Testes

The testes have two distinct functions: spermatogenesis and androgen production. Spermatogenesis occurs within distinct structures called **seminiferous tubules**. These tubules lie coiled within lobules whose ducts all exit the testis into the epididymis. Androgen production occurs within pockets of specialized cells that lie in the interstitium between the tubules.

The seminiferous tubules are surrounded by a basement membrane. Juxtaposed to the medial side of this basement membrane are the progenitor cells for sperm production. The epithelium containing the developing spermatozoa that line the tubules is known as the **seminiferous epithelium** or **germinal epithelium**. In a cross-section of the testis, spermatocytes within a given tubule are in varying stages of maturation. Mixed among the spermatocytes are **Sertoli cells**. These are the only nongerminal cells in the seminiferous epithelium. Sertoli cells were aptly called “nurse cells” when first described by Sertoli in 1865. They are responsible for the metabolic and structural support of the developing spermatozoa. All Sertoli cells make contact with the basement membrane at one pole and surround the developing spermatozoa at the other. Sertoli cells have large, complex cytoplasmic “fingers” that extend around many spermatozoa at one time.

A wide variety of substances that are normally present in the circulation are excluded from the fluid within the seminiferous tubule. This phenomenon is similar to that seen in the brain as the result of the blood–brain barrier. The male reproductive system displays its own **blood–testis barrier**. This barrier allows the testis to be one of very few immune-privileged sites in the human body. While the function of this barrier is incompletely described, its ultrastructural basis is known to be the tight junctions that form between adjacent Sertoli cells. The barriers created by these tight junctions divide the germinal epithelium into basal and luminal compartments. The basement compartment contains the spermatogonia and the adluminal compartment, the maturing germinal cells.

Spermatogenesis can be divided into three phases: (i) mitotic proliferation to produce large numbers of cells; (ii) meiotic division to produce genetic diversity; and (iii) maturation. The latter involves extensive cellular morphologic remodeling aimed at facilitating sperm transit to, and penetration of, the oocyte in the female tract. Primitive spermatogonial stem cells remain dormant in the testis until puberty.

At puberty, they are activated and maintained in rounds of mitoses at the basement membrane of the seminiferous tubule. From this reservoir of self-regenerating stem cells emerges several subtypes of spermatogonial clones until, after the final division, they exit mitosis as primary spermatocytes. Primary spermatocytes then undergo two meiotic cell divisions. These important divisions halve the number of chromosomes in the daughter cells. The first meiotic division produces secondary spermatocytes (II) and the second, early haploid spermatids. The spermatids then undergo remarkable cytoplasmic remodeling, during which a tail, mitochondrial midpiece and acrosome all develop. Almost all of the spermatid cytoplasm is expelled as residual bodies during this remodeling; only a small droplet of cytoplasm remains within the head of the mature spermatozoon. The surrounding Sertoli cells phagocytose the residual bodies, a process that may transmit information about the developing sperm cell to the Sertoli cell.

Development of the spermatozoa within the seminiferous epithelium is a complex and highly ordered sequence of events in most mammalian species. In humans, the process appears somewhat less orderly, but still follows the general principles found in other species.

In each, the number of mitotic divisions the spermatogonia undergo is fixed. In humans, four mitotic divisions occur. The length of time for an early spermatogonium to develop into a spermatozoon ready to enter the epididymis is also fixed and species-specific. In humans, it takes 64 ± 4 days for this process. As the spermatocytes move through the maturation process, they also move in waves toward the lumen of the seminiferous tubule.

The Sertoli cells enveloping the developing spermatozoa are homologs of the granulosa cells in the ovary. Sertoli cells phagocytose the extruded spermatid cytoplasm. They also function in aromatization of androgen precursors to estrogen, a product that exerts local feedback regulation on the androgen-producing (Leydig) cells. Sertoli cells also produce androgen-binding proteins.

Leydig cells perform the other major function of the testes – androgen production. The Leydig cells are homologous with the theca cells of the ovary. They produce large amounts of androgen from either circulating cholesterol or cholesterol made internally within their own smooth endoplasmic reticulum. Leydig cells are very large and, consistent with their intracellular activities, appear foamy by standard histologic assessment.

The most easily damaged cells in the testis are the spermatogonia. Irradiation, excessive alcohol intake, dietary deficiencies and local inflammation can rapidly induce degenerative changes in