general churning I have described, and like it is endoventricular and due to dilatation.

(c) As with aortic regurgitation the dilatation of the ventricle often raises the question of mitral disease, so with mitral regurgitation murmurs are sometimes heard at the base which raise the question of aortic regurgitation. In a case of undoubted mitral regurgitation there may be heard in the left third intercostal space, about an inch or so from the sternum, a double or continuous murmur. Although many aortic regurgitant murmurs are heard best, and sometimes only, in the left third intercostal space near the sternum, this murmur is continuous and double and not diastolic only, so that careful auscultation will soon show that aortic regurgitation alone will not explain it. Occurring as it does further from the sternum and over a larger area, there is nothing left for it but the left auricle, and it must be, I consider, a dilatation murmur produced in the dilated left auricle or appendix.

Fig. 5.

II. The Ventricular Dilatation Murmurs of the Right Side.

These are much more easy to deal with than those of the left side, for they are more superficial and the dilatation of the right side of the heart is more easily demonstrated.

Tricuspid regurgitation due to organic disease, though a very rare condition, yields very characteristic physical signs. The systolic murmur is well marked, and is propagated in a definite direction from the lower part of the sternum transversely outwards to the right, where the auricle can be shown clearly by percussion to be greatly dilated.

Tricuspid regurgitation is a very favourite diagnosis with some clinicians, but then on theoretical grounds and not on physical signs. The right side of the heart is greatly dilated as shown by percussion; there is epigastric pulsation; distension, and pulsation of the jugular veins. These physical signs are considered sufficient for the diagnosis even without any murmur whatever, but they may all be present without regurgitation.

Murmurs over a dilated right heart are by no means common, yet dilatation is an everyday phenomenon.

I do not know that I have ever seen the characteristic murmurs of tricuspid regurgitation without organic disease, and have in many cases confirmed the diagnosis by *post-mortem* examination. When murmurs over a dilated right heart do occur they are soft and blowing, heard over the ventricle especially and not over the auricle, and are not propagated as those of organic disease are across the sternum towards the right side. Therefore I maintain that on the right side, as on the left, they are not due to regurgitation through the auriculo-ventricular orifices, but are produced within the dilated chamber.

The considerations I have brought forward thus justify the conclusion I desire to establish—namely, that these ventricular-dilatation murmurs are not regurgitant, but are due to eddies set up within the dilated cavities; in other words, that they are not valvular but intra-ventricular. They are, of course, connected with defective muscular action, but only so far as this leads to dilatation. Varying degrees of dilatation associated with variations in the force of muscular contractions are adequate to explain all the phenomena met with.

Fig. 6.

THE Harben lectures of the Royal Institute of Public Health will be delivered on July 1st, 3rd, and 6th, by Dr. L. Vaillard, President of the Health Committee of the French army. The first lecture will deal with caries, the second with tetanus, and the third with house-flies. The lectures will be delivered at the Institute, 37, Russell Square, W.C., at 5 p.m. on each day, and are open to the public.

COMMON ERRORS IN DIAGNOSIS AND TREATMENT OF CARDIAC DISEASES.*

BY

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It is obviously impossible for me, in the short time at my disposal, to deal with all the common errors in the diagnosis and treatment of cardiac diseases. I shall only deal with those which are most common and of the greatest practical importance.

The Rheumatic Infection in Childhood.

I think we cannot do better than commence with the rheumatic infection of the heart in childhood—a subject of the utmost importance, for by far the larger number of cases of heart disease under 30 years of age, and a considerable proportion of those of later life, are a direct result of this infection.

Notwithstanding the fact that this subject has received a great deal of attention, it is still not sufficiently realized that it is very easy to overlook a rheumatic infection in children, and even when we are especially on the look-out for it it is not infrequently very difficult to come to a definite conclusion as to whether the heart is affected or not. This is very unfortunate, because the future welfare of the patient in large measure depends upon the medical attendant adopting sufficiently prolonged, careful, and adequate treatment during the stage of infection.

