THE CORRELATION OF FUNCTION :

WITH SPECIAL REFERENCE TO THE ORGANS
OF INTERNAL SECRETION AND THE
REPRODUCTIVE SYSTEM.

A BRITISH MEDICAL ASSOCIATION LECTURE DELIVERED BEFORE
THE PRESTON DIVISION ON MAY 21ST, 1920.

BY

W. BLAIR BELL, B.S., M.D.LOND.,

GYNAECOLOGICAL SURGEON TO THE ROYAL INFIRMARY AND LECTURER
ON CLINICAL GYNAECOLOGY IN THE UNIVERSITY, LIVERPOOL.

FIFTY years ago specialists were composed of a body of men who had been carried by their scientific bias to limit their practical work, as far as possible, but rarely completely, to medicine, surgery, or midwifery; and I venture to think that men who shot over the rough before attempting to bring down driven partridges and rocketing pheasants made specialists who had a wider outlook and greater power of practical deduction than would have been the case had they been fed on high game from the cradle. Yet, with the tremendous and rapidly accumulating knowledge that came like an avalanche at the end of the Victorian era, and has continued ever since, it became inevitable that, unless the brain of the practitioner of medicine expanded proportionately, some must devote themselves to narrow issues in order to advance knowledge along special lines and to render themselves available for consultation on certain points. But there has been one evil in the tendency to the ultra-specialism of to-day—a tendency which I am glad to believe is not likely to go further—and it is that, driven by the force of circumstances, and also no doubt in obedience to the dictates of professional etiquette, men have attached themselves too rigorously to their own little bit of anatomical territory, and have not dared to take into consideration what may be called the Correlation of Function. That an eye is an eye, and a tooth is a tooth, is not the whole truth, though the refinements of specialism have almost made it appear so. An eye functions on behalf of the body; a tooth, likewise, serves and is served by the whole organism.

I hope I have expressed myself clearly; if so, it will be understood how it has come about that some of us have been forced to look beyond the narrow confines of our special region for a solution of our many difficulties, and I do not think I am wrong in advising everybody, whether he be a general practitioner or specialist, to remember that not only the structure but also the function of every part of the body is in close correlation with the rest. I believe, if this truth be held in the forefront, our work becomes more interesting and more capable of improvement, for it must be clear to all general practitioners, with the splendid example of men like Sir James Mackenzie in front of them, that to each a scientific career of discovery lies at hand, especially, as that great physician has said, in regard to beginnings of disease. And this is essentially true in regard to the subject of the ductless glands: the shadow of their influence is over all; every patient you see has her metabolism reflected in her system of ductless glands.

It may be asked how I, a surgeon, came to be specially interested in the organs of internal secretion. May I now justify what I dare say some have considered nothing more than a useful hobby, and at the same time say that all surgeons should be as conversant with physiology as with anatomy?

It is hard to understand the difficulties that others have faced, but I feel sure my own difficulties represent a common picture. Had I been orthodox I should have kept my eyes on the pelvis and not have looked outside for an explanation of the function of menstruation and other difficult problems with which my speciality has so long been burdened. Nevertheless I have often been handicapped, partly for the want of certain knowledge that would bear on the subject, but even more because I have felt that what was still looked upon as a primary process might really be secondary, could we go back to the beginning. It is still a debatable point, for instance, whether in many definite cases of mental disease, such as dementia praecox, the primary lesion is in the brain, or whether it is a lesion in the genitalia or elsewhere that produces the mental disturbance. Who is to decide if it be not the man who sees the early phases of these complicated conditions?

Once we grasp the fact that, as Weismann, Ray Lankester, and others have insisted, the individual exists to perpetuate the species, it is not difficult to realize that the metabolic factors concerned in reproduction are the same as those related to the individual metabolism. In other words, as I have stated elsewhere, the individual metabolism is the reproductive metabolism. It follows, therefore, that the ductless glands which regulate the individual metabolism concern equally the reproductive. So it is that we must seek in the metabolism of the mother—or hostess as we may call her—and in the regulation of her own metabolism, the factors that are most closely concerned in the preparation for and performance of reproduction. Moreover, closely linked to the individual and reproductive processes is the mind of the hostess; its normality is dependent on the integrity of the internal secretory organs and the metabolism; and what obtains physiologically is emphasized pathologically.

