EMBRYOLOGY OF THE FEMALE REPRODUCTIVE SYSTEM

Important Explanation

SEXUAL DIFFERENTIATION.

The first step in sexual differentiation is the determination of the genetic sex (XX or XY)

- **sexual development does not depend on the presence of ovaries**
- **sexual development depend on the presence of functioning testes & responsive end organs**
- **the exposure to androgens in- utero will bring about masculinization**

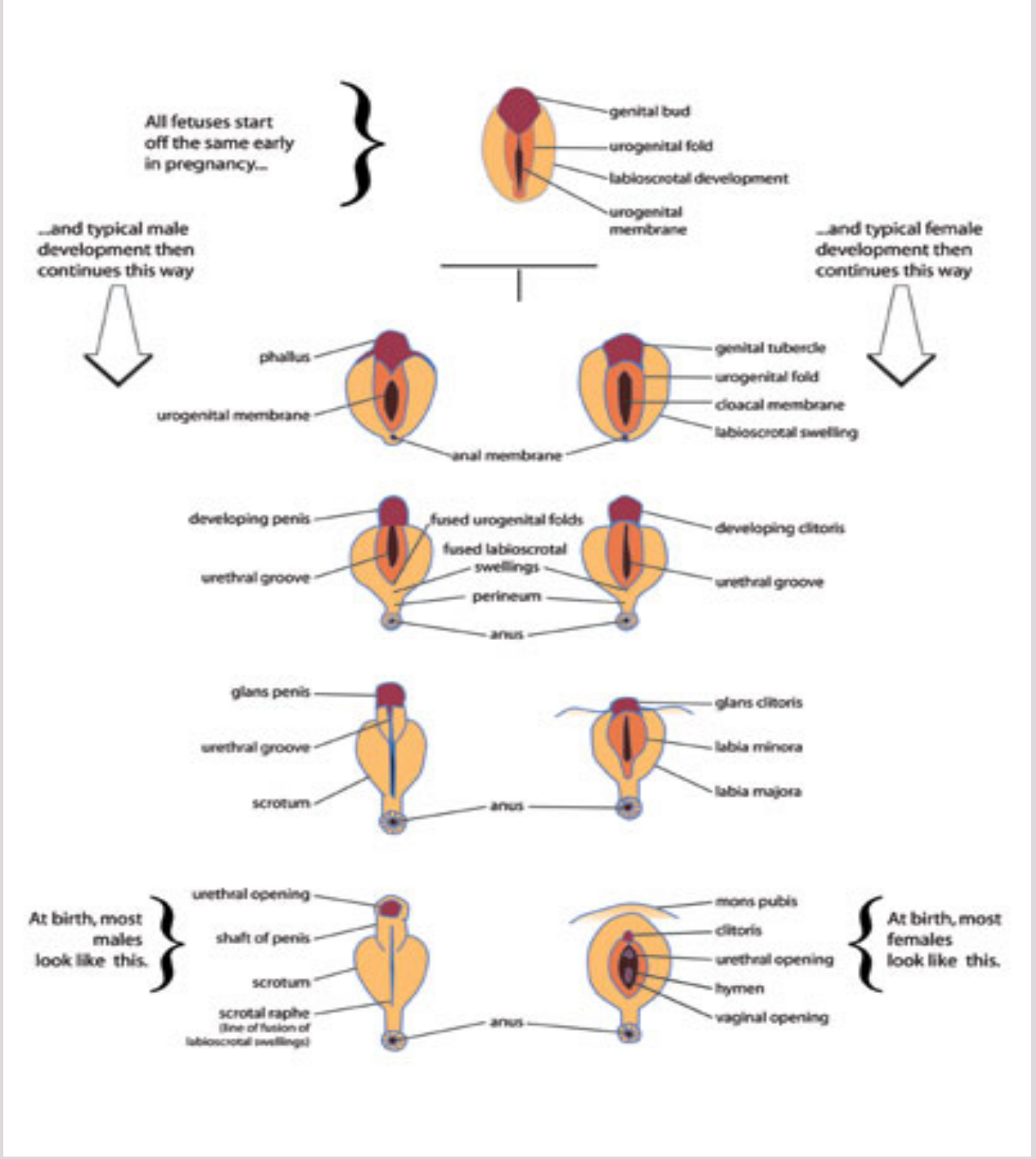
Neutral external genitalia (4-8 weeks)	Differentiated genitalia (9-12 weeks)
neutral genitalia includes: 1. Genital tubercle 2. Labioscrotal swelling 3. Urogenital folds 4. Urogenital sinus	by 12th of week of gestation the genitalia begins to differentiate upon the presence of androgens particularly DHT, made from the conversion of testosterone by 5A-reductase male genitalia develops and in the absence of androgens female genitalia develops

