A Lecture ON CARDIAC ARRHYTHMIA.

DELIVERED AT THE HOSPITAL FOR CONSUMPTION,
BROMPTON.

BY

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GENTLEMEN,—As you are aware, the normal action of the heart is rhythmical and nearly regular, the beats following one another at tolerably equal intervals so long as the rate of the heart's action is unaltered. This regularity is maintained in the average healthy subject, whatever the rate at which the heart is working, whether fast or slow. The same regularity is met with in many cases of heart disease, whether functional or organic, valvular or myocardial; the heart itself is such a well trained organ, and its nervous centre is such a well trained mechanism, that approximate regularity of action, whether at a rapid or a slow rate, is one of the most striking or persistent characters of its pulsation, whether the heart itself is healthy or diseased. Hence what I have to say on the subject of cardiac arrhythmia has no bearing on the action of the great majority of healthy hearts or of a large number of diseased hearts; there only remain for consideration the minority of instances, those in which the cardiac rhythm is abnormally irregular. It is not necessary to remind you that a slight degree of irregularity is always to be seen in the heart's action; for example, the normal pulse quickens a little during inspiration and slows during expiration, and the action of swallowing is accompanied by a slowing of the pulse due to vagus inhibition. These alterations in the rhythm of the heart are normal when they are of slight degree, and will not be further considered. It is only in extreme cases when the respiratory irregularity is very marked that it can give rise to the suspicion of cardiac disease, and that it certainly does at times.

Analysis of the causes of irregular action of the heart shows that they are very various but that they may be divided up into two great classes: (1) Those arising within the heart and due to changes in the state or nutrition of its walls, or of the Purkinje cells that form the bundle of His. (2) Those arising outside the heart, and due either to alterations in the nervous impulses coming to it from the central nervous system, or to changes in the case with which the blood enters or leaves it.

In many cases the irregularity is a transient and unimportant matter, but in others it is an important and serious sign indicating a definite downward stage in the course of a patient with heart disease. Before going more deeply into the matter, it will be best to lay before you what is known about the regulation of the heart's activity under normal conditions.

The first question to be asked and answered is this: What is it that originates and maintains the rhythmical contractions of the heart? The human heart, as you know, goes on beating throughout life, and after death it can be made to go on beating again for many hours if transfused with a warm solution containing oxygen, dextrose, and a mixture of salts of the three metals, sodium, calcium, and potassium, in the right proportions. The fact has received two explanations, embodied respectively in the neurogenic and the myogenic theories of its action. According to the neurogenic theory, the stimulus to contract is generated in the nerve plexuses and ganglion cells that are found scattered throughout the tissue of the heart, and is communicated from the nerve tissue to the muscle of the heart. It is certain that the heart can go on beating quite normally when it has been taken out of the body, and so is separated from all the nervous connexions—the vagus and sympathetics—that connect it with the central nervous system; hence the impulse to contract cannot arise there. The other theory, or myogenic theory of the heart's action, states that the rhythmical impulse to contract originates in certain fibres of the cardiac muscle quite independently of the nervous tissue

and ganglion cells in the heart. Both theories agree in the statement that the contractions start in a certain region of the heart—the sino-auricular region—and spread thence by way of the auriculo-ventricular bundle of His to the muscle of the ventricles. In favour of the myogenic theory may be quoted the fact that the heart of the embryo chicken beats before any nerve fibres have entered it, and also the observations that stimulation of the ganglion cells of the heart does not alter its rhythm. But there appears to be no conclusive evidence either way to show whether the neurogenic or the myogenic theory is most nearly correct; and the question is, perhaps, of academic rather than practical interest.

