A Lecture

ON

ANGINA PECTORIS AND THE POSSIBILITIES OF ITS SURGICAL RELIEF.

DELIVERED BEFORE THE ROYAL COLLEGE OF PHYSICIANS OF LONDON ON MAY 5TH

BY

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It is so great a pleasure to me to find myself in London again amongst many old friends, exchanging views and, as in olden times, fighting by strength of argument with many a member of the British profession, that I am in danger of overlooking the great and exceptional honour bestowed upon me by being allowed—nay, invited—to address this highly illustrious Royal College of Physicians, of which William Harvey was and is the everlasting glory. I want to acknowledge my great appreciation of this invitation, my great indebtedness to your President, to my friend Dr. McNee, and to all of you who have honoured me by your presence.

It seems madness that I should endeavour to bring new notions, personal conceptions about my chosen subject, to England, the classical country of angina pectoris, where it was and still is a favoured subject of investigation and controversy. However, it is exactly this fact which made me wish to bring our problems, our schemes, before a British audience, where I feel sure to find interest, good advice, and help. Here I knew I would meet the best authority on angina pectoris of this time—your highly honoured, even right honourable, Nestor of teachers of medicine, my faithful friend in sunny and in dark years, Sir T. Clifford Allbutt.

There is a special reason why I want to say my say concerning a subject about which I have been silent until now. In the *Lancet* a few years ago Dr. Alexander Morison wrote to the editor:

"Whatever [the] disadvantages of such maturity, one must have attained one's fifth or sixth decade before, under the most favourable circumstances from the point of view of personal experience, one can have seen, I shall not say many, but a sufficient number of cases of Heberden's disease to be in a position to speak with authority on this always interesting affection."

Now I happen to find myself exactly at that time of life which the authority I have quoted thinks the moment of dawn of knowledge. In my younger years I saw many cases of angina in Holland, but not so many by far as my English friends did in this country. It is chiefly in the last ten years, spent in Vienna during its struggle for life, that I have had the opportunity of seeing even more than the sufficient number of cases of which Morison speaks. As nobody can possibly give me a guarantee of reaching with sound brain the age of Heberden or Clifford Allbutt, I should speak now or perhaps never.

As to what we should mean by angina pectoris, I do not think that there will be any danger of being misunderstood here in England. In other countries quite different forms of heart paroxysms are called by this name. Cardiac asthma, any kinds of sudden pain in the cardiac area, even paroxysmal tachycardia, or other irregularities associated with sensations of anxiety, are packed together under the name of "stenocardia" or "angina pectoris." This fact makes discussion very difficult, and so confused that the poor pathologist, if asked to name the lesions characteristic of angina pectoris, is at a loss for an answer. Here, I think, angina pectoris is always and only characterized by pain—pain of a definite kind and with a typical localization, coming on in attacks, as was described by Heberden. It is this purely clinical entity which is the chief subject of my lecture. In my description of it I will first of all try to delineate angina pectoris as it is seen in general and private practice, much rarer in hospitals, but covering certainly 70 to 80 per cent. of all cases that might be called angina pectoris.

A. THE COMMON, MOSTLY "CHRONIC," FORM OF ANGINA PECTORIS.

(a) *The Patient's Sensations.*

At first the sensation is spoken of as a pressure, a heavy weight, always a very disagreeable, somewhat alarming sensation; it may be constricting or a stress. Sooner or later, sometimes from the first attack on, there is a definite sensation of pain, that may be tearing, piercing, or burning as hot fire; you never will hear the expression of "stabbing pain," which is so typical in heart neuroses and in some kinds of irregularities. Sometimes it is a spasmodic pain or as if the breast would burst. It may irradiate as in neuralgia, and may start or remain in the form of definitely circumscribed hyperaesthesias.

A good observer, who knows how to get precise answers out of his patient, will easily recognize this kind of pain, were it only by the grave face and awed respect with which the patient speaks about it. It is quite different from the pain of the neurotic patient, who with dramatic emphasis and sweeping gestures wants to make an impression upon his doctor, and points with the finger to that part of the chest where he thinks his heart is to be found.

(b) *Localization of Pain.*

The centre of the pain is never at the apex or in what we call the cardiac area. It is nearly always somewhere on the sternum, at a higher or lower level, mostly at the manubrium, sometimes beginning at the xiphoid and rising to the middle or the upper parts of the sternum. It may be at a spot lying to the "north-east" of the heart, in the level of the third and fourth ribs, where the patient will place three or four fingers. In light cases the patient may move his pointing finger across the chest in the level of the angulus Ludovici, speaking of a tearing pain. These movements are characteristic and of great diagnostic significance.

Irradiation, the most typical quality of anginal pain, spreads first into the back, where it covers an area opposite the painful spot on the chest; it runs up to the left shoulder, down at the inner side of the arm, and may go down as far as the wrist or the little finger. It may ascend to the left or to both sides of the neck, to the angle of the jaw, or even as high as the scalp. These sensations in the neck are often felt as a kind of strangulation. At the height of the attack the pain may spread over the whole chest, to the right side and arm, sometimes in the same intensity as in the left (angina duplex), or the whole irradiation may be localized and limited to the right side from the very beginning (angina dextra).

The typical segmental areas of hyperaesthesia and hyperalgesia, or, in chronic cases, also of hypoaesthesia or analgesia, may be accompanied by tenderness on compression and pinching of skin, muscles, and nerves. These areas of changed sensibility correspond with the posterior roots of the lower cervical and the first one or two thoracic segments. Typical pain points may be present—for instance, above and under the clavicle, where the cervical and brachial plexuses are running down (R. Schmidt), and at below the mastoid over the styloid (Libman).

