THE IMPORTANCE OF HORMONES IN MENORRHAGIA *

BY

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Speaking from my experiences in my own special work I wish to indicate quite shortly the possible significance of hormones in menorrhagia.

Apart from such other hormones as, for example, those of the thyroid and the suprarenal cortex—perhaps, also, the so-called circulatory hormone to which I shall refer later—there are two endocrine glands, the ovary and the pituitary, which have a particular action on the female genital apparatus.

THE OVARIAN HORMONE

Since Allen and Doisy employed their well-known test on castrated rats and mice to prove the action of this hormone on oestrus production it has become possible to prepare it in crystalline form. The best source of the hormone is the urine of pregnant women or pregnant animals, in which Zondek and Aschheim first demonstrated it, and in which it is present in large quantities. For therapeutic purposes it is not absolutely necessary to use a crystalline preparation, the manufacture of which entails a great deal of waste. I myself have had a good deal of experience with the ovarian preparation unden, which contains 100 mouse units in every tablet. The work of the biochemist in his laboratory is limited to the preparation, free from poisonous impurities, of any desired hormone and its standardization as well as possible by animal tests.

Only the practising doctor can form an opinion of the therapeutic value of such preparations. It is for him to diagnose the occurrence of cases in which the symptoms point to the presence of too little ovarian hormone, and in which the administration of a standardized preparation would be of value. According to experiences up to the present a certain number of cases can be benefited by the administration of ovarian hormone. There also occur cases in which by no means all the symptoms, and not even all cases of menorrhagia, can be thus improved.

CORPUS LUTEUM

Apart from the oestral hormone there is at least one other hormone present in the ovary which is formed in the corpus luteum. The researches of Allen and Corner, in particular, have shown that this hormone is necessary to promote the fixation of the ovum in the mucous membrane of the uterus. Some authors believe that it also has an inhibitory effect opposite to that of the oestral hormone, possibly also to that of the pituitary, to which we shall return later. A few authors hold that there is a co-operation between oestrous hormone and corpus luteum. Corresponding to the uncertainty surrounding the theoretical basis of the corpus luteum hormone, its therapeutic value is as yet little known. Since the corpora lutea are primarily very difficult to procure, the isolation of this hormone in sufficient quantities is for the most part almost impossible. However, according to my opinion, the hormonal function of the corpus luteum can, to a very large extent, be taken over by the anterior pituitary lobe, the function of which I now intend to discuss.

ANTERIOR PITUITARY LOBE

Theory.—As is well known, Evans proved that a hormone affecting growth is secreted by the anterior lobe of the pituitary. Aschheim and Zondek, almost simultaneously with Smith, also found in this gland a hormone

governing the genital function. B. Zondek, with whom I have worked in the most pleasant relationship for many years, has therefore designated the anterior pituitary lobe as the seat of the motor of the sexual function. Moreover, he also proved the presence of this hormone, which he called prolán, in the urine during pregnancy. Together with Aschheim he evolved a method of diagnosing early pregnancy by this fact. You see, during pregnancy in human beings there are two hormones present in the urine. But the diagnosis of pregnancy is only based on the early appearance of the pituitary hormone. There are important biological differences between these two hormones. For example, prolán, in contradistinction to the ovarian hormone, has no action in castrated animals. In infantile female animals it causes early maturity. According to our experiences the best experimental animal on which to prove the action of prolán is the rat. A rat unit is the smallest amount which in 66 per cent. of the animals tested under special conditions brings about complete oestrus with the formation of large follicles in the ovary. If larger doses are injected there is actually an inhibition of oestrus, and the formation of corpora lutea takes place. Zondek believes that there are two different hormones in prolán—factor A, which induces ripening of the follicles, and factor B, which stimulates lutein formation. However, it is possible that it is only a question of quantity. My experience is that any preparation which in small doses produced follicle ripening, in large doses, particularly if given for some length of time, always caused luteinization. Prolán, as it is at present recovered from the urine of pregnant women, always contains these two factors. It contains, however, no growth hormone, since this is only found in the gland itself, and is not excreted in the urine of pregnant women. Even preparations subjected to repeated purification still contain factors A and B. We succeeded in making preparations containing 20,000 to 30,000 rat units in 1 gram. They can be dissolved in water and injected subcutaneously. In contradistinction to the ovarian hormone prolán is easily dissolved in water, but insoluble in lipoid solvents. However, the watery solution of prolán is not very stable, being very sensitive to high temperatures and the least change in the H-ion concentration. Oral administration in animals has also proved effective, but here larger doses must be given. Even in the purest products it has so far been impossible, in spite of many endeavours, to isolate the two fractions A and B by chemical means. This points to the possibility of there not being two separate substances A and B in prolán, but only a quantitative difference in one uniform hormone.

Therapeutic Uses.—The following rules apply to the therapeutic use of prolán. When one wishes to stimulate the ovary to renewed activity small doses should be given, so that the so-called factor A action is obtained. If one desires to inhibit the activity of the ovaries large doses of prolán should be given, thus producing a luteinizing action. By this method, therefore, it is possible, in a roundabout manner, to obtain the specific effect of the corpus luteum hormone, which in itself is difficult to achieve. Thus every case of menorrhagia resulting from over-activity of the ovary should with advantage be treated with large doses of prolán. Already clinical experiences have proved the truth of this observation. It is therefore now possible to achieve that hormonal sterilization which has for some time been sought. By combining treatment with unden and prolán together it is at least theoretically possible to regulate disturbed ovarian function.