We may take it as proved, then, that the rhythmical impulses to contract start in the sino-auricular area of the heart and travel to the ventricles by way of the bundle of His under normal circumstances. As it happens that in a good many cases of cardiac arrhythmia the irregularity of the heart's action is due to pathological interference with the transmission of these impulses, it is advisable to give more careful consideration to this area. In many of the lower animals, such as the frog, you will remember that the venae cavae join the heart by means of a chamber called the sinus venosus, and that the frog's cardiac contractions start in this sinus. The human heart has no definite sinus venosus, but the analogous part has become incorporated in the wall of the right auricle, roughly corresponding with the area bounded by the superior vena cava, the inferior vena cava, the Eustachian valve, and the coronary sinus; much of it is on the interauricular septum. The cardiac impulses originate here and travel to the auricular walls by small bundles of Purkinje fibres; they travel on to the ventricles by a single bundle of Purkinje fibres known as the auriculo-ventricular bundle, described first by Kent in 1893 and later in the same year by His. If this bundle of His is interfered with in any way, if it is cut across, or if it is invaded by fibrosis or destroyed by a gumma or other new growth, one gets a condition known as "heart-block." In heart-block the auricles continue to beat at their normal rate, about 70 times in a minute. But the ventricles no longer beat in unison with the auricles, but at their own rate, which is from 28 to 32 beats per minute. When the bundle of His is only partially infiltrated and destroyed the condition of partial heart-block results. So much, then, for the intracardiac mechanism whereby the impulse to rhythmical contraction is originated and maintained in the heart.

A few moments must now be given to the consideration of the extra-cardiac mechanism or control from the central nervous system, which regulates but does not originate the heart's action. The nerve supply of the heart comes from two sources—the vagus or tenth nerve and the sympathetic, both of which are normally in a state of activity, and continuously regulate the heart's action. The vagus inhibits, slows, or weakens the contractions of the heart, causing a fall in blood pressure; it also lessens the conductivity of the heart muscle, preventing impulses from passing from the auricle to the ventricle, so that if the vagus is stimulated to a certain definite extent it is often possible to bring about a condition of affairs in which the ventricle only beats once to every two beats of the auricle—in other words, to establish a functional or neurogenic heart-block. The sympathetic nerves of the heart have the opposite action; when they are stimulated they quicken and strengthen the heart beat, raise the blood pressure, and improve the conduction of stimuli from auricles to ventricles. Both the vagus and the sympathetic are under normal circumstances at work regulating the beat of the heart, the vagus endeavouring to slow it, the sympathetic to make it beat faster, the balance between the two giving the normal rate of heart beat. It is by means of these two nerve supplies that the common reflex quickening or slowing of the heart's rate occurs. Thus, severe pain causes reflex quickening of the heart because the normal tonic inhibitory impulses coming down the vagus are lessened, while the accelerating sympathetic impulses are increased. The action of emotion and of other forms of sensation, and of gentle exercise in quickening the pulse-rate is similarly reflex. Almost all the experiments on the mode of action of the heart and on its regulation by the vagi and sympathetic system have been made on animals, and very few of

the conclusions arrived at have been made from observations in man. But there are certain drugs which stimulate and others that paralyse the vagus nerve endings, and by use of these in man it is possible to find out, in certain cases, whether the vagus is or is not responsible for changes in the heart's rate of beating. The drugs muscarin and physostigmin stimulate the vagus and so bring about slowing of the heart. On the other hand, atropine, and to a less extent oureare, paralyse the vagus and prevent it from slowing the heart, and this action of atropine is sometimes useful to one clinically. For example, in some cases of irregular heart it is found that the subcutaneous injection of $\frac{1}{100}$ or $\frac{1}{50}$ grain of atropine removes the irregularity for a time, and this is taken as indicating that the cause of the irregularity lay in the inhibitory action of the vagus, and not, for example, in some lesion of the conducting fibres of the bundle of His. But it must be remembered that if the dose of atropine fails to regularize the heart beat, it may do so because the dose was not large enough to paralyse the vagus nerve endings; hence it is not invariably safe to conclude that a cardiac arrhythmia is not neurogenic because it is not set aside by atropine.

Having thus cleared the ground by considering the physiology of the heart's action and of its nervous control, we may go on to consider the various examples of cardiac irregularity that one is likely to meet with in practice. As I have already said, the causes of irregular heart may be divided into two main classes: the intracardiac, or those arising within the heart; and the extracardiac, or those arising outside it. Most cases of cardiac arrhythmia are of extracardiac origin, and so these may be considered first.

