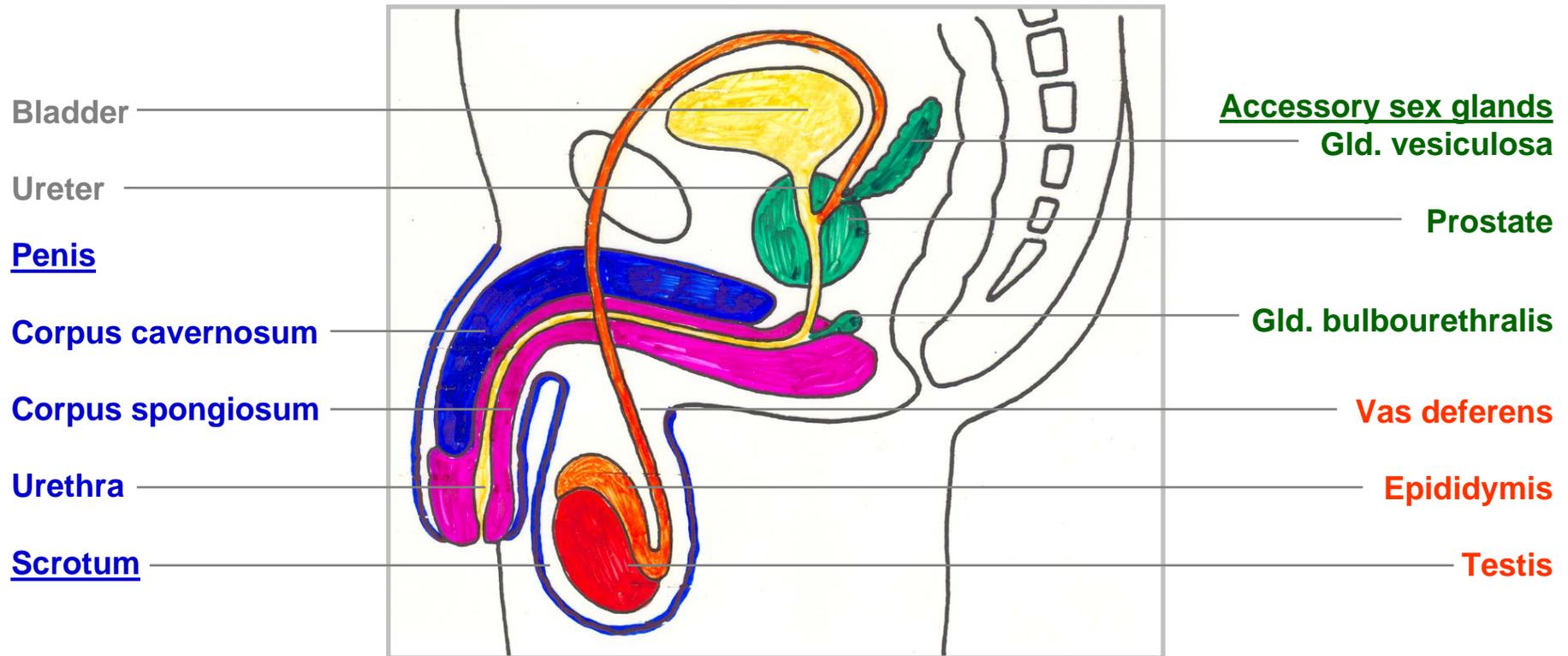


MALE REPRODUCTIVE ORGANS



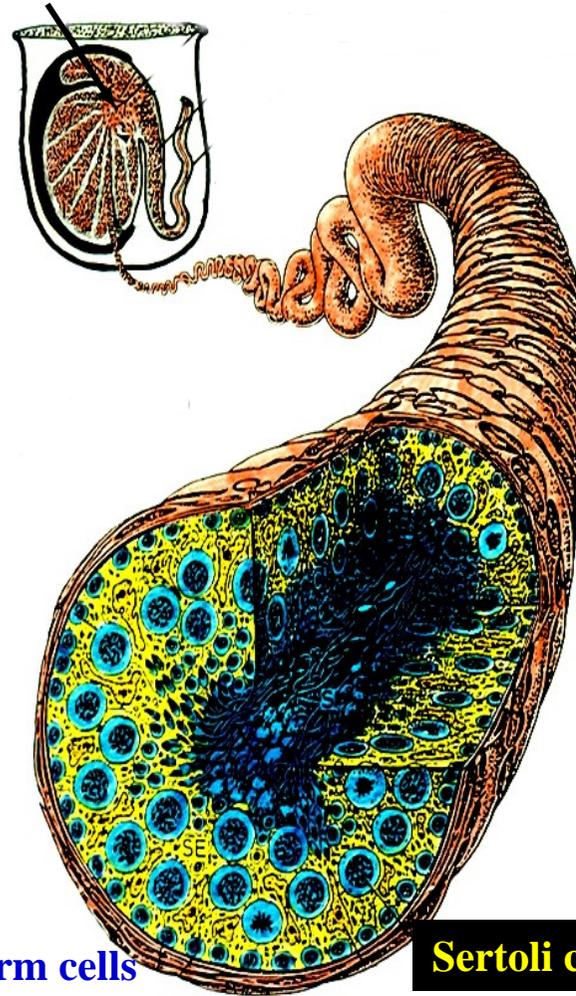
Male mammals have two testicles which are components of both the reproductive and the endocrine system. Therefore, the two main functions of the testicles are: producing sperm (approximately 1 million per hour) and male sex hormones (e.g. testosterone).

