The vaso-dilators differ from the constrictors physiologically in several ways. When stimulated, the latent period seems somewhat longer, the effect reaches a maximum more slowly and it persists much longer. Their irritability is also of a different kind, disappearing more slowly after section of the nerve or on cooling and making them more sensitive to weak, slowly repeated stimuli. These differences furnished the means of tracing these nerves even in the mixed trunks and of determining their anatomical paths. Some of them appear to run much the same course as the vaso-constrictors. Such are the vaso-dilator fibres running in spinal nerves like the sciatic and brachial, those which seem to be present in the splanchnics, and certain fibres of the cervical sympathetic which act as dilators to parts of the mouth and face. All of these issue from the cord in the anterior roots of the lower cervical, thoracic, and upper lumbar spinal nerves and pass in their course outward through the sympathetic system in essentially the same way as the constrictor fibres.

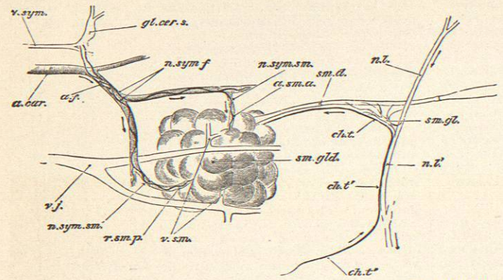

FIG. 1356.—Diagrammatic Representation of the Submaxillary Gland of the Dog with Its Nerve and Blood-Vessels. *sm.gld.*, The submaxillary gland, into the duct (*sm.d.*) of which a cannula has been tied. The sublingual gland and duct are not shown. *n.l.*, *n.l'*, the lingual branch of the fifth nerve, the part *n.l.* is going to the tongue; *ch.t.*, *ch.t'*, *ch.t''*, the chorda tympani. The part *ch.t'* is proceeding from the facial nerve; at *ch.t'* it becomes conjoined with the lingual *n.l'* and afterward diverging passes as *ch.t.* to the gland along the duct. The continuation of the nerve in company with the lingual *n.l.* is not shown. *sm.gl.*, the submaxillary ganglion with its several roots; *a.car.*, the carotid artery, two small branches of which, *a.sm.a.* and *v.sm.p.*, pass to the anterior and posterior parts of the gland; *v.s.m.*, the anterior and posterior veins from the gland, falling into *v.j.*, the jugular vein; *v.sym.*, the conjoined vagus and sympathetic trunks; *gl.cer.s.*, the upper cervical ganglion, two branches of which, forming a plexus (*a.f.*) over the facial artery, are distributed (*n.sym.m.*) along the two glandular arteries to the anterior and posterior portions of the gland.

The more distinct and notable vaso-dilators, however, do run a different course. These are found in the nerves coming from the cranial and sacral regions of the central nervous system whence no vaso-constrictor fibres are known to issue. Thus the vaso-dilator fibres for the submaxillary may be traced back through the chorda tympani to the facial or seventh cranial nerve (see Fig. 1356). By the same path vaso-dilator fibres are supplied to part of the tongue also. Of the remaining cranial nerves the glosso-pharyngeal contains vaso-dilator fibres for the parotid gland, the trigeminal for the eye and part of the face (although the latter also receives dilator fibres for the lips, etc., from the second to fifth thoracic nerves through the cervical sympathetic), and the vagus for the coronary arteries of the heart. The vaso-dilator fibres which pass into the nervi erigentes leave the sacral region of the cord by the anterior roots of the sacral nerves and reach the penis by way of the hypogastric plexus. In these instances the vaso-dilator fibres, as they leave the central nervous system, are like the vaso-constrictor fibres, fine, medullated nerves; but unlike the majority, at least, of the vaso-constrictors, they retain their medulla for the greater part of their course and lose it only near their termination in the tissue whose blood-vessels they supply. It should be mentioned also as a curious and remarkable anomaly that some of the vaso-dilator fibres leave the spinal cord in a number of the posterior roots. First discovered in the lumbar region (Stricker, Morat), they have been recently shown[23] to occur in the posterior roots of the fourth, fifth, sixth, and seventh lumbar and first sacral nerves for the posterior extremity, and also in the roots of the cervical and brachial plexuses, especially the seventh cervical and first thoracic, for the anterior extremity.

