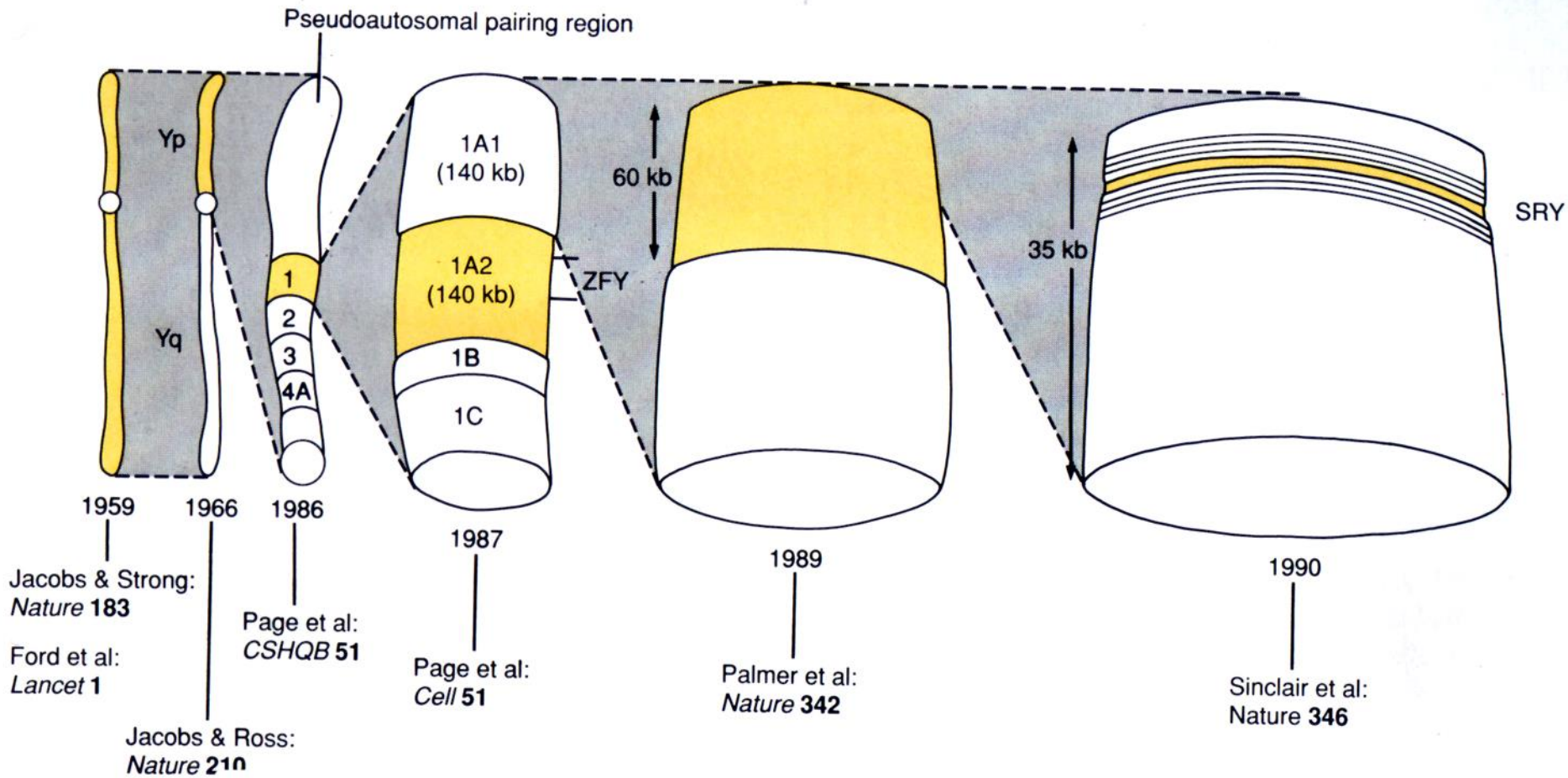


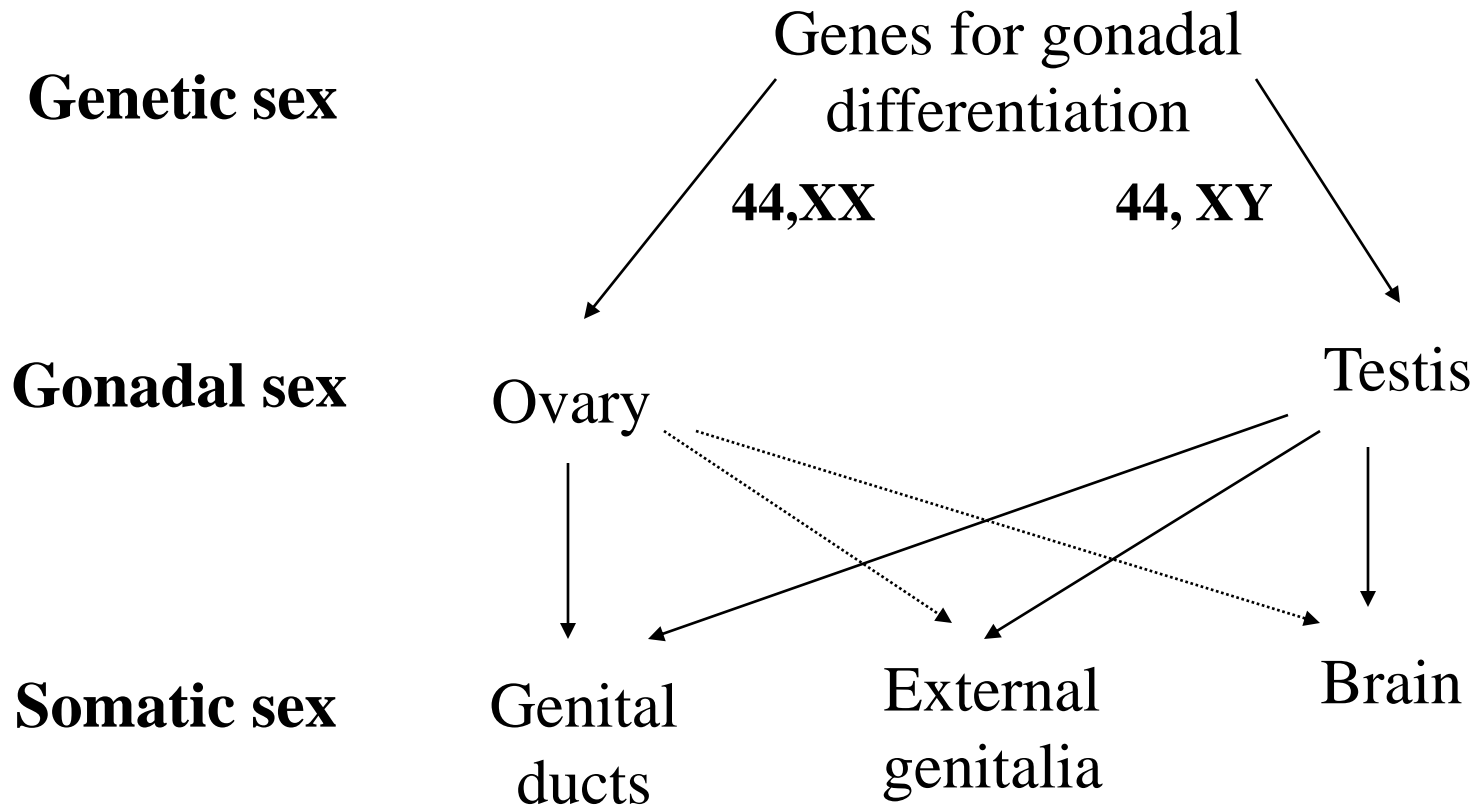
# Development of the Genital System

1. Sexual differentiation
2. Differentiation of the gonads
  - a. Germ cells – *extragonadal* in origin
  - b. Genital ridge – intermediate mesoderm consisting of bipotential cell types to differentiate into testis/ovary
3. Differentiation of genital ducts – two independent duct systems (male & female) and two patterns of morphogenesis