A certain number of perfectly healthy people seem to have naturally irregular hearts without ever having had any disease, either local or general, whereby the arrhythmia can be accounted for. They present no cardiac symptoms, and the irregularity of their pulse is generally found out by accident. It is presumably neurogenic in origin.

The next arrhythmia to which I wish to direct your attention is the respiratory irregularity. We have already seen that in the majority of normal persons inspiration causes a quickening of the pulse, and expiration a slowing. This depends on two separate factors. It is due partly to the fact that inspiration increases the supply of venous blood reaching the heart by the venae cavae; the act of inspiration increases the negative pressure or suction power in the thorax, and tends to draw venous blood into the right auricle, with the result that it fills up with blood more rapidly while inspiration proceeds, and the whole cycle of cardiac operations is thereby accelerated, while in expiration the converse takes place. But this is not the only factor concerned in the inspiratory quickening, for it is lessened or even abolished if atropine is given; the inference from this fact is that a certain amount of vagus inhibition of the heart occurs during expiration in these persons. In a minority of cases respiration has no effect on the rate of the heart, and in a few normal persons inspiration may cause slowing of the heart, and expiration quickening. This respiratory arrhythmia of the heart is oftenest and best seen in children and young people, and is worth mention because it is sometimes so marked and leads to so great an irregularity in the pulse that the patient is labelled "heart disease," and treated accordingly. But such mistakes are not likely to occur if one remembers that they may be made, and the true cause of the irregularity will be easily made out by observing the pulse and respiration together, and noting how they vary together.

Neurogenic arrhythmias, the third group of the reflex arrhythmias, are still commoner than the respiratory. In certain patients almost any severe mental or sensory stimulation may bring on an attack of rapid or intermittent action of the heart. This is particularly so with nervous and excitable people. In many cases the patient will say that he or she has an attack of palpitations; but the two things are not necessarily the same, for these reasons: On the one hand a patient may have palpitations—that is to say, perceptible and painful cardiac action—without any change in the rate of the pulse; on the other hand, patients may have an attack of rapid or irregular pulse, without being aware of the fact. A good many of these neurogenic reflex arrhythmias have got into the textbooks under the headings, "Cardiac

Neuroses," or "Functional Affections of the Heart"; many of them are associated with precordial referred pain, and it is often this pain that brings the cardiac arrhythmia to the patient's notice. In certain patients it is some toxic influence that brings on these attacks of intermittent or irregular action of the heart. The use of strong tea or coffee is an extremely common cause of irregularity of the heart in the edentulous middle-aged women and men who crowd hospital out-patient departments and come up complaining of pain under the heart. One has known a great many middle-aged people, 40 years of age or so, who have had to give up taking afternoon tea because it so often brought on attacks of palpitation; and these attacks of palpitation are often accompanied by an intermittent action of the heart.

Another toxic cause of intermittent heart-beat is excessive tobacco smoking, usually in young men, particularly when the smoke is inhaled. These patients often complain of faintness and dizziness with palpitations; either tachycardia or irregularity of the heart may occur, and physiological experiments go to prove that it is the nicotine in tobacco smoke that produces the disturbance of the heart, and that it does it by stimulating the sympathetic nerves—in other words, the accelerator nerves of the heart. The bad effects pass off as soon as the smoking is discontinued, and are not accompanied by any permanent muscular weakness of the heart. Tobacco heart sometimes occurs in older people, and may lead them to give up tobacco; but here the pathological picture is less simple, for these older patients often have arterio-sclerosis and high blood pressure, and very likely some sclerosis of their coronary arteries. So that it is not safe to say that the irregularity of the tobacco heart in older people is a neurogenic reflex as it is in adolescents; probably it is also due in part to myocardial changes in the old.

The excessive use of alcohol is another common toxic cause of irregularity of the heart.

