Determination Of Sex & Intersex

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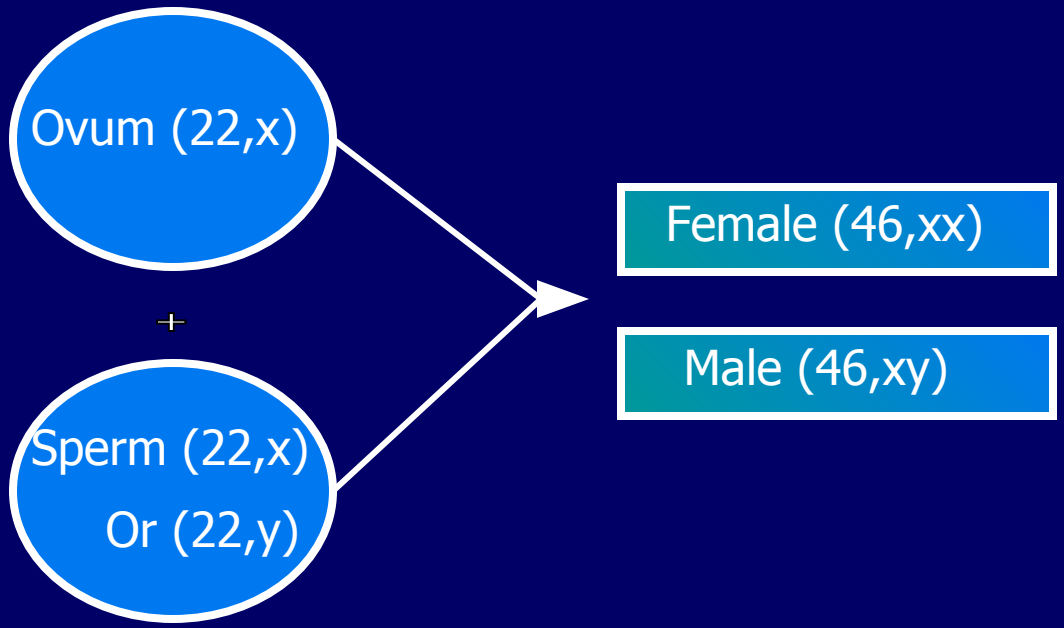
Determination Of Sex & Intersex

Normal sexual differentiation

:Chromosomal sex.1



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Normal sexual differentiation

:Gondal sex .2

- Gonds develop from the gondal ridge.
- Presence of (XY) sex chromosomes influence the gonads to develop into testes.
- Presence of (XX) sex chromosomes influence the gonads to develop into ovaries.

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Normal sexual differentiation

Internal Genital Sex .3

:External Genital Sex .4

- When the testes develop and function normally in the early fetus, the fetus will develop phenotypically into a male.
- If the testes are absent or not function the fetus will become phenotypically a female.
- The testes carry out their intrauterine function by producing two substances: testosterone and Mullarian inhibitory factor (MIF).

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Normal sexual differentiation

:In the normal female fetus

- Mullerian ducts will develop into the uterus, tubes & upper two thirds of the vagina.
- Cloaca will form the external genitalia and lower part of vagina.

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Normal sexual differentiation

In the normal male fetus:

- Mullerian ducts will regress.
- Wolffian ducts will develop into Vas deferens, Seminal vesicles, and epididymis.
- The cloaca will musculinize to form male external genitalia.

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Normal sexual differentiation

- If the gonads are removed before the stage of gonadal differentiation, and irrespective of chromosomal sex, development will be into female.
- Male development depends on the presence of functioning testes.
- Male external genitalia differentiation is mediated through the action of fetal testosterone.

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Normal sexual differentiation

5.Sex Of Rearing:

Is determined from simple inspection of the external genitalia at birth.

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Abnormal sexual differentiation

Intersexuality may occur because of:

1. Abnormality in sex chromosomes.
2. Gonadal defects.
3. End organ resistance.
4. Deficiency in the production of Mullerian Inhibitory Factor.
5. Abnormal hormonal stimulus in utero.
6. True hermaphroditism.
7. Rarely, in a genetic female, genes (capable of producing the H-Y antigen) may be found on an autosome, leading to the condition known as the 46, XX male.
8. Behavioral intersex.

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Definition of intersex

An intersex is an individual where there is conflict at any level between chromosomal sex, gonadal sex, internal genital sex, external genital sex or the sex of rearing.

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Types Of Intersex

1. At the chromosomal level:

- Sex chromosome deletion.
- Sex chromosome addition.

a. Turner Syndrome Features:

- Short stature.
- Sexual infantilism.
- Cubitus vulgus.
- Webbing of the neck.