## The history of the search for the sex-determining region of the Y chromosome

# SEXUAL DIFFERENTIATION



# Gonadal Sexual differentiation

## Hormones

- Testosterone
- Antimullerian hormone
- Ins13



Testis with Sertoli  
& Leydig cells

*Cyp26b1*

*Fgf9*

*Sox9*

*Sry*

Ovary

*Stra8*

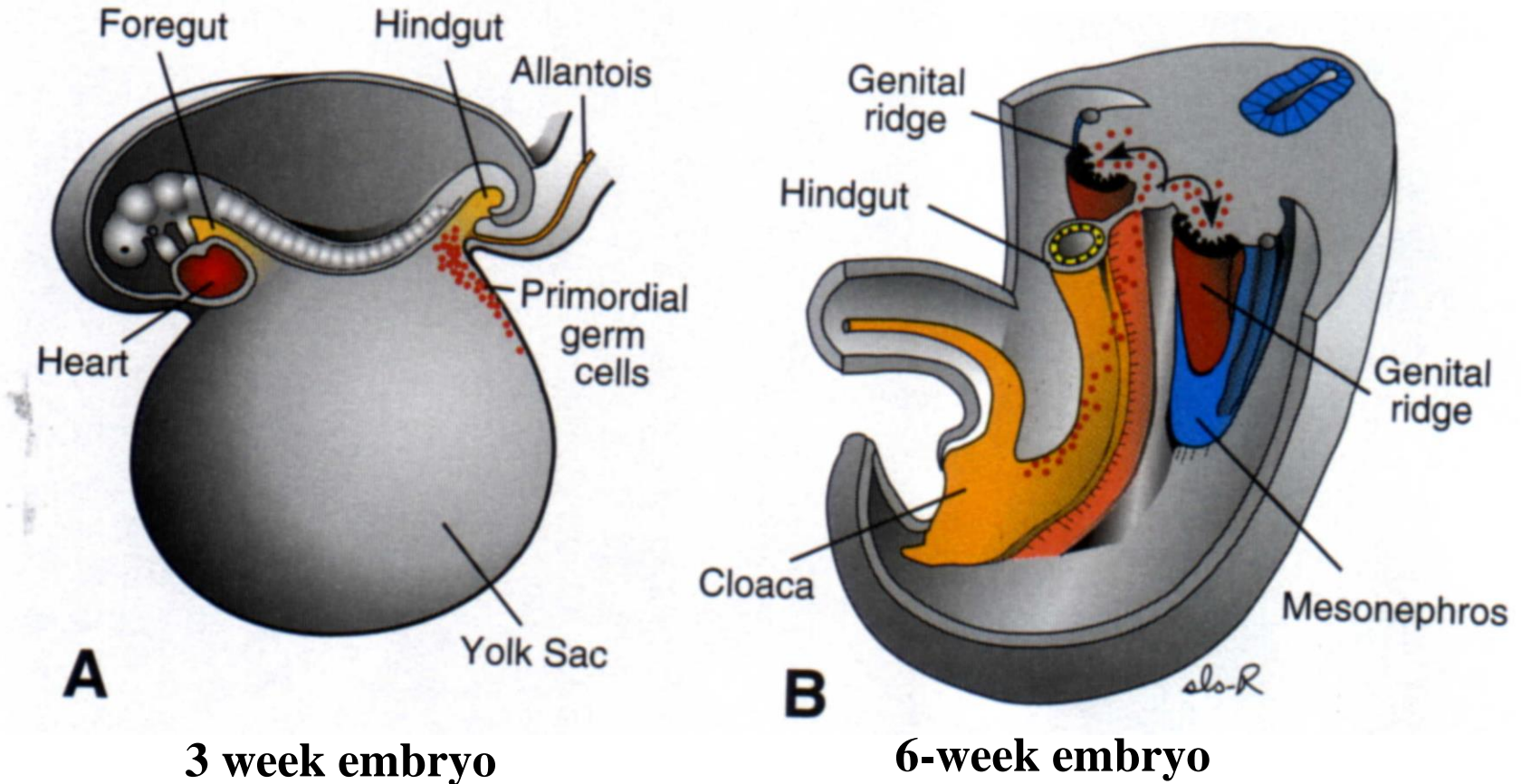
*Dmc1*

*Retinoic acid*

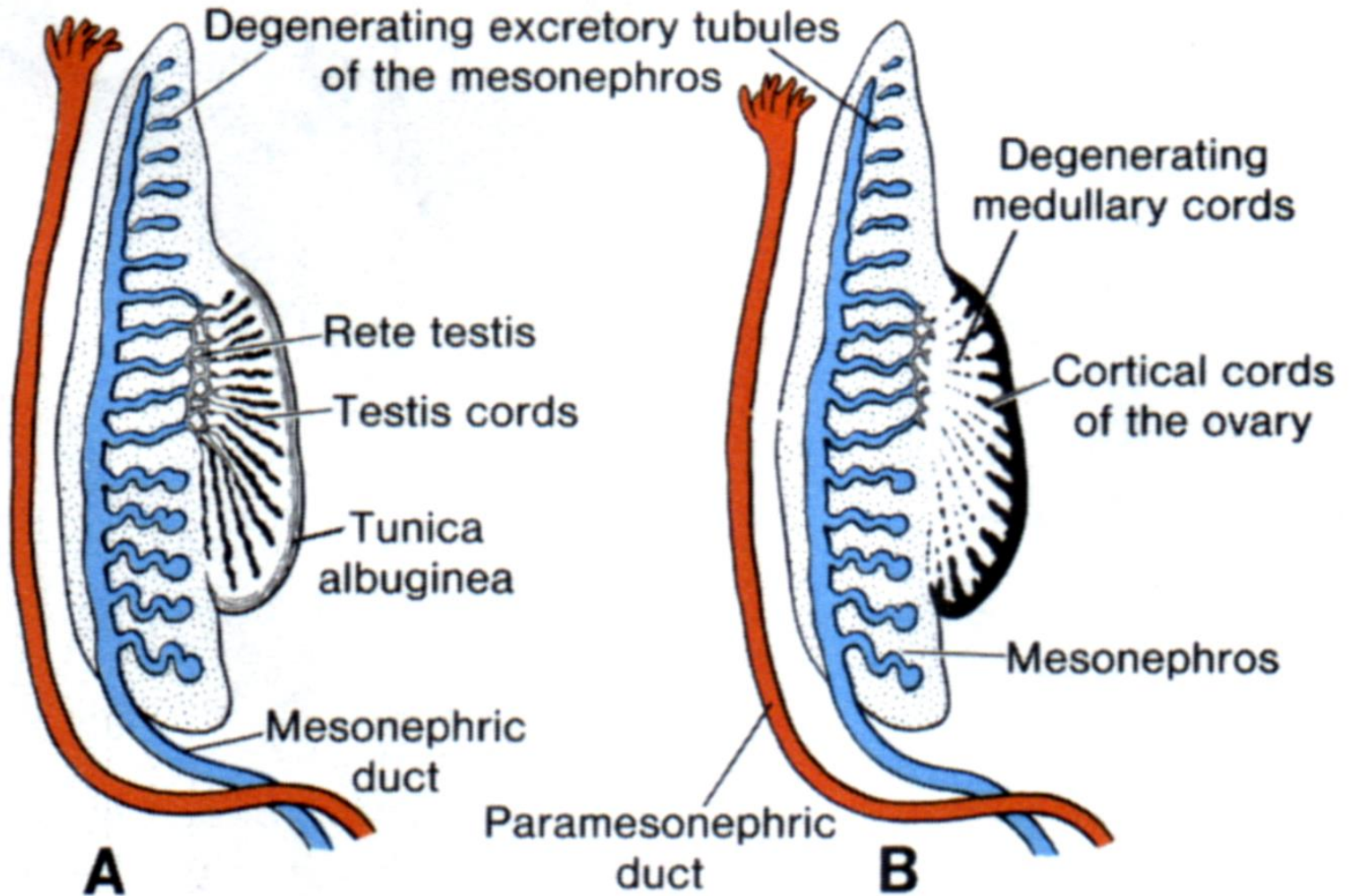


<b>Mouse</b>	11.5	12.51	13.5	14.5	<i>days pc</i>
<b>Man</b>	42	45	48	51	days post fertilisation

