Brit. J. Pharmacol. (1957), **12**, 293.

THE EFFECT OF INHALATION OF 30% CARBON DIOXIDE ON THE PERIPHERAL CIRCULATION OF THE HUMAN SUBJECT

BY

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(RECEIVED FEBRUARY 12, 1957)

Inhalation of 30% carbon dioxide for 1 to 2 min. caused a transient increase followed by a marked fall in blood flow through the normal forearm and calf. Since there was an associated large increase in arterial blood pressure, the fall in flow was due to intense vasoconstriction. It is likely that the vasoconstriction in the forearm occurred deep to the skin because the oxygen saturation of the superficial venous blood did not fall during the inhalation. Since there was a slight decrease in flow through the nerve-blocked forearm in spite of the increased blood pressure, it is unlikely that nervous vasoconstriction can completely account for the marked decrease in muscle flow.

The inhalation of 20 to 30% carbon dioxide in oxygen is occasionally used in the treatment of patients with nervous disorders (Meduna, 1948; Fay, 1953a and b). The present experiments describe some effects of 30% CO_2 on the cardiovascular system in two young men who were undergoing a course of such treatment for stammering.

METHODS

30% CO_2 in oxygen was administered from a cylinder connected to a large breathing bag and a close-fitting face mask. The subject lay on a couch in a room at 20 to 22° C. and breathed this mixture for 1 to 1½ min. (20 to 30 breaths) during each session. The respiratory movements were recorded by two stethographs, one around the chest and the other around the abdomen, connected to a single volume recorder. Forearm, hand and calf blood flow was measured by venous occlusion plethysmography using temperature-controlled plethysmographs (Greenfield, 1954). Digital heat flow was determined in some experiments with Hatfield (1950) heat flow discs fixed to the finger pulp. The fingers were immersed in water at 29° C. In one experiment on one of the subjects the radial, median and ulnar nerves of one side were infiltrated with local anaesthetic solution (Roddie, Shepherd, and Whelan, 1957a). Direct measurement of brachial arterial blood pressure was made with a capacitance manometer. The oxygen saturation of blood samples taken from a superficial forearm vein was determined by a spectrophotometric technique (Roddie, Shepherd, and Whelan, 1957b).

TABLE I

THE EFFECT OF 30% CO_2 ON FOREARM, CALF AND HAND BLOOD FLOW

The observations marked with an asterisk were made with plethysmograph temperatures of 44°.

Blood flow is expressed in ml./100 ml./min.

Subject	Blood Flow								
	Forearm			Calf			Hand		
	Before CO_2	During CO_2	Peak Flow after CO_2	Before CO_2	During CO_2	Peak Flow after CO_2	Before CO_2	During CO_2	Peak Flow after CO_2
O'N. ..	2·5	0·5	5·5	—	—	—	3·0	8·5	19·0
O'N. ..	5·0	1·0	12·0	4·0	1·5	9·0	—	—	—
O'N. ..	5·0	0·2	10·7	—	—	—	—	—	—
O'N. ..	4·0	0·2	13·0	4·2	0·5	10·0	—	—	—
O'N. ..	3·0	0·3	12·0	—	—	—	—	—	—
O'N. ..	—	—	—	3·0	0·4	11·5	2·0	2·0	10·0
O'N.* ..	13·5	13·0	19·0	—	—	—	21·0	30·0	38·0
M. ..	3·0	0·7	7·5	—	—	—	—	—	—
M. ..	6·5	3·6	12·0	—	—	—	11·0	6·5	24·0

RESULTS

Both subjects had had a previous course of treatment and did not appear apprehensive before the inhalation. During the inhalation there was a striking increase in the depth and to a lesser extent in the rate of respiration. Apart from the increased activity of the respiratory muscles there were no other involuntary muscular movements either during or after the inhalation and, though consciousness was dulled, it was not lost. The subject was sweating profusely at the end of the inhalation.

