

Gametogenesis

THE CHROMOSOME THEORY OF INHERITANCE

Traits of a new individual are determined by specific genes on chromosomes inherited from the father and the mother. Humans have approximately 23,000 genes on 46 chromosomes. Genes on the same chromosome tend to be inherited together and so are known as **linked genes**. In somatic cells, chromosomes appear as 23 **homologous** pairs to form the **diploid** number of 46. There are 22 pairs of matching chromosomes, the **autosomes**, and one pair of **sex chromosomes**. If the sex pair is XX, the individual is genetically female; if the pair is XY, the individual is genetically male. One chromosome of each pair is derived from the maternal gamete, the **oocyte**, and one from the paternal gamete, the **sperm**. Thus, each gamete contains a **haploid** number of 23 chromosomes, and the union of the gametes at **fertilization** restores the diploid number of 46.

SEXUAL REPRODUCTION

Sexual reproduction occurs when female and male gametes (oocyte and spermatozoon, respectively) unite at fertilization. Gametes are direct descendants of **primordial germ cells**, which are first observed in **the wall of the yolk sac** at week 4 of embryonic development and subsequently migrate into the future gonad region. Gametes are produced by **gametogenesis** (called **oogenesis** in the female and **spermatogenesis** in the male). Gametogenesis employs a specialized process of cell division, **meiosis**, which uniquely distributes chromosomes among gametes.

Gametogenesis:

It is mean the Conversion of Germ Cells Into Male and Female Gametes. Gametes are derived from primordial germ cells that are formed in the epiblast during the second week and that move to the wall of the yolk sac . During the fourth week these cells begin to migrate from the yolk sac toward the developing gonads, where they arrive by the end of the fifth week. Mitotic divisions increase their number during their migration and also when they arrive in the gonad. In preparation for fertilization, germ cells undergo gametogenesis, which includes meiosis, to reduce the number of chromosomes and cytodifferentiation to complete their maturation.

Mitosis

Mitosis is the process whereby one cell divides, giving rise to two daughter cells that are genetically identical to the parent cell. Each daughter cell receives the complete complement of 46 chromosomes. Before a cell enters mitosis, each chromosome replicates its deoxyribonucleic acid (DNA). During this replication phase

the chromosomes are extremely long, they are spread diffusely through the nucleus, and they cannot be recognized with the light microscope. With the onset of mitosis the chromosomes begin to coil, contract, and condense; these events mark the beginning of prophase. Each chromosome now consists of two parallel subunits, chromatids, that are joined at a narrow region common to both called the centromere. Throughout prophase the chromosomes continue to condense, shorten, and thicken, but only at prometaphase do the chromatids become distinguishable. During metaphase the chromosomes line up in the equatorial plane, and their doubled structure is clearly visible. Each is attached by microtubules extending from the centromere to the centriole, forming the mitotic spindle. Soon the centromere of each chromosome divides, marking the beginning of anaphase, followed by migration of chromatids to opposite poles of the spindle. Finally, during telophase, chromosomes uncoil and lengthen, the nuclear envelope reforms, and the cytoplasm divides. Each daughter cell receives half of all doubled chromosome material and thus maintains the same number of chromosomes as the mother cell.

Meiosis

Meiosis is the cell division that takes place in the germ cells to generate male and female gametes, sperm and egg cells, respectively. Meiosis requires two cell divisions, meiosis I and meiosis II, to reduce the number of chromosomes to the haploid number of 23. As in mitosis, male and female germ cells (spermatocytes and primary oocytes) at the beginning of meiosis I replicate their DNA so that each of the 46 chromosomes is duplicated into sister chromatids.

In contrast to mitosis, however, homologous chromosomes then align themselves in pairs, a process called synapsis. The pairing is exact and point for point except for the XY combination. Homologous pairs then separate into two daughter cells. Shortly thereafter meiosis II separates sister chromatids. Each gamete then contains 23 chromosomes. Crossover

Crossovers, critical events in meiosis I, are the interchange of chromatid segments between paired homologous chromosomes. Segments of chromatids break and are exchanged as homologous chromosomes separate.

As separation occurs, points of interchange are temporarily united and form an X-like structure, a chiasma. The approximately 30 to 40 crossovers (one or two per chromosome) with each meiotic I division are most frequent between genes that are far apart on a chromosome.

As a result of meiotic divisions,

(1) genetic variability is enhanced through crossover, which redistributes genetic material, and through random distribution of homologous chromosomes to the daughter cells.

(2) each germ cell contains a haploid number of chromosomes, so that at fertilization the diploid number of 46 is restored.

Polar Bodies

Also during meiosis one primary oocyte gives rise to four daughter cells, each with 22 plus 1 X chromosomes. However, only one of these develops into a mature gamete, the oocyte; the other three, the polar bodies, receive little cytoplasm and degenerate during subsequent development. Similarly, one primary spermatocyte gives rise to four daughter cells, two with 22 plus 1 X chromosomes and two with 22 plus 1 Y chromosomes .

