exceptionally large. It measures 14·5 mm. in antero-posterior length and is 16 mm. across. It has four large cusps with a well-marked posterior fovea. The 3rd molar has been detached from the bone but it is preserved in perfect condition and unworn. It has three well-developed cusps, but the hypocone is relatively small owing to the invasion of the large fovea. The tooth measures antero-posteriorly 13·7 mm. and transversely 15·5 mm. The crown in this unworn condition is extremely wrinkled.

The whole premolar and molar series measures 59 mm.

This newly-found primate probably agrees fairly closely with the Taungs ape, but the only parts that we can compare are the brain casts and the 1st upper molars. The brain cast of the new form is considerably wider, especially in the frontal region, and the molar teeth differ in a number of important details. Further, the associated animals found at Taungs are all different from those found at Sterkfontein. I think the Taungs deposit will probably prove to be Lower or Middle Pleistocene, while the Sterkfontein deposit is most probably Upper Pleistocene. I therefore think it advisable to place the new form in a distinct species, though provisionally it may be put in the same genus as the Taungs ape.

This discovery shows that we had in South Africa during Pleistocene times large non-forest living anthropoids—not very closely allied to either the chimpanzee or the gorilla but showing distinct relationships to the Miocene and especially to the Pliocene species of *Dryopithecus*. They also show a number of typical human characters not met with in any of the living anthropoids.

The Control of the Circulation of the Blood*

By Prof. R. J. S. McDowall

Variations in the Activity of the Heart

THE heart is not like an ordinary pump which sucks fluid from one tube and pushes it into another. The veins are so thin that any degree of suction would cause them to close. The heart is filled by the pressure of the blood which reaches it during the time it is relaxed, and adjusts the force of its stroke to the amount of blood in it at the beginning of contraction. The more blood reaching it, the more it pumps out, within limits. This is made possible by the fact that the force with which the heart contracts is increased if the heart muscle is stretched.

The heart can also change its rate. In the past it has been usual to describe the heart as being under two sets of controlling nerves, one the sympathetic, which when stimulated makes the heart go fast, and the other the vagus, which makes the heart go slower. Now we know that this is only part of the story. The evidence is almost complete that the heart is really under the control of two sets of reflexes which have this function. The difference between these statements is that the second involves an afferent pathway to the central nervous system, for the sympathetic and the vagus are constantly carrying down impulses to the heart, and if they are cut off the heart goes slow or fast as the case may be. In the case of the sympathetic, we do not know accurately as yet the exact source of the afferent impulses, but the fact that stimulation of any sensory nerves causes cardiac acceleration suggests that the source is stimulation from the outside world. This is not necessarily conscious, for it has been shown that a sound may accelerate the heart of a person who is asleep, but during waking hours the higher centres undoubtedly play a part in the acceleration. I shall refer to this further in relation to the vaso-motor centre. In the case of the inhibitory impulses which slow the heart, the source of the afferent impulses is known. These arise from certain sensitive regions within the circulation itself. These are situated in the left side of the heart, the arch of the aorta and the carotid sinuses, which are small dilatations at the bifurcation of the common carotid artery in the neck.

When exercise is taken, two changes occur : the sympathetic accelerator impulses increase and in particular the vagus impulses are reduced. The evidence for this rests on the effect of exercise and other procedures on the heart rate before and after section of the vagi, and with and without the sympathetic. It has been shown, for example, that if the vagus nerves have been cut the increase of the heart rate is, during the exercise, not nearly so great as it was before they were cut. It is not possible for me to discuss here how the change is brought about, except to say that it is in part due to the action of the higher centres and to a rise of venous pressure. The increased temperature of the blood and adrenaline liberated by the suprarenal gland enhance the effect of the nervous changes.

* From the presidential address to Section I (Physiology) of the British Association, delivered at Blackpool on September 11.

