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ENDOCRINES IN GYNAECOLOGY *

BY

ALECK BOURNE, M.B., F.R.C.S., F.R.C.O.G.

There is no doubt that the discovery of the sex hormones has conferred an enormous boon on the drug manufacturers, but we cannot be so confident of the benefit to the suffering patient. After the early experiments which demonstrated their striking effects on the structure and function of the genital system of laboratory animals we had high hopes that they would exert comparable effects when used for the treatment of pelvic disorders in women. But with some well-defined exceptions we have been grievously disappointed. The reasons why this should be are not far to seek. This branch of medicine was initiated in 1917 by the observation by Stockard and Papanicolaou that injection of the liquor of the Graafian follicle produced oestral changes in the vaginal mucosa. From this fundamental discovery has been built up our knowledge of the secretions of oestrogen and progesterone; of their effect on the development of the genital tract, and on the cyclic changes of the endometrium; later, of the gonadotrophins of the pituitary and their relation to the ovary. The greater part of this work during thirty years has been done by experimental work on small animals and monkeys.

Difficulties in Clinical Use

Herein lies the first reason for clinical disappointment. It was hoped and expected that the precise result obtained by injecting this or that hormone into rats and rabbits would be similarly obtained with the human patient. But the mechanism of the endocrine system is infinitely complex, not only in the individual species but also in its variations in different species even closely allied. It was soon realized that deductions made from observation of one animal could not safely be made for another species, and still less where the other species was human. Moreover, the experimental work has been done on either normal animals or those which have suffered a severe and totally mutilating operation, such as ablation of the pituitary gland. Our patients are not normal animals nor have they been subjected to severe surgical mutilation, except, rarely, by removal of both ovaries. Clinical experience has shown that deductions made from the reactions of animals to hormone treatment cannot be applied to parallel treatment of the pelvic disturbances of women.

A further difficulty is adequate dosage for the human subject. Whereas the synthetic oestrogens can now be given in any amount it is probable that the substitute pituitary hormones (chorionic gonadotrophin and mare's serum hormone) can be given only in doses totally inadequate for the proportional weight of a woman. As the pituitary hormones—the gonadotrophins—are the prime movers of ovarian function, it is impossible to influence ovarian function, for example folliculation, except by the appropriate gonadotrophin in sufficient dosage. So far it has been impossible to synthesize these extremely complex bodies, and I am told there is also little prospect of success in the future. Fortunately, hormones can be extracted from the urine of pregnant women and the serum of the pregnant mare, which can be obtained in larger amount for clinical purposes than from the pituitary itself, but the available doses of even these pituitary-like hormones are probably far too small to exert an appreciable clinical effect.

The rhythmical secretion of the sex hormones of the pituitary and ovary introduces a further complication in therapy. It is necessary to know the details of the rhythm of normal secretion if we wish, with some hope of success, either to apply reinforcement to subnormal activity or to counter the action of an oversecretion. During the first fortnight of the menstrual cycle the pituitary produces its follicle-stimulating hormone and the ovary oestrogen, while during the second two weeks the pituitary secretes its luteinizing hormone and the ovary progesterone with less oestrogen. For any given complaint, therefore, we should know not only whether there is an excess or deficit of the particular hormones responsible but also the time in the cycle when the therapeutic hormone should be given. In other words, unless the correct hormone is given at the right time in the menstrual cycle there cannot be any improvement; indeed, the patient may be worse.

But after we have noted the difficulties dependent upon the differences of the species, inadequate dosage, and timing, perhaps the greatest of all is the complexity which arises in the human subject by reason of the profound effect of the highly organized emotional system on the hormonal function of the pituitary. We see this in our gynaecological practice almost every day. Amenorrhoea and certain cases of menstrual excess so often follow emotional storms of one kind or another that it is impossible to deny the association. It is probable, too, that toxic goitre, even sterility and many other states, similarly depend on interference with pituitary function by anxiety, fear, and anger; while, *per contra*, we may perhaps attribute a smooth function—or euphoria, as the Greeks called it—to contentment, exaltation, and translation out of ourselves. We may be correct in assuming the basic effect of oestrogen in man from the experimental evidence gained from the small animals, but the result of any given treatment may be totally different from what we should expect from purely physiological considerations, because of the incalculable effect of emotional interference with the functions of the pituitary body. A good example is the treatment of the

