III. "The Innervation of the Pulmonary Vessels." By J. Rose Bradford, M.B., D.Sc., George Henry Lewes Student, and H. Percy Dean, M.B., B.S., B.Sc. Communicated by E. A. Schäfer, F.R.S. (from the Physiological Laboratory of University College, London). Received February 13, 1889.

Although hitherto most physiologists have considered that the pulmonary vessels probably possessed a system of vaso-motor nerves, yet no direct experimental proof of the existence of such a system has been obtained. Still less has any evidence been adduced to demonstrate the actual anatomical paths by which such nerves, if they exist, reach the lungs. Hence it seemed that the whole question was one deserving a further attempt for its solution. When this research was commenced, there were practically only two facts which could be appealed to in support of the existence of these nerves.

Firstly, Lichtheim observed that in asphyxia a rise of blood-pressure may occur in the pulmonary artery unaccompanied by any rise in the aorta.

Secondly, it has been shown that in the frog, irritation of the skin causes a contraction of the pulmonary vessels.

It is clear that this second fact could not be used as an argument in support of the existence of these nerves in the mammal, since the anatomical relations are so different in the two cases.

With regard to Lichtheim's observation, it is evident that it affords no very direct proof, since other conditions, such as venous distension, might easily account for the rise of pulmonary pressure.

It was felt by us that the only really reliable method would be to excite one by one the roots of the spinal nerves, and to observe the effects of such stimulation on the aortic and pulmonary blood-pressures simultaneously.

The following method was employed:—A cannula, placed in the carotid artery in the usual manner, was connected with a mercurial manometer. In a similar manner a second mercurial manometer was then connected with the branch of the left division of the pulmonary artery distributed to the lower lobe of the left lung. This vessel was reached from the back by resecting portions of two or sometimes three ribs. In this way a record of the pressure in the left division of the main artery was obtained, and also a means of detecting changes of pressure in the main artery. At the same time, the minimum amount of lung tissue was thrown out of gear.

The upper dorsal nerves were then exposed inside the spinal canal, and were ligatured outside the dura mater. By cutting through the

nerves between the spinal cord and the ligature, the peripheral ends could be easily arranged for excitation.

In this way the fibres of both anterior and posterior roots are excited, but, as previously shown by one of us, no efferent vaso-motor fibres can be demonstrated to exist in the posterior roots. Hence for our purposes this mode of excitation is practically equivalent to exciting the anterior roots alone, and inasmuch as a comparatively long stretch of tough nerve can be obtained, the danger of the exciting current spreading to the spinal cord, and so producing reflex effects, is avoided. The nerves were excited on the right side, on the same side as the uninjured lung.

The two blood-pressure curves were recorded simultaneously on the same blackened surface, together with a time tracing and a lever marking the duration of the excitation.

The anæsthetics used were chloroform and morphia, and after the nerves had been prepared, a small dose of curare was injected, and artificial respiration maintained before opening the chest to insert the pulmonary cannula.

Before describing the results following excitation of the upper dorsal nerve roots, it will be necessary to describe shortly the relations existing between the systemic and pulmonary blood-pressures, and more especially what effects are produced on the pressure in the pulmonary artery by sudden alterations of the blood-pressure in the systemic vessels. It is necessary to do this, as otherwise in many cases it might be urged that the effects of a given nerve excitation on the pulmonary pressure were simply due to the reaction of the pulmonary vessels to the accompanying carotid rise. In some cases this objection has no force whatever, since there is no carotid rise or there may even be a carotid fall. In other cases, *e.g.*, in stimulation of the fifth dorsal nerve, there is often a rise of blood-pressure in both vessels, and so we see how important it is to get a clear notion as to what effect a given rise of arterial tension has on the pulmonary blood-pressure.

Before describing the results we have obtained in this direction, it will be convenient to consider shortly the actual amount of the pulmonary blood-pressure, and the manner in which it is influenced by artificial inflation of the lungs.

The pressure is found to vary between 16 mm. and 20 mm. of mercury in different dogs, these being the animals we have always used in our experiments. The pressure in the main artery is a few millimetres higher than this.

