The Oliver-Sharpey Lectures

ON

THE ACTIVITY OF THE CAPILLARY BLOOD VESSELS,

AND ITS RELATION TO CERTAIN FORMS OF TOXAEMIA.

DELIVERED BEFORE

THE ROYAL COLLEGE OF PHYSICIANS OF LONDON

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LECTURE I.

It is fitting that the Oliver-Sharpey Lectures should deal with the application to medical problems of some physiological development of current interest. Among fresh developments of recent years has been a rather remarkable awakening of interest in the function of the capillary blood vessels as an active factor in the circulation. But a few years ago discussion of a possible activity of the capillaries was almost limited to the question whether their primary function, of facilitating chemical interchange between the blood and the tissues, involved an active secretion, or could wholly be explained by the physical processes of filtration, osmosis, and diffusion. There were not wanting, indeed, records in detail of appearances seen under the microscope, which were difficult to interpret except by attributing to the capillary walls an independent power of contracting, relaxing, and maintaining a tonus. But the prevailing tendency was to find alternative explanations for these appearances, or, in so far as a contractile function of the capillaries was admitted as a possibility, to regard it as a remnant of an embryonic condition, which, if it persisted in the fully differentiated vascular system of the higher vertebrates, played no real part in the regulation of the blood stream.

As long ago as 1858 Lister,¹ in his classical work on inflammation, described appearances which, I think, we should to-day not hesitate to attribute to active changes in capillary tone; but tradition was strong enough to lead him to interpret them as secondary to changes of pressure, produced by changes in the tone of the arterioles. Stricker,² in 1865, was the first observer to claim that changes in the capillary lumen took place independently of the blood pressure, since he was able to see them in the nictitating membrane of the frog, even when excised from the body. The soundness of the observation was challenged by the authority of Cohnheim,³ and a series of workers—Golubew,⁴ Tarchanoff,⁵ Severini⁶—who confirmed and extended Stricker's observation, were so far reluctant to attribute the narrowing of the capillary lumen to contraction of the wall in the ordinary sense, that they described it as due to the swelling of the nuclei of certain fusiform elements, which produced a partial or complete blockage.

In contrast to these, and in conformity with the most recent observations, was the description given by Rouget⁷ of special flat contractile cells, applied to the outside of the capillary endothelium, and encircling the vessel by delicate protoplasmic processes. Roy and Graham Brown,⁸ whose elaborate investigation was published in an early volume of the *Journal of Physiology* (1879), produced convincing evidence of the independent tone and contractility of the capillaries, but, apparently in ignorance of Rouget's work, were content to ascribe the function to the capillary wall as a whole. Rouget's work, indeed, was practically forgotten until Mayer,⁹ nearly thirty years later, repeated and confirmed his observations, describing not only the special form of contractile cell seen on the true capillaries, but all intermediate forms between this and the true plain muscle fibres of the arterioles and venules respectively. Steinach and Kahn¹⁰ then renewed observation of the living capillaries, and demonstrated contraction in response to stimulation, the contraction being in accord with the descriptions given by Rouget and by Mayer, in that the endothelial wall was seen to become folded and creased by an external con-

stricting force. They added the important point that the capillaries, like the arterioles, have a motor nerve supply from the sympathetic system.

This body of direct evidence, produced up to the year 1903, seems to have had little effect on physiological teaching. Attention being naturally concentrated on the picture of the capillaries, as that part of the vascular system in which the blood performs its respiratory, nutritive, and cleansing functions, it was apparently assumed that their walls had become so differentiated to facilitate filtration, diffusion, and osmosis, as to have lost the primitive contractile function, so that their state of patency or collapse was held to be determined entirely by the pressure in the arteries or the veins. For the next fourteen years this conception was only disturbed by observations which did not seriously influence the general trend of opinion. The observations of Heubner¹¹ on the type of circulatory collapse, produced by certain metallic and bacterial poisons which injured the capillary wall, were apparently not regarded as having a bearing on normal conditions. Langley's¹² suggestion that the intense local ischaemia produced by adrenaline seemed to involve an active participation of the capillaries in the vasoconstriction, and¹³ that this intrinsic capillary tone might be of importance under conditions of very low arterial pressure, seemed to lie rather aside from the main current of interest in the physiology of the circulation. From the point of view of the normal regulation of the blood flow, the rôle of the capillaries was regarded as one of passive obedience to external forces; and to emphasize the contrast between this view and that to which the work of recent years had led us I entitled these lectures "The activity of the capillary blood vessels."

