2. Where there are lesions due to such states, healing does not commence until the ionic calcium of the blood approximates to the normal figure.

3. By parathyroid therapy it is possible to rectify the calcium balance of the blood much more effectively than by the injection of calcium salts.

4. The therapeutic use of parathyroid substance in the cases described is essentially physiological. It does not appear to act specifically against any one organism, nor any one toxin. Its action is to place the tissues of the patient under conditions more suitable for the performance of their normal functions, and for combating the effects of toxic processes.

NOTE (by W. R. G.).—The septic foci believed to be the primary cause of the calcium deficiency have in various diseases been found in a chronic ear discharge, the tonsils, the accessory sinuses of the nose, a chronic appendix, the gall bladder, probably the colon (as evidenced by colitis), possibly the uterus, but most often in the teeth. In this connexion the ulceration of the gums (pyorrhoea) has often been the cause, since the removal of the tooth has materially altered the condition of the disease for the better. When a red oedematous line leading from the ulcerating margin outlining the tooth is found suspicion should be at once aroused. From personal observation in these cases the apex of the tooth has always shown erosion.

REFERENCES.

¹ Vines: *Journ. Physiol.*, 1921, 55, 86. ² Grove and Vines: *BRITISH MEDICAL JOURNAL*, 1921, II, 687.

CARDIAC DISEASE AND OCCUPATION.

BY

R. O. MOON, M.D. OXON., F.R.C.P.,

SENIOR PHYSICIAN TO THE NATIONAL HOSPITAL FOR DISEASES OF THE HEART, LONDON.

ONE of the most important problems which confront the physician in regard to diseases of the heart is to give sound advice as to occupation. In former days the great importance of rest in heart disease was perhaps somewhat indiscriminately and unconditionally emphasized; nowadays it would seem that more stress is laid upon the advisability of exercise. This does not mean, of course, that medicine has swung violently from one extreme to the other of treatment, but that in days gone by physicians in their writings were more particularly concerned with advanced cases of heart disease, for which rest must always be the prime requisite. The increased facilities for discovering cardiac abnormalities have not unnaturally led medical men to regard such abnormalities as more serious than often they really are, and consequently to apply to them the same line of treatment which would only be suitable in the case of a quite definite disease.

The profession has been gradually learning that cases with cardiac disability are capable of doing much more work than was formerly supposed; true, there have always been wonderful cases of damaged hearts doing extraordinary things, but no prudent physician would base his advice upon abnormal and exceptional cases.

In the case of any cardiac abnormality what one wants to know is whether the abnormal finding indicates any really serious disability at the moment or in the near future. There are quite a number of hearts which it would be well to regard not as diseased but as handicapped, and in much the same condition as a limb impaired by infantile paralysis which limits but does not prevent one's power of walking; no doubt in the case of infantile paralysis it is easier for the patient to discover unaided what he can and what he cannot do than is at first possible for heart cases. Such cardiac conditions would include not only certain valvular lesions and some arrhythmias, but also many hearts with no physical signs which for want of a better term one might describe as "subnormal hearts," where the functional capacity of the myocardium is less than normal, such cases being formerly described perhaps as weak or flabby hearts. Patients with such hearts insensibly drift into sedentary occupations, which suit them fairly well, and it is only when some sudden and unusual output of energy (as occurred so frequently in the army, when cases of this type were enlisted) is called for that the intrinsic cardiac weakness becomes manifest. Many of these cases, however, need not be confined to sedentary work only: they might be much more active, provided they could take their own time over the work. Many of them can earn as good wages as if they had no disease at all.

In a rough sort of way we may think of any given cardiac lesion as of a static or dynamic type, by which, of course, we

mean that in the one case the condition seems comparatively stationary, while in the other it is likely to progress. Cases which are likely to be of the static kind are usually those due to rheumatism, chorea, or scarlet fever occurring in early life; while those of the progressive type are in the main the cases which originate from arterio-sclerosis, or in which syphilis is admitted as a cause. Clearly very different occupations will be adopted for these two categories of cases, and it is only for the static ones that much activity can be permitted. Contrary to what is generally supposed, aortic regurgitation, when due to rheumatism, in a young adult has one of the best prognoses of all valvular lesions from the point of view of work; the reason why it has had such a bad prognosis in the past is that such cases have not been sufficiently distinguished from those of arterio-sclerotic and syphilitic origin, which certainly furnish the larger number of aortic lesions, and their prognosis is specially bad.