Now, in my view, the reason why the practitioner so frequently overlooks infection of the heart by the rheumatic poison is that the clinical picture of acute and subacute rheumatism was originally exclusively drawn from the disease as it appears in adult life, and the result is that many practitioners do not realize that rheumatism as it appears in childhood presents many and important points of difference. It is important to recognize the following facts: In adult life arthritis is the chief manifestation of the rheumatic infection, and is looked upon as constituting a typical attack, while cardiac involvement is regarded as a complication. In children, on the other hand, arthritis is usually slight, and may be even entirely absent, while affections of other organs and parts are more frequent, and constitute a more prominent part in the disease. Thus endocarditis, myocarditis, and pericarditis are much more frequent, and should not be looked upon as "complications"; they are just as much part of the disease as is affection of the joints. Subcutaneous nodules, certain exudative erythematata, and purpura rheumatica are also more frequent manifestations of the rheumatic infection; chorea is common in connexion with the rheumatism of childhood; and tonsillitis is perhaps more common in connexion with the rheumatic state in youth than in adult life.

Endocarditis, myocarditis, or pericarditis may accompany the slightest affection of the joints. There is often a little pain, stiffness, and tenderness, with no perceptible swelling; acid perspirations are usually very slight, and the pyrexia is in most instances moderate. Sometimes the affection is confined to the tendons of the fascia in the neighbourhood of the joint, as, for example, the tendons of the hamstring muscles under the knee, causing the child to walk on the tips of the toes, with the knees bent. This may be mistaken for incipient talipes equinus or paresis. On the other hand, we should be careful to exclude infantile scurvy, acute anterior poliomyelitis in its early stages, syphilitic disease of the ends of the long bones, and other affections of the joints in children. Involvement of the heart may also be associated with subcutaneous nodules, certain exudative erythematata, chorea, or merely with an indeterminate febrile attack. Indeed, carditis may occur alone, that is, it may be the only manifestation of rheumatism at the time.

While endocarditis may occur acutely in children as it does in adults, it often occurs in a subacute and insidious form, and therefore its existence is frequently not known or suspected until the heart is examined because of some other rheumatic manifestation. There is frequently an

* The substance of a lecture given at the Medical Graduates' College and Polyclinic, February, 1914.

absence of subjective symptoms, and even when present they are often very insidious. Therefore, the diagnosis rests largely upon physical signs. Now, if these be facts, it is clear that when a child complains of pain in the joints, muscles, or tendinous structures, or of what are called "growing" pains; or has subcutaneous nodules on the tendons or round the joints, or subperiosteal nodules on the bones; or exhibits an erythematous eruption; or whose behaviour suggests chorea; or if he suffers from malaise and unexplained pyrexia; or complains of pain in the chest, or shortness of breath; or presents marked pallor; he should at once be put to bed, and a systematic and most careful examination of the heart should be performed daily in every case. If there is any doubt about the heart being involved or not, the patient should be kept in bed until all doubt is over. When there is no doubt that the heart is affected by rheumatism, absolute rest in bed is essential. A common error is that the rest is not sufficiently prolonged. In the majority of cases a period of three months is essential, and in some cases even a longer period is necessary.

Afterwards, the amount of exertion should be most carefully graduated, and if at any stage exertion is accompanied or followed by undue breathlessness, palpitation, sense of fatigue, precordial pain or distress, or maintained increased frequency of the pulse, the patient is doing too much, and the amount of exertion should be reduced.

PHYSICAL SIGNS.

Let us now consider cardiac affections in general; and we will deal first with physical signs.

With regard to the pulse: The pulse of mitral stenosis and of aortic stenosis are important from the view of diagnosis. In mitral stenosis the pulse is small, the up-stroke being short and soon attaining its maximum, the pulse wave is long, and dicrotism is absent; the maximum pressure is usually rather below the normal, but the minimum pressure is usually rather high, so that the pulse is full between the beats. In aortic stenosis, frequently the pulse is of small amplitude, the impression conveyed to the finger is that the rise is gradual and slow, the percussion wave is oblique, the summit is gradual, and the pulse is full between the beats. A common error still, notwithstanding the fact that much has been written and spoken with regard to the subject in recent years, is to misunderstand the significance of the irregularity of the pulse.

Cardiac Irregularity.

