FERTILITY

Investigation of

MALE REPRODUCTIVE HORMONE DYSFUNCTIONS

from diagnosis,
the seeds of better health

BIOMÉRIEUX

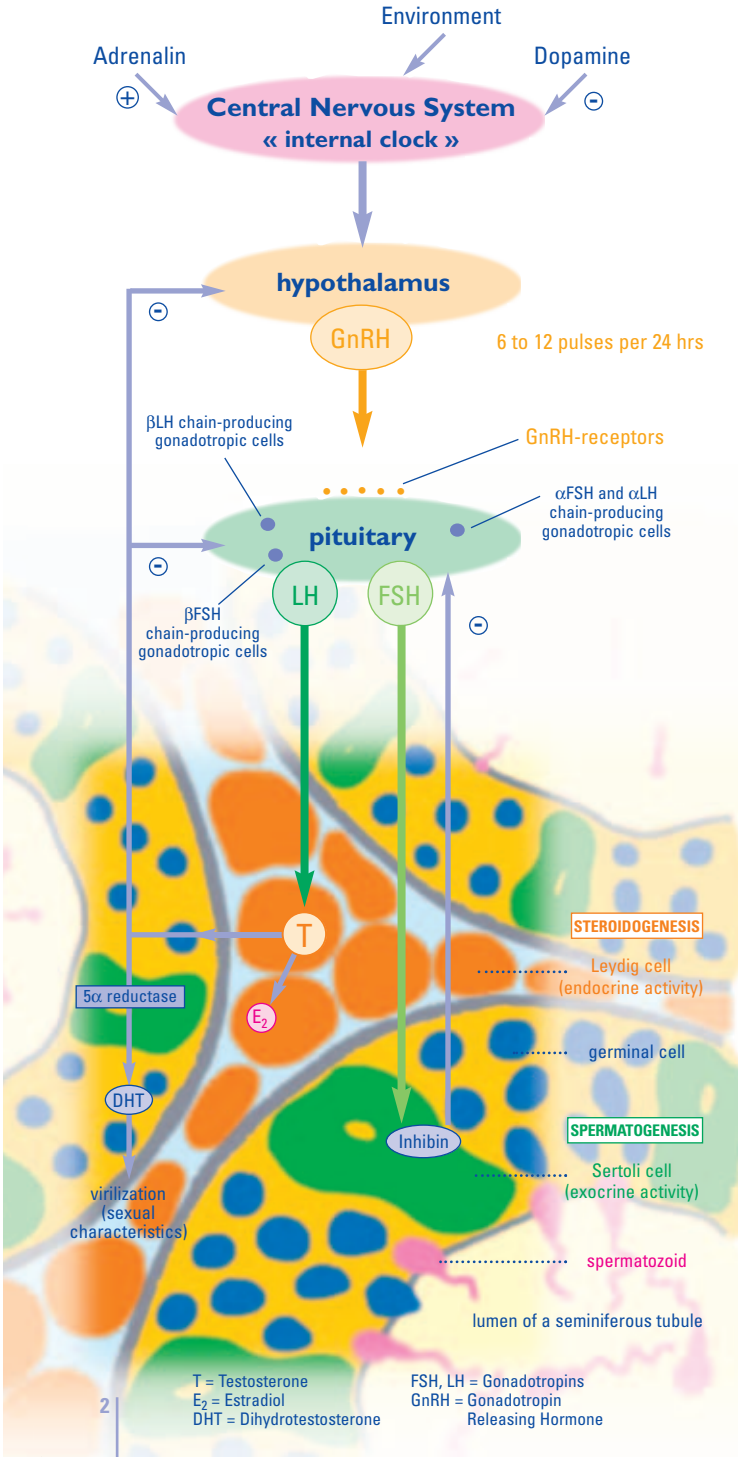
contents

The approach used for each of the subjects discussed in this booklet is identical :

