Obstetrics & Gynecology
TEAM

Embryology of female genital tract, congenital malformation & intersex

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◆very important ◆mentioned by doctor ◆team notes ◆not important

Part 1: Embryology of ♀ genital tract

SEXUAL DIFFERENTIATION

- The first step in sexual differentiation is the determination of 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
- ♀ exposed to androgens in- utero will be masculinized.

EXTERNAL GENITALIA

1-UNDEFERENTIATED STAGE (4-8 WK)

Before the 7th week of development, the appearance of external genital area is the same in males & females.

The neutral genitalia includes:

genital tubercle (phalus)
labioscrotal swellings
urogenital folds
urogenital sinus

2-♂ & ♀ EXTERNAL GENITAL DEVELOPMENT (9-12 WK)

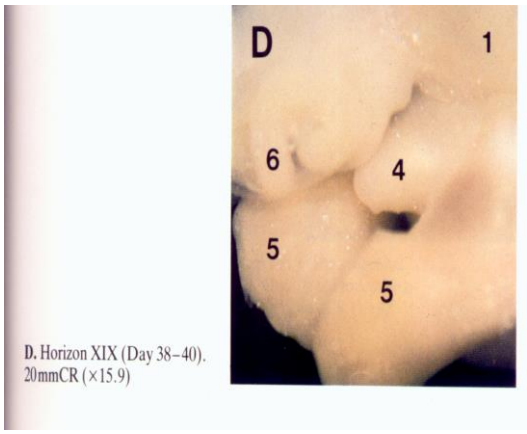
- By 12 wk gestation ♂ & ♀ genitalia can be differentiated
- In the absence of androgens ⇨♀ external genitalia develop
- The development of ♂ genitalia requires the action of androgens, specifically DHT

5 alpha reductase

Testosterone ⇨ ⇨ ⇨ ⇨ ⇨ DHT

EXTERNAL GENITALIA (INDIFFERENT STAGE)

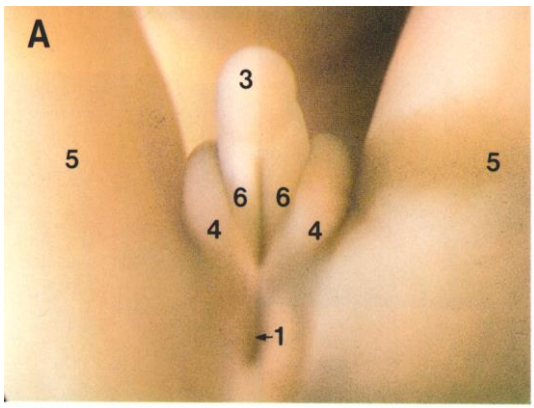
1-abdomen
4-genital tubercle
5-leg bud
6-midgut herniation to the umbilical cord



FEMALE EXTERNAL GENITALIA

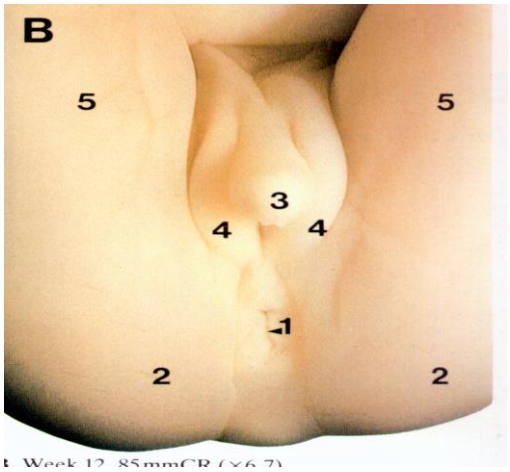
Week 9

1-anus
2-buttocks
3-clitoris
4-labioscrotal swelling (labia majora)
5-leg
6-urogenital fold (labia minora)

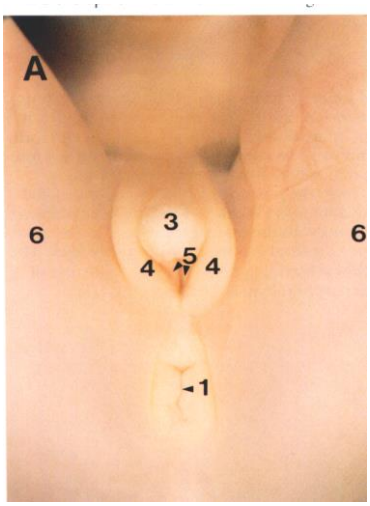


Week 12
1-anus
2-buttocks
3-clitoris
4-labioscrotal swelling (labia majora)
5-leg
6-urogenital fold (labia minora)

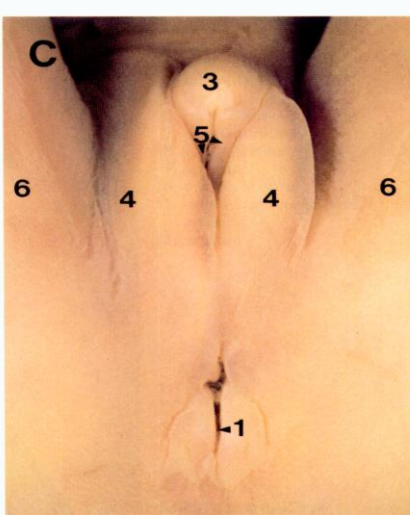
The external genitalia of female is distinguishable at about 12



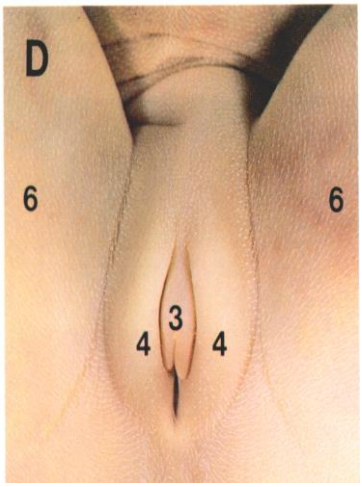
Week 13
1-anus
2-buttocks
3-clitoris
4-labia majora
5-labia minora
6-leg



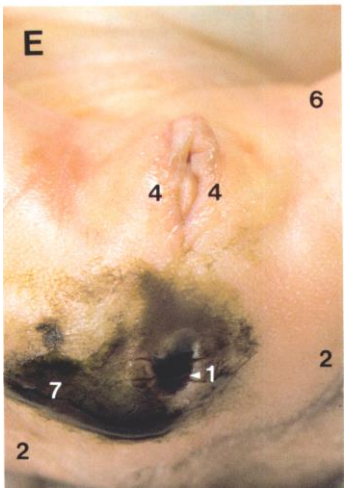
Week 17
1-anus
2-buttocks
3-clitoris
4-labia majora
5-labia minora
6-leg



Week 20
1-anus
2-buttocks
3-clitoris
4-labia majora
5-labia minora
6-leg



Week 35
1-anus
2-buttocks
3-clitoris
4-labia majora
5-labia minora
6-leg
7-meconium



