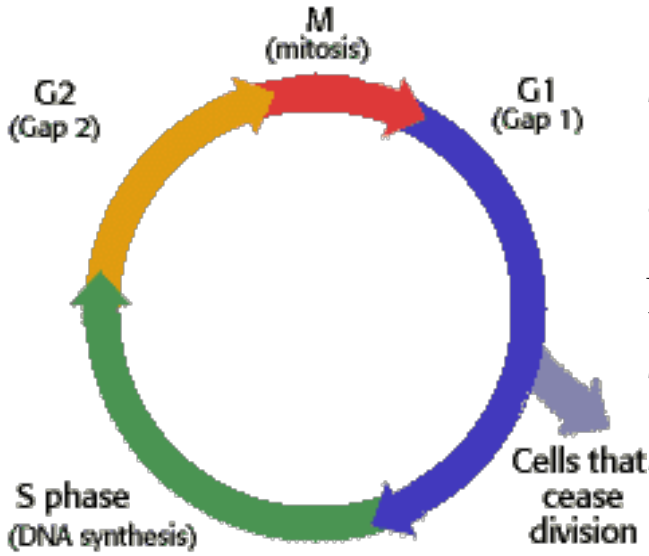
The Cell Cycle

Stages of the cell cycle

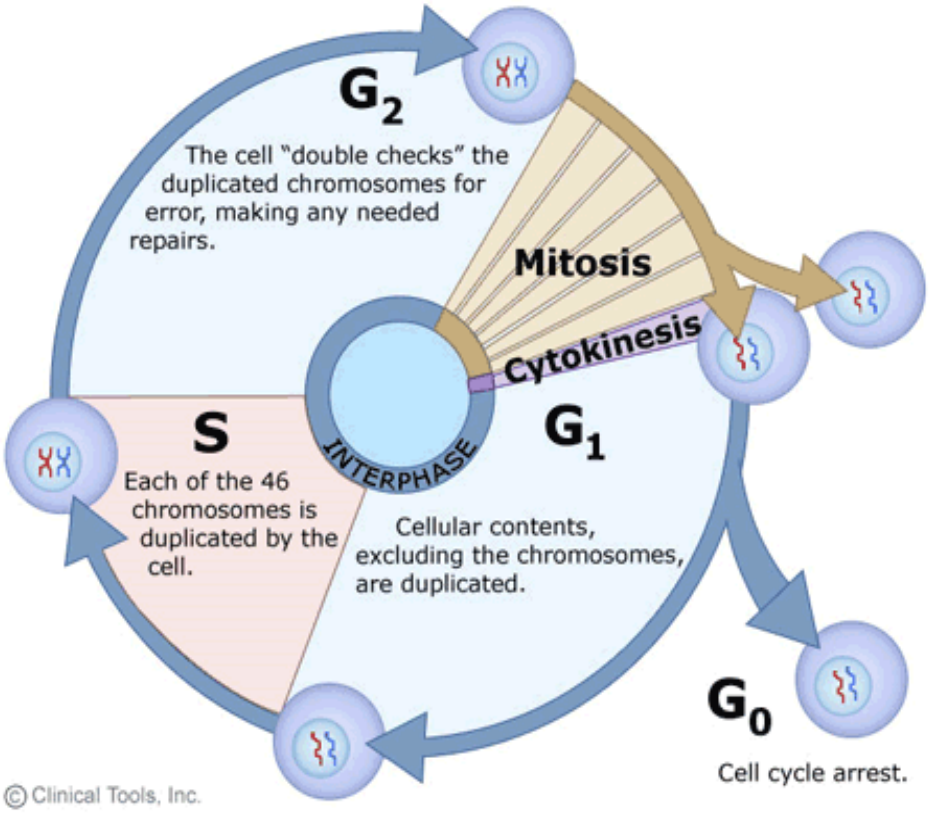


The cell cycle includes cell growth and division into two daughter cells.

Non-dividing cells not considered to be in the cell cycle.

The stages: G1-S-G2-M.

The G1 stage stands for "GAP 1". The S stage stands for "Synthesis". This is the stage when DNA replication occurs. The G2 stage stands for "GAP 2". The M stage stands for "mitosis", and is when nuclear (chromosomes separate) and cytoplasmic (cytokinesis) division occur.

