

Lecture 3: Cell cycle. Cell division

1. Cell reproduction
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The ability of organisms to reproduce their kind is the one characteristic that best distinguishes living things from non-living matter.

In 1855, **Rudolf Virchow** (1821-1902), a German physician, founder of cellular pathology and one of authors of Cell Theory, put it into words: "Where a cell exists, there must have been a preexisting cell, just as the animal arises only from an animal and the plant only from plant". He summarized with the Latin axiom: *Ômnis cellula e cellula*.

The continuity of life is based on the reproduction of cell, or cell division.

Reproduction results in the creation of new individuals, or offspring, from either one or two parent organisms.

Unicellular organisms such as *Amoeba* divide to form duplicate offspring; division of one cell reproduces an entire organism. Unicellular organisms are reproduced by **cell division**. Cell division enables sexually reproduced organisms to develop from a single cell . the fertilized egg, or zygote. And after an organism is fully grown, cell division continues to function in renewal and repair, replacing cells that die from normal wear and tear or accidents.

So, functions of cell division are:

1. *Reproduction.*
2. *Growth and development.*
3. *Renewal and repair.*

Offspring can either be genetically identical to the parent, as is the case in asexual reproduction, or vary genetically from their parents, as is the case in sexual reproduction. In both cases, genetic material is passed on from one generation to the next. Asexual reproduction is very common in microorganisms (bacteria). Sexual reproduction occurs only in eukaryotes.

Prokaryotes (bacteria) reproduce by a type of cell division called binary fission, meaning division in half.

The prokaryotic chromosome is a single DNA molecule that first replicates, then attaches each copy to a different part of the cell membrane. When the cell begins to pull apart, the replicate and original chromosomes are separated. Following cell splitting (cytokinesis), there are then two cells of identical genetic composition (except for the rare chance of a spontaneous mutation).

Genetic identity of all microorganisms in a colony is one of conditions of use of antibiotics in medicine. When treating a bacterial disease, a drug that kills one bacteria (of a specific type) will also kill all other members of that clone (colony) it comes in contact with.

Eukaryotic chromosomes occur in the cell in greater numbers than prokaryotic chromosomes. Due to increased numbers of chromosomes, organelles and complexity, **eukaryote cell** division is more complicated, although the same processes of replication, segregation, and cytokinesis still occur.

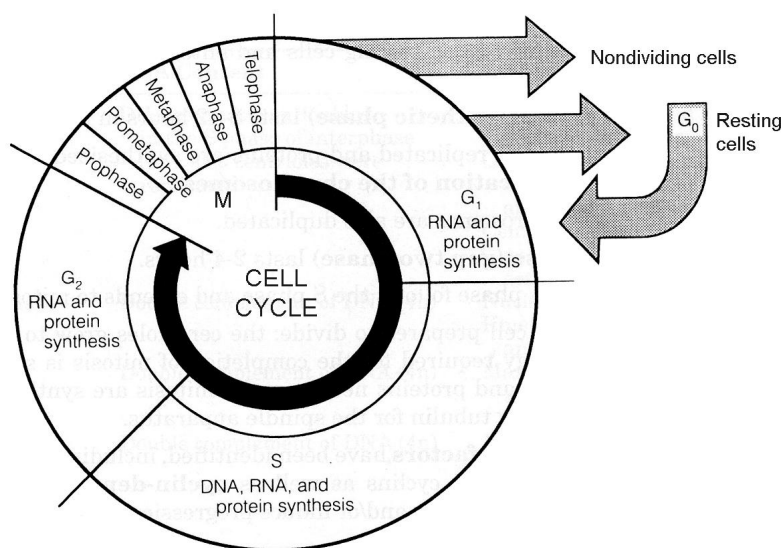
Despite differences between prokaryotes and eukaryotes, there are several common features in their cell division processes:

1. *Replication of the DNA must occur.*
2. *Segregation of the "original" and its "replica" follow.*
3. *Cytokinesis ends the cell division process.*

Cell cycle . an ordered sequence of events in the life of a eukaryotic cell, from its origin in the division of a parent cell until its own division into two.

Cell Division distributes identical sets of chromosomes

A cell's endowment of DNA, its genetic information, is called its *genome*. Although a prokaryotic genome is often a single long DNA molecule, eukaryotic genomes usually consist of a number of DNA



molecules. Yet before the cell can divide, all of this DNA must be copied and then the two copies separated so that each daughter cell ends up with a complete genome.