In an address entitled, "Recent advances in the diagnosis, prognosis, and treatment of heart disease," which I had the honour of giving in Toronto, and which was published in the *BRITISH MEDICAL JOURNAL* of March 8th, 1913, I pointed out that formerly there was great confusion in regard to the significance of cardiac irregularity—that it was known that cardiac irregularity might signify serious impairment or disease of the heart on the one hand, or, on the other hand, it might be of little or no importance. And yet, notwithstanding the advance in recent years, many practitioners still do not understand that it is now possible to classify the vast majority of cases of irregularity into types, and that it is known what each type signifies.

In my address I explained that all cases of cardiac irregularity, apart from comparatively rare exceptions, fall into one of five groups. They are: (1) What are called sinus irregularities; (2) irregularity due to what is called extra-systole; (3) irregularity due to depressed conductivity; (4) irregularity due to the pulsus alternans; and (5) the irregularity associated with auricular fibrillation.* There are a few points with regard to this subject which I should like to repeat. First, the importance of auricular fibrillation—importance with regard to the diagnosis, prognosis, and treatment of cardiac affections—should be recognized. Auricular fibrillation is a specific clinical condition, which accounts for approximately 50 per cent. of all cases of persistent irregularities of the heart, and is found in at least 60 per cent. of all cases of serious cardiac failure with dropsy. It may be present in any organic disease of the heart (mitral, aortic, and myocardial); while on the other

hand any organic disease may be present without the existence of fibrillation. When the condition has once set in, in the great majority of cases it persists for the remainder of life, and it produces a marked effect on the heart's efficiency. The condition may be diagnosed with absolute certainty by means of the polygraph or electrocardiograph. But, also, we may be reasonably certain of its existence from the presence of complete irregularity of the pulse. I will speak of the importance of auricular fibrillation from the point of view of treatment when I deal with the subject of digitalis. What I want to impress upon you is that although auricular fibrillation is a condition of the utmost practical importance, and although its nature and diagnosis have been made abundantly clear, many clinicians still fail to grasp its significance.

A few words about an "intermittent" pulse or "dropped beats." The expression is often used, and yet how rarely is any attempt made to explain what it signifies! Now, the commonest cause of an intermittent pulse is an extra-systole which fails to reach the wrist, and the next most common cause is partial heart-block. These two causes account for the vast majority of cases of intermission of the pulse. A differential diagnosis can readily be made by means of the polygraph. But in the great majority of cases there is a much easier method than this, all that is necessary being careful auscultation. In the case of an extra-systole which is not palpable at the wrist, heart sounds are heard during the pause, because the ventricle has contracted; but in the case of partial heart-block no heart sounds are heard during the pause, because the ventricle has failed to contract. It is important to distinguish between an intermission of the pulse due to an extra-systole which fails to reach the wrist and that which is due to partial heart-block, because apparently there is no evidence for supposing that extra-systoles are indicative of an impaired heart or add to the gravity of an already diseased heart, whereas partial heart-block occurring during the course of infective diseases is a sign, and may be the only sign, of myocardial damage. The only other points which I would reiterate with regard to cardiac irregularity are that sinus irregularity is of no practical importance, and pulsus alternans is of grave omen.

Errors frequently occur with regard to the apex-beat. It is sometimes forgotten that displacement of it may be due to extrinsic causes, such as adherent pleura, chronic interstitial pneumonia or fibroid tuberculosis on the one hand, or pleural effusion or pneumothorax on the other hand. A diagnosis of hypertrophy should not be made merely from a displacement of the apex-beat. Neither should it be made from an increase in area of pulsation, for here again the cause may be extrinsic to the heart. It should always be remembered that the only pathognomonic sign, as far as the apex-beat is concerned, of hypertrophy of the left ventricle is increased force of the beat.

A not uncommon error is to suppose that indrawing of the area of the apex-beat during cardiac systole is necessarily indicative of adherent pericardium.

With regard to percussion, I should like to refer to two points only: First, it is of great importance to accurately percuss the left border of the heart in cases in which the apex-beat is faint or absent. I have seen several cases in which a dilated heart associated with cardio-sclerosis was missed because of an omission to do this. Secondly, it should not be forgotten that an increase in the area of cardiac impairment may be caused by morbid conditions in the lungs or pleura, as well as by disease of the heart or pericardium.

Cardiac Murmurs.