In another large class of cases the neurogenic arrhythmia is due to reflexes from the viscera. A great many dyspeptics suffer far more from the painful irregular action of their hearts than they do directly from the indigestion that is the *fons et origo* of their complaint. To some extent the palpitations are caused mechanically; the stomach or intestines, or both, become distended with flatus and press the diaphragm upwards, embarrassing the action of the heart. But, in addition, there is a reflex nervous factor, abnormal stimuli spreading up by the vagus from the unhealthy viscera to the nucleus of the vagus in the medulla, and upsetting the action of the heart by means of impulses transmitted down the cardiac branches of the vagus. A similarly caused irregularity of the heart is not rare in constipation; in both cases suitable treatment does away with the arrhythmia. Other reflex arrhythmias are seen with meningitis, intracranial tumour, and in any condition increasing the intracranial pressure, and the heart's action tends to be slower and more intermittent as the pressure increases; this is, no doubt, due to the increased stimuli descending from the vagus nucleus. The cardiac arrhythmia so common in exophthalmic goitre may have two causes. On the one hand, the enlarged thyroid gland may press on the sympathetic in the neck and so lead to the transmission of accelerating impulses to the heart. On the other hand, the victim of exophthalmic goitre has an excess of thyroid secretion in his system, and this gives rise to a toxic irregularity of the heart. Another and rarer cause of irregular heart lies in the common childish complaint of adenoids. Children with adenoids, as is well known, are liable to attacks of nocturnal dyspnoea, and probably some of these are due to irritation of a particular spot on the nasal septum opposite the middle turbinal bones. It is found that stimulation of this area on the septum brings about vagal inhibition of the heart, with consequent arrhythmia. A number of cases have been reported in which the cure of the local septal disease or the removal of the adenoid growths have resulted in the disappearance of the attacks of cardiac irregularity. It is clear, then, that a great many cases of irregular heart may be explained as reflexes from peripheral stimulation. The irregularity is usually in the general rhythm of the heart rather than in its individual beats. That is to say, groups of rapid beats occur, preceded and followed by groups of beats at a

normal rate, or slower than the normal. As a rule, all the beats are about equal in force, and in most cases the arrhythmia becomes regular again when atropine is given and the cardiac terminations of the vagus are paralysed.

The diagnosis of these reflex arrhythmias depends upon two things. In the first place, an accurate history of the conditions under which it is observed must be obtained from the patient, when some reflex or toxic cause for the irregularity will very possibly be found. And, in the second place, a careful examination of the patient's pulse and heart must be made, to exclude organic disease as far as possible, and to find the characteristic irregularity of rhythm by groups of beats, and not by the interpolation here and there of single disorderly beats. If only it were possible, it would be an excellent thing to take polygraph tracings of the pulsations in the jugular vein and carotid artery of the neck, and also of the inspiratory movements in all these cases. But a good deal of time and skill are necessary to use the polygraph recorder, and much experience is needed in the interpretation of the tracings obtained, so that for the general practitioner the use of the instrument seems to be impracticable. So much, then, for the neurogenic arrhythmias, which form the largest and, from a clinical point of view, the least serious group of cases of irregular heart.

We now come to the second group of arrhythmias—the vascular arrhythmias—and they are very few in number and need not delay us long. In these the irregularity of the heart is brought about by interference with the passage of blood to it or from it. In certain rare cases of pericardial adhesions it happens that the newly-formed inflammatory tissue is deposited round the points where the superior and inferior venae cavae enter the pericardium, and it may happen that these adhesions are dragged upon at some phase of respiration so as to kink these thin-walled vessels and prevent the venous blood from reaching the heart in proper quantity. This will cause slowing of the heart and, if it happens during inspiration, will produce what was called the “paradoxical pulse” by Kussmaul (1873), in which the pulse is slowed—and even a beat or two may be dropped—in inspiration. If the adhesions are between the heart and the anterior chest wall, according to Riegel, the pulse will be abnormally slowed in expiration. It must be remembered that both Riegel's and Kussmaul's form of pulse may occur in normal persons. In a few recorded cases of dropping of the diaphragm, with or without enteroptosis, the heart has apparently sunk so low in the thorax as to drag on the arch of the aorta on inspiration, kinking the vessel and preventing the left ventricle from emptying itself, and so producing paradoxical pulse. This cause of irregular heart must be very rare.

