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The hepatic anaphylatoxin. Final evidence of its rôle in canine anaphylaxis.

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In previous papers,[1, 2] it was shown that typical anaphylactic contractions of certain smooth muscle structures do not take place on intravenous injection of specific foreign protein into dehepatized anaphylactic dogs. The conclusion was drawn that the characteristic smooth muscle contractions in intact dogs are due to chemical products (hepatic anaphylatoxins), explosively formed or liberated by the anaphylactic liver. We have obtained additional evidence in support of this conclusion by cross-circulation, hepatic transplantation and blood transfusion tests.

As a preliminary to these tests it was shown that primary reactions between specific foreign protein (horse serum) and anaphylactic blood are in themselves insufficient to produce recognizable anaphylactic reactions in normal canine tissues. If a normal dog is exsanguinated as completely as possible and transfused from an anaphylactic donor, the normal dog will show no recognizable anaphylactic phenomena on immediate intravenous injection with specific foreign protein. This finding is in line with the well-known latent period in passive anaphylaxis.

If the isolated hind-quarters of a normal dog are connected by means of paraffined rubber tubes with the general circulation of an anaphylactic dog, typical anaphylactic contractions of the normal urinary bladder and of the normal rectum occur on intravenous injection with specific foreign protein. If the isolated liver of an anaphylactic dog is connected with the general circulation of a normal dog, the normal dog will show a typical anaphylactic fall in arterial blood pressure, typical contractions of the urinary bladder and of the gastro-intestinal tract, and a typical loss of blood coagulability, on intravenous injection with specific

[1] Manwaring, W. H., Hosepian, V. M., Enright, J. R., and Porter, D. F., PROC. SOC. EXP. BIOL. AND MED., 1924, xxi, 536.

[2] Manwaring, W. H., Enright, J. R., Porter, D. F., and Moy, H. B., PROC. SOC. EXP. BIOL. AND MED., 1924, xxii, 61.

foreign protein. We believe these experiments furnish conclusive evidence of the existence of toxic hepatic products in the general circulation, at least during the initial stage of canine anaphylactic shock.

If blood is drawn from the carotid artery of an anaphylactic dog from two to five minutes after throwing the dog into anaphylactic shock, and this blood is immediately transfused into a partially exsanguinated normal dog, no recognizable anaphylactic phenomena usually occur. This finding is in line with the negative results previously reported by Weil.[3] If, however, the foreign protein is injected directly into a mesenteric vein of the anaphylactic dog and shock blood is collected as it escapes from the liver, this blood, transfused into a normal dog, will reproduce all of the characteristic features of canine anaphylaxis. One hundred cc. of this hepatic blood, transfused into a 10 kg. normal dog, will cause a typical fall in arterial blood pressure lasting thirty minutes, typical contractions of the urinary bladder and of the gastro-intestinal tract, and a typical, usually complete loss of blood coagulability. The toxic hepatic products in themselves, therefore, are apparently sufficient to account for all of the observed anaphylactic phenomena.

The shock in normal dogs connected with an anaphylactic liver is less prolonged than the shock in intact anaphylactic controls. The toxic hepatic products, therefore, are presumably not the only factors operative in canine anaphylaxis.

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Changes in glycogen content of the liver in anaphylaxis.

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Changes in the glycogen content of the liver in canine anaphylactic shock were followed by routine histological and chemical methods.

[3] Weil, R., *J. Immunol.*, 1917, ii, 399.