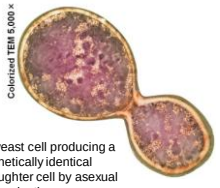
CELL DIVISION AND REPRODUCTION

Cell division plays many important roles in the lives of organisms

- **Cell division** is at the heart of the reproduction of cells and organisms because cells originate only from preexisting cells.
- Some organisms reproduce through **asexual reproduction**, producing offspring that are all genetic copies of the parent and identical to each other.
- Other organisms reproduce through **sexual reproduction**, creating a variety of offspring.



A yeast cell producing a genetically identical daughter cell by asexual reproduction

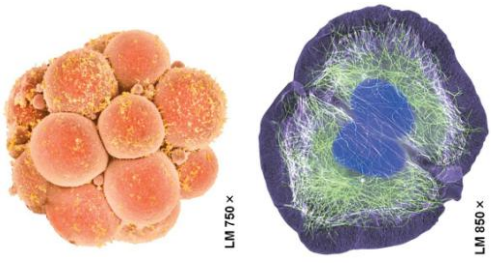
A sea star reproducing asexually via fragmentation and regeneration of the body from the fragmented arm

An African violet reproducing asexually from a cutting

Cell division plays many important roles in the lives of organisms

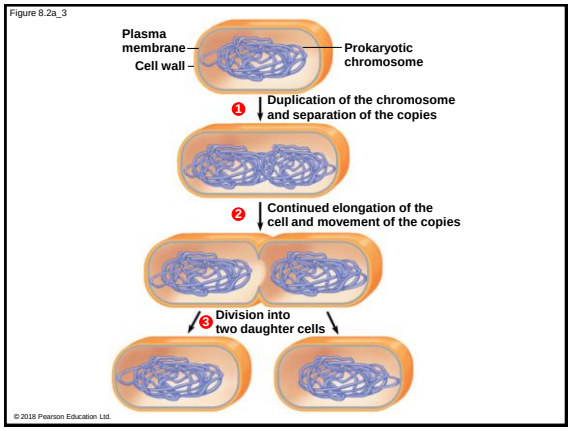
- **Checkpoint question** Why do fully-grown human cells continue to divide?

Figure 8.1e



Prokaryotes reproduce by binary fission

- Prokaryotic cells reproduce asexually by **binary fission**, a term that means “dividing in half.”
- In typical prokaryotes, most genes are carried on one circular DNA molecule that, with associated proteins, constitutes the organism’s chromosome.
- As the cell replicates its single chromosome,
  - the copies move apart,
  - the plasma membrane pinches inward, and
  - more cell wall is made, which eventually divides the parent cell into two daughter cells.



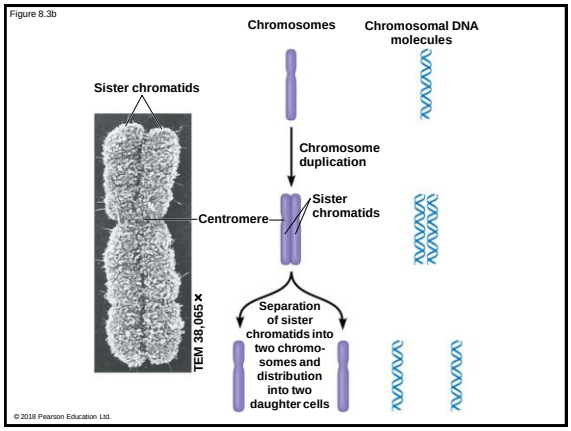
The Eukaryotic Cell Cycle and Mitosis

The large, complex chromosomes of eukaryotes duplicate with each cell division

- A eukaryotic cell has many more genes than a prokaryotic cell, and they are grouped into multiple chromosomes in the nucleus.
  - Each chromosome contains one long DNA molecule.
  - Individual chromosomes are visible under a light microscope only when the cell is in the process of dividing; otherwise, chromosomes are thin, loosely packed **chromatin** fibers too small to be seen.