The pulmonary pressure is very constant in its height, not only in the same animal during the course of an experiment, but also in different animals. In this point it contrasts strongly with the aortic pressure, since the latter is very variable in amount after the necessary

operative procedure described above. The aortic pressure must fall very low indeed for the pulmonary pressure to be appreciably diminished in amount. The following is an instance bearing out the truth of this statement.

Section of spinal cord at level of seventh dorsal nerve caused the aortic pressure to fall from 106 mm. Hg to 52 mm. Hg. The pulmonary pressure fell from 16 mm. to 14 mm. Hg. Thus, while the aortic pressure fell to half its previous height, the pulmonary pressure only diminished by one-eighth of its previous amount.

Artificial inflation of the lungs causes a rise of pressure in both systems followed by a fall during the subsequent expulsion of the injected air. The pulmonary rise is more sudden and marked in character than the aortic rise, but the rise and fall of pressure in the two vessels are, as far as can be determined, quite synchronous.

The effect of artificial inflations is the same, whether the vagi are intact or whether they have been previously divided.

We will now turn our attention to the effects produced on the pulmonary blood-pressure by a sudden increase in the aortic pressure. It is evident that this rise of pressure in the systemic circulation must be produced in such a way as to avoid stimulating, if possible, the vaso-motor centre reflexly, although, as we shall see later on, the results obtained by reflex excitation are also valuable in deciding this question.

Three methods have been used by us to produce a large rise of blood-pressure in the systemic circulation, and so to determine the passive effect of this rise on the pulmonary circulation. They are as follows :—

I. The excitation of the peripheral end of a divided splanchnic.

II. The excitation of the lower end of the spinal cord divided in the middle of the dorsal region, and care being taken that no spreading of the current to the central end occurs.

III. Compression of the thoracic aorta.

I. *Results obtained by Excitation of the Peripheral End of a divided Splanchnic.*

The rise of systemic blood-pressure is of course considerable, in many cases it is doubled. The rise of pressure in the pulmonary artery is not, however, very marked. Thus in one case an excitation lasting 48 seconds produced a rise of aortic pressure amounting to 54 mm. Hg. The accompanying rise of pulmonary pressure was only 3 mm. Hg.

The aortic pressure was rather more than doubled, having risen from 50 mm. Hg to 104 mm. Hg, on the other hand, the pulmonary rise was from 13 mm. Hg to 16 mm. Hg, the mean rise being, however, 2·5 mm. Hg.

These results are curiously similar to those mentioned above, where

a fall of aortic pressure from 105 mm. to 52 mm. Hg was accompanied by a pulmonary fall of only 2 mm. Hg.

Thus in two different animals sensibly the same effects were produced in the pulmonary pressure in opposite directions by practically equal changes of pressure in opposite directions produced in the aortic pressure.

II. *Results obtained by Excitation of the divided Spinal Cord.*

Excitation of the lower end of the divided cord produces an enormous rise of general blood-pressure, but the accompanying rise of pulmonary pressure is not only always small but it is frequently absent.

Thus in one case stimulation for 38 seconds caused a rise of general blood-pressure amounting to 180 mm. Hg, and the simultaneous pulmonary rise was 6 mm. Hg. This is an extreme case. In many instances the pulmonary rise was less than this, even when the aortic rise was quite as marked. In this case the aortic pressure rose from 52 mm. Hg to 232 mm. Hg, and the pulmonary pressure from 20 mm. Hg to 26 mm. Hg, thus although the aortic pressure was quadrupled, the pulmonary pressure was only raised by less than one-third of its previous amount.

III. *Results obtained by Compression of Thoracic Aorta.*

When this vessel is compressed about the middle of the dorsal region by the finger introduced through the wound, the aortic pressure measured in the carotid undergoes a great and sudden rise, followed on removing the finger by a transitory fall. If the compression be maintained for only a short time, *e.g.*, 10 seconds, then there is no rise of pulmonary pressure, although, of course, the aortic pressure will have been greatly augmented, in this case from 104 mm. to 169 mm. Hg, a rise of 65 mm. Hg.

