THE LOCATION AND FUNCTION OF THE CHEMORECEPTORS 
OF THE AORTA

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Although Heymans and Heymans (1927) demonstrated the presence of chemically sensitive nerve receptors in the region of the aortic arch several years before Heymans et al. (1931) discovered similar receptors in the carotid sinus area, the former have received little attention since that time while the latter have been investigated repeatedly. Consequently the localization and physiological significance of the carotid receptors are now fairly well understood, but even the existence of the aortic receptors has been denied (Dautrebande and Wegria, 1937; Beyne, Gautrelet and Halpern, 1933), and their localization and significance are both uncertain. A number of investigators (Selladurai and Wright, 1932; Schmidt, 1932; Jongbloed, 1936; Gesell and Moyer, 1937; Lambert and Gellhorn, 1938) have confirmed the presence of extracarotid chemoreceptors by showing that, even after complete carotid denervation, anoxemia still produces some increase in respiration which disappears when the vagodepressor nerves are cut. However no attempts at precise physiological localization have been reported since the work of Heymans and Heymans (1927). Anatomical studies made by Penitschka (1931), Palme (1934), Muratori (1934), Seto (1935), Nonidez (1935, 1937), and Boyd (1937) have demonstrated the presence about the aortic arch of cell groups which are similar in appearance to the chemoreceptors of the carotid bodies—a structural relationship which has led to the suggestion that these cells represent the chemically sensitive areas of the aortic region. Until now this suggestion lacked physiological confirmation.

The objects of the present experiments were to ascertain the anatomical

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and physiological characteristics of the aortic chemoreceptors, i.e., to determine their location, blood and nerve supply, and to obtain information about their significance to the organism. Owing to the relative inaccessibility of the aortic reflex zone, the various perfusion methods which have been successfully employed by a number of workers in investigating carotid reflexes, when applied to the aortic region, involve such wide departures from normal conditions that the results are of limited value beyond an indication that reflexes are aroused there by certain chemical agents. We hoped that useful information could be obtained by simple methods, now that the characteristics of the carotid reflex mechanism are fairly well understood; this hope was justified.

The experiments were performed on dogs and cats under anesthesia by chloralose (about 50 mgm. per kilogram) supplemented by urethane (about 0.6 gram per kilogram, this and the chloralose being given together intraperitoneally in dogs and cats) or by morphine (2 mgm. per kilo intramuscularly in dogs, following which the chloralose was given intravenously). A valved tracheal cannula was inserted; blood pressure was recorded by a mercury manometer from a femoral artery with thiosulfate or heparin-saline in the cannula; respiration was recorded by a pneumograph and tambour and occasionally the volume of expired air was measured by a gas meter. The sinus and aortic nerves and their receptor fields were scrupulously avoided until it was desired to inactivate them.

I. The physiological significance of the aortic chemoreceptors in the dog. Information on this point was obtained by testing the responses of respiration and blood pressure to systemic anoxemia (produced by inhalation of nitrous oxide) and to intravenous injections of α-lobeline and sodium cyanide, before and after complete bilateral carotid denervation. The responses after the denervation were assumed to be due to aortic reflexes—an assumption which appears to be justified, as will be seen below.

It should be emphasized at the outset that the results elicited by these simple procedures were quite variable from animal to animal, not only in the intensity of the total response (hyperpnea and hypertension) produced by the same agency in different animals, but also in the partition of the total response between the carotid and aortic receptors. However, three results were consistently obtained:

1. The hyperpneas produced by acute anoxemia and by α-lobeline and cyanide were usually reduced considerably though never completely abolished by carotid denervation.

2. The hypertension during acute anoxemia was usually intensified, and that produced by intravenous injections of α-lobeline and cyanide was always greatly intensified, after carotid denervation.

3. The hyperpnea and hypertension elicited by any of these agents after carotid denervation as a rule were abolished by section or blocking
of the depressor or vagodepressor nerves and pure depression of respiration and blood pressure occurred.2

The type of evidence upon which these statements are based is illustrated in figure 1. In the intact dog (fig. 1a) anoxemia caused intense hyperpnea and marked hypertension. When both vagi were blocked with procaine (fig. 1b) anoxemia still caused marked hyperpnea but the hypertension was completely lacking although the carotids were untouched. After the vagus block wore away (fig. 1c) anoxemia again produced both hypertension and hyperpnea. When both carotids were denervated with vagi intact (fig. 1d) the hyperpnea of anoxemia was greatly reduced though not abolished, while the hypertension was greater than before. Finally when both vagi were again blocked after carotid denervation, (fig. 1e), anoxemia failed to cause any increase in either blood pressure or respiration.

