E-content for Programme: M.Sc. Zoology (Semester-III)

Core Course (CC-11): Gamete and Developmental Biology

1.1 Cellular basis of spermatogenesis and Biochemistry of semen

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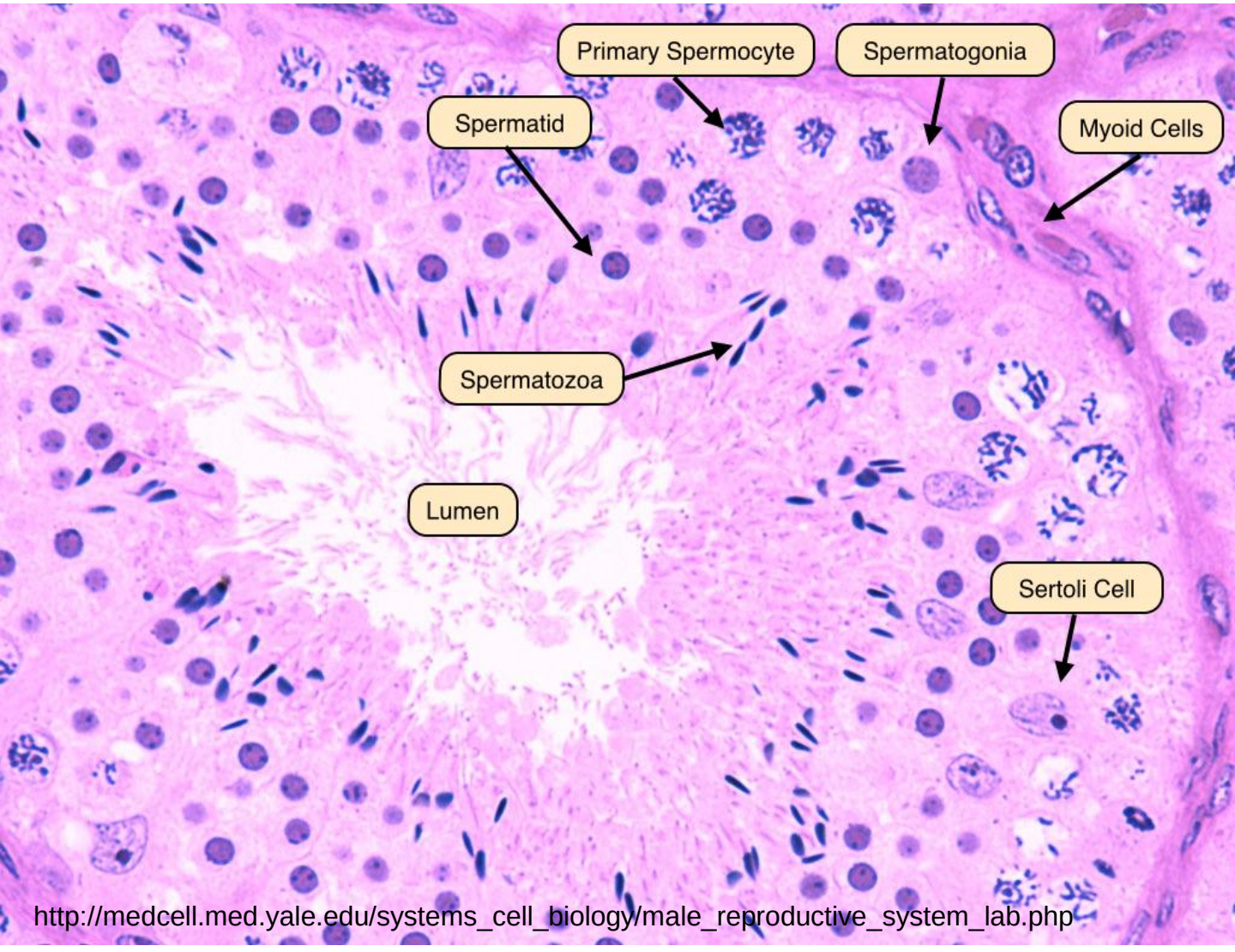


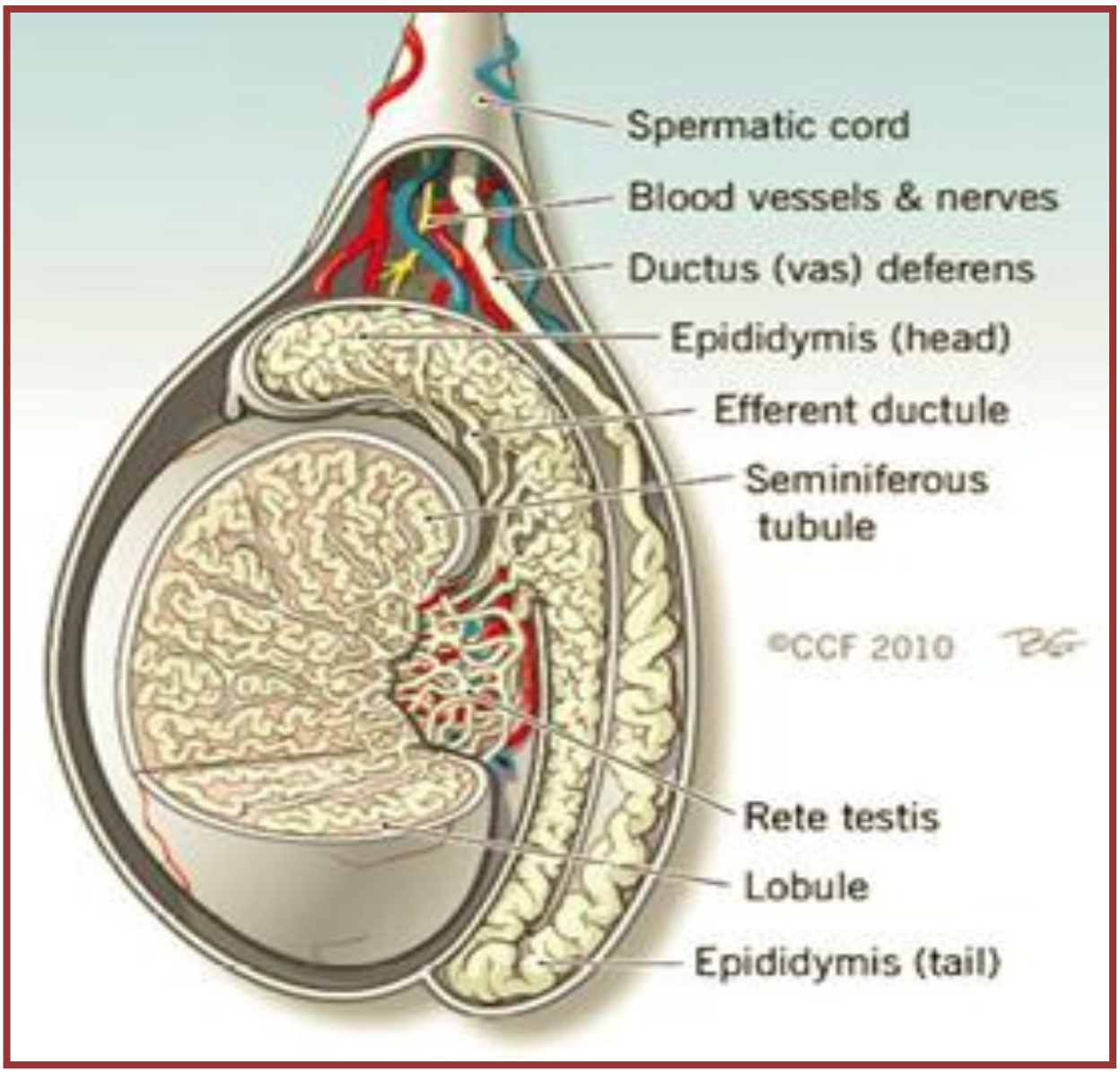
http://medcell.med.yale.edu/systems_cell_biology/male_reproductive_system_lab.php

Introduction: The Testis and The Epididymis

- The testes are the male gonads, normally found outside the body proper in a sac called the scrotum. Each testis is composed of two distinct compartments.

  - the tubular compartment that contains the seminiferous tubules.

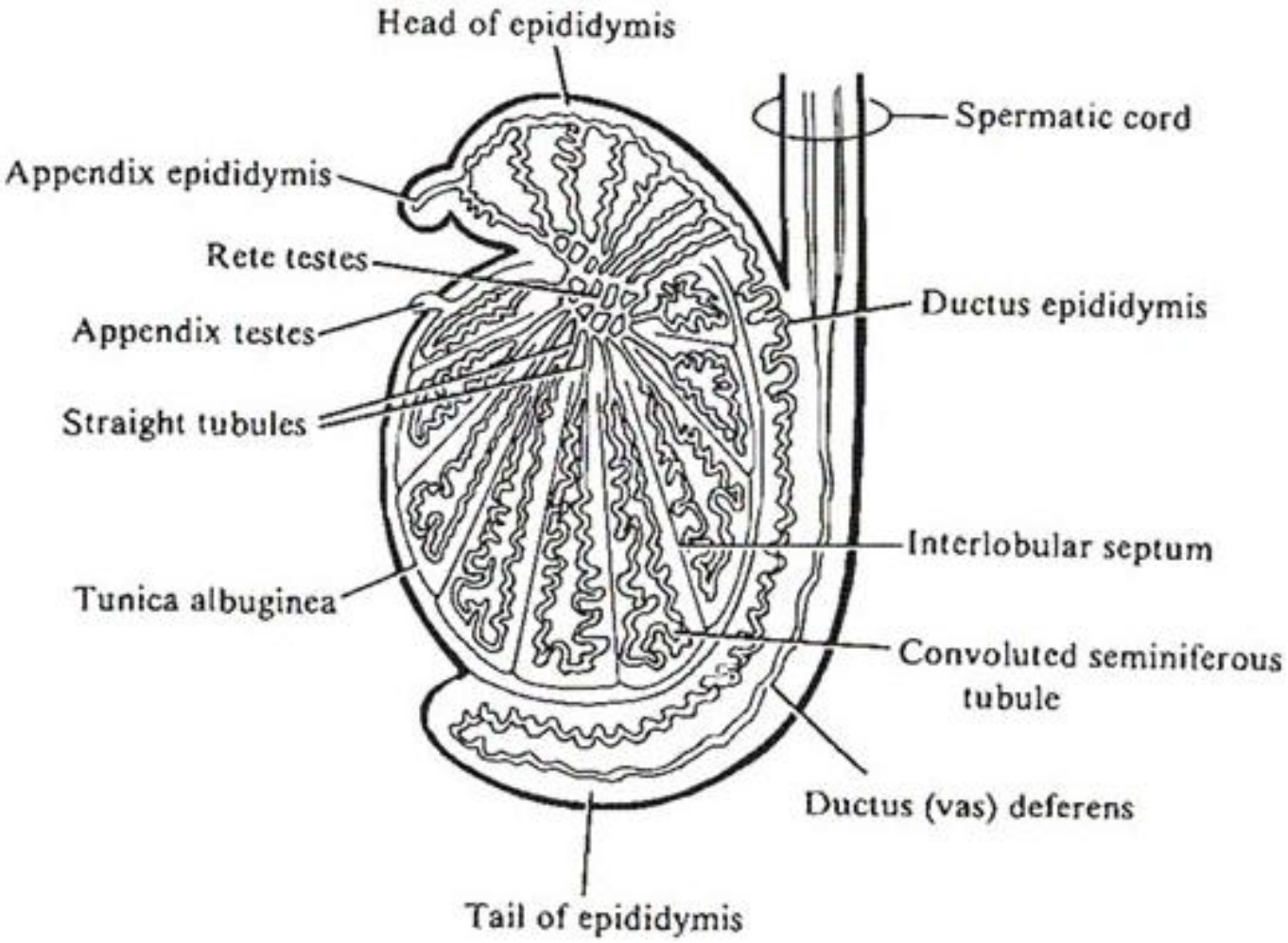
  - the intertubular compartment that lies between the seminiferous tubules and contains the interstitial tissue.