The ductless glands are concerned, then, not only in such gross manifestations as disorders of the reproductive system and of the characteristics of sex, but also in the more elusive disorders of the emotions—that is, of the mind. There is a wide field of study for those who see the beginnings of these disturbances, and it will make the study more interesting and more instructive, and certainly more complete, if it be remembered that the beginning of a disorder of an organ of internal secretion is shown in triplicate, as it were—in the mind, in the body, and in the reproductive system, all inseparably linked together.

What, then, do we know of the connexion between the ductless glands and the reproductive system? There is much left for us to discover. Most of our information is based on the results of animal experiments and on pathological investigations; and I propose to relate some of the more important facts obtained in the laboratories, and then indicate how these facts may be turned to use in practice.

WHAT IS A WOMAN, AND WHY IS SHE NOT A MAN?

This is the first point of interest that presents itself in a consideration of the genital functions. We ask ourselves whether the organs of internal secretion have any influence in this respect, and in reaching our present physiological knowledge on the subject we have worked backwards: we have discovered certain facts in regard to pathological conditions, and we now know that what is seen as an abnormality represents a disturbance of normal physiological processes.

Further advances in our knowledge have made it more and more clear that sex differences are pronounced. I dare say a good many of you know that I hold strong views in regard to the functions of woman, and that I look upon any divergence, sociological or otherwise, as abnormal.

I have spoken of the triplication of effects, and in considering the question of the differences between a man and a woman we find that these differences exist in the ductless glands, in the metabolism, and in the mental processes. I do not propose to consider the matter in detail, for I have often done so in other publications; but I will call attention to those remarkable instances in which a woman is or becomes masculine in her secondary characteristics, and males feminine. This is seen in the congenital abnormality known as partial hermaphroditism, and in acquired lesions of the pituitary and suprarenal glands.

Partial hermaphroditism is a very curious and interesting state. I have been fortunate enough to have under my close observation one of the three or four authentic cases of so-called "true hermaphroditism." There is no such thing in the higher animals as true hermaphroditism, although this is seen low down in the scale of evolution. But in the few cases of this type of hermaphroditism, so called, in Man, better known as partial glandular hermaphroditism, we have found what are known as ovotestes—that is to say, the gonads are composed of both ovarian and testicular elements. In my case the patient commenced life as a girl, and menstruated for a year or two regularly. Then menstruation stopped, she grew a moustache and much hair in other parts of the body, and the voice became bass. Removal of the genital organs caused a return to femininity, with slight symptoms of the artificial menopause. The other form of partial hermaphroditism, known as tubular partial hermaphroditism,

is not uncommon. In these cases the gonads are usually testicular in structure, whereas the secondary characteristics are invariably those of the opposite sex, and the external genitals most commonly conform with the secondary characteristics. I have seen a beautiful girl, as was thought, whose gonads were testes.

In passing I must make allusion to the practical side of these conditions. It has usually been taught that, owing to the frequency with which the gonad is testicular, the subject from childhood should be brought up as a boy. With the best will in the world it is impossible to suspect or to know in a majority of these cases the nature of the gonad, unless an operation be performed and part of the genital gland removed. As a result, most partial hermaphrodites reach adult life as girls, and look the part. I have known a case in which a hermaphrodite of this type was married. Legally, that marriage could have been annulled, and I am waiting with interest for the time when one of these abnormal individuals will be entitled, in accordance with the structure of the gonad, to be considered the heir as the eldest son. I am prepared to argue that the structure of the gonad is not necessarily the criterion of sex. I believe it would be better at once to put the question on a proper legal footing. I call your attention to this important matter because any one may come across such a case at any time.

The most outstanding of the acquired lesions producing masculinity in women are hyperplasia or neoplasia of the suprarenal cortex. I can best describe the changes which occur in previously normal women by repeating the description of a French writer: The voice, which was previously soprano, became like that of a lieutenant, and the woman, previously gentle and amenable, became rough and aggressive. Practically all these persons develop excellent beards, and no doubt in the days gone by the bearded woman of the country fair was one who had a lesion in her suprarenal cortex. If further confirmatory pathological evidence were required, we have it in the cases of so-called infant Hercules—boys with suprarenal tumours who are often fully-grown men at the age of five or six; that is to say, excessive masculinity is produced in males suffering with lesions in this and certain other organs. My friend and colleague, Professor Ernest Glynn, has written a classical paper on the pathological aspect of such lesions in the suprarenals.

