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HEPATIC REACTIONS IN ANAPHYLAXIS

VIII. ANAPHYLACTIC REACTIONS IN ISOLATED CANINE ORGANS

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To find a tissue that would serve as a reliable reacting index for the serological analysis of anaphylactic phenomena in dogs, tests were made of anaphylactic reactions in the principal isolated canine organs.

The dogs were sensitized by a subcutaneous injection of 0.3 to 0.5 cc. horse serum per kilogram of body weight, followed two days later by an intravenous injection of the same dose. The isolation tests were made between the seventeenth and twenty-fourth day after the intravenous injection. During this period all control dogs thus far tested have given typical anaphylactic reactions on intravenous injection of horse serum, about a third of them reactions of the fatal type (1). The isolation tests were made by perfusion methods. The perfusion fluid was well-aerated Locke's solution containing 0.04 to 2.5 per cent horse serum. The perfusion technic was otherwise the same as that described in a previous paper (2).

BLOOD-FREE PERFUSIONS OF ISOLATED ANAPHYLACTIC ORGANS

Distinct anaphylactic phenomena have been demonstrated in all isolated canine organs thus far tested. The following parts have been studied:

a. Lungs: Slight preliminary decrease in perfusion resistance, increasing the perfusion rate about 12 per cent (fig. 1). This is followed in from thirty to ninety seconds by a marked increase in perfusion resistance, reducing the perfusion flow fully 70 per

cent. With larger serum doses (A, fig. 1), this reduction reaches its maximum by the end of ninety seconds. With smaller serum doses (B, fig. 1), the maximum is not reached till the fourth to tenth minute.

During the perfusion, the lungs take on a rubber-like consistency. On releasing the tracheal clamp, practically no pulmonary collapse takes place. A large amount of clear, frothy fluid now escapes from the trachea. If the perfusion is continued with the tracheal clamp removed, fluid continues to pour out of the trachea almost as rapidly as it escapes from the efferent cannula.

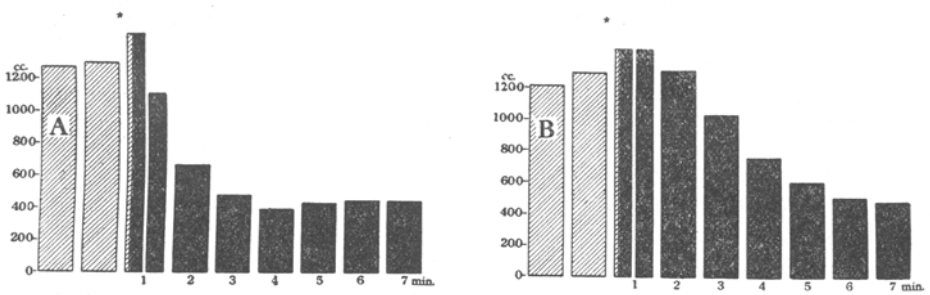

FIG. 1. REACTIONS IN ISOLATED ANAPHYLACTIC LUNGS

Cross-hatched areas show perfusion flow per minute with Locke's solution. Black areas show rate per minute (or half-minute) with Locke's solution plus horse serum. Stars (*) show time of changing the perfusion clamps. Temperature, 38°C., perfusion pressure, 25 mm. Hg.

A = Composite picture of three perfusions with 2.5, 1 and 0.5 per cent horse serum respectively. Control perfusions of normal lungs show no change in perfusion rate within the limits of the experimental error.

B = Composite picture of three perfusions with 0.25, 0.125 and 0.06 per cent horse serum respectively.

On gross section, each large blood vessel of the lungs is seen to be partially collapsed and surrounded by an edematous zone. Whether or not the increased perfusion resistance is due to increased local tissue pressure from this perivascular edema, cannot be determined from our present data. A histological study of these reactions will be reported later.

b. Intestines: Gradual increase in perfusion resistance reducing the rate of perfusion flow from 20 to 40 per cent by the end of

seven minutes, depending upon the serum concentration used (fig. 2). Marked peristaltic movements. Increased tone of the intestinal musculature. Distinct edema of the intestinal walls. Peritoneal transudation. Marked increase in the volume of the intestinal contents.