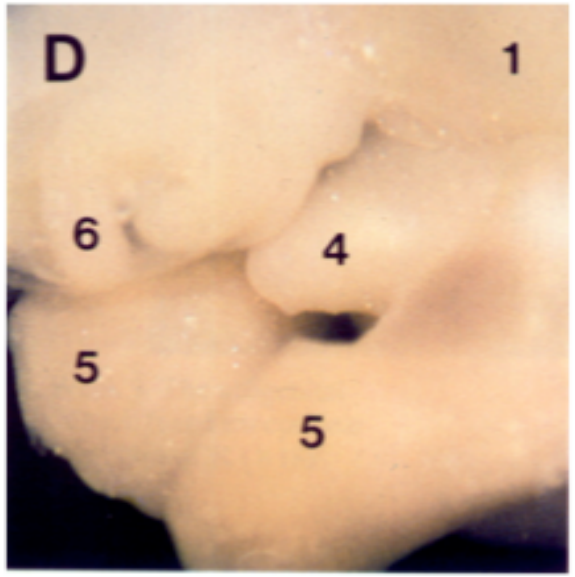
1- genital tubercle develops into the clitoris

2- urogenital folds develop into the labia minora

3- labioscrotal swelling fuse to form labia majora that later forms the anterior, posterior labial commissures

** estrogen produced from the ovaries and the placenta helps in the feminization process





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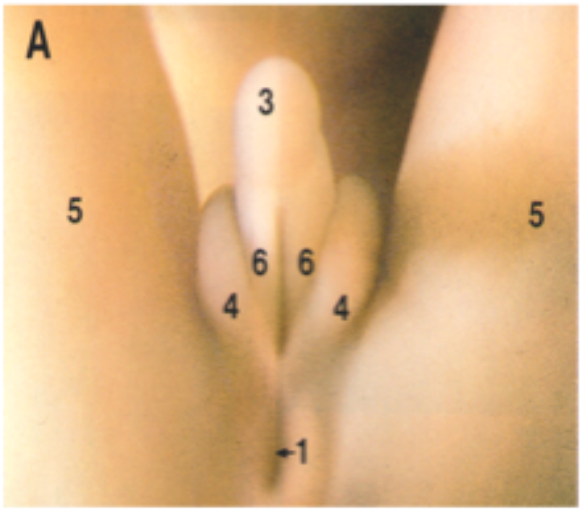

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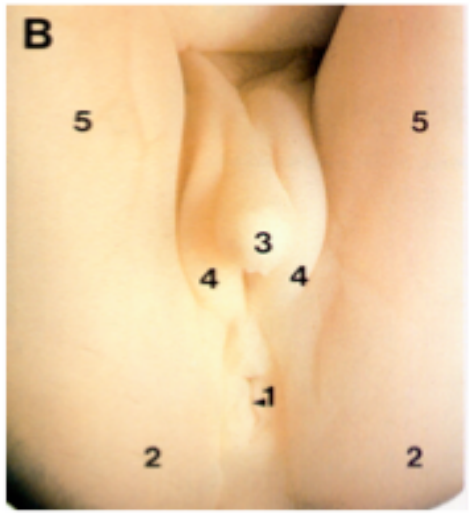

