The Effect of Hypocapnia on Arterial Blood Pressure

By J. F. Burnum, M.D., J. B. Hickam, M.D., and H. D. McIntosh, M.D.

In man, hypocapnia induced by hyperventilation causes a drop in arterial pressure. The calculated peripheral resistance is decreased, indicating a net vasodilatation. The forearm blood flow is markedly increased, and the vascular resistance of the forearm is much reduced. Persons with impaired function of the sympathetic nervous system continue to show these effects. The increase in forearm flow is not prevented by brachial block. These results suggest that hypocapnia acts directly on blood vessels to produce a net over-all vasodilatation and fall in blood pressure, and that this effect is not mediated through the nervous system, as usually supposed.

Breathing carbon dioxide raises the blood pressure and hyperventilation lowers it in man and experimental animals. Changes in blood carbon dioxide are supposed to affect vessels both directly and by way of the vasomotor centers. These actions are thought to be opposite in direction, with the central effect being the stronger. That is, a high carbon dioxide level causes an over-all vasoconstriction because of its effect on the vasomotor centers, even though the direct action is to dilate vessels. Loss of carbon dioxide has opposite effects, both centrally and locally. These conclusions are based on animal experiments.

It is the purpose of this paper to describe the effects on vascular tone of lowering carbon dioxide by hyperventilation in (1) normal subjects and (2) patients in whom portions of the nervous system have been destroyed by disease or surgery or blocked by drugs. The results of this study do not support the conventional concept of the means by which carbon dioxide affects vascular tone.

Methods

Hyperventilation studies, unless otherwise specified, were conducted on recumbent subjects during one-minute periods of maximal voluntary forced breathing of either room air or a 5 per cent carbon dioxide, 21 per cent oxygen gas mixture. Procedures included simultaneous measurements of forearm blood flow by plethysmography, intrarterial pressure, pulse rate, cardiac output by dye dilution method and arterial blood pH and carbon dioxide content; from the latter blood carbon dioxide tension was calculated. Local forearm vascular resistance was calculated as

\[
\frac{\text{mean blood pressure (mm. Hg)}}{\text{forearm blood flow (cc./min./100 cc. tissue)}}
\]

and over-all peripheral resistance as

\[
\frac{\text{mean blood pressure (mm. Hg)}}{\text{cardiac output (L/min.)}}
\]

Forearm blood flows at 37 C. with hand excluded, central venous pressure and intra-arterial pressures were measured with the use of strain gauges and a Sanborn Poly-Viso oscillograph. Single determinations of cardiac output were separated by 15-minute intervals, and the Evans blue dye was injected through a standard cardiac catheter threaded into one of the intrathoracic great veins (subclavian or superior vena cava) or right atrium. Arterial blood samples for dye analysis were collected from the brachial or femoral artery.

Brachial plexus block was achieved by infiltration with 20 cc. of 2 per cent xylocaine containing 1:300,000 epinephrine.

Results

Control Subjects

After a period of one minute of forced breathing, the arterial blood carbon dioxide tension was commonly halved, falling to around 20 mm. Hg, and the pH rose to around 7.6. Maximal forced voluntary hyperventila-
HYOCAPNIA AND ARTERIAL BLOOD PRESSURE

Table 1.—Circulatory Changes during Hyperventilation (Air). Control Subjects

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<tr>
<th>Case no.</th>
<th>State</th>
<th>Mean B.P. mm. Hg</th>
<th>Pulse rate, per. min.</th>
<th>Cardiac output, L./min.</th>
<th>Forearm blood flow, cc./min.</th>
<th>Vascular resistance</th>
<th>Over-all Peripheral Mean B.P.</th>
<th>Forearm Mean B.P.</th>
<th>Forearm Cardiac Output</th>
<th>Mean circ. time, sec.</th>
<th>pH 37°</th>
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* Essential hypertension.

Hyperventilation. In 16 patients forced over-breathing of a 5 per cent carbon dioxide mixture caused no change in pressure. Hyperventilation on air caused a striking increase in heart rate; on 5 per cent carbon dioxide only a moderate increase.

The cardiac output during hyperventilation on air was measured in nine subjects. It increased an average of 50 per cent. The circulation time was halved (average decrease 43 per cent). Measurements were made on three subjects hyperventilating on 5 per cent carbon dioxide; the output decreased in two of the three subjects and was unchanged in one.