A VASOMOTOR HORMONE

I would like to refer also, very briefly, to the substance which Frey and Kraut isolated some years ago from the urine of healthy individuals, and which proved to be

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a product of the pancreas which lowers blood pressure. They called it kallikrein—a vasomotor hormone. Since this hormone dilates the peripheral blood vessels, thus lowering the blood pressure, its therapeutic use in disturbances of the climacteric may possibly be of value. Whether this applies also to menorrhagia has so far not been investigated thoroughly.

CONCLUSION

In the short time at my disposal it has been impossible to give more than a short survey of a mere part of the whole hormone question. I have only touched upon those factors which I consider to be of special importance in gynaecology. How great is the interest in hormones, particularly anterior pituitary, was demonstrated at the German Gynaecological Congress which I attended two months ago in Frankfurt-on-Main. Twelve papers were read, and a further thirty speakers took part in the discussion on this subject alone. Most of the papers dealt with animal experiments and were more theoretical than practical, showing that we are still at the beginning of our knowledge. The new tests which the physiologist plans and works out facilitate the preparation by the biochemist of standardized hormonal preparations which can be used by the doctor. Vice versa, the observations and suggestions of the doctor amplify the theoretical laboratory investigations. I see in this very collaboration of several sciences the most practical way of arriving at a correct understanding of the whole hormone question. Not only is this a matter of several branches of science working together in perhaps each separate land, but collaboration between the different countries too. It has therefore given me especial pleasure to appear at the Annual Meeting of the British Medical Association as a German physiologist speaking to English gynaecologists, and I am grateful for the invitation which brought this about.

SOME POINTS IN CONNEXION WITH THE TREATMENT OF GLAUCOMA

BY

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From the earliest days of the operative treatment of glaucoma, dating back over seventy years, there has always been a tendency towards the establishment of two schools of thought: that which favours operative measures and that which relies on medical treatment alone. Formerly there was the strongest antagonism between the two. The more generally adopted view of to-day is a compromise in which both methods are made use of, each case being judged on its own merits. It may be said, without fear of challenge, that no case should be submitted to operation if the use of miotics, the employment of massage, and attention to the patient's general health suffice to arrest the course of the disease and to keep the case *in statu quo*.

MIOTICS

Of the two miotic drugs pilocarpine is to be preferred to eserine in the great majority of cases for several reasons: (1) It causes less conjunctival irritation. (2) It does not give rise to the same measure of spasm and headache, for it acts more quietly and evenly. (3) Suitably employed, it maintains the necessary contraction of the pupil quite as well as its more powerful rival.

When it is a question of producing miosis as rapidly as possible in a patient with congestive glaucoma, the case is quite different, and eserine is the drug to employ. Pilocarpine should be used in the weakest doses that will maintain efficient miosis, and should be given last thing

at night, first thing in the morning, and about 3 o'clock in the afternoon. This timing is important, for, (a) rises in pressure occur frequently during sleeping hours, owing to the withdrawal of the pumping action on the canal of Schlemm exerted by the ciliary and iris muscles; and (b) the afternoon is, for many patients, a time of fatigue in which the vasomotor tone falls, and the pressure in the eye is consequently in danger of rising. If medical treatment is to be fairly tried, miosis must be sustained. Sometimes trouble is experienced owing to conjunctival irritation set up by the drug. This can best be combated by the use of silver collosol, alternated with hazeline eye-drops (40 minims to the ounce of rosewater). It sometimes, however, though fortunately rarely, becomes a very serious factor in the case, making the maintenance of miosis difficult, if not impossible. Operative intervention may then become a necessity.

MASSAGE

The importance and value of ocular massage in glaucoma does not seem, even now, to be sufficiently appreciated. There are certainly quite a number of cases under treatment for raised tension of the eye in which massage is either not being used at all or else not to the fullest advantage. The technique is simple, and any patient can be taught to use it for himself. Both hands should be used, and the index or middle fingers should be placed on the upper lid as far apart as possible and with the eyes looking downward. Alternate pressure with each finger in turn will rapidly lower the tension of most eyes, but the pressure must be made toward the centre of the eye, whereas the great majority of patients employ a stroking movement which is of little value. Strong pressure should not be used; light, quick, almost butterfly movements will do more good and will not hurt the patient at all. In fact, he often offers the comment that he "hardly felt the massage, and does it much stronger himself." It is, however, the light, quick pressure, with the fingers far apart and with every stroke toward the centre of the eye, that is by far the most effective.

GENERAL RULES

Remembering the influence of vasomotor exhaustion on glaucoma, there are certain practical rules which should be impressed on every patient; indeed, it is well to write these down for them.

1. *Avoid Over-fatigue*.—Few things are more dangerous to the man who is threatened with congestive glaucoma than allowing his vital energy to run low. He should work within reason; indeed, this is much better for him than idleness, but he should never exhaust himself. Exhaustion means a lowering of the vasomotor control and a consequent provocation of local congestion, especially in the cerebral circulation. On the other hand, to cut him off from work which engages his attention, diverts his mind from his trouble, and fills his time profitably, is bad and not good, though it is often done. Moreover, the intermittent action of his iris and ciliary muscles is a safeguard of which he is to some extent deprived if he is stopped from reading and writing, and kept in the shade. I have often released a patient from this strict regime of doing nothing, and have never seen harm follow. On the contrary, the patient has benefited materially, and has become more cheerful and brighter in his outlook. The influence of the mental on the physical condition in glaucoma is a psychological factor of great importance. The unoccupied man not only has time to fret, but the very fact that occupations are forbidden predisposes him to do so. Allow him to engage his mind and you cut the vicious circle.

2. *Get Regular Sleep*.—Much of what has been said under the last heading applies again here. If necessary, the aid of drugs, such as luminal, should be invoked. Glaucoma patients are often elderly, and the boggy of