INTERNAL GENITAL ORGANS

1-GONADS

- Undifferentiated gonads begin to develop on the 5th wk
- Germ cells originate in the yolk sac & migrate to the genital ridge
- In the absence of Y chromosome the undiff gonad develop into an ovary
- 45XO embryo the ovaries develop but undergo atresia ⇨ streak ovaries **Turner Syndrome**
- The gonads develop from the mesothelium on the genital ridge ⇨ 1ry sex cords grow into the mesenchyme ⇨ outer cortex & inner medulla
- The ovary develop from the cortex & the medulla regress
- The testes develop from the medulla & the cortex regress
- The development of the testes requires the presence of SRY gene (Sex determining region Y) found on Y chromosome
- The ovary contains 2 million 1ry oocytes at birth

2-UTERUS & FALLOPIAN TUBES

- Invagination of the coelomic epithelium on the cranio-lateral end of the mesonephric ridge ⇨ Paramesonephric ducts
- Fusion of the two PMN ducts (mullerian ducts) ⇨ uterus, cx & F tubes (at 8-11 wk)
- 12-16 wks ⇨ proliferation of the mesoderm around the fused lower part ⇨ muscular wall
- In the male fetus the testes secrete the mullerian inhibiting factor ⇨ regression of the mullerian ducts

-The upper vagina, cervix & fallopian tubes are formed from the paramesonephric "PMN" (mullerian) ducts.
-the absence of Y chromosomal influence leads to the development of PMN system & total regression of the mesonephric system.

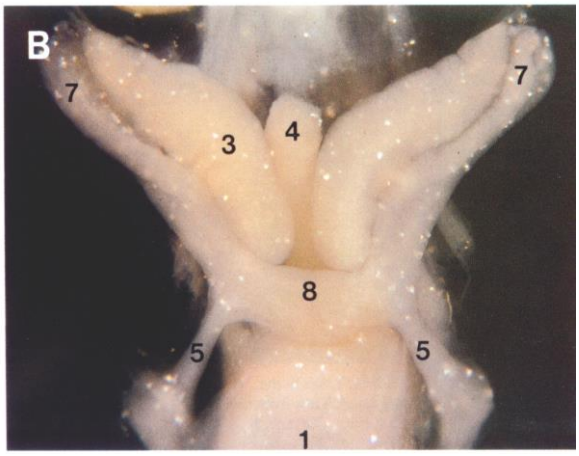
3-VAGINA

- 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 ⇨ 16-18 wk the central core breaks down ⇨ vaginal lumen
- The upper 2/3 of the vagina ⇨ formed by mullerian tubercle
- The lower 1/3 ⇨ urogenital sinus

FEMALE INTERNAL GENITAL ORGANS

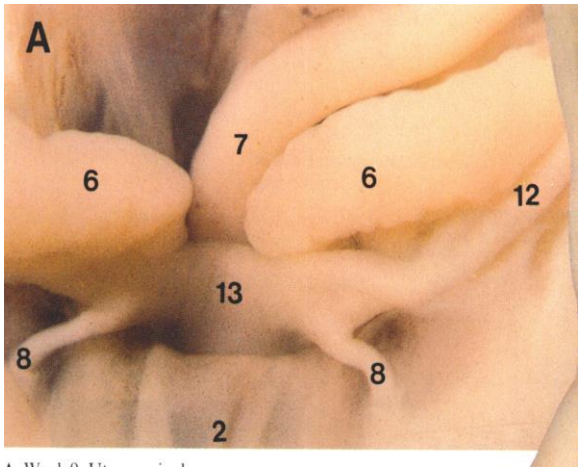
Week 8

1-bladder 2-kidney
3-ovary 4-rectum
5-round ligament of the uterus
6-adrenal gland
7-Fallopian tube
8-utero vaginal primordium



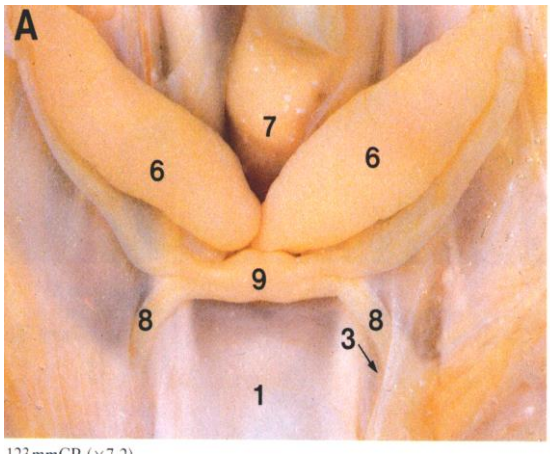
Week 9

2-bladder
6-ovary
7-rectum
8-round ligaments
12-uterine tube
13-uterovaginal primordium



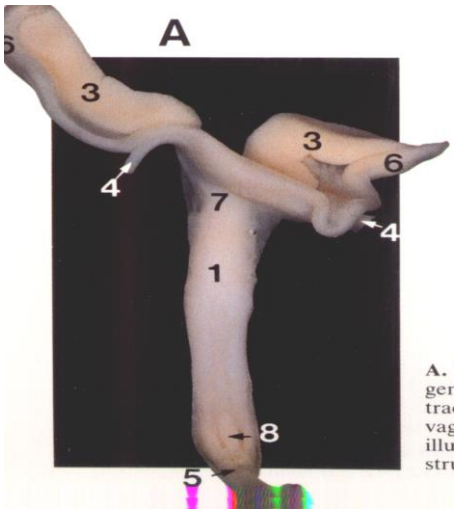
Week 15

1-bladder
2-clitoris
3-vaginal process
4-labia majora
5-leg
6-ovary
7-rectum
8-uterine round ligament
9-uterovaginal primordium

