A VAGO-PRESSOR REFLEX. By R. J. S. McDOWALL.

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In 1915 Bainbridge(1) described a nervous relation between the venous pressure and the pulse rate. He showed that a rise in venous pressure caused a diminution of vagal and an increase in accelerator tone, and pointed out the importance of this factor in the regulation of the cardiac output during muscular exercise. In the course of experiments made for another purpose the possibility arose as to whether the vagus was not also an important factor in the maintenance of blood-pressure under conditions of poor inflow. I am indebted to Dr G. V. Anrep for the information that Pavlov in 1879 had observed that the alterations in arterial pressure which occur as the result of bleeding or of the injection of defibrinated blood were both increased if the vagi were cut. For example, he noted that in dogs the withdrawal of blood to the extent of 1·5 p.c. of their body weight only caused a small or temporary fall of blood-pressure when the vagi were intact but that there was a large fall if the vagi were cut.

It is well known that in hæmorrhage there is constriction of arterioles and this is usually alleged to be due to increased action of the vaso-motor centre. There is also a fall of venous pressure but no one appears to have suggested that this fall is responsible for keeping up of the vaso-motor tone. A series of experiments have been carried out to investigate this point. In all experiments cats anæsthetised with chloralose, and under artificial respiration, were used. Various methods have been adopted to reduce venous pressure.

Alcohol. I have shown elsewhere that a certain amount of alcohol causes a profound fall of venous presssure, although the arterial pressure may be unchanged. The latter observation is well known. If after the administration of alcohol (say 5 to 10 c.c. of a 50 p.c. solution) the vagi be cut there is a marked fall in arterial pressure. This fall may be permanent or may to some extent be recovered from for reasons which will be put forward below.

Histamine. In partial shock caused by the injection of one or two milligrams of histamine there is a fall of venous pressure(3), and inadequate supply of the heart(4). If sufficient histamine is given to reduce

the arterial pressure to 60 or 80 mm. Hg then the cutting of the vagi causes a further fall in arterial pressure.

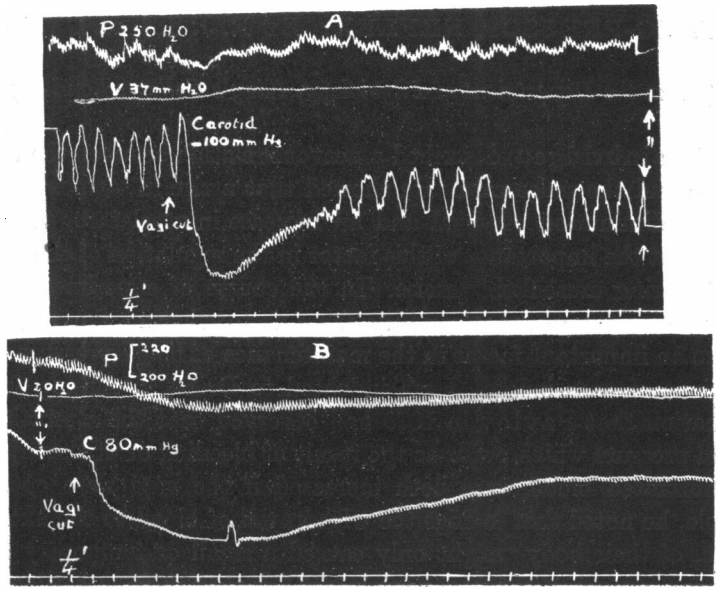


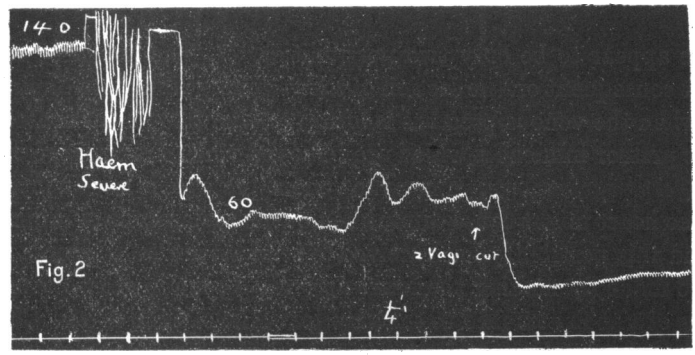
Fig. 1. Effect of alcohol. 8 c.c. of 50 p.c. alcohol had been injected. Tracings of pressure, in pulmonary artery, superior vena cava and carotid artery. Section of the vagi causes a large fall of arterial pressure without a corresponding large rise of venous pressure. In *A* there is no change of pulmonary pressure. In *B* there is a fall.