Forearm and Calf Blood Flow.—The forearm blood flow was measured at a plethysmograph temperature of 34° C. during inhalation of 30% CO_2 on eight occasions (Table I). There was an initial transient increase followed by a fall in blood flow which was maintained throughout the period of inhalation (Fig. 1). On some occasions the blood flow through the forearm almost ceased. When the inhalation of CO_2 was stopped a large transient increase in blood flow occurred. The changes in flow were found to be symmetrical on the two sides. Similar changes in flow were observed in the calf. The arterial pressure rose markedly, for example in one experiment from 125/75 to 205/110 (Fig. 1). Since the blood flow had decreased and the arterial blood pressure had increased, the resistance blood vessels of the forearm and calf must have been strongly constricted.

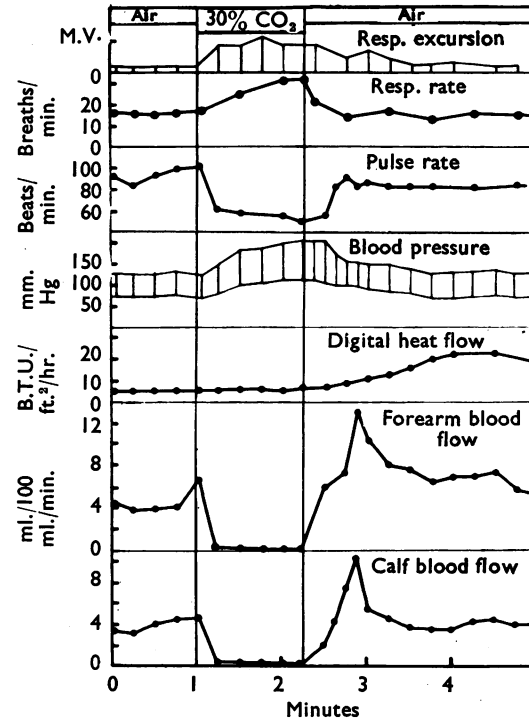

FIG. 1.—The effect of breathing 30% CO_2 in O_2 on respiratory excursion and rate, pulse rate, arterial blood pressure, digital heat flow and forearm and calf blood flow. The respiratory excursion obtained by maximal voluntary inspiration is designated M.V. Digital heat flow was measured by heat flow discs.

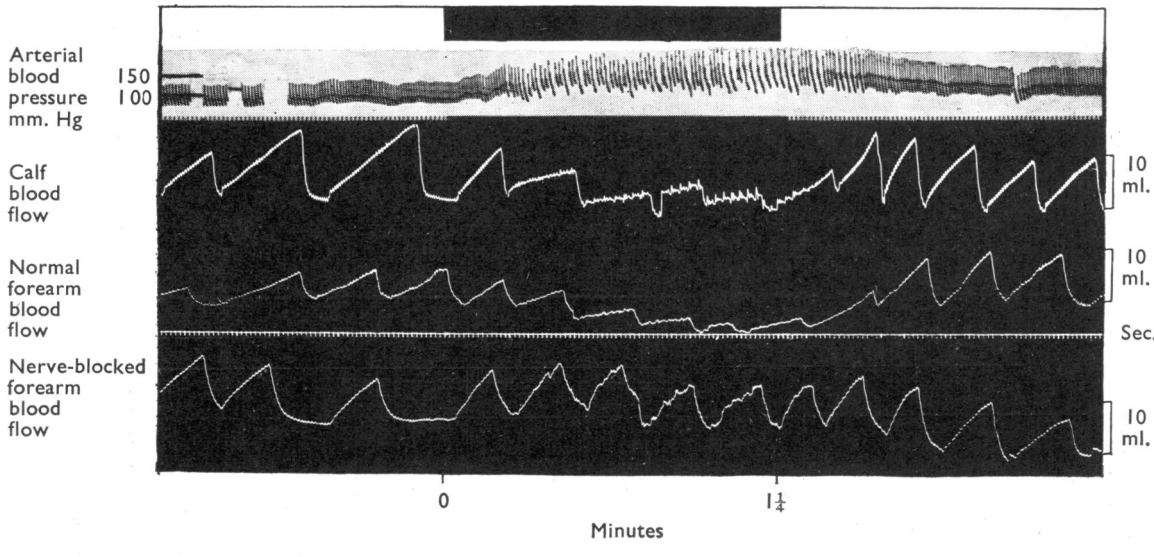

FIG. 2.—Arterial pressure and plethysmographic records obtained before, during, and after inhalation of 30% CO_2. The black rectangle represents the period in which CO_2 was administered.