A feeling of dissatisfaction with the accepted teaching seems to have been in the scientific atmosphere in the early years of the war; for about the year 1917 evidence pointing in another direction began to appear from at least four different and independent sources. Early in that year Cotton, Slade, and Lewis¹⁴ published a very important communication on the reaction of the capillaries in the skin of man, as exhibited in the phenomena long known as "dermatographism"—the local vasomotor response following non-traumatic pressure. They showed that both the red and the white tache, representing reactions to different degrees of pressure, or different degrees of sensitiveness, and often appearing alongside one another in the same individual, must be attributed to intrinsic relaxation and contraction of the capillary walls, since they were produced, often with little or no impairment, in a limb with the circulation completely arrested by closure of the arteries. Only the diffuse flush, surrounding the tache, was obliterated by arterial obstruction, and, like the flush developing round a painful, punctiform stimulus, which it closely resembled, must be attributed to reflex relaxation of the arterioles. They found, further, that, in a limb in which the circulation had been brought to a standstill, a small injection of a dilute solution of adrenaline still produced an area of characteristic pallor. Mere constriction of arterioles or venules containing stationary blood could not thus empty the capillaries, so that Langley's suggestion that these also contracted actively in response to adrenaline was definitely established, and, by inference, the motor sympathetic innervation of their walls, described by Steinach and Kahn, was confirmed.

Later in the same year Ebbecke¹⁵ published, in *Pflüger's Archiv*, a paper which, owing to conditions then existing, only later became available in other countries. It covered much of the same ground and led him to conclusions, concerning the local vasomotor reactions of the skin vessels, very similar to those of Cotton, Slade, and Lewis. He added the important point that a closely similar reaction of the capillaries, by dilatation, to stroking pressure, could be observed on the surface of viscera, such as the liver and the kidney. Both these sets of quite independent observers noticed that a pronounced local dilatation of capillaries, thus produced, might result in a local oedema, with formation of a raised wheal. This increase of permeability, accompanying full relaxation of the capillary wall, is, as we shall see, a point of very general importance. In his long and suggestive paper Ebbecke also reviewed a wide range of phenomena in which the varying tone of the capillaries might participate,

mentioning, in this connexion, the action of poisons like peptone and histamine, and some of the features of the anaphylactic reaction.

It was this last aspect of capillary function—the connexion of changes in capillary tone with the action of certain poisonous protein derivatives—which at this same period had forced itself on the notice of my co-workers and myself. But it will be convenient if I depart a little from strict chronology, to mention another group of investigations which was also, at this same time, proceeding independently—namely, the beautiful series of observations by Krogh, which, though by accident their publication began a little later, were already in active progress, and which, with the help of his fellow workers in Copenhagen, have continued to the present day. Fortunately Professor Krogh, by the recent publication of his Silliman lectures,¹⁸ has made it unnecessary that I should give more than a general review of his work. We may note that he had been led to this question by yet another entirely different route, his original problem being that of the oxygen supply to the voluntary muscle fibre. He was impressed by the difficulty of accounting for the adjustment of the blood supply to the widely varying needs of the active and the resting muscle for oxygen, unless the capillary vessels were actively contractile, so that, with a large proportion closed and impervious to blood in the resting muscle, there would be a large reserve of potential channels, the opening of which would meet the need for a relatively enormous increase of blood in close relation to the muscle fibres, during and after contraction.

By an ingenious method of intravital injection with Indian ink Krogh was able to give a clear demonstration of this adjustment. He counted and measured the capillaries open to the blood flow in the resting and the working muscles of frogs and small mammals, and his figures show an impressive contrast. One actual count of the open capillaries in a guinea-pig's muscle at rest showed only 85 per square millimetre, while in the muscle at work no less than 2,500 were counted in the same area—a ratio of 1 to 30. Still more impressive was the disparity between the volumes of blood in the muscle capillaries under the two conditions, calculated from measurements of the sectional areas and lengths of the capillaries open to the circulation. The blood volume, given as a percentage of the muscle volume, varied from 0.02 per cent. in the resting muscle, to 5.5 per cent. in the active muscle, and 15 per cent. in the muscle with all the capillaries fully dilated. In other words, the volume held by the capillaries open for transmission of blood in a normal, resting muscle, may be as little as one 750th part of the total capacity of the whole capillary network in the muscle, if all were fully dilated. We may note the obvious inference. If we suppose that, under normal conditions of rest, the capillary vessels in the voluntary muscles hold at any moment no more than 1/750 of the blood in circulation, if all, for any reason, were simultaneously relaxed to the fullest extent they would accommodate the whole of the blood in the body.

