Disorders of puberty.

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Puberty

Adrenarche:

Adrenal maturation

(DHEA, androstenedione)

- Pubic hair
- Oiliness of hair and skin
- Acne
- Axillary hair
- Body odour

Gonadarche:

Maturation of hypothalamic-pituitary- gonadal axis

- Enlargement of gonads
- Gonadal steroid secretion: E♀, T♂ secondary sex characteristics

Gonadotropin control

In females:

FSH- ovarian production of estrogens

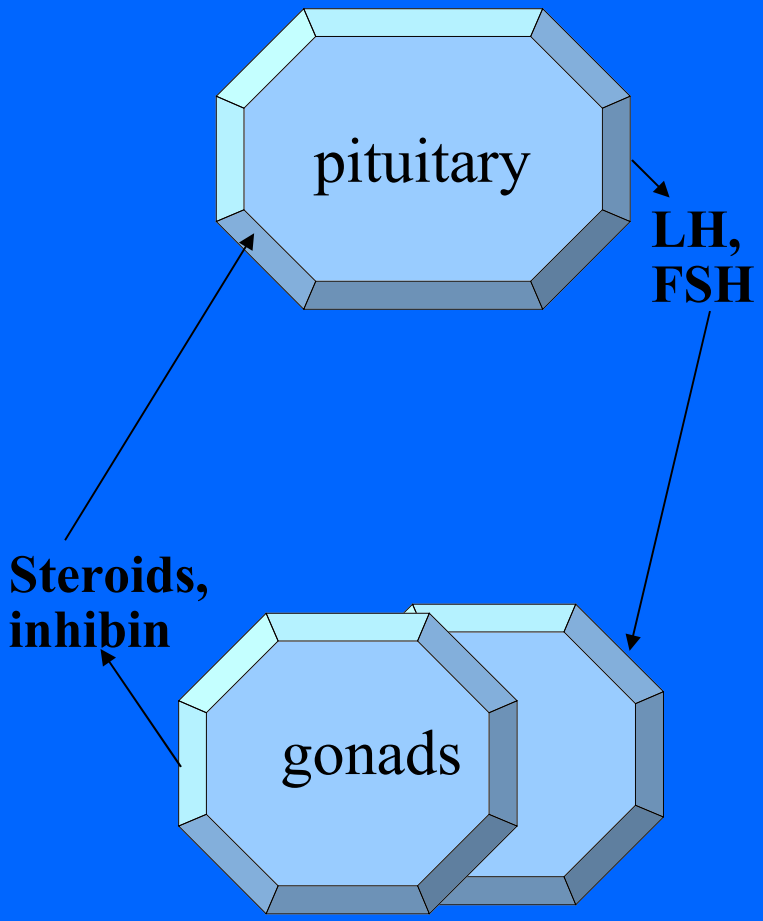
LH- formation and support of corpus luteum

In males:

LH- testosterone production in Leydig cells

FSH- stimulation of development and support of seminiferous tubules

pituitary- gonadal feetback



Normal puberty in girls

Start: after completion of 8 years- to the end of 13th year of life

First sign: breast development

Pubertal growth spurt: breast development -II in Tanner scale

Menarche: breast development - IV in Tanner scale

Normal puberty in boys

Start: after completion of 9 years- to the end of 14th year of life

First sign: testicular enlargement >4ml

Pubertal growth spurt:

by testicular volume 9ml

Marshall and Tanner scale
[B] breast development

B1- prepubertal

B2- breast bud stage- elevation of breast and papilla, enlargement of areolar diameter

B3- further enlargement, breast tissue around areolas

B4- areola and papilla form a secondary mound above the level of the breast

B5- mature stage; projection of papilla only

Marshall and Tanner scale
[G] male genital development

G1- prepubertal

G2- the scrotum and testes enlarged, change in the texture and some reddening of the scrotal skin

G3- the penis enlargement in length and some in breadth, further growth of testes and scrotum

G4- the penis enlargement in length and girth with development of glans

G5- genitalia adult in size and shape

Marshall and Tanner scale
[P] pubic hair development

P1- prepubertal

P2- long slightly pigmented, straight hair

P3- hair darker, coarser and curled

P4- hair adult in type, the area covered by it is still considerably smaller than in adults

P5- hair is adult in quantity and type

Delayed puberty

Lack of any signs of puberty at the age

> 13y. In girls

> 14y. In boys

The most common cause = constitutional delay in growth and adolescence.

