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THE ESSENTIAL FACTOR IN THE CAUSATION OF
ANGINA PECTORIS.

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The object of the following **T**hesis is to discuss, and if possible determine more exactly than has hitherto been done, the essential cause of cardiac pain; with a view to doing so I propose relating as shortly as possible what we already know, and the theories that have been evolved by various writers on the subject, of the conditions frequently associated with this symptom; drawing especial attention to that degree of cardiac pain which originally attracted the attention of Heberden and which he named Angina Pectoris. I approach the subject with considerable diffidence knowing as I do the work that has already been done by so many of the ablest physicians, both those of the past and those no less distinguished who are still adding to our knowledge of the subject, such as Powel, Fraser, Gibson, Morison, Russel, Mackenzie etc., in this country, and others in America and on the continent.

I do not propose reporting a series of cases and then discussing them, nor going into the question of

treatment except in so far as it may help us to elucidate the cause or causes of this comparatively rare but particularly interesting disease; but will give a general account of the History, Anatomy, Physiology, Aetiology and Symptomatology of the affection, with mention of my own observations, concluding with the conclusions which seem to me to result from this study of the subject.

A satisfactory definition of Angina Pectoris is impossible to give since we are ignorant of the precise anatomical or pathological conditions on which the symptoms of the disease depend, in spite of the attention it has attracted since it was first described by Heberden in 1768. Some authors extend the application of the term to such an extent as to include all pains felt in the cardiac region that are of an anginal character; one cannot help feeling that this is distinctly unfortunate, and that as some writer has said, these pseudo angina affections stand in much the same sort of relationship to angina proper as epileptiform convulsions do to true epilepsy.

By many (Latham, Osler, etc.) it has been looked upon as "an assemblage of symptoms with no constant pathological condition."

It has been described under various names, the

following being some of them Pectoris dolor, Syncope anginosa, Angor Pectoris, Cardiodynia, Neuralgia cordis, Asthma dolorcum, Suffocative Breast pang, Hyperaesthesia plexus cordis, Stenocardia, Cardiac epilepsy. French, Angine de poitrine. German, Brust braune. The name "Angina" has been objected to on the grounds that it is "singularly inappropriate inasmuch as neither the symptoms nor the danger have aught to do with strangulation"; this objection seems to me to be quite uncalled for, as taking "Angina" to be the same as "Angor" we find the latter is used for anguish or torment of a transitory nature as opposed to "anxietas" differt anxietas ab angore: neque enim omnes anxii, qui anguntur aliquando; nec qui anxii, semper anguntur. Cic Tusc. 4. 12. 27.

The whole subject of cardiac pain has interested me greatly for a good many years both in hospital and private practice, and I have been much struck with the difference that one finds in the subjective phenomena complained of by the two types of patients; one noticeable point being that the lesser degrees of cardiac pain are relatively much more common in the out-patient department than in one's private practice, this I have attributed to anaemic conditions, from improper or

insufficient food, being more commonly met with amongst the class of patients that come to hospital for advice; on the other hand it is the rarest thing possible to come across the more acute and paroxysmal forms amongst the latter. That one does so rarely come across the more striking and dramatic forms one regrets from the scientific point of view, but one feels that the less fortunate members of society are to be sincerely congratulated that they are to such a great extent saved from falling victims to what is by many considered the most appalling disease of all those that flesh is heir to.

Since writing the above I have met with two cases at hospital.

The Cardiac Innervation.

The heart derives its innervation from the Pneumogastric, Spinal accessory and Sympathetic, these nerves have a close relationship and are connected with each other in the medulla, in their course; in the superficial and deep cardiac plexus, in the cardiac ganglia and in their distribution to the heart; they also have communications with other cerebral nerves and with the cervical and brachial plexus, they send branches to the lungs and all the abdominal viscera, in the medulla they are connected at the cardiac and vaso motor centres. **The**

superior cardiac nerve is supplied by the pneumogastric, the inferior cardiac nerve by the spinal accessory; the superior cardiac nerve is an afferent nerve conveying impressions from the heart to the central nervous system, these impressions or their results, are conveyed by the inferior cardiac nerve which is inhibitory to the heart; the impressions are also reflected by the vaso motor nerves from the vaso motor centre causing relaxation of arteries, especially the abdominal, thereby relieving the pressure on the heart.

The superior cardiac nerve is supposed to be the sensory or the chief sensory nerve of the heart (in health), Head has pointed out that "the sensory nerves of the heart are in relation with the spinal cord from the first to the eighth dorsal roots, namely auricle with fifth to eighth dorsal, ventricle second to fifth dorsal, ascending aorta first to third dorsal and third and fourth cervical; in the early tubal form of the heart the auricles are placed below (posterior to) the ventricle and their nerve supply is lower in the cord." In Angina Pectoris we shall notice that the nerve roots which receive the most intense impressions are the second dorsal roots, the painful impressions are referred to the corresponding surface areas of nerve distribution, and Powel says:

"taking the left ventricle as the most common primary seat of the pain and the second dorsal as the chief recipient of the disturbance, when intense enough to pass beyond the cervical cardiac ganglia, we can account for the most common reflected surface pains." Morison has recorded a case in which disease of the right side of the heart was accompanied by symptoms of angina affecting the corresponding side of the chest and arm.

Before going on to the consideration of the main subject of my thesis viz: Angina Pectoris, I should like to make a few remarks upon some of the slighter and more common varieties of cardiac pain, or pain that is apt to be referred by the patient to the heart.

One of the commonest is that felt by neurotic patients or those suffering from nervous debility, it varies considerably in character being generally dull and constant, on the other hand it may be sharp and darting, exertion as a rule increases the discomfort; accompanying it is a feeling of anxiety or oppression in the praecordium, called by the Germans "herz angst". There are generally indications of vaso motor disturbance such as palpitation and coldness of hands and feet.

Another variety is the sharp pain felt under the

mamma accompanied by palpitation, and is particularly common amongst epileptics and persons suffering from hysteria. It is not accompanied by any evidence of organic change in the heart, and its origin is considered by most observers to be probably in the central nervous system.

Neuralgia and Neuritis of the intercostal nerves cause paroxysmal pains, it may precede the development of herpes zoster; there are often points of tenderness, these tender points being where the greatest pain is felt, correspond anatomically with the positions where the nerves have their exits through the fascia to the surface. This variety is usually found in people with a gouty or rheumatic diathesis but may also occur with anaemic and neurasthenic patients.