Again, if a woman have acromegaly, which we believe is the result of hyperplasia or neoplasia in the anterior lobe of the pituitary, she shows well marked masculine traits. Her voice becomes deep, her skin coarse, and her metabolism, especially in regard to the deposition of calcareous salts, closely akin to that of man. In these women there is amenorrhoea, simply and solely because they have become masculine, and not because of the lesion in the pituitary as such; indeed, hyperplasia in the anterior lobe should, if it did not produce masculinity, stimulate activity in the genitalia. It is these facts which give rise to the apparent paradox that destructive lesions, as well as hyperplastic lesions in the anterior lobe of the pituitary, produce amenorrhoea. It is interesting to note that acromegaly in the male is often associated with increased sexuality, whereas destructive lesions in the same region in men produce impotence and a change towards femininity as far as possible in the male—that is to say, the skin becomes soft, hair on the face falls out, and the fingers become fine and tapering.

Another interesting sex-characteristic or distinction in regard to the pituitary is of considerable medico-legal importance, although I do not think it has yet found its way into the textbooks on jurisprudence. It is that once a woman has a child the pituitary becomes and remains larger than normal; indeed the average size of the pituitary of multiparous women is considerably greater than the average size of that of men. Moreover, the staining reactions of the cells of the pars anterior are much altered, so much so that an expert in the histology of the pituitary gland cannot fail to recognise the effect and cause.

The subject of the sex-characteristics and the ductless glands is so extensive, being related not only to the glands mentioned but also to the pineal, the thyroid and to some extent to the gonads, that I fear I cannot discuss it further. I have brought forward these details to show that my bias on the subject of the differences in the two sexes is produced by weight of scientific evidence.

ASSOCIATED DISTURBANCES IN THE DUCTLESS GLANDS AND GENITAL ORGANS.

We come now to the gynaecological disturbances due to the correlations of internal secretions and their disorders.

The Ovaries.

In the first place, what have we learned from experiments on animals regarding the place of the ovary in the system of ductless glands? My deductions lead me to look on the ovary as a connecting link in the chain—a link that is only temporarily employed during the reproductive period; that is to say, the metabolism of boys and girls is probably not greatly different, nor is that of women after the menopause much different from that of men in late life. During the reproductive period, however, a woman is called upon for great metabolic effort in order that she may be able to nourish her child in the womb, and, after parturition, at the breast; consequently, the ovary is concerned in keeping the other organs of internal secretion and the resultant metabolism in touch with the genital system and its needs. In my mind menstruation represents merely the monthly excretion of substances that would be concerned in the building up of a child were the woman pregnant. For this reason a woman usually has amenorrhoea for, at any rate, five months of lactation, and should she nurse for more than nine months her metabolism is apt to be drained if she be menstruating at the same time; she suffers, in other words, with the symptoms of superlactation.

What, then, happens at the menopause? Nature is gentle in her methods, and woman is usually let down, so to speak, by degrees. A majority of women suffer with flushes and other disturbances, many of them due to instability in the vasomotor system.

Experiments on animals have shown that if the ovaries be removed changes are produced in the other ductless glands, especially in the pituitary and thyroid. It appears, therefore, that the menopausal disturbances are due to an upheaval of the internal secretory system. The symptoms usually indicate the line of treatment. Many women after the menopause show an unusual degree of atrophy in the thyroid, coincidental with ovarian atrophy, with the result well known to all; not only are the reproductive organs concerned, but also the ductless gland system, and the mind—the patient becomes depressed and melancholy. The obvious treatment is the administration of thyroid extract. This specific example is interesting, for it shows clearly not only the triplication of effects, but also how these effects are produced by an easily recognizable lesion. It has been shown recently by Mott that in all such cases the cells of the brain and nervous system undergo definite changes.