What I want to emphasize is that the range of acceleration is determined by the degree of activity of the cardio-inhibitory reflexes: indeed, it has been recently shown in Belgium that the capability of dogs to withstand sustained activity is apparently enhanced by removal of the sympathetic. The extent to which the animals have then to rely on the reduction of vagus activity is thereby increased. This, of course, does not mean that the maximum effort for short periods is increased. To show this it is necessary to time the running of the animal over short distances. It has been shown that in athletes during mild exercise the cardiac output is increased with a trivial increase in cardiac rate—that is, the increase is chiefly produced by an increased output per beat. I shall, however, return to this point. Meantime I should like to leave you with the question: The heart increases its output; where does it get its blood?

Experimentally it can be demonstrated that the vagus restraint of the heart is extremely variable—not only in different animals, but also in the same animal under different conditions, as may be seen if we block the vagi. For example, if we give an animal nitrogen to breathe, the normal vagus restraint can be shown to have disappeared. Or we can increase the restraint by previous sensory stimulation. This last experiment is of special interest, as it may give a clue as to how the normal vagus restraint is built up. We know that animals and human beings which take large amounts of exercise have slow hearts. How exactly this slow heart is produced is not yet clear. All we can say at the moment is that certain procedures such as sensory stimulation or asphyxia increase the heart rate, partly by reducing vagus activity, but that afterwards this reduction is followed by an increase in the activity of the vagus.

Variations in the Calibre of the Blood Vessels

It may be taken as a general principle that in physical exercise the blood is distributed to the active tissues at the expense of the less active tissues. This local dilatation of vessels, combined with a rise in the general blood pressure which is the result of increased cardiac output and constriction of vessels in less active tissues, results in an enormous increase in blood flow through the active muscles.

The cause of the chemical dilatation has been a matter of considerable debate. It has been demonstrated that blood issuing from tetanized limbs has a vasodilator action. There are first to be considered the products of carbohydrate metabolism—carbon dioxide and lactic acid. Each of these has been observed to cause vasodilatation if applied in suitable concentrations to capillaries under the microscope. I emphasize the concentration, because larger concentrations have the opposite effect. It may be demonstrated also that, if the vessels of the hind limb of a chloralosed animal are perfused with the nerves intact and carbon dioxide is administered, the perfused vessels constrict because of the action of the carbon dioxide on the vasomotor centre, but the blood-pressure does not necessarily rise, presumably because there has been a compensatory dilatation of vessels in the rest of the animal. A number of workers, especially Fleisch, have demonstrated that vessels are sensitive to most minute changes of hydrogen ion concentration, even that which is produced by the addition of the normal amount of carbon dioxide to the blood, and personally I think that normally this is the most important factor concerned.

There is, however, evidence that certain substances of protein origin may be involved. Of these the most important is histamine. It has recently been shown by Anrep that the vasodilator substance which is liberated into the venous blood gives all the known biological reactions for histamine, and it is possible to demonstrate that extensive tetanization of muscles may produce a state which is a very similar one to histamine shock. There is at the same time a constriction of pulmonary vessels such as is produced by histamine. This liberation of histamine—if it be histamine—is of interest, as biochemists have reported that, compared with other tissues, muscles contain relatively little histamine. It is, however, somewhat doubtful if we are justified in considering that what happens during a severe artificial tetanus necessarily occurs in normal exercise.

The nervous dilatation is, judging from the work of Cannon and his associates, probably sympathetic. Here we see a dual function of the sympathetic, for its constrictor action is much better known. It has been known for some time that the sympathetic contained vasodilator fibres. In order to show the vasodilator fibres in the sympathetic, it is necessary to paralyse first the vasoconstrictor fibres with ergotoxine (Dale), or to use slow rates of stimulation. In this connexion it may be remarked that this slow rate of stimulation may be an imitation of what normally occurs, since presumably ordinary muscle contraction may give rise to similar stimuli.

Once the exercise has begun, it seems likely that local vasodilator reflexes, similar to Loven reflexes, are set up by afferent impulses arising within the muscles themselves, possibly as a result of the mechanical and chemical changes which take place. The evidence is somewhat scanty, but it is impossible to ignore any longer the possibility of the

existence of a nutrition reflex as suggested by Hess and supported more recently by Fleisch. By this is meant the fact that oxygen lack in a part sets up afferent impulses which result in reflex dilatation.