The replication and distribution of so much DNA is manageable because the DNA molecules are packaged into chromosomes. DNA-protein complex, called chromatin, is organized into a long, thin fiber. After a cell duplicates its DNA in preparation for division, the chromatin condenses, making the chromosomes visible in light microscope. Every eukaryotic species has a characteristic number of chromosomes in each cell nucleus. For example, the nuclei of human **somatic cells** (all body

cells except for reproductive cells) each contain 46 chromosomes. Reproductive cells, or gametes . sperm cells and egg cells . have half as many chromosomes as somatic cells, or 23 chromosomes in humans. Set of chromosomes in somatic cells is diploid ($2n$). Set of chromosomes in sex cells is haploid (n).

A eukaryotic cell preparing to divide duplicates each of chromosomes. A duplicated chromosome consists of two *sister chromatids*, which narrow at their centromeres. The DNA molecules of the sister chromatids are identical. The chromatids separate during cell division (*mitosis*), becoming the chromosome of the new daughter cells.

Eukaryotic cell division consists of:

1. **Mitosis** (division of the nucleus)
2. **Cytokinesis** (division of the cytoplasm)

Commonly the two processes of cell division are confused. Mitosis deals only with the segregation of the chromosomes and organelles into daughter cells. Mitosis is just one part of the cell cycle. Mitotic cell division alternates with a much longer interphase, which often accounts for 90% of cell cycle. It is during interphase that the cell grows and copies its chromosomes in preparation for cell division.

Interphase . interval between cell divisions.

- is considerably longer than the **M** (mitosis) phase
- is the period during which **the cell doubles in size and DNA content**.
- Interphase is divided into three separate phases (G_1 , S, and G_2),

G_1 phase (gap one phase) lasts from hours to several days.

Occurring after mitosis, it is the period during which the cell grows and proteins are synthesized, thus restoring the daughter cells to normal volume and size.

S phase (synthetic phase) lasts 8-12 hours in most cells.

DNA is replicated and proteins are synthesized, resulting in **duplication of the chromosomes**.

Animal cells (except for a group of worms known as nematodes) have a centrosome which is composed of two centrioles. Plants and most other eukaryotic organisms lack centrioles. Prokaryotes, of course, lack spindles and centrioles; the cell membrane assumes this function when it pulls the by-then replicated chromosomes apart during binary fission. Centrioles are also duplicated.

G_2 phase (gap two phase) lasts 2-4 hours.

The cell prepares to divide: the centrioles grow to maturity; energy required for the completion of mitosis is stored; and RNA and proteins necessary for mitosis are synthesized, including *tubulin* protein for the microtubules of spindle apparatus.

Mitosis lasts 1-3 hours. Mitosis is the process of forming (generally) genetically identical daughter cells by replicating and dividing the original chromosomes, in effect making a cellular xerox.

Structure and main features of a spindle apparatus

The condensed replicated chromosomes have several points of interest. The area where both sister chromatids are in contact with each other is known as the **centromere**; the **kinetochore** . a complex protein structure where microtubules of the spindle apparatus attach . is on the outer sides of the centromere.

There are **2 types of microtubules**: *kinetochore microtubules* that the kinetochores of the chromosomes interact with and *non-kinetochore microtubules (polar microtubules)* from opposite poles that do not attach to the kinetochores but do overlap at the midpoint between the two poles. The microtubules have the 9+2 arrangement.

Cells that contain centrioles also have a series of smaller microtubules, the aster, that extend from the centrioles to the cell membrane. The aster is thought to serve as a brace for the functioning of the spindle fibers and presumably help anchor the centrosome. Polar microtubules are responsible for elongation of whole cell during anaphase.

Although kinetochore structure and function are not fully understood, it is known that it contains a molecular motor. When a microtubule connects with the kinetochore, the motor activates, using energy from ATP to "crawl" up the tube toward the originating centrosome. The kinetochore provides the pulling force necessary to later separate the chromosome's two chromatids.

Mitosis consists of 5 major stages: Prophase, Prometaphase, Metaphase, Anaphase, Telophase. They are sometimes difficult to separate. The process is a dynamic one, not the static process displayed of necessity in a textbook.

Prophase is the first stage of mitosis proper. Chromatin condenses (remember that chromatin/DNA replicate during Interphase); centrioles (if present) divide and migrate.