With regard to murmurs, a not uncommon error is to suppose that a murmur necessarily means an impaired or diseased heart. Let me remind you of three points: (1) On severe muscular exertion a natural function of the tricuspid valve is to provide for a certain amount of regurgitation, and thus a tricuspid systolic bruit may appear under physiological conditions; (2) it should never be forgotten that murmurs may be haemic in origin; and (3) in every case of suspected valvular disease we should exclude cardio-pulmonary murmurs. A cardio-pulmonary murmur is a murmur which is due to some condition of the lung, the pleura, or the mediastinum, and not to any morbid state of the heart. In cardio-pulmonary

* During the last few years a condition called "auricular flutter" has attracted attention, the term having been first used clinically by Jolly and Ritchie. The condition is probably not an uncommon one, and it may give rise to irregularity of the pulse.

murmurs the point of maximum intensity and the direction of selective propagation do not coincide with those of organic bruits; the murmurs are not exactly synchronous with systole or diastole, they are more distinct during expiration, and disappear when the breath is held after deep inspiration, and they often disappear when the patient lies down. The last point makes it incumbent that in every case of suspected valvular disease the patient should be examined both in the standing and recumbent positions.

A common mistake is to diagnose aortic stenosis from the mere presence of a systolic bruit with its area of maximum intensity in the aortic area. This is not justifiable; other evidence is required, for an aortic systolic bruit may be due to other causes besides aortic stenosis—such as a mere roughening of the aortic cusps or orifice, fusiform dilatation of the aorta just above the valve, aneurysmal dilatation of the ascending aorta, anaemia, or pressure upon the aorta by a mediastinal tumour. Other physical signs of aortic stenosis are the characteristic pulse (already referred to), evidence of hypertrophy of the left ventricle, a gradual slow and sustained rise of the apex-beat, an aortic systolic thrill, and a diminished or absent second sound. The direction of the selective propagation of the murmur is upwards along the vessels in the neck. The presence of a thrill alone is almost sufficient to make the diagnosis of aortic stenosis.

A systolic murmur due to aortic stenosis may have its point of maximum intensity in the pulmonary area, and when this is the case the condition may be mistaken for pulmonary stenosis or patent ductus arteriosus.

With regard to aortic incompetence, may I remind you that not infrequently the point of maximum intensity of the murmur is in the pulmonary area, and then the condition may be mistaken for pulmonary incompetency? The essential points which should be remembered in the differential diagnosis are that in pulmonary incompetence the pulse is not collapsing in character, there is an absence of greatly exaggerated pulsation of the arteries and of capillary pulsation, there is evidence of hypertrophy of the right but not of the left ventricle, and the murmur is very rarely propagated so far down as the apex of the heart, and is never audible over the carotid artery.

Not very infrequently I have seen a diagnosis of mitral stenosis made in cases of aortic incompetence when the point of maximum intensity of the diastolic bruit—especially when the bruit is only audible towards the latter part of the long pause—is as low as or lower than half-way down the sternum and on the left side of the middle line, and of course especially when it is near the apex-beat. But the differential diagnosis is easy. In mitral stenosis the pulse is quite different from that of aortic incompetence; there is an absence of greatly exaggerated pulsation of the arteries and of capillary pulsation, there is evidence of hypertrophy of the right and not of the left ventricle, the murmur is harsher than in the case of aortic incompetence, the first sound is short, sharp, and clear, and the area of the thrill and murmur is usually small.

Mitral stenosis is often unrecognized because the area over which the murmur is audible is almost always very limited, and in some cases there is from time to time a complete absence of a thrill and murmur. In the latter case we are justified in inferring that in all probability mitral stenosis is present from the character of the pulse, the first sound—short, sharp, and clear, like a sudden snap—the evidence of hypertrophy of the right ventricle, and the accentuation or reduplication of the second sound. I have not infrequently seen a mere reduplication of the first sound mistaken for mitral stenosis.