TESTIS

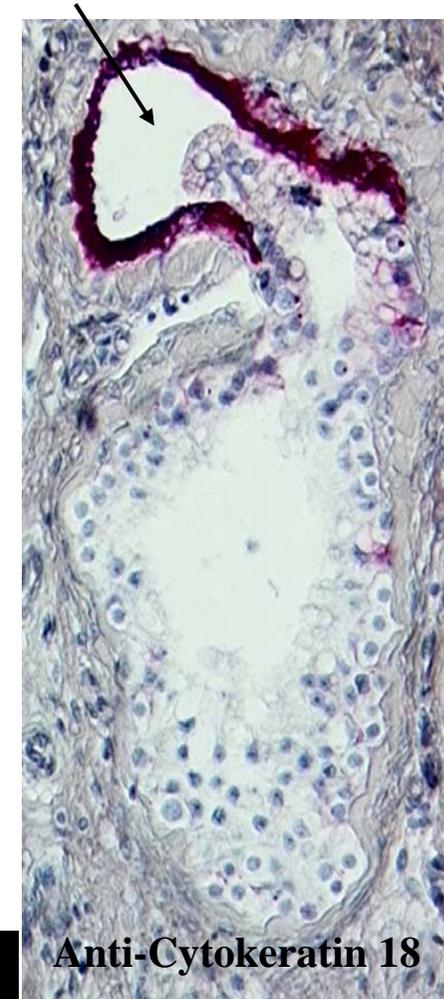
Seminiferous tubules



Rete testis



Rete testis



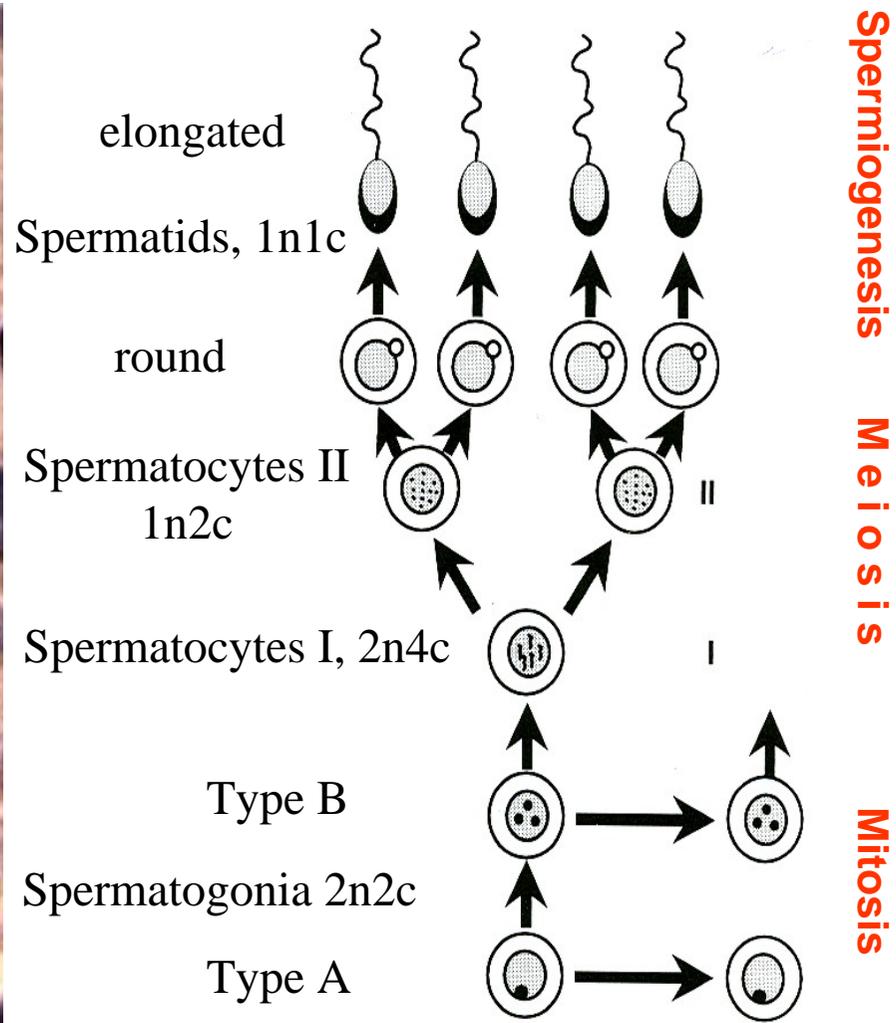
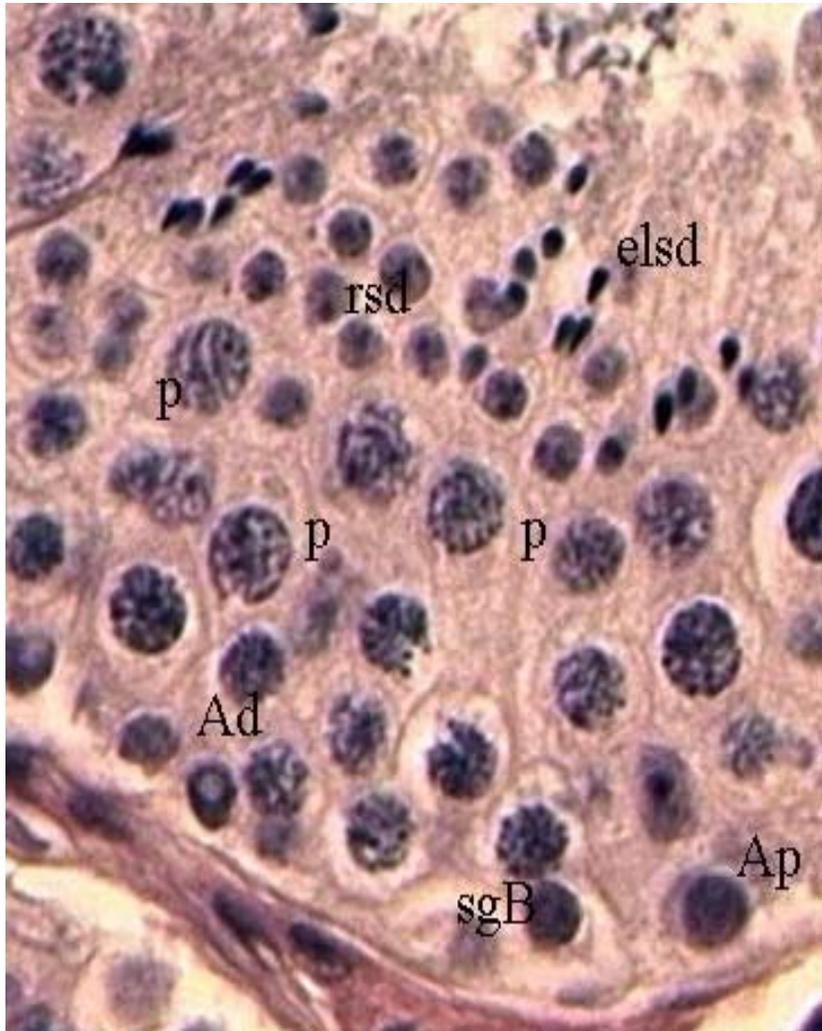
Spermatogenesis occurs within the seminiferous epithelium on the surface of the somatic Sertoli cells. Functional Sertoli cells are required for normal spermatogenic progression resulting in the continuous production of numerous fertile spermatozoa which, in turn, is necessary to maintain Sertoli cells in their functional differentiation state. Adjacent Sertoli cells form Sertoli-Sertoli junctional complexes dividing the seminiferous epithelium into a basal and an adluminal compartment. During spermatogenesis, germ cells migrate through the Sertoli-Sertoli junctional complexes successively passing through the following three developmental stages:

Mitosis: Following mitosis of a spermatogonial stem cell, one spermatogonium is conserved as a spermatogonial stem cell, while the other spermatogonium undergoes further mitoses and, subsequently, enters meiosis.

Meiosis: During the first meiotic division, one primary spermatocyte gives rise to two secondary spermatocytes. During the second meiotic division, each of the two secondary spermatocytes gives rise to two round spermatids.

Spermiogenesis: Round spermatids do no longer divide, but differentiate into mature spermatozoa undergoing numerous morphological, biochemical, and physiological modifications. Nuclear chromatin condensation, development of the acrosome, and formation of the flagellum occur simultaneously in haploid spermatids.

