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The fundamental physiological mechanism of anaphylaxis.

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The following is our conception of the fundamental physiological mechanism of canine anaphylaxis, and constitutes our present working hypothesis with other animal species.

We assume that the capillary endothelium is the initial point of anaphylactic attack and defense. We further assume that in dogs the different capillary systems have different susceptibilities to the anaphylactic insult, the capillaries of the liver having the greatest susceptibility.

On intravenous injection of the usual doses of specific foreign protein into sensitized dogs, the hepatic endothelium alone is unable to resist the anaphylactic insult. There is a sudden increase in capillary permeability in this organ, with the rapid passage of foreign protein and altered blood plasma into the hepatic tissue spaces.

The hepatic parenchyma, in consequence, is immediately thrown into exaggerated, possibly atypical functional activity. The chemical products from this activity pass rapidly into the circulating blood, on account of the increased hepatic capillary permeability. These products, acting in conjunction with the circulating foreign protein and altered blood plasma, break down the endothelial defenses in the extra-hepatic tissues, with the resulting rapid passage of atypical products into the extra-hepatic tissue spaces.

This conception, we believe, fully accounts for the clinical picture of canine anaphylaxis. Thus, the suddenly increased local tissue pressure from hepatic edema with the resulting passive narrowing of the hepatic capillaries, coupled with the suddenly increased local blood viscosity from plasma loss, would account for the characteristic hepatic stasis. The suddenly reduced available blood volume from hepatic stasis and resulting gastro-intestinal passive congestion, coupled with the reduced blood volume from hepatic and extra-hepatic plasma losses, would account for the characteristic fall in arterial blood pressure.

This conception of the fundamental mechanism of anaphylaxis tends to unify anaphylactic phenomena in different animal species. The dominant clinical manifestations in different species would depend upon the relative anaphylactic susceptibility of the capillary endothelium in these species, with the resulting promptness and completeness with which atypical chemical products are brought into contact with the secondary tissues.

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An experimental study of the effect of stenosis upon the respiratory changes induced by muscular exercise.

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Dyspnea from muscular exercise results when the increased respiratory demands can no longer be met without effort. In the present series of experiments the ability to meet these demands was artificially restricted by having a normal individual (A. W. H.) breathe through small apertures. For this purpose two perforated corks were used, the diameters of the bores being 8 mm. and 6 mm. respectively. The first of these caused no effort so long as the subject of the experiments was at rest. It caused moderate respiratory effort when stairs were climbed at the rate of approximately 80 per minute. The second caused slight effort at rest and considerable distress during stair climbing. The latter culminated in discontinuance of the exercise after two or three minutes.

During rest, the respiratory rate was not influenced by the milder obstruction but in some experiments was somewhat slowed by the more marked obstruction. During exercise, the respiratory rate was definitely slowed by each, average figures being: without stenosis 27 respirations per minute, with 8 mm. stenosis 21 respirations per minute, and with 6 mm. stenosis 17 respirations per minute.

During rest, the minute volume of respiration was not altered by the lesser stenosis but in some experiments became somewhat