Before leaving the problems connected with the ovaries, I wish to call attention to a matter that, in this country at any rate, has been strangely neglected: I refer to the transplantation of ovarian tissue, a procedure based on physiological experiments. All who have studied the question in animals have found that if the ovaries be removed and some ovarian tissue transplanted the uterus, a section of which is taken at the time when the ovaries are removed, does not undergo atrophy as is the case when the ovaries are removed and no graft is made. We know, too, that in rodents it is the interstitial cells and not the follicles that are important in respect to the integrity of the uterus. The ovaries of rodents, in contrast with the human ovary, contain much of this interstitial tissue, and this is probably the reason why transplantation is almost invariably successful in the lower animals and not constantly so in women. After an ovarian graft has been made, the uterus is an important indicator, for if this organ remains normal no changes are to be observed in the other organs of internal secretion, such as occur after oophorectomy alone; in other words, an autogenous ovarian graft may be as effective as undisturbed normal ovarian tissue, except, of course, in regard to reproduction. It is, however, important to remember that the best—indeed, the only satisfactory—results are obtained with autogenous grafts, and that a graft taken from one woman's ovary and placed in the muscles of another woman rarely grows. We are only now learning how remarkably individual people are in regard to their blood and other tissues. I have not time to discuss this interesting subject which may account for selective sterility and many other hitherto obscure phenomena.

Unfortunately, as I think, many gynaecologists in this

and in other countries have not much respect for the ovaries in the presence of other pelvic lesions; should they be operating for pyosalpinges, for instance, they invariably remove all the ovarian tissue. I know of a sad case of a young girl who had both ovaries removed for dysmenorrhoea. I can hardly control my words in stating what I think of such an unscientific procedure. This girl has been in an asylum for more than twenty years. No doubt she had a neuropathic tendency. But I doubt if she would ever have broken down if her ovarian tissue had been left alone. There is no reason for removing the whole of the ovarian tissue in any woman, unless the lesion be malignant. In malignant disease the lesser evil is chosen, in view of the fact that we have therapeutical measures which can lessen to some extent the symptoms of the artificial menopause, and probably prevent such a disaster as that of which I have just spoken.

I never leave an ovary in the pelvis if infection be present. I remove all the diseased structures, and, as the ovary can play no further part in reproduction because the tubes have been destroyed so far as their function is concerned, I transplant a piece of healthy, or even infected ovarian tissue, into the muscles of the abdominal wall or some other vascular site. I think I have cause to be satisfied with this procedure, for many of the patients have menstruated, although part of the uterus has been removed in most of the cases; so far as I know at present, no patient has complained of pronounced menopausal symptoms. There may be difficulty in deciding this point. We must not pay attention to agreement with a leading question; but, if the patient volunteers the statement that she is sorely troubled with hot flushes, I would immediately consider that she had menopausal symptoms. Nevertheless, even this is not an absolute indication that the ovarian transplantation has failed. I have in mind at the moment the cases of two private patients, from both of whom I removed double ovarian abscesses with pyosalpinges, and in whom I implanted infected ovarian grafts. Some two or three months subsequently to the operation they complained of discomfort and flushing, yet both of them menstruated shortly afterwards with fair regularity, and the disturbing symptoms ceased. In these cases, as in all in which complaint of such symptoms is made, I administer ovarian and thyroid extracts, which are discontinued when the patient recommences to menstruate.

There are other uses for ovarian transplantation of which I have had satisfactory experiences, but time will not allow of my giving the facts in detail. Transplantation of ovarian tissue is no doubt a complicated surgical problem, and deserves much further consideration. I hope one day to make use of an opportunity such as the present to bring forward a collection of these cases of ovarian transplantation, with which I and those who assist me always endeavour to keep in touch.

I now come to the consideration of primary disorders of the ductless glands which affect the genital functions.

Through the courtesy of many friends I have had an unusual opportunity of seeing a large number of these cases. Generally the patient has complained of amenorrhoea and sterility. It is interesting to speculate as to what happened to all these patients in the days gone by. I notice that in the textbooks of twenty years ago, even in some of those of to-day, obesity, without qualification, occupies a considerable importance in regard to amenorrhoea. I do not say that amenorrhoea and sterility cannot be produced in animals by overfeeding, but, after all, obesity in these circumstances is probably a reflection in the organs of internal secretion of some disturbance in metabolism. It is interesting to note that the two disorders associated with obesity and amenorrhoea, that are seen every day in practice, are connected with the pituitary and thyroid glands. With any considerable insufficiency in these organs the carbohydrate tolerance increases, and the patient becomes obese, as not infrequently happens after the menopause.

I shall now consider these derangements as primary lesions in the ductless gland concerned. I have already considered the other side of the picture.

The Pituitary.

This wonderful little organ, about which so much has been written of recent years, has, as we have

already seen, an important influence on sex-characterization and on the reproductive functions. I wish now to discuss the question of insufficiency of its secretion or secretions, and in so doing I shall first call attention to certain important physiological observations which have helped us greatly in forming clinical conclusions; and in these observations you will recognize at once the difference between scientific deduction and guessing.