Veno-Motor Nerves.—The statements made thus far concerning vaso-motor nerves apply entirely to the arterial portion of the vascular system. Now the veins are also provided with muscular fibres and contain plexuses of nerve fibres in their walls. It has, moreover, been known for a long time that they contract in response to various stimuli, and that in certain localities, as in the wing of the bat, rhythmical contractions are displayed. It has only recently been shown physiologically that the veins are supplied with vaso-motor nerves, and the instances on record are still too few to justify any general statements. In 1892 Mall demonstrated the vaso-constrictor fibres to the portal vein in the splanchnic nerve, and showed that through their stimulation as much as twenty-seven per cent. of the total blood could be displaced from the splanchnic area and driven forward to the right heart. Since that time, similar fibres have been traced for the veins of the hind limb,[24] and their general course and arrangement found to correspond to that of the arterial vaso-motor fibres to that limb. In this connection it may be interesting to refer to the observations of Bert and Laffont in 1882 and the more recent work of Camus and Gley,[25] according to which the receptaculum chyli and thoracic duct both receive dilator and constrictor fibres through the thoracic sympathetic chain and splanchnic nerves. It seems plausible to conjecture that the distribution of these two kinds of fibres may be general to all parts of the vascular system.

As to the mechanism through which the vaso-motor nerves influence the calibre of the vessels, little can be said. The constrictor fibres represent the motor fibres, whose impulses increase the tone or degree of contraction of the involuntary muscle tissue in the coats of the vessels, while the removal of constrictor influences previously exerted is followed by a passive dilatation under the influence of the blood pressure from within. Whether the

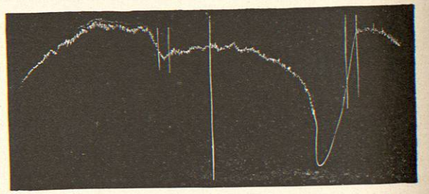

FIG. 1357.—Plethysmograms (Hind Limb of Cat). To be read from right to left. On the left hand is shown the effect of slow stimulation of the sciatic (1 per second); on the right hand the effect of rapid stimulation (64 per second).

influence of these fibres is a direct one on the muscle cells themselves, or whether a peripheral ganglionic mechanism is interposed, must be left undecided as in the case of the cardiac nerves.

The dilator nerves are usually compared to the inhibitory fibres of the heart and the dilatation which they produce is considered a passive one. It has been maintained, however, that they cause an active dilatation of the vessels which is independent of the pressure within, and in support of this view there are on record some interesting observations on the frog's tongue by Frey (1876), which have been recently repeated and perfected by Siawcillo.[26] According to these observers an active expansion of the smallest arteries and capillaries made sufficient suction to start a current in the vessels after the blood had come to absolute rest under a uniform zero pressure. An active elongation of the muscle cells and of the capillary endothelium in response to the nerve stimulus alone could account for such an active dilatation, and if proven this would be the first instance of the kind on record.

Vaso-Motor Centres.—The vaso-dilator nerves, whose use is simplified by the absence of habitual tonic influences, occur in connection with organs used chiefly at least as parts of reflex mechanisms, and arise from centres placed in different regions of the central nervous system. Thus the reflex centre for the fibres descending in the chorda tympani lies in the medulla oblongata, while the centre of origin of the fibres in the nervi erigentes is placed in the lower part of the cord; and in general the centre may be said to lie in the central nervous system, not far from the superficial origin of the nerves in which the vaso-dilator fibres run. Nothing more definite can be said, although it is possible that a chief centre for these nerves may exist in the medulla, where the centres for so many vegetative functions are concentrated.

