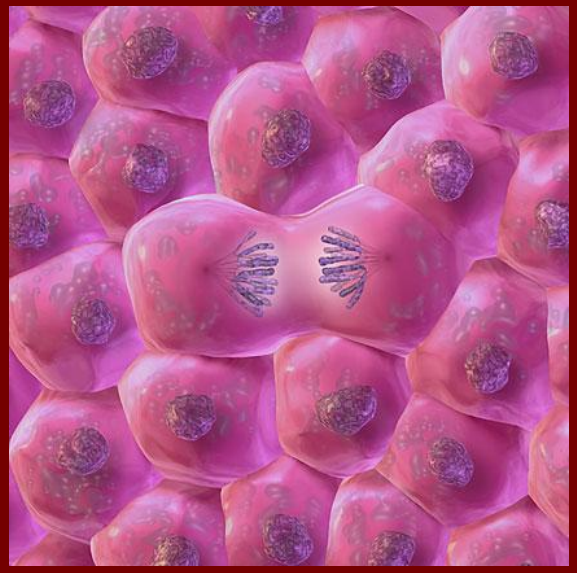
BIOLOGY I

Chapter 12: THE CELL CYCLE AND CELLULAR REPRODUCTION



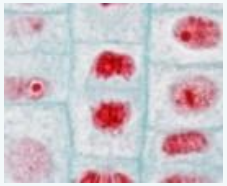
Evelyn I. Milian

Instructor

Basic Terms

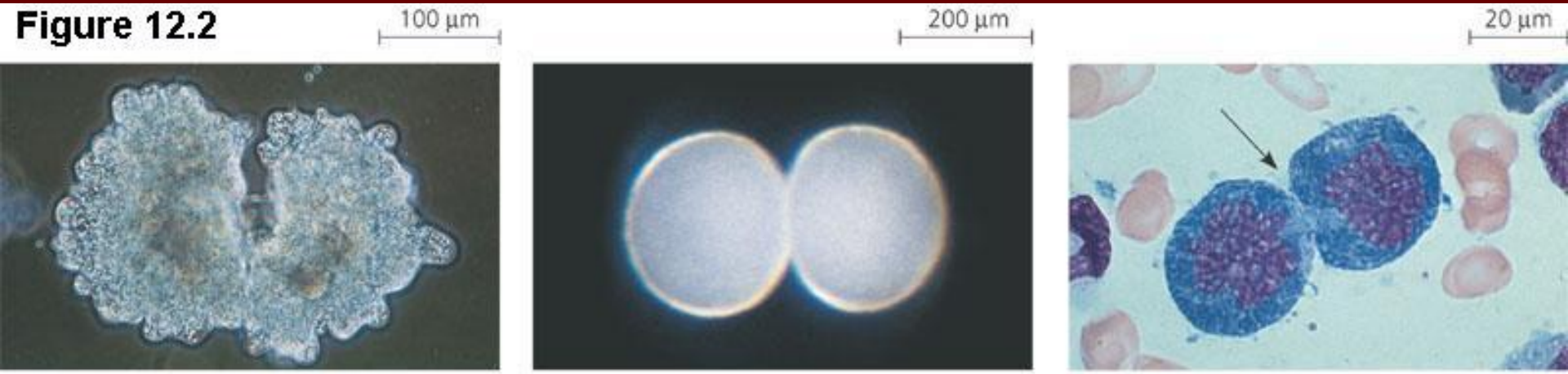
Cell division	The ***reproduction*** of cells.
Cell cycle	An ordered, repeating sequence of events in the life of a ***eukaryotic*** cell (cell with a membrane-bound nucleus containing the genetic material) that involves ***cell growth***, ***nuclear division*** and ***cytoplasmic division***; it consists of the stages **G_1, S, G_2,** and **M**.
Gene	A functional ***segment of DNA*** located at a particular place on a chromosome; it is a unit of hereditary information that encodes the information needed to specify the amino acid sequence of proteins and hence particular traits. ✓*Remember*: DNA is the abbreviation of **deoxyribonucleic acid**, a molecule of nucleotides that contains information for the cell's functions and metabolism. DNA is the genetic material of cells. All the information for the structure and function of an organism is coded in its genes.
Genome	The entire **set of genes** carried by an organism.

Basic Terms

Chromosome 	The cellular threadlike structure that contains the **genetic material** of cells (in the nucleus of an eukaryotic cell, or the nucleoid region of prokaryotic cells). Each chromosome consists of one very long **DNA molecule** and **associated proteins**. In other words, chromosomes contain the genes.
Chromatin 	The network of **DNA strands and associated proteins** observed within the nucleus of a cell that is not dividing. In a cell that is dividing, chromatin *condenses and coils* and becomes observable **chromosomes**.
Chromatid (Sister chromatids)	The two **genetically identical chromosomal units** that are the result of DNA replication and are attached to each other at a narrow centralized region called the **centromere**.
Somatic cells	All **body cells** in a multicellular organism ***except*** the reproductive cells (egg and sperm, or *gametes*).
Gametes	**Reproductive cells: eggs** (female) and **sperm** (male). Gametes unite during sexual reproduction, or fertilization, to produce a cell called **zygote**. Sometimes called "**germ cells**" or "**sex cells**".

The Key Roles of Cell Division: *Why is Cell Division Important?*

Figure 12.2



(a) Reproduction. An amoeba, a single-celled eukaryote, is dividing into two cells. Each new cell will be an individual organism (LM).

(b) Growth and development. This micrograph shows a sand dollar embryo shortly after the fertilized egg divided, forming two cells (LM).

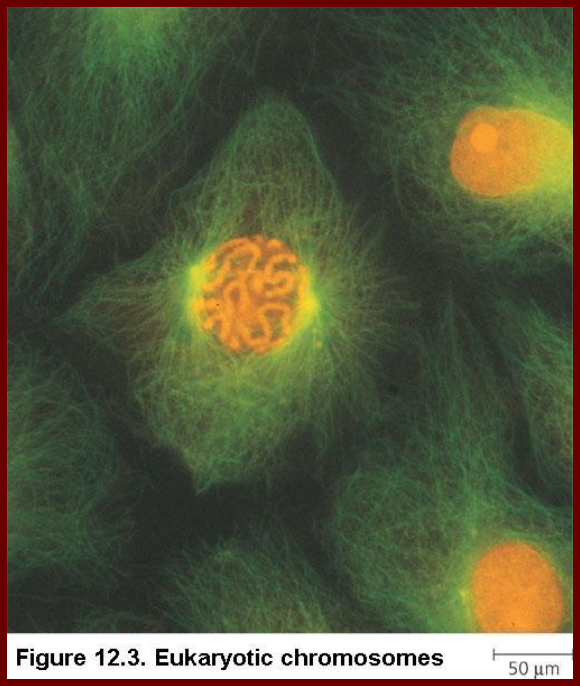
(c) Tissue renewal. These dividing bone marrow cells (arrow) will give rise to new blood cells (LM).

a) **Reproduction:** Cell division enables a single cell to eventually produce many cells; for example, to form a new unicellular organism by asexual reproduction (from a single parent).

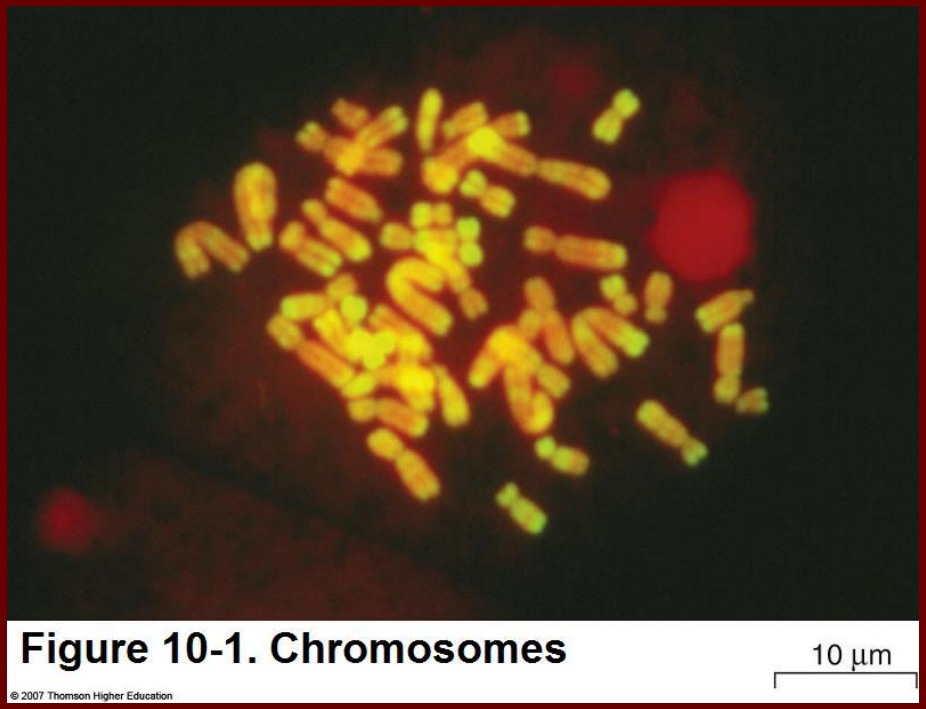
b) **Growth and development:** Cell division also enables sexually reproducing organisms to develop from a single cell—the fertilized egg, or zygote. The organisms can then grow and develop.

c) **Tissue renewal and repair:** Replacing cells that die from normal wear and tear or accidents; repairing tissues.

Cellular Organization of the Genetic Material: **Chromosomes**



- **Chromosomes** (stained orange) are visible within the nucleus of a kangaroo rat epithelial cell in the center of this micrograph. The cell is preparing to divide.



- **Human chromosomes** from an unidentified cell are shown in this fluorescence light micrograph. Chromosomes are the cellular threadlike structures that contain the **genes** (DNA segments).

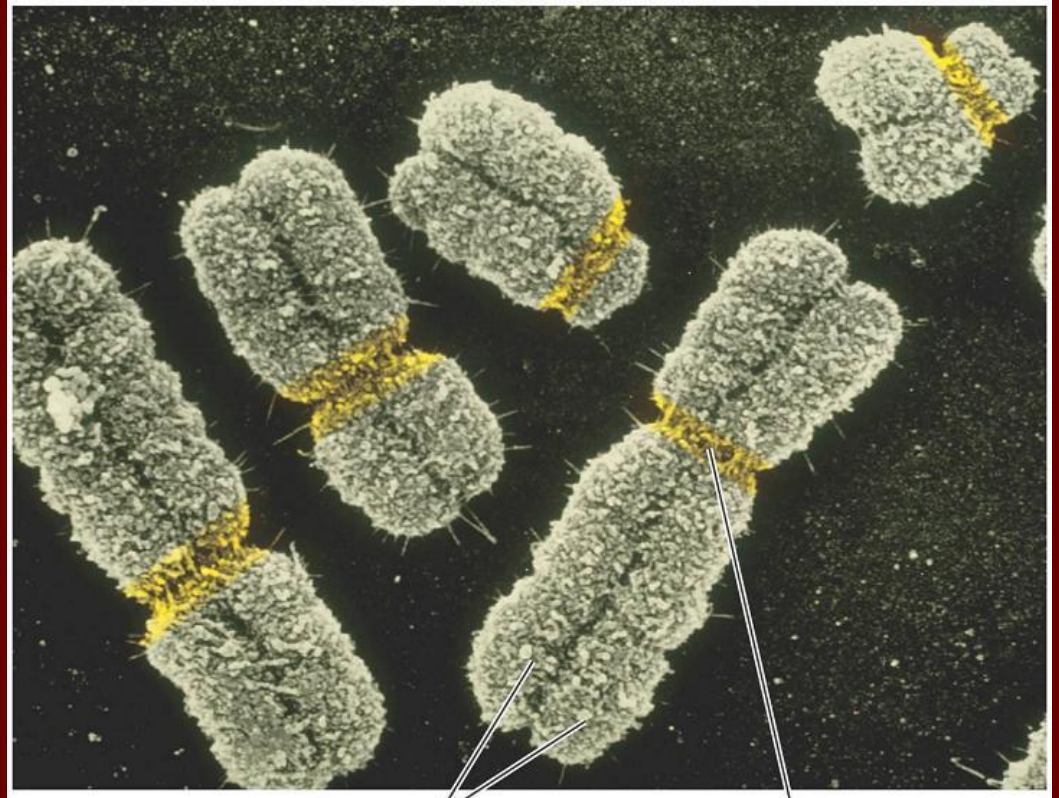
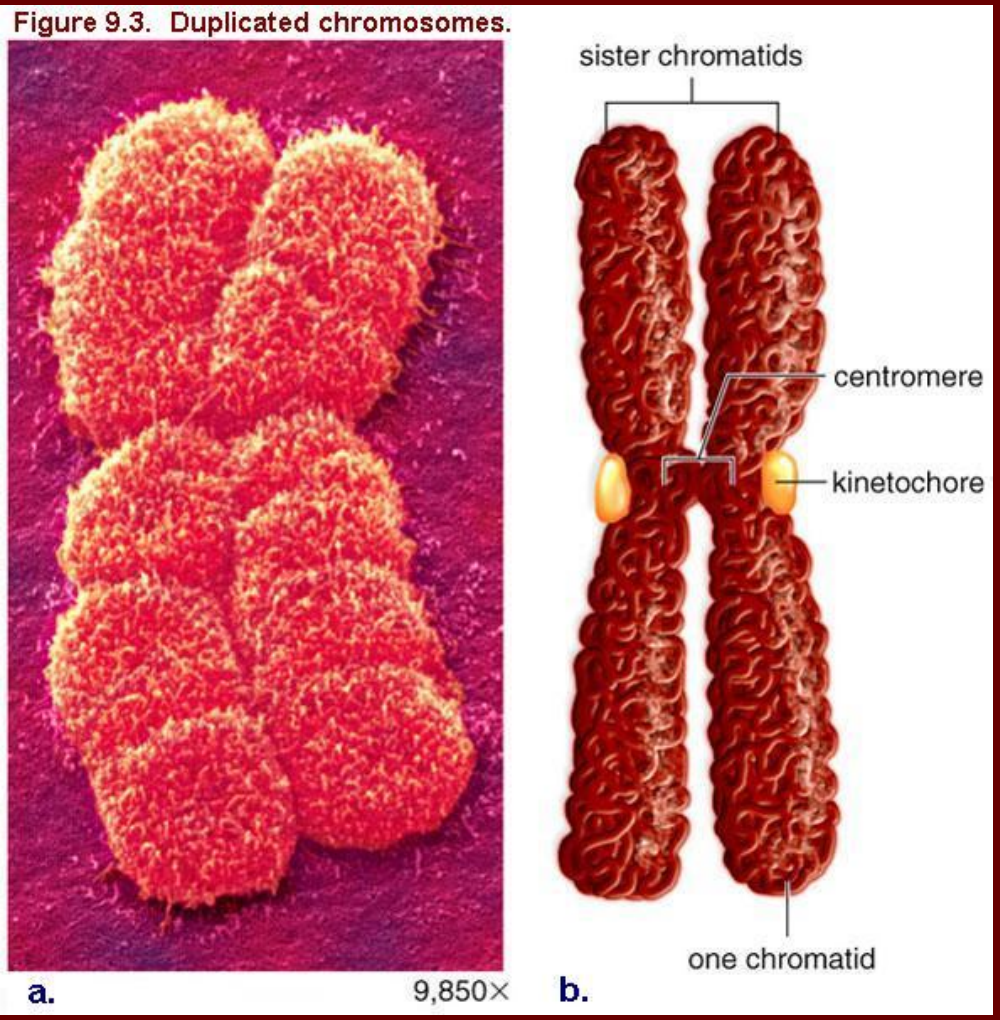


FIGURE 11-6. Human chromosomes during mitosis

- **Human chromosomes during mitosis.** The DNA and associated proteins in these duplicated human chromosomes, have coiled up into the thick, short **sister chromatids** attached at the **centromere**. Each visible strand of "texture" is a loop of DNA. During cell division, the condensed chromosomes are about 5 to 20 micrometers long. At other times, the chromosomes uncoil until they are about 10,000 to 40,000 micrometers long.

Duplicated Chromosomes



- A duplicated **chromosome** contains two **sister chromatids**, each with copies of the same genes.

a. Electron micrograph of a highly coiled and condensed **chromosome**, typical of a nucleus about to divide.

b. Diagrammatic drawing of a condensed chromosome. The chromatids are held together at a region called the **centromere**. The **kinetochore** is the portion of the chromosome centromere to which mitotic spindle fibers attach (during cell division).

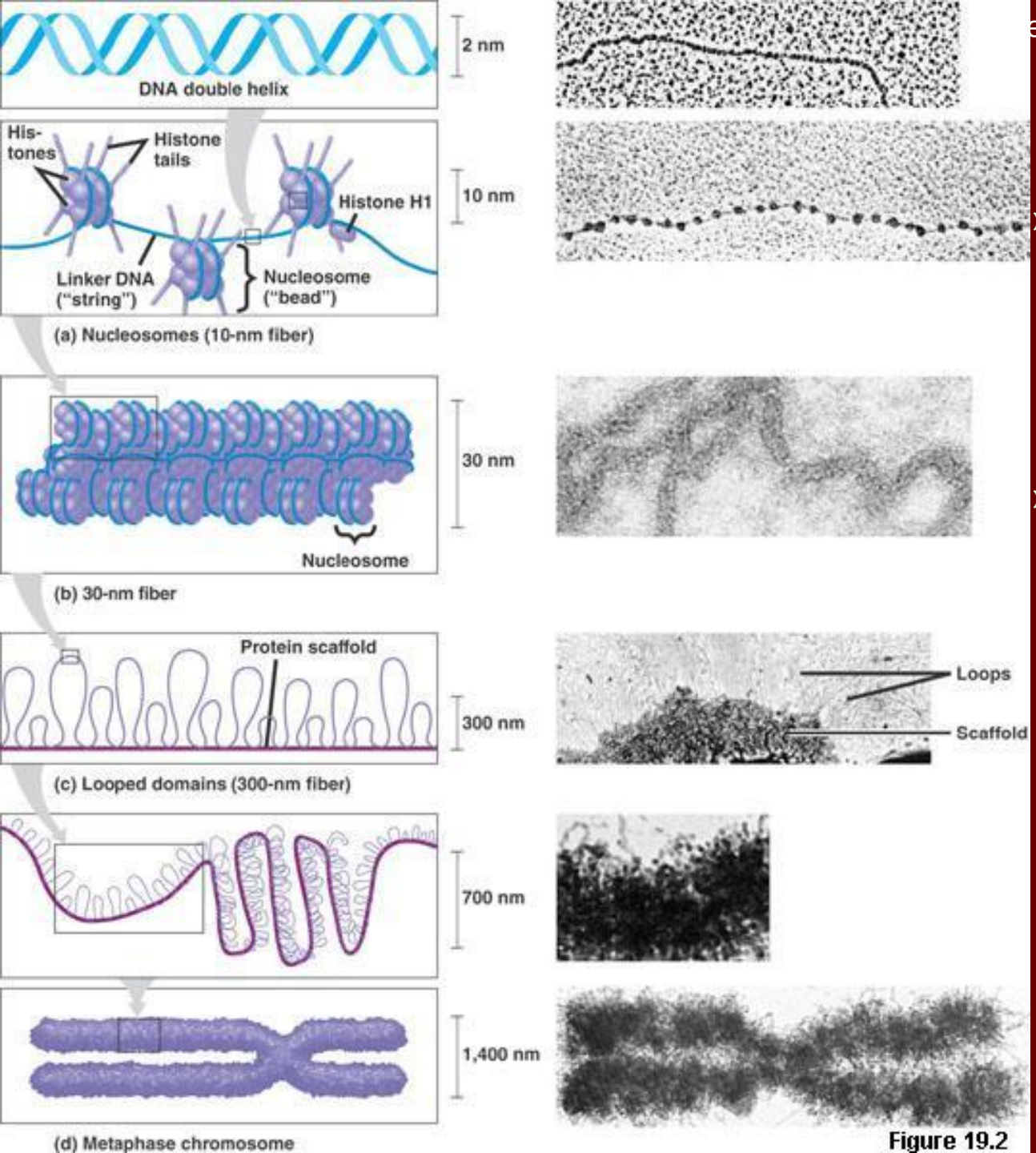


Figure 19.2

Organization of a Eukaryotic Chromosome

- These diagrams and transmission electron micrographs depict a current model for the progressive stages of DNA coiling and folding.
- Eukaryotic chromosomes have several levels of organization. The DNA is associated with **histones** (basic proteins) to form **nucleosomes**, each of which consists of a histone bead with DNA wrapped around it. The nucleosomes are organized into large, coiled loops held together by non-histone **scaffolding proteins**.