Introduction (Cont'd)

➢The male tubes begin with the seminiferous tubules; from which the spermatozoa are collected and transported via the following tubes (sequentially):

- ✓The straight tubules to the rete testis to the efferent ductules of the epididymis.
- ✓The epididymis is a coiled, C-shaped long tube found inside the scrotal sac, consists of a head, a body, and a tail.
  - ▪While temporarily stored here, the spermatozoa mature and become mobile.
  - ▪All coiled epididymal ducts empty into a single duct, the ductus epididymis.



Introduction

✓The ductus (vas) deferens of the spermatic cord is a continuation of the ductus epididymis

- The ductus curves behind the urinary bladder, over the ureter, and just medial to the seminal vesicle. Each ductus dilates into an ampulla and joins with the seminal vesicle (one on each side) to form the ejaculatory duct.

✓The ejaculatory ducts pierce the glandular tissue of the prostate to open into the prostatic urethra at the urethral crest.

➢**Auxiliary male genital glands**

- The seminal vesicles are tortuous muscular tubes with small outpouchings in back of the bladder. They produce a thick, yellow secretion that forms most of the semen volume and helps nourish the spermatozoa.

- The prostate gland is a pyramid-shaped fibromuscular gland wrapped around the urethra at the base of the urinary bladder.

- Tubules from the gland enter the prostatic urethra and add prostatic secretion to the sex cells as they pass through and helps in maintaining motility.

Introduction (Cont'd)

- The bulbourethral or Cowper's glands are the largest of the mucus-secreting glands in the male reproductive system and are a pair of pea-shaped organs in the pelvic floor tissue just below the prostate gland. Their ducts empty into the urethra.

    - Other small urethral glands also secrete mucus into the penile urethra.

➢ The urethra and penis

The urethra serves a dual role: conveying urine from the bladder and carrying reproductive cells and their accompanying secretions to the outside.

The ejection of semen is made possible by the erection of the penis. The latter consists of a sponge like tissue containing many blood spaces that are relatively empty during organ flaccidity, but fill with blood and distend on erection.

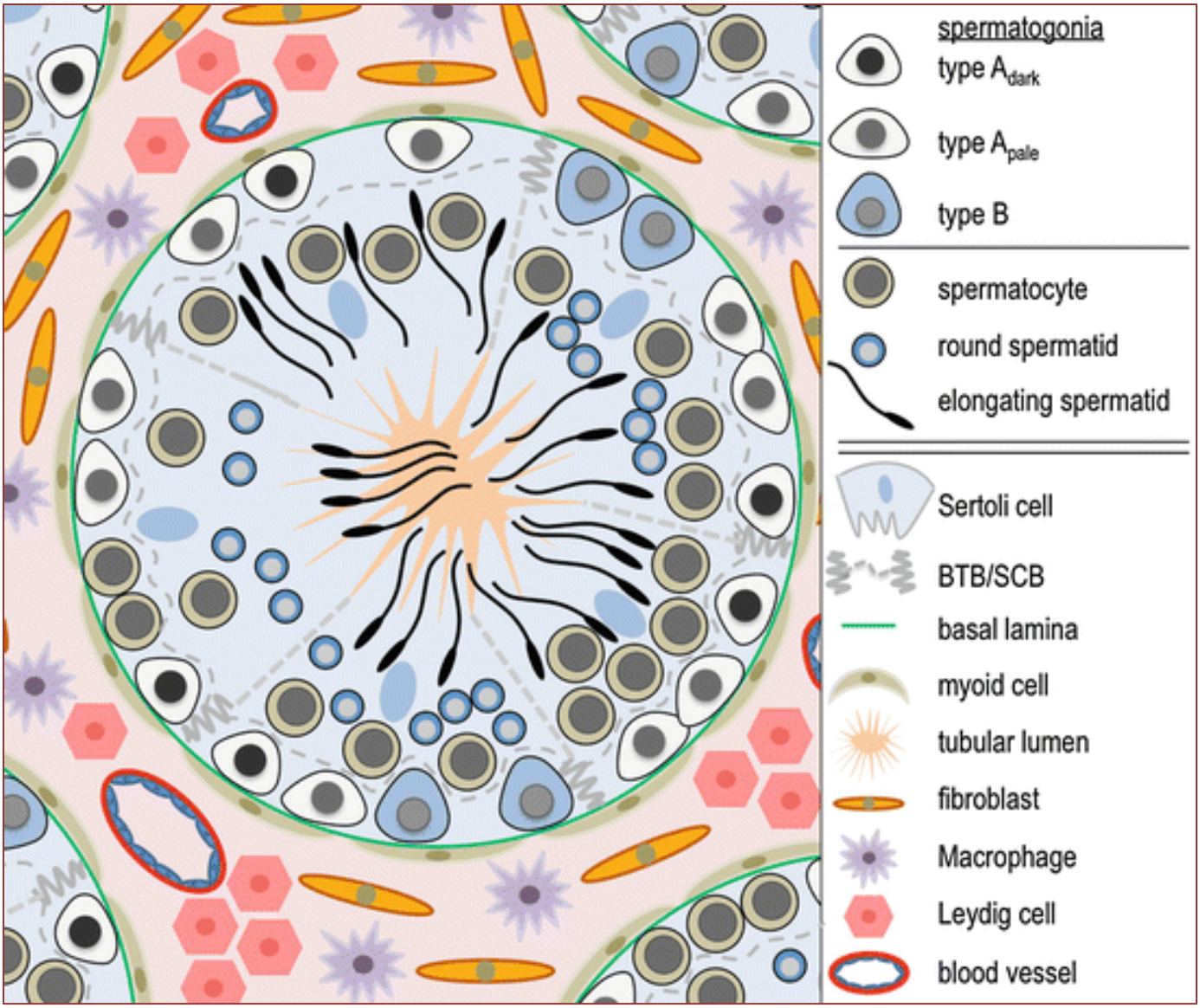
The penis and scrotum are the male external genitalia. The semen passes from the urethra to the membranous urethra to the penile urethra before it reaches the outside.

Seminiferous tubule

- The functional unit that produces sperm via spermatogenesis is the seminiferous tubule.

- Each testis contains about 250 functional units called lobules; each lobule contains about 4 seminiferous tubules.

- All somniferous tubules in a testis converge and form a channel called rete testis.



Seminiferous epithelium: Structure and cellular composition

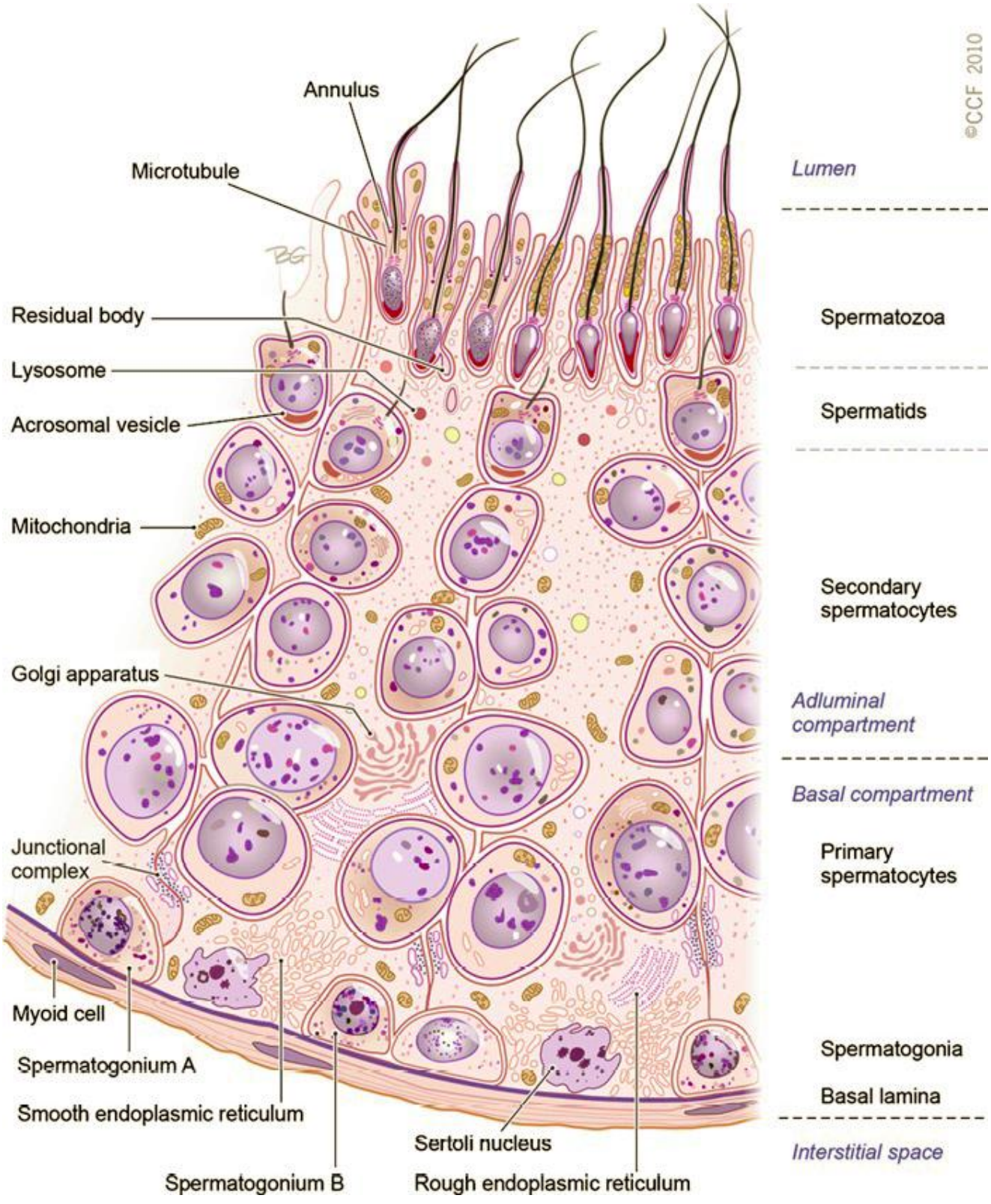
▪The seminiferous epithelium rest on the tunica propria, which is composed of an acellular zone namely basement membrane and type I collagen layer, and a cellular zone of peritubular myoid cell layer and the lymphatic microvessel.

▪The Blood–Testis Barrier (BTB) divides the seminiferous epithelium into the adluminal (apical) and basal compartments. BTB is constituted by actin-based tight junctions, basal ectoplasmic specialization (ES), and gap junctions, as well as the intermediate filament-based desmosome. The blood–testis barrier has three different levels:

- tight junctions between Sertoli cells, which helps separate premeiotic spermatogonia from the rest of the germ cells,
- the endothelial cells in both the capillaries and,
- peritubular myoid cells.