SPERMATOGENESIS

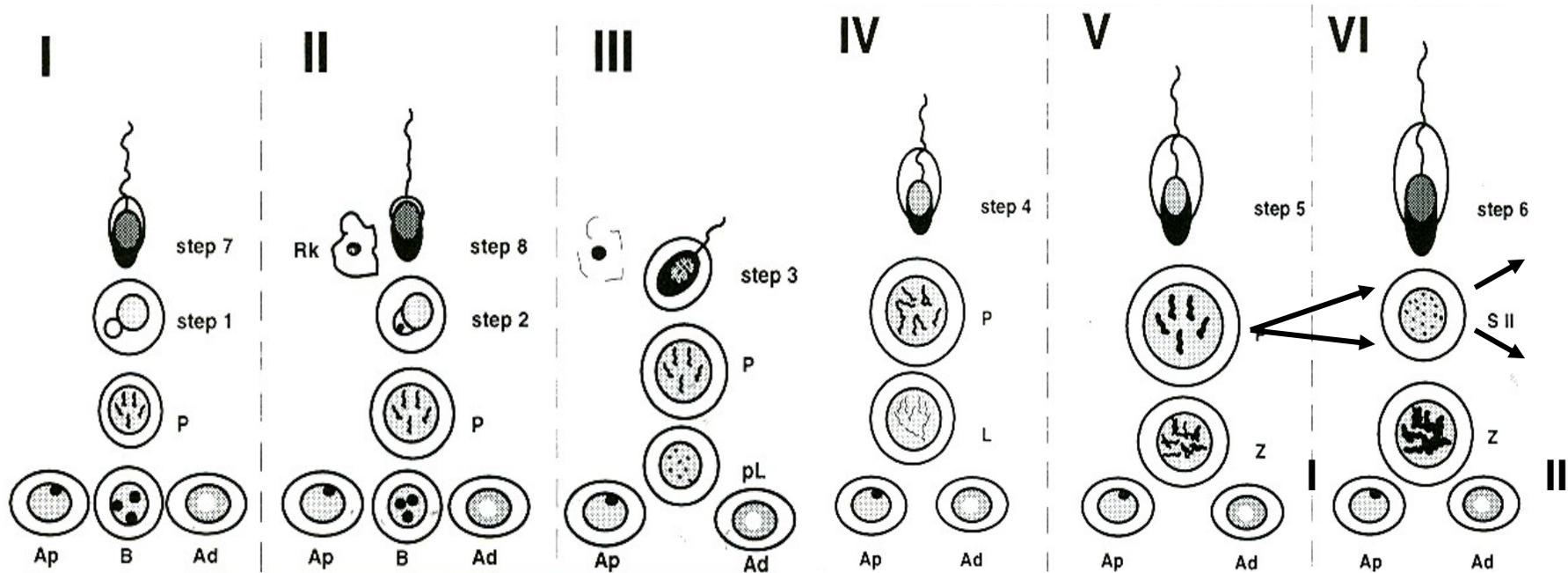


Each cell division – from spermatogonium to spermatid – is incomplete, as germ cells remain connected to each other by intercellular bridges. This is a prerequisite for synchronous development.

Germ cells are subjected to permanent proliferation and differentiation processes resulting in the appearance of various germ cell populations each representing a particular phase of germ cell development. A defined arrangement of germ cell populations is called the stage of the seminiferous epithelium. A complete series of changes in stages arranged in the logical sequence of germ cell maturation is called the cycle of the seminiferous epithelium. In men, the seminiferous epithelial cycle is divided into six stages (I-VI). Due to the nuclear morphology of the spermatids and the reactivity of spermatid nuclei with periodic-acid-Schiff (PAS), spermatid differentiation is further subdivided into eight steps (1-8).

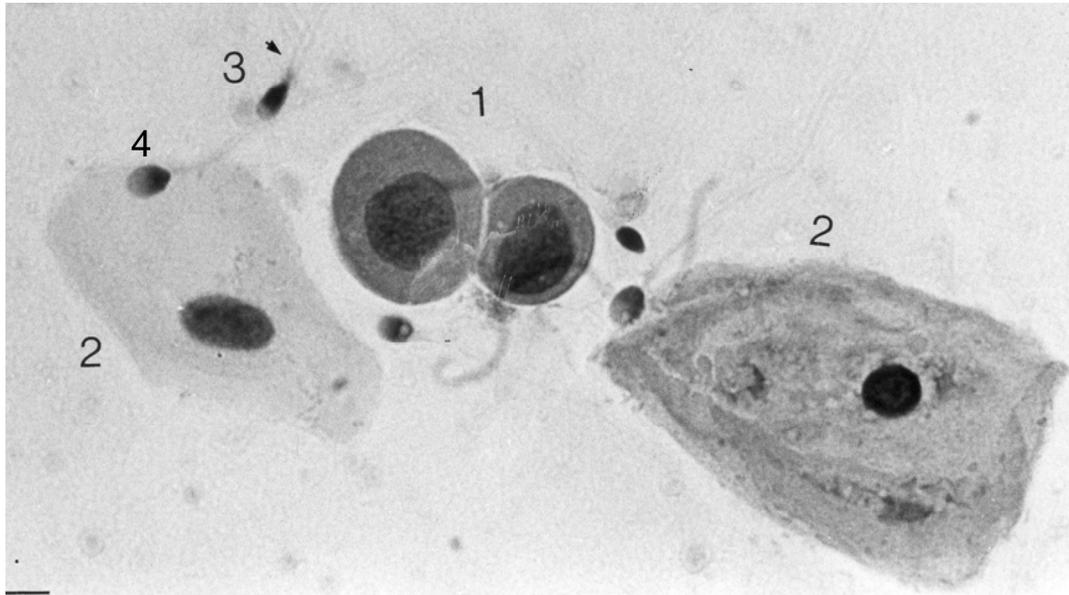
Development from spermatogonium to spermatozoon lasts 74 days. As maturation within the epididymidis lasts 8-17 days, the generation of a spermatozoon from a stem spermatogonia lasts at least 82 days.

STAGES OF SEMINIFEROUS EPITHELIAL CYCLE - MAN -



Spermatogonia type A-pale (Ap), type A-dark (Ad) and type-B (B); Primary spermatocytes in preleptotene (pL), leptotene (L), zygotene (Z) and pachytene (P); Secondary spermatocytes (SII); Spermatids in step 1 to step 8; Residual bodies (Rk); First (I) and second (II) meiotic division. Bergmann M, Spermatogenese. From: Andrologie. Krause W, Weidner W, eds., Ferdinand Enke, Stuttgart, 1998.

SPERM



Ejaculate under light microscope

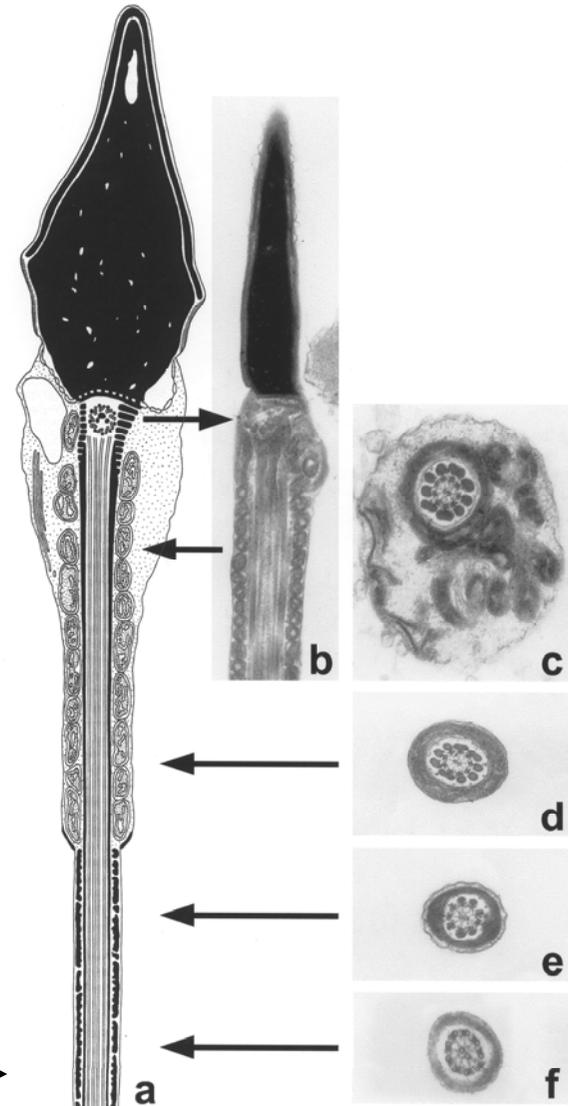
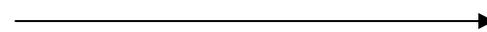
1: Spermatid