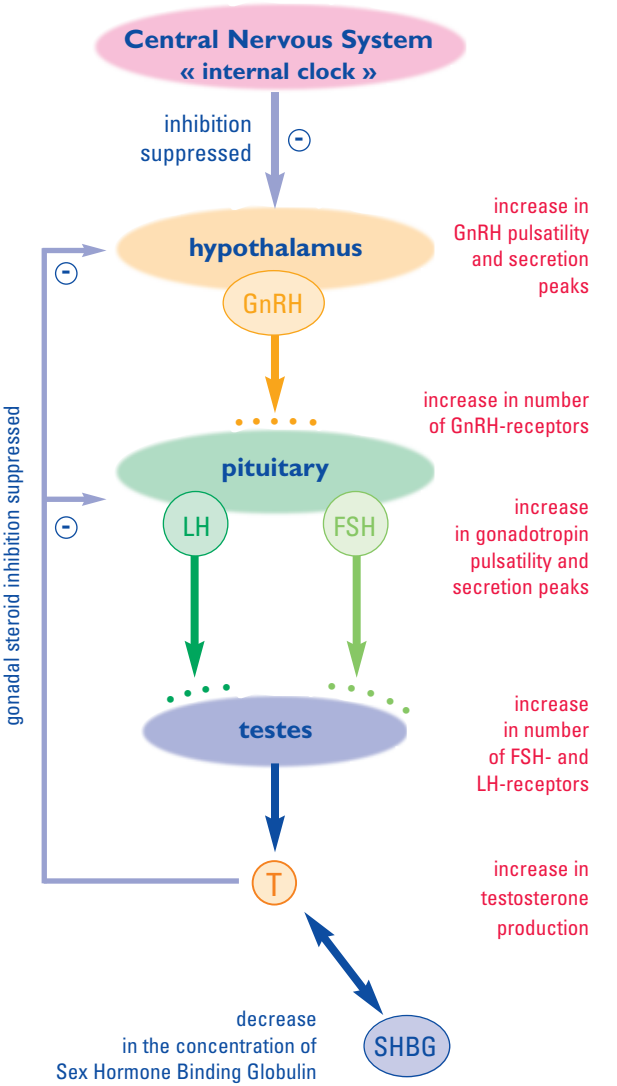
- brief physiological description
- clinical approach
- basic biological profile
- interpretation of results
- secondary tests, if required
- treatment

Dynamic tests and a list of the main hormone assays are given at the end of the booklet.

gonadotropic axis (adult)



gonadotropic axis (puberty)



Complete pubertal development takes 2 to 3 years.
It is preceded by an adrenal maturation phase (at the age of 7 or 8), known as the adrenarche, biochemically characterized by an increase in circulating DHEAS*.

* Dehydroepiandrosterone sulfate.

precocious puberty

Onset of puberty before the age of 9
(European population)

Clinical signs

Growth of pubic hair, and possible signs of gynecomastia.

Growth of testes and/or development of the penis and scrotum.

