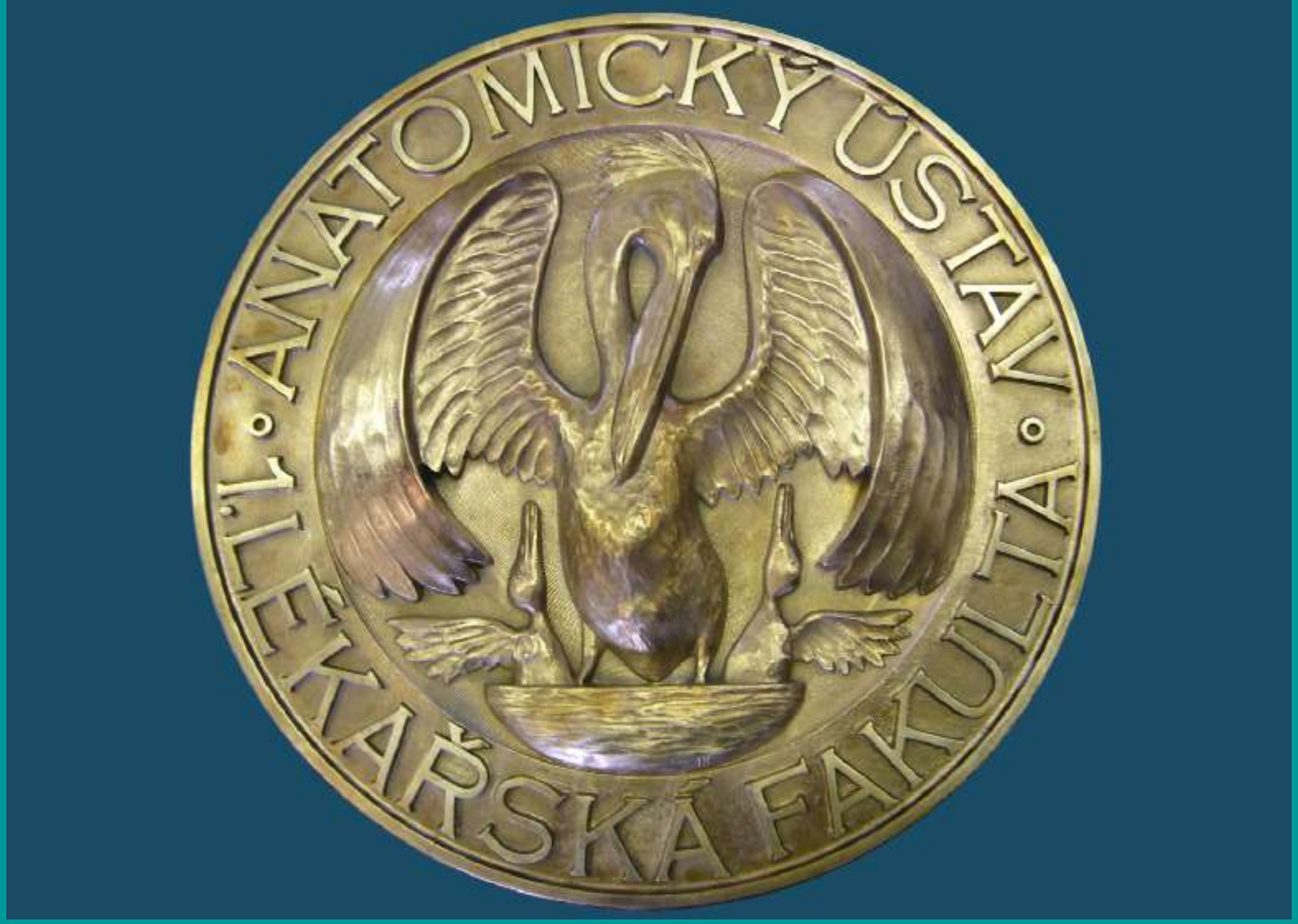
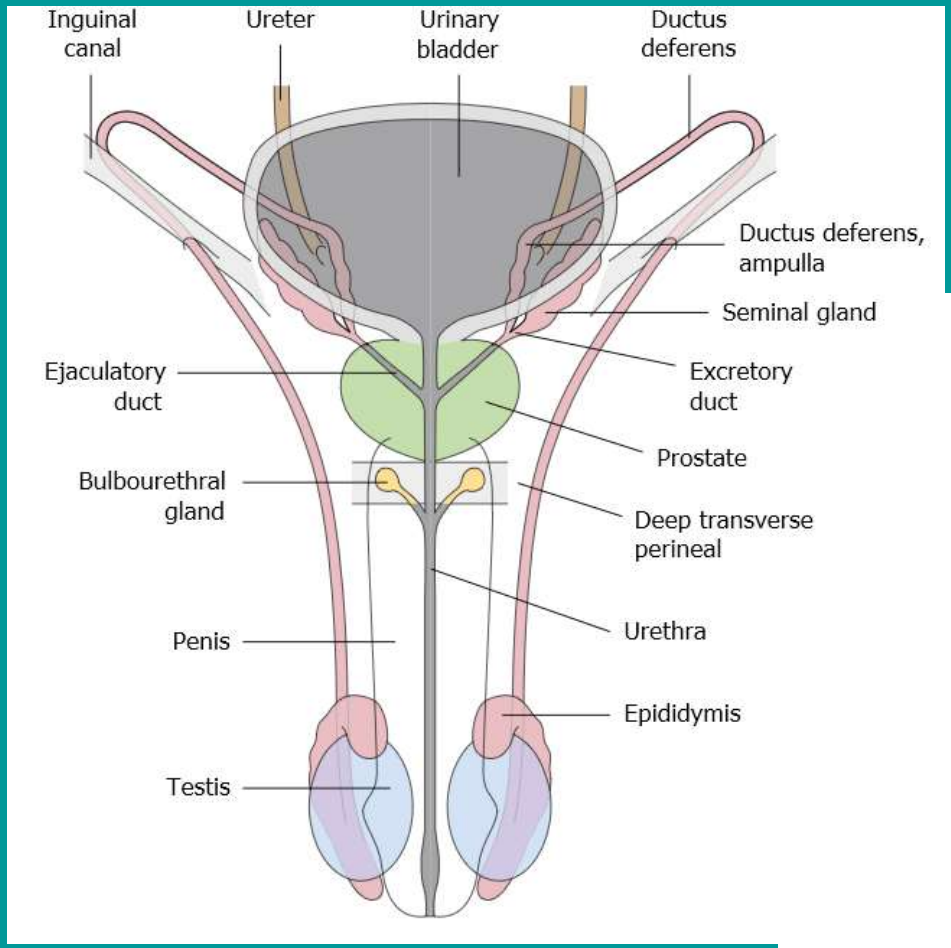
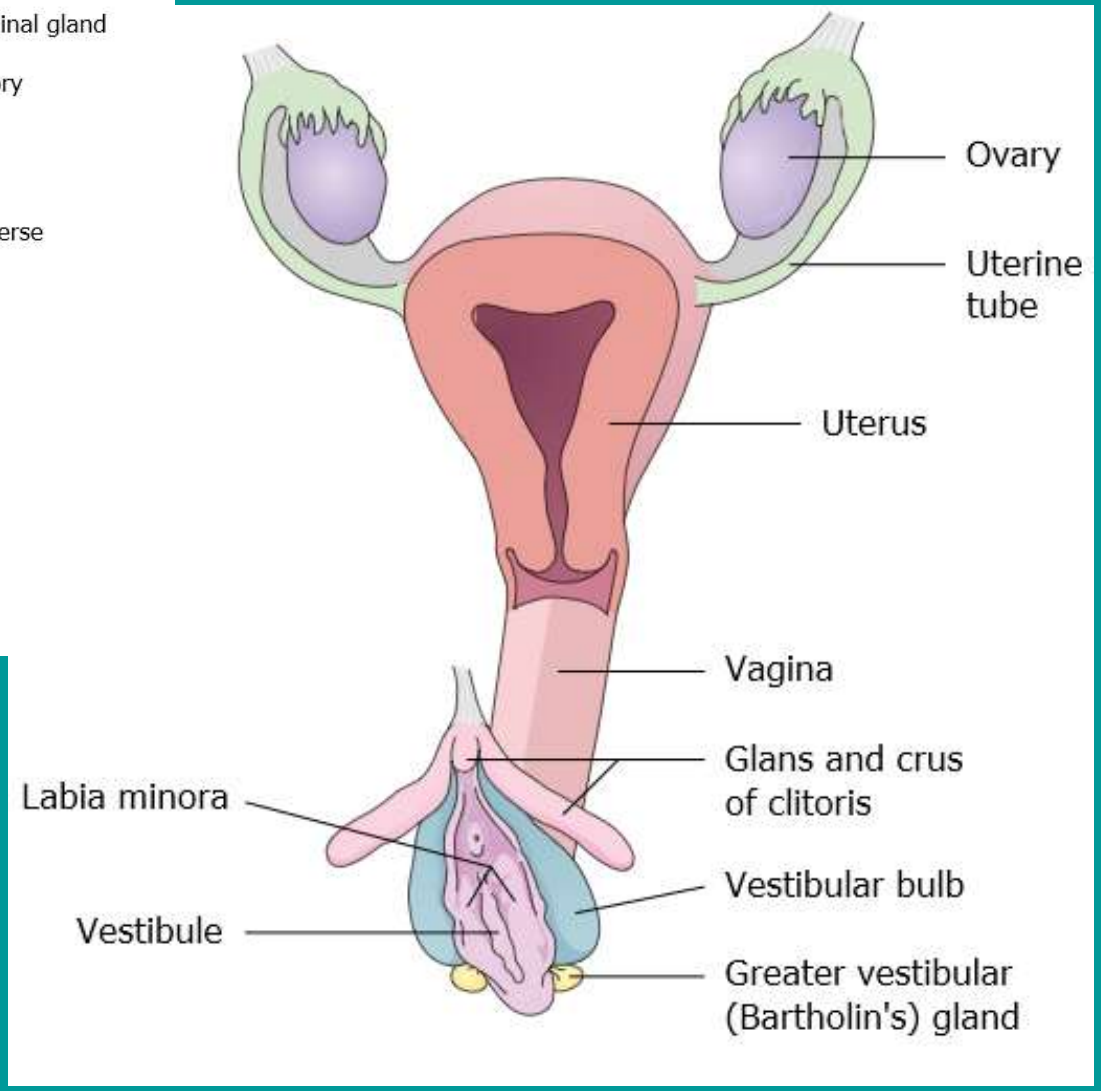


Development of genital organs
lecture for students of general medicine and dentistry

Miloš Grim
Institute of Anatomy, First Faculty of Medicine, Summer semester 2016 / 2017

Genital systems (reproductive organs)
Organa genitalia masculina et feminina
internal + external organs
Gonads –
gametogenesis (spermatozoa, oocytes),
endocrine function (testosteron, estrogenic hormones, progesterone),
Gonadal ducts -
transport of gametes,
retention and nutrition of embryos
penis and vagina - internal fertilization
Accessory glandular structures -
specific secrets


Inguinal canal
Ureter
Urinary bladder
Ductus deferens
Ductus deferens, ampulla
Seminal gland
Ejaculatory duct
Excretory duct
Prostate
Bulbourethral gland
Deep transverse perineal
Urethra
Penis
Epididymis
Testis


Ovary
Uterine tube
Uterus
Vagina
Glans and crus of clitoris
Labia minora
Vestibular bulb
Vestibule
Greater vestibular (Bartholin's) gland

The male and female genital organs originate from the same undifferentiated embryonic primordium

Two sets of ducts are formed in the undifferentiated developmental stage: **Mesonephric duct** (Wolffian duct) – primordium of male gonadal ducts and **Paramesonephric duct** (Mullerian duct) - prmordium female gondal ducts. A choice between them is made accorging to karyotype

Female phenotype develops spontaneously in the absence of chromosome Y (the absence of SRY gene expression)

Male phenotype requires masculinization factors (SRY gene expression, testosterone activity)

Genetic sex determination depends on the X and Y chromosomes.

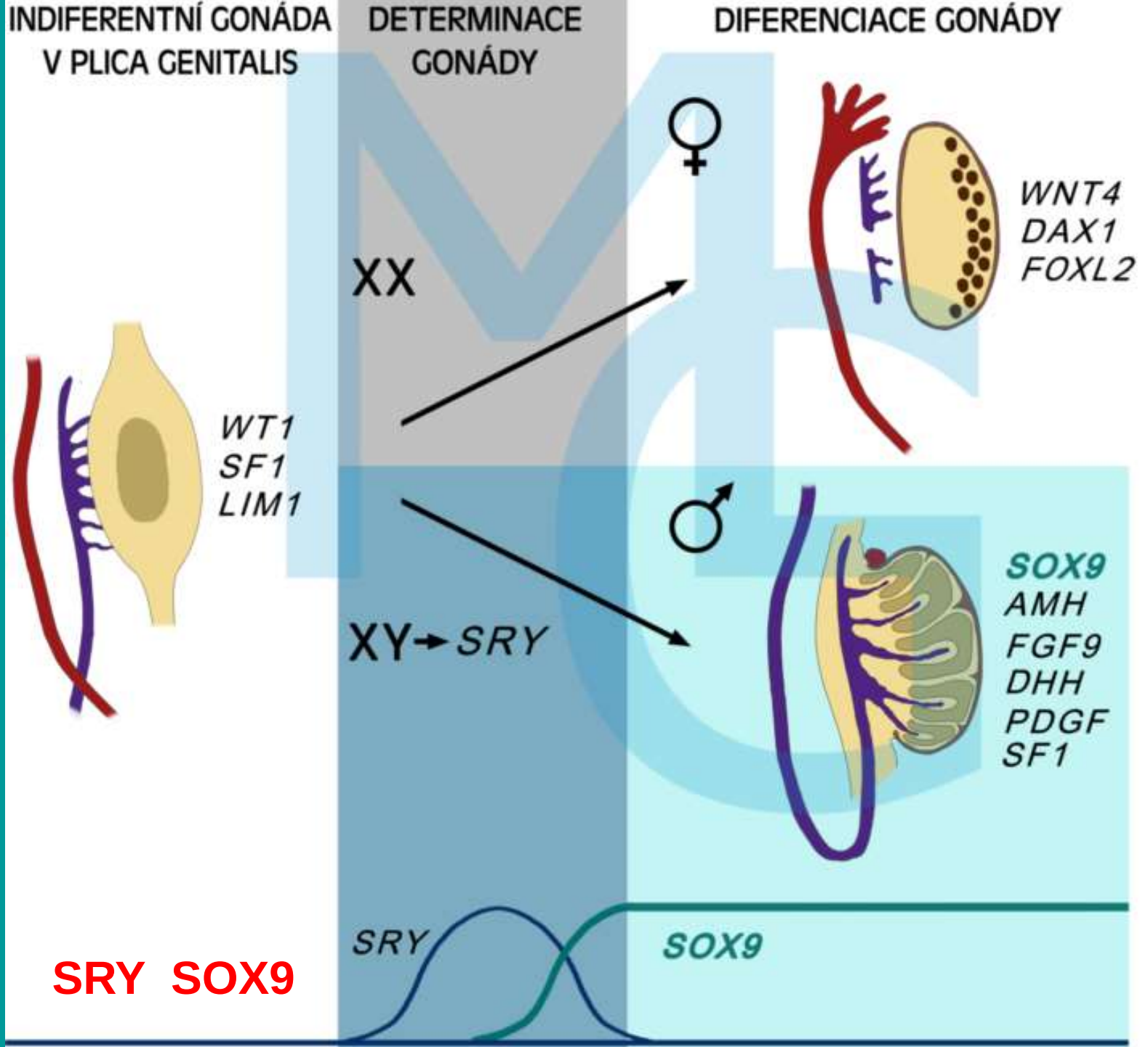
XX female katryotype develops female phenotype spontaneously

XY male karyotype leads to male phenotype under the influence of expression of the SRY gene, which determines the development of testis.

Developing testis produce

- **Testosterone** - stimulates development of the mesonephric duct and the external genitalia,
- **AMH (anti-Müllerian-hormone) –** stimulates regression of the paramesonephric duct,

External genital organs develop from:
genital eminence, genital folds, genital ridges and urogenital sinus


INDIFERENTNÍ GONÁDA
V PLICA GENITALIS
DETERMINACE
GONÁDY
DIFERENCIACE GONÁDY
♀
XX
WNT4
DAX1
FOXL2
WT1
SF1
LIM1
♂
XY→SRY
SOX9
AMH
FGF9
DHH
PDGF
SF1
SRY
SOX9
SRY SOX9

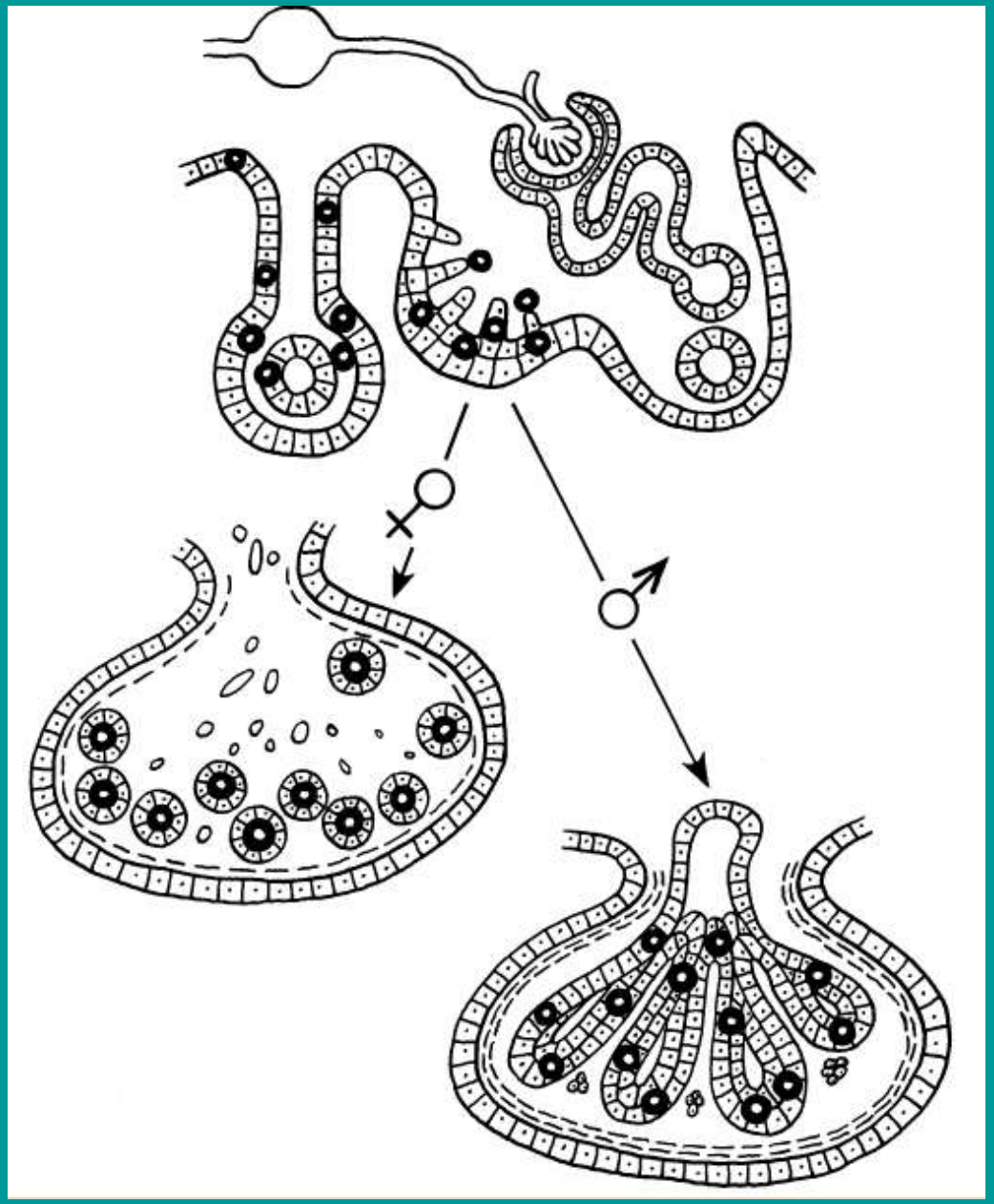
SRY gene is expressed for a short time (about 6 to 8 weeks) in somatic precursor cells of the cell line of Sertoli cells.

SRY gene induces ***SOX9*** gene expression, which controls differentiation of the **Sertoli cells**.

FGF9 produced by Sertoli cells promotes **Leydig cells** differentiation.

Two hormones determine further development of masculine phenotype**:** : The **AMH (anti-Müllerian hormone)** secreted by Sertoli cells and **testosterone** from the Leydig cells.

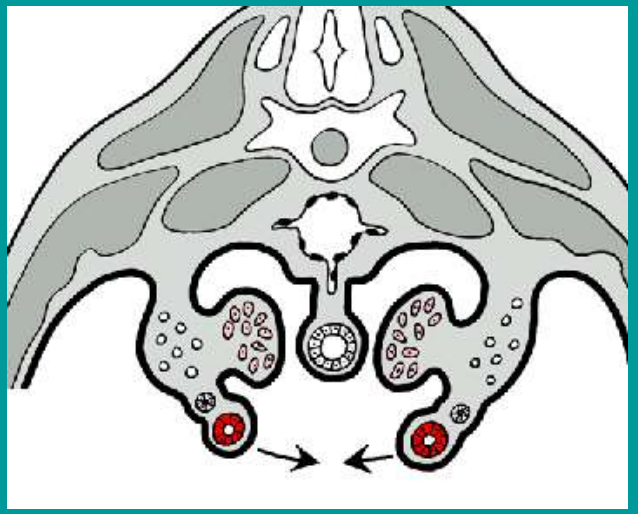
In female fetuses the indifferent gonad develops **spontaneously** as the ovary.



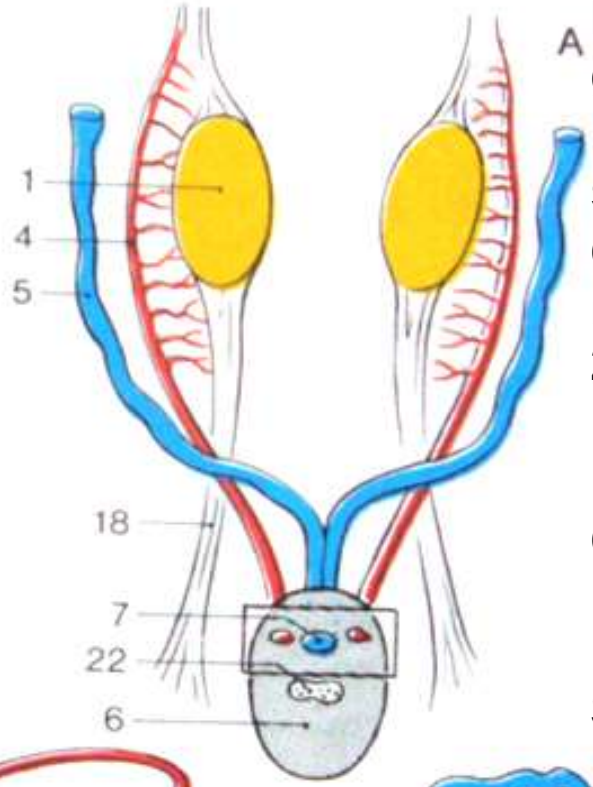
Primordial germ cells migrate into gonads from the yolk sac

Differentiation of indifferent gonads into ovary and testis

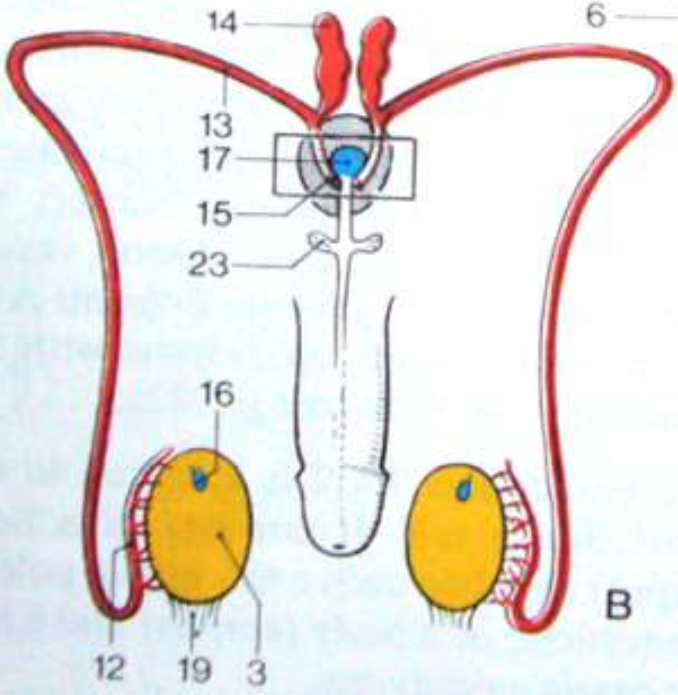
Ovary: ovarian follicles
Testis: seminiferous tubules, tunica albuginea