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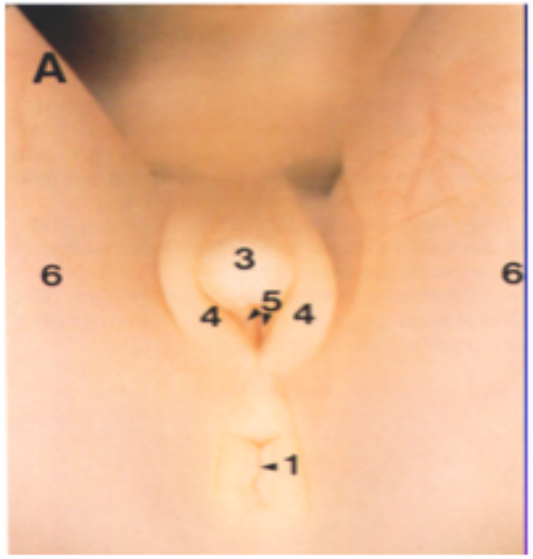

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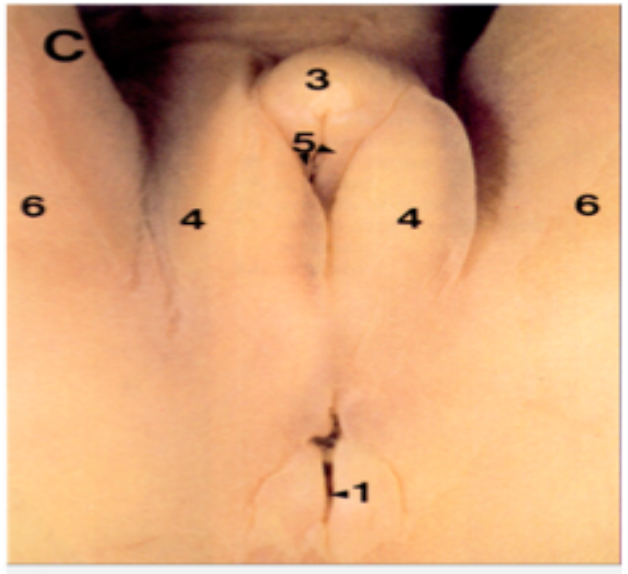

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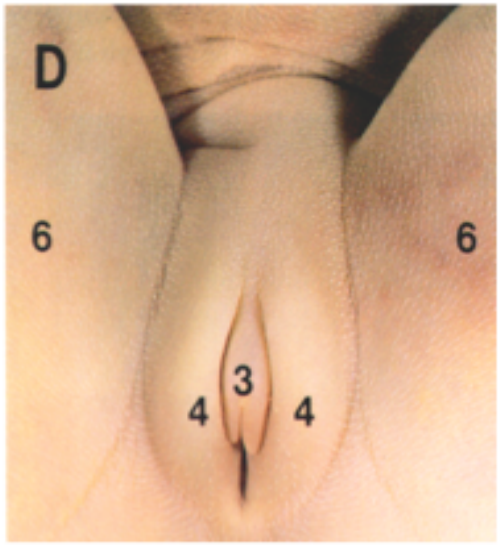

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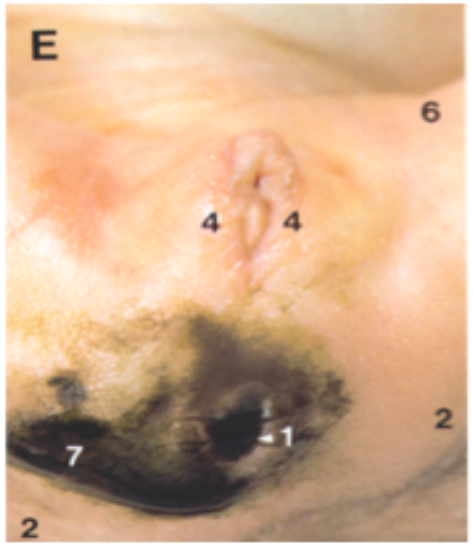