- Delayed bone age
- Family history of delayed puberty
- Start of puberty by bone age

  11y in girls

  12 y in boys

- Other causes eliminated

Hypogonadotropic hypogonadism

Low levels of sex steroids without elevated gonadotropins at the age of puberty

= „secondary" hypogonadism

Causes of hypogonadotropic hypogonadism

Multihormonal hypopituitarism

- CNS disorders: tumours, congenital malformations, irradiation.

Isolated hypogonadotropism

- Kallmann's syndrome

Functional gonadotropin deficiency

- Malnutrition, hypothyroidism, diabetes mellitus, anorexia nervosa, exercise amenorrhea

CNS abnormalities

CNS tumours:

pituitary adenoma,

germinoma,

glioma,

prolactinoma,

craniopharyngioma

CNS abnormalities

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Craniopharyngioma

- Peak incidence in teenagers
- Symptoms of hypopituitarism (anterior and/or posterior)
- Calcifications inside tumour, erosion of sella turcica.
- Optic chiasm injury (hemianopsia, optic atrophy, blindness).

Germinoma

Hypothalamic and pineal tumours

Without calcifications

Production of chorionic gonadotropin in some cases (hCG)

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Kallmann's syndrome

Isolated gonadotropin deficiency with disorders of olfaction

Mutation in KAL gene (Xp22.3)

Heterogeneity of genetic and clinical picture:

Infertility, decreased sense of smell, eunuchoid body proportions, mirror hand movements, shortened 4th metacarpal bone, absent kidney.

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Hypergonadotropic hypogonadism

Elevated gonadotropins and low sex steroid levels

= primary gonadal failure

Hypergonadotropic hypogonadism

Elevated gonadotropins and low sex steroid levels (after normal time of puberty)

= primary gonadal failure

Gonadal failure

Gonadal dysgenesis

galactosemia

irradiation

chemotherapy

after surgical removal

The most common causes of gonadal failure

In girls-

Turner syndrome 1:2500 female births

In boys –

Klinefelter syndrome 1:500 male births

Turner syndrome

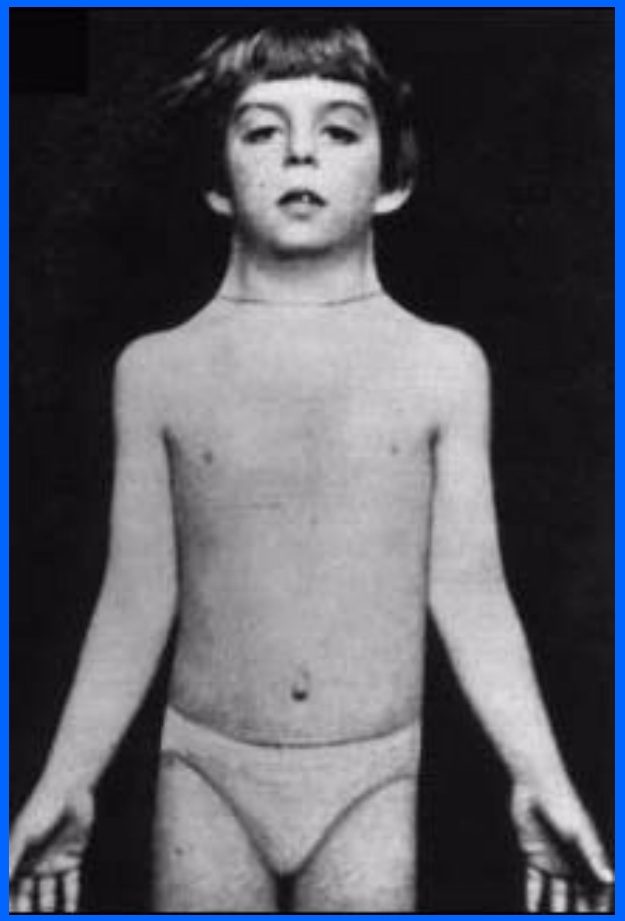
short stature; ovarian failure; webbed neck;

low posterior hairline;