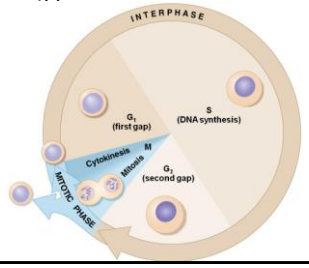
The large, complex chromosomes of eukaryotes duplicate with each cell division

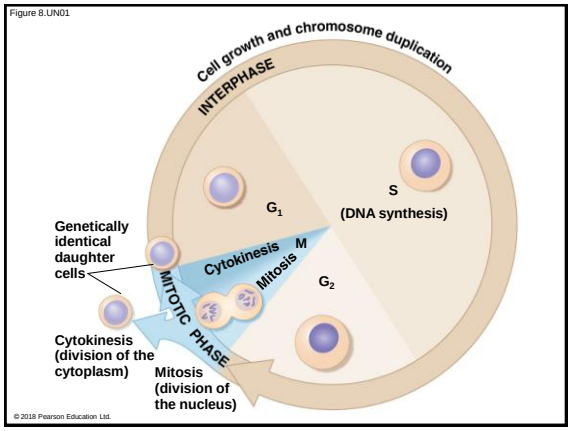
- Before a cell starts dividing, the chromosomes duplicate, producing **sister chromatids** (containing identical DNA) that are joined together along their lengths by proteins, most closely at a region called the **centromere**.
- Cell division involves the separation of sister chromatids and results in two daughter cells, each containing a complete and identical set of chromosomes.



The cell cycle includes growth and division phases

- The **cell cycle** is an ordered sequence of events that extends from the time a cell is first formed from a dividing parent cell until its own division.

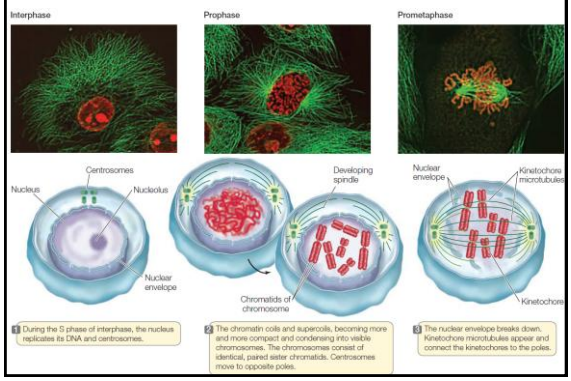




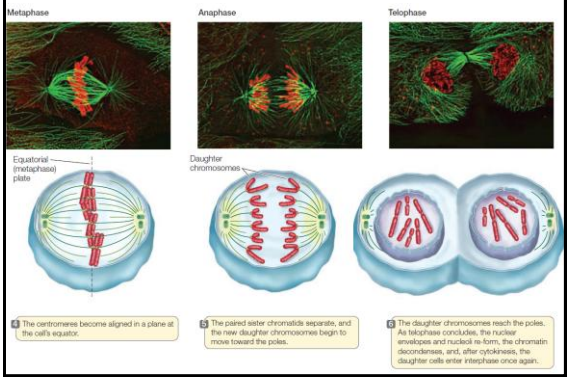
Cell division is a continuum of dynamic changes

- Mitosis distributes duplicated chromosomes into two daughter nuclei.
- After the chromosomes are coiled up, a **mitotic spindle** made of microtubules moves the chromosomes to the middle of the cell.
- The sister chromatids then separate and move to opposite poles of the cell, at which point two new nuclei form.

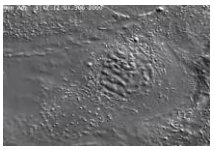
Mitosis



Mitosis (cont'd)



Video: Animal Mitosis



Cytokinesis differs for plant and animal cells

- Cytokinesis, in which the cell divides in two, overlaps the end of mitosis.
  - In animals, cytokinesis occurs when a cell constricts, forming a **cleavage furrow**.
  - In plants, a membranous **cell plate** forms and then splits the cell in two.

Figure 8.6a Cleavage of an animal cell

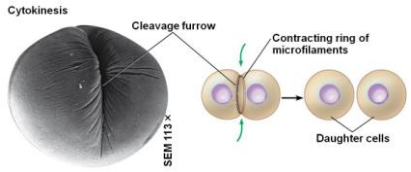
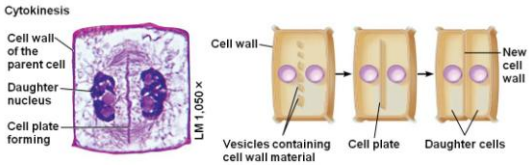


Figure 8.6b Cell plate formation in a plant cell



Cell Cycle Control

- The control of the system is regulated by brakes that can stop the cycle at specific *checkpoints*.