Are there any general principles which can guide us in the selection of work for cardiac cases? As a rule, all kinds of work which involve sudden spurts, although there may be comparatively long intervals of rest, are bad for most cardiac patients; the life of the docker and of the soldier, just to take two types, is liable to periodical rushes with unduly slack intervals, and such occupations should of course be avoided. In selecting an occupation it is specially important to consider whether the hours are regular and the work more or less the same from day to day and hour to hour, while there need be no undue sense of hurry in the doing of it. This question of regularity in work requires quite as much consideration as the number of foot-pounds of energy which the work may require to be put forth. Work which places a fairly heavy strain upon the lower extremities is much more easily tolerated than that in which the main strain falls upon the arms. Most forms of aortic disease, and undoubtedly those of the degenerative type, seem to be very unfavourably affected by any work which involves even a moderate strain upon the arms, such as carpentering, and this is particularly the case where there is any suspicion of angina. It should also be borne in mind that aortic cases, when otherwise doing fairly well, are often liable to transient attacks of giddiness, which should rule out the numerous occupations which necessitate going up ladders or close contact with machinery. It is unfortunate that there seem to be so many occupations in which "heavy lifting," though by no means the essential part of the work, yet is often required incidentally; thus a man is suddenly asked to move a heavy piece of furniture, and it is this which does the damage and not the regular work itself.

Apart from the actual occupation one should further inquire into how great the distance is at which a man lives from his work, for often it is not so much the occupation *per se* which proves too much for him as the long walk to and from it, with, it may be, a heavy uphill grind at the end of the day, or there may be the added excitement and anxiety about catching trains or omnibuses. Then, too, at the end of the day it makes a good deal of difference if a man lives in a two-storied cottage or has to ascend to the top floor of some model dwelling. In the case of women, the vast majority even nowadays are occupied in some way with a home, the complicated activities of which are not easy to curtail; often, however, the omission of one single item of household labour, such as "washing," may make all the difference to a woman being able to carry on or having to give up her work. Women as a rule are not good organizers of their own work, but the task is difficult, and they might say with Frau von Stein in a letter to Goethe, "It is not perceived that to discharge the thousand little details of life which we have to attend to more ability (for which we get no credit) is required than for the doings of a genius who is at once accorded honour and fame."

As will be gathered from what has been said, it is a great mistake to suppose that cardiac cases can only do sedentary work; many more active forms of work are open to them, but they require selecting and being carefully gone into. Clearly the most important thing to do is to make some attempt to estimate the power of the myocardium. The significance of the myocardium in the estimate of the seriousness of any cardiac lesion was recognized as far back as the time of Stokes of Dublin, who said:

"It is in the vital and anatomical condition of the muscular fibres that we find the way to cardiac pathology; for, no matter what the affection may be, its symptoms mainly depend on the strength or the weakness, the irritability or the paralysis, the anatomical health or disease, of the cardiac muscles."

Such, too, has been the teaching in the medical schools for the last thirty years, but it has certainly been more emphasized during the last few years by Sir James Mackenzie and Sir Thomas Lewis. Yet with the more generally diffused recognition of the importance of the myocardium one cannot say that our ability to appraise the strength of the heart muscle has increased in the same ratio; still, by a careful inquiry into the patient's symptoms and study of the reaction to exercise an approximate estimate of its power can be obtained.

In considering whether a man with a cardiac lesion should remain at his work, one must not take too abstract a view as to how many foot-pounds of energy are required, but how far the work seems to suit the man—how far, if we may so express it, he is psychically attuned to it, for there are many forms of work which might seem intrinsically too heavy, and so they would be for a beginner, yet by long custom and a natural aptitude they have become easy for the particular individual, who has found out how to accomplish a great deal with the minimum amount of exertion; one must, therefore, hesitate long before removing such a case from his work. We must, unfortunately, among other things, distinguish between a man's keenness about his work and his keenness for the wages which his work brings in, for he will continue at work long after he is quite unfitted for it when the wages are particularly good, and it is astonishing how difficult it is to persuade such cases to take on lighter work, with shorter hours, when any sacrifice of wages is involved.

When the question arises as to the future occupation of a boy with valvular disease, which in early life is usually of rheumatic origin, it is always advisable to recommend some sedentary or quasi-sedentary work, for one can never be sure that a second attack of rheumatism may not occur quite soon and damage the heart still further; also boys are only too ready to overstrain themselves if the work they have been started upon is at all heavy.

In advising work for any given case much must depend on the man's education, previous training, general mental equipment, and temperament. It is obviously more difficult to find work for the unskilled than for the skilled, as the former requires more actual physical exertion than such cases should be allowed to give. It is of course most important that a man should work well within the limits of his capacity so that there may be a margin of safety. Nor should it be forgotten that mental and emotional stresses in many occupations may cause a cardiac case to break down nearly as often as physical overexertion.

Men suffering from a cardiac lesion who can be up and about are far too readily sent off to some convalescent home in the country, when what is really most required is some suitable occupation near their own home. It is quite possible for hearts to be underworked as well as overworked. Cardiac convalescent homes should be primarily for women and children, while for men training centres for occupation with an occupational bureau are indicated, such as have been started in the United States by the Association for the Prevention and Relief of Heart Disease.

FURTHER RESEARCHES ON DETOXICATED VACCINES.