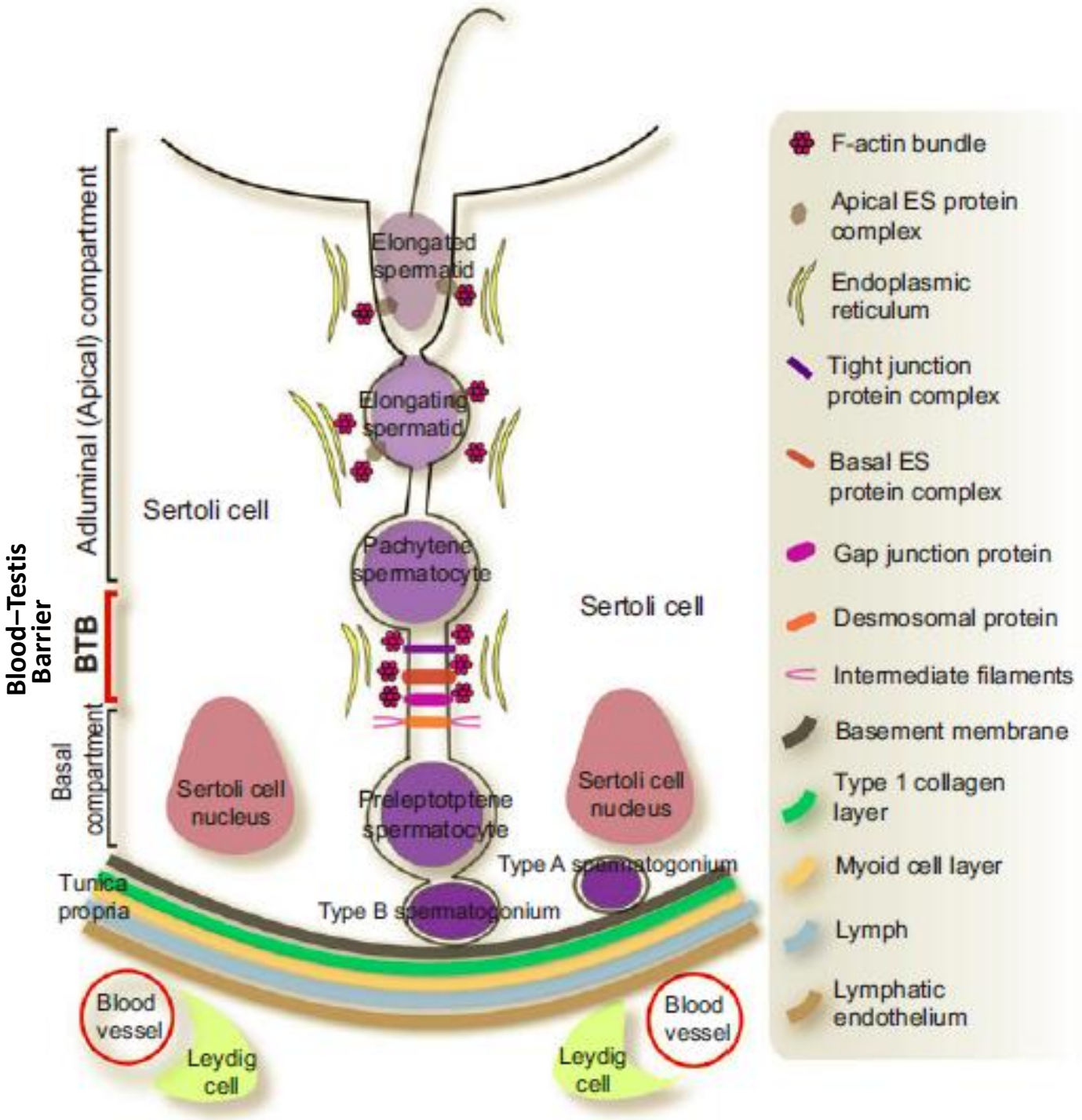
▪Spermatogonia (both type A, B and undifferentiated) and preleptotene spermatocytes reside in the basal compartment, whereas the other primary and secondary spermatocytes and post-meiotic haploid spermatids are found in the apical compartment.

Seminiferous epithelium: Structure and cellular composition (Cont'd)



Section of the germinal epithelium in the seminiferous tubule.

Seminiferous epithelium: Structure and cellular composition (Cont'd)



Structure and cellular composition of the seminiferous epithelium in the human testis.

Seminiferous epithelium: Structure and cellular composition (Cont'd)

The seminiferous epithelium is composed of :

- ✓ **Sertoli cells**
  - Located in the germinal epithelium.
  - Have multiple roles in germ cell development, ranging from physical support and immunoprotection to the supply of nutrients and other factors.
  - Targets of pituitary-derived follicle-stimulating hormone (FSH) and testosterone, produced in Leydig cells of testicular interstitium under control of luteinizing hormone (LH), and they transduce these signals and other stimuli into paracrine regulation of spermatogenesis and coordinate gene expression in germ cells.
  - Energetic imbalance and disturbances of the reproductive axis (hypothalamus–pituitary–testis axis) severely affect Sertoli cells functions

- ✓ **Germ cells** at different stages of development: germ cells are arranged in a highly ordered sequence from the basement membrane to the lumen.

Other cell types:

- ✓ **Interstitial or Leydig cells** are located in the connective tissue surrounding the seminiferous tubules. Blood vessels and nerve fibres are restricted to the interstitial space between seminiferous tubules. Leydig cells produce testosterone under the influence of luteinizing hormone (LH).
- ✓ **Myoid cells** surround the tubules and generate rhythmic contractions to propel spermatozoa and fluid.

Sertoli cells vs. Leydig cells

Functions of the Sertoli cells:

- Maintains the integrity of seminiferous tubules epithelium
- Secretion of hormones—inhibin and androgen-binding protein (ABP)
- Secretes tubular fluid into the tubular lumen for transport of sperm within the duct
- Delivery of nutrients to germ cells
- Steroidogenesis and steroid metabolism
- Aids in process of phagocytosis and elimination of cytoplasm
- Regulates the spermatogenic cycle
- Acts as a hormonal target for LH, FSH, and testosterone

Functions of the Leydig cells:

- Initiation and maintenance of spermatogenesis
- Activation of the hypothalamus–pituitary–gonadal axis
- Production of testosterone—manifestation of male secondary sex characteristics
- Differentiation of male genital organs
- Masculinization of the brain and sexual behavior

Common terms in sperm formation

Spermatogenesis:

The process of differentiation of a simple diploid spermatogonium into a spermatid is known as Spermatogenesis. It is a complex, temporal event whereby primitive, totipotent stem cells divide to either renew them or produce daughter cells that are transformed into a specialized testicular spermatozoon. This takes place in the basal compartment.

Spermiogenesis:

Spermiogenesis is the process of differentiation of the spermatids into spermatozoa with fully compacted chromatin. During this process, morphological changes occur once the process of meiosis is completed. It is a complex process that transforms round spermatids after meiosis into a complex structure called the spermatozoon.

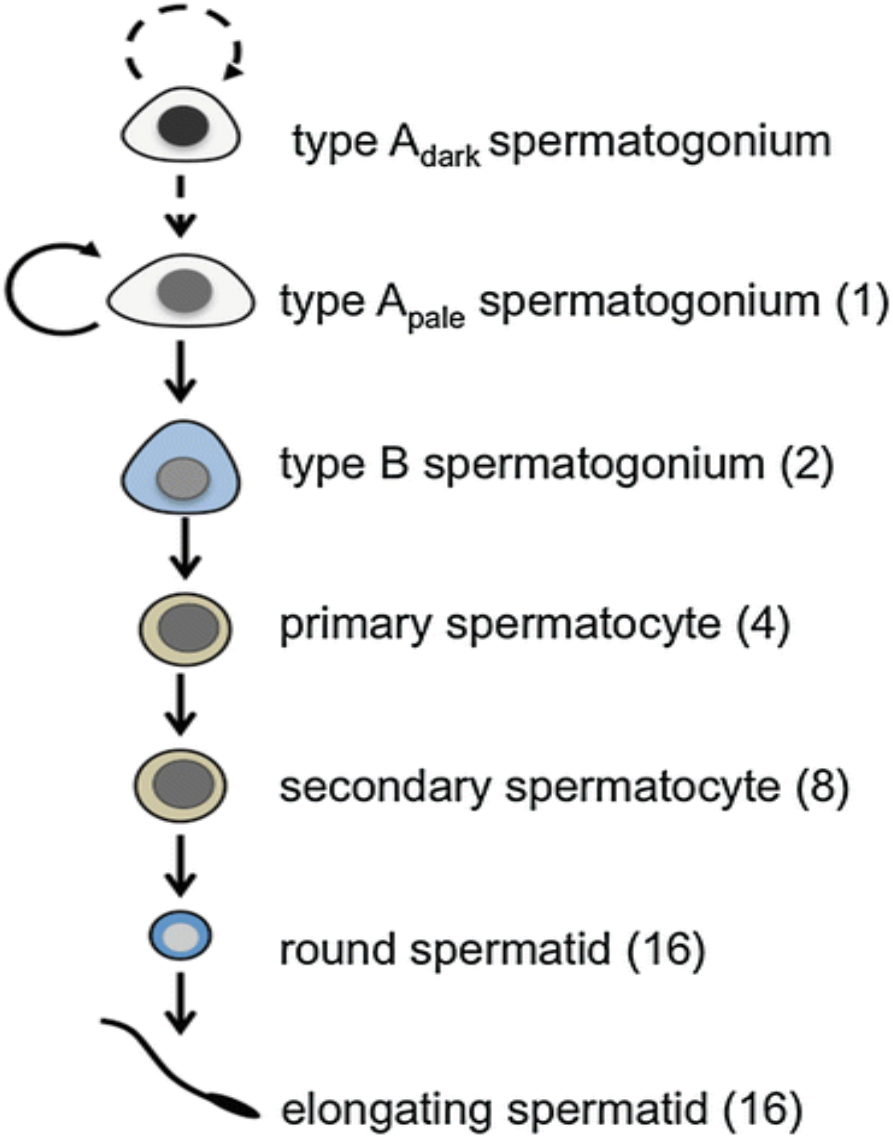
Spermiation:

A mature spermatid frees itself from the Sertoli cell and enters the lumen of the tubule as a spermatozoon in a process called spermiation. The excess cytoplasm, known as residual bodies, is phagocytosed by surrounding Sertoli cells in the testes under the influence of testoterone. The mature spermatozoa are released from the protective Sertoli cells into the lumen of the seminiferous tubule. The resulting spermatozoa are mature but lack motility. These non-motile spermatozoa are transported to the epididymis in testicular fluid secreted by the Sertoli cells where they acquire motility and become capable of fertilization.

Types of Spermatogonia

▪Spermatogonia are designated type A and type B. In humans, type A spermatogonia are further categorized into progenitor dark type A spermatogonia (Ad) and pale type A spermatogonia (Ap) which are capable of undergoing self-renewal through mitosis, and Ap also give rise to type B spermatogonia which differentiate to form preleptotene spermatocytes.

▪In the human testis, preleptotene spermatocytes of the epithelial cycle are transported across the BTB to enter the adluminal compartment to prepare for meiosis I/II. In the human, only 16 sperms are derived from one type A spermatogonium.



Spermatogenesis

- Production of male gametes, i.e., spermatogenesis, takes place in the seminiferous tubules of the testis.

- A multifaceted, process that takes ~2.5 months to complete in man.

- The seminiferous epithelium is in constant turnover as new generations of germ cells start to differentiate on the basal lamina and mature gametes are released from the apical part to the tubular lumen.

