

Histology

Male Reproductive System - Part 2

Spermiogenesis

This is the final phase of sperm production. It is a temperature-sensitive process by which spermatids differentiate into spermatozoa, which are highly specialized cells that deliver male DNA to the ovum. No cell division occurs during this process, and as with spermatogenesis the cells involved remain associated with Sertoli cells.

The haploid (early) spermatids are rounded small (7-8 μm in diameter) cells near the lumen of the seminiferous tubules. Spermiogenesis includes formation of the acrosome, condensation and elongation of the nucleus, development of the flagellum, and the loss of most of the cytoplasm. The end result is the mature spermatozoon, which is released from the Sertoli cell surface into the tubule's lumen. Spermiogenesis is commonly divided into four phases:

1. Golgi phase:

In this phase the cytoplasm contains a prominent Golgi apparatus near the nucleus, mitochondria, paired centrioles, and free ribosomes. Small **proacrosomal vesicles** from the Golgi apparatus fuse as a single membrane-limited **acrosomal cap** close to one end of the nucleus. The centrioles migrate to a position farthest from the acrosomal cap and one acts as a basal body, organizing the axoneme of the flagellum which is structurally and functionally similar to that of a cilium.

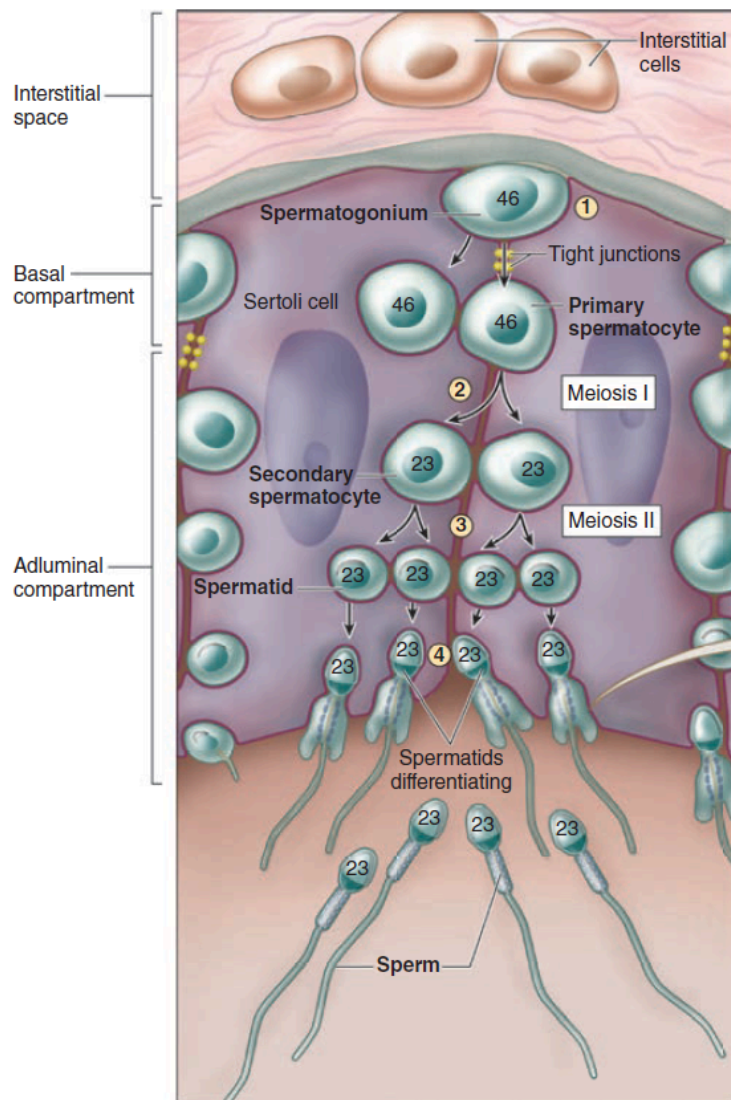
2. Cap phase:

The acrosomal cap spreads over about half of the condensing nucleus. The acrosome is a specialized type of lysosome containing hydrolytic enzymes (mainly hyaluronidase and acrosin). These enzymes are released when the spermatozoon reaches the oocyte, where they dissociate cells of the corona radiata and digest the zona pellucida to enable the spermatozoon to enter the oocyte. This "acrosomal reaction" is one of the first steps in fertilization.