A systolic bruit audible over the apex of the heart is often interpreted as indicative of organic disease of the mitral valve when it is due merely to relative mitral incompetence or the presence of a haemic or cardio-pulmonary murmur. In order to say that a mitral systolic murmur is indicative of organic disease of the valve we must satisfy ourselves that certain other physical signs are present. There are three main distinguishing features between a systolic murmur due to organic disease of the mitral valve and a bruit due to other causes—namely, (1) the position and character of the apex-beat, (2) the area of propagation of the murmur, and (3) the existence or absence of accentuation

of the pulmonary second sound. In the case of a mitral systolic murmur due to organic valvular disease there is evidence of hypertrophy of the left ventricle, and the apex-beat is more forcible than normal. The area of propagation of the murmur is significant. If it is propagated towards the angle of the scapula beyond the mid-axillary line we may be practically certain that it denotes the existence of organic disease. A definite accentuation of the pulmonary second sound, provided there is no condition of the lungs to account for it, is in favour of the view that we are dealing with organic disease of the mitral valve.

SYMPTOMS.

The symptoms of cardiac diseases do not receive the attention which they deserve. In this connexion it should be remembered that, while the seat of cardiac failure is in the myocardium, the custom has been to consider valvular lesions too much as specific affections in themselves, the relation which they bear to the myocardium being largely lost sight of. Diseases of the valves not only act as a source of embarrassment to the cardiac muscle, but, as a rule, along with the valvular defects there are coincident changes in the cardiac musculature, the aorta, or coronary arteries. In any case of valvular disease, a question which should invariably be asked is whether the lesion which has invaded the valve has also affected the myocardium or large vessels. Indeed, it is necessary to remember that myocardial disease may occur independently of a valvular affection.

Another question which should invariably be asked in regard to cardiac diseases is whether the lesion (valvular, myocardial, or arterial) is stationary or progressive; and, if the latter, at what rate.

Two Facts of Importance.

Now, with regard to these two important questions, Mackenzie has pointed out that, while the results of physical examination—such as evidence of the size of the heart—are important, the most important question of all is the efficiency of the working power of the heart, and that the best method of testing this is to see how the heart responds to effort; in other words, is the patient able to undergo physical exertion without distress? Careful and detailed inquiries should be made in regard to this. In making such inquiry it is essential to remember two facts—namely, (1) the natural standard of the heart's strength varies in each individual; and (2) symptoms of cardiac distress on exertion may be due to some temporary or extrinsic cause, such as deficient tone from lack of physical exercise, temporary physical or mental overstrain, and anaemia. With regard to the first, one healthy individual can normally perform only a moderate amount of exertion without experiencing symptoms of cardiac distress, while a second can do more, and a third can do still more. The point of our inquiry should be to ascertain whether the normal standard of a particular individual has decreased, and, if so, in what degree. To sum up: Provided temporary and extrinsic causes can be excluded, the fact and degree of a departure from the normal standard of an individual may be taken as fairly indicative of the presence and degree of myocardial impairment or disease; and, further, provided there is no other cause to account for it, and the patient has had the advantage of an adequate amount of rest, increasing severity of the symptoms is indicative of a progressive lesion.

Some symptoms are of much greater importance than others. Lack of time prevents me from dealing with them at all fully. The most common symptoms are undue breathlessness or fatigue, palpitation, precordial distress or pain, and a sense of tightness across the chest, on or after exertion.

Breathlessness on exertion is one of the most important symptoms. It should be remembered, however, that dyspnoea on exertion is a symptom common to many affections besides heart disease. Also, not infrequently errors with regard to the differential diagnosis of what is often termed "cardiac asthma" and bronchial asthma may arise. Palpitation is not a reliable sign of heart failure. It may occur, for example, in neurotic people, and is often reflex in origin. While pain in the precordium is a frequent symptom of cardiac failure, it often occurs in functional heart affections, and is frequently absent in

organic disease. The most characteristic feature of pain due to heart disease is that it is brought on by exertion; though it may not come on until some hours after the exertion which has induced it. I have seen more than one case of angina pectoris in which the pain has been strictly limited to the epigastrium. There may be tenderness with the pain; and a sense of constriction or oppression of the chest may occur with or independently of it.

May I remind you that the most common cause of haemoptysis in pulmonary tuberculosis is mitral stenosis? With regard to cerebral symptoms, which are numerous and are due to a diminished supply of blood to the brain, all I should like to say is that they may be present in cerebral anaemia, apart from heart disease. For example, syncope is far more frequently indicative of some temporary and functional derangement than of organic heart disease; it may be due also to reflex disturbances.

