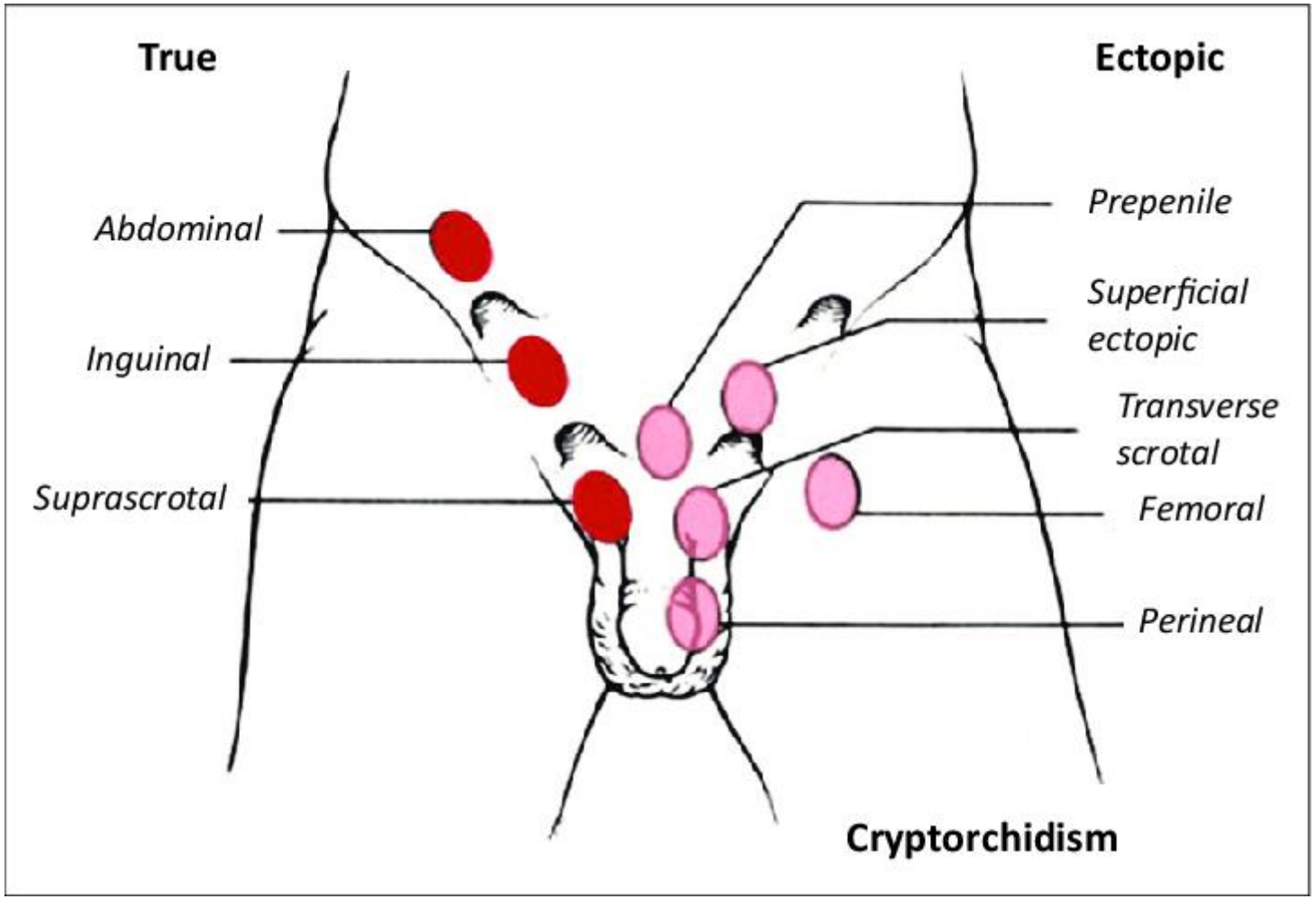
Cryptorchidism

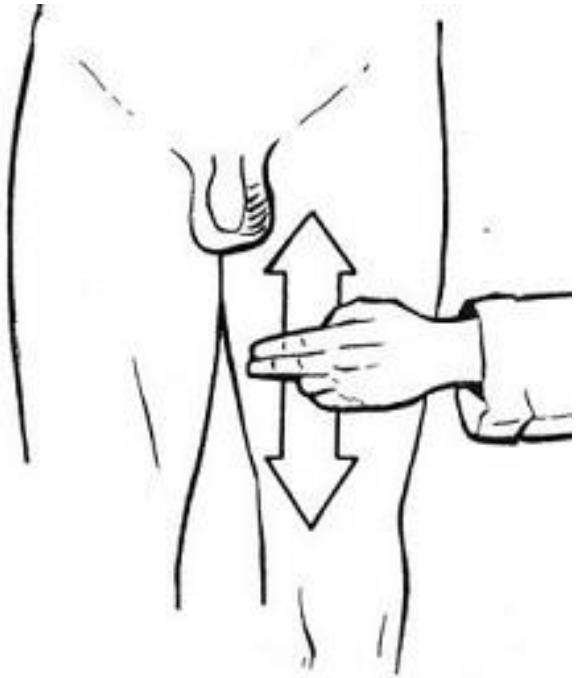
- Ectopic
- Retractile testes
- Undescended
- Absent

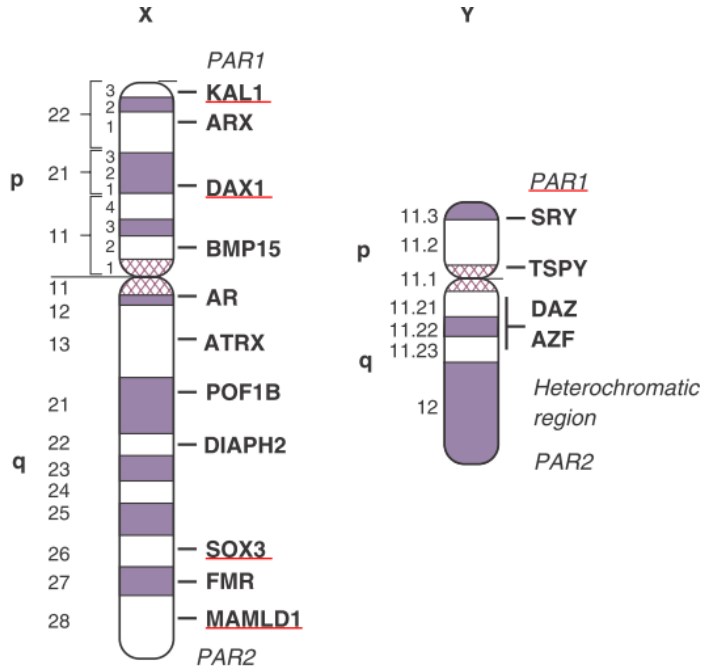


Retractile (pseudocryptorchidism)

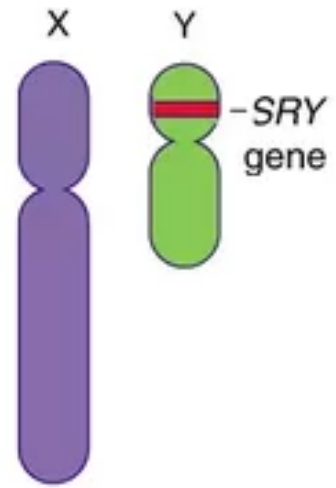
- Boys older than age 1 yr often have a brisk cremasteric reflex
- not at increased risk for infertility or malignancy.
- it can become an acquired undescended testis (1/3, < 7 years)
  - Risk for infertility or malignancy
  - monitored every 6-12 mo with follow-up