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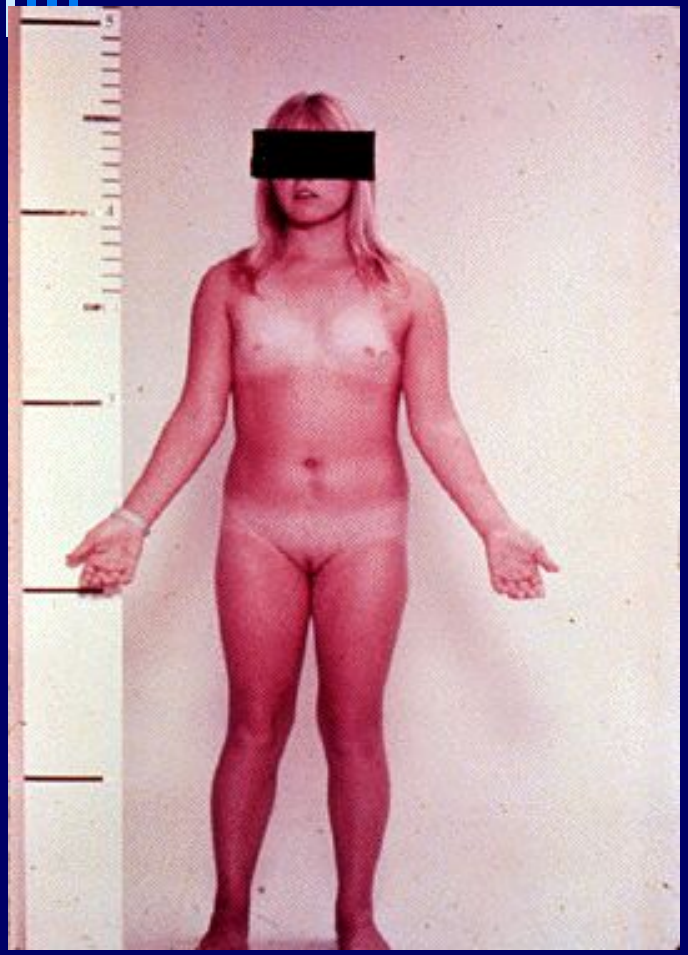
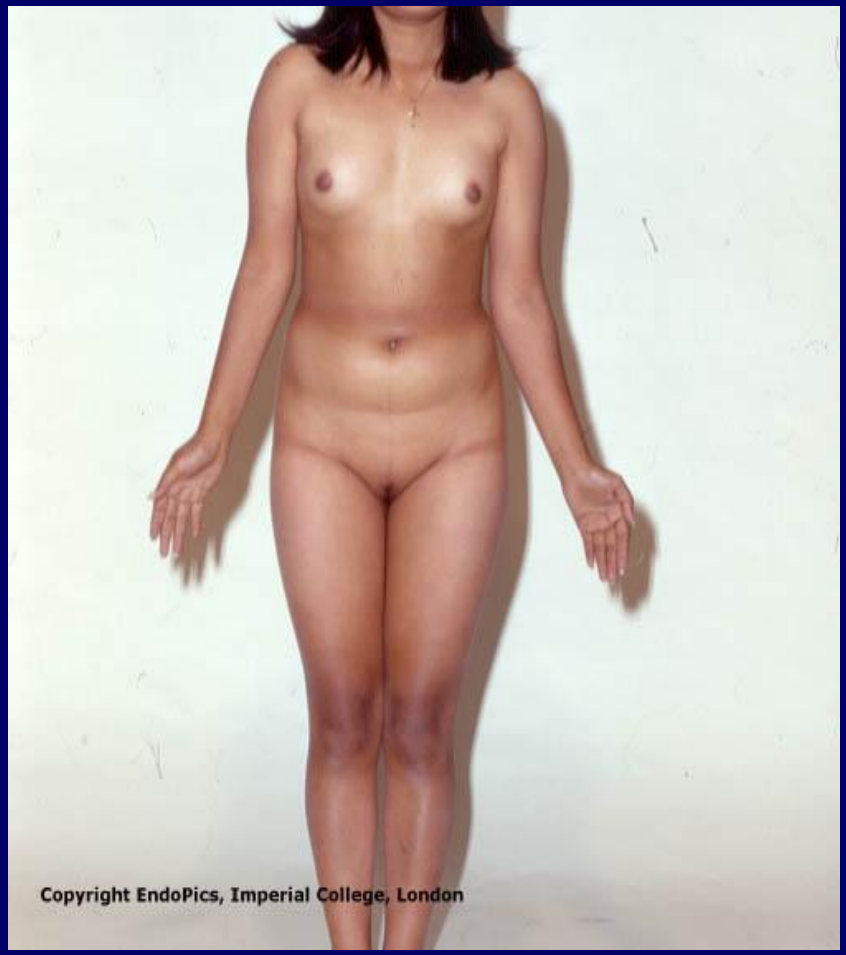
Turner Syndrome Features:

- Widely spaced nipples.
- Congenital cardiac defects.
- Karyotype 45, XO.
- Others mosaics 45, XO/ 46, XX.
- Some have partial deletion of the second X chromosome.
- No gonads are present (instead, streaks of fibrous tissue).
- Primary Amenorrhoea.