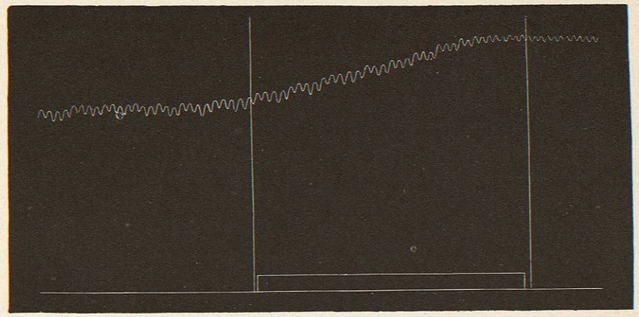

FIG. 1358.—Blood-Pressure Record during Electrical Stimulation of the Depressor Nerve. To be read from right to left. The time of stimulation is indicated by the vertical lines (⎓ = 10 seconds).

The vaso-constrictor nerves are distinctly under the control of a general centre situated in the medulla, occupying a region which extends from a point 4 to 5 mm. above the point of the calamus scriptorius to within 1 to 2 mm. of the corpora quadrigemina. This centre is in continued tonic activity, so that section of the cord below the medulla results in a general loss of tone throughout the vascular system and a great fall of blood pressure. The existence of one presiding centre confers upon the constrictor mechanism the power of producing general effects, and its utility is further increased by reason of its tonic activity, since the same fibres may by an increase in the impulses passing along them be the means of constriction and by the removal or diminution of the tonic influence be the means of dilatation. When an animal whose cord has been divided in the thoracic region is kept in good condition, the arteries of the hind limbs and hinder part of the body which became dilated at the time of the section after a while re-establish a normal or nearly normal tone. This and the fact that they undergo reflex changes of calibre indicate that there are other centres for the vaso-constrictor nerves scattered along the spinal cord. These centres seem to be less irritable than the medullary centre under whose control they normally stand, but their great power of endurance would indicate that they may play an important rôle in maintaining a normal vascular tone. Finally, experiment has shown that the vessels may slowly recover their tone after extirpation of a very large part of the spinal cord. They are at first completely paralyzed and maximally distended; gradually, however, their tone returns and they begin to react to local applications of heat or cold much as they do under normal conditions. It follows that the vessel walls themselves possess the power of exhibiting independent tonic contractility, or else this recovery indicates the existence of vaso-motor centres of a third order in the peripheral ganglia distributed along the course of the nerve trunks. Such a tone of peripheral origin would explain the additional dilatation observed on stimulating vaso-dilator nerves to parts whose vaso-constrictor nerves had previously been divided. From what has been said it follows that the simplest efferent path along which vaso-motor impulses can pass may be considered as built up of two neurones, one with its cell body in the central nervous system and the other in a sympathetic ganglion. Since, however, the spinal vaso-motor centres are under the control of the chief centre in the medulla, the axis-cylinder processes of the cells of the bulbar centre must come into relation with the spinal vaso-motor cells, and so the complete efferent path comes to include three nerve units.

Vaso-Motor Reflexes.—The activity of the centres in the medulla and cord from which the vaso-constrictor and vaso-dilator fibres take their origin is determined in large measure by the impulses falling into them along various afferent nerve channels giving rise to reflex vaso-motion.

The possible afferent paths include practically every centripetal nerve in the body, those distributed to the vessel walls not excepted; while the response may vary from a slight local effect in the region whence the afferent impulse started to a change involving an extensive vascular area sufficient to produce variations in the general blood pressure.