(c) *Under What Circumstances does this Pain come on?*

The most important peculiarity of the pain is its absence in rest and during the night. As long as the patient keeps quiet, bodily and mentally, he may feel perfectly well; as soon as he starts moving the pain comes on—at first on severe exertion only, as on going uphill or running after a tram-car; later a quiet walk or even the least effort—dressing, writing, chewing—causes the pain, so as to make life quite unbearable.

In exciting these attacks there are three other conditions which make themselves felt in the great majority of cases. First, a *full stomach*; the business man may, before noon, run into his office, manage his affairs, and bustle about; after a copious lunch, in the afternoon, he is nearly paralysed, the slightest movement or excitement giving rise to terrible attacks; belching brings relief. This factor is so obvious that sometimes angina

pectoris is looked upon as a disease of purely abdominal origin.

In the second place *excitement* and nervousness, alone or combined with bodily work, may cause the most terrible pain. This is so much the case that the whole condition is sometimes regarded as one of nervousness only. On the way to the railway station the mere idea of perhaps missing his train is sure to cause an attack; the same thing happens the moment he finds that he has left his nitroglycerin bottle at home.

A third factor of great importance is *cold*. Nearly every patient tells us that cold weather, a cold room, makes him suffer more. Leaving a warm room and going into cold open air invariably brings about the pain. Sometimes going to bed has the same effect, which I did not understand until I found out that it is the undressing in a cold bedroom, and especially the cooling of the skin by stretching himself between the cold sheets, which is the active agent. A fire in his room and a hot-water bottle in bed prevent this untoward event.

From these facts we see that everything which stimulates the action of the heart, increases its output, or raises the blood pressure, causes the pain.

(d) *The Course and Subsidence of the Attack.*

Just as the onset of the attack is caused by exertion, excitement, cold, a full stomach, and abdominal tension, or the combination of these factors, anginal pain will disappear as soon as these causal influences are removed. Therefore the attack generally lasts only a short time: a warm room, a hot stove, a healthy belching or other depletion of the abdomen, mostly have an immediately favourable effect. As soon as the patient stands still in the street and keeps quiet, the distress disappears. These peculiarities give anginal attacks a typical aspect, the more so as anginal pain is of the most excruciating character, and so dominates its victim that he is forced to stand still immediately. The patient does not stop in the street because he finds it convenient or because he knows that it will do him good, but because he *must*. Therefore this stopping in the street is one of the most reliable symptoms in the patient's history. The man with heart failure and dyspnoea, as soon as he is conscious of overexertion, will slow his pace and make his way to a quiet spot; the subject of angina must stand stock still and can only move when he is out of the devil's clutches; should he not keep quiet long enough the attack will come on again before he has taken a step or two. In doubtful cases we should try to get a history out of the patient, or if still in doubt take him by the arm and walk a mile with him.

(e) *There is no Dyspnoea in the Attack.*

Symptoms that are absent during the attack are not less important than the characteristic symptoms we see. Dyspnoea does not belong to angina pectoris. The patient may tell about a loss of breath; he may even mention some curious sensations of suspended respiration and a feeling of constriction which makes respiration nearly impossible (symptoms on which we have to talk later); close observation shows that there is not a single sign of overfilling of the lung circulation or typical forced breathing. With the subsidence of the attack these respiratory symptoms immediately disappear, and a deep sigh is the signal of the patient's release and the onset of normal breathing. There is a general acknowledgement of these facts, and we will therefore have to look on a pulmonary stasis coming on during the attack as an *event grafted on the attack* and not as an essential part of it. The absence of dyspnoea in the typical, most frequent form of angina eloquently speaks against the hypothesis that brings angina in connexion with heart muscle weakness of any kind.

(f) *The Action of Nitrites.*

The miraculous action of nitrites is diagnostic for angina. In no other condition do these drugs act so wonderfully; in dubious cases the presence or absence of this effect may be of almost decisive importance for diagnosis.

(g) *Physical Diagnosis.*

The clinical findings in our patients are not in any way characteristic. Percussion and the x-ray screen may or may not show a wide aorta or enlarged heart. We may find sclerotic or weak arterial walls, a high or a low blood pressure; you get angina in a body of athletic build as well as in that of a weakling. Symptoms may be absent or present in the most different combinations of anginal patients. Hence the impossibility of reaching a correct diagnosis by means of a physical examination alone.

(h) *The Course of the Disease.*

A small percentage only of cases of this group die in the first or one of the first attacks. On the other hand, if the patient survives, a lasting cure is extremely rare. The pain may disappear for a short time; nearly always it comes back. I do not mean that the patient dies always under the symptoms of angina; we will see later that the pain may disappear and may be replaced by symptoms of developing heart failure. In favourable cases a long but necessarily quiet life is possible. In a goodly number of instances (in private practice, not in hospital cases) patients may live for a number of years if they will accept our advice and avoid bodily exertion, mental excitement, full meals, and some of our sweet poisons.

This full clinical picture belongs to the cases that visit the general practitioner. Taking all cases that show the typical paroxysmal pain, in my opinion 80 per cent. belong to this type, which I call common angina, or at least belonged to it in the first phases of the disease. The changes in the course of the disease and its various aspects are to be explained from superadded factors. It was the observation of a very great number of cases which has made it possible for me to reach the essentials and to eliminate conditions which are exceptional, superadded, or which may complicate or lead to a total change of symptoms in certain cases: these essential features of angina are fully portrayed in the classical picture drawn by Heberden.

