Endocrine disease of the gonads

Primary Testicular Disorders

Clinical manifestations of testicular dysfunction and their examination

- Manifestations of prepubertal androgen deficiencies: lack of development of secondary sexual characteristics, development of eunuchoid skeletal proportions, penis and testes remain small, typical scrotal folds do not develop, voice remains high, musculature does not fully develop, impotence disorder and infertility.
- Manifestations in post-pubertal androgen deficits: decrease in libido, potency and infertility, slows down beard growth, development of osteopenia and osteoporosis .

***Laboratory examination*:** basic determination of hormones – testosterone, FSH, LH, prolactin, estradiol, free testosterone, dihydrotestosterone, SHBC, hCG.

Dynamic tests:

- Stimulation test with hCG – administered 3 days in a row after 3000 jim → stimulation of synthesis and secretion of steroids by Leydig cells → with a two-fold increase in plasma testosterone there is a normal response.
- Test with GnRH - 0.1mg of GnRH is administered i.v. → 2–5× rise in LH and double rise in FSH.

Bilateral Anarchy

- occurs in approximately 1 in 20,000 men,
- **the disappearance of the testicles during the development of the fetus**,
- testosterone level, ↑ gonadotropin.


Anorchia

therapy:

- long-term androgen replacement,
- implantation of testicular prostheses.

Cryptorchidism

- **testicular dystopia** (retention of the testes in the descent path, 77%) with **ectopia** (outside the normal descent path, 23%);

complication:

- torsion,
- trauma,
- the development of a malignant tumor of the testicle (about 20-30x higher incidence than in healthy men) - untreated can be the cause of infertility;

therapy - as soon as possible:

- hormonal – intramuscular human chorionic gonadotropin (hCG), or intranasal treatment with gonadotropin hormone (GnRH),
- surgical - recommended between 12.-18. month of age.

Klinefelter syndrome (47,XXY)

🔎 *For more information see Klinefelter Syndrome.*

- the most common cause of male hypogonadism,
- the classic karyotype is 47,XXY, but there are other variants 48,XXXY, 49,XXXXY, 48,XXYY, possibly mosaic 47,XXY/46,XY;

symptoms:

- manifestation usually during puberty,
- eunuchoid habitus,
- development of gynecomastia in puberty,
- small testicles with azoospermia, infertility, decreased libido,
- sparse pubic and axillary hair,
- long-term → development of osteopenia,
- 20 times higher incidence of breast cancer compared to healthy men;

therapy:

- androgen substitution: most recently – transdermal patches,
- infertility treatment within assisted reproduction methods.

Failure of seminiferous tubule function in adulthood

Etiology:

- inflammation as complications of mumps, gonococcal, irradiation, uremia, alcoholism, narcotics, paraplegia, lead poisoning, chemotherapy, varicocele;
- idiopathic

symptoms:

- infertility,
- with more severe damage, testicular atrophy with androgen deficiency;

diagnosis:

- oligospermia to azoospermia,
- hormones usually normal,

therapy:

- removing the cause,
- in hypogonadism, androgen replacement therapy.

Decline of Leydig cell function in adulthood and old age – climacterium virile

- gradual **decline in gonadal function** during aging → decline in libido, potency, emotional lability.

Central (hypothalamic–pituitary) causes of testicular dysfunction

Hypogonadotropic hypogonadism

- it is caused by a disorder in the secretion of gonadotropins both at the level of the pituitary gland and in the hypothalamus or higher centers of the brain,
- **isolated LH** luteotropic hormone **deficiency** (Pasqualini syndrome, fertile eunuchoidism) – secretion of LH and testosterone is affected,
- part of a disorder of the secretion of multiple pituitary hormones,

symptoms: depends on whether it develops pre- or post-puberty, ***diagnosis***:

- LH, FSH (follicle-stimulating hormone),
- with GnRH stimulation in the case of a hypothalamic lesion, there will be LH and FSH (in contrast to a pituitary lesion),

therapy:

- application of FSH, LH,
- in hypothalamic disorders of GnRH application.