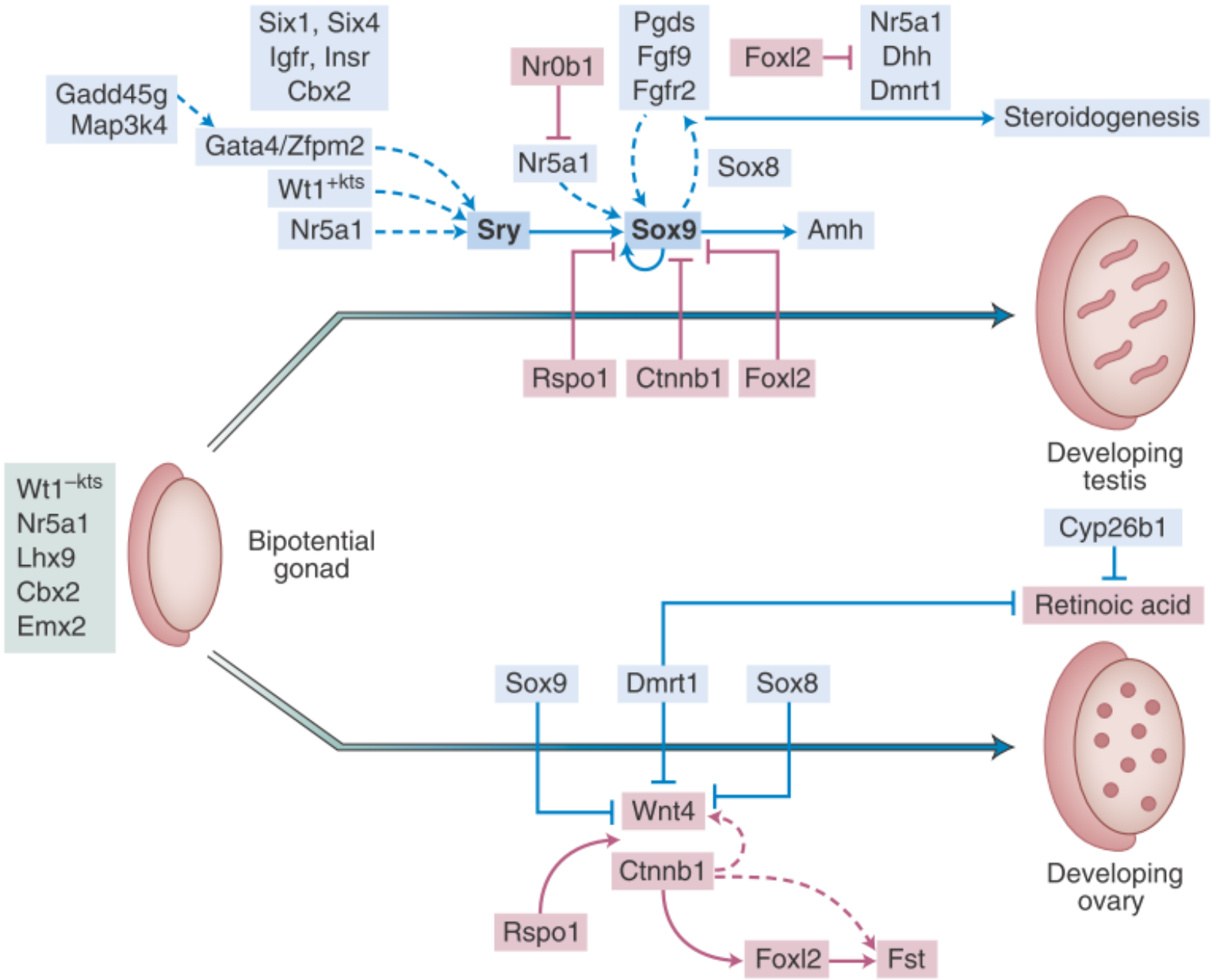
PE: Valsalva maneuver for retractile testes / Hot bath