# Germ cells originate from the epiblast during early gastrulation



**Migration of primordial germ cells during development**



**Genital ducts in the sixth week in the male (A) and female (B)**

## Testis in the male:

- Germ cells: 44,XY

mitosis 3<sup>rd</sup>-12<sup>th</sup> week

- Genital ridge

**Mesenchyme form cords enclosing germ cells**



**Medullary cords proliferates(6<sup>th</sup> week)**



**Seminiferous tubules & Leydig cells**

# Ovary in the female:

- Germ cells: 44,XX

mitosis 3<sup>rd</sup> – 8<sup>th</sup> week

meiosis 8<sup>th</sup> week – 4<sup>th</sup> month

- Genital ridge

Mesenchyme form cords enclosing germ cells



Cortical cords proliferate (7<sup>th</sup> week)



Cords break up into segments



Germ cells separated individually  
(primordial follicles)

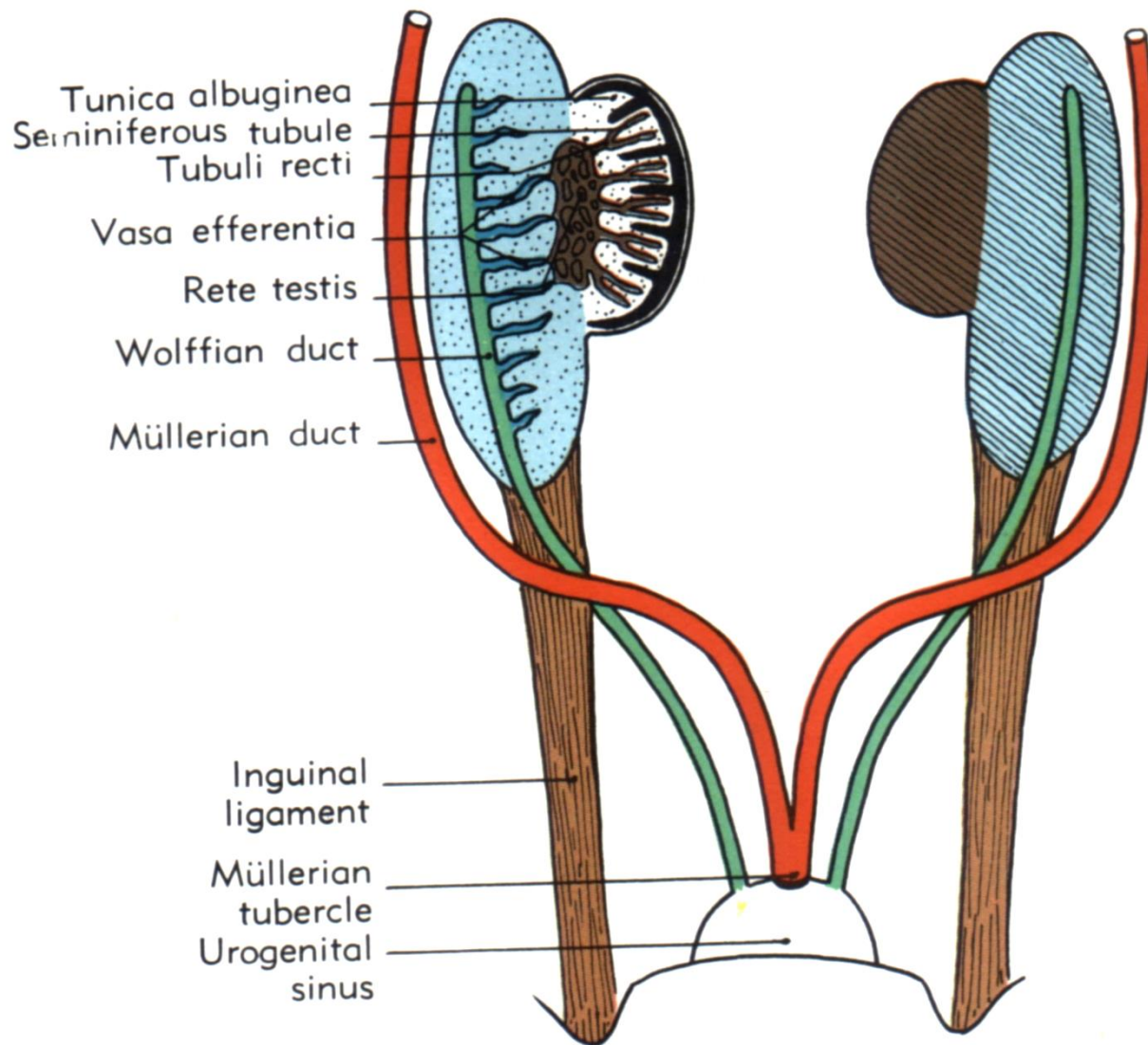


# **Genital ducts:**

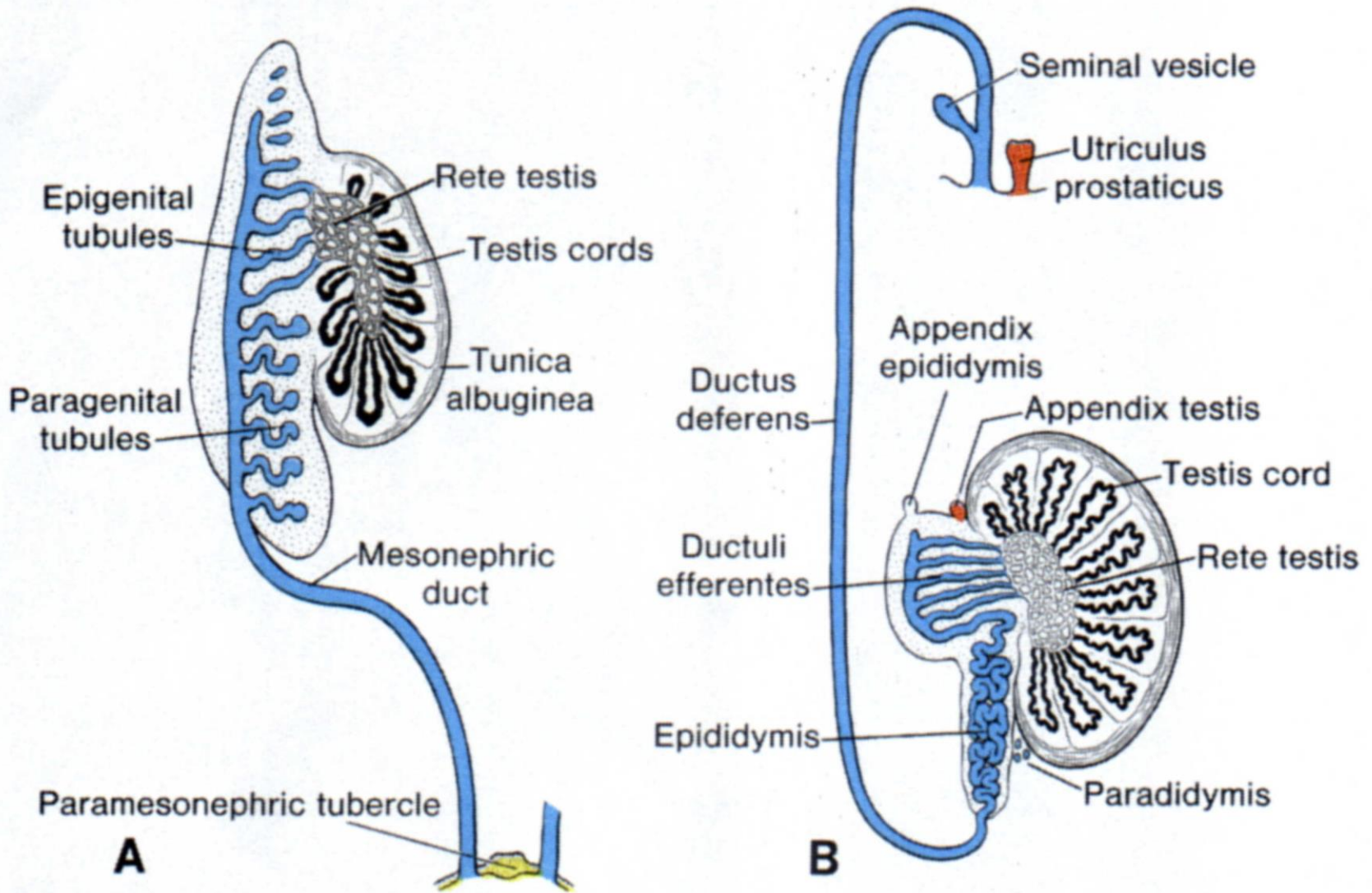