The local reflexes, such as the congestion of the skin on the application of warmth, are commonly dilatations, although constrictions also occasionally result. Of the general reflexes those occurring in the great splanchnic area are perhaps the most frequent, sensory stimulation causing constriction there with special ease. Stimulation of sensory nerves may, however, cause reflex dilatation in the splanchnic region, while in the vessels of the skeletal muscles this is the rule. In them the reaction affects first the muscles which stand in a more or less intimate functional relation with the stimulated nerve, but it may become general and so become an efficient means of bringing on a general fall of blood pressure. It is apparent that the effect on the blood pressure of stimulating a sensory nerve will depend on the relative extent of the antagonistic changes, both of which are usually present, and the

question as to the conditions which determine the preponderance of vaso-dilatation in one case and of vaso-constriction in another is one of unusual interest.

We know at present but one nerve, the so-called depressor nerve of Cyon, which with all degrees of stimulation regularly brings on a fall of blood pressure. This is the sensory nerve of the heart which has already been referred to as causing reflex inhibition of the heart. The effect on blood pressure is not dependent on this heart action, as it still occurs after section of both vagi, but is due to an extensive vaso-dilatation in which the splanchnic area has a prominent share, although the vessels of other parts of the body also participate. The dilatation appears to be due to an inhibition or depression of the tonic activity of the vaso-constrictor centre, since the effect is diminished or abolished by agencies which reduce or destroy the irritability of this centre, and hence the name of "depressor" for this nerve. Since sensory nerves in general produce both kinds of effects, "pressor" and "depressor," the interesting discussion has arisen as to whether they contain two distinct varieties of nerve fibres or whether the different results depend entirely on the condition of the centres and the character of the stimuli used. That both of the latter factors may influence the result can be easily shown. A sensory nerve like the sciatic, whose stimulation regularly produces vaso-constriction and rise of blood pressure in an animal under curare, will frequently give a fall of pressure when chloral or ether is used for the anæsthetic. Again, mechanical stimulation of the sensory nerves in muscles by kneading or massage regularly causes reflex vaso-dilatation, while electrical stimulation of the same nerves gives reflex constriction.

On the other hand there is strong evidence for the view that there are both "pressor" and "depressor" or "reflex vaso-dilator" fibres in the sciatic and similar nerves.[27] The pressor fibres ordinarily have the upper hand, but by subjecting the nerve to the action of cold or stimulating the nerve at a certain stage of regeneration after section, the depressor effect may be obtained. The depressor fibres seem to retain their power of conduction longer than do the pressor fibres when cooled, and when the nerve is cut and sutured they regenerate earlier. There is also a certain amount of evidence to indicate that the fall of pressure from stimulation of the sciatic and similar nerves is of a different nature from that resulting from stimulation of the depressor nerve of the heart. In the former case the dilatation occurs largely in the limbs and is probably due to a reflex stimulation of dilator fibres, so that the name "reflex vaso-dilators" has been suggested

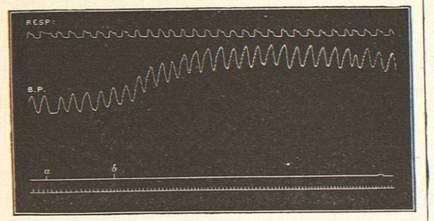

FIG. 1359.—Pressor Effect Produced by Stimulating the Central End of the Sciatic of a Curarized Cat Under Morphine. Time tracing in seconds. Reduced one-half.

for this class of fibres to distinguish them from the "depressor" fibres proper which act by inhibiting the vaso-constrictor centre.

The complicated nervous mechanisms thus associated with the circulatory apparatus enable the nervous system, directed by the afferent impulses which reach it along various channels, to coordinate the action of the heart and vessels and to direct the blood flow according to the needs of the body. The blood supply of the organs is continually shifting according to their varying activity; but dilatation and increased blood flow to the active organs is met by compensatory constriction elsewhere, thus preventing a wasteful use of cardiac energy which would otherwise be required to keep up the general blood pressure. This reciprocal relation is particularly conspicuous between the blood-vessels of the somatic and those of the splanchnic divisions of the body, thereby providing the chief means by which the blood pressure is regulated and by which the maintenance of a normal body temperature is in large measure secured.

