

We believe, therefore, that these observations, in conjunction with present known facts regarding the stimulating action of alcohol upon gastric secretion, warrant the theory that alcohol has a "histaminergic" action and that its stimulating action upon gastric secretion depends upon this mechanism.

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**Peptone Shock in Fetal Dogs and its Significance in the Metabolism of Histamine.**

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It has previously been shown<sup>1, 2</sup> that "peptone" shock in dogs, which is produced by the intravenous injection of proteoses, is accompanied by and due to the liberation of histamine from the tissues of the injected animals. The source of, and the reasons for, the storage of histamine in the tissues are only incompletely understood. It seemed, therefore, of interest to determine whether histamine is present in the tissues of fetal animals, and if it is present, to determine whether it can readily be liberated with resulting shock reactions such as occur in adult animals. The studies of Code<sup>3</sup> indicate that the traces of histamine which are normally present in the blood of dogs occur in the cellular elements and not in the plasma. This would imply that the histamine normally circulating in the blood of a pregnant dog would not be accessible to the fetus. As there is no opportunity for the formation of histamine within the fetus by bacterial decomposition of histidine in the fetal intestine, it may be presumed that any histamine occurring in fetal tissues has been produced by local mechanisms such as histidase.<sup>4</sup>

The skeletal muscle and liver of a 200 g fetus, obtained by Caesarian section, were assayed for histamine by the method of Best<sup>5</sup> and Best and McHenry.<sup>6</sup> The skeletal muscle assayed less than 0.1

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<sup>1</sup> Dragstedt, C. A., and Mead, F. B., *J. Pharm. and Exp. Ther.*, 1937, **59**, 429.

<sup>2</sup> Dragstedt, C. A., and Mead, F. B., *J. Pharm. and Exp. Ther.*, 1938, **63**, 400.

<sup>3</sup> Code, C. F., *J. Physiol.*, 1937, **90**, 349.

<sup>4</sup> Holtz, P., and Heise, R., *Archiv. f. exp. Path. u. Pharm.*, 1937, **186**, 377.

<sup>5</sup> Best, C. H., *J. Physiol.*, 1929, **67**, 256.

<sup>6</sup> Best, C. H., and McHenry, E. W., *J. Physiol.*, 1930, **70**, 349.

mg histamine base per kilo of tissue. It is, therefore, somewhat doubtful whether any histamine was present. The liver assayed 5.0 mg of histamine base per kilo of tissue.

Three 400 g fetuses, obtained at term, were anesthetized with ether and arranged for the recording of the carotid blood-pressure. Two cc per kilo of peptone solution were injected intravenously in each case, and the resulting reactions recorded. The peptone solution used was a 10% solution of Bacto-Protone-Difco, which had previously been acidified, shaken with permutit, filtered, and then neutralized. Such solutions contain negligible quantities of histamine, are rich in proteose and have been found very satisfactory.<sup>2</sup> A severe reaction occurred in each instance. The reaction was fatal in one, and probably would have been fatal in the others, although in these any possible recovery was prevented by bleeding them to death so that histamine determinations of the blood could be made. The blood was incoagulable in each instance. The plasma in each instance had a histamine activity equivalent to 0.6 gamma histamine base per cc when tested on the etherized and atropinized cat.

*Discussion.* Histamine occurs in the liver, if not in the skeletal muscle of the dog fetus. The quantity appears to be less than that occurring in adult dogs, although more information is necessary to establish the average relationship. Peptone shock can occur in the dog fetus and, as is the case in the adult dog, it is associated with the liberation of histamine. These findings would seem to have a bearing on the question of the metabolism of histamine, indicating that an appreciable part, at least, of the histamine store in the tissues owes its existence to other than bacterial production.

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### Toxic and Therapeutic Response of Blood and Bone Marrow to Sulfanilamide.

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Sulfanilamide may produce an acute hemolytic anemia, which comes on rapidly after therapy and may terminate fatally. More commonly, however, the drug causes a mild type of anemia which is