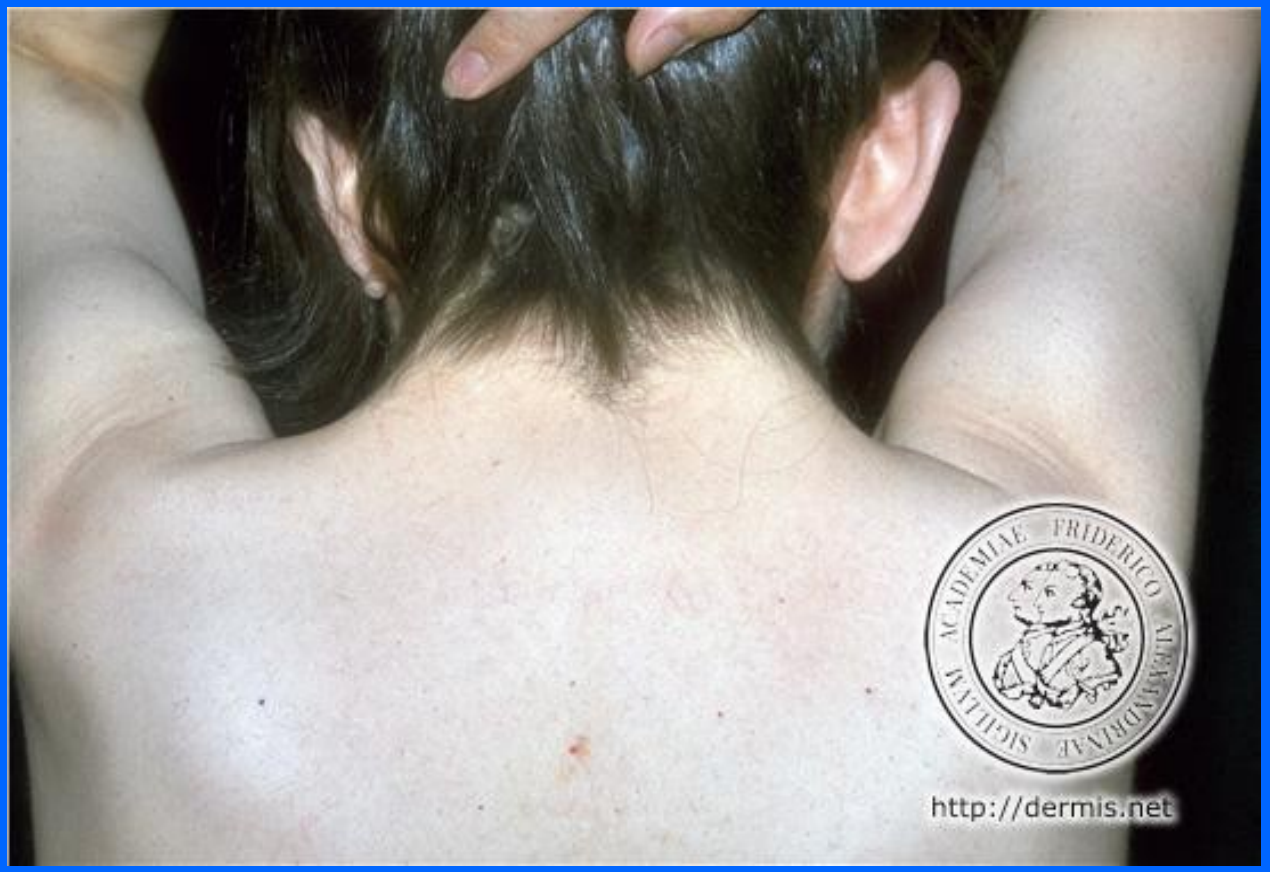
broad chest; lymphedema;