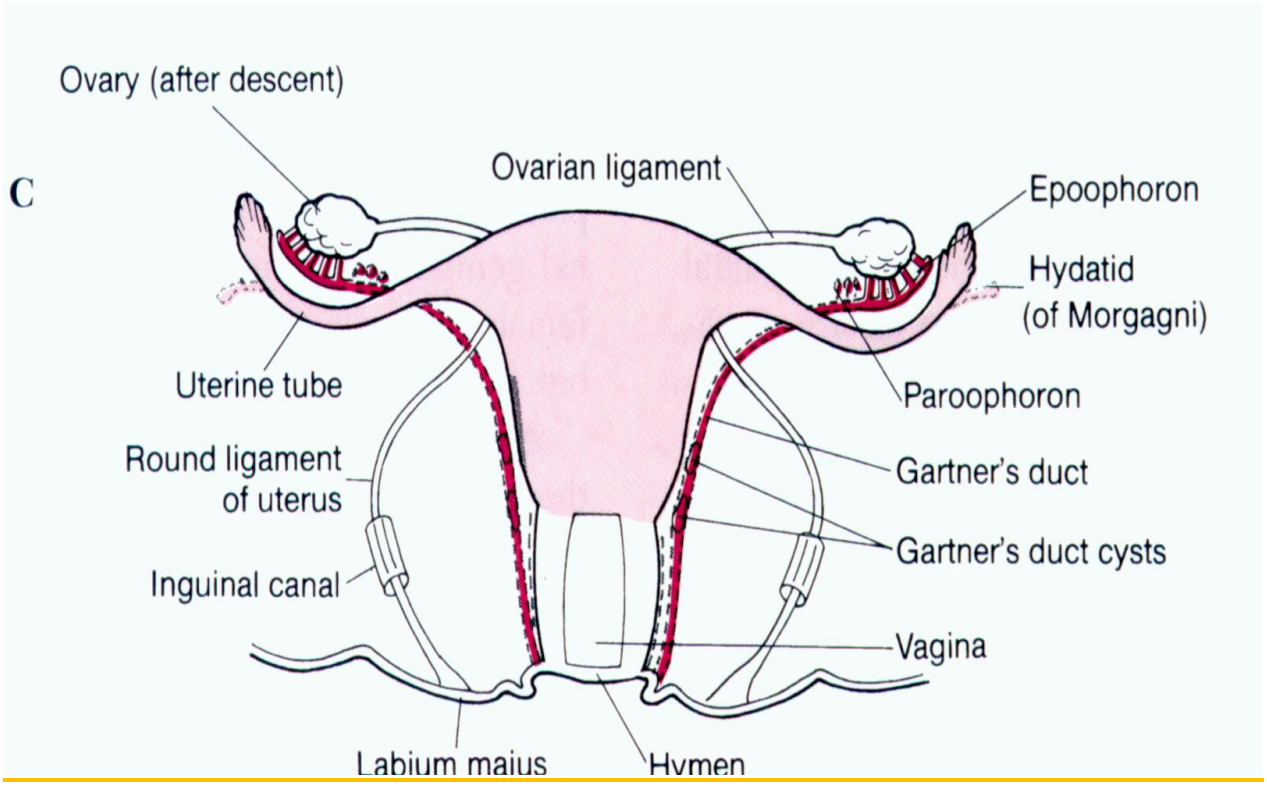


Week 13 (dissected genital tract)

1-body of uterus
2-clitoris
3-ovary
4-round ligament
5-solid epithelium (vagina meets urogenital sinus)
6-fallopian tube
7-uterus
8-vagina



FEMALE INTERNAL GENITAL ORGANS (Newborn)



Male & Female Derivatives of Embryonic Urogenital Structures

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	—
Mesonephric tubules	Ductuli efferentes Paradidymis	Ureter, renal pelvis, calyces, and collecting system Epoophoron Paroophoron
Undifferentiated gonad	Testis	Ovary
Cortex	Seminiferous tubules	Ovarian follicles
Medulla	—	Medulla
	Rete testis	Rete ovarii
Gubernaculum	Gubernaculum testis	Round ligament of uterus

Part 2: Congenital Malformation of the ♀ Genital Tract

OBJECTIVES

- To be able to differentiate the various types of congenital malformation of female internal genital organs
- To know the abnormalities due to lateral and vertical fusion of the mullarian ducts as well as failure of mullarian duct development
- To know the clinical presentation and management of congenital anomalies of the female genital tract

1-MULLERIAN AGENISIS

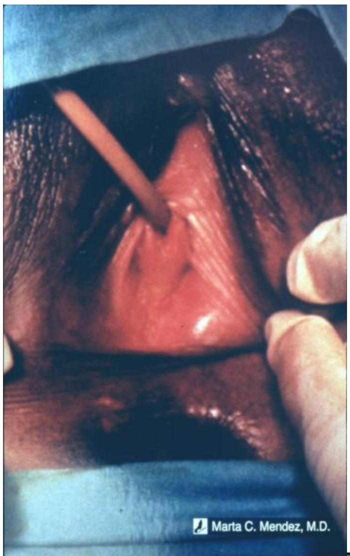
To read more about Vaginoplasty click the link below: http://en.wikipedia.org/wiki/Vaginoplasty

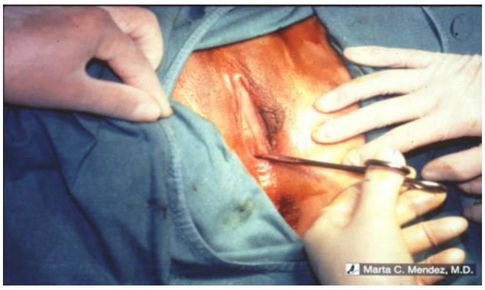
Mayer –Rokitansky-Kuster-Huser syndrome

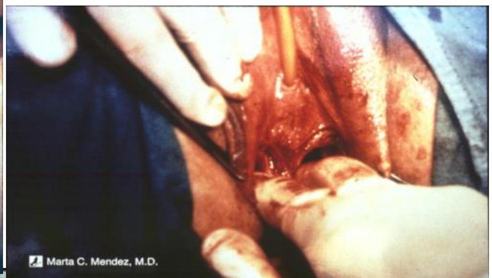
Etiology ?

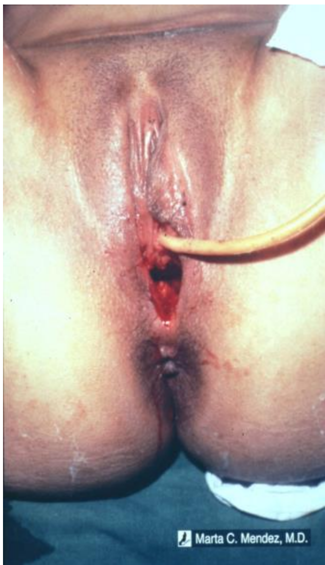
- Failure of mulleria n duct development ⇨ absence of the upper vagina, cx & uterus (uterine reminants may be found)
- The ovaries & fallopian tubes are present
- Normal 46XX ♀ with normal external genitalia
- Pt present with 1ry amenorrhea
- 47% have associated urinary tract anomalies
- 12% skeletal anomalies
- Rx ⇨
  - Psychological counseling
  - Surgical ⇨- vaginoplasty
    - - Excision of utrine reminant (if it has Functioning endometrium)
    - -vaginal dilators

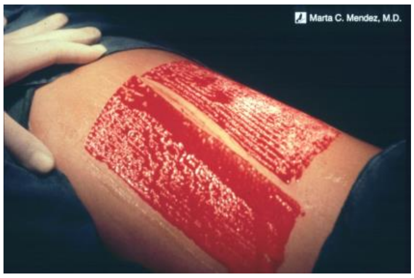
-Pt with 1ry amenorrhea, breast development & a 46XX karyotype have levels of testosterone appropriate of females.
-The clinical diagnosis may be caused by mullerrian defects that cause obstruction of the vaginal canal (e.g., imperforated hymen of a transverse vaginal septum) of by the absence of a normal cervix or uterus & normal fallopian tubes.