![Fig. 1. Effects of systemic anoxia with all chemoreceptors intact (A and C'), with only carotid chemoreceptors intact (B), with only aortic chemoreceptors intact (D), with all chemoreceptors denervated (E). See text. Dog. Morphine and chloralose. Pure nitrous oxide inhalation given between marks. From above downward: Respiration (pneumograph), femoral B.P., signal, time in 5 sec. intervals.]

As pointed out above, the results of this simple experiment were quite variable from animal to animal. To show the nature and extent of these variations it will be necessary to take up the respiratory and circulatory effects separately. The respiratory effects shown in figure 1 are typical of

2 There are several exceptions to this statement: (1) A smaller, more gradual increase in blood pressure followed intravenous injections of large doses (1.0 mgm.) of a lobeline, presumably due to direct sympathetic ganglion stimulation. (2) An increase in respiration sometimes occurred during systemic anoxemia even after denervation of the carotid and aortic chemoreceptors. Occasionally this occurred only after the N\textsubscript{2}O inhalation was carried to the point of an abrupt fall in blood pressure, and was probably due to the accumulation of metabolic products in the respiratory center because of reduction in its blood supply (Gesell, 1925; Schmidt, 1928, 1932). In a few instances a slight, delayed increase in respiration occurred without fall in blood pressure. In the absence of other known peripheral chemoreceptors this probably represents a direct stimulation of the respiratory center as described by Gesell (1939).
those obtained in 12 out of 49 dogs (24 per cent) subjected to inhalation of \(\text{N}_2\text{O}\) or to intravenous injection of \(\alpha\)-lobeline or cyanide, before and after carotid denervation. In such cases the hyperpnea of aortic origin (fig. 1d), while distinct, was decidedly less than that arising in the carotids. In another 18 of these 49 animals (37 per cent) the aortic component of the total respiratory response was even less marked than this, though still perceptible. Thus in 61 per cent of these unselected animals the major portion of the hyperpnea produced by anoxemia, \(\alpha\)-lobeline, or cyanide, arose from the carotid chemoreceptors. In 14 of the 49 dogs (28 per cent) the respiratory response was approximately half as great after carotid denervation as before, indicating that the carotid and aortic areas contributed about equal shares to the total respiratory effect. In 5 of the 49 animals (11 per cent) the respiratory response was almost as great after carotid denervation as before; in these exceptional animals the aortic component of the respiratory response evidently exceeded the carotid.

The circulatory effects shown in figure 1 are typical of those obtained in 19 out of 36 dogs in which \(\text{N}_2\text{O}\) inhalation was tested before and after aortic denervation. The rise in pressure produced by the inhalation with all nerves intact in these 36 dogs ranged from 18 to 126 and averaged 48 mm. Hg. After inactivation of the vagodepressor nerves the corresponding range was 0 to 76, average 12 mm., this representing the carotid body component. In 19 of these 36 dogs (53 per cent) the carotid component did not exceed 5 mm., in 13 of the 36 (36 per cent) the carotid component ranged from 5 to 30 mm. Hg, and in only 4 of the 36 dogs (11 per cent) did it exceed 30 mm. Thus in our series of unselected dogs, under conditions not far removed from the normal, only exceptional animals showed signs of strong vasomotor reflexes arising from the carotid chemoreceptors in response to acute systemic anoxia. Even in these exceptional cases, the hypertension of carotid body origin was not immediate and sharp, but began 10 to 30 seconds after the onset of the reflex hyperpnea and then progressed gradually; apparently the carotid vasomotor chemoreceptors have a higher threshold than those of the aortic region, or else their influence is too weak to produce hypertension in the face of increasing anoxia of the heart muscle. Certainly in the great majority of our animals the aortic component of the total vasomotor response to systemic anoxia was much more important than the carotid.3

3 This does not mean that reflexes from the carotid bodies are incapable of affecting the circulation reflexly. Evidence has been presented that such reflexes can produce strong reflex bradycardia (Heymans et al., 1933) and reflex vasoconstriction (Heymans et al., 1933, 1935; Bernthal, 1934, 1938). In the present experiments abundant confirmation of these findings was obtained, but the reflex bradycardia (effective through the vagi) was by far the stronger component; it usually overshadowed com-
A diagrammatic representation of the usual parts played by the various chemoreceptor groups in the circulatory and respiratory responses of the dog to acute systemic anoxia is shown in figure 3.