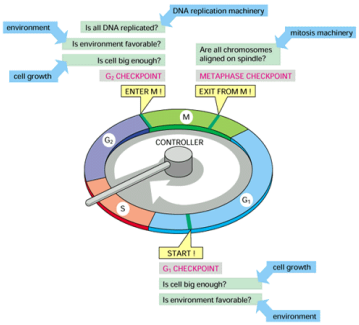
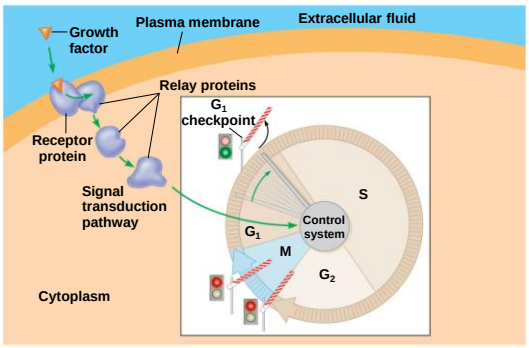
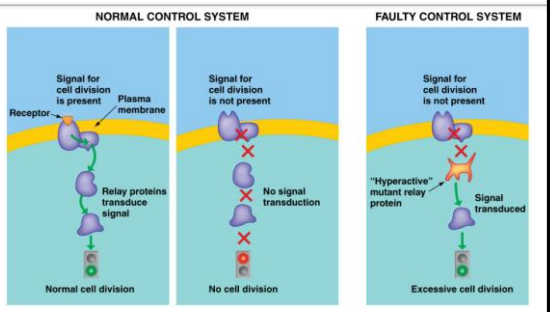


Figure 8.8b

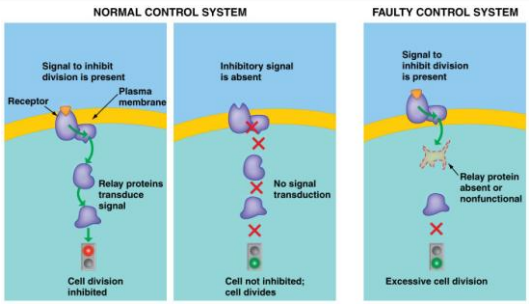
How a growth factor signals the cell cycle control system



The stimulative signaling system is faulty



The inhibitive signaling system is faulty



Cell death

- Cells die in one of two ways:

1. ***Necrosis***: cells are damaged by mechanical means or toxins, or are starved of oxygen or nutrients. These cells usually swell up and burst, releasing their contents into the extracellular environment.
2. ***Apoptosis***: (More typical) programmed series of events that result in cell death (=self-distruction).

Apoptosis

- Occurs for 2 reasons:

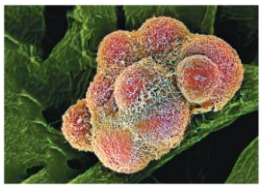
1. **The cell is no longer needed by the organism.** For example, before birth, a human fetus has web-like hands, with connective tissue between the fingers. As development proceeds, this unneeded tissue disappears as its cells undergo apoptosis in response to specific signals.
2. **The longer cells live, the more prone they are to genetic damage that could lead to cancer**. This is especially true of epithelial cells of the surface of an organism, which may be exposed to radiation or toxic substances. Such cells normally die after only days or weeks and are replaced by new cells.
   - Apoptosis is a critical defense against cancer

Cell Cycle Control

- **Some proteins regulate cell cycle:**
  - **Positive regulators** such as growth factors stimulate the cell cycle: they are like "gas pedals."
  - **Negative regulators** such as 'retinoblastoma' inhibit the cell cycle: they are like "brakes."
- Just as driving a car requires stepping on the gas pedal *and releasing* the brakes, a cell will go through a division cycle only if the positive regulators are active and the negative regulators are inactive.
- The two regulatory systems ensure that cells divide only when needed.
  - In cancer cells, these two processes are abnormal.