If, however, the compression be maintained longer, then the pulmonary pressure rises as we see from the following experiment:—The aorta was compressed for 30 seconds, and the aortic pressure rose from 71 mm. to 128 mm. Hg, and that in the pulmonary artery from 19 mm. to 22 mm. Hg.

In all three of the preceding series of experiments the pulmonary rise is very small when compared with the enormous effects produced in the aortic pressure. In all these cases the pulmonary rise was roughly one-twentieth of the simultaneous rise in the systemic circulation. Not only is the rise of pulmonary pressure small when compared to the aortic rise, but the actual pulmonary rise is but a small fraction of the total pulmonary pressure. Thus, although some of the above methods may double or even quadruple the aortic pressure,

yet none of them causes anything like a doubling of the pulmonary pressure.

In other words, when a great aortic rise has succeeded in producing a pulmonary rise, the latter is not only small relatively to the aortic rise but also relatively to the pulmonary pressure itself. We may conclude that not only must a great rise of aortic pressure occur in order to produce any appreciable rise of pulmonary pressure, but also that this rise must be of some duration.

The further discussion of the mode in which a rise of aortic pressure produces a rise of pulmonary pressure will be entered into at the close of this communication. Having thus described shortly what may be called the mechanical effects of rises of aortic pressure on the pulmonary circulation, we will now consider the results of reflex excitation of such nerves as the *sciatic* and *vagus*.

Results of Excitation of the Central End of the divided Sciatic.

It is well known that the rises of aortic pressure produced by the excitation of this and other afferent nerves are frequently very considerable. This is especially the case with the sciatic nerve.

In one case the stimulation of the central end of this nerve gave an aortic rise of 36 mm. Hg, and the accompanying pulmonary rise was only 2 mm. Hg, *i.e.*, one-eighteenth of the aortic rise, that is to say, nearly the same ratio as that obtained in the previous experiments described above in the passive reaction of the pulmonary vessels to rises of general arterial tension. In another instance, with an aortic rise of 30 mm. Hg, there was no simultaneous pulmonary rise.

Results following Excitation of the Central End of divided Vagus.

With this nerve somewhat different results are obtained.

Thus, in one case, the aortic rise was 32 mm. Hg and the pulmonary rise 4 mm. Hg, *i.e.*, the relative ratio of the two effects being one-eighth. This result was obtained in the same animal that previously gave with the sciatic a ratio of one-eighteenth. In the case of the vagus the pulmonary rise was double that observed with the sciatic, although the aortic rises were almost the same in the two cases, *i.e.*, 36 mm. and 32 mm. Hg. It is clear then that, although in this animal the vagus and sciatic gave on stimulation practically equal effects in the systemic vessels, yet the results on the pulmonary vessels were by no means the same in the two cases. Hence the only conclusion is that excitation of the central end of the divided vagus caused a reflex contraction of the pulmonary vessels and thus caused a heightened pulmonary tension.

In the cat frequently and in the dog occasionally the stimulation of the central end of the vagus causes a fall of blood-pressure instead of a rise, in many cases the fall of aortic pressure is considerable. Thus

in one experiment the central end of left vagus was excited for 28 seconds and the aortic pressure fell from 112 mm. to 66 mm. Hg, *i.e.*, a fall of 56 mm. Hg. The pulmonary pressure fell from 17 mm. to 14 mm. Hg, *i.e.*, a fall of 3 mm. Hg.

This pulmonary fall is rather greater in amount than that previously described as occurring after section of the cord in the dorsal region, but it is not too large to be explained on the grounds of a passive effect owing to the large aortic fall.

It is, however, with stimulation of the posterior surface of the spinal cord that the greatest relative effects are seen. When this mode of excitation is used the rise of pulmonary pressure is frequently as much as one-tenth of the simultaneous aortic rise, *i.e.*, the ratio is higher than with any of the previous methods of experimentation.

No doubt part of this effect may be due to the direct excitation of the pulmonary vaso-motor fibres, as will be shown below. Probably, however, the result is mostly due to reflex effects dependent on the cord stimulation, and this is confirmed by the fact that excitation of the central end of a divided posterior root of the upper nerves will cause a great relative rise of pulmonary pressure.