II. Localization of the aortic chemoreceptors in the dog. The procedures used for this purpose were the same as those already enumerated (p. 177) with the following additions: Both carotids were denervated at the outset,

Fig. 2. Vasomotor reflexes from carotid body. Representative tracings of effects produced by intracarotid injections of lobelin (0.1 mgm.). The figures refer to blood pressure changes only; they indicate the number of observations in a large series which were similar to those pictured. Thus, so long as the cardioinhibitory fibres were intact (first two records) no significant change in B.P. occurred in 93 per cent and 88 per cent of the cases. (See footnote1.) When these nerves were severed (vagodepressors cut) a slight or no increase in B.P. occurred in 54 per cent, a rise of 10-20 mm. Hg occurred in 28 per cent, and an increase of more than 20 mm. Hg in only 18 per cent. A marked hyperpnea was observed in 100 per cent of all 5 groups.

Comroe and Schmidt (1938) found no reflex hypertension in dogs during perfusion of the carotid body with anoxic blood, but in those animals one or both vagi were intact (although the depressors were cut) and only one carotid body was perfused. In recent experiments (unpublished) on vagotomized dogs with carotid pressure receptors denervated, we have frequently seen reflex hypertension upon perfusion of both carotid bodies with anoxic fluid; injection of cyanide into the fully oxygenated perfusion stream produced some hypertension in 89 per cent of 46 cases, and the average rise in pressure was 34 mm.; in 60 per cent the hypertension exceeded 20 mm. These circumstances are ideal for obtaining maximum reflex hypertension (i.e., perfusion of all functionally active chemoreceptors in an animal with the opposing aortic and carotid pressure receptors denervated and vagi cut). Since no comparable experiment can as yet be done with the aortic chemoreceptors we do not know how greatly the reflex hypertension arising from them would be exaggerated under equivalent circumstances.
so that any reflexes of chemical origin could be attributed to the aortic receptors. A small soft rubber catheter, filled with lobeline or cyanide solution, was passed down a common carotid or subclavian artery, or up the abdominal aorta toward the heart, and with the tip of the catheter at various points lobeline or cyanide was injected through it repeatedly (0.1–0.2 cc. at a time) until the region of maximum reactivity was ascertained. At this point the response was similar to that elicited by intravenous injections of lobeline or cyanide after carotid denervation but the hyperpnea and hypertension following intra-arterial injection appeared immediately and were more intense (fig. 4A). After such a reaction was obtained the catheter was withdrawn measured distances until the response disappeared. In most animals an opening was made in the superior mediastinum and through this the position of the tip of the catheter could be palpated during the experiment; in all cases the position was checked at autopsy.

Experiments of this sort were performed on 38 dogs. Figure 4A shows the positions of the catheters at which positive responses were obtained in each of 33 dogs, while figure 4B shows the positions at which no responses could be obtained, with only 5 exceptions, in the 38 animals. Excepting
these 5, in which some receptors apparently were supplied from the brachio-cephalic trunk, the chemosensitive area could always be localized in the ascending aorta or in the first portion of the aortic arch. Confirmation of this finding was obtained in another way, as shown in figure 5.

a. The blood supply of the aortic chemoreceptors. At postmortem examination a small vessel was regularly found to arise from the dorsocaudal aspect of the aorta at the level of the brachiocephalic orifice, which corresponds to the region of maximum sensitivity (fig. 4). In only 2 out of 35 dogs examined was this vessel lacking, and in these it arose from the first portion of the brachiocephalic; its subsequent course and distribution were the same in all the animals.

