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THE CARDIOVASCULAR EFFECTS OF HYPOXIA IN THE DOG WITH SPECIAL REFERENCE TO THE CONTRIBUTION OF THE CAROTID BODY CHEMORECEPTORS

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In the dog inhalation of a gas mixture of low oxygen content causes an increase in respiratory minute volume, tachycardia, hypertension, an increase in cardiac output and a decrease in peripheral vascular resistance (Harrison & Blalock, 1927; Lewis & Gorlin, 1952; Nahas, Visscher, Mather, Haddy & Warner, 1954; Leusen & Demeester, 1955). There is general agreement that the hyperpnoea is largely, if not entirely, reflex in origin through stimulation of the carotid and aortic bodies (Heymans & Neil, 1958). The tachycardia, however, cannot be explained on this basis. Neil (1956) found in the cat that the cardio-acceleration evoked by inhalation of 5 % O_2 in N_2 was not affected by withdrawing the carotid body chemoreceptor 'drive', achieved by changing the carotid body perfusate from hypoxic blood to oxygenated Ringer–Locke's solution. In the dog, on the other hand, changing the perfusate from hypoxic to oxygenated blood was found to cause a further tachycardia (Daly & Scott, 1959). Both Neil (1956) and Daly & Scott (1959) concluded that the carotid bodies do not contribute to the tachycardia of systemic hypoxia.

The aim of the present experiments was to study in more detail the role of the carotid bodies in the cardiovascular responses evoked by systemic hypoxia. Some of the results have been reported briefly elsewhere (Daly & Scott, 1960, 1963*b*).

METHODS

Dogs, of either sex, varying in weight from 23·4 to 36·5 kg were anaesthetized with a mixture of chloralose (Roche Products, Ltd. 0·05 g/kg) and urethane (British Drug Houses Ltd., 0·5 mg/kg) intravenously, after premedication with morphine hydrochloride (2 mg/kg subcutaneously). Systemic blood pressure was recorded from a femoral artery with either a mercury or a Hürthle manometer. Heart rate was measured continuously by means of a drop timer (Gaddum & Kwiatkowski, 1938) using the method of Daly & Schweitzer (1950), or was counted over a period of $\frac{1}{2}$ min from the blood pressure trace taken on a fast-moving paper. Tidal volume was recorded on the kymograph by means of a balanced spirometer

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using the method described by Donald & Christie (1949) as modified by Bacon, Daly & Scott (1962). All gas volumes are expressed at A.T.P.S.

In some experiments artificial respiration was applied by means of a Starling 'Ideal' pump. Spontaneous respiratory efforts were prevented by decamethonium iodide (0·25 mg/kg I.V., Light & Co. Ltd.) and anaesthesia was maintained in these experiments by regular injections of the anaesthetic, the dose having been determined previously in a series of experiments on spontaneously breathing dogs.

A double-lumen cannula was inserted through the right external jugular vein into the right atrium. The right atrial pressure was measured by means of a vertical saline manometer, the open end of which was connected to a small volume recorder. The zero reference point was taken from the tip of the cannula established post mortem.

Perfusion of the carotid bodies

Both carotid bifurcation regions were isolated from the circulation and perfused with blood by means of a roller pump. The arrangement of the perfusion circuit was such that the carotid bodies could be perfused with blood from an artery of either the same (recipient) animal or a donor dog. The carotid sinus pressure, measured with a mercury manometer, was automatically maintained at the same level as the recipient dog's systemic blood pressure or was maintained at a constant level. Full details of the method have been described previously by Daly & Scott (1958).

Measurement of cardiac output

Cardiac output was measured by the dye-dilution method (Moore, Kinsman, Hamilton & Spurling, 1929). The dye (T-1824, Evans Blue, British Drug Houses Ltd.), in doses of 6·25–6·91 mg according to the weight of the animal, was injected into the right atrium through one lumen of the double-lumen catheter inserted through the right external jugular vein. The exact amount of dye injected was determined by taking the difference in the weight of each syringe before and after injection. Blood from the arch of the aorta was continuously sampled via a catheter inserted through the right common carotid artery, and collected in a series of small tubes arranged on a moving kymograph drum. An equal volume of blood was transfused at the end of each sampling period. The concentration of dye in each sample of blood was estimated at a wave-length of 600 mμ (Ilford 607 filter) by means of a Spekker absorptiometer (Hilger and Watts, Ltd.). A calibration curve was obtained at the beginning of each experiment, with the blood of the recipient animal.