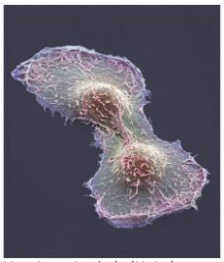
Cancer cells

- Cancer cells start as normal cells, but genetic mutations cause them to lose the ability to regulate their division.
- Cancer cells divide and may spread, invading other tissues, disrupting organ function, and killing the host.
- Although uncontrolled cell division is harmful, normal cell division is necessary in all forms of life.



Henrietta Lacks's cervical cancer cells: an intriguing example of immortal cells

Henrietta Lacks



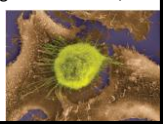
Henrietta Lacks's (HeLa) cells dividing

Cancer cells

- Cancer cells differ from the normal cells in two ways:
  - They lose control over cell cycle/division.
  - They can migrate to other locations in the body (*metastasis*).
- Most cells in the body divide only if they are exposed to extracellular signals such as growth factors. Cancer cells do not respond to these controls, and instead divide more or less continuously, ultimately forming **tumors** (large masses of cells). By the time a physician can feel a tumor or see one on an X-ray film or CAT scan, it already contains millions of cells. Tumors can be ***benign*** or ***malignant***.

Tumors

- **Benign tumors:** resemble the tissue they came from, grow slowly, remain localized where they develop. They can be removed by surgery.
  - E.g., a lipoma is a benign tumor of fat cells that may arise in the armpit and remain there. Benign tumors are not cancers, but they must be removed if they invade on an organ, preventing its function.
- **Malignant tumors:** do not look like their parent tissue. They can spread.
  - E.g. A flat, specialized epithelial cell in the lung wall may turn into a relatively featureless, round, malignant lung cancer cell. Malignant cells often have irregular structures, such as variable nucleus sizes and shapes.



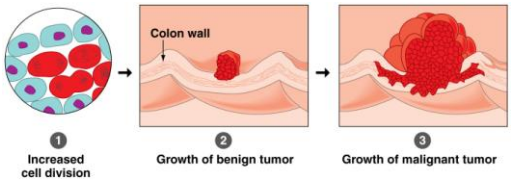
11.23 A Cancer Cell with its Normal Neighbors This lung cancer cell (yellow-green) is quite different from the normal lung cells surrounding it. The cancer cell can divide more rapidly than its normal counterparts, and it can spread to other organs. This form of small-cell cancer is lethal, with a 5-year survival rate of 10 percent. Most cases are caused by tobacco smoking.

Benign tumors

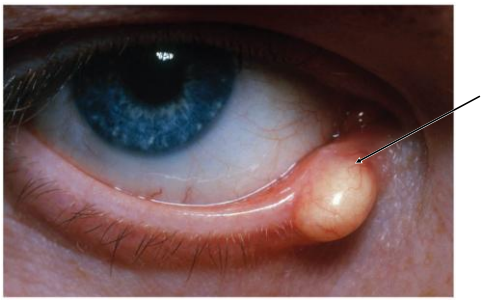
- Clean boundary between tumor and the tissue
- Remain at the original site

Malignant tumors

- Invade surrounding tissue
- Migrate into other tissues = metastasis



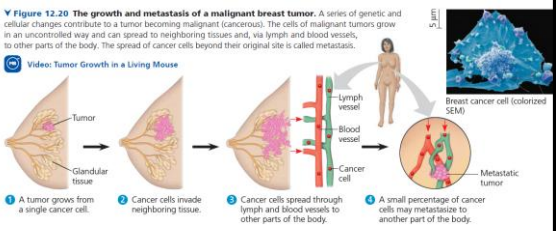
A benign tumor near the eye



Malignant tumors

- The changes that have occurred in cells of malignant tumors show up in many ways besides excessive proliferation.
- These cells may have unusual numbers of chromosomes.
- Their metabolism may be altered, and they may stop to function in any constructive way.
- Abnormal changes on the cell surface cause cancer cells to lose attachments to neighboring cells and the extracellular matrix, allowing them to spread into nearby tissues.
- Cancer cells may also secrete signaling molecules that cause blood vessels to grow toward the tumor.
- A few tumor cells may separate from the original tumor, enter blood vessels and lymph vessels, and travel to other parts of the body. There, they may proliferate and form a new tumor, which is called as **metastasis**.