On the other hand, the excitation of the central end of a divided intercostal nerve causes but slight effects both on the pulmonary and on the aortic blood-pressures. Occasionally the central end of an intercostal produces depressive effects similar to those just described for the vagus.

Having thus determined the relation existing between a given rise of aortic pressure and the coincident passive pulmonary rise, and also the effects resulting from reflex excitation of the cord, vagus and sciatic, we will now pass on to the question of the existence and paths of the vaso-motor fibres.

If the upper part of the medulla oblongata be excited it will, of course, be found that a large rise of aortic and pulmonary pressure will be observed. If, now, the spinal cord be divided at about the level of the 7th dorsal nerve and its lower end excited, then just as great or perhaps greater rise of aortic pressure will be observed, but the pulmonary rise will be either very small indeed or else entirely absent.

If the upper part of the medulla be now again excited, the rise of aortic pressure is small owing to the section of the cord, but the pulmonary rise is as great as before. With stronger excitation this rise of pulmonary pressure becomes greater whilst the accompanying aortic rise is still comparatively small. Thus, in one case, the excitation of the lower end of the divided cord caused an aortic rise of 150 mm. Hg. The accompanying pulmonary rise was less than 2 mm. Hg. On now exciting the medulla in the same animal the aortic pressure rose 55 mm. only, owing to section of the cord, but the pulmonary pressure

rose from 16 mm. to 22 mm. Hg, *i.e.*, 6 mm. Thus in the latter case the aortic rise was one-third of what it was in the previous experiment, but the pulmonary rise was three times as great.

This experiment then clearly demonstrates that the pulmonary pressure is not dependent on the aortic rise, since the latter can be obtained without the former, and a pulmonary rise, very considerable in amount, can be obtained when the aortic rise is either small or large.

Hence this result points strongly to the conclusion that the vaso-motor centre can influence the pulmonary vessels directly. In the light of Gaskell's work on the sympathetic, we naturally turn to the roots of the upper dorsal nerves, and we are enabled to map out the paths by which these vaso-motor nerves reach the lung.

When the peripheral end of such a nerve as the 6th or 7th dorsal is excited a rise of pressure in both the pulmonary and aortic system is observed. The pulmonary rise, although considerable, *e.g.*, 3 or 4 mm. Hg, is not out of proportion to the aortic rise which, with these nerves, may be as much as 30 or 40 mm. Hg. On ascending, however, very different results are obtained. Thus in one case the 5th dorsal gave an aortic rise of 10 mm. Hg only, but the pulmonary rise was 3 mm. Hg. Clearly the latter was not a passive effect of the former. In another case the 4th dorsal gave an aortic rise of 20 mm. Hg, and a pulmonary rise of 4 mm. Hg.

Perhaps, however, the most marked and conclusive result is seen with the 3rd dorsal nerve. This nerve frequently causes no aortic rise, and, indeed, sometimes actually a fall, *e.g.*, 10 mm. Hg, but in both these cases there is a distinct pulmonary rise of 3 or 4 mm. Hg. We sometimes get such a fall in the aortic pressure accompanied by a pulmonary rise with the 4th nerve and twice we have seen it with the 5th nerve.

As a rule these effects cannot be obtained when the accelerators produce marked effects, and hence no very definite results have been obtained from stimulation of the 2nd dorsal nerve. Often, however, the heart is already beating rapidly, so that irritation of the accelerator nerves causes no further increase in rate, and it is under these circumstances that the pulmonary vaso-motor fibres can be most easily demonstrated. Thus, as we pass from the 7th to the 2nd nerve, the effect of their excitation on the aortic pressure diminishes as we pass from below upwards, and the upper nerves may even cause a fall of pressure in systemic circulation. On the other hand, the effect on the pulmonary pressure seems to increase as we pass from below upwards. Hence we may conclude that the vaso-constrictor fibres for the lungs leave the spinal cord in the roots of the dorsal nerves from the 2nd to the 7th.

An attempt was made to separate the pulmonary nerves from the

cardiac nerves in the branches of the ganglion stellatum and in the annulus Vieussenii. As yet, however, we have not been able to separate the pulmonary vaso-motor fibres from the accelerator fibres.

