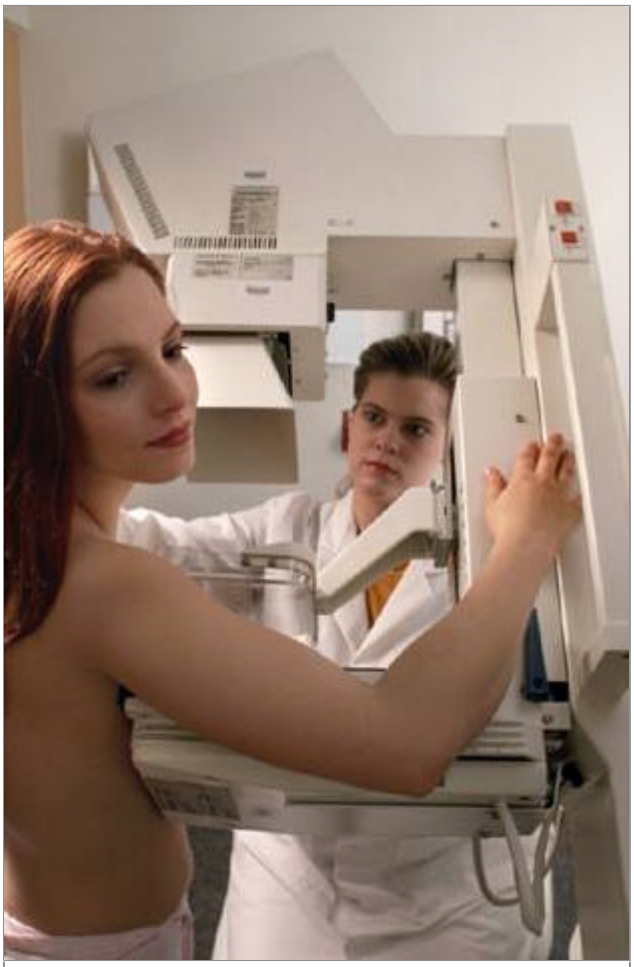
Cancer (medicine)

INTRODUCTION

Cancer (medicine), any of more than 100 diseases characterized by excessive, uncontrolled growth of abnormal cells, which invade and destroy other tissues. Cancer develops in almost any organ or tissue of the body, but certain types of cancer are more lethal than others. Cancer is the leading cause of death in Canada and second only to heart disease in the United States. Each year, more than 1.2 million Americans and 132,000 Canadians are diagnosed with cancer, and more than 1,700 people die from cancer each day in the United States and Canada. For reasons not well understood, cancer rates vary by gender, race, and geographic region. For instance, more males have cancer than females, and African Americans are more likely to develop cancer than persons of any other racial and ethnic group in North America. Cancer rates also vary globally—residents of the United States, for example, are nearly three times as likely to develop cancer than are residents of Egypt.



Tony Stone Images/Charles Thatcher

Woman Receiving a Mammogram

Fifty years ago few people diagnosed with cancer survived longer than one year. Today, 60 percent of Americans diagnosed with cancer live five years or longer. This remarkable turnaround is due, in part, to our ability to detect cancerous tumors early, before they have spread to other parts of the body. Using regular screening tests, even in the absence of any cancer symptoms,

Americans are finding and treating cancers more successfully than ever before. One such screening test, the mammogram, detects tumors and other abnormalities in the breast before they can be felt as a lump by a woman or her doctor. Because catching breast tumors early dramatically improves a woman's chances for survival, the American Cancer Society recommends that women over the age of 40 have an annual mammogram.

Although people of all ages develop cancer, most types are more common in people over the age of 50. Cancer usually develops gradually over many years, the result of a complex mix of environmental, nutritional, behavioral, and hereditary factors. Scientists do not completely understand the causes of cancer, but they know that certain lifestyle choices can dramatically reduce the risk of developing most types of cancer. Not smoking, eating a healthy diet, and exercising moderately for at least 30 minutes each day reduce cancer risk by more than 60 percent.

Just 50 years ago a cancer diagnosis carried little hope for survival because doctors understood little about the disease and how to control it. Today 60 percent of all Americans diagnosed with cancer live longer than five years. While it is difficult to claim that a cancer patient is disease free, long-term survival significantly improves if the patient survives five years. The National Cancer Institute of the United States (NCI) estimates that as many as 8.4 million Americans are living with cancer or have been cured of the disease thanks largely to advances in detecting cancers earlier. The sooner cancer is found and treated, the better a patient's chance for survival. In addition, advances in the fundamental understanding of how cancer develops have reduced deaths caused by certain cancers and hold promise for new and better treatments.

HOW CANCER DEVELOPS

A healthy human body is composed of 30 trillion cells, most of which are in constant turnover as cells die and others reproduce to replace them in an orderly fashion. Healthy cells of the skin, hair, lining of the stomach, and blood, for example, regularly reproduce by dividing to form two daughter cells (*see* Mitosis). This cell division cycle proceeds under the regulation of the body's intricately tuned control system. Among other functions, this control system ensures that cells only divide when needed, so that organs and tissues maintain their correct shape and size. Should this system fail, a variety of backup safety mechanisms prevent the cell from dividing uncontrollably. In order for a cell to become cancerous, every one of these safety mechanisms must fail.

Cancer begins in genes, bits of biochemical instructions composed of individual segments of the long, coiled molecule deoxyribonucleic acid (DNA). Genes contain the instructions to make proteins, molecular laborers that serve as building blocks of cells, control chemical reactions, or transport materials to and from cells. The proteins produced in a human cell determine the function of each cell, and ultimately, the function of the entire body.

In a cancerous cell, permanent gene alterations, or *mutations*, cause the cell to malfunction. For a cell to become cancerous, usually three to seven different mutations must occur in a single cell. These genetic mutations may take many years to accumulate, but the convergence of mutations enables the cell to become cancerous.

A Safety Systems Fail

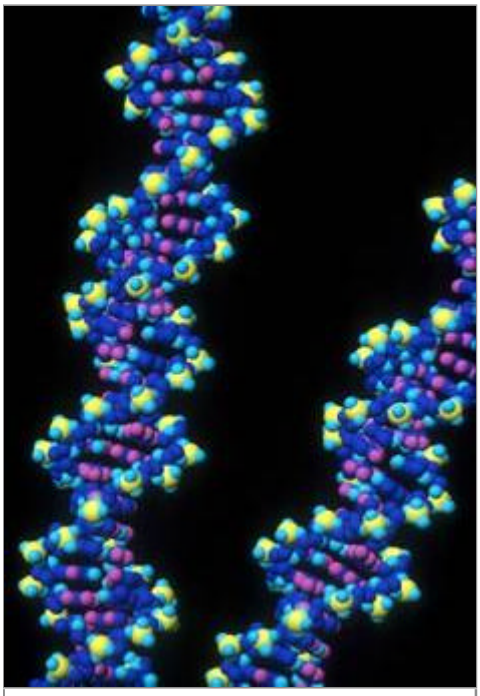


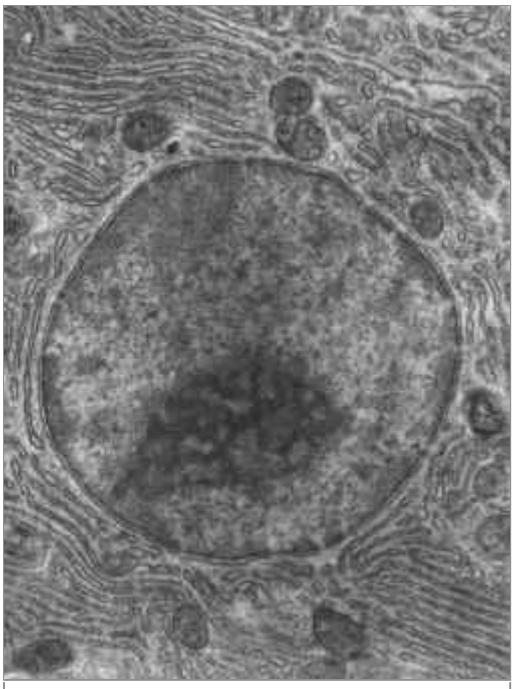
Photo Researchers, Inc./Ken Eward

DNA and Cancer

Cancer begins in the genes, segments of the long, coiled molecule known as deoxyribonucleic acid (DNA). Genes govern the body's development and specific characteristics by providing critical instructions that trigger the production of proteins within the body. In cancer, certain genes fail to perform their jobs correctly. This computer-generated model shows two strands of deoxyribonucleic acid (DNA) and its double-helical structure.

While each human cell performs its own specialized function, it also exerts influence on the cells around it. Cells communicate with one another via receptors, protein molecules on the cell surface. A cell releases chemical messages, which fit into the surface receptors of cells nearby, much as a key fits into a lock. A cell may instruct other cells in its neighborhood to divide, for example, by releasing a growth-promoting signal, or *growth factor*. The growth factor binds to receptors on adjacent cells, activating a message within each individual cell. This message travels to the nucleus, where a cell's genes are located.

A1 Proto-Oncogenes Become Oncogenes



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Nucleus of a Cell

The nucleus, present in eukaryotic cells, is a discrete structure containing chromosomes, which hold the genetic information for the cell. Separated from the cytoplasm of the cell by a double-layered membrane called the nuclear envelope, the nucleus contains a cellular material called nucleoplasm. Nuclear pores, present around the circumference of the nuclear membrane, allow the exchange of cellular materials between the nucleoplasm and the cytoplasm.

When the growth factor message reaches the cell nucleus, it activates genes called proto-oncogenes. These genes produce proteins that stimulate the cell to divide. In cancerous cells, mutations in proto-oncogenes cause these genes to malfunction. When a proto-oncogene mutates, it becomes an *oncogene*—a gene that instructs the cell to grow and divide repeatedly without stimulation from neighboring cells. Some oncogenes overproduce growth factors, causing the cell to divide too often. Other oncogenes stimulate the cell to reproduce even when no growth factor is present. Cancer researchers have identified about 100 different types of proto-oncogenes and their cancer-causing oncogene counterparts.

A2 Tumor Suppressor Genes Stop Working

When runaway cell division occurs, it does not necessarily lead to cancer. Neighboring cells respond by excreting a growth inhibitor. This chemical binds to receptors in the malfunctioning cell, sending a signal to the nucleus that activates tumor suppressor genes. Tumor suppressor genes are like brakes for cell growth. When activated, these genes halt the cell cycle, preventing further cell division.

But if tumor suppressor genes malfunction due to mutations, the rapidly dividing cell ignores messages from its neighbors telling it to stop dividing. Malfunctioning tumor suppressor genes are not

enough to cause cancer—the cell still must overcome a host of other safety mechanisms before it can cause truly significant damage.

A3 Cell Cycle Clock Malfunctions

The cell nucleus contains a collection of interacting proteins that control cell division. Sometimes called the cell cycle clock, this group of proteins interprets incoming messages at several checkpoints in the cell division cycle. At these checkpoints, the clock evaluates the health of the cell. If conditions are right, the clock activates certain proto-oncogenes, which produce proteins that trigger the cell to enter the next stage of the cell cycle. If conditions are not right, certain tumor suppressor genes produce proteins that prevent the cell from proceeding with cell division.