**Indifferent stage: 2 sets of ducts**

**Wolffian ducts (mesonephric ducts)**

**Mullerian ducts (paramesonephric ducts)**



## Undifferentiated urogenital system



**Development of the male genital ducts**

# Male reproductive ducts:

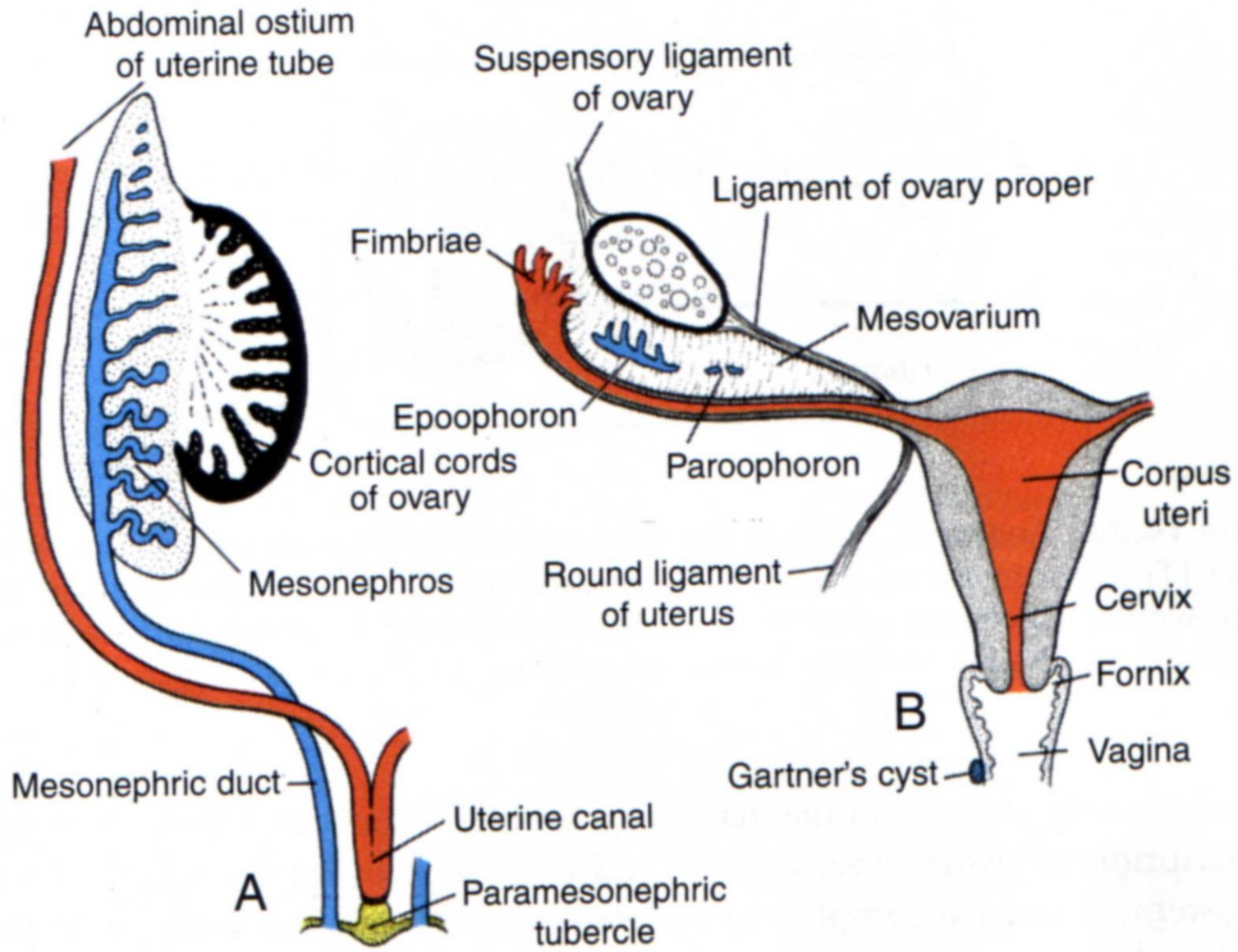
**Sertoli cells** —→ **Mullerian Inhibitory Factor**  
(regression of Mullerian ducts)

**Leydig cells** —→ **Testosterone**  
(stimulate differentiation of  
Wolffian ducts)

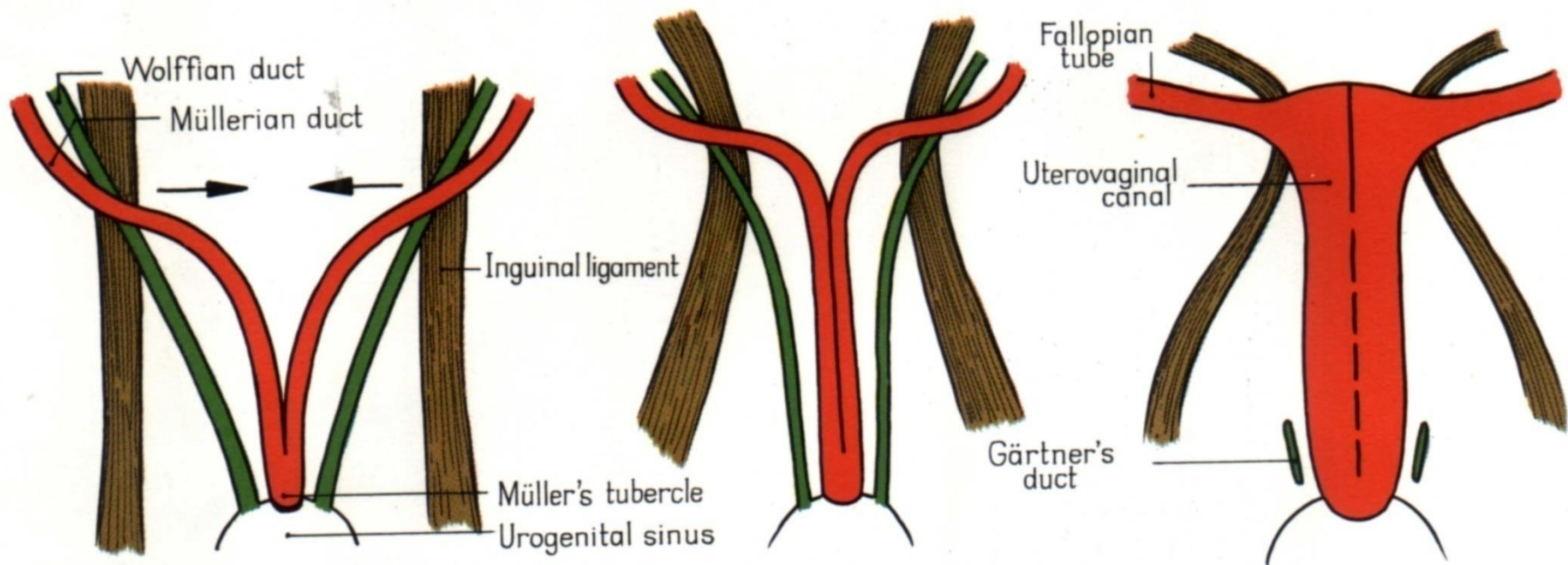
**Wolffian duct** —→ **Ducti efferentus, epididymis,  
ducti deferens, seminal vesicle**

**Mesonephros remains** —→ **appendix epididymis,  
paradidymis**

**Mullerian remains** —→ **appendix testis, prostatic  
utricle**



**Development of the female genital ducts**



**Fig. 1. — Formation of uterus.**

# Female reproductive ducts:

No MIF → Mullerian ducts develop

No testosterone → Wolffian ducts do not develop

Distal part of → fuse to form uterus

Mullerian ducts (uterine septum degenerates)