The objection will of course be made that the effects are slight, and no doubt they are, but when we consider that enormous changes in the aortic pressure produce such extremely slight effects, it is clear that, small as these effects are, they conclusively show that they are dependent on the contraction of the pulmonary vessels, and not on any passive effect from the slight rises in the aortic pressure.

There seems no doubt that the vaso-constrictor mechanism of the lungs is not very highly developed. It is impossible to get anything like a doubling of pulmonary blood-pressure by any kind of nerve excitation, although the systemic blood-pressure can easily be doubled or even quadrupled. The amount of possible contraction of the pulmonary arterioles is probably not nearly so great as that of the systemic vessels, and this view is confirmed by the results of asphyxia on the pulmonary circulation.

Results of Asphyxia on the Pulmonary Circulation.

In asphyxia both the aortic and the pulmonary blood-pressures undergo a considerable rise, but the rise of pressure in the pulmonary vessels lasts longer than that in the systemic, so that when the aortic pressure is falling rapidly, the pulmonary may be at its highest point.

The rise of pressure occurs synchronously in the two sets of vessels, and the general course of the two curves is the same, except that the pulmonary rise is more gradual than the aortic rise. As a rule, the sudden and great elevations seen on the aortic blood-pressure curve are not well seen on the pulmonary trace, but notwithstanding this, the maximum rise of the pulmonary pressure may be very considerable, *e.g.*, it may be doubled.

If, however, so large an effect as this is seen, the aortic pressure will have undergone a very much greater relative rise, *i.e.*, it will have been quadrupled.

The Traube curves, so well marked on the aortic blood-pressure tracing, are but faintly marked in the case of the pulmonary artery, and hence it is difficult to say whether the effects are direct or due simply to passive reaction from the systemic circulation. It is probable, however, that they are direct.

The curious maintenance of the pulmonary pressure at such a height as death approaches, when the aortic pressure has fallen perhaps to half its previous height, is probably due to venous distension as much as to the increased peripheral resistance, but this is a point we wish to investigate further.

Conclusions.

The pulmonary vessels of the dog are supplied with vaso-motor fibres leading the cord through the roots of the uppermost dorsal nerves. No efferent vaso-motor fibres have been detected in the vagus nerve.

The pulmonary circulation is comparatively independent of the systemic, and alterations in the blood-pressure of the latter must be of large amount to affect the pulmonary blood-pressure. It is probable that no rise of aortic pressure can materially influence the pulmonary blood-pressure, unless it is so great in amount or duration that the heart muscle and valves are unable to cope with it, and so an actual regurgitation is produced.

It is possible that the pulmonary blood-pressure can also be affected by rises of systemic pressure causing venous distension, and hence an increased supply to the right side of the heart.

Finally, although it is undoubted from the results of this research that the mammalian pulmonary vessels receive vaso-motor nerves, yet it is probable that the vaso-motor mechanism is but poorly developed as compared with that regulating the systemic arteries.

In this respect it may be that the pulmonary system holds an intermediate position between the systemic arteries on the one hand and the veins on the other.

This question we hope to elucidate by a further research. We also hope that, shortly, we shall be able to give the results of our researches on the vaso-dilator nerves of the lungs.

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Transactions.

Adelaide:—Royal Society of South Australia. Transactions and Proceedings. Vol. X (1886–7). 8vo. *Adelaide* 1888.
The Society.

Albany:—New York State Museum of Natural History. Bulletin. Nos. 4–6. 8vo. *Albany* 1888; Report, 1887. 8vo. *Albany* 1888.
The Museum.

Baltimore:—Johns Hopkins University. Circulars [Various numbers to meet deficiencies]. 4to. 1879–88; Studies (Historical and Political Science). Seventh Series. Nos. 1–3. 8vo. *Baltimore* 1889. The University.

Belgrade:—Royal Servian Academy. Bulletin. Nos. 1–9. 8vo. *Beograd* 1888; Annual. 1887. 8vo. *Beograd* 1888; Obituary of J. Pančić. 8vo. *Beograd* 1888. [In the Servian language.]
The Academy.

Bergen:—Museum. Aarsberetning. 1887. 8vo. *Bergen* 1888.
The Museum.