Total peripheral (systemic) vascular resistance (T.P.R.) was calculated thus:

$$\text{T.P.R.} = \frac{\text{systemic blood pressure} - \text{right atrial pressure (mm Hg)}}{\text{cardiac output (ml./min)}}.$$

In the experiments made on preparations with open chest, changes in cardiac output were inferred from changes in blood flow to one lobe of the lungs (Hürlimann & Wiggers, 1953; Daly, 1957). Blood flow to the left diaphragmatic lobe was measured and recorded continuously by means of a Shipley & Wilson (1951) type of rotameter in which were incorporated the modifications of Bell (1954). The calibration of the rotameter and measurements of mean left and right atrial pressures and mean pulmonary arterial pressure were made as described previously (Daly, 1957).

In all experiments heparin ('Liquemin', Roche Products Ltd.) was given in doses of 10 mg/kg to render the blood incoagulable.

Blood gas analyses

Estimations of arterial blood Po_2 and Pco_2 were made from determinations of pH, haemoglobin concentration, oxygen and carbon dioxide content and oxygen capacity using the same methods as described by Daly & Scott (1963*a*).

Experimental procedure

The recipient animal breathed room air and its carotid bodies were perfused with its own arterial blood. The donor dog breathed room air or O_2. After taking control measurements of tidal volume, heart rate, blood pressure, right atrial pressure and cardiac output, hypoxia was induced in the recipient animal by substituting 7–12 % O_2 in N_2 for room air. When a steady state had been reached, a second series of measurements was taken. The carotid body perfusate was then changed from hypoxic blood to oxygenated blood obtained from the donor animal while the recipient continued to breathe the low-oxygen gas mixture, and a third series of measurements was taken. Hypoxic blood perfusion of the carotid bodies was re-established and another series of measurements was taken. Finally, room air was substituted for the low-oxygen gas mixture.

RESULTS

Effects of hypoxia

In five spontaneously breathing dogs whose carotid bodies were perfused with their own blood, hypoxia was induced by substituting 7–12 % O_2 in N_2 for room air. The results of nine tests in five experiments are summarized in Table 1 and the typical response is shown in Fig. 1*A* and *B*. There was an increase in respiratory minute volume of 52–148 % of the control value.

The cardiovascular effects included tachycardia, the increase in heart rate varying from 24 to 75 beats/min, and a rise in blood pressure of 5–30 mm Hg. The mean control value for cardiac output, expressed as cardiac index, was 4·18 l./min/m^2 (range 2·58–5·25). In eight tests, substitution of the low oxygen mixture for room air resulted in an increase in cardiac output of 0·14–2·10 l./min/m^2; in the remaining test (Expt. no. 76) it decreased slightly from 5·00 to 4·82 l./min/m^2. The changes in total peripheral vascular resistance were more variable. In six tests in three experiments (nos. 70, 71 and 73) the vascular resistance decreased whereas in three tests in two experiments (nos. 72 and 76) it increased.

Effects of withdrawing the carotid body 'drive' during hypoxia

While the recipient animal continued to breathe the low-oxygen mixture, the carotid body perfusate was changed from hypoxic blood to oxygenated blood from the donor dog. The results are summarized in Table 1. In seven of eight tests in which respiration was recorded, a reduction in respiratory minute volume occurred; in the remaining test, rapid shallow breathing occurred which resulted in a slight increase in respiratory minute volume (Fig. 1). In eight of nine tests an increase in heart rate of 15–75 beats/min took place; in the remaining test in Expt. no. 73*a*, no change in heart rate occurred. Changes in blood pressure were variable. These results confirm those of Daly & Scott (1959).

As shown in Table 1 and Fig. 1, withdrawing the carotid body 'drive'

TABLE 1. Respiratory and cardiovascular effects of hypoxia and of withdrawing the carotid body 'drive' during hypoxia. *C*, control values, ventilation with room air. E_1, values during hypoxia, ventilation with 7% O_2 in N_2 (Expt. no. 70), 10% O_2 in N_2 (Expt. nos. 71 and 72) or 12% O_2 in N_2 (Expt. nos. 73 and 76). E_2, values during hypoxia, the carotid bodies being perfused with oxygenated blood from donor animal

