FATS IN RELATION TO THE GENESIS OF GOITRE.*

BY

ROBERT McCARRISON, M.D., D.Sc., LL.D., F.R.C.P.,
LIEUT.-COLONEL I.M.S.,

IN CHARGE DEFICIENCY DISEASES INQUIRY, INDIAN RESEARCH FUND
ASSOCIATION, DEPARTMENT OF PHYSIOLOGY, UNIVERSITY
OF OXFORD.

In a paper published in the *Indian Journal of Medical Research* in January, 1920, I drew attention to the effect of a diet containing an excess of butter in favouring the development of thyroid hyperplasia of the Graves's disease type. The experiment which led to this observation was carried out at Coonoor, Nilgiri Hills, Madras—6,000 ft. above sea-level—where goitre is practically unknown. It was made on pigeons and lasted 248 to 250 days, at the end of which period the birds that had survived were killed; several had died in consequence of maltreatment by their fellows.

EXPERIMENT.

1. Eighteen semi-wild pigeons were confined in a large netted wire cage, 5 ft. by 3 ft. by 2 ft. They were fed on a mixture of grains consisting of white millet seeds 12 oz., small dark millet seeds—known in India as *ragi*—8 oz., and split peas, of the variety known in that country as *mungdal*, 8 oz.; 3 oz. of fresh butter were intimately mixed by hand with the grains. The birds received this mixture daily. No sand nor grit was provided.
 2. Eighteen other semi-wild pigeons were similarly confined and fed on the same mixture of seeds and butter, but with the addition to it of a daily allowance of $6\frac{1}{2}$ oz. of freshly chopped onions. These also received neither sand nor grit.
 3. Forty-two pigeons similarly confined and fed on millet seeds only, without the addition of butter, onions, or sand, acted as controls to the experiment.
- In all three cases water was supplied in shallow troughs suspended a few inches above the bottoms of the cages.

Results.

1. The average weight of the thyroids per kilogram of body weight was 82 mg. in control birds receiving mixed millet seed only; in those which received mixed grains with butter and onions it was 128 mg.; and in those which received mixed grains with butter only, 183 mg.
2. Of fifteen pigeons which received *butter and onions* the weight of both thyroids exceeded the maximum weight in controls in five cases. Goitre was present in 33½ per cent. and absent in 66½ per cent. of cases.
3. Of seventeen pigeons which received *butter without onions* the weight of both thyroids exceeded the maximum weight in controls in eleven cases. Goitre was present in 65 per cent. and absent in 35 per cent. of cases.
4. On histological examination the enlarged thyroids of pigeons that received *butter and onions* presented a picture showing moderate congestion with the formation of many new acini whose epithelium did not exceed in height, or but slightly, that of the normal actively secreting gland. There was slight tendency to acinar budding. Colloid was comparatively scanty, thin, and pale-staining. Multiplication of acini was the essential feature of this type.
5. On histological examination the enlarged thyroids of pigeons that received *butter without onions* presented a picture showing little or no colloid, increase in height of the acinar epithelium, pronounced vesicular budding, irregularity in shape of the acini and plications of their walls—a picture similar to that characteristic of Graves's disease. Hypertrophy of acinar epithelium was the essential feature of this type of goitre.

The excessive richness of the food in butter was in this experiment a determining factor in the production of the thyroid hyperplasia and of the pronounced acinar budding.

A not less noteworthy result was the protective influence exerted by the onions. The addition of this vegetable to the diet of mixed grains and butter tended to lower the incidence of goitre, to reduce the average size of the thyroid enlargement, to restrain the intensity of the hyperplasia and the tendency to acinar budding, and to alter the character of the histological picture from an epithelial hypertrophy to a multiplication of acini without notable hypertrophy of their epithelial lining.

Variations in the histological types of goitre may thus be brought about by variations in the components of a goitre-inducing food.