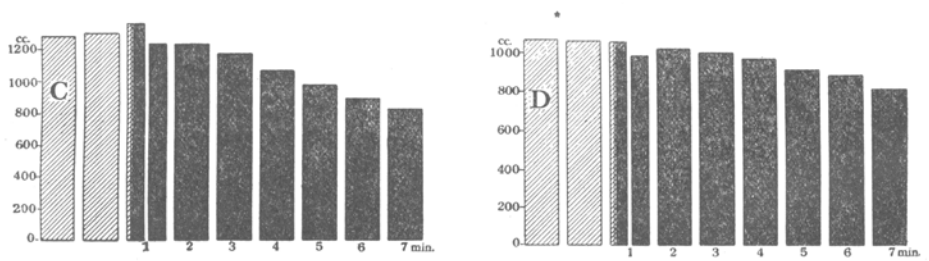

FIG. 2. REACTIONS IN ISOLATED ANAPHYLACTIC INTESTINES

Afferent perfusion pressure, 80 mm. Hg; efferent perfusion pressure, 10 mm. Hg.
C = Perfusion with 2.5 per cent horse serum.
D = Composite picture of two perfusions with 0.5 and 0.25 per cent horse serum respectively.

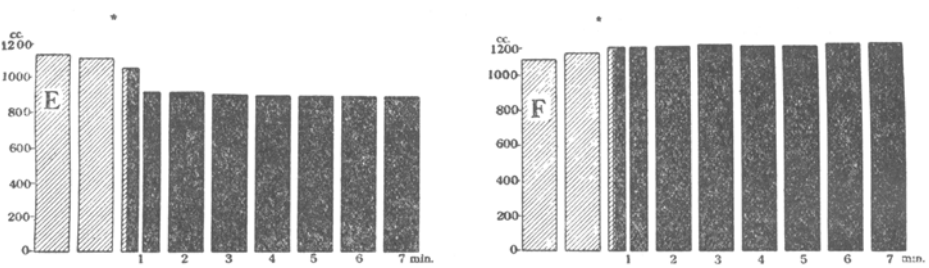

FIG. 3. REACTIONS IN ISOLATED ANAPHYLACTIC LIVERS

Perfusion pressure, 15 mm. Hg.
E = Composite picture of three perfusions with 2.5, 1 and 0.5 per cent horse serum respectively.
F = Composite picture of two perfusions with 0.25 and 0.125 per cent horse serum respectively.

c. Liver: With the larger serum doses (E, fig. 3), an increased perfusion resistance, reducing the rate of perfusion flow about 20 per cent by the end of thirty seconds. With smaller serum doses (F, fig. 3), no demonstrable change in perfusion rate within the limits of the experimental error. Distinct hepatic edema. Peritoneal transudation.

d. Hind quarters: On control perfusion of the hind quarters with Locke's solution, the rate of perfusion flow usually increases rapidly during the first two minutes. After the second minute, the flow usually remains fairly constant till the end of the test. The maximum variation during the next seven minutes is usually not more than 5 per cent.