B. ANGINA PECTORIS CAUSED BY CORONARY EMBOLISM.

In a number of cases—very small compared with that of the common form of angina pectoris—we find typical anginal pain, but its onset, its duration, and its consequences are easily (but not commonly) discriminated from the more chronic form. There is little doubt about its causation, because generally emboli, or sudden thrombosis of coronary arteries are found in these cases. Relatively often there is the opportunity of getting a *post-mortem* examination. To these cases the doctor is summoned as only in cases of extreme emergency. Until the attack came on the patient may have been in seemingly perfect health; perhaps there had been already some premonitory signs of beginning heart disease, perhaps the patient just "felt his heart" or found himself short of breath on stronger exertion. However this may be, suddenly and without any obvious cause a most severe pain in the chest, increasing into a most horrible paroxysm, sets in. The patient is unable to move about, sometimes collapsing from weakness, or he may even become unconscious. Speaking from personal experience, I may mention a case where a man was seized while quietly sitting in the train on his way to a hunting party and had to be carried from his compartment to the nearest hospital. In another case the subject of an attack broke down in the street and was brought to a neighbouring chemist; or a third case—a doctor on his way to a patient is suddenly overwhelmed by pain, and has to be carried to his home. In all such cases there is no apparent cause for the onset of the attack, nor is the duration a short one, nor do nitrites relieve the pain in any marked way; the attack does not pass off, but lasts for hours, sometimes days, without any real amelioration. Only repeated injections of morphine are able to help him. In many of these cases digitalis, caffeine, and injections of other analeptics are necessary to keep up the fluttering heart action. The patient may die in this first attack, or the pain, burning like a fire in his breast, disappears after terrible suffering. When at last the patient recovers he never, as in our common form, returns to his previous state of health, but

almost invariably becomes a broken man. And after that? After lighter, rapidly passing attacks the patient may *seem* a healthy man. I have seen a case in which, five years after such a seemingly complete recovery, a new attack left the patient with such a damaged heart that he died of heart failure three weeks later, but without any manifestation of pain. In this case all the symptoms of heart failure were present.

The most striking feature is that after such a terrible attack the patient nearly always is without pain, but instead shows the well known symptoms of a damaged heart muscle. In recent years electro-cardiographic tracings have often disclosed such changes in the ventricular complex as are now known to give proof of changes in the function of the ventricular muscle wall—*changes that in some cases did not exist a short time before the attack, and sometimes disappear sooner or later after the attack is over.*

The pain in these attacks is mostly, not always, the severe but usual form of anginal pain, with its typical localization and the same terrible qualities. As far as my experience goes, it may sometimes be localized in lower segments of the chest, lower down on the sternum, and even in the heart region. Irradiation in *both* arms seems to be not at all a rare occurrence.

This variety of angina has so much impressed itself on the mind of the clinician that he has come to regard it as the typical form of the disease, and hence the evil prognosis he has come to attach to the disease. Having learned and heard about such angina pectoris as a student I was greatly astonished at finding how rarely these cases occurred. The overwhelming majority of cases show the more chronic character of the common form first described. Nevertheless the typical character and localization of the pain compels us to include this form in the chapter of angina pectoris—well understood, as a form in itself, to be set apart from the more common form. Without this distinction we will never be able to come to a satisfactory agreement on the subject of angina pectoris.

I will not dwell on other forms of heart pain, nor on the relation of pericarditis to anginal or seemingly anginal pain. In Clifford Allbutt's book enough is said on this subject, and to discuss it fully would lead me too far. It is time to come to a discussion on the origin of anginal pain and of the attack.

C. THE ORIGIN OF ANGINAL PAIN.

What is the constellation of causes, what the pathological anatomy and the pathological physiology of angina pectoris, and how can we explain the attack and its many peculiar manifestations? We must discuss the three chief explanations which have been offered:

1. Pathological conditions of heart muscle.
2. Disease of the coronary arteries.
3. Disease of the proximal part of the aorta.

An agreement on the subject is reached neither in literature nor in the manifold discussions in medical societies; on the contrary the defendants of the various hypotheses stand for their opinion. So it seems necessary to test these opinions at the hand of the *clinical facts* that ask for explanation.

1. Heart Failure.

Heart weakness, insufficient action of the heart muscle—let the pathological factors be what they may—cause certain definite invariable symptoms, these symptoms being dependent upon the part of the heart which is affected. In left-sided insufficiency there will be greater filling and higher pressure in the pulmonary circulation, attended by different grades of dyspnoea. In failure of the right ventricle the lung will not be so much overfilled, and stasis will be found in the venae cavae, with enlargement of the liver and oedema. If the whole heart is damaged the symptoms will be a mixture of these sequelae, dependent on the preponderance of left- or right-sided heart failure. These facts are known to all of us, but we should not forget to apply them to our problem and to ask: Are these invariable sequelae of heart failure regular constituents of the anginal attack? There can be only one answer: No!

In the very large majority of cases dyspnoea is absent. From the very beginning this point has been emphasized by the first and by the most conscientious observers, especially here in England. There are exceptions: by raising the blood pressure and by efferent impulses to the heart the attack itself may lay such a stress on the left ventricle that consequently this compartment of the heart breaks down. In the midst of the paroxysm the well known short cough may appear, moist râles may be heard first at the base, later in the higher parts of the lungs, and the sputum may be rose-coloured and frothy. The patient even may be choked instantly by oedema of the lung. But we dare not forget that this breakdown of the left ventricle is not the cause, but a consequence of the attack. We will find that this complication occurs almost regularly in angina due to embolism of the coronary arteries; but it does not belong to the common form of angina. The difficulties of respiration, the curious sensation of not being able to breathe, frequently associated with anxiety and uneasiness, sometimes found in angina, are not signs of insufficient heart function, but probably reflex disturbances which, as we will see, may be otherwise explained.