Having become convinced of the importance of this variable intrinsic tone of the capillaries in regulating the flow of blood, Krogh and his fellow workers proceeded to investigate its finer mechanism, by physiological studies carried out under the microscope, with the aid of the facilities for illumination now available. They have confirmed, on all points, the description given by earlier workers, such as Steinach and Kahn, of the response of the capillaries to minutely localized stimuli by variations of their proper tonus. They have demonstrated the possibility of making an individual capillary relax by gentle local stimulation. They have confirmed, as also has Hooker²⁰ of Baltimore, the presence of a motor supply to the capillaries in the sympathetic nerves, and have added the highly significant observation that stimulation of true sensory nerve fibres, arising in the dorsal root ganglia, not only causes dilatation of arterioles, as Stricker²¹ had first shown, and Bayliss²² much more convincingly, but independent relaxation of the capillary walls as well. The dilator effect on capillaries of stimulating sensory roots was first described by Doi,²³ working in Starling's laboratory. Krogh and his colleagues have related this sensory supply to the spread of the capillary dilator reaction from a punctiform stimulus, which disappears when the nerves are degenerated. Krogh¹⁹ suggests the existence of a peripheral nervous network, formed by

anastomosis of these branches from sensory fibres. There are here many points of detail still needing elucidation.

Of at least equal interest is the fact that Vimtrup,²⁴ at Krogh's suggestion, has reinvestigated the minute histology of the capillary motor mechanism, and has fully confirmed and extended the descriptions of contractile cells given by Rouget and by Mayer. It seems no longer possible to question the presence of these flat, branching contractile cells, applied externally to the endothelial wall of the capillary, and girdling it with fine processes. Equally certain seems the continuity of this contractile coat of the capillaries with the plain muscle coats of arterioles, on the one hand, and venules on the other, all intermediate forms between the fully differentiated plain muscle fibre and the flat, branching Rouget cell being found at the transition in either direction. There are vessels, indeed, in the subpapillary plexuses of the skin, which from their size would be counted veins, but from their structure must rank as giant capillaries (Krogh¹⁹).

Such evidence is making it inevitable that we should abandon the conception of contractile function, active regulation of the blood flow, as ceasing abruptly where an arteriole opens into the capillary network. We cannot longer, I think, regard the capillaries as passive, membranous tubules, opening or collapsing merely in response to rise or fall of pressure, whether internal pressure of the blood, as has generally been assumed, or external pressure due to swelling or deturgescence of the surrounding tissues, as in the view put forward by Leonard Hill²⁵ in a highly suggestive lecture. I think we must accept it as established that the capillaries have their own contractile coat, continuous with the plain muscle coats of the arterioles and venules—more delicate and less fully differentiated than these, indeed, but similarly supplied with motor and inhibitor nerve fibres.

This contractility of the capillaries being accepted as proven, we have to inquire into its function and its significance for the control of the circulation. It can hardly be doubted that its normal function is a fine adjustment of the circulation, supplementing the relatively coarse adjustment effected by the varying tone of the arteries. We have seen that, under normal conditions, only a small proportion of the capillaries in any tissue must be regarded as simultaneously open for the transmission of blood; and we must suppose that, as the metabolic demand shifts from one cell or tissue unit to another, some capillary paths close down, while others open. The fact, demonstrated by Krogh, that the capillary tone is not only under nervous control, but finely responsive to chemical stimuli, obviously fits it for that purpose.

These results of direct observation of the individual capillaries correspond in a very striking manner with conclusions to which my fellow workers and I had found ourselves driven by evidence of a very different kind, and which, indeed, we had already put forward a few months before the publication of Krogh's investigations began. Dr. Laidlaw and I²⁶ had been interested and puzzled for some years by the action of the intensely active base histamine, which reproduced a type of action exhibited by a large group of poisonous protein derivatives—a complex of symptoms which, at the outset of our work, had recently come into renewed prominence in the guise of the so-called "anaphylactic shock." The occurrence of a kind of toxæmic collapse in a proportion of severely wounded soldiers²⁷ had given, in the early years of the war, a new keenness to our desire to clear up outstanding difficulties in the action of histamine, which was capable of producing a condition in many ways so similar.