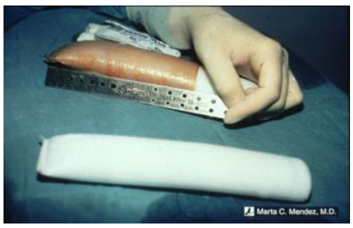


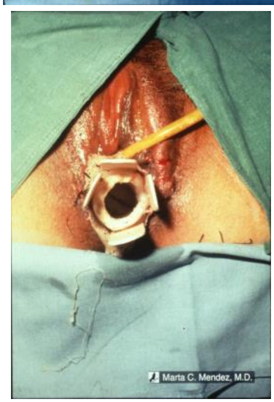


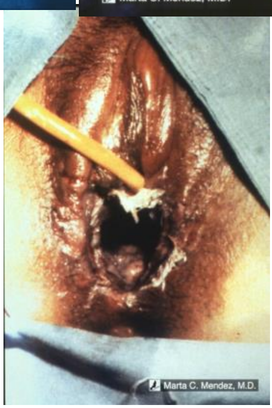


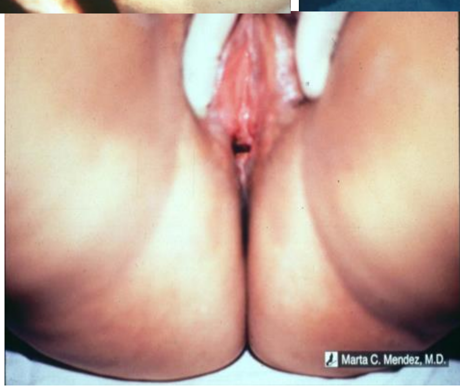


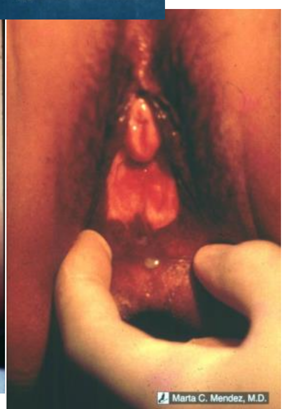


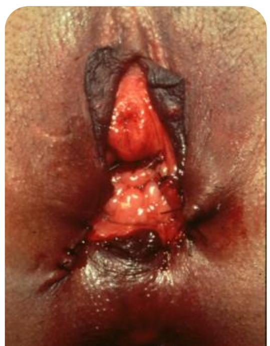












2-DISORDERS OF LATERAL FUSION OF THE MULL DUCTS

Incidence ? 0.1-2%
4% of infertile pt
6-10% recurrent abortion pt

Most pt can conceive without difficulty

↑ Incidence of:
◊ recurrent abortions
◊ premature birth
◊ fetal loss
◊ fetal malpresentation
◊ C S
◊ cx incompetence

CLINICAL PRESENTATION

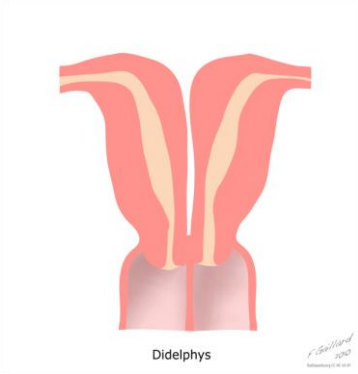
♣Shortly after menarche ⇨if there is obstruction to uterine blood flow
♣Difficulty in intercourse ⇨ longitudinal vaginal septum
♣Dysmenorrhea or menorrhagia
♣Abnormality detected on D&C
♣U/S, laparoscopy or laparotomy
♣Palpable mass
♣Complications of pregnancy
♣HSG ⇨ during infertility or RFL investigations

NON OBSTRUCTIVE MALFORMATIONS OF THE MULLERIANE DUCTS

2-DISORDERS OF LATERAL FUSION OF THE MULL DUCTS

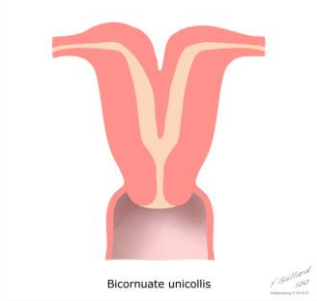
A-Uterus didelphus:

- Complete duplication of uterus, cx & vagina (due to failure of fusion of the two Mull ducts)
- ? ↑ pregnancy wastage
- Dx ⇨ HSG or at laparoscopy / laparotomy
- Rx ⇨ If affecting pregnancy outcome ⇨ surgical correction (metroplasty)



B-Bicornuate uterus

- Incomplete fusion of the two Mull ducts
- ↑ pregnancy wastage
- Dx ⇨ HSG or at laparoscopy / laparotomy
- Rx ⇨ If affecting pregnancy outcome ⇨ surgical correction (metroplasty)



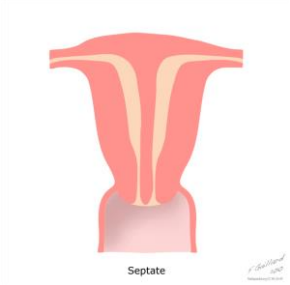
C-Septate uterus

External contour of the uterus is normal but there is intrauterine septum of varying length & thickness

Worst pregnancy outcome

Dx ⇨ both HSG & laparoscopy

Rx ⇨ Hystroscopic excision of the septum



D-Unicornuate uterus

Due to development of only one Mull duct

Almost all pt have associated single kidney

Pregnancy outcome ⇨ similar to pt with didelphic uterus

Dx ⇨ HSG or surgery

Rx ⇨ NO corrective surgery

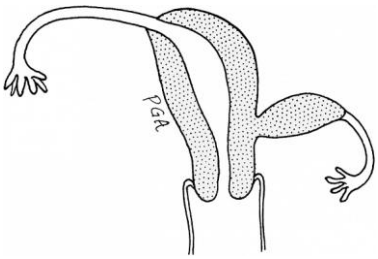
⇨ if pt has associated cx incompetence ⇨ cx cerclage

E-Unicurnuate with rudimentary horn

Noncommunicating horn 90%

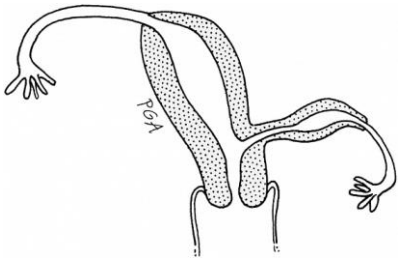
Present with cyclic pelvic pain, mass, ectopic pregnancy in the rud horn or endometriosis