Expt. no. ...		70*a*	70*b*	71*a*	71*b*	72*a*	72*b*	73*a*	73*b*	76
Dog wt. (kg) ...		36·6		26·0		25·2		23·4		24·6
Respiratory minute volume (l./min)	*C*	6·15	5·95	5·30	5·98	4·14	4·57	5·25	4·34	4·65
	E_1	15·3	12·5	8·05	10·3	8·20	8·52	11·2	7·61	16·1
	E_2	8·30	—	4·46	9·08	4·08	5·30	8·90	8·20	10·6
Heart rate (beats/min)	*C*	108	111	138	138	123	126	138	135	135
	E_1	183	180	162	162	168	165	192	171	180
	E_2	204	204	204	228	240	240	192	186	220
Blood pressure (mm Hg)	*C*	125	130	125	120	125	120	120	120	110
	E_1	155	150	130	125	140	140	125	135	120
	E_2	115	120	105	125	115	115	145	145	135
Cardiac output (l./min)	*C*	3·04	3·80	4·26	4·04	4·62	3·92	4·29	4·62	4·55
	E_1	5·26	4·62	4·68	5·00	4·95	4·05	4·82	6·47	4·38
	E_2	5·15	5·66	7·12	7·98	5·73	5·13	8·71	7·78	6·86
Total peripheral vascular resistance (mm Hg/ml./min × 100)	*C*	4·10	3·42	2·94	2·97	2·70	3·06	2·80	2·60	2·24
	E_1	2·94	3·25	2·78	2·50	2·83	3·45	2·59	2·08	2·75
	E_2	2·23	2·12	1·48	1·57	2·01	2·24	1·66	1·86	1·97
Arterial blood P_{O_2} (mm Hg)	*C*	—	—	77	77	73	73	100+	100+	100+
	E_1	—	—	38	42	35	32	50	41	46
	E_2	—	—	20	21	25	23	31	34	39
P_{CO_2} (mm Hg)	*C*	—	—	36	36	42	42	47	47	46
	E_1	—	—	26	27	32	29	39	41	34
	E_2	—	—	43	37	43	40	52	47	38
pH	*C*	—	—	7·31	7·31	7·35	7·35	7·32	7·32	7·27
	E_1	—	—	7·41	7·38	7·50	7·48	7·37	7·39	7·34
	E_2	—	—	7·30	7·32	7·39	7·41	7·31	7·35	7·32

