Development of genital organs
lecture for students of general medicine and dentistry
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Institute of Anatomy, First Faculty of Medicine, Summer semester
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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
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) - primordium female gonadal ducts. A choice between them is made according 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 karyotype** 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
**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. Female 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 insensitivity syndrome** - testicular feminisation – mutation of gene for androgen receptor (pseudohermaphroditism)
Klinefelter syndrome – 47 XXY

47, XXY

Turner syndrome – 45 X

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

Expression of Hoxd13 at E12.5
<table>
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<th>Indifferent Structure</th>
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<th>Female Derivative</th>
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<td>Lig. uteroovaricu, lig. teres</td>
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<tr>
<td>Mesonephric (Wolffian) ducts</td>
<td>Appendix of Epididymis</td>
<td>Appendix of ovary</td>
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<td></td>
<td>Epididymal duct</td>
<td>Gartner's duct</td>
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<td></td>
<td>Ductus deferens + Ejaculatory duct</td>
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<tr>
<td>Paramesonephric (Müllerian) ducts</td>
<td>Appendix of testis, Prostate utricle</td>
<td>Uterine tubes, Uterus + Upper vagina</td>
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<td>Urogenital sinus (upper part)</td>
<td>Urinary bladder</td>
<td>Urinary bladder</td>
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<td>Urogenital sinus (middle part)</td>
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<td>Genital folds</td>
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<td>Genital tubercle</td>
<td>Corpus and glans penis, Preputium</td>
<td>Clitoris, Preputium</td>
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<td>Genital swellings</td>
<td>Scrotum</td>
<td>Labia majora</td>
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</table>
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.

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)


In many mammalian species females with shorter AGD are more fertile.
AGD AS: center of anus to posterior base of the scrotum (point 2 to 3).
AGD AP anus – penis (point 1 to 3)

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

Male genital system
lecture for students of general medicine and dentistry
Miloš Grim
Institute of Anatomy, First Faculty of Medicine, Summer semester
2014 / 2015
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 length 30-70 cm, total length 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
**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 occurred 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)
Seminiferous 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 parenchyma**, 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
Parenchyma of the prostate: dense fibromuscular stroma and tuboalveolar glands
Penis - dorsum, urethral 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, spongry part,
external orifice
semenal colliculus,
prostatic sinus,
internal urethral sphincter,
external urtehral sphincter,
urethral glands,
urethral lacunae,
navicular fossa
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, innervation
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. helicinæ), 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.
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:
or
and
Junqueira´s Basic Histology 12th Edition, 2010