skeletal, cardiac,

and renal anomalies



low posterior hairline



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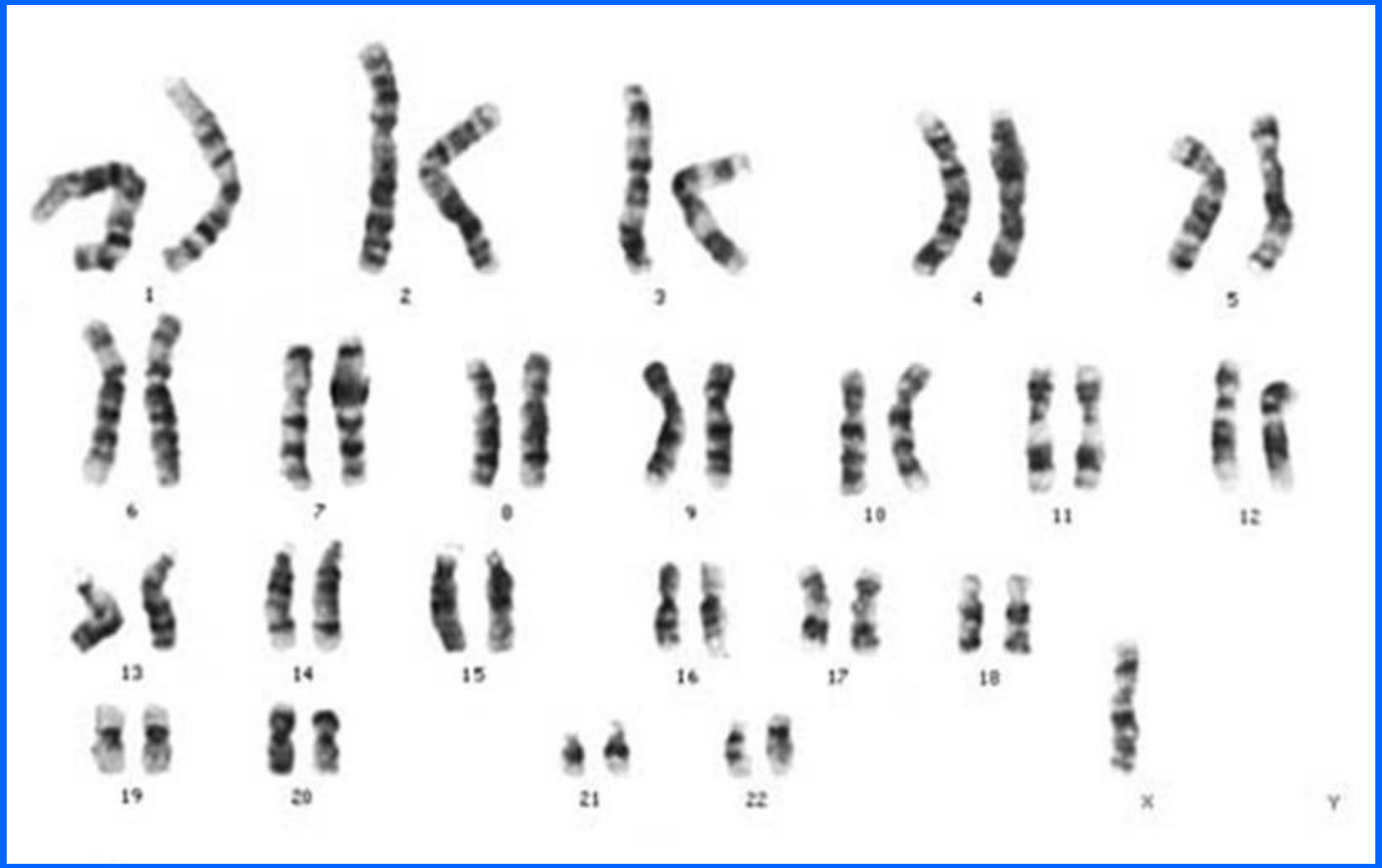