Rx ⇨ surgical excision



Communicating horn

Present with ectopic pregnancy in the rud horn or ↑ pregnancy wastage



3-DISORDERS OF VERTICALE FUSION OF THE MULLERIAN DUCTS

A- VAGINAL SEPTUM

- Faults in the junction between the Mull. Tubercle & the urogenital sinus ⇨ could be very thick or thin
- 85% in upper two third of the vagina
- Pt present 1ry amenorrhea, hematocolpus, mass or cyclic abdominal pain
- ↑ incidence of endometriosis
- Rx ⇨ surgical excision

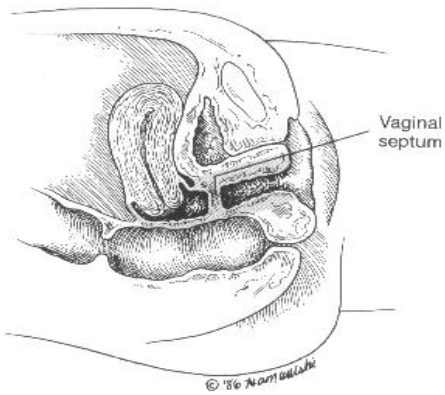
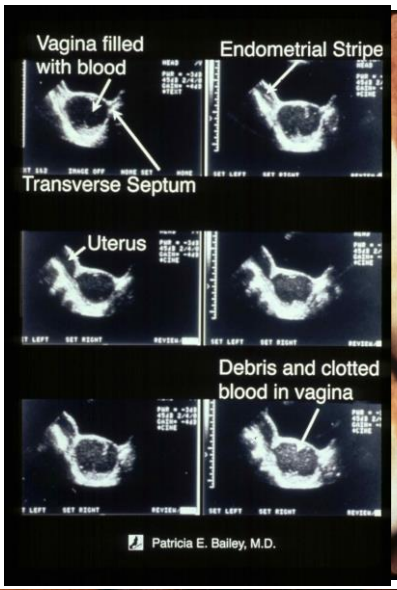
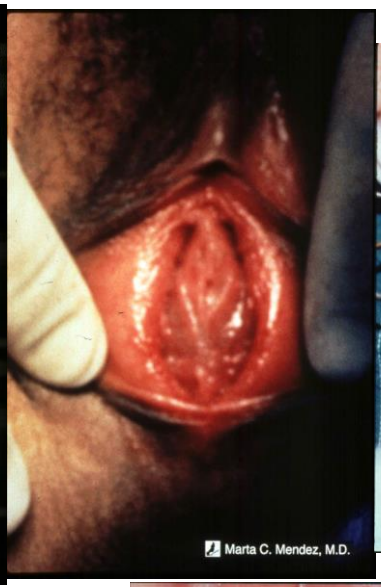


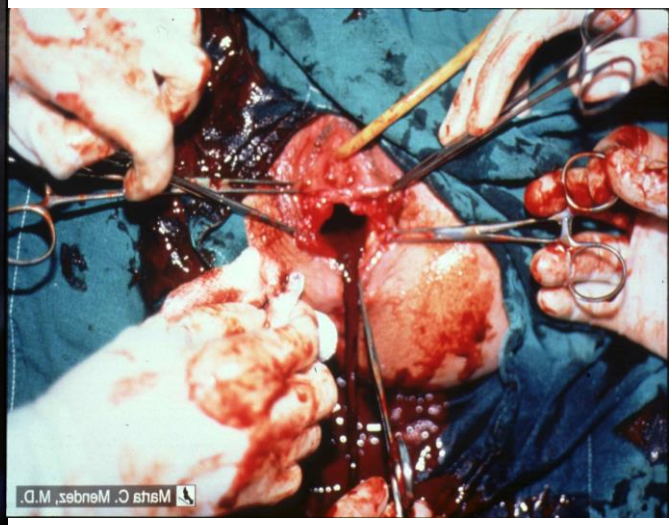
FIGURE 10-7
Diagram of transverse vaginal septum.

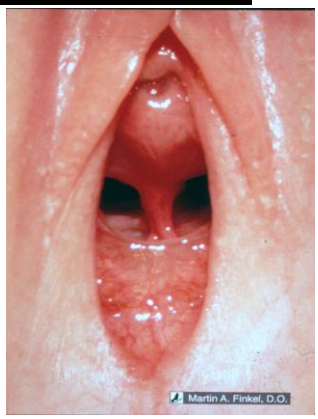
B-Cx AGENISIS / DYSGENISIS

- V rare
- Difficult, unsuccessful surgical correction
- Rx ⇨ hysterectomy





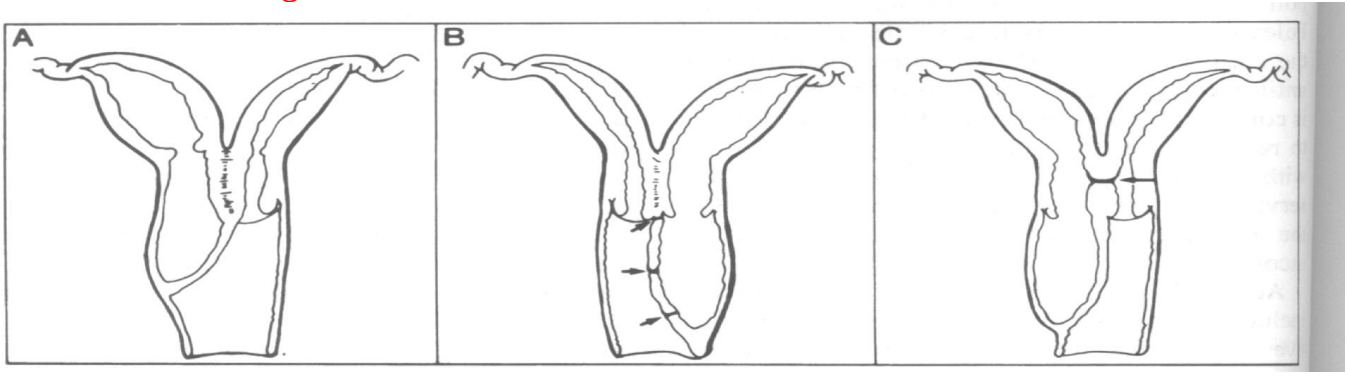




4-UNUSUAL CONFIGRATION OF VERTICAL/LATERAL FUSION DEFECTS

- Combined lateral & verticle defects
- Do not fit in other categories
- EXAMPLE, double uterus with obstructed hemivagina

Double uterus with vaginal obstruction



A-Complete vaginal obstruction B-Incomp vag obst C-Comp obst with comm double uterus