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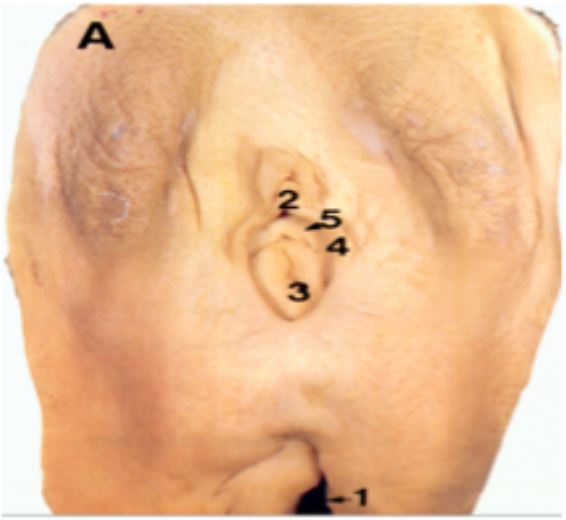

Neonatal genitalia

Development of the internal gonads.
1- begins on the 5th week at the sex determining region of the Y-chromosome SRY. If the y chromosome is absent ovaries develop.
- Neonates with the genetic variation 45 XO develop what is known as gonadal dysgenesis that is characteristically linked with the presence of streak ovaries. (turner syndrome) usually presents with primary amenorrhea at the age of 16 and no secondary sexual characteristics.
2- germ cells migrate from the yolk sac to the genital ridge. Gonads develop from the mesothelium of the genital ridge to form the primary sex cord that eventually forms the mesenchyme, the mesenchyme later forms the medulla and cortex.
3- the ovary develops from the cortex with the regression of the medulla. Testis develop from the medulla with the regression of the cortex
4- ovaries carry 2 million oocytes at the time of birth, this number decreases over the years there is no increase in number throughout the females life.

Uterus, fallopian tubes	Vagina
Invagination of the coelomic epithelium on the cranio-lateral end of the mesonephric ridge ⇨ to form Paramesonephric ducts due to the absence of mullerian inhibiting factor. Fusion of the two PMN ducts (mullerian ducts) ⇨ uterus, cervix & Fallopian tubes (at ٨-١١ wk) ١٢-١٦ wks ⇨ proliferation of the mesoderm around the fused lower part ⇨ muscular wall The end&myometrium are formed from the mesoderm	The caudal ends of the mullerian ducts form the mullerian tubercle at the dorsal wall of the urogenital sinus Mullarian tubercle is obliterated ⇨ vaginal plate ⇨ ١٦-١٨ wk the central core breaks down ⇨ vaginal lumen The upper ١/٣ of the vagina ⇨ formed by mullerian tubercle The lower ١/٣ ⇨ urogenital sinus

TABLE 1-2
Male and Female Derivatives of Embryonic Urogenital Structures

Embryonic Structure	Derivatives	
	Male	**Female**
Labioscrotal swellings	Scrotum	Labia majora
Urogenital folds	Ventral portion of penis	Labia minora
Phallus	Penis	Clitoris
	Glans, corpora cavernosa penis, and corpus spongiosum	Glans, corpora cavernosa, bulb of the vestibule
Urogenital sinus	Urinary bladder Prostate gland Prostatic utricle Bulbourethral glands Seminal colliculus	Urinary bladder Urethral and paraurethral glands Vagina Greater vestibular glands Hymen
Paramesonephric duct	Appendix of testes	Hydatid of Morgagni Uterus and cervix Fallopian tubes
Mesonephric duct	Appendix of epididymis Ductus of epididymis Ductus deferens Ejaculatory duct and seminal vesicle	Appendix vesiculosis Duct of epoophoron Gartner's duct —
Metanephric duct	Ureter, renal pelvis, calyces, and collecting system	Ureter, renal pelvis, calyces, and collecting system
Mesonephric tubules	Ductuli efferentes Paradidymis	Epoophoron Paroophoron
Undifferentiated gonad	Testis	Ovary
Cortex	Seminiferous tubules	Ovarian follicles
Medulla	—	Medulla
	Rete testis	Rete ovarii
Gubernaculum	Gubernaculum testis	Round ligament of uterus

