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THE OBESITY, MENSTRUAL IRREGULARITY AND HIRSUTISM SYNDROME

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Until the pathogenesis of this endocrinopathy is understood and defined, the designation of this fairly common condition as the *obesity, menstrual irregularity and hirsutism syndrome* seems sufficient to fulfil the interim need. The syndrome usually manifests itself in young women with the sudden onset of obesity followed by menstrual anomalies and not infrequently accompanied by the development of slight hirsutism. Various patterns of development are encountered in this syndrome, the most typical being the post-marital type and the post-pregnancy variety.

1. *Post-marital Type.* The history usually obtained in this type of case is that of a young woman who has a normal puberty and menstrual pattern until marriage, and develops this condition soon afterwards. These patients develop a voracious appetite almost immediately after marriage and obesity follows during the next few months. The weight may increase by 30-100 lb. Soon they start experiencing menstrual anomalies, most frequent in the form of oligomenorrhoea. Not infrequently they notice the concomitant development of slight hirsutism. Furthermore, they often complain of an inability to become pregnant.

2. *Post-pregnancy Type.* A similar train of events not infrequently follows pregnancy, usually full-term but in some cases an abortion. Soon after the birth of the baby, and often also during pregnancy, the woman allows her weight to increase tremendously. Often lactation is unsatisfactory. During the ensuing months her periods become abnormal. The obesity increases and the oligomenorrhoea persists. In due course she finds she is unable to become pregnant again. It is then, or even earlier, that she is given various hormone preparations, whereas in actual fact the

whole trouble can often be cured by plain and simple reduction of weight.

3. *Other Types.* Although the post-marital and post-pregnancy types are the most typical, various other patterns of development are also found. Often the history is obtained that the patient underwent an operation (not necessarily of any special nature) and after this she develops obesity with its consequences (*post-operative type*). At other times the history of a severe emotional upset is obtained, followed by a similar train of events (*post-stress type*).

SYMPTOMATOLOGY

Obesity is a classical component of the syndrome. It seems to affect the trunk and proximal parts of the limbs more than the distal parts.

Oligomenorrhoea is the usual menstrual pattern, i.e. infrequent menses occurring at intervals of less than 3 months. Often these intervals are more than 3 months; that is to say, periods of *secondary amenorrhoea* occur. On occasion, even with the history of oligomenorrhoea, the periods are clinically ovulatory in character and cramp-like pains are experienced on the first day of the flow. This, however, is exceptional. Usually the menses are completely painless and anovular. The occasional ovulatory character of these menses no doubt explains the rare occurrence of pregnancy when this syndrome has become established. Sometimes these infrequent periods are of a *metrorrhagic* type of bleeding. In rare cases regular menstruation is found. When this occurs it is more commonly anovular than ovular in nature.

Hirsutism, although frequently present, should not be regarded as a classical component of the syndrome. When present it is usually only slight in amount and takes the form of an abnormal growth of hair over the upper lip, chin, sternum and nipple regions, abdomen, lumbo-sacral region and limbs. Often the abdominal hair growth is attributed to shaving before an abdominal operation. It is revealing, if the point is enquired into, how frequently patients will state that the hirsutism started at about the

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same time as the obesity. Sometimes these patients volunteer that other members of their family are also hirsute. Whether patients with this familial trait are more inclined to develop this syndrome is not known.

Headache is another frequent complaint. Mostly it is situated over the vertex, but often it is typically migrainous in character. A family history of *diabetes* is not infrequently found.

DIFFERENTIAL DIAGNOSIS

Although the onset of hirsutism in any young woman may herald a serious disorder,^{1,2} in the vast majority of cases the underlying endocrinopathy is not of such serious concern. It would be ideal if an estimation of the urinary 17-ketosteroids could be obtained in all hirsute patients in order to rule out those few cases where the basis of the disorder were a major *adrenocortical disturbance—neoplasia or hyperplasia*. This, however, is not practical except in institutions with facilities for endocrinological investigation, and a different approach to the problem has to be made. Should the history conform to that given above, there are for practical purposes only two conditions which merit consideration in the differential diagnosis, *viz.* the '*obesity, menstrual irregularity and hirsutism syndrome*' and *ovarian hyperthecosis*. The latter is not an uncommon condition. There is a great possibility that these two endocrinopathies are of an identical nature, being only different in the stage of development reached or in the emphasis on the various target glands. The only clinical point of distinction between the conditions is the fact that in ovarian hyperthecosis bilateral ovarian enlargement is present, whilst in the obesity, menstrual irregularity and hirsutism syndrome the ovaries are supposed to be normal. For this reason the importance of a careful vaginal examination must be emphasized. This may also lead to the discovery of the very rarely occurring *androgenic ovarian tumour*.

Since many of these patients are obese, and since the proper evaluation of the state of the internal pelvic organs is at times a very difficult, if not impossible, matter on ordinary vaginal examination, examination under relaxant anaesthesia is essential. Curettage (and possibly salpingography and pelvic aerography) done at the same time may aid in establishing the diagnosis. Should the ovaries be palpable as firm, enlarged, globular or elongated masses, most often lying in the pouch of Douglas (ovarian hyperthecosis), *bilateral subtotal ovariectomy* should be seriously considered; strict reduction of weight is then also essential. Should no ovarian enlargement be ascertained under these favourable conditions, *strict weight reduction* is of paramount importance. In many cases this will be all that will be required in the way of therapy.

So-called '*partial gynaecography*'³ has been extensively used in America in the investigation of these cases. In this procedure the uterine cavity is outlined by a radio-opaque substance, followed by the induction of a pneumoperitoneum to display the internal pelvic organs radiographically. Theoretically it should be of immense value, particularly in the obese patient, in view of the pitfalls of a vaginal examination, even if carried out under anaesthesia. However, the attempts at the procedure made at Groote Schuur Hospital have been disappointing.

PATHOGENESIS

The pathogenesis of this common and interesting condition is still obscure. The most reasonable explanation seems to be that it is a 'stress' reaction with a consequent upset in the hypothalamic-pituitary axis and resultant dysfunction of the adrenal cortex and ovaries. It seems to be most feasible that there is an adrenocortical dysfunction without neoplasia or hyperplasia. Jones and Jones⁴ found increased quantities of pregnanetriol excreted in the urine in patients corresponding to these described types. Pregnanetriol is the urinary excretory metabolite of 17-hydroxyprogesterone, an androgenic substance found in the adrenal cortex during the synthesis of 17-hydroxycorticosterone.⁵ Our own observations have shown that there is an increased excretion of so-called 'pregnenediol' in the urine of patients with ovarian hyperthecosis.⁶ The method⁷ used, however, might have resulted in pregnenediol being misinterpreted for pregnanetriol.^{8,9} Another possible pointer to the probability of adrenocortical dysfunction in these cases is the finding that some of them respond to the administration of cortisone.^{10,11}

Further work on this matter is at present being conducted at Groote Schuur Hospital.

SUMMARY

1. The '*obesity, menstrual-irregularity and hirsutism syndrome*' is described.
2. The view is put forward that it develops as a consequence of a 'stress reaction' with resultant dysfunction of the adrenal cortex and ovaries.
3. The possibility that this endocrinopathy is basically the same as the condition of ovarian hyperthecosis, being only different in the stage of development reached or in the emphasis on the various target glands, is mentioned.

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