Hæmorrhage. If blood is withdrawn from the animal to lower the arterial pressure to 60 or 80 mm. Hg and, as stated above, also the venous pressure, section of the vagi causes a further fall of arterial pressure (Fig. 2).

Mechanical. A loop of thin twine was placed round the thoracic vena cava and attached to a screw arrangement by which the tension on the loop could be increased and the vena cava compressed. In this way the venous pressure close to the heart could be lowered to any required extent. When the vena cava was sufficiently compressed the arterial pressure fell to 60 mm. Hg, but rose slightly as the compression was maintained. On section of the vagi the arterial pressure at once fell (Fig. 3).

It will be seen from these experiments that under a variety of conditions section of the vagi causes a fall of arterial pressure, whereas normally such section causes, as is well known, a rise in pressure. From

the alcohol experiments it is seen that the effect of the vagal section is not necessarily dependent on a previous fall of arterial pressure. From



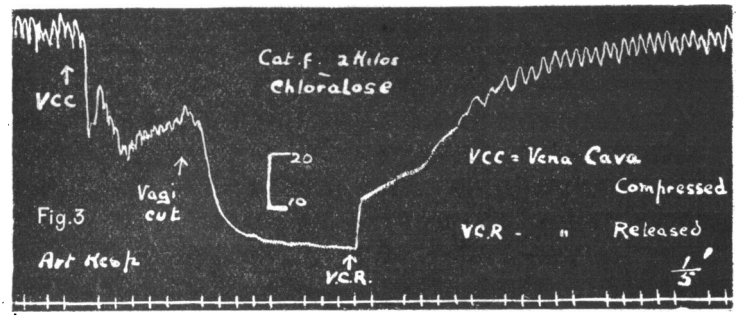


Fig. 2. Effect of hæmorrhage. After a reduction of blood-pressure from 140 mm. Hg to 60 mm. by hæmorrhage, section of the vagi causes a further fall.

Fig. 3. Effect of lowering the venous pressure near the heart. Compression of inf. vena cava at *V.C.C.* On section of the vagi the pressure falls nearly to zero. *V.C.R.*, vena cava released.

the histamine experiments it is seen that the effect is not due to any specific action of the alcohol, while the hæmorrhage and mechanical experiments exclude any effect of capillary dilation or a fall of peripheral venous pressure. All the experiments have in common a fall in pressure close to the heart. How then can a fall of venous pressure influence the result of vagal section on arterial pressure?

It cannot be considered that the depressor nerve, or what corresponds to it in the cat, is concerned. In those experiments in which the aortic pressure was reduced the diminution would tend to increase the tone of the vaso-motor centre, but section of the vagi in the cat would still further cause an increase in vaso-motor tone.

That the nerve section itself was not responsible for the results was shown by the fact that a similar fall occurred when the vagus paths were interrupted by the application of cocaine to the nerve trunk in the neck.

There appear to be only two possibilities. (1) The increased rate of the heart consequent on the section of the vagi may result in a diminished output when the venous pressure is low. (2) The vaso-motor centre may be under pressor influences which are removed when the vagi are cut.

Changes in cardiac rate. When the venous pressure is low an increased rate of the heart might cause diminished output as a result of diminished filling and this possibility has received special attention. Records of the rate were made by making the heart activate a system of two tambours by means of a hook attached to the anterior surface of the organ. Changes in rate were brought about by the application of hot and cold fluids to the region of the pacemaker. As the peripheral resistance is not affected and may be presumed constant, the blood-pressure may be considered to be an indication of the output of the heart. In this way it is comparatively easy to demonstrate, as pointed out by Henderson, that when the venous pressure is normal or high, an increased rate of the heart increases the output since the organ is still completely filled during the shortened diastole. When the venous pressure is low the rate of the heart within physiological limits makes no difference to the blood-pressure, as would be inferred from Starling's *Law of the Heart.* Of course, if the cooling is excessive, say with iced saline, and the heart rate enormously reduced, the blood-pressure may fall whatever the venous pressure, but in no instance has it been found possible with