This portion of the aorta was submitted to serial sectioning in 8 dogs, and it was regularly found (Addison and Comroe, 1938) that a large cell mass lay in the aortic adventitia surrounding the numerous small branches of this vessel, less than a millimeter from its aortic orifice. This cell mass corresponds closely with the paraganglion aorticum supracardiale of Penitschka (1931) or the aortic body of Nonidez (1937). The structure of the aortic body is very similar to that of the carotid body, both being essentially vascular in nature and containing many nerve endings in intimate relationship with blood spaces (fig. 6).

Nonidez (1937) described other smaller cell groups, lying in newborn
dogs at the very origin of the aorta, which receive their blood supply from a branch of the left coronary artery. We have not as yet been able to confirm the presence of these cell groups in full-grown dogs, though in a few experiments we found that aortic injections produced no response until the catheter was pushed almost to the aortic valves.

Since the aortic body lies between the aorta and the pulmonary artery there is reason to suspect that the receptors may receive blood from the pulmonary artery. This possibility was investigated in 3 dogs by passing one catheter down the right jugular vein into the right ventricle, another up the abdominal aorta into the left ventricle, and injecting lobeline or cyanide through these catheters. The results showed clearly that the receptors do not receive blood from the pulmonary artery, for the responses (hyperpnea and hypertension) from right ventricular injections were delayed 12 to 13 seconds while left ventricular injections were effective in 3 to 4 seconds. Furthermore, examination of the pulmonary artery and its two main subdivisions in 30 consecutive dogs revealed no branches visible with a hand lens.

Fig. 5. Localization of aortic chemoreceptors in dog. After injection of lobeline at the mouth of the brachiocephalic had produced no response (A), the catheter was pushed into the ascending aorta (B) and injection of lobelin at this site produced marked hypertension and hyperpnea. In C, although the left subclavian was ligated at its origin and the aorta occluded by inflation of a strong rubber balloon pushed up the abdominal aorta, lobelin produced an immediate and even more pronounced hyperpnea (catheter in same position as in B). The hypertension (C) of course was decreased because of the huge reduction in the vascular bed. Since the brachiocephalic and its branches had previously been found to be insensitive (A), the chemoreceptors or their afferent artery were necessarily located in the ascending aorta (see fig. 4).
b. The nerve supply of the aortic chemoreceptors. In dogs whose carotids were previously denervated, section of either vagodepressor nerve in the neck diminished, and section of both nerves usually abolished the circulatory and respiratory responses to N₂O inhalation, lobeline and cyanide. If, however, the vagi were cut below the point of entrance of the recurrent laryngeal nerves but were intact above that point, the responses were not altered in the least. This shows clearly that the afferent pathways for the aortic body reflexes are the aortic or cardiac branches of the vagi. In 4 favorable subjects it was possible to dissect out a nerve running from the aortic body to the right vagus (entering the latter along with the right recurrent laryngeal nerve, fig. 6) and to stimulate it electrically in a spon-
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Simultaneously breathing animal: the result was the same as that of an intra-aortic injection of lobeline or cyanide, i.e., intense hyperpnea and distinct hypertension (fig. 6). On the left side we have been unable to identify the corresponding nerve, but believe that it runs with the left recurrent laryngeal because section of the vagus below this level does not alter the systemic or intra-aortic response and stimulation of all branches of the left vagus accessible above the aorta has not as yet reproduced the hyperpneic-hypertensive response.

In one experiment on a dog with denervated carotids it was possible, by crushing the nerves in the vicinity of the aortic body, to abolish completely the aortic chemical reflexes without inactivating the pressure reflexes, as shown by abrupt rise in blood pressure when the vagi were subsequently cut. This observation, together with the occurrence of hyperpnea and hypertension upon stimulating the aortic body nerves directly, indicates that in the aorta, as in the carotids, the pressoreceptors and chemoreceptors are anatomically separable though closely associated.