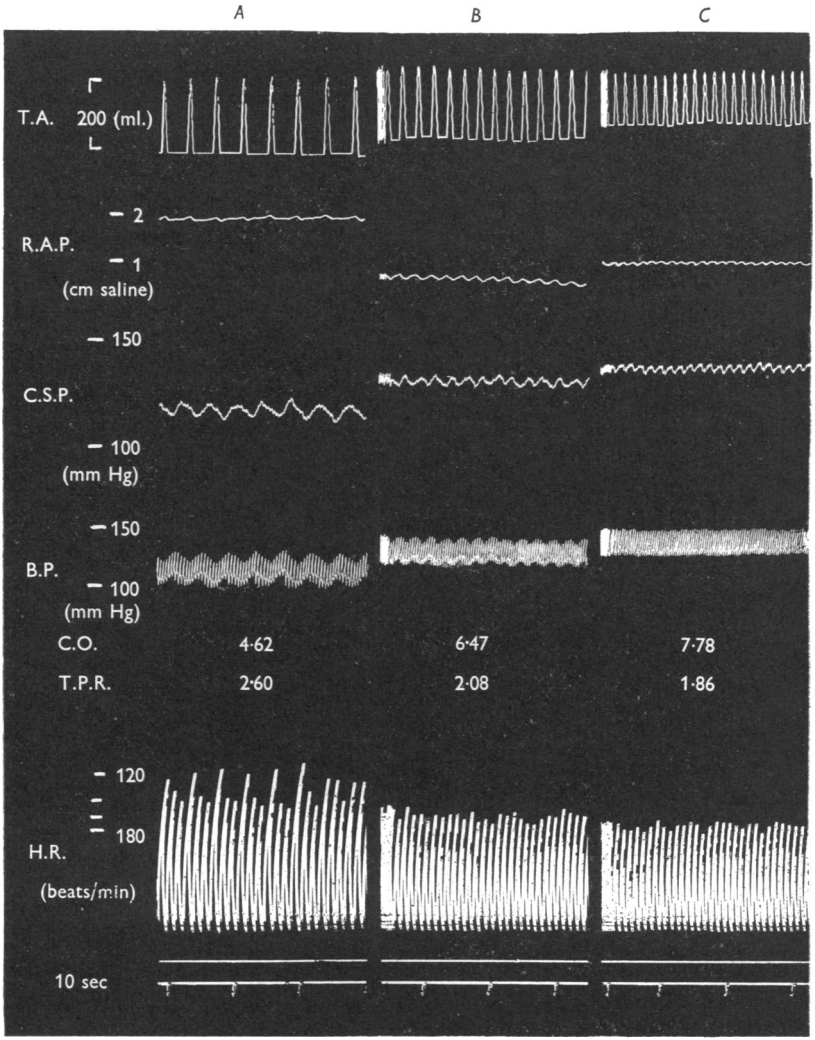

Fig. 1. Dog, ♀, 23·4 kg. Morphine–chloralose–urethane. Spontaneous respiration. Bilateral perfusion of the carotid sinus and body. *A*, control; ventilation with room air; perfusion of the carotid bodies with arterial blood from the same (recipient) animal (Po_2, 100+mm Hg, Pco_2 47 mm Hg, pH 7·32). *B*, record taken during period of systemic hypoxia while breathing 12 % O_2 in N_2 (arterial blood Po_2 41 mm Hg, Pco_2 41 mm Hg, pH 7·39). *C*, ventilation with 12 % O_2 in N_2 (arterial blood Po_2 34 mm Hg, Pco_2 47 mm Hg, pH 7·35); record taken 4 min after starting perfusion of the carotid bodies with oxygenated donor arterial blood (Po_2 100+ mm Hg, Pco_2 47 mm Hg, pH 7·25). The values below the blood pressure trace are those for cardiac output (l./min) and total peripheral vascular resistance (mm Hg/ml./min $\times$ 100).

In this and in subsequent figures: T.A., tidal air volume; R.M.V., respiratory minute volume; R.A.P., right atrial pressure; C.S.P., carotid sinus perfusion pressure; B.P., systemic blood pressure; C.O., cardiac output; P.A.P., pulmonary arterial pressure; P.L.F., pulmonary lobar blood flow; T.P.R., total peripheral vascular resistance; H.R., heart rate. Time marker, 10 sec.