The incidence of goitre in pigeons fed on mixed grains and butter, but without onions, was 65 per cent.; in the remaining 35 per cent. there was no goitre; and judged by two samples taken from this minority there was no appreciable departure of the thyroid gland from normal. The cases that did not develop thyroid hyperplasia have a significance second

only in importance to those that did. They suggest that the excess of butter was not in itself the cause of the goitre, but that it was made a potent contributing or determining cause by the operation of some other factor or factors. My previous work had indicated the important part played by bacteria introduced into the alimentary tract in the causation of goitre. The restriction of such bacterial intervention would afford an explanation of the protective influence exercised by onions in restraining the thyroid hyperplasia; in view of the minute content of iodine in onions it seems unlikely that a sufficient explanation is to be found in an increased iodine intake consequent on the addition of onions. I think it well to insist on this probability of bacterial intervention, for my recent work on "deficiency disease" has impressed upon me the necessity for bearing in mind not only the conditions of faulty food to which animals or man may be subjected, but also the variable character of the bacterial flora with which the faulty food may be associated in the digestive tract. Here we are concerned with faulty food in relation to goitre production—in relation, that is, to a malady whose prevention is dependent on the provision of an adequate supply of iodine for the needs of the thyroid gland. It is necessary, therefore, to take account of every means by which this supply may be interfered with. I interpret the results of this experiment to mean that in conditions of overfeeding (with butter in excess in the dietary), of lack of exercise, and of imperfect hygiene, the food must, for some reason, provide, in a high proportion of cases, an additional supply of available iodine for the normal functional activity of the thyroid gland.

So much, then, for my original observation with regard to the effects of a diet excessively rich in butter in contributing to the production of thyroid hyperplasia of a type similar to that found in Graves's disease; but this hyperplasia did not involve the discharge from the gland of an amount of thyroid secretion in excess of the requirements of the tissue cells. The pigeons presenting the thyroid hyperplasia did not exhibit any other signs of Graves's disease. The resemblance to this malady ended with the similarity of the histological picture of the thyroid gland in the two cases.

This observation as to the part played by food excessively rich in butter in producing hypertrophic goitre has recently received confirmation from the work of E. and M. Mellanby, who have reported similar results in puppies. They found that of the fats used by them butter induced the greatest degree of hyperplasia. They found, moreover, that cod-liver oil did not produce thyroid hyperplasia, and attributed this protective action to the oil's content of iodine. They comment also on the fact that the thyroid enlargement tended to be less marked when the fat-fed puppies had ample opportunity for exercise and an out-of-door life.

In pursuance of my original observation and of the more recent results of the Mellanbys I devised an experiment to contrast the action on the thyroid gland of free oleic acid with that of butter and of cod-liver oil. A small shelter, 6 ft. square and open at one side, was built on the roof of the laboratory at Oxford. In contrast to Coonoor, where the first experiment was carried out, simple goitre is common in Oxford. A number of small netted wire cages, approximately 16 in. square, and having a netted-wire bottom beneath which was a removable zinc tray, were placed in this shelter. The cages were piled one on top of another in columns of three. Two pigeons were placed in each cage. The amount of movement possible to the birds was thus more limited than in the first experiment and the hygienic conditions less perfect. The conditions under which the birds lived were, in short, highly favourable to the production of goitre, as the results noted in control birds at the conclusion of the experiment show. Some of the pigeons used were highly bred casters from among show birds, descended from a stock that had always lived a confined life; the tendency to goitre production was thus enhanced by hereditary factors. Twenty-eight birds were employed in the experiment, which commenced on April 4th, 1921, and terminated on August 26th (a period of one hundred and forty-four days). The birds were fed on a shop mixture of buckwheat, wheat, split peas, barley, maize, dari, and white African maize. Each bird consumed of this mixture approximately 50 grams a day. Six were in addition each given 1.6 c.cm. of oleic acid a day mixed with the grains; six each received 4 grams of butter a day, and six 1 drachm (3.55 c.cm.) of cod-liver oil in admixture with the grains; the birds ingested the major part of the several fats given. The cod-liver oil was the so-called "cattle cod-liver oil," and contained 0.002 per cent. of iodine. Six birds acted as controls; these

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received the same grains, in the same proportion, but no fats. They were confined in the same way (two to a cage) and in the same shelter as the birds receiving fats. One bird from each batch was killed during the course of the experiment in order to ascertain how the experiment was proceeding. The remainder were killed on the 143rd and 144th days; their thyroids and other organs were removed and weighed. It was found first that goitre, sometimes of large size, was

FIG. 1.—Showing the effect of cod-liver oil, butter, and oleic acid in retarding the growth of tadpoles.