How far we are off the right track when we ascribe the anginal syndrome to weakness of the heart is seen in long-standing cases. Here heart failure, developing in the course of time, completely alters the clinical aspect: *the patient loses his pain and becomes short of breath.* Not rarely there is first a period in which the attacks consist partly of anginal, partly of heart failure symptoms, until, sooner or later, the pain disappears completely and the patient complains of dyspnoea on exertion. I could tell you about a very great number of such cases, and every one of the colleagues in my clinic is, by ever-repeated experience, convinced of the reality of these events: the debility of the heart is a safeguard and prevents the onset of anginal pain. In literature a great number of observations lead us to the same conclusion. The last writer on this subject, Daniélopou, says in his recently published book:

"We see often angina patients who show no single sign of what we call heart insufficiency. On the contrary, as long as the patient's heart is strong he has numerous attacks of the classical type, which disappear the moment the symptoms of insufficiency appear. In the end dyspnoea takes the place of pain. To a certain extent both forms of attacks come on in turn. Far from being of common origin, they (angina and heart failure) are antagonists."

Further observation at the bedside shows the correctness of this view; it explains many curious events in the course of angina: patients who first showed typical angina and later get heart failure may benefit greatly from rest and digitalis treatment. It is not at all rare to find that by pushing digitalis the dyspnoea subsides completely, but the half-forgotten pain comes back. These are the well known cases in which we have to be very careful with digitalis and where we must find out the exact dose which controls dyspnoea and leaves the anginal pain still dormant. A few weeks ago I was treating a doctor who, at the outset of his illness, suffered for some months from severe anginal attacks. After a very serious attack, probably of coronary embolism, he lost his pain but became greatly short of breath. Digitalis answered well, but to his great disappointment the patient told me (exactly at the moment I demonstrated him in a post-graduate lecture) that the pain had come back two days before—that is, with the return of better function of the left ventricle. The puzzling fact, often mentioned in literature, that so many angina patients die at the end without attacks and without pain, is easily explained along the same lines. We can thus understand how it is that all those thousands of cases of myocardial disease have no angina; that among thousands of cases of valvular disease it is only the aortic ones which may show typical angina, whether the disease be of rheumatic, luetic, or toxic origin; that all such factors that diminish the output of the heart are inconsistent with anginal pain—for instance, I never saw angina pectoris in cases of lasting auricular fibrillation. *What damages the heart muscle wards off angina.*

Apart from these purely clinical arguments, other facts, of perhaps more "scientific" character, speak strongly against the heart itself being the starting point of anginal pain. Its typical localization is that of the affections of the aorta, especially of aneurysm of the ascending part of it.

Asking for the localization of affections of the heart itself, we get the answer from nobody less than Henry Head¹: afferent stimuli coming from the heart enter the upper cervical segments of the spinal cord, skip the four lower cervical and two upper thoracic segments, these being the segments associated with angina, and reappear at the second and succeeding thoracic segments. Thus it is explained how an overfilled auricle in mitral stenosis, a heart so large as to be confined by the chest, a sudden dilatation, or a ventricular extra-systole in a strong heart, if there be sensations at all, they will irradiate into the lower segments of the chest covering the heart. Cases which demonstrate the different localizations of referred pain in heart and in aortic disease abound in English literature, and in my opinion afford a very strong argument against the ventricular hypothesis of angina pectoris.

2. Coronary Disease as the Cause of Angina Pectoris.

There are three different forms of disease of the coronary arteries which are supposed to cause the anginal syndrome: (a) embolism or sudden thrombosis; (b) chronic sclerosis or syphilis, with more or less marked narrowing of the vessels; (c) vasomotor spasm of the coronary system.

(a) *Coronary Embolism*.—As we have seen, there can be no doubt that sudden obstruction of one or both coronary arteries can bring about the most terrible attacks of angina pectoris. A sudden termination frequently gives us the opportunity of finding the fresh plugging of the artery, and of reconstructing the pathological event and its after-effects. In longer standing cases we find myomalacia, demonstrating the damage done to the heart muscle. That there should be during the attack most marked symptoms of disordered and weakened heart function is not to be wondered at. The problem is: Why is there invariably associated with this pathological condition the terrible pain of angina? Some ascribe it to an insufficient blood supply to a heart which is still in full action. Among them Daniélopou², in his recent book on angina, rejects heart failure and Mackenzie's "exhaustion" of the heart, but speaks of "fatigue," by which he means the effect of a poisoning of the heart muscle by fatigue toxins. We will return to this question when I come to discuss spasm of the coronary arteries.

We might think, with Clifford Allbutt, that in such cases there will always be some lesion of the aorta, but I must say that my experience has convinced me that this is not always the case. I have had autopsies where our attention was mostly directed to the aortic wall, but no lesion of this structure was present. I think we may admit that the coronary arteries, put under abnormal stress by their sudden occlusion, are themselves the seat of, or better the starting point of, the pain. This matter also we shall have occasion to return to.

It is quite clear that this supposed pathogenesis of anginal pain is not inconsistent with Clifford Allbutt's views: the coronary arteries spring from the aorta immediately above and still within reach of the aortic valves. They are found in higher vertebrates only, represent a direct extension of this part of the aorta, and are of very late phylogenetic origin. Therefore we may expect that the central nervous localization of these vessels in the spinal cord should be the same as that of the aorta itself.

(b) *Chronic sclerosis or syphilis with more or less marked narrowing* is one of the most frequent pathological findings in elderly people. Every observer must sometimes have wondered how cases with high-grade narrowing or even occlusion of large branches, accompanied by widespread loss of muscle tissue, were completely devoid of symptoms of angina pectoris. Coronary sclerosis is such a frequent condition, where there has never been angina, that we must conclude that something apart from coronary sclerosis must be present to cause angina. For many years it has been acknowledged that normal coronary arteries may be found in patients who have suffered from typical angina pectoris during life. The conclusion must be that there must be other causes for angina, apart from coronary sclerosis. In order to adapt anatomically normal coronary arteries to this explanation of angina, two hypotheses have

been brought forward: some say that such cases cannot have been true angina (vera!), but only a pseudo form, which of course is an obvious *petitio principii*. Others take for granted that in such cases angina was due to paroxysmal spasm of the coronary arteries. This last hypothesis is very popular in many countries, especially on the Continent, and in Vienna is accepted as the explanation of angina pectoris. It will be discussed separately.