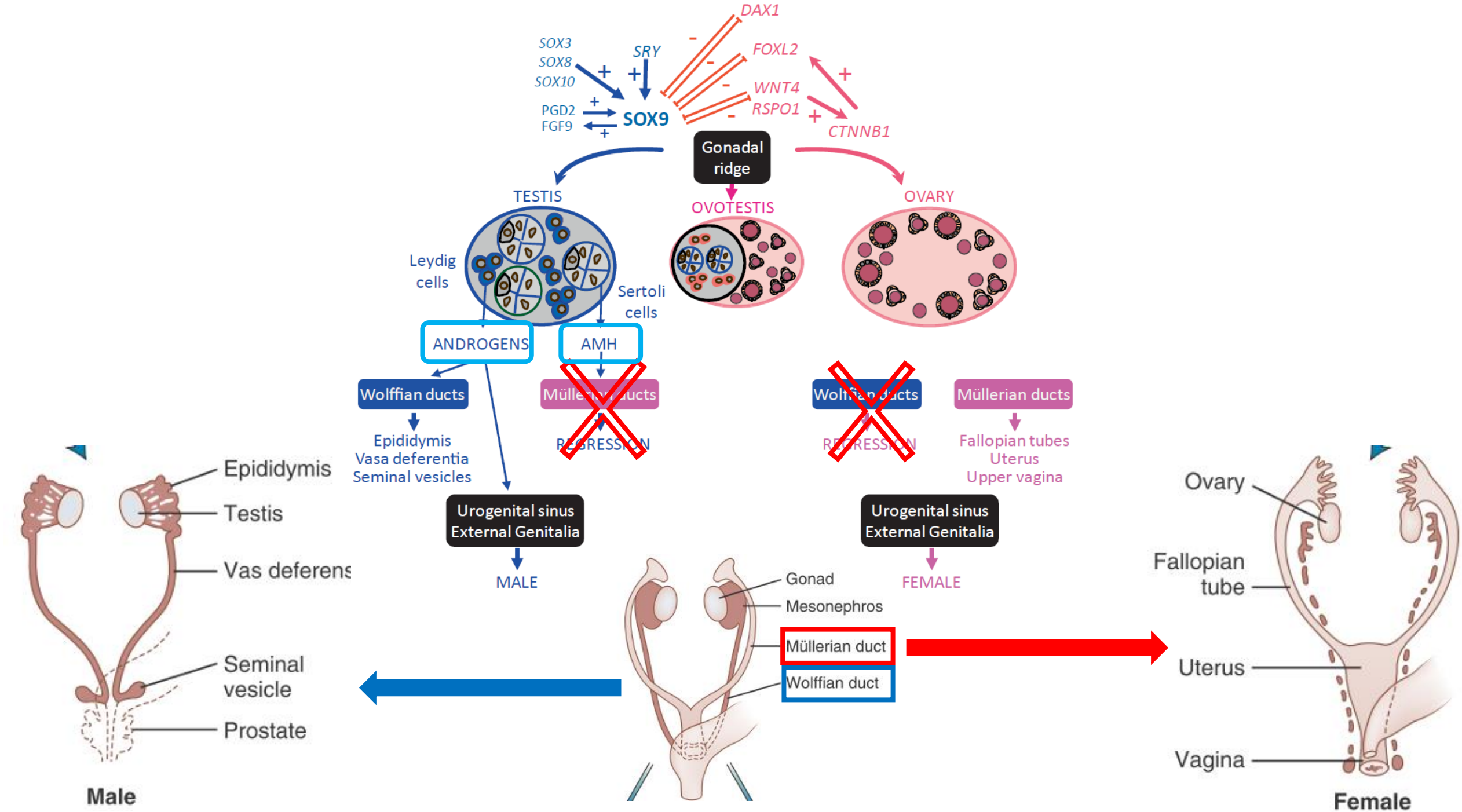




sex-determining region on the Y chromosome

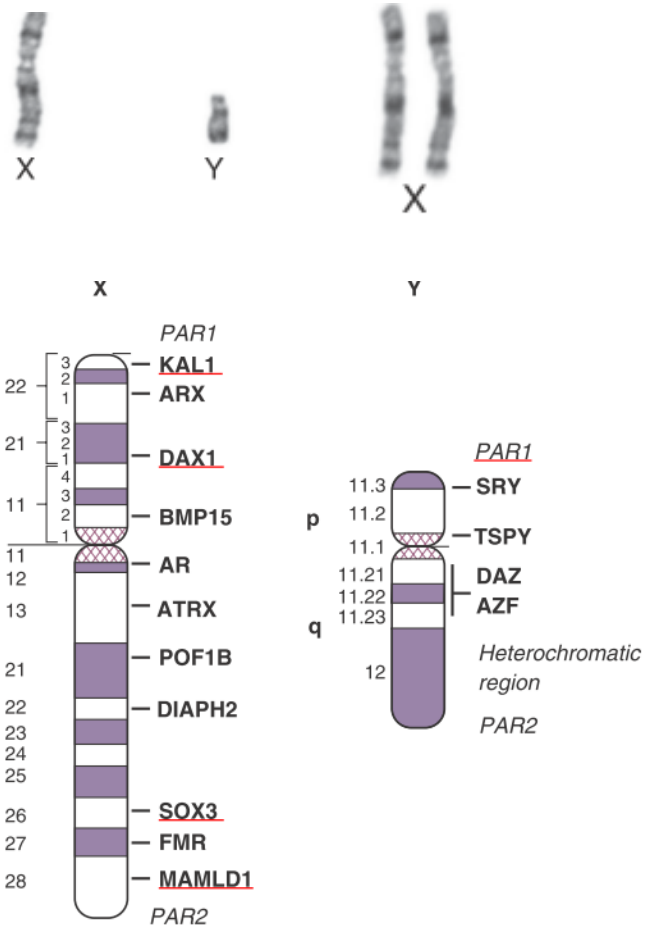




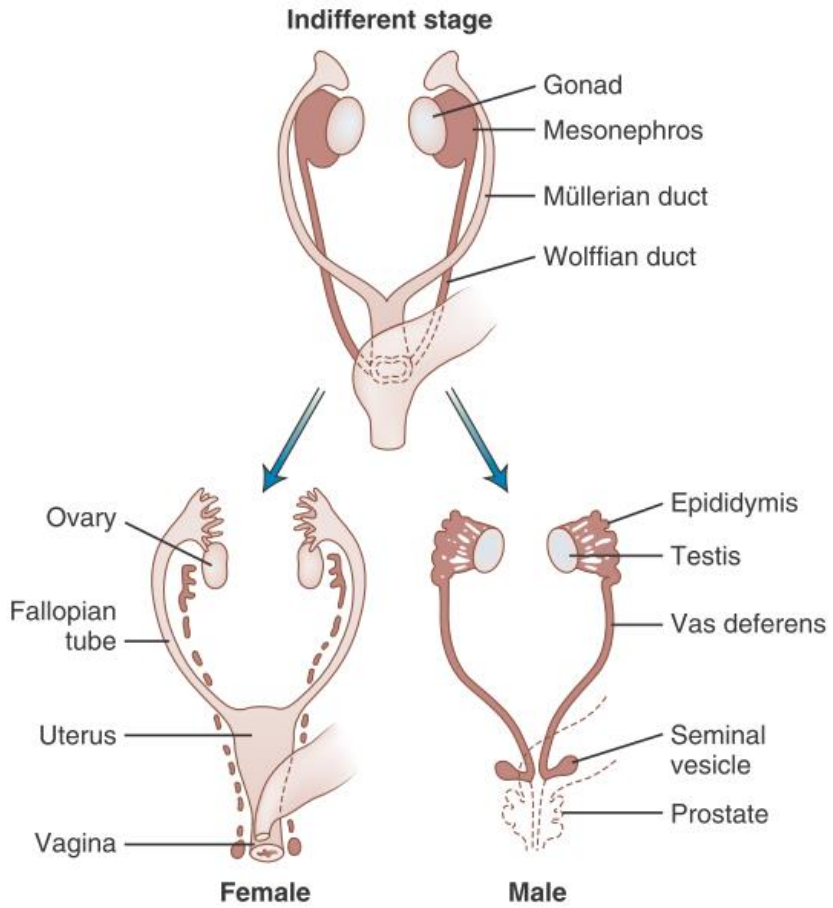

DAX1
SOX3
SOX8
SOX10
SRY
FOXL2
WNT4
RSPO1
CTNNB1
PGD2
FGF9
SOX9
Gonadal ridge
TESTIS
OVOTESTIS
OVARY
Leydig cells
Sertoli cells
ANDROGENS
AMH
Wolffian ducts
Müllerian ducts
REGRESSION
Epididymis
Vasa deferentia
Seminal vesicles
Urogenital sinus
External Genitalia
MALE
Fallopian tubes
Uterus
Upper vagina
FEMALE
Epididymis
Testis
Vas deferens
Seminal vesicle
Prostate
Male
Gonad
Mesonephros
Müllerian duct
Wolffian duct
Ovary
Fallopian tube
Uterus
Vagina
Female