2: Epithelial cell

3: Sperm with two flagella

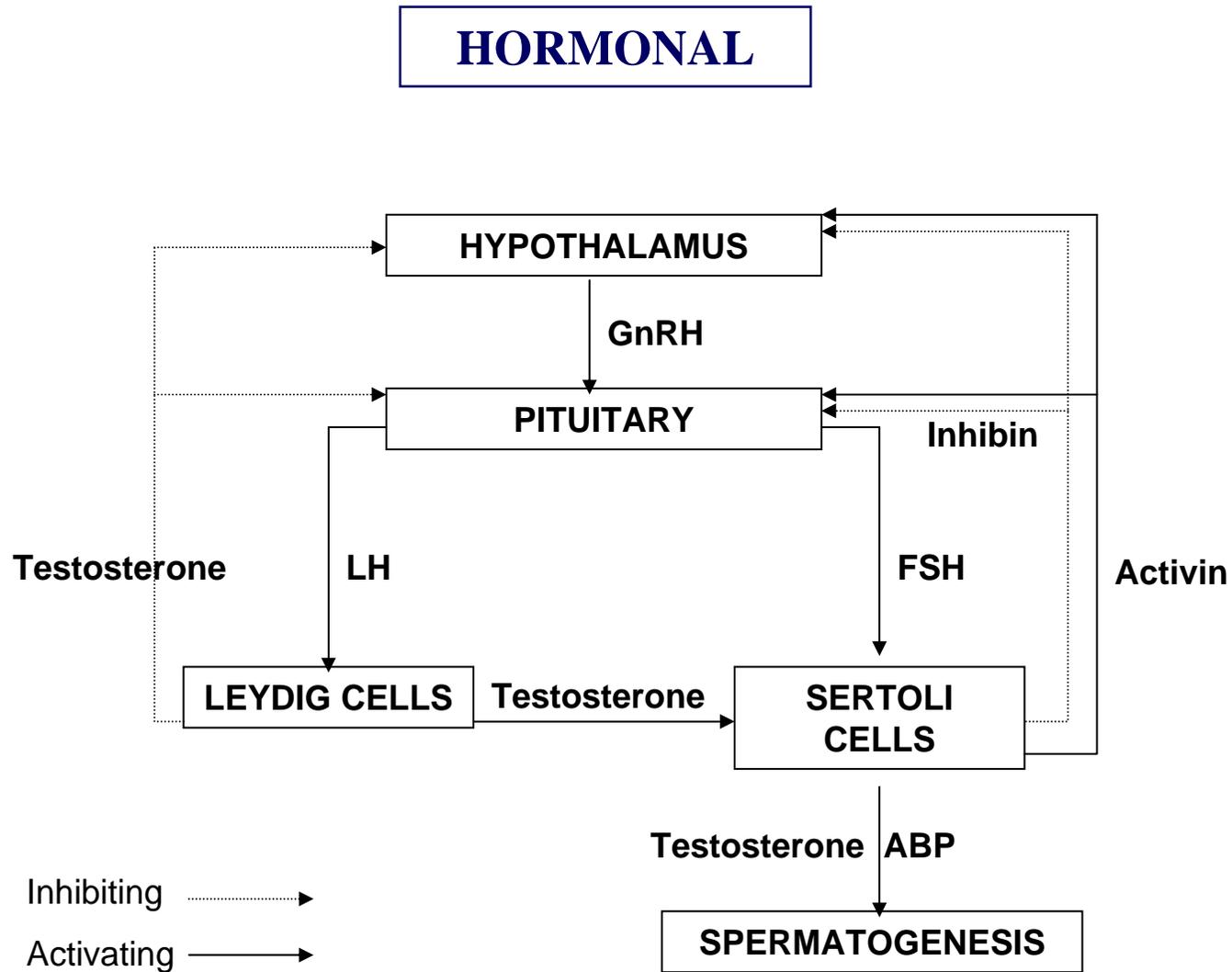
4: Normal sperm

Sperm under electron microscope



REGULATION OF SPERMATOGENESIS

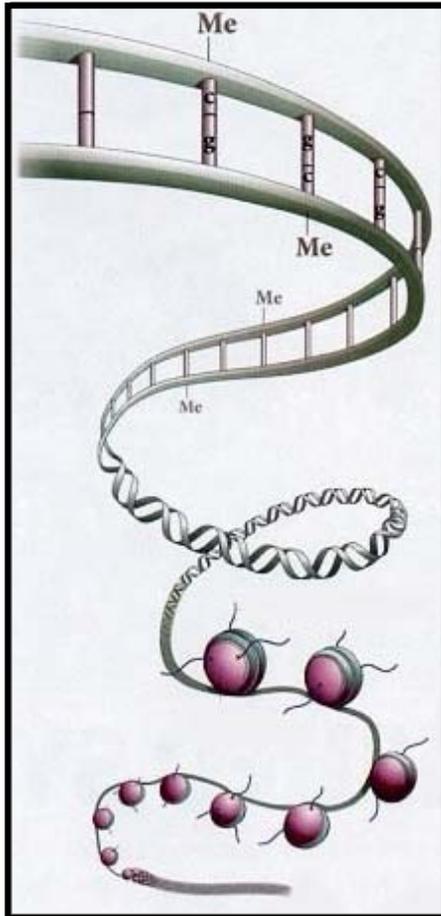
HORMONAL



Hormonal regulation of spermatogenesis is organized as control circuit with a negative feed-back mechanism involving hypothalamus, pituitary, and testis. Specific neurons of the hypothalamus synthesize gonadotropin releasing hormone (GnRH) which induces the production of two hormones within the pituitary, luteinizing hormone (LH) and follicle stimulating hormone (FSH). While high pulse rate of GnRH release (1 impulse per 1 hour) results in the production of LH, low pulse rate of GnRH release (1 impulse per 2 hours) results in the production of FSH. Within the testis, LH causes synthesis of testosterone by intertubular Leydig cells which negatively influences hormone release in hypothalamus and pituitary. By contrast, FSH acts on intratubular Sertoli cells. It induces the production of androgen-binding protein (ABP) by means of which testosterone can pass the Sertoli-Sertoli junctional complexes, as well as the production of activin and inhibin by Sertoli cells which both influences hormone release in hypothalamus and pituitary.