Capacity effects.—Now it has been shown by Krogh that when a muscle is active an enormous number of hitherto closed capillaries open up. This opening up of vessels previously closed necessitates the provision of blood, and as there is only a limited amount of blood in the body, it must be provided from other regions, otherwise the blood pressure would fall and the circulation through the tissues be reduced.

It is probable that practically all parts of the body, except possibly the voluntary muscles, the heart muscle and the brain, provide the blood necessary for the active muscles. It has been shown that any exercise, actual or even contemplated, causes vasoconstriction. Constriction of the spleen and of the intestine in animals has been observed. In man it has been shown that the vessels of the skin constrict under any emotional stress or even anticipated activity.

In regard to the sympathetic constriction of the vessels, we are in the same difficulty as we were in relation to the sympathetic acceleration of the heart. We do not know how the actual nerve impulses which originate the constriction arise. For convenience we say that they begin in the higher centres of the brain. It is, however, probably preferable, it seems to me, to consider that it is a sensory stimulation from the outside world, which is the point in time determining the psychical reaction which results in motor movement. Certainly we know that stimulation of a sensory nerve causes generalized vasoconstriction and commonly a rise of blood pressure, and that similar changes but of lesser degree may be recorded in a sleeping man.

It has been usual to ascribe the shutting down of the blood vessels solely to sympathetic activity, just as it was usual to ascribe cardiac acceleration solely to such action. In the case of the heart we have clear evidence that the reduction of the vagus restraint is just as important by increasing the range of cardiac activity and creating a cardiac reserve. It has now become evident that there probably exists an exactly parallel mechanism which increases the range of vascular activity and similarly enhances the reserve.

Maintenance of the Vascular Reserve

Just as we have the restraint of the heart by the vagus, which determines the range of cardiac acceleration, so we have in relation to the blood vessels a set of reflexes which determines the magnitude of the vasoconstriction of the blood vessels; that is, they maintain the vessels of the body generally in an actively dilated state. The afferent impulses which are concerned in these reflexes have an exactly similar origin to those responsible for the vagus restraint of the heart. They arise from the cardio-aortic region and the carotid sinuses, and pass up the medulla by the aortic and carotid depressor nerves. Like the cardio-depressor reflexes, the vascular-depressor reflexes are operated by the intravascular pressure in these regions.

It has been generally assumed that the primary function of this control of the vessels is to maintain the arterial pressure at a constant level, and this is quite reasonable, for a constant mean pressure is desirable to maintain a steady flow of fluid at rest from the capillaries to the tissues.

More recently it has become evident that these reflexes may have another and possibly more important function. Several facts led to this suggestion: (1) in physical exercise or mental stress, the blood pressure, like the heart rate, does rise in spite of the reflexes; (2) the response of blood pressure to posture may be normal if the reflexes are destroyed—a fact which shows that the maintenance of mean pressure is not wholly dependent on the reflexes; (3) as in the case of the vagus, different animals, or even the same animals in slightly different circumstances, show great variability in the activity of the reflexes—often it is possible to throw the reflexes out of action without affecting the blood pressure materially; and (4), as might almost be anticipated, the conditions which reduce the activity of the vagus also reduce the activity of the depressor reflexes.

Now since in exercise the venous pressure is increased and, if the stress of the occasion is sufficient, adrenaline is secreted, we may consider what happens to the circulation when the vaso-depressor reflexes are thrown out of action. As I have said, there is a rise of arterial pressure and a generalized constriction of the vessels. It has become usual to consider that this rise of arterial pressure is the result of an increased peripheral resistance to the flow of blood from the arteries. Were this wholly true, we should expect to find that there is a reduced flow of blood to the veins. If the animal, however, is in good condition, the reverse is the case: there is an increased flow to the veins. It is as if there were at the periphery a sponge-like reservoir which, when it is contracted, drives its store of blood into the veins.

