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.

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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 antiserum 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 antiserum 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 Antisubstances or Immunity.

The following experiments were carried out in order to prove the great importance of dosage in the stimulation of antisubstances 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

was tested against sheep cells every few days after each inoculation, but the result was more or less negative.

Rabbit B was injected with doses of sheep cells corresponding in mass to doses of detoxicated vaccine varying from 1,000 to 100,000 million germs—that is, doses of 1/20,000 to 1/200 c.cm. There was no appreciable rise in the haemolytic titre of this rabbit's serum until doses of 1/400 c.cm., corresponding in mass to 50,000 million germs, had been given. With doses comparable in volume to 50,000 million germs and upwards in a man the haemolytic titre, however, rose in a very remarkable degree, so that the serum became potent even in a dilution of 1 in 100.

Rabbit C was inoculated with doses of sheep corpuscles corresponding to doses of 1,000,000 million (one billion) germs, or 1 c.cm. of the semi-solid wet germ substance aimed at in a man. (The rabbit being one-twentieth the weight of a man received actually 1/20 c.cm. doses of the semi-solid moist sheep cells.)

Each dose of this size produced a very marked rise in the haemolytic titre of the rabbit's serum, and after seven such doses the eventual immune power of this rabbit rose to the extent that its serum was capable of dissolving the sheep cells when it was diluted 1 in 480 parts with normal saline. In order to get much higher immunity in rabbits wherein the serum is haemolytic to sheep cells at a dilution of 1 in 10,000 to 1 in 20,000, it is necessary to inject cubic centimetre doses of the sheep corpuscles.

It is logical to assume from these experiments that, in order to obtain a similar highly potent antiserum in man towards bacteria, similar massive doses of germ substance must be injected. Furthermore, for successful immunity it is not necessary to get severe toxic reactions, as many imagine. Sheep corpuscles are very non-toxic. They are hundreds of times less toxic than the most efficient detoxicated vaccines ever produced. The inoculations which were given to the above rabbits produced no toxic reactions whatsoever, yet the graphs of Rabbits B and C showed an enormous immunity response.

With regard to vaccine therapy there is still another fallacy or heresy which is frequently preached—namely, that if one injects too much vaccine the system becomes tired and overworked so that it can produce no more antibody. If a rabbit can keep on producing antibody to doses of sheep cells totalling 5 c.cm. of the solid moist corpuscles, surely doses of germ substance amounting to a minute fraction of a cubic centimetre will not exhaust the immunity-producing powers of a man who is enormously greater in weight and size than a rabbit.

It would seem more near the truth to say that it is the toxins of the germs which tire and exhaust the system. These toxins require to be removed, so that enormous doses of the germ substance proper may be given. We wish to develop in our serum a quality which will destroy germs by dissolving or lysing them. Such an immune serum would be a much more valuable possession than a serum which simply neutralized the poison of the germs. In any case it is stated in practically every modern work on immunity that it is very doubtful if antisubstances can be produced against the endotoxins of germs. These endotoxins are allied to the amino-acid derivatives of proteins, and it is known that no antisubstances are formed against such simple derivatives. Again, even if antisubstances can be formed against them, they are too toxic to permit of large enough doses to obtain any appreciable amount of such an antisubstance. Against certain toxins it is true that good immunity is produced—for example, against diphtheria and tetanus toxins. These toxins, however, are highly complex protein substances, allied to snake venoms, and are quite different from the usual simple endotoxins of germs.

It is stated that antimeningococcal serum is an anti-endotoxic serum, but this perhaps is not quite correct. The so-called meningo-endotoxin which is injected into horses to obtain this antiserum is a watery extract of meningococci, and is likely to contain much non-toxic meningococcus protein, such as proteoses, etc., as well as the true endotoxin. In the serum of the injected horses, therefore, there will be developed a considerable amount of antisubstance to the protein material of the meningococcus, and this may account for its successful therapeutic results when injected into human beings suffering from this disease.