The average weight of the thyroids per kilogram of body weight was, however, different. It was:

In controls	...	...	...	537 mg.
In butter fed pigeons	...	...	...	675 mg.
In oleic acid fed pigeons	...	...	...	909 mg.
In cod-liver oil fed pigeons	...	...	...	93 mg.

Great variation in size of the goitres in the first three categories was a notable feature.

The outstanding results of this experiment are: (1) The potency of the conditions of close confinement, want of exercise, overfeeding, and faecal contamination of the food in causing goitre. (2) The completeness of the protection against goitre afforded by cod-liver oil. (3) The influence of butter in favouring the development of the thyroid swelling, and the still greater influence of free oleic acid in so favouring it. (4) The pronounced individual idiosyncrasy to the disease as evidenced by size of the goitre. The last feature is one to which I have drawn attention in the case of congenital goitre produced in kids and in rats by feeding their mothers throughout pregnancy on cultures of faecal bacteria from goitrous persons.¹ It suggests the possible influence of

FIG. 2.—Showing the effect of iodine in compensating for the retardation of growth induced in tadpoles by an excess of oleic acid in their food. Dotted line: Controls receiving 1.0 mg. iodine per gram of food mixture, but without oleic acid.

tract in hampering the absorption or utilization of iodine. The fact that free oleic acid appears to be more potent in favouring goitre production than butter, suggests that it may be by means of the free unsaturated fatty acid derived from butter in the digestive tract that the latter exerts its harmful action on the thyroid gland.

The two main facts brought into prominence by this second experiment—namely, that the free unsaturated fatty acid (oleic acid) is peculiarly potent in respect to goitre production (in certain cases only), and that cod-liver oil, containing 0.002 per cent. of iodine, is peculiarly beneficial in respect to goitre prevention, both point to iodine as a common factor concerned in the results. It would seem that in the presence of an excess of free oleic acid the iodine in the food is in certain cases either rendered unavailable for use by the thyroid gland or a larger amount of iodine is in these circumstances required by the thyroid gland; or that the absorption

of oleic acid in excess creates in certain cases an increased demand for thyroid secretion on the part of the tissues. In the presence of an excess of cod-liver oil, on the other hand, it would appear that a supply of iodine sufficient to resist goitre-producing influences of a high degree of intensity is provided by the oil. Further experimental evidence is available relative to both these points.

While the second experiment was proceeding others were in progress with the object of studying the relation between fat-excess and iodine-intake. For this purpose tadpoles were used. It was thought that their sensitiveness to the influence of iodine might serve as an index of the harmful effect exerted by fat-excess on the thyroid gland. The experiments yielded remarkable results.

EXPERIMENTS WITH TADPOLES.

The tadpoles used were of the same age—eleven days—and approximately the same size. Fifty were used for each test. They were kept in white pudding dishes, each containing one litre of tap water; great pains were taken to keep the dishes clean and the water fresh. They were fed on a mixture of flour 85 parts, and caseinogen 15 parts, with green pond weed q.s. The flour-caseinogen mixture was made into a soft dough with water, and pills of it were dropped into the dishes. These the tadpoles ate greedily; cannibalism was very rare. Among the fats tested were butter, oleic acid, and cod-liver oil. The several fats were mixed with the flour-caseinogen mixture in the proportion of approximately one part of fat to two of the mixture. The addition of the fat enabled small pills to be prepared as above mentioned. These the tadpoles ate greedily during the earlier part of the experiment, more sparingly during its later stage. Three series of experiments were carried out. In the first the effects on the developing tadpoles of the several fats were observed in contrast with controls receiving the same food without fats; in the second the effects of the several fats with the addition of 0.5 mg. of iodine per gram of food mixture were observed in contrast with controls receiving the same amount of iodine but no fats; and in the third the effects of the several fats, with the addition of 1.0 mg. of iodine per gram of food mixture were observed in contrast with controls receiving the same amount of iodine but no fats. Details of the experiments have recently been published in the *Proceedings of the Royal Society*.