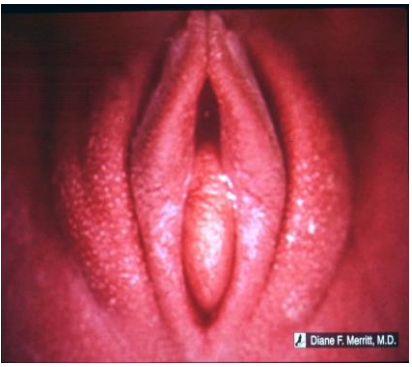
5-DEFECTS OF THE EXTERNAL GENITALIA

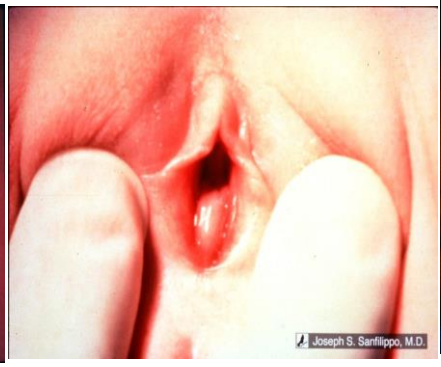
- Ambigious genitalia ⇨ congenital adrenal hyperplasia
  hermaphrodites
- Defects of the clitoris ⇨ uncommon ⇨ bifid clitoris
  hypertrophied ⇨ androgen effect
- IMPERFORATE HYMEN

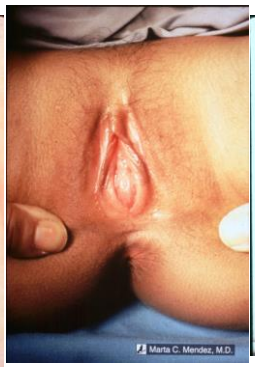
Hymen is formed at the junction of the urogenital sinus & sinovaginal bulbs

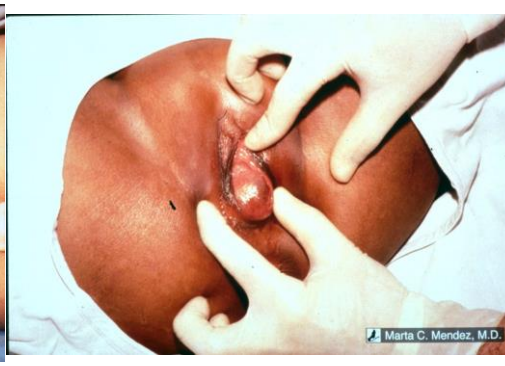
Pt presents with 1ry amenorrhea with cyclic abdominal pain or hematocolpus /hematometra

Rx ⇨cruciate incision









Part3: INTERSEXUALITY

OBJECTIVES

- To understands the defects that result in abnormal development of the external genitalia in male and female fetuses
- To be able to differentiate the types of male and female hermafrodites
- Causes presentations and management of various types of intersex

ABNORMAL SEXUAL DEVELOPMENT

1-Sex chromosome abnormality
Mosaicism associated with gonadal dysgenisis ⇨ 45X/46XY

2-Testis incapable of producing testosterone.

3-End organs incapable of utilizing testosterone eg. 5α reductase deficiency, failure of testosterone binding to receptors (androgen insensitivity)

MIF = Mullerian Inhibiting Factor.

4-Defficient production of MIF ⇨ ♀ internal genital organs in otherwise normal ♂

5-Musculanization of the ♀ external genitalia due to #↑ androgen eg. Congenital adrenal hyperplasia (CAH).

6-Rarely 46XX male due to the presence of a gene the SRY gene (Sex determining Region Y)

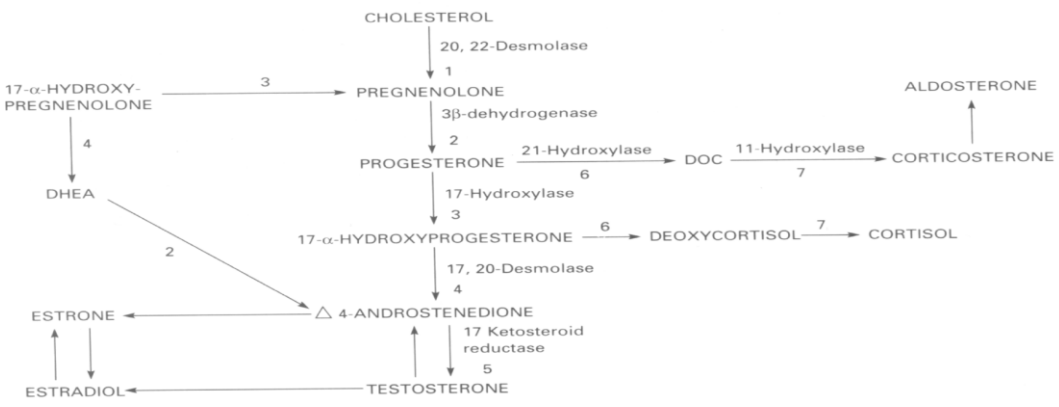
7-True hermaphroditism ⇨ the presence of testicular & gonadal tissue in the same individual

1-MUSCULINIZED ♀ (♀ PSEUDOHERMAPHRODITES)

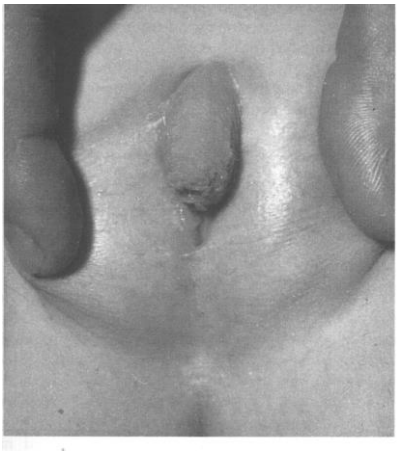
-46XX
-Exposed to androgens in utero ⇨ varying degrees of musculinization of the external genitalia

A-CONGENITAL ADRENAL HYPER PLASIA (CAH)

- The most common cause of ♀ intersex
- Deficiencies of the various enzymes required for cortisol & aldosterone biosynthesis (21-hydroxylase, 11β-hyroxilase , 3βhydroxisteroid dehydrogenase)
- 21-hydroxylase deficiency is the commonest defect 90%
- Affected ♀ may present at birth with ambiguous genitalia
  -enlargement of the clitoris
  -excessive fusion of the genital folds obscuring the vagina & urethra



A-CONGENITAL ADRENAL HYPER PLASIA (CAH)



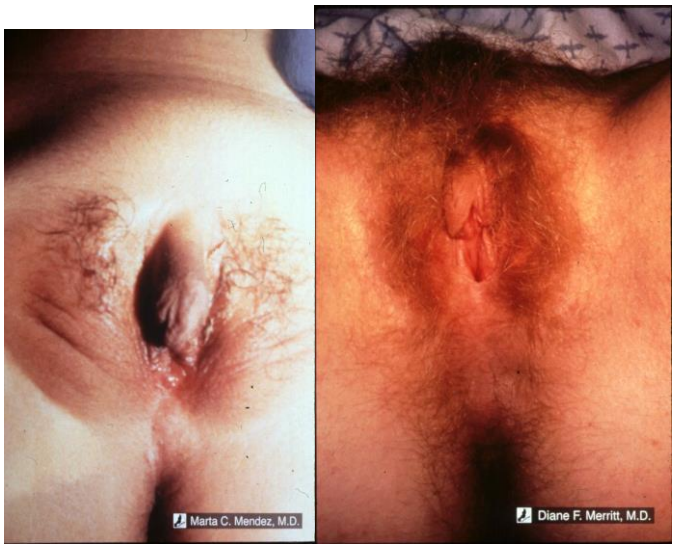
-thickening & rugosity of the labia majora resembling the scrotum