When we try to explain the clinical aspect and symptoms of angina pectoris by means of chronic coronary disease, we encounter the greatest difficulties. Omitting embolism, which we have discussed already, I cannot see any other way in which coronary sclerosis can affect the heart muscle except by a diminished blood supply. I cannot see that any other result could follow from a diminished blood supply, except a damage to the function of the heart muscle. We have also seen, and supported with numerous arguments, that diminished strength of the heart certainly does not cause anginal pain; nay, it may even abolish it. It must always be kept in mind that angina pectoris is not heart failure—the condition of the heart being one of hyperkinesis rather than of hypokinesis; with hyperkinesis the blood supply of the heart cannot be inadequate. Nor must we forget that subjects of angina may live many years without suffering from dyspnoea or from stasis of the great veins or of the venous system of the liver. Thus I cannot see how it is possible to accept sclerosis of the coronary arteries as the cause of angina pectoris.

(c) *Vasomotor Spasm of the Coronary Arteries*.—This is a favourite hypothesis of anginal pain. If we accept it we should at first try to find an explanation of the mechanism of the pain. There are two possible sources of the pain: (1) ischaemia of heart muscle; (2) the spasmodic contraction of the vessels. In so-called "vascular crises" (Pal) it is the ischaemia which is mostly looked upon as being the cause of the pain, along the same lines as in intermittent claudication. Concerning this last condition there is clear experimental evidence. MacWilliam and Walker showed that during suspended circulation in the bloodless arm muscular action becomes very painful, even before the muscle reaches a point of complete exhaustion. They compared this condition, as others have done, with angina pectoris. Although at first this explanation seems almost convincing, it will not stand more critical examination. There is a wide difference between the sensory nerve supply to voluntary muscle and to the heart. In voluntary muscle the pain is localized in the muscle and is never irradiating, while in heart muscle it is the opposite. It must not be forgotten that the segmental localization of pain in heart muscle differs from that in angina. Can the coronary arteries themselves be the starting point of the pain? We have admitted that in embolism of the coronary arteries this may be the case. Embolism, however, is a well recognized pathological condition, but of vasomotor spasm in general we have little knowledge. We must await the results of recent experimental work on the peripheral circulation before attempting to explain seemingly well known phenomena in certain painful conditions. Let me remind you that the frozen bloodless limb is not painful—it becomes so only when the blood begins to flow into the vessels and distends them. In Raynaud's disease it is not when the fingers are white and bloodless that pain is present, but when they become suffused by a sudden reflux of the circulation. These and other facts seem to suggest that it is not the contraction but the distension of vessels which gives rise to pain.

There are, too, pertinent arguments against the hypothesis of constriction of the coronary vessels; no one has ever succeeded in obtaining evidence of the existence of vaso-constrictor nerves in the heart (Bayliss).³ When the fact has to be considered that a local application of adrenaline does cause a coronary constriction,⁴ the wider fact remains that adrenaline, exhibited through the circulation, affects the coronary vessels in an exactly opposite way to the effect produced in the vessels in the rest of the body. Peripheral vaso-contraction causes a rise of blood pressure in the aorta and widens (by this rise of blood pressure) the aorta and coronary vessels; this dilatation of the coronary arteries is accompanied by an increased blood flow through the blood vessels of the heart. There is thus an antagonism

between the peripheral and the coronary circulation. As far as angina is concerned, it is much more in keeping with the present state of our knowledge to suppose that *peripheral vaso-constriction*, a condition called "vasomotor angina," by increasing the blood content of the aorta and coronary arteries and thus distending their walls, *may be the condition which excites the attack*. In brief, I hold that the theory which ascribes angina to a spasm of the coronary arteries is, in the present state of our physiological knowledge, destitute of substantial evidence.

3. Diseases of the Proximal Part of the Aorta.

Shortly after the appearance of Heberden's first description there were communicated to the Royal College of Physicians accounts of two autopsies made on patients who had suffered from angina of the common form described by Heberden. The only lesions found were, in one case, "patches in the supravulvular part of the aorta"; in the second, severe disease of the aortic valves and of the adjacent part of the aorta itself, with also extensive calcification and destruction. In both cases the left ventricle was hypertrophied but otherwise quite healthy. One hundred and fifty years later Clifford Allbutt looked up the problems of angina and found that his experience in the wards and in the *post-mortem* rooms led him to verify the findings of his predecessors of a century and a half before. As time goes on an ever-increasing number of physicians are adopting Clifford Allbutt's views, but even now there is no sort of general agreement as to the exact cause of angina. From my own experience, both clinical and pathological, I am convinced that Clifford Allbutt has put us on the right track. I hold the opinion, at least for the time being, that all symptoms, all peculiar features of angina pectoris, are best explained on the theory of disease of the proximal aorta. Pathological conditions of the heart muscle, and of the coronary arteries, become of secondary importance, for nearly always there is also disease of the proximal aorta. These pathological conditions may complicate cases; they may dominate their clinical aspect; they may even kill the patient. Nevertheless, they cannot be regarded as the cause of angina. In autopsies on patients who have died during an attack of angina I have always been impressed by the condition of the proximal aorta—the presence of syphilitic atheromatous or end-arteritic lesions, by which the coronary orifices are often narrowed or the coronary walls affected—still more convincing if we compare them with those cases where there has never been angina, where the ascending aorta is free from disease, and yet the heart muscle has undergone extensive damage and the coronary arteries are the seats of marked sclerosis.