This brings me to the intracardiac group of cases of irregular heart—namely, those arising from lesions of the heart itself. The bulk of the work on this subject has been done in the last few years, and is due very largely to the clinical studies and stimulus of Mackenzie. It is to this group of cardiac arrhythmias that the more serious and more frequently fatal cases belong, for the condition is associated with organic disease of the valves or of the myocardium, or of both.

We have already gone into the function of the bundle of His. Its duty is to transmit the impulse to contract, which arises in the sinus region, from the auricles to the ventricles. Now the bundle may be the subject of either functional or organic disease, and may then partially or completely fail to transmit these impulses to the ventricles, and if this occurs some form of cardiac arrhythmia is likely to result. To consider the irregularities caused by functional disorders of the bundle, it may first be said that digitalis, when pushed, may cause irregularity of the heart by lessening the conductivity of the cardiac muscle, and so preventing the normal passage of the impulses to contract. Digitalis first acts on the heart by stimulating the vagus nerve and so slowing the heart; it also increases the force of contraction and the tone of the heart muscle. When given in these therapeutic doses digitalis slows and regularizes and strengthens the heart's action. If the drug is pushed beyond these limits the heart beats faster and more irregularly. The reason for this, according to Cushman, is that the ventricle begins to beat with a rhythm of its own independently of and in addition to the impulses

to contract which it goes on receiving from the auricle. This stage of digitalis poisoning is sometimes seen in cardiac patients who are taking digitalis, and is, of course, an indication for stopping the exhibition of the drug. If given in larger doses still, digitalis produces extreme irregularity of the heart, absolute heart-block is established, and the auricles and ventricles beat quite independently of one another. In both these last stages a functional paralysis of the bundle underlies the arrhythmia produced. It is probable that a similar functional diminution in the conductivity of the bundle occurs in patients with slow or irregular pulse after influenza or acute fevers.

If the bundle of His is seriously interfered with or destroyed by organic disease—for example, fibrosis, gumma or other new growth—absolute heart-block is likely to result, with slow or irregular action of the ventricles. In typical instances of heart-block the clinical picture produced is that of Adams-Stokes disease, or slow pulse—28 to 35 beats a minute—combined with syncopal attacks, when for a few seconds the heart ceases to beat at all, as it does from time to time. The diagnosis of this form of irregular pulse depends upon its occurrence in the form of a well-marked syndrome like the Adams-Stokes disease, on the one hand, and on the other upon the securing of evidence, best by means of jugular and carotid tracings, that the auricles and ventricles are not contracting in uniform succession, but independently of one another.

Another category of cases of irregular heart is that in which the irregularity is produced by the interpolation of extra beats or extra-systoles into the otherwise regular action of the heart. The extra-systole is a premature systole due to abnormal stimulation of the heart, and is followed by an abnormally long diastolic period. Extra-systoles occur in a variety of organic diseases of the heart, and probably always indicate myocardial disease or overstrain. Thus they may cause irregularity of the heart in patients with high blood pressure and renal disease in whom compensation is beginning to fail, when they are perhaps due to failure of the left ventricle to empty itself in systole, the residual blood acting as an abnormal stimulus, making the ventricles beat again, but more feebly, before the normal auricular impulse has come down to the ventricle. Such an extra-systole, arising in the ventricle, is known as “ventricular.” In patients with mitral disease and dilatation of the left auricle the dilatation may cause the occurrence of “auricular” extra-systoles in an analogous way. It is the interpolation of extra-systoles such as those that make the pulse of mitral disease so irregular, and cause the sounds heard at the apex of the heart to be so very various and confusing in these patients. Many extra-systoles in mitral disease, particularly when they arise from dilatation or paralysis of the left auricle, are very feeble, and of short duration. They may be strong enough to open the aortic valves for a fraction of the normal time, but usually do not get up enough pressure in the left ventricle to open them at all. As I have said, there is always dilatation of the left auricle in these mitral cases, and often the auricle is paralysed as well. This has been shown by tracings taken from a tambour introduced into the oesophagus and placed in contact with the left auricle, and also by venous tracings from the jugular vein; microscopically, the left auricular wall usually shows signs of fibrosis. The question as to what part of the auricle it is that originates these extra-systoles is much disputed. According to Mackenzie they arise because the automatic contractions of the heart cease to originate, as they normally do, in the sinus region, but start instead in the thickened middle part of the bundle of His known as its nodal point.