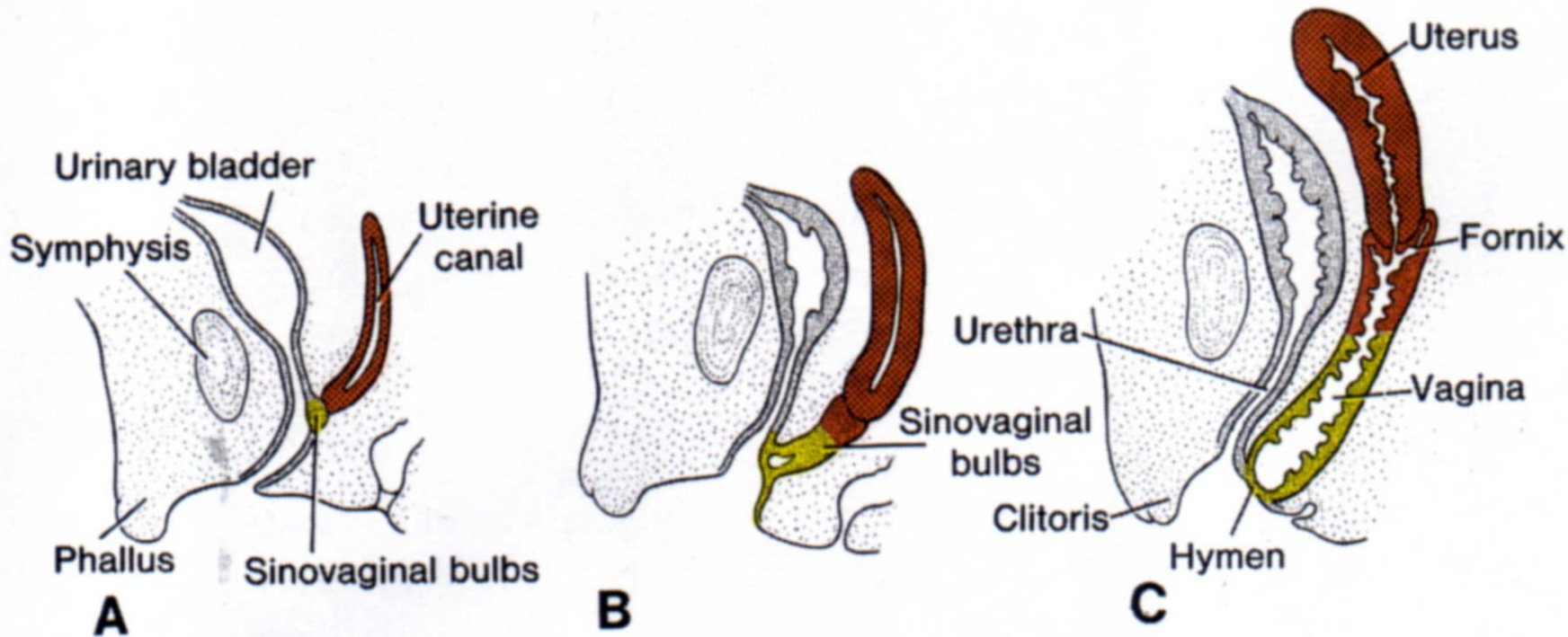
Proximal part of → oviduct

Mullerian duct

Distal end of → vagina

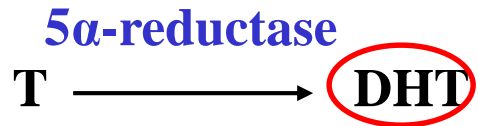
Mullerian duct (with urogenital sinus)

Mesonephros remains - epoophoron; Gartner's duct (paraoophoron)