In endocarditic disease of the aortic valves I have occasionally found a singularly convincing proof that angina is of aortic origin: I have seen angina in two young people—one a boy of 16, another a young woman of 22; a third instance was in a man under 40. In all three there was the most marked incompetence of the aortic valves, but there was no sign of heart failure; on the contrary, the heart was beating tumultuously during the anginal attacks; the proximal vessels were so under the stress of the enormous pulse waves that a loud systolic arterial sound, centred under the manubrium, was audible at a distance of several metres. Nine years ago I relieved the attacks of angina in the young woman by giving her amyl nitrite; the drug has successfully prevented her fearful attacks throughout the intervening years. In her case I do not expect her anginal attacks to cease until the final breakdown of her left ventricle. In the case of the boy I have just alluded to severe anginal attacks, lasting fifteen to twenty minutes, were instantly relieved by the intravenous injection of half a gram of quinine, which also at the same time caused a marked fall in the systolic and diastolic arterial pressure.⁵ I do not see that the pain of these cases can be explained in any other way than by supposing that the exaggerated action of the heart has brought about a stretching of the badly dilated aortic wall.

We have seen that all factors which ensure a greater filling of the aorta, thus increasing the stress on its walls, will give rise to pain, so long as the heart is equal

to its increased task. The hyperkinesis of the heart, manifested during the attack, may be explained by the influence of two factors—psychical reactions brought about by the pain, and a direct action on the reflex pressor centres in the spinal cord. Every influence which lowers the action of the heart, diminishes its output, allays excitement, releases peripheral vaso-constriction, reduces abdominal tension, will help in bringing the attack to an end. Nitroglycerin owes its efficacy to its power to bring about dilatation of the peripheral vessels, thus relieving the over-distended aorta. The alleviating action of atropine, emphasized by Clifford Allbutt, is not so easily explained. It is probable that this drug shuts off vagal influences, which in all likelihood play a role in the dramatic events of angina. I have found atropine most useful in cases of angina where the pulse was slow. I have a tracing of a case of angina where attacks came on after short periods of slowing of the pulse—periods extending beyond some ten or fifteen beats. Accepting anatomical lesions of the aortic wall—which may be limited to small areas—as the cause of anginal pain, we can understand how it is that physical signs may be absent, and how patients who live quietly, avoiding mental excitement and bodily exertions, may have long and apparently healthy lives.

This conception of the mechanism of the pain of angina and its specific localization are in keeping with what is known concerning the central localization of afferent impulses from the aorta (*vide* Head, *loc. cit.*); the area of irradiation of afferent impulses, in cases where the heart itself is involved, is quite different.

THE TREATMENT OF ANGINA BY SURGICAL METHODS.

As I regard the lesion of the aorta as the starting point of the pain I cannot agree with those who regard angina as a neuralgia. In severe toothache we may find the pain distributed as in trigeminal neuralgia, but we do not apply the name "neuralgia" to such cases; and as regards treatment, we attend to the tooth, not to the fifth nerve. It is the same in angina. In its treatment we must concentrate our attention on the aortic lesion which is the source of the pain. We cannot remove such a lesion as we do a diseased tooth, but we can search for the pathway which carries pain-evoking stimuli from the proximal aorta to the spinal cord, and having found it cut or block this *via dolorosa*.

The proposal to extirpate part of the sympathetic cardiac nerve system to abolish pain is not new. Long ago the idea occurred to François Franck; it was put into practice for the first time in 1916 by Jonnesco of Bucarest, who before then had gained a wide experience of operations on the cervical sympathetic system. His first operation for the relief of angina was a complete success, but for a long time no further cases were undertaken.

Our conception of angina pectoris, based on Clifford Allbutt's conception of it, leads us to attach an ever-diminishing significance to heart failure and to disease of the coronary arteries, and to attach an ever-growing importance to the afferent nerve supply of the proximal aorta. It has been known for long that the depressor branch of the vagus is the principal afferent nerve of the proximal aorta. It seemed, therefore, worth considering whether a resection of the depressor branch of the vagus might be the means of abolishing the pain of angina. The considerations which weighed with me—both for and against such an operation—were the following. I must admit straight away that there is no *curative* treatment of angina. It is true that cases may improve; by adopting reasonable habits of life patients may successfully stave off attacks; but in the majority of cases, sooner or later, the attacks come back. Normal life becomes impossible; life may become a drawn-out agony. The attacks themselves damage the heart further, hasten the progress of various affections of the organ, and often kill the patient. He who has reached the ripeness of experience to which I alluded in the opening part of this lecture must acknowledge that our attention must be directed, first and most, to the bringing of relief to such patients, even if we have to resort to surgical operations which are attended by great risks.

The depressor nerve, discovered by Ludwig and Cyon, is

a branch of the vagus, one root splitting off from the main trunk, while the other issues from the superior laryngeal. There is proof that this nerve, on stretching of the aortic wall by high blood pressure, brings about a rapid fall, thus relieving the stress on the aortic wall. I will mention, ever so briefly, some of the more important results yielded by experimental investigations—some of them old, some quite recent. Tschermak, who was one of the first to carry out a systematic investigation of the depressor nerve, published only a few weeks ago⁶ the results of renewed experiments. As far as it is possible to tell, the depressor has its distribution confined to the proximal part of the aorta. Its distribution has never been seen to extend to the heart. Its upper termination is in a group of cells contained in the jugular (higher) ganglion of the vagal trunk. A second group, lying close to the depressor group, belongs to fibres of the superior laryngeal nerve. There are numerous communications between the depressor and branches of the cervical sympathetic system described by Tschermak (loc. cit.), Bräucker,⁷ Shawe,⁸ and many others, which would account for afferent impulses from the aorta being conducted by sympathetic tracts to the spinal cord. Tschermak is still of opinion that the depressor nerve is the only sensory nerve of the aorta, and admits that its stimulation may give rise to sensation and to pain.* Another effect of stimulating the depressor is slowing, or even arrest, of respiration. Here the curious respiratory phenomena of angina pectoris, which have already been mentioned, and which include difficult breathing or even the lack of any desire to breathe, find a rational explanation.