If the cell cycle clock detects DNA damage in a cell, a tumor suppressor gene called p53 prevents the cell from reproducing until the damage is repaired. If the cell is unable to repair the DNA damage, p53 instructs the cell to undergo programmed cell death, or *apoptosis*, putting a stop to runaway cell division before it starts. Programmed cell death is a normal part of cell life and is tightly controlled by many genes, primarily p53.

In a cancerous cell, one or more mutations prevent these genes from doing their jobs. When mutated, p53 allows a cell to continue to divide, even with damaged DNA. This can lead to additional mutations in proto-oncogenes or tumor suppressor genes. In some cases, mutations occur in genes that produce proteins to repair damaged DNA. Such mutations can lead to yet other mutations because the faulty DNA cannot duplicate properly during cell division.

A4 Cells Achieve Immortality

A normal cell has a life span of about 40 cell divisions. This life span is controlled in part by telomeres, protective segments at the ends of the cell's DNA. Telomeres shorten with each cell division until they can no longer protect the DNA. At this point cell division severely damages the DNA, ultimately killing the cell. This normal process ensures that older cells, which may have accumulated mutations, no longer reproduce. Cancer cells escape this protective mechanism by producing a protein called telomerase. Telomerase extends the length of telomeres indefinitely, rendering the cells immortal and capable of never-ending cell division.

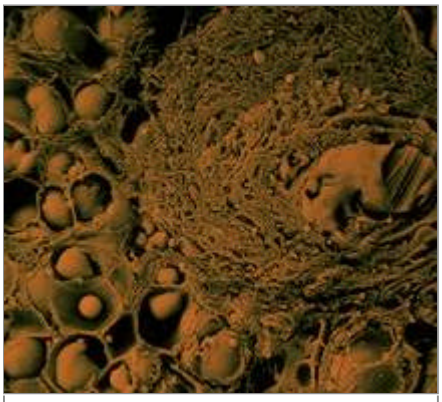
B Cells Break Free and Spread

Evading the many obstacles that guard against runaway cell division is still not enough for cancer to develop. A malfunctioning cell must also skirt a number of safety mechanisms designed to prevent cells from growing where they are not supposed to in the body.

Normal cells adhere to each other and to a fibrous meshwork called an extracellular matrix. This matrix exists throughout all tissues and provides the structural support on which cells grow and form organs and other complex tissues. While a normal cell will often die if it cannot adhere to an

extracellular matrix, cancer cells survive without this matrix.

B1 Tumor Forms



Oxford Scientific Films/Manfred Kage

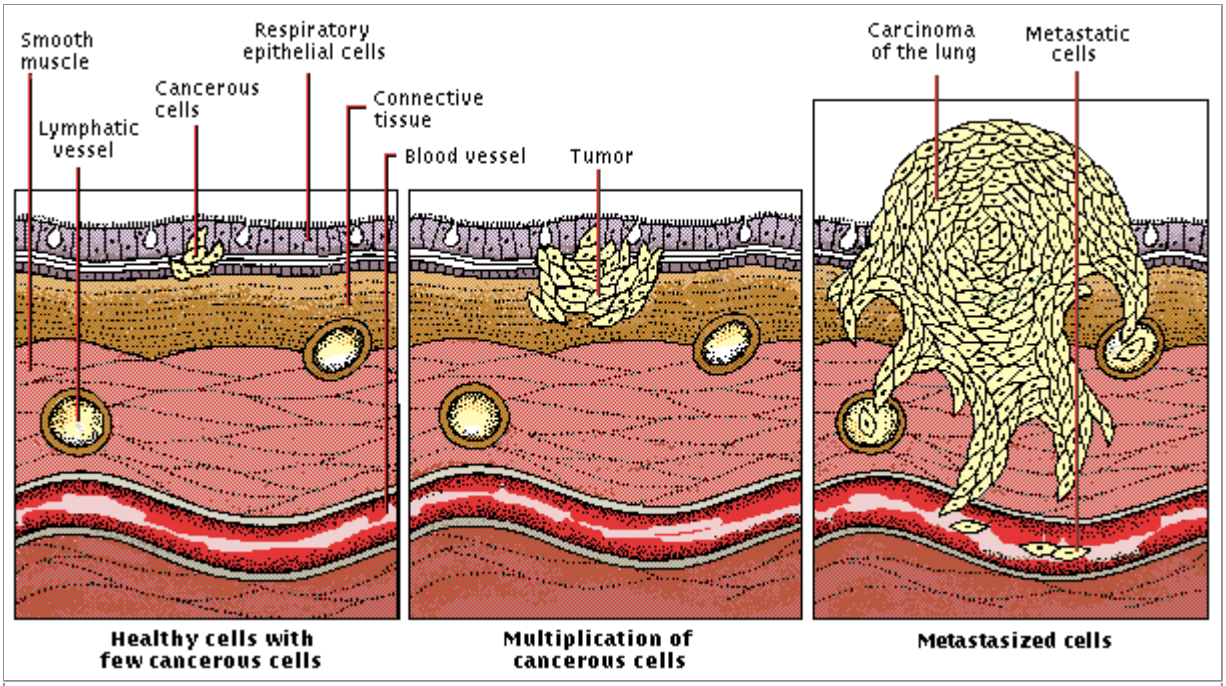
Abnormal Cells and Cancer

Cancerous cells usually become much different from the tissue from which they arise. The ovarian tumor pictured here bears no resemblance to the normal tissue of the ovary.

A tumor is a mass of cells not dependent upon an extracellular matrix. These cells can grow on top of each other, creating a mass of abnormal cells. Often a tumor develops its own network of tiny blood vessels to supply itself with nutrient-rich blood, a process called *angiogenesis*.

There are two general types of tumors. Benign tumors do not invade other tissues and are limited to one site, making surgical removal possible and the odds for a full recovery excellent. Some benign tumors are quite harmless and are not surgically removed unless they are unsightly or uncomfortable. For example, warts are benign tumors of the outer layer of the skin. Although they are usually not dangerous, warts may cause discomfort. Other benign tumors are thought to be precursors to cancerous, or malignant, tumors.

B2 Tumors Spread



The Development and Spread of Tumors

Lung cancer begins when epithelial cells lining the respiratory tract start to reproduce in an uncontrolled fashion. These cells invade surrounding tissue, forming a mass called a tumor and, when hardened, a carcinoma. Cancerous cells may penetrate blood and lymph vessels, to be carried through the body until they reach a juncture through which they cannot pass. At this point, they lodge and new tumors form. Metastasis, the spreading of cancer from its original location to other parts of the body, is the disease's most destructive characteristic.

Tumors are malignant only if they can invade other parts of the body. Malignant tumors extend into neighboring tissue or travel to distant sites, forming secondary growths known as metastases. To metastasize, tumor cells break through a nearby blood vessel to enter the circulatory system or through a lymphatic vessel wall to enter the lymphatic system. Most metastases occur in organs that are the next site downstream in the circulatory system or the lymphatic system and contain a network of capillaries, or small blood vessels. For example, cancer of the large intestine often travels through the bloodstream to the liver, the organ immediately downstream from the intestines. In the lymphatic system, tumor cells can spread to surrounding lymph nodes, or lymph glands. Normally, lymph nodes filter out and destroy infectious materials circulating in the lymphatic system.

The unique receptors on the surface of a cell may also play a role in where tumors metastasize. Specialized molecules on a cell's surface identify where in the body the cell belongs. Similar cells adhere to one another when their surface receptors are compatible. Most often cells from different tissues and organs have incompatible surface receptors. However, some tissue types share similar surface receptors, enabling cancerous cells to move between them and proliferate. Prostate cells and bone cells, for example, have similar surface receptors. This gives prostate cancer cells a natural affinity for bone tissue, where they can settle to form a new tumor.

Many cancers shed cells into the bloodstream early in their growth. Most of these cells die in the

bloodstream, but some lodge against the surface of the blood vessel walls, eventually breaking through them and into adjacent tissue. In some cases, these cells survive and grow into a tumor. Others may divide only a few times, forming a small nest of cells that remain dormant as a micrometastasis. They may remain dormant for many years, only to grow again for reasons not yet known.

III CAUSES OF CANCER

Scientists do not fully understand the causes of cancer, but studies show that some people are more likely to develop the disease than others. The incidence of cancer varies enormously among different regions. The highest death rate from all cancers in males is 272 per 100,000 men in Hungary while the lowest death rate of 80 men per 100,000 is found in Mauritius, an island off the coast of eastern Africa. For women the highest cancer rate is 140 per 100,000 women in Denmark compared to only 63 per 100,000 women in Azerbaijan in western Asia. The figures for the United States are 156 per 100,000 men and 108 per 100,000 women. For particular cancers, the difference between countries may be as high as 40-fold. Differences also occur within populations. Cancer rates vary between sexes, races, and socioeconomic groups, for example.

Scientists called epidemiologists study particular populations to identify why cancer rates vary (*see* Epidemiology). One method they use is to compare behavior and characteristics such as the gender, age, diet, or race of cancer patients to those of healthy people. Population studies provide useful information about risk factors that increase the likelihood of developing cancer.

A Carcinogens

One of the greatest risk factors for cancer is prolonged or repeated exposure to carcinogens—chemical, biological, or physical agents that cause the cellular damage that leads to cancer. The details of how carcinogens cause cancer remain unclear. One theory is that exposure to carcinogens, when combined with the effects of aging, causes an increase in chemicals in the body called free radicals. An excessive number of free radicals causes damage by taking negatively charged particles called electrons from key cellular components of the body, such as DNA. This may make genes more vulnerable to the mutating effects of carcinogens.

A1 Tobacco Smoke

Smoking causes up to 30 percent of cancer deaths in the United States and Canada, making tobacco smoke the most lethal carcinogen in North America. Smoking is associated with cancer in the lungs, esophagus, respiratory tract, bladder, pancreas, and probably cancers of the stomach, liver, and kidneys. The risk of cancer increases depending on the number of cigarettes smoked per day, the cigarette's tar content, and how many years a person smokes. Starting to smoke while young significantly increases the risk of developing cancer.

Each year in the United States, about 3,000 nonsmoking adults die of lung cancer caused by exposure

to the smoke of others 'cigarettes, called secondhand smoke or environmental tobacco smoke. Nonsmoking spouses of smokers are 30 percent more likely to develop lung cancer than those married to nonsmokers. Breathing secondhand smoke also increases the risk of cancer in the children of smokers and in nonsmokers who work in smoky places, such as restaurants and bars.

Cigars, pipes, and smokeless tobacco have also been implicated in increased risk for cancer. Cigars contain most of the same cancer-producing chemicals as cigarettes, and people who smoke cigars have a 30 percent higher risk of developing cancer than nonsmokers. Oral cancers occur more frequently in people who use smokeless tobacco, or *snuff*. Snuff users, for example, are 50 times more likely to develop cancers of the cheek or gum than nonusers.