Initial profile

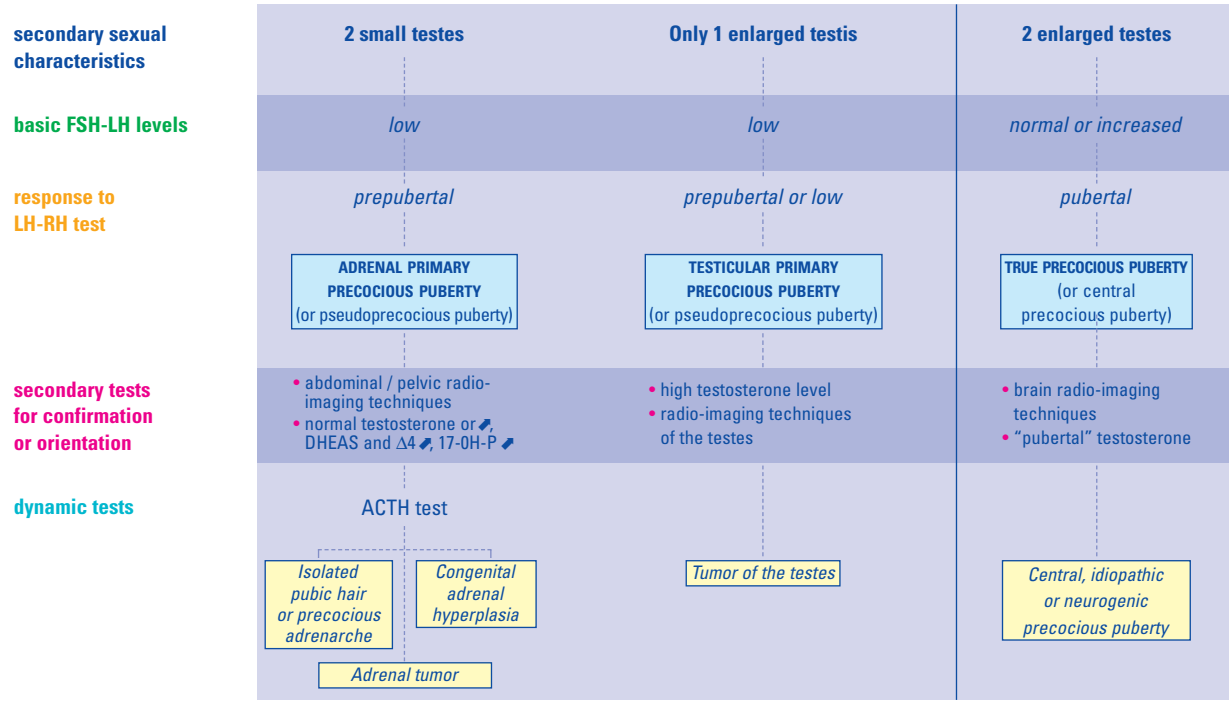
This profile aims to differentiate between :

- central precocious puberty.
- primary precocious puberty or pseudoprecocious puberty.

It comprizes :

- basic FSH and LH levels + LH-RH test (GnRH).
- Testosterone.
- DHEAS to evaluate adrenal maturation or adrenarche.
- evaluation of stature and bone age.

Interpretation of Results



Treatment

Treatment of the tumor, if required.
In cases of true central precocious puberty, pubertal development is halted by using an LH-RH agonist (an annual LH-RH test controls the degree of pituitary blockage).

Treatment of congenital adrenal hyperplasia.

delayed puberty

No signs of puberty after the age of 15
(European population)

Clinical signs

No growth of pubic hair, nor development of other secondary sexual characteristics.