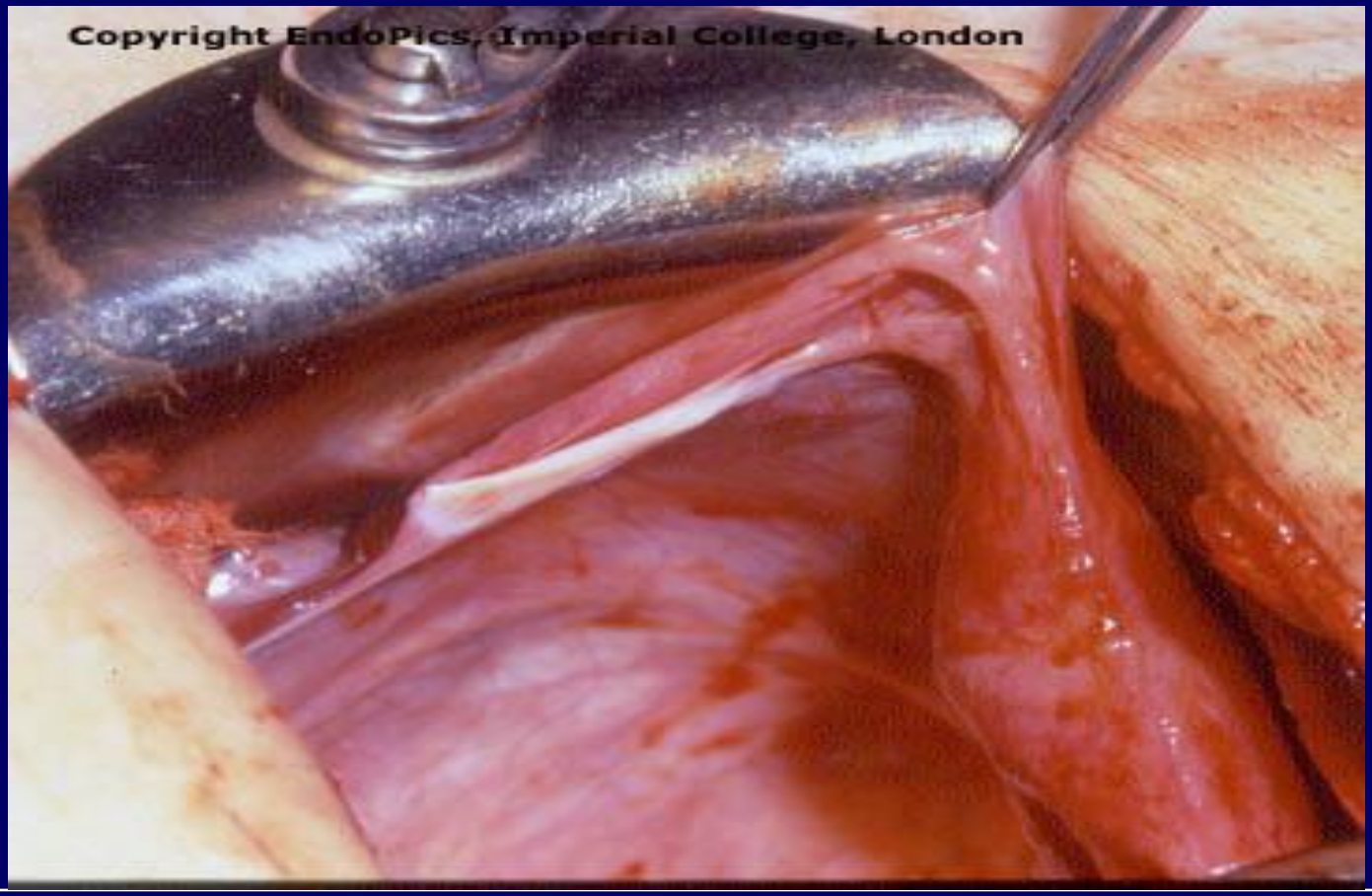
Turner's syndrome





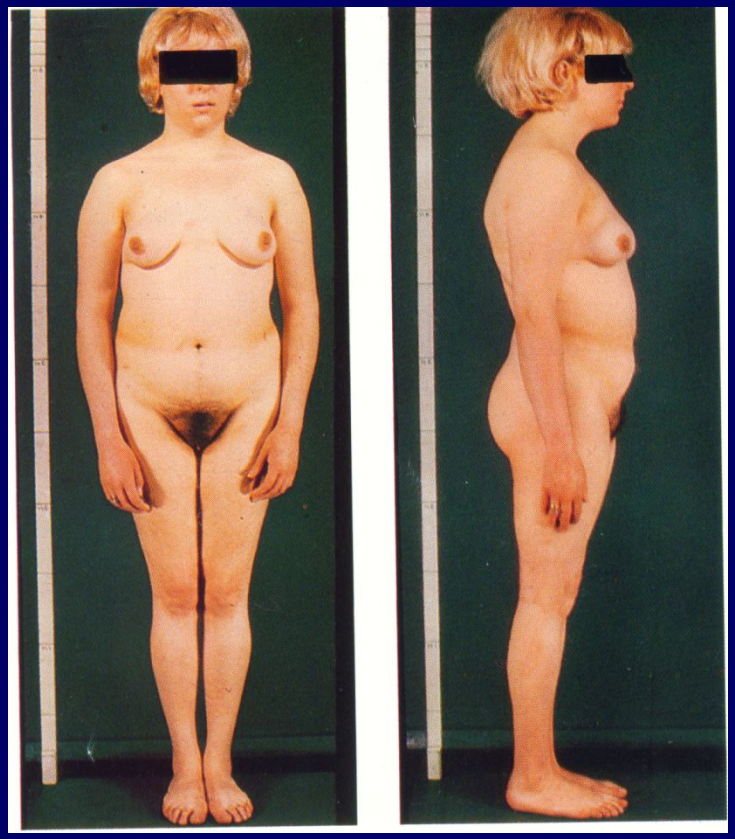
(Classic 45-XO) Mosaic (46-XX / 45-XO)