When the depressor reflexes are cut off, the reverse, however, does not necessarily occur experimentally. An increased flow into the veins does not necessarily result in a rise of venous pressure, because at the same time the heart is stimulated and the increased pressure is rapidly

dealt with. It can, as might be expected, be shown at the same time that there is an increased output of the heart. It is not possible to measure the output of the heart by the cardiometer method without there being some degree of shock or permanent increased capacity of the circulation from the absorption of toxic products. As a result, the increased cardiac activity more than balances any increased flow in the veins, and the venous pressure may actually fall. Commonly it remains unchanged in such experiments. However, if the animal is not subjected to any severe operative procedure, a small rise of venous pressure is the rule. Perhaps I should say that several workers using the Fick method have shown an enormously increased output of the heart when the impulses from the carotid sinus are cut off.

What we can imagine happens in exercise or emotion is, then, that just as the vagus restraint of the heart becomes reduced, so also the depressor restraint of the vessels becomes reduced, more blood is thrown into the circulation and is dealt with by the heart, which at the same time increases both its rate and its output per beat. It is to be anticipated that we shall eventually get evidence that the extent of the activity of the vasodilator reflexes varies in different animals just as the activity of the vagus varies.

The sympathetic and adrenaline.—All the mechanisms which I have described are probably still further enhanced by the vasoconstrictor action of the sympathetic and the action of adrenaline, which is apparently secreted whenever the emotional stress of the occasion is sufficient. Adrenaline in physiological amounts constricts the vessels of the skin and splanchnic region and dilates the vessels of the muscles. Here I should like to emphasize that probably the physiological dose of adrenaline is minute, and may even be insufficient to raise the blood pressure. Certainly the dilatation of muscle vessels is not a result of the rise of blood pressure which may occur, for it can be shown that the dilatation occurs with doses which do not raise the arterial blood pressure. An increased blood flow through the limbs can also be shown to be brought about by doses which do not raise the blood pressure. In such circumstances the constriction just counterbalances the dilatation. Why adrenaline should constrict some blood vessels and dilate others is a major problem in the study of the circulation. Since so far as we know the vessels themselves have the same structure in different parts of the body, we must assume that the difference is due to the different environment. I had hoped by this time to have obtained some definite evidence on this point, but so far the experiments have not been completely successful.

It is interesting to observe the effect of adrenaline on the depressor reflexes. If the hormone is injected, it is found that some minutes afterwards, even after the usual rise of blood pressure has passed off, it is not possible to affect the heart by a degree of stimulation of the vagus which was previously effective, and at the same time the effects of cutting off the impulses from the carotid sinus are markedly reduced or completely abolished. This, of course, is exactly what would be expected if adrenaline were secreted in the same circumstances in which the action of the depressor reflexes and the vagus are reduced, as in exercise.

A further corroboration of this somewhat new view of the function of the vasodilator reflexes comes from a study of the effect of exercise and of emotion on man. It is well known that when a man takes exercise on a stationary bicycle his systolic blood pressure goes up, but falls even below normal the moment the exercise stops. This fall has been explained by Cotton, Slade and Lewis as due to the accumulation of blood in the vessels of the dilated muscles, but from what I have said in relation to the diminution of the peripheral resistance in muscle, it is evident that the fall is in part due to a diminution of this resistance. Now if a careful comparison be made of the psychical effect of intended exercise and that of exercise, it has been found by Gillespie that there is no difference. In other words, the rise of arterial pressure in exercise is the result of psychical changes.

If exercise could be taken without psychical zest being involved, we might expect the blood pressure to fall. This, indeed, has been found to occur in the horse. In man, too, it has been found that if the exercise is slight, although the systolic arterial pressure rises, the diastolic pressure falls. This means that more blood is being pumped out of the heart per beat, but that blood escapes from the arteries more rapidly than normally before the next systole. In other words, from psychical causes alone there is a rise of arterial pressure from an increased cardiac output per beat, which can only be the result of more blood reaching the heart. In emotion, too, it is known that the systolic pressure rather than the diastolic rises. Since we have seen from the experiments of Mosso with the plethysmograph, of Barcroft on the exteriorized spleen and of Florey and Florey on the exteriorized colon, that generalized vasoconstriction is an accompaniment of psychical effort, we must assume that the increased output of the heart is in part, if not wholly, the result of the vasoconstriction which calls into use the reserves of blood, and thus the circulation is maintained in spite of the greatly increased capacity of the active muscles.