The nerves of the pleura may also be subject to neuralgia, the pain is diffuse and is said to be relieved by pressure with the whole hand but increased by pressure with the finger tips, personally I have found it impossible to diagnose from the next variety of pain referred to the cardiac region and that is, Intercostal myositis or Myalgia, here too the pain is diffuse and is relieved by uniform pressure, it is frequently seen in phthisical

patients brought on apparently by severe bouts of coughing, there is often a tendency to rheumatism, and similar kinds of pain may occur in other parts, such as lumbago.

Pleurisy if localized, and empyema, in the cardiac region may also be referred to as pain in the heart; various other rarer, localized conditions may cause pain which at first sight might be attributed to a cardiac origin, such as periostitis of rib, a localized tuberculous abscess between pericardium and the walls of the thorax.

Pericarditis. The pain here varies to a marked extent, often being entirely absent, at other times it is acute and lancinating or it may be dull and persistent, it may radiate to the left shoulder and down the arm; it is increased by movement, by pressure and by the action of the diaphragm.

Aortitis in the acute form causes a severe and continuous pain which often extends along the aorta, often radiates to the shoulder and may be referred to the sternum and extend along the spine.

Atheroma of the aorta may also cause paroxysmal pain in the same situation.

Aneurism of the aorta causes pain chiefly by pressure on adjacent structures, it is generally dull, aching

and boring in character, and is increased by movement; when nerves are pressed upon the pain may be acute and neuralgic in character, it may follow the course of the nerves and be associated with numbness and tingling.

In disease of the heart itself the pain may be due to

I. Disturbance of the rhythm.

II. Valvular disease.

III. Angina.

In the first division the palpitation may cause pain and distress, and often is very alarming to the patient, this is very noticeable in Graves's disease and in some cases of anaemia.

In Valvular disease it may be noticed how much more commonly it is associated with a lesion of the aortic valves than any of the others, here the pain is referred usually its site of origin, and is much aggravated by exertion. In mitral stenosis too pain is a common symptom, the pain may be dull and constant, or there may be pseudo anginoid attacks.

HISTORICAL.

Angina pectoris was first recognised and systematically described by Heberden in 1768, but previous to that several writers had described cases, for instance Seneca

gives a graphic account of the paroxysmal attacks from which he suffered and which are considered by many to have been angina; Morgagni in 1707 in describing a case of aortic aneurysm mentions the paroxysms of pain which the patient suffered; Rougnon in 1768 when writing to a friend described the death of a certain Captain Charles who seems to have suffered from the same disease.

Jenner in 1799 suggested that the essential cause of angina was sclerosis, calcification or some obstruction of the coronary arteries interfering with the blood supply of the heart; though he only published his views in 1799 he had come to this conclusion some 20 years previously, as is shown in a letter of his to Parry and soon after in a letter he wrote to Heberden but did not send for fear his friend John Hunter should see it, as he believed that John Hunter was suffering from this condition, which afterwards proved to be the case.

Parry agreed with Jenner and considered that the heart owing to faulty blood supply was unable to cope with any extra strain put upon it, he considered the condition to be one of heart failure or paralysis of the heart, and called the disease "syncope anginosa."

Allan Burns writing in 1809 agreed with the above views and considers the cartilaginous arteries act upon

the heart like a ligature tied tightly round a limb, which would only be able to work under the most favourable conditions.

In 1808 Baumes asserted that it was essentially a neuralgia; Desportes held a similar view.

Laennec writing a few years later agreed, and called the disease "neuralgia cordis," looking upon it as an affection of the sympathetic system.

Amongst others who have classed it as one of the neuroses is Jurine who writing in 1815 considered it to be "an affection of the pulmonary nerves"; Bouilland considered that the lesion was in the phrenic nerves.

Forbes in 1832 and Hope 1839 also agreed with Laennec's views.

Gintrac writing in 1834 gave it as his opinion that the pain was caused by an irritation of the fibres of the cardiac plexus.

To Walshe 1881 we owe the word "Pseudo-angina" or "imitation of the true disease"; he considered true angina to be a "paroxysmal neurosis in which the heart is essentially concerned"; he draws attention to the frequent occurrence of "Pseudo-angina", while on the other hand he points out that true angina is a very rare disease.

Landois writing in 1863 divides angina into four

groups, I. Cases caused by disturbance of the excito-motor or accelerator nerves of the heart. II. Those due to irritation of the cardiac branches of the vagus. III. Those arising from reflex irritation of the abdominal viscera "angina reflectoria", and IV. Such as arise from vaso-motor disturbance in various parts of the body "angina vaso motoria."

Trousseau regarded it as an idiopathic neuralgia, and called it "cardiac epilepsy", he advised long continued employment of belladonna.

Lancereaux writing in 1863 agreed with the views expressed by Gintrac 30 years previously, he published three cases in which the autopsy revealed inflammatory changes in the cardiac plexus.

Romberg's view is that it is a neuralgia of the cardiac plexus; while Friedreich looked upon it as a hyperaesthesia of the cardiac plexus.

Peter agreed with Bouilland as to the phrenic nerves being often the nerves affected; but considered other cases to be due to a neuritis of the cardiac nerves.

Sansom looks upon the paroxysms as nerve storms provoked by impulses conveyed to certain cerebrospinal centres.

Having quoted so many of those who hold to the

neuralgic or neuritic origin of the pain, I will now return to some of the earlier writers who held one of the other two theories that have been most generally favoured, namely that it was due to I. An interference with the blood supply of the cardiac muscle or II. That it was due to a spasm, convulsion, or cramp of the cardiac muscle or part of it.

We find that in 1816 Kreysig looked upon the complaint as due to Ischaemia of the myocardium in consequence of defective blood supply from sclerosis of the coronary arteries; a few years later Reeder (1821) amplified this theory of cardiac ischaemia by maintaining that the condition could be brought about by any lesion interfering with the blood supply to the heart muscle. - Tiedmann (1843) was of the same opinion; in reference to this theory of Ischaemia Boullaz in 1831 when discussing the relation between lessened blood supply and pain introduced the name "Intermittent claudication"; he observed that a mare which suffered from obliteration of the femoral arteries, if made to trot after a few minutes exercise would fall, the limbs being seized with engourdissement and severe pain, the collateral arteries of the limbs which in repose could carry on the circulation sufficiently well, with exercise were compressed and could

not furnish sufficient blood.