TABLE 9.1

Diploid Chromosome Numbers of Some Eukaryotes

Type of Organism	*Name of Organism*	*Chromosome Number*
Fungi	*Aspergillus nidulans* (mold)	8
	Neurospora crassa (mold)	14
	Saccharomyces cerevisiae (yeast)	32
Plants	*Vicia faba* (broad bean)	12
	Pisum sativum (garden pea)	14
	Zea mays (corn)	20
	Solanum tuberosum (potato)	48
	Nicotiana tabacum (tobacco)	48
	Ophioglossum vulgatum (Southern adder's tongue fern)	1,320
Animals	*Drosophila melanogaster* (fruit fly)	8
	Rana pipiens (frog)	26
	Felis domesticus (cat)	38
	Homo sapiens (human)	46
	Pan troglodytes (chimp)	48
	Carassius auratus (goldfish)	94

Chromosomes

- Chromosome number and informational content differ among species.
- Most human body cells have exactly **46** chromosomes.

Diploid (*2n*) number = Cell condition in which two of each type of chromosome are present.

The karyotype of a human male

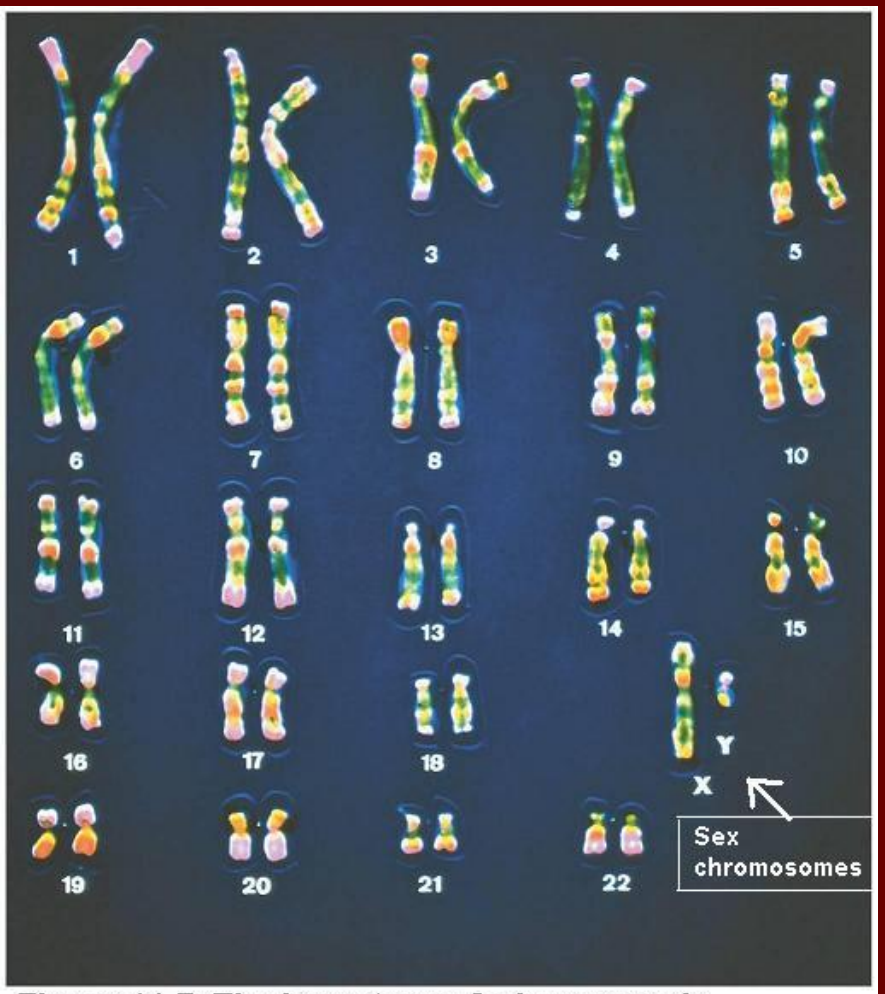
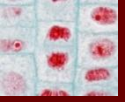


Figure 11-7. The karyotype of a human male.

- Staining and photographing the entire set of duplicated chromosomes within a single cell produces a **karyotype** (the chromosomal composition of an individual). Pictures of the individual chromosomes are cut out and arranged in descending order of size. The chromosome pairs (homologues) are similar in both size and staining pattern and have similar genetic material. Chromosomes 1 through 22 are the **autosomes**; the X and Y chromosomes are the **sex chromosomes**. Notice that the Y chromosome is much smaller than the X chromosome. If this were a female karyotype, it would have two X chromosomes.



Group Collaborative Activity: ***M Phase (Mitosis and Cytokinesis)***

- Organize a small group of 4-5 students.
- The instructor will assign a topic to each small group for discussion and presentation to the class.
- Prepare a brief summary of the topic and draw a sketch illustrating the most important aspects of the topic assigned. Use your textbook, previous knowledge, and any other resources available.
  - *Group 1*: Prophase
  - *Group 2*: Prometaphase
  - *Group 3*: Metaphase
  - *Group 4*: Anaphase
  - *Group 5*: Telophase and Cytokinesis

THE CELL CYCLE: **Interphase and Mitotic Phase**

- Repeating sequence of events in **eukaryotic** cells that involve cell growth, nuclear division and cytoplasmic division.
- It consists of the following stages:

1. **Interphase:** Three subphases of growth and DNA replication. It is the longest part; it usually accounts for **90%** of the cycle.
   a) **G_1 phase ("first gap"):** Cell growth; cell performs everyday functions such as producing proteins, organelles, substances.
   b) **S phase ("synthesis"):** Growth and DNA replication or synthesis (results in duplicated chromosomes)
   c) **G_2 phase ("second gap"):** Growth, more protein synthesis, and final preparations for cell division
2. **Mitotic (M) phase**: Cell division (nucleus & cytoplasm divide)
   a) **Mitosis:** Nuclear division. Its stages are: ***prophase***, ***prometaphase***, ***metaphase***, ***anaphase***, and ***telophase***.
   b) **Cytokinesis:** Division of the cytoplasm (the cell contents), resulting in two daughter cells; overlaps the last stage of mitosis.

THE CELL CYCLE: **Duration for a Particular Human Cell**

- A particular human cell might undergo one division in 24 hours.
- The duration of each phase depends on the type of cell.

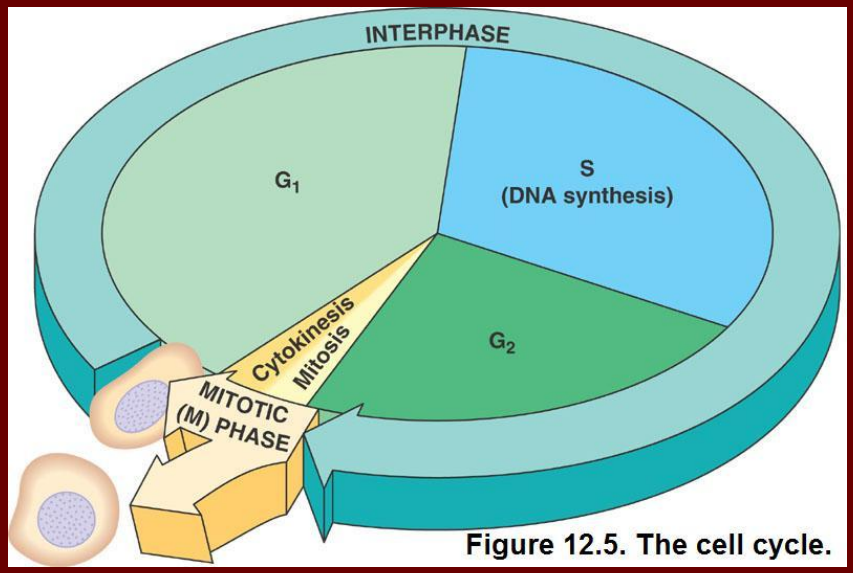


Figure 12.5. The cell cycle.

- **G_1 phase (growth):** 5-6 hours; the most variable in length in different types of cells
- **S phase (DNA synthesis):** About 10-12 hours (or about half the cycle)
- **G_2 phase (growth):** 4-6 hours
- **Mitotic (M) phase (nuclear and cytoplasmic division):** Less than 1 hour

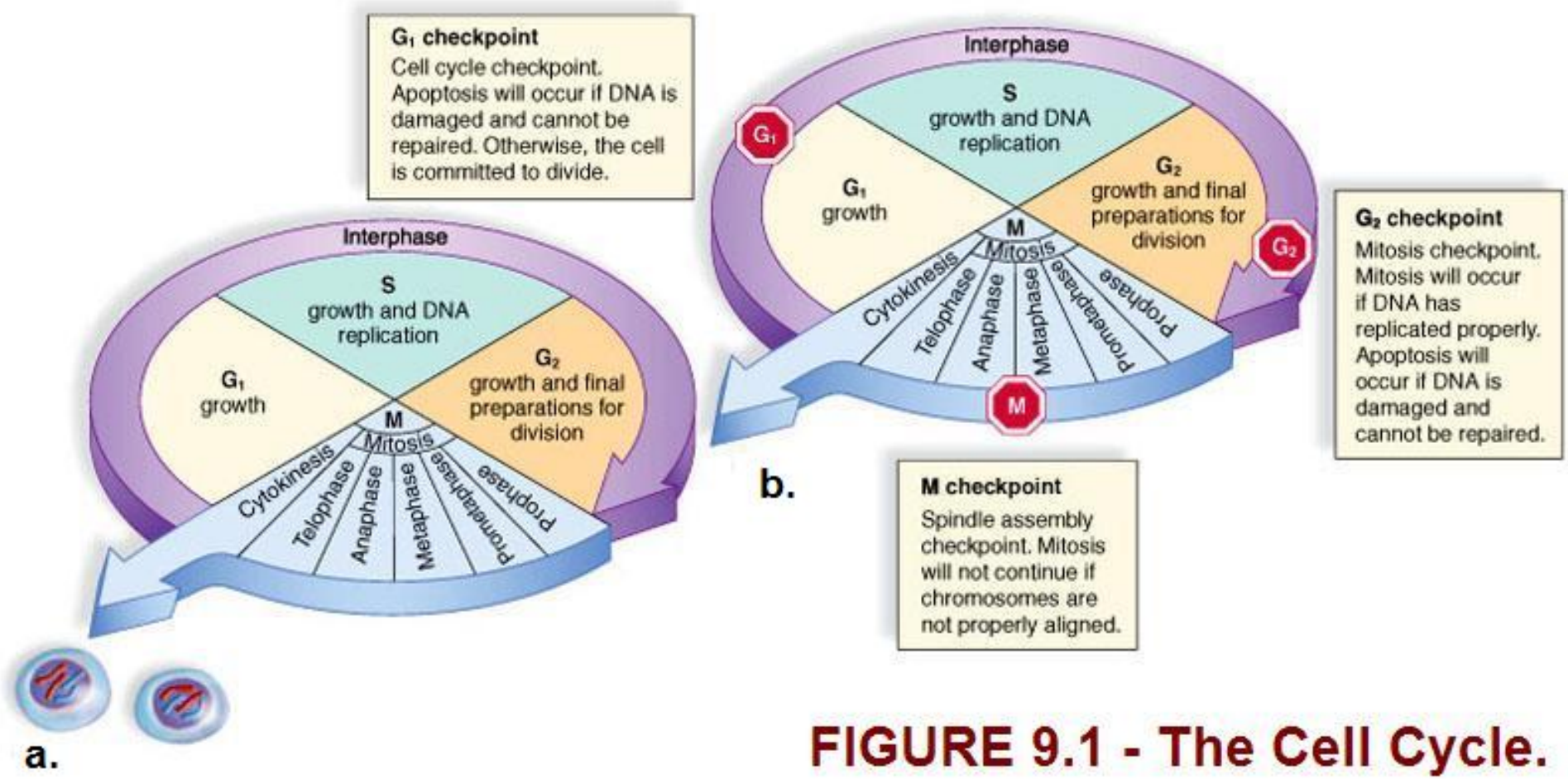


FIGURE 9.1 - The Cell Cycle.

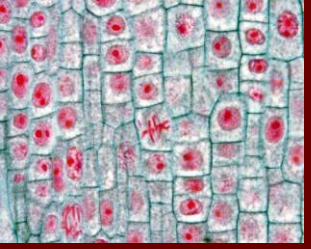
a) The cell cycle is an ordered, repeating sequence of events in the life of a ***eukaryotic*** cell (cell with nucleus) that involves ***cell growth***, ***nuclear division*** and ***cytoplasmic division***; it consists of the stages **G_1, S, G_2,** and **M**.

b) The cell cycle stops at checkpoints (in red) if necessary. *Apoptosis*, or programmed cell death, occurs if the cell is damaged in some way.

MITOSIS: *Basic Terms*

Mitotic spindle	An assemblage of **microtubules** (protein fibers) that brings about chromosomal movement during nuclear division.
Centrosome	Central *microtubule organizing center* of cells. In animal cells it contains two **centrioles** (organelles that help organize the mitotic spindle; not essential for cell division and absent in plant cells).
Centromere	Constriction or region of the chromosome where the two **sister chromatids** (chromosomal units) are held together.
Kinetochore	**Disk-shaped protein structure** within the centromere of a chromosome to which spindle microtubules become attached during mitosis and meiosis.
Metaphase plate	An **imaginary plane** (like a disk) formed during metaphase in which all of a cell's chromosomes are located midway between the two poles.

**** Note:*** *This is a summary of some terms that will help you understand mitosis. Review other terms in your book. *** Study the figures.*



MITOSIS

- *** Study all the figures here and in your book to make sure that you understand all the stages of **mitosis**, one of the stages of the cell cycle.
  - **Prophase, prometaphase, metaphase, anaphase**, **telophase**.
  - **Cytokinesis**, the division of the cytoplasm, is usually well under way by late telophase.
- Remember that mitosis is one of the subphases of the **cell cycle**. *** Study and understand all the stages and subphases of the cell cycle.
- *** Compare mitosis with meiosis and make sure that you understand the similarities and the differences between these two processes.

**** Study the figures carefully!***

SUMMARY OF THE PHASES OF MITOSIS

1. **Prophase:** Chromatin condenses into chromosomes; nuclear envelope (membrane) starts to fragment; nucleolus disappears: mitotic spindle begins to form (it will be involved in movement of chromosomes).
2. **Prometaphase (Late Prophase):** Nuclear membrane fragments even more; chromosomes even more condensed; some microtubules attach to kinetochores of chromatids.
3. **Metaphase:** Chromosomes are aligned at the *metaphase plate* (cell's "equator"); *kinetochores* of *sister chromatids* are attached to microtubules coming from opposite poles. Longest stage (about 20 minutes).
4. **Anaphase:** The two sister chromatids separate and become daughter chromosomes that move toward the poles (opposite ends) of the cell's mitotic spindle. The cell elongates. Shortest stage (a few minutes).
5. **Telophase:** Daughter cells are almost formed when nuclei begin to form; nuclear membrane and nucleoli reappear; chromosomes decondense (extend) and become indistinct chromatin. **Mitosis**, the division of one nucleus into two genetically identical nuclei, is now **complete**.

- **Cytokinesis**, division of cytoplasm, generally begins during late telophase.

FIGURE 9.4 - Phases of Mitosis in Animal and Plant Cells.

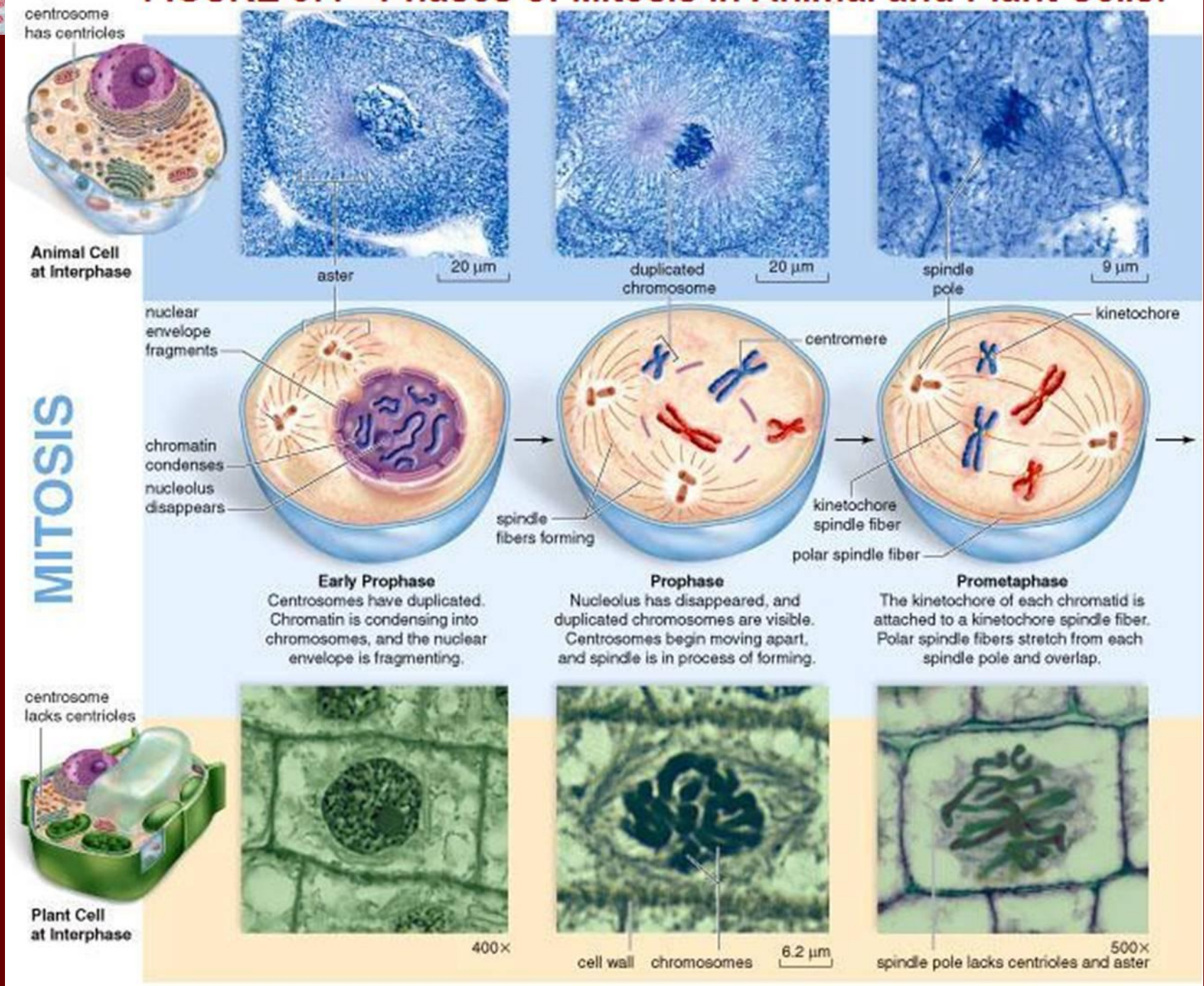
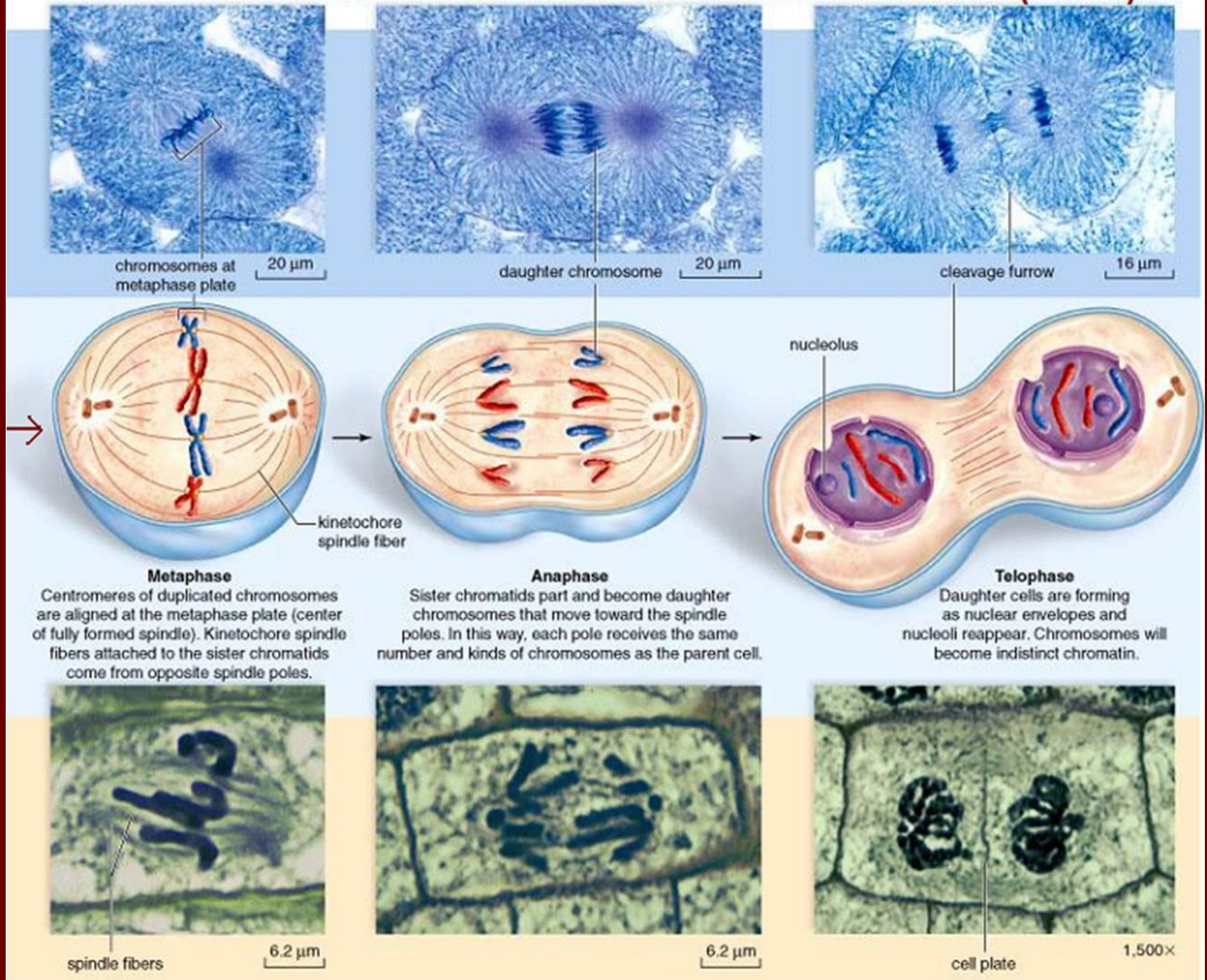


