CELLULAR BASIS OF SPERMATOGENESIS

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Spermatogenesis, the origin and development of the sperm cells within the male reproductive organs, the testes. The testes are composed of numerous thin tightly coiled tubules known as the seminiferous tubules; the sperm cells are produced within the walls of the tubules. Within the walls of the tubules, also, are many randomly scattered cells, called Sertoli cells, that function to support and nourish the immature sperm cells by giving them nutrients and blood products. As the young germ cells grow, the Sertoli cells help to transport them from the outer surface of the seminiferous tubule to the central channel of the tubule. Rounded immature sperm cells undergo successive mitotic and meiotic divisions (spermatocytogenesis) and a metamorphic change (spermiogenesis) to produce spermatozoa.

Mitosis and meiosis. Mitosis is the process of cell duplication - two daughter cells are formed with exactly the same DNA and chromosomal content of the original diploid (2N) mother cell. Human cells contain 46 chromosomes - 22 pairs of homologous autosomes and one pair of sex chromosomes.

During mitosis: chromosomes condense, the nuclear envelope disappears, and spindle fibers begin to form from microtubules (prophase); centromeres of duplicate sister chromatids align along the spindle equator (metaphase); chromatids separate and migrate toward opposite poles (anaphase); the mitotic apparatus is disassembled, autonomous nuclear envelopes are established, and the chromosomes uncoil (telophase). The final stage of the cell cycle, when cell division actually occurs, is called cytokinesis (C).

Meiosis is a special process of reductional cell division; it results in the formation of four gametes containing half (1N) the number of chromosomes found in somatic cells. Haploid gametes unite at fertilization to create a diploid zygote. Remember that in mammals the heterogametic male (XY) determines the sex of the embryo. Approximately one-half of spermatozoa contain either an X or Y chromosome (the sex chromosomal complement of mammalian females is XX, and therefore, ova can only contribute an X chromosome to the offspring). Genes carried on the X chromosome that inhibit spermatogenesis are inactivated in XY somatic cells.

Steps of meiosis

Meiosis differs from mitosis in two critical respects. During prophase of meiosis I, chromosomes pair along their length and come in contact in discrete areas of synapsis (chiasmata). Chromatids can exchange base pairs by crossing-over. The recombination of segments of chromosomes allows for continual generation of genetic variability (ie., rapid evolutionary progress) and provides a mechanism for correcting damage in the DNA helix. Secondly, nonidentical sister chromatids do not replicate between serial nuclear divisions. Meiosis II is essentially mitotic.

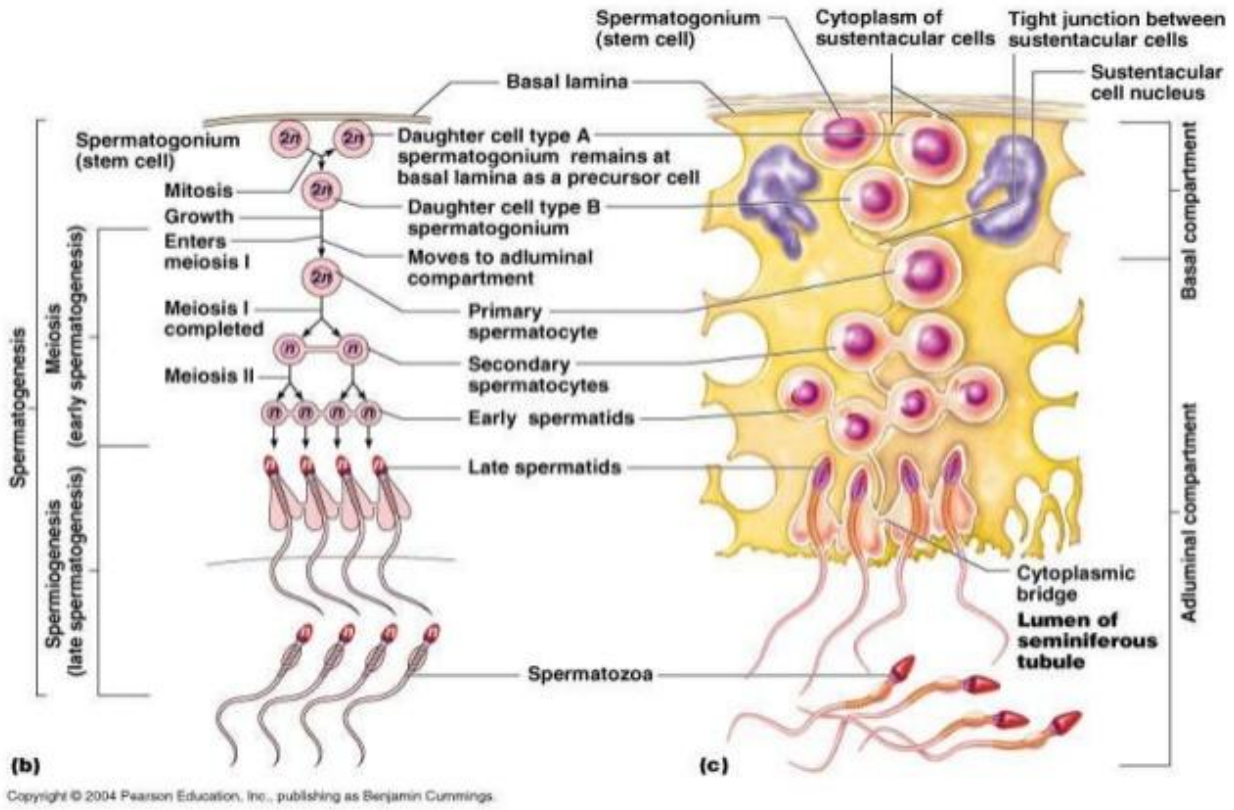

Fig: Spermatogenesis

Spermatocytogenesis. During spermatocytogenesis primitive cells called spermatogonia proliferate by mitosis. Several different types of spermatogonia have been identified (A-0 through A-4, intermediate [IN], and B). Only the discriminating anatomist can actually distinguish among types of spermatogonia. Mitosis ends when a B spermatogonium yields two primary spermatocytes.