Sir Benjamin Brodie 1846 in considering the nature and cause of the pain often met with in senile gangrene, compared the same with that of angina pectoris.

Latham when writing about the same time, considered the disease to be due to no constant pathological condition; he thought the pain was due to a spasm of the heart and says "in spasms of smaller degree the heart fails to close freely upon the blood and to impel it freely into the arteries; in its spasm of greater degree it fails to project it altogether."

Stokes in 1854 differed from this view of Latham's as to its being a spasm, and agreed with Parry.

Leyden considers the attack to be due to degenerative and inflammatory changes in the heart's muscle depending upon disease of the coronary arteries.

Rosenbach's views I will give rather more at length: his view is that there is some alteration in the contractions of the cardiac muscle, which alteration may, but does not necessarily, lead to functional weakness; in consequence of this change, irritation is imparted to the sensory tract, and this stimulus sets free the various forms of pain and anxiety felt. He considers that this true heart pain is an indication of the heart muscle being

less able than usual to accommodate itself to sudden change taking place in the performance of its work. Now and then obstacles residing in the heart itself and capable of interfering with its perfect action may give rise to the phenomena of angina pectoris.

One of the most important additions to our knowledge of the disease more especially as regards treatment is that of Sir Lauder Brunton who in 1867 discovered that the pain and distress of many cases of angina could be relieved by the dilatation of the peripheral arteries by nitrite of amyl; the fact that relief follows the administration of this drug and others of the same nature has been used as an argument that the angina is due to arterial spasm but this does not necessarily follow, in many cases it causes no relief when there is distinctly high arterial tension and in other cases it brings relief when the tension is not high, its efficacy in these cases may be due to diminishing the accumulation of blood in the heart-centres.

Morison though "supporting no single theory of angina pectoris" introduces another factor, namely an intravascular aneurism of one of the coronary arteries pressing upon adjacent nerve fibres.

Russel has recently brought forward the interesting

line between cardiac and angina pectoris.

hypothesis that the angina is due to a hyper-sensitive-ness of the vaso motor centre causing an increase of the normal arterio cardiac reflex, which is induced by digestive disturbance, in addition to the more usual causes of angina, physical exercise and mental emotion.

Musser emphasizes the relationship between cardiac dilatation and angina and holds (1) that the pain of the latter is mainly due to increased intraventricular pressure (2) that dilatation is attended with subsidence of pain, because of the relief of this pressure (3) that angina may occur in a patient who has had dilatation of the heart when the organic condition (dilatation) is removed by treatment and (4) true angina when it occurs in dilatation of the heart admits of more favourable prognosis than if associated with other mural changes in the absence of dilatation.

Kennig lays stress on the importance of complete physical rest for some days or longer after a severe attack on account of the important cardiac changes that not infrequently follow, for instance myocarditis, dilatation of one or another cavity, acute pericarditis, functional derangements such as oedema and diminution of the amount of urine.

Gibson holds that it is impossible to draw a distinct line between between cardialgia and angina pectoris.

Huchard classifies Angina as follows: (A) True Angina which he maintains is in all instances caused by coronary disease inducing ischaemia of the heart muscle. (B) Pseudo-angina, the latter he regards as being composed of three varieties The Reflex, The Vasomotor and The Toxic; in all three he considers the starting point to be not in the heart but some peripheral or visceral nerve, the impulse passes to the medulla and on reaching the sensory centres evokes a sensation of pain that radiates into the chest or down the arm with phenomena that point to a coincident stimulation of the vaso motor and vagus centres; he particularly emphasizes the fact that tobacco is a common cause of the toxic variety; and he describes three subvarieties Angina gastro-tabagique where there are merely digestive disturbances, Angina spasmo-tabagique, here he considers there is spasm of the coronary arteries, and Angina sclero-tabagique where there is sclerosis of the coronary arteries. He insists on the fact that none of the Pseudo-anginas are due to effort.

In True Angina he considers that the heart itself is the starting point of the attack and that the angina is originated in all cases by more or less sudden anaemia of the heart muscle due to atheroma or imperfect circulation in the coronary arteries; - from the heart the

stimulus ascends by way of the sensory centres and finally reaches the medulla, thence it is reflected along the intercostal nerves and brachial plexus as a manifestation of pain; the stimulus next reaches the vagus centre and from here an inhibitory impulse is sent down to the heart and declares itself by slowed and it may be intermittent action of the heart. Such an inhibitory action explains the sense of constriction and impending death, as well as the dilatation of the cardiac cavities so often noticed. He considers the nocturnal seizures are apt to be more severe as well as of greater duration because "the rise of blood pressure incident to the recumbent position does not subside quickly even after the patient leaves his bed, whereas that due to effort or emotion yields promptly to the removal of the cause." Another interesting point that he notices is the occurrence of attacks of pain of an hysterical nature in a patient suffering from cardiac or vascular disease, and the difficulty that naturally arises in coming to a correct diagnosis of the case.

Here I should like to point out that I think Huchard is wrong in his explanation of the nocturnal seizures when he says that there is a rise of blood pressure in the recumbent position. I have made a considerable number of observations as to the effect of position

on blood pressure and find that there is a considerable rise of blood pressure on assuming the erect position, averaging about 10 mm., the instrument that I have chiefly used being Oliver's Haemomanometer and I have got practically the same results with the Riva Rocci instrument.

Aetiology.

The classifications into which Angina Pectoris has been divided are numerous, one of the commonest being as follows: I. True Angina. II. Pseudangina or False angina, and subdividing the True variety into A. Primary cardiac Angina and B. Secondary cardiac Angina.

Personally I agree with those authors who object altogether to the term "False Angina" unless it be meant to denote some neuralgic condition of the thoracic wall.

Still the above classification being so commonly accepted for the present we may agree to adopt it.

Pseudangina the Angina Pectoris vasomotoria described by Eulenberg, Nothnagel and others is looked upon as a neurosis of the vaso-motor system in which occurs a paroxysmal contraction of "the systemic, pulmonary and cardiac vessels", thus causing embarrassment of the heart's action.

Primary cardiac angina in which the heart is the

primary seat of the disease, the lesion being any one of numerous valvular and muscular affections.

Secondary Cardiac Angina is looked upon as caused by the same neurosis as in Angina Pectoris vasomotoria in addition to which the heart has some serious valvular or textural disease.