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menopause by stilboestrol. Sometimes the patient finds complete relief from her flushes and sweats; but those women who are emotional or "temperamental," especially if they have had unhappy years, will find little improvement. But at this period the basic physiology is the same in most if not all women. The ovaries atrophy, probably owing to the cessation of the secretion of pituitary gonadotrophins. Menstruation ceases, and usually there are various subjective symptoms. The latter, however, are extraordinarily variable both in degree and in responsiveness to hormone treatment. Their intensity depends less on the actual hormonal imbalance than on the influence of temperament and the level of happiness and content during previous years of married life.

Endocrine Receptors

There is still one more unknown factor which may be important in endocrine therapy. I have seldom seen it mentioned, and never considered, in therapeutics. I refer to what I call endocrine receptors. When, for example, a large dose of oestrogen is injected into an adult female certain definite changes are found in certain organs, and those organs only. The endometrium proliferates, the uterus of the immature animal grows, and the vaginal mucosa cornifies. But there are no other demonstrable changes (except possibly indirect) in most other tissues of the body. It is doubtful if after millions of units the alimentary mucosa, for example, would show the slightest change at all. It is necessary, therefore, to postulate the existence of receptor substances in the vaginal mucosa, the endometrium, and a few other tissues, which are able to grasp the oestrogenic molecule and, perhaps by chemical union, enable it to perform its specific function. I visualize the characteristic changes in the reproductive organs as being the result of a dual and co-ordinated action of two substances—the activator and the receptor. In our therapeutics we consider only the activator—the hormone—but it may be that failure of the expected result to follow is due to absence of its vaginal or uterine receptor, without which it is powerless to exert its specific function. How far subsequent research may reveal and identify visceral receptors we do not know, but until we know something about them our endocrine therapy must remain largely empirical. It is possible that many pathological disturbances, such as amenorrhoea, are due to failure not of the appropriate hormonal secretion but of their necessary receptors in the ovary and uterus.

I have recently investigated a case which illustrates the existence and absence of these receptor substances. Briefly, a woman of 36 had had amenorrhoea for five years due to no apparent cause. Radiography and the sound show the uterus to be atrophied, and the curette could not remove more than the smallest fragments of endometrium for the microscope. The sections reveal no evidence whatever of oestrogenic action, and as the uterus has atrophied both in structure and in function we must assume that it has not received the oestrogenic stimulus. But in this woman the curious thing is that the vaginal mucous membrane manifests quite strongly that oestrogen is circulating in the blood stream. For example, the acid reaction gives a reading of the normal *p*H 4.5 by the universal indicator; the smear of its secretion shows an enormous number of Doederlein's acid-forming bacilli, and the histology of the epithelium reveals a very large amount of glycogen, similar to that of normal women during the child-bearing period. These features of the vagina are proof that oestrogen is present in the body in normal amounts, and yet the uterus is unable to receive it and so exhibit the ordinary histology and development characteristic of the presence of the circulating oestrogen. My inference is that, while the vagina is able to react, the uterus lacks something by which it also can react.

If this inference is true, should we not review some of our endocrine therapeutic failures from a different angle? From the evidence of animal experiments we are entitled to expect certain results from the sex hormones, especially when we work with ostrogen and progesterone, which can be injected in reasonable doses. But often in clinical medicine we are disappointed. Is this failure possibly due to the fact that we are using the wrong substance, and if we could replace a missing receptor—as in my illustrative case—should we not immediately see the expected reaction? It is obvious that we need more research on the tissues or soil on which the sex hormones normally act. The earlier years of the science of bacteriology were conspicuous for the same omission. The organisms were explored in the minutest detail, but the tissue cell and fluid resistance was largely neglected. Now we know that in the phenomena of infection the organism is only part, perhaps a small part, of the whole process of infective disease. Indeed, in this branch of medicine it is now recognized that the reaction of the tissues to the microbic assault is at least equal in importance to the biology of the microbes themselves. When, therefore, we consider all the difficulties which beset endocrine therapy—the correct hormone, its dosage and timing in the menstrual cycle, the effect of the emotional life, and the ignorance and neglect of receptors—it is surprising not that we find many failures but that we have any success at all.