Klinefelter's syndrome

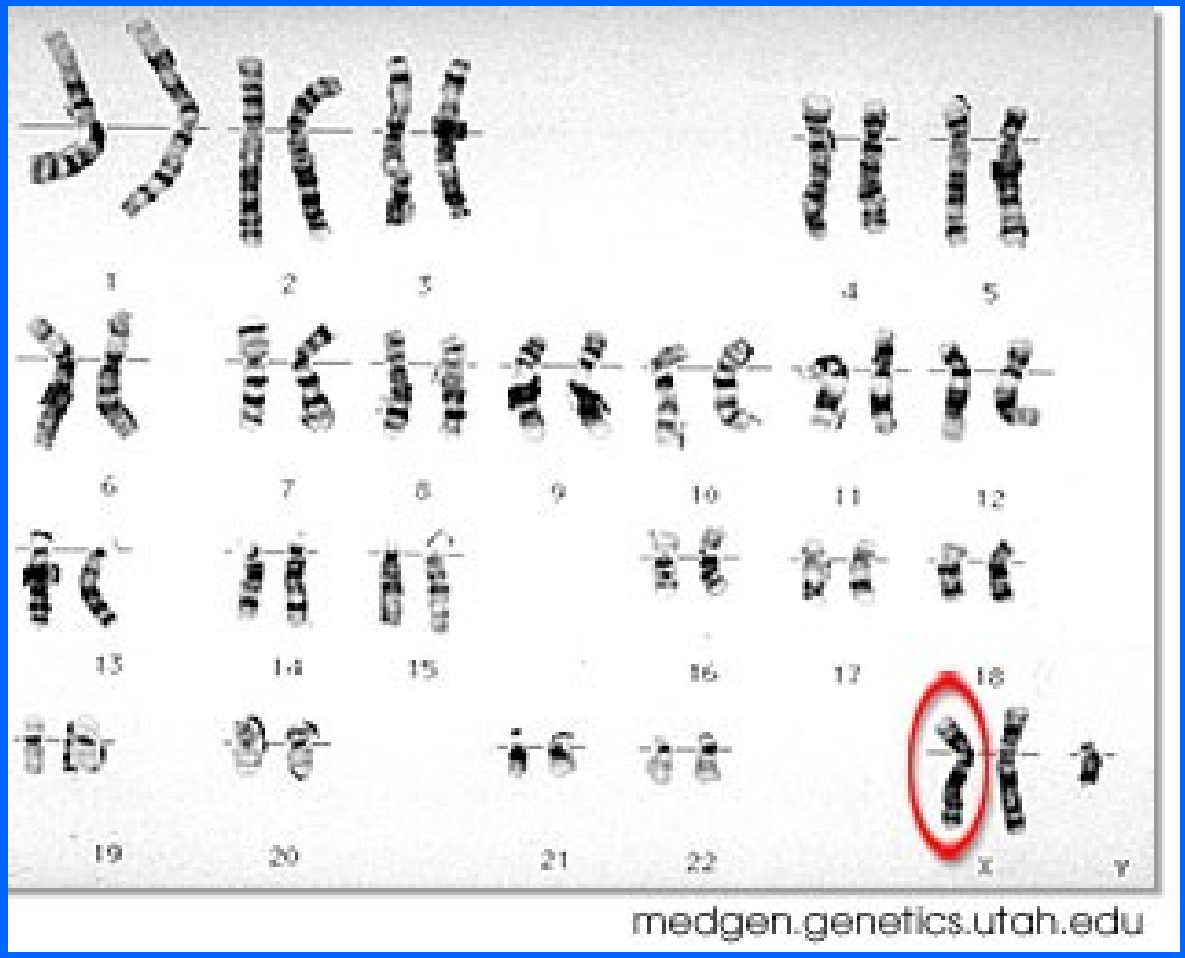
Seminiferous tubular dysgenesis

Karyotype 47 XXY or variants with more X or mosaics

FSH >>LH

Decreased testicular volume at puberty, tall stature, eunuchoid body proportions, arm span greater than height, gynecomastia.

Klinefelter's karyotype



Investigation in delayed puberty

Basal serum gonadotropin levels

Hypo-

Bone age

pelvic Usg

Hyper-

karyotype

pelvic Usg

Hormonal tests

Treatment

Replacement with sex steroids

In girls- increased doses of estradiol beginning from very low doses, when bleeding appears- whole cycle substitution.