The diploid number of primary spermatocytes is halved during meiosis. A primary spermatocyte is transformed into two secondary spermatocytes during meiosis I -

these cells then in turn are converted into (1N) spermatids during meiosis II. The second meiotic division is rapid (and therefore very few secondary spermatocytes can be identified in histological sections). Spermatocytes and spermatids tend to be larger than their ancestral spermatogonia.

Males have an almost unlimited capacity to produce germ cells; this is accomplished by replenishment of A spermatogonia early in mitosis. Although the mechanics of renewal are not totally understood, it appears that a stem cell (A-0) divides into an A-1 spermatogonia and an operative copy of itself. The A-1 cell becomes dedicated to spermatocytogenesis and the A-0 cell is kept in reserve for future divisions.

Endogenous damage to the the genetic material (eg., base deamination, depurination, methylation, oxidative insult) is inevitable in proliferative cells - a battery of repair mechanisms assure that the DNA fidelity of gametes is sustained.

Spermiogenesis. Throughout spermatocytogenesis cells retain a rounded configuration . Spermatids undergo a dramatic change in form during spermiogenesis - into the streamline spermatozoa adapted for fertilization. Spermiogenesis involves nuclear condensation, formation of the acrosomal cap, and development of a tail. The acrosome is derived from the Golgi apparatus. Centrioles (points of organization of spindle fibers) migrate to a postnuclear region after the completion of meiosis. The distal centriole provides a template for accretion of cytoskeletal elements comprising the contractile lattice of the tail. Mitochondria become concentrated into the sheath of the middle piece. Cells do not divide during spermiogenesis

Spermatogenic cycle and wave. If one closely examines serial cross-sections of a seminiferous tubule you will discover that sperm cells differentiate in distinctive associations. Each spermatogenic association has been classified as a stage of the seminiferous epithelial cycle. A spermatogenic cycle is defined as the time it takes for the reappearance of the same stage within a given segment of the tubule. Each stage of the cycle follows in an orderly sequence along the length of the tubule. The distance between the same stage is called the spermatogenic wave. One tubule can contain numerous complete waves. Adjacent segments of the tubule evidently communicate in some unknown manner.

The number of stages within a spermatogenic cycle and the number of cycles required for the completion of spermatogenesis varies between species. There are 12 different stages of the cycle in the bull of about 14 days each; approximately

four cycles within a given region of the tubule occur before an A1 spermatogonia is transformed into a spermatozoa. Six stages have been noted in man; four 16-day cycles are needed to complete spermatogenesis. The linear pattern of the spermatogenic cycle is less ordered in man than in farm animals or rodents.

Hormonal regulation. Spermatogonia continue to divide, but in reduced numbers, after hypophysectomy. Spermatocytogenesis is completely arrested at the primary spermatocyte stage in hypophysectomized animals; this step is restored by testosterone. Androgen-binding protein (the testicular counterpart of SHBG) sequesters testosterone within the seminiferous tubule (and caput epididymis). Meiosis II is hormonally-independent. Follicle-stimulating hormone participates in spermiogenesis. Estradiol and DHT are also involved in the spermatogenic process.

Hormonal effects on sperm cells are not direct, but are mediated through Sertoli cells. Biochemical and biophysical facets of sperm-Sertoli interactions in spermatogenesis are largely unknown. Rate of production of spermatozoa is not influenced by endocrine therapy.

Effect of temperature. Sperm cells will not mature at core body temperature in most mammals (spermatogenic DNA polymerase b and recombinase activities exhibit unique temperature optima); to adapt, the testes assume an external position. Testicular descent from the abdomen normally transpires during fetal or neonatal life.

Testicular descent is permanent in many mammals (eg., domesticated animals and primates). Sometimes high ambient temperatures are associated with infertility. A transient condition of "summer sterility" is common in rams. In other species (eg., rodents) the inguinal canals remain patent, and the testes periodically descend or retract; this activity is coordinated in the wild with the mating season. The testes of hibernating mammals often descend when body temperature begins to rise after awakening. A few mammals do not have scrotal sacs (eg., monotremes, armadillos, sloths, elephants, rhinoceroses, seals, dolphins, and whales) and the testes remain within the abdomen.; these animals have a low body temperature. Notwithstanding, the internal testes of birds produce viable gametes in spite of very high abdominal body temperatures. From an evolutionary perspective it is difficult to reconcile the hazardous location of pendulous testes.

Spermiation. Spermiation is the process by which spermatozoa are released from the seminiferous epithelium into the lumen of the tubule. Most of the "excess baggage" (cytoplasm and organelles) of the spermatid is discarded within the seminiferous epithelium in the form of a residual body. A small amount of cytoplasmic material, the cytoplasmic droplet, remains attached within the neck region or around the middle piece as the spermatozoon makes its way into the epididymis.

Further maturations. Seminiferous spermatozoa lack motility and fertilizing capacity. During transit through the epididymis, which takes approximately two weeks, the cytoplasmic droplet migrates distally along the tail of the spermatozoon and falls off; this event is correlated with an increase in cellular motility (normal motility and morphology of an ejaculate should be > 60-70%). Nevertheless, in some species the full fertilizing potential of spermatozoa is not gained until cells are affected by secretions of the female reproductive tract; these spermatozoa are said to be "capacitated."