Treatment by endocrine hormones has, however, definite fields of usefulness, and there is a wide fringe of partial or occasional success which will vary according to the faith of the patient in her doctor and to his confidence in the value of his injection. Endocrinology offers perhaps the widest scope in the whole of medicine for treatment by confidence. Where symptoms rather than signs are the object of treatment—such as the menopausal syndrome as opposed to the undeveloped uterus—we find the chief success. On the other hand, in the certain suppression of lactation there is a specific organic result of the action of oestrogen.

Hormones and Their Functions

Let us consider, first, what hormones we have at our disposal. By far the most important is one or other of the oestrogens. The natural oestrogens commonly used are oestradiol benzoate, oestrone, and oestriol, sold under different trade names by different makers. The synthetic oestrogens are stilboestrol, hexoestrol, and dienoestrol, the two latter being one-sixth and one-tenth as potent, weight for weight, as stilboestrol. They have the advantage over the natural oestrogens in that they are soluble in water and can be given by mouth. Oestrogen therapy is convenient, precise, and sufficient in dosage. The second ovarian hormone is progesterone, the product of the corpus luteum. In the process of its metabolism it is "denatured" and finally excreted in the urine as the inert water-soluble pregnanediol. Unfortunately for therapeutics, progesterone must be extracted from the corpus luteum, which means that the available dosage will be small and expensive. The synthetic product, sold as ethisterone, can be given by mouth; but it is much less potent, and is also scarce and expensive. It is indeed unfortunate that we have no adequate treatment by the corpus luteum, for it is one of the most important of all the sex hormones from the point of view of therapeutics. Lack of progesterone in adequate dosage is responsible for most of the failures in treating common conditions like amenorrhoea and dysmenorrhoea. The two hormones oestrogen and progesterone work so closely together—as, for example, in forming the progesta-

tional endometrium and the decidua—that, with two or three exceptions, it seems almost hopeless to produce any therapeutic results by giving oestrogen alone, as is so often done.

The anterior pituitary secretes two well-recognized sex hormones. One is the follicle-stimulating hormone formerly called prolan A, which stimulates the maturation of the Graafian follicle and production of the ovum; the other is a hormone which initiates the corpus luteum after rupture of the follicle. It was formerly known as prolan B, but is now commonly known as the luteinizing hormone. If we were dependent upon the pituitary alone as the source of these hormones there would be no practical use for them in clinical medicine, as the gland is so small and the yield insignificant. But it so happens that the serum of the pregnant mare during the middle of her pregnancy contains large quantities of the follicle-stimulating hormone, which can be extracted and put up in fair dosage. It is sold by various makers as "serogan," "antostab," "gestyl," and "gonadyl" in doses of from 200 to 3,000 units. The second gonadotrophin, the luteinizing hormone, can be obtained from the urine of pregnant women. It is not precisely the same substance as that secreted by the pituitary, but is very similar in its effect. It is produced by the chorionic cells of the placenta, whence its name—chorionic gonadotrophin.

Before we dwell upon the practical value of the sex hormones in therapeutics let us pause to consider their chief functions. The proximal group is the pituitary secretions. It is believed that during the first two weeks of the menstrual cycle the follicle-stimulating hormone is produced. Under its influence a single immature Graafian follicle ripens, secretes oestrogen, and dehisces the ovum on the 13th day, though this date is by no means constant. At the moment of rupture of the follicle the secretion of this hormone ceases by reason of a reciprocal inhibitory action of the follicular oestrogen on the secretion of the pituitary follicle-stimulating hormone. During the second fortnight is secreted the luteinizing hormone, whose function is to convert the follicle and maintain the corpus luteum and its hormone, progesterone. In its turn the secretion of the luteinizing hormone ceases, the corpus luteum degenerates during the next thirty-six hours, and menstruation begins. So far as we know, the pituitary gonadotrophins have no other function than these actions upon the ovarian follicles and corpus luteum. It is improbable that the story is as simple as the alternating action of two separate hormones. It is more likely that other ovariotrophic hormones exist which, for example, control the rupture of the follicle and together form a complex group of gonadotrophins. Of the "terminal" ovarian hormones, oestrogen is the best known. It is essentially the oestrus-producing hormone, but other changes it induces are the growth of the genital tract at puberty, the conversion of the endometrium into its proliferative phase after menstruation, and the cornification of the vaginal epithelium. Its action, preceding that of progesterone, is necessary for the appearance of menstruation.