Improved Detoxication Process whereby Doses of 100,000 million Germs may be given.

About eight months ago it was discovered that in the first stage of the detoxication process—namely, the solution of the germs in NaOH—some of the germs invariably escaped the solvent action of the alkali, and that when acid was added, a certain number of unautolysed germs were carried down in

the precipitate of germ metaprotein. In other words, the non-toxic precipitates of the germ substance contained a small proportion of the unaltered toxic germs themselves. The presence of these unchanged toxic bacteria, though few in number, was nevertheless responsible for a large amount of the toxic action residing in the so-called detoxicated vaccines. In other words, the detoxicated vaccines of a year ago were really a mixture of the non-toxic fractions along with a small proportion of the unchanged toxic germs.

This defect has now been avoided by passing the solutions of each germ fraction through a Chamberland filter before precipitating them. The precipitates obtained in this way after porcelain filtration were found to be about ten times less toxic than before. This filtration process alone, therefore, has brought about a tenfold increase in the dosage of the detoxicated vaccines.

This success, as already stated, leads one to hope that still more efficient detoxication will be attained whereby the ultimate aim of giving 1 c.cm. doses of the semi-solid wet germ protein will be reached. The rabbit experiments described lead one to hope that such massive doses will confer on man an extraordinarily powerful immunity, and that they will exert a very efficient curative action on various diseases.

Machine for Crushing Germs.

In order to remove the poisons which reside within the bodies of germs, the latter must be entirely disintegrated or autolyed. For this disintegration of the bacteria we have up to the present relied entirely upon the dissolving or disintegrating action of chemicals, such as weak alkalis, acids, alcohol, etc. Where weak chemicals are used the protein substances of the germs are not so injured or changed as to effect their specific immunizing properties. For example, it has been demonstrated by Balls and Korns (1918) that if red cells are dissolved in weak NaOH and the protein substance is then precipitated with weak HCl, this protein precipitate when injected into rabbits has still the power of causing the formation of specific haemolysins in the latter. Similarly it has been shown by Kolmer (1917) that specific immunity is produced against certain tissue cells when animals are inoculated with the metaprotein of these cells treated in this manner.

It so happens, however, that certain germs require very strong alkali, and even antiformin, to dissolve or disintegrate them, and such powerful chemicals are likely to have a deleterious effect upon the specific antigenic properties of the germ proteins. For this reason during the past two years strenuous endeavours have been made to find some mechanical means of disintegrating germs, in order, so far as possible, to avoid the use of strong chemicals in the detoxication process. Several machines were devised and constructed for this purpose with varying degrees of success. A machine was devised recently by Plauson which was claimed to have the power of smashing substances into colloidal form. Through the courtesy of Messrs. Plausons, Ltd., the disintegrating effect of this machine on germs has been tested. Emulsions of yeast and staphylococci were subjected to the smashing effect of the machine for thirty minutes, and they came through the test unaffected. It is the insignificance of germs which saves them, since they measure about 1/30,000 to 1/50,000 of an inch in diameter.

With the aid of a designing engineer, Mr. Macfie, one of us has been able to construct a small machine which has a cutting as well as a grinding action. It is capable of giving from 5 to 20 million cuts in the emulsion a minute. This machine, in the first few tests made, appears to be more efficient than the Plauson smasher, and it has enabled the writers to employ much weaker chemicals in dissolving the germs than hitherto used. With the present design, however, it is still incapable of smashing the germs in water—that is, without the aid of some chemical. When very fine carborundum powder, however, is added to the watery germ emulsion and the mixture smashed in the machine the disintegration effect on yeasts or germs was very considerable without the aid of any chemicals at all. There is no doubt that this machine should mark a very considerable advance in the detoxication process, and much better vaccines will be obtained by its use. It has been returned to the maker for some alterations in design which are calculated to make it more efficient, and it is hoped that the end in view—namely, the disintegration of germ emulsions with very weak chemicals or even without them—will very shortly be attained.