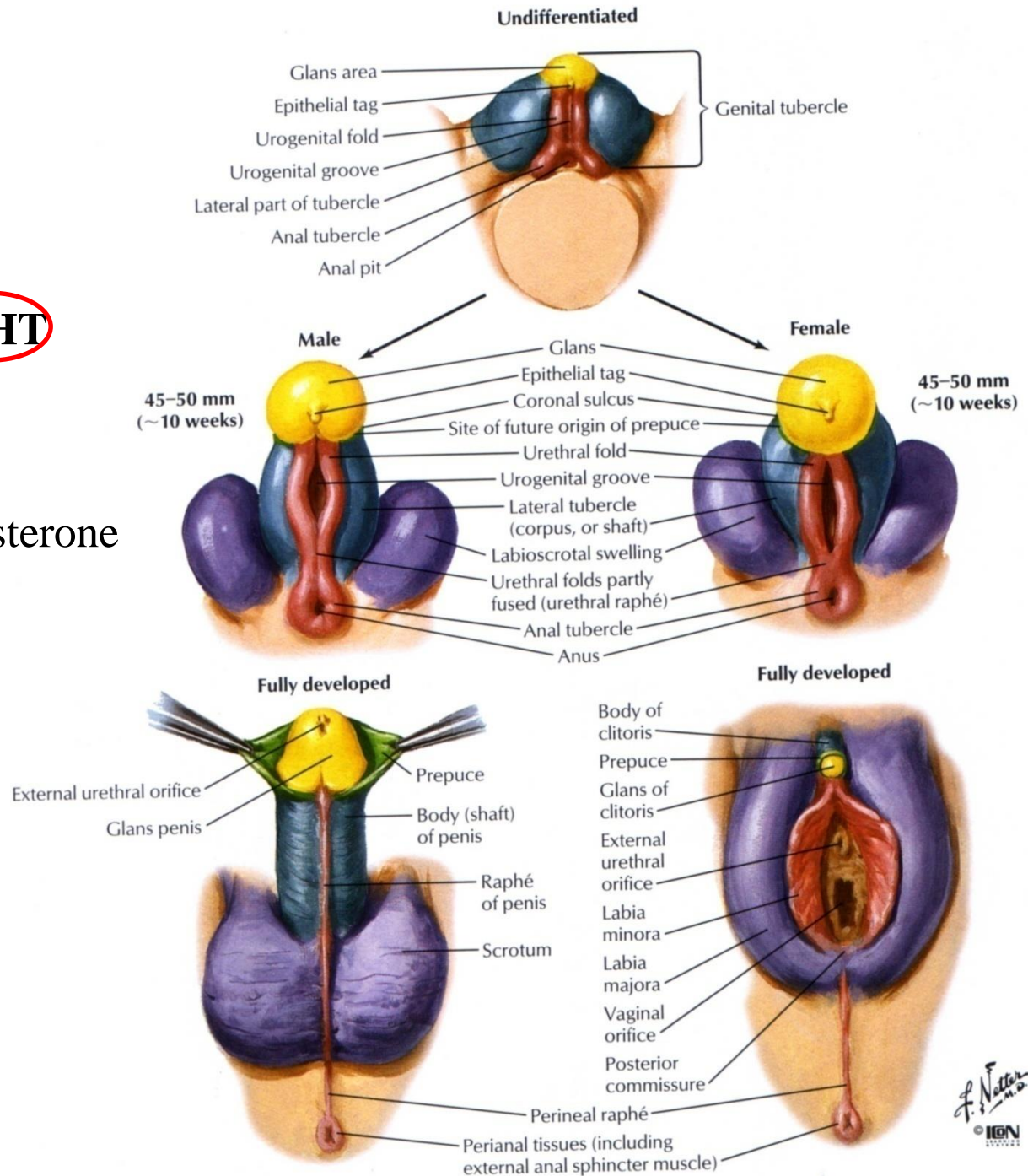


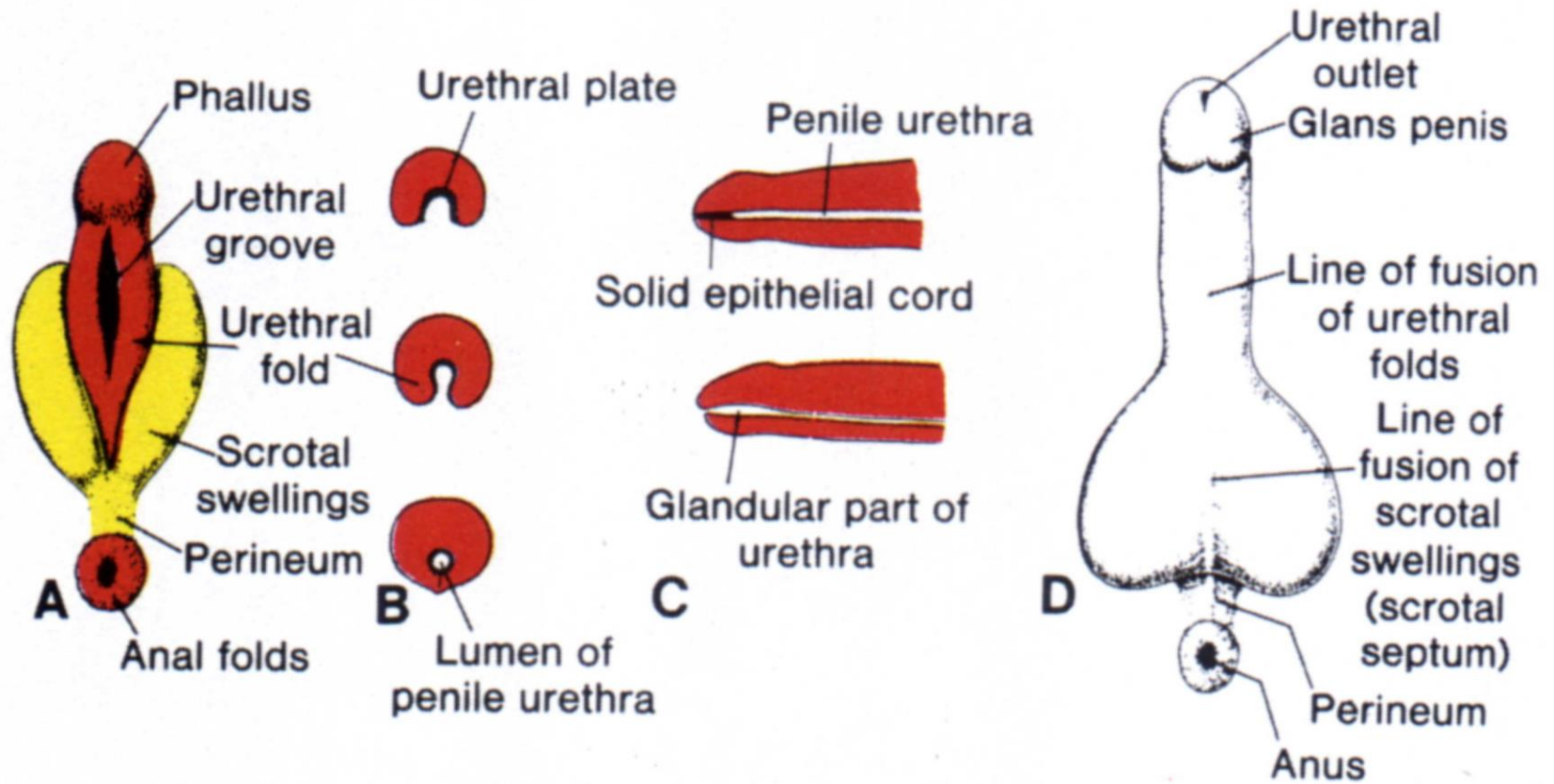
## Formation of vagina





DHT= dihydrotestosterone





## Development of the penile urethra

# Summary of External Genitalia Sexual Differentiation

The differentiation is directed by  
**Dihydrotestosterone (DHT)**

Indifferent state	Male with DHT	Female with no DHT
Cloacal folds (urethral/genital folds)	Penile urethra	Labial minora
Genital tubercle	Penis	Clitoris
Genital swelling	Scrotum	Labial majora

# Descent of testis

## Chronology of descent

- 3<sup>rd</sup> month – descend to iliac fossa
- 4<sup>th</sup>-7<sup>th</sup> month - at internal inguinal ring
- 7<sup>th</sup> month – travels through inguinal canal
- 8<sup>th</sup> month – at external inguinal ring
- 9<sup>th</sup> month - enter scrotum

# Cryptorchidism

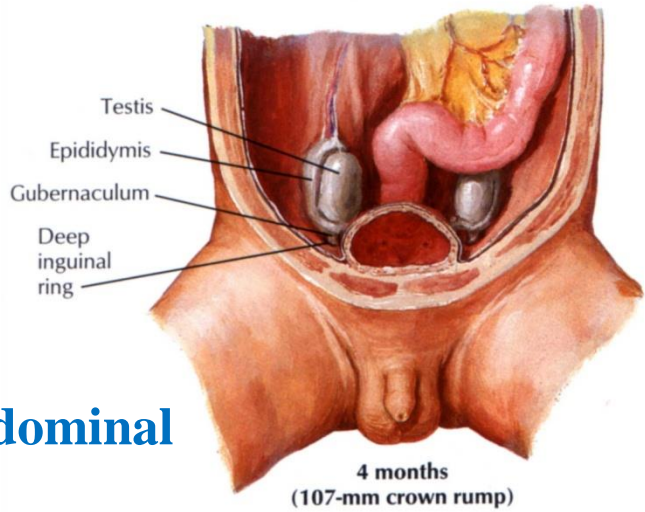
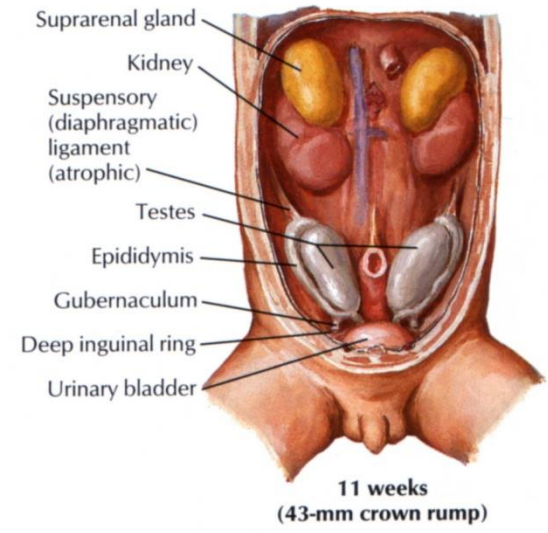
**No descent 1 year after birth**

**4% in full term births**

**33% undescended testis in premature births**

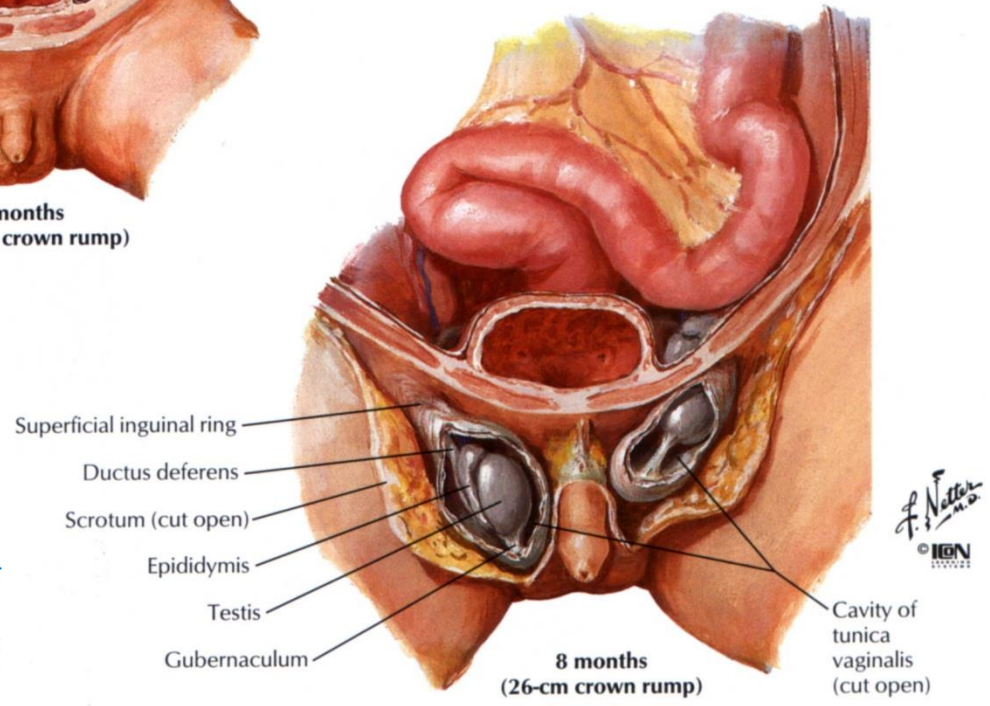
**(0.7% remain undescended in 3 months)**