BY

DAVID THOMSON, O.B.E., M.B., CH.B. EDIN.,
D.P.H. CAMB.,

DIRECTOR OF THE "PICKETT-THOMSON" RESEARCH LABORATORY, AND
HONORARY PATHOLOGIST, ST. PAUL'S HOSPITAL, LONDON;

AND

ROBERT THOMSON, M.B., CH.B. EDIN.,
CLINICAL PATHOLOGIST, ST. PAUL'S HOSPITAL, LONDON.

Preliminary Note.

In an article upon the biochemistry of germs and other proteins by one of us (D. T., *Lancet*, i, 1921, p. 849) it was pointed out that all germs could be split up into several non-toxic yet antigenic fractions, and it appeared that a detoxicated vaccine composed of all the non-poisonous fractions was better than one which contained a single fraction only, as was the case with the earliest detoxicated vaccines.

During the past year researches which have been successful have been made with the object of producing more efficient detoxication. Twelve months ago the average dosage of detoxicated vaccines was from 5,000 million to 20,000 million. As a result of more efficient methods of detoxication the

average dosage has been increased at least five times—namely, to 25,000 million to 100,000 million. It seems reasonable to hope that in the near future the detoxication process will be so efficient that doses of one billion germs will be attainable—that is, one million million organisms.

Numbers of this nature convey a very vague impression, but if translated into terms of mass of the semi-solid wet germ substance the actual dose is better appreciated. One million million germs represents roughly a mass of one cubic centimetre of the semi-solid wet bacteria. One hundred thousand million represents, therefore, one-tenth of this value—namely, 1/10 c.cm. of the semi-solid wet germs. Ten thousand million is equal to 1/100 c.cm. of the substance, one thousand million equals 1/1,000 c.cm., and one hundred million equals a dose of 1/10,000 c.cm. These figures vary according to the size of the germ and are only approximate. They are, however, sufficiently correct to convey to the mind a fairly clear idea of the actual doses of germ substance which are represented by hundreds and thousands of millions.

The dose of the ordinary toxic vaccines which have been in general use for the past ten to twenty years averages from five million to one thousand million germs—that is, from 1/200,000 to 1/1,000 c.cm. of the wet germ substance. Now 1/200,000 of a cubic centimetre is practically invisible, and 1/1,000 of a cubic centimetre is about the size of the head of a small pin.

It has seemed to us that injections of such small doses into a comparatively large animal like a man could only produce an infinitesimal amount of antistubstance or immunity. The maximum doses of the first detoxicated vaccines—namely, 10,000 to 20,000 million—represent 1/100 to 1/50 c.cm. of the wet germ mass. This is still in reality a very small dose. The dose attained by more efficient detoxication—namely, 100,000 million—represents 1/10 of a cubic centimetre, and the mind begins to appreciate that a dose of this size may conceivably stimulate the formation of a considerable quantity of antistubstance producing immunity, and experiments detailed below prove that this is the case.

It is our ambition, however, to reach such an efficiency of detoxication that doses of one billion germs, or 1 c.cm. of the wet germ mass, may be inoculated at a time. There can be little doubt that when such doses are attained the immunity produced will be so great as to produce very remarkable curative results. In the domain of preventive medicine, by such massive inoculations we may hope to be able to guarantee a complete and certain immunity from a given disease for a very considerable period of time.

The Importance of Dose in the Production of Antistubstances or Immunity.

The following experiments were carried out in order to prove the great importance of dosage in the stimulation of antistubstances to any foreign protein. Germs are composed of protein material, and it should be remembered that it is a well-proved law that when any highly complex foreign protein is injected into a living animal that animal has the power of developing a contrary substance, or, in other words, immunity to that foreign protein material. The animals used in these experiments were rabbits, and the foreign protein employed was sheep red corpuscles. Sheep red cells are non-toxic in nature, and very large doses can be injected without making the animals suffer in any way.

If we take the serum of an ordinary normal rabbit and mix it with sheep red cells the serum as a rule exerts no solvent or haemolytic action on these foreign cells. If, however, we inject that rabbit with large doses of sheep cells—namely, a total of 5 c.cm. of the semi-solid wet sheep cells—then the rabbit forms a large quantity of antibody (haemolysin) towards the foreign corpuscles. Indeed, the inoculated rabbit becomes so surcharged with the haemolysin that its serum becomes in many instances capable of dissolving the sheep cells, even when it (the serum) is diluted 10,000 to 20,000 times with normal saline. The smaller and smaller the doses of sheep cells injected, however, the smaller and smaller is the amount of haemolysin produced. This is well proved in the following experiments:

Rabbit A was injected with doses of sheep cells corresponding in mass to the doses of ordinary toxic vaccines given to a man. The mass of toxic germs given to a man, as already stated, amounts to 1/200,000 c.cm. to 1/1,000 c.cm. A rabbit, however, is on the average at least twenty times smaller than a man, so corresponding doses of sheep cells would be 1/4,000,000 to 1/20,000 c.cm. of the semi-solid wet cells. Doses of this size, however, were apparently too minute to stimulate the formation of any appreciable or detectable amount of haemolysin. The haemolytic titre of this rabbit's serum