In boys- testosterone intramuscularly or transdermally

Fertility

Patients with hypogonadotropic hypogonadism- gonadotropin therapy or pulsatile LH-RH therapy administered by a programmable pump.

Precocious puberty

Secondary sex characteristics before the age of:

8 years in girl

9 years in boys

Precocious puberty

Central;

Complete;

GnRH- dependent

Premature activation of Hypothalamo- pituitary -gonadal axis

Peripheral;

Incomplete;

GnRH- independent

Precocious puberty

Isosexual

Masculinisation in a boy

Feminisation in a girl

Heterosexual

Masculinisation in a girl

Feminisation in a boy

Central precocious puberty (CPP)

- Tall stature
- Advanced bone age
- Increased sex steroids
- Increased gonadotropin secretion
- Increased response of LH to GnRH

Time of appearance of CPP

A few months earlier-

probably constitutional, familial, obesity

Much earlier-

other forms of CPP

If no cause can be determined – idiopathic CPP.

Causes

Idiopathic CPP

CNS disorders:

Tumours (hamartomas)

Hydrocephalus

After meningitis, encephalitis

Suprasellar cysts,

After head trauma,

Irradiation

Causes

In girls- the most common cause idiopathic CPP

In boys- higher incidence of CNS disorders: tumours (hamartomas)

Hamartoma of tuber cinereum

Characteristic appearance on CT or MRI

A mass of GnRH secreting neurons –
as an ectopic hypothalamus

Hamartomas do not grow, but lead to the intracranial hypertension

Treatment: GnRH agonists, rarely surgery

Other CNS tumours

Optic or hypothalamus gliomas

Ependymomas

Treatment- radiotherapy

Additionally- GnRH agonists

GnRH independent PP

McCune -Albright syndrome

Adrenal carcinomas

Adrenal adenomas

In boys: familial GnRH independent PP with premature Leydig cell maturation

HCG secreting tumours (CNS, liver: hepatoblastoma)

Ovarian and testicular tumours

McCune -Albright syndrome (♀>♂)

Somatic mutation in the G protein intracellular signaling system (G-alpha subunit)

- Precocious gonadarche
- Bone disorder (polyostotic fibrous dysplasia)
- *Café au lait* spots
- Hyperthyroidism

Familial GnRH independent PP with premature Leydig cell maturation

A constitutive activation of the LH receptor

A continuous production and secretion of testosterone independently on the presence of LH or hCG.

Investigation

A physical examination (sex characteristics, testes volume, height and growth velocity).

Hormonal tests: T, E_2, DHEA, LH,

FSH,TSH.

GnRH test- answer of LH and FSH

CT or MRI of CNS, pelvic, testes USG

Treatment

In CPP –

long acting superactive analogues of GnRH.

In boys with testotoxicosis or McCune Albright sy- inhibitors of testosterone biosynthesis (ketoconazole), antiandrogens (spironolactone), or aromatase inhibitors (testolactone),

In girls with Mc Cune Albright sy- antiestrogens, tamoxifen.

In tumours - surgery

Isolated forms of pubertal precocity

Premature breast development – premature thelarche

Benign- between 6mths -3 yrs

No other signs

Diagnostics: USG, bone age, re-evaluation at intervals 6-12 mths

gynecomastia

Brest tissue in a boy.

Before puberty: exogenous source of oestrogens, tumours secreting oestrogens

Benign – at early puberty

But remember about Klinefelter sy.

Isolated premature adrenarche (pubarche)

Appearence of pubic hair before age 6-7 in girls and before 9 years in boys.

Benign- premature adrenarche (premature activation of DHEA secretion from adrenals)

High risk of malignancy, when other symptoms of virilisation: clitoral or penile enlargement,

advanced bone age,

Acne,

Rapid growth,

Voice change.

Pathological causes of virilisation

Adrenocortical carcinoma

Congenital adrenal hyperplasia

Virilising ovarian tumours

Diagnostics:

Bone age

DHEA

17 OH progesterone

Testosterone

ACTH

USG of adrenal glands and gonads (ovaries)