Müllerian Dysgenesis or Agenesis : Mayer –Rokitansky-Kuster-Huser syndrome;

Path; idiopathic agenesis or hypoplasia of the mullerian ducts, with the agenesis of the cervix, uterus and upper vagina or it could be due to the exposure of the mother to drugs such diethylstilbestrol(DES) which increase the risk of a small T-shaped endometrial cavity or cervical deformity

Clinical picture; normal breasts and secondary sexual characteristics, patients usually complain of dyspareunia, amenorrhea, recurrent abortions, normal external genitalia. Fallopian tubes and ovaries are present, but at times they may be present in the pelvic brim as a result of failure of descent. Check using MRI/CT.

Phenotype; 46 XX

Investigations; US to confirm, HSG-hysterosalpingogram-during infertility
or Recurrent Fetal Loss and FSH/LH hormone

TX; vaginal dilatation, if that doesn't work preform surgical dilatation

As most of them have 10% increase chance for developing skeletal abnormalities and urinary system deformities which is why an US and an intravenous pyelogram is indicated.

• excision of uterine remnant (if it has functioning endometrium)

*Both of these methods should be performed close to the time when the patient anticipates having vaginal intercourse

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FAILURE OF THE LATERAL FUSION OF THE MULLERIAN DUCTS

The female reproductive system develops from two ducts known as mullerian ducts, they lie lateral to wolffian ducts. The pair grow in a medial caudal direction. The most cephalad parts remain separated to form the Fallopian tubes.

Two fusion processes take place

Lateral fusion

the lower parts of the ducts fuse in a laterally. The midline septum disappears, leaving a single canal that later gives rise to the uterus, cervix and upper vagina.

Vertical fusion;

Failure of the fusion of the ascending sinovaginal bulb and descending mullerian duct e.g imperforate hymen

Types:	A. Uterus didelphys	B. Bicornuate uterus	C. Septate uterus	D. Unicornuate uterus	E. Unicurnuate with rudimentary horn
Cause	**failure of fusion of the two Mull ducts**	**Incomplete fusion of the two Mull ducts**	**Incomplete dissolution of the midline fusion**	**Failure of formation lead to development of only one Mull duct**	**1) Noncommunicating horn 90%** Present with: ✓ cyclic pelvic pain. ✓ Pelvic mass. ✓ **Ectopic pregnancy in the horn .** ✓ Endometriosis. Rx ⇨ **surgical excision**
Presentation	**two separate uterine bodies, each with its own cervix and attached fallopian tube and vagina.(Complete duplication)** ↑ pregnancy wastage	↑ pregnancy wastage	External contour of the uterus is normal but there is **intrauterine septum of varying length & thickness** Worst pregnancy outcome	Almost all patient have associated **single kidney.** ↑ pregnancy wastage	
Diagnosis	**HSG or at laparoscopy / laparotomy**		**HSG >shows 2 cavities laparoscopy> normal shape ouside**	**HSG or surgery**	**2) Communicating horn :** Present with **ectopic pregnancy in the rud horn** ↑ pregnancy wastage
Management	**If affecting pregnancy outcome ⇨ surgical correction (metroplasty)**		**Hysroscopic excision of the septum**	**NO corrective surgery ⇨** if pt has associated **cervix incompetence ⇨ cervix cerclage***	