Progesterone has been employed to a smaller extent than oestrogen because the difficulty of synthesis makes it impossible to provide large enough doses. Its chief function is to produce the secretory or progestational phase of the endometrium, in readiness to receive the fertilized ovum. Immediately the ovum is fertilized the endometrial change is carried a step further to form decidua. The integrity of the decidua is dependent upon the secretion of progesterone until about the fifth month; for if during this time the corpus luteum is removed or fails in its secretion—as shown by a low excretion of pregnanediol in the urine—the decidua breaks down and haemorrhage follows as the uterus aborts. It was formerly thought that progesterone was a kind of uterine sedative, but it is now known that the uterus is irritated through the influence of posterior pituitary extract to a greater extent during the luteal phase of the cycle than during the oestrogen or post-menstrual phase. A practical example is that usually progesterone given for dysmenorrhoea before the period makes the pain worse. It is incorrect to think of the ovarian hormones as having wholly separate and independent functions. They certainly induce different changes in the endometrium; but no normal function, whether it be menstruation, conception, pregnancy, or, probably, labour, can take place unless they work in harmony. The earlier view that oestrogen and progesterone were "antagonistic," though correct in a limited sense, has impeded the progress of successful endocrine therapy by leading us to neglect the idea of their synergism, and to think only of their antagonism.

Therapeutic Value of Sex Hormones

Having sketched the great difficulties of practical clinical application of the sex hormones and touched on their functions, what now of their therapeutic value? The main clinical problems, such as amenorrhoea, menorrhagia, dysmenorrhoea, sterility, and the menopause, seem to be due to deficiency or excess and disordered rhythm of their production. But of this we are not sure, for the disturbance may be due to disproportion of secretion of one hormone relative to another. It always amazes me to hear some physicians talk of the hormonal defects of one or other of their patients. They say with confidence and precision which hormone is lacking or excessive and just how the trouble can be compensated by giving a grain of this or a milligram of that.

If we divide the sex-organ disabilities into those which are functional or subjective and those which are objective or organic, and examine the effects of treatment by hormones of each group, we shall be better able to appraise their true value. It is not easy to draw a sharp line between the so-called functional and organic conditions, for there are always likely to be some structural changes, even if at the beginning they are only microscopic. But in general we mean by functional conditions those which are not associated with organic conditions discoverable by ordinary clinical, *x*-ray, or other examination. Of the organic states often treated by hormones the chief are pelvic hypoplasia or underdevelopment as a cause of amenorrhoea or sterility, lactation when it is necessary to suppress it, atrophy of the vulvo-vagina (kraurosis), leucoplakia, and metropathia. If we are honest with ourselves we must admit that the only certain success in treatment is the suppression of lactation by the oestrogens. If we give 15 mg. of stilboestrol daily for three or four days we can assume that engorgement will disappear and lactation will cease.

In cases of pain in older women due to atrophy of the vulva (kraurosis), or senile vaginitis due to a pyogenic infection, there is frequently either complete cure or much relief following oestrogen therapy, within three or four weeks. Similarly, some cases of chronic vulvo-vaginal infection in children will also clear up after the use of vaginal pessaries of 1,000 units of oestrogen.