REGULATION OF SPERMATOGENESIS

EPIGENETIC

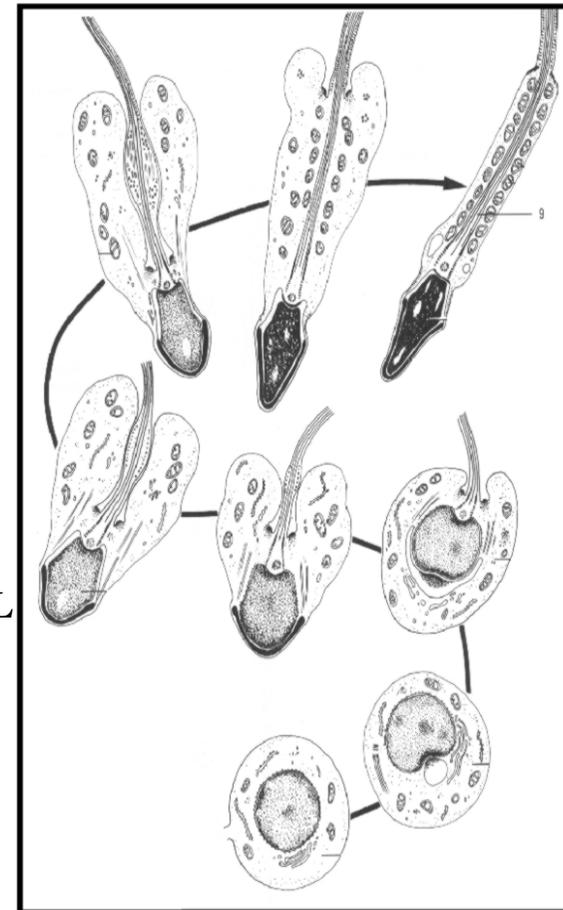


**DNA
METHYLATION**

**HISTONE
MODIFICATION:**

- ACETYLATION
- METHYLATION

GENETIC



PROTAMINES

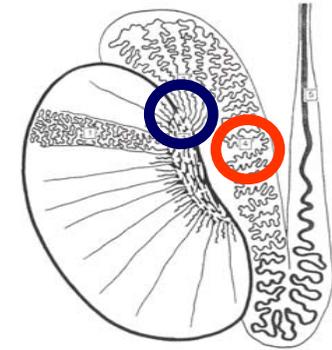
**TRANSLATIONAL
REGULATION**

**TRANSCRIPTIONAL
REGULATION**

HISTONES

MALE REPRODUCTIVE ORGANS

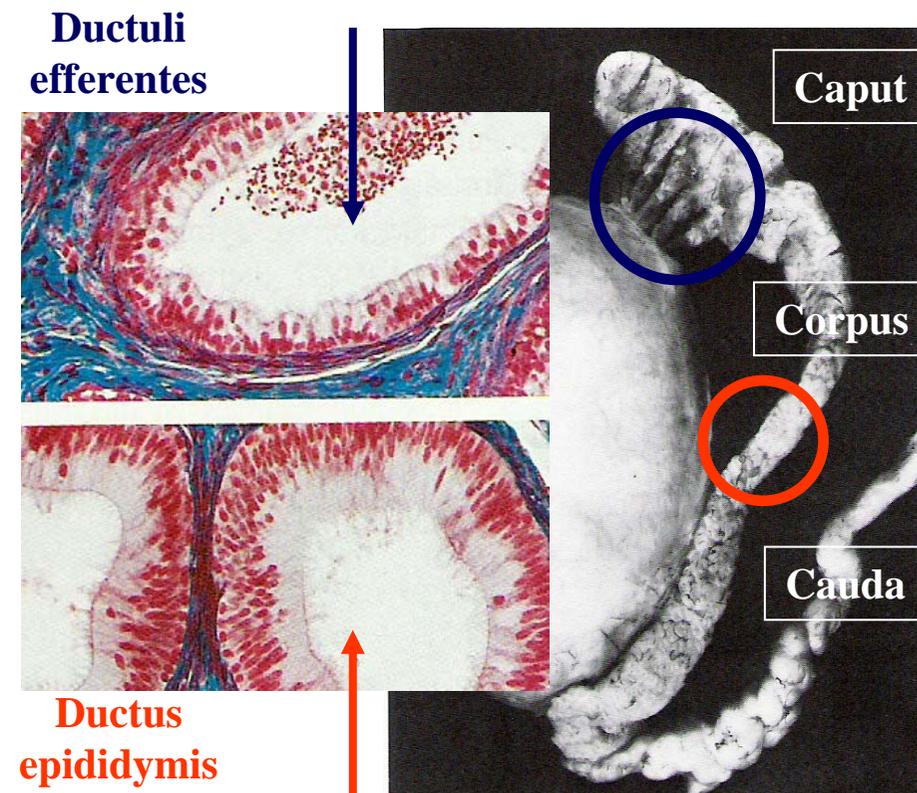
DUCTULI EFFERENTES AND EPIDIDYMIS



The columnar epithelium of the **ductuli efferentes** is underlined by smooth muscles and consists of two cell types: absorptive cells with microvilli and cells with kinocilia responsible for the transport of still immotile spermatozoa and estrogen dependent fluid resorption. As the height of these two cell types is variable, the lumen shows a characteristic wavy outline.

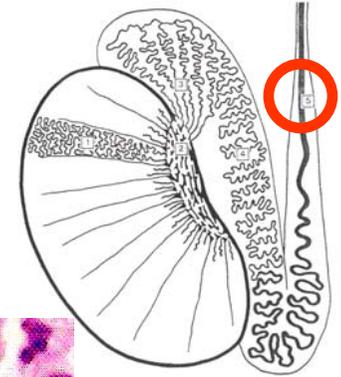
Spermatozoa are transported into the **epididymis** via the head (caput), progress to the body (corpus) and finally reach the tail (cauda), where they are stored. During their passage, spermatozoa undergo maturation to acquire motility necessary for fertilizing an egg. Note that final maturation is completed within the female reproductive tract (capacitation).

The **ductus epididymidis** is about 6 m long and is lined by a tall columnar epithelium which is underlined by smooth muscles and consists of basal cells and principal cells with non-motile stereocilia. From caput to cauda, the height of the epithelium decreases, while the diameter of the ductus and the lumen increases.

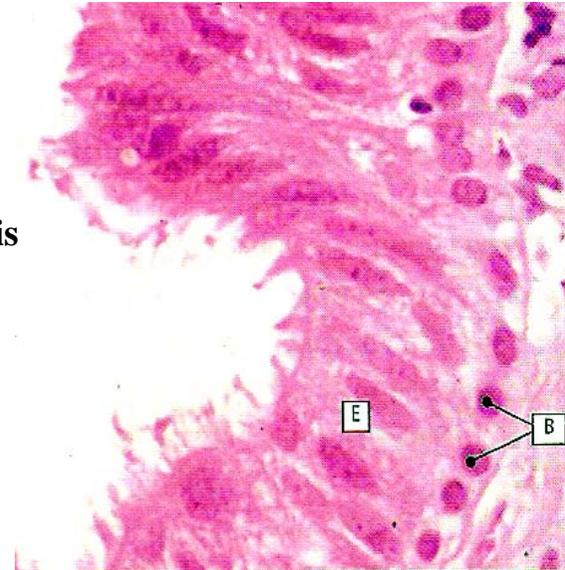


MALE REPRODUCTIVE ORGANS

DUCTUS DEFERENS



Ductus deferens:
Three-layered lamina muscularis
and two-layered epithelium
consisting of basal cells (B) and
epithelial cells (E)
with stereocilia (microvilli)

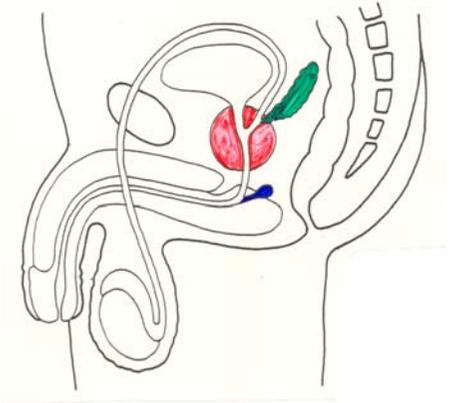


The two deferent ducts (ductus deferentes) or vasa deferentia – each about 30 cm long – connect right and left epididymis to the ejaculatory ducts. The deferent ducts can be divided into pars funiculi spermatici, pars inguinalis, pars pelvina, ampulla ductus deferentis, and ductus ejaculatorius which opens within the prostate into the urethra (colliculus seminalis).