To illustrate the great importance of symptoms in cardiac affections I cannot do better than briefly mention one case. A few years ago a carman, aged 37, was admitted to the Mount Vernon Hospital complaining of pain in the epigastrium and left arm, on exertion. There was no history of rheumatism, chorea, or scarlet fever. The patient denied having had venereal disease, but a positive Wassermann reaction was obtained. For rather more than three months he had been subject to attacks of pain in the upper part of the epigastrium and left arm on exertion, the pain in the arm being of a dull aching character, and accompanied by feelings of numbness and uselessness of the limb. There was no sensation of constriction or of impending death. Ultimately the attacks were induced by such slight forms of exertion as washing himself or lacing his boots; and later, tenderness in the epigastrium was observed. The patient was a well-built, muscular man, and on examination of the cardio-vascular system absolutely nothing abnormal was discovered. The systolic blood pressure was 118 mm., there was no evidence of thickening of the vessel wall or of enlargement of the heart, no bruit, and no accentuation of the aortic second sound. A polygraphic tracing revealed nothing abnormal. I had no doubt whatever that the patient was suffering from angina pectoris. He died in an attack, and *post-mortem* examination revealed extensive syphilitic aortitis (the cusps of the valves having escaped), and gummatous changes in the myocardium.

It is important to recognize the symptoms which may be present in extra-systoles. The patient may complain of a sensation of gripping of the throat or fluttering in the chest; or he may be conscious of the long pause following the premature beat, and complain that the "heart stops"; or the contraction of the heart following the pause may be accompanied by the consciousness of a thud in the region of the precordium, and this may be followed by a feeling of exhaustion. A common error is to attach a serious significance to these symptoms; whereas, as has been pointed out, there is no evidence so far for supposing that extra-systoles are indicative of an impaired heart or add to the gravity of an already diseased heart. Patients with auricular fibrillation may complain of fluttering in the chest, or of irregular action of the heart.

ERRORS OF TREATMENT.

There is only time for me to touch upon a few common errors in the treatment of cardiac diseases.

The first is an error mainly on the part of the public. One of the most unfortunate things we have to face is the fact that such a large proportion of patients with cardiac affections endeavour to live beyond the limits of the heart's power. A constant strain is thus thrown upon the organ, for it is well known that, after cardiac systole, the power of contraction is for a short period abolished, and that when the pause following contraction is prolonged the succeeding contraction is more powerful; in other words, the power of the heart is increased by a period of rest. It is of supreme importance that this should be avoided, and that the patient should acquire the habit of each day living within the limits of the heart's strength. One is constantly asked what amount of bodily exertion should a patient with a cardiac affection be allowed to undergo. I should like to enunciate a cardinal principle which, in

my opinion, is of inestimable service. It is that any exertion which the patient indulges in should not be attended or followed by undue breathlessness, palpitation or fatigue, a sense of tightness across the chest, or precordial pain or distress. On the other hand, exertion short of producing these is usually not harmful. Another error of treatment, in my opinion, is on the part of those who believe that certain waters of Nauheim, on account of their ingredients, possess a specific therapeutic value in cardiac affections. I do not for a moment deny that many patients undoubtedly derive great benefit from a stay at Nauheim. But in my judgement this is not due to any specific value of the waters, but rather to the change of air, the rest, the regular mode of life and exercise, the careful dieting, and other factors. I have not the least doubt that, given the same conditions of life, similarly good results may be obtained anywhere.

Administration of Digitalis.

Let us now consider the subject of the administration of the digitalis series of drugs. In spite of careful investigations and of what has been written on this subject, I am afraid there are still many who do not understand and appreciate the importance of recent advances. The extraordinary difference in the results of the administration of digitalis and its allies in persons suffering from identically the same lesions, and complaining of precisely the same symptoms, was formerly a cause of great perplexity to the clinician. It was thought by some that the drug was capricious in its action or uncertain in its strength on the one hand, or that some particular preparations are active while others are inert, and for this reason special preparations have been prepared and advertised as being more uniformly certain in their action. It has been clearly proved that both these opinions are wrong. The profession as a whole still do not realize that the question of the extraordinary differences in the results of the administration of digitalis has been practically solved. Put briefly, the response to digitalis differs according to the condition of the heart and character of the rhythm; those cases of cardiac failure which show wonderfully good results are, in the vast majority of instances, cases of auricular fibrillation.

