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Observations on the relation of the adrenal glands to the blood-pressure response during cerebral anæmia in cats and rabbits.

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The blood-pressure response during cerebral anæmia was analyzed by Pike, Guthrie and Stewart a number of years ago. Recently Winkin in studying some of the nervous factors involved in the cardio-vascular changes which take place during cerebral anæmia observed that after repeated occlusions of the head arteries for short periods, the curve of the anæmic rise may become dissociated into two distinct parts.

The question was raised by Winkin whether the second part of this anæmic rise may not be due to increased availability of some product of adrenal activity which the "cardio-vascular relations found in the mammalian organism under extreme conditions of stress" would call forth. With this in mind, we have carried out a series of experiments on cats and rabbits when:

1. The adrenal glands are tied off, or excised during an acute experiment.
2. The adrenal veins are clipped.
3. The remaining adrenal is excised (one having been previously excised and the animal allowed to recover).
4. One adrenal is excised and the other denervated (and the medulla of it curetted out or a large part of the remaining gland excised in addition to denervation) and the animal allowed to recover.
5. : Both adrenals are excised (rabbit) and the animal allowed to recover.

In cases 3, 4, and 5 the animals were operated upon from two to four weeks before the acute experiments were performed. The technique of the acute experiment was that devised by Stewart, Guthrie, and Pike in which the arteries are secured as they emerge from the thorax. It is well known that in the cat and rabbit, when the carotid and subclavian arteries (proximal to the origin of the vertebrals) are occluded, circulation to the head

is completely interfered with and cerebral anæmia with the attendant anæmic rise of blood-pressure ensues rapidly. The high level of blood-pressure is maintained until the fall to the spinal level of pressure indicates the failure of bulbar function. If the occlusion has not been carried on for too long a time, release of the head arteries with the maintenance of artificial respiration results, eventually, in restoration of the bulbar and cerebral function, the degree of restoration of function depending on the amount of injury that has been inflicted by the occlusion.

In our experiments, the beginning of the fall in blood-pressure, after the anæmic rise induced by occluding the head arteries, was the signal for the restoration of cerebral circulation, and the return of the blood-pressure to the previous level (or nearly so), together with the return of an active corneal reflex were usually the criteria for the beginning of the next occlusion of the head arteries. Artificial respiration was constantly maintained after the beginning of the first occlusion.

By employing this technique a number of occlusions (up to about thirty) can be made before there is a lack of response from the medulla to cerebral anæmia. In a large number of cases, after the first few occlusions, the curve of the anæmic rise has been observed to dissociate into two parts, each occupying about half the time which an undissociated curve would occupy, as reported by Mrs. Winkin. This type of dissociation curve we have obtained, however, not only in normal animals, but with equal success in the animals in which epinephrin secretion had been suppressed or abolished.

Moreover, animals in which adrenal function had been greatly interfered with or abolished by the operations above mentioned are able to respond in the usual manner to as many occlusions of the head arteries as normal animals. We have found that the number of definite responses to cerebral anæmia is largely dependent upon the general blood-pressure level existing just before the occlusion and that when this has fallen to spinal level so that no rise in blood-pressure can be obtained on occlusion of the head arteries, it is possible to obtain good responses by raising the basal level through injection of Ringer's solution, so long as the Ringer's solution is capable of sustaining a higher level of blood-pressure. But when a condition is reached when the blood-pressure improvement is transient, the usual responses are

no longer obtainable on occlusion of the arteries. Resuscitation can frequently be repeated with Ringer's solution a number of times before a condition is reached when it is no longer effective.

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Barium-epinephrin antagonism on the excised surviving intestine.

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Experiments conducted recently on the excised surviving intestine of the frog, showed that the barium contraction could be wholly or partially removed by epinephrin (Arch. Inter. de Pharmacodyn. et de Therap. Paper in press).

Inasmuch as the frog's intestine in Tyrode's solution, reacted to pilocarpine in an unexpected, heretofore undescribed manner, namely, to produce relaxation, it was thought that the barium-epinephrin antagonism was peculiar to the frog.

Further experiments, in which excised surviving intestinal segments, from the turtle and rabbit were used, showed that the barium-epinephrin antagonism could be demonstrated in these animals. For example, in the turtle, the contraction caused by 10 mg. of barium chloride was completely antagonized by 0.4 mg. of epinephrin. This is, of course, contrary to the current conception that barium act, directly on the contractile substance and epinephrin on the receptive mechanism.

This antagonism does not seem to have been previously described in the literature; however, Professor A. N. Richards informs me that he also had observed it in the excised rabbit's intestine.