Ovarian dysgenesis



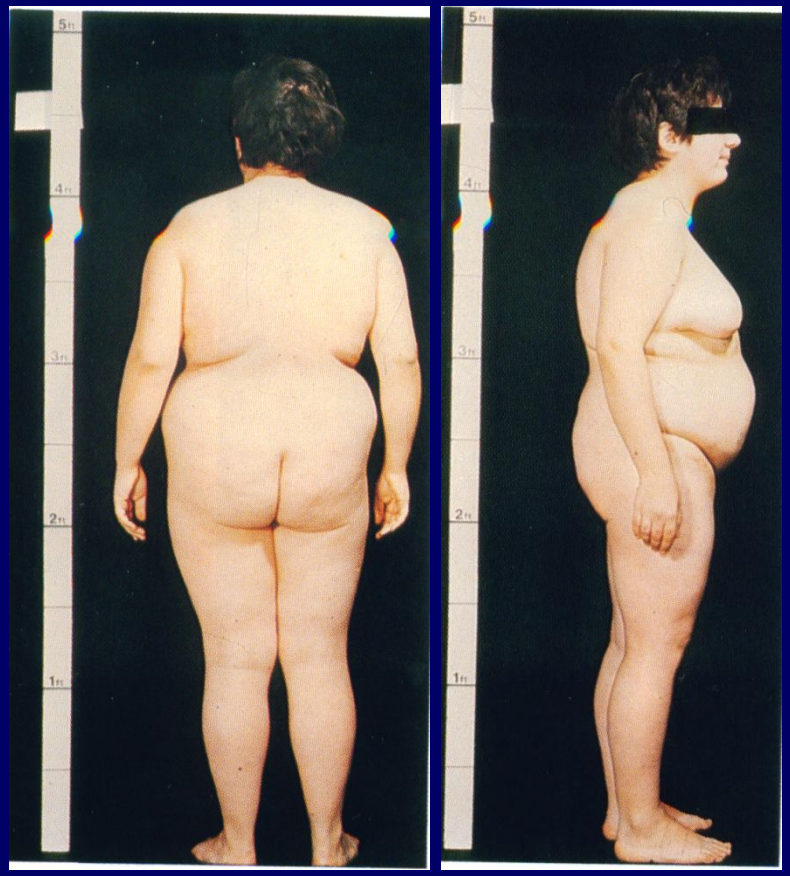
Atypical Turner's syndrome

This patient was 162.6 cm In height. One of the most common forms of mosaicism in Turner's syndrome is sex chromatin positive gonadal dysgenesis (XO/XX mosaic). This was the reason for this patient's gonadal dysgenesis. The secondary sex characteristics were reasonably well developed despite here prime symptoms of amenorrhoea and infertility.



Turner's syndrome

Despite the Cushing – like appearance , this patient is a typical Turner's syndrome (45 chromosome XO).



Gonadal dysgenesis

	Classic Turner's	Turner Variant	True gonadal Dysgenesis	Mixed Dysgenesis
phenotype	Female	Female	Female	Ambiguous
Gonad	Streak	Streak	Streak	Streak - Testes -
Hight	Short	Short - Normal -	Tall	Short
Somatic stigmata	Classical	±	Nil	±
karyotype	XO	XX/XO or abnormal X	XX(Pure)-46 XY (Swyer)-46	XO/XY

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b. Tripple X female:

- Rare.
- Patients may have amenorrhoea.
- Mental retardation is common.
- 2 Barr bodies are seen in buccal smear.
- Karyotype 47XXX.

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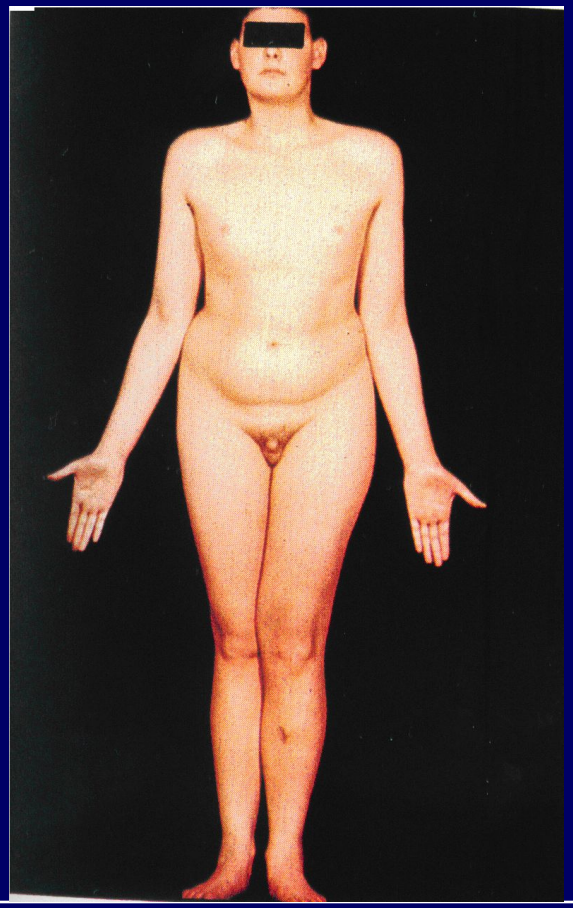
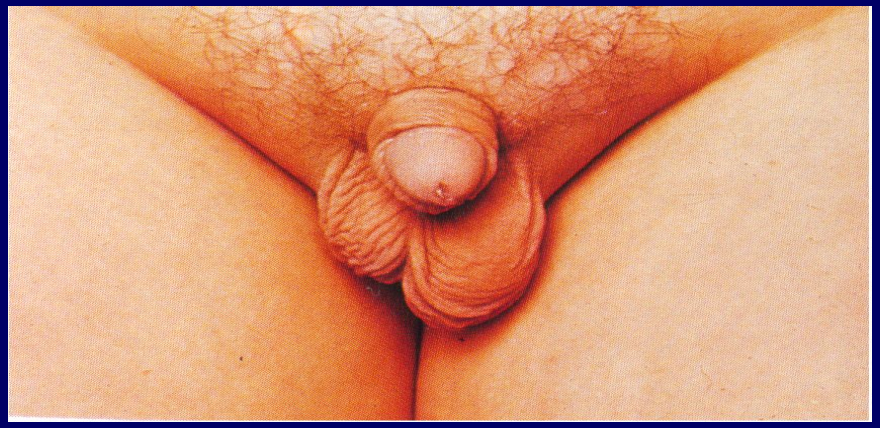
c. Klinefelter's Syndrome :

- Karyotype 47XXY.
- Arophy of seminiferous tubules.
- Azospermia.
- Gynaecomastia.
- Mental retardation is common.