A2 Diet

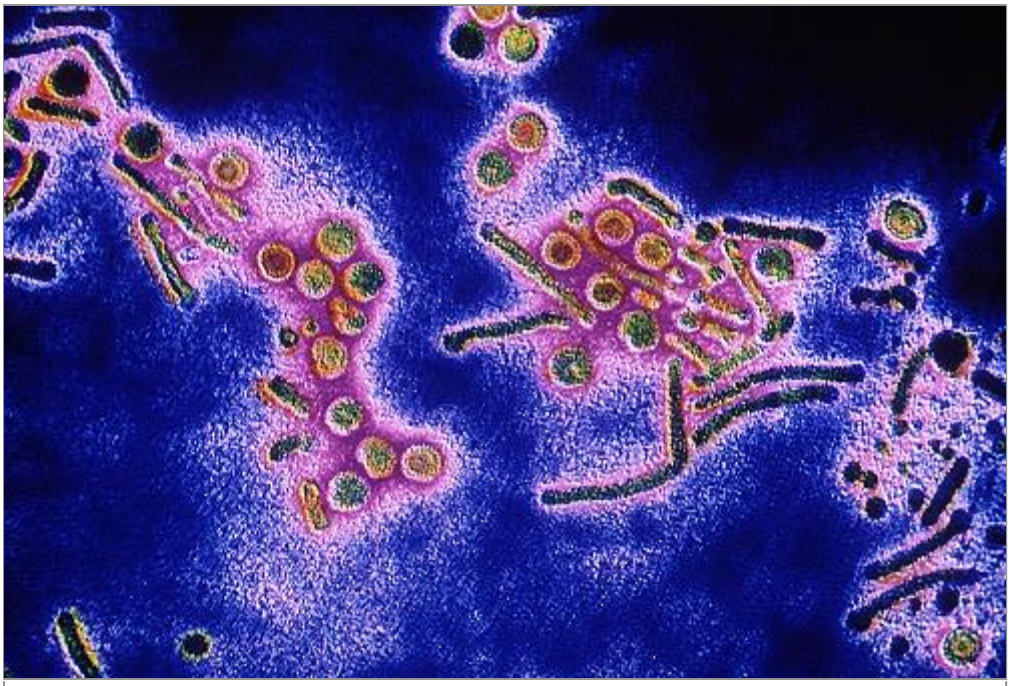
Corbis/Owen Franken

Hamburger and Fries

A diet high in fatty foods, such as what some consider to be the quintessential American meal—a hamburger and fries—can contribute to many cancers.

Diet accounts for about another 30 percent of cancer deaths in the North America. Saturated fats from red meats, such as hamburger or steak, and other animal products are linked with several cancers. High salt intake increases the risk of stomach cancer. Adult obesity increases the risk for cancer of the uterus in women and also appears to increase the risk for cancers in the breast, colon, kidney, and gallbladder. Alcohol consumption increases the risk of cancer of the esophagus and stomach, especially when combined with smoking.

A3 Pathogens



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Hepatitis B Virus

The hepatitis B virus (HBV), recognizable under magnification by the round, infectious "Dane particles" accompanied by tube-shaped, empty viral envelopes, causes nearly 80 percent of liver cancers worldwide.

Some carcinogens are living organisms. Certain viruses, bacteria, and parasites account for about 15 percent of all cancer deaths in the United States. Cancer-causing viruses include the human papilloma virus (HPV), a sexually transmitted virus responsible for 70 to 80 percent of all cases of cancer of the cervix. Hepatitis B and C viruses cause almost 80 percent of all liver cancer in the world. Epstein-Barr virus can also be carcinogenic, causing cancer of the lymphatic system. Human immunodeficiency virus (HIV) or a type of herpesvirus can lead to rare cancers of the lymphatic and circulatory systems. *Helicobacter pylori*, a bacterium associated with stomach ulcers, likely causes cancer of the stomach.

In developing countries, parasitic organisms are major carcinogens. In parts of Africa, China, and southern Asia, infestation with the liver fluke *Clonorchis sinensis* causes a form of liver cancer. In North Africa, infection with the parasite *Schistosoma haematobium* causes cancer of the bladder.

A4 Radiation

Exposure to electromagnetic radiation, invisible, high-energy light waves such as sunlight and X rays, accounts for about 2 percent of all cancer deaths (*see* Radiation Effects, Biological). Most cancer deaths from radiation are from skin cancer, which is triggered by too much sun exposure. Sunlight that reaches the Earth's surface contains two kinds of ultraviolet (UV) radiation. UV-A and UV-B both contribute to sunburn and skin cancer as well as to conditions such as premature wrinkling of the skin. Depletion of the ozone layer, which absorbs ultraviolet radiation in the upper atmosphere, will continue to increase skin damage and skin cancer rates in the future.

Radon, a colorless, odorless, radioactive gas, seeps from the Earth in some regions of the United States. Breathing the gas over a long period has been linked to a small number of lung cancer cases. Providing adequate air circulation in a building reduces exposure to radon. Infrequently, radiation exposure associated with medical treatments, such as therapeutic radiology, leads to cancer. This type of exposure is responsible for about 1 percent of all U.S. cancer deaths.

A5 Environmental and Occupational Chemicals

Air pollution, water pollution, and pollutants in the soil account for about 2 percent of all cancer deaths in the country, particularly due to lung and bladder cancer. Lung cancer rates are generally higher in cities, where increased industry and automobile traffic produce air pollution. Some people encounter carcinogenic chemicals in their working environment. Occupational carcinogens account for about 5 percent of all U.S. cancer deaths and include such industrial chemicals as benzene, asbestos, vinyl chloride, aniline dyes, arsenic, and certain petroleum products (*see* Occupational and Environmental Disease).

B Hereditary Factors

Evidence suggests that heredity plays a role in developing cancer. Some gene mutations associated with cancer are inherited. For example, inheritance of the mutated tumor suppressor genes BRCA1 or BRCA2 greatly increases the risk of breast cancer in young women. About 50 to 60 percent of women with inherited BRCA1 or BRCA2 mutations will develop breast cancer by the age of 70. Inherited mutations in the genes MSH2, MLH1, PMS1, and PMS2, all of which repair DNA, are especially prevalent in a rare form of hereditary colon cancer.

Scientists suspect that many other hereditary factors contribute to cancer. In addition to inherited mutations, other genetic variations, particularly those influencing how the body responds to carcinogens, may create a greater susceptibility to cancer. The identities of the majority of these genetic variations are not yet known.

C Steroid Hormones

Medical research suggests that cancers of the reproductive organs may be affected by naturally occurring steroid hormones produced by the endocrine system. These hormones stimulate reproductive organ cells to divide and grow. In women, relatively high or long exposure to the female sex hormone estrogen seems to increase the risk of breast and uterine cancers. Thus, early age at first menstruation, late age at menopause, having children after age 30, and never having children, all of which affect the duration of estrogen exposure in the body, increase the risk for these cancers. Some evidence also suggests that estrogen replacement therapy (ERT), in which women take estrogen to offset the unpleasant effects of menopause, may also increase the risk of some cancers of the reproductive organs. The risk appears to go down significantly, however, when estrogen and another female sex hormone, progesterone, are taken together. At one time studies showed a link between birth control pills and cancer. However, these studies examined early forms of birth control

pills, which contained high levels of estrogen. Today's birth control pills contain progesterone, as well as lower levels of estrogen, and carry very little risk of cancer. Male sex hormones, particularly testosterone, also appear to play a role in cancers of the male reproductive organs, but this role is not yet well understood.

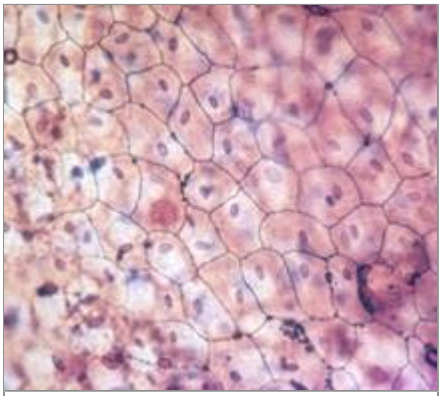
D Population Demographics

Population studies show that a person's age, race, and gender affect the probability that he or she will develop cancer. Most cancers occur in adults middle-aged or older. The risk of cancer increases as individuals age because genetic mutations accumulate slowly over many years, and the older a person is, the more likely that he or she will have accumulated the collection of mutations necessary to turn an otherwise healthy cell into a cancerous cell. Women aged 20 to 29, for example, account for just 0.3 percent of all cases of breast cancer, but women over age 50 account for more than 75 percent of breast cancer cases. Cancer of the prostate gland shows similar age discrimination. According to the American Cancer Society (ACS) and the National Cancer Institute of Canada (NCIC), more than 75 percent of all prostate cancers are diagnosed in men who are over the age of 65.

Statistics show that men are more likely to develop cancer than women. In the United States, half of all men will develop cancer at some point in their lifetimes. About one-third of all American women will develop cancer. Cancer statistics for Canada are similar. Stomach cancer is about twice as common in men than in women, as are certain types of kidney cancer. However, the reasons for the discrepancy between the sexes are unknown.

Some cancers are more prevalent in particular races than others. In the United States, for example, bladder cancer is twice as common in white people than it is in black people. White women are slightly more likely to develop breast cancer than are black women, but black women are more likely to die of the disease. Asian, Hispanic, and Native American women have the lowest breast cancer risk. On the whole, African Americans, especially men, are more likely to develop cancer—and more likely to die from it—than members of any other group in the United States. Reasons for the discrepancies between races are still not entirely clear, but many epidemiologists trace them to differences in diet and exercise, unequal access to medical care, and exposure to carcinogens.

IV TYPES OF CANCER



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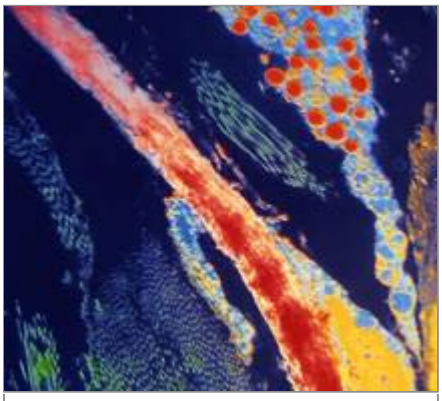
Epithelial Cells

Epithelial tissue forms a protective layer of cells that covers organ surfaces and lines body cavities. Shown here is a layer of simple *squamous* (scaly) epithelium under magnification. Cancers that arise in epithelial tissues, called carcinomas, account for approximately 90 percent of all human cancers.

More than 100 types of cancer develop in the various organs in the body. Cancers are described according to where in the body the cancer originated, what type of tissue it originated in, and what type of cell it started in. For example, breast cancer describes any cancer that originated in the breast. If the cancer spreads to a new organ, such as the lungs, the tumor is called metastatic breast cancer, not lung cancer.