RESULTS.

1. An excess of the several fats in the food of tadpoles caused remarkable retardation in their rate of growth (Fig. 1).
2. Iodine in amounts of 0.5 to 1.0 mg. per gram of food mixture tended to prevent the retardation of growth induced by butter and oleic acid, but not that induced by cod-liver oil (Figs. 2, 3, and 4).
3. The compensating action of iodine varied in the case of the several fats; it was complete in the case of oleic acid (Fig. 2), almost so in the case of butter (Fig. 3).
4. So far from iodine exercising any compensating action on the retardation of growth induced by cod-liver oil, the retardation was increased by the iodine (Fig. 4).
5. The normal rate of metamorphosis was only slightly affected by the harder fats, such as butter; but was delayed by the fluid and less saturated fats, oleic acid and cod-liver oil.
6. The delayed rate of metamorphosis induced by oleic acid was compensated for by the presence of 1 mg. of iodine per gram of food mixture, but was not compensated for by this amount of iodine in the case of cod-liver oil.
7. The retardation of growth induced by the fats was associated with delayed development of the thyroid gland. Iodine in the above proportion compensated for the retardation of thyroid development induced by butter and oleic acid, but did not compensate for that induced by cod-liver oil.

FIG. 3.—Showing the effect of iodine in compensating for the retardation of growth induced in tadpoles by an excess of butter in their food. Dotted line: Controls receiving 1.0 mg. of iodine per gram of food mixture, but without butter.

FIG. 4.—Showing the effect of iodine in accentuating the retardation of growth induced in tadpoles by an excess of cod-liver oil in their food. Dotted line: Controls receiving 1.0 mg. of iodine per gram of food mixture, but without cod-liver oil.

8. Finally, in a further experiment, in which tadpoles were fed on flour-caseinogen mixture 100 parts and metallic iodine 1 part, the abnormally rapid metamorphosis induced by the high iodine intake was considerably hastened by a high proportion of butter in the food mixture, but markedly delayed by a similar proportion of cod-liver oil.

From these results the general conclusion may be drawn that, in so far as butter and oleic acid are concerned, an intake of iodine approximately proportionate to the intake of these fats in the food is requisite for the maintenance of normal metabolism, and for the normal functional perfection of the thyroid gland. The influence of iodine in further retarding bodily growth and development of the thyroid gland in the case of cod-liver oil, when administered in dosage favourable to both in the case of butter and oleic acid, is not yet understood. It is to be noted, however, that this effect of iodine was the more marked the larger the dose of this element. A further contrast in the behaviour of butter and cod-liver oil is afforded by their action in the presence of a high iodine intake by tadpoles. The abnormally rapid metamorphosis induced by the iodine was hastened by a high proportion of butter in their food, but was delayed by a similar proportion of cod-liver oil. While it is not yet possible to afford a complete explanation of these reverse effects of butter and cod-liver oil, the facts as they stand indicate an important relationship between thyroid function and the metabolism of iodine and fats. Free oleic acid and cod-liver oil also, in respect to their relations with the thyroid gland, have reverse effects; the former favours thyroid hyperplasia, the latter protects against it. In respect to iodine they seem also to have reverse relations: the former when ingested in excess requires to be combined with iodine in the approximate proportion of one part of this element to 3,000 of the unsaturated fat, in order that it may be rendered harmless to tadpoles; the latter when ingested in excess by tadpoles becomes more harmful if combined with this amount of iodine.

Oleic acid also seems to have an effect on the thyroid gland of tadpoles which has not been observed in the case of cod-liver oil, nor in the same degree in the case of butter; it would appear, from the limited number of observations I have so far made, to cause a diminution of the colloid-content of the gland out of proportion to its retardation in development. This observation was made as follows: The tadpoles were serially sectioned, each section being 10 μ thick. The area occupied by the thyroid could thus be measured and the total number of vesicles counted. By measuring with the micrometer eye-piece the diameter of the colloid in each more or less circular vesicle, and adding the figures so obtained together, an arbitrary figure was reached which in the case of tadpoles that received oleic acid was one-third less per gram of tadpole than in controls. The addition of iodine to the food mixture containing oleic acid restored the colloid-content of the thyroid gland to normal. This observation suggests that oleic acid has a special tendency to prevent the storage of iodine-containing colloid in the thyroid gland.