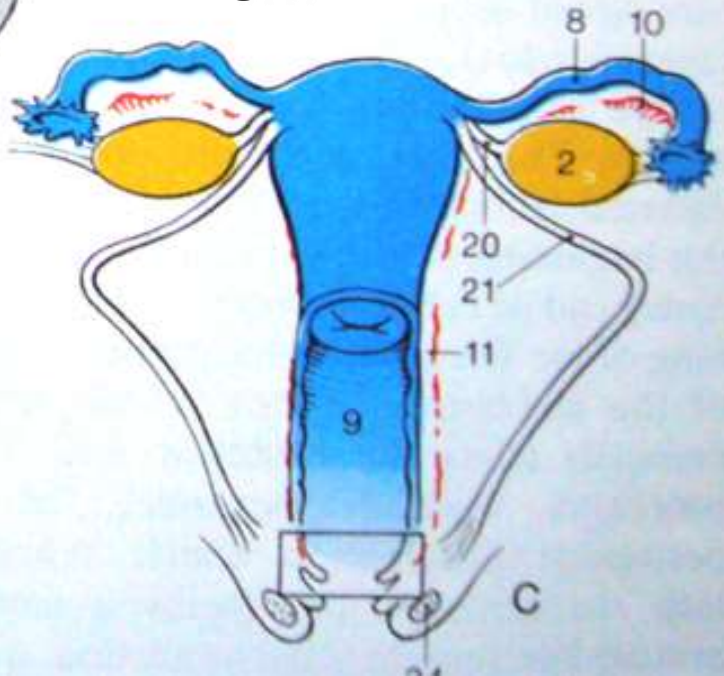


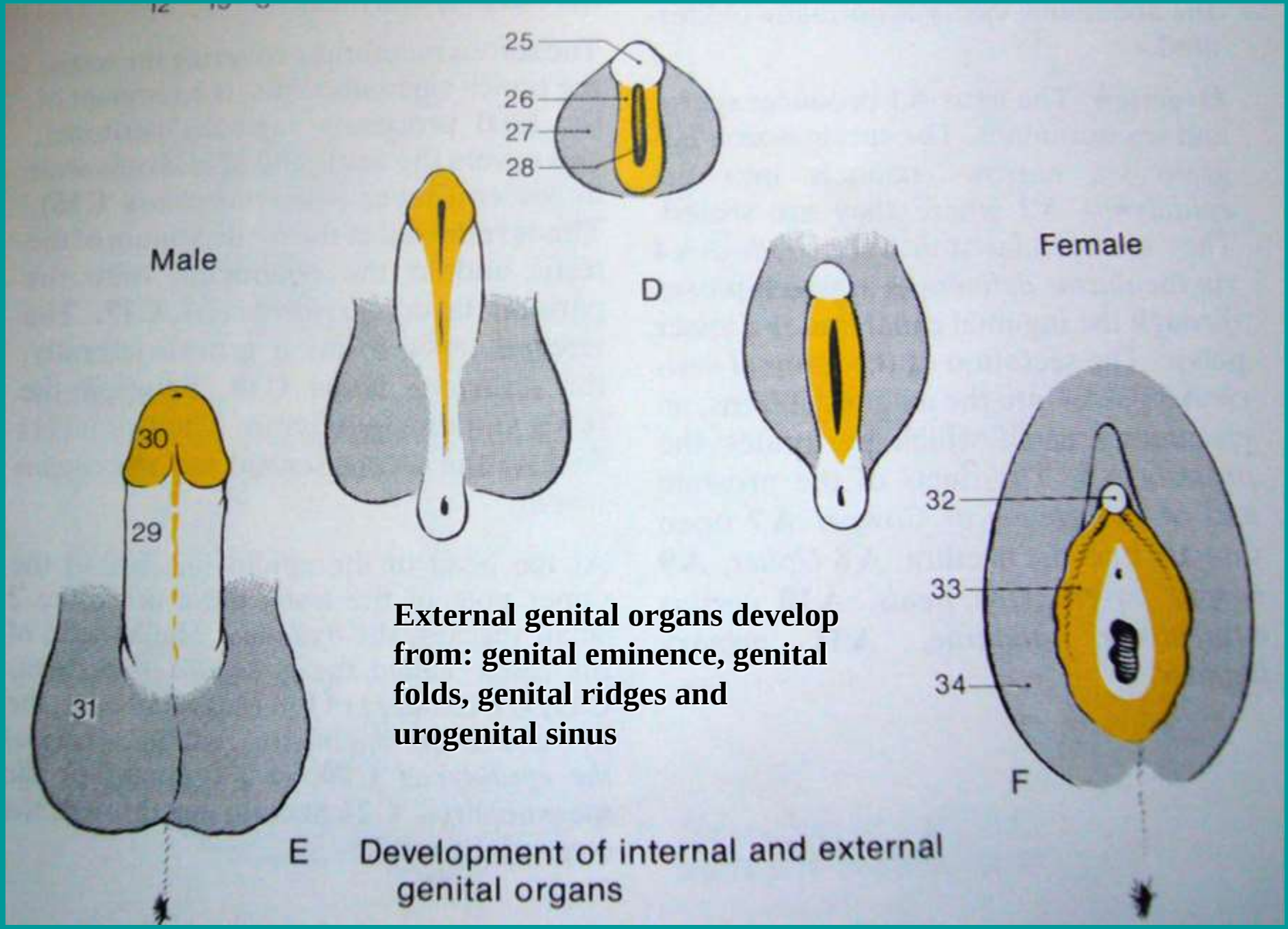
Descent of gonads
Two sets of ducts (mesonephric - Wolffian, paramesonephric - Mullerian) are formed early in development and a choice between them is made



Developing male **gonads produce 1) testosterone - stimulates development of mesonephric duct, 2 AMH – activate regression of paramesonephric duct. *Femal* phenotype develops in the absence of SRY**







External genital organs develop from: genital eminence, genital folds, genital ridges and urogenital sinus

Deviation of differentiation of sexual organs:

Abnormal karyotype

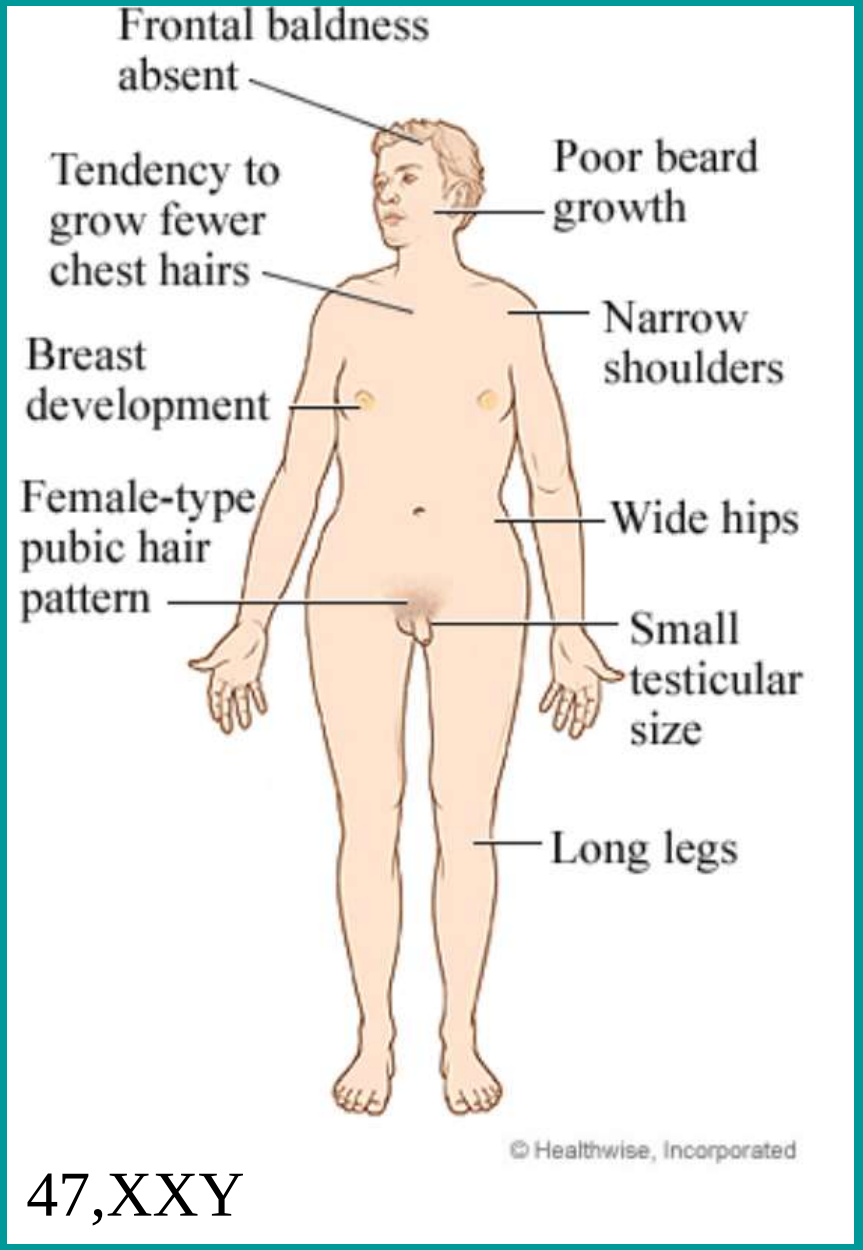
Klinefelter syndrome, karyotype 47 – XXY

Turner syndrome, karyotype 45 – X

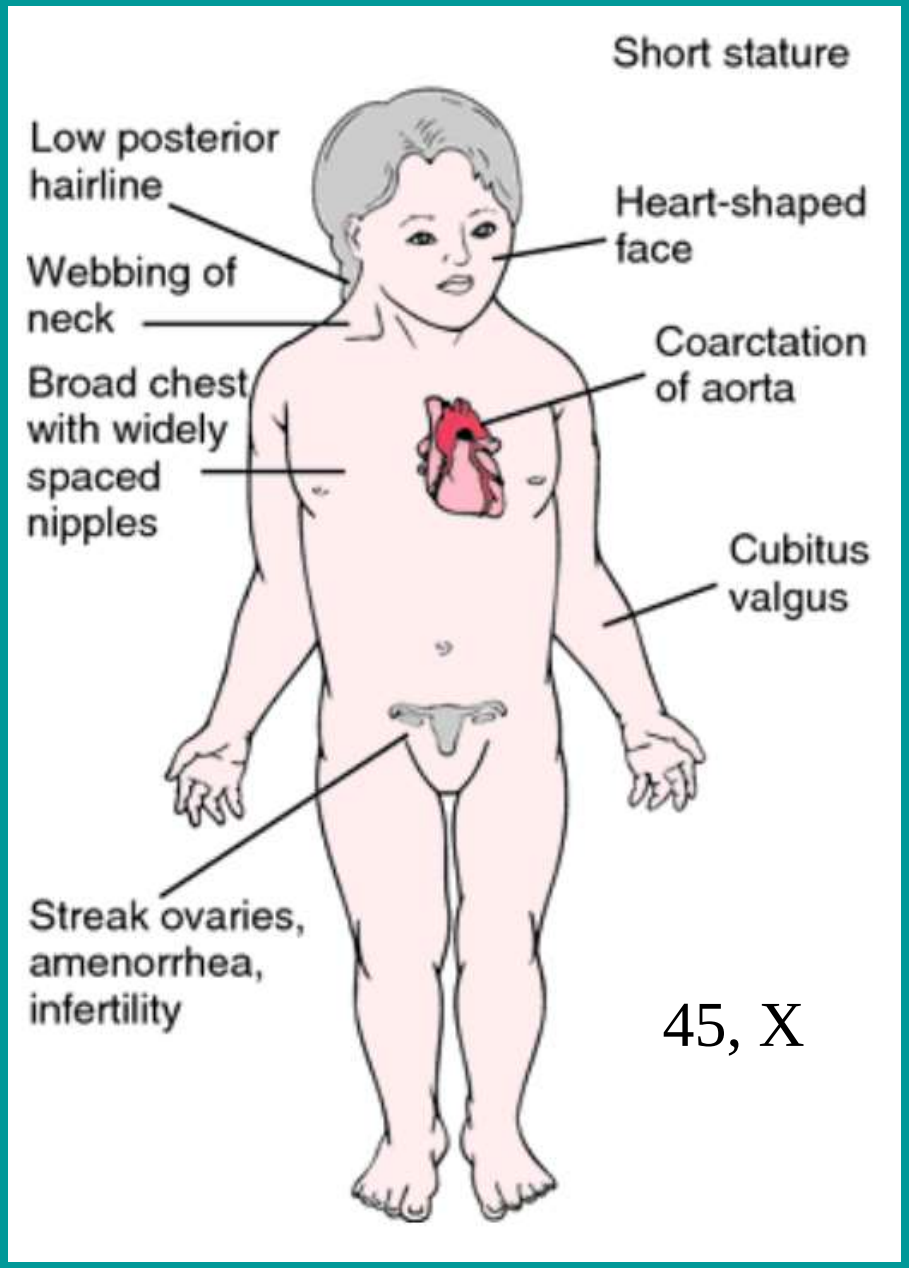
Normal karyotype – abnormal phenotype :
the result of disturbances of sex hormones and their receptors

AIS – androgen insensivity syndrome - testicular feminisation – mutation of gene for androgen receptor (pseudohermaphroditism)

Klinefelter syndrome – 47 XXY



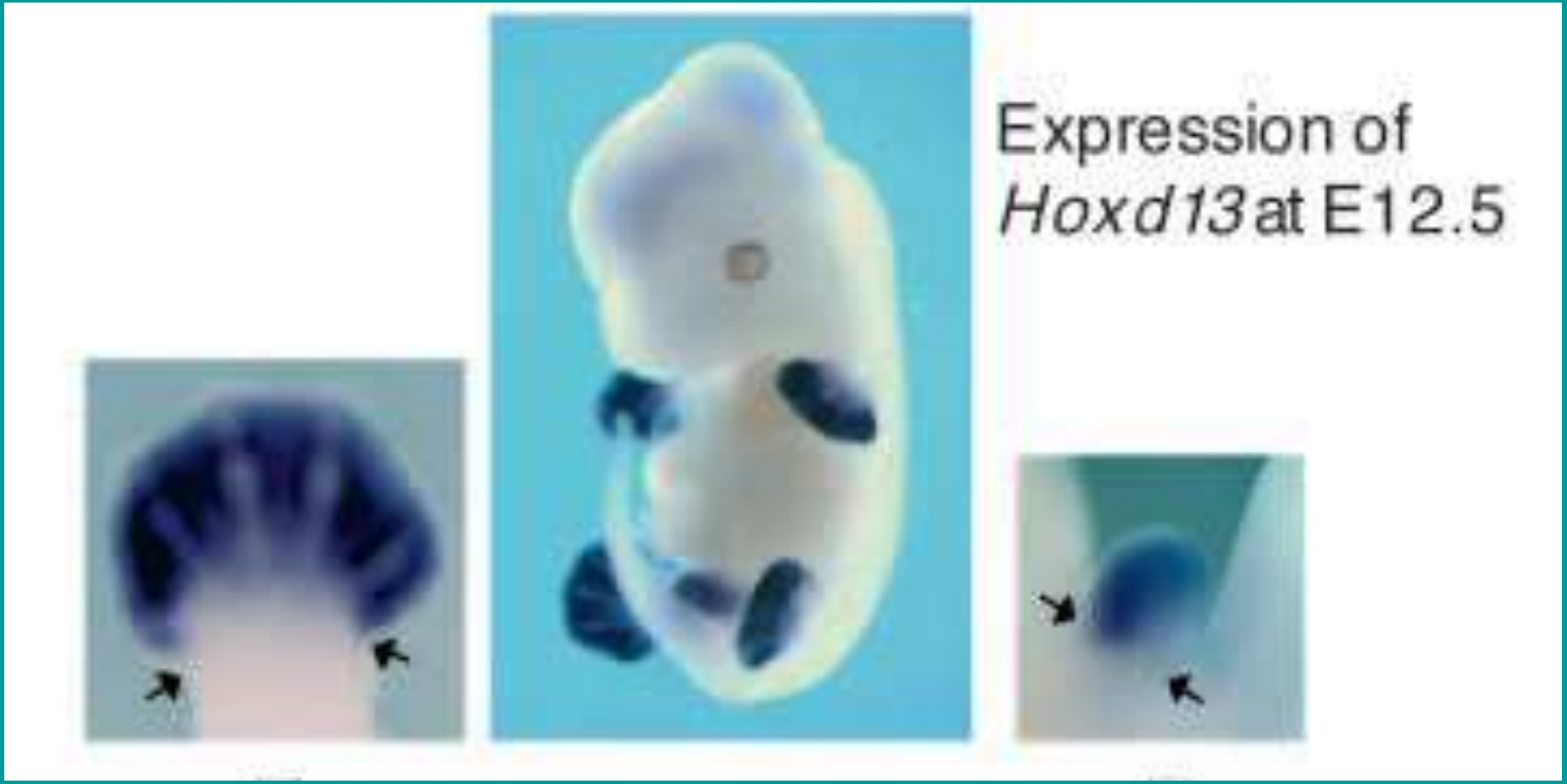
47,XXY



45, X

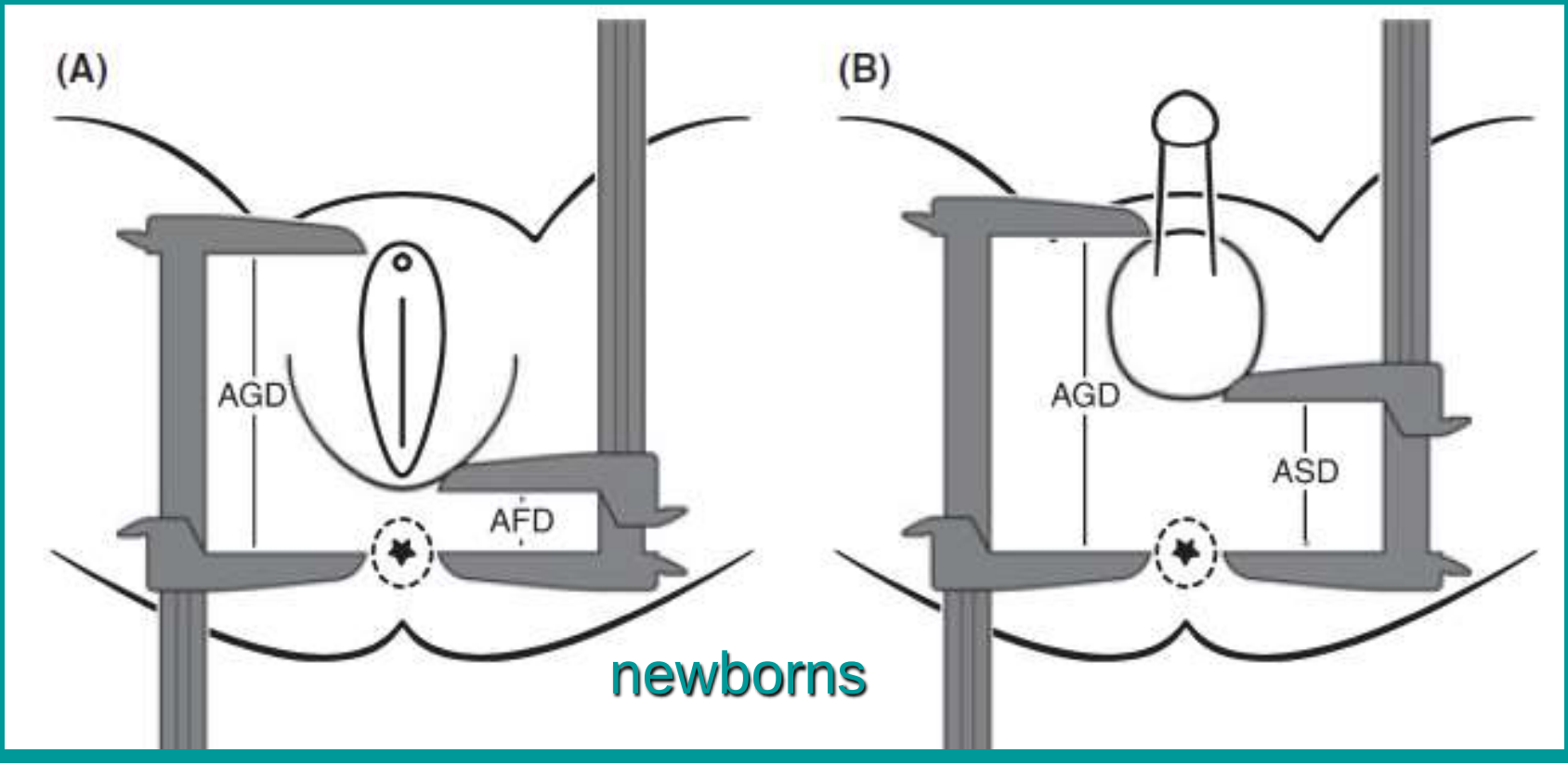
Turner syndrome – 45 X

John Cobb and Denis Duboule:
Comparative analysis of genes downstream of the Hoxd cluster in developing digits and external genitalia.
Development 132, 3055-3067, 2005



Homologies in the Male and Female Urogenital Systems

Indifferent Structure	Male Derivative	Female Derivative
Genital ridge	Testis	Ovary
Primordial germ cells	Spermatozoa	Ova
Gubernaculum	Lig. scrotale	Lig. uteroovaricum, lig. teres
Sex cords	Seminiferous tubules (Sertoli cells)	Follicular (granulosa) cells
Mesonephric tubules	Efferent ductules, Paradidymis	Oöphoron, Paroöphoron
Mesonephric (Wolffian) ducts	Appendix of Epididymis	Appendix of ovary
	Epididymal duct	Gartner's duct
	Ductus deferens + Ejaculatory duct	
Paramesonephric (Müllerian) ducts	Appendix of testis Prostate utricle	Uterine tubes Uterus + Upper vagina
Urogenital sinus (upper part)	Urinary bladder	Urinary bladder
Urogenital sinus (middle part)	Prostatic urethra (upper part)	Urethra feminina
Urogenital sinus (lower part)	Prostatic urethra (lower part)	Vaginal vestibule, lower vagina
Genital folds	Penile urethra	Labia minora, Bulb of vestibule
Genital tubercle	Corpus and glans penis, Preputium	Clitoris, Preputium
Genital swellings	Scrotum	Labia majora



newborns

An-ogenital distance/ano-scrotal distance/ano-fourchette distance diagrams. (A) Center of the anus to the anterior clitoral surface (AGD) and the center of the anus to the posterior fourchette (AFD) measurements made in female subjects. (B) Center on the anus to the anterior base of the penis (AGD) and the center of the anus to the junction of the perineum with the rugated scrotal skin (ASD) measurements made in male subjects.

The mean AFD was 15.1 mm (SD ± 2.9) and ASD was 23.0 mm (SD ± 3.8) and– in newborns.

S. Sathyanarayana,* L. Beard, C. Zhou* and R. Grady: Measurement and correlates of ano-genital distance in healthy, newborn infants. International Journal of Andrology 33 (2010), 317–323

AGD AC (mm) 80.4 ± 10.5 (SD) **79.2** - 59.5 - 96.1 (Median)
AGD AF (mm) 37.7 ± 6.3 (SD) **37.2** - 27.9 - 48.6 (Median)

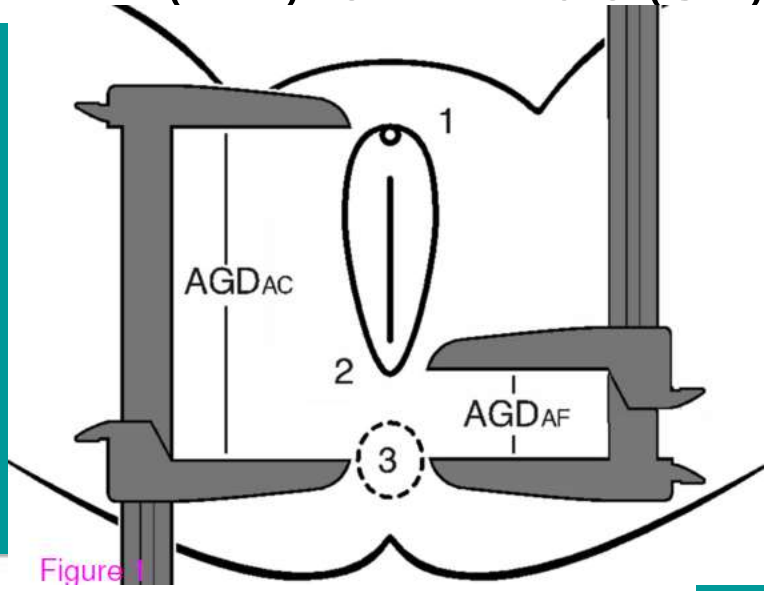


Figure 1

Mendiola J, Roca M. et al.: Anogenital distance is related to ovarian follicular number in young Spanish women: a cross-sectional study. Environ Health 2012 Dec ;11(1):90.

In many mammalian species females with shorter AGD are more fertile.