3. Acrosome phase:

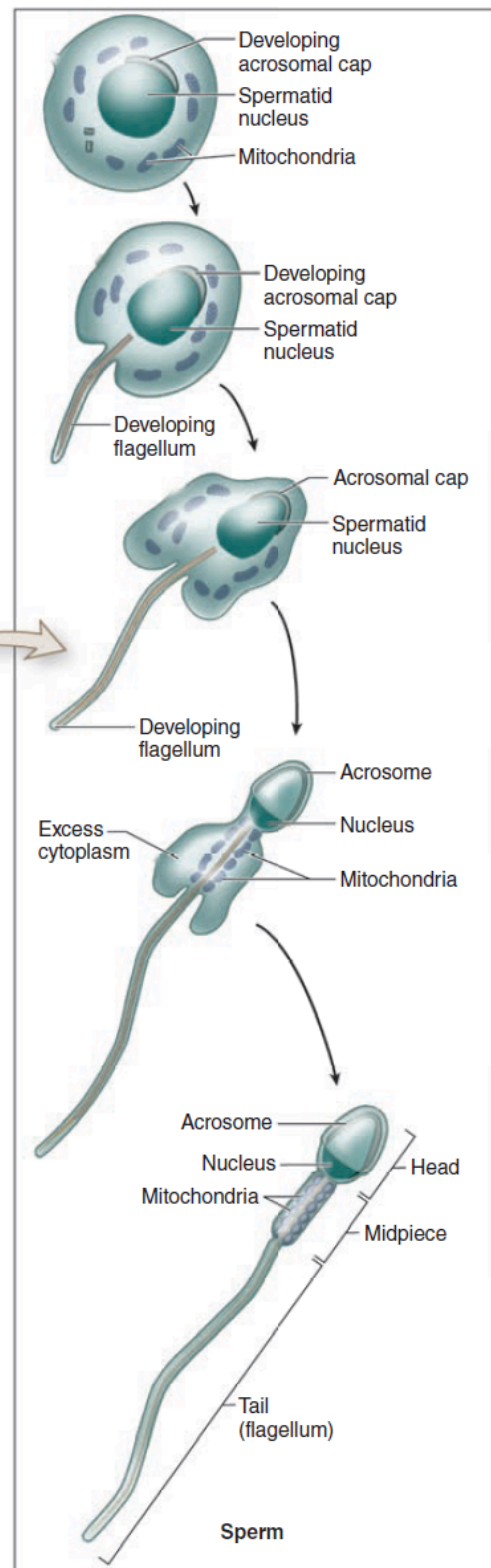
The head of the developing sperm, containing the acrosome and the condensing nucleus, remains embedded in the Sertoli cell while the

growing axoneme (future flagellum) extends into the lumen of the tubule. Nuclei become more elongated & very highly condensed, with the histones



(a) Spermatogenesis

- 1 The spermatogenic progenitor cells, called spermatogonia, are diploid cells containing 46 chromosomes (23 pairs). Mitotic divisions of these cells produce new spermatogonia and cells called primary spermatocytes which are committed to meiosis.
- 2 Each new primary spermatocyte transiently disassembles the tight junctions of the blood-testis barrier and moves from the tubule's basal compartment to the adluminal compartment. At the same time these cells replicate their DNA, enter meiosis I, and undergo synapsis. The first meiotic division produces two haploid secondary spermatocytes each with 23 chromosomes.
- 3 Meiosis II is rapid as chromatids in the secondary spermatocyte chromosomes separate into two smaller haploid cells, the spermatids.
- 4 Near the lumen but still embedded in Sertoli cells, the spermatids differentiate and undergo the morphological changes required to become motile and capable of fertilization.