The diagnosis of this extra-systolic irregularity of the heart depends upon the discovery of the appropriate physical signs. The pulse is markedly irregular in both frequency and force. Sometimes the pulse is what is called a bigeminal pulse, when the beats occur in groups of two; sometimes it is trigeminal, when the rhythm consists of three beats close together and followed by a pause. If the pulse is bigeminal one extra-systole occurs, and if trigeminal two extra-systoles occur, after each normal contraction of the heart. If one or two extra-systoles occur regularly after each normal contraction of the heart, as a rule atropine does not abolish these extra-

systoles, while it does do away, for the time, with neurogenic irregularities of the heart.

A very similar irregularity of the heart may occur in overstrain of the heart or in chronic myocarditis. Here the left heart fails, dilatation of the left auricle occurs, and injury is thus inflicted on the bundle of His as well as on the auricular myocardium generally. The heart's action becomes irregular in force and frequency, and extra-systoles occur just as they do in the cases of mitral disease already considered. This paralysis of the auricles occurs when the blood pressure within them rises to 15–20 mm. of mercury.

There is only one more example of irregular heart that we need consider, and that is the rare disease known as paroxysmal tachycardia, in which the patient is liable to sudden attacks of very rapid pulsation of the heart. Here the rate of the pulse, which was previously normal, suddenly doubles or trebles, and reaches 150 to 250; and at the end of the attack it is as suddenly halved or reduced to a third. It is this suddenness in the change of rhythm that is the characteristic feature of paroxysmal tachycardia. The tachycardia up to 140 that comes on in highly nervous or in convalescent patients on slight exertion or excitement is quite different, inasmuch as it comes on gradually and goes away gradually; it is neurogenic in origin and due to temporary loss of the vagus control. It is not possible to say with any certainty what is the mechanism of the arrhythmia in paroxysmal tachycardia. It may be due, as Mackenzie supposes, to a state of affairs in which the auriculo-ventricular bundle of His becomes more excitable, and initiates the cardiac rhythm instead of the sinus region. The heart muscle seems to be abnormally irritable, and it is possible that to some extent paroxysmal tachycardia is neurogenic. The whole subject of the diagnosis of these arrhythmias is extremely difficult, and depends in the last resort upon the interpretation of the pulse tracings obtained from the jugular vein and carotid artery. I do not propose to go into the subject at all—you will find it discussed in most of the recent textbooks on heart disease, and also in a small special volume, which I show you, by Dr. Hay.¹

As regards prognosis, one has seen a great many cases of mitral disease with irregular pulse live a quiet life for years without any marked symptoms or any deterioration of their condition. But the irregularity which comes on with dilatation and failure of the hypertrophied heart is usually of much more serious importance.

REFERENCE.

¹ *Graphic Methods in Heart Disease.* J. Hay. London: H. Frowde, 1909.

A Lecture

ON

THEORY AND PRACTICE IN THE TREATMENT OF PULMONARY TUBERCULOSIS.

DELIVERED AT THE HOSPITAL FOR CONSUMPTION,
BROMPTON.

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THE title of this lecture may suggest to you that I have taken in hand an unduly vast subject, and, indeed, volumes might be filled—and have been filled—with a discussion of theory and practice in relation to tuberculosis. Within the limits of an hour's lecture I can only hope to draw your attention to certain points which seem to be of interest in this connexion. Since by "theory" we mean a connected account of the phenomena of the disease, unified by reference to the underlying cause at work, it is clear that our practice can only be looked on as scientific in so far as it is the outcome of, or at least in accordance with, the accepted theory of the disease. All other modes of treatment must be classed as merely empirical.