On perfusing anaphylactic hind quarters, two types of reaction have been obtained. Type 1 (G, fig. 4): A decreased perfusion resistance increasing the perfusion rate about 12 per cent by the end of three minutes. No demonstrable edema except a slight edema of the genitalia. Type 2 (H, fig. 4): A rapid increase in

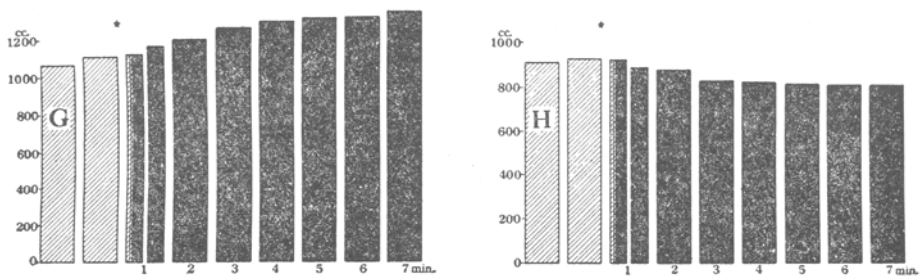

FIG. 4. REACTIONS IN ISOLATED ANAPHYLACTIC HIND QUARTERS

Perfusion pressure, 80 mm. Hg.

G = Composite picture of two perfusions with 2.5 per cent horse serum.

H = Composite picture of two perfusions with 0.5 and 0.25 per cent horse serum respectively.

perfusion resistance, decreasing the perfusion flow about 10 per cent in from thirty to ninety seconds. Pronounced edema of the hind quarters, particularly of the foot and genitalia.

It is believed that the differences between these two types are merely quantitative, depending upon differences in serum concentration and degree of sensitization. Our data, however, are insufficient to establish this fact.

COMPARISON WITH HISTAMINE REACTIONS

The above anaphylactic reactions differ quantitatively and in some cases qualitatively from the histamine reactions previously reported (3). For example, the anaphylactic edema

and vasoconstriction in the lungs are much more pronounced than the corresponding histamine vasoconstriction and edema. An initial vasodilation was not observed in our histamine tests.

The intestinal reactions are approximately equal in the two cases.

The anaphylactic reactions in the liver are much less pronounced than the corresponding histamine reactions.

The histamine reactions in the hind quarters are a marked vasodilation with very pronounced edema. These reactions are uniformly more marked than the slight vasodilation and edema in anaphylaxis. Vasoconstriction of the hind quarters was not observed in our histamine tests.

PHYSIOLOGICAL DEDUCTIONS

We conclude from the above observations that one of the important factors in canine anaphylaxis is an increased specific permeability (susceptibility to specific injury) of the capillary endothelium (4). The capillary endothelium of different parts of the body apparently differs widely in this acquired hyperpermeability. The endothelium of the hind quarters shows the least change from the normal. The hepatic and intestinal endothelium occupy an intermediate position. The pulmonary endothelium shows the most marked alterations.

The vasoconstriction in the different parts of the body varies roughly with the severity of the edema. We believe, therefore, the vasoconstriction is possibly secondary to increased tissue pressure from edema.

Histamine reactions in blood free perfusions of isolated organs differ from histamine reactions in defibrinated blood perfusions (5, 6). No attempt will therefore be made to draw conclusions from the above anaphylactic tests as to the probable mechanism of anaphylactic shock in intact dogs. Defibrinated blood perfusions will be reported later.

CONCLUSIONS

From these tests it would appear that the only isolated canine organs giving anaphylactic reactions sufficiently pronounced to

be used in the serological analysis of anaphylactic phenomena in dogs are the isolated lungs. Serological analyses by means of the isolated lungs will be reported later.

SUMMARY

1. The isolated organs of horse serum sensitized dogs, perfused with Locke's solution containing 0.04 to 2.5 per cent horse serum, give the following reactions:

a. Lungs: Slight preliminary vasodilation, followed by a pronounced vasoconstriction. Marked edema.

b. Intestines: Distinct vasoconstriction. Marked edema.

c. Liver: Slight vasoconstriction. Slight edema.

d. Hind Quarters: Either: (1) slight vasodilation without edema or (2) slight vasoconstriction with marked edema.

2. The vasoconstriction in these organs may possibly be secondary to increased tissue pressure from edema. If so, increased specific capillary permeability must be looked upon as the dominant underlying physiological factor in these reactions.

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