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**Analysis of the anaphylactic and immune reactions by means of the isolated mammalian heart.****By W. H. MANWARING, ARTHUR R. MEINHARD and HELEN L. DENHART.***[From the Department of Bacteriology and Immunity, Leland Stanford, Jr., University.]*

The heart of a rabbit sensitized to goat serum, tested in a blood-free condition by perfusion with 7 per cent. to 10 per cent. goat serum, is more resistant than a normal rabbit heart similarly tested. The increased resistance is shown by the absence of the initial tachycardia, the absence or delayed development of the secondary tachycardia, and a prolongation of the life of the isolated organ.

Hearts of rabbits sensitized or immunized by repeated injections with goat serum, are more resistant than those sensitized with a single injection.

Normal rabbit serum, corpuscles or defibrinated blood, added to the perfusion fluid, decreases its toxicity. The antitoxic action of defibrinated blood is apparently equal to the sum of the antitoxic actions of its serum and corpuscles.

Anaphylactic rabbit serum similarly added usually markedly increases the toxicity of the perfusion fluid. Such an anaphylactic serum mixture may completely inactivate a normal heart within from two to four minutes. Hearts of anaphylactic and immune rabbits are more resistant than normal hearts to such mixtures.

The active principle of the anaphylactic serum responsible for this increased toxicity is thermo-labile, the toxin-increasing or toxin-producing power being completely lost, if the serum is heated to 60° C. for 30 minutes.

The active principle is not complement, since such inactivated anaphylactic sera cannot be reactivated by the addition of unheated normal serum.

The active principle is presumably not precipitin, since the specific precipitins of rabbit serum are not destroyed, or at least not completely destroyed, by heating the serum to 60° C. for 30 minutes.

Such inactivated anaphylactic sera are strongly antitoxic. The presence of a thermo-stable antitoxin in the unheated anaphylactic serum is apparently masked by the relatively strong thermo-labile toxin-increasing or toxin-producing substance.

This thermo-stable antitoxin is present in larger amounts in the sera of rabbits sensitized or immunized by multiple injections, than in rabbits sensitized by a single injection.

Sera of partially immunized rabbits (3-5 injections) added to the perfusion fluid, usually give a non-fatal shock with normal hearts. The heart may come to a complete standstill by the end of four minutes, may remain inactive<sup>1</sup> for from two to four minutes, and then recover completely within two or three minutes. A heart that has passed through such a non-fatal shock will usually continue to beat strongly and regularly for an hour or more.

Sera of highly immunized rabbits (8-12 injections) added to the perfusion fluid, usually give no shock, and show only a marked antitoxic action.

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#### **Autolysis of anaphylactic and immune tissues.**

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The post-mortem autolysis of normal, anaphylactic and immune guinea pig livers was followed by determining the changes in the relative amounts of coagulable and non-coagulable nitrogen (Kjeldahl method). The anaphylactic guinea pigs had been sensitized by a single injection of egg-white or goat serum. The sensitizing dose varied from 0.1 c.c. to 2 c.c. Analyses were made from 11 to 17 days after the injection. The immunized guinea pigs had been injected at 4-7 day intervals with from 3 to 7 doses of the same antigens. They were analyzed from 8 to 12 days after the final injection. A summary of the data so obtained is shown in the following table:

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<sup>1</sup> The coronary perfusion is made under constant pressure, and is only partially dependent upon heart action. The perfusion of the myocardium, therefore, continues during the inactive period.