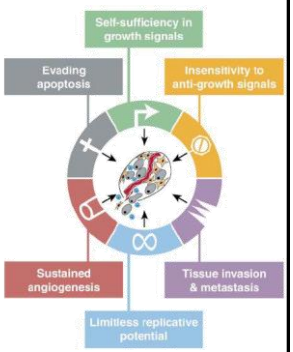
Tumors



- As a common sense, an individual with a malignant tumor is said to have cancer

Hallmarks of Cancer

- Six changes are found in most cancers

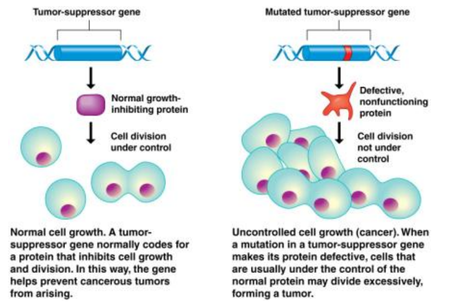


Hanahan and Weinberg (2000)

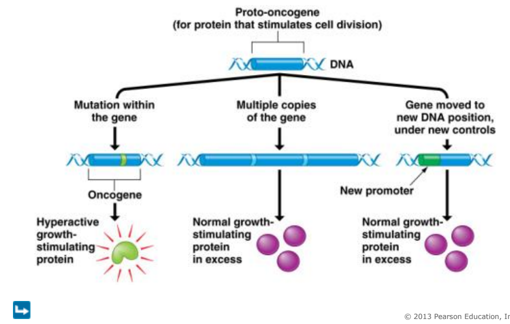
Cancer cells lose control over the cell cycle and apoptosis

- ***Oncogenes:*** positive regulators for cancer (e.g. ras, myc, cdk)
  - Signals for cell division
  - Signals for cell movement
  - Signals for formation of blood vessels
- ***Tumor supressor genes:*** negative regulators for cancer (e.g. Rb, p53, BRCA)
  - Stop cell division
  - Death signals

Tumor-suppressor genes

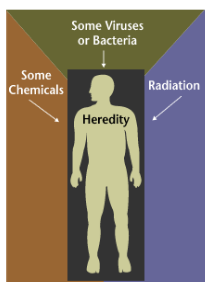


How a proto-oncogene can become an oncogene



Causes of Cancer

- Environmental factors, like radiation, tobacco, alcohol, toxic chemicals (carcinogens), diet
- DNA Mutations
  - Somatic mutations (random)
  - Germ line mutations (germ-line)
- Infections
  - Viral
    - HPV – cervical cancer
    - Hepatitis – liver cancer
  - Bacterial
    - H. pylori – stomach cancer

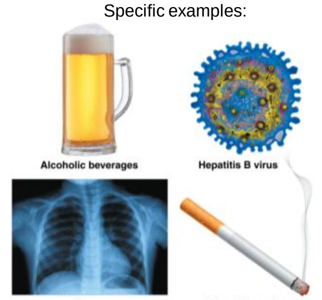


Carcinogens

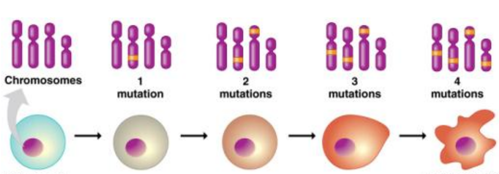
General categories:

- Radiation
- Tobacco smoke
- Diet
- Pollution
- Viruses

Specific examples:



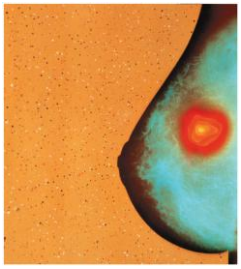
Accumulation of mutations in the development of a cancer cell



Warning signs of cancer (CAUTION)

- Change in bowel (intestine) or bladder habits
- A sore throat (pharyngitis) that does not heal
- Unusual bleeding or discharge (release of body fluids)
- Thickening or mass formation in the breast or elsewhere
- Indigestion or difficulty in swallowing
- Obvious change in wart or mole.
- Nagging (severe) cough or hoarseness (abnormal voice change).