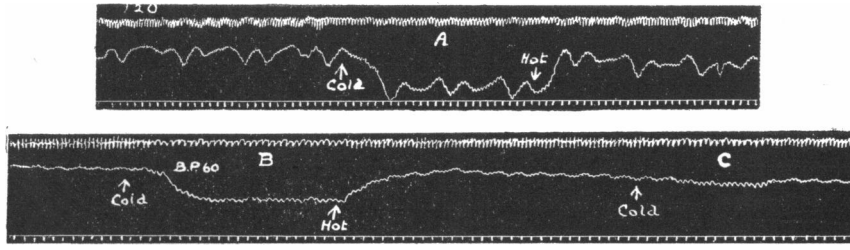


Fig. 4. Effect of varying the rate of heart beat with normal and with low venous pressure. Upper tracing, heart rate. Lower tracing, carotid pressure. Time $\frac{1}{10}$ secs. *A*. Venous pressure presumably normal since arterial pressure normal; slight slowing of the heart causes a marked fall of blood-pressure. *B* and *C*. Venous pressure low after hæmorrhage; in *C* greater slowing of the heart than in *A* causes a mere trace of fall; the absence of fall is not due to mechanical conditions since great slowing of the heart produced at *B* causes a moderate fall.

intact vagi so to increase the rate of the heart as to diminish the diastolic filling and the output. The effect of changes in rate are seen in Fig. 4.

To return to the effect of section of the vagus, were the fall of arterial pressure due to the increased rate and a diminished output of the heart it would be possible by again slowing the heart to recover the pressure by peripheral stimulation of the cut vagus (suggested to me by Dr Hewitt) by pilocarpine or direct applications to the pacemaker as above. This has not been found to occur, a fact which is in accordance with the results in relation to the heart rate stated above. When the venous pressure is low it is possible to slow the heart appreciably without affecting the blood-pressure as the increased diastolic filling increases the output per beat and makes up for the diminution in rate (Fig. 5).

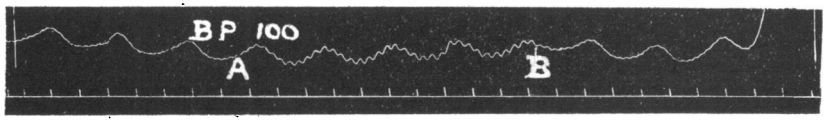


Fig. 5. Carotid blood-pressure after hæmorrhage. From *A* to *B*, peripheral end of vagus stimulated; slowing of the heart but no fall of blood-pressure. Time $\frac{1}{10}$ sec.

Were the effect of the section due to diminished output it would certainly give the characteristic abrupt rise of venous pressure. This does not occur. Rather there is the equally characteristic slow rise (since smooth and not cardiac muscle is concerned) which I find to be typical of diminished resistance in the arterioles. Fig. 1 also shows that the pressure in the pulmonary artery is not necessarily affected as it certainly would be if the diastolic filling were reduced. In this experiment there was an increased venous inflow to the heart which counterbalanced any fall of pulmonary pressure which may have occurred from pulmonary vaso-dilatation.

The effect of the rate of the heart may further be excluded by increasing the rate by hot applications to the pacemaker prior to the section of the vagi. Then there is the same fall of arterial pressure while the change in the heart rate is negligible (Fig. 6).

The second possibility that the vagi carry pressor influences remains for consideration. That the vaso-motor centre is concerned is shown by the fact that if the centre is cut off by section of the spinal cord in the upper dorsal region, section of the vagi under conditions of low venous inflow does not cause a further fall of arterial pressure. Tone of the peripheral arteries is then, as would be expected, an essential part of the

reflex. For complete confirmation of this and the participation of the peripheral arteries it may be shown that on section of the vagi there is