Prometaphase is the phase of mitosis following prophase and preceding metaphase. The nuclear envelope breaks into fragments and disappears. Microtubules emerging from the centrosomes at the poles (ends) of the spindle reach the chromosomes, now highly condensed. Some of the spindle microtubules attach to the kinetochores, throwing the chromosomes into agitated motion. Other spindle microtubules make contact with microtubules coming from opposite pole. Forces exerted by protein "motors" associated with spindle microtubules move the chromosomes toward the center of the cell.

Metaphase. The chromosomes (which at this point consist of chromatids held together by a centromere) migrate to the equator of the spindle, where the spindles attach to the kinetochore fibers.

Anaphase begins with the separation of the centromeres, and the pulling of chromosomes (we call them chromosomes after the centromeres are separated) to opposite poles of the spindle.

Telophase is when the chromosomes reach the poles of their respective spindles, the nuclear envelope reforms, chromosomes uncoil into chromatin form, and the nucleolus (which had disappeared during Prophase) reform. Where there was one cell there are now two smaller cells each with exactly the same genetic information. These cells may then develop into different adult forms via the processes of development.

A typical mitotic figure is symmetric and well formed. Cancer cells frequently have abnormal quantities of DNA and thus form abnormal or atypical mitotic figures.

Cytokinesis is the process of splitting the daughter cells apart. Whereas mitosis is the division of the nucleus, cytokinesis is the splitting of the cytoplasm and allocation of the Golgi, plastids and cytoplasm into each new cell.

The cell cycle varies in length in different types of cells, but is repeated each time a cell divides. Some cells divide rapidly (beans, for example, take 19 hours for the complete cycle; red blood cells must divide at a rate of 2.5 million per second). The cells that divide rapidly are also embryonic cells; marrow; cells of mucous tunics; skin cells (basal layer of epithelium); lymphoid tissue; cells of malignant neoplasms. Others, such as nerve cells, lose their capability to divide once they reach maturity. Some cells, such as liver cells (hepatocytes), retain but do not normally utilize their capacity for division. Liver cells will divide if part of the liver is removed. The division continues until the liver reaches its former size.

1. **It is temporarily suspended** in non-dividing resting cells (e.g., peripheral lymphocytes), which are in the G_0 state. Such cells may reenter the cycle and begin to divide again.
2. **It is permanently interrupted** in differentiated cells that do not divide (e.g., cardiac muscle cells and neurons).

Regulation of the cell cycle

Regulation of the cell cycle is accomplished in several ways:

- I. A molecular control system drives the cell cycle.
- II. Cyclical changes in regulatory proteins work as a mitotic clock.

As they divide, cells must proceed through the various stages of the cell cycle, including the G_1 , G_2 , and M phases. All phases are controlled by **checkpoints** . *critical control points where stop and go-ahead signals can regulate the cycle*. Triggers at each checkpoint assess the cell's readiness to

proceed to the next stage. Regulation also ensures that each cell obtains the proper number and type of chromosomes and organelles.

Without the controlled timing of cell division, an organism would be a shapeless blob of uncoordinated cells.

A cell uses **3 main checkpoints** to both assess the internal state of the cell and integrate external signals.

1. The G_1/S checkpoint is the primary point at which the cell decides to divide.
2. the G_2/M checkpoint represents a commitment to mitosis.
3. the spindle checkpoint ensures that all chromosomes are attached to the spindle in preparation for anaphase.

| | | |
|------------------|--|--|
| G_1 checkpoint | the end of G_1 phase | If conditions are not suitable for replication, the cell will not proceed to S phase but will instead enter a resting phase, G_0 . |
| G_2 checkpoint | the end of G_2 phase | If conditions are not suitable, transition to the M phase will be delayed. If DNA is damaged, cell division will be delayed to allow time for DNA repair. |
| M checkpoint | between metaphase and anaphase stages of mitosis | If the chromosomes are aligned properly and ready for division, the cell will proceed from metaphase to anaphase, during which it will divide. If the chromosomes are not aligned properly, the anaphase stage will be delayed |

Defects in the checkpoints that normally maintain the fidelity of the cell cycle can lead to chromosomal instability and cancer.

Proteins that regulate the cell cycle

Cell cycle is paced by rhythmic fluctuations in the **abundance** and/or **activity** of control protein molecules.

Two main families of proteins involved in regulation of cell cycle are:

1. **Cyclins**
2. **Cyclin-dependent protein kinases** (Cdk's)

Cells also receive protein signals (**growth factors**) that affect cell division.