In animals and birds periodic variations in pituitary activity are normal, even as we have seen variations are normal in connexion with reproduction in women. As I have said, in such cases it is usual to find adiposity when the pituitary is inactive; I shall mention certain apparent exceptions directly.

It has been shown, and I myself have observed, that during hibernation in animals the pituitary gland undergoes remarkable retrogression, which cannot be mistaken by those conversant with the normal active organ. In the hedgehog, which I have studied, there is a remarkable deposition of fat throughout the tissues of the body, most evident perhaps in the subcutaneous tissues. In such circumstances this small animal has a coat of fat as much as one and a half inches in thickness. No doubt this protects the creature from the winter cold and provides nutriment. Associated with this, as I have said, is atrophy of the pituitary.

Fat deposition and somnolence, so well seen in the hibernating animals, are the chief characteristics of acquired insufficiency in the pituitary. It has been suggested, and is indeed probable, that the other organs of internal secretion also undergo some retrogression in hibernation. I have found, too, that the pituitary of the broody hen shows similar changes, but in this case fat does not appear usually to be deposited, perhaps because food is still to be obtained.

Now what is normal in animals may be pathological in Man. I shall not refer here to the wonderful clinical results which have been obtained with the extract of the posterior lobe of the pituitary. They are well known; the subject is one in which I have been specially interested, and it is summarized in my book on the pituitary.

Experiments on animals, apart from the histological investigations to which reference has just been made, have afforded information of the highest importance in regard to the interpretation to be placed on corresponding clinical signs and symptoms. Unfortunately, but few successful series of cases have been published in which operations on the pituitaries of animals have been performed. To Paulesco belongs the credit of being the pioneer in this matter, although he was by no means the first to attempt such experiments. I shall briefly summarize the results of lesions experimentally produced on the pituitary, which are now accepted as being correct; and I may say the conclusions formed from the experiments of Paulesco, Cushing, and myself differ in only one or two important respects.

It is known that extirpation of the whole pituitary is inconsistent with life. The removal of large portions of the pars anterior may lead to the death of the animal, but if it does not do so, intense genital atrophy ensues, and in young animals general stunting. Cushing and Paulesco also observed obesity in these circumstances, but, on the other hand, I did not observe this result of carbohydrate tolerance. Removal of the posterior lobe causes no symptoms. There is a divergence of opinion concerning the results of compression of the stalk of the pituitary: Paulesco considered this to be a fatal operation; Cushing believed it produced effects similar to those following removal of the whole pituitary with immediate transplantation.

In my experiments the operation of compression of the stalk, whereby the blood supply to the pituitary is cut off, was found to lead to the syndrome of dystrophia adiposogenitalis—somnolence, obesity, and total atrophy of the genitalia—an exact counterpart of the disease in Man. I may add that Cushing has privately conceded the correctness of my experiments and deductions, as opposed to his own and those of Paulesco. Cushing is only concerned with the truth, and his work on the various aspects of the pituitary activity is an imperishable monument to his genius.

I have conducted a few experiments whereby an artificial tumour was introduced into the cranial cavity in the neighbourhood of the pituitary. When there was pressure on the stalk symptoms of dystrophia adiposogenitalis were

produced; when irritation from the proximity of the tumour was caused there was glycosuria and emaciation.

We occasionally see in Man congenital insufficiency of the pituitary, in which there is genital inactivity, often associated with poor somatic development. I have seen several cases of this sort. When there is general somatic underdevelopment, that in the pituitary may simply be part of universal insufficiency; but in other cases the patient may be finely developed, yet have inactive functions. I remember an interesting example of this. The patient was about 18 years of age and had not menstruated. She was beautifully developed, but had an infantile uterus. A radiograph showed the sella turcica to be one-third of the normal average size. She was fed on pituitary extract for a long time, and at the age of 22 years, sometime after discontinuing treatment, she commenced to menstruate regularly and freely.