The mucosa forms longitudinal folds and is lined by a columnar epithelium. The lamina muscularis is up to 1.5 mm thick and consists of a thick circular layer of smooth muscles between inner and outer longitudinal layers. The muscularis is covered by an adventitia. During ejaculation, smooth muscles within the wall of the ductus deferens contract reflexively and propel the sperm forward into the urethra. The prominent muscularis, in addition, makes the ductus deferens palpable within the spermatic cord.

ACCESSORY SEX GLANDS

The male reproductive system includes three different accessory sex glands, namely a pair of **seminal vesicles**, a pair of **bulbourethral glands** and the **prostate**.

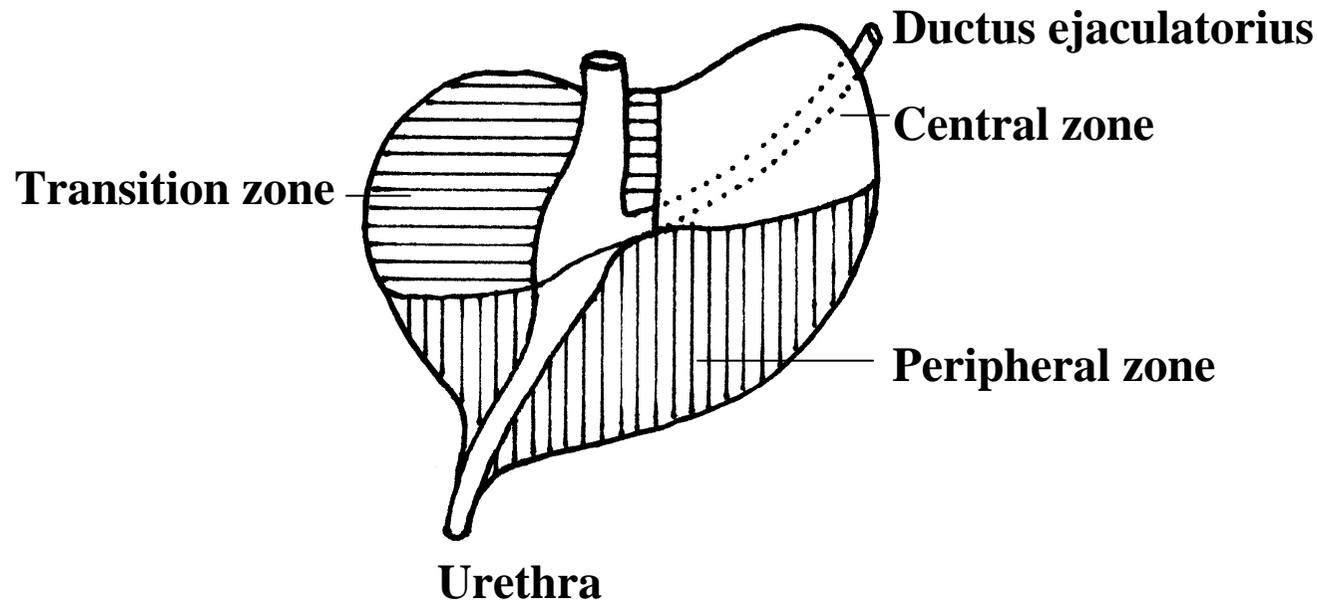
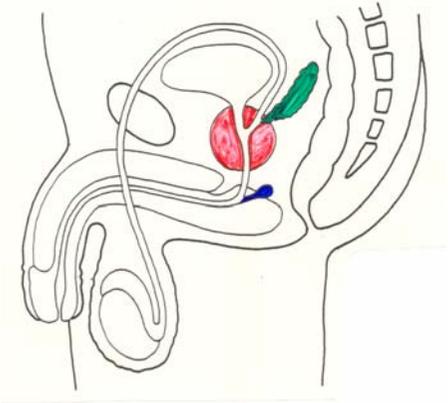


The secrete of **seminal vesicles** or **glandulae vesiculosae** is strongly acidophilic and constitutes 60-80 % of the ejaculate volume. It contains several proteins and enzymes, as well as mucus and vitamin C. The yellow fluorescing pigment flavin is of use in forensic medicine for the detection of semen stains. Prostaglandins stimulate smooth muscles of the female genital tract to enhance the migration of sperm from the vagina to the uterus. The large amount of fructose serves as an energy source for the sperm. The fructose concentration within the seminal plasma serves as indicator for the function of the seminal vesicles (reference $> 13 \mu\text{mol} / \text{ejaculate}$).

Bulbourethral glands or **Cowper's glands** are homologous to Bartholin's glands in the female.

ACCESSORY SEX GLANDS

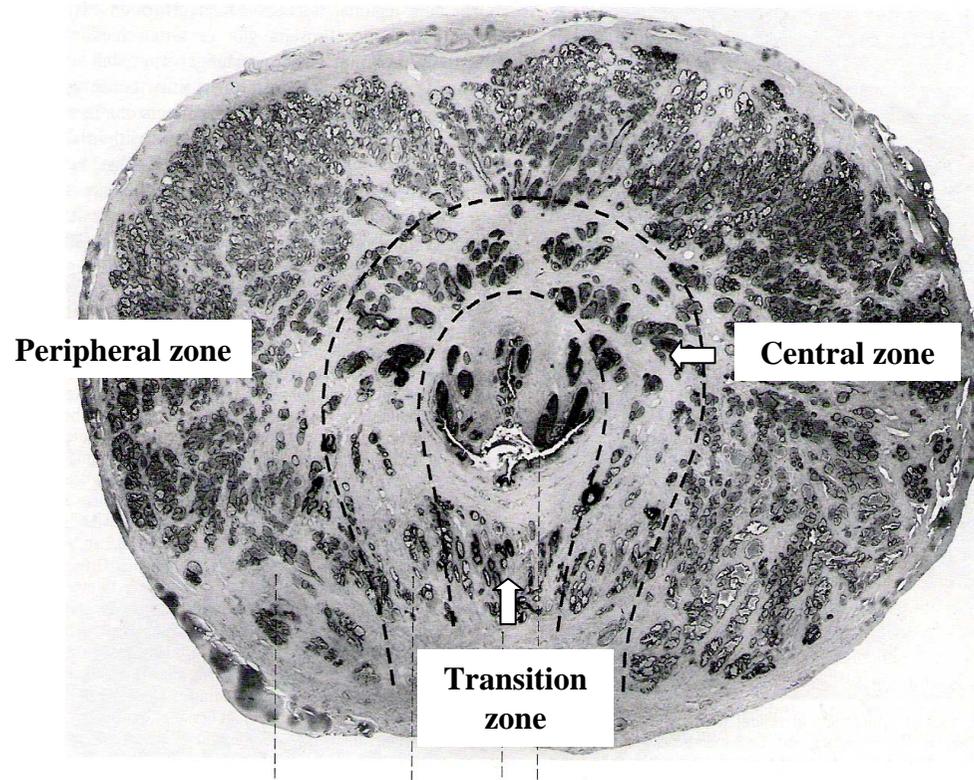
According to Mc Neal (1983), the **prostate** can be divided into three concentric zones: a central zone, a transition zone and a peripheral zone. The latter comprises 30–50 tubuloalveolar glands that empty into 15–30 independent excretory ducts which are lined by a simple columnar epithelium and open into the urethra.