1. Cyclins are named such because these proteins undergo a constant *cycle of synthesis and degradation* during cell division. When cyclins are synthesized, they act as an *activating protein* and bind to **cyclin-dependent protein kinases** forming a cyclin-Cdk complex. Eventually, the cyclin degrades, deactivating the Cdk, thus signaling exit from a particular phase. There are two classes of cyclins: *mitotic cyclins* and *G_1 cyclins*.

2. Cyclin-dependent kinases (Cdks) are proteins (enzymes) which phosphorylate (add a phosphate, $-PO_4$) other proteins to **activate** or **inactivate** them.

Now the group of protein kinases includes 11 proteins (Cdk1-Cdk11).

- Cdks levels are usually constant.
- Cdks are inactive in the absence of cyclin.
- Cdks are activated by binding to cyclins and regulated by phosphorylation and dephosphorylation.
- Cdks will be regulated the G_1 , G_2 and M checkpoints.

An example of cyclin-Cdk complexes is **maturation promoting factor (MPF, also called mitosis-promoting factor or M-Phase promoting factor)** which is composed of a *regulatory subunit* Ë cyclin B and a *catalytic subunit* . cyclin-dependent kinase (CDK1, also known as Cdc2 or p34 kinase) that stimulates the mitotic and meiotic cell cycles. MPF promotes the entrance into mitosis from the G_2 phase by phosphorylating multiple proteins needed during mitosis. MPF is activated at the end of G_2 by a *phosphatase* enzyme, which removes an inhibitory phosphate group added earlier.

External Signals

Growth factors are proteins released by certain body cells that stimulate other cells to divide.

Density-dependent inhibition . phenomenon when crowded cells stop dividing.

Anchorage dependence . phenomenon when cells to divide must be attached to substratum. The anchorage is related to plasma membrane proteins.

Cancer cells have escaped from cell-cycle controls

Cancer cells are those which undergo a series of rapid divisions such that the daughter cells divide before they have reached "functional maturity". Environmental factors such as changes in temperature and pH, and declining nutrient levels lead to declining cell division rates. When cells stop dividing, they stop usually at a point late in the G₁ phase, the R point (for restriction).

Transformed cells have lost their ability to respond to regulatory signals controlling the cell cycle. They may undergo cell division indefinitely, thus becoming *cancerous* and forming *tumors*. Malignant tumors invade surrounding tissues and can metastasize, exporting cancer cell to other parts of the body

Scientists have discovered one reason behind this uncontrolled growth: a defective **tumor-suppressor gene - p53 gene**, the "guardian of the genome". Proteins produced by the p53 gene assess the cell's DNA for damage at the G₁ checkpoint.

- If the DNA is intact, cell division proceeds.
- If the DNA is damaged, however, the p53 proteins halt cell division until the DNA is repaired or the cell is destroyed.
- If the p53 gene itself has been damaged, as in the case of cells that are cancerous, the G₁ checkpoint will fail and a malignant cancer cell may develop. The p53 is mutated in over 50% of all human cancers.

Other group of genes related with cancer is **proto-oncogenes**. Proto-oncogenes are normal cellular genes that become *oncogenes* when mutated due to genetic accidents or viruses. Oncogenes dominate the normal alleles (proto-oncogenes), causing a **deregulation** of cell division, which leads to a cancerous state, e.g., bladder cancer and acute myelogenous leukemia are caused by oncogenes.

Some medications, such as **Vinca alkaloids** (from common periwinkle *Vinca minor* plants or autumn crocus *Colchicum autumnale*), may arrest tumor cells in mitosis, destroying the microtubules of mitotic spindle. Other drugs (e.g., Methotrexate and 5-MP) that block purine and pyrimidine synthesis may arrest cells in the S phase.

Asexual and Sexual Reproductions

The parent passes on an exact replica of its genetic material to the offspring, resulting in an offspring, genetically identical to the parent organism. **No genetic variation** exists from one generation to the next in organisms that reproduce asexually, apart from variation introduced by random and uncontrollable mutations during gene replication.

The advantage of asexual reproduction is that it allows the rapid reproduction of numerous offspring in the absence of a partner. An isolated organism reproducing asexually can colonize an ideal habitat very quickly. In addition, the relatively low rate of genetic variation is beneficial to organisms inhabiting marginal or harsh environments to which they are already ideally suited. The lack of genetic variation in asexual reproduction, however, inhibits species adaptation that results from advantageous traits being passed down to subsequent generations, as is the case in sexual reproduction.