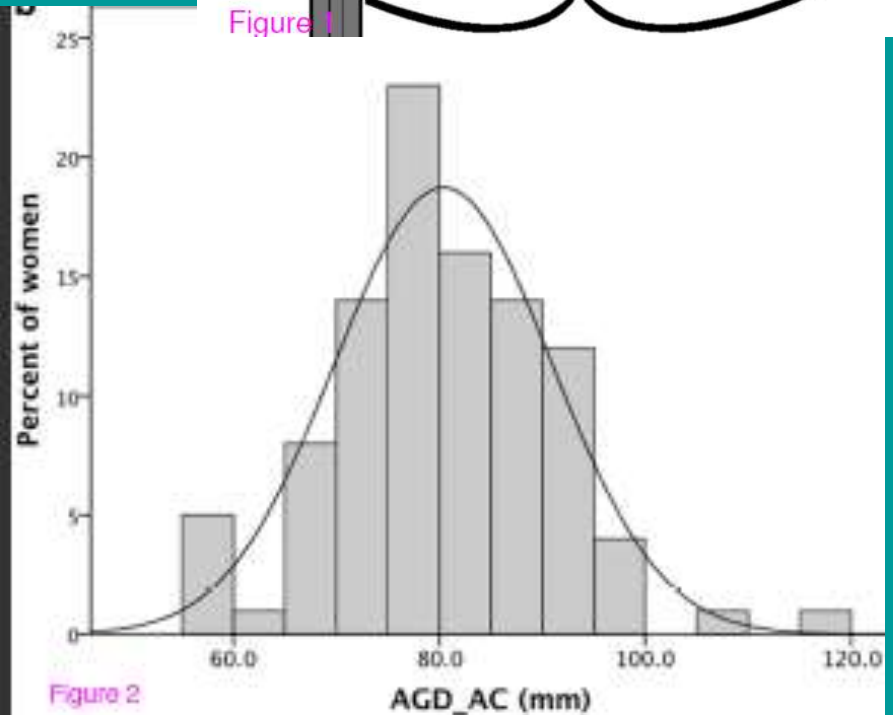
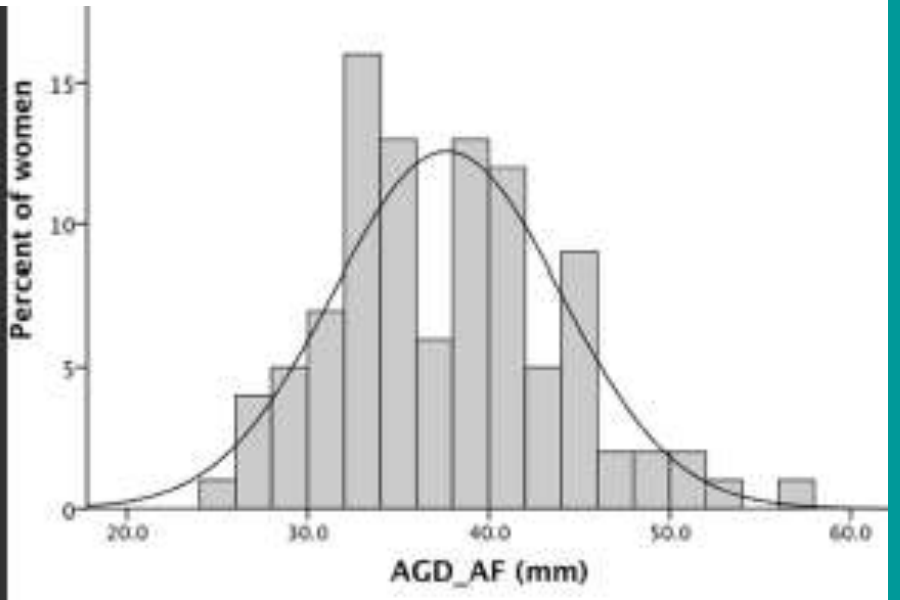
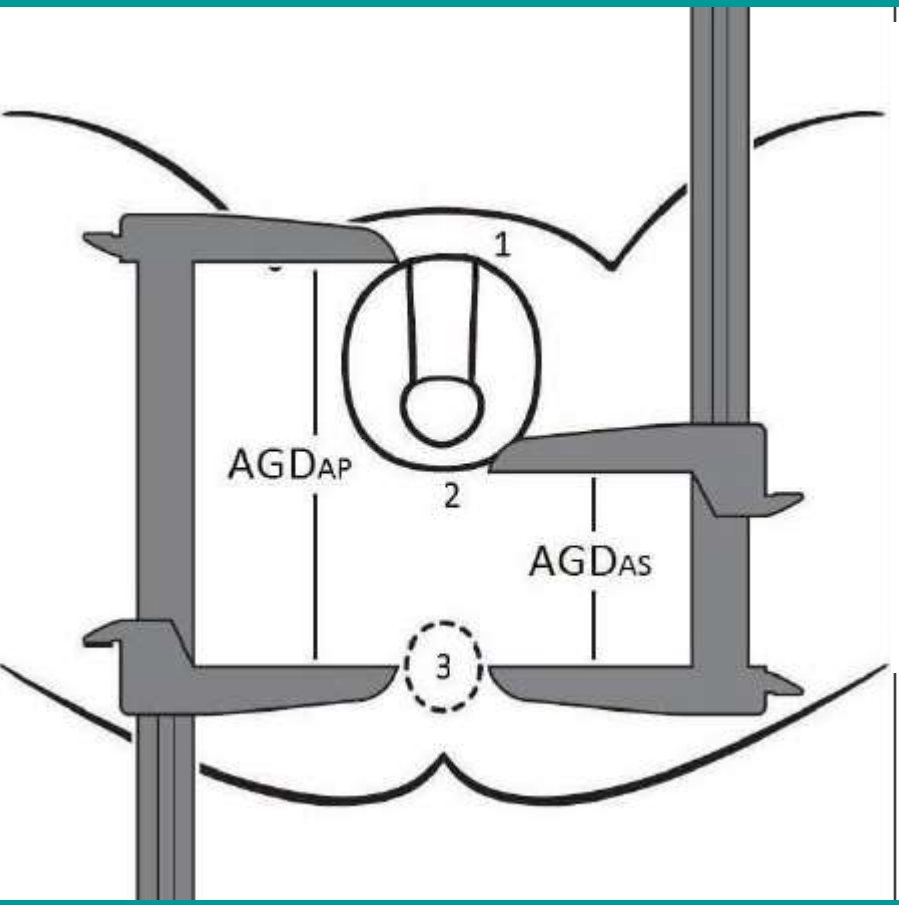
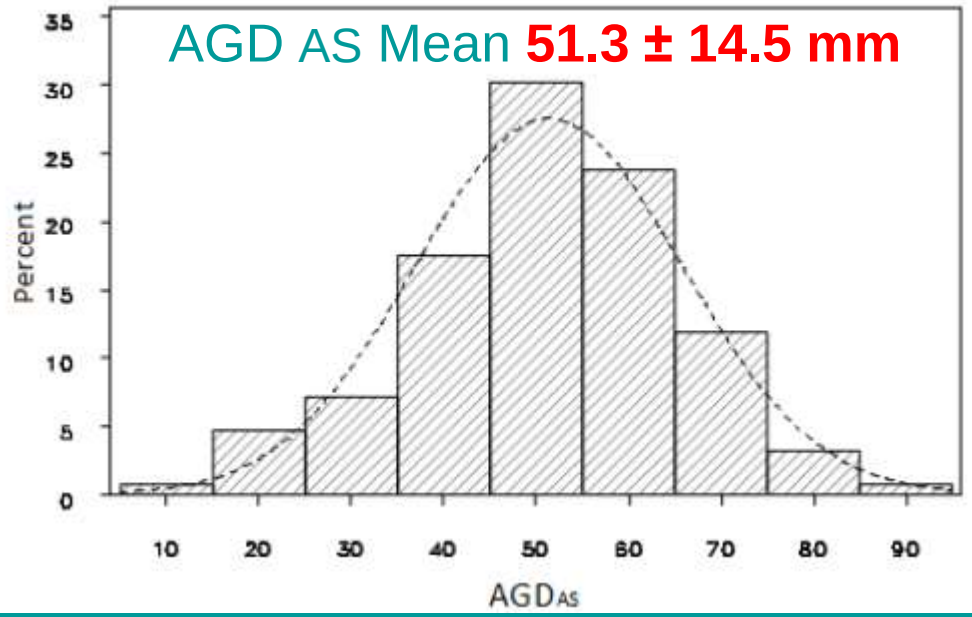


Figure 2





AGD AS: center of anus to posterior base of the scrotum (point 2 to 3).
AGD AP anus – penis (point 1 to 3)

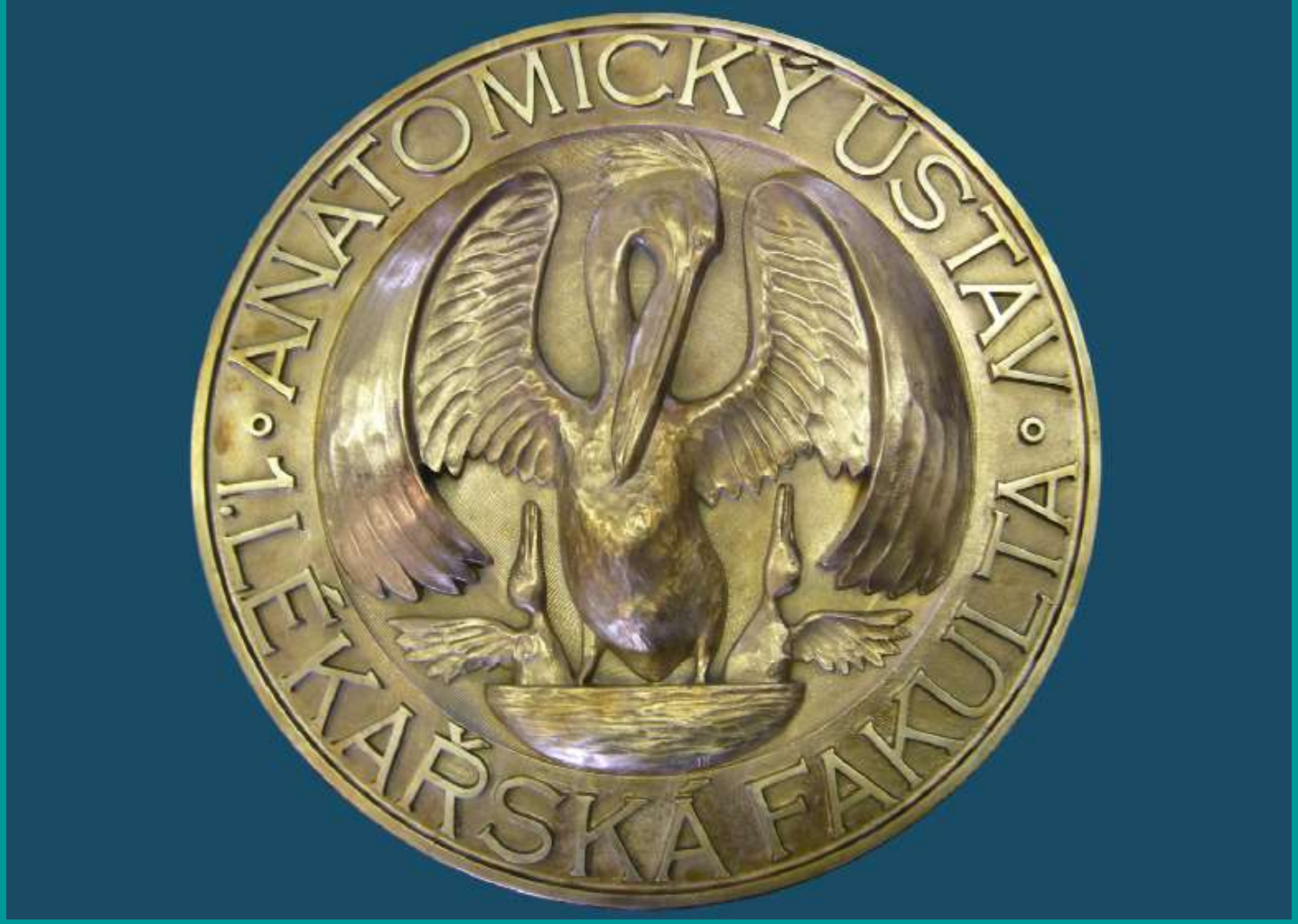


Frequency distributions of measures of anogenital distance

Mendiola J et al.:**Shorter Anogenital Distance Predicts Poorer Semen Quality in Young Men in Rochester, New York**. Environ Health Persp 119: 958 - 963 (2011)

Men with AGD AS below the median were 7.3 times more likely to have a low sperm concentration

Funded by the European Union 7th Framework Program Developmental Effects of Environment on Reproductive Health"

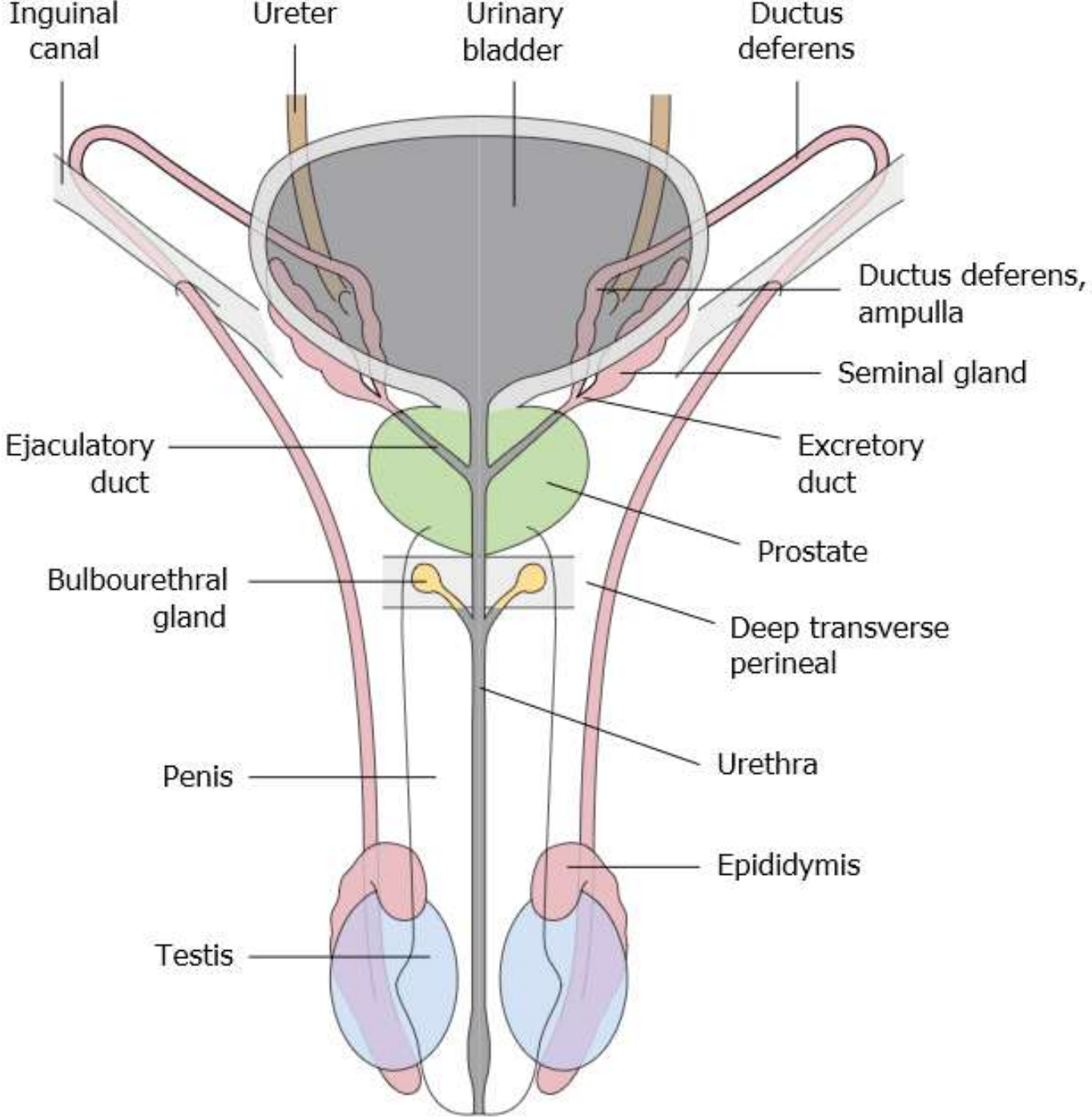


Male genital system

lecture for students of general medicine and dentistry

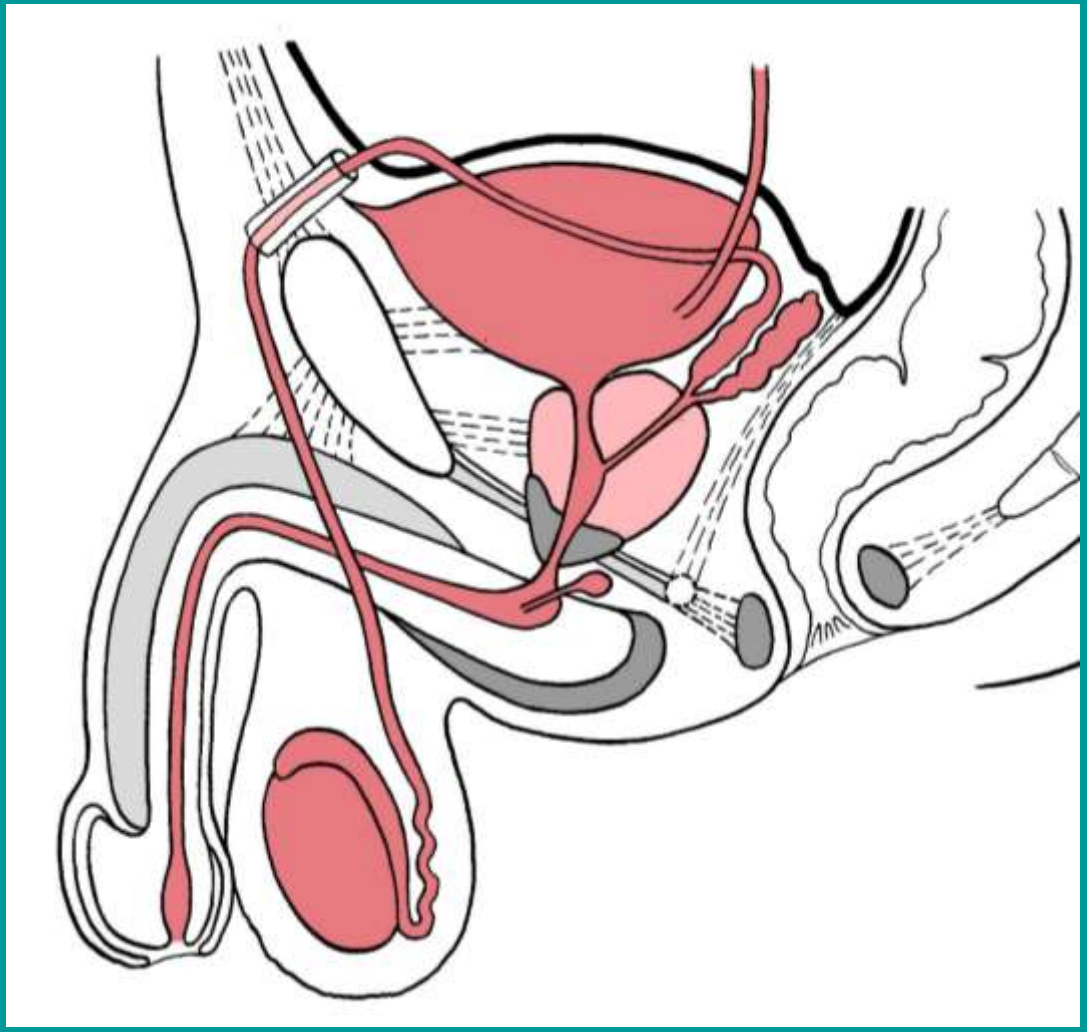
Miloš Grim

Institute of Anatomy, First Faculty of Medicine, Summer semester 2014 / 2015


Inguinal canal
Ureter
Urinary bladder
Ductus deferens
Ductus deferens, ampulla
Seminal gland
Excretory duct
Prostate
Deep transverse perineal
Urethra
Epididymis
Ejaculatory duct
Bulbourethral gland
Penis
Testis

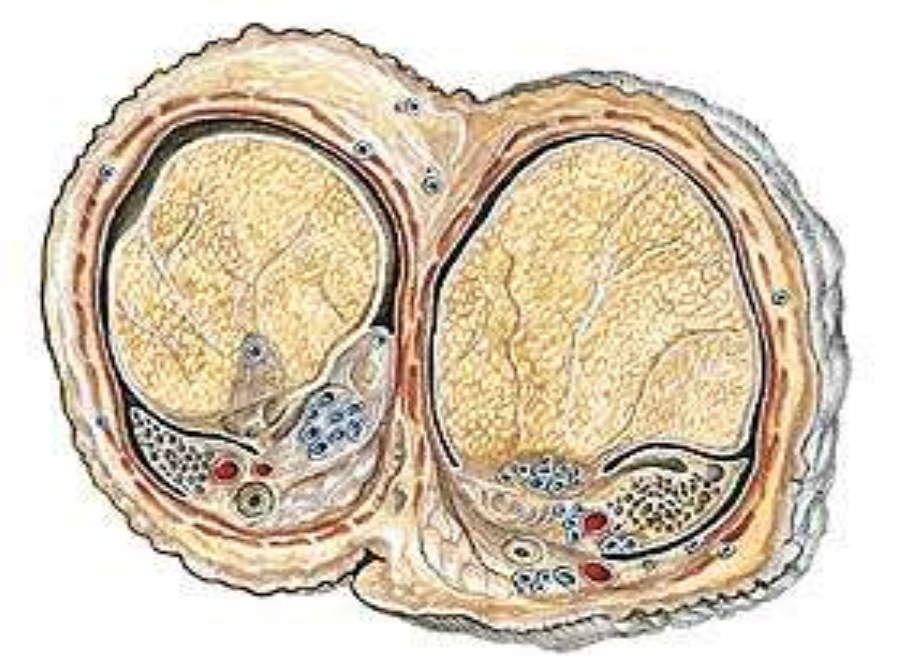
Male genital system, organa genitalia masculina

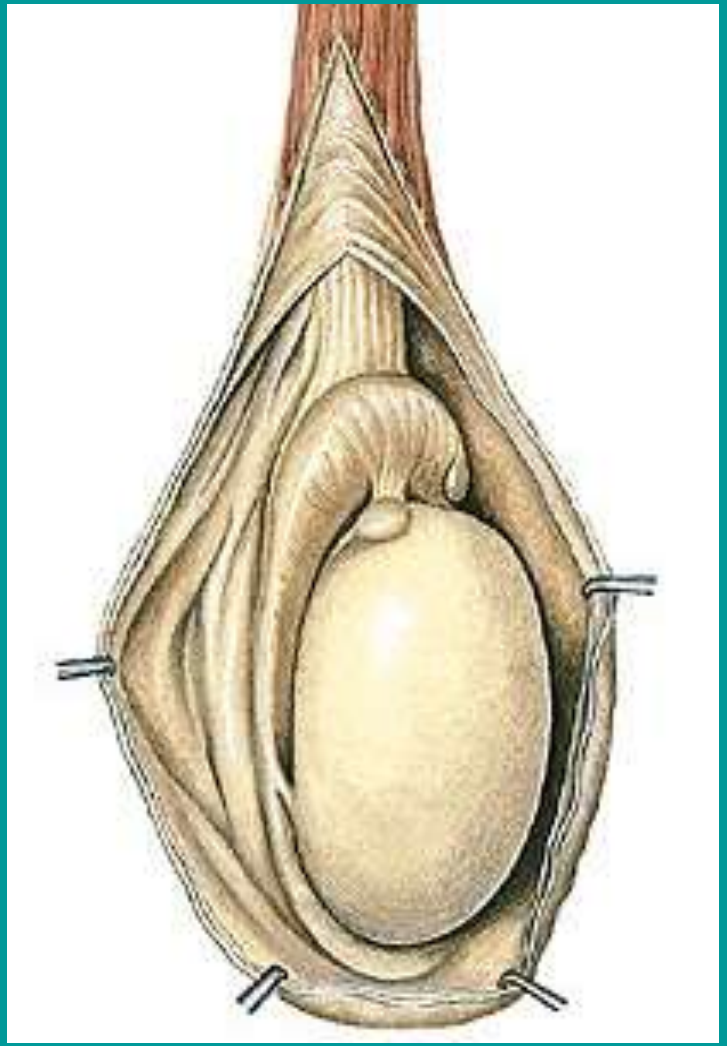
- Testis (orchis)
- Epididymis
- Vas (ductus) deferens
- ejaculatory duct
- Seminal gland (vesicle)
- Prostate
- Bulbo-urethral gland
- Penis
- Scrotum
- Spermatic cord



Testis (orchis)

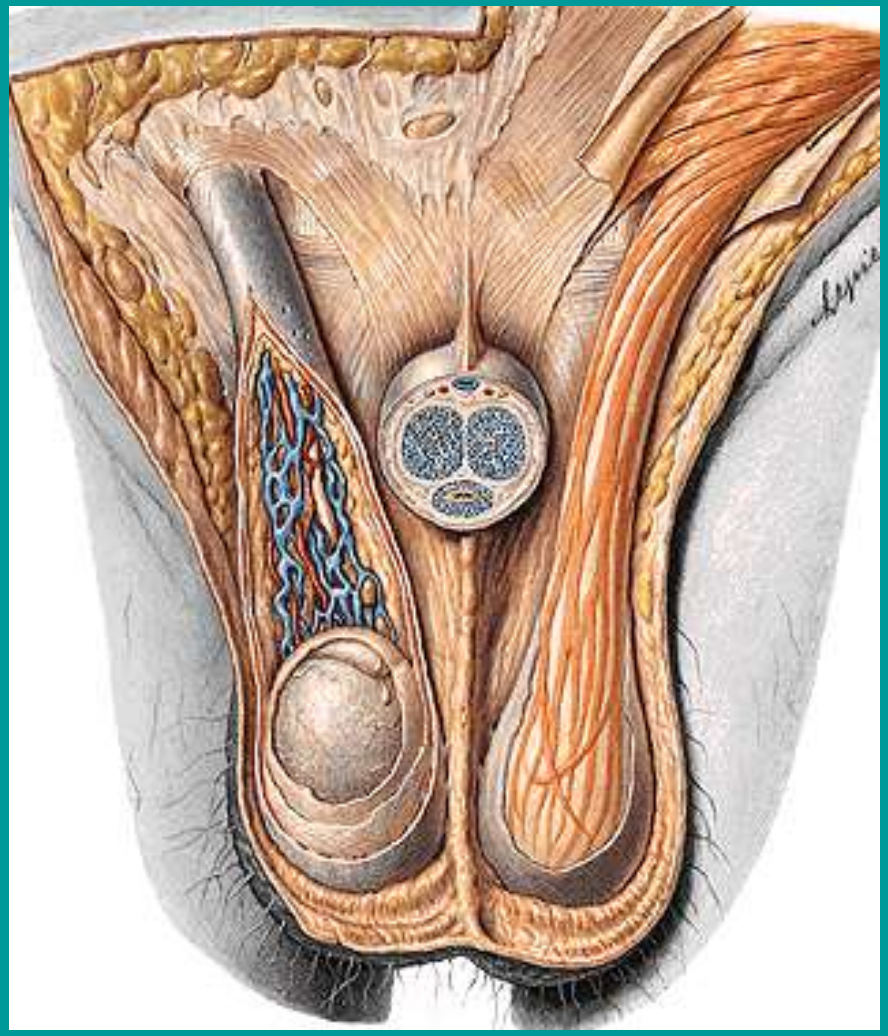
Upper, lower pole, lateral, medial surface, anterior, posterior border, Tunica vaginalis – parietal, visceral layer (epiorchium, periorchium), sinus of epididymis



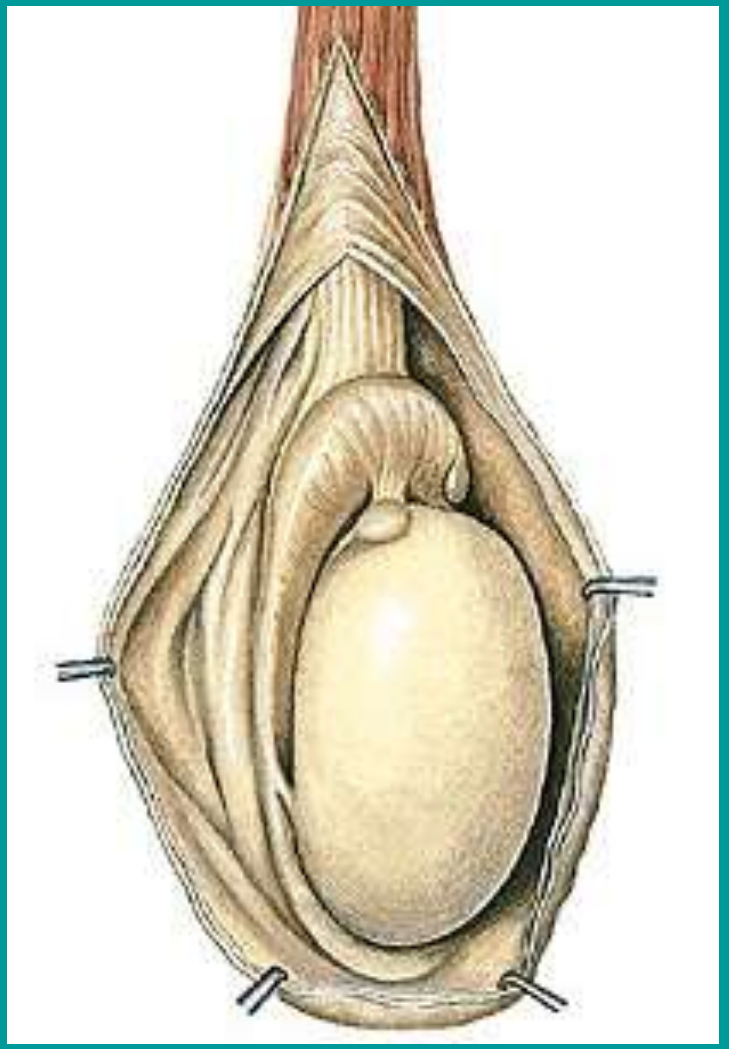


Epididymis

Head, body, lobules, tail, duct of epididymis



Testes in scrotum – elimination of intraabdominal pressure, lower temperature than intraabdominal

