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Hormonal development therapy (HDT) in hypogonadism in long-term view

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Since the 1960s, oestrogen deficiency in hypogonadism in girls has been successfully treated by a sort of analogous application of the menopausal hormone replacement therapy (HRT) scheme, here however, to induce and support sexual development in puberty and adolescence. The essential distinction between goals, ways and means of the two distinct hormonal treatments caused by menopause and by hypogonadism in puberty also suggests that the latter treatment is more characteristic of defining hormonal development therapy (HDT). Moreover, specific HDT in hypogonadism is essential for longitudinal growth of girls, functions of female reproductive system, bone and lipid metabolism and the immune, central nervous and cardiovascular systems. By contrast, the aim of menopausal replacement therapy in elderly women is treating negative effects of physiological loss of oestrogens as hot flush, lacks of female well-being and osteoporosis, while in hypogonadal girls there is of course nothing that might be replaced eventually.

Especially in cases of absolute oestrogen deficiency, as in Turner syndrome and in other cases of premature ovarian failure, HDT has to be started at the age of expected puberty. An international consensus suggests possibly lifelong HDT for the lasting support of female development and functions. However, neither reliable studies about possible risks and side effects of continuous hormonal therapy in adult women with hypogonadismus nor a more precise consensus have emerged yet. Emphasising the term HDT particularly aims at putting more effort in getting over these paucities simultaneously.

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Indications, hormonal therapy, dosage, application and timing in puberty are described in this article. Aspects of long-term hormonal treatment are critically discussed.

Oestrogens play a major role in pubertal development and function of the female reproductive system. They also have a profound effect on bone, longitudinal growth and lipid metabolism. Furthermore, oestrogens modulate immune functions, the central nervous system and the cardiovascular system (Table 1).

The essential distinction between hormonal development therapy (HDT) in puberty and hormone replacement therapy (HRT) in menopause

There are two important as well as completely different aims of therapeutic application of oestrogens or progestins in girls and in elderly women (Fig. 1).

On the one hand, oestrogens and progestins in girls are indicated for induction and lasting support of the sexual maturation process in cases of hypogonadism or hormone deficiency due to disturbances of the hormonal axis in puberty.

On the other hand, oestrogens and progestins are also indicated in menopausal women for hormonal maintenance and protective level by physiologic hormonal loss of own hormone production, which is often accompanied by osteoporosis and disturbances of female well-being in elderly women.

Thus, the aims of HDT and the well-known HRT should be clearly distinguished.[1] HDT should be customised to the individual and might require different application of oestrogens and/or gestagens due to the actual stage of sexual development. Moreover, the duration of hormone application for lasting support is supposed to be lifelong. However, there is a large paucity of knowledge about the long-term use of real HDT; hence, there is not much information to be found among all publications about HRT for elderly women particularly. Moreover, mothers of girls with hypogonadism are often misinformed and confused by the media about the risks of HDT and are therefore worried about the prospect of 'HDT treatment' in their daughters. Furthermore, it is often difficult for doctors to find adequate hormonal dosage for hypogonadism in girls among all replacement recommendations.

Indications of HDT

HDT is indicated in girls with disorders of pubertal development, congenital anomalies or delayed puberty with oestrogen deficiency and in girls with physiological instability of hormonal axis caused by progesterone deficiency.

It has to be distinguished between absolute and relative oestrogen deficiency.

Absolute deficiency is present in primary ovarian insufficiency due to gonadal dysgenesis such as Turner syndrome (45,X0), ovarian dysgenesis (46,XX), Swyer syndrome (46,XY), autoimmune oopheritis, ovarian insufficiency due to chemotherapy or radiation therapy of childhood malignancies, complete androgen insensitivity syndrome (CAIS) and in other 46,XY disorders of sex development with decision for the female sex after gonadectomy, FMR1 premutations, autosomal disorders,

Table 1
Why to treat estrogen deficiency in hypogonadism in girls in long-term view of HDT.

- to start puberty by inducing sex chracteristics
- to enhance normal growth and to facilitate pubertal growth spurt
- to support normal bone maturation and maintain normal bone mineral density
- to induce and maintain normal menstruation
- to maintain normal brain cell growth
- to support female's psycho-sexual well being