The theory of tuberculosis at the present day is, of course, founded on the discovery of the *Bacillus tuberculosis* by Robert Koch, whose recent death we have to deplore. Where there is no bacillus there is no tuber-

culosis. On the other hand, it is quite possible for the bacillus to enter the human body and yet fail to produce recognizable disease. There is, therefore, more than one factor to be considered, and we must not unduly concentrate our thoughts on the bacillus and forget the patient whom we have to treat. Starting, however, with the bacillus, we know that it produces disturbances in the living body—the sum of these disturbances being the disease tuberculosis—by means of the poisons to which it gives rise, but about these poisons we know little or nothing. This may seem an unduly pessimistic statement in view of the existence of preparations of poisonous bodies formed by the bacillus, to which the name "tuberculin" has been applied, and which can be submitted to chemical analysis; nevertheless it is not inaccurate, as may be seen by considering the nature of the principal tuberculins. The old tuberculin (T. or T.O.A.) is made by growing the bacilli in a fluid medium, filtering off the organisms themselves, and concentrating the filtrate to a small bulk. It thus contains the poisons formed by the bacilli in their growth on an artificial medium. It has been analysed, but the essential toxic principle is still undetermined, though the fever-producing substance is stated to be of the nature of an albumose, a body formed by breaking down of albumen. It is said that albumoses from other sources can induce the same rise of temperature in the tuberculous patient as does the albumose present in tuberculin. It is unlikely, then, that the albumose here is the specific poison of tuberculosis, and no other toxin has been isolated.

A peculiarity, indeed, of tuberculin is that it is not very toxic to healthy animals, whereas it is rapidly fatal in minute amounts to those which are infected with tuberculosis. It seems that the essential poison of the disease is formed by the interaction of two separate bodies. Its action may be compared with the process which has been called "anaphylaxis." If an animal is injected with a small quantity of the serum of one of another species, no harm seems to result; but if at the end of about twelve days a second injection of the same foreign serum is given, serious symptoms and even death may result. The nature of the phenomenon is not well understood, but it is likely that not only the action of tuberculin, but also the peculiar condition known as the "incubation period" of an infective disease, may be ultimately brought into relation with it.

The second form of tuberculin (T.R.) is produced by grinding up the actual bodies of the bacteria, and dissolving or emulsifying them with water; it contains the poisonous substances present in the bacilli. Its action differs somewhat from that of the old tuberculin, and it is therefore different in composition. Either it contains a different poison, or, if the same is present in both, its action is modified by mixture with other substances. Now if the poison formed in a culture differs from that extracted from the bacilli themselves, it is quite possible that the toxin formed within a living body, the actual poison of the disease, differs from both, and we cannot say that we know anything definite about it. We know, however, some of its effects. On the one hand, it produces a local destruction of tissue, which usually takes the form of caseation; and, on the other, it gives rise to constitutional symptoms, such as fever, wasting, sweating, and so forth. Possibly different poisons are at work in the two instances. The disease thus consists of two factors: there is the injury resulting from gradual destruction of some organ necessary for life, and there is also a general toxæmia or condition of poisoning of the whole system. When the malady affects the lungs the destructive process is acting on a large organ, with a considerable margin of tissue beyond what is absolutely needed for ordinary use, so that the disease can go on for a long time without causing death. It is a more chronic disease than, for example, tuberculosis of the kidneys usually is. There are, of course, acute cases of spreading miliary tuberculosis of the lungs in which death is due to toxæmia.

Now, with regard to the treatment of tuberculosis, two courses are theoretically open to us—we may endeavour to attack and kill the bacillus, or we may devote our efforts to strengthening the resistance of the patient. Actually, the former course is impracticable. We cannot bring bactericidal substances into contact with the bacilli in the living body in sufficient strength to kill them without at the same time killing the cells of the tissues. Attempts