All this evidence gives support to the idea that section of this nerve should bring relief to the sufferers from anginal pain. On the other hand, it must seem strange that in a disorder attended by permanent or paroxysmal hypertension we should cut the one nerve which is concerned in the lowering of blood pressure. But what holds true for the normal healthy body is not necessarily valid for one which is altered by disease. There is definite evidence that the depressor action of this nerve may be reversed and converted into a pressor one under the influence of strychnine and other poisons (Sherrington, Bayliss⁹). In angina the nerve endings, the reflex arcs, and the corresponding spinal centres are thrown into a pathological state—one of over-irritability. Head (loc. cit.) has pointed out how much the normal functions of the affected centres in the spinal cord must be changed by widespread irritations set up by abnormal stimuli. The excruciating pain associated with attacks may also play an important part in converting depressor into pressor effects. It seems to me that there cannot be any serious objection to section of the depressor nerve in angina, seeing that it has lost all its useful action—that of a depressor.

There is another difficulty in carrying out this operation—one of an anatomical nature. The formation of the depressor nerve is extremely variable, not only in different mammals, but in individuals of the same mammalian species. This is particularly true of man; in him the depressor nerve has no constant recognizable entity. Nevertheless, Eppinger and Hofer, convinced of the aortic origin of angina, made an exact study of the topography of the depressor nerve in man and animals, and on the knowledge thus gained applied the operation of section of the depressor to a case of severe angina (August, 1922). In this case there was pain both on the left and right sides of the body. The operation was carried out on both sides of the neck. In this case the depressor nerve was differentiated and recognizable on both sides. The result was most gratifying; both attacks and pain vanished at once. The patient had good health after the operation. Some months ago she died of intercurrent disease.

Section of the depressor nerve for the relief of angina has now been performed on some fourteen cases. Single cases have been reported from Halle and Basel; in both the result of the operation was satisfactory. Detailed histories of the Viennese cases have been reported to the Society of Internal Medicine, Vienna, only a few weeks

ago.¹⁰ The chief results which emerge from these cases are: The operations were well borne; no complications occurred. Two patients died. In the first case of double-sided angina resection of the left depressor gave a perfect result. At the second operation, performed on the right side, no isolated depressor nerve was found; the vagus was divided below the point of origin of its inferior laryngeal branch. The pain disappeared, but a fortnight later the patient died suddenly without obvious cause of death. In a second case of right-sided angina no depressor was found. In this case "sympathectomy" was performed—an operation which has been performed for angina with varying degrees of success. In this case extirpation of the whole sympathetic cord was followed by a rapidly developing failure of the heart. Five hours after the operation the patient died of pulmonary oedema.

Although not unexpected, the absence of a clearly differentiated depressor nerve in so many cases proved a great disappointment. This renders it impossible to perform the operation of division of this nerve. It is remarkable that it was mostly at the right side that the depressor was found undifferentiated. In those cases where a somewhat haphazard resection of communicating twigs between vagus and sympathetic was carried out, the operation failed to relieve the pain of angina. But in all those cases where the depressor nerve appeared in its individualized form, as described by Tschermak and others, the pain *disappeared at once on the side operated on*, and in most cases the success was enduring. Further, it was observed, where there was an opportunity of comparing the two sides, that the left nerve was thicker than the right. The results as a whole I regard as of great promise. Failure resulted in those cases where the depressor fibres were not isolated to form a separate trunk.

A detailed analysis of the individual cases brings out in quite a striking way the beneficial effects of dividing the depressor fibres. If a depressor trunk was recognizable its section gave immediate and complete relief. The effects of operation on one case of angina duplex were very instructive. The patient had clearly marked segmental areas of exquisite hyperalgesia on both sides of the body. Some days after an operation on the left side—a well marked depressor nerve being encountered and divided—the hyperalgesia had completely disappeared on the corresponding side of the body, but on the opposite and unoperated side the areas gave the old reaction when pinched or tested by pin-prick, the right-sided hyperalgesia ending sharply at the mid-line over the sternum.

Quite apart from the bearing such a case has on the possibilities of operative treatment for the relief of angina, we obtain, in this instance, evidence of a kind which we cannot hope to elicit by experiments on animals. We have here definite proof that the left depressor nerve was the sole pathway for the impulses which gave rise to anginal pain and all its sequelae. Knowing that this nerve has its distribution in the proximal aorta, we must conclude that, at least in such cases, the starting point of the pain and of the attack is situated in this structure and in no other.

In other words, we are in the possession of experimental evidence which gives the strongest proof of the truth of Clifford Allbutt's theory of angina. This, indeed, is my chief motive for laying this communication before my professional brethren in England.

QUESTIONS TO BE SOLVED.

Of the many matters which require further elucidation only a few can be mentioned now. *Is there only one depressor nerve or are there several of them?* In his work on the vasomotor system, Bayliss has summed up all we know concerning depressor reflexes obtained from more peripheral vessels (loc. cit., p. 41). In one particular way such peripheral depressor reflexes have a bearing on angina pectoris. The condition which has been named "angina abdominalis" has all the essential characters of angina pectoris, save only that its localization is different. This form of angina is supposed to be produced by a vaso-constrictor spasm of part of the splanchnic arterial field, but the existence of such a spasm has never been verified.

* Sharpey Schafer's investigation makes it highly probable that the depressor nerve contains afferent fibres only. *Quart. Journ. Exper. Physiol.*, 1922, vol. xii, p. 69.

May there not be concerned here a depressor mechanism similar in kind to that attached to the proximal aorta? There are facts mentioned by Bayliss which support such a surmise. This problem deserves investigation.