In acquired lesions of the pituitary there is usually enlargement of the sella turcica, and I have mentioned radiography of this region. This is valuable when carried out by a skilled radiographer, and I am indebted to my colleague, Mr. Thurstan Holland, for the trouble he has so often taken and the skill with which he has helped me in many difficult cases. It must not be forgotten that hemianopia, which may go on to complete blindness, occurs with enlargements of the pituitary fossa, and headache may be persistent and severe. But it will be remembered that pressure on the stalk can be experimentally produced, and that this lesion causes dystrophia adiposogenitalis. It is interesting, therefore, to note that in Man all the symptoms of dystrophia adiposogenitalis, without expansion of the sella turcica, may be caused by a suprasellar tumour. In such cases a definite diagnosis can be made by the symptoms and the absence of enlargement of the sella turcica on radiographic examination.

There are other methods of investigation which may help. I have spoken of carbohydrate tolerance, by which is meant the power to retain carbohydrates and deposit fat in the tissues instead of the ability to excrete carbohydrates in excess of the usual limit. The normal person is able to take about 110 grams of dextrose without the appearance of glycosuria. The power to retain more than about 150 grams may be considered pathological. The carbohydrate tolerance, then, of a patient may be measured, and it will be found to be raised in cases of pituitary insufficiency. I have known a patient swallow—with difficulty be it admitted—500 grams of sugar without subsequently passing sugar in the urine.

Then, again, we have what is known as the "thermic reaction." All cases of severe pituitary insufficiency show a subnormal temperature, which may be raised by the intramuscular injection of an extract of the anterior lobe. I cannot affirm, however, that this reaction is always striking. Moreover, the blood pressure is often very low, but can be raised with an extract of the posterior lobe—that is, by infundibulin injected intramuscularly. But, of course, this alone is not a specific test, as infundibulin administered intramuscularly will always raise a reduced blood pressure.

With regard to serious lesions of the pituitary and their effects on the genitalia, treatment is not always satisfactory. If there be a cyst in the pars anterior it may be safely evacuated, and the patient may recover completely. In other cases, feeding with whole-gland pituitary extract may give good results, especially if associated with operation.

Our knowledge of the minor disorders of the pituitary is less definite, because the conditions do not lend themselves so well to experimentation as do the grosser lesions. We have, however, the important facts of the physiological states of hibernation in animals and brooding in birds to help us, for we see in them a temporary phase of insufficiency, and we are led to realize that similar conditions may be found in Man. I have already mentioned that the opposite state—that of hyperplasia—occurs in women during gestation. Furthermore, experiment has shown that changes occur in the pituitary as the result of inoculations with bacteria. I would call special attention to this point in regard to the pituitary, without considering the coincidental changes that are seen in the suprarenals and elsewhere in the ductless gland system, for I feel sure many of the minor insufficiencies seen in practice may be the immediate sequel of bacterial infections. The lesions may be slight and curable. It is not always possible,

however, to get a definite history, but "a cold" is frequently mentioned as the starting point of secondary amenorrhoea.

When the fact that the organ chiefly at fault is the pituitary can be established, then treatment is, I believe, fairly satisfactory. I have seen patients in whom regular menstruation has been induced by pituitary feeding.

The Thyroid.

As intimate as the relation of the pituitary to the genital functions is the association between the thyroid gland and the genitalia. Here again we are to a great extent indebted to experimental research, but no less to pathological investigations; moreover, clinical observers have had a good chance to advance our knowledge of the thyroid, for this organ is accessible to ordinary physical examination.

A matter of considerable interest has come to light as the result of experimental extirpation of the thyroid; in rodents, such as the rabbit, removal of this gland is not only compatible with continued existence, but appears hardly to disturb the animal. Three reasons may be suggested for this comparative immunity to the effect of thyroidectomy, as opposed to the disastrous effects of the same operation in carnivora. First, it is known that a meat diet makes a greater call than a purely herbivorous on the activity of the thyroid. Second, in herbivorous animals the parathyroids usually escape removal with the thyroid itself, whereas in carnivorous animals it is not always possible to conserve all the parathyroids, which are closely adherent to the thyroid. Third, the thyroid is not so active in herbivorous animals as in carnivorous animals, perhaps primarily because of the diet, but also because the ovarian interstitial tissue in these mammals is more in evidence than in the carnivores.

Man being omnivorous should come half way between the two orders in regard to thyroid activity, if it were purely a question of diet; but I do not think it is. In Man we have seen there is little interstitial ovarian tissue, which, from a genital point of view, means a very active thyroid. Extirpation of the thyroid in animals is followed by a considerable degree of atrophy of the uterus, but strangely enough ovarian retrogression is not seen.