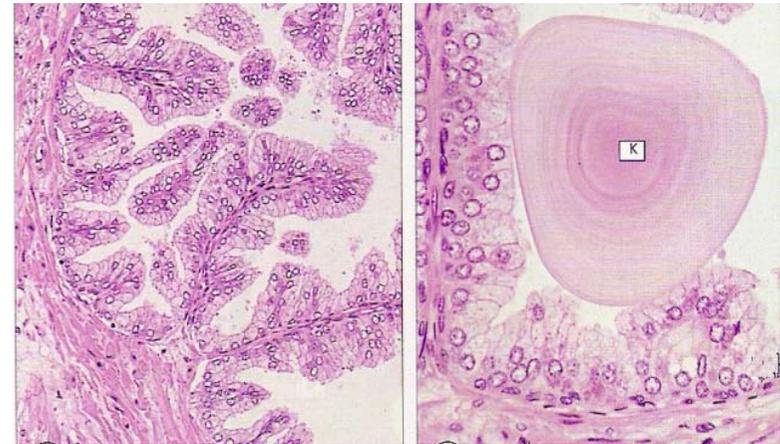
CLINIC

Benign prostatic hyperplasia (BPH) is the disease of the periurethral zone, whereas prostatitis and prostate cancer (PCa) are mainly located in the peripheral zone.

ACCESSORY SEX GLANDS



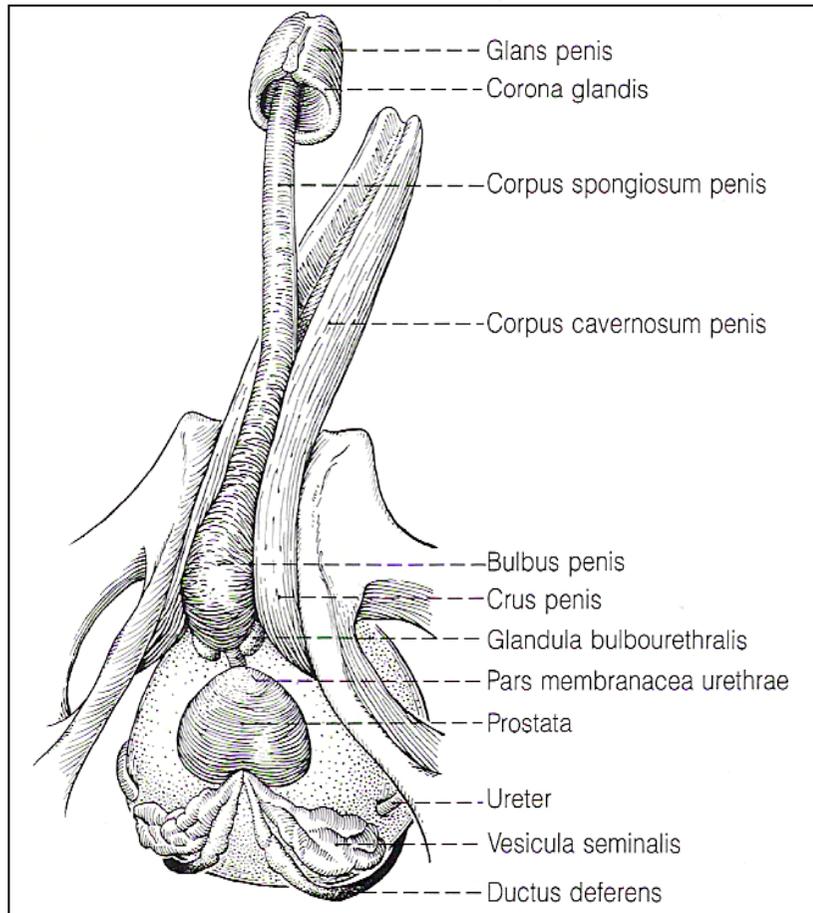
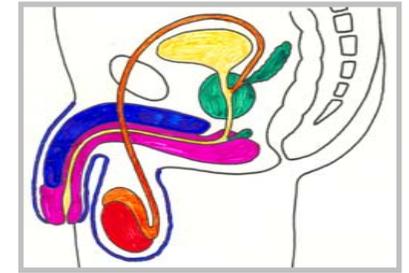
Round eosinophilic bodies (K), called corpora amylacea, represent a characteristic feature of secretory alveoli. These bodies may undergo calcification and may appear in semen.



The secretory cells contain granules which among other molecules produce prostate-specific acid phosphatase. The secrete, therefore, is acidic (pH 6.4). It constitutes approximately 30 % of the seminal fluid and contains many enzymes, as well as citric acid, prostaglandins that stimulate smooth muscles of the female genital tract to enhance the migration of sperm, zinc which is involved in the testosterone metabolism, spermine which accounts for the typical smell of the seminal fluid and fibrinolysin which liquifies the semen. Secretion is regulated by dihydrotestosterone (DHT).

