Meiosis in Humans [1]

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Meiosis, the process by which sexually reproducing organisms generate gametes (sex cells), is an essential precondition for the normal formation of the embryo. As sexually-reproducing, diploid, multicellular eukaryotes, humans [5] rely on meiosis [6] to serve a number of important functions, including the promotion of genetic diversity and the creation of proper conditions for reproductive success. However, the primary function of meiosis [6] is the reduction [7] of the ploidy [8] (number of chromosomes) of the gametes from diploid (2n, or two sets of 23 chromosomes) to haploid (1n or one set of 23 chromosomes). While parts of meiosis [6] are similar to mitotic processes, the two systems of cellular division produce distinctly different outcomes. Problems during meiosis [6] can stop embryonic development and sometimes cause spontaneous miscarriages, genetic errors, and birth defects [9] such as Down syndrome [10].

The process of meiosis [6] was first described in the mid-1870s by Oscar Hertwig, who observed it while working with sea urchin [11] eggs. Edouard Van Beneden expanded upon Hertwig’s descriptions, adding his observations about the movements of the individual chromosomes within the germ cells [12]. However, it wasn’t until August Weismann’s work in 1890 that the role that meiosis [6] played was recognized and understood as essential. Some twenty years later, in 1911, Thomas Hunt Morgan [13] examined meiosis [6] in Drosophila [14], which enabled him to present evidence of the crossing over of the chromosomes.

Both males and females use meiosis [6] to produce their gametes, although there are some key differences between the sexes at certain stages. In females, the process of meiosis [6] is called oogenesis, since it produces oocytes and ultimately yields mature ova(eggs). The male counterpart is spermatogenesis, the production of sperm [15]. While they occur at different times and different locations depending on the sex, both processes begin meiosis [6] in essentially the same way.

Meiosis occurs in the primordial germ cells [12], cells specified for sexual reproduction and separate from the body’s normal somatic cells. In preparation for meiosis [6], a germ cell goes through interphase, during which the entire cell (including the genetic material contained in the nucleus [16]) undergoes replication. In order to undergo replication during interphase, the DNA (deoxyribonucleic acid, the carrier of genetic information and developmental instructions) is unraveled in the form of chromatin [17]. While replicating somatic cells follow interphase with mitosis [18], germ cells [12] instead undergo meiosis [6]. For clarity, the process is artificially divided into stages and steps; in reality, it is continuous and the steps generally overlap at transitions.

The two-stage process of meiosis [6] begins with meiosis [6] I, also known as reduction [7] division since it reduces the diploid number of chromosomes in each daughter cell by half. This first step is further subdivided into four main stages: prophase I, metaphase I, anaphase I, and telophase I. Each stage is identified by the major characteristic events in its span which allow the dividing cell to progress toward the completion of meiosis [6]. Prophase I takes up the greatest amount of time, especially in oogenesis. The dividing cell may spend more than 90 percent of meiosis [6] in Prophase I. Because this particular step includes so many events, it is further subdivided into six substages, the first of which is leptotene. During leptotene, the diffuse chromatin [17] starts condensing into chromosomes. Each of these chromosomes is double stranded, consisting of two identical sister chromatids which are held together by a centromere; this arrangement will later give each chromosome a variation on an X-like shape, depending on the positioning of the centromere. Leptotene is also the point at which each chromosome begins to “search” for its homologue (the other chromosome of the same shape and size that contains the same genetic material).

In the next stage, zygonema, there is further condensation of the chromosomes. The homologous chromosomes (matching chromosomes, one from each set) “find” each other and align in a process called rough pairing. As they come into closer contact, a protein compound called the synaptonemal complex forms between each pair of double-stranded chromosomes.

As Prophase I continues into its next substage, pachynema, the homologous chromosomes move even closer to each other as the synaptonemal complex becomes more intricate and developed. This process is called synopsis, and the synapsed chromosomes are called a tetrad. The tetrad is composed of four chromatids which make up the two homologous chromosomes. During pachynema and the next substage, diplonema, certain regions of synapsed chromosomes often become closely associated and swap corresponding segments of the DNA in a process known as chiasma. At this point, while still associated at the chiasmata, the sister chromatids start to part from each other (although they are still firmly bound at the centromere; this creates the X-shape commonly associated with condensed chromosomes).

The nuclear membrane starts to dissolve by the end of diplonema and the chromosomes complete their condensation in preparation for the last substage of prophase I, diakinesis. During this part, the chiasmata terminalize (move toward the ends of their respective chromatids) and drift further apart, with each chromatid now bearing some newly-acquired genetic material as the result of crossing over. Simultaneously, the centrioles, pairs of cylindrical microtubular organelles, move to opposite poles and the region containing them becomes the source for spindle fibers. These spindle fibers anchor onto the kinetochores, a
macromolecule that regulates the interaction between them and the chromosome during the next stages of meiosis \(^6\). The kinetochores are attached to the centromere of each chromosome and help move the chromosomes to position along a three-dimensional plane at the middle of the cell, called the metaphase plate. The cell now prepares for metaphase I, the next step after prophase I.