As with the removal of the ovaries and also with partial removal of the pituitary, thyroidectomy is followed by definite changes in the other ductless glands, and these changes are particularly noticeable in the pituitary, which undergoes hyperplasia in all parts.

It is a too common observation in the experience of every one for me to do more than recall the curious enlargement often seen in girls during menstruation; but I believe that it is important to bear in mind that this enlargement may exist in two forms. It is either a primary lesion in the thyroid which persists between the monthly periods, in which case menstruation is profuse; or it may be due to a temporary state of hyperplasia, when the ovaries are not very active and supplementary action is required to establish menstruation. In the last-named circumstances menstruation is usually scanty and painful.

The treatment, of course, is obvious; in the first type of case attempts must be made to reduce thyroid activity, if symptoms are sufficient to warrant interference, because I believe exophthalmic goitre may supervene. Radiations of x-rays carefully managed appear to be a valuable method of treatment. I have also found intramuscular injections of infundibulin and the administration of calcium salts efficient in many cases. In the second type there is an attempt, as I have said, on the part of the thyroid to supplement ovarian insufficiency; consequently, we must treat the case by the administration of thyroid and ovarian extracts. I believe ovarian extract alone is useless, and this, I think, is the general experience of most clinicians; but I have seen excellent results when whole ovary extract is given in conjunction with thyroid extract. We must remember that in the blood stream the internal secretions meet and activate, or inhibit.

In myxoedema the most wonderful results are obtained with the administration of thyroid extract. A melancholic, obese, non-menstruating sterile woman, becomes happy, is reduced in weight, menstruates and may even conceive. An illustration again of the triplication of effects. But it is, after all, the minor degrees of insufficiency in organs of internal secretion that escape notice while they are still easy to treat, and I beg you to

be on the look-out for the protean signs and symptoms that are discernible very early.

I have not time to deal with insufficiencies of the other ductless glands; nor have I time to mention some of these glands at all. You will find in my book, *The Sex Complex*, especially in the new edition about to be issued, a more complete picture. I shall be amply satisfied if I have been lucid in this hasty sketch with which I have sought to attract your attention to the triplication of effects—in the mind, in the soma, and in the reproductive organs—which forms such striking evidence of what I have called the Correlation of Function.

THE COMMONER COMPLICATIONS OF BACILLARY DYSENTERY IN MILITARY PRACTICE.

BY

PHILIP MANSON-BAHR, D.S.O., M.D., M.R.C.P.,

ASSISTANT PHYSICIAN, HOSPITAL FOR TROPICAL DISEASES, ENDSLEIGH GARDENS, AND ALBERT DOCK HOSPITAL; LECTURER, LONDON SCHOOL OF TROPICAL MEDICINE.

THE complications of bacillary dysentery have received scant attention from medical writers in the past, but since the recent campaigns in the East many symptoms, apparently due to the absorption of the toxins of the *Bacillus dysenteriae*, have occurred with considerable frequency in military practice.

Arthritis in Bacillary Dysentery.

Of these complications, monarthrititis, or more generally polyarthrititis, have been frequently noted during the Egyptian and Palestine campaigns.

That such an arthritis may supervene during the course of a bacillary dysentery, even of a mild type and untreated by any specific serum, and that the joint disintegration so produced may persist for a long time—even a year or more—and may result in permanent disability, has long been recognized, though in many epidemics in India and elsewhere such occurrences have been rare. Davidson,¹ who wrote mainly from Indian experiences, remarked upon the tolerable frequency of arthritis in dysentery unaccompanied by any involvement of the endocardium. This, he noted, may be ushered in by pyrexia, either during the acute stage of the disease, or when, apparently, the bowel condition has once more become normal. In the Döberitz epidemic in Germany, in 1900, arthritis supervened in 3.75 per cent. of all cases, and the condition persisted from four days to four months. It is significant that, writing in 1913, Sir Leonard Rogers² mentions only a single case of arthritis of an obstinate character as having occurred to his knowledge during the course of such an epidemic in India.

In a bacillary epidemic of a more virulent character, which visited the Fiji Islands in 1897, I was informed by Daniels that fully 10 per cent. of the patients developed arthritis, whilst in 1910, during a study of 300 cases in the same colony, I did not see a single one.

During the war on the eastern European front 7 cases of arthritis out of a series of 600 have been reported. A streptococcus is said to have been isolated from the blood of one case, and the joint symptoms were regarded therefore as a result of streptococcal septicaemia secondary to the bacillary infection.