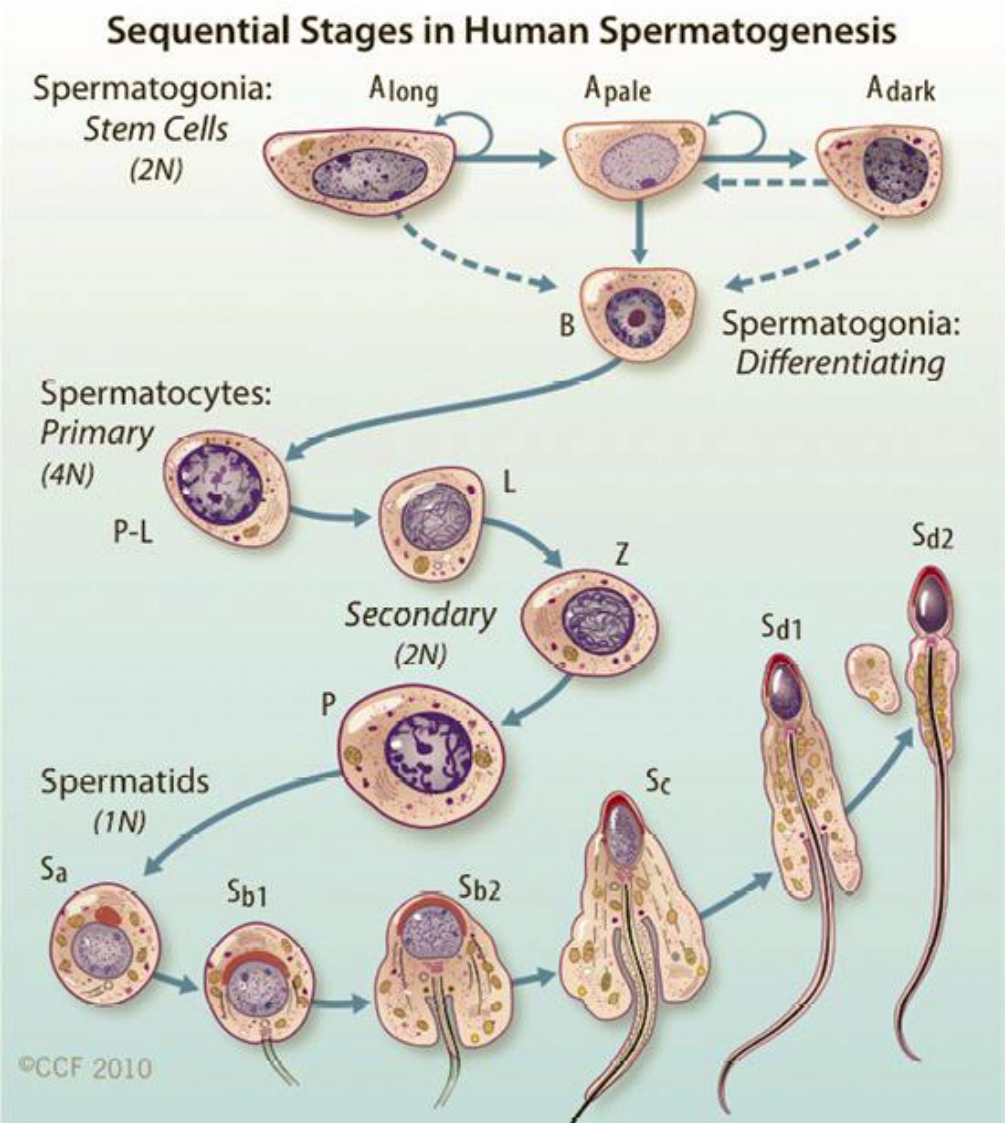
- Different generations of germ cells ensue spermatogenesis in synchrony and therefore over a period of time, called the cycle, the seminiferous epithelium has the same appearance.

- Ability to produce sperm ultimately depends on germ-line stem cell (GSC) self-renewal.

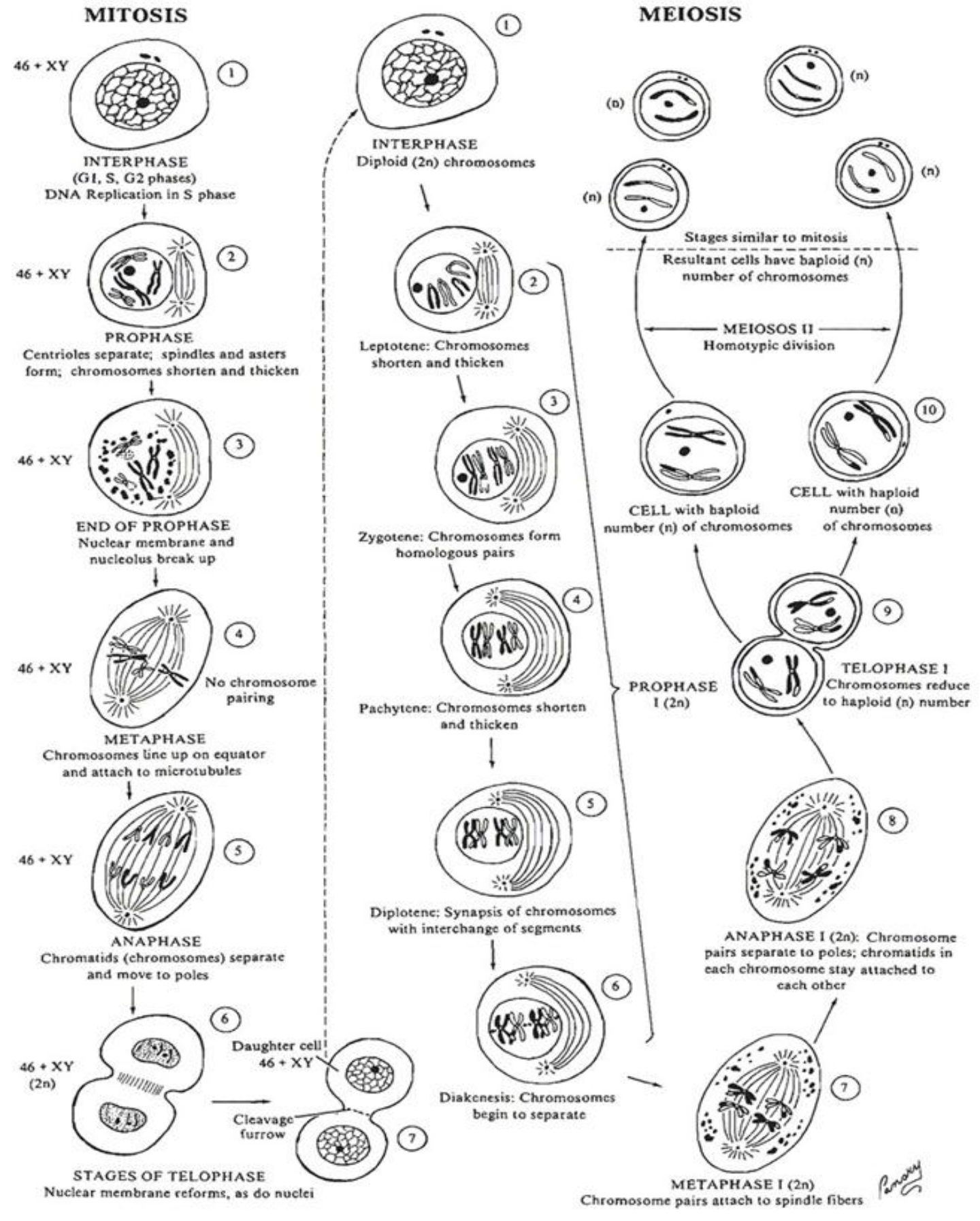
Spermatogenesis: Major events

Spermatogenesis is composed of a series of cellular events which includes

(i) Self-renewal of spermatogonial stem cells and spermatogonia via mitosis,
(ii) Transformation and differentiation of spermatocytes,
(iii) Generation of haploid spermatids via meiosis I/II, and
(iv) Morphological maturation of spermatids through round Sa spermatids, Sb1, Sb2, Sc, Sd1, and Sd2, to become spermatozoa via spermiogenesis.



Spermatogenesis: Mitosis and Meiosis



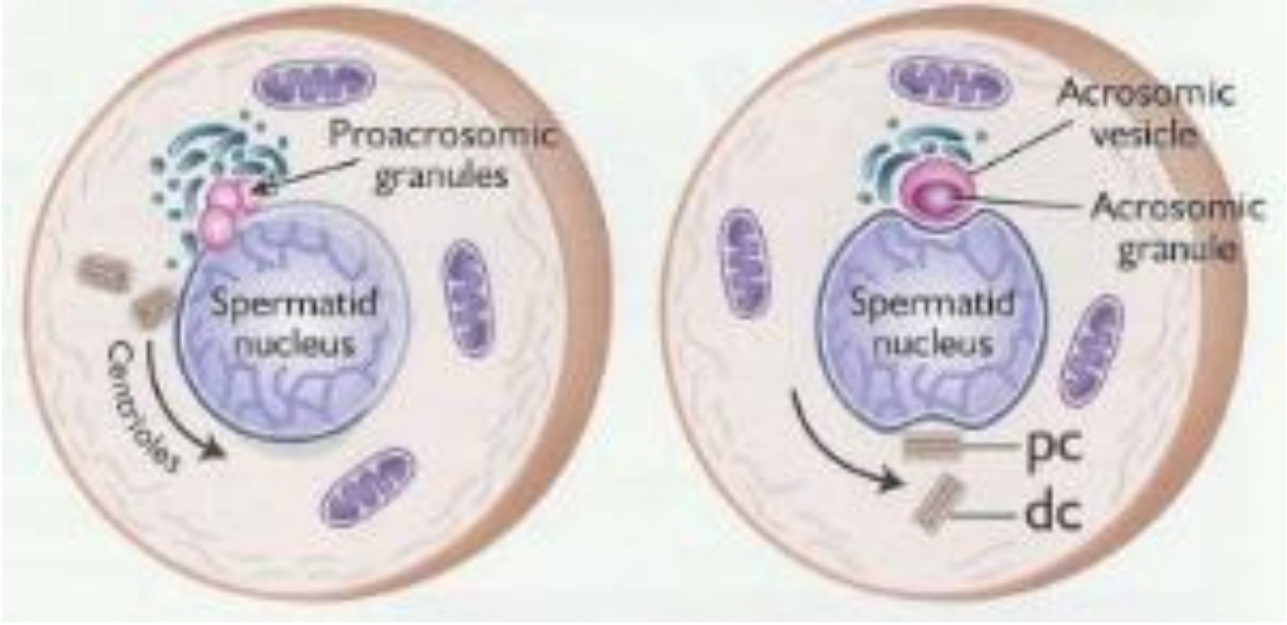
Spermiogenesis: Spermatid differentiation

Spermiogenesis:

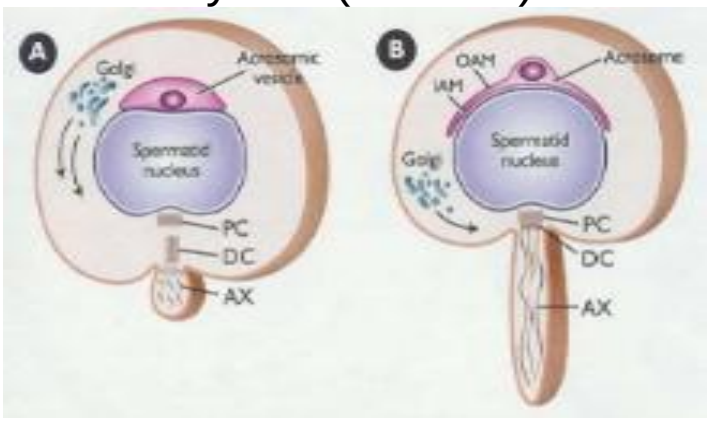
- Takes place in the adluminal compartment of the seminiferous tubule.
- A cell differentiation process in which round spermatids mature and become elongated spermatids.
- DNA becomes highly condensed, the acrosome is formed, flagellum (tail) is formed, and cells become potentially motile.
- Elongated spermatids move closer to the lumen of the seminiferous tubule.

Spermiogenesis comprises four phases:

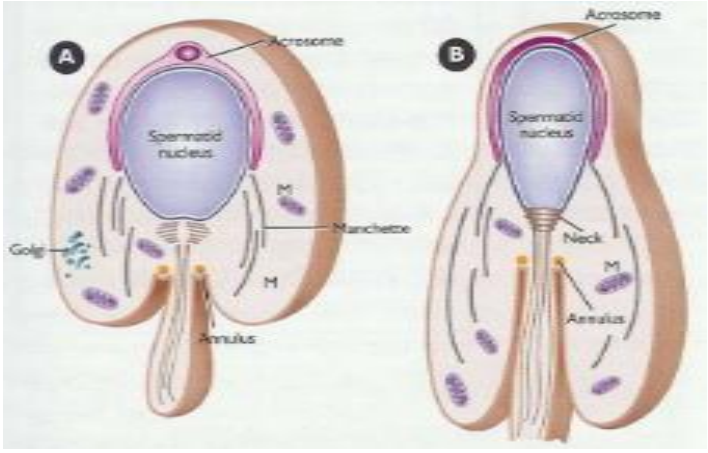
Golgi phase: Small vesicles of the Golgi fuse to form pro-acrosomic granules. Centrioles migrate to the pole opposite to the acrosomic vesicle. Large acrosomic vesicle is formed containing a dense acrosomic granule. The proximal centriole (PC) will give rise to the attachment point of the tail. The distal centriole (DC) will give rise to the developing axoneme (AX) or flagellum.