Mammogram of breast tissue



Breast cancer. In this mammogram, normal breast tissue appears as greenish-blue, while the tumor is highlighted yellow and red.

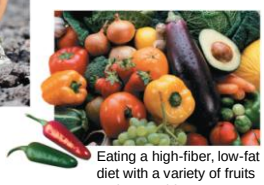
Lifestyle choices affect one's risk of cancer

HPV vaccination protects against cervical, anal, and oral cancer

Cancer prevention

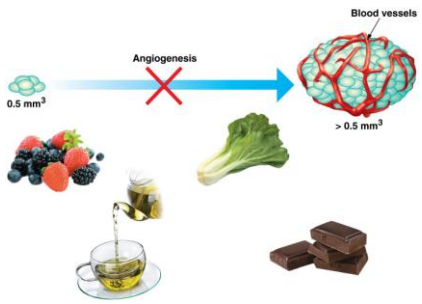
Maintaining a healthy weight

Regular exercise



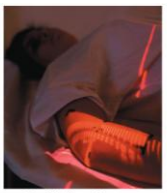
Eating a high-fiber, low-fat diet with a variety of fruits and vegetables

Foods that specifically starve cancer?



Three cancer treatments: "Slash, burn, and poison"

Surgery removes many (but often not all) cancerous cells.



Radiation therapy disrupts cell division.

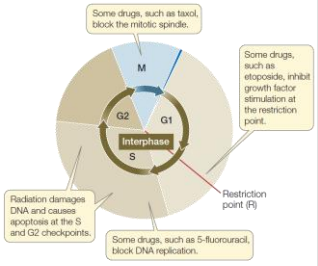
Chemotherapy involves drugs that disrupt cell division.

Cancer treatments

- **Surgery**: If cancer is localized it can be removed. If it has spread then surgeon can remove large portions to reduce symptoms. Potentially healthy tissue is also sometimes removed in case some cancer cells have spread to the tissue.
- **Radiotherapy**: Radiation alters body cells so they are destroyed or cannot reproduce.
- **Chemotherapy**: Drugs targeted at cells that reproduce rapidly (oral or injection)
- Depend on size & site(s)

Cancer treatments

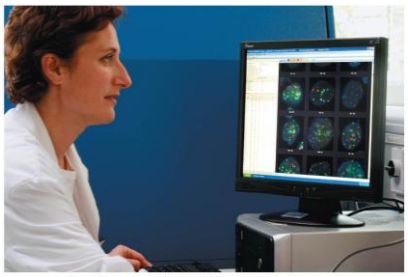
- The most successful and widely used treatment for cancer is surgery. While physically removing a tumor is optimal, it is often difficult for a surgeon to get all of the tumor cells. (A tumor about 1 cm in size already has a billion cells!) Tumors are generally embedded in normal tissues. Added to this is the probability that cells of the tumor may have broken off and spread to other organs. This makes it unlikely that localized surgery will be curative. So other approaches are taken to treat or cure cancer, and these generally target the cell cycle.



11.25 Cancer Treatment and the Cell Cycle To prevent cancer cells from dividing, physicians use combinations of therapies that attack the cell cycle at different points.

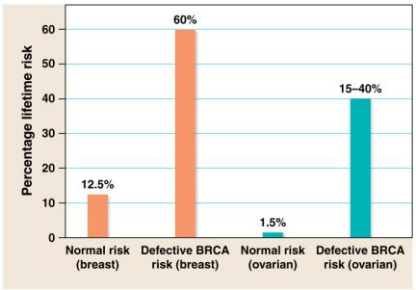
- The drug taxol prevents the functioning of microtubules in the mitotic spindle.
  - inhibit the cell cycle, and apoptosis causes tumor shrinkage.
- More dramatic is radiation treatment, in which a beam of high-energy radiation is focused on the tumor. DNA damage is extensive, and the cell cycle checkpoint for DNA repair is overwhelmed. As a result, the cell undergoes apoptosis.
- A major problem with these treatments is that they target normal cells as well as the tumor cells. These treatments are toxic to tissues with large populations of normal dividing cells such as those in the intestine, skin and bone marrow (producing blood cells).

