

THE FORMATION OF PRECIPITATES IN THE BLOOD IN VITRO BY ACID SALVARSAN SOLUTIONS.*

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H. E. Hering¹ called attention to the difference in toxicity between the acid and the alkaline solutions of salvarsan. Since that time, numerous writers have commented upon the comparative toxicity of these two solutions, but as far as I have seen, only two—Willige² and Auer³—have mentioned the concentration of the acid solution in connection with its toxicity. Auer showed recently that the toxicity of this solution varies inversely with the dilution.

In connection with the experiments described in a former paper,⁴ a large number of mixtures, *in vitro*, of blood and acid solutions of salvarsan of different concentrations were examined for precipitates. In the course of these experiments, the following facts were noted which may be of importance and which may possibly be connected with Auer's observations on the relation between toxicity and the concentration of the acid solution.

Very weak solutions of acid salvarsan (0.1 per cent.) produce with blood *in vitro* no precipitate, or at least no precipitate that is easily seen. The blood retains its normal consistency. This is true even if the volume of the salvarsan solution be from one to three times that of the blood to which it is added. The amount of precipitate produced in the blood increases with the concentration of the acid salvarsan solution employed, so that after the addition of a 1 per cent., or stronger, solution of salvarsan, the precipitate may be so heavy that the blood practically loses its fluidity and the test tube can sometimes even be inverted without spilling its contents.

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¹ H. E. Hering, *München. med. Wchnschr.*, 1910, lvii, 2621.

² Willige, *München. med. Wchnschr.*, 1910, lvii, 2403.

³ Auer, *Arch. Int. Med.*, 1911, vii, July number.

⁴ Joseph, *Jour. Exper. Med.*, 1911, xiv, 99.

The loss of fluidity is due to the formation of a precipitate and not to clotting.

While, as stated before, a comparatively large volume of a 0.1 per cent. solution of acid salvarsan may be added to blood without a precipitate being formed, a very small amount of a more concentrated solution of salvarsan (0.5 to 1 per cent. or over) gives a definite precipitate. For example, in one experiment, equal parts of a 0.1 per cent. solution of acid salvarsan and blood gave no precipitate, while 1 part of a 0.5 per cent. acid solution to 54 parts of blood gave a definite precipitate. The precipitate is formed apparently before the salvarsan can be diluted by the large volume of blood to which it is added.

In brief, then, there is a fairly definite relation between the concentration of the acid salvarsan solution used, and the quantity and consistency of the precipitate which it forms when added to the blood *in vitro*.

In the paper⁵ mentioned above, it was shown that a precipitate is formed in the blood stream by acid salvarsan solutions, just as *in vitro*; also, that the precipitate nearly always disappears from the blood stream during its passage through the lungs. Now if the more concentrated solutions of acid salvarsan produce heavier precipitates than more dilute solutions when injected intravenously, one might expect concentrated solutions to be the more dangerous. As a matter of fact, in a number of cases in which death was reported in man and animals, following intravenous injections of acid salvarsan solutions, we find that solutions of high concentration were used. Fraenkel and Grouven⁶ reported the death of a patient who received a 2.5 per cent. solution; Willige⁷ lost a case after using a 2 per cent. solution; and Miessner⁸ reported the death of several cattle that received a 5 per cent. solution.

⁵ Joseph, *loc. cit.*

⁶ Fraenkel and Grouven, *München. med. Wchnschr.*, 1910, lvii, 1771.

⁷ Willige, *loc. cit.*

⁸ Miessner, *Deutsch. med. Wchnschr.*, 1911, xxxvii, 491.