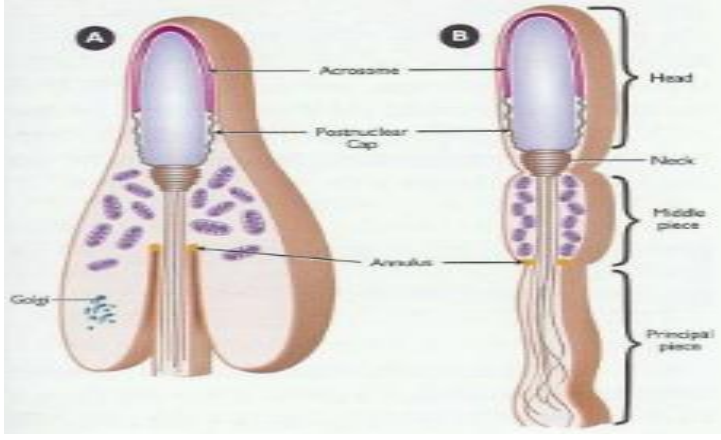
Cap phase: DC forms the axoneme. The acrosomic vesicle flattens and starts to form a distinct cap consisting of an outer acrosomal membrane (OAM) and inner acrosomal membrane (IAM) & the acrosomal enzymes (A and B).



Acrosomal phase: Nucleus elongates and acrosome covers majority of the anterior nucleus. The manchette forms in the caudal half of the nucleus. The neck and annulus (future juncture between the middle and principal piece) are formed (A and B).

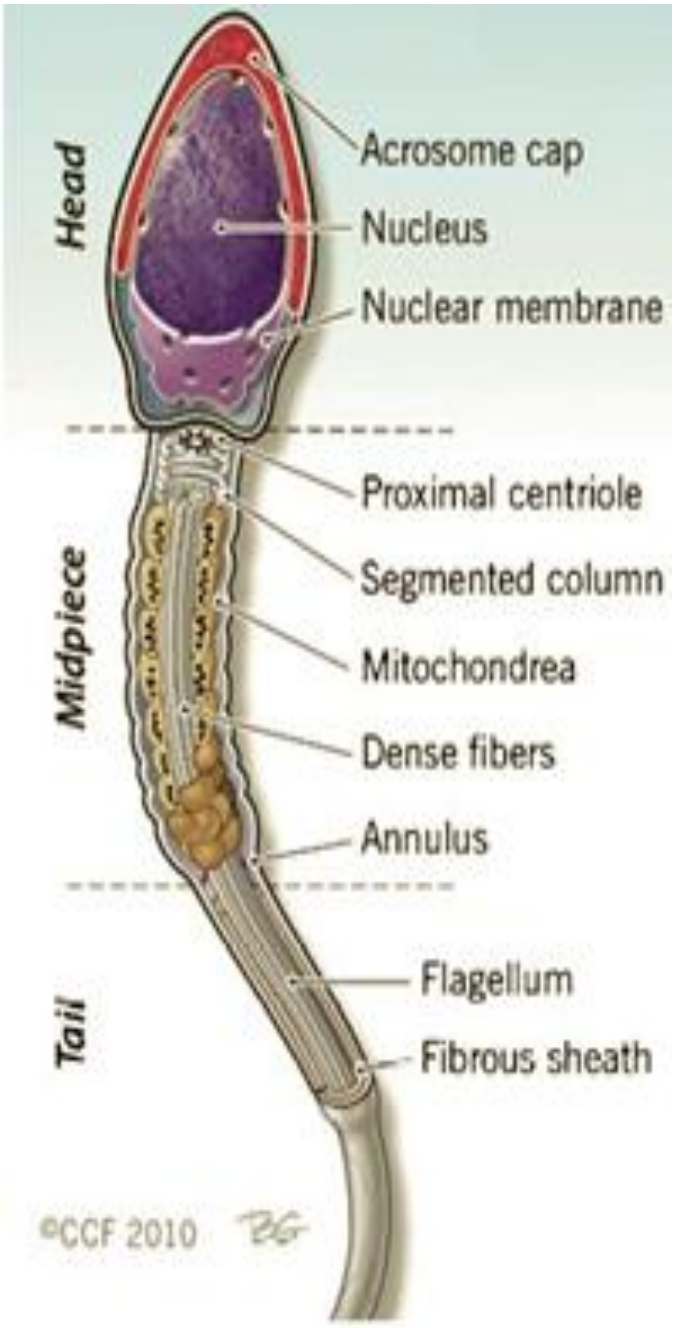


Maturation phase: Mitochondria are assembled around the flagellum and the flagellum is completely formed (A and B).



Normal human spermatozoa

- **Biological characteristics**
  - Length: 65 mm
  - Number: 100 million per ml of semen
  - Motile at emission: more than 80%
  - Rate of movement in the genital tract: 5 mm per minute
  - Survival in the genital tract: 3 to 4 days



Diagrammatic representation of a fully mature spermatozoon

Epithelial cycle of spermatogenesis

- Staging of the epithelial cycle is largely defined according to changes in the Golgi region of developing spermatids, namely the acrosome.

- A cycle of spermatogenesis involves the division of primitive spermatogonial stem cells into subsequent germ cell types through the process of meiosis.

- Type A spermatogonial divisions occur at a shorter time interval than the entire process of spermatogenesis. Therefore, at any given time, several cycles of spermatogenesis coexist within the germinal epithelium.

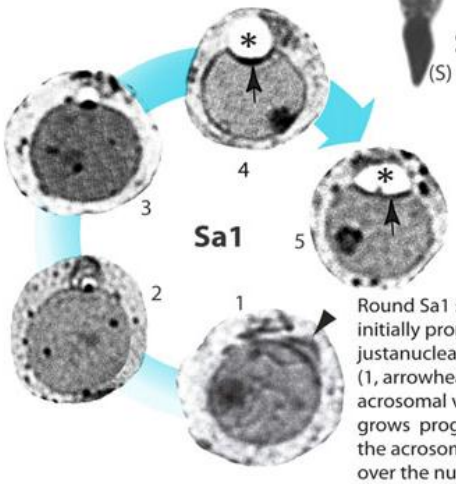
- Each stage is recognized by development of the acrosome; meiotic divisions and shape of the nucleus and release of the sperm into lumen of the seminiferous tubule.

- In the testis of humans, an epithelial cycle is composed of I-VI stages.

Stage I of the epithelial cycle

Germ cells at Stage I under HRLM

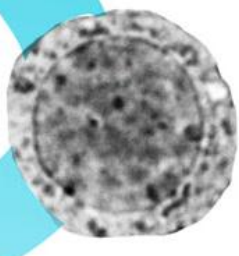
Sd1 elongated spermatid at frontal (F) and sagital (S) views. The chromatin is strongly condensated making it difficult to distinguish between Sc2 (stage VI) and Sd2 (stage II) spermatids.

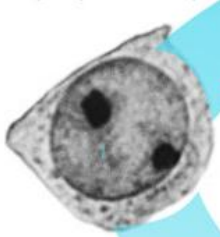


Round Sa1 spermatids show initially prominent justanuclear Golgi complex (1, arrowhead). The acrosomal vesicle (asterisks) grows progressively while the acrosome spreads out over the nucleus in a concave way (4 and 5, arrows).

Pachytene

Chromatin: appears as lightly stained, small spots homogeneously spread throughout the nucleus. **Nucleolus:** small and compact. Genetic recombination (crossing over) occurs along the pachytene development.



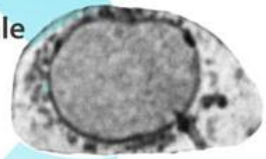


B

Chromatin: clumps of heterochromatin randomly distributed in the nucleus; euchromatin is more granular compared with type A spermatogonia

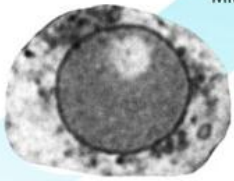
Mitosis

Apale



Mitosis

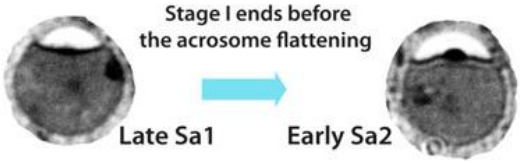
Adark



Nucleoplasm: homogeneous and deeply stained in Adark; lightly rough and poorly stained in A pale.

5 µm

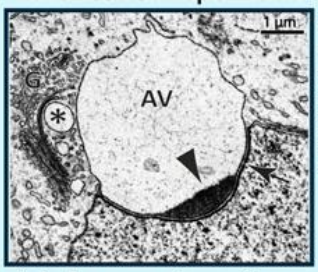
Cut-off between stages I and II



At stage I the acrosomal vesicle of Sa1 spermatid is always concave over the nucleus and when the acrosome becomes flattened, it is classified as stage II.

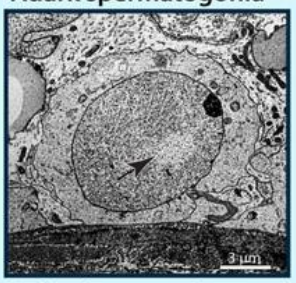
Ultrastructural features

Advanced Sa1 spermatid



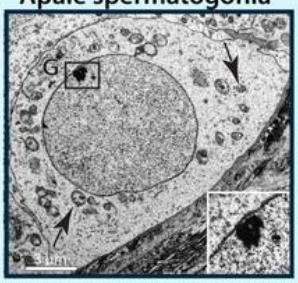
Evident acrosomal vesicle (AV) with dense material (arrowhead) close to the thickened nuclear envelope (arrow). A prominent Golgi complex (G) with proacrosomal granules (*) is seen in the vicinity.

Adark spermatogonia



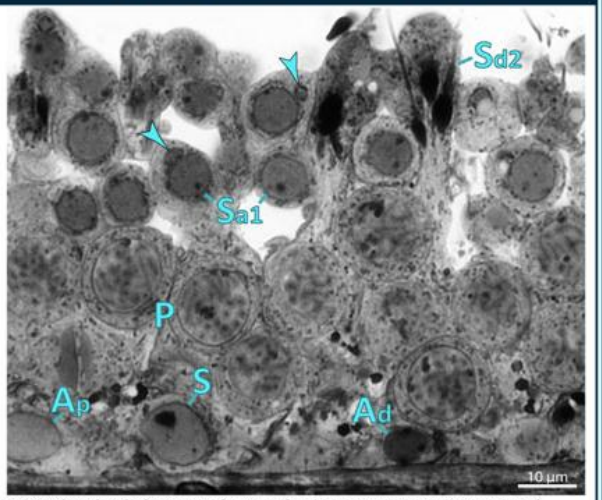
Nucleoplasm: more electron -dense compared to Apale with a central electron- lucent area (arrow). **Nucleolus** in close apposition to the nuclear envelope.

Apale spermatogonia



Nucleoplasm: homogeneous and finely granular. **Nucleolus** (box) undergoes initial disarrangement. **Mitochondria** (arrows) and **Golgi** complex (G) are frequent.

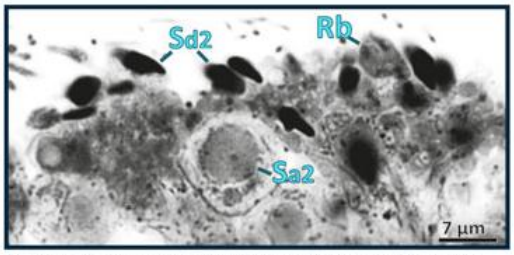
Stage I - Seminiferous tubule view



S, Sertoli; Ad, Adark; Ap, Apale; P, pachytene spermatocyte; Sa1, round spermatid; Sd1, elongated spermatid; Arrowheads, Golgi complex.

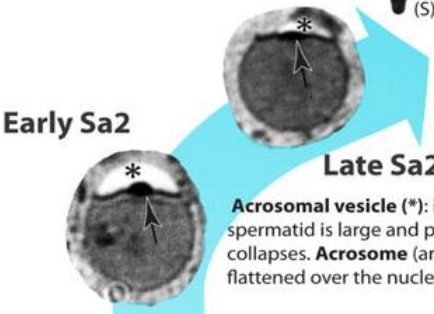
Stage II of the epithelial cycle

Germ cells at Stage II under HRLM

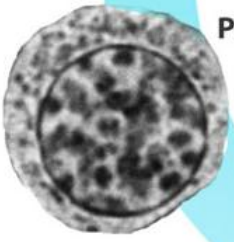


At the end of stage II, Sd2 elongated spermatids are no longer deeply embedded in the crypts of Sertoli cells, being released afterall. Sa2, round spermatid; Rb, residual body.