Chromosomal sex

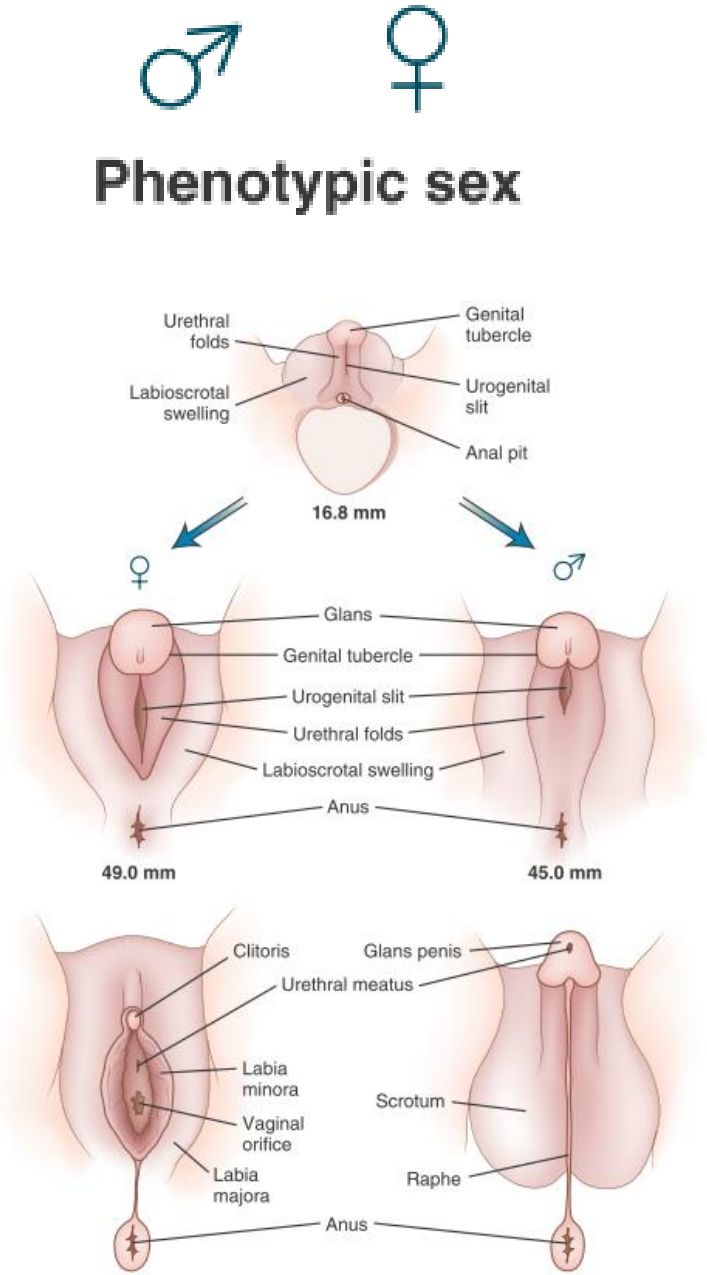
XY XX

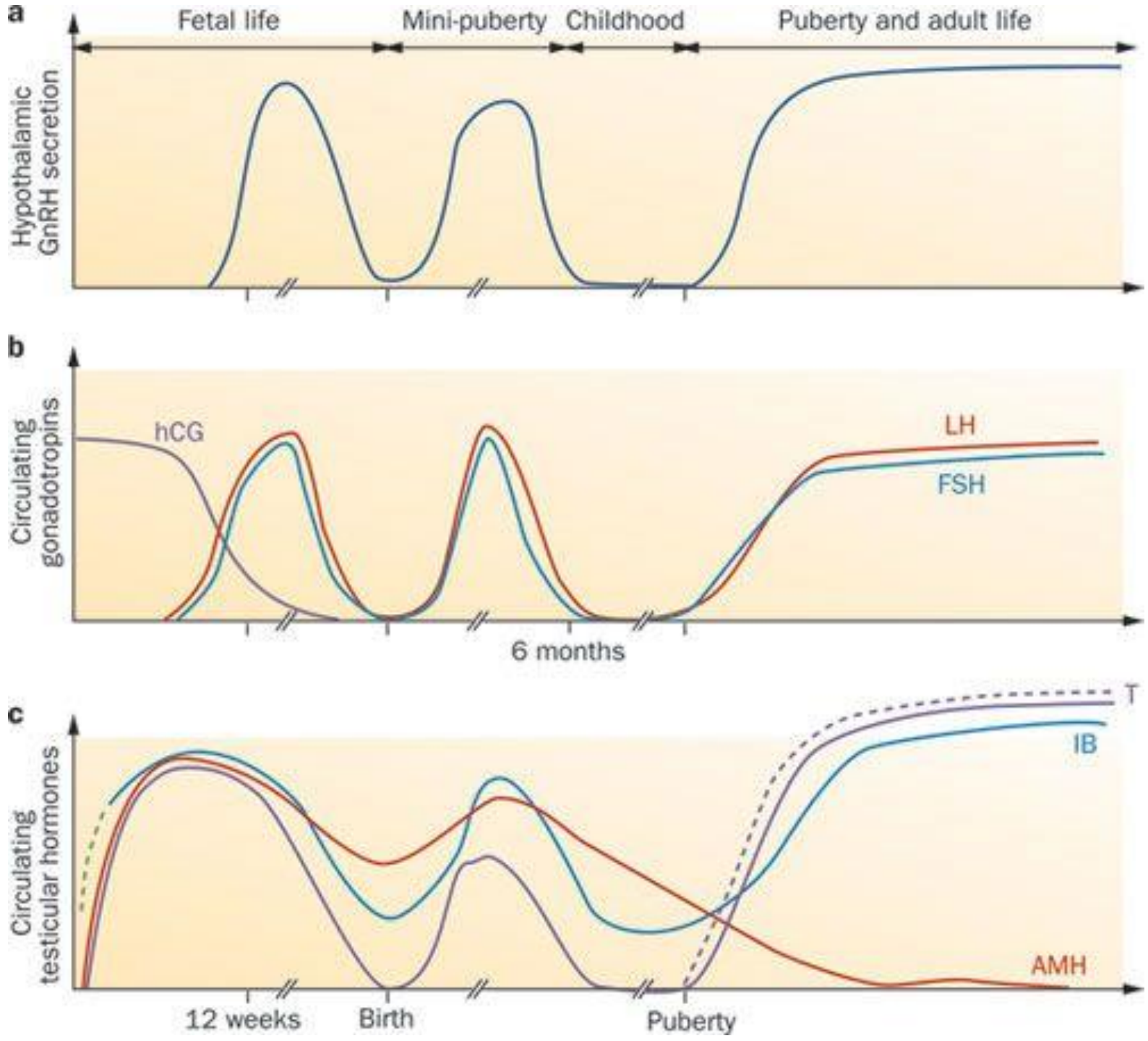


Gonadal sex



Phenotypic sex




a
Fetal life
Mini-puberty
Childhood
Puberty and adult life
Hypothalamic GnRH secretion
b
Circulating gonadotropins
hCG
LH
FSH
6 months
c
Circulating testicular hormones
T
IB
AMH
12 weeks
Birth
Puberty

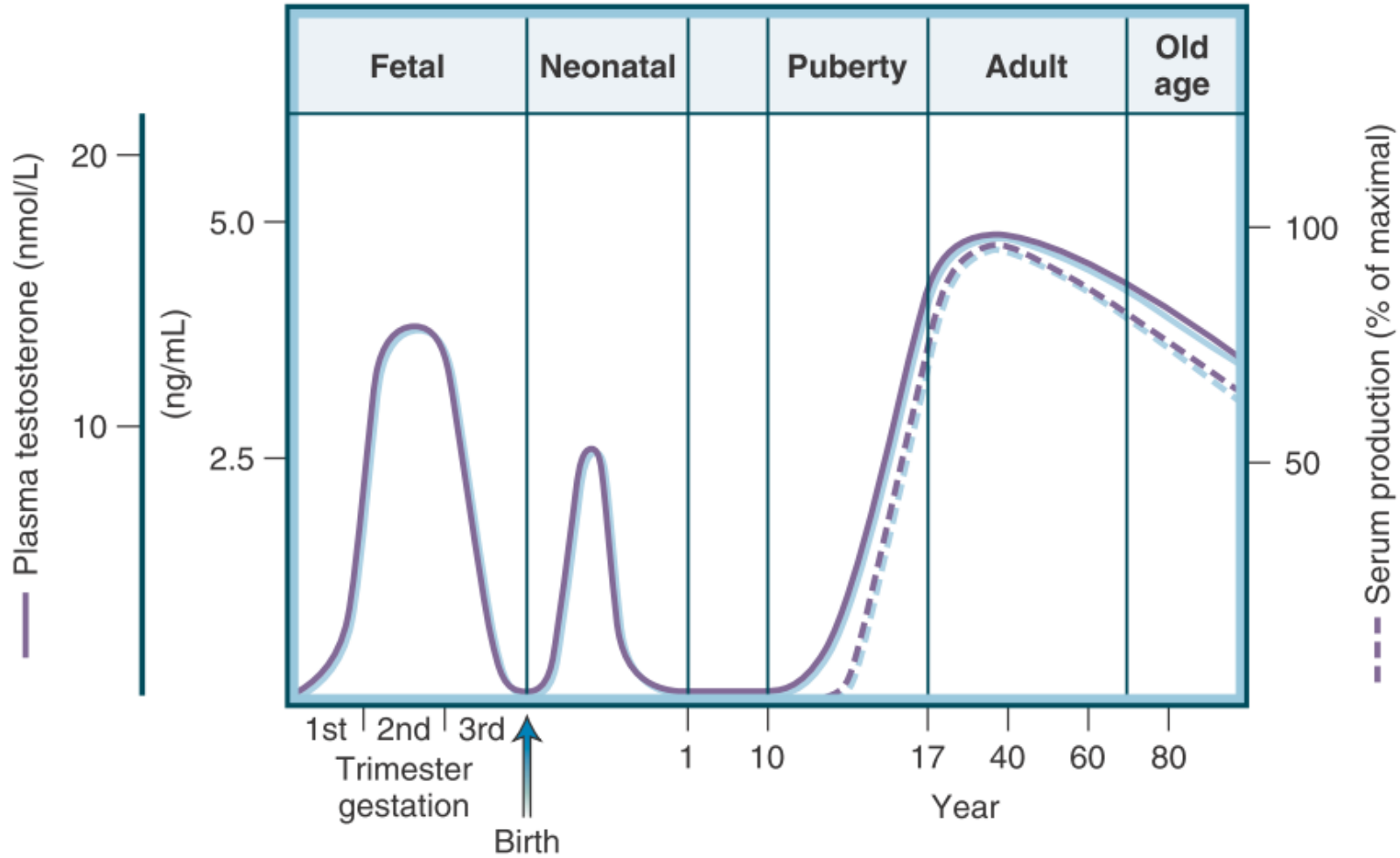
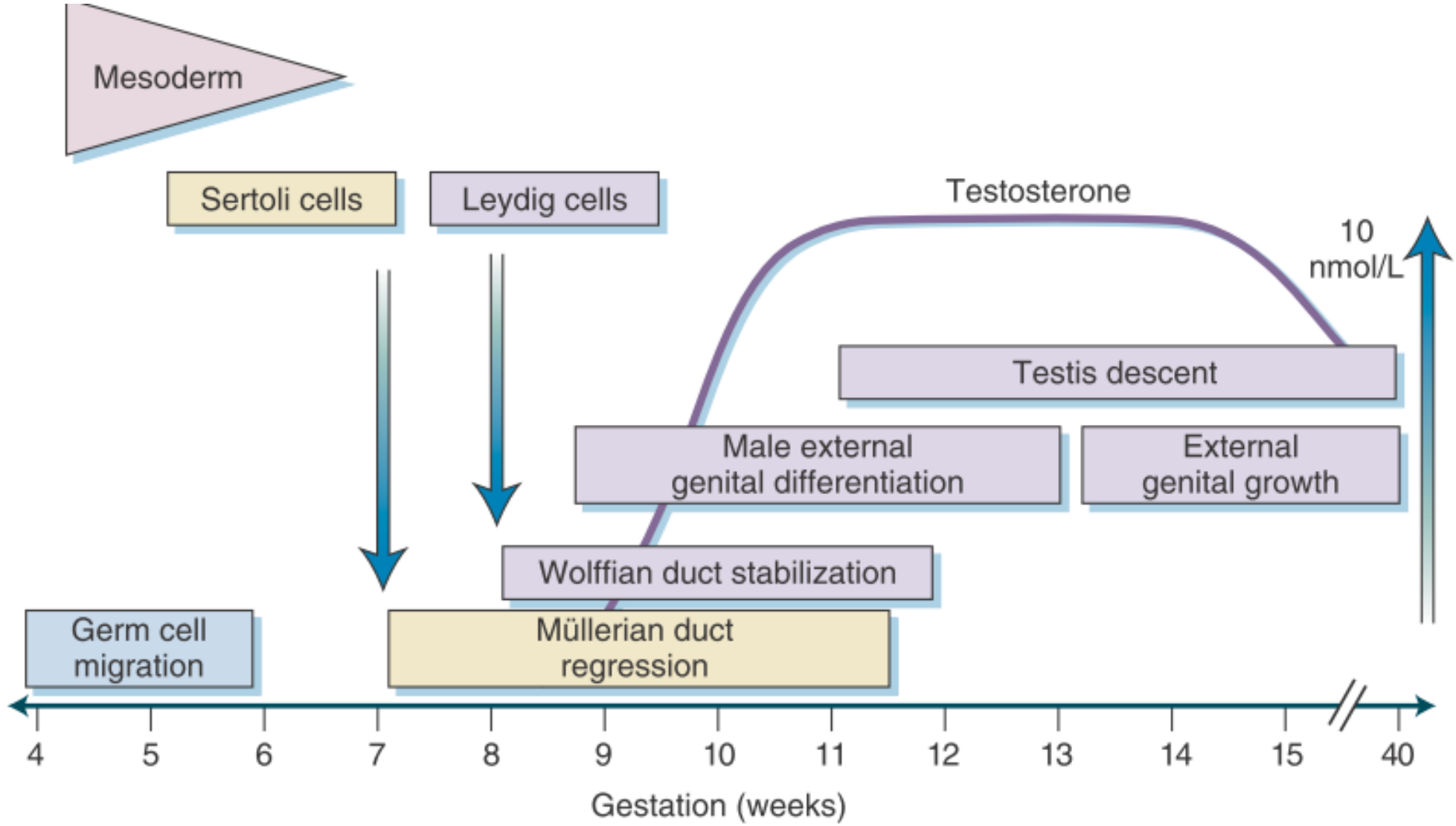