Vertical fusion defects

A. Vaginal Septum:	B. Cervix Agenisis / Dysgenisis: rare
• **Failure in the junction between the Mull, Tubercle & the urogenital sinus ⇨ could be very thick or thin.** • 85% in **upper two third of the vagina**. • Patient present **primary amenorrhea, hematocolpus*, mass or cyclic abdominal pain.** • ↑ incidence of endometriosis. • Rx ⇨ **surgical exision**.	• **complete lack of development of the paramesonephric system.** • Difficult, unsuccessful surgical correction . • Rx ⇨ hysterectomy .Because we can't create a functional cervix and the blood we accumulate in the uterus

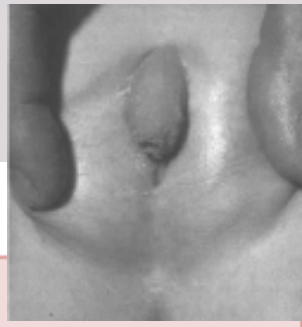
Hematocolpos; blood in the vagina
Hematometra; blood in the uterus

External genitalia anomalies

Mucocele may be present at the time of birth

Ambigious genitalia	Defects of the clitoris	Hermaphrodites	imperforate hymen:
• Most common cause : congenital adrenal hyperplasia.	• bifid clitoris : rare • Hypertrophied(Clitoromegaly)* ⇨ **androgen effect.** • Clitoral agenesis : result from the failure of the genital tubercle to develop • Incomplete development of the genitalia can result in a cloaca with no separation of the bladder and the vagina . *determined by the relative size of the clitoris in relation to the other vulvar structure	The presence of testicular and ovarian tissue in the same individual.	• the mildest form of these canalization abnormalities. • After birth, a **bulging, membrane-like structure may be noticed in the vestibule, usually blocking egress of mucus** and **a midline cystic mass on rectal examination** • An imperforate hymen should be suspected in adolescents who ***report monthly dysmenorrhea in the absence of vaginal bleeding (1ry amenorrhea)*** **or hematocolpus /hematometra** • Dx: Ultrasonography confirms the presence of **a normal uterus and ovaries.** • Rx: hymenectomy/**cruciate incision**

FEMALE PSEUDOHERMAPHRODITE



A-CONGENITAL ADRENAL HYPER PLASIA (CAH) The most common cause of female intersex

Deficiencies of the various enzymes required for cortisol & aldosterone biosynthesis (21-hydroxylase (most common) , 11β-hyroxilase ,3βhydroxisteroid dehydrogenase) ⇨ ✖ cortisone &aldosterone,↑Androgen	✓ Affected female may present at birth with ambiguous genitalia: • Enlargement of the clitoris • Excessive fusion of the genital folds obscuring the vagina & urethra • Thickening and rugosity of the labia majora resembling the scrotum. ✓A dangerous salt losing syndrome due to deficiency of aldosterone may occure . ✓ Delayed menarche & menstrual irregularities	INVESTIGATIONS: ✓ Karyotyping ✓ ↑17-α hydroxiprogestrone. ✓ 17-ketosteroids (androgens) in urine. ✓ Electrolytes ✓ U/S for internal organs	Management: 1.Cortisol or its synthetic derivatives (hormone replacement) ⇨ suppress the adrenals⇨ lower androgen production. 2.Corrective surgery. • *Clitroplasty* (at the neonatal period to reduce the size of it) • Division of the fused labiocsrotal folds to create the vagina (delayed till puberty)

B-EXPOSURE OF THE MOTHER TO ANDROGENS Rare

-**Androgen secreting tumours** , eg. Luteoma,arrhenoblastoma

-**Drugs**

male pseudohermaphrodite

Anatomical	Enzymatic	End-organ insensitivity
1. Failure of the descent of the testis 2. Gonadal dysgenesis 3. The presence or absence of a uterus, fallopian tubes etc depends on the testis secretion of MIF 4. SRY gene mutation with 46 XY with normal external genitalia	5-a-reductase deficiency causes androgen resistance and it varies from mild to severe with infertility with or without gynecomastia . 46 XY External female genitalia at puberty there's an increase in the production of testosterone and hence an increase in virilization	Complete androgen insensitivity known as testicular feminization syndrome takes place.