Chemoreceptors in the cat. The respiratory and circulatory responses of the cat to anoxia, like those of the dog, are dependent upon aortic and carotid reflexes, but the relative parts played by the carotid and aortic bodies are much more variable in the cat. Taking first the respiratory response, the carotids appeared to contribute the greater portion of the total hyperpnea of anoxemia and cyanide in 12 out of 26 cats (46 per cent); in 5 of these the aortic response was insignificant. The aortic region was relatively more important in 9 (35 per cent); in 3 of these there was practically no carotid response. In the remaining 5 (19 per cent) each zone appeared to contribute about equally to the total hyperpnea. The average respiratory responses to anoxemia were a 61 per cent increase in minute volume from the carotid bodies alone (average of 23 determinations in 18 cats) and a 64 per cent increase from the aortic region alone (average of 33 inhalations in 20 cats) but the individual variations were much wider in cats than in dogs. It is quite apparent, however, that the aortic body of the cat contributes more to the hyperpnea of anoxemia than that of the dog.

The circulatory responses to anoxia in these cats differed from those of dogs similarly prepared in two respects:

First, the hypertension of anoxia was less marked in the cat than in the dog: the average rise in blood pressure produced by 87 N₂O inhalations in 20 cats with all nerves intact was only 22 mm. Hg (range 2–76 mm.), while that in 55 dogs was 40 mm. (range 12–126 mm.).

Second, the partition of this response between the carotid and aortic chemoreceptors was not so clear-cut as in the dog. Of 25 cats, the aortic region was relatively more important to the circulatory response in 11 (44 per cent); in two of these 11, the carotid response was negligible. The carotid region appeared to contribute more than the aortic to the total
circulatory response in 10 (40 per cent); in 3 of these the aortic response was insignificant. In the remaining four (16 per cent) the two zones appeared to contribute about equally. Here again extreme variations were encountered in individual cats, but the average anoxemia (NaO inhalation) increase in blood pressure due to the carotid region alone was 16 mm. (42 determinations in 17 cats), that due to the aortic region alone 15.2 mm. (50 determinations in 22 cats). Similarly, following intravenous NaCN, the average increase in blood pressure due to the carotid bodies was 12 mm. (35 determinations in 16 vagotomized cats); that due to the aortic factor was 13 mm. (36 determinations in 14 cats with carotids denervated).

It is evident that the carotid body is a more important factor in the vaso-motor response to acute systemic anoxemia in the cat than in the dog. This was confirmed by intracarotid injections of NaCN, which produced some reflex hypertension in 18 of 23 cats (78 per cent) even though the vagi were intact; in dogs similar injections rarely raised blood pressure as long as these nerves were intact. In only 3 cats however did the rise in blood pressure exceed 15 mm. (maximum 72 mm. Hg in one cat) and the average increase in 91 such injections in the 23 cats was only 9 mm. As in the dog, this was exaggerated by section of the vagodepressor nerves; the average increase in blood pressure following 29 intracarotid injections of cyanide in 14 vagotomized cats was 20 mm. Furthermore some increase in blood pressure was produced by 100 per cent of the injections under these conditions.

Physiological localization of the aortic chemoreceptors was accomplished in 4 cats by passing a fine ureteral catheter filled with NaCN down one common carotid into the left ventricle. In each case the carotids were denervated. Injection of NaCN through the catheter produced immediate hyperpnea and hypertension only when the tip of the catheter was within the left ventricle; the reaction disappeared when the catheter tip lay distal to the aortic valves. This indicates that the blood supply of the aortic body in the cat is derived from the coronary arteries, and this was confirmed by histological studies. Serial sections showed that these physiologically active chemoreceptors in the adult cat lie beneath the aorta near the coronary orifices.

As in the dog, the chemoreceptors do not appear to receive blood from the pulmonary artery, for right ventricular injections (via ureteral catheters passed down an external jugular vein) of cyanide or lobeline regularly showed a considerably longer interval between injection and response than left ventricular injections. The pulmonary artery region was also studied histologically in 6 adult cats: in one a patent vessel arose from the pulmonary artery and entered the chemoreceptor tissue, in another a similar vessel was found but the opening on the pulmonary artery side was obliterated; in the remaining four, no patent vessel or orifice could be found.
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The existence of supra-aortic bodies (described by Nonidez in new born kittens) has not yet been confirmed by our preliminary physiological and anatomical studies in adult cats.

As in the dog, the aortic body fibres enter both vagodepressor nerves; section of these invariably abolishes the aortic chemical reflexes in the cat. The course of the fibres from the aortic body to the vagodepressor trunks has not yet been traced.