Continuing temporarily to adopt for convenience the above classification, several very interesting points are brought out if one compares their aetiology, take first the question of Sex, we find that "Angina Pectoris Vasomotoria" occurs about equally commonly in both sexes, for while the women may show what one might call a natural tendency to the disease, man rights the balance to his disadvantage by alcohol, gout, syphilis, tobacco and overwork; as regards True angina a better name for which is Angina Pectoris Gravior man is said to suffer in the proportion of over 90 %, at least this is the proportion given by most observers but Trousseau says on the other hand "I do not think it has been proved that males are more subject than females to this singular affection." My own experience has been too limited to draw any conclusions.

Age. "Angina Pectoris Vasomotoria" may occur at any age but as one might expect in women it is very apt

to occur about the climacteric period; Angina Pectoris Gravior is distinctly a disease of middle life the great majority of cases occurring between the ages of 40 and 60.

Occupation, Habits, Station in life, as regards these points the incidence of both varieties fairly agree, the following conditions appearing to be distinctly predisposing causes, high living, sedentary occupation, anxiety, worry, mental strain while it has been a noticeable fact what a large number of distinguished men there has been amongst those who have fallen victims to the disease, on the other hand it is relatively far less common amongst the poorer classes especially amongst those employed in manual labour.

Heredity, That there is some slight tendency for the disease to be hereditary is maintained by some writers on the subject, but the rarity of the disease makes this difficult of proof, it may be stated, however, as a fact, whether it be regarded as a mere coincidence or not that patients who suffer from angina will assert that a parent had a similar complaint.

(Just after I wrote the above a gentleman came to see me whose uncle and grandfather had both died of angina).

Another point I should like to draw attention to

and that is in my limited number of cases a large proportion have occurred in particularly long lived families, I do not know if other observers have noticed the same thing.

Another point as regards the question of heredity. Eulenberg and Trousseau have pointed out that in certain families angina alternates with epilepsy and insanity, while other observers have shown that members of the same family in which the disease has occurred have shown traces of hysteria others have suffered from asthma and others again from neuralgia.

Poisons and Toxins such as those of Gout, Rheumatism, Alcohol, Syphilis, Plumbism, Influenza, Malaria, Tobacco, Uraemia and Constipation seem at times to be either predisposing or exciting causes.

Symptoms.

The symptoms both objective and subjective vary to a marked extent, more especially the former, the first attack nearly always comes on suddenly and whilst the patient is exciting himself slightly, especially after a meal; on the other hand it may come on when the patient is in bed or upon his first getting up, cold air is sometimes an exciting cause, as is violent emotion.

The pain is usually felt at the lower end or beneath the sternum, generally to the left of it, the pain is often excruciating, and is variously described as burning, tearing, stabbing, crushing and lancinating; with the pain there is generally a feeling of fear of impending death, the patient feels that if the pain does not quickly stop he must certainly die; the pain often extends up to the left shoulder and down the arm not so frequently to the right shoulder and arm, or to the head and neck, less commonly to the lower limbs or the region of the abdominal viscera.

The breath is held for fear of aggravating the pain, for the same reason he feels that it is necessary for him to stand absolutely still leaning against or holding to anything he can for support; - as the attack passes off he may feel a numbness or tingling in those parts to which the pain had radiated. As the attack ceases there is often the getting rid of flatulence; the duration of the attack may vary from a few seconds to several minutes, there may be less acute attacks lasting several hours, the attacks may keep on recurring or there may be no return for months or even years, on the other hand the first attack may be fatal; occasionally after the patient has been subject to them for years they may entirely cease.

The objective symptoms vary considerably more than the subjective; the agony the patient suffers is reflected on his face, which is usually pale, or an ashen grey or it may be flushed, the latter especially when the attack is passing off; the skin is usually cold and covered with sweat; at the end of the attack the patient generally passes a large quantity of urine; the mental faculties are not affected as a rule but the attack often leaves the patient frightened and nervous.

The pulse is usually fast, small and low tension, occasionally it is of high tension (a patient that I have just seen had a systolic blood pressure in his brachial artery of 230 mm. with Oliver's Haemomanometer), more rarely it is irregular or intermittent, it may be markedly slow, some writers maintain that this is the rule and not the exception, often it is not affected at all.

The above is a short sketch of what one usually meets with in an attack of "true angina", but the following symptoms may also be noted, and they are said by some observers to indicate that the patient is not suffering from any of the valvular or textural heart lesions referred to in the next section; instead of keeping still, holding himself in one position he writhes with the pain and throws himself about like a person is apt to do who is suffering

from any ordinary painful affection, he tries by changes of position to get relief from his agony; the pain too is said, I cannot say with what truth, to be less excruciating than in those cases where there is a gross heart lesion; it is also said that the patient has less of the fear of impending death.

Morbid Anatomy.

In the great majority of cases some organic disease of the heart or the aorta has been found, fatty degeneration of the heart wall being on the whole the most common, even more so than calcification or some form of obstruction (thrombosis, embolism, stenosis) of the coronary arteries, which at one time was considered to be the essential cause of the disease; as regards valvular disease it may be noted that aortic affections are much more commonly met with than mitral; in connexion with disease of the aorta and aortic valves I would draw attention to the close relationship of the cardiac plexus to the root of the aorta and of its continuation the coronary plexus to the coronary arteries, it has been pointed out that "the milder forms of angina are frequent in slow aortic sclerosis." As regards the frequency or **rarity** of the occurrence of angina in connexion with obstruction or regurgitant lesions at the aortic

orifice, it is difficult to decide, the number of cases recorded has not been sufficiently large to lead to a definite conclusion, some authors asserting the predominant influence of the one and others equally maintaining the frequent association of the symptom with the other kind of lesion; - cardiac dilatation and dilatation of the aorta are frequently met with, also aneurism of the aorta; the following conditions have also been noted fatty infiltration and fibroid disease, infarction and syphilitic arteritis in the heart wall, pericarditis and adherent pericardium, in fact nearly every lesion of the heart and aorta have been observed in connection with this striking but baffling disease; - the heart has generally been found to be relaxed and full of blood, on the other hand it may be, but very rarely, contracted and empty.

Various abnormalities have also been found in the nervous system connected with the innervation of the heart, amongst them being affections of the vagus, phrenics, cardiac plexus, and cardiac ganglia.

The Coronary Arteries.

It has long been a keenly debated point whether the coronary arteries of the heart have any direct nerve

supply, and whether they are under the influence of the vasomotor system, many authorities maintaining that there is no evidence of such action, others maintaining just as emphatically that there is ample evidence of their being so governed.