Central venous pressure was measured in the right atrium or superior vena cava in seven subjects. There was no change in six and a rise of 5 mm. Hg in one.
increased the blood flow in the forearm to an average of 2.5 times the control level. Hyperventilation on 5 per cent carbon dioxide also increased the flow, but the increase averaged only a third as much as when hypocapnia was allowed to develop. This effect on forearm flow is similar to that recently reported by Clarke.6

Comment. In normal subjects overbreathing on air causes tachycardia, fall in arterial pressure, increased cardiac output and increased forearm blood flow. The increase in cardiac output in the presence of a reduced mean blood pressure indicates an over-all fall in peripheral resistance. The forearm is one of the areas where the resistance is lowered.

These data are in general agreement with those in the literature. Henderson7 pointed out that Ewald in 1873 produced hypotension and apnea in dogs by hyperventilation, and Mosso found the same effects in man. The latter coined the word "acapnia" from the Greek kaphnos meaning "smoke." Henderson showed that the fall in blood pressure in both

![Fig. 1. Mean values of circulatory changes during recumbent hyperventilation in control subjects are presented as per cent change from resting measurements. During overbreathing on air the blood pressure falls and cardiac output and forearm blood flow rise; the calculated over-all and local forearm vascular resistance decrease. During hyperventilation on 5 per cent carbon dioxide there is only a small increase in forearm flow. These average changes were calculated from data on blood pressure in 35 subjects, forearm flow in 16 subjects, and cardiac output in 9 subjects.](image)

![Fig. 2. Continuous intra-arterial pressure tracings during recumbent hyperventilation in normal subjects. During hyperventilation on air the arterial pressure falls but may tend to recover while overbreathing continues, top record, or not until later, middle record. On 5 per cent carbon dioxide no significant fall occurs. (Arrows indicate period of hyperventilation.)](image)
dog and man was prevented by breathing a carbon dioxide mixture instead of air.

Roome overventilated dogs in a Drinker respirator and demonstrated that the fall in arterial pressure resulted from over-all peripheral vasodilation and was prevented by breathing carbon dioxide. The cardiac output was measured by the direct Fick method.

Dale and Evans found in the cat that hyperventilation hypotension was largely prevented by overventilation on 5 per cent carbon dioxide and that acutely raising the pH with sodium bicarbonate to levels attained during hyperventilation on air did not cause a fall in pressure. They postulated that loss of carbon dioxide caused the fall in pressure and that this effect of low carbon dioxide was a central one since hyperventilation on air after destruction of the spinal cord caused a small rise in pressure, supposedly due to the now unveiled peripheral effects of hypocapnia.

Standard physiology texts have accepted Dale and Evans' explanation that lowering of the arterial carbon dioxide tension tends to cause vasoconstriction through local effect on vessels, but this effect is not demonstrable in the intact animal because of vasodilatation induced by the central effects of the low carbon dioxide tension. If this explanation is correct for man, one would expect the vasodilator effects of a low carbon dioxide tension to be lessened or absent in patients with a large portion of the vasomotor nerves destroyed by disease or blocked by suitable drugs. This hypothesis has been tested on appropriate patients.

**Patients with Postural Hypotension**

Observations were made on three subjects complaining of postural fainting. Two subjects had the classic syndrome of orthostatic hypotension with fixed pulse, impotence and impaired sweating as described in the classic paper of Bradbury and Eggleston. The third patient was incapacitated 12 months after bilateral lumbar sympathectomy. The disturbances in reflex regulation were so marked that we believed she might have had poor postural regulation before operation. In each instance, at least partial paralysis of the vasomotor nerves was present. The Valsalva maneuver caused a major fall in arterial pressure and upon release of the strain, no overshoot in pressure occurred.

Hyperventilation on air in the recumbent position caused a large fall in arterial pressure with delayed recovery and no overshoot of pressure upon resumption of normal respiration (fig. 3). The cardiac output and forearm blood flow tended to increase, the circulation

![Fig. 3. Continuous intra-arterial pressure tracings in orthostatic hypotension during recumbent hyperventilation on air and 5 per cent carbon dioxide. A mean blood pressure fall of 60 mm. Hg occurs during overbreathing on air with a delayed recovery after resumption of normal respiration. No change occurs if hyperventilation is conducted on 5 per cent carbon dioxide. In both instances the pulse rate is fixed. (Arrows indicate period of hyperventilation.)](image)
time to shorten and the calculated local forearm and over-all peripheral resistance to decrease. Figure 4 gives a graphic presentation of the data.

Hyperventilation on 5 per cent carbon dioxide largely prevented any circulatory changes.

Patients after Sympathectomy

Studies were done on one patient before and seven weeks after the second stage of a bilateral sympathectomy from T-1 to L-1 (fig. 5). All changes are related to the preoperative resting values. Removal of this large portion of the sympathetic chains did not change the over-all decrease in peripheral resistance and in forearm resistance produced by hyperventilation on air. Hyperventilation on 5 per cent carbon dioxide did not lower the pressure.