Figure 19-13 Schematic diagram of changes in serum testosterone concentration and sperm production during different phases of life. During fetal life, testosterone levels increase almost to adult male levels, peaking during the first trimester and remaining elevated throughout the second trimester, after which they decline. During neonatal life, testosterone increases almost to adolescent levels at 3 to 6 months of age, then declines to prepubertal levels. During puberty, testosterone concentrations and sperm production increase to adult male levels over several years. With aging, there is a variable, gradual, and progressive decline in serum testosterone levels and sperm production, beginning at age 40 years. (From Griffin JE, Wilson JD. The testis. In: Bondy PK, Rosenberg LE, eds. *Metabolic Control and Disease*, 8th ed. Philadelphia, PA: WB Saunders; 1980:1535-7158.)


Mesoderm
Sertoli cells
Leydig cells
Testosterone
10
nmol/L
Testis descent
Male external
genital differentiation
External
genital growth
Wolffian duct stabilization
Germ cell
migration
Müllerian duct
regression
4
5
6
7
8
9
10
11
12
13
14
15
40
Gestation (weeks)

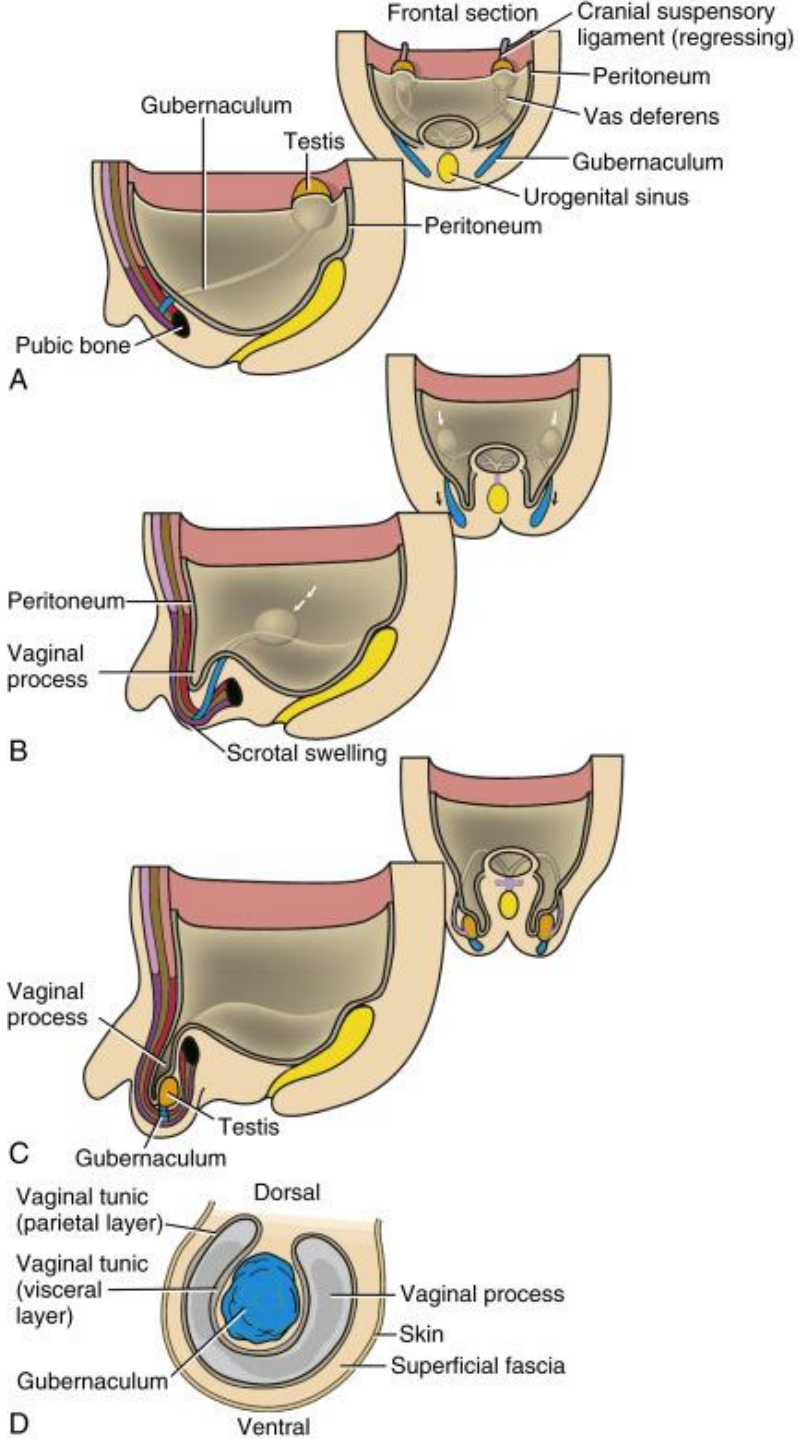
Testis develops at 7-8 wk of gestation [no testes]

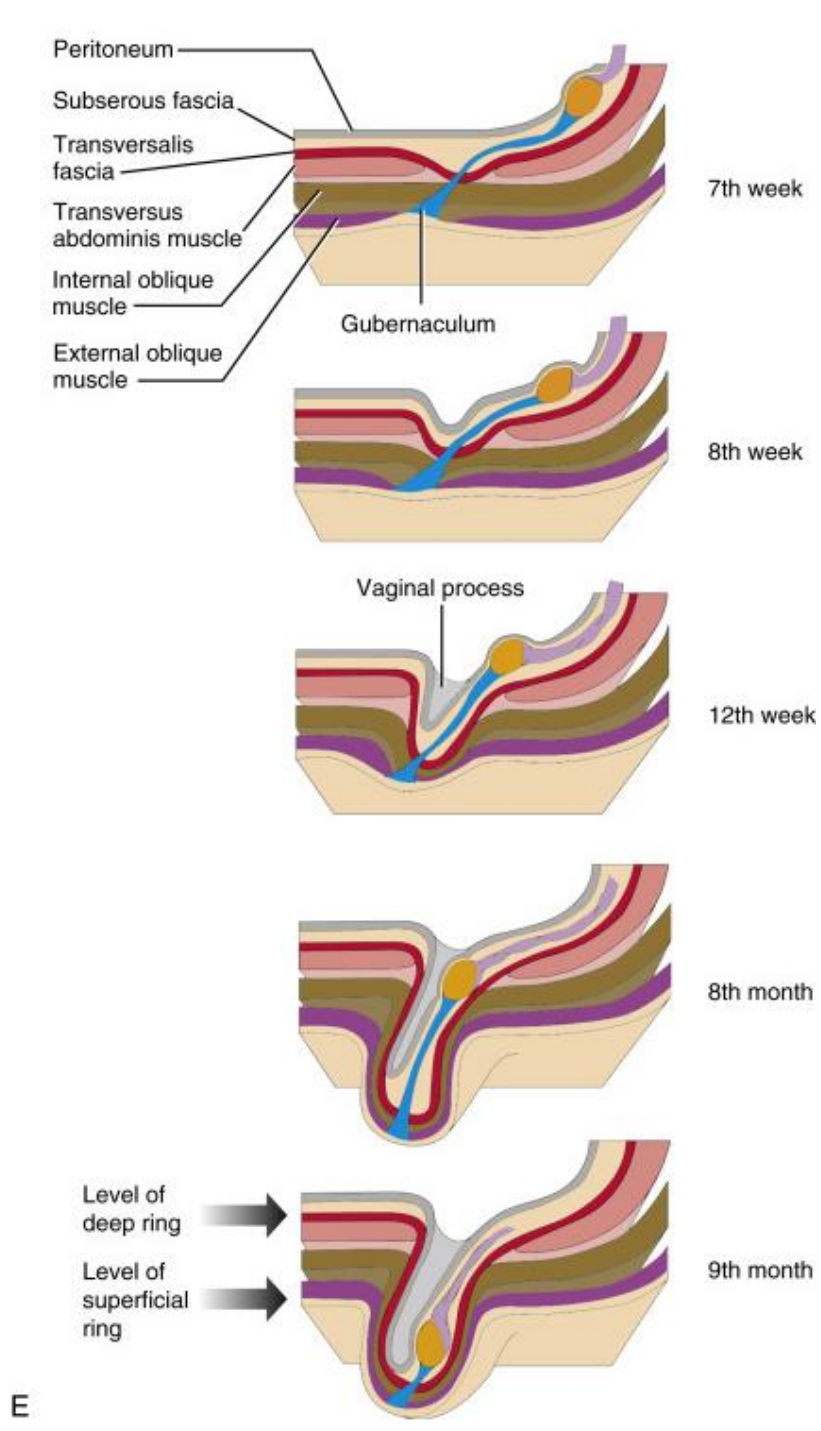
=> DSD:46 XX CAH => Ambiguous genitalia => Chromosome study