The main difficulty was briefly this. It was a powerful and general stimulant of plain muscle, of that of the arteries, so far as direct evidence could show, as well as of other organs. When added to blood or a saline solution perfused through the vessels of any excised organ it produced, in accordance with expectation, a simple retardation of the flow and diminution of the organ volume, by increasing the arterial resistance. Yet, when injected in a small dose into the vein or artery of an anaesthetized animal of the same species, it caused a simple fall of arterial pressure, having all the features of a pure vaso-dilator effect—that is, an action due to diminution of the peripheral resistance to the circulation.

There have been several attempts, some of them quite recent, to explain this paradox by representing this depressor

action of histamine as due, not to vaso-dilatation, but to constriction at some point on the venous side of the circulation, retarding the return of blood to the left side of the heart. These various constrictor actions—on the hepatic veins (Mautner and Pick²⁸), on the pulmonary arterioles (MacDowall²⁹), and on the mesenteric venules (Inchley³⁰)—do doubtless occur. Indeed, their occurrence was explicitly recognized by Laidlaw and myself as playing a minor part in effects seen at different stages of the action of large, shock-producing doses of histamine. But we satisfied ourselves that they were not seriously concerned in the evanescent effects produced by small doses. These in every respect—in the increase of the heart's output, the accentuated volume-pulse in a limb, the bright red flush which can be seen by simple inspection of the exposed intestine—resembled those of substances causing arterial dilatation.

A somewhat complex investigation, in which I had the great advantage of co-operating with Professor A. N. Richards³¹ of Philadelphia, drove us, in the face of the accepted physiological teaching, to the conclusion that this depressor action of histamine was due to a vaso-dilator action, not on arterioles, like the long familiar effect of nitrites and the more recently studied effect of acetylcholine, but on the capillaries. The failure hitherto to demonstrate this action of histamine on the artificially perfused organ was attributable to the fact that, under the conditions of such an experiment, the capillaries had not retained any of their normal tone, so that further relaxation was impossible, and only the constrictor effect on arteries appeared. By finding the conditions necessary for the artificial maintenance of the capillary tone—namely, the presence in the perfusion fluid of red corpuscles, to maintain a free supply of oxygen to the tissues, and a small proportion of adrenaline—we were able, in the perfused organ, to demonstrate the vaso-dilator action of histamine as in the whole animal. The perfusion pressure fell, the volume of the organ increased, and the venous outflow was accelerated. Venous constriction would not produce such an effect, since it would impede the outflow and raise the perfusion pressure. Arterial dilatation might do so, but it could be shown that this did not occur; a preparation consisting only of the arteries, down to the finest branches which could be separated from the tissues, perfused under identical conditions responded to histamine with simple constriction, while nitrites and acetylcholine caused prompt and wide relaxation.

There remained only, as the site of this demonstrated vaso-dilatation, the capillaries and possibly the microscopic arterioles immediately preceding them. Between these our methods could not distinguish; and, indeed, the evidence now to hand as to the structure and behaviour of the capillaries makes it doubtful whether the distinction would be a logical one. No sharp line, apparently, in relation either to structure or function, can be drawn between the ultimate arterioles and capillaries. At some point in the vascular system the response to histamine changes from the constriction, seen in the finest separable arteries, to dilatation; and whether we think of this change as occurring where vessels are still anatomically called arterioles, or at the level where arterioles are branching into capillaries is of comparatively little moment. That the capillaries share in the dilatation seems to be beyond doubt (Doi²³).