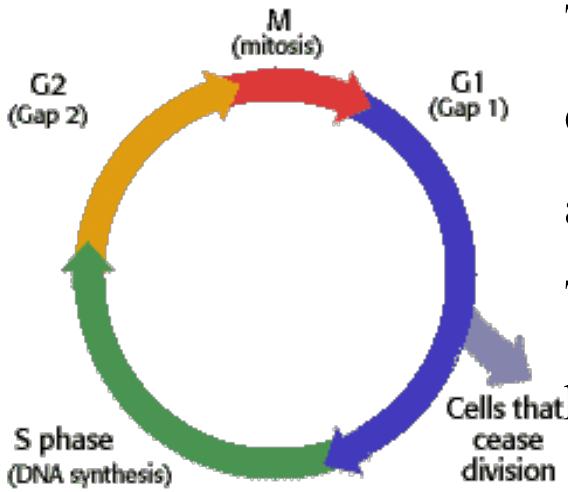


G1 phase :Metabolic changes prepare the cell for division. At a certain point - the restriction point - the cell is committed to division and moves into the S phase.

S phase. DNA synthesis replicates the genetic material. Each chromosome now consists of two sister chromatids.

G2 phase. Metabolic changes assemble the cytoplasmic materials necessary for mitosis and cytokinesis.

M phase. A nuclear division (mitosis) followed by a cell division (cytokinesis).



The control of cell division (and thus tissue growth) is very complex. When the normal control is lost, the cell cycle goes awry can develop cancer.

Terms and some of the features important in regulation, and places where errors can lead to cancer:

Cdk (cyclin dependent kinase, adds phosphate to a protein), along with cyclins, major switches for the cell cycle, causing the cell to move from G1 to S or G2 to M.

MPF (Maturation Promoting Factor) includes the CdK and cyclins that triggers progression through the cell cycle.

p53 is a protein functions to block the cell cycle if the DNA is damaged. If the damage is severe it can cause apoptosis. p53 levels are increased in damaged cells. This allows time to repair DNA by blocking the cell cycle. A p53 mutation is the most frequent mutation leading to cancer.

p27 is a protein that binds to cyclin and cdk blocking entry into S phase. Reduced levels of p27 predict a poor outcome for cancer patients.

Cell cycle checkpoints

Each part of the cell cycle features its own unique checkpoints.

During G_1, the cell passes through a critical checkpoint that ensures environmental conditions (including signals from other cells) are favorable for replication.

If conditions are not favorable, the cell may enter a resting state (**G_0**).

Some cells remain in G_0 for their entire lifetime: the neurons and skeletal muscle cells of mammals are typically in G_0.

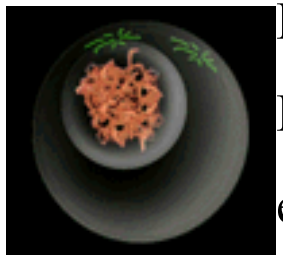
Another checkpoint takes place before the synthesis of the DNA. Before that can happen the integrity of the DNA is checked. The cell may pause at this point to allow time for DNA repair, if necessary, or if the DNA damage is severe the cell is killed by apoptosis.

When DNA is duplicated a number of proteins investigate again the cell's DNA, making sure it is structurally intact and properly replicated. Each DNA part is duplicated correctly and there is only one extra copy. The cell again may pause at this point to allow time for DNA repair.

Another cell cycle checkpoint takes place mid-mitosis. This check determines whether the chromosomes in the cell have properly attached to the **spindle**, or the network of microtubules that will separate them during cell division. This step decreases the possibility that the resulting daughter cells will have unbalanced numbers of chromosomes.

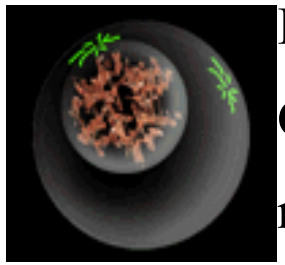
Mitosis

Mitosis is nuclear division plus cytokinesis, and produces two identical daughter cells.



Interphase

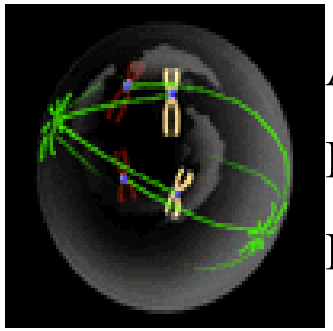
Encompasses stages G1, S, and G2 of the cell cycle, when the cell is engaged in metabolic activity and performing its prepare for mitosis. Chromosomes are not clearly discerned in the nucleus, the nucleolus may be visible. The cell may contain a pair of centrioles (microtubule organizing centers) an organizational sites for microtubules.