FIGURE 9.4 - Phases of Mitosis in Animal and Plant Cells (Part 2)



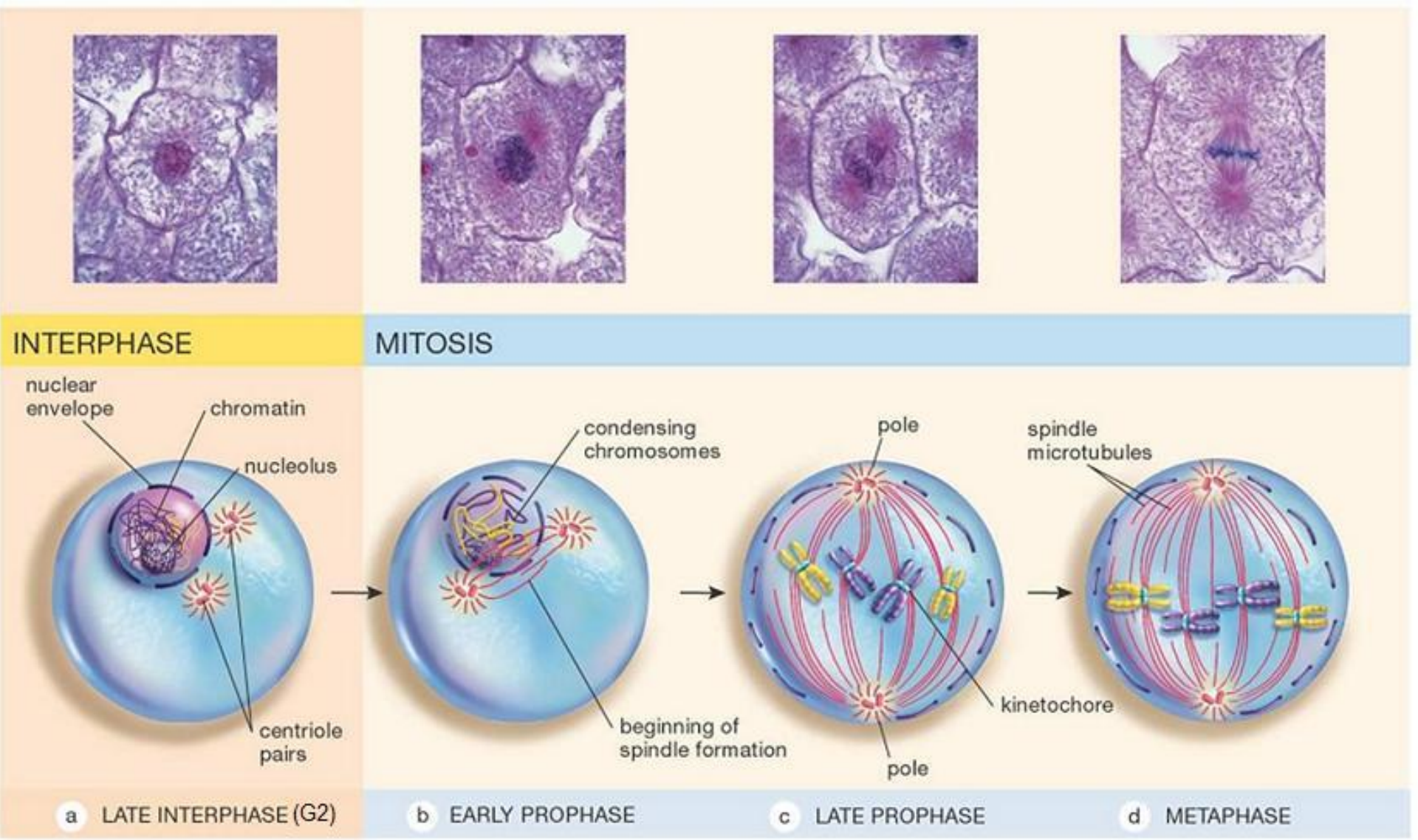


FIGURE 11-8. Mitotic Cell Division in an Animal Cell.

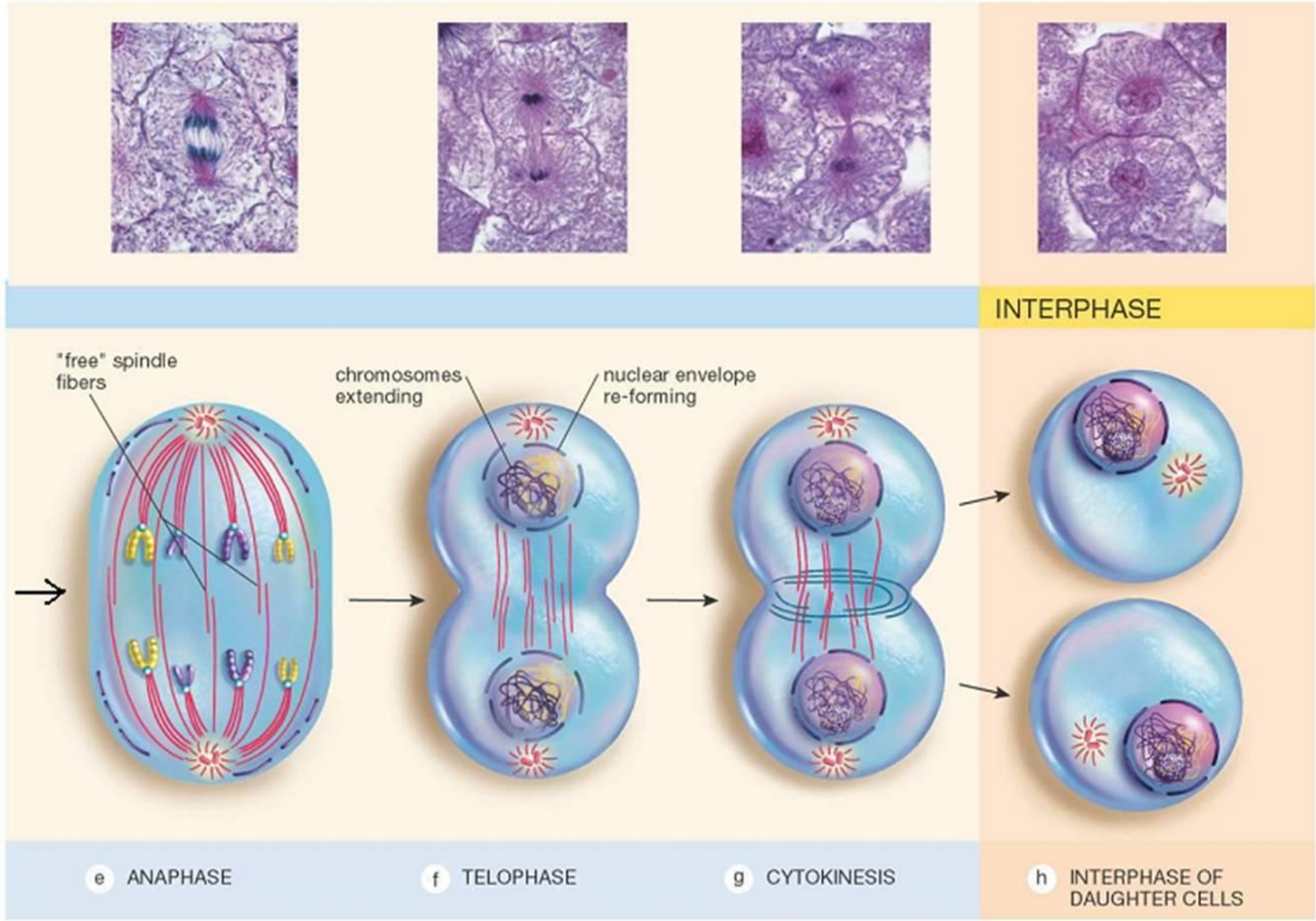
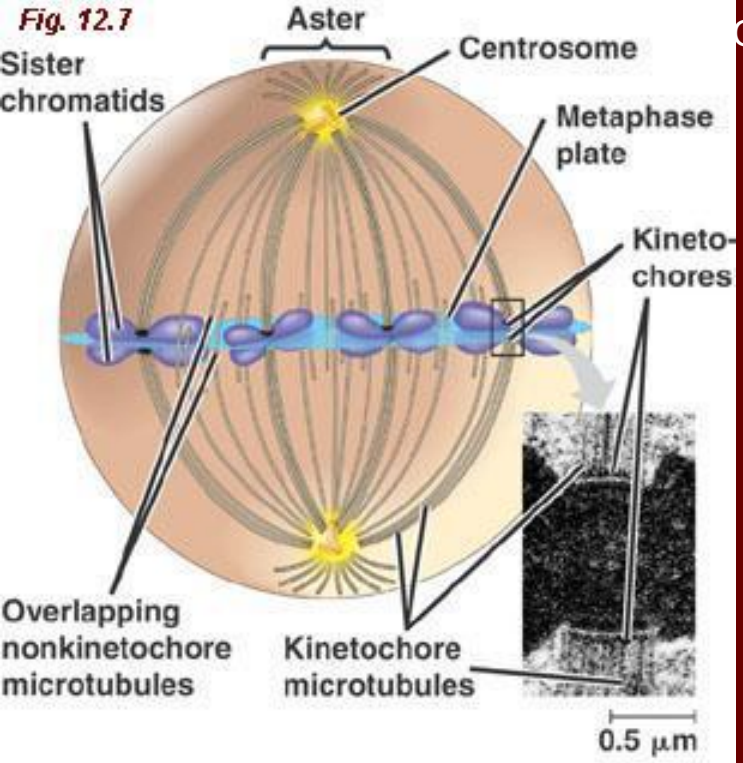
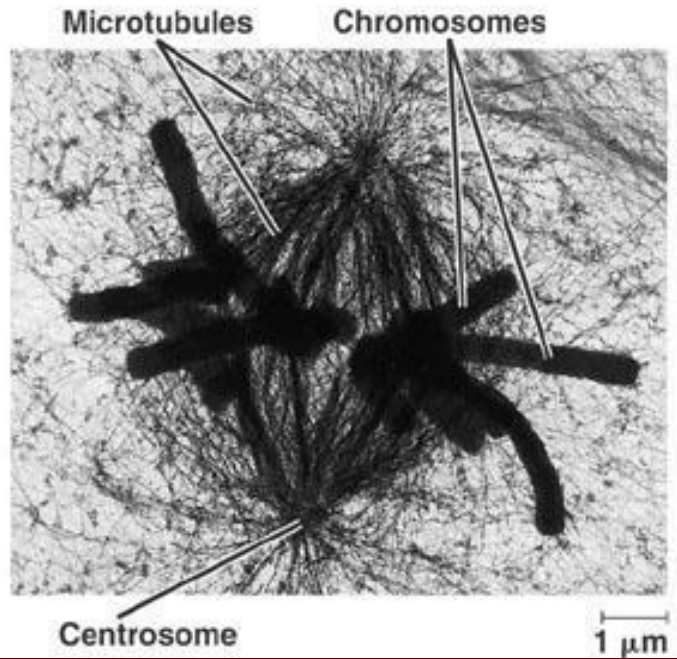


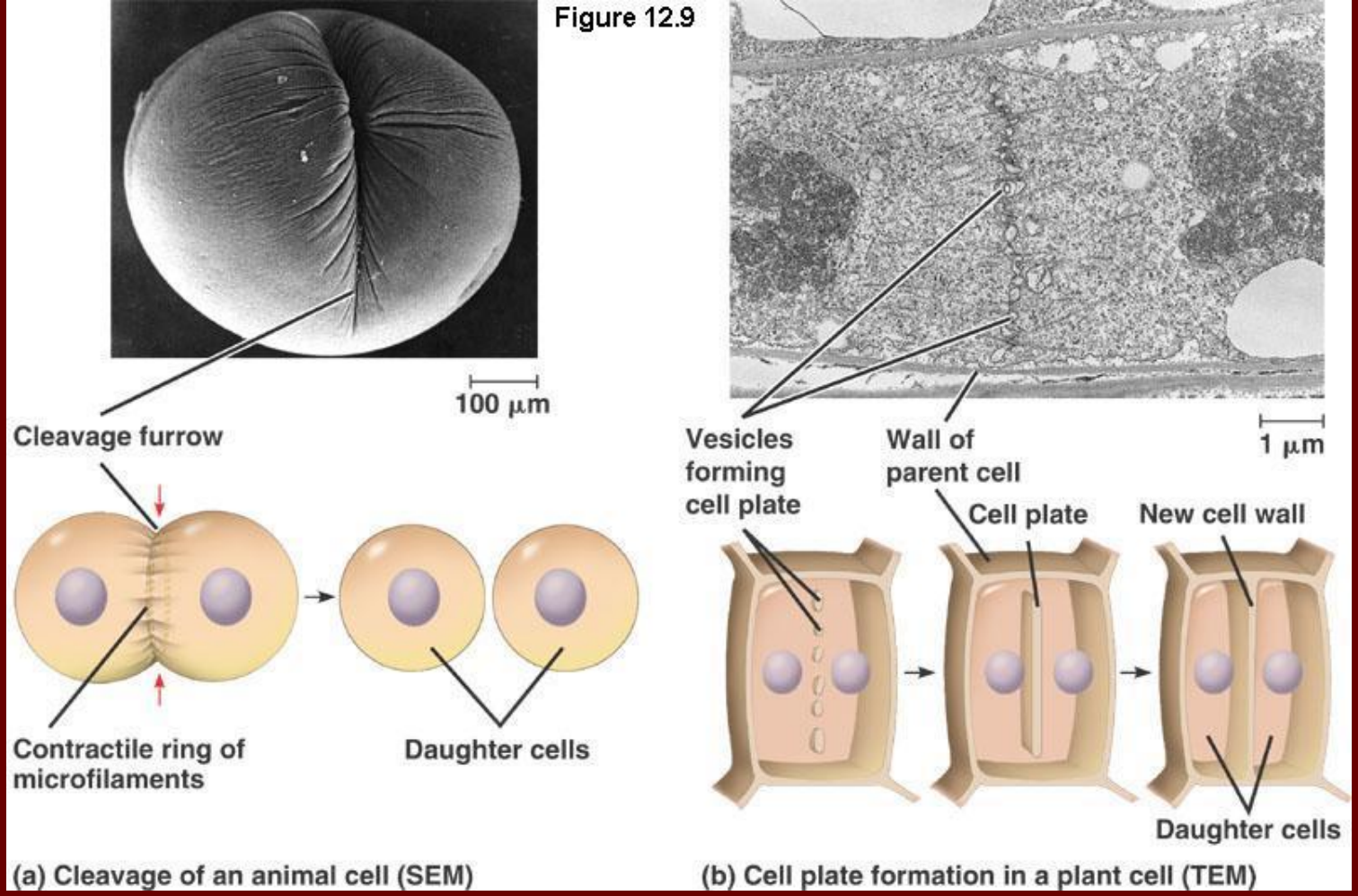
FIGURE 11-8. Mitotic Cell Division in an Animal Cell (Part 2)





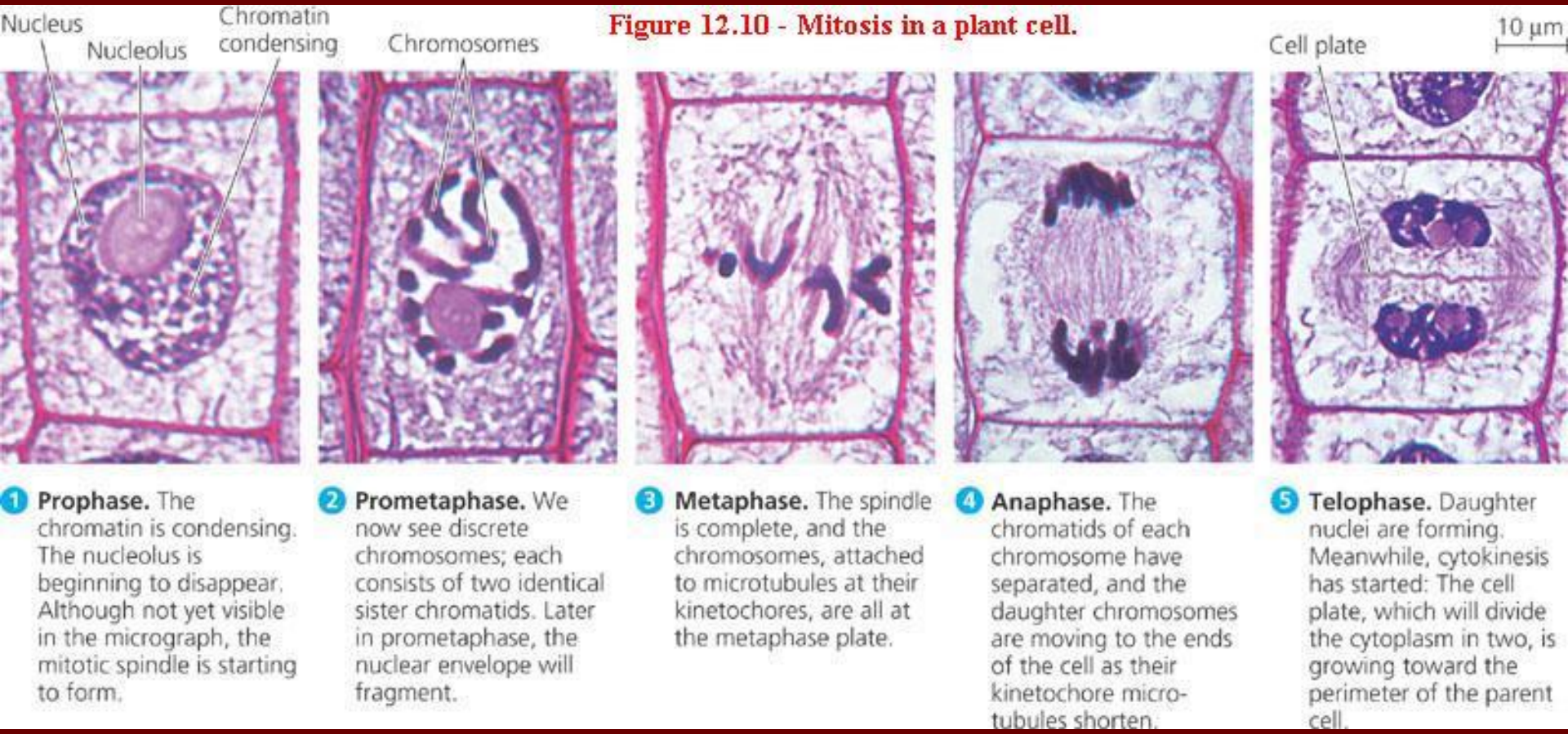
The Mitotic Spindle at Metaphase

- The **mitotic spindle** is an assembly of microtubules (protein fibers) that help chromosomal movement during nuclear division. It begins to form during prophase.
- In animal cells, the assembly of spindle microtubules starts at a *microtubule-organizing center* called the **centrosome**.
- An **aster**, a radial array of short microtubules, extends from each centrosome.
- Each of the two sister chromatids of a replicated chromosome has a **kinetochore**, a protein structure within the **centromere** that joins the chromatids. Each kinetochore is attached to a cluster of microtubules extending from the nearest centrosome.
- In metaphase, the duplicated chromosomes align on an imaginary plane midway between the spindle's 2 poles, the **metaphase plate**.