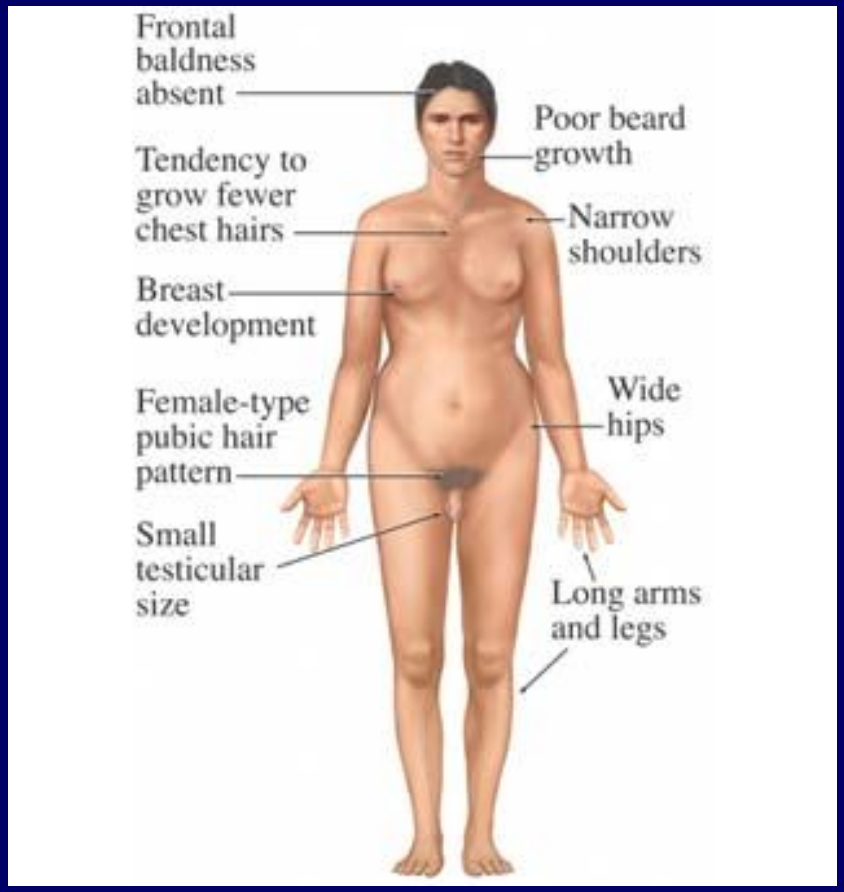
Klinefelter's syndrome





The typical picture of a tall, eunuchoid individual with poor development of the genitalia. The testes descended and are small, the right is extremely small, the left is less than a third of the normal size.

Klinefelter's syndrome



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2.At the gonadal level

True Hermaphroditism:

- Essential diagnostic criteria are presence of true testicular tissue and true ovarian tissue.
- External genital sex and Internal genital sex, Vary widely.
- Internal genital organs may be Uterus, Testes, Ovaries.
- External genital organs may be male or female.
- Karyotype: Variable 46,XX ; Mosaics 46,XY /47,XXY ; rarely 46,XY.

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3. End organ resistance:

Testicular feminization:

- Most cases present at puberty.
- Karyotype 46,XY.
- Females of normal height.
- Have well developed breasts.
- Have scanty or absent axillary and pubic hair.
- Female external genitalia.
- Vagina is short and blind.
- No uterus, no tubes.

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Testicular feminization:

- Bilateral testes may be present in the inguinal canal.
- Buccal smear : chromatin negative.
- The condition may be familial.
- Testosterone level is normal male level.
- Actiology is due to deficiency of androgen receptors in the target organs due to absence of the gene for the androgen receptor.

Androgen insensitivity

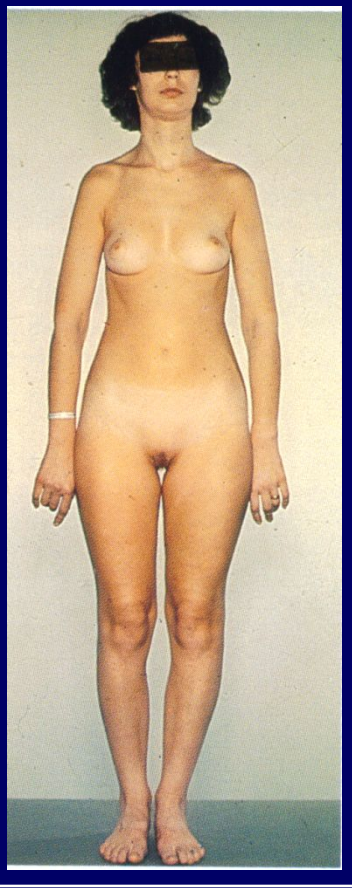
Testicular feminization syndrome

- X-linked trait
- Absent cytosol receptors
- Normal breasts but no sexual hair
- Normal looking female external genitalia
- Absent uterus and upper vagina
- Karyotype 46, XY
- Male range testosterone level
- Treatment : gonadectomy after puberty + HRT
- Vaginal creation (dilatation *VS* ? Vaginoplasty)

Testicular feminization syndrome

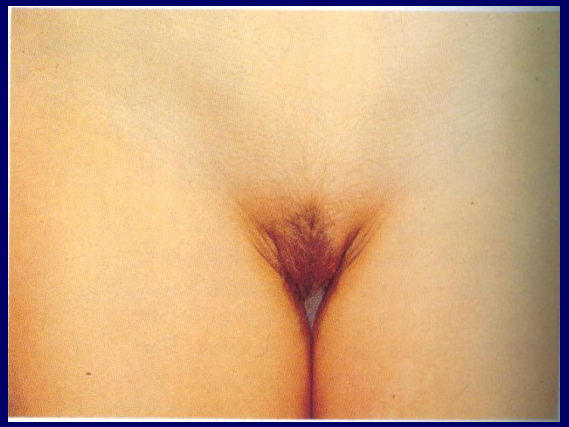
A woman with well developed breasts and minimal pubic hair.

Kariotype 46 XY and chromatine negative buccal smear.