Fig. 2 shows typical examples of plethysmograph and blood pressure records on one of the subjects.

In one experiment, the forearm blood flow on one side and the % oxygen saturation of superficial venous blood draining the skin of the opposite side were measured during CO_2 administration (Fig. 3). The circulation was arrested at both wrists by pneumatic cuffs inflated to 200 mm. Hg. During the CO_2 inhalation, the forearm blood flow decreased in the usual manner, but the oxygen saturation of the superficial venous blood increased from 80 to 91%. The increase in arterial blood oxygen content with 70% oxygen inhalation could at the most account for this increase. Even if it is assumed that it does so, it can be concluded that, provided the metabolism of the forearm skin remains constant, the blood flow through the skin is unchanged or possibly increased. The decrease in total forearm flow must be due to constriction of vessels deep to skin presumably in the skeletal muscles. On one occasion, with the plethysmograph temperature at 44° C., there was no change in forearm blood flow during the inhalation of CO_2. It is possible that under these conditions the increase in skin flow resulting from the rise in pressure combined with the dilatation of the skin vessels by the local heating was sufficient to balance the decrease in muscle flow.

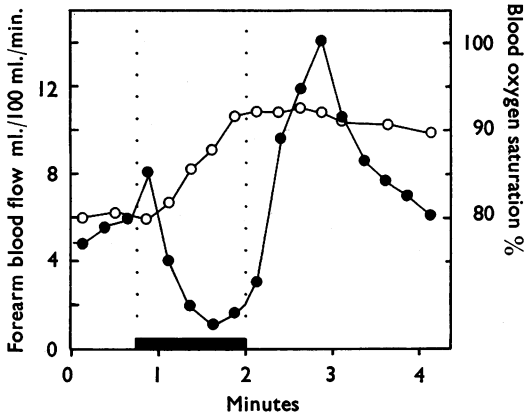

FIG. 3.—The effect of inhalation of 30% CO_2 for duration of black rectangle on forearm blood flow (●) and the oxygen saturation of the blood in a superficial forearm vein (○).

In one experiment (Figs. 2 and 4*a*) the flow through the normal and the nerve-blocked forearm was compared during CO_2 administration. There was the usual marked decrease in flow through the normal forearm and a small decrease through the nerve-blocked side. That the changes were not due to the mechanical effects of the hyperventilation is shown by the fact that hyper-