Observations were made on five patients who had had bilateral sympathectomy for hypertension from T-1 to L-1 from one to eight years previously and on one patient with essential hypertension with his vasomotor responses blocked by hexamethonium. In all cases, release of Valsalva maneuver caused no overshoot or bradycardia, indicating continued interruption of the visceral sympathetic pathways. Data from the control and sympathectomized groups are compared in figure 6. Measurements are averaged and presented as per cent changes during hyperventilation from resting values. The two groups are similar, except that the sympathectomized subjects showed no substantial recovery of arterial pressure during the course of hyperventilation, such as occurs in some normal subjects. No significant changes occurred when over-breathing a 5 per cent carbon dioxide mixture.

Subjects after Brachial Plexus Block

Brachial block was performed on one patient with an old hand injury, in whom the rest of the
extremity was normal, and on one normal subject. In each case the effectiveness of sympathetic block was indicated by the skin of the arm becoming hot, dry and flushed. The arm was anesthetized and almost totally paralyzed. In addition there was a Horner's syndrome and phrenic paralysis on the blocked side in one case. The data are summarized in table 2. In both cases before block, hyperventilation on air produced the usual fall in blood pressure, rise in forearm blood flow and fall in forearm resistance. After block the resting forearm flow increased, but not to the extent of that produced by preblock hyper-ventilation. After block, during overbreathing the blood pressure fell as usual, and the forearm flow increased and the local resistance fell to precisely the same levels reached before block.

**Comment**

These data indicate that in man a loss of carbon dioxide from overbreathing has an over-all vasodilating effect. In normal subjects the fall in pressure is restricted by a combination of an increase in cardiac output and the expected effect of vasoconstriction in various areas secondary to the fall in arterial pressure. These are the familiar homeostatic adjustments which keep the arterial pressure at its surprisingly constant level. The importance of these adjustments for regulating the arterial pressure is well shown in the patients with symptoms of postural hypotension and in the patient with the recent extensive sympathectomy, who had greater and more prolonged falls in pressure during hyperventilation than did the normal subjects. The fact that a fall in carbon dioxide tension causes a marked fall in peripheral resistance in patients with destruction of a large portion of the autonomic nervous system argues against a central effect and suggests that lowering carbon dioxide tension causes vasodilatation because of a direct effect on certain vessels. Brachial blocks established the fact that at least in the forearm a lowering of carbon dioxide tension caused vasodilatation by local action.

These data are not to be interpreted as meaning that lowering of the arterial carbon dioxide tension causes vasodilatation in all organs. It is well known that in the cerebral vessels where vasomotor activity is low, acapnia causes a rise in resistance. It does appear that the sum of all the changes in resistance add up to vasodilation and that if the nervous system is not working properly this vasodilation is sufficient to cause a marked fall in arterial blood pressure.

Neither do these data shed any light on the effects of high carbon dioxide tension on the blood vessels. The fact that a low carbon dioxide tension causes a fall in peripheral resistance does not mean that sufficiently high carbon dioxide tension might not have the same effect. For example, both too much potassium and too little potassium cause paralysis.

These data are convincing evidence that the role of carbon dioxide tension in arterial pressure homeostasis needs further investigation.

**Summary and Conclusions**

1. Hypocapnia, induced by voluntary hyperventilation, causes a substantial decrease in the peripheral vascular resistance and blood pressure of normal subjects, and a substantial increase in forearm blood flow.

2. These effects of hypocapnia persist in subjects who have extensive loss of function of the sympathetic nervous system, resulting from disease, surgery, or the use of autonomic blocking drugs.

3. Brachial block does not substantially
change the response to hypocapnia of forearm vascular resistance and forearm blood flow.

4. It is probable that vasodilatation produced by hypocapnia in man is the net result of direct action on the vessels in different vascular areas and is not mediated by the nervous system.

SUMARIO ESPAÑOL

En el hombre la hipocapnia inducida por la hiperventilación causa un decremento en presión arterial. La resistencia periférica calculada esta disminuida, indicando una vasodilatación neta. La circulación del antebrazo es marcadamente aumentada, y la resistencia vascular muy reducida. Personas con función deteriorada del sistema simpático continuan demostrando estos efectos. El aumento en circulación del antebrazo no se evita por medio de un bloqueo braquial. Estos resultados sugieren que la hipocapnia actúa directamente en los vasos para producir una vasodilatación neta y un decremento en presión arterial, y que este efecto no es mediado por el sistema nervioso como se había supuesto.

REFERENCES


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