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Connective Cell Tissues

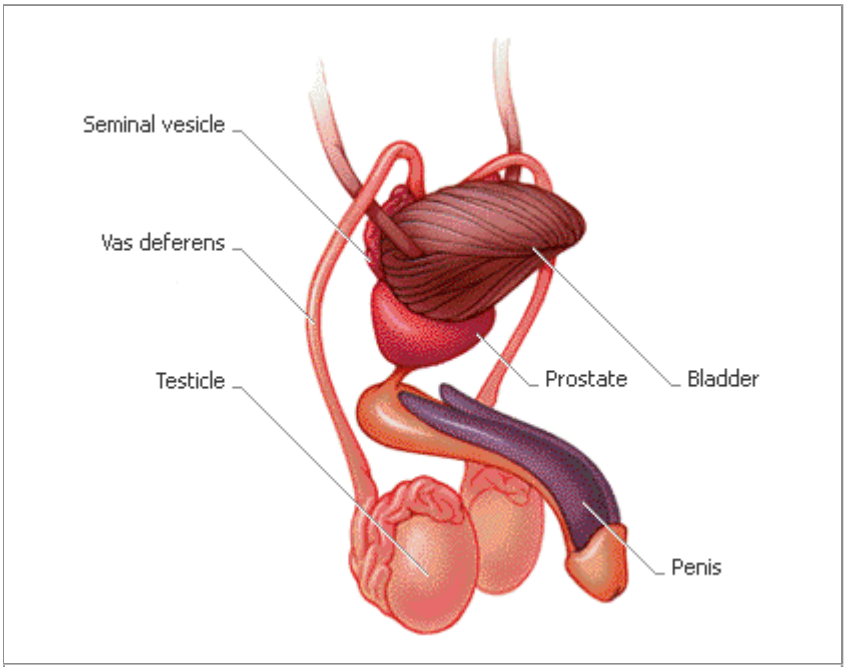
Connective tissues include bone, cartilage, fat, ligaments, and tendons. These tissues support and connect parts of the body. The structure varies depending on the purpose of the tissue. The diagonal red band in this image shows elastin fiber, which allows connective tissue to spring back into shape following deformation. Cancers called sarcomas orginate in connective tissues. Rare, sarcomas constitute only about 2 percent of all human cancers. Sarcomas are elusive in their early stages. They may arise deep within connective tissues, making them more likely to spread to distant parts of the body before they are detected.

Each organ in the body is composed of different types of tissue, and most cancers arise in one of three main types—epithelial, connective, or blood-forming tissue. Carcinomas are cancers that occur in epithelial tissues—the skin and inner membrane surfaces of the body, such as those of the lungs, stomach, intestines, and blood vessels. Carcinomas account for approximately 90 percent of human cancers. Sarcomas originate in connective tissues—such as muscle, bone, cartilage, and fat—that support and connect other parts of the body. Much rarer than carcinomas, sarcomas account for less than 2 percent of all cancers. Leukemias develop in blood cells, and lymphomas originate in the lymphatic system. Combined, these cancers of the blood-forming tissues account for about 8 percent of all human cancers.

Cancers are further identified according to the type of cell affected. For example, squamous cells are flat, scalelike cells found in epithelial tissue. Cancers that originate in these cells are called squamous cell carcinomas. Adenomatous cells are glandular or ductal cells, and carcinomas that originate in

these cells are called adenocarcinomas. Sarcomas that develop in fat cells are called liposarcomas, and those that develop in bone cells are called osteosarcomas.

A Prostate Cancer



Prostate Gland

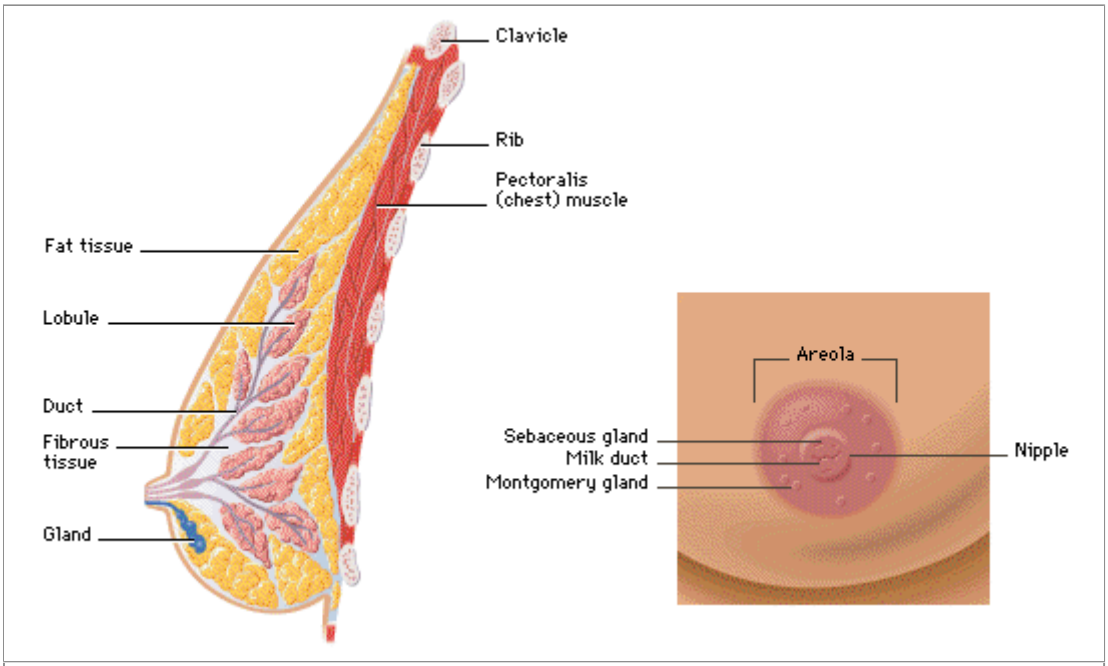
The prostate gland is a walnut-sized organ that rings the male urethra. The secretions of the prostate and Cowper's glands add nutrients to semen, the fluid in which sperm is ejaculated from the body. Cancer of the prostate gland is a common type of cancer in men.

Cancer of the prostate gland, a walnut-sized organ surrounding the urethra in males, is the most common cancer in North American males. About 180,000 new cases of prostate cancer in the United States and 16,900 in Canada are diagnosed every year. For unknown reasons, the prevalence in black men is nearly twice as high as in white men. Prostate cancer risk increases with age, and some evidence suggests that high-fat diets may increase the risk of developing the disease.

Most prostate cancers are adenocarcinomas, cancers that arise in glandular cells of the prostate's epithelial tissue. Prostate cancers usually progress slowly and produce no symptoms in the initial stages. Eventually, the tumor may enlarge the prostate gland, pressing on the urethra and causing painful or frequent urination and blood in the urine or semen. Sometimes pain in the lower back, pelvis, or upper thighs may signal that prostate cancer cells have spread to the ribs, pelvis, and other bones. All these symptoms, however, may have other causes, such as infection of the prostate or prostate enlargement, a natural result of the aging process.

The prognosis for prostate cancer is quite good if it is caught and treated early. The five-year survival rate for American men with prostate cancer is almost 92 percent, but this number rises to almost 100 percent if the tumor is caught early.

B Breast Cancer



Human Female Breast

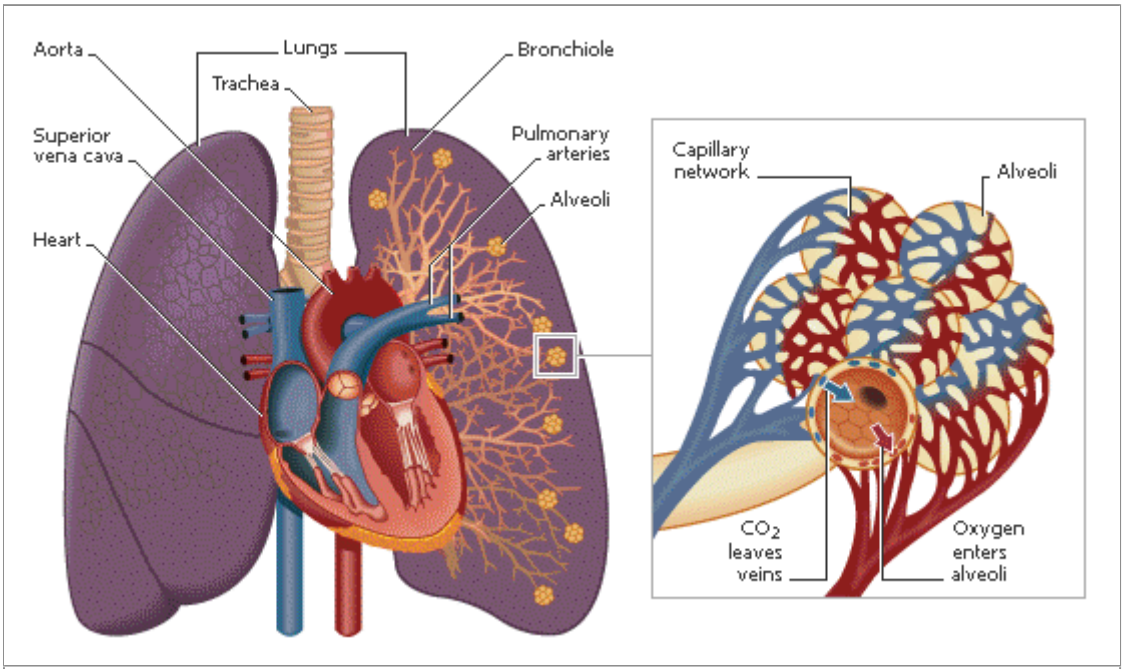
In the center of the human female breast is the protruding nipple, which is surrounded by a pigmented circular area called the areola. Internally, the breast is composed of milk glands surrounded by fatty tissue and some connective tissue. Produced by the lobules in the interior of the breast, milk is carried to the nipple by a collection of tubes known as ducts. Breast cancers may start in the milk glands, milk ducts, fatty tissue, or connective tissue. Cancers of the breast are the most common cancers in women, affecting 1 in every 8 American women who live to age 80.

Breast cancer is the most common type of cancer in women, and the second most common cancer in North America. Every year 183,000 new cases of breast cancer are diagnosed in the United States, and 19,200 cases are diagnosed in Canada. The majority of cases occur in women over 50, and as with most cancers, the risk of developing breast cancer increases with age. An American woman who lives to age 80 has a one in eight chance of developing breast cancer. Breast cancer strikes men as well as women, but male breast cancer accounts for less than 1 percent of all breast cancer cases. Cancer researchers have found that approximately 5 percent of all breast cancer cases are associated with inherited mutations in genes such as BRCA1, BRCA2, and p53. The protein HER-2 (also called HER2/neu), produced by oncogenes, is present in about one-third of all breast cancers. Other risk factors include a family history of the disease, early onset of menstruation, late menopause, never having children, or having a first child after age 30, conditions that seem to extend the duration of estrogen exposure in the body.

The breast is made up of milk-secreting glands called lobules; ducts that connect the glands to the nipple; and fatty, connective, and lymphatic tissue. Breast cancer occurs in any of these components of the breast. Ductal carcinomas account for 80 percent of all breast cancers. Between 10 and 15 percent of breast cancers are lobular carcinomas. Other types of breast cancer are much more rare; combined, they make up the remaining 5 to 10 percent of all breast cancer cases.