The evidence I am putting before you is nearly five years old, and I have forbore to trouble you with details. My immediate object is to point out to you that it involved somewhat new assumptions, concerning the nature of the capillary circulation, which the more recent, direct evidence has fully upheld. We were accustomed to the diagram in which the gradient of the blood pressure fell ever more steeply as the blood passed into finer and finer arteries, to become suddenly flattened and almost horizontal where the arterioles branched out into the relatively enormous capillary network. This conception, and the corollary that change in the tone of the capillaries, if it occurred, would have little effect on the peripheral resistance, and hence on the arterial pressure, would be inevitable on the view that a large proportion of the capillaries were regularly open for the passage of blood. Our conception of the capillaries as the site of an important part of the peripheral resistance, so that the steep

portion of the pressure gradient was shifted to cover the arterial side of the capillary zone, necessarily involved the assumption that only a very small proportion of the available capillaries are simultaneously open under normal conditions, so that no great and abrupt increase, of the total sectional area of the path open to the blood, occurs in passing from arterioles to capillaries. This assumption, which was vital to our argument, was unfamiliar at the time, and, I believe, made it difficult for many to accept our conclusions. Krogh's work has provided its much needed justification by direct evidence.

There was a further inference, of much greater significance, to which this conception of the capillary circulation necessarily led us. In dealing with the simple vaso-dilator action of small doses of histamine we had supposed that the small proportion of capillaries which, at the moment, were actually transmitting blood, underwent a dilator relaxation, with an effect resembling an arterial dilatation in all but quantitative details. If such a reaction should spread beyond the immediate path of the blood and involve the whole of the capillary network, so that all the capillaries in the body became simultaneously relaxed, the mere capacity thus developed should, we argued, be sufficient to accommodate practically the whole of the blood at the periphery, where a large part of it would lie stagnant, removed from effective circulation. I have already shown you how Krogh's actual measurements, subsequently published, have given a quantitative reality to this conception of the capacity of the generally dilated capillaries. The condition so produced would correspond exactly with that which Laidlaw and I had for some time been studying, and which followed the injection into an anaesthetized cat or dog of a large dose of histamine.³² The circulation failed, in this instance, not because the peripheral resistance was low, but because the output from the heart gradually fell to minimal proportions. The muscular action of the heart, and the tone of the arteries remained good; the output, and with it the blood pressure, failed because the blood was accumulating at the periphery, in dilated capillaries and venules, while the larger arteries and veins were alike collapsed and empty. The shortage of the blood available for circulation was accentuated by a phenomenon which, again, the more recent work of Krogh has brought into the scheme of the general physiology of the capillaries. We found that the capillaries became not merely relaxed in tone but abnormally permeable. We were inclined, not realizing the importance of the contractile cells as responsible for capillary tone, to regard the relaxation and the morbid permeability as due alike to poisoning of the capillary endothelium, as Heubner also had assumed in describing a very similar condition. It would appear from Krogh's observations that not only the diameter of the capillaries, but the power of the endothelial wall to retain the constituents of the blood is conditioned by the maintenance of an adequate tone by the Rouget cells. Loss of capillary tone, however produced, seems to result in oedema in the area of relaxation. To what extent the abnormal permeability, which we observed, is the result of the loss of the supporting tonus of the Rouget cells, directly modifying the porosity of the endothelial filter, and to what extent, on the other hand, it is due to a poisonous action on the endothelium, or to secondary nutritional changes, caused by the inefficient circulation, is a matter on which evidence is incomplete and difficult to procure. That increase of permeability due to relaxation of tone is an important factor, is strongly suggested by the rapidity with which the loss of plasma through the capillary walls appears; within a few minutes of the injection of histamine as much as one-half of the plasma may have passed from the blood vessels, probably leaving many of the capillaries clogged with a viscid corpuscular cream.

This picture of the histamine shock, which I believe to be the picture of a condition having a wide pathological and clinical importance, was drawn by us chiefly from data obtained by macroscopic methods—measurements of blood pressure, of blood volumes both general and local, of changes in corpuscular content. It has been closely confirmed by the microscopic observations of Hooker²⁰ and of Rich³³ in America. Inchley³⁰ has quite recently raised the question of constriction of the venules as the essential factor in pro-

ducing the condition. That constriction of the smaller veins occurs irregularly when the shock is already well advanced, and the circulation is reduced to a slow trickle, was observed by Laidlaw and myself. The venules, properly so called, are shown by the microscopic observations of Hooker and of Rich, as well as by our own naked-eye description, to be dilated and full of blood. When once the peripheral stagnation has occurred, it is obvious that a constriction of the arteries, on the one hand, and of the veins on the other, if it occurs, will intensify the condition and render recovery from it more difficult; but I am still convinced that the primary and essential factor is the loss of the tone of the capillaries.