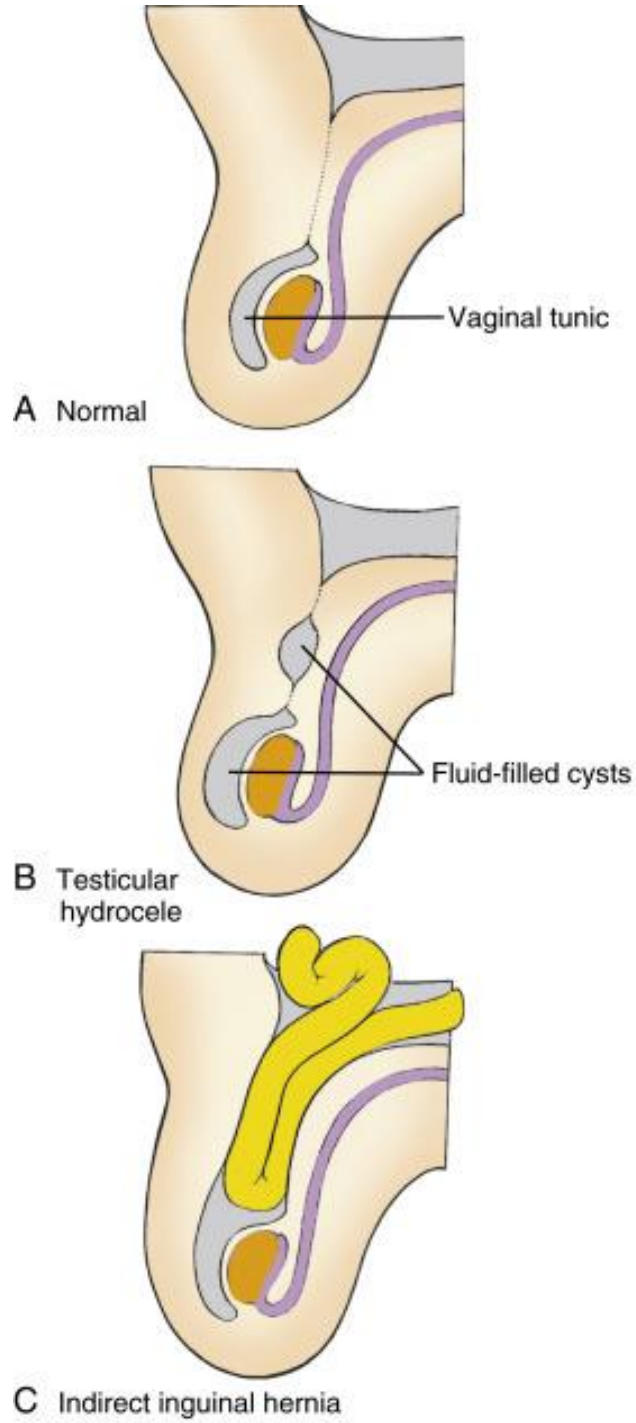
=> Vanishing : torsion/ischemia/atrophy (no Mullerian structure, penile length)

Descend : 2 phases

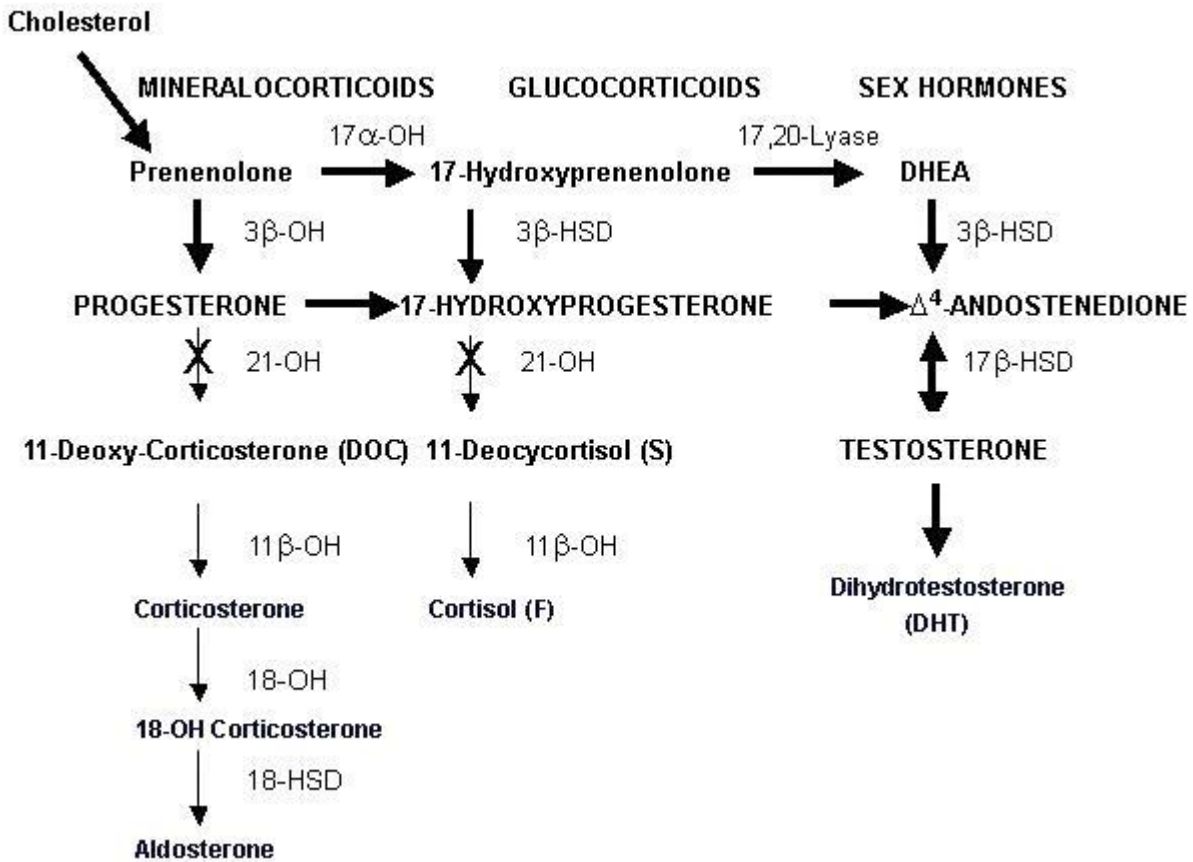
- Phase 1 : transabdominal phase: 10-23 weeks of gestation [Intra-abdominal]
  - craniosuspensory ligament (testosterone)
  - thickening of the gubernaculum (Leydig cell: INSL3/RXFP2) => INSL3 or RXFP2 mutations
  - => internal ring of inguinal canal
- Phase 2: inguinoscrotal phase: 26-35 weeks [inguinal]
  - Preterm
  - gubernacular shortening (testosterone depend)
    - Testosterone deficiency (46XY: 17 hydroxylase deficiency/ 5a-reductase / Klenefileter)
    - Resistant (androgen insensitivity)
    - gonadotropin deficiency (Kallmann syndrome / Prader-Willi)