- **Cytokinesis (division of cytoplasm) in animal and plant cells**
  - In *animal and fungal cells*, cytokinesis occur by a process known as **cleavage**; an actomyosin ring contracts forming a **cleavage furrow**.
  - In *plant cells*, there is no cleavage but the formation of a **cell plate**, a partition that grows laterally towards the cell wall.

Mitosis in a Plant Cell (*Onion Root*)



⌑ **Figure 12.10. Mitosis in a plant cell.** These light micrographs show mitosis in cells of an **onion root**.

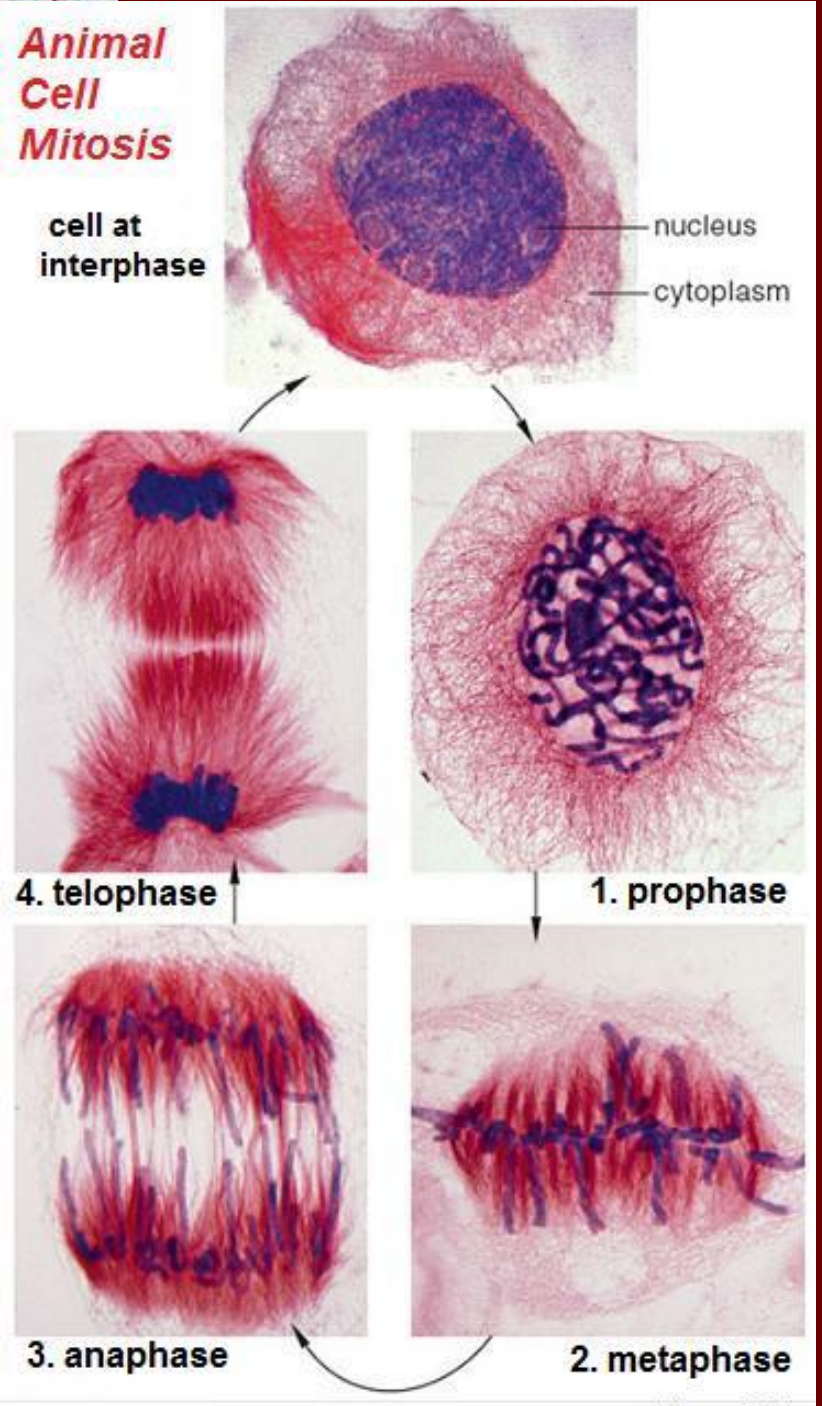


Figure 8.14

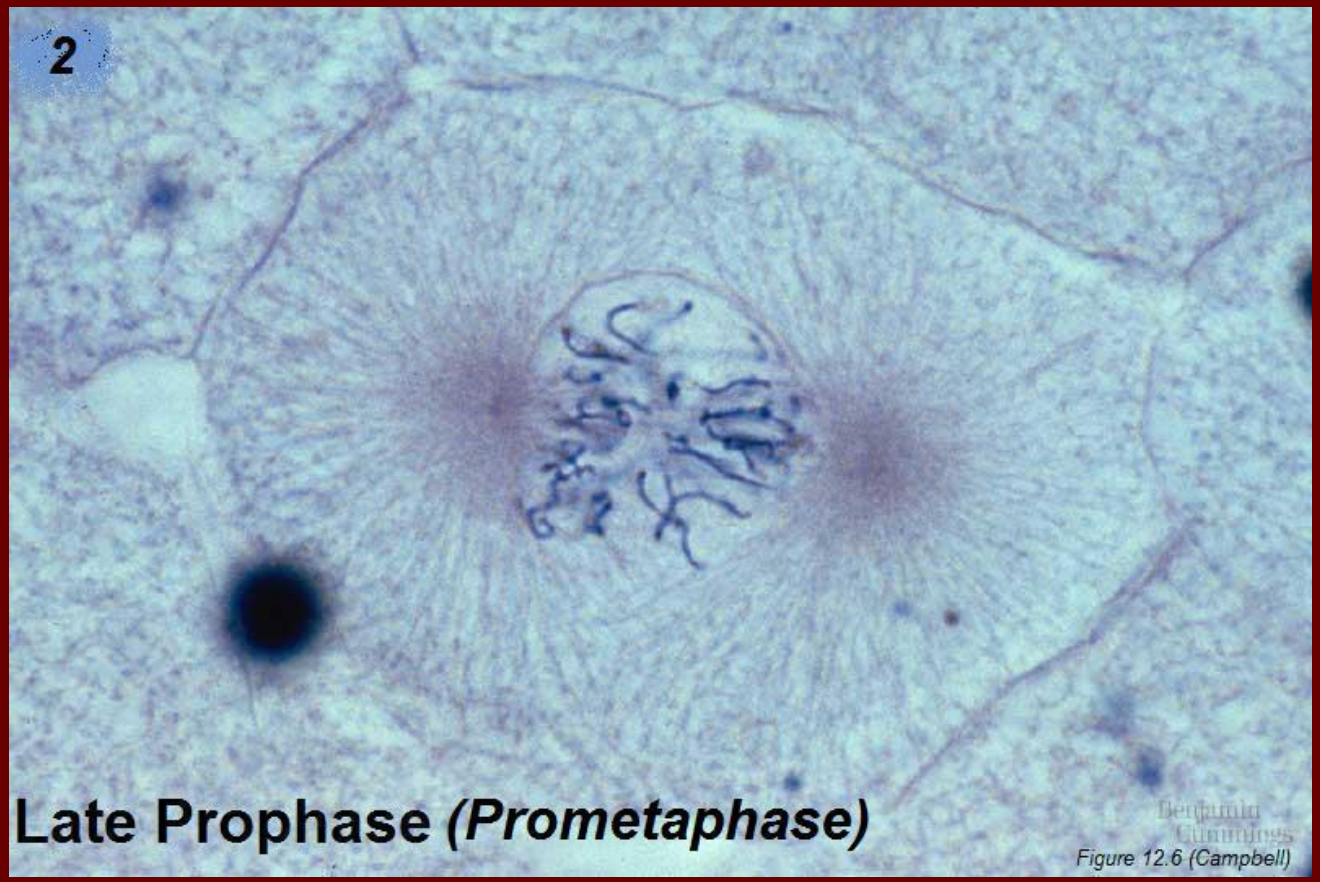
Mitosis in an Animal Cell

1. **Prophase:** Chromatin is condensing; nuclear membrane fragments; mitotic spindle starts to form.
2. **Metaphase:** Chromosomes more condensed and aligned at metaphase plate; chromatids attached to microtubules from opposite poles.
3. **Anaphase:** Sister chromatids separate and move to opposite poles of mitotic spindle; cell elongates.
4. **Telophase:** Daughter cells almost formed when nuclei begin to form; nuclear membrane reappears; chromosomes decondense (become chromatin). Mitosis, the division of one nucleus into two genetically identical nuclei, is now complete. ***Cytokinesis*** generally begins during telophase.

PHASES OF MITOSIS: *Review*

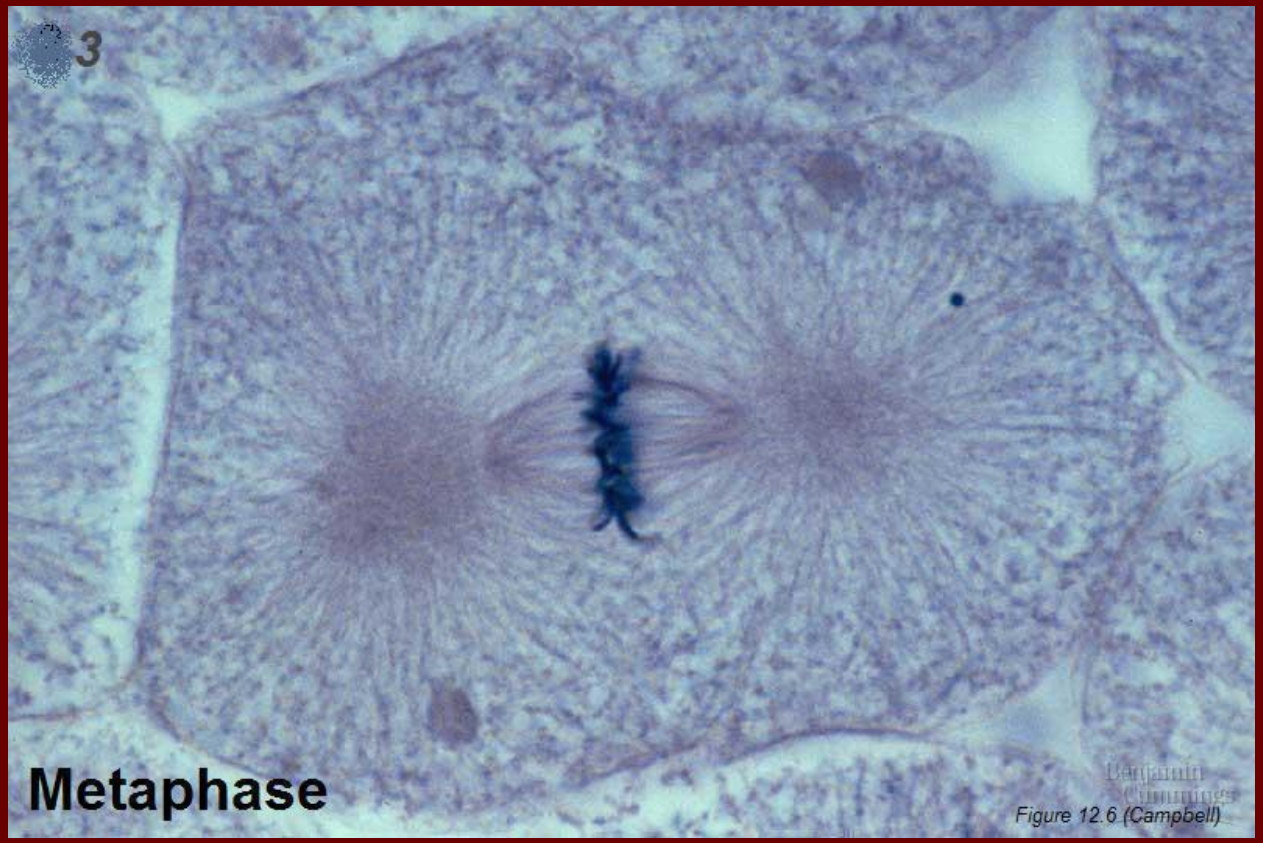
1. **Prophase:** Chromatin **condenses** into chromosomes; nuclear envelope (membrane) is **fragmenting**; nucleolus disappears: **mitotic spindle** begins to form (it will be involved in movement of chromosomes).

PHASES OF MITOSIS: *Review*



2. **Prometaphase (Late Prophase):** Nuclear membrane **fragments**; chromosomes even more condensed and defined; some **microtubules attach** to kinetochores of chromatids.

PHASES OF MITOSIS: *Review*



3. **Metaphase:** Chromosomes are **aligned** at the *metaphase plate* (cell's "equator"); *kinetochores* of *sister chromatids* are attached to microtubules coming from opposite poles. Longest stage (about 20 minutes).

PHASES OF MITOSIS: *Review*

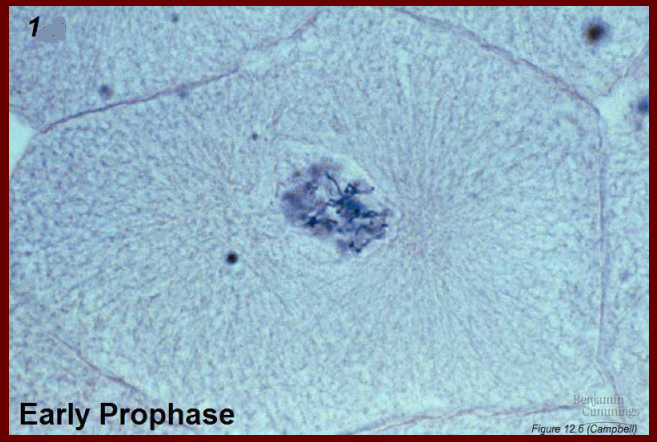
4. **Anaphase:** The two ***sister chromatids*** **separate** and become daughter chromosomes that **move toward the poles** (opposite ends) of the mitotic spindle. The cell elongates. Shortest stage (a few minutes).

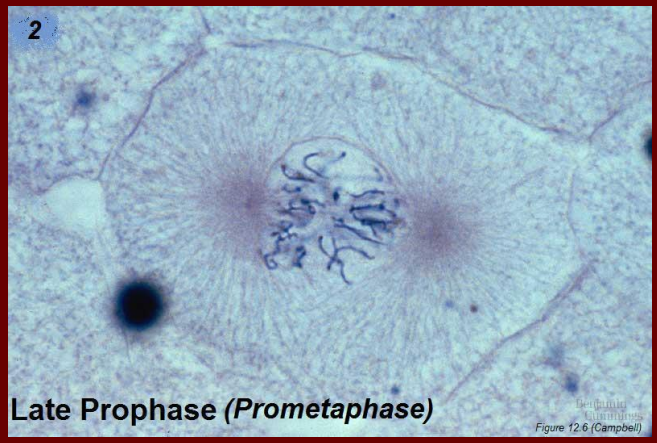
PHASES OF MITOSIS: *Review*

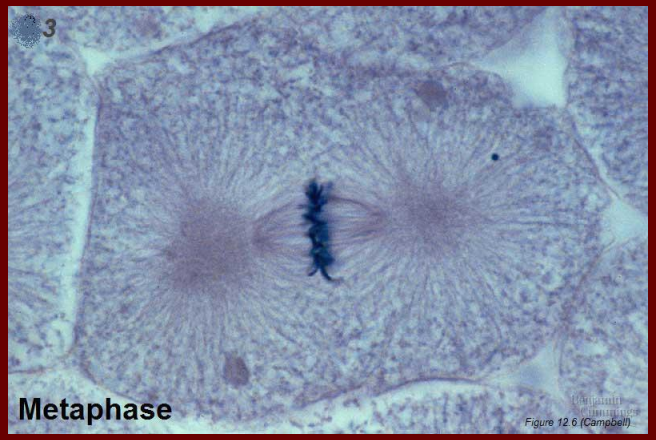
5. **Telophase:** Daughter **nuclei** begin to form; nuclear membrane and nucleoli reappear; chromosomes **decondense** and become indistinct **chromatin**. Mitosis, the division of one nucleus into two genetically identical nuclei, is now complete.

PHASES OF MITOSIS: *Review*

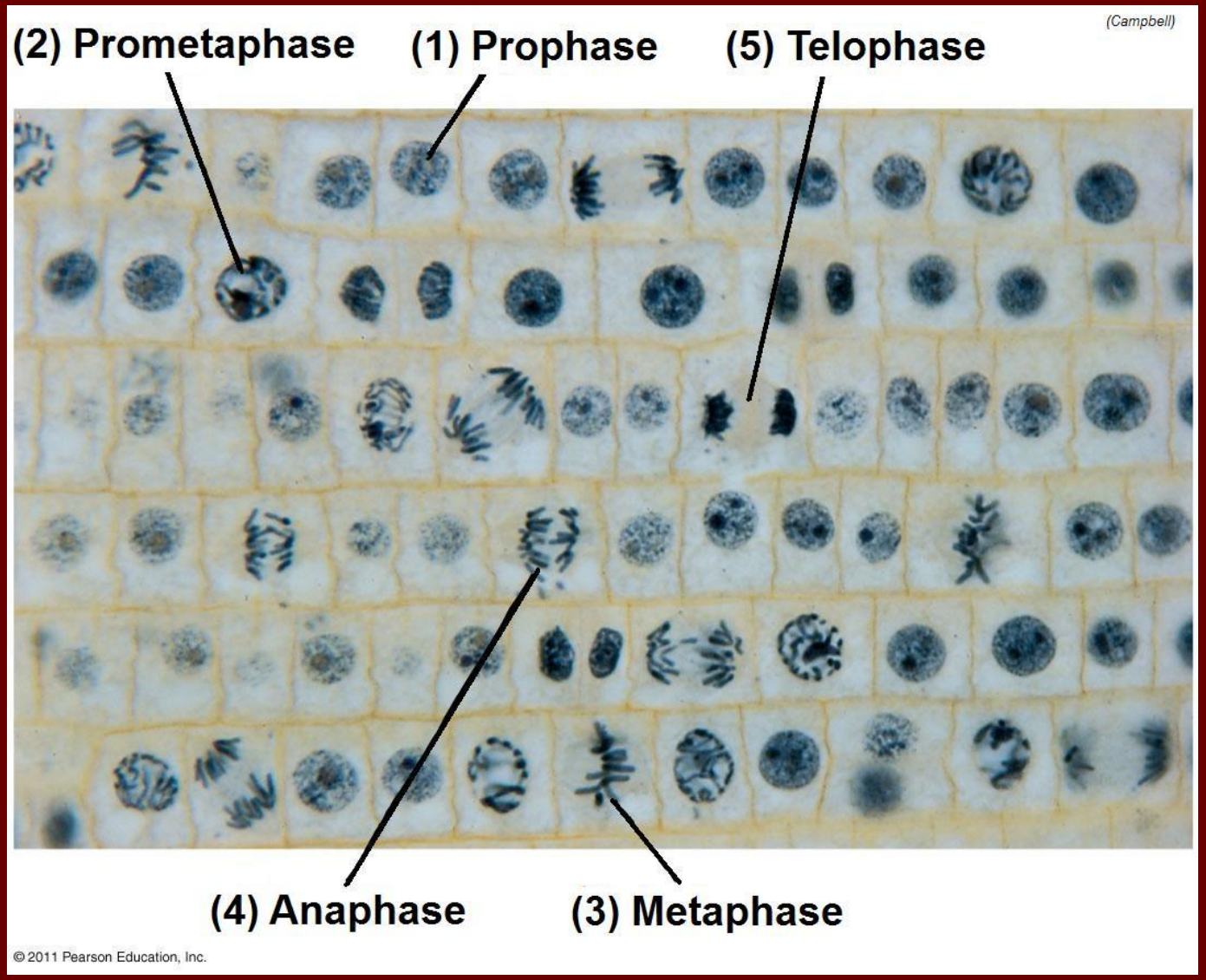
1) **Prophase**
2) **Prometaphase**
3) **Metaphase**
4) **Anaphase**
5) **Telophase**







PHASES OF MITOSIS: *Review*



Prokaryotic Cell Division: **Binary Fission**

- **Prokaryotic** organisms (microorganisms without a cell nucleus, such as ***archaea*** and ***bacteria***) reproduce **asexually** through **binary fission**, the splitting of a parent cell into two daughter cells that are identical to the original parent cell.
- In summary, in binary fission:
  - First, the circular DNA replicates, and as the cell lengthens, the two identical chromosomes separate, moving to opposite ends of the cell. Then, the cell becomes divided. The two resulting bacteria are identical.