REFERENCES.

- ¹Lister: *Phil. Trans.*, 148, p. 645, 1858. ²Stricker: *Sitzungsber. d. Akad. d. Wissensch. Wien*, 52, ii, p. 379, 1865. ³Cohnheim: *Virchow's Archiv*, 40, p. 1, 1867. ⁴Golubew: *Arch. f. Mikr. Anat.*, 5, p. 49, 1869. ⁵Tarohanoff: *Pfuger's Archiv*, 9, 1874. ⁶Severini: *Ricerche sulla innervaz. d. vasi sang.*, Perugia, 1878. ⁷Rouget: *Comptes Rendus*, 79, p. 559, 1875. ⁸Roy and Graham Brown: *Journ. of Physiol.*, 2, p. 323, 1879. ⁹Mayer: *Anat. Anzeiger*, 21, p. 442, 1902. ¹⁰Steinach and Kahn: *Pfuger's Archiv*, 87, p. 105, 1903. ¹¹Heubner: *Arch. f. exp. Path. u. Pharm.*, 56, p. 370, 1907. ¹²Langley: *Journ. of Physiol.*, 27, p. 248, 1901. ¹³Langley: *Ibid.*, 41, p. 483, 1911. ¹⁴Cotton, Slade, and Lewis: *Heart*, 6, p. 227, 1917. ¹⁵Ebbecke: *Pfuger's Archiv*, 169, p. 1, 1917. ¹⁶Krogh: *Journ. of Physiol.*, 52, pp. 391, 405, 457 (1919); 63, p. 399 (1920); and 65, p. 412 (1921); also papers in Danish. ¹⁷Krogh and Harrop: *Journ. of Physiol.*, 54, Proc. Phys. Soc., 1921. ¹⁸Krogh, Harrop, and Rehberg: *Journ. of Physiol.*, 56, p. 179, 1922. ¹⁹Krogh: *The Anat. and Physiol. of the Capillaries*, New Haven, 1922. ²⁰Hooker: *Amer. Journ. of Physiol.*, 54, p. 30, 1920. ²¹Stricker: *Sitzungsber. d. Akad. d. Wissensch. Wien*, 74, iii, 1876. ²²Bayliss: *Journ. of Physiol.*, 26, p. 173, 1901; and 28, p. 220, 1902. ²³Dole: *Ibid.*, 54, p. 227, 1920. ²⁴Vimtrup: *Zeit. f. d. ges. Anat.*, 65, p. 150, 1922. ²⁵Hill: *BRITISH MEDICAL JOURNAL*, 1921, i, p. 767. ²⁶Dale and Laidlaw: *Journ. of Physiol.*, 41, p. 318 (1910); and 43, p. 182 (1911). ²⁷Medical Research Council Special Reports, No. 25, 1919. ²⁸Mautner and Pick: *Munch. med. Woch.*, 62, p. 1141, 1915. ²⁹MacDowall: *Journ. of Physiol.*, 57, p. 146, 1923. ³⁰Inchley: *BRITISH MEDICAL JOURNAL*, 1923, i, p. 679. ³¹Dale and Richards: *Journ. of Physiol.*, 52, p. 110, 1918. ³²Dale and Laidlaw: *Ibid.*, 52, p. 355, 1919. ³³Rich: *Journ. of Exp. Med.*, 33, p. 287, 1921.

ON LIMITATION OF EFFORT IN HEART DISEASE.*

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THIS subject is one on which medical opinion, both individual and collective, has never been uniform, and is by no means uniform now. Fifty years ago, while Oertel sent patients with serious heart disease to climb mountains, the general trend of practice was seriously to limit all who showed either murmurs or irregularities, let alone more obvious signs and symptoms; and it was further very generally assumed that once restricted meant always restricted.

Of late years murmurs have been perhaps too much discounted, for the pendulum is apt to swing, while the differentiation of the irregularities—which, apart from evidence of physiological efficiency, throws more light upon this question than any other single consideration—is as yet not fully comprehended except by those who have made it a special study. It is not a simple matter, and the busy practitioner welcomes something simple and easily recognized to guide him. And the latter-day specialists—or some of them—have given him a sign which seems easy enough to recognize, and which has to some extent replaced the systolic murmur. The sign is enlargement.

ENLARGEMENT OF THE HEART.