Oogenesis

Maturation of Oocytes Begins Before Birth; Once primordial germ cells have arrived in the gonad of a genetic female, they differentiate into oogonia. These cells undergo a number of mitotic divisions and, by the end of the third month, are arranged in clusters surrounded by a layer of flat epithelial cells . Whereas all of the oogonia in one cluster are probably derived from a single cell, the flat epithelial cells, known as follicular cells, originate from surface epithelium covering the ovary.

The majority of oogonia continue to divide by mitosis, but some of them arrest their cell division in prophase of meiosis I and form primary oocytes. During the next few months, oogonia increase rapidly in number, and by the fifth month of prenatal development, the total number of germ cells in the ovary reaches its maximum, estimated at 7 million. At this time, cell death begins, and many oogonia as well as primary oocytes become atretic. By the seventh month, the majority of oogonia have degenerated except for a few near the surface. All surviving primary oocytes have entered prophase of meiosis I, and most of them are individually surrounded by a layer of flat epithelial cells . A primary oocyte, together with its surrounding flat epithelial cells, is known as a primordial follicle.

Maturation of Oocytes Continues at Puberty; Near the time of birth, all primary oocytes have started prophase of meiosis I, but instead of proceeding into metaphase, they enter the diplotene stage, a resting stage during prophase that is characterized by a lacy network of chromatin. Primary oocytes remain in prophase and do not finish their first meiotic division before puberty is reached, apparently because of oocyte maturation inhibitor (OMI), a substance secreted by follicular cells. The total number of primary oocytes at birth is estimated to vary from 700,000 to 2 million. During childhood most oocytes become atretic; only approximately 400,000 are present by the beginning of puberty, and fewer than 500 will be ovulated. Some oocytes that reach maturity late in life have been dormant in the diplotene stage of the first meiotic division for 40 years or more before ovulation. Whether the diplotene stage is the most suitable phase to protect the oocyte against environmental influences is unknown. The

fact that the risk of having children with chromosomal abnormalities increases with maternal age indicates that primary oocytes are vulnerable to damage as they age.

At puberty, a pool of growing follicles is established and continuously maintained from the supply of primordial follicles. Each month, 15 to 20 follicles selected from this pool begin to mature, passing through three stages:

1- primary or preantral

2- secondary or antral, also called vesicular or Graafian

3-preovulatory.

The antral stage is the longest, whereas the preovulatory stage encompasses approximately 37 hours before ovulation. As the primary oocyte begins to grow, surrounding follicular cells change from flat to cuboidal and proliferate to produce a stratified epithelium of granulosa cells, and the unit is called a primary follicle. Granulosa cells rest on a basement membrane separating them from surrounding stromal cells that form the theca folliculi. Also, granulosa cells and the oocyte secrete a layer of glycoproteins on the surface of the oocyte, forming the zona pellucida. As follicles continue to grow, cells of the theca folliculi organize into an inner layer of secretory cells, the theca interna, and an outer fibrous capsule, the theca externa. Also, small, finger-like processes of the follicular cells extend across the zona pellucida and interdigitate with microvilli of the plasma membrane of the oocyte.

As development continues, fluid-filled spaces appear between granulosa cells. Coalescence of these spaces forms the antrum, and the follicle is termed a secondary (vesicular, Graafian) follicle. Initially, the antrum is crescent shaped, but with time, it enlarges. Granulosa cells surrounding the oocyte remain intact and form the cumulus oophorus. At maturity, the secondary follicle may be 25 mm or more in diameter. It is surrounded by the theca interna, which is composed of cells having characteristics of steroid secretion, rich in blood vessels, and the theca externa, which gradually merges with the ovarian stroma.

With each ovarian cycle, a number of follicles begin to develop, but usually only one reaches full maturity. The others degenerate and become atretic. When the secondary follicle is mature, a surge in luteinizing hormone (LH) induces the preovulatory growth phase. Meiosis I is completed, resulting in formation of two daughter cells of unequal size, each with 23 doublestructured chromosomes. One cell, the secondary oocyte, receives most of the cytoplasm; the other, the first polar body, receives practically none. The first polar body lies between the zona pellucida and the cell membrane of the secondary oocyte in the perivitelline space. The cell then enters meiosis II but arrests in metaphase approximately 3 hours before ovulation. Meiosis II is completed only if the oocyte is fertilized; otherwise, the cell degenerates approximately 24 hours after ovulation. The first polar body also undergoes a second division.

Spermatogenesis

Maturation of Sperm Begins at Puberty. Spermatogenesis, which begins at puberty, includes all of the events by which spermatogonia are transformed into spermatozoa. At birth, germ cells in the male can be recognized in the sex cords of the testis as large, pale cells surrounded by supporting cells. Supporting cells, which are derived from the surface epithelium of the gland in the same manner as follicular cells, become sustentacular cells, or Sertoli cells. Shortly before puberty, the sex cords acquire a lumen and become the seminiferous tubules. At about the same time, primordial germ cells give rise to spermatogonial stem cells. At regular intervals, cells emerge from this stem cell population to form type A spermatogonia, and their production marks the initiation of spermatogenesis.