Discussion of Results.

The results of these three experiments possess a number of interesting features. If the question of goitre production be considered simply from the point of view of iodine available for the needs of the thyroid gland, then it may be concluded that under the conditions of the first experiment the food contained a sufficiency of iodine for these needs when butter was absent from the dietary, but not always when it was present. The excessive richness of the food in butter thus became in a relatively high proportion of cases a determining factor in the production of thyroid hyperplasia. In the second experiment on pigeons the results appear to incriminate oleic free acid as a peculiarly harmful derivative of butter, and in this the influence of the unsaturated fatty acid was apparently exerted in increasing in certain cases the difficulties of the thyroid in securing the requisite amount of iodine under the goitre-producing conditions of the experiment. When a sufficiency of iodine was provided, as in cod-liver oil, these difficulties ceased and goitre did not arise. The results of the experiments on pigeons may, I think, be correlated with those in tadpoles; they emphasize the dependence of the animal organism and of the thyroid gland upon an amount of iodine approximately proportionate to the amount of edible fat or of free unsaturated oleic acid ingested. When the available iodine is not sufficient then the organism and the thyroid gland suffer; when it is rendered sufficient,

but not excessive, then metabolism and thyroid function proceed normally.

The results of the experiments indicate that there is such a thing as a "fat-thyroid-iodine balance," and that this balance may be disturbed either by an intake of iodine insufficient for the needs of the body in the particular circumstances in which it finds itself, or by the presence in the digestive tract of an excess of fat, and more especially of an excess of free unsaturated oleic acid. Goitre may arise, therefore, either from actual or from relative deficiency of iodine. We thus have an example of a deficiency disease (goitre)—due to an insufficient supply of one essential element of the food (iodine)—arising in consequence of, or favoured in its development by, excess of another essential element of the food. It has become usual of late in connexion with goitre to read of "relative deficiency of iodine in the food" as though the conditions under which it may arise had been known. The present results indicate one means by which such relative deficiency may be brought about—namely, by an excess of edible fat or of free oleic acid in the digestive tract.

But if free oleic acid in the digestive tract is to be incriminated as a determining cause of goitre in actual practice, and as a derivative of digested fat peculiarly harmful to the thyroid gland, it is necessary to ascertain how it becomes relatively excessive to the available iodine in the food. People do not ordinarily ingest the excessive amounts of fats eaten by the animals in these experiments; nor is free oleic acid used as a food. Provided that fats are ingested in normal amounts it seems unlikely that in the ordinary processes of their digestion free oleic acid would normally be relatively excessive to the available iodine in the digestive tract. It is possible, however, that abnormal conditions may arise in this situation in consequence of bacterial action that would render by one means or another the small amount of available iodine in the food relatively deficient, or free oleic acid relatively excessive. A number of possibilities as to the mode of action of bacteria introduced into the digestive tract suggest themselves. What, for instance, is their effect on the iodine-holding elements of the food? Do they rob these elements of available iodine, absorb it in some way, and pass with it out of the body? Or, do they split up the components of the food in such a way as to enable some cleavage product to absorb iodine and pass with it out of the body? What effect have they on ingested fats? Do they interfere with that combination of fatty acids with alkali or bile salts that is necessary for the solution and absorption of these acids? Do they, by some means, lead to a relative excess of free oleic acid over the available iodine in the digestive tube? And, if oleic acid be absorbed in excess, in what way does it increase the difficulties of the thyroid gland in securing an adequate supply of iodine? Or in supplying the demands of the tissues for thyroid secretion? And why are these difficulties greater in some cases than in others? These are among the questions that suggest themselves; their solution will, I think, materially advance our knowledge of the mechanism of goitre production.