Sd2 elongated spermatids on frontal (F) and sagittal (S) section. **Nucleus:** strongly stained as seen in Sc2 and Sd1 spermatids. It is not possible to differentiate them from their predecessors.

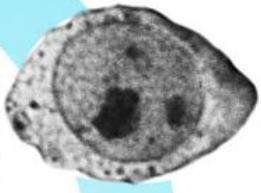


Acrosomal vesicle (*): in early rounded Sa2 spermatid is large and progressively collapses. **Acrosome** (arrows): remains flattened over the nucleus.



Pachytene

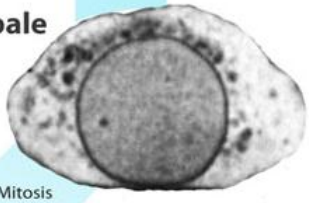
Chromatin: organized in patches and weakly stained. **Nucleus**: along its development (stage I to V) become highly synthetic and grows progressively in size.



B

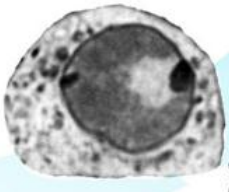
Nucleoli: less compact and bigger than in type A spermatogonia and frequently detached from nuclear envelope

Mitosis



Apale

Mitosis



Adark

Only Adark spermatogonia show evident **nuclear vacuole**.

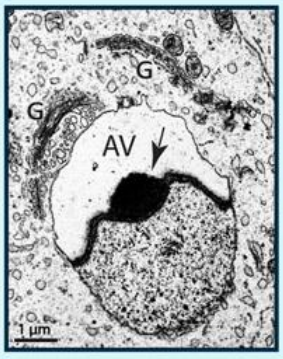
5 µm

Cut-off between stages II and III

Stage II ends when the acrosome assumes a convex shape

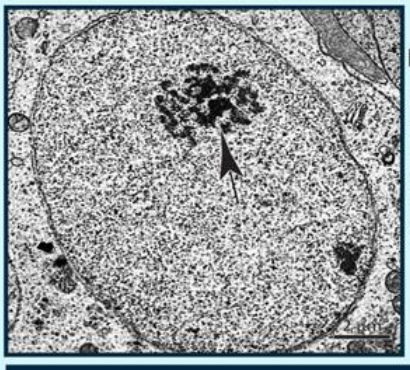
In the late Sa2 (stage II), acrosomal vesicle is almost collapsed and the acrosome is flattened while in early Sb1 (stage III) the acrosome assumes a convex shape over the nucleus.

Ultrastructural features



Other forms of round Sa2 spermatids

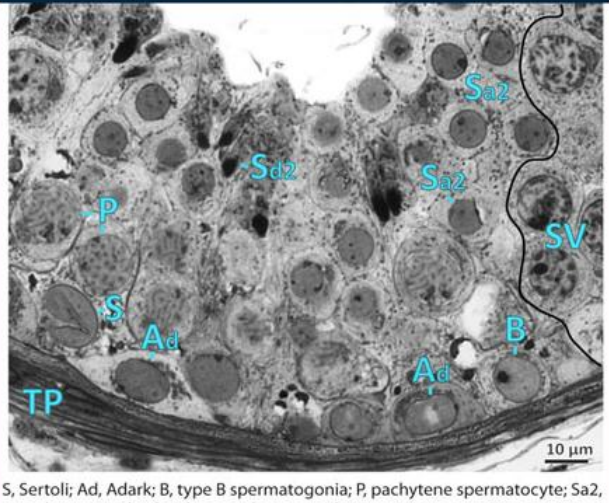
Acrosome (arrow): spreads out over the nucleus with a pattern of waviness. **Golgi complex** (G): well developed and commonly seen nearby large acrosomal vesicle (AV).



B spermatogonia

Euchromatin: rough appearance. **Nucleolus:** reticulated (arrow) and frequently detached from the nuclear envelope .

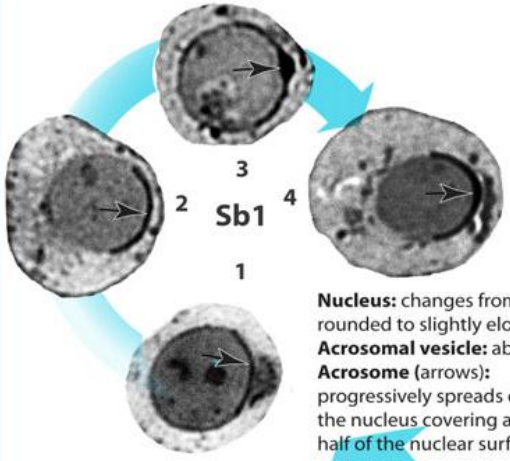
Stage II - Seminiferous tubule view



S, Sertoli; Ad, Adark; B, type B spermatogonia; P, pachytene spermatocyte; Sa2, round spermatid; Sd2, elongated spermatid; TP, tunica propria; SV, stage V.

Stage III of the epithelial cycle

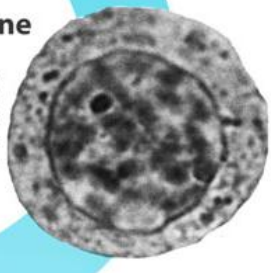
Germ cells at Stage III under HRLM



Nucleus: changes from rounded to slightly elongated. **Acrosomal vesicle:** absent. **Acrosome** (arrows)**:** progressively spreads out over the nucleus covering almost the half of the nuclear surface.

Pachytene

Chromatin: arranged in cords, moderatly stained and associated with clear areas; very distinctive when compared with those from previous stages.



Preleptotene

They are rounded and smaller than spermatogonia, sometimes a bit far from the basal membrane. **Euchromatin:** mottled. **Hetrochromatin:** clumped and ramdonly distributed in the nucleus. **Nucleoli:** bigger than in spermatogonia; markedly scattered in the nucleus and detached from the nuclear envelope.

Apale

Nucleolus: usually Apale shows only one nucleolus while two of them can be seen in Adark.

Mitosis

Adark

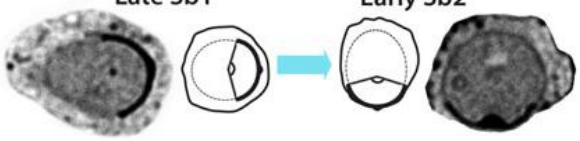
Nucleolus: condensed in both Adark and Apale and usually lies close to the nuclear envelope.

5 µm

Cut-off between stages III and IV

Stage III ends when the nuclear envelope contacts the plasma membrane

Late Sb1 — Early Sb2

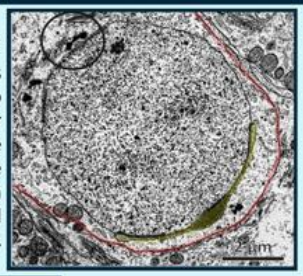


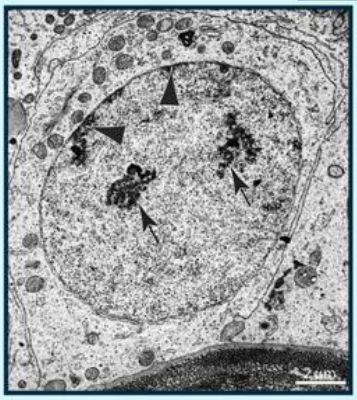
In late stage III, the nucleus of elongating Sb1 spermatids is far from the plasma membrane while in the stage IV the early Sb2 nucleus contacts the plasma membrane.

Ultrastructural features

Sb1 spermatid

The **acrosome** is clearly seen as an electron dense cap (highlighted in yellow) and far away from cellular membrane (red). The **flagellar pole** of the nucleus, in which the flagellum will be implanted, is observed (circle).

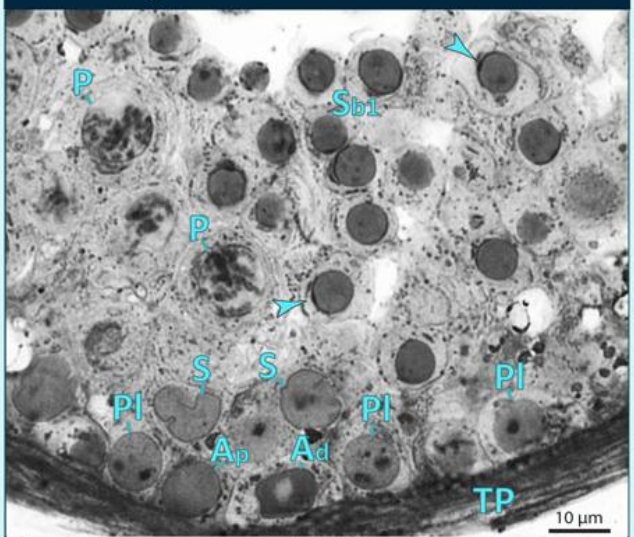




Preleptotene spermatocyte

The **nucleoli** (arrows) are usually scattered and detached from the nuclear membrane. The amount of **heterochromatin** (arrowheads) is increased when compared with spermatogonia.

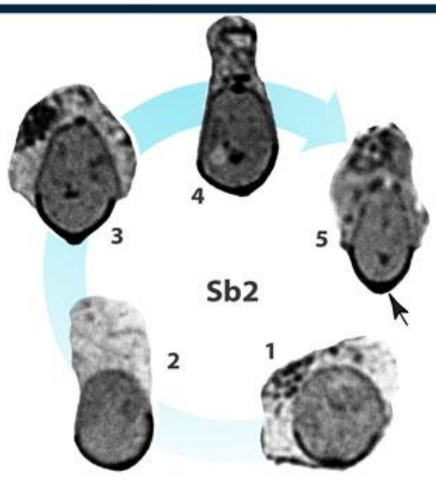
Stage III - Seminiferous tubule view



S, Sertoli; Ad, Adark spermatogonia; Ap, Apale spermatogonia; PL, preleptotene; P, pachytene; Sb1, round spermatid; TP, tunica propria; Arrowhead, acrosome.

Stage IV of the epithelial cycle

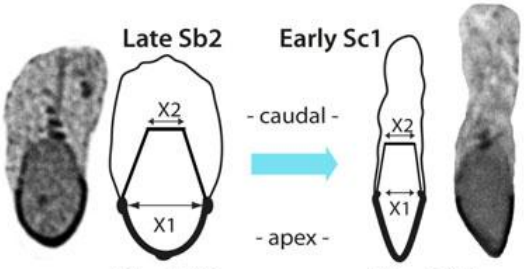
Germ cells at Stage IV under HRLM



Sb2 elongating spermatid is characterized by the presence of acrosome contacted to the plasma membrane (1), facing toward the basal lamina of the tubule. Early Sb2 spermatid shows an oval nucleus that elongate progressively (2-4). Late Sb2 spermatid (5) shows elongated nucleus and evident acrosomal granules on the apex surface of the nucleus (arrow).

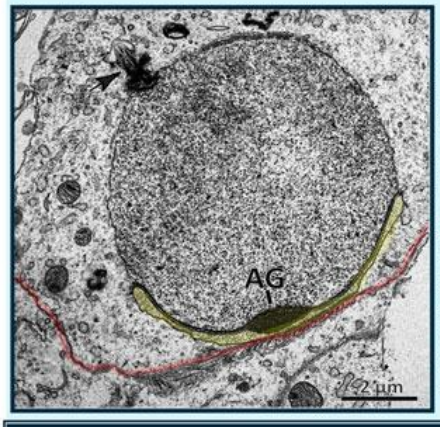
Cut-off between stages IV and V

Stage IV ends when the apex axis becomes narrower than the caudal axis



In the late elongating Sb2 spermatids (stage IV), the length of the transversal axis at acrosomal apex (X1) is at least twice longer than the transversal axis at caudal apex (X2). In early Sc1, spermatid (stage V) this ratio is less than 2 times.