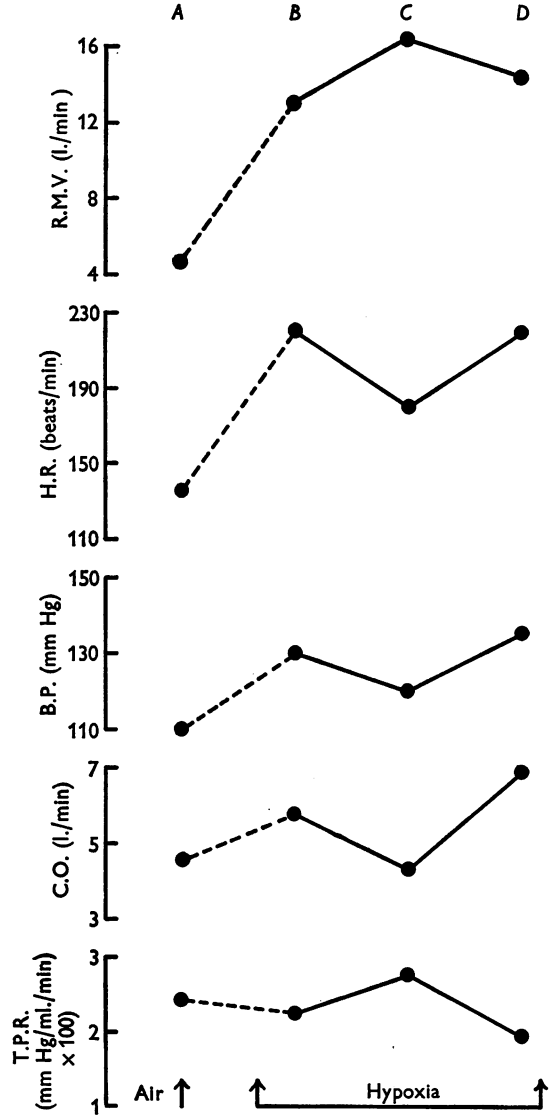

Fig. 2. Dog, ♀, 24·6 kg. Morphine–chloralose–urethane anaesthesia. Spontaneous respiration. Bilateral perfusion of the carotid sinus and body. Effects of stimulation of the carotid bodies and of withdrawing the carotid body 'drive' during systemic hypoxia. Donor dog ventilated with room air. *A*, control. Recipient animal ventilated with room air (arterial blood Po_2 95 mm Hg, Pco_2 46 mm Hg, pH 7·27). Carotid bodies perfused with oxygenated blood from donor dog (Po_2 85 mm Hg, Pco_2 43 mm Hg, pH 7·33). *B–D*, recipient ventilated with 12 % O_2 in N_2. *B*, carotid bodies perfused with oxygenated blood from donor animal (recipient arterial blood Po_2 39 mm Hg, Pco_2 38 mm Hg, pH 7·32). *C*, carotid bodies perfused with recipient's arterial blood (Po_2 46 mm Hg, Pco_2 34 mm Hg, pH 7·34). *D*, carotid bodies perfused with oxygenated donor blood (recipient arterial blood Po_2 24 mm Hg, Pco_2 45 mm Hg, pH 7·31).

caused a considerable increase in cardiac output compared with the value obtained during hypoxia with the carotid bodies perfused with hypoxic blood. In eight tests the increase varied from 0·86 to 4·30 l./min/m^2; in the remaining test (Expt. no. 70*a*), the cardiac output fell slightly from 4·46 to 4·36 l./min/m^2. The total peripheral vascular resistance diminished in all nine tests (Table 1). These effects were reversed when hypoxic blood perfusion of the carotid bodies was re-established.

When the values for the various parameters during the control state, the recipient animal breathing room air, are compared with those observed during systemic hypoxia in the absence of chemoreceptor excitation, the cardiac output is 1·22–4·91 l./min/m^2 higher in the hypoxic state. The total peripheral vascular resistance is lower in spite of variable changes in respiration and systemic blood pressure (Table 1, rows *C* and E_2).

These results indicate, therefore, that systemic hypoxia causes an increase in cardiac output and usually a reduction in total peripheral vascular resistance, both responses being greater in the animal whose carotid bodies are excluded from the circulation.

These findings were confirmed in two tests in one experiment with a slightly different experimental procedure. The recipient animal was made hypoxic by substituting 12 % O_2 in N_2 for room air while its carotid bodies were perfused with oxygenated blood from the donor dog. This resulted in hyperpnoea, tachycardia, hypertension, an increase in cardiac output, and a small reduction in total peripheral vascular resistance (Fig. 2*A*, *B*). While the recipient animal continued to breathe the low-oxygen gas mixture the carotid bodies were stimulated by changing the perfusate from oxygenated donor blood to hypoxic recipient blood. As shown in Fig. 2*C*, this resulted in an increase in respiratory minute volume, bradycardia, hypotension, a reduction in cardiac output and an increase in peripheral vascular resistance. When oxygenated donor blood perfusion of the carotid bodies was re-established, the responses were reversed (Fig. 2*D*).

The evidence presented in Table 1 shows that withdrawing the carotid chemoreceptor 'drive' usually caused a reduction in respiratory minute volume and consequently a fall in arterial blood P_{O_2} and a rise in P_{CO_2}. To find out to what extent changes in arterial-blood gas tensions affected the responses to oxygenated-blood perfusion of the carotid bodies during systemic hypoxia, a series of experiments was carried out in which pulmonary ventilation was maintained constant artificially.

Dogs ventilated artificially

In experiments carried out on dogs with open chest and ventilated artificially, changes in cardiac output were inferred from alterations in