Hyperprolactinemia

- is the cause of infertility in about 4% of infertile men,

symptoms:

- loss of libido and potency,
- reduced ejaculate volume, oligospermia,
- rarely gynecomastia, galactorrhea,

diagnosis:

- ↑ prolactin, ↓ testosterone,
- LH and FSH reduced or within the norm,

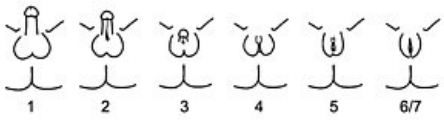
therapy:

- dopaminergic agonists,
- possibly substitution of androgens or gonadotropins (to achieve fertility).

Androgen effect disorders

- can be at any stage of androgen action on target tissues → lead to male pseudohermaphroditism.

Complete androgen insensitivity syndrome (testicular feminization syndrome)



Grades of androgen insensitivity syndrome

- disorder at **the androgen receptor** level,

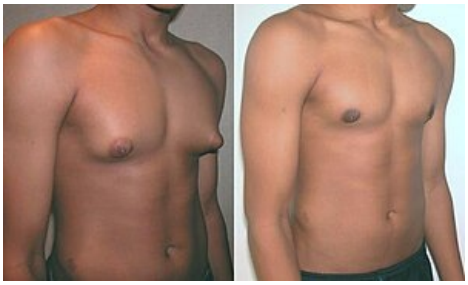
***symptoms*:**

- karyotype **46,XY**, female phenotype,
- blind ended sheath,
- ectopically located testicles,
- primary amenorrhea,
- axillary or pubic hair is sparse or completely absent.

Incomplete forms of androgen insensitivity

- patients with **testicular feminization** to **normal men** with evidence of hypogonadism and spermiogenesis disorders.

Gynecomastia



Gynecomastia is an enlargement of the mammary gland in men. We distinguish:

1. *True gynecomastia* - proliferation of the mammary gland;
2. *Pseudogynecomastia* – increased fat deposition in the breast area;

- the cause is an absolute or relative **increase in estrogen** concentration.

Physiological

- in newborns;
- in puberty;
- in men at the transition to senium.

Pathologically:

- certain estrogen-producing tumors of the testicles or kidneys;
- cirrhosis;
- thyrotoxicosis;
- drugs (spironolactone, cimetidine, psychotropic drugs);
- gynecomastia occurs in 56–88% of Klinefelter syndrome cases.

Therapy:

- elimination of the underlying cause;
- in pubertal gynecomastia – androgens, antiestrogens (*Tamoxifen*);
- surgical therapy.

The course of surgical removal

Gynecomastia in men can also be removed surgically by performing plastic surgery, where an incision is made around the areola. This operation takes place under general anesthesia

Primary ovarian disorders

- *manifestation of disorders of the endocrine function of the ovaries*

1. manifestation of premature and delayed secretion of estrogens,
2. estrogen deficiency → in the long term leads to osteoporosis, acceleration of atherosclerosis, atrophy of the lower urogenital tract with infections and dysfunction, skin atrophy, alopecia and hirsutism, psychological changes, vasomotor climacteric symptoms – hot flushes, sweating, flushing,
3. menstrual cycle disorders in adult women and infertility,
4. excessive secretion of androgens → emergence of hirsutism, acne, alopecia, cycle disorders.

Turner syndrome

- **karyotype 45,X**, structural chromosomal aberrations of chromosome X or chromosomal mosaic with line 45,X are also possible

symptoms:

- absence of puberty, small height (average final height is 143 cm),
- skin fold on the neck – pterygium coli,
- micrognathia,

- lymphedema of hands and feet after birth,
- kidney abnormalities,
- coarctation of the aorta,
- arterial hypertension,
- pigment nevi,

biochemistry:

- ↓ estradiol, ↑ gonadotropins,

therapy:

- affecting final height (growth hormone),
- hormone replacement (estrogens + progestogens).