Most breast cancers are first detected as an unusual mass or lump in the breast. If the cancer is detected and treated early, the odds of recovering from breast cancer are quite good. The American five-year survival rate for all breast cancers is 83 percent, but if the tumor is detected early, it rises to 96 percent.

C Lung Cancer



Human Lungs

Lung cancer is the leading cause of cancer death in the United States and Canada. The two branches of the trachea, called bronchi, subdivide within the lobes into smaller and smaller air vessels. These lobes terminate in alveoli, tiny air sacs surrounded by capillaries. When the alveoli inflate with inhaled air, oxygen diffuses into the blood in the capillaries to be pumped by the heart to the tissues of the body, and carbon dioxide diffuses out of the blood into the lungs, where it is exhaled. Most lung cancers originate in the lining of the bronchi, but cancer can also begin in the trachea, bronchioles, or alveoli.

With 164,000 new cases in the United States and 20,600 new cases in Canada diagnosed each year, lung cancer is the third most common type of cancer in North America. Although it ranks below prostate cancer and breast cancer in prevalence, lung cancer is the leading cause of cancer death in the United States and Canada. In the United States, the five-year survival rate for lung cancer is quite low at 14 percent, and that number climbs only to 50 percent if the cancer is detected early.

The single largest risk factor for lung cancer is cigarette smoking, a behavior that accounts for 85 to 90 percent of all cases. Long-term exposure to secondhand smoke also causes lung cancer. Other major risk factors include workplace exposure to carcinogenic chemicals, particularly asbestos and organic chemicals such as vinyl chloride. Exposure to radon gas and other air pollutants also increases lung cancer risk, particularly among smokers.

Phototake NYC/Martin Rotker

Cancerous Human Lung

This dissection of human lung tissue shows light-colored cancerous tissue in the center of the photograph. At bottom center lies the heart. While normal lung tissue is light pink in color, the tissue surrounding the cancer is black and airless, the result of a tarlike residue left by cigarette smoke. In their cancerous state, lung cells lack the cilia that normally catch and eliminate foreign particles inhaled into the lung. Mucus ordinarily cleared by bronchial cilia becomes trapped, blocking air passages. Epidemiologists estimate that cigarette smoking is directly responsible for about 85 percent of all lung cancer.

Oxygen reaches the blood through a series of tubes and passages in the lungs. The trachea, commonly known as the windpipe, brings air into the lungs. It divides into tubes called the bronchi, which divide into smaller branches called the bronchioles. At the end of the bronchioles are tiny air sacs known as alveoli. Most lung cancers start in the lining of the bronchi, but cancer can also begin in the trachea, bronchioles, or alveoli. About 20 percent of people with lung cancer have small cell carcinoma, a type of lung cancer that usually starts near the bronchi. Squamous cell carcinoma also often originates near the bronchi. It accounts for about 30 percent of all lung cancers. Adenocarcinomas, usually found in the outer region of the lung, account for about 40 percent of all lung cancer. Several rare types of lung cancers make up the remaining 10 percent of lung cancer cases.

Lung cancer often goes unnoticed in its early stages. The patient may develop a persistent cough or find that a chronic cough is worsening. Other symptoms include chest pain, shortness of breath, hoarseness, bloody fluid coughed up from the respiratory tract, and frequent bouts of bronchitis or pneumonia. Sometimes the first symptoms of lung cancer are bone pain, headaches, dizziness, or other signs that the disease has metastasized.

D Colorectal Cancer

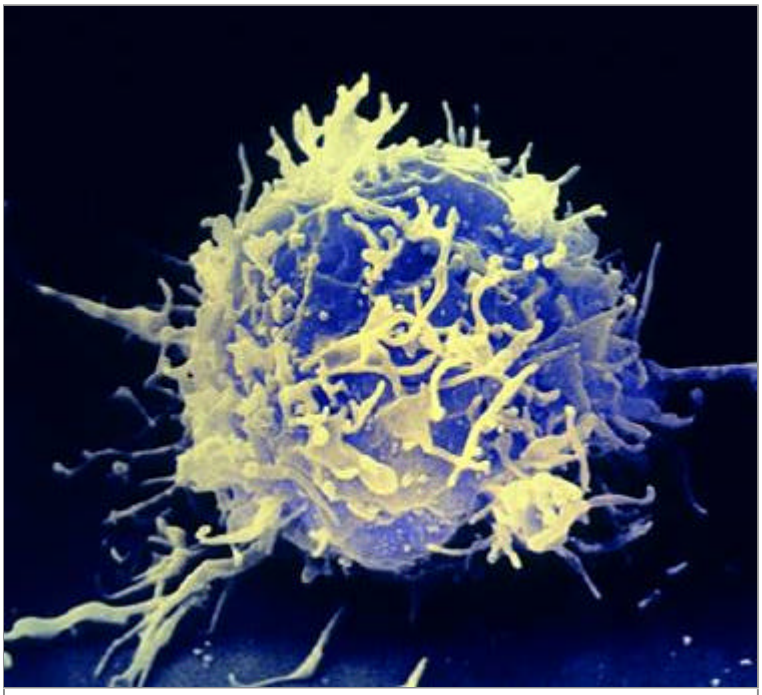
Colorectal cancer, cancer of the large intestine, is the fourth most common cancer in North America, accounting for about 130,000 new American cancer cases and about 17,000 new Canadian cases of cancer each year. Many cases of colorectal cancer are associated with low levels of physical activity and with diets that are low in fruits and vegetables. Individuals with a family history of the disease have a higher risk. High rates of colorectal cancer are also found in people who have colorectal polyps, fleshy growths on the inside lining of the large intestine, and in those who have inflammatory bowel

disease, a condition causing pain and inflammation of the small intestine and the colon.

The large intestine consists of the colon and the rectum. The colon is a muscular tube about 1.5 m (5 ft) long. Digestive wastes from the small intestine pass through the colon and the rectum before being expelled from the body. Over 95 percent of colorectal cancers are adenocarcinomas, cancers of the glandular cells lining the inside of the colon and rectum. Other cancers of the large intestine, such as sarcomas, are much more rare.

Colorectal cancer usually develops slowly and may not produce noticeable symptoms in its early stages. Some individuals with undiagnosed colorectal cancer may detect blood in their feces. They may also experience persistent constipation or diarrhea, abdominal pain, or unexplained weight loss. Eventually the tumor may grow so large that it obstructs the intestine or causes it to rupture. In the United States the five-year survival rate for colorectal cancer is 60 percent, but it climbs to 90 percent if the cancer is detected early.

E Lymphoma



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Lymphocyte

Lymphomas develop in the cells of the lymphatic system. This scanning electron micrograph shows one of the primary cells of the lymphatic system, a T lymphocyte. T lymphocytes are specialized white blood cells that identify and destroy invading organisms such as bacteria and viruses. Some T lymphocytes directly destroy invading organisms, whereas other T lymphocytes regulate the immune system by directing immune responses. Cancers of the T lymphocytes, which comprise 15 percent of all lymphomas, spread through the lymphatic system to other parts of the body.

An estimated 62,000 Americans and almost 6,000 Canadians are diagnosed each year with lymphoma, also known as non-Hodgkin's disease, a group of related cancers involving the lymphatic system. The

lymphatic system consists of many organs—including lymph nodes, the spleen, the tonsils and adenoids—and of cells in the bone marrow and in the digestive and respiratory systems. The main cell type found in the lymphatic system is the lymphocyte. There are two main types of lymphocytes, B lymphocytes (B cells) and T lymphocytes (T cells). Lymphomas develop in both types of lymphocytes—B-cell lymphomas make up 85 percent of all lymphoma cases, and T-cell lymphomas constitute the remaining 15 percent.

Lymphomas interfere with the function of healthy lymphocytes and spread to other organs in the body, where they compress and destroy healthy tissue. The most common symptom of lymphoma is a painless swelling in the lymph nodes in the neck, underarm, or groin. Other symptoms include fevers, night sweats, tiredness, weight loss, itching, and reddened patches on the skin. Sometimes there is nausea, vomiting, or abdominal pain.

Lymphoma risk increases with decreasing immune function, such as that caused by acquired immunodeficiency syndrome (AIDS) or exposure to certain infectious agents. Organ transplant recipients are also at higher risk because they take drugs that weaken the immune system as part of the transplantation process (*see* Medical Transplantation). The overall five-year survival rate for lymphoma in the United States is 51 percent, but people with less-severe tumors have a good chance of surviving longer than ten years.

Hodgkin's disease, or Hodgkin's lymphoma, is a less severe lymphoma diagnosed in approximately 7,000 Americans and 800 Canadians each year. Although the symptoms are similar to those of other lymphomas, the cancer cells in Hodgkin's disease look different under a microscope. Hodgkin's disease is easier to treat than other types of lymphomas, a factor reflected in the five-year survival rate—more than 80 percent of people diagnosed with Hodgkin's disease survive five years or longer.

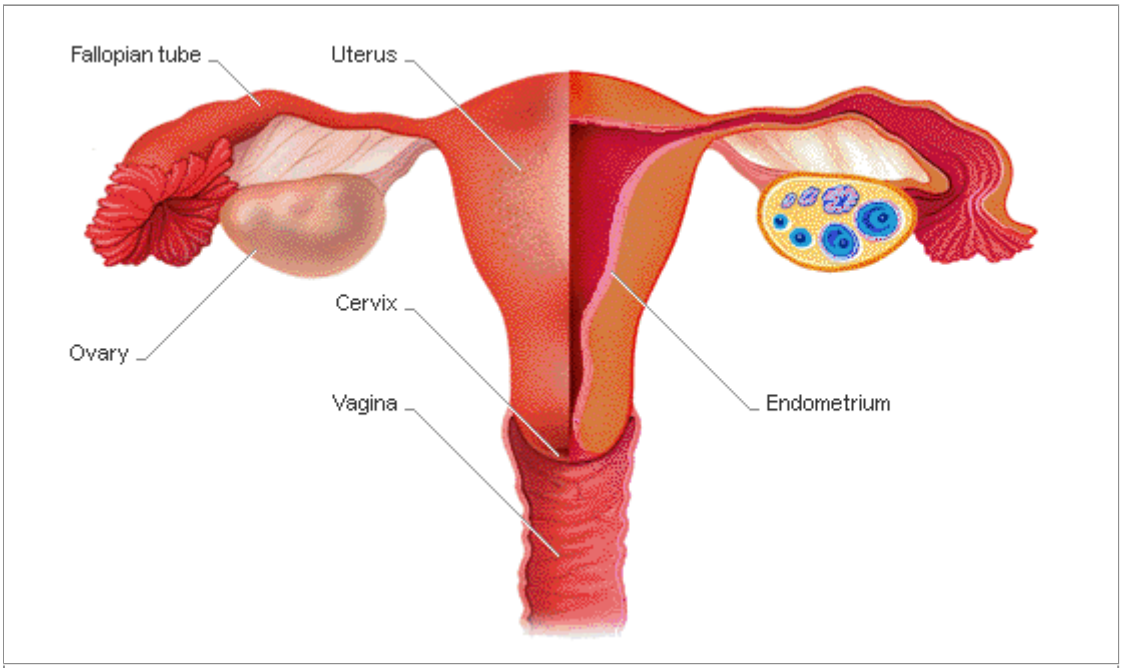
F Bladder Cancer

Bladder cancer is diagnosed in about 53,000 people in the United States and 4,800 people in Canada every year. White Americans are afflicted at almost twice the rate of African Americans, and men are two to three times more at risk than women. The disease is two to three times more likely to affect smokers than nonsmokers. Occupational exposures also appear to increase risk. People who work in the rubber, leather, and chemical industries are at greater risk, as are hairdressers, machinists, metal workers, printers, painters, and textile workers. Chemicals used in these industries become concentrated in the urine, causing bladder cells to become cancerous.