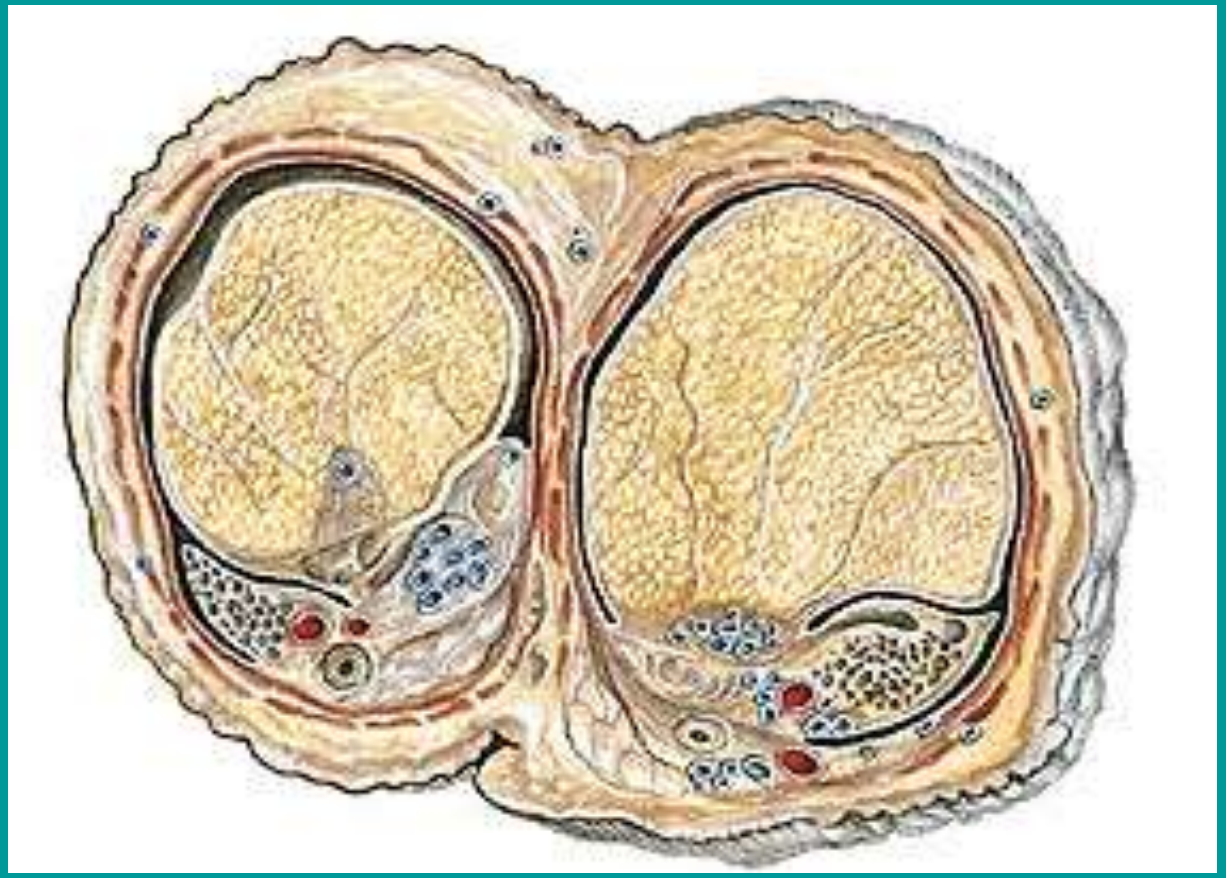


Epididymis

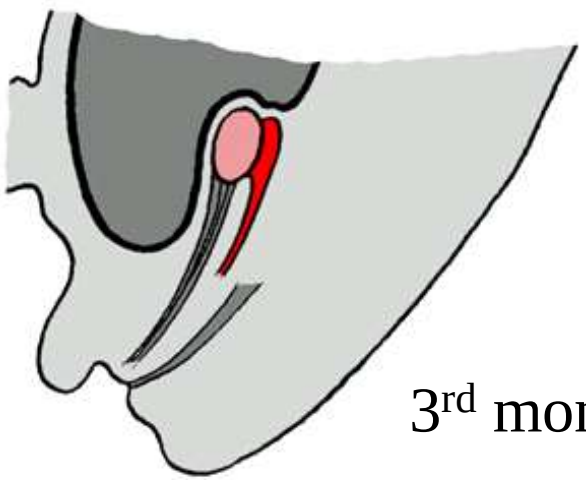
Head, body, lobules, tail, duct of epididymis

Scrotum

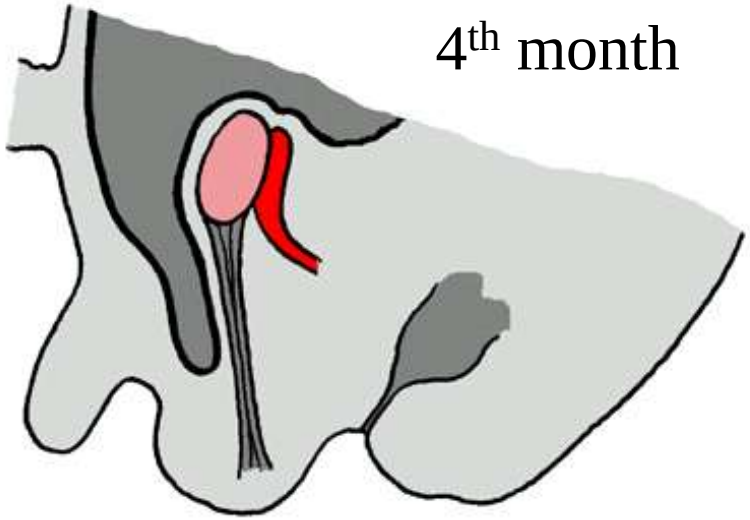
Cutaneous + muscular pouch, raphae, dartos fascia, septum, dartos muscle, external + internal spermatic fascia, cremaster, cremasteric fascia, rudiments of vaginal processus;



Descent of the testes: the role of the gubernaculum testis

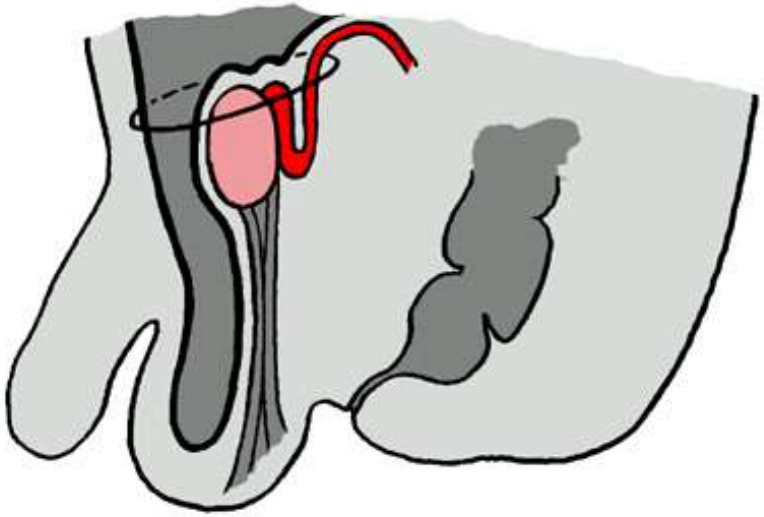


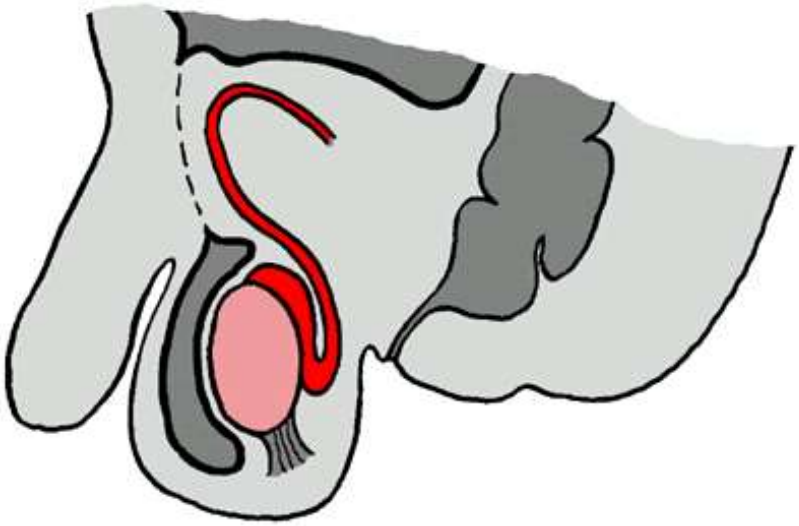
3rd month



4th month

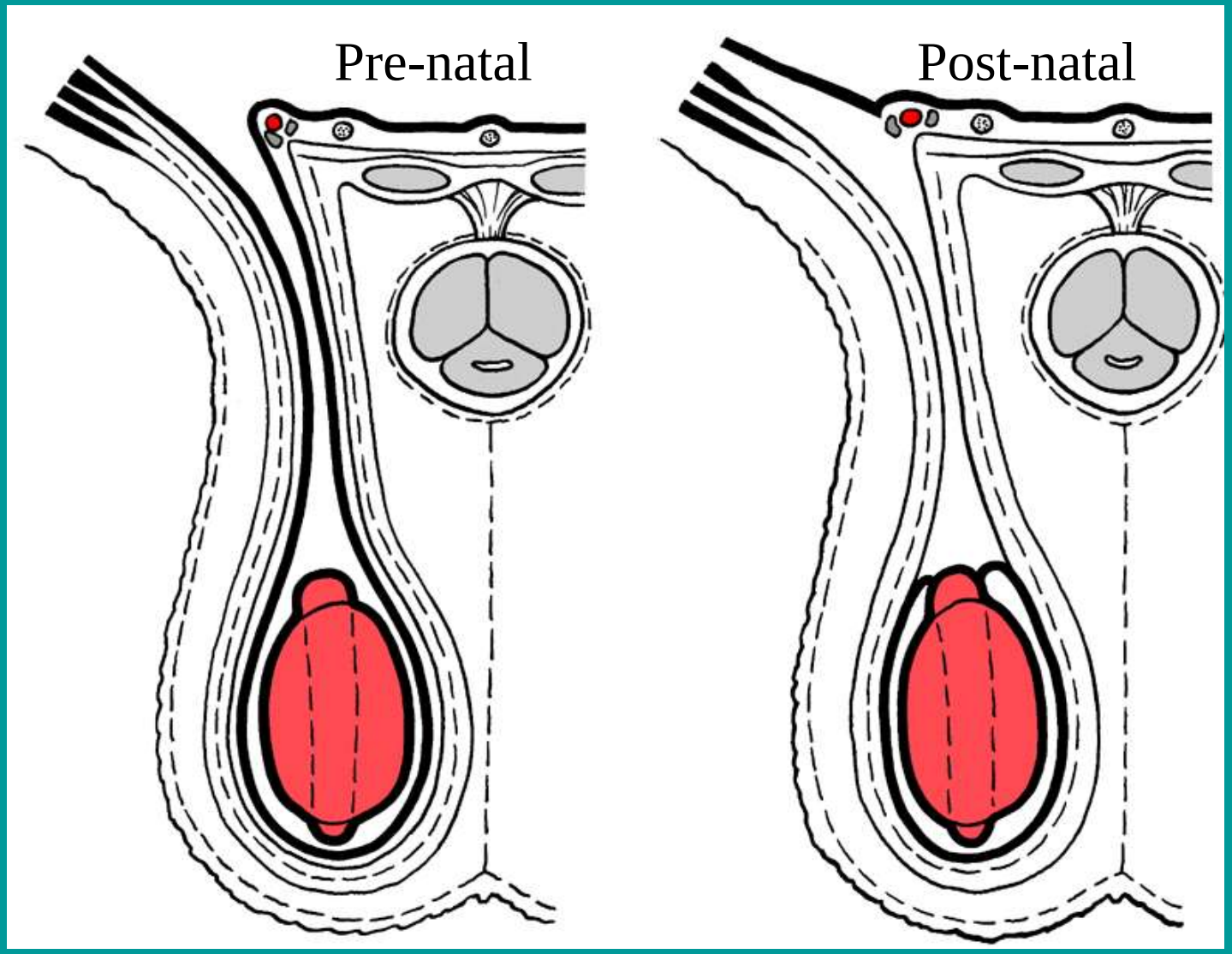
7th month

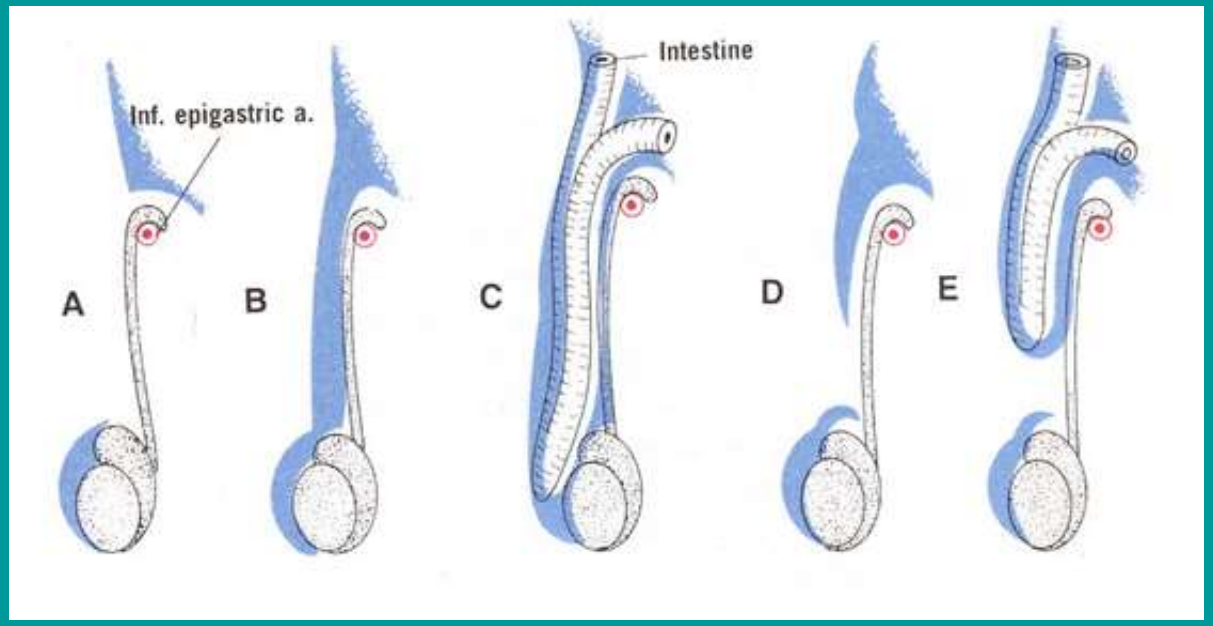


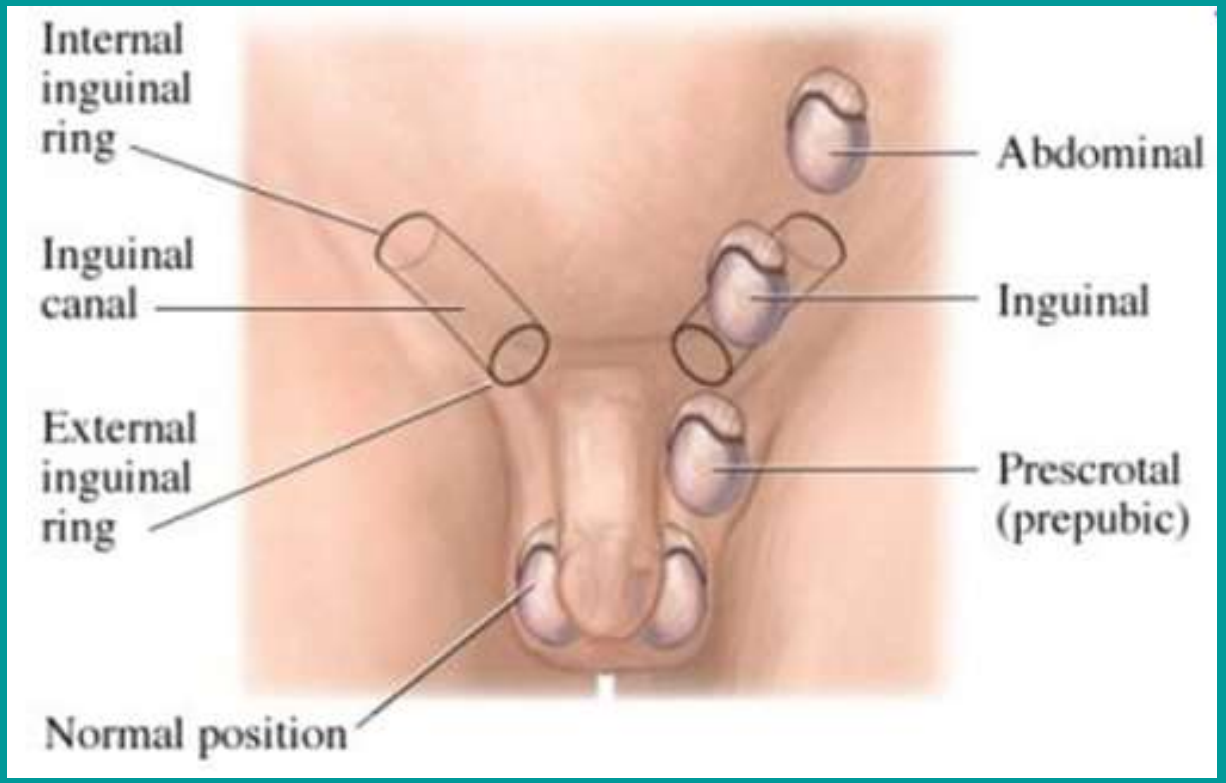


8-10th month

Skin, dartos muscle + fascia, external spermatic fascia, cremaster muscle + fascia, internal spermatic fascia rudiments of vaginal processus



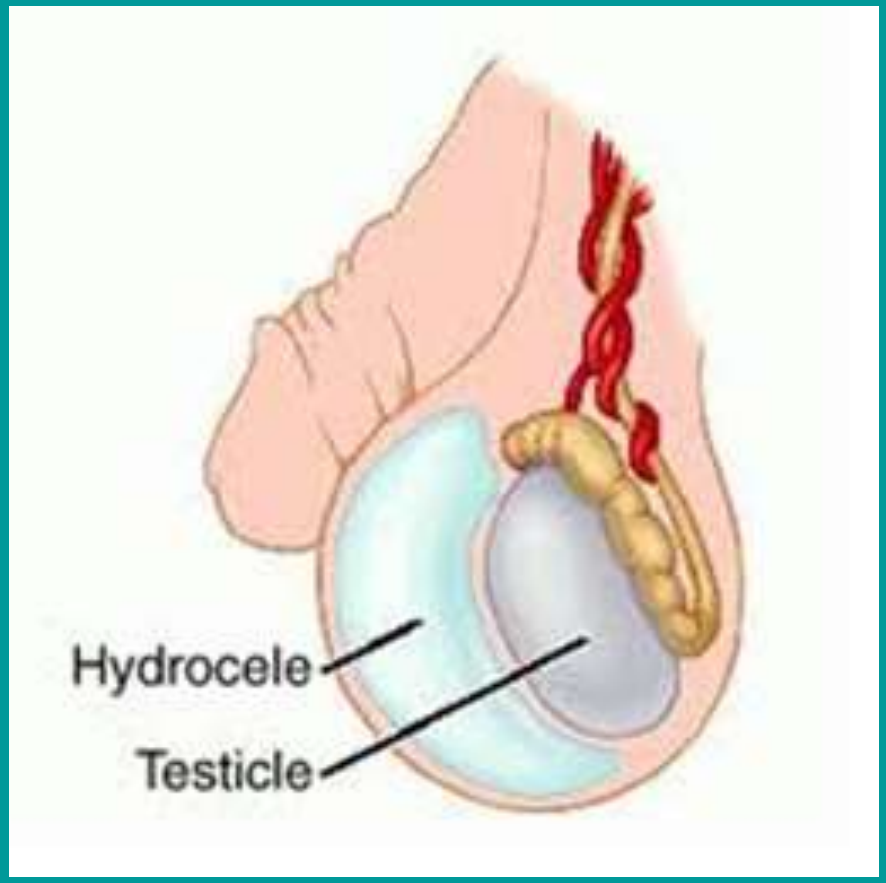


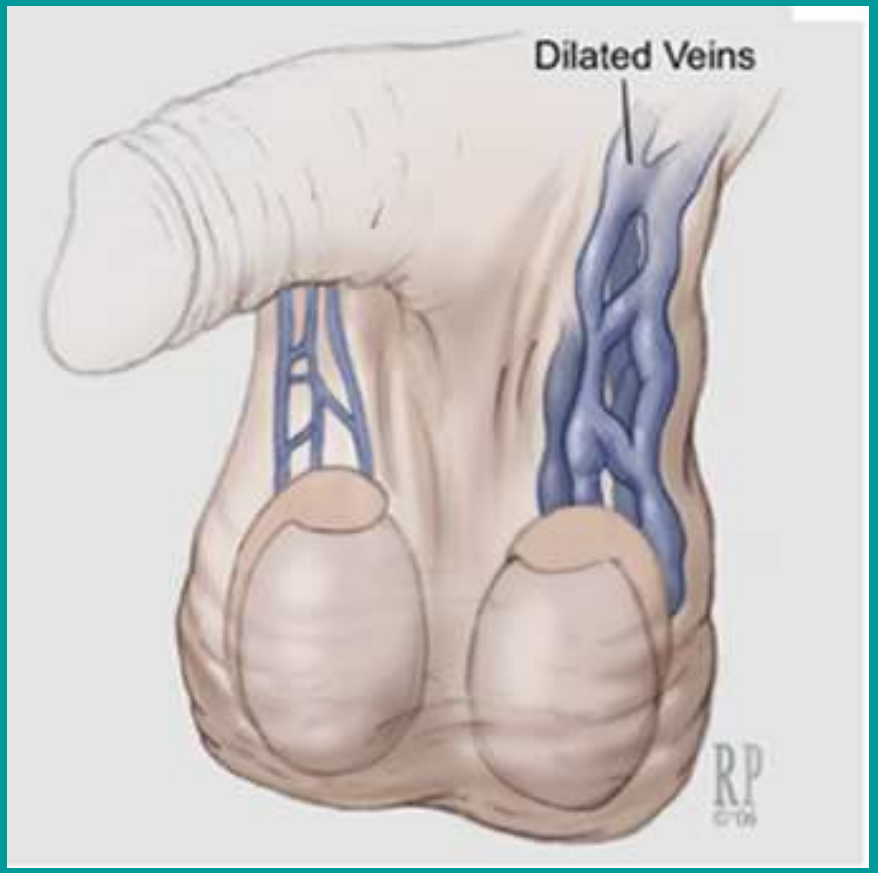


Congenital inguinal hernia

Cryptorchism,
Retention of testis,
Ectopia testis,

Inversion of testis





Hydrocele – the cavity of the scrotum filled by pathological serous effusion

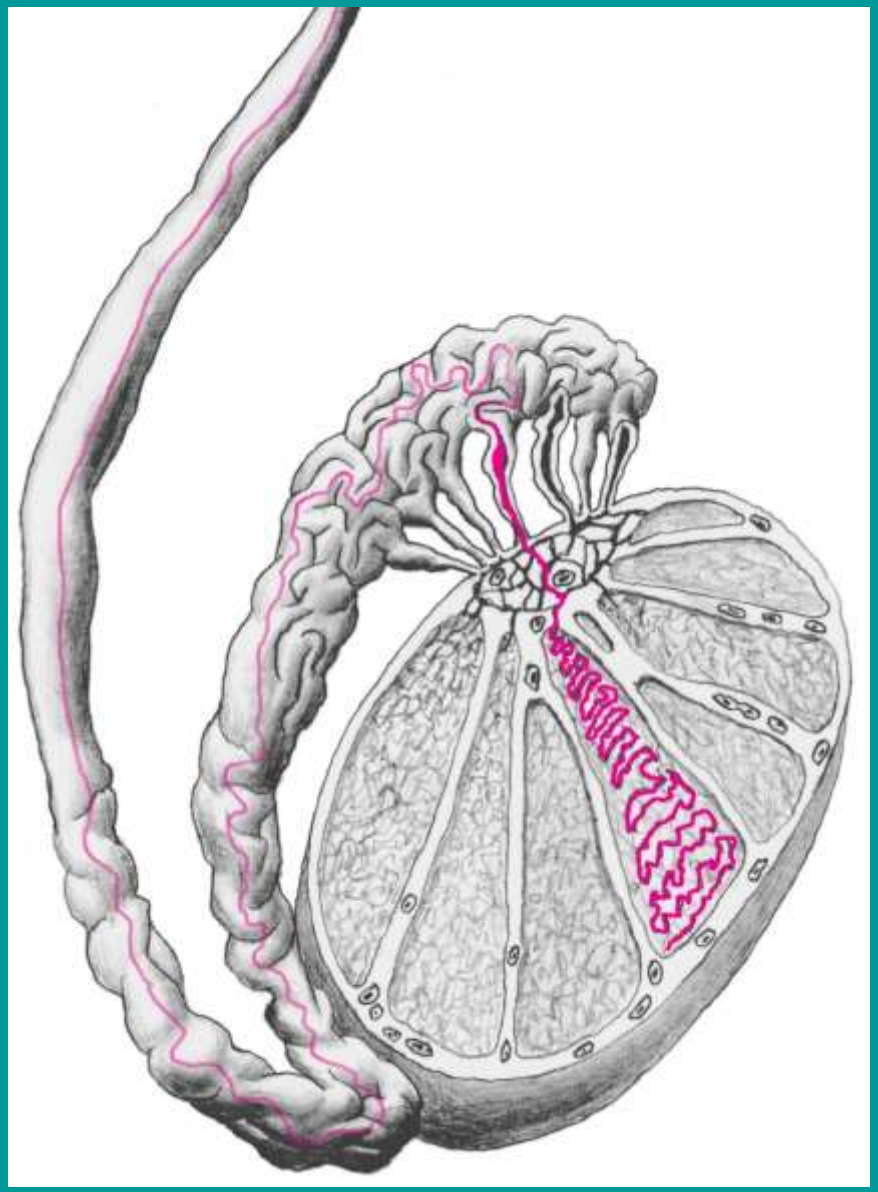
Varicocele – varicose condition of pampiniform plexus – alteration of spermatogenesis