Consulting the literature on the subject I find that Martin observed that the coronary arteries dilated on excitation of the peripheral end of the vagus nerve, and during asphyxia; in the latter case the dilatation occurred before the rise of aortic pressure. These effects Martin ascribed to the influence of coronary vasomotor nerves: Roy and Adami also obtained some evidence of the existence of vaso dilators passing to the heart by the vagus, and vaso-constrictors by the sympathetic. Brown Sequard 1854, and Porter 1896 state that stimulation of the vagus in the lower cervical region causes contraction of the coronary arteries. These effects on the heart and blood vessels, says Gaskell, may possibly be due to fibres running to the vagus from the superior cervical ganglia. Maas states that in the cat vaso dilator fibres pass to the coronary artery from the ganglion stellatum and that vaso-constrictor and some vaso-dilator fibres pass to it from the vagus.

Wishing to satisfy myself histologically of the

presence or absence of nerves in the coronary arteries I have examined the hearts of the following animals Lamb, Pig, Bullock, Calf, I dissected out both right and left coronary arteries with several of their branches, these I prepared in the following manner; I first macerated the arteries in acetic acid, glycerine and a 1% solution of chloral hydrate in distilled water, in the proportions of one each of the two first to six of the last, in this solution they were left for a fortnight; they were then placed in a second solution differing from the first in containing Ehrlich's haematoxylin instead of the acetic acid, in this they were left for ten days; they were then allowed to soak in pure glycerine; parts of the specimens to remove overstaining were treated with acetic acid.

This is the method for nerve staining recommended by Sihler and has been employed by several who have investigated the innervation of both voluntary and involuntary muscular structures. I send a few specimens out of many which I have examined.

I have found stripping the vessel from the intima outwards in the longitudinal direction gives the best results, the transverse sections stained by this method gave less definite results, still some nerve fibres are to be made out in the latter.

I should like to point out that the nerve trunks which are shown in these specimens are not extra vascular but intra vascular, and the size of the larger trunks shows that their ultimate distribution must be in distant ramification of the coronary system, and therefore that these vessels have a direct innervation is I think evident.

The fibres are of the non-medullated variety, and unless physiologists can prove to the contrary, I see no reason why the majority of them should not be vaso-motor, as the non-medullated fibres usually are when found in connection with other arteries.

I have not been able to demonstrate any medullated fibres, which according to Schäfer are afferent.

From the literature which I have quoted at some length one sees that there have been many elaborate and ingenious hypotheses raised as to the pathology of this most interesting disease. Take first the "neuralgic" hypothesis; it has been objected to on the ground that for a neuralgia to prove habitually fatal is without precedent, but this objection is scarcely valid, as the fatality of morbid action depends not so much upon the nature of the affection, as on the nature of the function of the organ affected; for instance the gravity of a pneumococcic infection (or pneumococcosis as the Americans call it) of a localized patch of the lung would be very different from a pneumococcic meningitis, or a streptococcic infection of the skin, as in pustular acne, would be very different to the same form of infection of the pericardium.

Again it might be argued that those cases in which no changes have been found post mortem either in heart, blood vessels or nerves (and here the changes might be molecular and therefore not visible to the naked eye or demonstrable by the microscope), are comparable to the arrest of the frog's heart after injury to the intestines, and death is due to shock. In any case holders of this theory have this advantage over those who hold that

angina is due to an intraventricular distension or to a cramp of the heart wall except a very localized one, in that it is compatible with those cases in which there is little or no change in the pulse.

Let us next take the ischaemic theory, especially when caused by some disease of the coronary vessels; here too one is confronted by the statistics of post mortem examination, coronary disease in all its forms is not uncommon while true angina is one of the rarest of diseases; surely this should convince us that one must look for some other underlying cause and not attribute the angina to any of the numerous and varying organic lesions of the heart that have been met with.

The theory of acute intraventricular distension assumes that the heart is unable to cope with and propel the amount of blood in its cavities, which are thus distended and this distension causes pain like the pain caused by an overdistended bladder.

There are several objections to accepting this view, many people have weak hearts, and though on exertion their hearts may become interfered with in function causing palpitation etc., it is the rarest thing possible for

their exertions to be followed by an angina attack; again others who die in an attack of angina have nothing wrong with their hearts as far as the most careful examination can make out.

Again acute cardiac dilatation is not an uncommon occurrence and here too we very rarely meet with angina, which one might reasonably expect, at least before the dilatation takes place when there is merely great increase of intraventricular pressure.

A combination of the neuralgic theory with that of "relative cardiac ischaemia" is an explanation that has in many ways appealed to me; briefly it is as follows; in spite of possibly coronary, aortic or other disease the heart muscle is ordinarily supplied with sufficient blood for its needs, and with the muscle the nerve filaments and ganglia with which it is so richly supplied; now if through ⁽¹⁾ vaso motor spasm acting on the systemic arteries or (2) any extra exertion on the part of the individual throwing more work on the heart or (3) the coronary arteries themselves being affected by the vaso motor spasms, the heart muscle suffers from ischaemia, ~~such being the case~~ ^{then} if the nerves or ganglia are in a state of irritability whether from anaemia or

other cause, these nerves not getting their proper supply of blood ^{will} send an impression through the cardiac plexus to the cardiac centre, which ^{will} then send impulses down the efferent nerve trunks and through them to their terminal filaments, and we get the various phenomena we recognise as angina; this theory agreeing with Romberg's dictum "neuralgia is the cry of the nerves for blood".

In connection with our present investigation it is interesting to study and compare the action of various drugs that have been found useful in the treatment of angina, I do not propose discussing all, as their number is legion, but will mention a few, take first Chloral.

Chloral. This we know when given in large doses both relieves the attacks and also helps to avert them to a marked extent; it has according to ^{pharmacologists} ~~physiologists~~ the following action; Even when given in large doses it has no specific effects on algæic areas, the reflex response to irritation is very much lowered; the reflexes of the spinal cord are depressed and finally paralysed, the blood pressure is little affected except by very large quantities, which reduce it considerably and at the same time cause marked slowness of the pulse; this depression of the blood pressure is caused in part by paresis of the vaso motor centre, in part by the effects on the cardiac

and being so much better neglected to take the prescrip-

muscle, and possibly in part by a direct action on the muscular walls of the vessels.