Discussion. These experiments show clearly that the chemoreceptors first described by Heymans and Heymans (1927) in the cardio-aortic region are localized in the aortic body just as definitely as the carotid chemoreceptors are confined to the carotid body. This is a matter of considerable interest because these two chemoreceptor zones are very similar, not only in function, but in embryological derivation, structure, and relationship to the vascular and nervous systems. Although the localization of the aortic chemoreceptors seems to be accomplished, final conclusions concerning their physiological significance must be postponed. However, several points of value have emerged from the present studies. These will now be considered.

The first point is concerned with the relative physiological importance of the carotid and aortic chemoreceptor areas. There seems to be an unmistakable tendency in the dog for the carotid body to affect the respiratory center more than the vasomotor, and for the aortic body to affect the vasomotor center more than the respiratory. Only the carotid chemoreceptors act directly upon the cardio-inhibitory center. In the cat, the partition of the circulatory and respiratory responses between the two chemoreceptor zones appears in average figures to be much more nearly equal than is the case in the dog, but the averages include wider extremes in the cat.

The second point is the matter of individual variation among different animals of the same species. The experimental conditions under which these observations were made were certainly closer to normal than would have been the case in the perfusion or crossed-circulation experiments that have been used so extensively in investigating these chemoreceptors. In all the present experiments, the chemoreceptor zones and nerves were carefully avoided until we desired to inactivate them. Clearly the weak responses cannot be ascribed to damage to the reflex mechanisms and discarded in favor of the strongest ones, which would then be taken to be representative of the normal state. Instead, the variations must be accepted as inherent in the animals themselves and the factor of individual variability deserves greater prominence than it has been accorded in evaluating results of such experiments. For example, in one dog of this series the aortic respiratory response to anoxemia was far greater than the carotid respiratory effect in many of the animals, yet in only 5 of 49 dogs did the aortic respiratory response exceed the carotid, and in no other
animal did the aortic response closely approach this one in intensity. On the other hand, in 18 of the 49 dogs the aortic respiratory response was barely perceptible. Obviously in a small series one exceptional result of either of these types would incorrectly influence the observer's viewpoint, and conclusions of lasting value can be drawn only from studies on a series of animals sufficiently large to permit determination of the general tendency amid individual variations.

Because of these natural variations individual investigators in this field, having different purposes in view, may arrive at conclusions which seem to be widely divergent but which actually are not at all at variance. An excellent illustration of this is the vasomotor reflex originating in the carotid bodies. If one wishes to demonstrate the maximum influence which this can exert, one may find an occasional dog in which, under suitable conditions, chemical stimulation of the carotid bodies will cause a tremendous rise in blood pressure; in one dog of this series a rise of 138 mm. Hg was observed. Yet this turned out to be distinctly unusual in a large series, and it occurred only after bilateral vagotomy and after selective denervation of the carotid pressure receptors. Heymans and Bouckaert (1939) emphasize the necessity for preventing reduction in the CO₂ tension of the blood (consequent on the simultaneous hyperpnea) by curare and artificial respiration if the carotid body hypertension is to be seen in its fully developed state. Yet if the investigator's purpose is to estimate the importance of this reflex to the intact animal, he cannot base his conclusions on results which are intentionally exaggerated or admittedly exceptional. In the present series it was clear that in the intact anesthetized dog the carotid body receptors alone are incapable of stimulating the circulation in times of acute anoxia, despite marked rises in blood pressure obtainable from them in selected animals under highly abnormal conditions. On the other hand the aortic chemoreceptors of the dog can and regularly do maintain an increased blood pressure during acute anoxemia, and this despite the opposing influence of the carotid and aortic pressoreceptors, the bradycardia arising from the carotid chemoreceptors, the increasing anoxia of the heart muscle, and the reduction in the CO₂ tension of the blood produced by the concomitant hyperpnea. The carotid chemoreceptors can do this only exceptionally, and then only after the opposing tendencies of aortic pressoreceptors and reflex bradycardia have been eliminated by bilateral vagotomy.