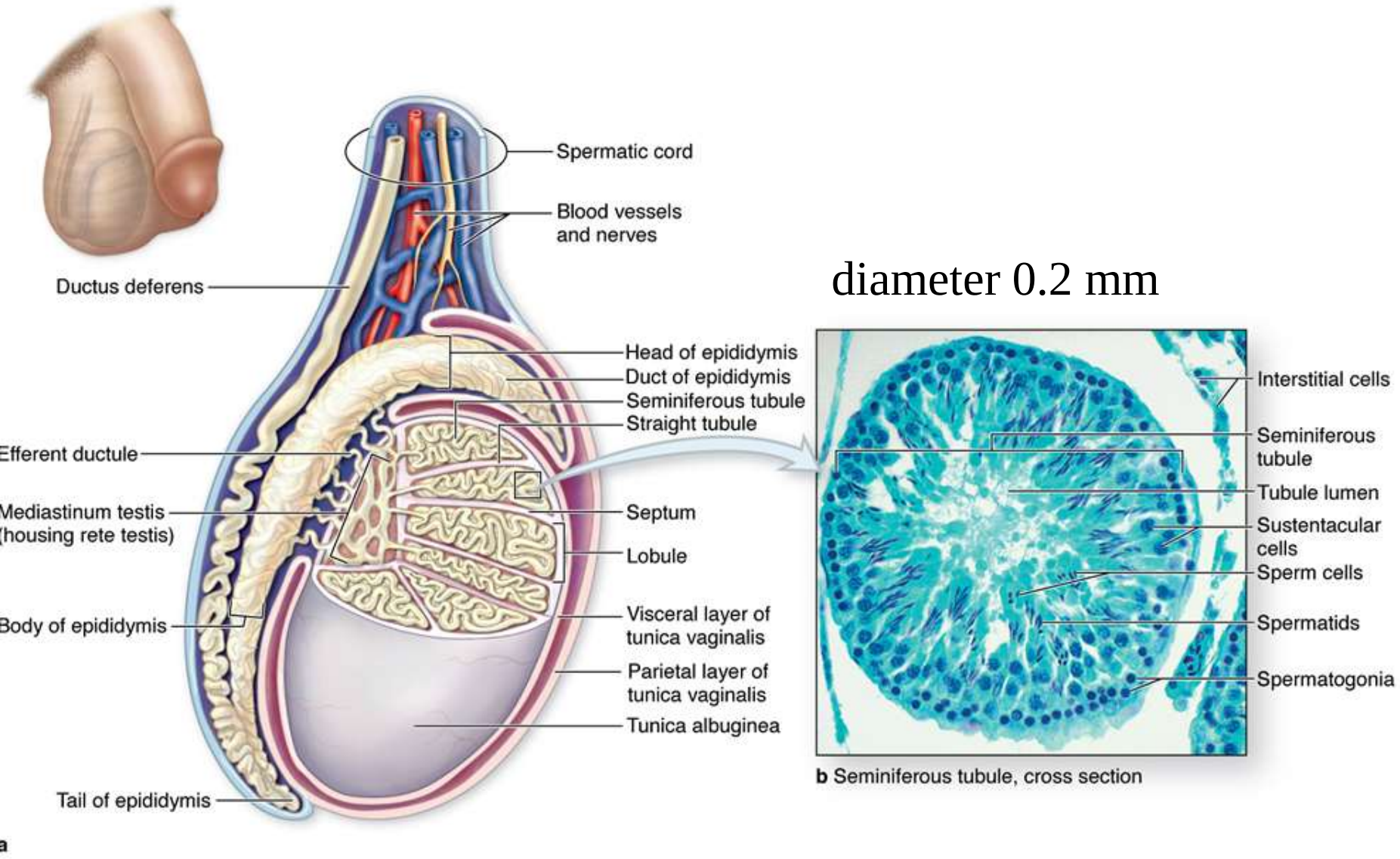
Structure of testis

tunica albuginea, vascular layer, mediastinum, septa, lobules, seminiferous tubules, rete testis, efferent ductules, germinal epithelium, spermatogenic cells, sustentacular cells of Sertoli

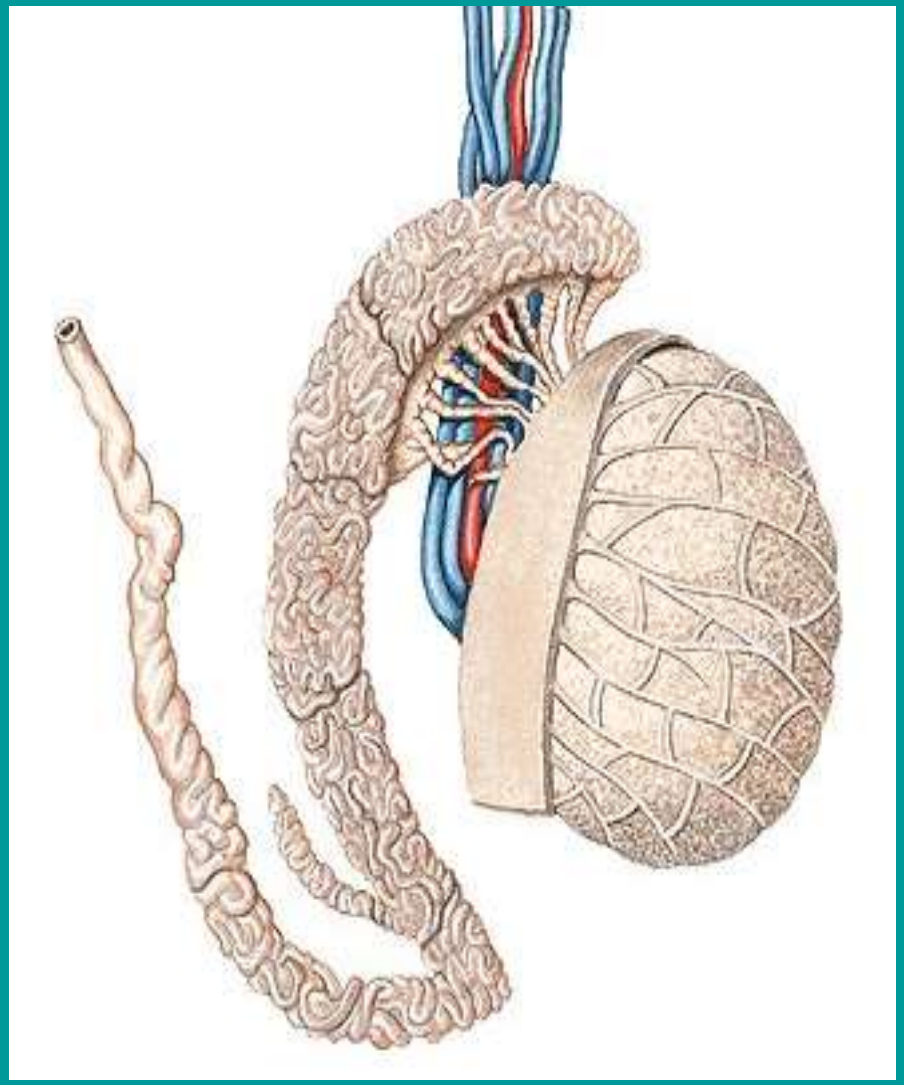
Interstitial endocrine cells of Leydig

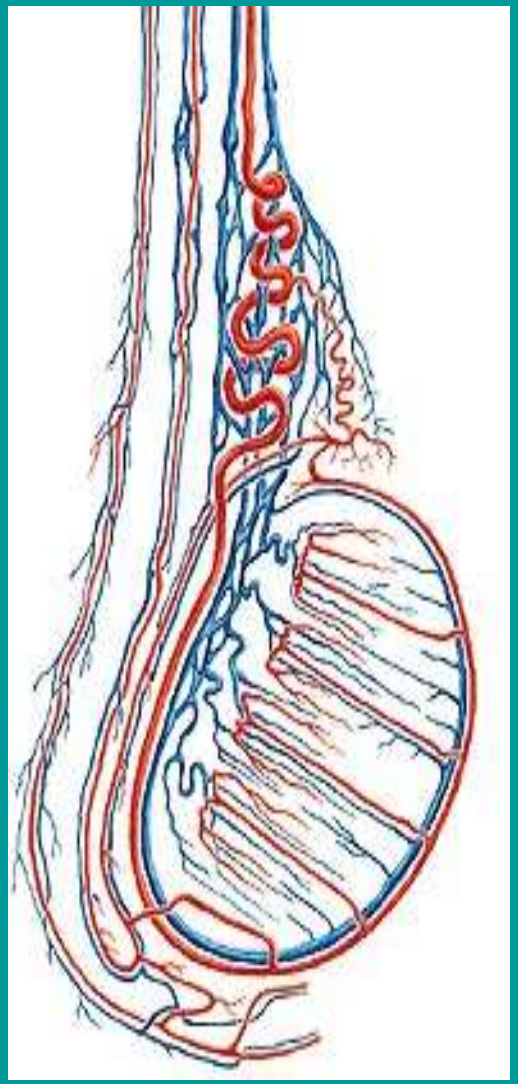
Epididymis –duct of epididymis



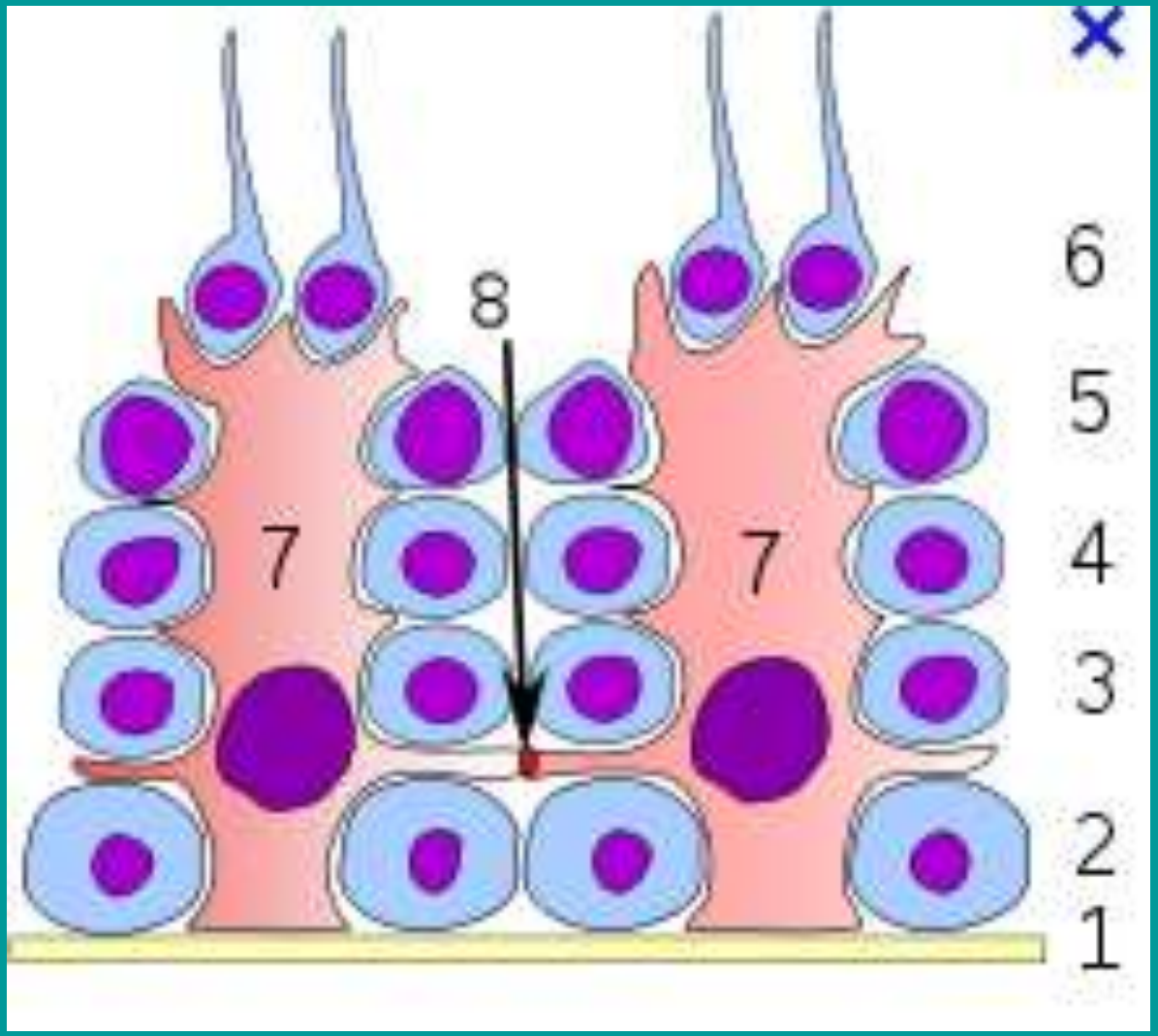


Testis and seminiferous tubules (individual lenght 30-70 cm, total lenght 300 m)





Spermatic cord: testicular a. + v., pampiniform venous plexus, vas deferens, a.+ v. of deferent duct



1 - basal lamina
2 – spermatogonia
3 – spermatocyte I
4 – spermatocyte II
5 – spermatide
6 – mature spermatide
7 – Sertoli cell
8 – tight junction

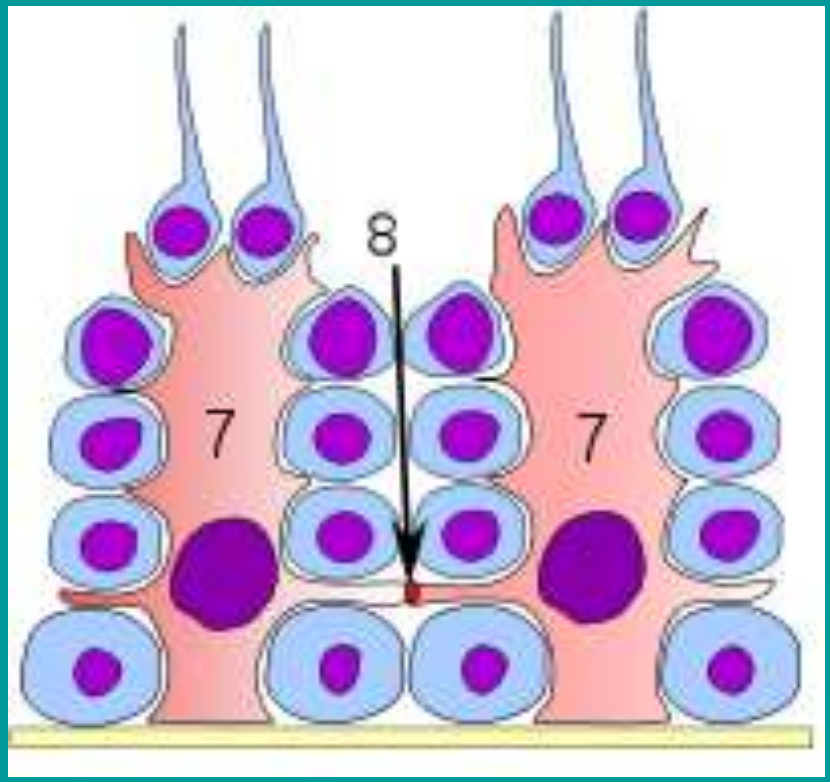
Function of the Sertoli cells

Essential cells in the regulation of spermatogenesis

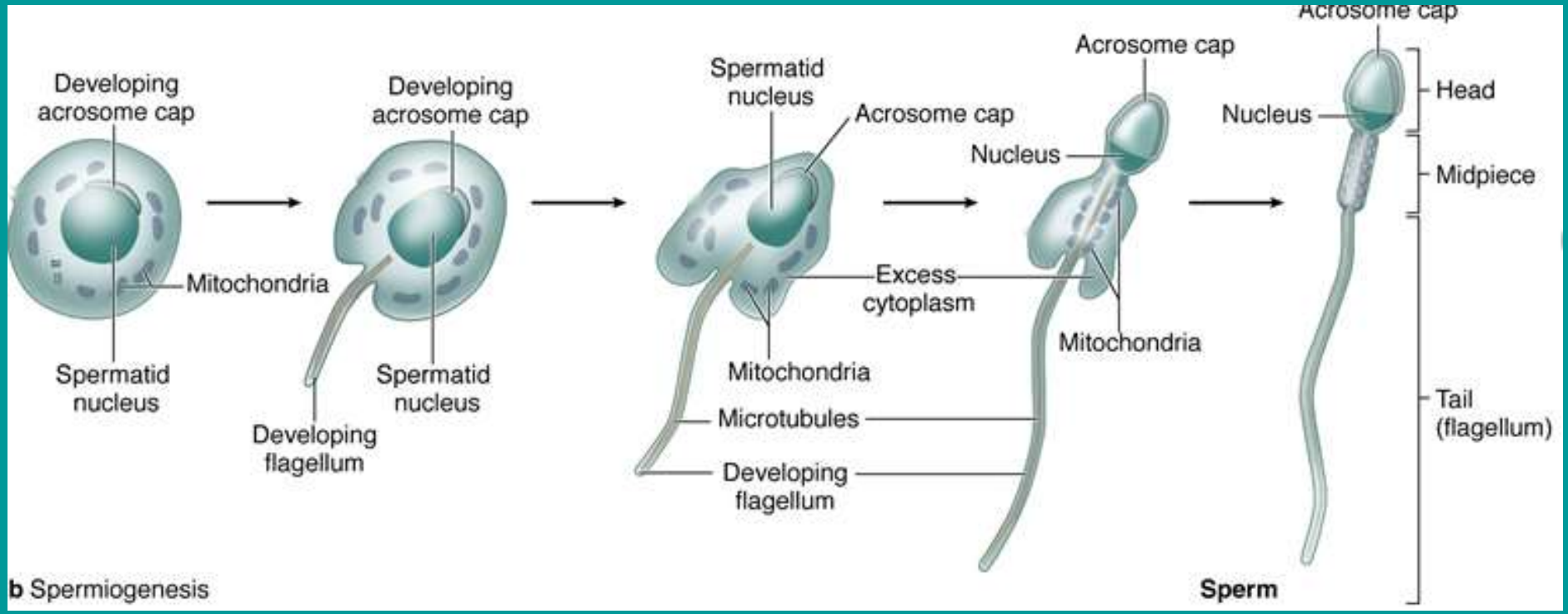
Blood-testis-barrier

Production of the seminal fluid containing Androgen-binding protein

Production of AMH (Anti-Müllerian hormone) during development of the male phenotype



Spermiogenesis
Spermatides
Motile sperm



Spermatogenesis: 1 million of spermatozoa / 1h

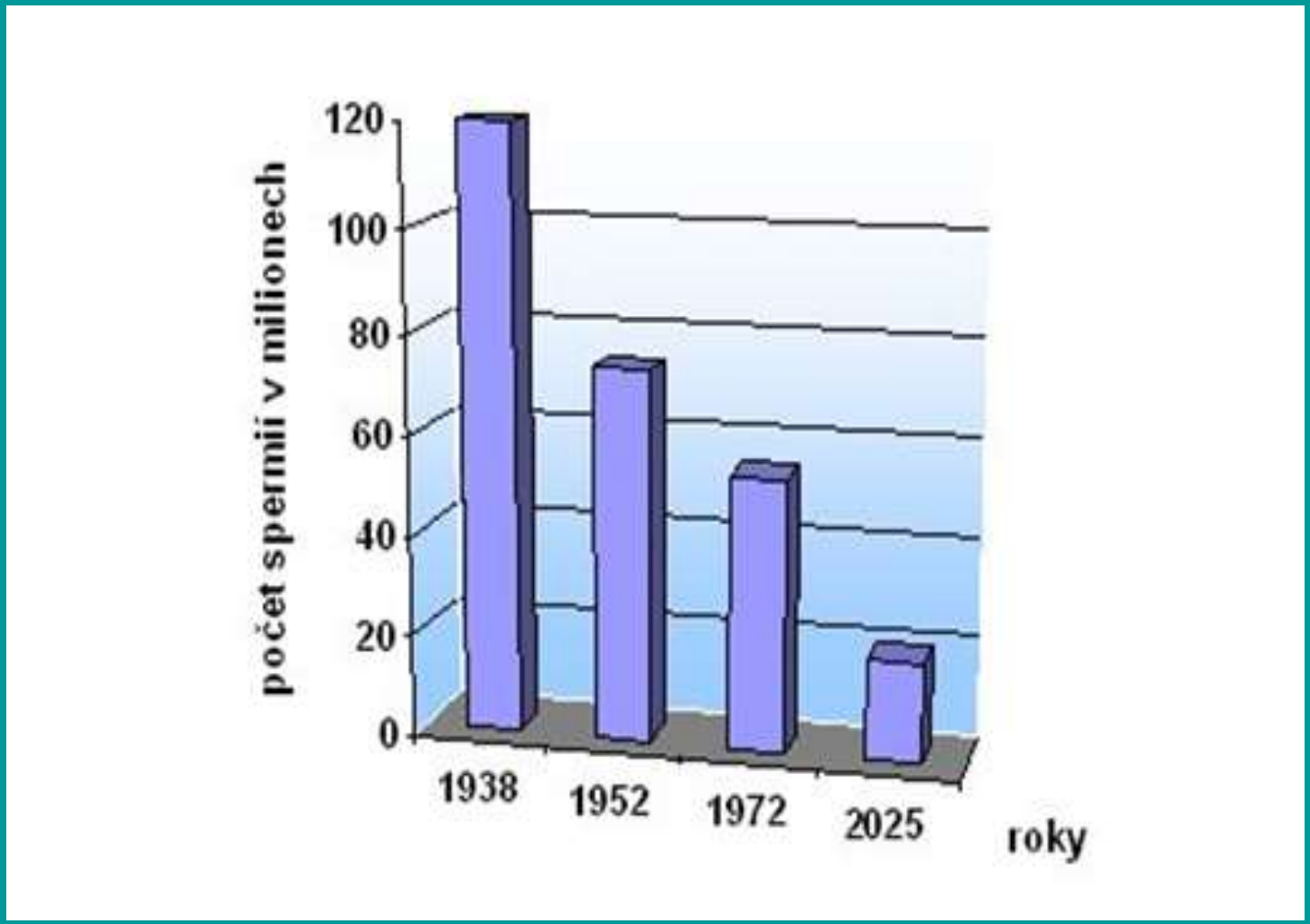
Differentiation and maturation lasted 82 days.

Ejaculate, semen (2–6 ml) 35 – 200 mil. spermatozoa

Less than 10 mil /1 ml = oligospermia, sterility

WHO 2006

Historical development of spermatozoa number in the 1 ml of ejaculate (2006 – 20 000 000/1 ml)



Environmental effects on gonadal development

Disorders of development of the testis and reproductive tract in the male fetuses are increasing in incidence. The most dramatic change that appears to have ocurred over the past 60 years is a fall in sperm counts of around 40-50%.

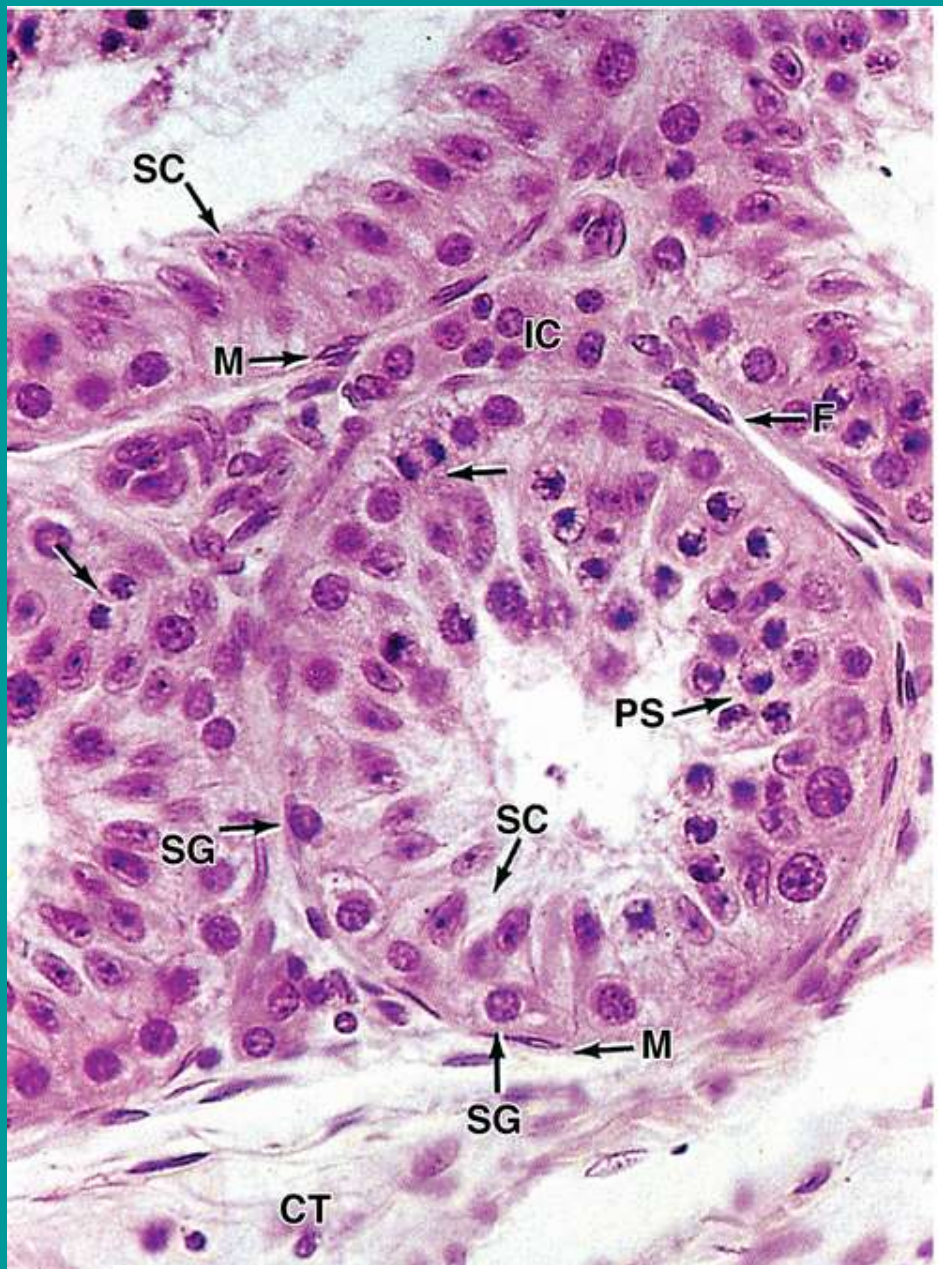
These developmental disorders are attributed to feminising factors affecting prenatal development.