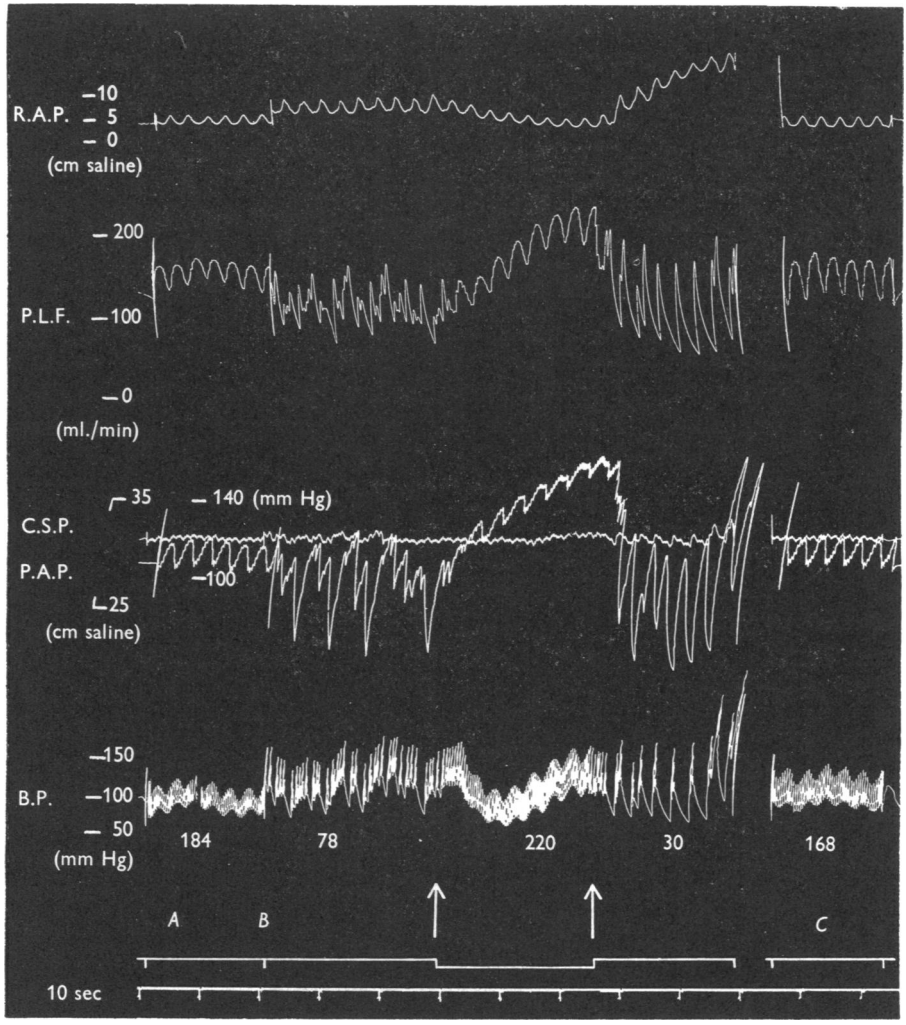

Fig. 3. Dog, ♀, 15·3 kg. Morphine–chloralose–urethane. Positive pressure artificial respiration. Bilateral perfusion of the carotid sinus and body. Carotid sinus pressure maintained constant. Measurement of blood flow to the left diaphragmatic lobe. Decamethonium, 0·25 mg/kg intravenously before recording began. *A*, control; ventilation of recipient animal with room air. At *B*, ventilation with 7 % O_2 in N_2 instead of room air. Carotid bodies perfused with blood from recipient animal. Kymograph restarted after a steady state had been reached. Between arrows ↑ ↑, the carotid bodies were temporarily perfused with oxygenated blood from donor dog breathing room air. *C*, control; ventilation of recipient animal with room air. The figures below the blood pressure record are those for heart rate (beats/min). Time marker, 10 sec.

blood flow to one lobe of the lung, measured with a rotameter flowmeter (Daly, 1957).

It was found that hypoxia induced by substituting 7–10 % O_2 in N_2 for room air caused variable changes in heart rate as found previously by Daly & Scott (1959). In eight of nine tests in six experiments, an increase in cardiac output occurred. A similar response has been observed recently by Penna, Soma & Aviado (1962) and by Murray & Young (1963). In these tests the systemic blood pressure increased and it is not possible therefore to determine from measurements of lobar blood flow whether or not there was any change in total peripheral vascular resistance. In the remaining test, however, a reduction in blood flow occurred and this response was also accompanied by a rise in systemic blood pressure. The total peripheral vascular resistance must, therefore, have increased. The response occurring in one experiment is shown in Fig. 3.

In six tests in four experiments the effects of changing the carotid body perfusate from hypoxic to oxygenated blood was observed during systemic hypoxia. In confirmation of our previous findings (Daly & Scott, 1959) an increase in heart rate occurred. The cardiac output increased in all six tests, whereas the systemic blood pressure fell in three tests and did not change in the remaining three. In all tests, therefore, the total peripheral vascular resistance must have decreased. When hypoxic blood perfusion of the carotid bodies was re-established, these responses were reversed. The typical response is shown in Fig. 3.

These results show that, in the dog with controlled ventilation, systemic hypoxia causes variable changes in heart rate, hypertension and an increase in cardiac output. As in dogs with natural breathing, withdrawal of the carotid chemoreceptor 'drive' during systemic hypoxia causes a further increase in heart rate and in cardiac output and a reduction in total peripheral vascular resistance.

DISCUSSION

There have been several recent reports of the effects of hypoxia on the cardiovascular system before and after denervation of the chemoreceptors. Penna *et al.* (1962) found in anaesthetized dogs ventilated artificially that inhalation of 5 % O_2 in N_2 caused an increase in cardiac output which was still present after denervation of the carotid and aortic body chemoreceptors.