- A dangerous salt losing syndrome due to deficiency of aldosterone may occure in some pt
- Delayed menarche & menstrual irregularities
- INVESTIGATIONS

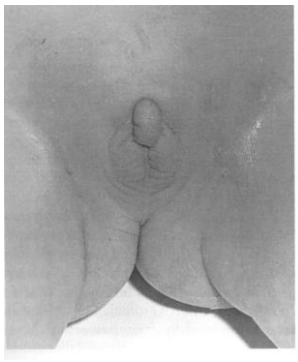
Karyotyping
17-α-hydroxiprogestrone ↑
17-ketosteroids (androgens) in urine
Electrolytes
U/S

- Rx

1- Cortisol or its synthetic drevatives
⇨ suppress the adrenals ⇨ ↓ androgen production
2-Corrective surgery
clitroplasty (neonatal period)
division of the fused labial folds
(delayed till puberty)



B- EXPOSURE OF THE MOTHER TO ANDROGENS



-Rare
-Androgen secreting tumours , eg. luteoma, arrhenoblastoma
-Drugs

2-UNDERMUSCULINIZED ♂ (♂ PSEUDOHERMAPHRODITES)

A-ANATOMICAL TESTICULAR FAILURE

-Pure gonadal dysgenisis
*normal chromosomes 46XY
*variable features – mild-severe
(normal ♀ , ♀ with mild musculinization)
*uterus present
-Mosaicism 45X/46XY
*Variable features
(normal ♀, ambiguous genitalia, nearly normal ♂)

B-ENZYMETIC TESTICULAR FAILURE

- Enzymetic defects in the biosynthesis of testosterone
- These defects are usually incomplete ⇨ Varying degrees of musculinization of the external genetalia
- Uterus & tubes ⇨ absent (MIF produced by the testes)

C-END-ORGAN INSINSITIVITY

1-5α REDUCTASE DEFICIENCY

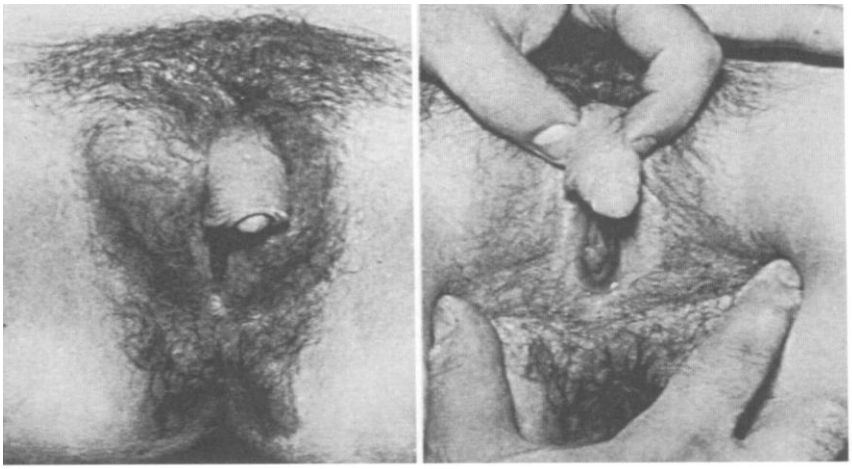
-Autosomal recessive

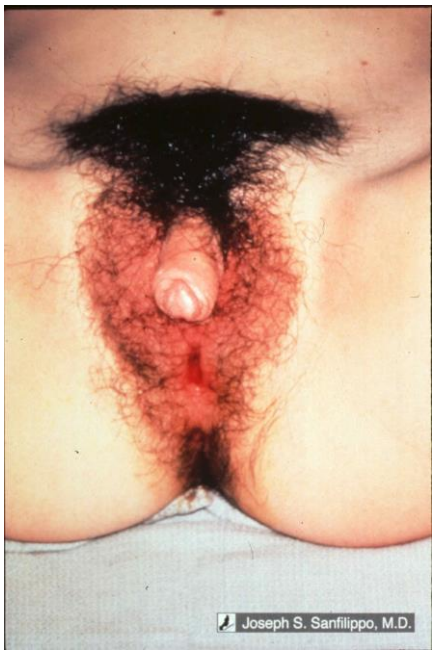
- Formation of the ♂ external genitalia requires 5α REDUCTAS testosterone ⇨ ⇨ ⇨ ⇨ dihydrotestosterone
- Formation of the internal wollfiane structures respond directly to testosterone

-External genitalia ♀ with mild musculinization

-Absent uterus

-At puberty ⇨ ↑ testosterone secretion ⇨ virilization





D-ANDROGEN INSINSITIVITY

2-ANDROGEN INSINSITIVITY (TESTICULAR FEMINIZATION)

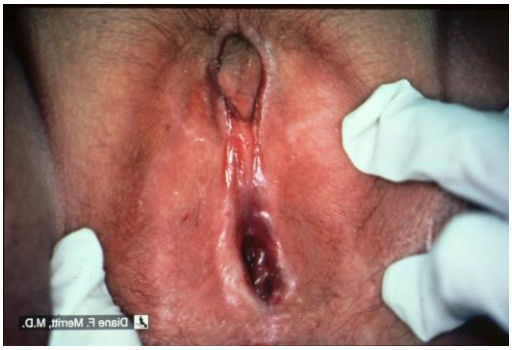
Etiology

- Lack of androgen receptors ⇨ complete (classical TF)
- -Receptors are present but low in NO. or inactive

⇨ incomplete androgen insensitivity

Clinical features of Complete Androgen Insinsitivity

Normal ♀ external genitalia with blind vagina
Absent uterus
Breast development
Present with 1ry amenorrhea
Testes found in abdomen or inguinal canal
Normal ♂ Testosterone level



Rx

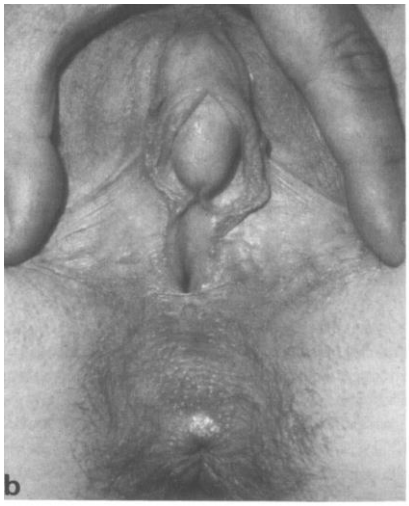
Gonadectomy after puberty due to ↑ incidence of malignant change (5%)
Oestrogen replacement