But if the pain of kraurosis is relieved by oestrogen it is certain that leucoplakia, which is an epidermal hypertrophy and always a new growth in its late stages, not only is not improved but is probably increased. No form of anaerobic infection of the vagina, as by the common enterococcal streptococcus—sometimes associated with the symbiotic *Trichomonas*—is touched by oestrogen therapy, because these organisms can live comfortably in the acid

medium of the vagina, which is increased by oestrogen. One of the commonest and most serious states is pelvic hypoplasia. Here we have failure of complete development of the uterus, and often of the vagina and vulva. There may be full development of the secondary sex characters, or the woman may show some degree of virilism. Usually she is apparently a normal woman except that puberty was late, menstruation is imperfect, perhaps absent, sometimes but by no means always painful, and if she is married she may complain of vaginal dyspareunia and sterility. It is difficult to diagnose uterine hypoplasia by clinical examination: it can be proved only by comparative *x*-ray shadow or the uterine sound. I am convinced that no amount of combined oestrogen and progesterone treatment can add half a centimetre to the uterine stature. In some of these cases amenorrhoea can be apparently cured, so long as the oestrogens are given, by producing the so-called withdrawal haemorrhage; but primary amenorrhoea can never be cured, and that form of amenorrhoea which is secondary to early uterine atrophy—not necessarily a true menopause—also can never be cured by the sex hormones. Where, therefore, amenorrhoea is "organic" it can seldom if ever be replaced by a normal regular and permanent menstruation.

Sterility offers a different problem. It is certain that the underdeveloped uterus presents no difficulty to embedding of the fertilized ovum, even if the progestational phase of the endometrium is imperfect, because we know that the ovum can embed itself in the tube or even the ovary. The failure of conception is probably due to the associated failure of ovulation where the uterus is underdeveloped. The small uterus is the chief clinical evidence of smallness of function, including ovulation. The problem of sterility in these cases is therefore how to treat function by producing ovulation; the condition of underdevelopment is less important. In the follicle-stimulating hormone of the pregnant mare's serum we hoped that we might have a means of inducing ovulation. I have used it many times in doses of 1,000 units in carefully selected cases during the post-menstrual ten days, but in only one woman has conception occurred after treatment during three months. Pregnancy progressed to term, and at last, after eight years of trying to conceive, she has got her baby. In no other case can I honestly say that the serum gonadotrophin has possibly worked. Many schemes of hormone therapy have been used for sterility of all kinds, and here and there successes have been claimed, but we must remember that the arm of coincidence is long, especially when dealing with such a condition as sterility.

Another organic condition is metropathia (it should be named oophoropathia), causing profuse and irregular haemorrhage. It is probably true that the irregularity of haemorrhage in cycle, duration, and amount is due to disordered rhythm of production of the follicle and corpus luteum. During the periods of bleeding no corpus luteum exists in either ovary, and the endometrium shows an intense oestrogenic stimulus. One ovary contains unruptured follicles the fluid of which is much more highly charged with oestrogen than the normal Graafian follicle. The obvious endocrine treatment is therefore to give an anti-oestrogen—progesterone or testosterone. Scowen (quoted by Bishop) has shown that very large doses of progesterone (20 mg. on alternate days) will effect improvement lasting for many months after ceasing the injections. A more certain remedy is testosterone propionate, but again the doses must be large (20 mg. twice weekly). This male hormone acts by overcoming the female oestrogen and ultimately inducing genital atrophy and virilism. It must therefore be used with great caution. Whatever improvement short of atrophy may be induced is temporary in moderate or advanced cases, and most of these patients must submit to *x* rays or hysterectomy according to their age. Mild cases of excessive loss with irregularity can often be controlled for a while with progesterone, but the treatment is expensive and unreliable. Among the truly functional conditions there are the menorrhagia of puberty and the subjective symptoms of the menopause. Certain cases of spasmodic dysmenorrhoea form a large group, and many attempts have been made to treat repeated threatened abortion and inertia in labour, of which many cases are functional. As a means of inducing premature labour oestrogen is quite unreliable even when given in such doses as half a million units. The disorders which can be grouped as sexual frigidity or "functional" dyspareunia are entirely unresponsive to oestrogen. The haemorrhage of puberty, like that of metropathia, is probably due to failure to establish ovulation, with the consequent deficient secretion of progesterone. The child is under the influence of an uncontrolled action of oestrogen which produces oestral haemorrhages and not true menstruation. When investigating these cases many years ago Dr. Charles Wilson (now Lord Moran) and I found evidence that these patients were in a state of hypothyroidism as measured by the basal metabolic rate. If this is generally true it may be that thyroid deficiency is no more than a side issue of general endocrine incoordination. Some enlargement of the thyroid is often seen at the age of puberty, and in such cases I always give small doses of thyroid extract or iodine. The logical treatment, as in the case of metropathia, is to give large doses of progesterone, but in my experience this is seldom the right course. Most of these children are being pushed for school examinations. They are overworked, tired, thin, pale, and sometimes anxious about the school certificate. The best treatment is to rest them by removing them from school for a term and keeping them in bed during the days of worst bleeding. Really serious cases are very rare, and nearly all of these patients soon become normal.