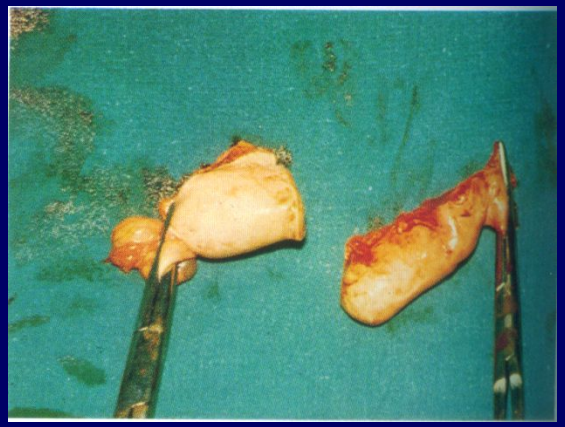


Testicular feminization syndrome

A well – developed vulva with minimal pubic hair.



The gonads (testes) removed from the same patient. They were intra – abdominal.



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4. 5-alpha reductase deficiency:.

- Affects only chromosomaly males (Karyotype 46XY).
- Caused by mutation of the 5-alpha reductase type 2 gene.
- This gene encodes an enzyme that converts Testosterone to Dihydrotestosterone.
- This leads to failure of conversion of testosterone to dihydrotestosterone by 5-alpha reductase.
- Dihydrotestosterone is necessary for the development of male genitalia in utero.
- External genitalia could be either female with enlarged clitoris capable of ejaculation , ambiguious or poorly developed male organs.
- Internal Genitalia :No uterus, no tubes & no vagina due to MIF production.
- Sex of rearing most of the time is female.

Determination Of Sex & Intersex

5. Female Intersexuality

a. Congenital Adrenal Hyperplasia:

- Due to congenital deficiency in enzymes essential for the transformation of progesterone to cortisol.

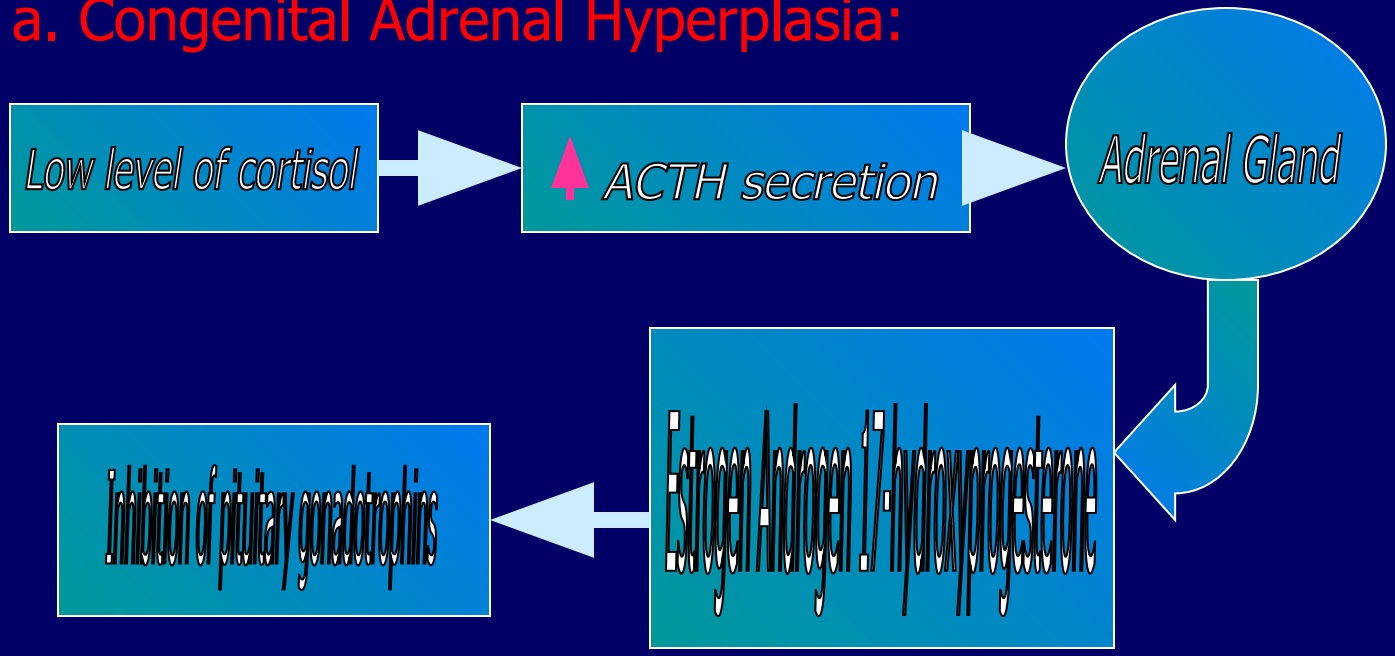
  Most commonly in 21-hydroxylase enzyme.

  less commonly in 11-hydroxylase enzyme.

- 17-hydroxyprogesterone ⟶ cortisol by hydroxylation at C21 then at C11.

Determination Of Sex & Intersex

a. Congenital Adrenal Hyperplasia:



- Result: ovarian function doesn't get established.