INCOMPLETE ANDROGEN INSINSITIVITY

Ambiguous genitalia with varying degrees Breast development
Musculinization at puberty

3-TRUE HERMAPHRODITES

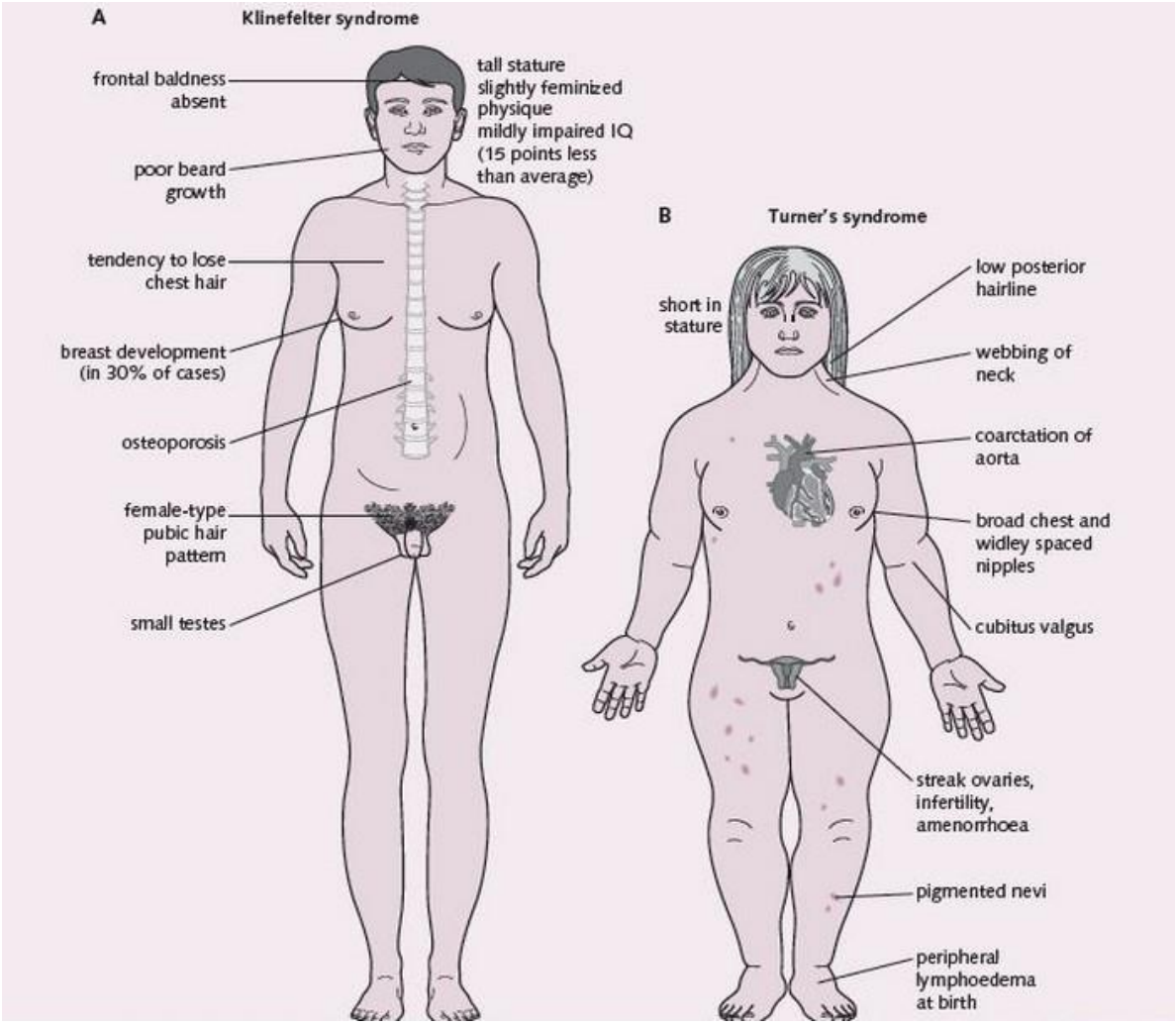
HAVE BOTH OVARIAN & TESTICULAR TISSUE
Ovotestes on one side & ovary or testes on the other
Ovary on one side & testes on the other
Bilateral ovotestes
Varying degrees of sexual ambiguity



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

Klinefelter Syndrome

47XXY
Normal male external genitalia
Tall stature
Gynecomastia
Azospermia (infertility)



♀ Pseudohermaphrodites	♂ Pseudohermaphrodites	True Hermaphrodites
Musculinized ♀ (46XX) ⬆ androgens in utero	Undermusculinized ♂	Have Both Ovarian & Testicular Tissue
A-Congenital Adrenal Hyper Plasia (CAH) -thickening & rugosity of the labia majora resembling the scrotum -A dangerous salt losing syndrome due to deficiency of aldosterone may occure in some pt -Delayed menarche & menstrual	A-Anatomical Testicular Failure Pure gonadal dysgenisis -normal chromosomes 46XY (normal ♀ , ♀ with mild musculinization) -uterus present -Mosaicism 45X/46XY -Variable features (normal ♀, ambiguous genitalia, nearly normal ♂)	Ovotestes on one side & ovary or testes on the other Ovary on one side & testes on the other Bilateral ovotestes
B- Exposure Of The Mother To Androgens: -Rare -Androgen secreting tumours , eg. luteoma, arrhenoblastoma -Drugs	B-Enzymatic Testicular Failure -Defects in the biosynthesis of testosterone -incomplete defect ⇨ Varying degrees of musculinization of the external genetalia -Uterus & tubes ⇨ absent (MIF produced by the testes	Varying degrees of sexual ambiguity
	C-Endorgan Insinsitivity (1-5α Reductase Deficiency) -Formation of the ♂ external genitalia requires 5α REDUCTAS testosterone ⇨ dihydrotestosterone (DHT) - Formation of the internal wollfiane structures respond directly to testosterone -External genitalia ♀ with mild musculinization -Absent uterus -At puberty ⇨ ↑ testosterone secretion ⇨ virilization	KARYOTYPING 46XX ⇨ most common 46XX/XY 46XY 46XY/47XXY

	D-Androgen Insinsitivity - Lack of androgen receptors ⇨ complete (classical TF) -Receptors are present but low in NO. or inactive. Complete Androgen Insinsitivity -Normal ♀ external genitalia with blind vagina -Absent uterus -Breast development Present with 1ry amenorrhea -Testes found in abdomen or inguinal canal -Testosterone level Incomplete Androgen Insinsitivity -Ambiguous genitalia with varying degrees Breast development Musculinization at puberty