An individual's cancer cells are genetically tested



Breast cancer cells are being examined to see if they possess extra copies of a particular gene.

BRCA mutations dramatically increase the lifetime risk of developing breast and ovarian cancer



Data from National Cancer Institute, *BRCA1 and BRCA2: Cancer Risk and Genetic Testing, Factsheets: Risk Factors and Possible Causes*, 2009, from http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA#r4

Cancer incidence, United States, 1975–2009

Year of Diagnosis	All Races		
	Both sexes	Males	Females
1975	400.44	466.85	365.68
1976	407.40	481.15	367.40
1977	407.78	486.53	363.75
1978	407.32	488.40	362.21
1979	412.54	496.46	365.60
1980	418.07	505.83	368.11
1981	425.27	510.84	377.13
1982	424.51	511.10	376.22
1983	431.20	520.01	380.81
1984	440.07	525.53	392.53
1985	448.94	531.35	403.23
1986	451.49	538.35	402.41
1987	468.11	563.28	413.36
1988	463.95	558.51	409.33
1989	467.88	567.19	408.44
1990	482.07	592.84	415.60
1991	503.24	637.65	419.13
1992	510.80	658.40	415.04

Year of Diagnosis	All Races		
	Both sexes	Males	Females
1993	493.62	622.34	408.53
1994	483.69	589.96	413.70
1995	477.12	571.84	415.03
1996	479.39	572.79	418.28
1997	486.82	576.02	428.82
1998	488.63	573.22	434.24
1999	491.05	581.30	431.04
2000	486.68	580.44	422.68
2001	490.36	581.38	427.74
2002	488.15	575.04	428.77
2003	475.57	560.05	417.77
2004	476.25	557.78	420.17
2005	472.02	548.60	419.35
2006	475.18	554.24	419.38
2007	480.97	564.97	420.93
2008	474.08	545.12	424.32
2009	474.95	537.88	431.29

Rates are per 100,000 and are age-adjusted to the 2000 U.S. standard population

Source: Surveillance Research Program, National Cancer Institute, http://surveillance.cancer.gov

Cancer death rates, United States, 1975–2009

Year of Death	All Races			Year of Death	All Races		
	Both sexes	Males	Females		Both sexes	Males	Females
1975	199.14	258.43	160.03	1993	213.45	275.89	174.55
1976	202.30	262.23	162.70	1994	211.74	272.12	174.11
1977	203.02	264.23	162.94	1995	209.89	268.50	173.35
1978	204.42	267.07	163.76	1996	207.00	263.75	171.21
1979	204.53	268.65	163.06	1997	203.55	258.13	169.00
1980	206.96	271.08	165.75	1998	200.82	253.63.	166.93
1981	206.40	269.78	165.90	1999	200.72	252.75	167.24
1982	208.32	272.89	167.45	2000	198.76	248.41	166.67
1983	209.21	274.09	168.27	2001	196.09	244.83	164.42
1984	210.91	275.08	170.55	2002	194.03	241.35	163.03
1985	211.35	275.68	170.96	2003	190.46	235.56	160.68
1986	211.79	276.04	171.59	2004	186.37	230.11	157.34
1987	211.91	276.34	171.54	2005	184.72	228.06	155.79
1988	212.62	276.89	172.53	2006	181.55	222.71	153.93
1989	214.30	278.50	174.25	2007	178.70	219.51	151.19
1990	214.95	279.82	174.65	2008	175.78	215.65	148.42
1991	215.06	279.15	175.30	2009	173.09	211.90	146.43
1992	213.46	276.51	174.39				

Rates are per 100,000 and are age-adjusted to the 2000 U.S. standard population

Source: Surveillance Research Program, National Cancer Institute, http://surveillance.cancer.gov

ANCILLARY SLIDE (3 of 4)

Trends in current cigarette smoking in adults, United States, 1965–2010

Source: Centers for Disease Control and Prevention, National Health Interview Survey, 1965–2010.
www.cdc.gov/tobacco/data_statistics/tables/trends/cig_smoking/index.htm