Frontal section
Cranial suspensory ligament (regressing)
Peritoneum
Vas deferens
Gubernaculum
Urogenital sinus
Peritoneum
Gubernaculum
Testis
Pubic bone
A
Peritoneum
Vaginal process
Scrotal swelling
B
Vaginal process
Testis
Gubernaculum
C
Vaginal tunic (parietal layer)
Vaginal tunic (visceral layer)
Dorsal
Vaginal process
Skin
Superficial fascia
Gubernaculum
Ventral
D


Peritoneum
Subserous fascia
Transversalis fascia
Transversus abdominis muscle
Internal oblique muscle
External oblique muscle
Gubernaculum
7th week
8th week
Vaginal process
12th week
8th month
Level of deep ring
Level of superficial ring
9th month
E


Vaginal tunic
A Normal
Fluid-filled cysts
B Testicular hydrocele
C Indirect inguinal hernia

In females, the cranial suspensory ligament persists as the suspensory ligament of the ovary. Exposure of XX fetuses to androgen does not promote significant ovarian descent in humans, as evidenced by normal ovarian position in females with congenital adrenal hyperplasia.



Nonpalpable testis

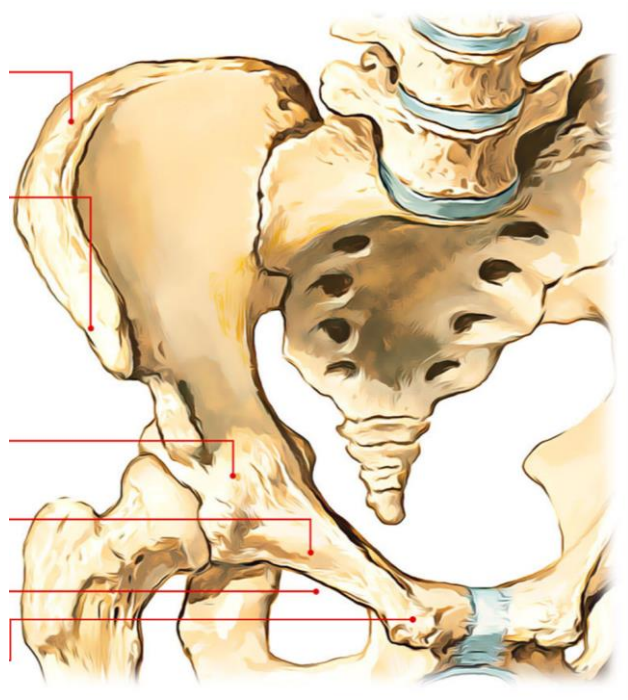
- 10% of undescended testes are nonpalpable testis.
- 50% are viable testes in the abdomen or high in the inguinal canal, and 50% are atrophic or absent (secondary to spermatic cord torsion in utero (vanishing testis))
- If the nonpalpable testis is abdominal, it will not descend after 3 mo of age.
- Inguinal scrotal sonography might be beneficial in obese boys with a nonpalpable testis
- CT / MRI
- In boys with a nonpalpable testis, diagnostic laparoscopy is performed in most centers

Clinical Manifestations

- 2% to 4% of full-term male infants
- 30% of premature male infants (7-8 months descend)
- Descend spontaneously during the 1st 3 mo of life, and by 6 mo the incidence decreases to 0.8% (temporary testosterone surge during the 1st 2 mo, which also results in significant penile growth)
- If the testis has not descended by 4 mo, it will remain undescended
- Patent processus vaginalis => 50-80% hernia
- Maternal diabetes mellitus, including gestational diabetes, may be a risk factor.

Clinical Manifestations

Most undescended testes are palpable just distal to the inguinal canal over the pubic tubercle.



Bilateral

Cryptorchidism is bilateral in 10% of cases

Secondary hypogonadism
- IHH
- Kallmann syndrome

Genetic anomalies
- Prader-Labhart-Willi syndrome
- Laurence-Moon-Biedl syndrome
- Androgen resistance syndromes

Primary hypogonadism
- Klinefelter syndrome
- Noonan syndrome

DSD
- virilized girl with CAH

Mutations of the Leydig cell product, INSL3, which controls growth of the gubernaculum, or of its receptor (RXFP2) in up to 5% of cases

Unilateral

Up to 50% of men with a unilateral, nonpalpable testis in the scrotum have a severely atrophic or absent testis rather than cryptorchidism; in these instances, the contralateral testis may be relatively large (by about 2 mL).

Unilateral or bilateral => associated with infertility and testicular cancer

DSD

- In a boy with midpenile or proximal hypospadias and a palpable undescended testis, disorder of sexual development is present in 15%, and the risk is 50% if the testis is nonpalpable.

Consequence

- poor testicular growth, infertility, testicular malignancy, associated hernia, torsion of the cryptorchid testis, and the possible psychologic effects of an empty scrotum.

- The undescended testis is normal at birth histologically, but pathologic changes can be demonstrated by 6-12 mo.

- Delayed germ cell maturation, reduction in germ cell number, hyalinization of the seminiferous tubules, and reduced Leydig cell number are typical

Infertility

Primary hypogonadism, causing isolated impairment of sperm production associated with low sperm counts, normal testosterone concentrations, a selective elevation in FSH levels, and, occasionally, high LH levels as well.

Rarely, cryptorchidism causes Leydig cell failure and androgen deficiency (e.g., in adults with uncorrected bilateral cryptorchidism), producing low serum testosterone with high LH and FSH levels

Infertility

After treatment for a unilateral undescended testis, 85% of patients are fertile, which is slightly less than the 90% rate of fertility in an unselected population of men. In contrast, following bilateral orchiopexy, only 50-65% of patients are fertile

Azoospermia occurs in 50% to 60% and oligozoospermia in 75% to 100% of men with bilateral cryptorchidism; among men with unilateral cryptorchidism, these figures are, respectively, 15% to 20% and 20% to 40%.

Cancer

The risk of a germ cell malignancy developing in an undescended testis is 4 times higher than in the general population and is approximately 1 in 80 with a unilateral undescended testis and 1 in 40-50 for bilateral undescended testes.

In **some** instances of unilateral cryptorchidism, abnormal histology is apparent in the contralateral normally descended testis. However, it is unclear if these features represent consequences or causes of cryptorchidism.

In patients with a history of unilateral cryptorchidism, the risk of malignancy in the contralateral testis is also increased, by about **70%**

The risk remains higher even after the testis is surgically relocated into the scrotum, supporting the notion that cryptorchidism is a manifestation of a underlying testicular disorder (i.e., testicular dysgenesis)

If orchiopexy is performed before puberty, the risk of testicular cancer is reduced but is still increased **twofold to threefold**

Orchidopexy at 9 months of age results in greater testicular volume and increased number of germ cells compared to orchidopexy at 3 years of age.

It is uncommon for testis tumors to occur if the orchiopexy performed before the age of 2 yr.

Adolescents should be instructed in testicular **self-examination**. The peak age for developing a testis tumor is 15-45 yr.