(b) Spermiogenesis

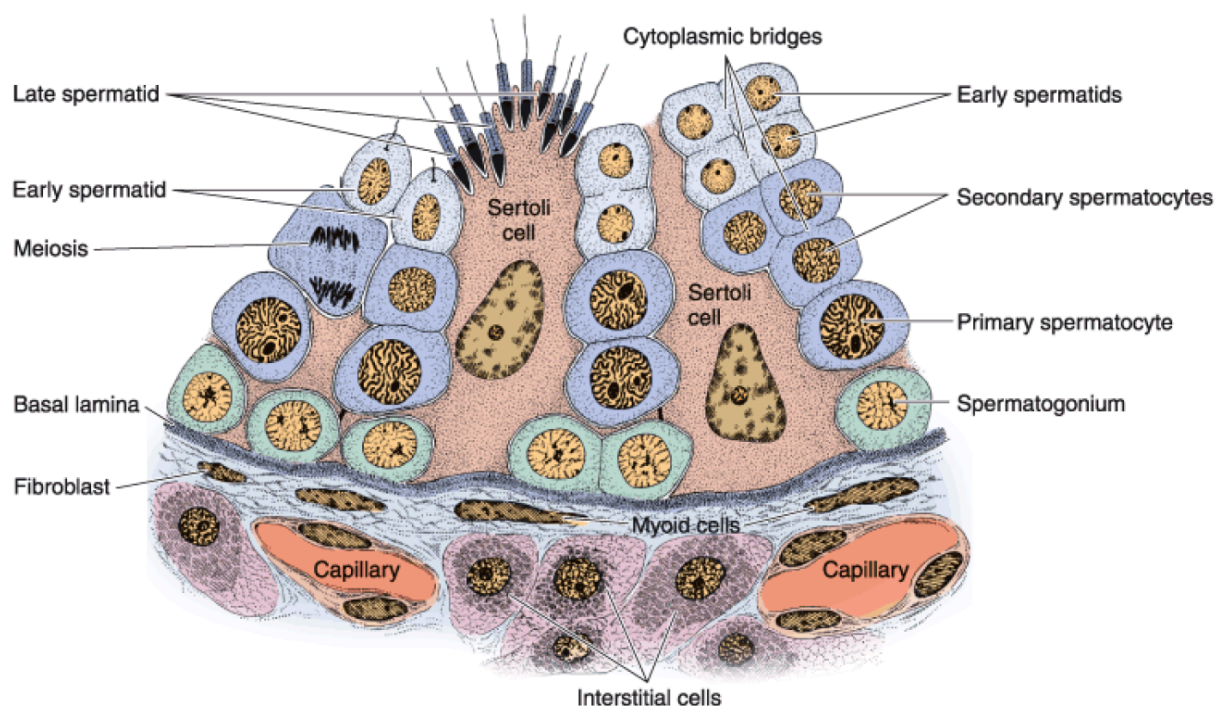
of nucleosomes replaced by small peptides called **protamines**. Flagellum growth continues distally in the tail and mitochondria aggregate around it proximally to form a thickened **middle piece** where the ATP for flagellar movements is generated. The cells are now called (late) spermatids.

4. Maturation phase:

In this phase of spermiogenesis, unneeded cytoplasm is shed as a residual body from each spermatozoon and remaining intercellular bridges are lost. Fully formed, but not yet functional or mobile, sperm are released into the lumen of the seminiferous tubule.

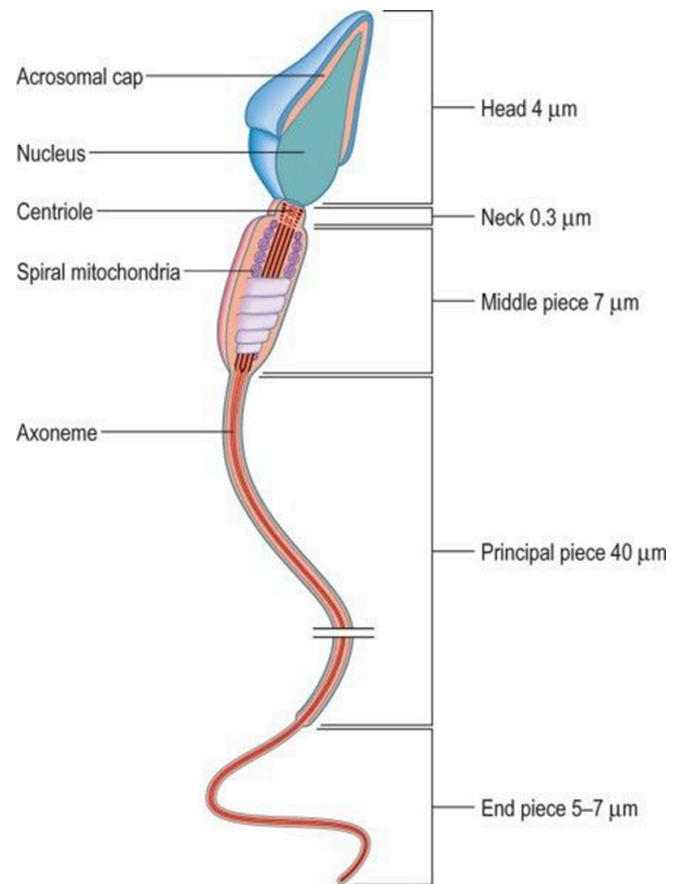
Sertoli Cells

The Sertoli cells are tall columnar epithelial cells, which surround, support, and nourish the spermatogenic cells. All cells of the spermatogenic cells are closely associated with the extended surfaces of Sertoli cells and depend on them for metabolic and physical support. Sertoli cells adhere to the basal lamina and their apical ends extend to the lumen. In routine preparations, the outlines of Sertoli cells surrounding the spermatogenic cells are very poorly defined. Each Sertoli cell supports 30-50 developing germ cells. Ultrastructurally Sertoli cells contain abundant SER, some rough ER, well-developed Golgi complexes, numerous mitochondria, and lysosomes. Their nuclei are typically ovoid or triangular, euchromatic, and have a prominent nucleolus.



Sertoli cells have tight occluding junctions between their basolateral membranes, which form (with other junctional structures) a **blood-testis barrier** within the seminiferous epithelium, dividing the seminiferous epithelium into basal compartment (below the barrier) & adluminal compartment (above the barrier). This is the tightest blood-tissue barrier in the body, it prevents autoimmune attacks against the spermatogenic cells, which first appear after the immune system is mature and central self-tolerance is well established.

