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

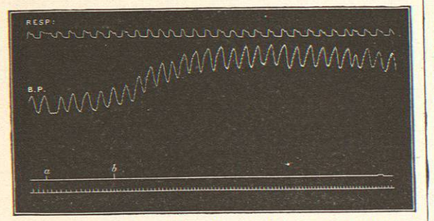

FIG. 1359.—Pressor Effect Produced by Stimulating the Central End of the Sciatic of a Curarized Cat Under Morphine. Time tracing in seconds. Reduced one-half.

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.

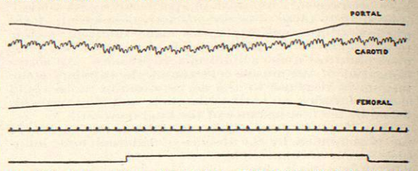

FIG. 1360.—Dog. Ether. Vagi intact. Fall of pressure in carotid and portal vein, and rise in femoral vein on stimulation of sciatic at 10ª. All the curves have the same base line; the curves of venous pressure being drawn to indicate the pressure in millimetres Na_2CO_3, the curve of arterial pressure 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

compensatory hypertrophy if conditions of nutrition are good. In stenosis of the mitral orifice the chief work falls upon the right ventricle, which becomes hypertrophied; in mitral insufficiency there is also hypertrophy of the left ventricle, caused by the increased amount of blood which comes to it from the greater flow sent through the lungs by the right ventricle. In stenosis of the pulmonary and aortic orifices the corresponding ventricle becomes enlarged. Since the auricles have but little power of hypertrophy, lesions of the tricuspid valve are most unfavorable inasmuch as they cannot be compensated. In any form of valvular disease compensation becomes inadequate as soon as the heart is driven to the point of fatigue; that is, as soon as the period of diastole becomes so shortened that the products of tissue metabolism cannot be removed and the building-up of the muscle take place in the proper degree. Besides the alterations in the circulation manifested by the pulse, valvular lesions give rise to marked changes in the sounds of the heart, pathological sounds (murmurs) of varying quality and intensity being produced.

Disturbances of Blood Pressure.—The blood pressure in both the systemic and pulmonary arteries varies within certain physiological limits. Through the influence of many widely differing pathological conditions these limits may be over-stepped, and an abnormal increase or diminution of arterial pressure may result. Increase of pressure in the aorta may be due to an obstruction in the aorta or in the larger arterial branches, or to vascular contraction involving the entire corporeal circulation or vascular areas large enough to affect the entire circulation. Increased aortic resistance may be caused by stenosis of any portion of the vessel, congenital hypoplasia of the entire aorta or of a portion of its course, aortic thrombosis, aneurism, changes in its wall due to arteriosclerosis and inflammation, or to dilatation of its lumen due to loss of elasticity of its walls following sclerotic changes. Contraction of the peripheral arterioles with resulting increase of pressure in the aorta may be caused by an excess of carbonic acid in the blood. In chronic nephritis there is a permanent increase in the general arterial pressure, the cause of which is as yet uncertain. It may be due to the direct action of retained urinary poisons upon the blood-vessel walls, or upon the vaso-motor centres, or to reflex stimulation of the vessels or heart. In whatever way it may be caused, the increase of arterial pressure has been conclusively shown to be due to increased peripheral resistance resulting from the contraction of the smaller arterioles. As a result of this increased resistance the heart undergoes a compensatory hypertrophy. It is possible, however, that the enlargement of the heart, in part at least, may be due to an increased stimulation of the heart itself. Chronic intoxications from various poisons as lead, ergot, etc., likewise lead to increased arterial pressure, which may be due either to the direct effect of the poison upon the vessel wall or nerves or to changes in the kidneys.

Arterial pressure in the systemic circulation may be diminished by severe hemorrhage, relaxation of arterial tone following paralysis of the vaso-motor system, syncope, shock, hysteria, injuries to the cervical cord, etc. When this decrease of pressure occurs, the blood passes too rapidly from the arteries into the veins, the pressure in the two systems tends to become equal, so that when a certain minimum of difference is reached stasis occurs.

Increase of pressure in the pulmonary circulation may be caused by obstruction of a portion of the lung capillaries, inflammatory conditions of the lungs and pleura, atrophy, emphysema, indurations and retractions, pleural adhesions and effusions, thoracic deformities, tumors, aneurisms, etc. When the pulmonary obstruction is but slight, it may be entirely overcome by collateral dilatation; if the obstacle is large enough to cause the pulmonary pressure to rise, compensatory hypertrophy of the right ventricle will follow.

The pulmonary pressure may be decreased as a result of valvular lesions of the right heart, thrombosis, weakness of the muscle of the right heart, etc. A decrease in the negative pressure in the right side of the thorax, caused by pneumothorax, pleural effusions, high position of the diaphragm, etc., hinders the aspiration of blood into the right heart, and causes a general damming back of the venous blood and a deficiency in the pulmonary and arterial systems. If this decrease of negative pressure is very sudden, as in right sided pneumothorax, the blood may flow back out of the right auricle into the veins.