These experiments confirm the belief that the aortic and carotid chemoreceptors together constitute the main and in many cases the sole source of the hyperpnea and hypertension associated with anoxemia and with the action of chemicals such as cyanide; when both sets of receptors are inactivated, systemic anoxia is always much less stimulant than before to respiration and blood pressure; most frequently it is purely depressant
in anesthetized animals. The conclusion that anoxia does not directly stimulate the medullary centers has been fairly generally accepted with regard to respiration, but not to circulation. Our results confirm the conclusions of Brewer (1937) and Lambert and Gellhorn (1938) that the characteristic vasomotor response to anoxia, like the respiratory, is due to reflexes, not to direct central stimulation.

The fact that powerful vasopressor nerve impulses originate in the aortic body and are carried in the vagodepressor nerves is interesting in connection with the reflex described by McDowall (1924). Information obtained from the present experiments indicates that at least a portion of the phenomena described by McDowall originates in the aortic body as a result of chemical changes in the blood. If the vagi are cut when the blood pressure is normal or high, a rise in blood pressure is the rule, for inactivation of the more powerful pressoreceptors occurs simultaneously with inactivation of the chemoreceptors. But if the vagi are cut when blood pressure is low, a further fall in blood pressure usually results, for only the chemoreceptors are now inactivated by vagotomy (the pressoreceptors being already partially or wholly inactivated by the subthreshold level of blood pressure). This is in conformity with the observations of Reed (1925) that the McDowall reflex is most consistently observed at the end of long experiments with a low arterial blood pressure. As evidence that removal of vasopressor impulses from aortic chemoreceptors is indeed responsible for the fall in blood pressure when the vagi are cut under such circumstances, an experiment may be cited in which the aortic chemoreceptors of a dog were denervated without severing the vagi or interfering with the innervation of the great veins. In this case, vagotomy led to a rise—and not a fall—in blood pressure even though performed at the end of a long experiment with a low arterial blood pressure.

Furthermore, O₂ inhalation as well as vagotomy may cause an abrupt fall in blood pressure in a cyanotic dog with denervated carotids—an effect presumably due to inactivation of aortic chemoreceptors. It must be pointed out however that oxygen inhalation does not lower pressure as consistently as bilateral vagotomy under similar circumstances, indicating that systemic anoxia is not the only factor in these vagal pressor reflexes. In view of the findings of Bernthal and Weeks (1938) that the carotid chemoreceptors are tonically active under similar experimental conditions, it is probable that the aortic chemoreceptors also set up a continuous discharge of impulses to the vasomotor center. Interruption of this discharge by vagotomy of course would tend to lower blood pressure. In those cases in which vagotomy does, but O₂ inhalation does not lower blood pressure, some other chemical influence, probably increased CO₂, lowered pH, or stagnant anoxia acting through the aortic body, may have been the driving factor. Evidence on this point is not yet available.
SUMMARY

1. The extra-carotid chemoreceptors of the dog have been localized by physiological and anatomical studies in the aortic body, a structure fundamentally similar to the carotid body.

2. Both carotid and aortic bodies set up reflexes to the respiratory and vasomotor centers in response to anoxia, whether this be produced systemically by oxygen lack in the inspired air, or locally by interference with tissue oxidations.

3. The major rôle of the aortic chemoreceptors in the dog is the initiation of powerful reflexes to the vasomotor center during anoxemia. By far the greater portion of the hypertension of acute systemic anoxia is produced by aortic body reflexes; vascular reflexes from the carotid body are inconstant and relatively ineffective. The carotid body, however, usually contributes by far the greater portion of the hyperpnea of anoxemia in the dog; the aortic body component, though invariably present, is often insignificant. In the cat the carotid chemoreceptors are relatively more important to the vasomotor response to anoxia than is the case in the dog.

4. The blood supply and afferent nervous pathways for the aortic chemoreceptors have been determined in the dog and cat. In the dog the blood supply is from the transverse aorta, in the cat from the coronary arteries. In both species the nerve fibers reach the vagus trunk close to (probably by way of) the recurrent laryngeal nerves.

5. The possibility that the McDowall reflex may result from chemical stimulation of the aortic body rather than from alterations in venous pressure has been discussed.

6. In view of the close functional and structural similarity to the carotid body, it is proper to use the term aortic body suggested by Nonidez, to designate structures now known as paraganglion aorticum supracardiale, paraganglion of Penitschka, paraganglion aorticum supracardiale superius.

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