Peripheral vasoconstriction which also occurs has been shown to be dependent on the integrity of the carotid and aortic chemoreceptors (Litwin, Dil & Aviado, 1960). Kahler, Goldblatt & Braunwald (1962) found that induced hypoxia in the systemic circulation, perfused at constant blood flow, caused a rise or a fall in perfusion pressure indicating

respectively an increase or decrease in peripheral vascular resistance. After denervation of the carotid and aortic bodies, a fall in perfusion pressure invariably occurred in response to hypoxia. In these experiments and in those of Penna *et al.* (1962), the chemoreceptors were denervated by division of the carotid sinus and cervical vagosympathetic nerves. This procedure, however, denervates not only the chemoreceptors in the regions of the carotid bifurcations and aortic arch, but the baroreceptors as well, which means that the responses of the cardiovascular system to hypoxia before and after denervation were made on a different 'background' because an increase in total peripheral vascular resistance must have occurred as a result of baroreceptor denervation (see Heymans & Neil, 1958). Furthermore, the results of experiments in which such denervation procedures are adopted cannot, in our opinion, be interpreted as being due solely to exclusion of the chemoreceptor reflexes. In this connexion Daly & Scott (1962*a*) have shown that the systemic blood-pressure responses to hypoxia after denervation of the carotid bifurcation regions are, in part at least, the result of denervation of carotid sinus baroreceptors.

In the present experiments a technique has been used which is similar in principle to that employed previously (Neil, 1956; Daly & Scott, 1959) in that the carotid body chemoreceptors during systemic hypoxia can be physiologically inactivated without affecting the functioning of the carotid sinus baroreceptors. In this way it is possible to separate the respective roles of the carotid chemoreceptors and baroreceptors in the cardiovascular responses to systemic hypoxia.

Daly & Scott (1959) showed that in the dog cessation of the hypoxic stimulus to the carotid bodies during systemic hypoxia caused acceleration of the heart. They concluded that the tachycardia of systemic hypoxia could not be attributed directly to excitation of the carotid chemoreceptors. Neil (1956) had earlier reached a similar conclusion based on his experiments carried out in the cat. The cardio-accelerator response which occurs in the dog on removal of the hypoxic stimulus to the carotid bodies during systemic hypoxia is probably due to abolition of the primary cardiac reflex originating from the carotid bodies (Daly & Scott, 1958, 1962*b*) since the acceleration is independent of changes in systemic blood pressure and in pulmonary ventilation.

The results reported here have confirmed and extended these observations. In the spontaneously breathing dog systemic hypoxia usually caused tachycardia, hypertension and increase in cardiac output and a reduction in total peripheral vascular resistance, responses similar to those observed by other workers (for references, see Introduction). When, in the presence of hypoxia, the carotid body chemoreceptor 'drive' was withdrawn by changing the composition of the carotid body perfusate from

hypoxic to oxygenated blood, a further tachycardia, increase in cardiac output and decrease in peripheral vascular resistance occurred. The responses to withdrawing the chemoreceptor 'drive' cannot be due wholly to the accompanying alterations in respiration as similar effects were observed in animals whose ventilation was maintained constant. Moreover, it is evident that, since the cardiovascular responses of induced hypoxia are not reversed by withdrawing the carotid chemoreceptor 'drive', they cannot be attributed to carotid body excitation.

This conclusion is supported by the observations of Korner & Edwards (1960), who, in the unanaesthetized rabbit, compared the effects of systemic (arterial) hypoxia produced by breathing gas mixtures of low oxygen content and of tissue hypoxia produced by inhalation of carbon monoxide. Both types of hypoxia caused an increase in cardiac output, but since carboxyhaemoglobinaemia fails to excite the carotid bodies (Duke, Green & Neil, 1952) they concluded that the arterial chemoreceptors play no part in the development of the increased cardiac output of systemic hypoxia.