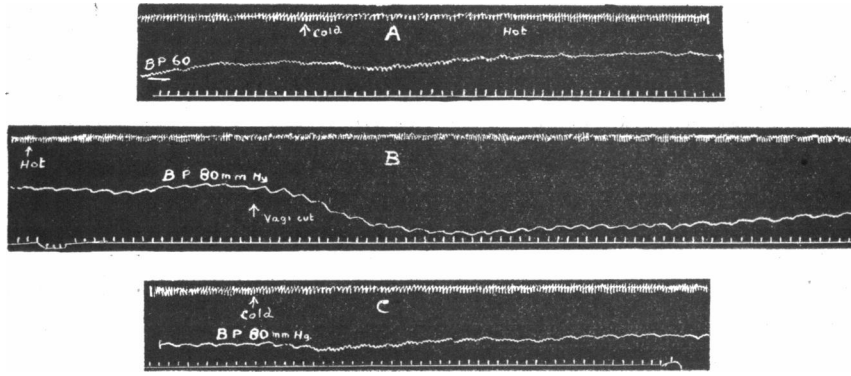


Fig. 6. Upper tracing heart rate, lower tracing carotid blood-pressure after the blood-pressures have been reduced by hæmorrhage. In (*B*) the typical effect of vagus section is seen. *A* and *C*, taken in the same animal immediately before and after the section, show that much larger changes in rate can occur without affecting the arterial pressure. Were the change in the vagal section (*B*) due to slowing of the heart, a similar change would be expected on slowing in (*A*), while if the fall in (*B*) were due to quickening, a recovery would be expected on slowing in (*C*). Time $\frac{1}{10}$ sec.

in plethysmographic experiments a distinct increase in the volume of a limb and, as is seen in Fig. 7, the increased volume of the limb is main-

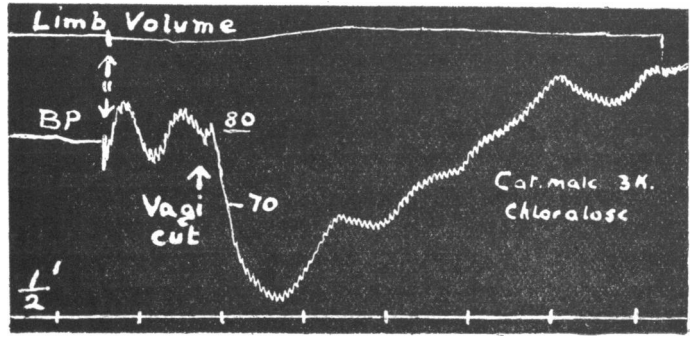


Fig. 7. After hæmorrhage. Section of the vagi causes a fall in arterial pressure accompanied by an increase in the volume of the hind limb.

tained although the arterial pressure may return to normal for reasons stated above. It can therefore be considered that under conditions of low venous pressure in the region of the right auricle, impulses pass up the vagi to the vaso-motor centre which is thereby stimulated and the tone of the arterioles and arteries is increased. An attempt has been

made to differentiate between the effect of a diminution in venous and a fall of pulmonary arterial pressure which necessarily occurs at the same time but the experimental difficulties have so far prevented any satisfactory conclusion being arrived at.

It is evident that the existence of such a reflex will be of considerable value in conditions of loss of blood actual or relative (*i.e.* when the vascular bed has been increased as in certain varieties of shock). By its means the arterial pressure and especially the pressure in the coronary and vertebral arteries will be kept as high as possible when the output of the heart is reduced. In this respect the vago-pressor reflex will supplement the well-known depressor reflex, but with this difference that it will continue to act when the arterial pressure has returned to normal if the venous pressure has not—as after hæmorrhage. Thus is explained a phenomenon which was difficult to understand, namely, how the vaso-motor centre is so stimulated as to maintain the arterial pressure when the normal has been reached again soon after hæmorrhage, *i.e.* when the depressor reflex is no longer active.

The possibility of the operation of the reflex in plethysmographic experiments has also to be remembered. Thus a drug which causes a fall in venous pressure may cause diminution in the volume of a limb and variations in the reflex may account for the many admittedly anomalous results which occur in relation to limb volume, with a drug such as histamine.

SUMMARY.

When the venous pressure in the large veins is low, section of the vagus causes a fall of arterial blood-pressure.

Reasons are put forward why this is to be considered a vago-pressor reflex, and not due to changes in the heart rate.

The evidence indicates that when the venous pressure is low impulses pass up by way of the vagus and stimulate the vaso-motor centre and so increase the arterial tone.

The importance of this reflex in supplementing the depressor reflex in conditions of blood loss is pointed out, and an explanation of the marked arterial constriction of secondary wound shock is afforded.

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(2) McDowall. Ibid. 58. Proc. Physiol. Soc. viii. 1923.
(3) —— Ibid. 57. p. 146. 1923.
(4) Dale and Laidlaw. Ibid. 52. p. 335. 1918.