In cases of chloral poisoning, at least in animals, even when the pulse has almost ceased, the circulation may be restored almost immediately by suprarenal extract.

I mentioned at the beginning of my paper that I did not intend reporting individual cases but I should like to make an exception as regards the following. My friend Dr. Alfred Eddowes to whom I was telling my views about the nature of angina, said that it reminded him of the extraordinary success he had (some 30 years ago when he was in general practice) in treating a most aggravated and persistent case of angina, the worst he had ever seen; he described to me the first attack he saw the patient have, and told me that he thought that it would certainly have been fatal; he tried many remedies, as others had done before him, with no avail; the patient's life was felt to be a burden and death was prayed for to bring relief from the suffering: finally he decided to try Chloral Hydrate and Tinct. Hyoscyamus to be taken at bedtime or at other times if necessary, he only gave moderate doses of the former 10-20 grains but the latter he gave up to two drachms; it had the most marvellous effect, so much so that the patient went out to Cannes and, being so much better, neglected to take the prescrip-

tion; after a time the attacks returned and again refused to yield to all the different remedies given by Dr. Bright of that town who wrote ^{to Dr. Eddowes} saying he had "exhausted the pharmacopeia without success", (I forget why the patient did not write to Dr. Eddowes in the first instance). On getting the chloral and hyoscyamus prescription and again taking it the result was as satisfactory as it had been previously; Dr. Eddowes could not tell me the future history of the case, which he lost sight of by having moved from the neighbourhood.

Of all the numerous drugs that have been administered for the relief of angina none according to most observers have given such good results as the Nitrites, this has been attributed to their marked action in lowering blood pressure; this they do, so physiologists tell us, by depressing the nerve ends and muscle of the arterioles but more especially the muscle, slightly also by depression of the vaso constrictor centre; it may be noticed that stimulation of a vaso constrictor nerve such as the splanchnic still produces some rise in blood pressure. One might imagine theoretically that the coronary

Large quantities of amyl nitrite slow and weaken the contractions of the heart owing to the direct depressing action on the muscle. there is more work thrown on the

heart. This is also stated "In very advanced degeneration of the cardiac muscle fibre, the administration of amyl nitrite is distinctly contra indicated for the blood pressure is low and any further reduction may lead to syncope, and to still greater weakness of the heart from the low pressure in the coronary arteries lessening its nutrition."

Possibly I misunderstand what the author means, if he intends us to understand that dilatation of the coronary arteries lessens the nutrition of the heart muscle I cannot think he is right, as surely the greater the calibre of the vessels the greater the quantity of blood they can carry to the cardiac muscle; of course he may mean that the blood pressure in the coronary arteries is lowered by the vis a tergo of the heart's contractions being lessened by the depressing action on the heart muscle itself.

There is a point here I should like to raise and that is do the coronary arteries dilate when the vessels of the head, neck and splanchnic area dilate?

One might imagine theoretically that the coronary arteries ought to act in a directly opposite manner to those of the systemic circulation, because when these latter are contracted there is more work thrown on the

heart, this requires more nutriment, and obeying the well known physiological law, that the supply of blood to an organ, gland etc., is in direct proportion to the work for which it is called upon, the coronary arteries ought now to dilate so as to allow the muscle to be flushed with blood; while on the other hand when the vessels of the extremities and still more so, those of the splanchnic area are dilated, the obstruction to the circulation is diminished, the heart's work is therefore lessened, it requires less blood, and as a result, as I have said before, theoretically the coronary arteries should be contracted. One knows that different parts of the circulation are governed in different ways by the vaso motor centre or centres; for instance blushes are confined chiefly to the head and neck; certain drugs and foods cause localized redness, for instance the nitrites themselves, and so do some emotions such as anger, pain etc.;

Of course some physiologists deny that the coronary arteries have any direct innervation, but after the observations I have made, I, personally, have no doubt but what they have, and such being the case I naturally conclude that the nerves have a vaso motor function; whether they act in the way I have suggested I do not know, and should be glad if some physiologist would enlighten me.

Belladonna, as recommended by Trousseau, has in the hands of certain observers given considerable relief in many cases, its physiological action, as far as the points about which we are concerned, seems to be shortly as follows; - it acts as a stimulant to the central nervous system and paralyses the terminations of a number of nerves, more especially those that supply involuntary muscle, secretory glands and the heart. The nerve fibres in the glands are paralysed not the ganglion cells. The nerve fibres of inhibitory terminations of the vagus in the heart are also paralysed. The terminations of the accelerator nerve are unaffected, exactly as the terminations of the sympathetic in the salivary glands are unaffected, and the heart muscle is neither stimulated nor depressed; the heart therefore is placed in the same position as if the vagus were divided in the neck, that is to say there is acceleration of the pulse (according to the age of the patient) increase in systole, decrease in diastole, augmentation of the output of the heart per minute. *is to raise the blood pressure considerably, and*

this All organs containing unstriped muscle (apart from that of the arterial walls) are affected by atropine. It has been suggested that "atropine acts on some still "unknown nerve terminations and that the violent movements

"which it arrests arise from stimulation of a mechanism
 "which is distinct from that presiding over the ordinary
 "peristalsis of the bowel."

Very large doses of the drug besides paralysing the
 vagus weaken and depress the heart muscle, the heart
 therefore beats slower and weaker and the output is less.

Hedborn states that large quantities accelerate the
 coronary circulation in mammals and increase the ampli-
 tude of the contractions. He is inclined to regard the
 latter alteration as due in part to the dilatation of the
 coronary vessels in part to a direct action on the heart
 muscle wall.

It has been pointed out that its action on the cir-
 culation is somewhat complex as besides the action on
 the heart there is an action on the central nervous
 system.

To me there seems one strong objection to the use
 of belladonna in angina if one believes the latter is
 due to increase of blood pressure, because the action of
 atropine is to raise the blood pressure considerably, and
 this it does by contracting the abdominal blood vessels
 and the resulting rise of blood pressure is not counter-
 acted by the dilatation of the vessels of the skin; the
 only way blood pressure is lowered is after long adminis-

tration of atropine or very large doses and then the drug only acts by weakening the heart muscle, which is certainly undesirable especially if it is already in a morbid condition.

There is a marked difference in the condition of the Hyoscyamus. I do not propose discussing this drug at length but merely emphasize its anti-spasmodic action and general depressant action on the nervous system; of course I quite allow that it may be argued that the beneficial results that have followed the use of hyoscyamus in large doses, have been caused by its lowering the blood pressure; which of course it does; I know for a fact that if the drug be pushed the dilatation of the cutaneous blood vessels may be so great as to cause an erythema.