During metaphase I, the tetrads finish aligning along the metaphase plate, although the orientation of the chromosomes making them up is random. The chromosomes have fully condensed by the point and are firmly associated with the spindle fibers in preparation for the next step, anaphase I. During this third stage of meiosis \(^6\) I, the tetrads are pulled apart by the spindle fibers, each half becoming a dyad (in effect, a chromosome or two sister chromatids attached at the centromere). Assuming that nondisjunction (failure of chromosomes to separate) does not occur, half of the chromosomes in the cell will be maneuvered to one pole while the rest will be pulled to the opposite pole. This migration of the chromosomes is followed by the final (and brief) step of meiosis \(^6\) I, telophase I, which, coupled with cytokinesis (physical separation of the entire mother cell), produces two daughter cells. Each of these daughter cells contains 23 dyads, which sum up to 46 monads or single-stranded chromosomes.

Meiosis II follows with no further replication of the genetic material. The chromosomes briefly unravel at the end of meiosis \(^6\) I, and at the beginning of meiosis \(^6\) II they must reform into chromosomes in their newly-created cells. This brief prophase II stage (isEmbeddedin) is followed by metaphase II, during which the chromosomes migrate toward the metaphase plate. During anaphase II, the spindle fibers again pull the chromosomes apart to opposite poles of the cell; however, this time it is the sister chromatids that are being split apart, instead of the pairs of homologous chromosomes as in the first meiotic step. A second round of telophase (this time called telophase II) and cytokinesis splits each daughter cell further into two new cells. Each of these cells has 23 single-stranded chromosomes, making each cell haploid (possessing 1N chromosomes).

As mentioned, sperm \(^{15}\) and egg \(^{19}\) cells follow roughly the same pattern during meiosis \(^6\), albeit a number of important differences. Spermatogenesis follows the pattern of meiosis \(^6\) more closely than oogenesis, primarily because once it begins (human males start producing sperm \(^{15}\) at the onset of puberty in their early teens), it is a continuous process that produces four gametes per spermatocyte (the male germ cell that enters meiosis \(^6\)). Excluding mutation and mistakes, these sperm \(^{15}\) are identical except for their individual, unique genetic load. They each contain the same amount of cytoplasm and are propelled by whip-like flagella.

In females, oogenesis and meiosis \(^6\) begin while the individual is still in the womb \(^{20}\). The primary oocytes, analogous to the spermatocytes in the male, undergo meiosis \(^6\) I up to diplonema in the womb \(^{20}\), and then their progress is arrested. Once the female reaches puberty, small clutches of these arrested oocytes will proceed up to metaphase II and await fertilization \(^{21}\) so that they may complete the entire meiotic process; however, one oocyte \(^{22}\) will only produce one egg \(^{19}\) instead of four like the sperm \(^{15}\). This can be explained by the placement of the metaphase plate in the dividing female germ cell. Instead of lying across the middle of the cell like in spermatogenesis, the metaphase plate is tucked in the margin of the dividing cell, although equal distribution of the genetic material still occurs. This results in a grossly unequal distribution of the cytoplasm and associated organelles once the cell undergoes cytokinesis. This first division produces a large cell and a small cell. The large cell, the secondary oocyte \(^{22}\), contains the vast majority of the cytoplasm of the parent cell, and holds half of the genetic material of that cell as well. The small cell, called the first polar body, contains almost no cytoplasm, but still sequesters the other half of the genetic material. This process repeats in meiosis \(^6\) II, giving rise to the egg \(^{18}\) and to an additional polar body.

These differences in meiosis \(^6\) reflect the roles of each of the sex cells. Sperm must be agile and highly motile in order to have the opportunity to fertilize the egg—and this is their sole purpose. For this reason, they hardly carry any cellular organelles (excluding packs of mitochondria which fuel their rapid motion), mostly just DNA. The egg \(^{18}\), on the other hand, is “in charge” of providing the necessary structures and environment for supporting cell division once it is fertilized. For this reason, only a single, well-fortified egg \(^{19}\) is produced by each round of meiosis \(^6\).

Meiosis is a process that is conserved, in one form or another, across all sexually-reproducing organisms. This means that the process appears to drive reproductive abilities in a variety of organisms and points to the common evolutionary pathway for those organisms that reproduce sexually. It is vitally important for the maintenance of genetic integrity and enhancement of diversity. Since humans \(^5\) are diploid (2N) organisms, failure to halve the ploidy \(^8\) before fertilization \(^{21}\) can have disastrous effects. For this reason, only very select types of abnormal ploidy \(^8\) survive (and do so with noticeable defects); most combinations containing abnormal ploidy \(^8\) never make it into the world. The correct reduction \(^7\) of the number of chromosomes insures that once fertilization \(^{21}\) takes place, the correct amount of genetic material is established in the fertilized egg \(^{23}\) and, eventually, in the person resulting from it.

**Sources**

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