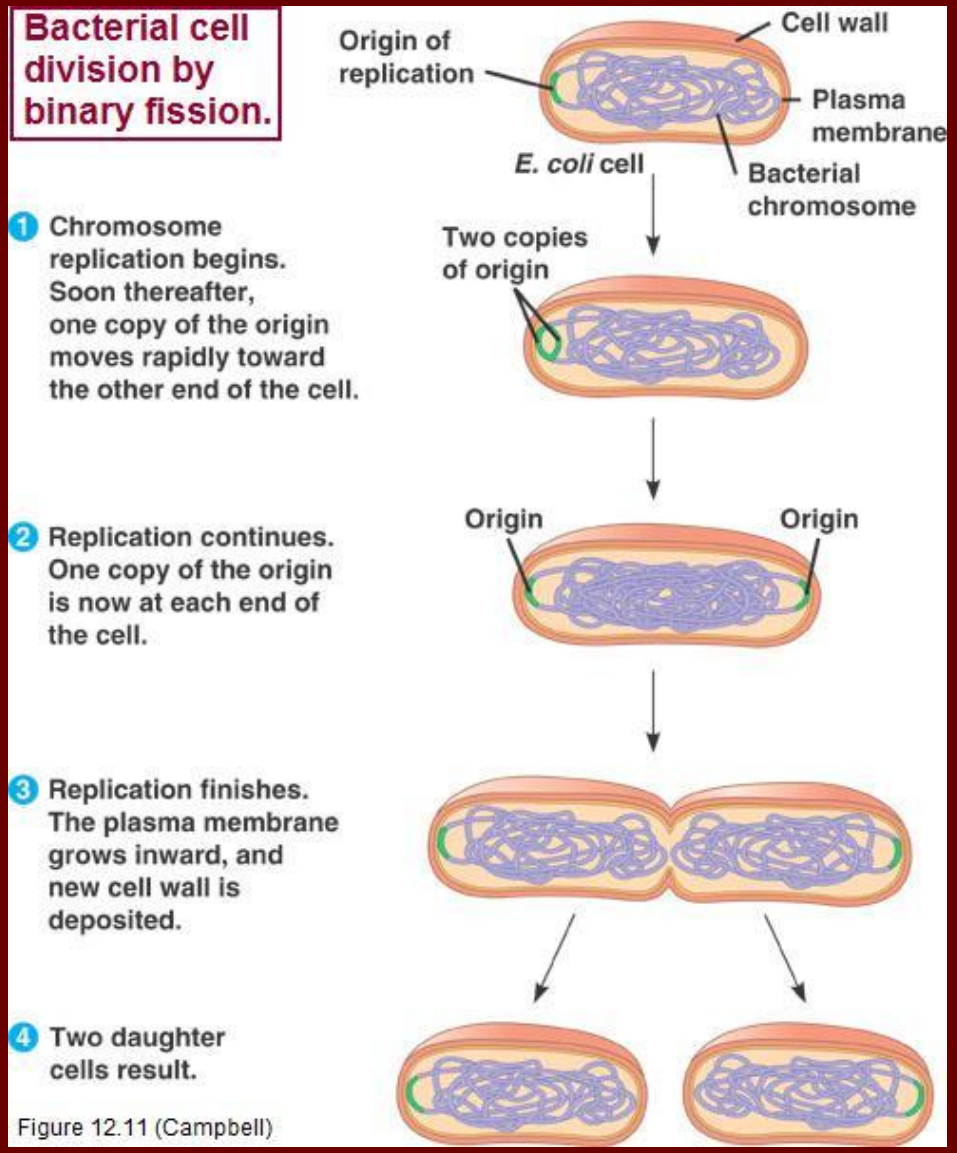


Figure 12.11 (Campbell)

Figure 9.9. Binary fission.

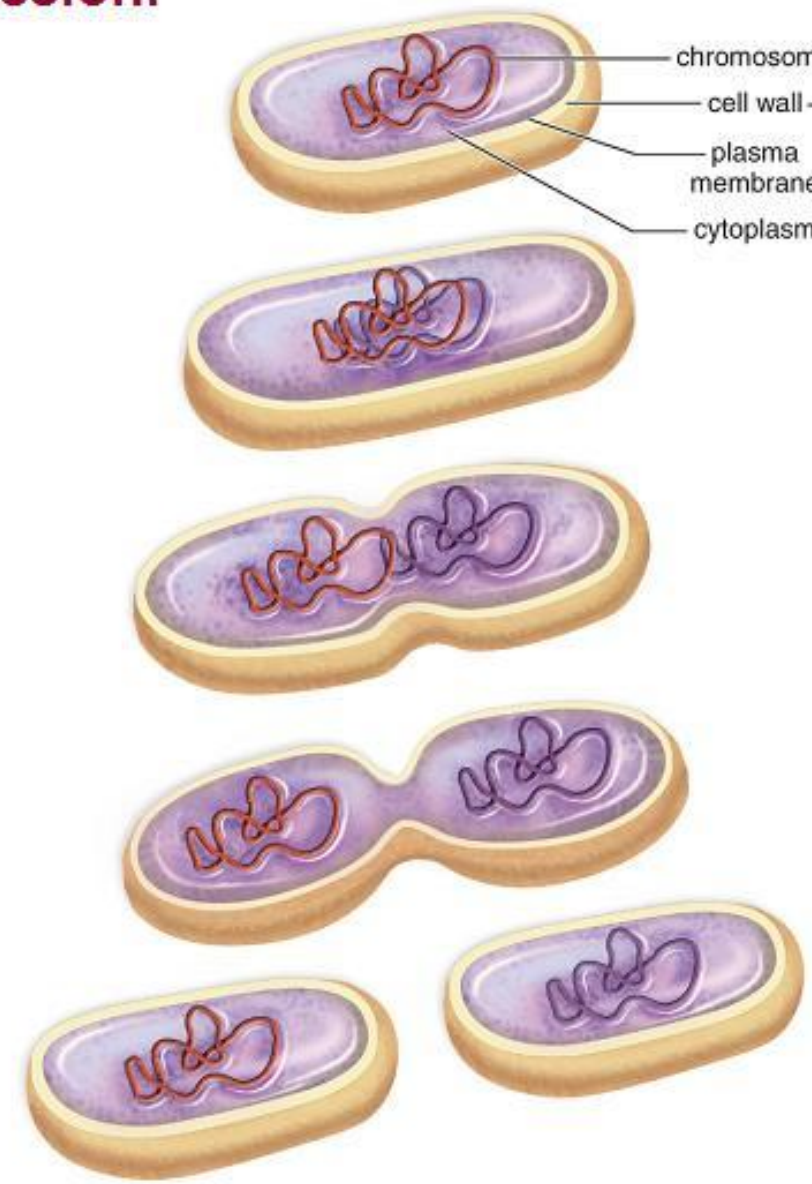
1. Attachment of chromosome to a special plasma membrane site indicates that this bacterium is about to divide.

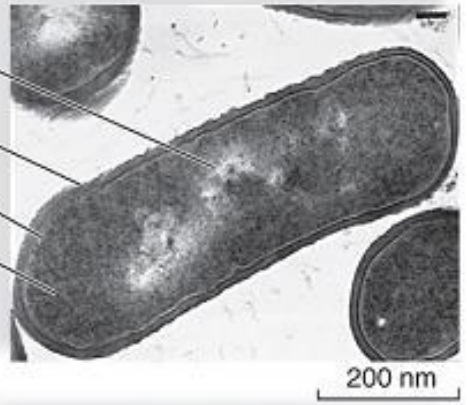
2. The cell is preparing for binary fission by enlarging its cell wall, plasma membrane, and overall volume.

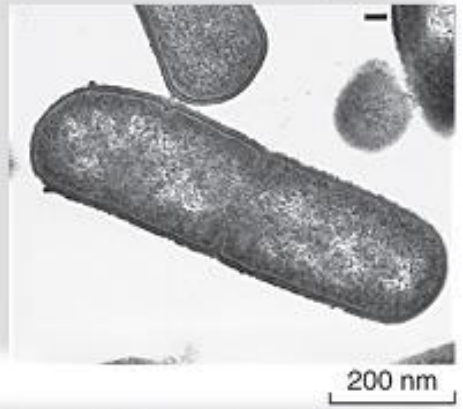
3. DNA replication has produced two identical chromosomes. Cell wall and plasma membrane begin to grow inward.

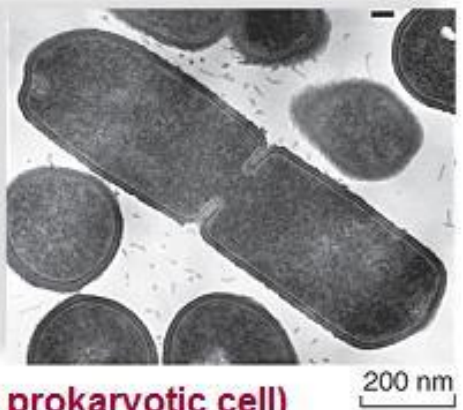
4. As the cell elongates, the chromosomes are pulled apart. Cytoplasm is being distributed evenly.

5. New cell wall and plasma membrane has divided the daughter cells.









Cell division by binary fission in a bacterium (a prokaryotic cell)

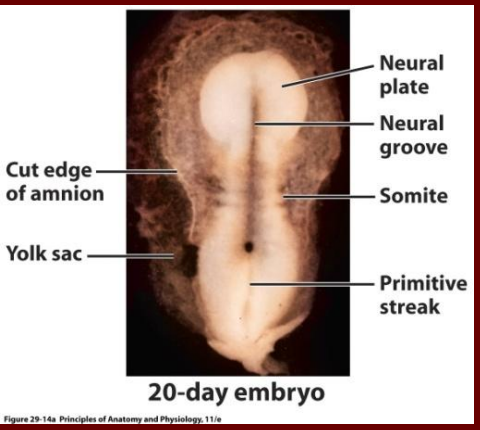
TABLE 9.3

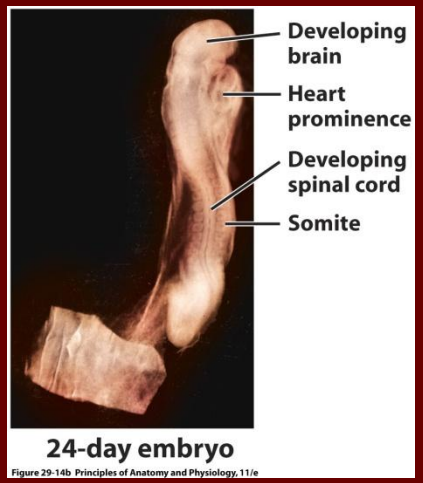
Functions of Cell Division

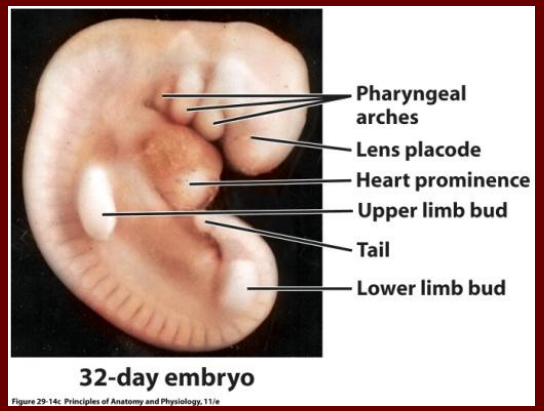
Type of Organism	*Cell Division*	*Function*
Prokaryotes Bacteria and archaea	Binary fission	Asexual reproduction
Eukaryotes		
Protists, and some fungi (yeast)	Mitosis and cytokinesis	Asexual reproduction
Other fungi, plants, and animals	Mitosis and cytokinesis	Development, growth, and repair

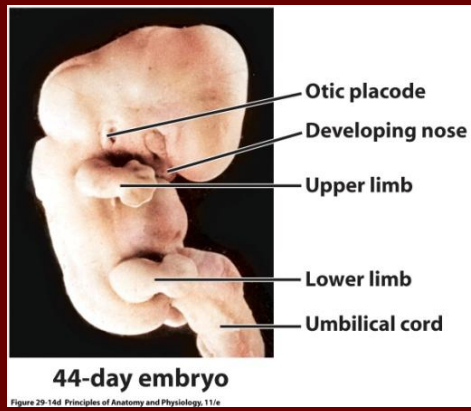
Appreciate the Process!

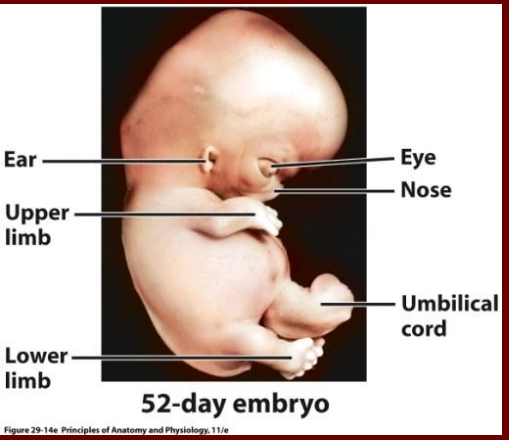
Human Embryonic Development: Cell Division and Cell Differentiation

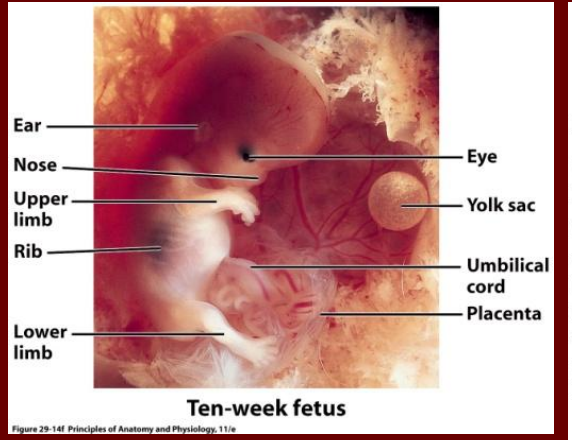


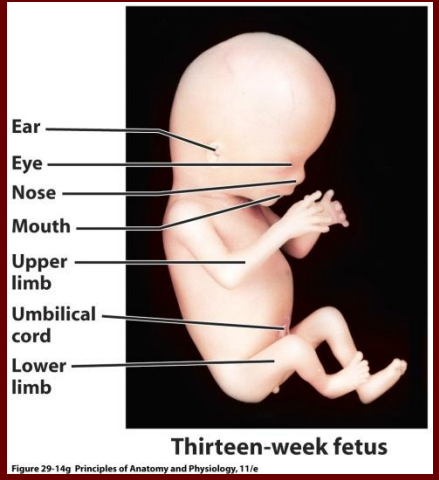


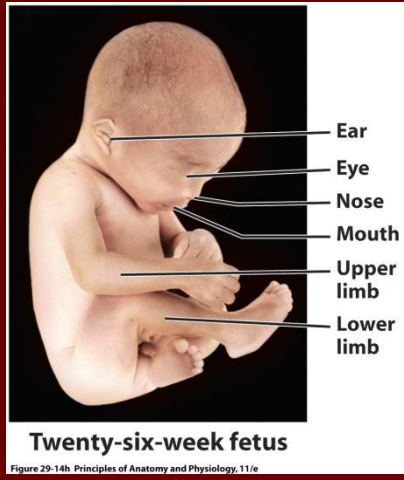








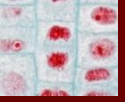




The process of differentiation (specialization in form and function) does not happen all at once. Body parts and organs emerge gradually.

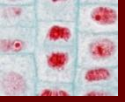
Regulation of the Eukaryotic Cell Cycle

- The timing and rate of cell division in different parts of a plant or animal are crucial to normal growth, development, and maintenance.
- The **frequency** of cell division varies with the type of cell.
  - *Skin cells* divide frequently, while *liver cells* divide when an appropriate need arises, for example, to repair a wound.
  - The most specialized cells such as *nerve cells* and *muscle cells* do not divide at all in a mature human.
- These cell cycle differences result from **molecular regulation** (specific molecules control the cell cycle).



Regulation of the Eukaryotic Cell Cycle

- The cell cycle is regulated at certain **checkpoints** (control points) by both **internal and external signals**.
- A **signal** is a molecule that stimulates or inhibits a metabolic event. These signals ensure that the stages follow one another in the normal sequence and that each stage is properly completed before the next stage begins. For example:
  - **Growth factors:** Proteins that act as external signals received at the plasma membrane (cell membrane); they stimulate cell proliferation and differentiation.



The Cell Cycle Control System

- The **cell cycle control system** is a cyclically operating set of molecules in the cell that both triggers and coordinates key events in the cell cycle.
  - Compare it to the control device of an automatic washing machine.
- Cyclic changes in regulatory proteins work as a **"cell cycle clock"**.
- There are specific **checkpoints**, critical control points in the cell cycle where *stop and go-ahead signals* can regulate the cycle.
- *** The key **regulatory molecules** in the control of the cell cycle are **cyclins** and **cyclin-dependent kinases (Cdks)**.
  - The activity of a **Cdk** rises and falls with changes in the concentration of its **cyclin** partner.
  - **M-Cdk, or MPF (maturation-promoting factor):** cyclin-Cdk complex that was discovered first (in frog eggs). We can think of it as "M-phase promoting factor" because it triggers the cell's passage past the G_2 checkpoint into M phase.