The authors wish to express their thanks to Mr. E. S. Dean and Mr. F. T. Downing, who have been associated with them in this research.

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STRANGULATED DIRECT INGUINAL HERNIA.

BY

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THE formation of a direct inguinal hernia is due, in the majority of cases, to repeated distension of a weak point in the posterior wall of the inguinal canal. In such cases the abnormal opening in the abdominal wall is usually large, and the edges of the opening offer little resistance to the protrusion of bowel or omentum within the hernial sac. Occasionally, however, when the intra-abdominal pressure is suddenly increased, the weak point in the posterior wall of the inguinal canal undergoes instant rupture, and it is in these cases that strangulation is apt to occur.

In the case to be described the strangulation was probably caused simultaneously with the origin of the hernia—that is to say, a split occurred in the medial portion of the posterior wall of the inguinal canal (conjoined tendon) which allowed of the protrusion of a knuckle of gut—covered, of course, by a layer of parietal peritoneum—into the inguinal canal. The tension of the conjoined tendon tended to approximate the edges of the split and thus prevented the reduction of the hernia and also imperilled the blood supply of the herniated gut, producing its strangulation. Strangulation of a direct inguinal hernia is an event of somewhat uncommon occurrence, and the following case, which was recently under my care, may be regarded as a fairly typical example of this condition.

The patient, a carter, aged 62, was admitted as an urgency case under my care at the Ancoats Hospital, complaining of a painful swelling in the right groin. He stated that, about eight hours previously, whilst loading a cart, he felt a sudden pain in the lower part of his abdomen. At first he endeavoured to disregard the pain, but as it did not disappear he left his work and returned home. Here he noticed a swelling in the right groin, and on going to his doctor was advised to seek treatment immediately at Ancoats Hospital. He gave a previous history of a hernia which was easily reducible, on the left side, but he was quite sure there had never been one on the right side.

On examination the patient was a fairly muscular man, but looked decidedly ill. Over the inner third of Poupart's ligament on the right side there was a rounded tender swelling, tense, elastic, quite free above and below, and apparently not communicating with the internal abdominal ring. There was no impulse on coughing, and gentle taxis failed to have any effect on its reduction.

On the left side there was an easily reducible direct inguinal hernia. Operation was immediately carried out. The inguinal canal was opened by division of skin and external oblique aponeurosis. The hernial sac at once presented itself, and on isolation was found to be entirely free from, and external to, the spermatic cord. The neck of the sac was traced to the conjoined tendon. The sac, which was extremely thin, was then opened. A quantity of the usual blood-stained peritoneal fluid escaped, and a knuckle of bowel of the Richter type, and plum-coloured, was seen. Digital examination of the neck of the sac from within showed that the constriction was due to tension of the conjoined tendon. A hernia director was passed within the sac, and the tendon was divided in a medial direction. The gut was drawn out of the abdominal cavity, found to be viable, and then reduced. An attempt at a radical cure for the hernia was made by ligaturing the sac, suturing the split in the conjoined tendon, and then suturing the internal oblique muscle to Poupart's ligament.

The patient made an uninterrupted recovery, and was discharged from hospital seventeen days after admission.

THE Fifth Italian Congress for Industrial Diseases will be held at Florence from June 11th to 14th, when the following subjects will be discussed: (1) Rural hygiene since the war, especially in relation to malaria, introduced by Professor A. Monti; (2) new and old views on lead poisoning, introduced by Professor C. Biondi; (3) reform of legislation relating to industrial accidents, introduced by Professor Borri; (4) prevention of disabilities following disease, introduced by Professor L. Devoto. An exhibition will be held illustrating the most recent methods for preventing industrial accidents.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

TUBERCULOUS PERICARDITIS.

MEDICAL literature contains so few references to tuberculous pericarditis that I feel justified in recording the case mentioned below as being of interest.