Ultrastructural features



Sb2 spermatid

Typical early Sb2 showing slightly oval nucleus and the acrosome (highlighted in yellow) in contact with the plasma membrane (red). The flagellum is partially seen arising from the flagellar pole of the nucleus (arrow). AG, acrosomal granule

Pachytene

Nucleoplasm: seen as large clear areas in late pachytenes due to the progressive chromosomal condensation.

Leptotene

Chromatin: thin and loosely stained; organized in threads or small splotches when cross-sectioned; corresponds to chromosomes that still remain unpaired. Leptotene is rounded and dislocated away from the base of the tubule.

Apale

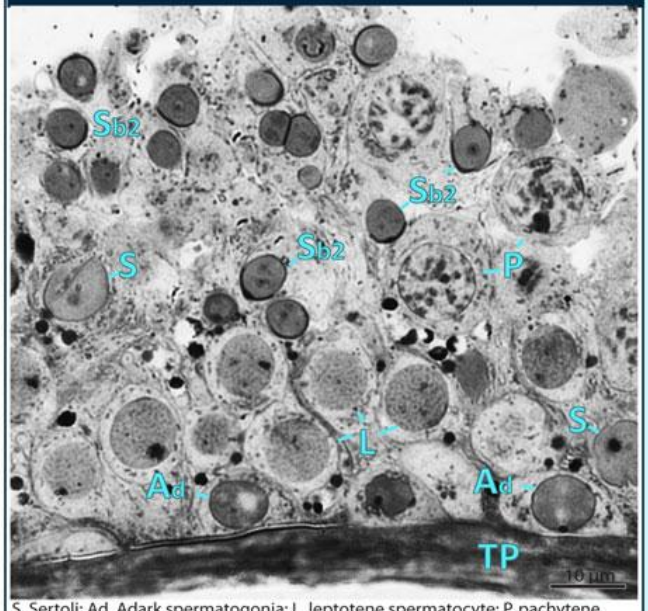
Mitosis

Adark

Nucleus: rounded in Adark and bigger and slightly oval in Apale.

5 µm

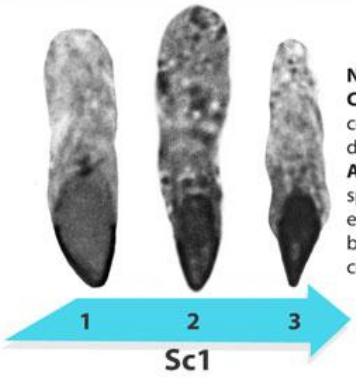
Stage IV - Seminiferous tubule view



S, Sertoli; Ad, Adark spermatogonia; L, leptotene spermatocyte; P, pachytene spermatocyte; Sb2, elongating spermatid; TP, tunica propria.

Stage V of the epithelial cycle

Germ cells at Stage V under HRLM



Nucleus: elongated.
Chromatin: progressively condensated and dark-stained.
Acrosome: visible in early Sc1 spermatids (arrow) and less evident in most advanced Sc1 because of the chromatin condensation.

Pachytene

Nucleus: round with thick cords of dark-stained chromatin intermingled with large clear spaces.
It reaches the maximum size compared with those from previous stages.

Leptotene/Zygotene

The transition between leptotene and zygotenes occurs in this stage. In sections, they are frequently similar in terms of morphology.

Apale

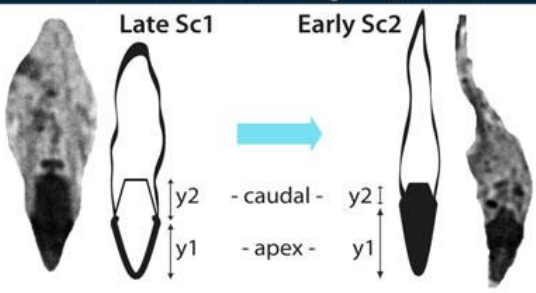
Mitosis

Adark

Nuclear envelope: thicker and darker in Adark compared with Apale and B spermatogonia.

5 µm

Cut-off between stages V and VI

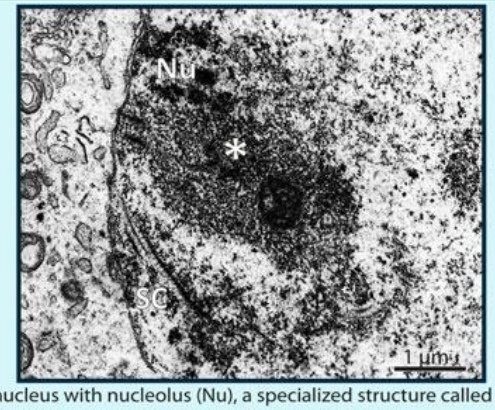


The transition from Sc1 (stage V) to Sc2 (stage VI) spermatids occurs when the longitudinal axis at caudal nucleus (Y2) is shorter in Sc2 spermatids. Once this characheristic is not easy to be noticed due to the darkness staining of the nucleus, the staging is not confidently recognized based only on Sc1 and Sc2 elongated spermatids. Other parameters must be taken into account:

Stage V
Sc1 spermatid
Late pachytene

Stage VI
Sc2 spermatid
Diplotene
Mitotic divisions
Secondary spermatocyte

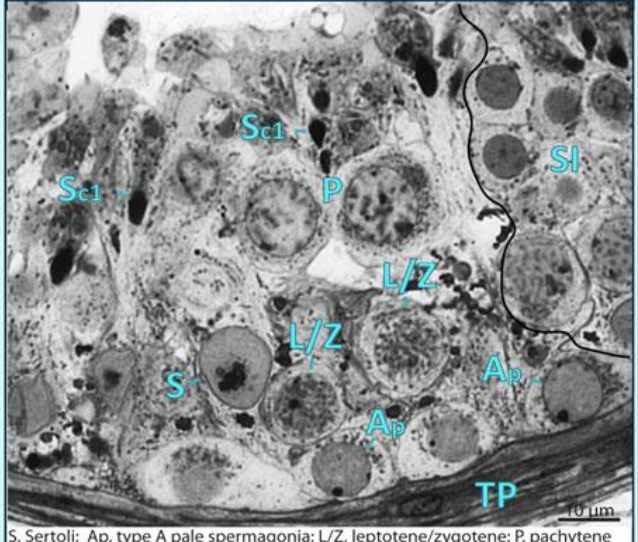
Ultrastructural features



Pachytene

View of the nucleus with nucleolus (Nu), a specialized structure called sex chromatin (asterisk) and a tripartite structure konwn as synaptonemal complex (SC).

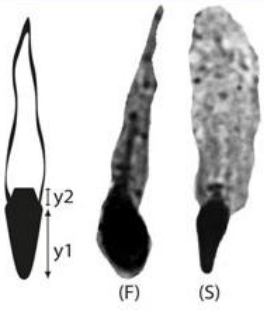
Stage V - Seminiferous tubule view



S, Sertoli; Ap, type A pale spermagonia; L/Z, leptotene/zygotene; P, pachytene spermatocyte; Sc1, elongated spermatids; TP, tunica propria; Sl, stage I.

Stage VI of the epithelial cycle

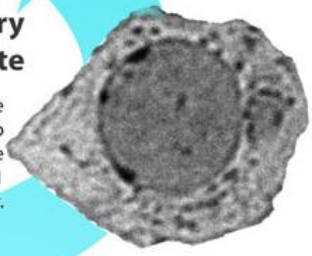
Germ cells at Stage VI under HRLM



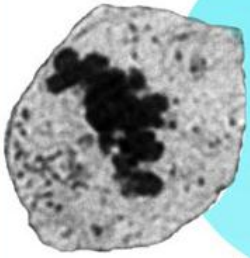
Sc2 elongated spermatids on frontal (F) and sagital (S) view show condensed and heavily stained chromatin and very sharp nuclear apex surface . Their longitudinal axis at the apex (Y1) is longer when compared with caudal one (Y2).

Sc2

Secondary spermatocyte



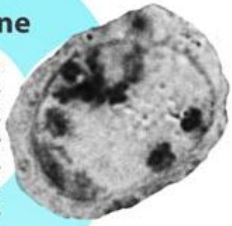
These cells are hardly seen in the seminiferous epithelium due to their short duration. They are similar in appearance to step Sa1 spermatid, however 25% larger.



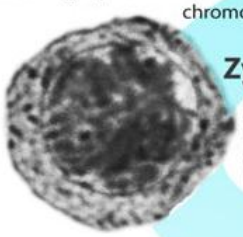
Meiotic division

Large dividing cells. Nuclear envelope disappears and chromosomes are arranged in subsequent phases of the meiotic division: metaphase, anaphase and telophase. Here a metaphase.

Diplotene



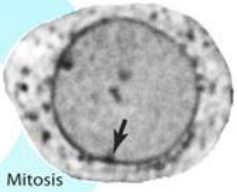
Nucleus: oval and bigger than in pachytenes with large interchromosomal clear areas.
Chromatin: distribution restricted to the nucleus periphery.
Diplotene has brief duration when the synaptonemal complex dissipates allowing separation of homologous chromosomes.



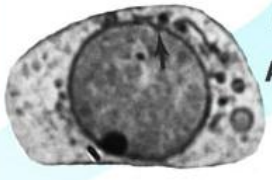
Zygotene

Chromatin: thicker and bulkier when compared with leptotene´s one. The homologous chromosomes have become paired.

Apale



Mitosis

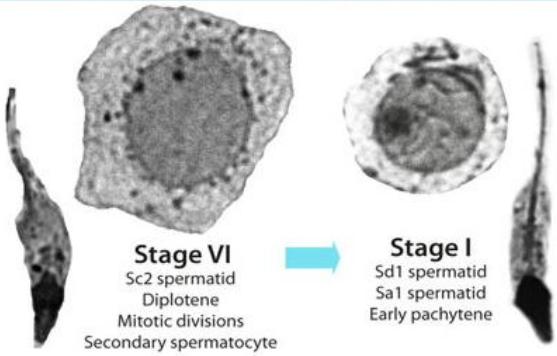


Adark

Heterochromatin: occasional clumps (arrows) randomly seen in both Adark and Apale nuclei.

5 µm

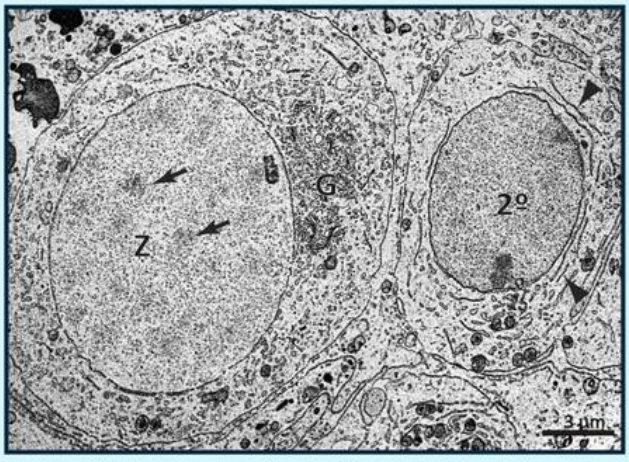
Cut-off between stages VI and I



Stage VI
Sc2 spermatid
Diplotene
Mitotic divisions
Secondary spermatocyte

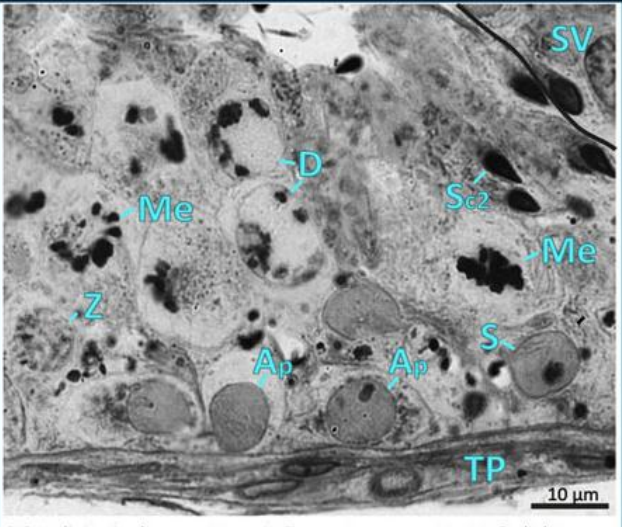
Stage I
Sd1 spermatid
Sa1 spermatid
Early pachytene