Digitalis should not be administered in a mere rule-of-thumb fashion in cases of cardiac failure. First, it is possible to do harm in cases of diminished conduction. Secondly, if auricular fibrillation is present (whether there is mitral disease, aortic disease, or disease of the myocardium), as long as there is a rapid pulse, digitalis is in the vast majority of cases a therapeutic agency of wonderful potency. The administration of the drug is followed by a rapid fall in the pulse-rate and a concomitant improvement in the general symptoms. Certainly two exceptions are (1) cases of cardio-sclerosis in which the degeneration is so widespread that little healthy muscle remains; and (2) cases in which there is pyrexia. A very common error is to give the drug in too small doses. As a rule improvement can be started after a time by small doses of 5 minims of the tincture three times a day, but they always require a much longer period to do so than larger doses; and sometimes small doses produce no effect in cases which respond well to a full dose of the drug. It is advisable to begin with a drachm of the tincture per day, or in urgent cases with even $1\frac{1}{2}$ or 2 drachms per day, and to continue until there is nausea or vomiting, diarrhoea, headache, an unduly slow pulse, or what is called "coupling of the beats." Coupling of the beats is a danger signal. When a reaction is obtained the drug should be stopped until these symptoms have passed away. As a rule the patient relapses. The indication, then, is to find out what dose suits him best—that is, the dose sufficient to control the heart without producing toxic symptoms. Having discovered this dose, in the great majority of cases it will be necessary for the patient to continue taking the drug for the remainder of his life, for the reason that in the vast majority of cases auricular fibrillation persists for the rest of the patient's life. One of the most common errors in cardiac therapeutics is to stop the administration of digitalis in cases of cardiac failure with auricular fibrillation and a rapid pulse as soon as the patient has improved.

When auricular fibrillation is not accompanied by a rapid

pulse, no marked result should be expected to follow the administration of the drug.

What may be expected from the administration of digitalis in cases of cardiac failure unaccompanied by auricular fibrillation? Well, in exceptional cases auricular fibrillation develops during the administration of the drug, and then these cases respond in the same manner as do most of the other cases of auricular fibrillation. Apart from these exceptional cases, as a rule, though not in all cases, the beneficial results will be only moderate or slight, or none at all. And a very important point in this connexion is that, unlike cases of auricular fibrillation, the improvement can usually be maintained without continuing the drug.

Strophanthus and squills should be regarded as substitutes for digitalis. They may be tried when a patient is found to be peculiarly intolerant to digitalis. With regard to the so-called alleged active principles of digitalis, it is asserted by those most competent to judge that there is no pharmacological or clinical evidence that they are either pure substances or that different samples of them are uniform in their potency; and that there is no reason to believe that they are more reliable than, and possibly they are not so reliable as, different samples of the tincture of digitalis.

And, lastly, among the common beliefs which are held by the profession at large is the belief that the internal administration of digitalis increases the blood pressure in man by constricting the peripheral vessels. In two papers which I read at the annual meetings of the British Medical Association in 1912 and 1913, I showed from investigations that, judged by the methods in use for observing the blood pressure clinically, this is not true; and therefore there is no risk in employing the drug in cases of degeneration of the walls of the blood vessels or of supernormal blood pressure.

The subject of heart disease demands serious attention. In the *BRITISH MEDICAL JOURNAL* of February 7th, p. 335, reference was made to a paper by Dr. Karl Grassmann, in which it was pointed out that the death-rate from diseases of the circulatory system is high in all countries, and that heart disease causes a large amount of invalidity in all sections of the population. The subject is well worthy of your study, and I trust that the remarks which I have made during the limited time at my disposal will be of service to you in your private practice.

ON TINCTURE OF DIGITALIS (B.P.): ITS ACTIVITY AND STABILITY.

BY

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I.

INTRODUCTION.

THE subjoined observations deal primarily with the physiological activity, assayed on frogs, of a series of tinctures of digitalis, prepared according to the *British Pharmacopoeia* from leaves grown in the years 1911-1913 inclusive.