Spermatogonia lie in the basal compartment of the tubule, being exposed to the vascularized interstitial tissue containing lymphocytes and other immune cells. Newly formed primary spermatocytes temporarily disassemble the BTB and move into the tubule's adluminal compartment while still adhering to Sertoli cells, after which the BTB reforms quickly. Like the spermatogonia, all spermatocytes and spermatids lie within invaginations of the Sertoli cells surfaces. Sertoli cells are also connected and coupled ionically by

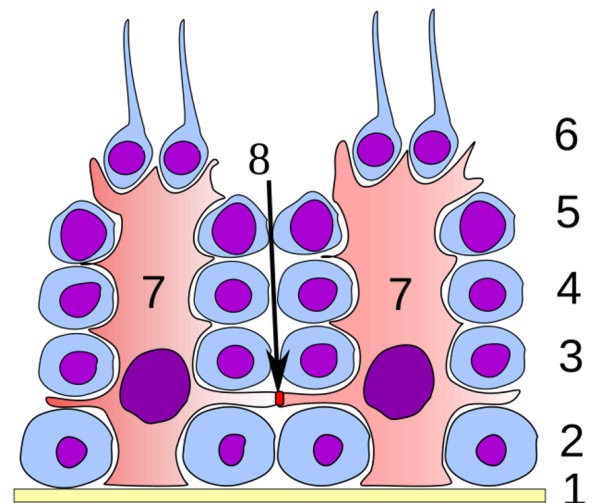


Blood-Testis Barrier

1. Basement membrane of seminiferous tubule
2. Spermatogonium
3. Primary spermatocyte
4. Secondary spermatocyte
5. Early spermatid
6. Late spermatid
7. Sertoli cell
8. Blood-testis barrier

• Adluminal compartment

• Basal compartment



gap junctions, which may help synchronize activities in the spermatogenic cells. The tails of late spermatids appear as tufts extending from the apical ends of the Sertoli cells into the lumen. Sertoli cells have 4 functions:

1. Support, protection, and nutrition of the spermatogenic cells:

Because spermatocytes, spermatids, and developing sperm are isolated from plasma proteins and nutrients by the blood-testis barrier, they depend on Sertoli cells for having nutrients & getting rid of metabolites.

2. Protecting spermatogenic cells from immune components:

By the effect of blood-testis barrier, Sertoli cells isolate the developing spermatogenic cells from the cells & antibodies of the immune system that may recognize those cells are foreign. Disruption of the BTB (due to trauma or surgery in the testis) can result in the formation of antisperm antibodies, which may negatively affect the sperm function.

3. Exocrine and endocrine secretion:

Sertoli cells continuously release into the seminiferous tubules water that carries new sperm out of the testis. Also, Sertoli cells produce nutrients and androgen-binding protein (ABP), which concentrates testosterone to a level required for spermiogenesis, under stimulation of follicle-stimulating hormone (FSH). As endocrine cells, they secrete inhibin, which feeds back on the anterior pituitary gland to suppress FSH synthesis and release. In the fetus, Sertoli cells also secrete a glycoprotein called müllerian-inhibiting substance (MIS) that causes regression of the embryonic müllerian (paramesonephric) ducts; in the absence of MIS, these ducts persist and become parts of the female reproductive tract.

4. Phagocytosis:

During spermiogenesis, excess cytoplasm shed as residual bodies is phagocytosed and digested by Sertoli cell lysosomes. No proteins from sperm normally pass back across the blood-testis barrier.

Interstitial Tissue

The interstitial tissue of the testis between the seminiferous tubules consists of sparse connective tissue containing fibroblasts, lymphatics, and blood vessels including fenestrated capillaries. During puberty interstitial cells, or **Leydig cells**, develop as large round or polygonal cells with

central nuclei and eosinophilic cytoplasm rich in small lipid droplets. These cells produce the steroid hormone testosterone, which promotes development of the secondary male sex characteristics. Testosterone is synthesized by enzymes present in the smooth ER and mitochondria similar to the system in adrenal cortical cells.

Testosterone secretion by interstitial cells is triggered by the pituitary gonadotropin, luteinizing hormone (LH). Testosterone synthesis thus begins at puberty, when the hypothalamus begins producing gonadotropin-releasing hormone that stimulates the pituitary secretion of gonadotropins (LH & FSH). In the embryonic testes (during the third and fourth months of pregnancy), gonadotropin from the placenta stimulates fetal interstitial cells to synthesize the testosterone needed for development of the male reproductive system. Then, these cells regress and become quiescent cells until puberty when they resume testosterone synthesis in response to the pituitary gonadotropin.