Mechanical Analogy for the Cell Cycle Control System

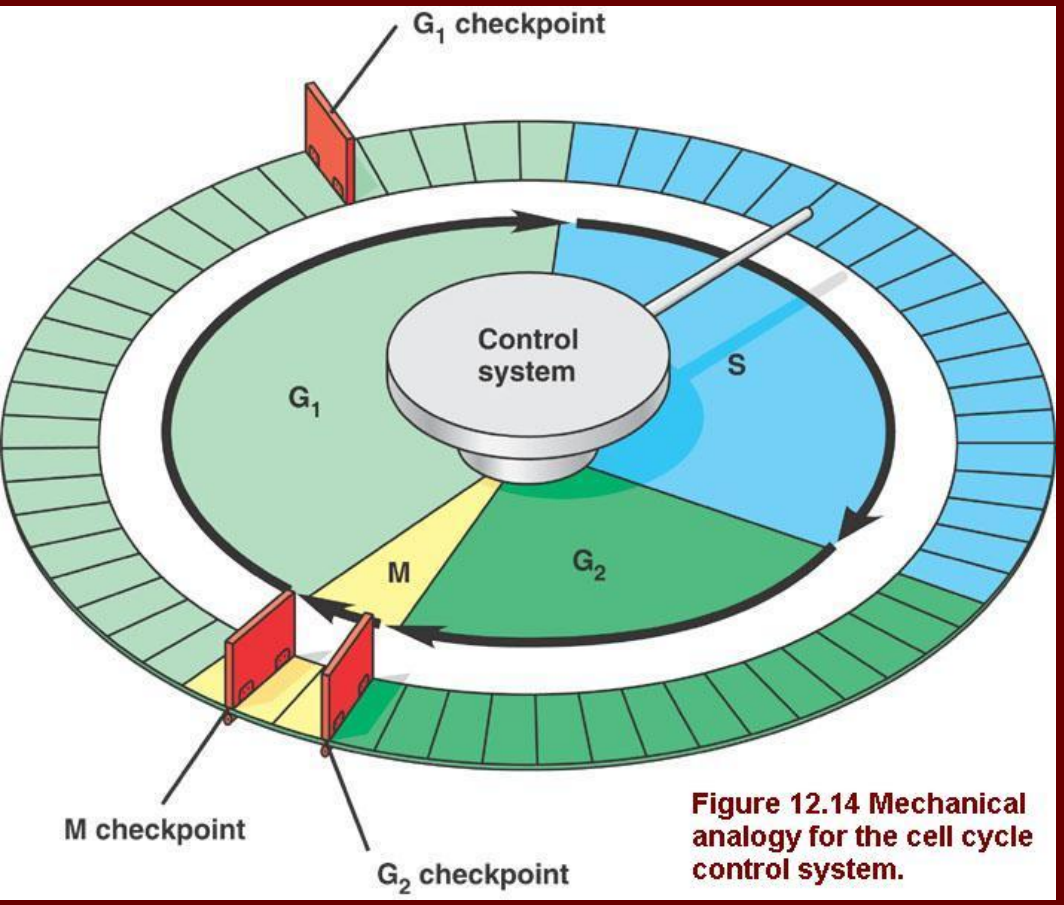


Figure 12.14 Mechanical analogy for the cell cycle control system.

- In this diagram of the cell cycle, the flat "stepping stones" around the perimeter represent sequential events. Like the control device of an automatic washer, the cell cycle control system proceeds on its own, driven by a built-in clock. However, the system is subject to internal and external regulation at various **checkpoints**, of which three are shown (in red).

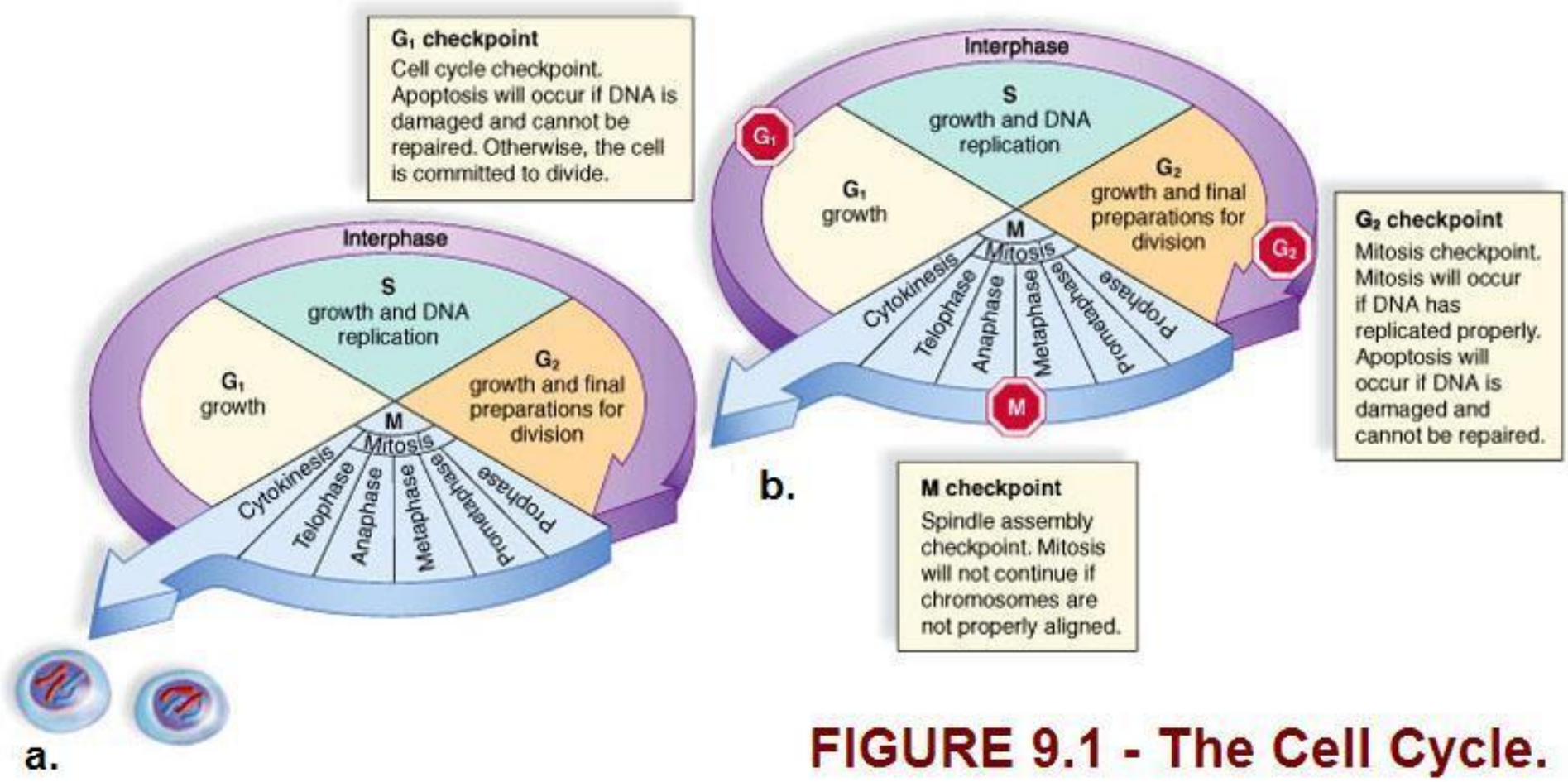
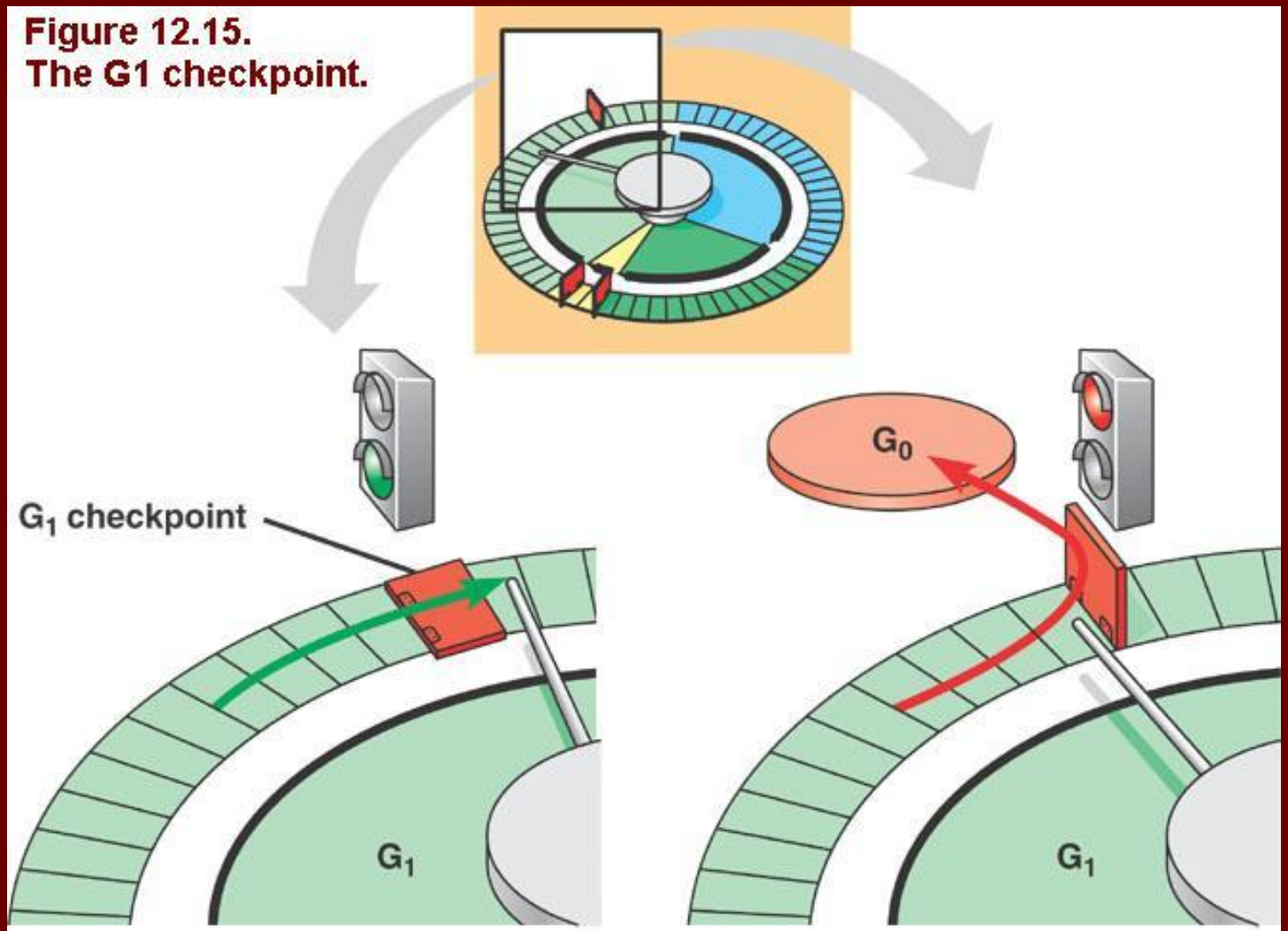


FIGURE 9.1 - The Cell Cycle.

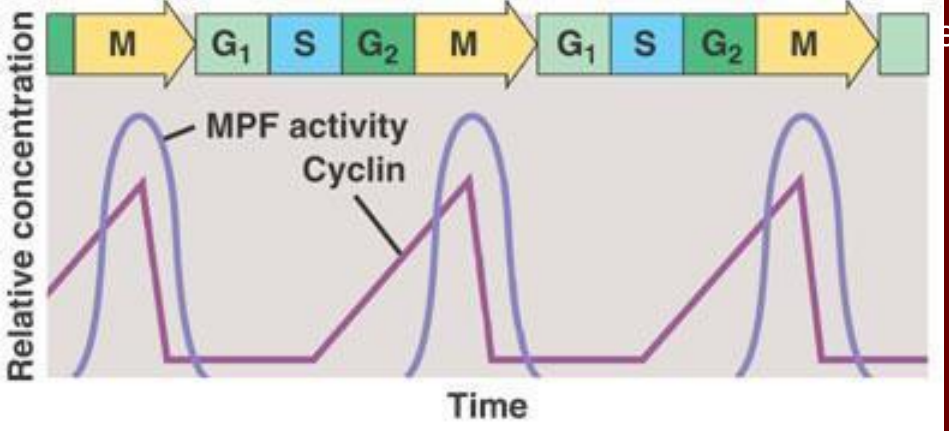
- Three cell cycle **checkpoints** (the cycle stops at these checkpoints if necessary):
  - **G_1 checkpoint:** In G_1 prior to the S stage.
  - **G_2 checkpoint:** In G_2 prior to the M stage.
  - **M checkpoint:** Near the end of mitosis.

Figure 12.15.
The G1 checkpoint.



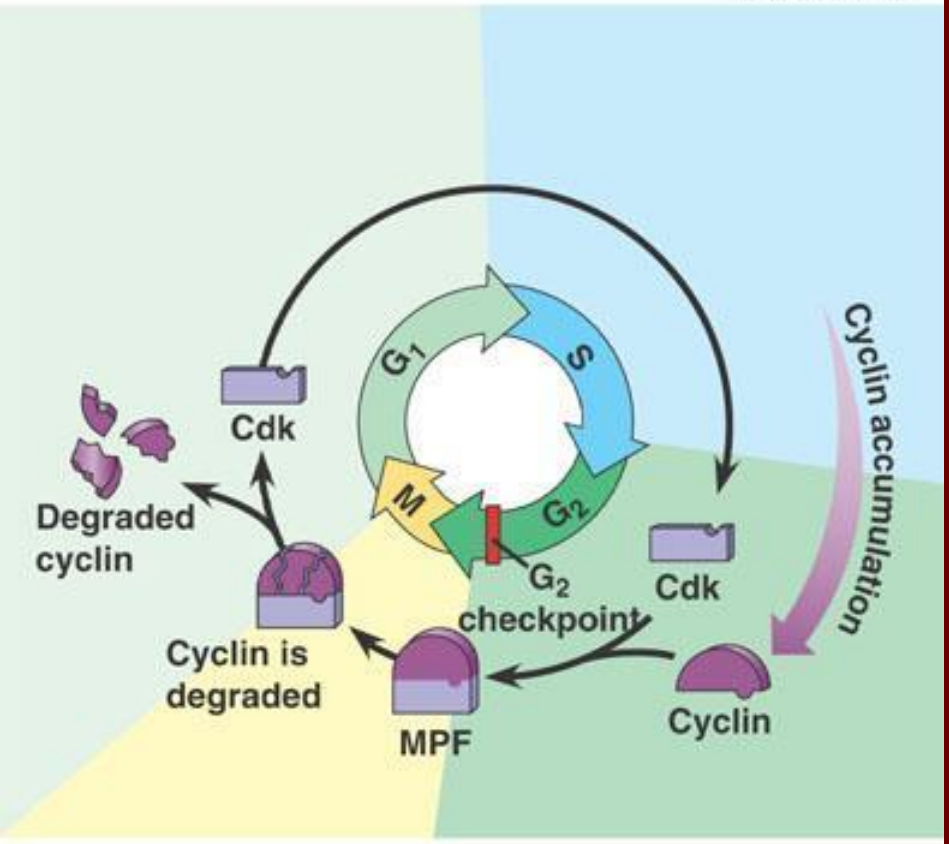
(a) If a cell receives a go-ahead signal at the G_1 checkpoint, the cell continues on in the cell cycle.

(b) If a cell does not receive a go-ahead signal at the G_1 checkpoint, the cell exits the cell cycle and goes into G_0, a nondividing state.



(a) Fluctuation of MPF activity and cyclin concentration during the cell cycle

Figure 12.16

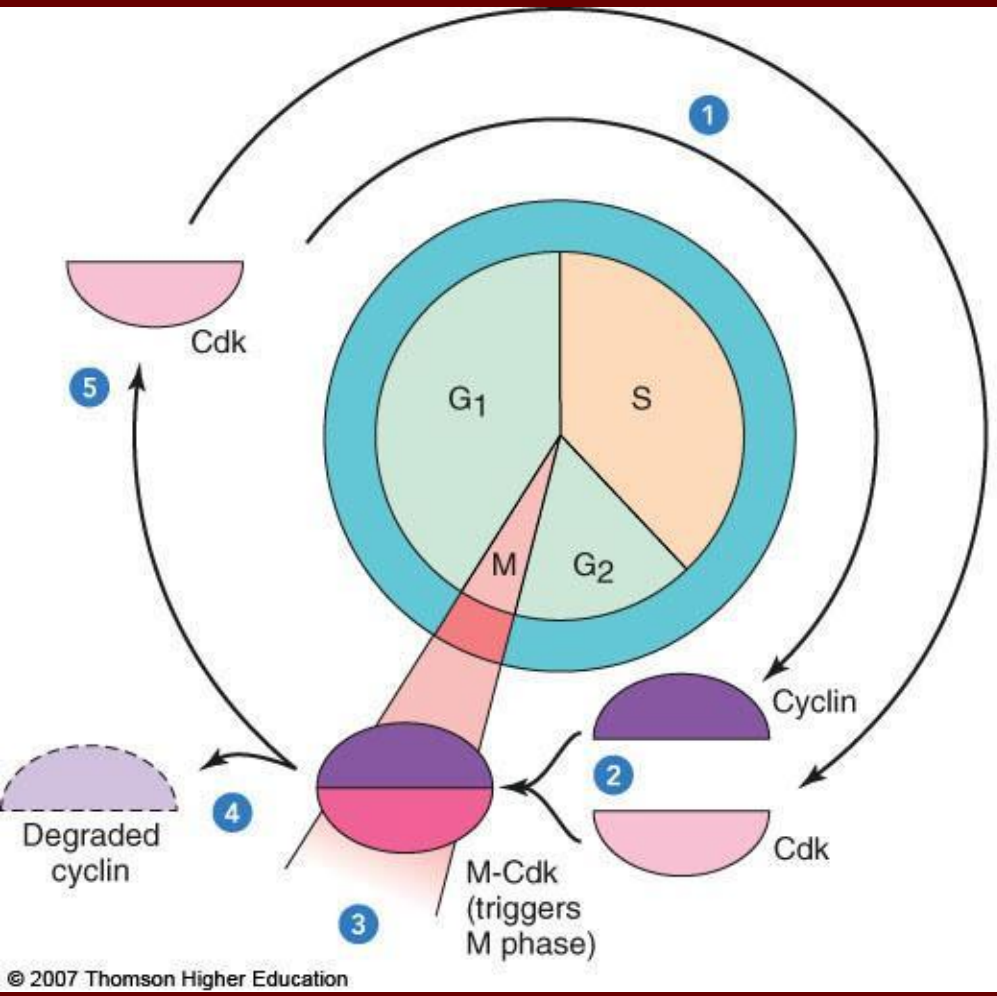


(b) Molecular mechanisms that help regulate the cell cycle

Molecular Control of the Cell Cycle at the G_2 Checkpoint

- The steps of the cell cycle are timed by rhythmic fluctuations in the activity of **cyclin-dependent kinases (Cdks)**. Here we focus on a cyclin-Cdk complex called **MPF** (maturation-promoting factor), which acts at the G_2 checkpoint as a go-ahead signal, triggering the events of mitosis.

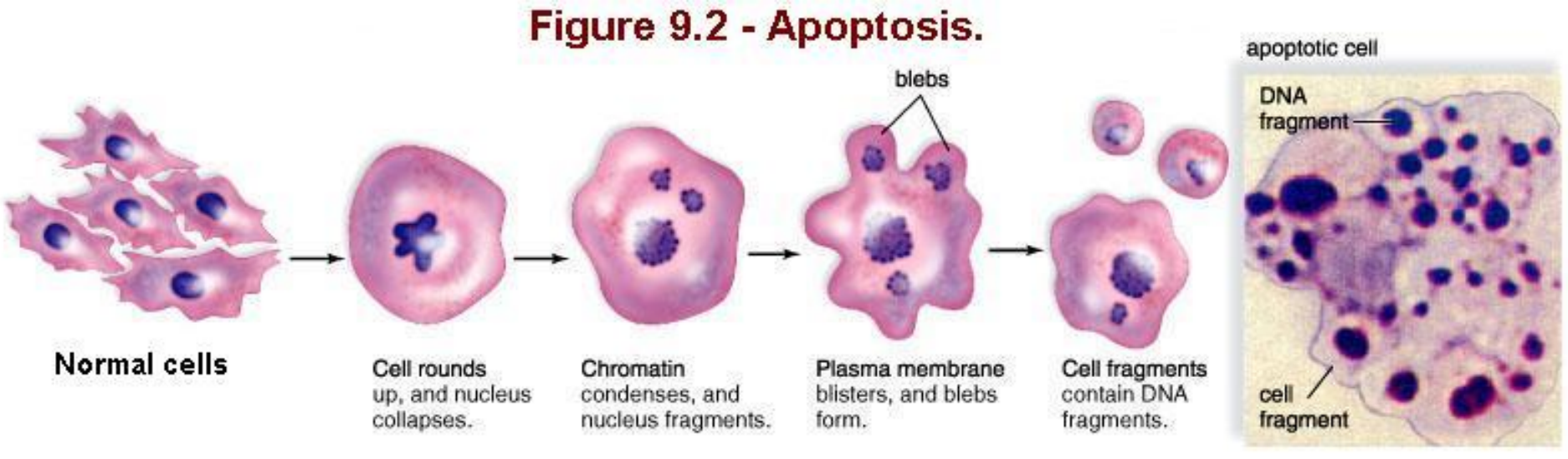
Molecular Control of the Cell Cycle



1. Cyclin is synthesized and accumulates.
2. Cdk associates with cyclin, forming a cyclin–Cdk complex, M-Cdk.
3. M-Cdk phosphorylates proteins, activating those that facilitate mitosis and inactivating those that inhibit mitosis.
4. An activated enzyme complex recognizes a specific amino acid sequence in cyclin and targets it for destruction. When cyclin is degraded, M-Cdk activity is terminated, and the cells formed by mitosis enter G_1.
5. Cdk is not degraded but is recycled and reused.