In dysmenorrhoea we have the biggest problem of all, as is manifest by the multiplicity of methods of endocrine treatment. Of the many theories advanced to explain severe first-day pain, my own view is that it is caused by intense uterine contraction with coincident spasm of the internal os—as we often see in painful first-stage labour—producing obstruction to the outflow and ischaemia of the muscle. It is indeed uterine colic. The uterus seems to lack polarity, or co-ordination between fundal contraction and cervical relaxation. The worst case of dysmenorrhoea I ever saw was in a woman, previously without any monthly pain, for whom I amputated the cervix. Severe pain immediately followed the operation, and on investigation, after the second painful period, under anaesthesia I had the greatest difficulty in passing a filiform bougie. When, however, I had finally dilated the stenosed os by a tent, the pain entirely disappeared. In the less severe cases almost any treatment, especially if given by injection, may be successful for a few months. The rational therapy would be some measure which relieved the irritability of the uterine muscle and at the same time relaxed the spasm of the internal os. In practice we find that progesterone before the period is not only useless but may actually increase the pain, just as it often expedites threatened abortion by stimulating the uterine response to posterior pituitary extract. It is also useless to treat dysmenorrhoea on the supposition that the uterus is underdeveloped, for Jeffcoate has shown that pain is caused by the normal uterus equally with the small uterus. Oestrogens, given during the post-menstrual week in rather large doses—5 mg. daily—may relieve pain by inducing an anovular cycle, but there is nothing

approaching certainty either by this or any other form of hormone treatment.

The subjective symptoms—flushing, sweating, and many nervous symptoms—of the natural menopause are nearly always relieved or even abolished by oestrogen. It is necessary to impress on the patient that stilboestrol or dienoestrol must be taken only intermittently—say for two weeks, followed by one week without treatment—and that it should not be continued indefinitely. Many cases of post-menopausal bleeding which we see to-day are found in women who have been taking stilboestrol literally for years. They suffer from an intensely oestrogenic proliferative endometrium which oozes blood by reason of its congestion. But while oestrogens are invaluable at the natural menopause they are disappointing when given after radium, *x* rays, or double oophorectomy. Implantation of oestrogen pellets is similarly useless, though this method has striking success for a year or so when used for the natural menopause. Implantation of oestrone is, however, a risky procedure as it may cause repeated irregular haemorrhages, and it may be necessary to remove the pellet.

Lastly we come to repeated abortion. During early pregnancy, excretion of pregnanediol—the final inert product of progesterone—increases greatly, up to 50 or 60 mg. daily. Where the excretion is markedly low it is stated that abortion is certain. It is well known, too, that removal of the corpus luteum before the 20th week will be immediately followed by abortion. It would therefore appear that for those patients who abort by reason of defective secretion by the corpus luteum progesterone given from the earliest weeks until the 20th week would provide an effective substitution therapy. The estimation of pregnanediol in the urine is difficult and expensive, and thus cannot be used as a test in many cases of early pregnancy of women who have had repeated abortions. Injection of progesterone has been disappointing, perhaps because it produces peak influences followed by "negative phases," but by implantation of a 100-mg. pellet of progesterone it is possible to preserve an even absorption of the hormone. Unfortunately progesterone is not well tolerated by the tissues, and it is always extruded from a fat embedding. It is possible, however, to increase the chance of its retention by embedding the crushed pellet beneath the rectus muscle sheath. The whole pellet may be extruded even from below the rectus sheath, but in only one case have the fragments of the crushed pellet been rejected. I have done too few cases to generalize, but I have evidence that implantation in suitable cases is at least associated with continuation of an undisturbed pregnancy.