The bladder is a hollow organ that stores urine. Its flexible, muscular walls consist of three layers: an epithelial lining (also known as the transitional lining), an intermediate layer of muscle, and an outer layer of connective tissue. Cancer can originate in any of these layers, but transitional cell carcinomas in the epithelial lining account for about 90 percent of all bladder cancers.

Bladder tumors may obstruct urine flow into the bladder or interfere with bladder function in other ways. When symptoms are present, they may include blood in the urine and painful or frequent urination. In the United States this cancer has an overall 81 percent five-year survival rate, which climbs to 93 percent when the tumor is detected early.

G Uterine Cancer



Female Reproductive System

A component of the female reproductive system, the uterus is a muscular organ with an expandable neck called the cervix. Two main types of cancer arise in the uterus—endometrial cancer orignates in the lining of the uterus, while cervical cancer begins in the epithelial cells of the cervix.

Uterine cancer includes both cervical cancer and endometrial cancer, cancer of the lining of the uterus. Nearly 49,000 women in the United States and 5,000 women in Canada are diagnosed with uterine cancer each year. The single greatest risk factor for cervical cancer is infection with the human papilloma virus (HPV). Other risk factors include sexual intercourse before age 18, having many sexual partners, and cigarette smoking. For reasons that are not entirely clear, the disease also seems to be more common in women of low socioeconomic status.

There are two main types of cancer of the cervix, the lower part of the uterus. Squamous cell carcinomas make up 85 to 90 percent of these cancers. The other 10 to 15 percent are adenocarcinomas. Most cervical cancers develop slowly and may not produce any noticeable symptoms in the early stages. As the cancer progresses, the woman may experience a watery vaginal discharge and painless bleeding. Over time, the bleeding becomes heavier and more frequent, and pain becomes noticeable in the lower abdomen or back. The five-year survival rate for cervical cancer in the United States is 71 percent but rises to 91 percent if the cancer is detected early. For unknown reasons, black women are twice as likely to die of the disease than are white women in the United States.

Nearly all endometrial cancers are adenocarcinomas. The risk of developing endometrial cancer is higher in women who take certain hormones during estrogen replacement therapy. Other risk factors include early onset of menstruation and late menopause, probably because these factors increase the number of years during which the endometrium is exposed to estrogen and other steroid hormones.

Obesity also increases the risk of endometrial cancer, probably because excess fat can increase the level of estrogens in a woman s body. Excess weight of 14 kg (30 lb) triples a woman's endometrial cancer risk. Similarly, diseases more common in women who are overweight, including diabetes mellitus and gallbladder disease, are also associated with a higher risk of endometrial cancer.

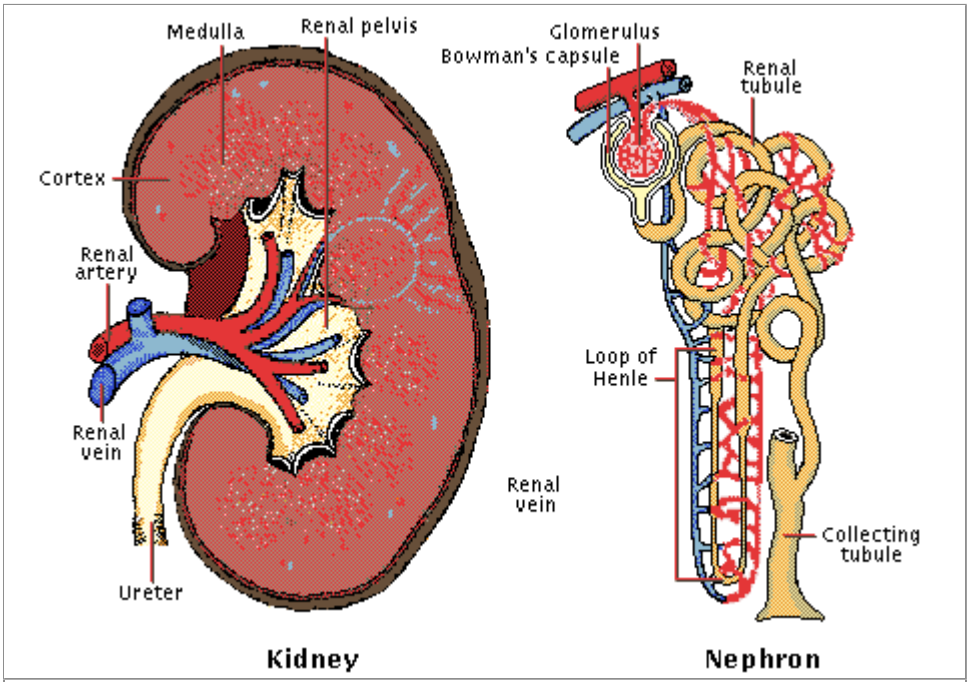
Endometrial cancer symptoms are similar to those of cervical cancer. Most often, they start with a watery vaginal discharge that has streaks of blood. In the United States, the five-year survival rate for endometrial cancer is 83 percent but climbs to 96 percent if the cancer is caught and treated at an early stage.

H Skin Cancer

There are three main types of skin cancer: basal cell carcinoma, squamous cell carcinoma, and melanoma. While basal cell and squamous cell carcinomas account for 95 percent of all skin cancers, melanoma is the most dangerous type of skin cancer and accounts for more than 75 percent of all deaths due to skin cancer. Each year about 48,000 cases of melanoma are diagnosed in the United States, and 3,700 cases are diagnosed in Canada. The single greatest risk factor is sun exposure, especially during childhood. Melanoma occurs more frequently in people with fair skin and freckles.

Melanoma begins in the melanocytes, cells that produce the skin pigment known as melanin, but is likely to spread to other parts of the body. Symptoms include any change in the size, shape, color, or texture of a mole or other darkly pigmented area of the skin. Any mole that begins to itch or becomes tender may be a sign of skin cancer. Other signs include sores that do not heal or black spots under a toenail or fingernail that extend beneath the cuticle. For melanoma patients, the five-year survival rate in the United States is 88 percent and climbs to almost 96 percent if the cancer is detected early.

I Kidney Cancer



Kidney

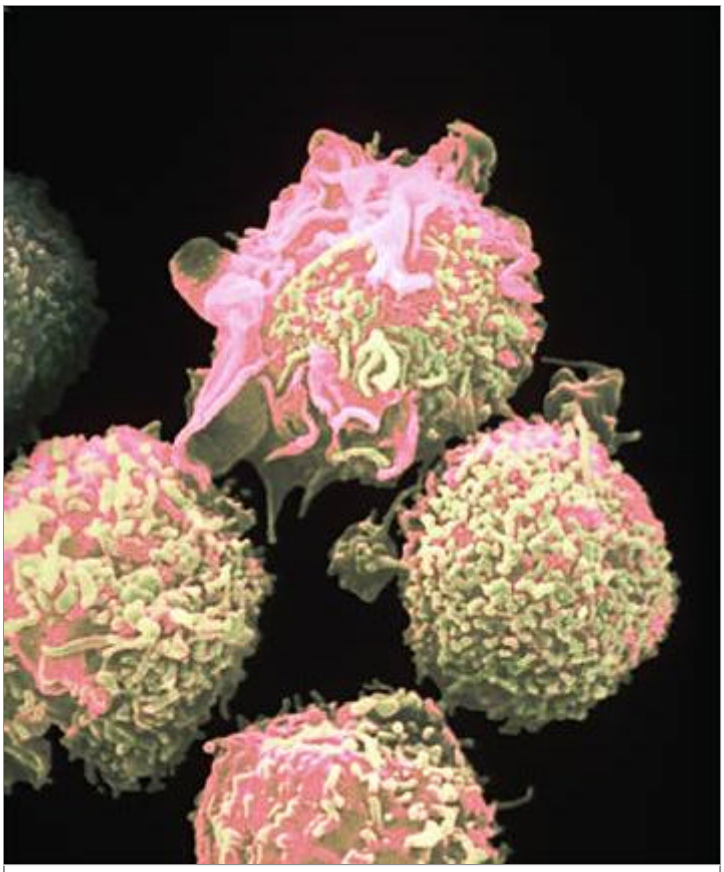
The kidneys filter the blood and rid the body of wastes. Approximately one million nephrons (*right*) compose each bean-shaped kidney (*left*). The filtration unit of the nephron, called the glomerulus, regulates the concentration within the body of important substances such as potassium, calcium, and hydrogen, and removes substances not produced by the body such as drugs and food additives. Cancers that originate in the filtration tissues of the kidney, called renal cell cancer, account for 85 percent of all cancers of the kidney. A small percentage of cancers originate in the renal pelvis, a cavity in the center of each kidney.

Cancer of the kidney is diagnosed in approximately 30,000 people in the United States and 3,900 people in Canada each year. Men have twice the risk of women, and smokers have twice the risk of nonsmokers. Excess weight also increases the risk of developing kidney cancer. Some studies show a link between occupational exposure to asbestos or cadmium and kidney cancer.

The kidneys, two bean-shaped organs on either side of the spine, filter the blood and rid the body of waste through urine. In adults, most kidney cancers develop in the tissues that filter blood and produce urine. This type of cancer is called renal cell cancer and accounts for 85 percent of all cancers of the kidney. Cancer of the renal pelvis, a cavity in the center of each kidney, is similar to certain cancers of the bladder and is called transitional cell carcinoma. Wilms' tumor, the most common kidney cancer in children, results when developing kidney cells fail to mature and instead divide uncontrollably, forming a mass of immature cells.

The most common symptom of kidney cancer is blood in the urine. A lump or a mass that can be felt in the kidney area may also be an indication of kidney cancer. As kidney cancer grows, it may invade organs near the kidney, such as the liver, colon, or pancreas. The five-year survival rate in the United States for adult kidney cancer is 58 percent but rises to nearly 88 percent if the tumor is detected before it spreads.

J Leukemia



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Hairy Cell Leukemia

Pathologists can distinguish various types of leukemia by the appearance of the cancerous cells underneath a microscope. Hairy cell leukemia, a rare form of chronic lymphocytic leukemia, is characterized by cells with minute, hairlike projections on their surface.