I am glad to find that the bacterial aspect of the goitre problem, to which I have devoted so much attention in the past, is at length receiving recognition. Dr. Plummer, whose work has contributed so much to our knowledge of disorders of the thyroid gland, has recently expressed himself as follows:

"That introduction of bacteria into the digestive tract is an important factor, if not the primary cause of endemic goitre, is fairly well established. As to how the organisms act in the host, there is no definite evidence. That the bacterial flora in the digestive tract may sufficiently interfere with the absorption of the small amount of iodine available in the diet is a possibility, particularly in areas in which this element is relatively small. The relation of the bacterial flora to the available iodine would explain the geographical distribution of goitre."

Formerly, I considered that the harmful effects of bacteria in the digestive tube on the thyroid gland were due to positive toxic agents produced by them in this situation. Of late, however, the possibility that their harmful influence may be due in some part to interference with iodine absorption or utilization has seemed to call for consideration.

I venture to think that the new facts I have brought to notice here throw a further light on the difficult problem of the genesis of goitre. They indicate that the composition of the food has an important bearing upon it; that the food must be considered both in relation to its content of available iodine and in relation to its content of fats; that the thyroid may enlarge not only from insufficient intake of iodine

(a comparatively rare occurrence), but from relative insufficiency of iodine consequent on the presence of an excess of certain edible fats or of free fatty acid (oleic) in the digestive tract; that the food must be considered in relation not only to the normal processes of digestion but in relation to abnormal processes that may arise from the introduction of bacteria into the digestive tube; and that variations in histological types of goitre may result from variations in the composition of a goitre-inducing food. They provide, too, a new point of view from which to consider the genesis of simple goitre, of sporadic goitre, and of exophthalmic goitre.

REFERENCE.

¹ McCarrison, R.: *The Thyroid Gland in Health and Disease*. London, 1917.

THE RECOGNITION OF AORTIC INCOMPETENCE.

BY

E. M. BROCKBANK, M.D., F.R.C.P.,

HONORARY PHYSICIAN, ROYAL INFIRMARY, MANCHESTER.

I HAVE on many occasions in recent years, in private and hospital work, found incompetence of the aortic valve which had not been previously recognized or even suspected. It has been present in several soldiers, officers and men, who had been demobilized or discharged as physically fit, although at that time they must have had aortic disease, judging from the condition of the heart when first seen by me. I also meet with it from time to time in insurance work in supposed healthy persons, men and women, and in people with known aortic stenosis but unsuspected incompetence. I think it worth while, therefore, to emphasize the importance of a most careful and systematic examination for this lesion, which is, in my experience, more commonly overlooked or unsuspected in its early stages than any other valvular lesion in proportion to the relative frequency of its occurrence.

The failure to recognize aortic incompetence in its early stages is most unfortunate, because the strain thrown by a leaking aortic valve on the ventricular muscle is greater than that produced by any other diseased valve, and steps should be taken to assist the muscle to withstand this strain at the earliest possible moment.

Aortic incompetence is most likely to be overlooked when it occurs, as it not uncommonly does, without any accompanying obstruction or stenosis to attract attention to the diseased aortic valve by its definite, easily recognized systolic murmur heard over the second right costal cartilage. But even when there is obstruction, and it is remembered that it is unusual for this condition to occur without some leaking of the valve as well, the diastolic murmur of incompetence is sometimes not found.

The chief reason why aortic incompetence is frequently overlooked in its early stages is that then its diastolic murmur—which is short, soft, and blowing in character—is generally heard only, or heard best, not at the aortic cartilage where the systolic murmur is heard, but down the left edge of the sternum, and often only in the fourth intercostal space against the sternum—that is, the so-called tricuspid area of the precordia.

With this source of error it is necessary to adopt some safeguarding rules for examining the heart of every patient, and those which I practise myself as well as teach every day are as follows:

I.

To ascertain as accurately as possible, by palpation and percussion, the position and nature of the cardiac impulse and apex beat, always feeling for the latter well out towards the axilla. To assume invariably that aortic valvular disease is present whenever, with no increase of blood pressure, there is any enlargement of the left ventricle with forcible impulse (even if the enlargement be slight in degree) and the heart's action is moderately slow and regular. The onus of proof to the contrary then rests with the clinician, but the assumption will be justified at least in four out of five of such cases.

Hearts which are enlarged with good compensation in aortic disease generally beat regularly and at a moderate rate as compared with enlarged hearts associated with mitral incompetence and auricular fibrillation.