2.Androgen insensitivity (TESTICULAR FEMINIZATION): 46,XY

Complete (classical TF): *Lack of androgen receptors.*

- ✓ **Normal female external genitalia with blind vagina**.**
- ✓ **Absent uterus.**
- ✓ **Breast development***.**
- ✓ **Present with 1ry amenorrhea.**
- ✓ **Testes found in abdomen (pelvic sidewalls) or inguinal canal.**
- ✓ **Normal male Testosterone level.**

Treatment:

- ✓ **Gonadectomy** after puberty due to ↑incidence of malignant change(5%).
- ✓ **Oestrogen replacement.**

incomplete androgen insinsitivity: Receptors are present but low in NO. or inactive.

- ✓ **Ambiguous genitalia with varying degrees.**
- ✓ **Breast development***.**
- ✓ **Musculinization at puberty.**

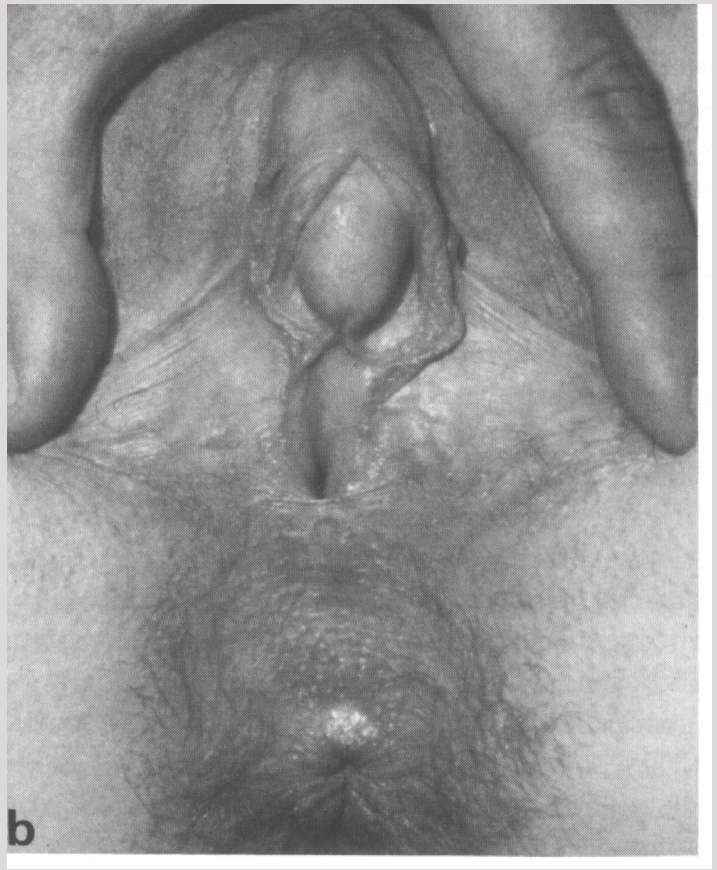
TRUE HERMAPHRODITES

HAVE BOTH OVARIAN & TESTICULAR TISSUE
Ovotestes on one side & ovary or testes on the other
Ovary on one side & testes on the other
Bilateral ovotestes
Varying degrees of sexual ambiguity
KARYOTYPING

- 46XX ⇨ most common
- 46XX/XY
- 46XY
- 46XY/47XXY

EXAMPLE; Klinefelter Syndrome
Karotype;47XXY
Normal male external genitalia

- Tall stature
- Gynecomastia
- Azospermia (infertility)



THANK YOU