Cancer

Because the risk of malignancy is two to six times higher in men who underwent orchiopexy **after puberty** and the fertility potential is poor, **some clinicians** recommend **orchidectomy** for men with cryptorchidism discovered after puberty

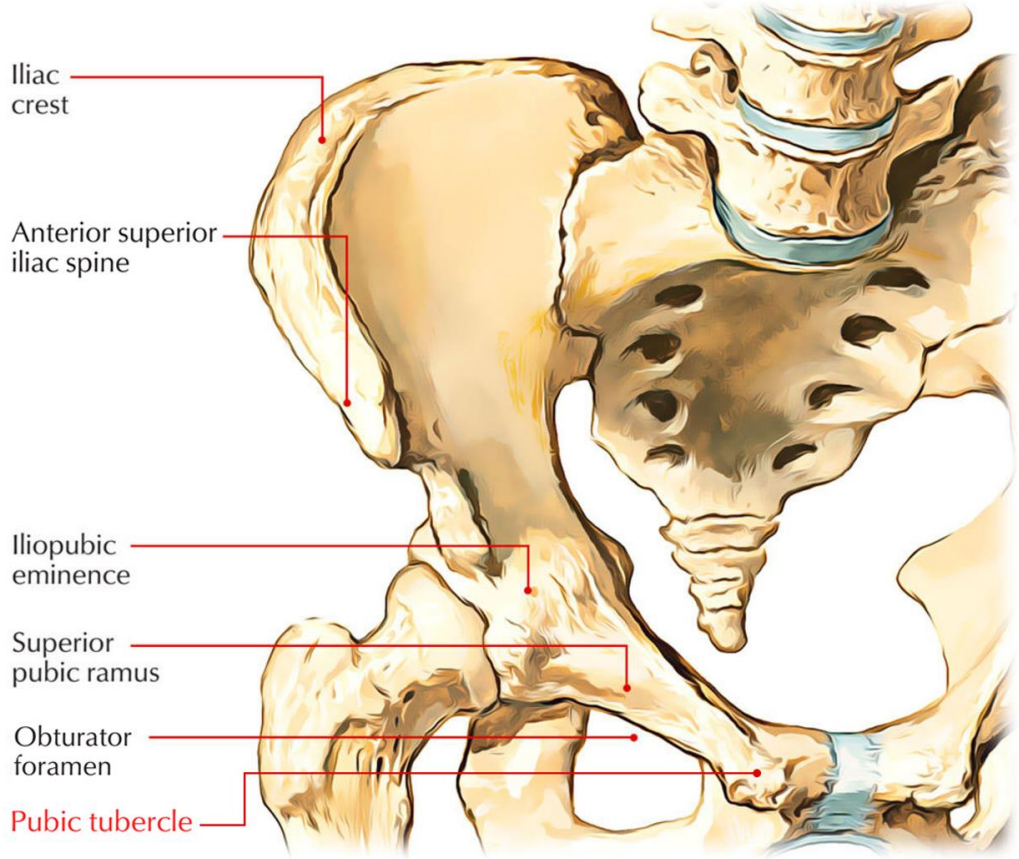
The majority of testis cancers found in persistently cryptorchid testes are **seminomas**, whereas those in cryptorchid testes after orchiopexy are mostly **nonseminoma** testicular cancers

Torsion

Torsion and infarction of the cryptorchid testis also are **uncommon** but can occur because of excessive mobility of undescended testes

inguinal pain and or swelling in a boy with an undescended testis should raise the suspicion of an incarcerated hernia or testicular torsion of the undescended testis

Physical examination



- Location
- Hernia, hydrocele, urethral meatus
- Penile size
- Valsalva maneuver for retractile testes
- Soap
- pulling on the scrotum
- High-resolution ultrasonography or MRI

* One soft sign that a testis is absent is contralateral testicular hypertrophy

Treatment

- Hormonal treatment with **hCG or GnRH** in prepubertal boys is effective in stimulating descent of a cryptorchid testis in approximately 10% to 20% of cases

- Orchiopexy (monitor cancer, preserve function)
- Surgically between 6 and 12 months of ages

- Testicular prostheses (saline testicular implant) : early in child-hood is recommended for boys with anorchia

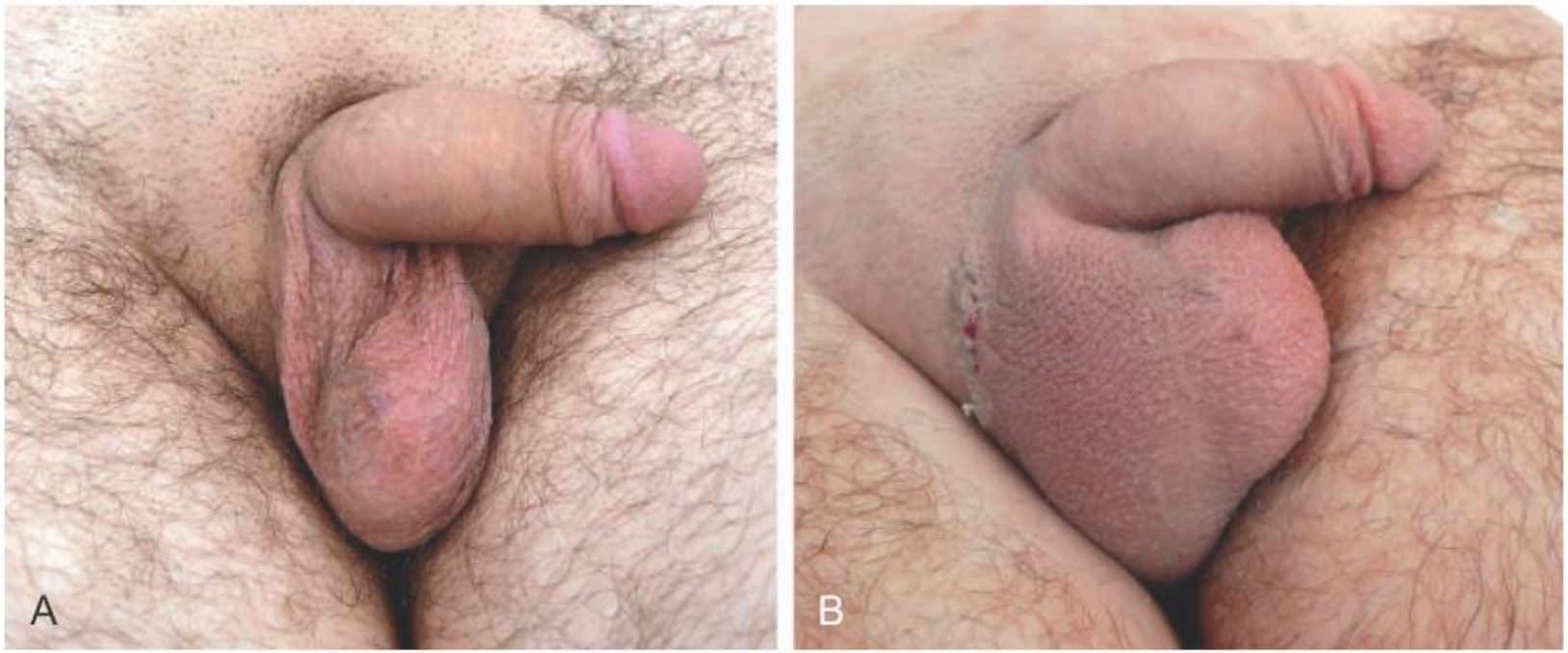


Figure 545-1 **A,** Adolescent with solitary left testis. **B,** Appearance following implantation of right testicular prosthesis.

Table 545-1 American Urological Association Guidelines for Evaluation and Treatment of Boys with an Undescended Testis

DIAGNOSIS

- Primary care providers should palpate testes for quality and position at each recommended well-child visit. (Standard)
- Providers should refer infants with a history of cryptorchidism (detected at birth) who do not have spontaneous testicular descent by 6 mo (corrected for gestational age) to an appropriate surgical specialist for timely evaluation. (Standard)
- Providers should refer boys with the possibility of newly diagnosed (acquired) cryptorchidism after 6 mo. (Standard)
- Providers must immediately consult an appropriate specialist for all phenotypic male newborns with bilateral, nonpalpable testes for evaluation of a possible disorder of sex development (DSD). (Standard)
- Providers should not perform ultrasound (US) or other imaging modalities in the evaluation of boys with cryptorchidism before referral because these studies rarely assist in decision making. (Standard)
- Providers should assess the possibility of a disorder of sex development (DSD) when there is increasing severity of hypospadias with cryptorchidism. (Recommendation)
- In boys with retractile testes, providers should monitor the position of the testes at least annually to monitor for secondary ascent. (Standard)

TREATMENT

- Providers should not use hormonal therapy to induce testicular descent, since evidence shows low response rates and lack of evidence for long-term efficacy. (Standard)
- In the absence of spontaneous testicular descent by 6 mo (corrected for gestational age), specialists should perform surgery within the next year. (Standard)
- In prepubertal boys with nonpalpable testes, surgical specialists should perform examination under anesthesia to reassess for palpability of testes. If nonpalpable, surgical exploration and, if indicated, abdominal orchidopexy should be performed. (Standard)
- In boys with a normal contralateral testis, surgical specialists may perform an orchiectomy (removal of the undescended testis) if a boy has a normal contralateral testis and either very short testicular vessels and vas deferens, dysmorphic or very hypoplastic testis, or postpubertal age. (Clinical Principle)
- Providers should counsel boys with a history of cryptorchidism and/or monorchidism and their parents regarding potential long-term risks and provide education on infertility and cancer risk. (Clinical Principle)