Initial profile

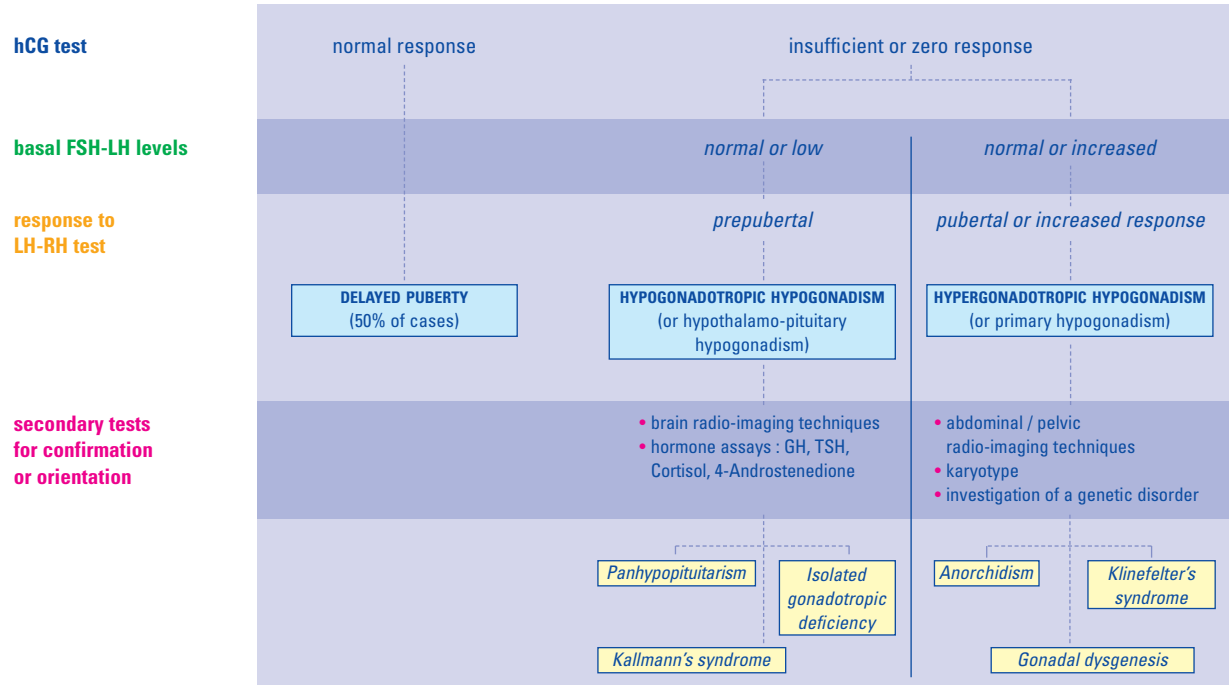
This profile aims to differentiate between :

- delayed puberty: hCG test.
- hypogonadotropic hypogonadism.
- hypergonadotropic hypogonadism.

It comprizes :

- an hCG test.
- basic FSH and LH levels + LH-RH test.
- Testosterone.
- DHEAS to evaluate adrenal maturation or adrenarche.
- evaluation of stature and bone age to orient a diagnosis of delayed puberty.

Interpretation of Results



Treatment

Substitutive (testosterone-based) for functional hypogonadotropic hypogonadism and some types of hypergonadotropic hypogonadism.

Clinical signs

- decreased libido
- sexual indifference
- impotence
- physical fatigue
- reduced muscle mass
- reduced testicular volume

Initial profile

Testosterone, FSH, LH, Prolactin, Inhibin B

Interpretation of Results

testosterone ↘↘ to ↘↘↘
(for info : Reference values = 3 to 12 ng/ml)

inhibin B ↘ to ↘↘
FSH and **LH** are normal to ↘↘

Etiologies

SUPRASELLAR LESIONS

- Tumoral (CT scan + NMR)
  - craniopharyngioma, visual disorders and/or panhypopituitarism
  - germinoma, (hCG, AFP)
  - glioma of optic chiasm or hypothalamus
- Post-infectious
  - tuberculous meningitis or other microorganism
- Infiltration processes (NMR necessary)
  - histiocytosis
  - sarcoidosis
- Post radiotherapy
- Section of the pituitary stalk

PITUITARY ORIGIN

- Hemochromatosis
  - ferritin > 1000 µg/l
  - investigation of C282Y mutation
  - ▶ gonadotropic cells affected by Fe deposition
  - ▶ no GnRH stimulation
- Hyperprolactinemia
  Prolactin = strong antigonadotropic effect on the hypothalamus
  - ▶ Prolactin adenoma (80% of pituitary adenomas)
- Secreting or non-secreting pituitary adenomas

FUNCTIONAL DEFICIENCIES

- Anorexia (rare in males)
- Nutritional disorders : celiac disease due to gluten intolerance
- Hypercorticism, long-term corticosteroid therapy
- Hyperestrogenemia
  - estrogen treatment (transvestites)
  - estradiol-secreting tumor

secondary tests for confirmation or orientation

- radio-imaging techniques, GnRH test

Treatment

- Pulsatile GnRH pump (1 to 2 years), if positive test response
- Long-term IM administration of testosterone
- Specific according to etiology

Clinical signs

Unilateral or bilateral enlargement of the male breast (normally undeveloped)
- Newborn (due to placental estrogen)
- Puberty (60 % of adolescents aged between 12 and 15)
- Adult : frequent, often asymptomatic, increasing incidence with age, occasionally with breast deformation and tenderness.