I had intended, as a prologue to this paper, a short discussion on enlargement, but the subject is too wide for such treatment, and it may suffice to say that—(1) it is often impossible to differentiate between dilatation and hypertrophy, or the amount of each in a given case; (2) data are as yet very incomplete as to the variations in size and position, and of the movements of the heart as a whole within the thorax in different positions of the body—matters which probably vary at varying ages and in different types of individuals; and (3) all the means at our disposal for estimating the size of the heart are open to fallacy. Percussion is perhaps the least reliable, for

differing outlines are often drawn by two or more skilled observers. The results of palpitation seem obvious, yet may be quite unreliable, for, apart from displacement, an impulse (presumably conducted) is sometimes felt well outside the nipple line when a skiagram will show the heart to be well inside it; and yet skiagraphy is often discredited because of its tendency to exaggerate the cardiac area.

In connexion with enlargement I would submit that—(1) it is easy to make mistakes as to size, (2) the condition may be temporary, and (3) many permanently and considerably enlarged hearts may be safely allowed such effort as is comfortably tolerated. I could cite cases illustrating all these points, but space forbids, and one must suffice.

What the evidence was I do not know, but presumably it must have been convincing, as three different R.A.M.C. boards, each confirming the previous decision, threw this officer out of the army in 1919 on account of "cardiac debility with great enlargement," and he was told that he must, for the rest of his days, lead a very quiet life. As he had been used in earlier years to climb mountains and wanted to do so again, he came to me in 1920, because he had been told that I was interested both in mountains and in hearts. I found him in poor condition generally, the result of illness and war conditions, and he had a systolic murmur, but I found no evidence of cardiac enlargement, and a skiagram by Dr. Robert Knox showed a heart of normal size. Clearly the army boards were mistaken, or else the enlargement was temporary. I allowed him to do some mild climbing in 1920, and it improved his condition wonderfully; while in 1921 I let him climb as much as he liked, when he made some fine ascents and came back very fit indeed. In 1922 he was a distinguished member of the Everest expedition, was never sick nor sorry for a day, and now looks ten years younger than he did in 1920.

GENERAL CONSIDERATIONS.

How difficult it often is to decide on the amount of liberty that may be safely allowed to a heart patient is evident, and it is hardly surprising that different practitioners should take different views. But that extreme divergence of opinion should be possible on individual cases—a fact that both we ourselves and the public recognize—does not bring credit to the profession. It should not be; and I offer this paper as a small contribution towards what I trust is a reasonable attitude.

To impose sufficient restriction "to be on the safe side" is the easy solution of each case; yet needlessly to restrict is not only to disobey the Golden Rule, but to depress the patient's health and spirits, to limit his life and his interests, to lower his money-earning capacity, and to bring anxiety to himself and his family. These are considerations which should ever be present in our minds when dealing with these cases, and I think it is good to form the habit of asking oneself before giving a decision, "Can he safely be allowed to do more?"

In approaching any individual case the first point to settle is whether it is or is not a cardiac case at all, or whether it is a mixed case. Dyspnoea on exertion at once suggests the heart; but many other conditions may be causal or contributory, and, though cardiac weakness may be present, it may be secondary. Chlorosis, pernicious anaemia, and the secondary anaemias of malignant and other serious diseases are not only direct causes of dyspnoea, but also of cardiac weakness, from lack of healthy blood supply to the coronaries. Phthisis and emphysema are probably not often overlooked, but a quiet pulmonary effusion may exist without suggestive symptoms; while, in cancer of the lung, dyspnoea is sometimes the earliest symptom and the one which brings the patient to the doctor. And then there is Graves's disease and the "effort syndrome," in which the heart is rapid and feeble, but only as part of a general asthenia—a mixture probably of neurasthenia and endocrine anomaly; and there is Addison's disease itself, and diabetes. In the early stages of many of these disorders breathlessness may be a prominent symptom, and the heart may be suspected, and perhaps there is a murmur. It behoves us to be wary and look all round.

And now let us come to the cases in which the heart itself has been carefully isolated as the seat of such mischief as there may be, and we shall find that each case demands individual consideration, and that the degree of effort restriction requisite varies from *nil* to complete immobilization; though even in the worst cases the hope may

*A paper read at a meeting of the Kent Branch of the British Medical Association at Tonbridge.