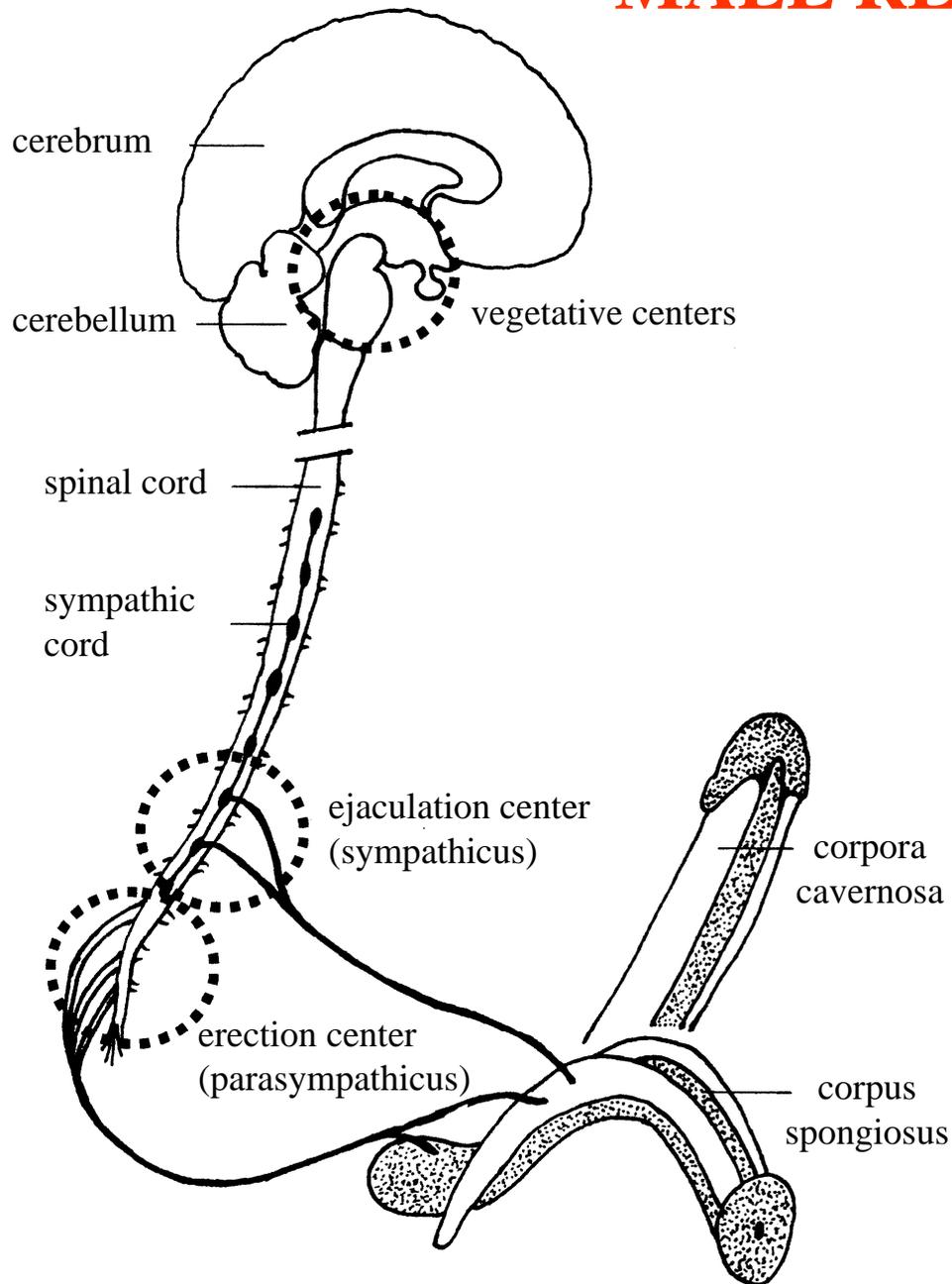
MALE REPRODUCTIVE ORGANS

PENIS



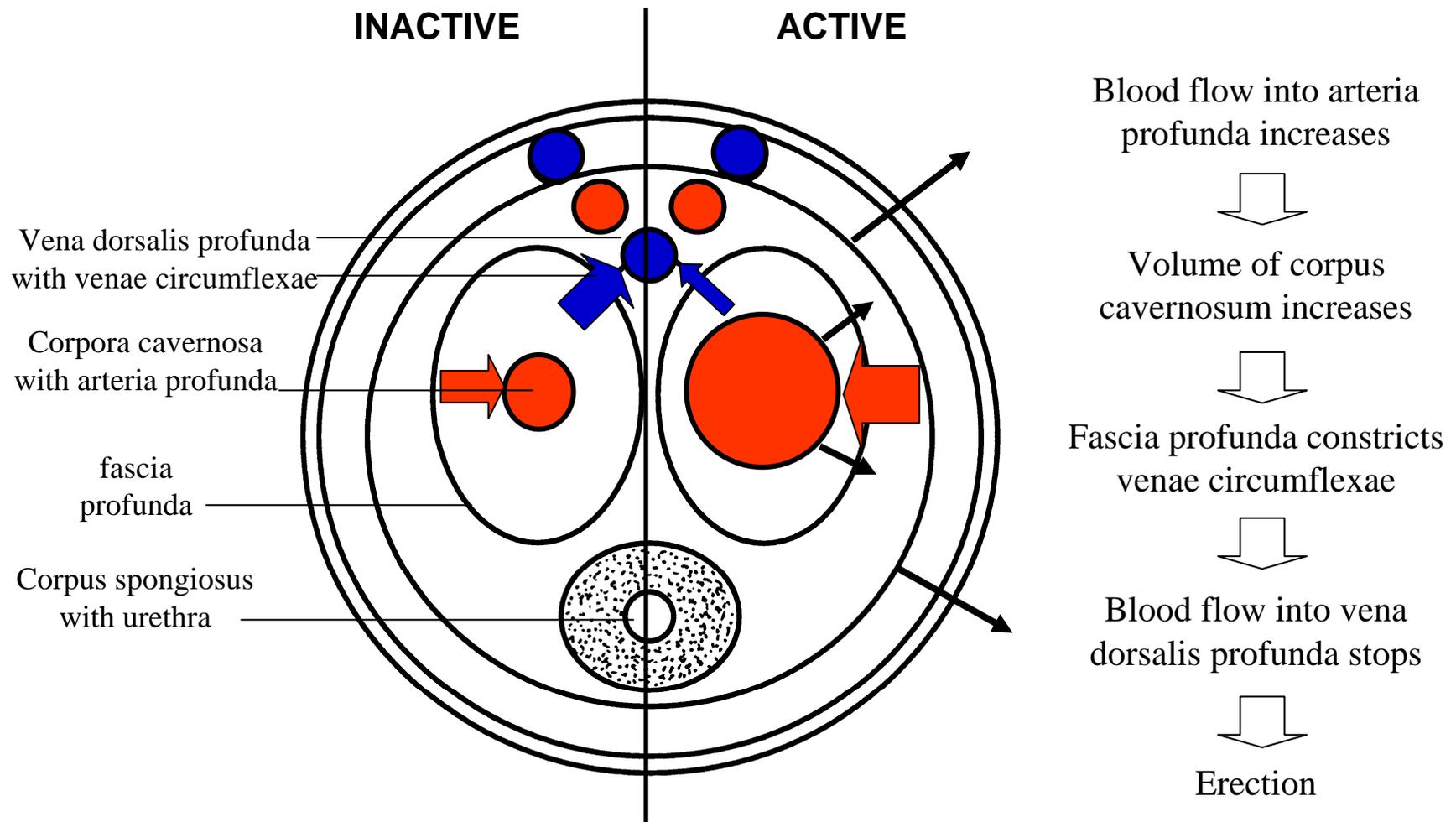
The human penis is made up of three columns of tissue: Two corpora cavernosa and one corpus spongiosum. The end of the corpus spongiosum is enlarged and forms the glans which supports the foreskin or prepuce, a loose fold of skin that in adults can retract to expose the glans. The area on the underside of the penis, where the foreskin is attached, is called the frenulum. The urethra traverses the corpus spongiosum and its opening lies on the tip of the glans. It is a passage for both urine and semen. The raphe is the visible ridge between the lateral halves of the penis, found underside of the penis running from the meatus (opening of the urethra) across the scrotum to the perineum (area between scrotum and anus).

MALE REPRODUCTIVE ORGANS



ERECTION

Erection is caused by the parasympathic (S3 of spinal cord) dilatation of the arteriae helicinae that supply blood to the chambers of the corpora cavernosa. As a consequence, more and more blood fills the chambers causing the penis to lengthen and stiffen. The now engorged erectile tissue presses against and constricts the veins that carry blood away from the penis. As a consequence, more blood enters than leaves the penis until an equilibrium is reached where an equal volume of blood flows into the dilated arteries and out of the constricted veins.



Ejaculation, in contrast to erection, is caused by the sympathetic nervous system (L2/3 of spinal cord) and is usually accompanied by orgasm. A series of contractions of the muscoli bulbospongiosus et ischiocavernosus delivers semen from the penis into the vagina.