Three main types of asexual reproduction are exhibited in species of the animal kingdom:

1. **Fission:** An individual organism splits into two roughly equal-sized organisms, which then grow to the size of the original. *E.g., amoebae and sea anemones* reproduce through fission.
2. **Budding:** Small individuals split off from a parent organism and develop into full-sized adults. *Cnidarians*, which includes *the jellyfish and corals*, can reproduce through budding.
3. **Fragmentation/regeneration:** A parent individual splits into several parts, each of which develops into an adult. Some *sponges* and *worms* reproduce through fragmentation.

Offspring created during **sexual reproduction** receive genetic material from two separate parent organisms, a male and a female, that are mixed together to form a fertilized cell, a **zygote**.

Females package their genetic material in an immobile haploid gamete (sex cell) called an **ovum**. Males package their genetic material in a mobile haploid gamete (**sperm**).

Meiosis

Whereas somatic cells undergo mitosis to proliferate, the germ cells undergo **meiosis** to produce haploid gametes . sex cells (the sperm and the egg). Meiosis results in the division of a diploid parental cell into haploid progeny, each containing only one member of the pair of homologous chromosomes that were present in the diploid parent.

Three distinct processes of major genetic importance occur during meiosis:

1. a reduction in chromosome number from diploid to haploid;
2. independent assortment of chromosomes of maternal and paternal origin into the gametes (or other haploid progeny of meiosis)

3. genetic recombination, or crossing-over

The stages of meiosis are

1. meiosis I (reductional division)
2. meiosis II (equatorial division).

Reductional division (meiosis I) occurs after interphase when the 46 chromosomes are duplicated, giving the cell a **4c DNA content**

Equatorial division (meiosis II) begins soon after the completion of meiosis I, following a brief interphase without DNA replication. The centromeres separate in this division, generating a haploid number of chromosomes, each of which consists of a single chromatid. The DNA content at this stage is 2c - one half that of a pre-replication diploid cell.

For meiosis, the phases prophase, metaphase, anaphase and telophase are identified, but because there are two divisions, there are two sets. These are designated by Roman numerals; thus Prophase I, Metaphase I, Anaphase I, Telophase I, Interphase, Prophase II, Metaphase II, Anaphase II and Telophase II. Interphase is normally not designated with a Roman numeral. Because of the significance of the chromosome pairing which occurs in Prophase I, it is further subdivided into 5 stages.

1. **Leptonema (leptotene stage)** (thin strings) is marked by the first appearance of the chromosomes when the chromosomes are in their most extended form (except for during interphase). They appear to be a string with beads. The beads are known as chromomeres. The chromatids have already replicated prior to this phase, but typically, the replicated chromatids can not be observed during the leptotene stage.
2. **Zygonema (zygotene stage)** (yoked strings). Zygos means "yoked," and during this stage, the homologous chromosomes are seen as paired units. The chromosomes are shorter and thicker than in leptotene, and in some cells they remain attached to the nuclear envelope at the points near the aster. This gives rise to an image termed the "bouquet." This attachment is rare in invertebrates and absent in plants, where the chromosomes appear to be a tangled mass.
3. **Pachynema (pachytene stage)** (thick strings). When the pairing of zygotene is complete, the chromosomes appear as "thick" strings. The chromosomes are about 1/4 the length they were in leptotene, and there are obviously two chromosomes, each with two chromatids in each bundle. The two chromosomes are referred to as a "bivalent," while the same structure viewed as four chromatids is known as a "tetrad." Genetic recombination - **crossing over** - occurs between maternal and paternal chromosomes. During crossing-over, chromatids break and may be reattached to a **different** homologous chromosome.
4. **Diplonema (diplotene stage)** (double strings) is characterized by the beginning of separation of homologues, with residual areas of close contact called **chiasmata** (singular = chiasma), which are sites of recombination; This stage results as the gap between the two homologous chromosomes widens. The homologs have already paired during zygotene, recombined during pachytene and are now beginning to repel each other. During this stage, the chromosomes of some species uncoil somewhat, reversing the normal direction typical of prophase. As the chromosomes separate, they are observed to remain attached at points known as "chiasmata." These are believed to be the locations where genetic recombination of the genes has taken place.
5. **Diakinesis** . shortening of the chromosomes, due to further condensation, and by migration of chiasmata toward the ends of the chromosomes Prophase I ends as the homologs completely repel each other. The chromosomes will continue to coil tightly (reversing the slight uncoiling of the diplotene) and will reach their greatest state of contraction. As diakinesis progresses, chiasmata appear to move toward the ends of the chromosomes, a process known as "terminalization." Since this stage is the end of prophase, the nucleolus usually disappears, along with the nuclear envelope.