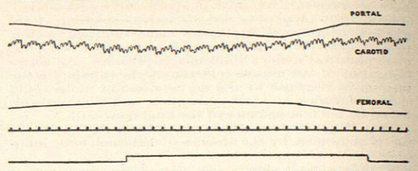

FIG. 1360.—Dog. Ether. Vagi intact. Fall of pressure in carotid and portal vein, and rise in femoral vein on stimulation of sciatic at 10ª. All the curves have the same base line; the curves of venous pressure being drawn to indicate the pressure in millimetres Na_2CO_3, the curve of arterial pressure in millimetres Hg. The changes of pressure in the curves must be multiplied by two to obtain the absolute changes. Tracing from right to left.

George P. Dreyer.

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CIRCULATION, PATHOLOGY OF.—The state of the circulation is dependent upon the work of the heart, the condition of the blood-vessels, and the amount and character of the blood. Through the rhythmical contractions

of the auricles and ventricles the blood is kept in motion within the vessels, where it flows under a certain pressure which is dependent upon the elasticity of the vessel walls and the amount of peripheral resistance. This pressure is relatively high throughout the systemic arterial circulation, but is low in the veins. The venous pressure, however, varies with the location of the vein, being greatest where the vessel supports a high column of blood. In the great veins of the thorax the pressure is very slight, or negative during inspiration when the negative pressure within the thorax causes an aspiration of the blood from the veins outside of the thoracic cavity. In forced expiration the pressure within both thoracic and systemic veins is increased. The factors directly controlling the blood pressure are: the mass of blood, the work of the heart, and the resistance of the blood-vessels. The latter factor is chiefly dependent upon the degree of tension exerted by the elastic contractile vessel walls. In the systemic circulation the tension is normally much greater than that in the pulmonary vessels; the pressure in the pulmonary artery being only about one-third of that in the aorta. The work of the heart is governed by the condition of its muscle and ganglia, and of the nerves and centres regulating its action. The blood-vessels are also under nervous control, and the circulatory conditions are influenced to a large extent by this innervation as well as by changes in the walls themselves. Every lesion of the heart or blood-vessels, as well as any disturbance of the nervous mechanism controlling the blood flow, will be followed by pathological disturbances in the circulation in case such lesions are not compensated by increased work of other parts of the circulatory apparatus. Further, the tone of the heart muscle and blood-vessels as well as that of the ganglia and nerve centres is directly affected by pathological changes in the amount or composition of the blood; therefore the pathological states of the circulation arise as the result of those pathological changes which lead either to disturbances of heart or blood-vessel function or to an altered state of the blood. These may be considered in the following order:

Increase of Heart's Action.—An increase in the rate of the heart's contractions without decrease in force causes an increased velocity of the blood flow with rise of arterial pressure. The force of each beat may or may not be increased at the same time, or it may be strengthened without change in the rate. The effect upon the circulation is the same at first in both cases. As a result of increased muscular activity the heart undergoes a compensatory hypertrophy in case its nutrition is properly kept up. When both rate and force are increased the compensatory reserve of the heart muscle is sooner exhausted, as the short diastoles lead to fatigue, the products of waste are not thoroughly removed, and the nutrition of the muscle suffers. As a result fatty degeneration may take place, and with this a failure of compensation. As long as the nutrition of the muscle is kept up to meet the increased demand compensation will be maintained. The left ventricle is the first to become hypertrophic, but as the right ventricle receives a larger amount of blood during diastole because of the quickening of the blood current its muscle has also an increased amount of work to perform and likewise becomes enlarged. The increased work of the heart may be caused by excessive bodily labor, over-exercise ("athletic heart"), high living, abnormal irritability of the cardiac nerves ("smoker's heart," "sexual heart,"), etc. Obstruction to the outflow of blood from the heart or in the aorta, abnormal positions of spine or thorax, chronic nephritis, etc., may also be accompanied by increase in rate and strength of the heart's action. In all of these conditions when compensation is fully maintained the pulse is full, quick, and of high tension. The heart sounds are increased in force, especially the aortic second sound. The first sound at the apex is frequently accompanied by a soft blowing murmur even when compensation appears to be perfect.