Conclusion

I began the address by emphasizing the difficulties and disappointments of endocrine therapy, and continued to show that few conditions can with certainty be cured. The obvious lesson is that we have plunged too quickly and with too high hopes from the endocrinology of animals to its application in clinical medicine. There are many difficulties in the way of clinical research, but it is badly needed. One of the chief obstacles is the complexity of biochemical assay whereby blood and urine levels of the endocrine secretions and their by-products can be measured accurately. A further field is the quantitative effect of emotional states on pituitary secretions and, as I have said, the role of the receptors of the hormones. The synthesis of stilboestrol is an indication of what great progress would follow the synthesis of other hormones. Finally, except in the case of the "trace element" iodine and the thyroid, the relation of nutrition and other "trace elements"—the ultimate source of all our secretions—to endocrine activity has yet been scarcely touched.

VOLVULUS OF THE CAECUM

BY

RALPH H. GARDINER, D.M., M.Ch., F.R.C.S.

Surgeon, Royal Buckinghamshire Hospital, Aylesbury

While volvulus of the sigmoid colon is a well-known condition, volvulus of the caecum is still classed as one of unusual occurrence, unknown to many members of our profession. Isolated cases are considered worthy of report as rarities, and in standard textbooks of surgery the condition is dismissed in a few lines or else entirely ignored. It is not nearly so uncommon as has hitherto been supposed. I have been able to collect reports of 15 cases in the past five years and have had three personal cases in the past two and a half years, and it is by no means a unique occurrence in the experience of other surgeons, many cases not having been reported. It should receive wider recognition, as it is a condition associated with a high mortality rate if treatment is withheld for long, and is apt to remain undiagnosed altogether until the abdomen is opened—frequently too late. Partial torsion often occurs in recurrent attacks over a period of years, sometimes culminating in an acute complete torsion, and may be the cause of obscure abdominal pain and discomfort, simulating in some cases subacute appendicitis. Furthermore, it can seriously complicate pregnancy and the puerperium, and is therefore of importance to obstetricians. A review of the condition dealing with its diagnosis and treatment will, I feel, be of value.

Mortality Rate and Incidence

Some idea of the incidence of the condition may be gained from a review by Wolfer *et al.* (1942), who found that 194 cases had been reported since 1913, with 110 previously, in the world's literature, making a total of 304. Mortality rates given are very high—50 to 60% in cases which had been operated on, rising to 100% in those which had not. A wider recognition of the condition, with prompt diagnosis and treatment, should certainly bring this high mortality rate down to a much lower figure.

Anatomical Factors in Causation

Normally, after the process of herniation of the midgut loop into the umbilical cord has taken place, with its subsequent rotation, it returns to the abdominal cavity, and the process of descent and fixation of the caecum occurs. This is called the third stage of rotation. The caecum lies beneath the liver on its return to the abdominal cavity and then descends to the right iliac fossa, finally becoming fixed to the posterior abdominal wall, its mesentery disappearing. If the fixation, with disappearance of the mesentery, fails to take place, the caecum and ascending colon are left with a variable degree of mobility depending on the length of this mesentery, and it may even be continuous with that of the terminal ileum, making a common ileocaeco-colic mesentery. Variable amounts of ascending colon may be included up to the hepatic flexure and extending to the transverse mesocolon. This will render the caecum and a variable portion of the right half of the colon liable to torsion. The terminal ileum may also be involved. Points of fixation at the base of this mesentery frequently act as hubs round which torsion occurs. Such fixed points are often found at the level of the hepatic flexure or at the point where the transverse colon crosses the duodenum.

Wolfer *et al.* investigated the frequency of this non-fixation of the caecum and right half of the colon, and concluded that it occurs in at least 15% of individuals; other workers give even higher figures—20 to 25%. Any