Metaphase I is when tetrads line-up along the equator of the spindle. Spindle fibers attach to the centromere region of each homologous chromosome pair. Other metaphase events are as in mitosis.

Anaphase I is when the tetrads separate, and are drawn to opposite poles by the spindle fibers. The centromeres in Anaphase I remain intact.

Telophase I is similar to Telophase of mitosis, except that only one set of (replicated) chromosomes is in each "cell". Depending on species, new nuclear envelopes may or may not form. Some animal cells may have division of the centrioles during this phase. In many species, the chromosomes do not completely uncoil. If the chromosomes do uncoil and enter a brief interphase, there is no replication of the chromatids.

After mitosis I each daughter cell contains 23 chromosomes (**n**) number, but has a **2C DNA content** (the diploid amount of DNA). Each chromosome is composed of two similar **sister chromatids** (not genetically identical).

Metosis II: Equatorial division

- The stages of meiosis II are similar to those of mitosis; thus the stages are named similarly (prophase II, metaphase II, anaphase II, and telophase II).
- In anaphase II, the centromeres of sister chromatids finally separate, and the sister chromatids of each pair, now individual chromosomes, move toward opposite poles of the cell
- Equatorial division produces 4 haploid ($n=23$) cells

Prophase II - Telophase II

These phases are essentially identical in meiotic and mitotic division: the only distinction is that the chromosome number is half of the number the cell had prior to meiosis. Each chromosome (homolog) is composed of two chromatids, and during Anaphase II, the two chromatids of each chromosome move apart and become separate chromosomes. There is a shift in the terminology applied to these units. While the two chromatids remain attached at the centromere, they are known as chromatids. Immediately upon separating, each chromatid becomes known as a chromosome and is no longer referred to as a chromatid. This is the reason that a cell can divide one chromosome (with two chromatids) into two cells, each with a chromosome - the term applied to the chromatid is changed.

Comparison of Mitosis and Meiosis

| MITOSIS | MEIOSIS |
|--|---|
| One cell division results in two daughter cells | Two cell divisions result in four cells |
| Chromosome number per nucleus is maintained following division | Chromosome number is halved in final products of meiosis |
| One S phase per division | One S phase per two divisions |
| Normally, there is no pairing of homologs | Full synapsis of homologs in prophase |
| Normally, no recombination or crossovers | At least one crossover per homologous pair |
| Centromeres divide at anaphase | Centromeres do not divide at anaphase I, but do at anaphase II. |
| Genetic composition of daughter cells is rigidly maintained | Independent assortment and crossover promote genetic variation |

Gametogenesis

Gametogenesis is the process of forming gametes (by definition *haploid, n*) from diploid cells of the germ line. **Germ cells** are progenitors of the gametes. These singled out cells move (migrate) through the gut to the developing gonads and undergo mitotic proliferation followed by meiosis and differentiation into mature gametes - either eggs or sperm.

Spermatogenesis is the process of forming sperm cells by meiosis in specialized organs . testes. After division the cells undergo differentiation to become sperm cells.

Oogenesis is the process of forming an ovum (egg) by meiosis in specialized gonads known as ovaries.

Spermatogenesis & Meiosis in males

1. **Spermatogenesis** takes about 74 hours. It occurs in the **seminiferous tubules** within the **testes**. 300 million are produce per day. Once ejaculated they live about 48 hours within female reproductive tract. It begins at the onset of **puberty** and continues throughout male's life.
2. **Spermatagonia** in seminiferous tubules of testes become **primary spermatocytes**, which enter **Meiosis I**.
3. At the end of **Meiosis I** there are 2 **secondary spermatocytes**.
4. Telophase of Meiosis II results in 4 **spermatids** of equal size and cellular material.
5. A **flagellum (tail)** forms and a **protein cap** which contains enzymes necessary to penetrate the coat of the **ovum**. The top of the head is called the **acrosomal cap** which contains the enzymes. The result is a mature **spermatozoon**.