Impairment of Heart's Action.—The efficiency of the work of the heart may be impaired by pathological changes in the heart muscle: anæmic infarction, fatty degeneration and infiltration, atrophy, coagulation necrosis, myocarditis, etc. In the acute infectious fevers and in many of the intoxications, trophic disturbances, prolonged over-work, etc., the heart may become inadequate without discoverable anatomical changes. Obstruction of the coronary vessels may lead to heart failure so rapidly that the anatomical changes produced may be too slight to be recognized. Likewise in the acute heart failure resulting from a sudden over-strain no microscopical changes may be found in the heart muscle. Pericardial and pleural adhesions and effusions, deformities of the thorax, thoracic tumors, aneurisms, high position of the diaphragm, etc., may hinder the filling of the heart during diastole, so that the blood becomes dammed back in the venous system while a less amount is supplied to the aorta. Pericardial adhesions may also hinder the amplitude of the systole. Stenosis and insufficiency of the valves of the heart are the most common and important causes of impaired heart's action. In stenosis of any valvular orifice the onward flow of blood is impeded; in insufficiency of the mitral and tricuspid the ventricular systole forces blood back into the auricles, and in pulmonary and aortic insufficiency there is during diastole a backward flow into the ventricles. Valvular vegetations, thrombi either free or situated upon the valves or between the trabeculæ of the heart muscle, may interfere with the free passage of the blood through the heart.

The effects of impairment of cardiac efficiency are in all cases the same: there is a decreased amount of blood supplied to the arteries, and an over-filling of the veins. This leads to a fall in arterial pressure, while the venous pressure rises. As a result of the engorgement of the veins and capillaries, the surface of the body becomes cyanotic, and stagnation œdema may occur. If the difference between arterial and venous pressure reaches a certain minimum, stasis results. When the cause of impaired efficiency is located in the left side of the heart there is first manifested an over-filling of the pulmonary circulation. This leads to increased work on the part of the right ventricle resulting in compensatory hypertrophy. When the cause is located on the right side the blood is dammed back into the systemic veins, while in the aorta and pulmonary circulation there is a fall of pressure and diminished supply of blood. The damming back of the venous blood into the large thoracic veins may cause an exaggeration of the normal venous pulse (negative venous pulse) in these veins, and in case the vessels are so distended that the valves of the jugular bulb become inadequate this pulse may extend beyond the bulb into the veins of the neck and head. It is presystolic in time, occurring synchronously with the auricular systole. If the dilatation of the right side of the heart becomes so great that the tricuspid valves are rendered inadequate, or if an organic insufficiency of these valves is present, a second venous pulsation (positive venous pulse) may be produced. This is systolic in time, being caused by a backward flow of blood through the tricuspid opening during the contraction of the right ventricle. The extreme engorgement of the veins in tricuspid insufficiency may lead to pulsations of the liver, which may become greatly enlarged from the over-filling of the hepatic veins.

In all conditions in which the contractions of the heart become infrequent and weakened, the arterial pulse is slow, soft, and small in volume. Such a pulse wave ("pulsus tardus") is seen in aortic stenosis. In insufficiency of the aorta or pulmonary artery a normal, or, as is usually the case, an increased amount of blood is thrown into the artery during systole, while in diastole a partial regurgitation into the ventricles occurs. This causes a sudden fall of tension in the artery which in aortic insufficiency is manifested in the so-called "water-hammer" pulse ("pulsus celer"). The sudden increase of pressure from the excess of blood thrown into the aorta causes a dilatation of the whole arterial system, and also of the capillaries, which may show marked pulsation. In all forms of valvular lesions that part of the heart which is called upon for increased work undergoes a