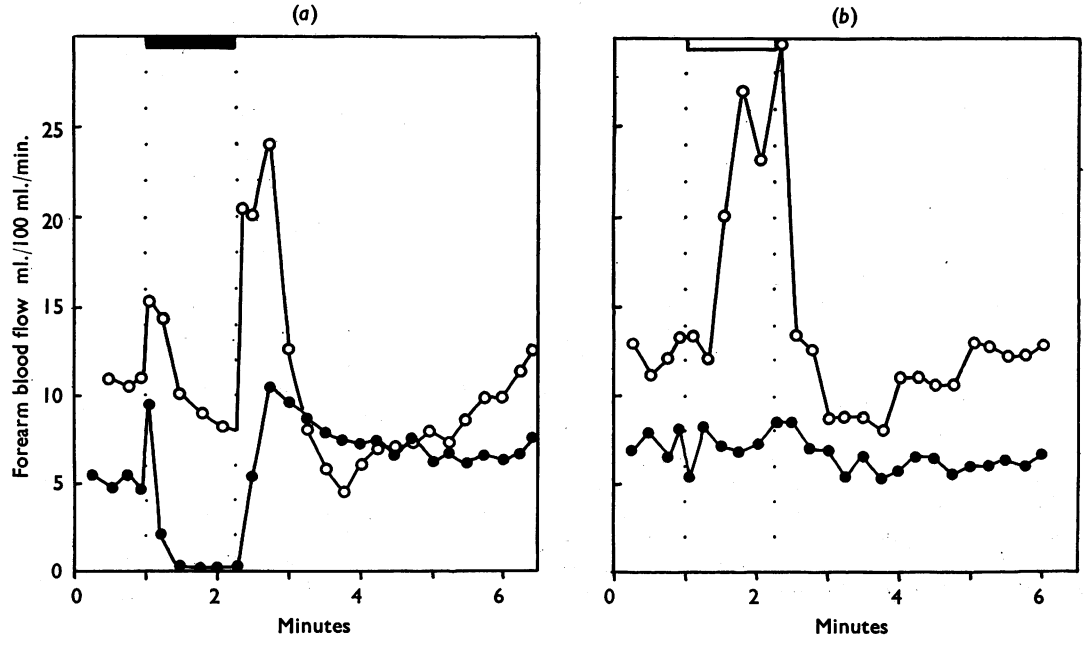

FIG. 4.—The blood flow through the normal (●) and nerve-blocked forearm (○). (*a*) During 30% CO_2 inhalation (black rectangle) and (*b*) during overbreathing air (clear rectangle).

ventilation in air at approximately the same rate and depth, which reduces the blood CO_2 level, produces a large increase in flow through the nerve-blocked forearm (Fig. 4*b*) (Roddie, Shepherd, and Whelan, 1957c).

Hand Blood Flow.—On three occasions the forearm and hand blood flows were measured simultaneously. Though the forearm blood flow always decreased, the hand blood flow on one occasion showed a transient fall, on another remained unchanged and on the third increased. Equivocal results were also obtained when digital heat flow was measured on two occasions. On one there was a fall in heat flow and on the other no change in flow during inhalation of 30% CO_2. As in the forearm, there was a transient increase in hand blood flow after the inhalation ceased. It is always difficult to distinguish changes in hand flow which result from emotional stimuli from changes due to other causes, but it seems that the response of these vessels was less marked and consistent than those of the forearm.

Discussion

It is generally believed that CO_2 by its action on either the vasomotor centre or the chemoreceptors can reflexly constrict peripheral blood vessels (Goodman and Gilman, 1955). Lennox and Gibbs (1932) found that breathing 4 to 8% CO_2 did not affect the blood flow through the leg and Abramson and Ferris (1944) found that, during inhalation of 7% CO_2, the forearm blood flow was either unchanged or increased. Abramson (1944) explained these findings on the basis that the blood vessels of the forearm are little, if at all, affected by vasoconstrictor impulses. Recent work, however, has shown that nervous control of skeletal muscle vessels plays an important part in the baroreceptor reflexes (Sharpey-Schafer, 1953; Roddie and Shepherd, 1956). While 30% CO_2 is outside the physiological range, the observation in the present experiments of intense constriction of normally innervated skeletal muscle vessels during inhalation of 30% CO_2 suggests that the sympathetic control of these vessels can play a part in the chemoreceptor reflexes.

It is unlikely that nervous vasoconstriction can completely account for the marked decrease in muscle flow since in the nerve-blocked forearm there was a slight decrease in flow in spite of the increased blood pressure. Failure to interrupt the sympathetic fibres by the nerve block is unlikely to explain these results; the forearm flow showed the characteristic increase after the block, the forearm and hand muscles were completely paralysed and there was a complete loss of sensation in the hand. Further, the increase in flow through this forearm with overbreathing room air was that typically seen in the denervated forearm (Fig. 4*b*).

During inhalation of 30% CO_2 there is a decrease in the arterial blood *p*H from 7.37 to 6.96 and the lactic acid changes from 8.0 to 8.75 mg. % (Gibbs and Gibbs, 1950). There is no evidence, however, that either of these changes would cause vasoconstriction. Liberation of noradrenaline could explain the decrease in flow through the nerve-blocked forearm as it has a direct constrictor action on muscle vessels. However, when given intravenously it often causes an increase in blood flow through the normal forearm due to an indirect dilator action (Barcroft, Gaskell, Shepherd, and Whelan, 1954).

It is most unlikely that there is a single explanation for the cardiovascular findings. Mechanical effects of the hyperventilation, emotional effects, the stimulation of chemoreceptors, the direct effect of carbon dioxide on the central nervous system, the chemical changes in the blood and the possible release of a humoral agent may all play a part in the final response.

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