Premature ovarian failure

- **cessation of ovarian function in women of reproductive age**,

Etiology:

- antibodies against ovaries – possible autoimmune etiology,

therapy:

- substitution of estrogens + progestogens.

Central ovarian disorders

Hypogonadotropic hypogonadism

- in an isolated disorder before puberty, puberty does not develop - symptoms:

  have ↓ gonadotropins and estradiol,
  normal height

- disorder in adulthood - symptoms:

  secondary oligomenorrhea to amenorrhea,

therapy:

- *substitution of estrogens and progestogens:*

  there must be a combination – estrogens alone increase the incidence of endometrial cancer (estrogens alone only in women after hysterectomy),

  - cyclic application

    either we administer estrogens continuously and add progestogens for half the month; or we administer estrogens for 3 weeks → skip 1 week → then add progestogens for 10–12 days in the second half of the cycle,
    interruption of treatment → cyclic uterine bleeding,

  - continuous application

    permanent administration of estrogens and progestogens,
    continuous administration of gestagen gradually leads to atrophy of the endometrium, the woman stops bleeding after a certain period of time,

    - *FSH and LH gonadotropin substitution:*

      we apply to achieve follicle maturation, ovulation and pregnancy in central forms of hypogonadism,

    - *GnRH substitution:*

      ovulation and pregnancy can also be achieved in this way.

Hyperprolactinemia

1. **mild hypersecretion** – causes anovulation,
2. **higher hypersecretion** – oligomenorrhea to amenorrhea; may be accompanied by galactorrhea,

therapy:

- depends on etiology,
- dopaminergic agonists.

Ovarian dysfunction associated with androgen hypersecretion

Polycystic ovary syndrome (Stein-Leventhal syndrome)

symptoms:

- infertility, hirsutism and acne, anovulatory cycles, or oligomenorrhea to amenorrhea,
- obesity, insulin resistance, ↑ incidence of DM,
- hypertension,

***diagnosis*:**

- ↑↑ LH, ↑ androgens in serum or their metabolites in urine,
- enlarged, shiny, white, polycystic ovary with thickened tunica albuginea,

***therapy*:**

- to control ovulation: clomiphene citrate,
- treatment of hirsutism and acne.

Hirsutism

***symptoms*:**

- **increased growth** of pigmented **hair in women** in places where male hair typically occurs (cheeks, upper lip, chin, neck, chest, back, inner thighs),
- acne, oily skin,
- oligomenorrhea to amenorrhea,
- **virilization** - somatic changes: hair angles, rougher voice, breast atrophy, enlarged clitoris, male muscle formation,

causes of hirsutism :

- increased production of androgens in the ovaries or adrenal glands,

therapy:

- antiandrogens – block the effect of androgens on receptors (cyproterone acetate),
- contraceptives.

Links

Reference

1. VISOOTSAK, Jeannie and John M GRAHAM. Klinefelter syndrome and other sex chromosomal aneuploidies. *Orphanet J Rare Dis* [online] . 2006, vol. 1, p. 42, also available from < https://ojrd.biomedcentral.com/articles/10.1186/1750-1172-1-42 >. ISSN 1750-1172.
2. ↑ Breast enlargement in men is common. *Idnes* [online]. Prague, 2007 [cit. 2021-10-27]. Available from: https://www.idnes.cz/onadnes/zdravi/zvetseni-prsou-u-muzu-je-bezne.A070920_095937_zdravi_bad
3. ↑ Gynecomastia. *Medicom Clinic* [online]. [feeling. 2021-10-27]. Available from: https://www.medicomclinic.cz/gynekomastie (https://www.medicomclinic.cz/gynekomastie)

References

- MAREK, Josef – BRODANOVÁ, Marie. *Internal medicine Volume VI..* 2nd edition. Prague : Galen publishing house, 2002. 102 – 111 pp. pp. 266. ISBN 80-7262-169-6.
- KÁBRT, Jan – KÁBRT, Jan. *Lexicon medicum..* 2nd edition. Prague : Galén, 1995. pp. 791. ISBN 80-85824-10-8.