Changes in the tension of the systemic circulation are recognized by the palpation of the radial pulse; those of the pulmonary system by the auscultation of the pulmonary second sound, which varies in strength according to the tension in the pulmonary artery. The clinical value of this sound is so great that it has been called the "pulmonary pulse."

Disturbances of Blood Supply.—The regulation of the amount of blood which an organ or tissue receives under normal conditions is effected by changes in the calibre of the afferent vessels. These changes are primarily dependent upon the elasticity of the vessel wall and the power of contraction possessed by its muscular coats. The latter are controlled by nervous impulses arising from the vessel plexuses or from the vaso-motor centres in the medulla and cord. These impulses may be direct or reflex, and either inhibitory or stimulative in character. As the total amount of blood in the body is not sufficient to fill all of the vessels to their fullest capacity at the same time, it follows that at certain times some of the organs may be richly supplied with blood, while others contain but little. The former condition is designated as hyperæmia, the latter as anæmia. When these conditions become protracted in time or of excessive degree, the hyperæmia or anæmia is to be regarded as pathological.

Hyperæmia.—This may be either active (arterial congestion) or passive (venous congestion). The former depends upon an increase in the arterial supply; the latter is caused by obstruction to the venous outflow.

Arterial congestion may be either collateral or idiopathic. The first plays but a slight rôle pathologically. It is merely the result of a diminished flow to other parts, and is found in the immediate neighborhood of parts whose blood supply has been decreased or entirely shut off, as around an anæmic infarct. An active hyperæmia of the internal organs may be caused by a contraction of the peripheral vessels as in a chill. In carbonic monoxide poisoning more than half of the volume of blood may be gathered in the blood-vessels of the abdominal cavity. Idiopathic active congestion is of much greater pathological importance. It depends upon a dilatation of the vessel, due either to paralysis of the vaso-constrictors, stimulation of the vaso-dilators, direct action upon the muscular coats, or a lessening of the external pressure exerted upon the vessels. Neuro-paralytic congestion may be caused by injury or section of the cervical sympathetic; as in a case of gunshot wound of the right cervical sympathetic, unilateral flushings of the face were caused by slight exertions. The unilateral congestions in migraine and various forms of neuralgias may also belong to this class; likewise the phenomena observed in shock, where paralysis of the splanchnic leads to an extreme active congestion of the abdominal vessels. Many of the local hyperæmias common in hysterical cases may also be explained as being of the nature of neurotic congestions, but between the paralytic form and that due to stimulation of the vaso-dilators no clear line can yet be drawn except in experimental work. Direct weakening of the muscles of the blood-vessel walls may be caused by the action of heat, trauma, disturbances of blood current, action of certain drugs, as atropine, chlorine, ammonia, etc. Active congestion of the abdominal vessels follows the removal of ascitic fluid; likewise, in stenosis of the upper respiratory tract, the decreased pressure in the alveoli of the lungs leads to active dilatation of the pulmonary arterioles and capillaries. Active congestion is manifested clinically by redness, swelling, and increased warmth of the affected area.

The color is that of arterial blood. The clinical picture resembles that of inflammation, in which process active congestion plays a very important rôle.

Passive hyperæmia may be produced throughout the entire systemic venous circulation as the result of imperfect compensation of valvular lesions, impaired efficiency of the cardiac muscle (fatty degeneration and infiltration), obstructions in the pulmonary vessels, decreased negative pressure in the right half of the thorax due to pleuritic exudates, etc. Lesions in the right side of the heart produce a direct damming back of the venous blood; those in the left side cause first a passive congestion of the lungs which, if not compensated by the right ventricle, will extend back through the right heart into the veins of the corporeal circulation.

Local venous hyperæmia may be caused by compression, ligation, direct pressure upon the vein by tumor or pregnant uterus, venous thrombosis, extension of malignant growths into the lumen of the vein, gummata, etc. In cirrhosis of the liver the obliteration of the intrahepatic branches of the portal leads to chronic passive congestion of all the branches making up the portal together with their collaterals (caput medusæ, œsophageal hemorrhoids, etc.). Pressure upon the superior vena cava by mediastinal tumors leads to a dilatation of the superficial veins of the thorax and abdomen from the establishment of a collateral venous circulation through these branches. The flow of blood from the lower extremities may be retarded by lack of proper aid from muscular action, as in the case of varicose veins in individuals who lead sedentary lives or who stand in one position for a great part of the time. This form of congestion is also favored by the anatomical peculiarities of certain veins: the hemorrhoidal, for example, containing no valves, are easily affected by disturbances of the venous circulation through the liver, since the blood from these vessels is obliged to traverse a second set of capillaries in this organ. Hemorrhoids are on this account one of the earliest symptoms of hepatic obstruction. The branches of the left spermatic vein are also predisposed to passive congestion, from the fact that this vessel empties at right angles into the left renal vein.