In advanced cases of aortic incompetence with marked cardiac enlargement and muscle failure there is often considerable irregularity, but then there is no difficulty in recognizing the condition.

II.

To examine, in the first place, over the aortic area for auscultatory evidence of valvular disease—namely, the systolic murmur of obstruction and the diastolic murmur of incompetence.

The diastolic murmur is generally, but not always, heard at the aortic area when there is accompanying actual aortic obstruction and the regurgitation is free. Unfortunately, however, in many cases where there is no obstruction and the regurgitation is slight, and also, but less frequently, when there is obstruction and free regurgitation, the aortic diastolic murmur is not heard at the aortic cartilage. The stethoscope must then be applied down the left edge of the sternum and in the fourth left intercostal space—that is, the tricuspid region of the precordia. In the cases in question a diastolic murmur will very likely be heard in this situation, but if one is not found, further search must be made, for this murmur is occasionally heard at a very limited area of any part of the precordia, sometimes nowhere but at the true apex beat. So when the conditions set forth above, which point to aortic disease, are present, the whole of the precordia, but especially that down the left region of the sternum, must be searched for a diastolic murmur.

If such a procedure be adopted there is little likelihood of aortic incompetence being overlooked. I have known an individual practitioner find it in this way in one of his ex-soldier patients when a medical board has not done so.

A diastolic murmur heard down the left edge of the sternum might, of course, be caused by incompetence of the pulmonary valve. This lesion is, however, very uncommon, but if it were present there would be evidence of pulmonary valve disease, especially of hypertrophy of the right ventricle with a heaving forcible impulse in the left of the epigastrium under the costal arch.

Mitral or tricuspid diastolic murmurs with their associated physical signs need rarely be mistaken for aortic diastolic murmurs.

In several of the cases I have observed there was no previous history of rheumatism in any form, of chorea, tonsillitis, scarlet fever or trench fever, the only illness remembered having been influenza or malaria. In one or two I could get no history of any previous acute illness or of venereal disease, and I was forced towards the conclusion that the very strenuous exertion of physical training and active service had caused some dilatation of the aorta and incompetence of the valve. I did not always use the Wassermann test to check statements, but I felt convinced that some of the young soldiers with aortic disease had not had syphilis.

In some of the soldiers I was much impressed by the fact that when aortic incompetence developed in muscular and vigorous men the heart muscle was evidently able to compensate so well for a time that there was no breathlessness on exertion and no sensation of over-action sufficient to attract attention and cause a visit to the medical officer.

I add notes of a few of the more interesting cases:

CASE I.

J. D., a motor driver, aged 33, who drove a Ford ambulance car in the Expeditionary Force from Mesopotamia to Baku was admitted to the Manchester Royal Infirmary in 1919 for a relapse from malaria. He had a forcible cardiac impulse, with extension of the heart to the left 4½ in. from the mid-sternal line; there was no increase in the blood pressure and no albumin in the urine. On auscultation the only evidence of valvular disease was in the fourth intercostal space at the left margin of the sternum. At this point was a definite soft aortic diastolic murmur, which I demonstrated at a post-graduate clinic. I advised him to inform any medical board before which he went of the existence of the valvular lesion, and I also told him that he was not fit for hard manual labour. He was readmitted to the infirmary the following year, when he informed us that his medical boards had not found the valvular disease. The murmur was more marked and the cardiac enlargement greater then. I saw the man at a later date, when the condition of the heart was worse. He had not had any other illness than the malaria to account for the aortic disease.

CASE II.

R. C., aged 29, served at Salonica, and was demobilized July 7th, 1919. He had had no malaria or other definite illness, but only pain in the back in May, 1919, for which he was given aspirin. He was discharged with "V.D.H." I saw him in November, 1919, at the request of his own doctor, who considered that there was mitral disease and aortic incompetence, although the medical board said there was no aortic disease present. The heart was enlarged, extending 5 in. from the middle line. I found that he had mitral stenosis and aortic incompetence, there being a definite soft diastolic murmur at the left of the sternum in the third intercostal space. There was a crescendo murmur but no diastolic murmur at the apex.