THE INFLUENCE OF OXYGEN SUPPLY ON THE RESPONSE OF THE ISOLATED INTESTINE TO DRUGS.

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THE isolated intestines of rats and rabbits were used in the following experiments. These were suspended in the usual manner in Tyrode's fluid. We found that cutting off the oxygen supply caused a lowering of the tonus of the gut although the pendulum movements continued unaltered, and that with the loss of tone the gut ceased to respond to adrenalin and pilocarpine.

A stream of air maintained the activity of the gut as well as a stream of oxygen, but the effects of cutting off the oxygen or air were not due to any mechanical effects, for the substitution of oxygen by a stream of nitrogen (Fig. 3) produced exactly the same effects as did the simple cutting off the oxygen supply (Fig. 1). When the supply of air or oxygen to the rat's or rabbit's gut is cut off, there is at first a slight rise in tonus and then a rapid fall. When the air is turned on, there is a slow rise of tonus (Fig. 2).

When the gut is relaxed by the lack of oxygen it is very insensitive to the action of adrenalin. Fig. 2 shows that adrenalin 1 in 25 million, which produces a strong effect on the normal gut, produces no effect on the relaxed gut. Fig. 5 shows that as the gut regains its tonus after oxygen lack it becomes progressively more sensitive to adrenalin.

The failure of the asphyxiated gut to respond to adrenalin might be due to its being in a state of maximum relaxation but the gut is equally insensitive to the action of stimulants such as pilocarpine, as is shown in Fig. 4. This figure shows that pilocarpine in moderate concentrations does not act on the asphyxiated gut, but that as soon as air is introduced the pilocarpine acts and the gut contracts violently. The asphyxiated gut is not paralysed for it can respond to the action of stimulants acting directly on the muscle. Fig. 1 shows this in the case of potassium chloride, and Fig. 6 shows the same effect with barium chloride.

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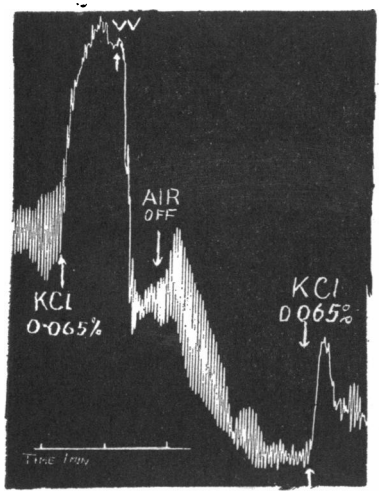

Fig. 1.

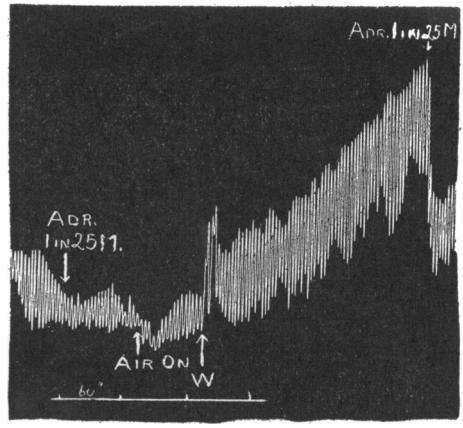

Fig. 2.

Fig. 1. Isolated gut of rabbit. Effect of increasing concentration of KCl from ·02 % to ·065 %. (1) Gut supplied with oxygen; (2) on asphyxiated gut.

Fig. 2. Isolated gut of rabbit deprived of oxygen for a few minutes. Action of adrenalin (1) on asphyxiated gut, (2) on gut supplied with air.

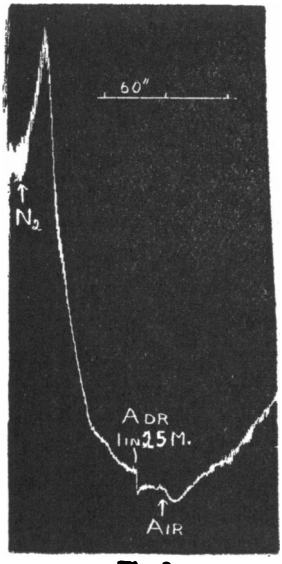

Fig. 3.

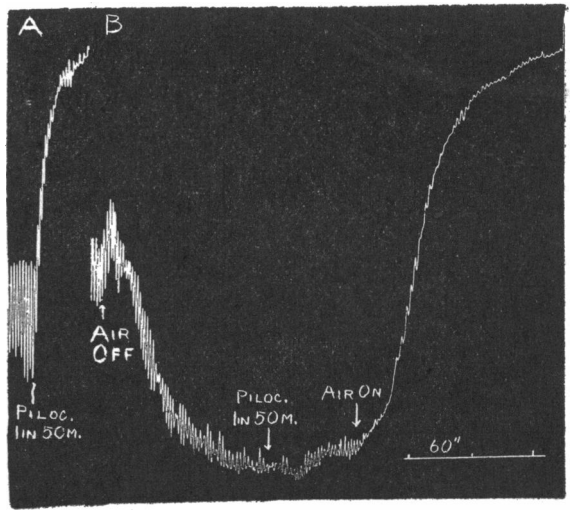

Fig. 4.