# Positions of the testis at different stages of development

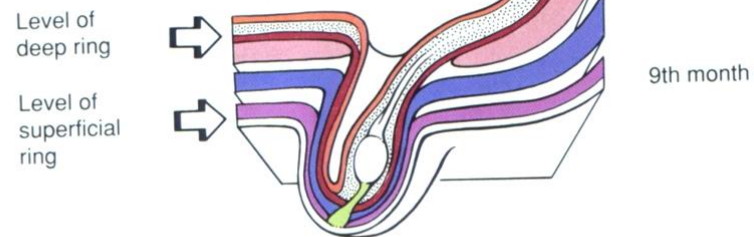
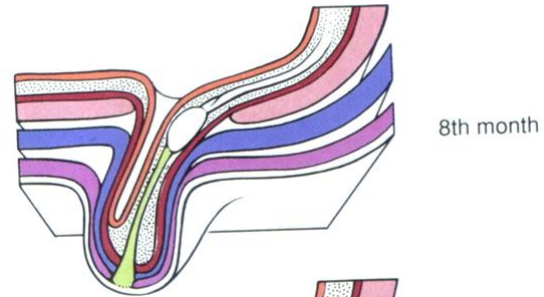
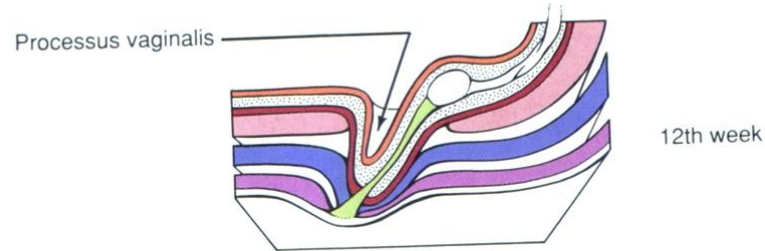
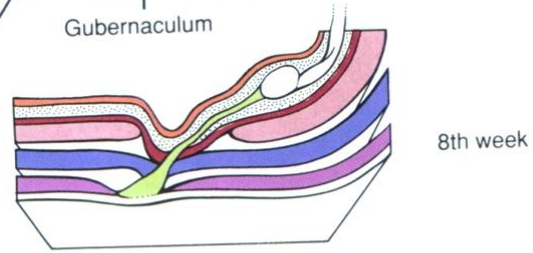
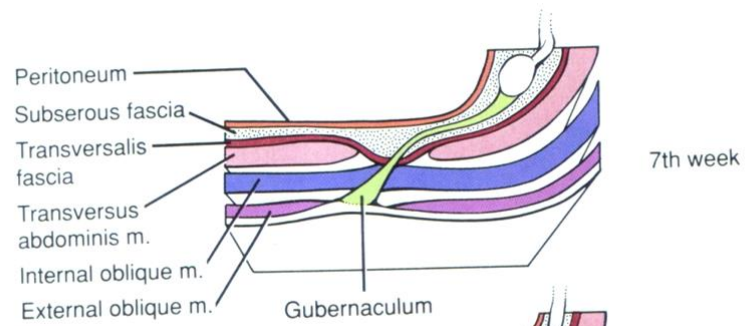


## Trans-abdominal phase

## Inguino-scrotal phase



# Testicular descent



# Mechanism of testicular descent:

Testicular descent occurs in two distinct and sequential phases:

- The *transabdominal phase* – the gubernaculum develops and grows pulling the testis toward the base of the abdomen.
- The *inguinal scrotal phase* – development of the cranial suspensory ligament is blocked leading to its regression. Involution of the gubernaculum allows the testis to go through the inguinal canal into the scrotum.

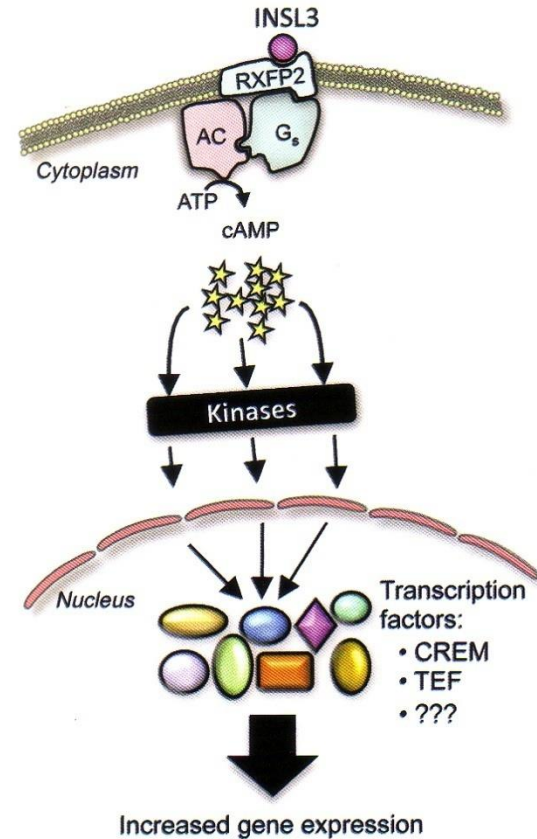


Each of the two phases of testicular descent is regulated by a hormone secreted by the Leydig cells:

- INSL3 regulates the transabdominal phase;
- Testosterone controls the inguino-scrotal phase.

**Other factors:**

- Direct effect of testosterone also cause lengthening of vas deferens and testicular vessels
- Maternal hormones (e.g. LHRH, lutenizing hormone releasing hormone; LH, lutenizing hormone) stimulate testosterone production.



cAMP	Neurogenesis	WNT	BMP
<i>Crem</i>	<i>Pnoc</i>	<i>Wnt2</i>	<i>Bmp1</i>
<i>Pde10a</i>	<i>Pcsk2</i>	<i>Wnt4</i>	<i>Bmp2</i>
<i>Pde8a</i>		<i>Wnt5a</i>	<i>Bmp3</i>
<i>Pde4d</i>		<i>Wnt9a</i>	<i>Bmp5</i>
		<i>Wnt16</i>	<i>Bmp7</i>
			<i>Chrdl2</i>