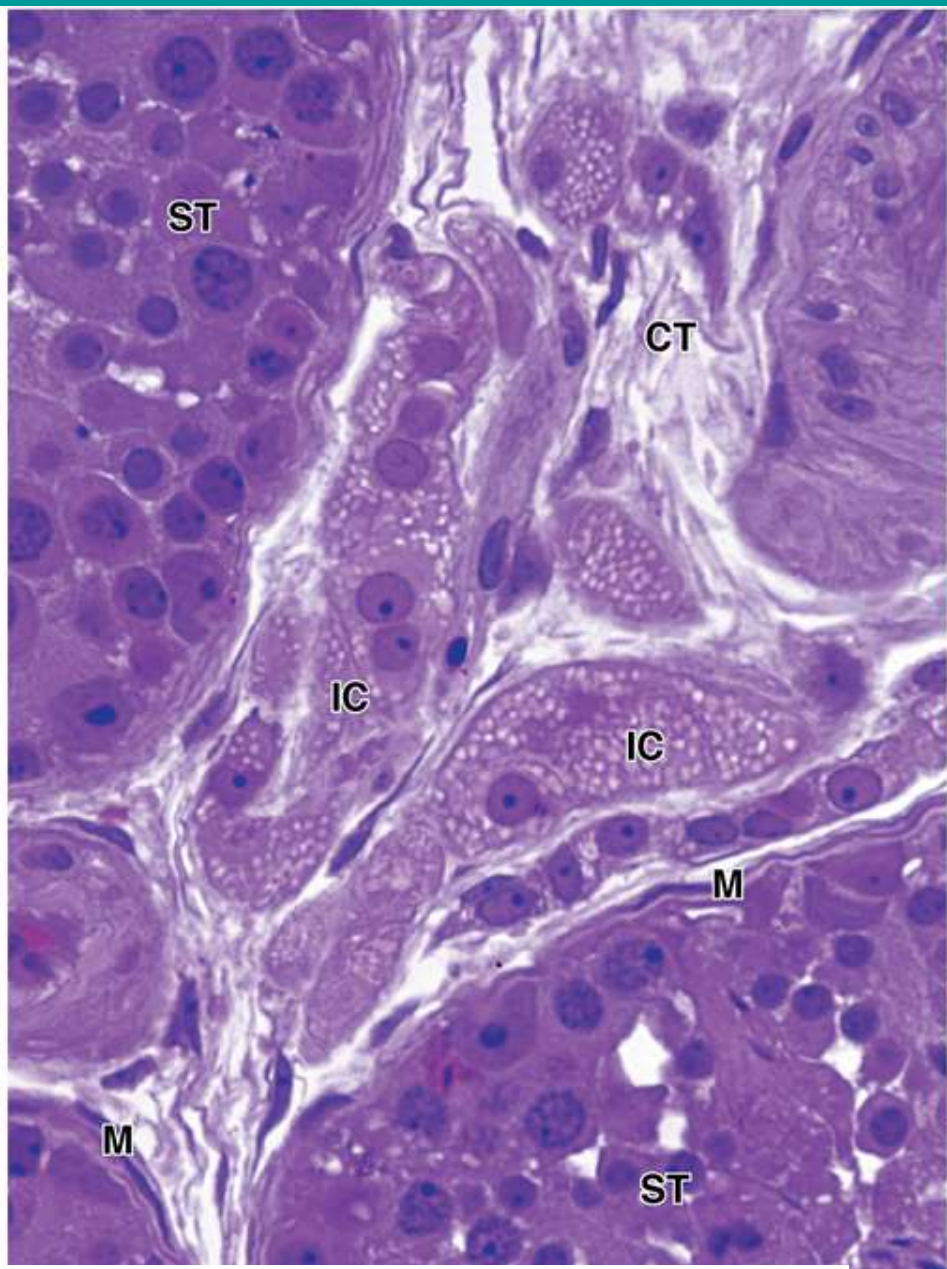
Feminising factors:

- exogenous estrogens produced by the pharmaceutical industry
- substances with estrogenic effects by binding to estrogen receptors: DDT, polychlorinated biphenyls, chlorinated hydrocarbons and detergents and cleaners

They are fat-soluble and accumulate in the food chain and in our body, which contains more fat than in the past.

It is therefore likely that the rising frequency of morphological and functional abnormalities of the male reproductive system, is the result of these changes (according to Gray's Anatomy, 38th edition)





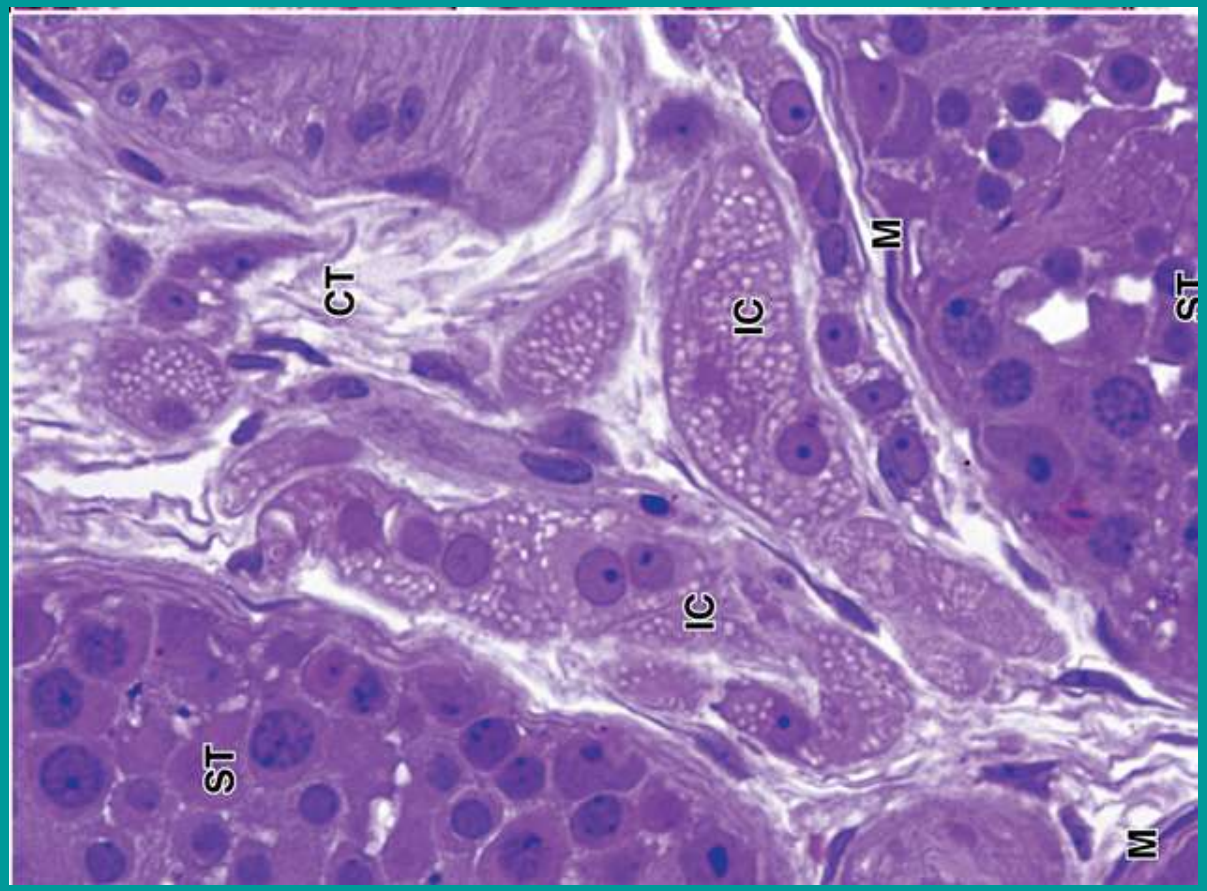
a

Seminiferious tubules (supporting Sertoli cells and germ cells of spermatogenic lineage); interstitial (Leydig) cells producing androgens

Leydig cells produce testosterone

a) in fetal weeks 8. - 14. – masculinization of genital tract

b) From puberty to adulthood – growth of genital organs, secondary sexual features, spermatogenesis



Epididymis - head, body, lobules, tail, duct of epididymis

Epididymis: highly coiled duct with temporarily stored sperm

Vas (ductus) deferens

(50-60 cm)
muscular layer, mucous membrane, adventitia
Emission - contraction waves during transportation of spermatozoa into urethra followed by ejaculation
Parts: scrotal, funicular, inguinal, pelvic, ampulla

Seminal gland (vesicle)

excretory duct

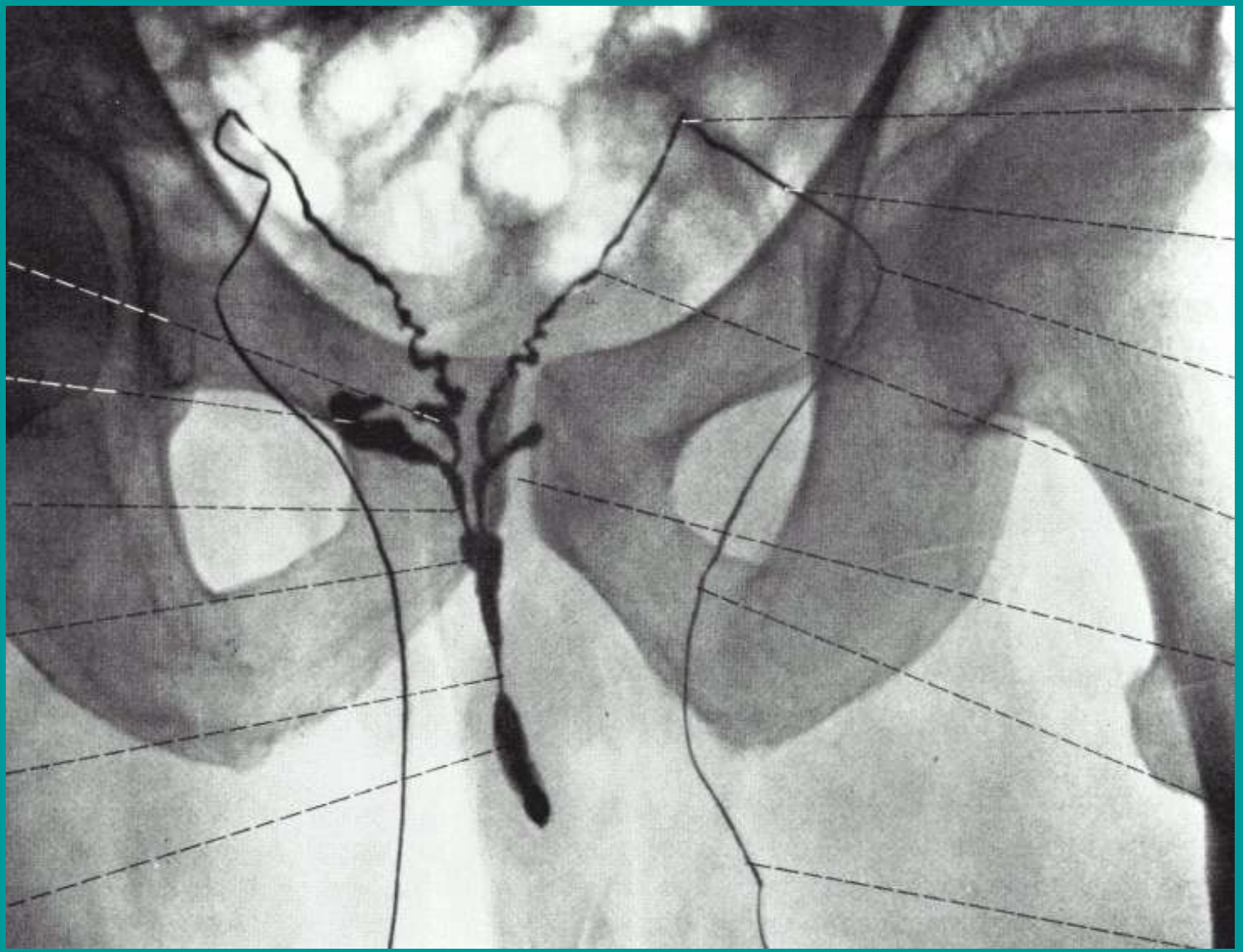
Ejaculatory duct

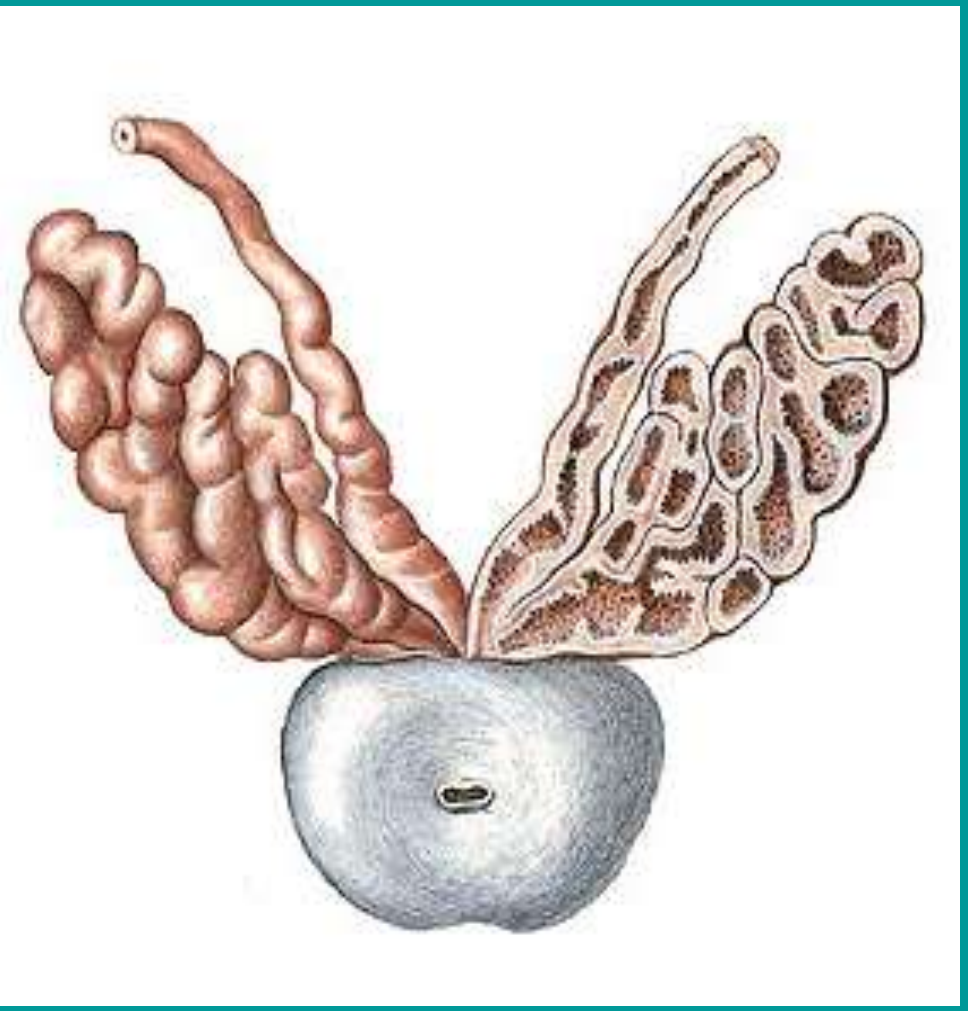
Spermatic cord

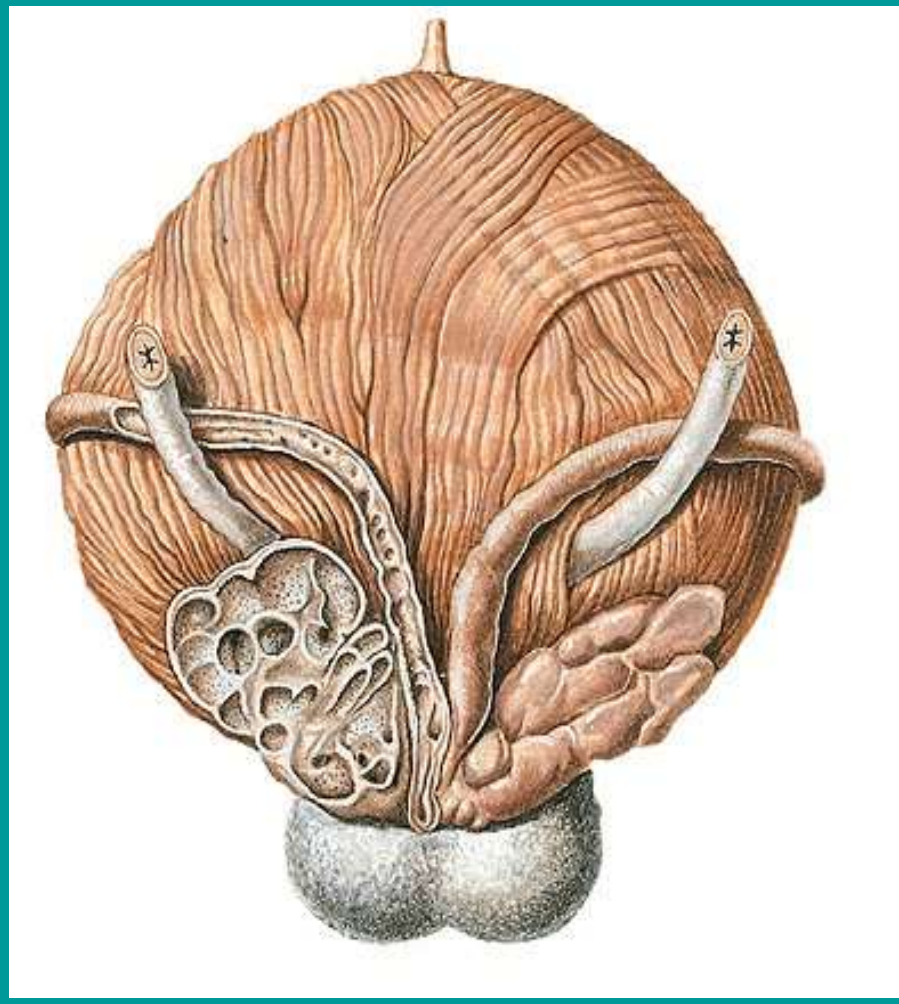
testicular a. + v., pampiniform plexus,
vas deferens, a.+ v. of deferent duct

Vas (ductus) deferens

scrotal, funicular, inguinal, pelvic part, ampulla

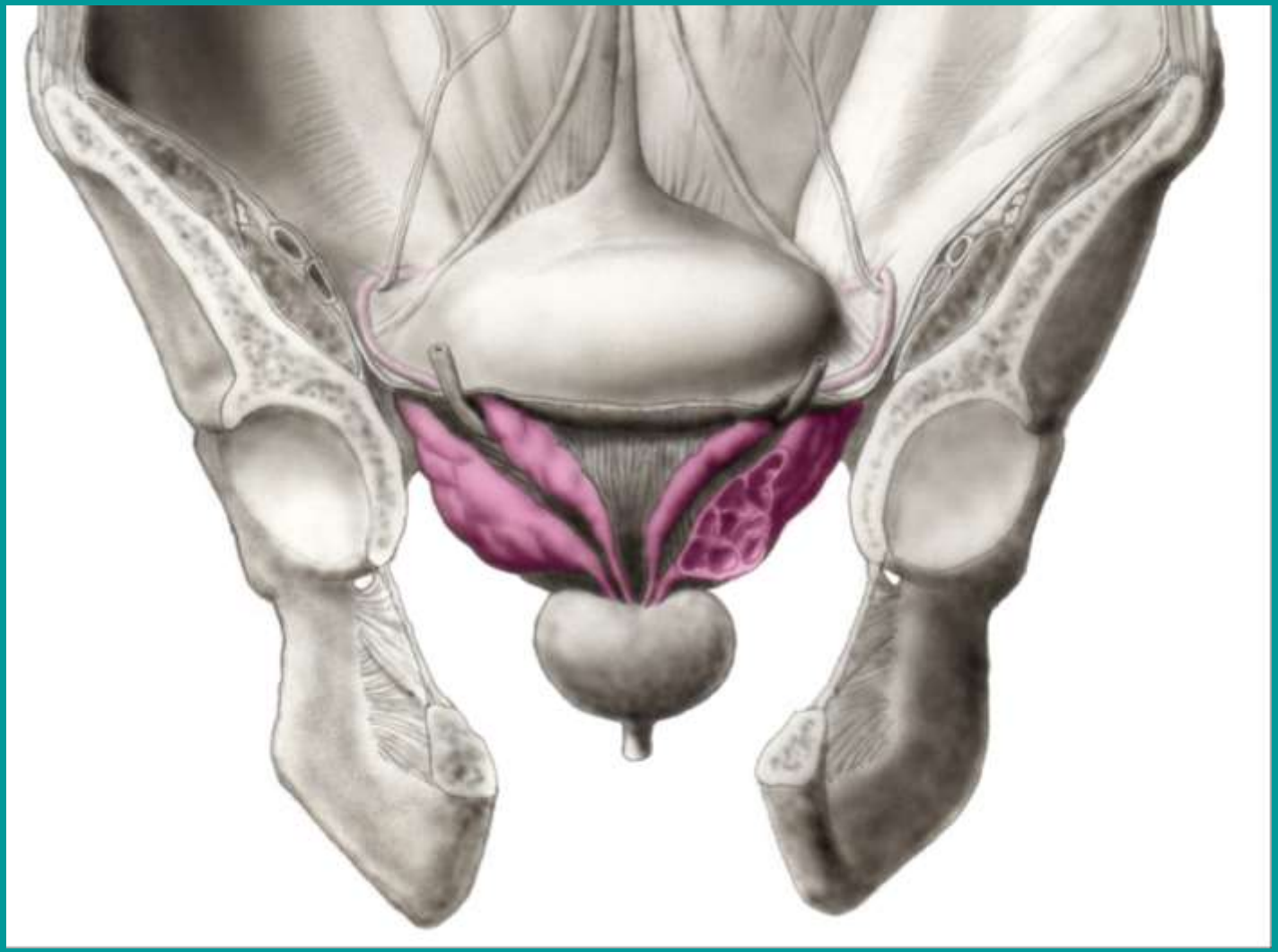


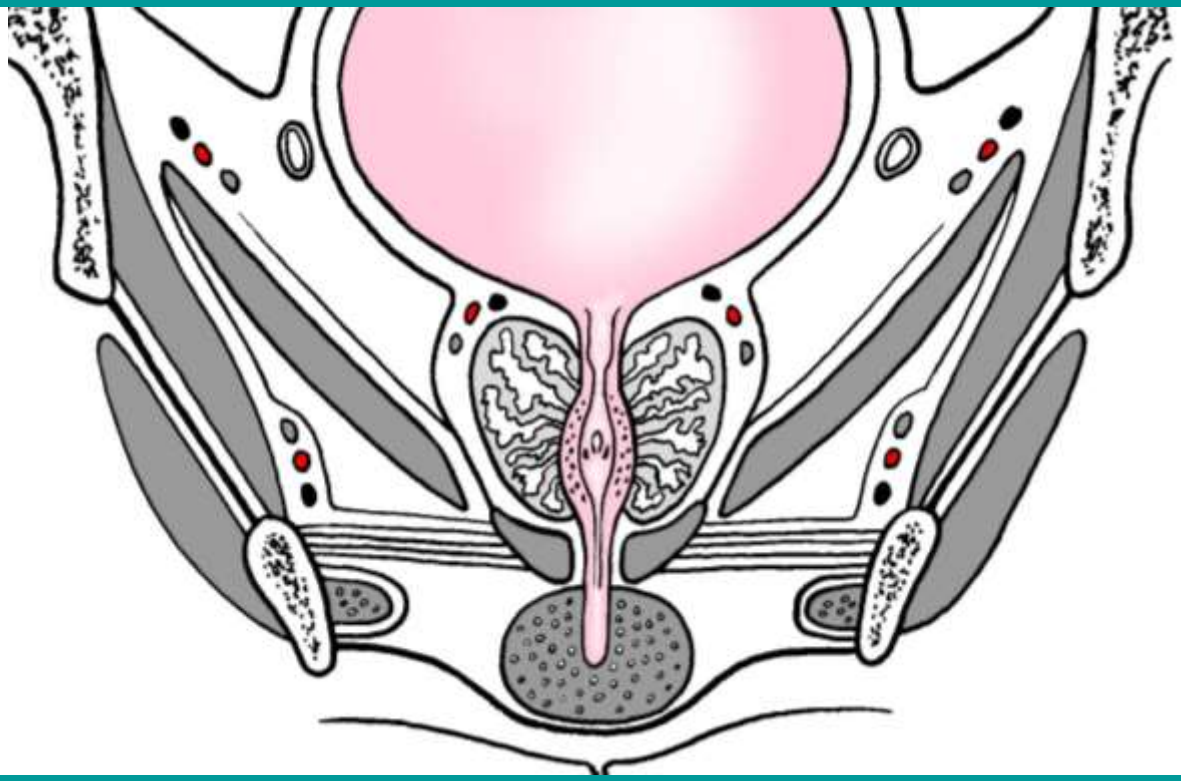




Seminal gland (vesicle), coiled ducts, excretory duct, ampulla of deferent duct, rectovesical septum, interampullar trigon