In the spontaneously breathing dog withdrawal of the carotid body 'drive' during hypoxia caused a decrease in peripheral vascular resistance. This response was also seen in animals whose ventilation was maintained constant and occurred whether the blood pressure increased, decreased or remained unchanged. It must be attributed, therefore, to peripheral vasodilatation, though our experiments do not enable us to state in which vascular territories this response takes place. It also follows that, because the blood pressure fell or remained unchanged in the majority of tests, the peripheral vasodilatation cannot be the result of a reflex arising from the carotid sinus and aortic arch baroreceptors. It is known that excitation of the carotid bodies causes a powerful primary vasoconstriction mediated via the sympathetic nervous system (Bernthal, 1938; Bernthal, Motley, Schwind & Weeks, 1945; Daly & Daly, 1959; Daly & Scott, 1962*b*), and a likely explanation of the peripheral vasodilator response occurring on withdrawing the carotid chemoreceptor 'drive' during hypoxia is, therefore, abolition of the primary vascular chemoreceptor reflex. This view is supported by the fact that re-establishing hypoxic blood perfusion of the carotid bodies causes peripheral vasoconstriction. The primary vascular reflex from the carotid bodies may therefore be a mechanism by which the peripheral vascular resistance is maintained in systemic hypoxia, thereby representing an important function of the chemoreceptors in their control of the circulation.

Comparison of the effects of elective stimulation of the carotid bodies in the present experiments during systemic hypoxia with those observed by Daly & Scott (1958, 1963*a*) in dogs breathing room air or 30% O_2 in N_2 indicate differences which appear to us to warrant further discussion.

When the carotid bodies were stimulated during systemic hypoxia, hyperpnoea, bradycardia, a reduction in cardiac output and an increase in peripheral vascular resistance occurred. On the other hand Daly & Scott (1963*a*) observed variable effects in dogs spontaneously breathing room air or 30% O_2 in N_2, but those effects which predominated were hyperpnoea, tachycardia, an increase in cardiac output and a reduction in peripheral vascular resistance. This apparent discrepancy between the results obtained in the two series of experiments may lie in the fact that there was a considerable difference in the size of the ventilatory response. In the present experiments, increases in respiratory minute volume of up to 101% were observed, whereas in those of Daly & Scott (1963*a*) the average increase was 211% (range 46–493%). In this connexion, Macleod & Scott (1963) found that in the spontaneously breathing cat the predominant response to carotid body stimulation was bradycardia, not tachycardia as in the dog; the increase in respiratory minute volume, however, rarely exceeded 100%, so their results fall into line with those of Daly & Scott (1958, 1963*a*) on the dog. The importance of the reflex changes in pulmonary ventilation determining the responses of the cardiovascular system to carotid body stimulation has been stressed previously by us (Daly & Scott, 1958, 1962*b*, 1963*a*). The primary cardiac and vascular reflex responses from the carotid bodies are bradycardia and peripheral vasoconstriction (Bernthal, 1938; Daly & Scott, 1958, 1962*b*). Thus when the accompanying respiratory minute volume is relatively small (less than about 200% of the control value) or even absent, such as when respiration is controlled artificially, stimulation of the carotid bodies causes bradycardia. With larger increases in respiratory minute volume, however, an increase in heart rate occurs which has been shown to be secondary to events initiated by the hyperpnoea and not to a primary reflex from the carotid bodies.

It is of interest, therefore, that stimulation of the carotid bodies in the present experiments carried out on a 'background' of systemic hypoxia caused an increase in respiratory minute volume, the degree of which falls within the limits found by Daly & Scott (1958) to favour the development of the primary cardiac response. In support of this hypothesis is the finding that the stimulation of the carotid bodies in preparations artificially ventilated with a low-oxygen gas mixture had a similar effect. Another possible explanation, however, is that the presence of systemic hypoxia modifies the interaction between the primary reflex effects from the carotid bodies and the secondary mechanisms initiated by the concomitant hyperpnoea (Daly & Scott, 1963*b*; Daly, 1964). Further studies are required to clarify this point.

SUMMARY

1. In dogs under chloralose and urethane anaesthesia, the carotid bodies were isolated and perfused with blood from either the same (recipient) animal or a donor dog.

2. Substitution of 7–12% O_2 in N_2 for room-air breathing caused an increase in respiratory minute volume, tachycardia, hypertension, an increase in cardiac output and a decrease in total peripheral vascular resistance.

3. If during systemic hypoxia the carotid body perfusate was changed from hypoxic blood to oxygenated blood obtained from a donor dog, a further increase in heart rate and cardiac output, and a reduction in peripheral vascular resistance occurred, together with a reduction in respiratory minute volume. Re-establishing hypoxic blood perfusion of the carotid bodies reversed these effects.

4. Similar effects occurred in animals ventilated artificially.

5. It is concluded that the cardiovascular responses observed in systemic hypoxia cannot be attributed to excitation of the carotid body chemoreceptors. These chemoreceptors do, however, play an important part in maintaining the peripheral vascular resistance reflexly in this condition.

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