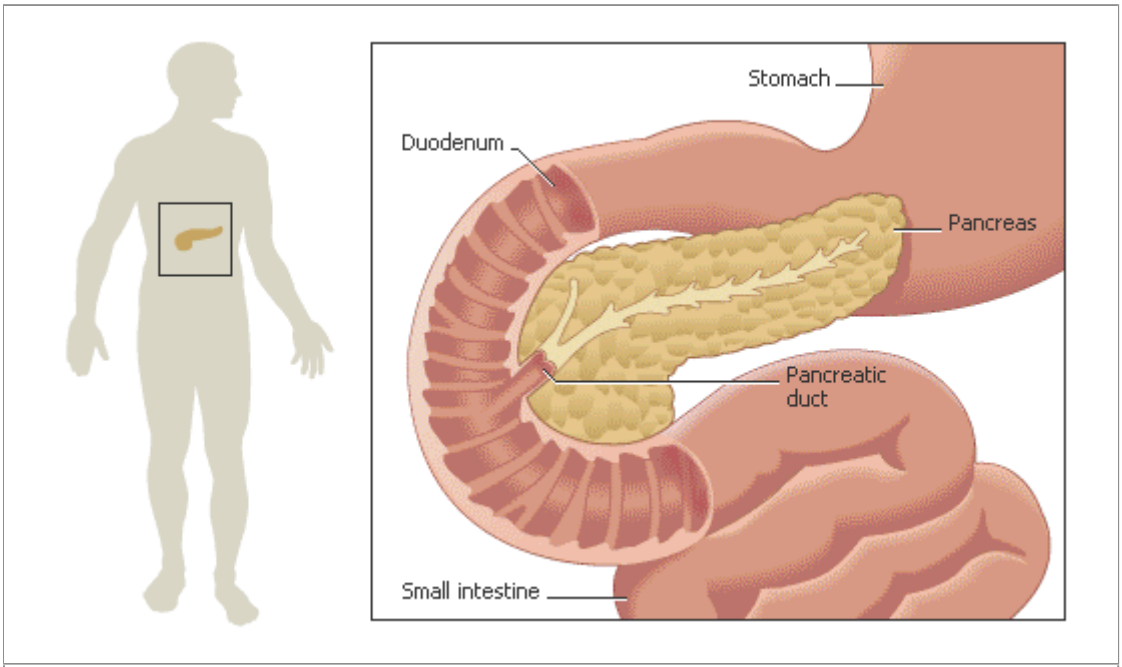
Leukemia is cancer of the blood cells. About 31,000 new cases of leukemia are diagnosed in the United States and 3,500 new cases are diagnosed in Canada each year. Leukemia is typically thought to be a childhood disease, but in fact it strikes many more adults. Smoking increases the risk of developing leukemia, as does long-term exposure to high levels of the chemical benzene and high-dose radiation exposure.

There are four types of leukemia, classified by the type of blood cell affected and whether the cells are mature or immature. The four major types are acute myelocytic leukemia (AML), chronic myelocytic leukemia (CML), acute lymphocytic leukemia (ALL), and chronic lymphocytic leukemia (CLL). AML and CLL are most common in adults, while ALL is the most common form in children. CML also affects adults. Acute leukemias progress rapidly, while chronic leukemias tend to develop slowly.

Most symptoms of leukemia result from the lack of normal blood cells that occurs when leukemia cells crowd out normal cells. General symptoms include weight loss, fever, and loss of appetite, and less often, profuse bleeding from the gums and mucous membranes under the skin. Low levels of red blood cells may also indicate the presence of leukemia.

In the United States the five-year survival rate varies according to the type of leukemia and the age of the patient. Almost 68 percent of the people diagnosed with CLL live at least five years. The five-year survival rate for adult ALL is almost 56 percent and is 70 percent for children with ALL. More than 27 percent of those diagnosed with CML survive five years or more. AML is the most fatal of the leukemias. The five-year survival rate for adults with this disease is just over 11 percent, while for children it is 40 percent.

K Pancreatic Cancer



Pancreas

Epidemiologists estimate that smoking causes 30 percent of all cases of pancreatic cancer, the fourth leading cause of cancer death in the United States. The pancreas has both a digestive and a hormonal function. Composed mainly of exocrine tissue, it secretes enzymes into the small intestine, where they help break down fats, carbohydrates, and proteins. Pockets of endocrine cells called the islets of Langerhans produce glucagon and insulin, hormones that regulate blood-sugar levels. About 95 percent of all pancreatic cancers begin in the exocrine tissue.

Each year about 28,300 Americans and 3,100 Canadians are diagnosed with cancer of the pancreas, a small gland sandwiched between the stomach and intestine that secretes chemicals used in digestion. Epidemiologists estimate that smoking causes about 30 percent of all cases of pancreatic cancer. Men are 30 percent more likely to develop this type of cancer than women, and in the United States, pancreatic cancer affects African Americans more than any other ethnic group.

The pancreas is composed of two different types of glands: exocrine and endocrine glands. Exocrine glands, which make up the bulk of the pancreas, produce enzymes that help the body break down fats and proteins. About 5 percent of the cells in the pancreas are endocrine glands. These cells secrete the hormones insulin and glucagon, which help control blood sugar levels. About 95 percent of all cancers that originate in the pancreas are adenocarcinomas of the exocrine glands. Cancers of the

endocrine glands are very rare, and the following discussion pertains to cancer of the exocrine glands.

Although rarer than many types of cancer, pancreatic cancer is the fourth leading cause of cancer death in the United States because it produces few if any symptoms before it metastasizes. When symptoms are present, they may include jaundice, a yellowing of the skin, eyes, and fingernails; abdominal pain; weight loss; and digestive problems. Usually by the time symptoms appear, the cancer has spread to distant organs in the body. For this reason, only about 4 percent of all people diagnosed with pancreatic cancer in the United States survive five years or more.

L Ovarian Cancer

About 23,100 cases of ovarian cancer in American women and 2,500 cases in Canadian women are diagnosed annually. Women over the age of 50 have a higher risk for ovarian cancer, as do women who have had breast cancer. Other conditions that increase the risk for ovarian cancer include early age at first menstruation, late menopause, having a first child after age 30, or having no children at all. Women with a close relative who has ovarian cancer are also at greater risk, as are women with inherited mutations in the tumor suppressor genes BRCA1 and BRCA2.

The ovaries, two almond-shaped glands on either side of the uterus, produce eggs and release hormones that regulate menstruation and pregnancy. Malignant ovarian tumors arise in the epithelial tissue of the ovaries, in the connective tissue, or in the germ cells—the egg-producing cells. Ovarian carcinomas, those that arise in the epithelial tissue, account for 85 to 90 percent of all ovarian cancer. Sarcomas account for less than 5 percent of all cases, and several different types of germ cell cancers account for the remaining 5 to 10 percent of ovarian cancers.

Ovarian cancer accounts for just under 5 percent of all cancer in women. While rare, it often does not produce symptoms and goes undiagnosed until the cancer has spread and become more deadly. At that point, a woman may experience any of a variety of symptoms, such as an enlarged abdomen, persistent abdominal discomfort, indigestion, nausea or vomiting, weight loss, diarrhea or constipation, and bleeding that is not part of a normal menstrual period. If diagnosed and treated before the cancer has spread, the five-year survival rate in the United States is 95 percent, but only about 25 percent of ovarian cancers are detected this early. Overall, the five-year survival rate is 50 percent.

M Stomach Cancer

About 21,500 Americans and 2,800 Canadians are diagnosed with cancer of the stomach each year. Stomach cancer is about twice as common in men as it is in women, and it occurs much more frequently in people who have experienced long-term infection with the *Helicobacter pylori* bacterium. Incidence of stomach cancer varies significantly between different populations. In Japan, for example, the disease is five times more common than it is in the United States. Researchers attribute these regional risk differences to dietary differences. Diets high in smoked or cured meats appear to increase the risk of stomach cancer. In the United States, stomach cancer is now only one-fourth as common as it was in 1930. This decline may be due, in part, to the increased use of refrigeration for

food storage and decreased use of salted and smoked foods.

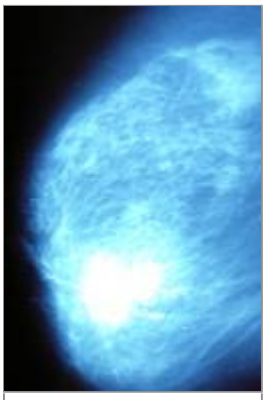
Approximately 90 to 95 percent of all cancers of the stomach are adenocarcinomas that develop in the lining of the stomach. Cancers of the immune tissue in the stomach wall, called gastric lymphomas, make up about 4 percent of all cancers of the stomach. Gastric sarcomas develop in the muscle tissue in the stomach wall, and account for only about 3 percent of all stomach cancers.

Like many cancers of the internal organs, stomach cancer rarely produces noticeable symptoms until it has spread to other sites in the body. When symptoms are present, they may include abdominal pain, heartburn, nausea, and vomiting. Stomach cancer is rarely detected early, and only about 20 percent of people diagnosed with stomach cancer in the United States live five years or longer.

V DIAGNOSIS

Diagnosis of cancer often begins when a person notices an unusual health symptom and consults a doctor. Early warning signs of cancer include changes in bowel or bladder habits, a sore that does not heal, unusual bleeding or discharge, thickening or a lump in the breast or any other part of the body, indigestion or difficulty swallowing, change in appearance of a wart or mole, or a nagging cough or hoarseness.

A Detection



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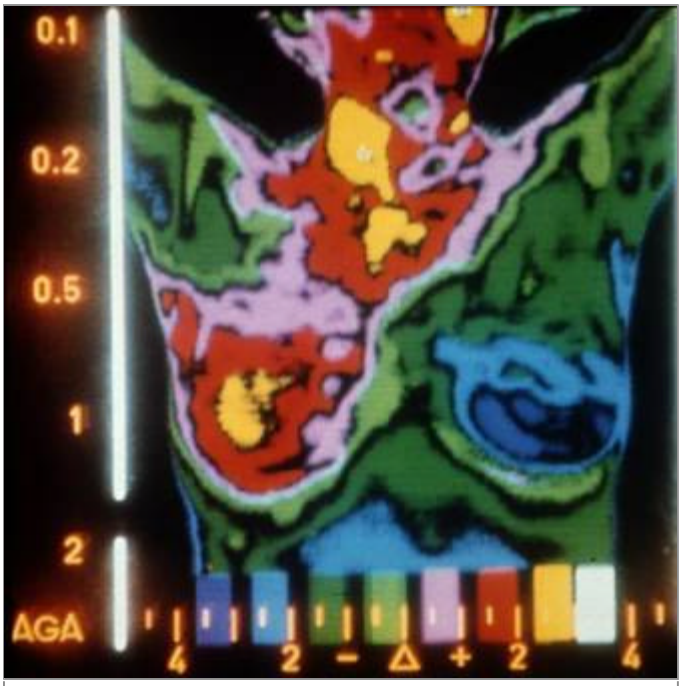
Mammogram

Mammography is a special X-ray technique that is used to visualize soft tissues of the breast as a means for screening women for breast cancer. This mammogram shows calcification (dense white flecks) in a cancerous tumor. The nipple is to the left. The majority of breast cancers originate in the duct of the mammary, or milk-secreting, gland. The remainder arise in the glands themselves. Most tumors of either type show early evidence of *invasive* (malignant) behavior, but both may also exist in noninvasive forms.