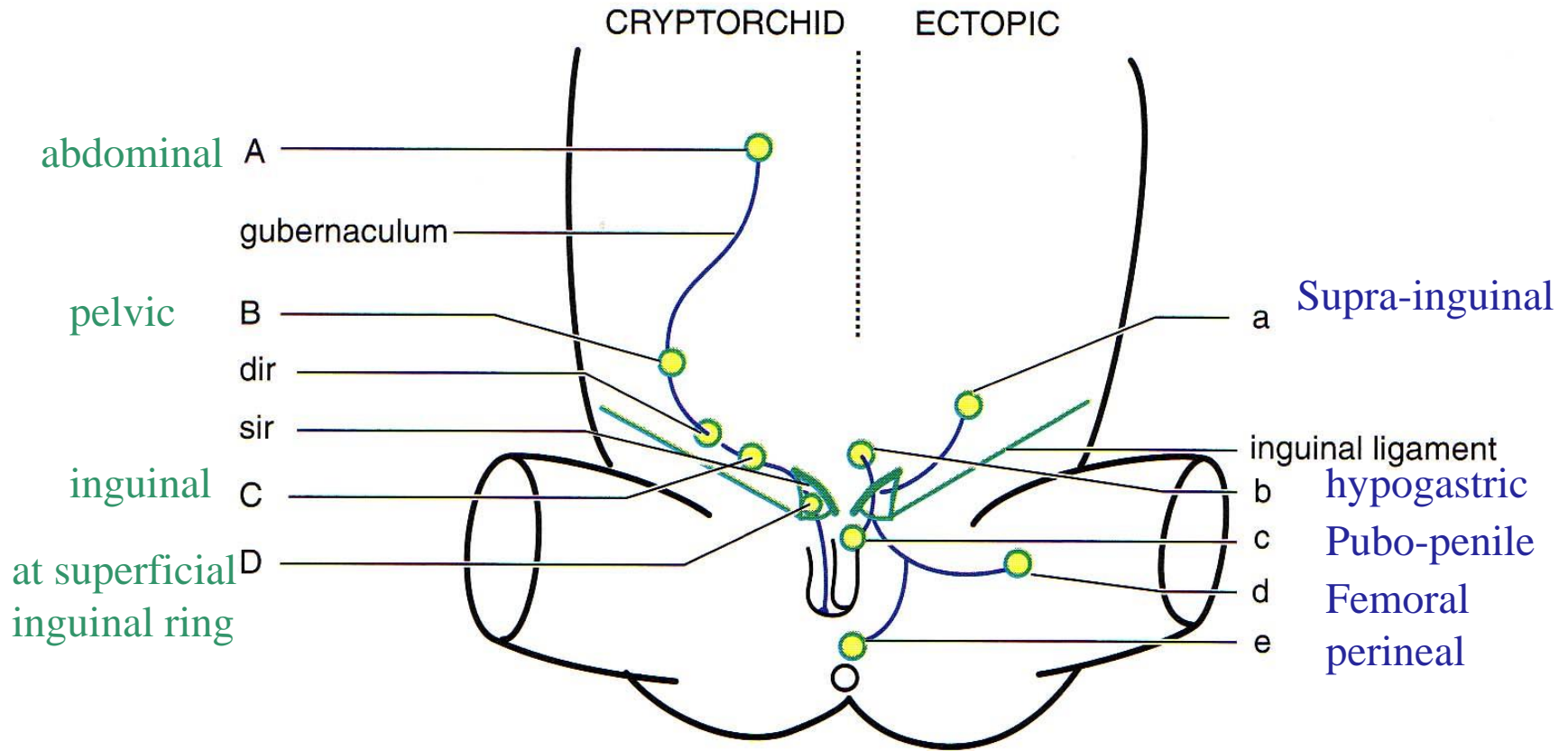
# Fate of processus vaginalis:

Processus vaginalis occludes at 2 points soon after birth:

- Internal inguinal ring
- Above the testis

## **Anomalous development**

- Indirect inguinal hernia
- Congenital hydrocoele
- Ectopic testis
- Cryptorchidism



## Abnormal descent of the testis

# Congenital anomalies:

## 1. Hermaphroditism

- True hermaphrodite (presence in one individual of both testicular and ovarian tissues)
- Pseudohermaphrodites (external genitalia are characteristic of one sex and gonads are of the other sex) e.g. androgen insensitivity, congenital adrenal hyperplasia.

## 2. Uterovaginal malformation

- Uterus didelphys
- bicornuate uterus
- Uterus bicornuate unicollis
- vaginal atresia

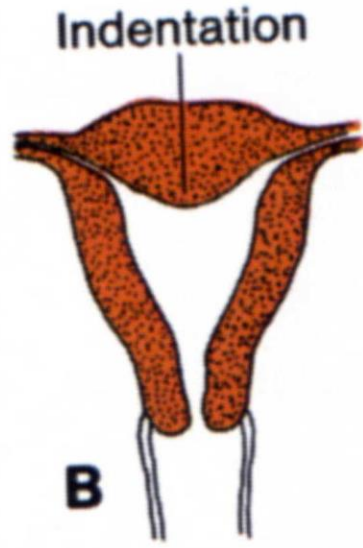
## 3. Testicular dysgenesis syndrome

- Cryptorchidism
- Hypospadias
- Infertility due to widespread Sertoli cell-only areas in the testis (results from germ cells fail to colonize)

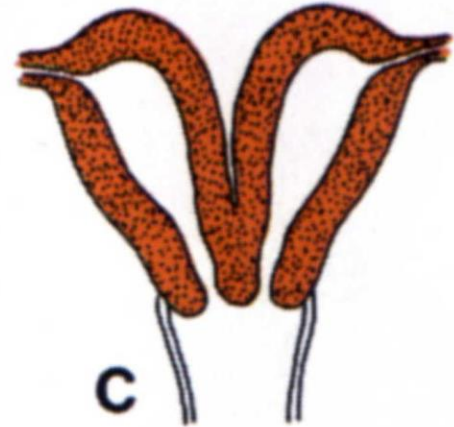
Uterine tube



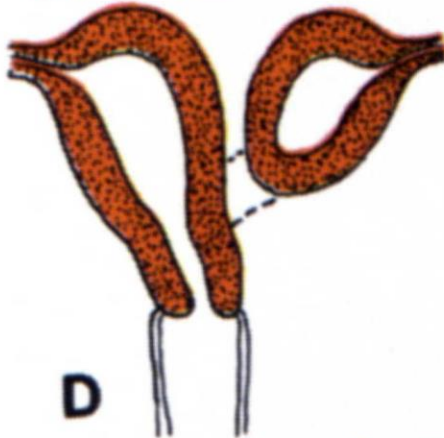
**A**  
Uterus didelphys  
with double vagina



**B**  
Uterus arcuatus



**C**  
Uterus bicornis



**D**  
Uterus bicornis unicollis  
1 rudimentary horn



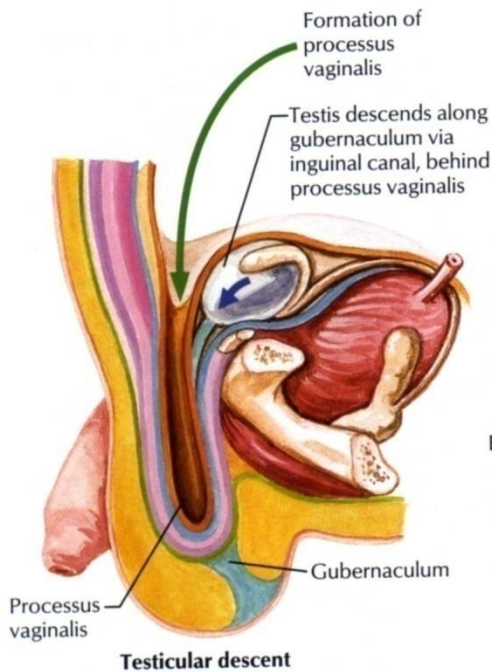
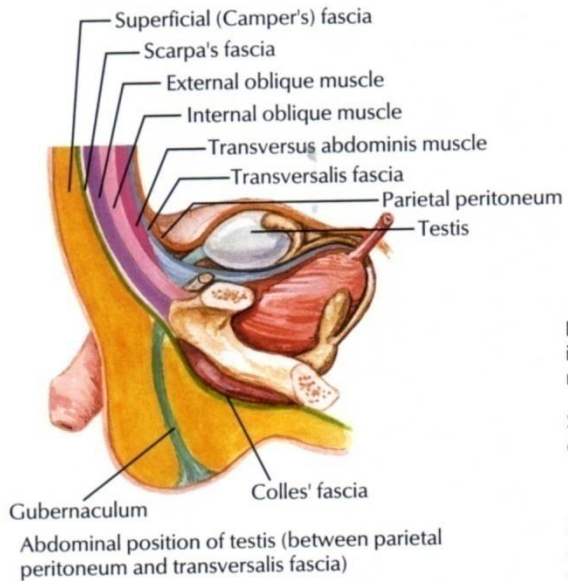
**E**  
Atresia of cervix



**F**  
Atresia of vagina

## *References:*

- Cochard LR (2002) Netter's Atlas of Human Embryology.
- Sadler TW (2005) Langman's Essential Medical Embryology. 9<sup>th</sup> edition Lippincott Williams & Wilkins



Layers of the abdominal wall and their counterparts in the scrotum or spermatic cord (indicated in parentheses):