Ultrastructural features



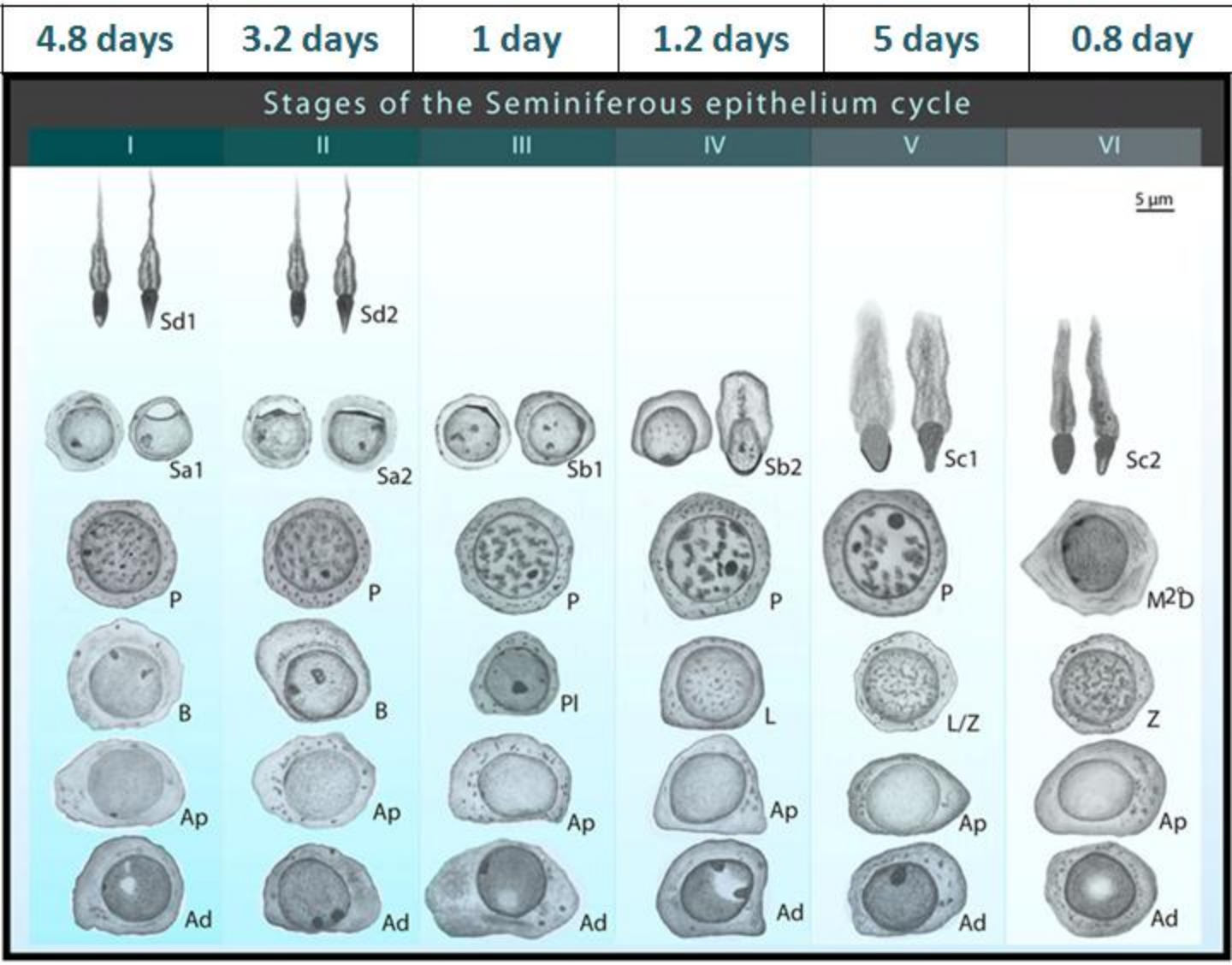
Zygotene (Z) showing a prominent Golgi complex (G) and chromatin condensation (arrows). Secondary spermatocyte (2º) presenting flat cisternae of the endoplasmatic reticulum (arrowheads) arranged concentrically around the nucleus.

Stage VI - Seminiferous tubule view



S, Sertoli; Ap, Apale spermatogonia; Z, zygotene spermatocyte; D, diplotene spermatocyte; Me, meiotic division; Sc2, elongated spermatids; TP, tunica propria; SV, stage V.

Summary: Epithelial cycle of Spermatogenesis

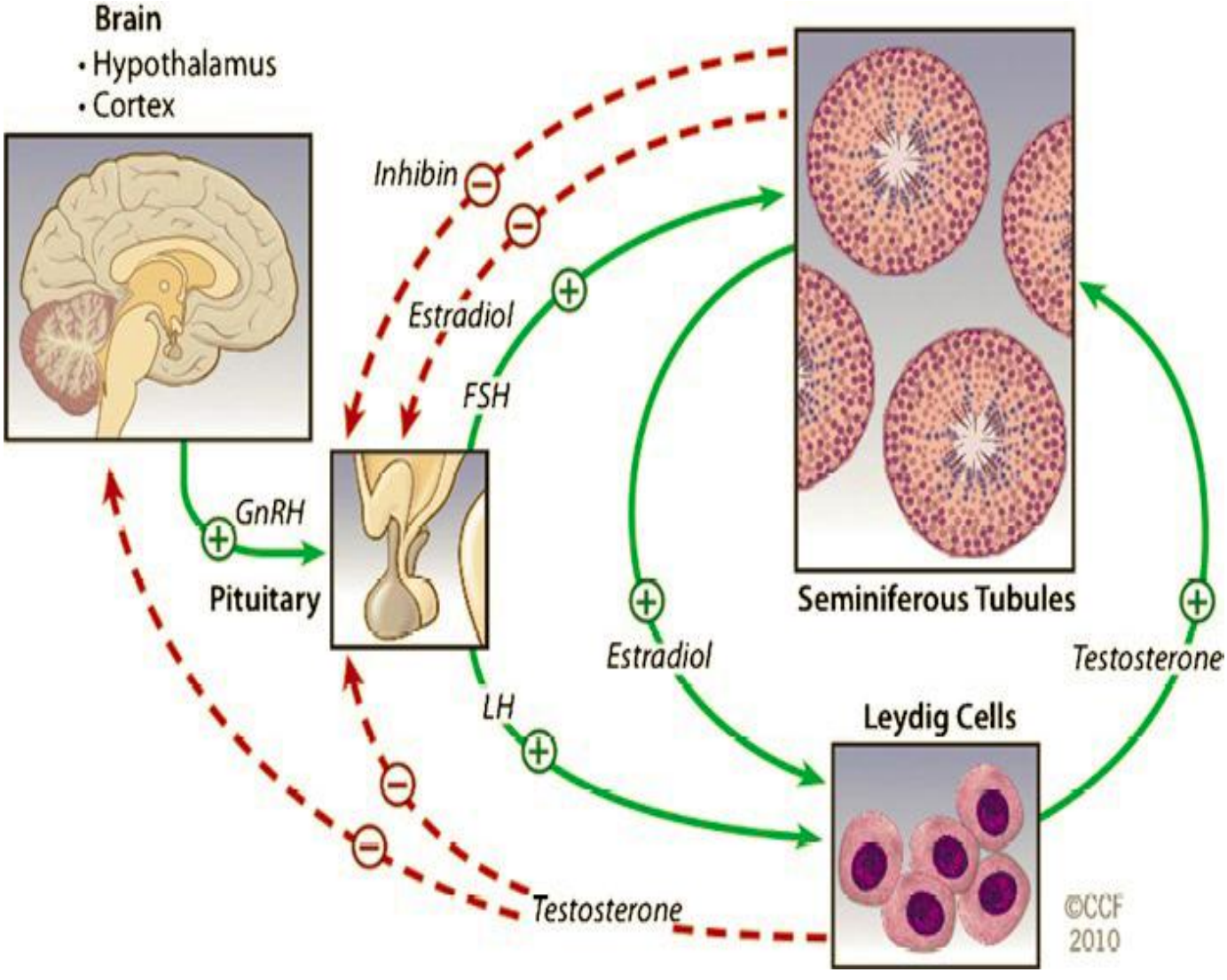


Map of germ cells distribution in the six stages of seminiferous epithelium in man. The duration of each stage, from I to VI, is also annotated.

A_d, A_{dark} spermatogonia; A_p, A_{pale} spermatogonia; B, B spermatogonia; Pl, preleptotene spermatocyte; L, leptotene spermatocyte; Z, zygotene spermatocyte; P, pachytene spermatocyte; D, diplotene spermatocyte; M, meiotic division; 2°, secondary spermatocyte; S_{a1}, S_{a2}, S_{b1}, S_{b2}, S_{c1}, S_{c2}, S_{d1}, S_{d2} spermatids.

Hormonal regulation of Spermatogenesis

The hypothalamic–pituitary–testicular axis exerts its regulatory effects on the testis through the release of gonadotropin-releasing hormone (GnRH) from the hypothalamus, that regulates the secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the pituitary gland. Testosterone produced by interstitial Leydig cells provides the feedback loop to modulate the production of GnRH from the hypothalamus and thereby LH and FSH from the pituitary gland. In humans and primates, testosterone has no direct feedback effect on the pituitary. Inhibin produced by Sertoli cells in seminiferous tubule provides selective feedback to the production of FSH.



Semen or seminal fluid

Semen is body fluid that contains sperm & secretion of seminal vesicle, prostate, Cowper's gland & urethral glands.

Fluid fractions:

Less than 5% of semen volume is contributed by Sperm cells (spermatozoa).

Testis & Epididymis: (5%) Spermatozoa are produced in the testis under the influence of testosterone, and then the epididymis provides a temporary storage site for the immature sperm that enter it from testis. This fraction still is in the inactive form until ejaculation.

Seminal vesicles: (produce about 60% of the fluid volume of semen) viscous, yellowish secretion is rich in fructose, vitamin C, prostaglandin, and other substances, which nourish and activate the sperm passing through the tract.

Prostate: Approximately 30% of the semen volume is acidic fluid produced by the prostate gland, the secretion contains acid phosphatase and proteolytic enzymes that act on the fluid from the seminal vesicles, resulting in the coagulation and liquefaction of the semen.

Urethral glands: (2-5%) are small mucus secreting glands.

Semen or seminal fluid (Cont'd)

The ejaculate can be divided into four fractions:

- **Pre–ejaculatory fraction**: Colourless secretion from the Cowper's glands; lower the acidity of the urethra..
- **Prelimnary fraction**: Originates from the prostrate gland. It gives semen it's characteristic. chestnut blossom odour. It contain enzymes which liquefies the spermatozoal coagulum.
- **Main fraction**: Oiginates from the seminal vesicles, testes, epididymis & partially from the prostate gland. The prelimnary fraction & the main fraction contain majority of spermatozoa.
- **Terminal fraction**: Secretions of seminal vesicles; gelatinous in consistency ,with large number of immotile spermatozoa.

Semen Biochemistry

- **Acid phosphatase:** marker for prostatic function.
- **Citric acid:** can indicate prostatic function – low levels may indicate dysfunction or a prostatic duct obstruction.
- **Zinc:** marker for prostatic function–colorimetric assay (WHO).
- **Fructose:** marker for seminal vesicle function, and is a substrate for sperm metabolism–spectrophotometric assay (WHO).
- **α-glucosidase**: marker for epididymal function–spectrophotometric assay (WHO).

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Zini A and Agarwal A (eds.), Sperm Chromatin: Biological and Clinical Applications in Male Infertility and Assisted Reproduction, DOI 10.1007/978-1-4419-6857-9_2.

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