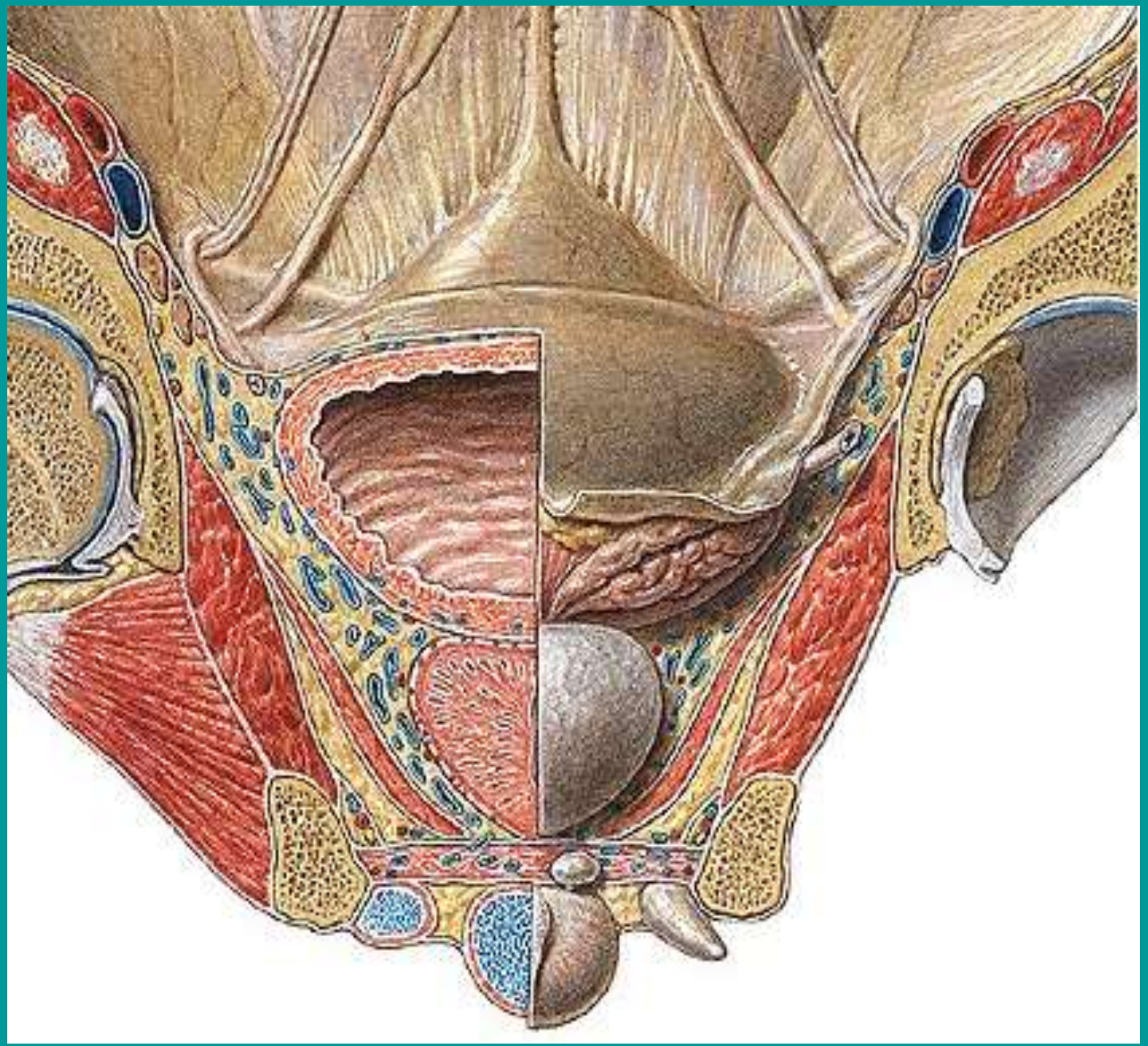
Interampullar trigon



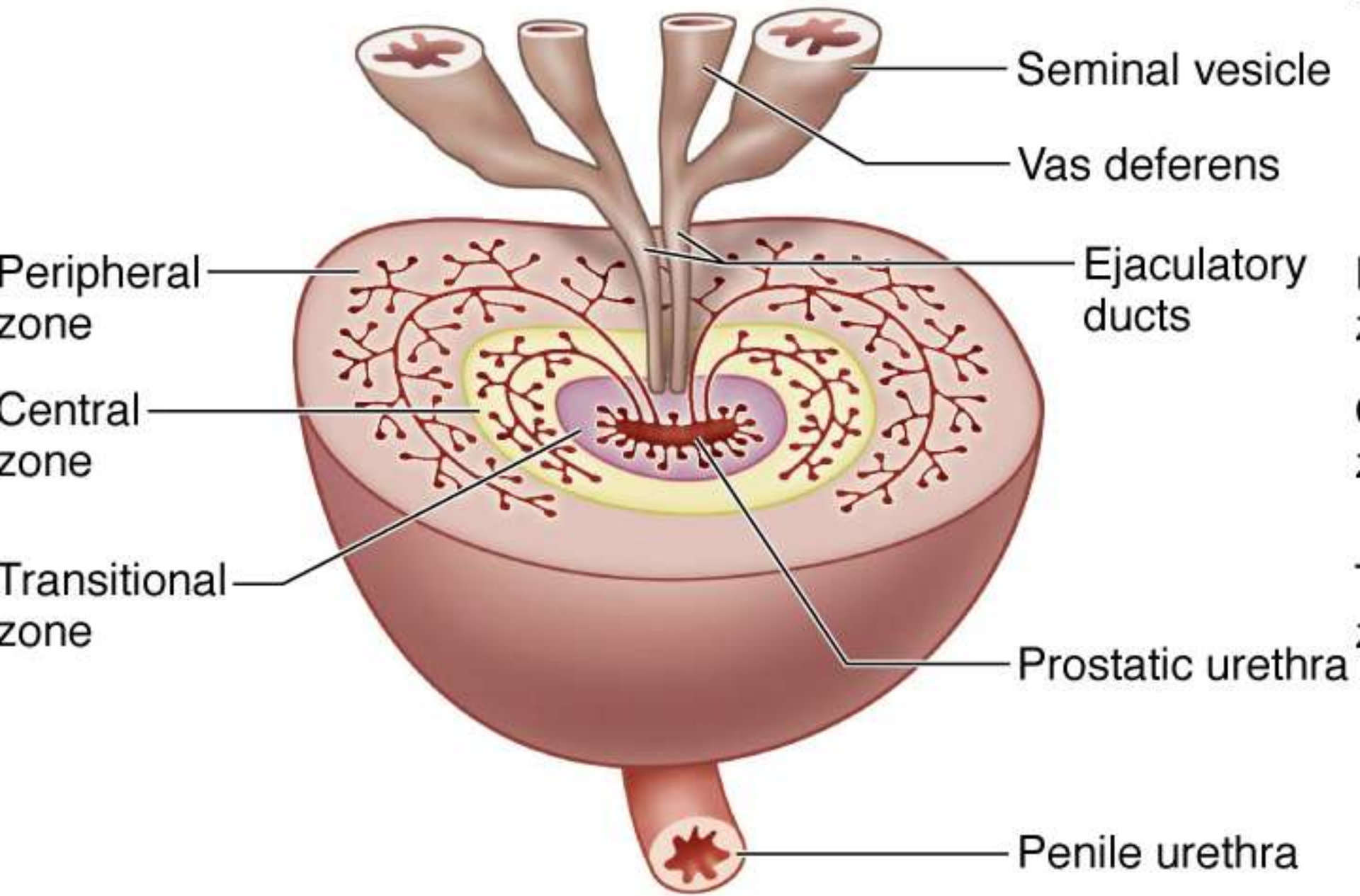


Prostate

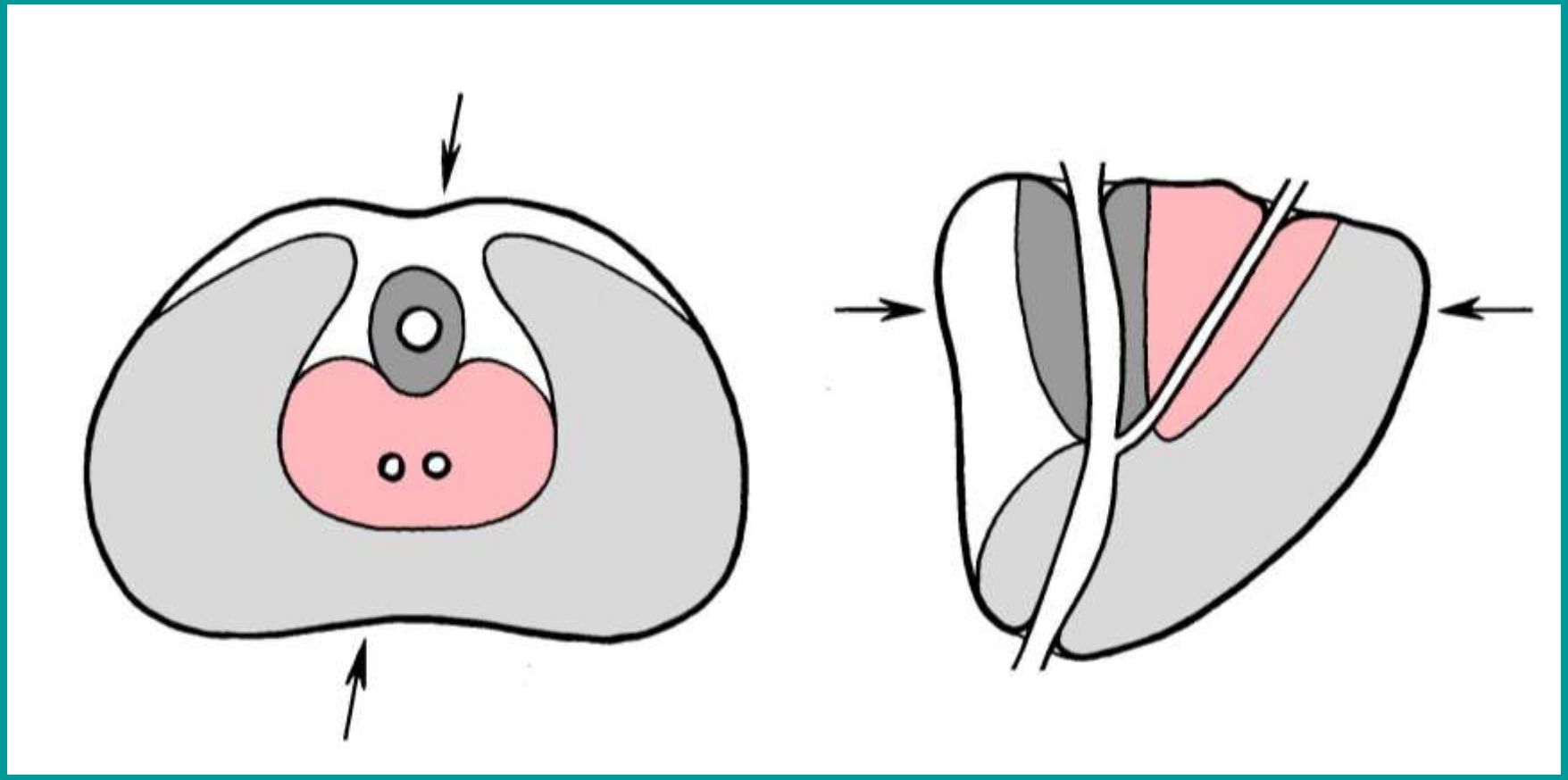
base, apex, anterior, posterior, inferolateral surface
capsule, glandular parenchyme, prostatic ducts,
muscular tissue,
right + left lobes, middle lobe,
puboprostaticus, vesicoprostaticus mm.



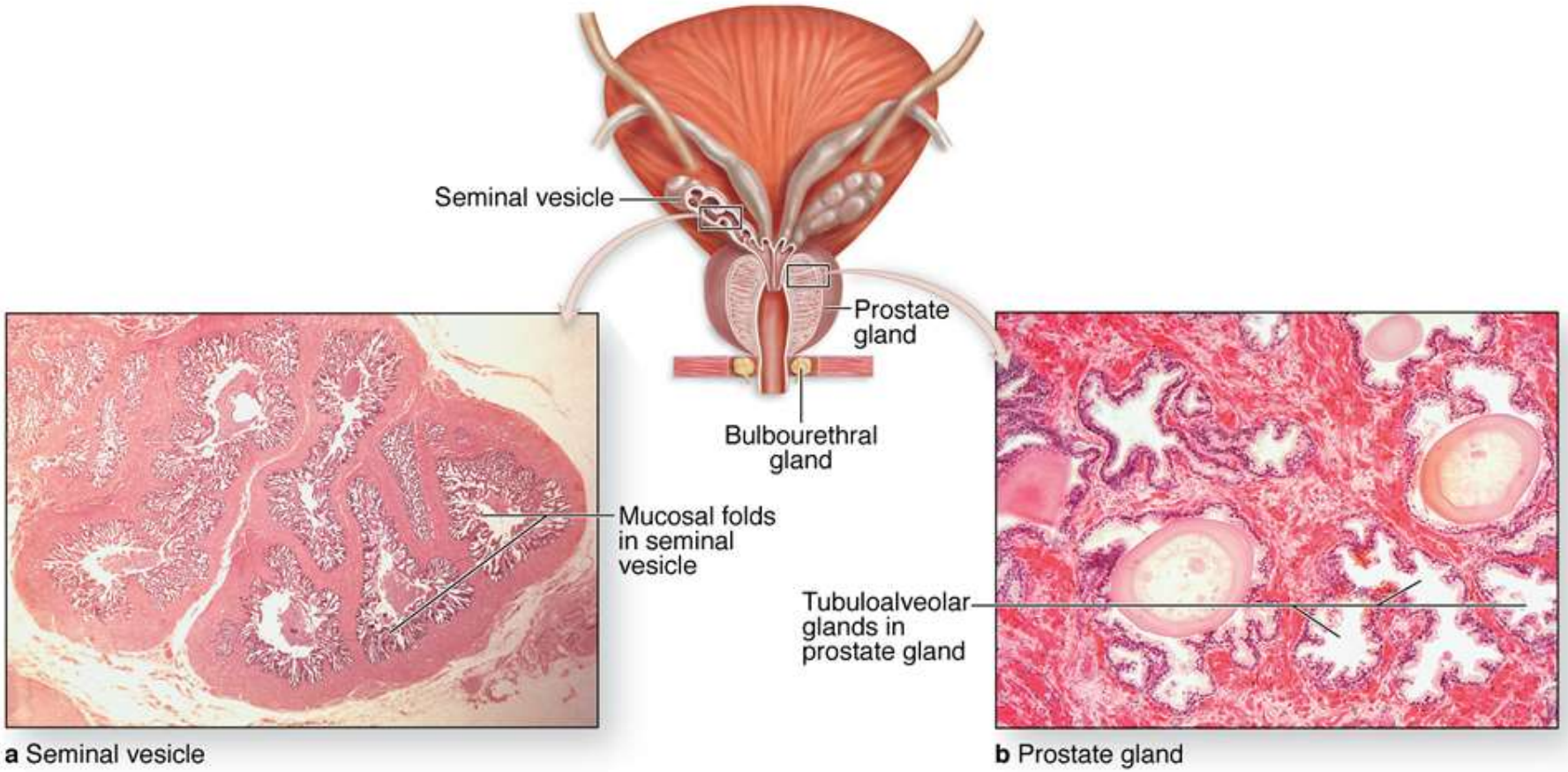
Syntopy of prostate



Organization of the prostate: mucosal glands, submucosal glands, main glands

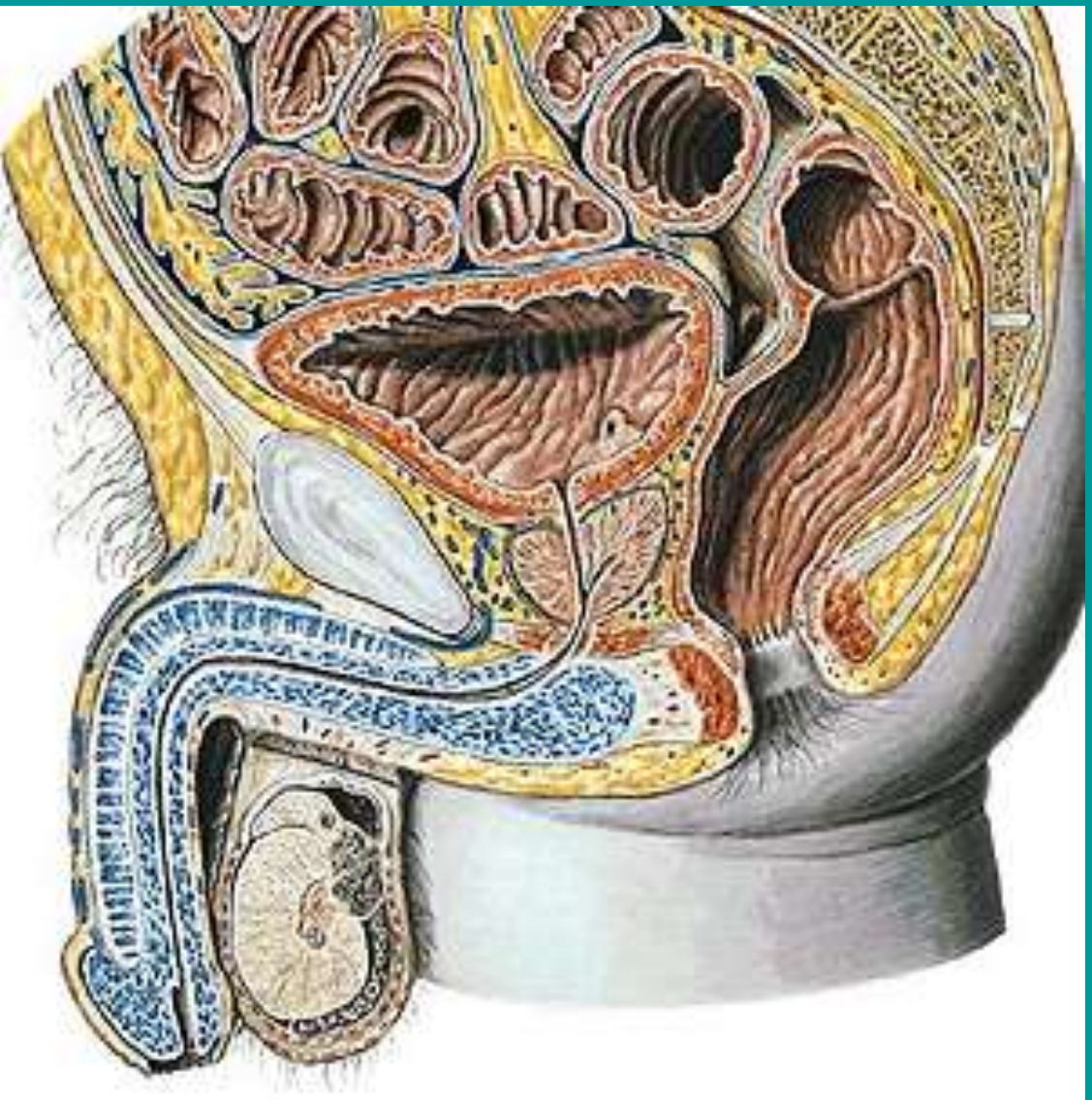


Zones of prostate: periurethral, central, peripheral

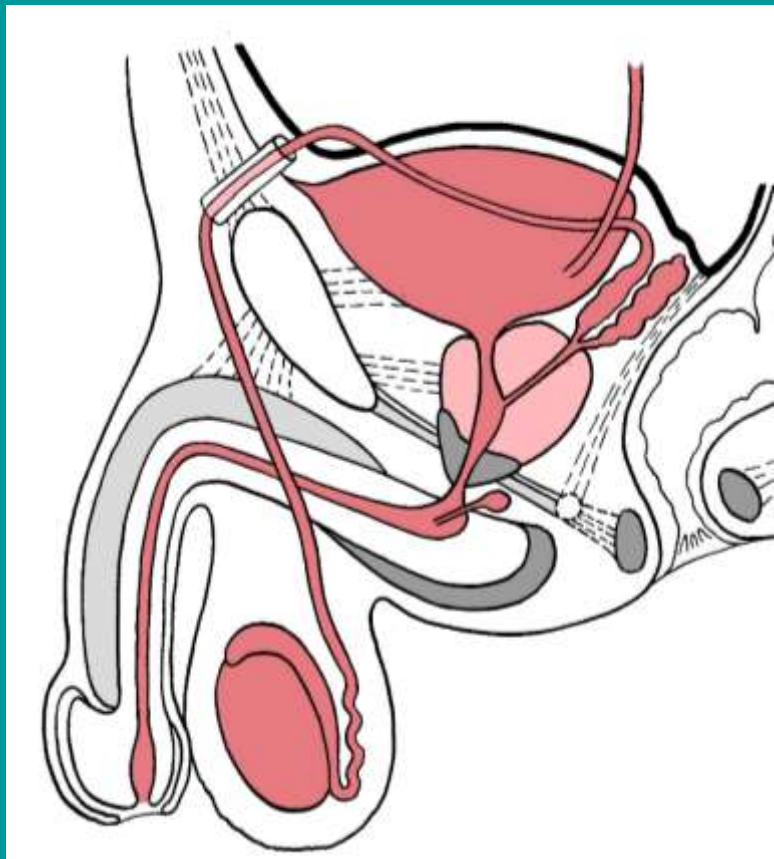


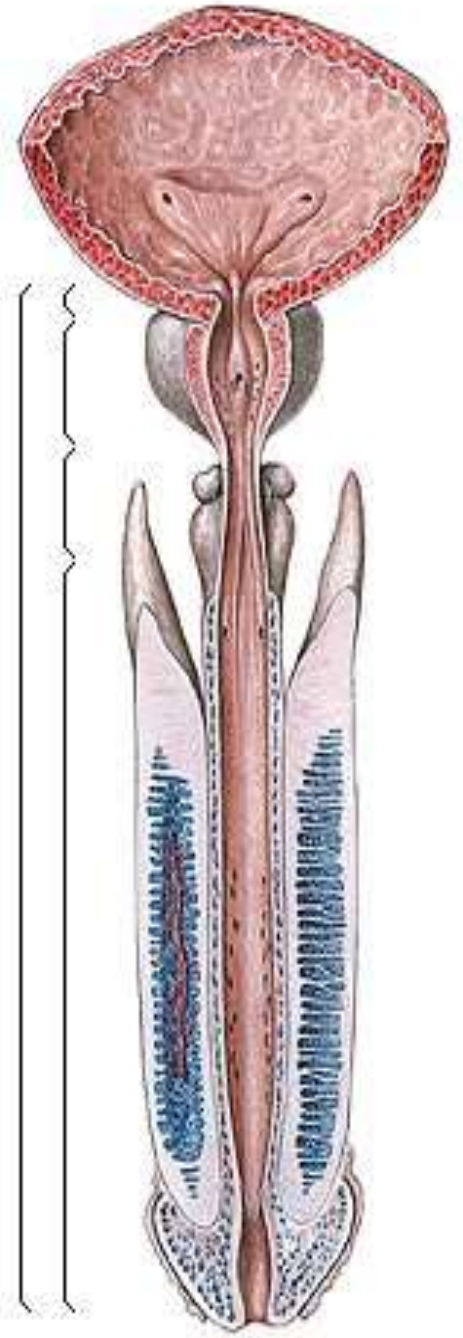
Parenchyme of the prostate:
dense fibromuscular stroma and tuboalveolar glands

Penis - dorsum, urtehral surface, root, body, raphae, suspensory lig., fundiform lig., subpubic + prepubic curve



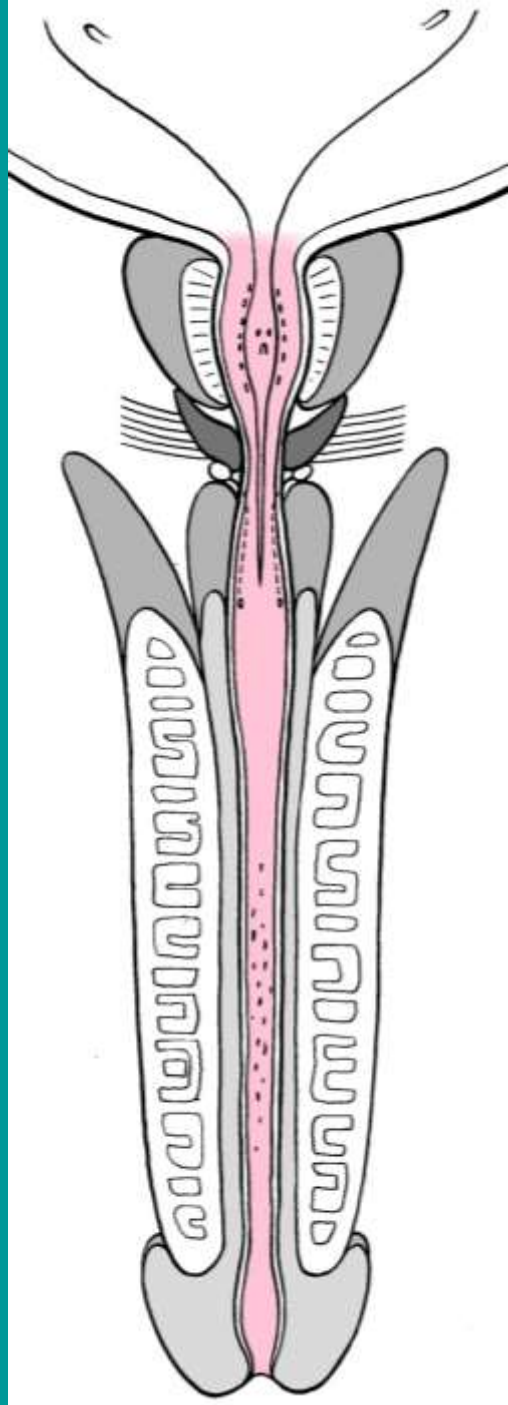
corpus cavernosum
corpus spongiosum
bulb, glans, prepuce

