Histamine-Independent Mechanisms in Shock in Guinea-Pigs

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Our investigations as to the role of histamine in anaphylactic, anaphylatoxin and Forssman shock detected some mechanisms which are not induced by the release of histamine. For example, in contrast to anaphylatoxin shock, large doses of antihistamines into saline perfused guinea-pig lungs did not influence the intensity either of the anaphylactic bronchospasm or of the constriction of lung vessels.

In the blood-perfused heart-lung preparation of guinea-pigs, the anaphylactic histamine release was as high as in the isolated lung, and the anaphylactic bronchoconstriction was not inhibited by antihistamines. In most preparations, the cardiac output and the blood pressure did not change until heart failure induced by anoxia was apparent. In some experiments heart failure was observed immediately after antigen injection. This early heart failure occurred more frequently in the presence of antihistamines, suggesting that an initial small anaphylactic damage to the heart may have been made visible, enlarged and aggravated by the antihistamine. The early heart failure may be the result of anaphylactic constriction of the pulmonary vessels.

In the heart-lung-liver preparation of guinea-pigs, anaphylactic constriction of the liver vessels probably occurred and resulted in decreasing cardiac output, diminished heart volume and depressed blood pressure in the right atrium.

In the intact animal, anaphylatoxin shock produced a decrease in the number of white blood cells but this decrease has nothing to do with the bronchospasm as this occurred when red blood cell

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suspensions were perfused in the heart-lung preparation. Anaphyla-toxin as well as anaphylaxis had an antihistamine-resistant effect on the liver vessels.

The acute mortality of guinea-pigs due to anaphylactic bron-chospasm was totally inhibited by antihistamines, but many of the animals died later with congestion of the abdominal organs and dilatation of the right ventricle, but no inflation of the lungs. Perhaps this form of protracted shock may be induced by the antihistamine-resistant constriction of the pulmonary and liver vessels.

Somewhat larger doses of antihistamines were needed to reduce the acute mortality in anaphylactic shock than in anaphyla-toxin shock but this may result from the fact that histamine released from the lung itself plays a major part in anaphylaxis in this species.

In the Forssman shock in the intact animal, histamine liberation was very small, lung oedema occurred, and antihistamines did not reduce the death rate, though they slightly delayed the onset of shock symptoms. Large doses of heparin also had a strong inhibitory effect in this type of shock, probably by inhibiting the activity of certain plasma factors. Thus this shock mechanism differs from those involved in anaphylactic and anaphylatoxin shock.