Anamnesis :
- hyperthyroidism
- renal insufficiency (dialysis)
- hepatic insufficiency
- therapeutic drugs or non-therapeutic substances *
- libido
- galactorrhea

Initial profile

Biological :
Testosterone, Estradiol, hCG
Radiological :
mammography

hCG secretion may orient diagnosis towards a secreting chorionic carcinoma or neoplasia (e.g. lung).
Mammography should identify an increase in adipose tissue linked to obesity or breast cancer (rare).

Interpretation of Results

Testosterone	↗	↘	↘	N	N
Estradiol	N	N	↘	N	↗
FSH-LH	N	↗	↘	N	-
SHBG	-	-	-	↗	-
Prolactin	N	-	↗	-	-
	ANDROGEN RESISTANCE ▼ Testosterone-receptor deficiency ▼ *Reifenstein's syndrome*	PERIPHERAL HYPOGONADISM: *Primitive karyotype (Klinefelter's syndrome)*; *Secondary - viral orchitis - castration - sarcoidosis*	HYPOGONADOTROPIC HYPOGONADISM: *Pituitary adenoma - with PRL secretion (galactorrhea) - other*	*Cirrhosis (Hepatic insufficiency)*; *Renal insufficiency*; *Hyperthyroidism*	SECRETING ESTRADIOL TUMOR: • Ultrasonography of the testes → *Leydig cell tumor*; • Adrenal CT scan

N = reference value

* Therapeutic drugs responsible for gynecomastia
- Estrogens
- Androgens, anabolic steroids (peripheral aromatizations)
- Spironolactone
- Cimetidine
- hCG therapy
- Antiandrogenic drugs
- Digitalis
- Isoniazid
- Cytostatics and irradiation (testicular lesion)
- Hyperprolactinemia drugs
- Neuroleptics, tricyclical antidepressant drugs

* Non-therapeutic substances
- Cannabis (marijuana)
- Heroin
- Estrogen-rich hair lotions
- Partner's local estrogen therapy (« vacation gynecomastia »)

The diagnosis of azoospermia is based on the absence of spermatozoa.

Clinical signs

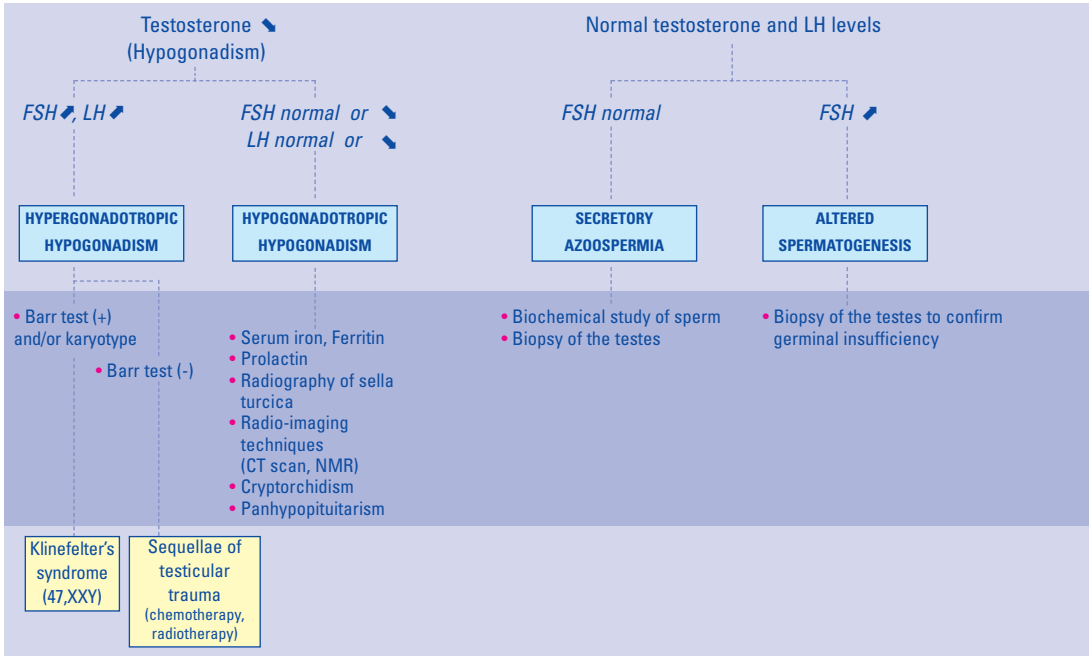
The clinical approach takes into consideration :