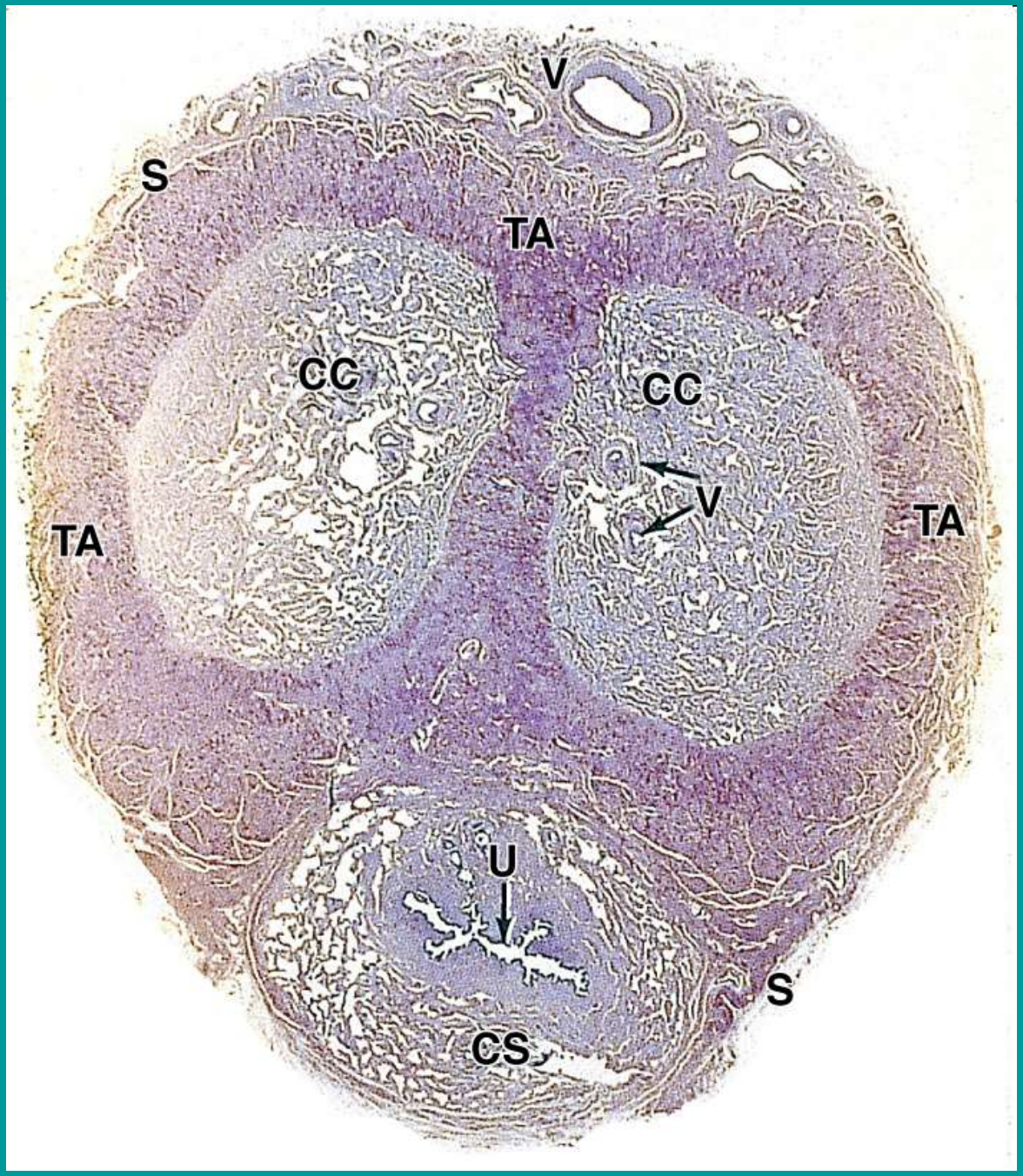




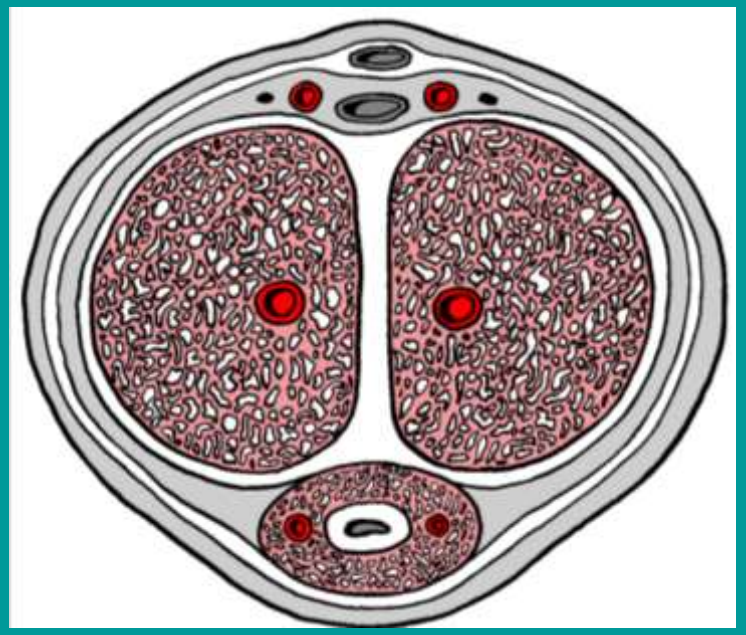
Male urethra

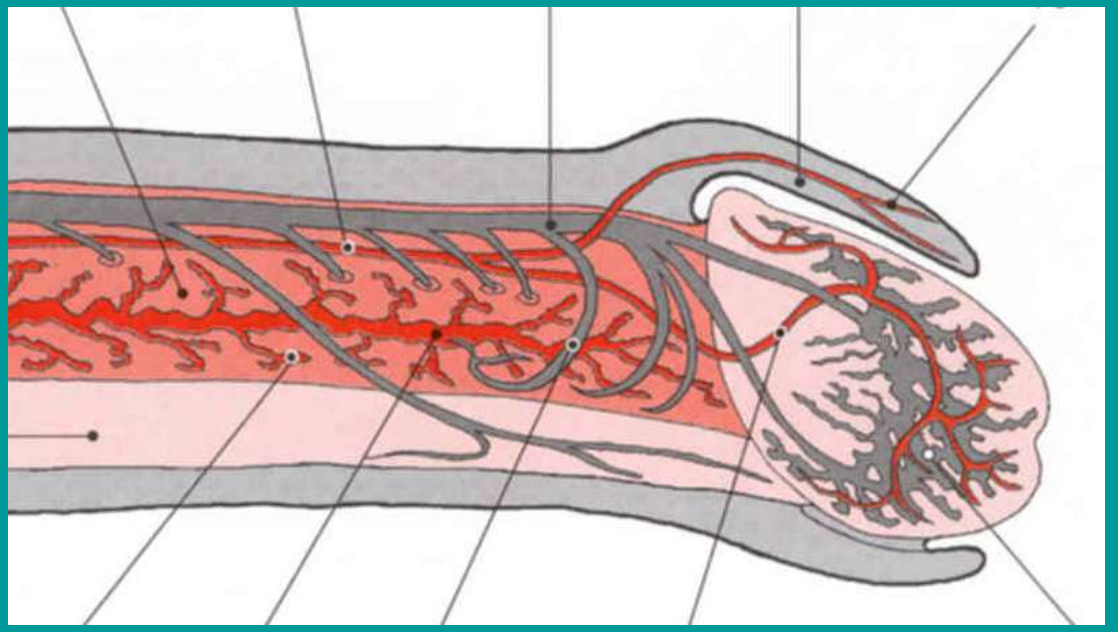
(urinary + seminal duct)
internal orifice, intramural,
prostatic, spongy part,
external orifice
seminal colliculus,
prostatic sinus,
internal urethral sphincter,
external urtehral sphincter,
urethral glands,
urethral lacunae,
navicular fossa




V
S
TA
CC
CC
V
TA
TA
U
S
CS

Cross section of penis: skin, tunica dartos, fascia penis superficialis, - profunda, tunica albuginea, septum penis, trabeculae, cavernae



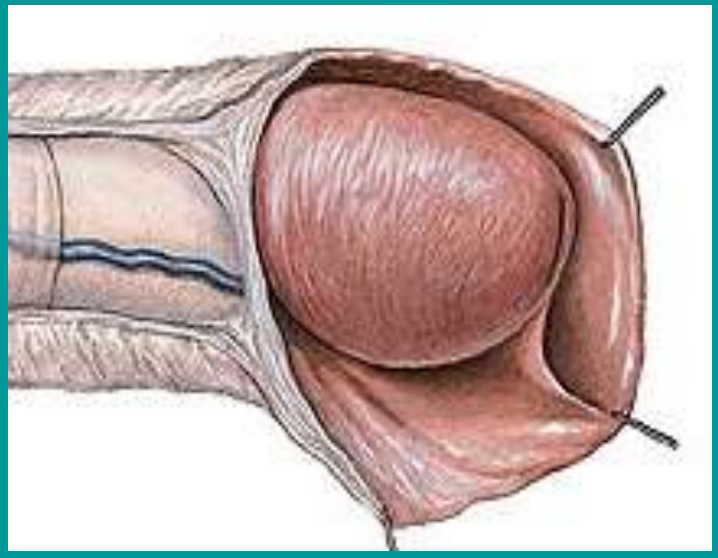


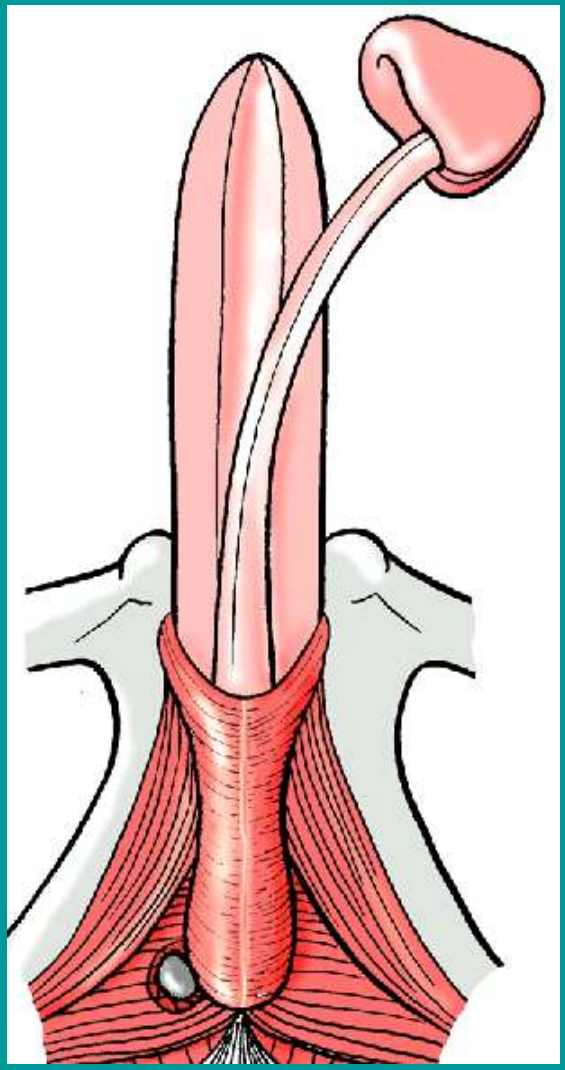
Blood vessels of penis

Arteries (paired) – branches of a. pudenda interna: a. dorsalis penis, a. profunda penis, aa.helicinae, a. bulbi penis, a. urethralis

Veins (unpaired) - v. dorsalis penis superficialis - vv. pudendae externae; vv. circumflexae, vv. cavernosae - v. dorsalis penis profunda -– plexus venosus prostaticus

Corpus cavernosum penis, crus, corpus spongiosum, bulbus, m. ischiocavernosus, m. bulbospongiosus, glandula bulbourethralis

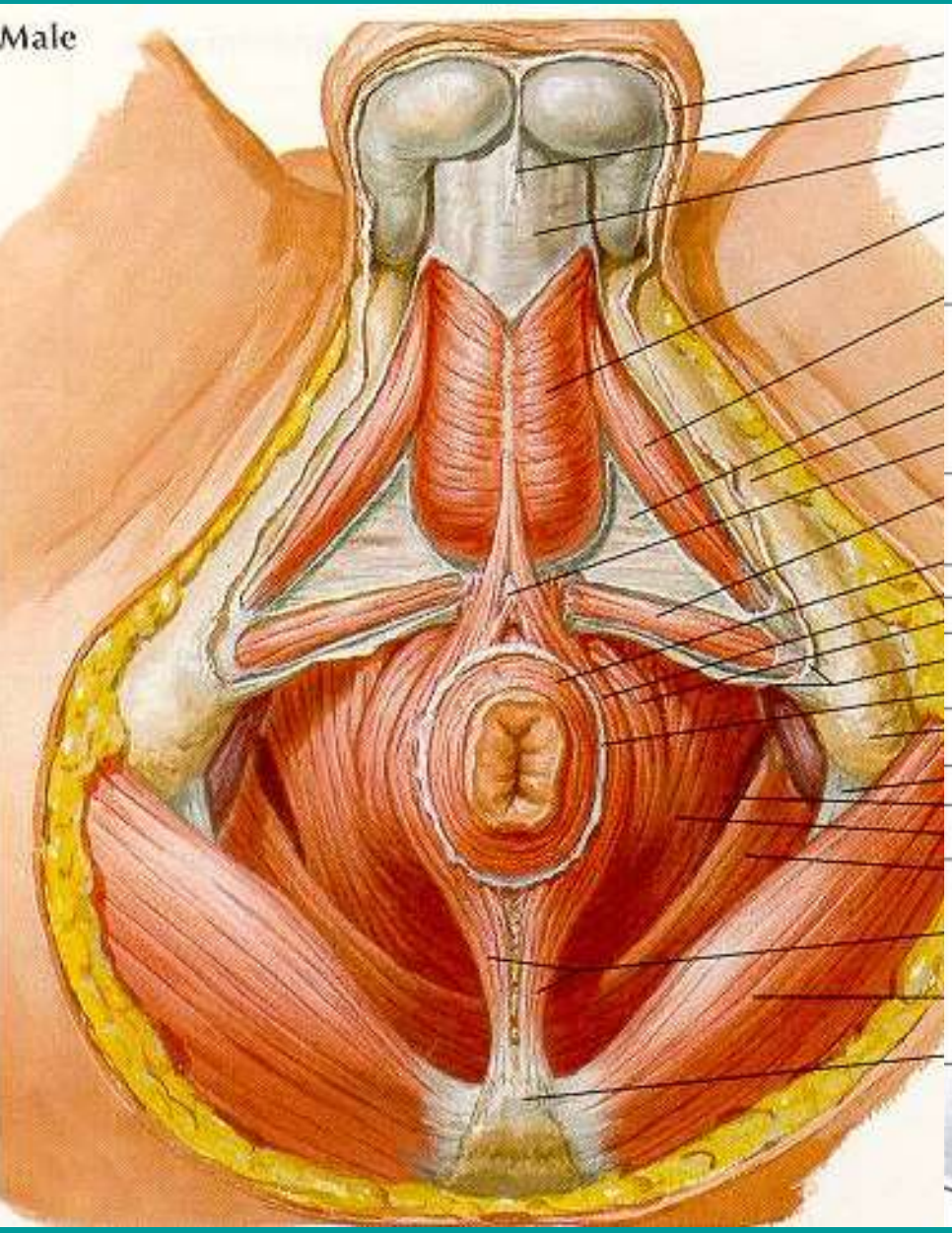


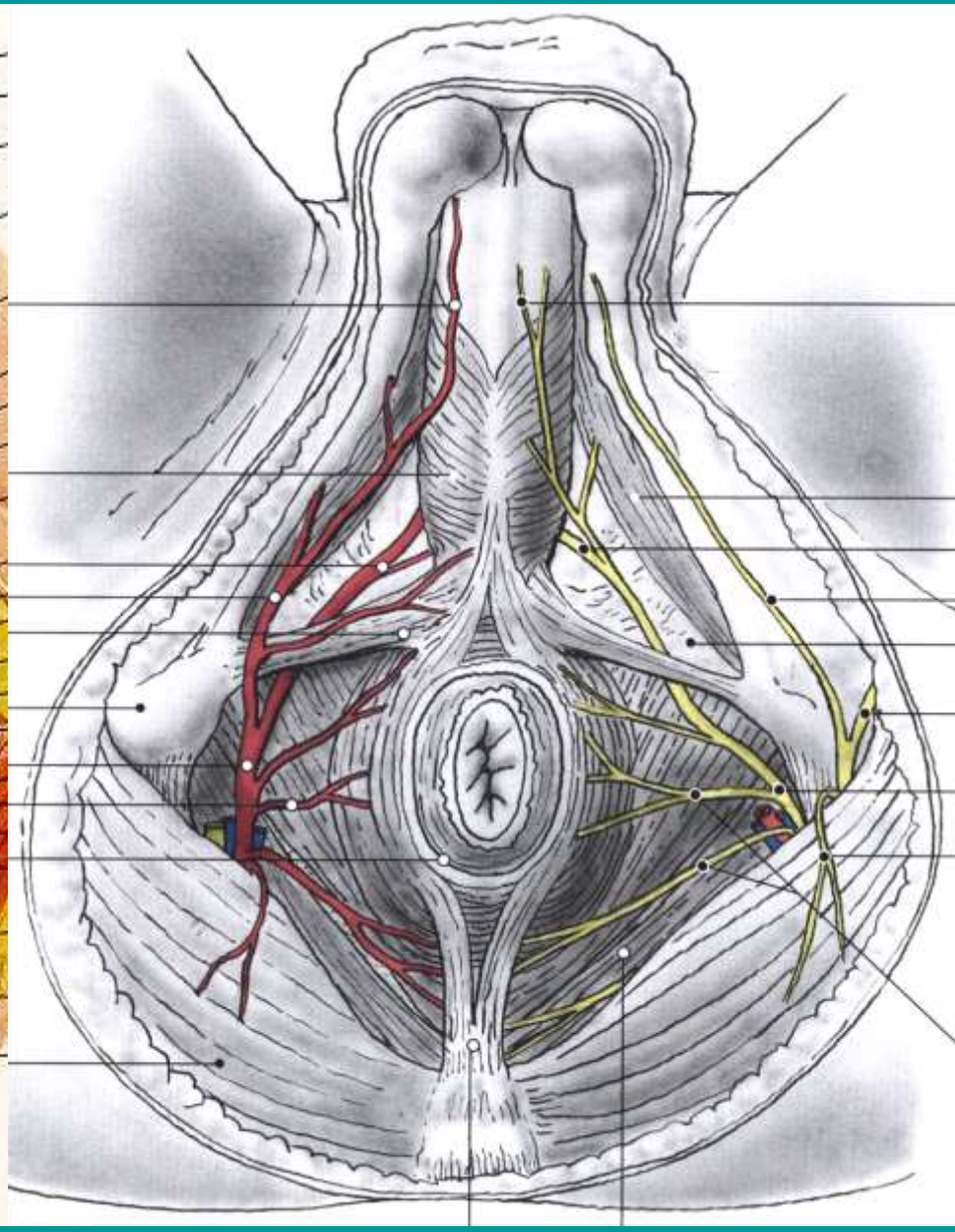


glans, corona glandis, preputium, frenulum

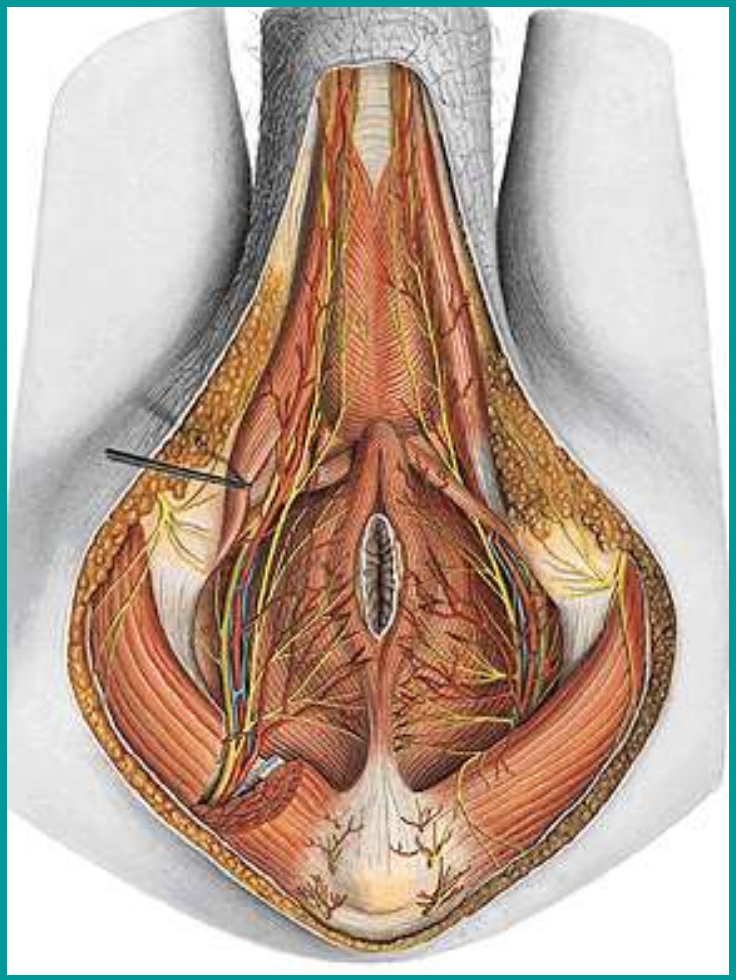
Separation of preputium from glans during 1. postnatal year, **circumcision, phimosis**

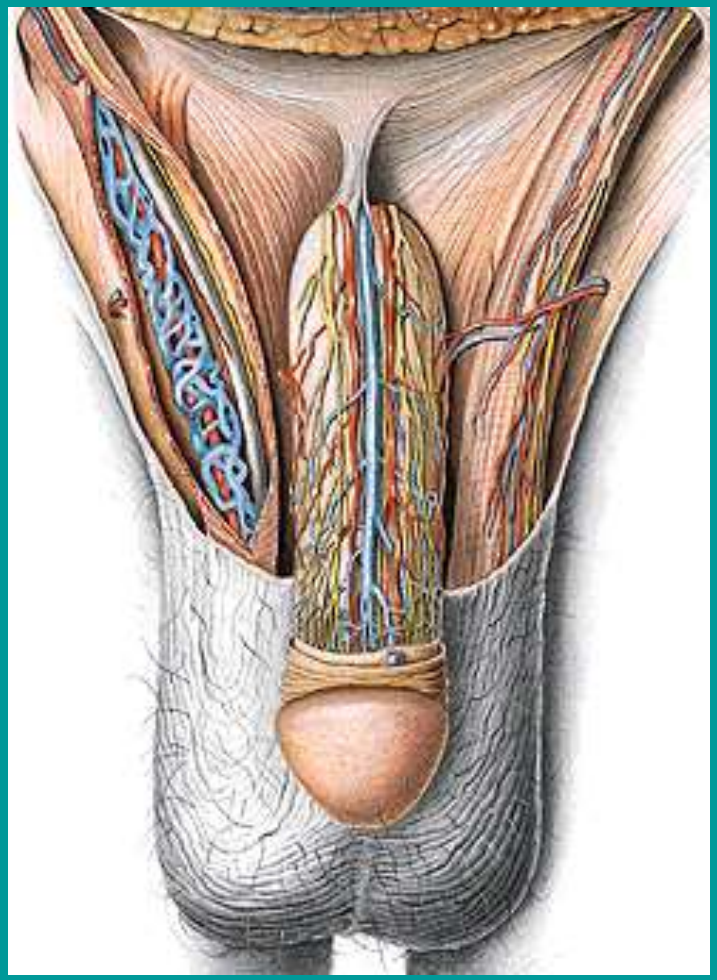
Radix of penis, perineal muscles, blood supply, inmnervation





N. pudendus – n. dorsalis penis (sensitive), plexus hypogastricus inferior (autonomous) - nn. cavernosi along vessels, parasympathetic nn. errigentes from S3, sympathetic from L1-3

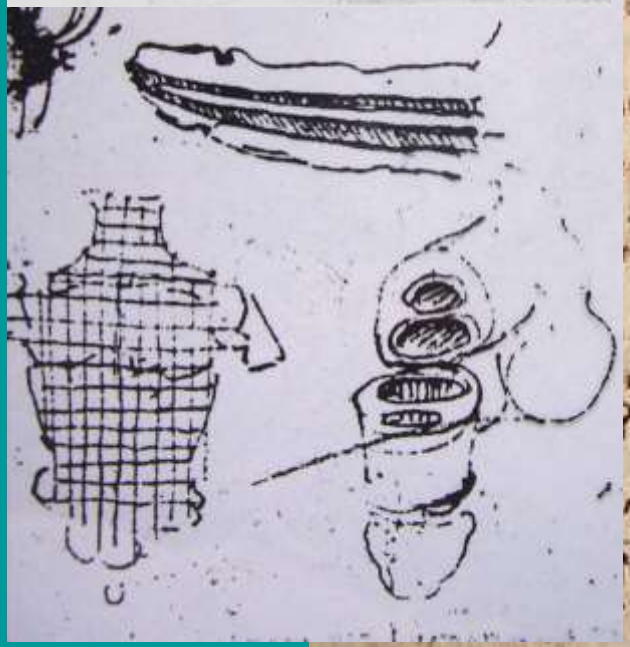


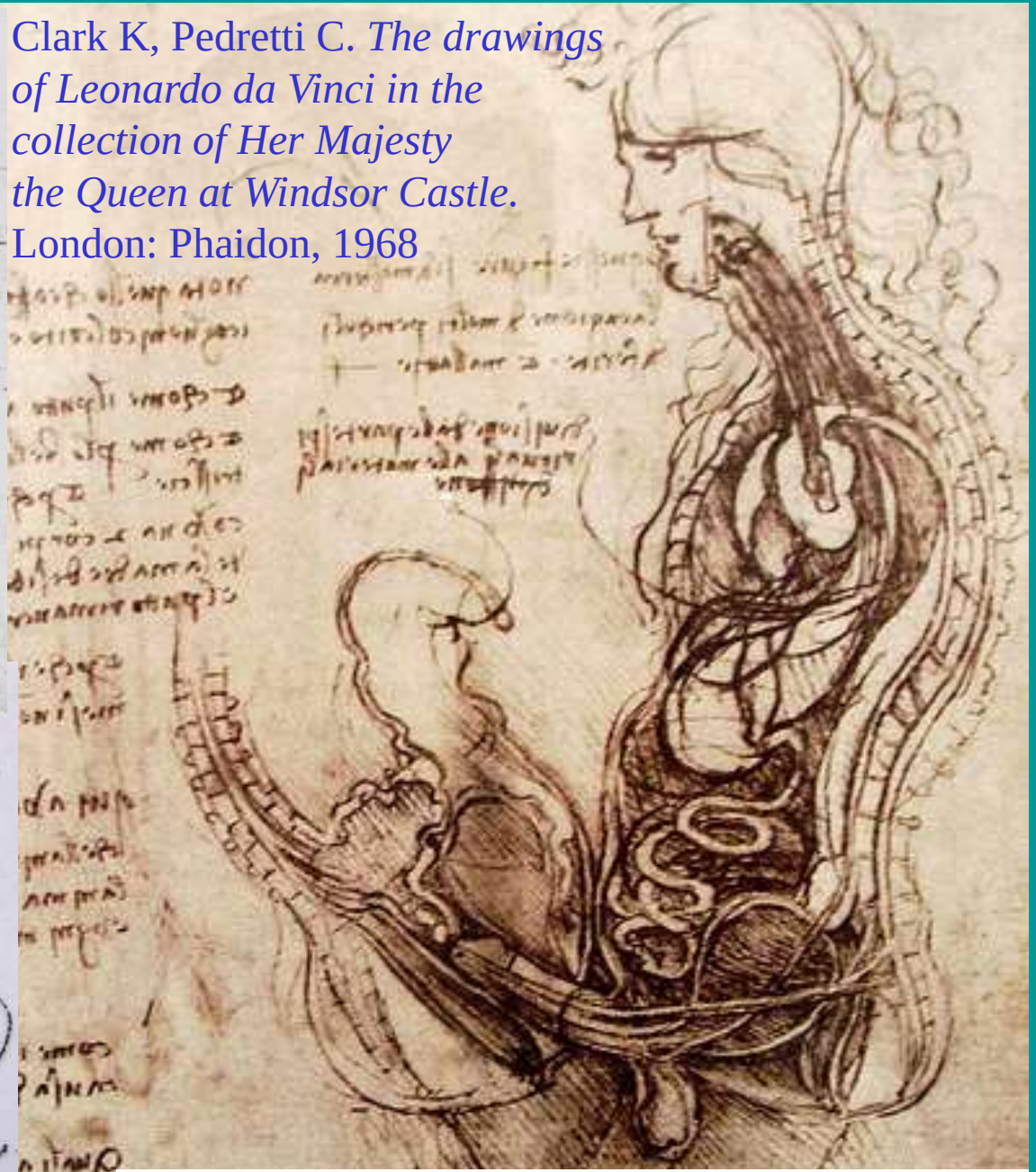


A. pudenda interna: a. dorsalis penis, a. profunda penis, a. urethralis, a. bulbi penis. V. dorsalis penis subcutanea, v. dorsalis penis profunda

Erection- hemodynamic process – dilatation of arterioles (aa. helicinae), accumulation of blood in cavernous bodies and restricted blood outflow.
Vasodilation caused by parasympathetic nitrergic nerves – release of nitric oxide (sildenafil).
Refectory activation from sensory impulses and by supraspinal psychogenic mechanisms.

Clark K, Pedretti C. *The drawings of Leonardo da Vinci in the collection of Her Majesty the Queen at Windsor Castle.* London: Phaidon, 1968





Leonardo´s drawing of human copulation

Sources of illustrations used :

Gray´s Anatomy,
Sobotta: Atlas der Anatomie des Menschen
Grim, Druga: Regional Anatomy, Galen, Prague 2012
Benninghoff, Drenckhahn: Anatomie I., II.
Carlson,B.M.: Human Embryology and Developmental Anatomy

Recommended Textbooks:

R. S. Snell: Clinical Anatomy. 7th Edition, Lippincott Williams & Wilkins, 2004, pp. 478 – 562
or
K. L. Moore: Clinically oriented Anatomy, 3rd Edition, Williams & Wilkins 1992, pp. 501 – 635
and
W. Kahle: Color Atlas/Text of Human Anatomy, Vol. 2 Internal organs. Thieme, 4th English Edition, 1993
Langman´s Medical Embryology,11th Edition, 2010
Junqueira´s Basic Histology 12th Edition, 2010