Figure 10-12. Molecular control of the cell cycle.

This diagram is a simplified view of the control system that triggers the cell to move from G_2 to M phase.



Control of the Cell Cycle: Apoptosis

- **Apoptosis** is "**programmed cell death**" involving a cascade of specific cellular events leading to death and destruction of the cell. It is a mechanism that occurs all the time and helps control the cell cycle.
- Apoptosis results in a fragmented cell. The fragments are phagocytized (ingested) by white blood cells of the immune system and neighboring tissue cells.
- Death through apoptosis prevents a tumor (abnormal growth of cells) from developing.

External Signals: The Effect of a Growth Factor on Cell Division

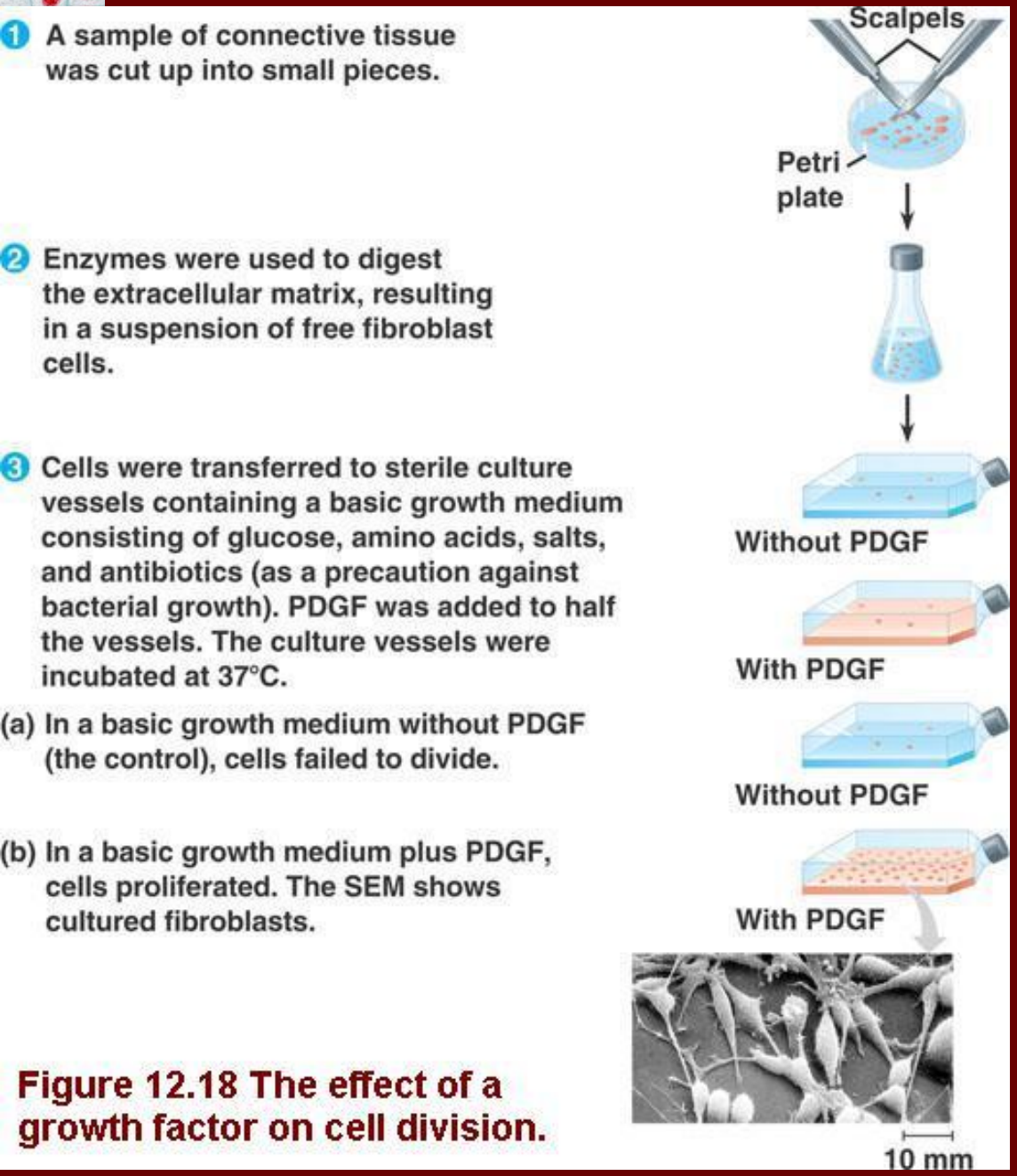


Figure 12.18 The effect of a growth factor on cell division.

- As this experiment shows, adding platelet-derived growth factor (PDGF) to human fibroblasts in culture causes the cells to proliferate. (Fibroblasts are cells of connective tissues.)

SEM = Scanning Electron Microscope

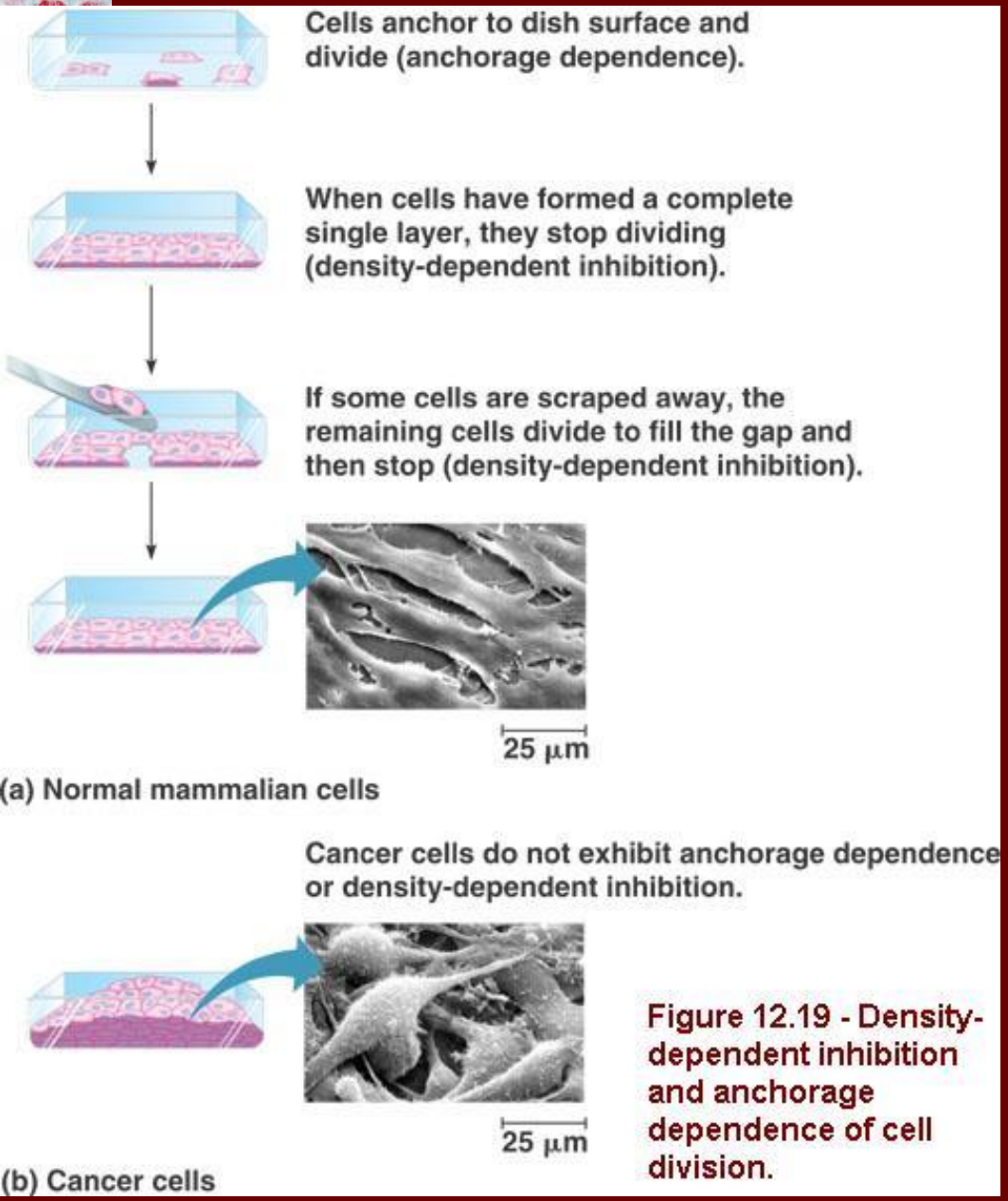


Figure 12.19 - Density-dependent inhibition and anchorage dependence of cell division.

Effect of An External Physical Factor

- Most cells exhibit density-dependent inhibition as well as anchorage dependence.
- **Anchorage dependance** is the requirement that a cell must be attached to a substratum in order to divide.
- **Density-dependent inhibition** is the phenomenon observed in normal animal cells that causes them to stop dividing when they come into contact with one another.

Loss of Cell Cycle Controls in Cancer Cells

- **Cancer:** A cell growth disorder resulting from the **mutation** (change in DNA) of genes responsible for regulating the cell cycle.
- **Transformation** is the process that converts a normal cell to a cancer cell.
  - Cancer cells ***do not respond*** to the body's control mechanisms; they divide excessively and invade other tissues. If unchecked, cancer cells can kill the organism.
- **Neoplasm = tumor:** An abnormal growth of cells or tissue without physiological function.
  - ***Benign neoplasm:*** Not cancerous tumor.
  - ***Malignant neoplasm:*** Cancerous tumor.
- **Carcinogenesis:** Development of cancer.

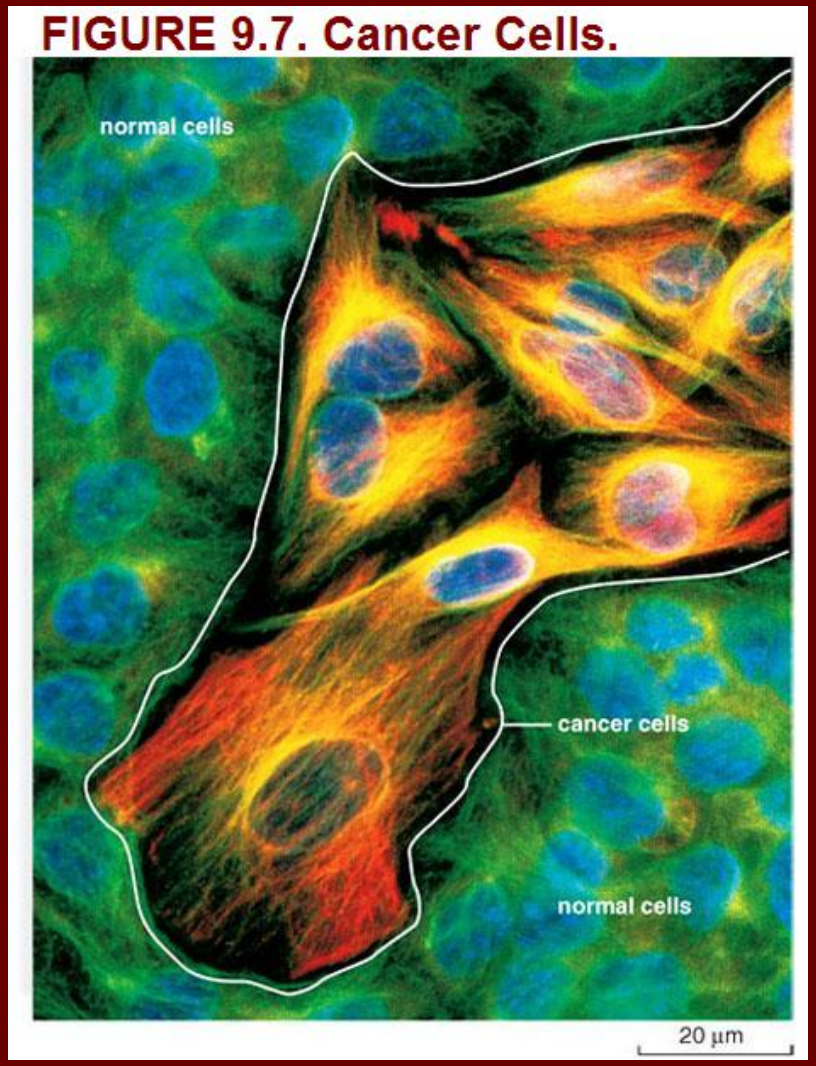
TABLE 9.2

Cancer Cells Versus Normal Cells

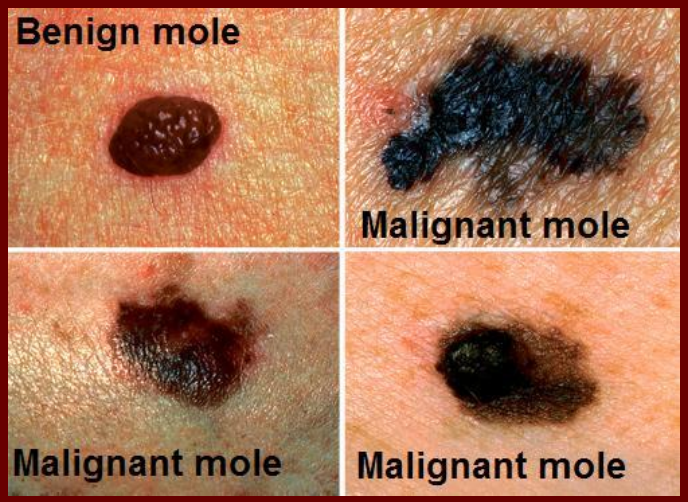
Cancer Cells	*Normal Cells*
Nondifferentiated cells	Differentiated cells
Abnormal nuclei	Normal nuclei
Do not undergo apoptosis	Undergo apoptosis
No contact inhibition	Contact inhibition
Disorganized, multilayered	One organized layer
Undergo metastasis and angiogenesis	

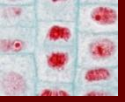
Metastasis: The spread of cancer cells to locations distant from their original site.
Contact inhibition: Normal animal cells stop dividing when they are too close to each other.
Angiogenesis: The formation of new blood vessels that carry nutrients and oxygen to cancerous cells.

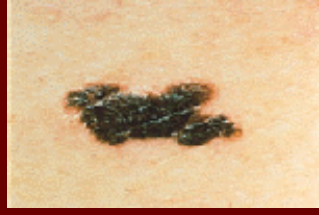
CANCER



- In this micrograph, the orange cells are *cancer cells*, and the other cells are normal cells.
- These cancer cells were detected by using a special fluorescent technique that detects abnormal proteins.







ORIGIN OF CANCER

1) Mutations in genes that encode **repair enzymes** (proteins involved in chemical reactions) that fix errors during DNA replication.

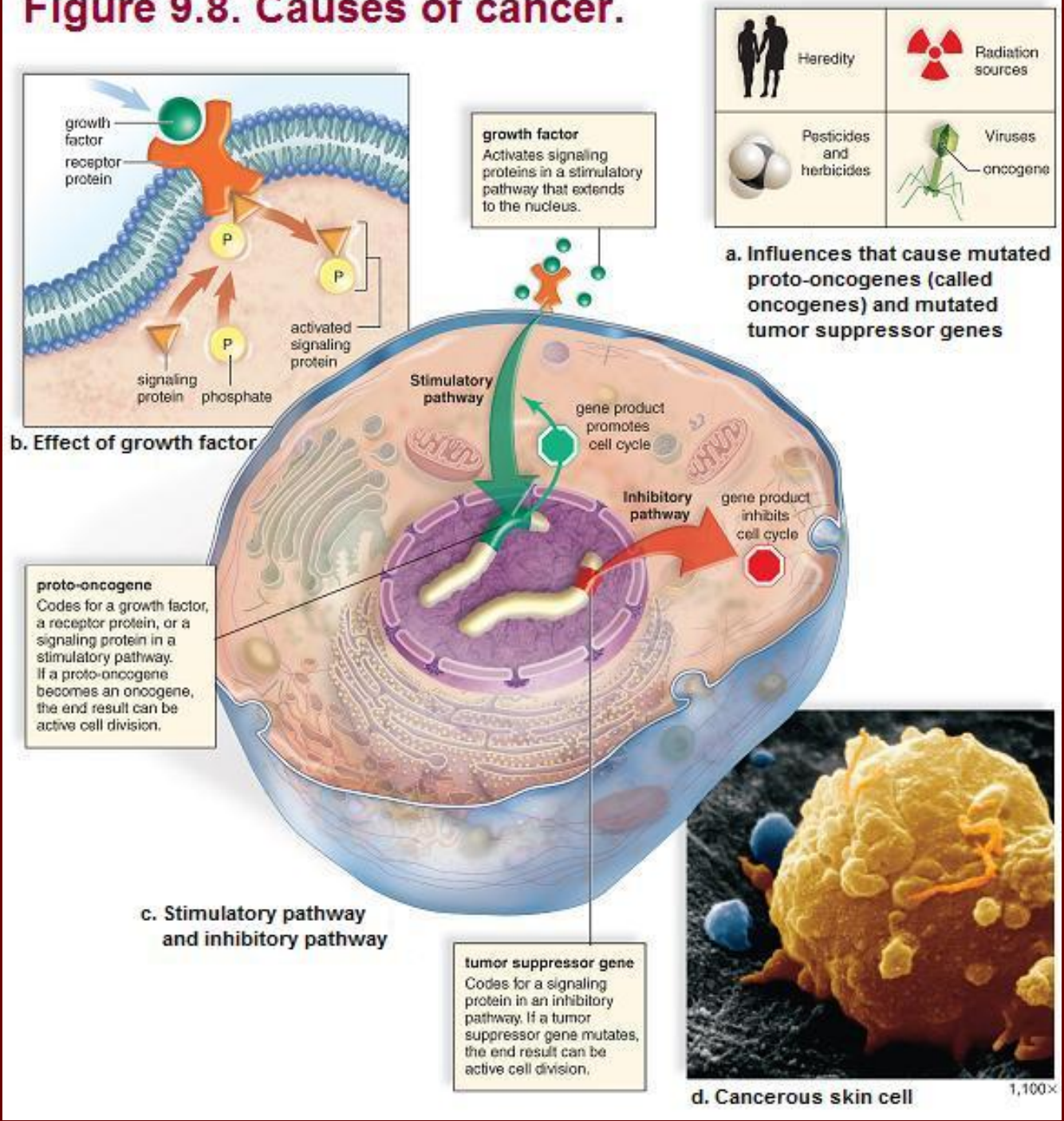
2) Mutations in **proto-oncogenes** and **tumor suppressor genes**.