The obstruction to the flow of blood in any single vein is usually of slight consequence if the vessel has free anastomosis with other veins, but if the collateral circulation is insufficient partial or complete stasis must result which may lead to thrombosis. Frequently the dilatations of the veins behind the point of obstruction may overcome this, and the flow become re-established, or the small anastomosing veins may become stretched until they are adequate to carry on the obstructed circulation. In this way small veins may become changed into vessels of large size. Even after thrombosis the lumen of the vein may be partly restored by contraction of the thrombus and formation of new channels in the tissue resulting from the organization of the thrombus. The contraction of this newly formed tissue also aids in the formation of new blood channels. Direct anastomosis between veins and arteries may also occur.

The clinical signs of passive congestion are most manifest in the extremities, tips of fingers, ears, and nose. When the congestion extends into the capillaries, the tissues acquire a reddish-blue color (cyanosis), become somewhat swollen, inelastic, and warmer to the touch. In thrombosis of either the superior or inferior vena cava the corresponding half of the body supplying these vessels becomes cyanotic. Enlargement of the liver, venous pulsations, stagnation œdema, etc., are important clinical features of genenal venous congestion. Both active and passive hyperæmia may disappear after death. The contraction of the vessel walls in rigor mortis forces the blood out of the smaller vessels into the large veins and auricles. Extreme passive congestion usually persists to a greater or less extent after death.

Hypostasis (Cadaveric Livedity).—After death the blood in the arteries is driven into the veins by the contraction of the arterial walls, so that within a short time after the beginning of rigor mortis the entire mass of blood is found in the veins and auricles, while the arteries and ventricles are contracted and empty. The blood thus collected in the veins tends, through gravity, to sink to the dependent portions of the cadaver, so that within a few hours after death reddish or bluish patches of coloration appear over these parts. If the body lies in the usual position upon its back, those portions of the back not pressed upon by the weight of the body become hypostatic. In a cadaver kept in an upright position the hypostasis would be confined to the lower extremities. Post-mortem hypostasis is more marked in those cases in which there has been a general passive congestion before death. Pressure upon the hypostatic areas causes them to become pale, and cutting into them with a knife produces hemorrhage from the dilated veins. In carbon monoxide poisoning the hypostatic areas are of a bright cherry-red color; in poisoning by potassium chlorate they are of a dirty chocolate brown. Post-mortem hypostasis also appears in the internal organs, to the most marked degree in the lungs and meninges. In these regions it is often mistaken at the autopsy for pathological conditions. Ante-mortem hypostasis of the internal organs, especially of the lungs, may result from weakened heart's action. This is most likely to occur in failure of compensation in chronic valvular disease and in prolonged fevers or severe cachexias. As the force of the blood flow becomes decreased, it is not able to drive the blood ahead with sufficient power to overcome the force of gravity, so that a hyperæmic condition of the lower portions of the lungs is produced which gradually leads to stasis. As a result the circulation is further impeded and death may be hastened.

Increase in the Volume of Blood.—An increase in the mass of the blood, so that the sum total comes to stand in an abnormally high proportion to the weight of the body, is known as plethora. It is very doubtful if this condition exists as a definite pathological state, but it is possible that as a result of over-eating and drinking or as a part of some diathesis there may be a temporary increase in the total mass of the blood. In such cases there is a compensatory hypertrophy of the heart and a dilatation of the arteries. As a result of the high tension and consequent overstretching of the vessels, early sclerotic changes may result. The metabolic powers of the body are in time decreased by excesses in eating and drinking, and with the deposit of a large amount of fat throughout the body the blood tends to become anæmic. Animal experiments show that an increase in the volume of the blood through injection of blood or normal salt solution produces only temporary changes in the circulation. The blood pressure quickly returns to its normal point as a result of the compensatory dilatation of certain vascular areas, especially of the abdominal vessels, and also because of the increased elimination of fluid through the kidney and intestine. Even when the volume of the blood is increased eighty per cent. the plethora is but temporary.

Anæmia.—A diminution in the total amount of the blood leads to marked disturbances in the circulatory system, which are in direct proportion to the amount of blood lost and to the rapidity of the loss. A sudden hemorrhage of 0.5 kgm. in the adult will cause syncope. The blood pressure becomes greatly reduced, the pulse becomes small, fluttering, and frequent, owing to the lessened stimulation of the vagus. The peripheral vessels are contracted, the skin becomes pale and cold, while in the abdominal vessels there is usually dilatation, *i.e.*, hyperæmia. This may lead to stasis as a result of the weakened heart's action. As soon as the amount of blood sent from the heart becomes too small to supply the respiratory centres in the medulla, symptoms of asphyxia appear, and death finally takes place. This may result when less than one-half of the normal amount of the blood in the body is lost if there is a sudden anæmia of the nerve centres. The loss of much larger amounts may be borne if the hemorrhage is extended over a long period of time. When the loss of blood is not excessive, the stimulation of the vaso-motor centre through local anæ-