Type A cells undergo a limited number of mitotic divisions to form a clone of cells. The last cell division produces type B spermatogonia, which then divide to form primary spermatocytes. Primary spermatocytes then enter a prolonged prophase (22 days) followed by rapid completion of meiosis I and formation of secondary spermatocytes. During the second meiotic division, these cells immediately begin to form haploid spermatids. Throughout this series of events, from the time type A cells leave the stem cell population to formation of spermatids, cytokinesis is incomplete, so that successive cell generations are joined by cytoplasmic bridges. Thus, the progeny of a single type A spermatogonium form a clone of germ cells that maintain contact throughout differentiation. Furthermore, spermatogonia and spermatids remain embedded in deep recesses of Sertoli cells throughout their development. In this manner, Sertoli cells support and protect the germ cells, participate in their nutrition, and assist in the release of mature spermatozoa.

Spermatogenesis is regulated by luteinizing hormone (LH) production by the pituitary. LH binds to receptors on Leydig cells and stimulates testosterone production, which in turn binds to Sertoli cells to promote spermatogenesis. Follicle stimulating hormone (FSH) is also essential because its binding to Sertoli cells stimulates testicular fluid production and synthesis of intracellular androgen receptor proteins.

Spermiogenesis

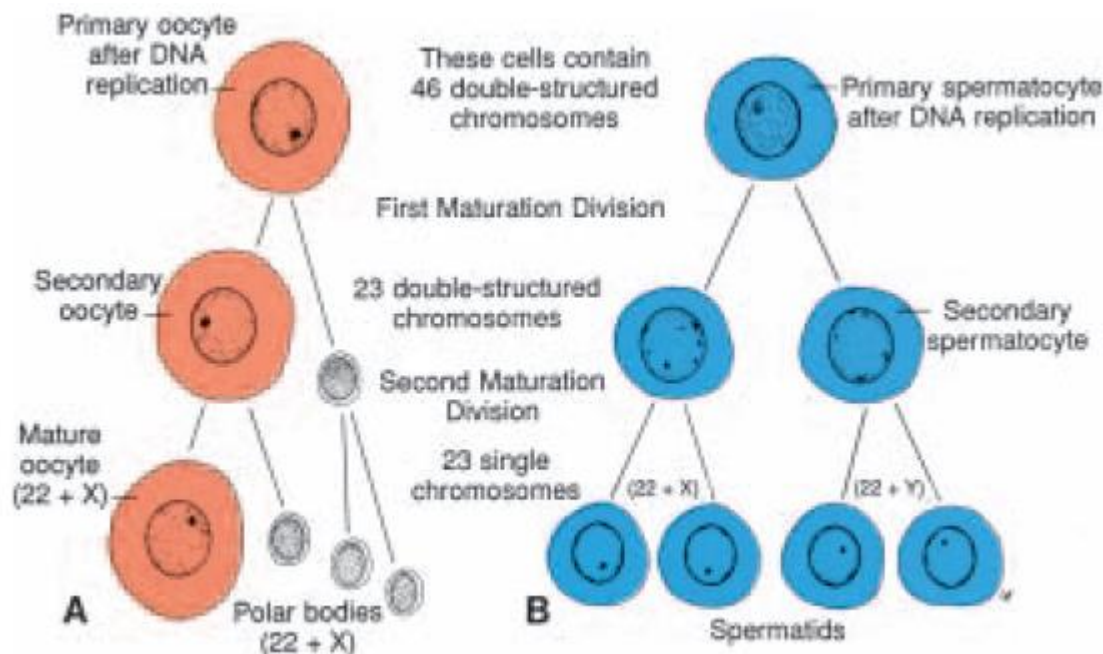
The series of changes resulting in the transformation of spermatids into spermatozoa is spermiogenesis. These changes include:

- 1- formation of the acrosome, which covers half of the nuclear surface and contains enzymes to assist in penetration of the egg and its surrounding layers during fertilization
- 2- condensation of the nucleus
- 3-formation of neck, middle piece, and tail

4- shedding of most of the cytoplasm.

In humans, the time required for a spermatogonium to develop into a mature spermatozoon is approximately 64 days.

When fully formed, spermatozoa enter the lumen of seminiferous tubules. From there, they are pushed toward the epididymis by contractile elements in the wall of the seminiferous tubules. Although initially only slightly motile, spermatozoa obtain full motility in the epididymis.



Events occurring during the first and second maturation divisions. A. The primitive female germ cell (primary oocyte) produces only one mature gamete, the mature oocyte. B. The primitive male germ cell (primary spermatocyte) produces four spermatids, all of which develop into spermatozoa.

