

# Illinois Branch.

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## Modification of Adrenalin Effect with Functional Status of Stomach.

SERGIUS ARQUIN. (Introduced by W. F. Petersen.)

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There has been a growing conviction among physiologists and pharmacologists that the reaction of an organ to stimulation will vary, within certain limits, with the state of tonus of the organ at the time of excitation. This conviction applies to drugs involving the autonomic nervous system, but by no means confined to them. A good part of the work has been done on strips of extirpated muscle, or the nerves of the organ have been cut, or numerous drugs influencing the autonomic system have been used in succession, so that, the results must be interpreted in the light of altered physiologic status.

Our work was done on a series of normal dogs trained to lie perfectly quiet under no restraint. A fine balloon at the end of a duodenal tube was passed by mouth (the dogs offer very little resistance after the first 3 or 4 times) and the duodenal tube was connected to a water manometer. The balloon was inflated with 100 cc. of air and the fluctuations of the manometer levels were recorded on a slowly revolving Kymograph. After a suitable control period an injection of 5 m. of 1:1000 Parke Davis Adrenalin was given intracutaneously, in the leg, forming a wheal. (Intracutaneous injection was chosen because a mild relatively prolonged action was desired.)

Controls. The animals' gastric functions were established over a period of one to two weeks under daily observation. They showed: (1) That hunger contractions in a starving animal last from 30 to 50 minutes, and periods of active motility are separated from each other by periods of relative quiescence. (2) These periods of quiescence last from 1 to 1½ hours. In a few instances, however, they were as short as 45 minutes. (3) There was at no time a complete relaxation of the stomach in a starving animal. During the period

of relative quiescence there were regular tonus waves occurring every 2 to 3 minutes. (4) For 3 to 4 hours after feeding, the stomach shows active digestive contractions, which lead directly into hunger contractions.

Results. The results obtained after the intracutaneous injection of adrenalin were as follows: (1) In a starving animal during the period of relative quiescence the administration of adrenalin intracutaneously resulted within 10 minutes after complete absorption of the adrenalin (as indicated by the disappearance of the wheal) in a rapid increase in gastric tonus and forcible hunger contractions. Usually the absorption of adrenalin would be complete 10 to 15 minutes after injection. (2) In a starving animal with active hunger contractions the administration of intracutaneous adrenalin resulted (after absorption) in a marked gastric dilatation, much greater than the physiologic inhibition observed in our controls. This inhibition lasted for 20 to 30 minutes, after which the stomach gradually returned to the former status. (3) A stomach in active digestive contractions is not influenced at all by the administration of adrenalin—even if the dose is increased to 15 m. intracutaneously or 10 m. intramuscularly. Apparently, therefore, adrenalin injection may be followed by diametrically opposed reactions on the part of the stomach musculature depending on the pre-existing status. This property is manifested, not only on isolated strips of gastric musculature, as has already been reported<sup>1</sup> but also on the intact organ of normal animals.

Most of the older observers explain this apparent paradox on the basis of a predominance in the tonus of either the sympathetic or the parasympathetic nerve group, resulting in variations in reaction to stimulation.<sup>2</sup> Schilf<sup>3</sup> concludes that there must be some change in the organ proper, not in the nerves, that causes this modification of reaction. Burn and Dale<sup>4</sup> attributed these phenomena to the variations in the state of tonus of the capillaries which in turn are controlled by the amount of histamine in the tissues.

None of the numerous theories is very conclusive. Until some very substantial proof is forthcoming no more theories should be given. We do feel, however, from these experiments, that the site of reversal must be in the organ cells, although the possibility of involvement of the terminal neuro muscular apparatus cannot be definitely eliminated.

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<sup>1</sup> McSwinnery and Brown, *J. Physiol.*, 1926, lxi, 261.

<sup>2</sup> Cow, D., *J. Physiol.*, 1918, lii, 301.

<sup>3</sup> Schilf, E., *Klin. Wochens.*, 1927, vi, 193.

<sup>4</sup> Burn and Dale, *J. Physiol.*, 1926, lxi, 185.