In concluding the discussion of the drugs that have been found of most use in this disease I will point out that in a certain number of cases considerable benefit results from the usual nerve tonics, Strychnine, Iron, Arsenic especially, Zinc, Phosphorus, Quinine, etc.

Leaving remedial drugs alone there is one more drug that I should like to consider shortly, because I think its physiological action is both interesting and suggestive, I refer to Adrenalin.

On examining an animal that has been given a poisonous dose intravenously one finds on post mortem examination the following appearances (the specimen that I have had an opportunity of examining being that of a cat).

There is a marked difference in the condition of the various organs, the cerebral blood vessels are scarcely affected, if anything they seem slightly dilated, the peripheral blood vessels are all noticeably constricted, but still more so are those of the abdominal organs which appear quite blanched and bloodless, on the other hand the vessels in the lung are markedly dilated, the lungs being a deep purple and evidently engorged, and what concerns us more in our present investigation the coronary arteries are widely dilated and engorged with blood. The above appearances are to me very significant; thinking the matter over I was ~~quite~~ struck by the fact that many of the phenomena were similar to those observed after stimulating the sympathetic.

On consulting the latest writers on the subject I come across the following, as the result of intravenous injection of adrenalin "the constriction of the vessels of the stomach, intestine and other organs whose blood flow is regulated by the splanchnic nerve, is apparently the chief factor in the rise of blood pressure". Now

adrenalin is known to act on a large number of forms of involuntary muscle causing constriction in many cases but inhibiting it in others, as it has been noted stimulation of the sympathetic nerves has similar results in most cases, for instance stimulation of the splanchnic nerves contracts the intestinal vessels but relaxes the muscular coats of the bowels. certain amount of freedom

It has been argued, in consequence of the above phenomena, that drugs of the adrenalin series act not by stimulating the muscle fibres directly but by stimulating the terminations of the nerves. Against this theory it may be pointed out that the action persists after the degeneration of the nerve endings, and this seems to indicate that the drug acts on the muscle fibres, and the difference in the results depends on fundamental differences in the chemical character of the fibres.

Again many of the secretions are increased; here physiologists consider that this is brought about by stimulation of the nerve terminations. Gottlieb has pointed out that in animals poisoned with chloral or chloroform until the pulse has almost completely ceased the circulation may be restored immediately by suprarenal extract.

Now we have seen that (1) the action of adrenalin is remarkably like in many ways the phenomena seen on

stimulation of the sympathetic (2) the pain of angina closely resembles that referable to the sympathetic e.g. Hepatalgia, Nephralgia, Enteralgia etc. (3) we know from experience that in certain cases at least drugs that act in a directly opposite manner to Adrenalin, such as Chloral, give marked relief in angina attacks, and taken between attacks confer a certain amount of freedom from the attacks; such being the case it raises an interesting point whether an angina attack is not caused by a toxin secreted and suddenly poured into the blood stream; this is not altogether impossible, there might be a sudden increase or change in the chemical composition of the secretion from the supra renals, and the action of adrenalin is as physiologists tell us of very short duration which would tally with the short duration of an anginal attack; so far I have been unable to make investigation as regards this question of the composition of the blood during an anginal paroxysm, but I hope to do so before long when I can have an angina patient under close observation.

On the other hand remembering how closely the pain of angina resembles that referable to the sympathetic nerve, the vaso motor phenomena, the alteration in the secretions, etc., it would seem probable that an anginal

paroxysm is caused by a stimulation acting through the sympathetic nerves, for instance there might be some degeneration of one of the nerve centres causing such an excitability and instability as is seen in epilepsy, this same degeneration being in some cases secondary to the aortitis, aortic valvular disease, coronary disease, fatty degeneration of the heart etc., in other cases being a primary disease of the nerve centre, possibly due to arterio sclerotic changes in the sympathetic system, sometimes in the cardiac plexus, sometimes the coronary plexus, in fact different parts of the sympathetic system may be affected in different cases, and according to the site of the lesion so will both the objective and subjective symptoms vary; I do not mean to infer that from the latter one could necessarily locate the site of lesion, because, as in other affections of the nervous system, the pain would likely be referred to other situations; as the pain caused by a decayed tooth may be referred to all the branches of the fifth nerve, and again hip joint disease may cause pain in the distribution of the sciatic nerve.

Since writing the above I have examined the blood of a patient who suffers from angina, he was sent to me by a friend and I understand has improved very much under

treatment, I was not able to get the blood during a paroxysm. I both examined the blood myself staining it with Jenner's stain, and also had it examined at the Clinical Research Association, the following is their report:-

"Small lymphocytes	= 18.0)	
Large "	= 17.0)	35.0
Polymorphonuclears			60.0
Eosinophiles			4.0
Mast cells			1.0
			<hr/>
			100.0
			<hr/>

There is no poikilocytosis or increase of blood platelets."

It will be noticed that there is a considerable difference from the normal in the relative proportion of the Small and Large lymphocytes.

I also took an exploratory-needleful of his blood from which I got the serum and with this I made a simple experiment, with the help of Mr. Lyle at King's College Laboratory who provided me with the apparatus; I pithed two frogs and having pinned them out I took cardiogram tracings of their heart's action, attaching the lever to their apices in the usual way; salt solution having no

effect, I tried the effect of the serum from the blood of the angina patient, with the result that there was no marked alteration but both Mr. Lyle and myself thought that after each application of the serum the heart beat faster; I do not at all emphasize the result of this simple experiment but hope in a few months to carry out some more experiments going more into detail; at present the exigencies of practice make it difficult for me to devote the necessary time to the work.

In coming to a conclusion as to the essential underlying pathological condition, allowing as we may that various cardiac lesions are contributing factors, one is helped by comparing the disease with those of an analogous paroxysmal nature, and the following are those that will, I think, occur to most of us, Tic douloureux, Epilepsy, Tabetie crises, Asthma and the various abdominal neuroses viz: Gastralgia, Enteralgia, Hepatalgia and Nephralgia.

The objection may be raised that by introducing a comparison with these diseases, the pathology of which is still doubtful, one only obscures the subject, personally I do not think so, and consider the comparison besides being interesting to be distinctly helpful.

