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Carotid Body Reflexes in the Dog.

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In vagotomized dogs anesthetized with morphine and chloralose the following results have been obtained:

1. Contrary to our previous belief[1, 2] carotid chemoreceptors of some of these animals were continuously active under normal experimental conditions because—

(a) Respiration was often momentarily depressed when both sinus nerves were inactivated by cooling or by injection of procaine. This occurred also in decerebrated animals or anesthetized dogs breathing oxygen, and when rise in blood pressure upon blocking the nerves was obviated by preliminary selective denervation of the pressure receptors.

(b) Respiration was temporarily depressed when the fluid perfusing both carotid bodies was cooled from 38° to 26°C or less (confirming Bernthal and Weeks[3]). Similar results were obtained when the perfusing fluid was phosphate-buffered Locke's solution at pH 7.5, free of CO_2 (less than 1 mm tension) and saturated with O_2 (more than 150 mm tension)—in brief, when the carotid chemoreceptors were subjected to much smaller amounts of the materials known to stimulate them than could ever be the case under physiological conditions. Part or all of the continuous activity revealed by these experiments may therefore have been contributed by something other than ordinary chemoreceptors; temperature receptors are suggested as a possibility.

2. The sensitivity of the carotid chemoreceptors was tested by perfusion of both carotid bodies with oxygenated Locke's solution of which either pH was kept constant and CO_2 tension was varied (according to the Hasselbalch equation) or CO_2 was removed and the pH varied by means of phosphate buffers. In those animals whose carotid bodies showed unusually great reactivity, the following results were obtained:

(a) *CO_2 tension:* The smallest change by which breathing was reflexly affected was 5 mm Hg, which was effective in one trial out

1 Comroe, J. H., Jr., and Schmidt, C. F., *Am. J. Physiol.*, 1938, **121**, 75.

2 Schmidt, C. F., *Macleod's Physiology in Modern Medicine*, 8th ed., pp. 505-516, St. Louis, 1938.

3 Bernthal, T., and Weeks, W. F., *Am. J. Physiol.*, 1939, **127**, 94.

of 8 on 5 animals. Changes of 10 mm were effective in 4 out of 8 trials in 4 animals. In all these cases the respiratory effects were slight (changes of 8-21% in minute volume). Changes of 15 mm were tested 22 times (in 8 animals) but only 8 tests gave positive results. Only at a 20 mm change were the results marked and consistent (11 positive results in 11 trials in 4 animals). In interpreting these results we realize that anesthesia, trauma, artificial perfusion, etc., all tended to reduce the sensitivity of the carotid bodies and that the most sensitive preparation might therefore be regarded as closer to the intact state than the others. Yet there are undoubtedly wide natural variations in the sensitivity of the chemoreceptors; this is revealed in the variability in normal men of the hyperpnea of anoxemia, which is essentially a chemoreceptor phenomenon. Choosing between these alternatives, we believe our results to indicate that in the average dog, under our experimental conditions, the smallest alteration in CO_2 tension that will change chemoreceptor activity sufficiently to produce a significant respiratory response, is probably closer to 20 mm than to 10 mm. An occasional response to a 5 mm change seems to represent exceptional reactivity, not that of the average animal.

(b) *Acidity:* Changes of 0.1 pH unit in either direction produced distinct though slight respiratory effects in 4 of 7 tests in 4 animals. Changes of 0.15 elicited greater and more consistent effects, 0.2 still more so. Changes smaller than 0.1 were not tried.

3. The threshold of the respiratory center of the dog under these conditions (vagotomy, morphine-chloralose anesthesia) has been tested by noting the change in CO_2 tension of arterial blood when respiration began to be stimulated distinctly during rebreathing of oxygen. In the experiments so far performed, this has been an increase of 2 to 3 mm in CO_2 tension; there were no changes in pH detectable by the glass electrode. After denervation of both carotid bodies these results were unchanged.

Although the carotid bodies of these animals showed greater sensitivity to changes in CO_2 tension and pH than any previously reported, the conclusion of our earlier experiments—that under all ordinary conditions the chemical control of breathing can be accomplished by the cells of the center without involving the relatively insensitive chemoreceptors—is reaffirmed.