added. Larger quantities again disperse the precipitate and then protect the colloidal metal from precipitation by subsequently added fresh serum.

The addition of further arsenic trisulphide to such protected mixture will disturb the balance and lead to precipitation.

It should be possible to make up two clear solutions, each containing the three bodies, but in entirely different proportions, such that upon mixing the two, the protective action of the heated serum is so reduced that precipitation will occur. Slight, slowly appearing precipitates have been produced in this way, but the results thus far obtained have merely sufficed to emphasize the likelihood of the explanation we offer. The protective action of the heated serum is so enormous that it requires a very accurate adjustment of relative amounts to ascertain the exact limit of protection.