A student, aged 23, who had arrived in England for the first time eighteen months previously from a colony, was admitted to the hospital of SS. John and Elizabeth on April 13th, 1921, with a history of having taken to bed for a week with marked malaise and rise of temperature. There were no other symptoms whatever. He had always enjoyed excellent health, and had never suffered from any pulmonary complaint. On admission his temperature was 103.6° F., pulse rate 120, and respiration rate 40. He was tall, thin, and of a pallid complexion. His breathing, though rapid, was unembarrassed. The tongue was clean.

On examination the right side of the chest was almost motionless and dull from the fourth rib downwards, where vocal fremitus was almost absent. Breath sounds were prolonged and high-pitched above and practically absent below the fourth rib. The apex beat of the heart was displaced to the left, and an exocardial to-and-fro murmur was heard. Aspiration of the right chest yielded 20 ounces of clear fluid, which on microscopic examination showed neither cells nor bacilli, and on culture this remained sterile. A diagnosis of pleural and pulmonary tuberculosis was made.

The murmur at the cardiac apex became more marked as time progressed, and seemed rougher and louder on expiration, and on May 19th some fine crepitations were heard in the right mid-axillary line, both on inspiration and expiration. These extended anteriorly on the 31st, when a very marked rough creaking pleural rub was also heard over the left base anteriorly. Night sweats at this date became very marked. Repeated examination of the sputum revealed no tubercle bacilli. The cardiac area of dullness appeared to increase gradually to the left and right, and on June 6th the exocardial murmur, which had been getting less audible, disappeared, and at the same time the heart sounds became less distinct. Breath sounds in the left mammary region were now harsh, and in the right scapular region almost tubular in character and accompanied by fine crepitations. Emaciation became more marked. Tuberculous pericarditis was now diagnosed.

X-ray examination on June 16th showed an enormous cardiac shadow, and loss of pulsation; this was suggestive of pericardial effusion. Paracentesis pericardii was performed on three occasions with obvious relief to the patient. The fluid obtained, altogether 8 ounces, was sanious in character, and sterile in direct films and culture. No tubercle bacilli were detected. The right base was also aspirated and a similar fluid obtained, which was shown to be sterile bacteriologically. The patient died on July 1st. During his illness the temperature was continued for the first ten days; subsequently it was intermittent, ranging between 97° and 102° F.; the pulse rate varied between 90 and 140, respirations from 18 to 35.

Post-mortem Examination.—The body showed extreme wasting. On opening the chest the parietal pericardium was found to be very thickened, in parts up to a quarter of an inch, and was fused with the thickened visceral pleura. The visceral pericardium was markedly thickened by a deposit of caseous material to the extent of half an inch. The pericardial cavity was dilated and contained approximately 8 ounces of sanious fluid. The heart muscle was very pale and flabby; the valves were competent. The pleurae were thickened and contained some free fluid; and the lungs, which were adherent to these in parts, especially on the left, showed numerous miliary tubercles, but practically no evidence of old tuberculosis. The mediastinal glands showed moderate enlargement. The liver, spleen, and kidneys showed amyloid degeneration; the latter had a few miliary tubercles, and the peritoneum was studded with these. Free fluid was present.

For kind permission to publish this case I am greatly indebted to Dr. A. Saunders, Physician to the Hospital of SS. John and Elizabeth.

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REFERENCE.

Adrien Forestier: "Études Cliniques de la Péricardite Tuberculeuse avec atteinte des autres Séreuses."

RUPTURED HEART.

THE following case seems to me of sufficient interest to place on record, as it illustrates how a fatal result may follow a very slight effort in a person who was not apparently seriously ill, her chief complaint being of shortness of breath.

On January 10th, 1922, I was called hastily and found a fairly well nourished woman lying on her back on a bed. She was quite dead. The only person in the house besides the dead woman was her husband. He said his wife was about 50 years of age, was almost a teetotaler, and had never been really ill before, but a few months ago had had an upset and had lately complained of shortness of breath. On this particular day, not feeling very well, she stayed in bed; during the morning he heard a noise as of someone falling,