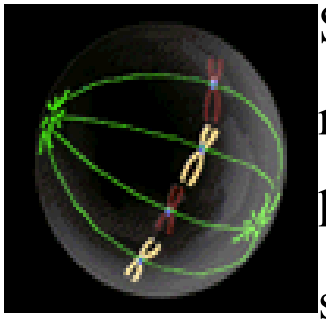
Prophase

Chromatin in the nucleus begins to condense and becomes visible in the light microscope as chromosomes. The nucleolus disappears. Centrioles begin moving to opposite ends of the cell and microtubules extend from the centromeres. Some fibers cross the cell to form the mitotic spindle.

Metaphase

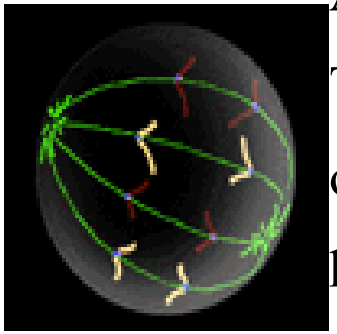


At the beginning of the metaphase the nuclear membrane dissolves. Proteins attach to the centromeres creating the kinetochores. Microtubules attach at the kinetochores and the chromosomes begin moving.

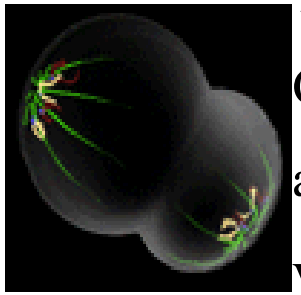


Spindle fibers align the chromosomes along the middle of the cell nucleus. This line is referred to as the metaphase plate. This organization helps to ensure that in the next phase, when the chromosomes are separated, each new nucleus will receive one copy of each chromosome.

Anaphase

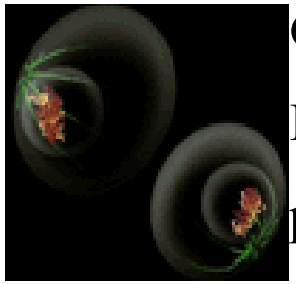


The paired chromosomes separate at the kinetochores and move to opposite sides of the cell. Motion results from a combination of kinetochore movement along the spindle microtubules and through the physical interaction of polar microtubules.



Telophase

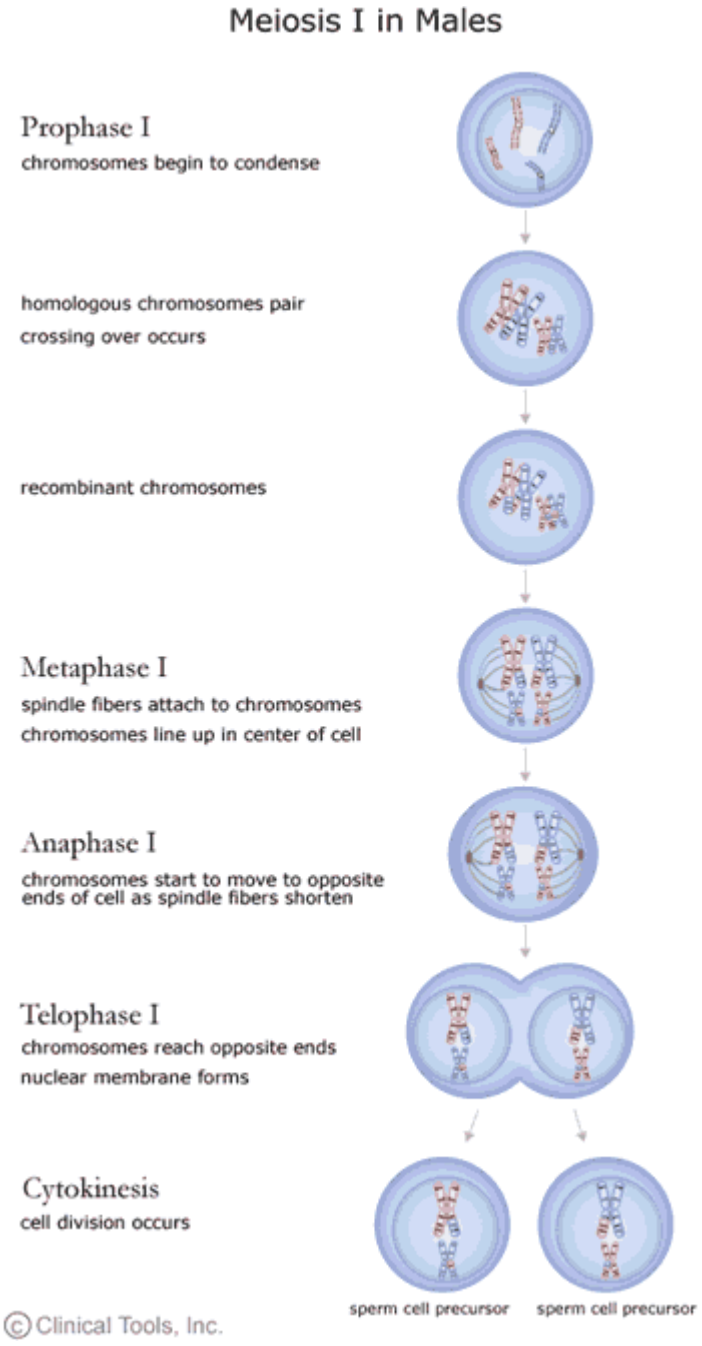
Chromatids arrive at opposite poles of cell, and new membranes form around the daughter nuclei. The chromosomes disperse and are no longer visible under the light microscope. The spindle fibers disperse, and cytokinesis or the partitioning of the cell may also begin during this stage.