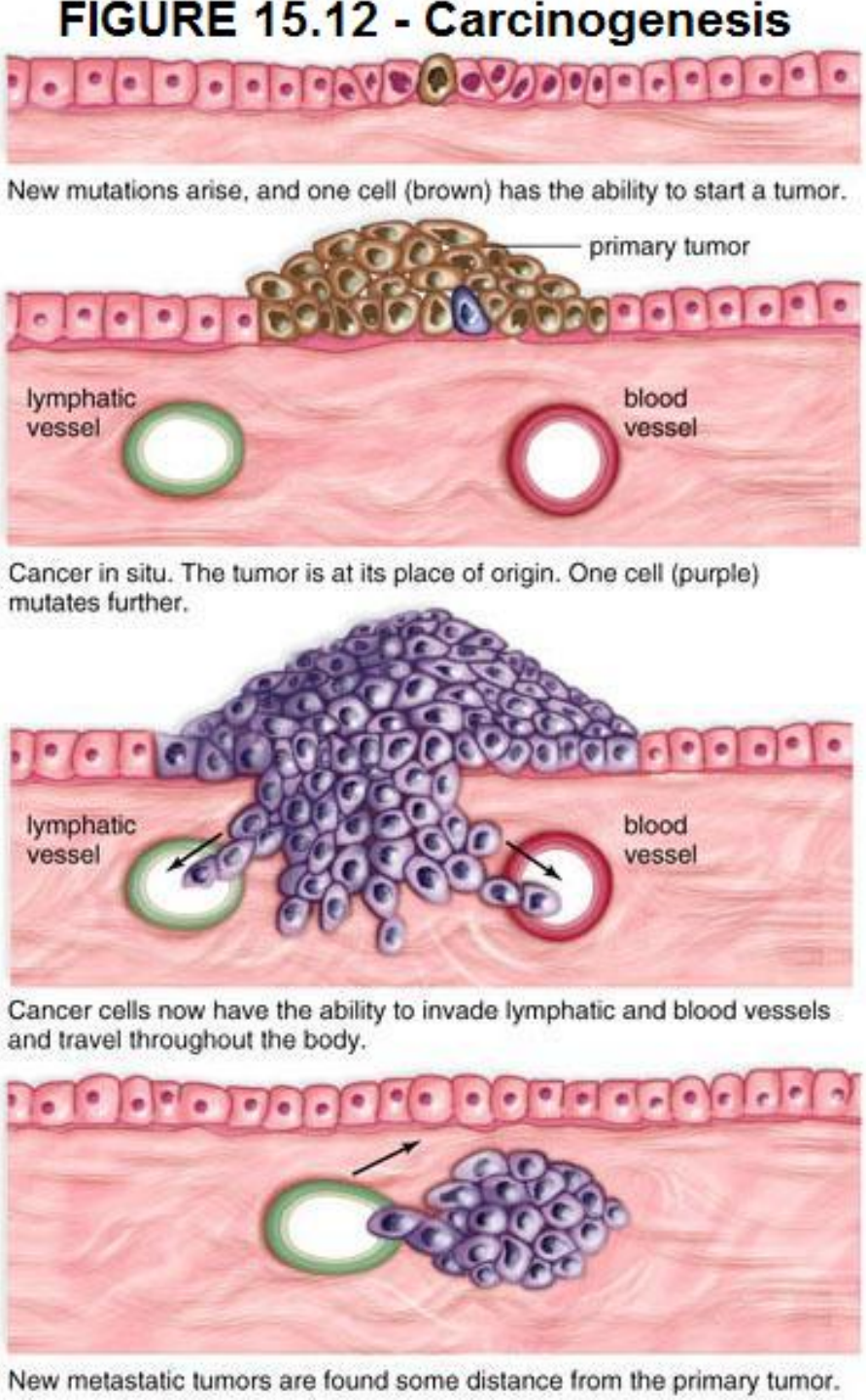
   - **Proto-oncogenes:** Normal genes that code for proteins that promote the cell cycle. When mutations occur in proto-oncogenes, they become **oncogenes**, or cancer-causing genes.

   - **Tumor suppressor genes:** Specify proteins that inhibit the cell cycle.

3) Mutation of the enzyme ***telomerase*** which regulates the length of **telomeres** (the ends of chromosomes), causes telomeres to remain at a constant length. Since cells with shortened telomeres normally stop dividing, keeping the telomeres at a constant length allows the cancer cells to continue dividing over and over again.

Figure 9.8. Causes of cancer.

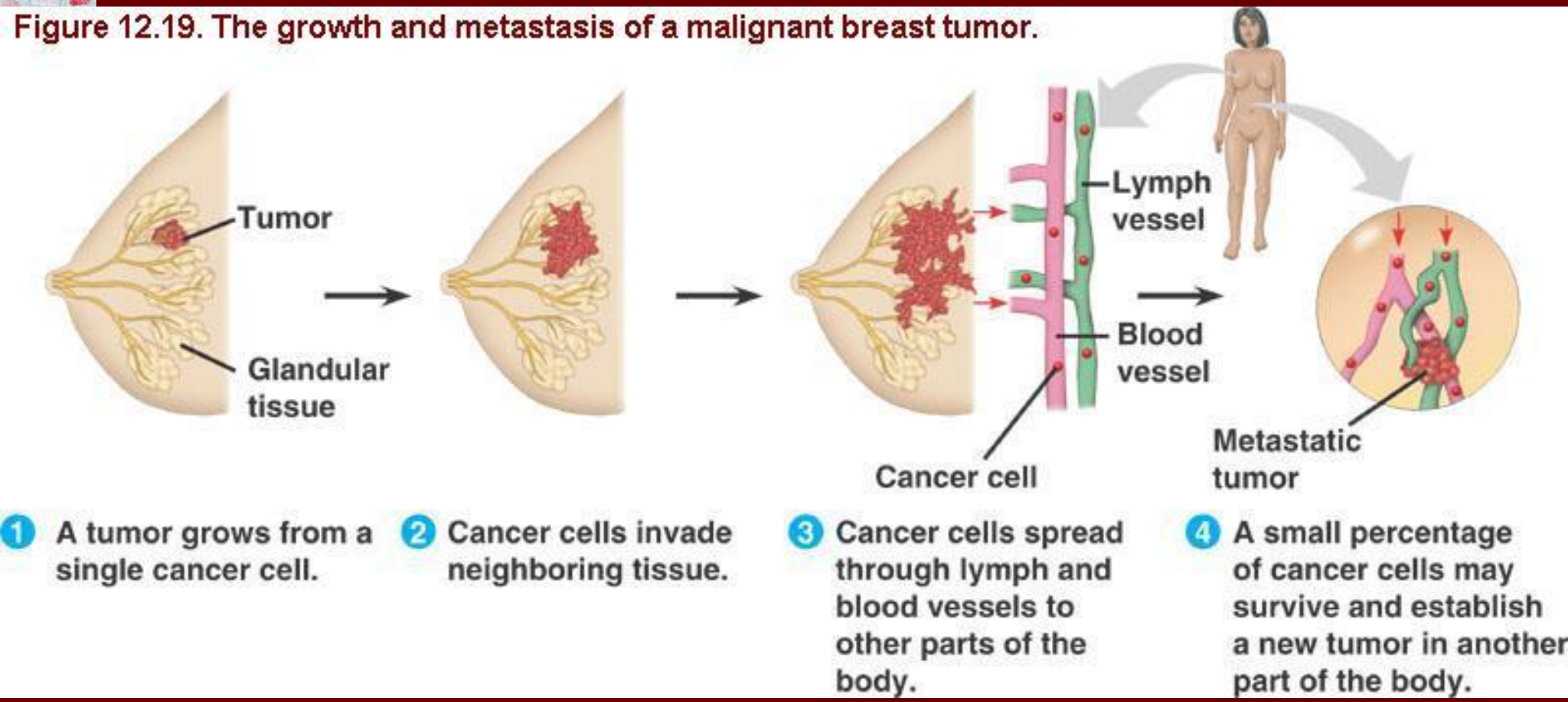




Carcinogenesis

- The development of cancer requires a series of *mutations* leading first to a **localized tumor** and then to **metastatic tumors**.
- With each successive stage toward cancer, the most genetically altered and aggressive cell becomes the dominant type of tumor.
- The cells take on characteristics of embryonic cells; they are **not differentiated**, they can **divide uncontrollably**, and they are able to **migrate** to new locations.

Figure 12.19. The growth and metastasis of a malignant breast tumor.



- The growth and metastasis of a malignant breast tumor.
  - The cells of ***malignant (cancerous) tumors*** grow in an uncontrolled way and can spread to neighboring tissues and, via lymph and blood vessels, to other parts of the body. The spread of cancer cells beyond their original site is called **metastasis**.

TABLE 12.2 Major Factors That Increase the Risk of Cancer

Factor	Examples of Implicated Cancers	Comments
Heredity	Retinoblastoma (childhood eye cancer) Osteosarcoma (childhood bone cancer)	Most cancers are not caused by heredity alone. Persons having family histories of certain cancers should follow physicians' recommendations.
Tumor viruses	Liver cancer Adult T cell leukemia/lymphoma Cervical cancer	Five viruses are initiators of certain cancers. (See Table 19.1)
Tobacco use	Lung cancer Cancers of the oral cavity, esophagus, and larynx Cancers of the kidney and bladder	Cigarette smoking is responsible for approximately one-third of all cancers. Nonsmokers have an increased risk of smoking-related cancers if they regularly breathe in sidestream smoke.
Alcohol consumption	Cancers of the oral cavity, esophagus, and larynx Breast cancer	The combined use of alcohol and tobacco leads to a greatly increased risk of these cancers. The mechanism of action in breast cancer is not yet known.
Industrial hazards	Lung cancer	Certain fibers, such as asbestos, chemicals such as benzene and arsenic, and wood and coal dust are prominent industrial hazards.
Ultraviolet radiation from the sun	Skin cancers	Those at greatest risk are fair-skinned persons who burn easily. However, everyone is at risk and should wear sunscreens and protective clothing when in the sun for extended periods of time. All types of UV radiation in tanning beds (UVA, UVB, & UVC) are harmful and may lead to skin cancer.
Ionizing radiation	Related to location and type of exposure	Eliminate unnecessary medical X rays to lower cancer risk. Infants and children are particularly susceptible to the damaging effects of ionizing radiation. Check your home to detect high levels of radon gas.
Hormones (estrogen and possibly testosterone)	Breast, cervical, ovarian, and prostate cancers	Estrogen-only and estrogen-progesterone hormone replacement therapies both increase the risk of breast cancer. Oral contraceptives increase the risk of breast cancer and cervical cancer, while reducing the risk of ovarian cancer. The role of testosterone in prostate cancer is unclear.
Diet	Breast and prostate cancers (weak association with high-fat diets), stomach and esophageal cancers (nitrites).	Nitrites found in salt-cured, salt-pickled, and smoked foods increase the risk of cancer.

Table 12-2 Biology: Understanding Life 1/e

TABLE 12.3

General Dietary Recommendations to Reduce the Risk of Cancer

1. Avoid obesity by balancing caloric intake with exercise.
2. Choose foods that are low in fat and that help maintain a healthful weight.
3. Limit consumption of meats, especially high-fat and processed meats.
4. Eat five or more servings of fruits and vegetables each day.
5. Eat other foods from plant sources, such as breads, cereals, grain products, soy products, rice, pasta, or beans, several times each day.
6. If alcohol is consumed, limit intake to one mixed drink or glass of wine per day for women and two for men.

Adapted from *Cancer Facts & Figures 2004*, the American Cancer Society.

Table 12-3 Biology: Understanding Life 1/e

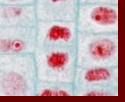


TABLE 12.4 The Seven Warning Signs of Cancer

Change in bowel or bladder functions

A sore that does not heal

Unusual bleeding or discharge

Thickening or lump in any tissue

Indigestion (chronic) or difficulty in swallowing

Obvious change in a wart or mole

Nagging hoarseness or cough

Table 12-4 Biology: Understanding Life 1/e

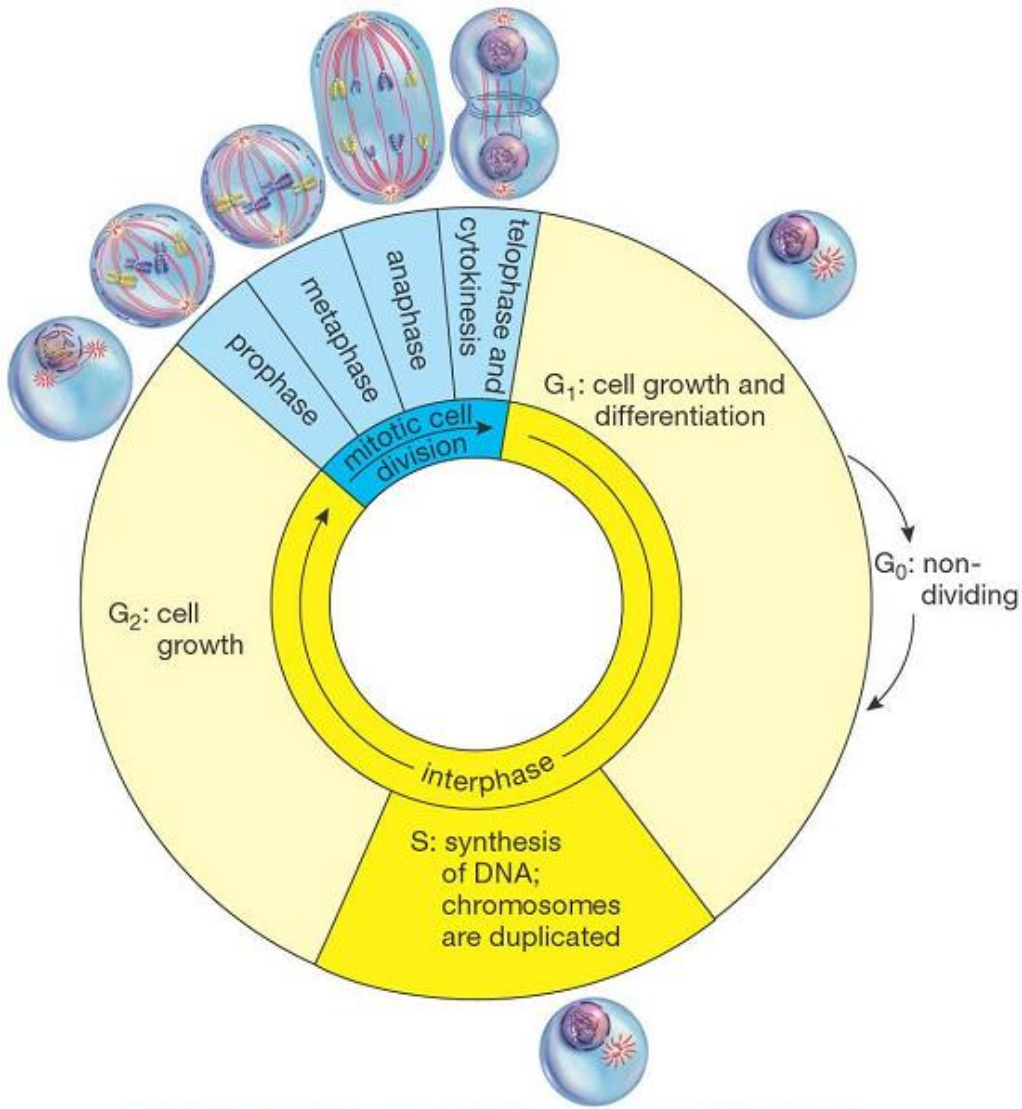
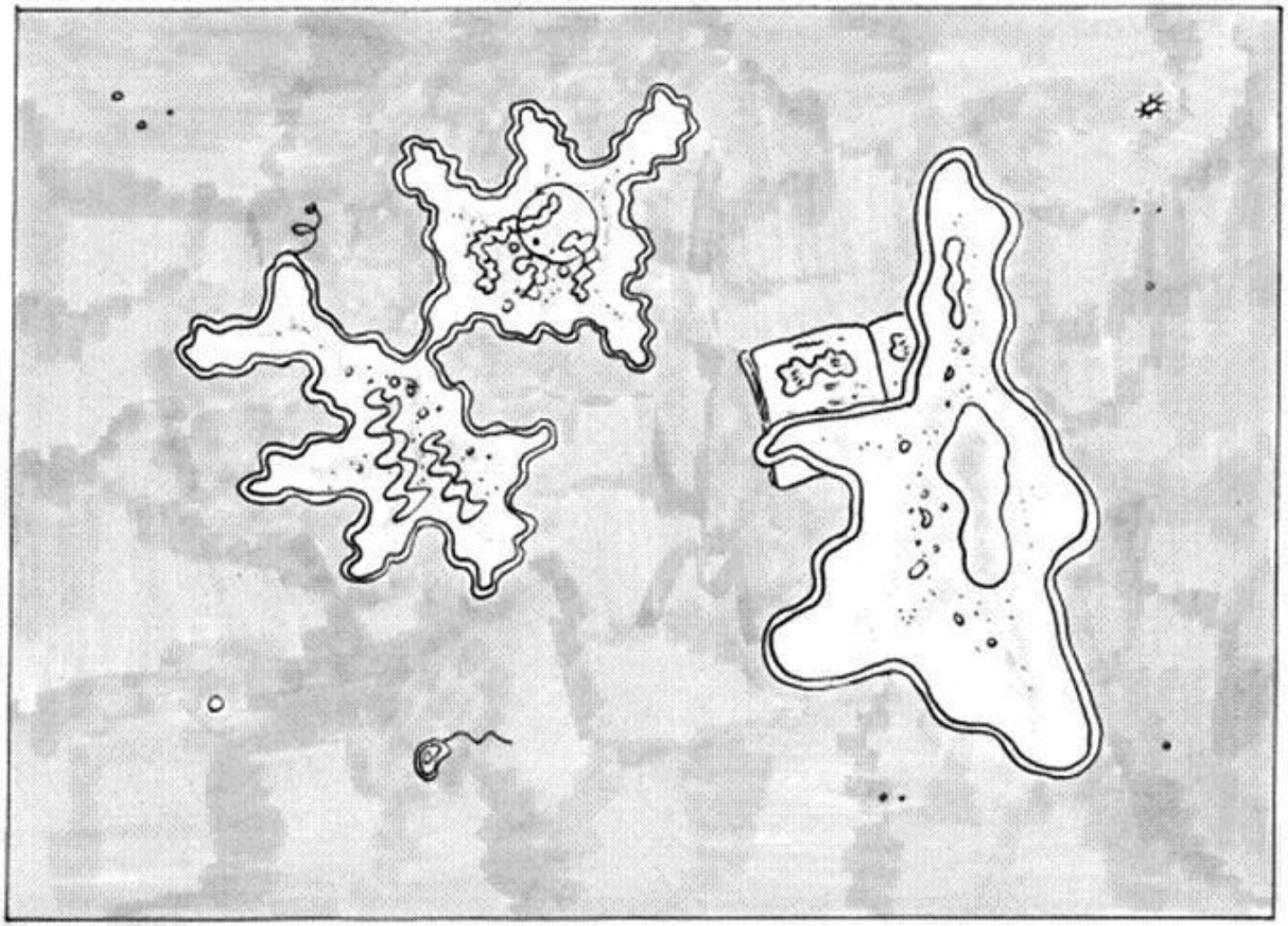


FIGURE 11-3. The Eukaryotic Cell Cycle.

The Cell Cycle: Final Review

- The eukaryotic cell cycle consists of **interphase** and **mitotic cell division**.
- Some cells, such as nerve cells and muscle cells, typically do not complete the cell cycle and are permanently arrested. They enter the **G_0** phase and may not divide again, but they continue to perform normal everyday processes.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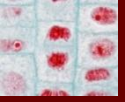
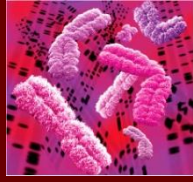
ght © 2001 David Farley, d-farley@ibiblio.org http://ibiblio.org/Dave/drfun.html
Here's where you screwed up - telophase comes after metaphase."





References

- **Audesirk, Teresa; Audesirk, Gerald & Byers, Bruce E.** (2005). ***Biology: Life on Earth*.** Seventh Edition. Pearson Education, Inc.-Prentice Hall. NJ, USA.
- **Brooker, Robert J.; Widmaier, Eric P.; Graham, Linda E.; Stiling, Peter D.** (2008). ***Biology*.** The McGraw-Hill Companies, Inc. NY, USA.
- **Campbell, Neil A.; Reece, Jane B., et al.** (2011). ***Campbell Biology.*** Ninth Edition. Pearson Education, Inc.-Pearson Benjamin Cummings. CA, USA.
- **Ireland, K.A.** (2011). ***Visualizing Human Biology*.** Second Edition. John Wiley & Sons, Inc. NJ, USA.
- **Mader, Sylvia S.** (2010). ***Biology.*** Tenth Edition. The McGraw-Hill Companies, Inc. NY, USA.
- **Martini, Frederic H.; Nath, Judi L.** (2009). ***Fundamentals of Anatomy & Physiology*.** Eighth Edition. Pearson Education, Inc. – Pearson Benjamin Cummings. CA, USA.
- **Solomon, Eldra; Berg, Linda; Martin, Diana W.** (2008). ***Biology.*** Eighth Edition. Cengage Learning. OH, USA.
- **Starr, Cecie.** (2008). ***Biology: Concepts and Applications, Volume I.*** Thompson Brooks/Cole. OH, USA.
- **Tortora, Gerard J.; Derrickson, Bryan.** (2006). ***Principles of Anatomy and Physiology.*** Eleventh Edition. John Wiley & Sons, Inc. NJ, USA. www.wiley.com/college/apcentral.