Fig. 3. Isolated gut of rat. Effect of replacing air by nitrogen, and action of adrenalin on asphyxiated gut.

Fig. 4. Isolated gut of rat. Effect of pilocarpine: *A*. on gut supplied with oxygen; *B*. on asphyxiated gut.

Asphyxia therefore appears to paralyse the sympathetic and parasympathetic nerve endings in the gut long before the gut muscle itself is paralysed. This result agrees with the work of Gunn and Underhill(1) who showed that the isolated gut, when kept for long periods, first became insensitive to parasympathetic stimulants, then to sympathetic stimulants and last of all to plain muscle stimulants. These workers also showed that the pendulum movements continued long after the nerve endings had become paralysed but that they ceased at the same time as the gut became insensitive to direct muscle stimulants. They adduced these facts as evidence of the myogenic origin of pendulum movements and our results support the same view. An examination of our tracings shows that the pendulum movements of the gut are not altered either in rate or extent at a stage in asphyxia when the gut no longer responds to either adrenalin or pilocarpine.

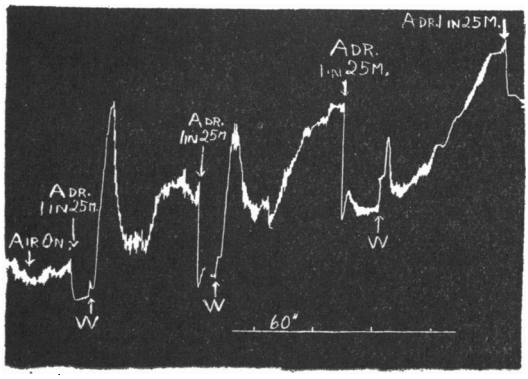

Fig. 5.

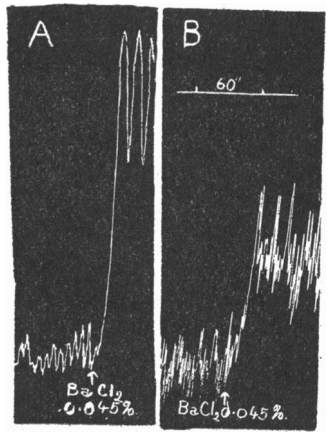

Fig. 6.

Fig. 5. Isolated gut of rat deprived of oxygen for a few minutes. Action of adrenalin with gradually increasing air supply.

Fig. 6. Isolated gut of rat. Action of barium on gut: *A.* when supplied with oxygen, *B.* when deprived of oxygen. The initial tonus of the gut in *B* was much lower than the initial tonus in *A*.

This paralysis of specific nerve endings by asphyxia was not observed in the other isolated organs tested, namely the uterus and heart. For example the isolated auricle of the rabbit is fairly rapidly affected by lack of oxygen, the height and rate of the contractions being diminished, and this effect is produced even more rapidly if nitrogen is substituted for oxygen. The asphyxiated auricle, however, responds to adrenalin

and pilocarpine in the same manner as does the normal tissue. The effect produced on the gut by lack of oxygen appears therefore to be peculiar to this tissue. Apparently there are in the isolated gut two independent mechanisms, one regulating the pendulum movements and the other regulating the tonus. The latter mechanism is intensely sensitive to the action of adrenalin and pilocarpine for these drugs alter tonus in concentrations far lower than those required to alter pendulum movements (Alvarez(2)). Lack of oxygen paralyses the tonus regulation mechanism very rapidly and hence renders the gut insensitive to low concentrations of the above mentioned drugs.

Evidence from other isolated tissues suggests that the sympathetic and parasympathetic nerve endings are not particularly sensitive to lack of oxygen. The effects observed with the gut can, however, be explained on the assumption that the tonus of the gut is maintained by the nerve cells in Auerbach's plexus: for nerve cells are known to be very sensitive to oxygen lack. The results in this paper support the view that the pendulum movements on the other hand are myogenic.

Conclusions.

(1) Cessation of oxygen supply, or the substitution of nitrogen for oxygen, causes an immediate loss of tonus in the isolated intestine.

(2) Lack of oxygen does not affect the pendulum movements of the gut for a long time.

(3) Lack of oxygen causes in the isolated gut a great diminution in sensitivity to adrenalin and pilocarpine, but no corresponding diminution in the reaction to direct muscle stimulants such as potassium and barium.

(4) These results support the view that the pendulum movements of the gut are myogenic, but suggests that the tonus of the gut is neurogenic.

REFERENCES.

(1) Gunn and Underhill. Quart. Journ. Exp. Physiol. 8. 275. 1914.
(2) Alvarez. The Mechanics of the Digestive Tract (Hoeber, New York). 1922.