Cytokinesis

In animal cells, cytokinesis results when a fiber ring composed of a protein called actin around the center of the cell contracts pinching the cell into two daughter cells, each with one nucleus. In plant cells, the rigid wall requires that a cell plate be synthesized between the two daughter cells.

Meiosis


Meiosis I in Males
Prophase I
chromosomes begin to condense
homologous chromosomes pair
crossing over occurs
recombinant chromosomes
Metaphase I
spindle fibers attach to chromosomes
chromosomes line up in center of cell
Anaphase I
chromosomes start to move to opposite ends of cell as spindle fibers shorten
Telophase I
chromosomes reach opposite ends
nuclear membrane forms
Cytokinesis
cell division occurs
sperm cell precursor
sperm cell precursor
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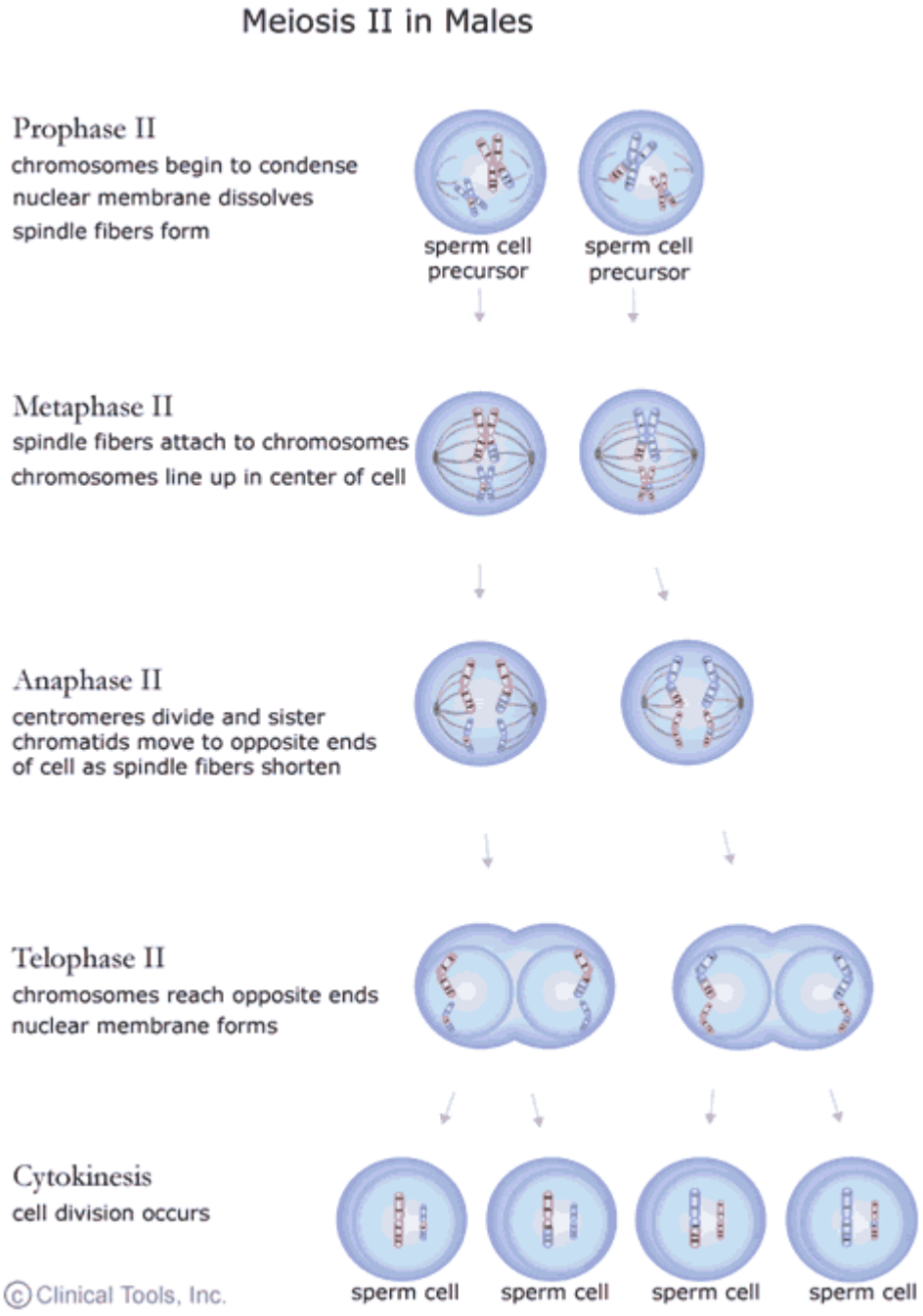
Meiosis II in Males
Prophase II
chromosomes begin to condense
nuclear membrane dissolves
spindle fibers form
sperm cell precursor
sperm cell precursor
Metaphase II
spindle fibers attach to chromosomes
chromosomes line up in center of cell
Anaphase II
centromeres divide and sister chromatids move to opposite ends of cell as spindle fibers shorten
Telophase II
chromosomes reach opposite ends
nuclear membrane forms
Cytokinesis
cell division occurs
sperm cell
sperm cell
sperm cell
sperm cell
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Meiosis

Eukaryotic cell division form that produces **haploid** gametes from **diploid** cells.

The process consist of one DNA replication followed by two successive nuclear and cellular divisions (Meiosis I and Meiosis II).

Meiosis is preceded by a process of DNA replication that converts each chromosome into two sister chromatids.

Meiosis I separates the pairs of homologous chromosomes.

Meiosis II separates each chromosome into two chromatids.

Meiosis generates genetic diversity through:

- the exchange of genetic material between homologous chromosomes during Meiosis
- the random alignment of maternal and paternal chromosomes in Meiosis I
- the random alignment of the sister chromatids at Meiosis II

Prophase I

The homologous chromosomes pair and exchange DNA to form recombinant chromosomes. Prophase I is divided into five phases:

- **Leptotene**: chromosomes start to condense.
- **Zygotene**: homologous chromosomes become closely associated (synapsis) to form pairs of chromosomes (bivalents) consisting of four chromatids (tetrads).
- **Pachytene**: crossing over between pairs of homologous chromosomes to form chiasmata (sing. chiasma).
- **Diplotene**: homologous chromosomes start to separate but remain attached by chiasmata.
- **Diakinesis**: homologous chromosomes continue to separate, and chiasmata move to the ends of the chromosomes.