- the size and consistency of the testes
- the possible existence of gynecomastia
- hypoandrism
- mental retardation
- pubic and axillary hair and muscle mass
- size of penis (micropenis)

Initial profile

Involves FSH, LH and Testosterone

Interpretation of Results



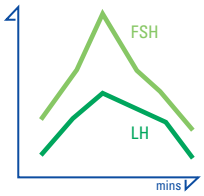
Reminder : characteristics of a normal spermogram (histological viewpoint)

- Ejaculate volume > 2.5 ml
- Number of spermatozoa : > 20 million/ml
- Percentage of motile spermatozoa after 4 hrs > 60 %
- Percentage of morphologically normal forms 40 - 70 %
- Percentage of living forms (vitality) 60 - 90 %

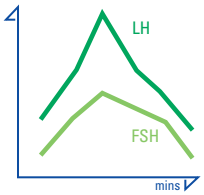
LH-RH (or GnRH) TEST

Intravenous injection at T_0 of 100 µg/m² (child)
or 100 µg (adult) of LH-RH

Assay of FSH or LH at T_{-15} , T_0 , T_{20} , T_{40} , T_{60} , T_{90} minutes



prepubertal type response



pubertal type response

hCG TEST

Intramuscular injection on D_1, D_3, and D_5 of 1500 IU of hCG,

Testosterone assay on D_1 and D_6 .

The testosterone level must be at least 3 ng/ml in prepubertal phase and may reach similar values to those of the adult (7 to 12 ng/ml) during puberty.

SYNACTHEN TEST (synthetic ACTH)

Intramuscular injection at T_0 of 0.25 mg of Synacthen (0.125 mg if ≤ 2 years old),

Assay of cortisol, 17-0H-progesterone, aldosterone, DHEAS, 4-Androstenedione at T_0, T_{30} and/or T_{60} minutes.

An objective normal response is obtained if there is an increase in cortisol and aldosterone (minimum factor 2) without any significant modification of the other parameters.

BLOOD HORMONE ASSAYS :

VIDAS hCG	**ref. 30 405**
VIDAS LH	**ref. 30 406**
VIDAS FSH	**ref. 30 407**
VIDAS Prolactin	**ref. 30 410**
VIDAS Progesterone	**ref. 30 409**
VIDAS Estradiol II	**ref. 30 431**
VIDAS Testosterone	**ref. 30 418**
VIDAS Cortisol	**ref. 30 417**
VIDIA hCG*	**ref. 38 300**
VIDIA LH*	**ref. 38 310**
VIDIA FSH*	**ref. 38 320**
VIDIA Prolactin*	**ref. 38 330**
VIDIA Progesterone*	**ref. 38 340**
VIDIA Estradiol*	**ref. 38 350**

Availability of some VIDAS tests may be restricted in certain countries due to registration requirements. Consult our local representatives for further information.
*In development.

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