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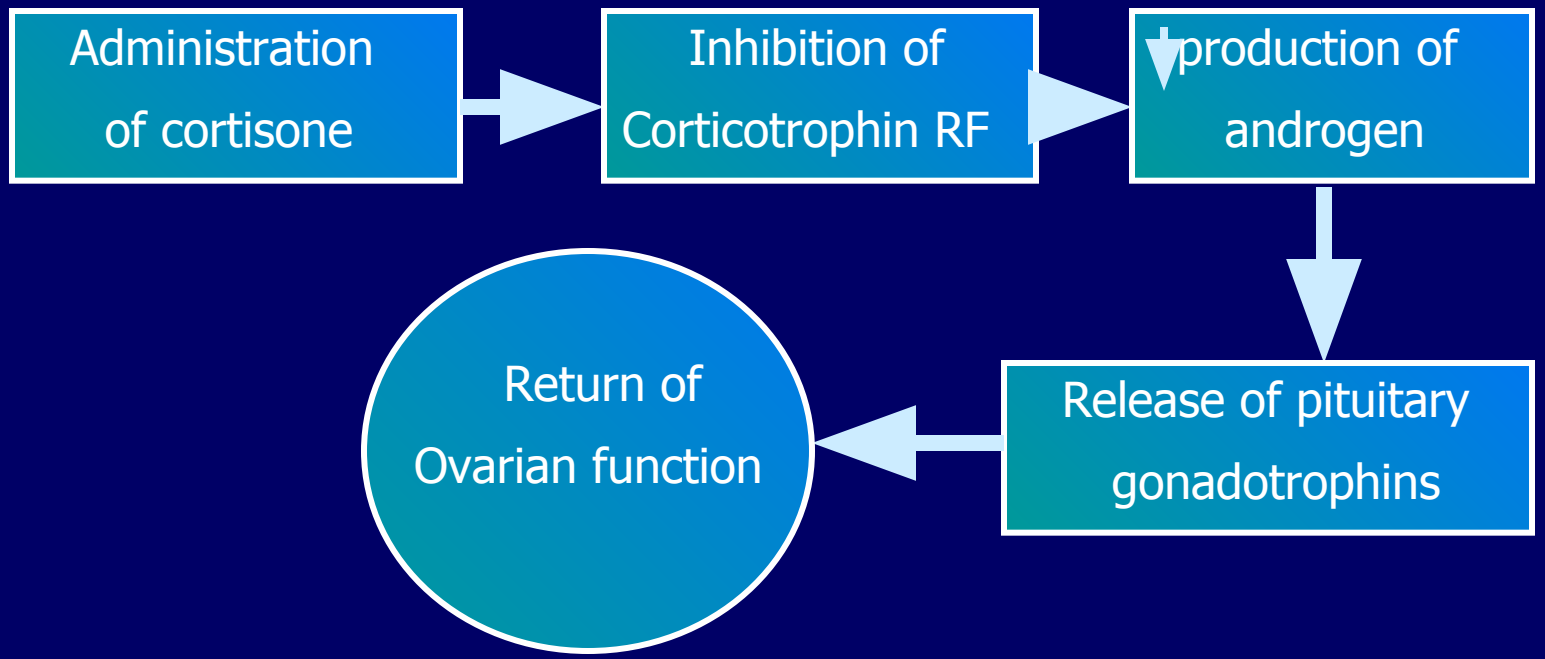
a. Congenital Adrenal Hyperplasia:



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a. Congenital Adrenal Hyperplasia:

Clinical picture:

- Usually seen in the newborn.
- Clitoral hypertrophy.
- Labioscrotal fusion.
- In severe cases, complete musculinization of external genitalia.
- Internal genital, gonadal & chromosomal sex are never affected.

Late onset congenital adrenal hyperplasia

- Autosomal recessive trait
- Most common form is due to 21-hydroxylase deficiency
- Mild forms Closely resemble PCO
- Severe forms show Signs of severe androgen excess
- High 17-OH-progesterone blood level
- Treatment : cortisol replacement and ? Corrective surgery

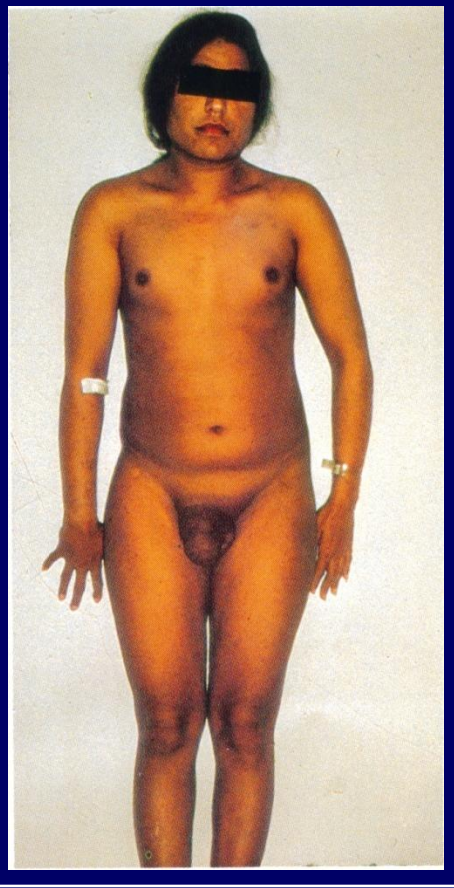
Determination Of Sex & Intersex

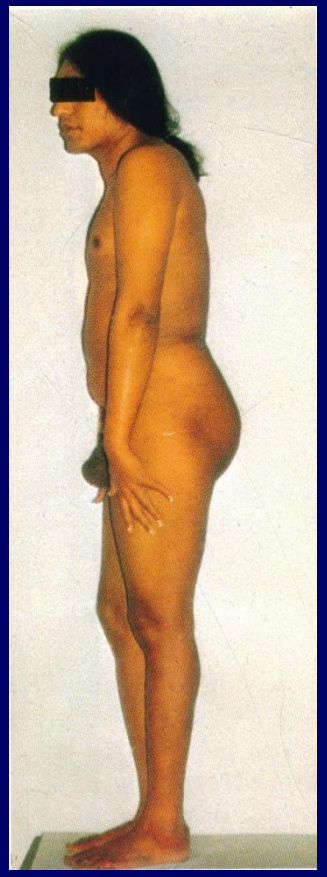
b. Non-progressive female intersex:

- Due to female fetus exposure to abnormal androgenic stimulus in utero.
- At birth the external genitalia are similar to cases of adrenal hyperplasia.
- The condition is not progressive.