Cell death

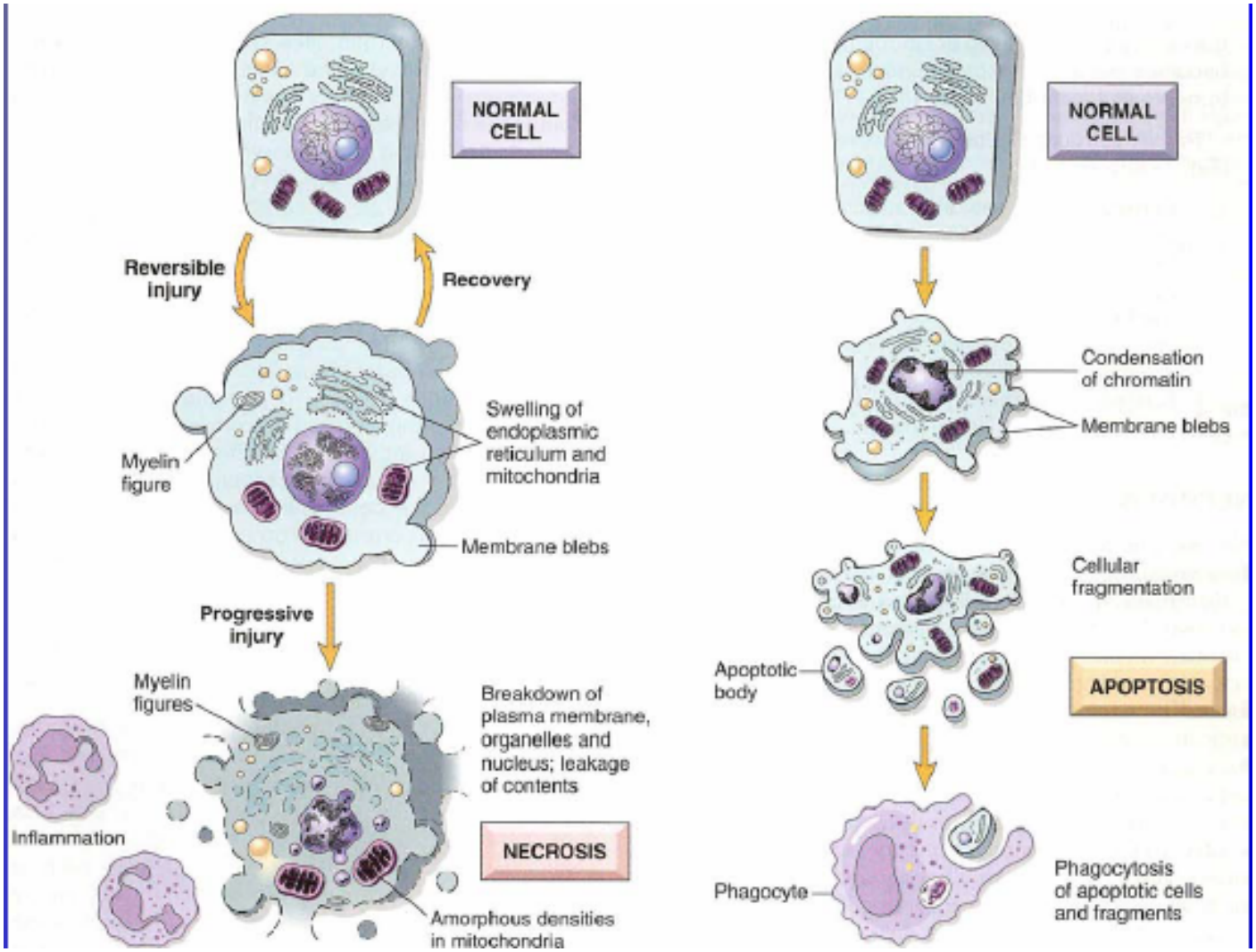
There are two ways that a cell can die: necrosis and apoptosis.

Necrosis occurs when a cell is damaged by an external force, (poison, injury, infection or shortage of O_2 and nutrition).

When cells die from necrosis, never only one cell is affected, usually there is a necrotic zone. The death causes inflammation that can cause further distress or injury within the body.

Apoptosis, practically the suicide of the cell. Individual cells die independently to each other. The cleanup is much easier, no imflammation or other complications occur.

It's sometimes referred to as **programmed cell death**, the process of apoptosis follows a controlled, predictable routine.


NORMAL CELL
Reversible injury
Recovery
Swelling of endoplasmic reticulum and mitochondria
Myelin figure
Membrane blebs
Progressive injury
Myelin figures
Breakdown of plasma membrane, organelles and nucleus; leakage of contents
Inflammation
NECROSIS
Amorphous densities in mitochondria
NORMAL CELL
Condensation of chromatin
Membrane blebs
Cellular fragmentation
Apoptotic body
APOPTOSIS
Phagocyte
Phagocytosis of apoptotic cells and fragments