Several hundred million sperm are produced **each day. Once sperm form they move into the epididymis, where they mature and are stored.**

Oogenesis & meiosis in females

1. Cells in **ovaries** that give rise to oocytes and ova are called **oogonia**. Oogonia begin in the in the embryos forming gonad as early as the 3rd month.
2. After 3rd month oogonia proliferate extensively by mitotic divisions and some of them develop into **primary oocytes**. These cells enter **prophase I** but do not continue until puberty.
3. **Primary oocyte** continues to develop at onset of puberty. Several primary oocytes continue each month in **menstrual cycle**. Only one survives per month to become ovum. Primary oocytes are present from week 10 until menopause at ~53 years.
4. Follicle-stimulating hormone (**FSH**) stimulates continuation. Result of meiosis I is one **secondary oocyte** and the **1st polar body**, which is essentially discarded nuclear material. It may develop further to **2 polar bodies**. A secondary oocyte is released each month from puberty until menopause, a total of 400-500 egg cells.
5. After Meiosis II the secondary oocytes produces 2 cells of unequal size - the **ootid and the second polar body**.
6. The ootid eventually becomes the **ovum**. All polar bodies disintegrate and die.

Comparison of Spermatogenesis and Oogenesis

Whereas in spermatogenesis all 4 meiotic products develop into gametes, oogenesis places most of the cytoplasm into the large egg. The other cells, the polar bodies, do not develop. These all the cytoplasm and organelles go into the egg. Human males produce 200,000,000 sperm per day, while the female produces one egg (usually) each menstrual cycle.

At birth each female carries a lifetime supply of developing oocytes, each of which is in Prophase I. A developing egg (secondary oocyte) is released each month from puberty until menopause, a total of 400-500 eggs.

| Spermatogenesis | Oogenesis |
|---|--|
| <i>Number of gametes</i> | |
| Principle: continuous production. Sperm production begins at puberty. Although from puberty to old age sperm cells are constantly being engendered, the production is subject to extreme fluctuations regarding both quantity and quality | Principle: Using up the oocytes generated before birth. Continual decrease of the oocytes, beginning with the fetal period. Exhaustion of the supply at menopause. |
| <i>Meiotic output</i> | |
| Four functioning, small (head 4 mcm), motile spermatozooids at the end of the meiosis | One large, immotile oocyte (ø 120 mcm) and three shriveled polar bodies are left at the end of the meiosis |
| <i>Fetal period</i> | |
| No meiotic divisions | Entering into meiosis (arrested in the <i>dictyotene</i> stage) |
| No germ cell production | Production of the entire supply of germ cells |

Errors of meiosis: non-disjunction of chromosomes

In *non-disjunction*, a chromosome may fail to separate during anaphase. One daughter cell will receive both sister chromosomes and the other will receive none. This results in the former cell having three chromosomes coding for the same thing (two sisters and a homologous), a condition known as *trisomy*, and the latter cell having only one chromosome (the homologous chromosome), a condition known as *monosomy*. These cells are considered aneuploidic cells. Aneuploidy can although cause cancer.

Examples of aneuploidy in human are chromosome diseases:

Down syndrome (trisomy 21) is characterized by mental retardation, short stature, stubby appendages, congenital heart malformations, and other defects.

Klinefelter syndrome (XXY) is aneuploidy of the sex chromosomes, characterized by male phenotype, infertility, variable degrees of masculinization, and small testes.

Turner syndrome (XO) is **monosomy** of the sex chromosomes, characterized by female phenotype, short stature, sterility, and various other abnormalities.

Cell death

Cells die in one of two ways: *necrosis* and *apoptosis*.

Necrosis occurs when cells either are damaged by poisons or are starved of essential nutrients. These cells swell and burst. Healing of the tissue may occur as seen in scabs forming around wounded areas.

Cell death more typically occurs in a controlled fashion, a process called **apoptosis**. Apoptosis is genetically programmed cell death. Cells need signals not only to proliferate, but also to survive. If deprived of these signals, cells die by an apoptosis. Developmentally, apoptosis is a necessary event leading to correct morphological development in an organism. An example of programmed cell death is the elimination of the cells of the weblike tissue between the fingers of a developing human fetus. In this example, cell death is necessary to properly form individual fingers. Another is when the cell is old or damaged and needs to be replaced.

There are signals controlling the process of apoptosis, such as the lack of a mitotic signal to divide.

The cell is isolated, chops up its own chromatin, and gets ingested by surrounding living cells.