Male pseudohermaphrodite

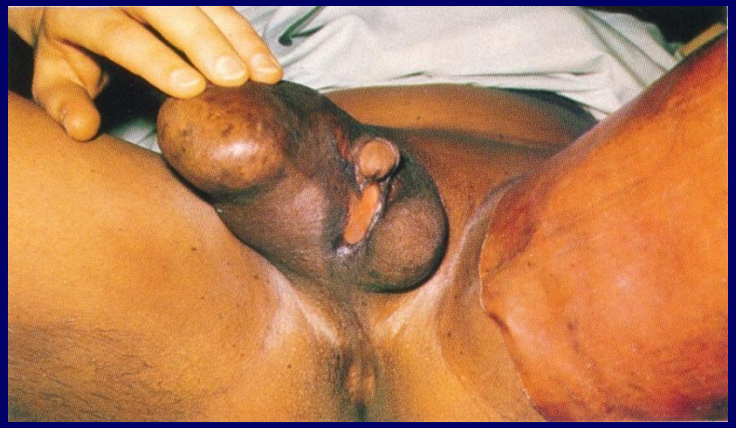
This patient had been brought up as a female. The side is less characteristic of a female, with poor breast development and suggestion of a male type phallus.



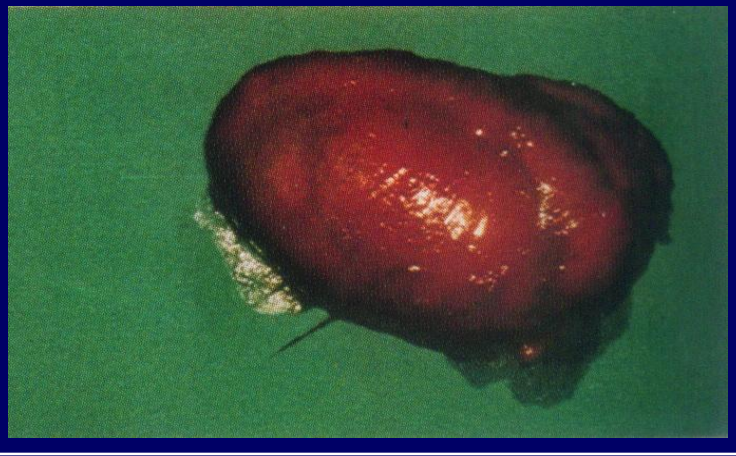


Male pseudohermaphrodite

Male type of genitalia with hydrocele on the right side.

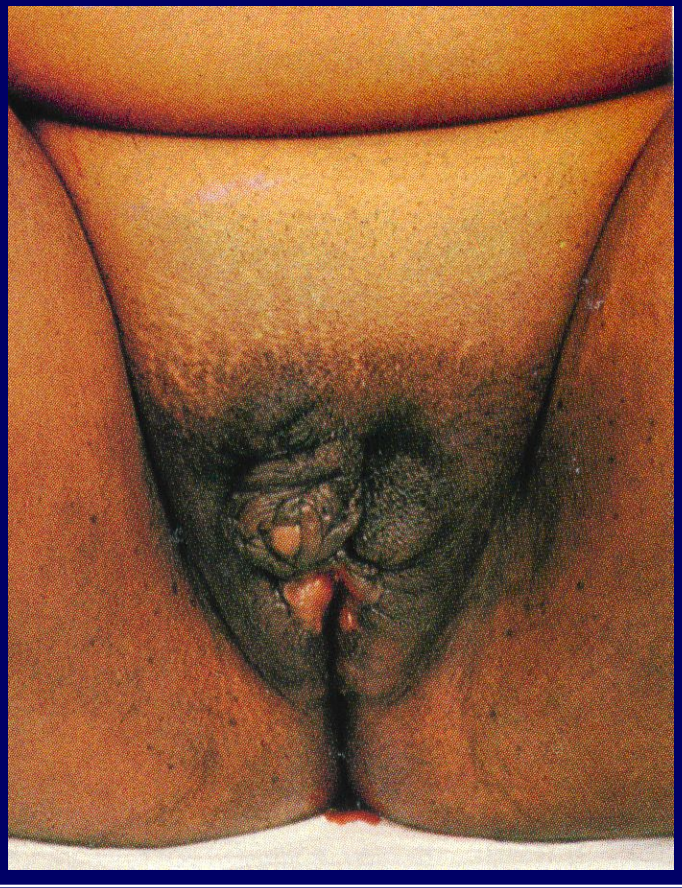


The left gonad of the same patient.



Male pseudohermaphrodite

The reconstructed genitalia of the same patient two months after operation.



Behavioral Intersex

Determination Of Sex & Intersex

Investigations:

- Buccal smears.
- Chromosome studies.
- Hormone studies.
- Ultrasonic studies.
- Imaging studies i.e. MRI, CT scanning.
- Diagnostic laparoscopy.
- Exploratory laparotomy.

Determination Of Sex & Intersex

Differential diagnosis & management:

- "Is it a boy or a girl?"

The answer should never be: I think it is a boy or a girl.

The answer should indicate ambiguity, & it will be resolved by further investigations.

- Proper assignment of the sex of rearing must be done as soon as possible.
- Careful counseling & discussion with the family is essential.

Determination Of Sex & Intersex

Differential diagnosis & management:

Sex assignment rules:

- Do not assign a newborn intersex to the sex for which it can't by surgery or other treatment be made coitally adequate. This rule applies regardless of genetic, gonadal or hormonal sex.
- Don't impose a sex reassignment on older hermaphrodite children & adults if psychologically it would be equivalent to announcement that you yourself should be reassigned.

Determination Of Sex & Intersex

Differential diagnosis & management:

Corrective surgery:

- Corrective surgery for external genitals should be undertaken before the child is old enough to notice his/her difference from others (2 – 3 years).
- Corrective surgery for internal genitals may be required.
- Gonadectomy in cases of male intersex showing virilism at birth if will be assigned as a female .

Medical treatment:

- Hormone therapy.