Let us first turn our attention to the distinctly analogous attacks that occur in Tic douloureux; here we

get the same kind of paroxysms of agonising pain; the same exciting causes, such as a breath of cold air, palpitation on one of the 'points douloureux' (as in certain cases of angina) slight movement or exercise, defaecation; there is the same rapid onset, in both the pain may disappear as suddenly as it came; and there are frequently as in angina marked vaso motor disturbance shown by flushing, sweating, etc.

Here again there is considerable doubt as to the exact pathology of the disease, some maintaining that it is an ascending neuritis this view being held by Sir Victor Horsley; Putnam and Dune have described endarteritis in the vessels of the nerve sheath; Krause found thickening of nerve sheath with some thickening of nerve fibres; others have described changes in the Gasserian ganglion; others again have been able to detect nothing abnormal either in the nerve or the ganglion; in fact the divergence of opinion is almost as marked as it is in angina, still most authorities are agreed that the Gasserian ganglion is finally at least at fault, be that as it may complete removal of the ganglion and in some cases injection of osmic acid into the nerve to cause degeneration of the nerve, removes all symptoms of the disease. In angina unfortunately we have hitherto been unable to locate the site of the lesion and if we did we should

probably be unable to deal with it surgically, at least not with our present knowledge.

The next affection or symptom which it is interesting to compare with angina is that of Tabes with its lightning pains; here too we get paroxysmal pains with often long intervals between the attacks; they are not so analogous to the pain of angina as tic douloureux being generally only momentary in duration, they are not limited to any special nerve districts as a rule, may be widely distributed, and may shift their seat rapidly.

Again we find there is considerable divergence of opinion as to their exact pathology, authorities differing as to whether they are due to central nerve changes or not, some authorities considering that in certain cases at any rate peripheral neuritis may contribute to their production; the more usual interpretation being that they are due to irritation of centripetal nerve fibres within the cord, namely the *bandalettes externes* which Pierret has shown to suffer early in the disease.

Epilepsy.

I will not discuss the vexed question of its pathology but will content myself with referring to some of the points

of similarity between it and angina.

We notice in both the sudden onset, the proxysmal character of the attack, and often the sudden disappearance, between the attacks there may be long intervals of perfect health, in both the exciting cause is generally trifling and in both the attack may come on while the patient is resting.

A form of Epilepsy called by Gowers Reflex Epilepsy occurring though it does nearly always in children would appear very analogous to what happens in angina; in the former the exciting cause such as tapeworm etc., will not cause any explosion of nerve force if the nervous system be in a normal state.

Conclusion.

As the burden of my thesis is the essential cause of that form of cardiac pain known as Angina Pectoris I will conclude by stating the views that have impressed themselves upon me from the preceding study of the subject; these views I have indicated to a certain extent when I was discussing the physiological action of Adrenalin, see pages 41, 43 It seems to me the main points we have to reconcile are the following:

Various cardiac lesions are usually associated with

this disease, but the disease may occur and be fatal with no gross cardiac lesion at all, on the other hand all these same cardiac lesions may occur with no angina symptoms. Though the pulse is frequently altered yet it is not so always.

The causes that generally bring on a paroxysm are trivial, not violent exercise etc.

The character of the paroxysm and its resemblance to certain nervous diseases.

The sudden onset and frequently its equally sudden cessation.

The long intervals of perfect health between the attacks, which may cease entirely.

The family history and the associated diseases.

The alleviating effects of certain drugs and the known physiological action of these.

The vaso motor disturbance and the alterations in the secretions.

And lastly and perhaps it will be considered scarcely worth mentioning, and that is the fact that it has been frequently remarked that the proportion of intellectual and even distinguished men who have fallen victims to this disease is noticeably large; now the old adage "Genius is akin to madness" has a certain amount of truth

in it, at least there is an abnormality of the nervous system, though what that abnormality consists of we do not know, still it is possible that the abnormal nervous system of these same distinguished men may have had some tendency to degenerative changes; be that as it may, a consideration of all the points I have enumerated leads me to the conclusion that the one essential cause of Angina Pectoris is certainly a neurosis, and without considering that there is an exact identity between Epilepsy, Tic douloureux and Angina I believe that the essential factor in each is an instability of some nerve centres; and it is interesting to note that cases have been recorded in which patients who originally suffered from attacks of angina later on were free from these but developed brain disease with epilepsy.

I believe that this excitability or instability causes an explosion of nerve force which produces the phenomena we recognise as angina and the degrees of the attack will be in proportion to the excitability of the nerve centres. If the excitability and instability of the nerve centres be extreme then any of the cardiac lesions associated with angina such as coronary disease interfering with the nutrition of the heart muscle, fatty degeneration of the heart etc., will easily provoke those

morbid reflex sensations, or actions in those cases where cramp or spasm of fibrils, fibres or larger portions of the heart muscle is induced, constituting angina pectoris. If on the other hand the nerve centres be normal, these same cardiac lesions would cause no such phenomena; and, as we know, all these lesions are frequently met with on post mortem examination when there has been no symptoms of angina during life.

Taking the above hypothesis to be true we see how the extent and intensity of the pain varies in different cases, depending as it does on the character and extent of the affection of the nervous centres. If the nerves more immediately supplying the heart be affected we shall have its action disturbed; if the sensory branches connected with the spinal nerves suffer there will be more pain and that more widely distributed; if branches of the nerves connected with the vaso motor system are especially involved, we shall have the various phenomena of vaso motor disturbance which are so constantly met with, such as the pronounced pallor of the skin followed by flushing, the feeling of chilliness, the cold sweat, and the excessive secretion of urine as the attack passes off.

As regards the changes in the nerve centres that

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cause such excitability and instability I would suggest, as I mentioned before, that they are sometimes secondary to arterio-sclerotic changes, and the fact that man is more subject to arterio-sclerosis accounts for the said difference in incidence of the disease in the two sexes. At other times it may possibly be caused by the various toxins that may circulate in the blood.

As regards the fact that in some cases the attacks may cease, this may be accounted for by the morbid nerve centres having undergone such a degree of degeneration as to be no longer able to respond to stimuli. On the other hand the cessation of the attacks may be due to the fall of blood pressure due to the yielding of the mitral valve or cardiac dilatation causing alteration in the nutrition of the nerve centres or diminishing their stimulation.

I own to a certain feeling of dissatisfaction at not having come to more definite conclusions, but console myself with the knowledge that many who have paid special attention to the subject have had to acknowledge that it is beset with questions which still await an answer.