"Second wind," a term which we owe to English athletes, often plays a part in angina pectoris. It is by no means uncommon to hear a patient say that he suffers most in the first ten minutes of an effort such as walking, and that he finds, if he persists in his effort, that he can walk a longer spell without being compelled to stop, until he may be able to walk for an hour or even longer without bringing on pain. I merely touch on this matter, contenting myself with the remark that we are here face to face with a problem which concerns the peripheral circulation, and more particularly its regulation. It may be, in such cases, that the heart and aorta, owing to some initial difficulty in opening up peripheral pathways, have a difficulty in discharging the greater amount of blood returned to them by the great veins. Indeed, the course of angina may depend not only on aortic conditions but also on circumstances which affect the peripheral circulation.

The sudden death of angina patients offers us a problem of its own, and cannot be dealt with extensively. We are not often present at the attack which kills the patient. I have myself seen death by pulmonary oedema caused by the breakdown of the left ventricle as a sequela of the attack. In chronic cases heart failure may be the cause of death; in these cases there is no pain. Sudden fulminating deaths I have myself never seen. Whether this sudden stopping of the heart is the result of vagus inhibition (Clifford Allbutt), or ventricular fibrillation, as is assumed by many authors, I do not know. It may be true that compression of the vagus of the neck often causes a very strong, even somewhat alarming, standstill of the heart (as I pointed out myself); it may be true that atropine is helpful in many cases (Clifford Allbutt). However, clear evidence of the cause of sudden death is rarely obtainable, and we should not decide too readily in favour of one or some other cause.

Can our medical conscience justify operative treatment of angina? This question, an ethical one, has been frequently brought to my notice. My American friends put the question in this form, "Is it right to extinguish the red light—the danger signal—on the trackway of life?" Is not pain the danger signal for the overtaxed heart? Many reactions, rightly regarded as protective, compensatory, or defensive, may in the course of disease become changed into processes which are highly injurious to the organism. This may become true of referred pain, *défense musculaire*, pyrexia, high blood pressure, and rapid action of the heart in infections and in cardiac disorders. All of these may reach such an intensity that life itself is endangered. Their amelioration becomes the most urgent object of our treatment. This view, which is generally accepted, must be permitted to guide us in the treatment of angina pectoris. As it is anatomically impossible to remove the cause of the pain, we must take such steps as will put to sleep such pain and attacks which threaten life itself, or which render existence quite unbearable. We see how the heart suffers with every repetition of the attack. Daniélopou has shown us, in the most convincing way, that pathological afferent impulses can bring about a discharge of efferent impulses which have a damaging effect on heart and on blood pressure. We cannot afford to neglect any means of giving relief to the most miserable of cardiac patients, particularly if the arguments urged against their adoption are founded only on theoretical considerations. It is a rule or commandment we must follow when the heart and aorta are diseased. The fact that we cannot mend a broken-down valve or patch up a damaged aorta is no reason why we should not make use of what means of treatment may be at our disposal.

What is the best form of operation? As we have seen, resection of the cervical sympathetic nerves was thought out by François Franck and put into practice by Jonnesco. When resection of the depressor nerve was first performed by Eppinger and Hofer (who independently and for different reasons adopted this method of treatment), the older operation on the sympathetic was being carried out by various surgeons in different countries.

Philip King Brown and Coffey of San Francisco published most interesting and partially successful cases of sympathetic resection. Jonnesco has reported several cases, two successful ones. In Germany Brüning introduced similar operations, looking on angina pectoris as an affection of the sympathetic system, or at least as a syndrome which might be treated by Leriche's "peri-arterial sympathectomy" for the same reason that the operation is performed for chronic ulcer, intermittent claudication, etc. In this country A. K. Henry of Dublin discussed the chances of this operation.

Daniélopou has published very important suggestions as to the part of the sympathetic system which should be excised. He points out the necessity of sparing as many efferent augmentory nerves as possible. From all these various operations performed on the cervical sympathetic system good results have been reported. There seems no doubt that the pathway of pain has been interrupted in the performance of many of these operations, and that patients have derived benefit. As to which is the safest and most effective operation it is too soon to give a decisive answer. There remains great need for a much fuller and more precise knowledge of the anatomy and physiology of the nerve pathways and ganglionic masses of the cervical sympathetic. Great differences are found in the structure of this nerve complex. It is our ignorance of this system, as well as of the depressor and other vagal pathways, which offers the greatest obstacles to our obtaining relief by the application of operative procedures. In recent literature we find articles which throw vagal and sympathetic nerves in the neck into one common system and even deny the existence of a depressor nerve.

Clearly we must wait until anatomists and physiologists, by means of experimental evidence and pathological investigation, can throw more light on the problems I have been dealing with in this lecture. A precise history of the results which follow every operation performed on man will place additional knowledge at our disposal. As far as the relief of pain is concerned, such means afford the only way of discovering the best operative procedure. What is necessary in this problem is that we should not be led by theory only, by hypothesis and speculation, or by a desire to push our personal preconceptions. The last word in such matters must rest on clinical evidence and on the facts we can elicit at the bedside.

Personally I am greatly in doubt whether resection of the depressor nerve will be the operation *de choix*, seeing how often it is difficult or even impossible to find. Theoretically it may be held that this is the safest form of operation because in it only afferent nerves are removed, and the essential augmentory nerves are left uninjured. However this may be, the matter most to be considered by us now is that there should be co-operation of effort and division of labour in the various departments of medicine concerned. Why should not this co-operation be international? Some weeks ago a number of men of different nationalities and schools met together, to the benefit of all concerned. Knowing well your famous school of physiology, your great and practical experience of angina pectoris, I thought it might be of value for the progress of knowledge if I might bring this problem in all its bearings and lay it before you. In Vienna we all hope that you will bring your results and lay them before us. Suffering humanity will be the gainer.

[At the conclusion of the lecture Sir Clifford Allbutt commented on some of the points dealt with. His remarks are reported at page 828.]

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