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GENERAL PRACTICE SERIES

DISEASES OF THE GONADS*

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Recent important advances in gonadal disorders include the application of methods of 'nuclear sexing', a clearer understanding of hermaphroditism, intersexuality and 'ovarian agenesis', and an appreciation of the frequency of hyperthecosis ovarii in secondary menstrual disorders. The treatment of undescended testes has been placed on a sounder footing.

1. EUNUCHOIDISM AND MALE HYPOGONADISM

The onset of puberty is heralded by increasing pituitary activity, as is indicated by rising gonadotrophin output. The testes respond to this by development of both seminiferous tubules and of Leydig cells. The latter produce testosterone, which in its turn induces secondary male characteristics and also acts 'thermostatically' on the pituitary, controlling gonadotrophin production by its inhibitory effect. Hence clinical hypogonadism may be the effect of a primary pituitary defect in which gonadotrophin production (measured by urinary F.S.H.) is low, or of a primary testicular defect in which gonadotrophin production is high, but the testes cannot respond to it.

The problem frequently presented to the practitioner is one of *delayed puberty*. Since perfectly normal puberty often occurs as late as the age of 16 (even up to 20 occasionally), there is no clinical reason for treatment under that age, unless there is collateral evidence of testicular damage. If there are no signs of puberty at all over the age of 16, the patient should be further investigated. His lack of development may be caused by a *primary testicular* or a *primary pituitary* disorder. In the former case, injection of gonadotrophins (e.g. 'Pregnyl') will be totally useless since the testes cannot respond. In the latter case, the continued use of testosterone, though producing male development, may condemn the patient to lifelong sterility, since no stimulation of seminiferous tubules will occur.

Over the normal age of puberty, the long limbs of eunuchoidism together with lack of male secondary characters indicate a hypogonadal state which started *before* pubertal age. If, however, the gonadal disorder started *after* puberty had occurred, the only complaints may be of infertility and shrinkage of the testes, sometimes with gynaecomastia. In all cases the differentiation of primary testicular and pituitary disorder is essential. (In the latter, gynaecomastia is very unusual.)

All this really means is that the practitioner should be able to diagnose hypogonadism, but cannot be expected to treat it without further specialized investigation of the basic cause.

Mumps not infrequently attacks the testes, and may damage them very severely. Any male, therefore, who develops mumps orchitis should be treated with cortisone or an analogue, while it is reasonable to add testosterone (one injection of 'depo-testosterone', 100 mg.) if the patient is adolescent or adult.

2. UNDESCENDED TESTES

Here it is vital to ascertain whether the testes are simply retractile or truly abnormally placed or fixed. The testes of all male infants should be examined at birth, since a retractile testis may be felt then, but not again for many years. The differentiation of these two conditions is often very difficult and an experienced paediatrician, paediatric endocrinologist or paediatric surgeon should be consulted. The true mal-descended testis requires operation, while the retractile testis will always descend later. Hormones are seldom indicated and certainly should not be used by the general practitioner.

* This is the last article in a series of 5 on endocrine disturbances by the same authors which have been appearing weekly.

3. GYNAECOMASTIA

This is quite common at puberty, and is often unilateral. It may not disappear on its own, and operation may be indicated if there is no regression after a year. Fat men develop 'pseudo-gynaecomastia' which is pure fat, and operation should not be recommended until general weight reduction has been achieved, when it may no longer be necessary. Other forms of gynaecomastia (except in the Bantu) are less common and need specialized investigation.

4. THE FAT BOY

Fat boys overeat, do not have delayed puberty, are not hypogonadal and suffer from no endocrine disorder. The disease is of the appetite, usually parentally induced. The apparently small penis becomes normal sized if the pubic fat is rolled back. The boys are often lazy and sleepy because of the soporific effect of too much food. This reduction in calorie expenditure itself induces further obesity. The patients need dieting (or, really, a more healthy diet), but it is usually more important to talk to the parents than to the children. You cannot expect to reduce a child's weight while the parents remain over 250 lb. apiece.

5. HYPERTHECOSIS OVARII

In this condition both ovaries are large and pearly white, with thick capsules, and contain multiple small cysts. This very common condition is found in combination with a variety of clinical phenomena.

1. The subject may be entirely normal gynaecologically.
2. There may be secondary amenorrhoea or oligomenorrhoea.
3. There may (less commonly) be menorrhagia.
4. The patient may be infertile.
5. There may also be hirsuties and obesity.
6. Sometimes real masculinization, with deepened voice, male hair distribution, powerful muscles and enlarged clitoris, develops.

There is much argument over the relation of the ovaries to the symptoms, but there is no doubt that the ovarian abnormality is common, particularly as a 'cause' of oligomenorrhoea with sterility. There is also no doubt that following wedge-resection of the ovaries many previously infertile women have conceived and their periods have become normal and regular. In these circumstances, and also in the true virilization group, it is important to be aware of the condition, and to resort to examination under anaesthesia or even to laparotomy if necessary for accurate diagnosis.

6. INTERSEX

No dissertation on the varieties of intersex will be attempted here. Intersex is, however, not uncommon (it has been reported to occur once in every 1,000 births) and the exact pathogenesis in every case must be worked out at an early age, if irremediable psychological harm is to be obviated. Consequently it behoves the practitioner or other person who delivers every baby to examine its genitalia carefully for any sign of intersexual development. Enlarged 'clitoris', hypospadias, non-descent of 'testes' in an apparent male may be as important as the obvious case in which there is a 'penis' with penile urethra together with a vagina.

Investigation of intersex may necessitate (1) the identification of the nuclear 'chromosomal' sex, (2) estimation of urinary 17 = ketosteroid output, (3) biopsy of any gonad, (4) visualization by opaque dye of the urinary and genital tracts, or (5) laparotomy.

It must be evident that, once again, the practitioner's role (and a very important one) lies in the recognition of an abnormality and in the referring of the patient for special investigation before he or she is 2 years old. The age of 2 is mentioned because it has been shown that over this age the child begins to develop an awareness of the sex in which it is being reared, and any subsequent change may result in very severe psychological distress.

7. OVARIAN AGENESIS (GONADAL DYSGENESIS)

We are beginning to think that 'ovarian agenesis' is the commonest cause of primary amenorrhoea. It is often, but not always, associated with shortness of stature and developmental anomalies such as webbing of the neck, a low nuchal hairline, or an asymmetrical face. Anyway it should be suspected in all cases of primary amenorrhoea, whatever the height or appearance of the patient.

The certain diagnosis, again, is a matter for the specialist. Most cases actually show *male* nuclear sex chromatin (i.e. the 'ovarian' agenesis in them is 'testicular' agenesis). Laparotomy may be necessary to establish the diagnosis.

This condition is important to recognize, because 'menstrual' bleeding, together with breast development and other advantages can be obtained from the long-continued cyclical use of oestrogens. Furthermore it is necessary to inform the patient that she can never become pregnant.