Arthritis occurring in the course of amoebic dysentery appears to be very rare. I have only been able to find a record of one case.

During the first nine months of 1916 a number of cases of arthritis occurred amongst patients suffering from bacillary dysentery in Egypt. The bacillus responsible was the Shiga bacillus in all cases which could be properly investigated, and it is noteworthy that no cases of arthritis were observed at the same time in Flexner-Y infections. Though the latter bacillus was commonly met with amongst the numerous cases of bacillary dysentery in Turks at the Prisoners of War Hospital, Heliopolis, Cairo, yet no instances of joint involvement were noted amongst these patients.

Arthritis in Cases Untreated by Serum.

The majority of the cases of arthritis encountered during the course of bacillary dysentery have been those previously injected with antidysenteric serum, though

arthritis was observed twice in cases untreated by serum of any kind.

In one such case the right knee alone was affected, and there was a large effusion into the subcrural pouch, which was very gradually absorbed. In the other cases all joints were affected, including the temporo-maxillary and the interphalangeal; there was also a uniform swelling of the right parotid gland. Arthritic symptoms in both instances supervened during convalescence from dysentery and while the stools were completely faeculent.

Arthritis occurring Subsequent to the Administration of Antidysenteric Serum.

According to my personal observation, arthritis occurring in a patient subsequent to the administration of antidysenteric serum, either by the subcutaneous or the intravenous route, can be classified under two headings:

- (a) Fugitive polyarthrititis, with or without joint effusions, occurring during the course of "serum sickness."
- (b) Intractable polyarthrititis, with effusion into joints and wasting of adjoining muscles, apparently due to absorption of dysenteric toxins.

(a) *The Fugitive Form.*—Eleven out of 29 acute cases of bacillary dysentery injected intravenously with doses of from 30 to 40 c.cm. of antidysenteric serum developed a fugitive polyarthrititis seven to twelve days after the injection; that is to say, the arthritis was ushered in with pyrexia, urticaria, general malaise, and hyperaesthesia of the muscles. This condition lasted as a general rule for two to three days and then cleared up, and might possibly be ascribed to the elimination of foreign proteins originally contained in the serum injected.

(b) *The Intractable Form.*—Eight out of 29 cases (or 27 per cent.) developed joint symptoms, often of a very intractable nature, with intra-articular effusions. This came on generally from the sixth to the tenth day after injection of serum. This is a much higher percentage of incidence of arthritis than in the series from France and Mesopotamia recently described by Klein³ and Waller⁴; the latter reported 12.4 per cent. of arthritis as occurring in his cases treated by serum.

The effusions in my cases took place with surprising rapidity, accompanied by acute pain and a rise of temperature to 102° to 103° F., especially when the knee-joint was involved. The one death in this series was preceded by profuse watery diarrhoea with a septic pyrexia ending finally in collapse.

In the knee-joint the effusion took place into the subcrural pouch and, in less than twenty-four hours from the commencement, the joint cavities were distended to their utmost capacity and the superjacent skin was stretched and shiny. There were no signs of local inflammation such as hyperaemia of the adjacent tissues. In the interphalangeal joints the swelling occurred into the tissues immediately surrounding the articulations, thus giving the spindle-shaped appearance of rheumatoid arthritis.

In one case large sterile effusions took place into the substance of the gluteus maximus and latissimus dorsi muscles, and subsided very slowly so that the patient was incapacitated for six months. The stage of the disease at which the arthritis supervenes is of importance; in all the cases I observed, the arthritic symptoms commenced at a time when the intestinal condition had considerably improved—even, in some cases, when the stools had been apparently normal for a week or more. The effusion was straw-coloured and slightly viscid, sterile on culture and containing a considerable number of polymorph cells. According to Klein this fluid agglutinates the specific bacilli in high dilutions.

In all cases observed, and especially in several cases not included in the series quoted above, intermittent pyrexia persisted as long as the joint symptoms were in evidence. Another characteristic seems to be that the pain, or, in some cases, a sense of stiffness, appears to be more marked at night time or in the early mornings.

As bearing on the etiology it is important to note that in two cases previous arthritis of rheumatic or traumatic origin had occurred a year or more before the onset of dysentery; it therefore seems probable that previous joint injury may exert a very definite predisposing influence on the supervention of joint symptoms in a subject subsequently attacked by a bacillary dysentery.