These tinctures, examined within a few days of manufacture, and repeatedly during the following months, showed marked variation not only in their initial activity but also in their stability. Many of them were in the first instance sent by the manufacturers to the Society of Apothecaries for physiological assay, and these were supplemented by samples purchased from wholesale firms of good repute. In comparison with the above there were also examined a small number of tinctures purchased from dispensing chemists and a few non-official solutions, including some prepared from so-called pure principles.

The mode of assay was based on the method practised by Houghton in 1895, and published three years later⁸—namely, that of injecting measured doses into a series of frogs and noting the smallest dose, in proportion to body-weight, which arrested the ventricle in systole. In the majority of initial assays only a single series of frogs was employed. Repetition of each assay would have

determined the "minimal lethal" dose with smaller error, but careful manipulation was found to yield such concordant results, and the variations found at the outset were so marked, that this appeared unnecessary, since it was of greater interest to test broadly the variability and stability of the whole series than to follow minutely the changes in a limited number of samples. The accuracy of the work was, however, controlled by occasional re-assays, after a few days' interval, on a fresh batch of frogs. The frogs employed (*R. temporaria*) were almost exclusively males, between 20 and 30 grams in weight. Within these limits the ratio of body-weight to body-surface is so nearly constant that no attempt was made to ascertain whether weight or surface is the better basis of dosage. Weight was chosen on account of its readier determination.

The activity of the tinctures is expressed in terms of the Dixon-Haynes standard²—that is, in terms of a tincture with a minimal lethal dose of 0.75 c.cm. per 100 grams body-weight. The number expressing activity is obtained from this by dividing 0.75 by the minimal lethal dose found in each case, and the latter (minimal lethal dose) is calculated as lying midway between the smallest dose that proved fatal, by arresting the ventricle in systole, and the largest that failed to kill. The alcohol of the tinctures was removed by distillation, *in vacuo*, at 40° C. In each initial assay the doses tested were six in number, ranging between 0.3 c.cm. and 1.0 (or 1.2) c.cm. per 100 grams body-weight. In early re-assays three doses were given—(1) the smallest dose that proved fatal at the preceding assay, (2) one larger, and (3) one smaller than the first. In re-assays of stale tinctures several series of frogs were at times necessary. The difference between consecutive doses was, at most, 0.2 c.cm. (per 100 grams), and no assay was taken as completed until at least one animal showed systolic arrest of the ventricle and unless the largest non-fatal dose was completely absorbed. Verification of absorption is a precaution of cardinal importance. A more detailed account of these procedures will be published elsewhere.

II.

INITIAL ACTIVITY OF THE TINCTURES.

Fifty-five tinctures were examined within a few days of manufacture, and are grouped according to their activity in Table I.

TABLE I.—Classification of Tinctures according to Initial Activity.

$$\text{Activity} = \frac{\text{Standard M.L.D.}}{\text{Observed M.L.D.}} = \frac{0.75}{x}$$

Group:	I.	II.	III.	IV.	V.
M.L.D. (c.cm. per 100 gm.)	1.3-1.0	0.9-0.75	0.7-0.6	0.55-0.45	0.4-0.3
Activity	0.6-0.75	0.8-1.0	1.1-1.25	1.4-1.7	1.9-2.5
Number of tinctures	2	9	12	18	14
Percentage	4	16	22	33	25

The distribution of the tinctures among the above groups in the three years taken separately was strikingly different. This matter is, however, of pharmaceutical rather than of clinical interest, and will be dealt with in detail in another publication.

A similar examination of twenty-three British tinctures, by Dr. Alexander Goodall,³ published in 1912, showed equally great variation. Classified as above, they were as follows:

In Group I	5 (22 per cent.)
„ Group II	12 (52 per cent.)
„ Group III	1 (4 per cent.)
„ Group IV	3 (13 per cent.)
„ Group V	2 (9 per cent.)

Within the same range, therefore, there was a much higher percentage of weak, and a much lower percentage of the very strong, samples than was found in the present work.

Taken broadly, the tinctures of Groups II and III may all be regarded as "standard" and make up (in Table I) between one-third and one-half of the total. Only 3 to 4 per cent. were much below standard. More than one-half of the total number (Groups IV and V) was very much above standard.