People with early warning signs should consult their family doctor, who will evaluate symptoms and may refer the patient to a physician who specializes in cancer. A physician will first take the patient's

medical history to learn about current symptoms, past history of disease, and family members diagnosed with cancer. The procedures used in a physical exam depend on the patient's clinical symptoms and may include a digital rectal examination, in which the physician uses a gloved finger to gently check the smoothness of the rectal lining. The physician may perform a breast exam on female patients, in which the breasts are gently probed to feel for lumps or unusual masses.

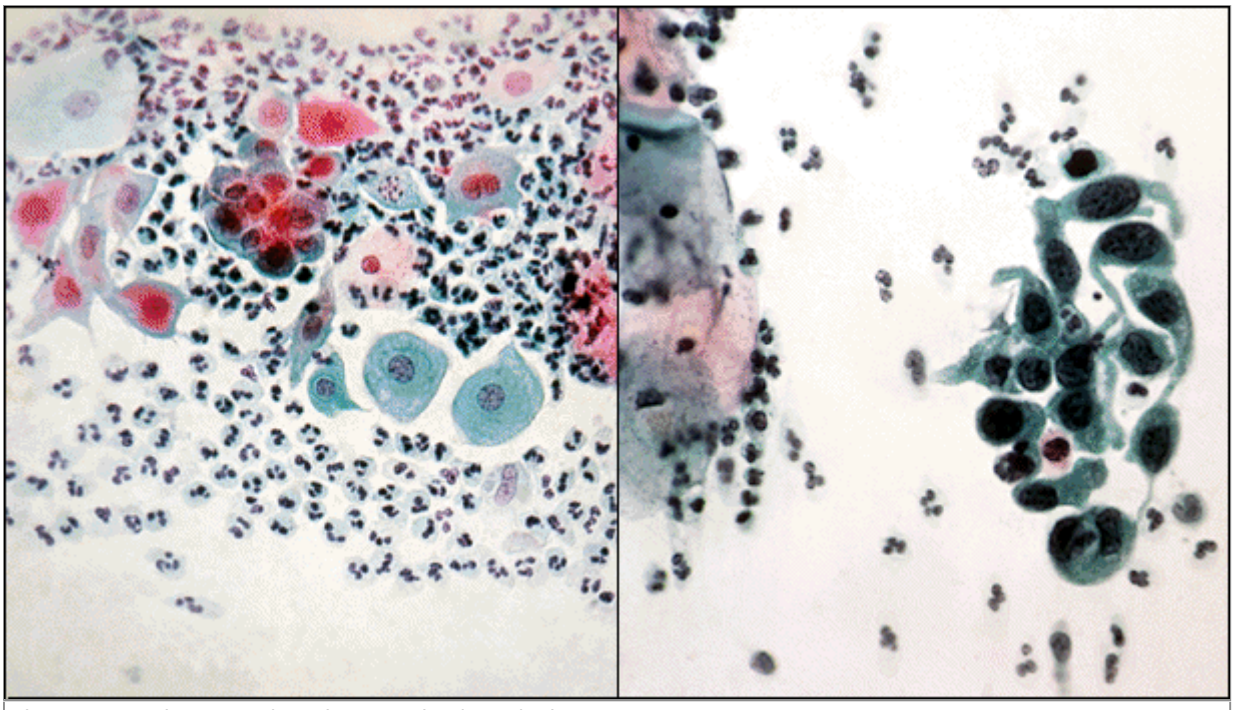


Phototake NYC/CNRI

Thermogram

Because the temperature of human skin changes in response to disorders in the underlying tissue, conditions such as poor circulation, swelling, and cancer are visible with cameras sensitive to infrared heat. In this thermogram, cancerous tissue (yellow) contrasts with the rest of the body's blue and green coloration.

During the examination the physician may use a thin, lighted tube called an endoscope to look for tumors in internal body cavities. The endoscopy procedure used depends on the organ or body cavity examined. In gastric endoscopy, the doctor feeds a specialized endoscope down the throat to examine the lining of the esophagus, stomach, and first part of the small intestine. Fiberoptic sigmoidoscopy, in which a flexible instrument is inserted into the lower intestinal tract through the anus, enables a physician to visually examine the interior of the colon and rectum. Colonoscopy uses a much longer flexible instrument to view the entire length of the large intestine.



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Cervical Cells

Healthy cervical cells *(left)* are fairly uniform in size and shape, while diseased cervical cells *(right)* are irregular and disfigured. Gynecologists use a Pap smear to detect abnormalities in cervical cells, which may signal cancer. Cells are scraped from the cervix, and then are spread on slides and studied with a microscope.

A number of laboratory tests help narrow the possible diagnoses. In a Pap smear, cells are removed from the cervical epithelium with a small plastic brush. These cells are examined under a microscope for cell changes that are a sign that cancer may be developing as well as signs of malignancy. If a patient ѕ clinical signs suggest colorectal cancer, the doctor may search for blood in the stool using a fecal occult blood test. A small sample of the patient ѕ stool is smeared on a card coated with a chemical called guaiac, which reacts with blood. The card is analyzed in a laboratory for occult (hidden) blood. Certain blood tests determine if levels of red and white blood cells are low, a possible indication of leukemia. Others test for the presence of *tumor markers*, chemicals that are present in higher levels when certain cancers are present. For example, a prostate-specific antigen (PSA) test measures levels of prostate-specific antigen in the blood. Prostate cancer cells overproduce this protein, causing an elevation of PSA levels in blood.

BBC Worldwide Americas, Inc.

Endoscopic Surgery

Physicians may use a fiber optic tool called an endoscope to look for tumors in internal body cavities or collect tissue samples. An endoscope provides the physician with an illuminated and magnified view of internal organs and body cavities without making sizable incisions. Endoscopes are easily maneuverable to reach inaccessible areas and they can be equipped with a variety of instruments, from knives to lasers.

Medical imaging techniques help doctors locate and evaluate a tumor. These include computed tomography (CT) and magnetic resonance imaging (MRI) scans. CT and MRI scans use computers to form a three-dimensional image of the tumor and surrounding tissues. X-ray images of the breast called mammograms help physicians detect and evaluate breast cancer. Ultrasound scanning bounces high-frequency sound waves off a tumor and surrounding tissue to create an image of the tumor. The multimodality display technique combines the images from several imaging tools into one picture, providing a final three-dimensional image with much greater detail. Computer-aided diagnosis uses complex computer programming technology called artificial intelligence to scan mammograms and X rays to help look for signs of cancer and offer an automated second opinion.

B Staging

When a tumor is detected, the physician takes a biopsy by removing a sample of the tissue. The biopsy sample is inspected under a microscope to determine if the tumor is benign or malignant. Cancerous cells usually appear abnormal in shape and no longer orient themselves in orderly configurations. If the tumor is cancerous, the physician assigns it a stage, indicating how far cancer has spread. The stage is a key factor in determining both the cancer's treatment and prognosis. Oncologists, physicians who specialize in the diagnosis and treatment of cancer, use several different staging systems. In one system, tumors are grouped into four stages denoted by Roman numerals I through IV. Stage I cancers are small localized cancers that are usually curable. Stage II and III tumors are usually locally advanced and may or may not have invaded nearby lymph nodes, and stage IV tumors have usually metastasized—that is, spread to distant tissues in the body.

The most widely used staging system is the Tumor, Lymph Node, and Metastasis system, commonly abbreviated TNM. This system uses numbers between zero and three to assess the size of the tumor

(T), the extent that it has spread to nearby lymph nodes (N), and the extent that it has spread throughout the body (M). A cancer's stage depends on a combination of these numbers. For example, a T-1, N-0, and M-0 tumor is a stage 1 tumor. This tumor is 2 cm (1 in) or less (T-1) and has not spread to nearby lymph nodes (accounting for N-0) or metastasized (M-0). The five-year survival rate for a patient with this stage tumor is accordingly excellent. A T-3, N-1, and M-0 tumor is a stage 3 tumor. This tumor is greater than 5 cm (2 in) and has spread to nearby lymph nodes, but there is no evidence that the cancer has spread to distant tissues. The five-year survival rate for a patient with this tumor is not as high as the T-1, N-0, M-0 patient. Stage 4 tumors are distinguished by an M-1 number. This means they have progressed to the point where metastasis is widespread, and the prognosis is usually quite poor.

VI TREATMENT

Oncologists select from a number of options when treating cancer, depending on the type and stage of the tumor involved. The major treatments currently available are surgery, radiation therapy, chemotherapy, hormone therapy, and immunotherapy. Often, targeting cancerous tumors requires the artful combination of more than one type of cancer therapy.

A Surgery

Surgery is the most effective and fastest treatment for tumors that are caught early and have not metastasized. It is the only option ensuring that the entire visible tumor is eliminated. However, there is no guarantee that all microscopic extensions of a tumor have been removed. For this reason, surgeons may also remove a large portion of healthy tissue that surrounds the tumor. This may not be possible if the tumor lies near or within a vital tissue, such as a major nerve or organ.

Often, cancer surgery requires general anesthesia, in which the patient loses consciousness, and a hospital stay of several days. For example, women with breast cancer may have a lumpectomy or mastectomy, surgical removal of part (or all) of the breast. Depending on the stage of the tumor, doctors may also remove the nearby lymph nodes and muscle tissue. As with any major surgery, mastectomies and other major surgical cancer treatments involve some risk, and doctors must consider the overall health of the patient, as well as the stage of the tumor.

Some cancers can be treated surgically with less-invasive techniques, such as laser surgery. Laser surgery uses a powerful beam of high-energy light to vaporize certain tumors of the cervix, larynx, and skin. Physicians perform laser surgery with an endoscope inserted through a small incision in the skin. Laser surgery and other less-invasive surgical procedures may require only local anesthesia, in which a patient loses feeling in one particular area of the body but never loses consciousness.

Sometimes oncologists recommend surgery to improve a patient's quality of life, even if it is not likely to rid the body of cancer. Surgery of this type aims to correct a problem that is causing discomfort or disability. For example, some cancers may spread to the spine, pressing on the spinal cord or nearby nerves. This pressure may cause severe pain, and in some instances, paralysis. Surgical removal of all or part of the tumor near the spine may alleviate these symptoms.

B Radiation Therapy

Photo Researchers, Inc./Martin Dohrn/Science Source

Radiation Treatment

Here, a patient undergoes radiation treatment for cancer of the spine. In this procedure the radioisotope cobalt 60 is used as the source of gamma radiation. A high dose of gamma radiation is guided by laser targeting to a localized area of treatment.

Therapeutic radiology uses high-energy particles or waves, such as X rays or gamma rays, to focus damaging radiation on the region of a tumor, inflicting genetic damage that kills cancerous cells. Radiation therapy damages rapidly dividing cells, mostly cancer cells but also healthy cells that reproduce quickly. This leads to side effects such as fatigue, skin changes, and loss of appetite. Other side effects usually are related to the treatment of specific areas, such as hair loss following radiation treatment to the head. Radiation therapy can also cause a decrease in the number of white blood cells, cells that help protect the body against infection. Most side effects are short-lived, as healthy tissues recover from radiation much better than cancer cells because healthy cells repair damaged DNA more efficiently.

Many short doses of radiation therapy, instead of fewer heavier doses, can minimize side effects. The total dose and the number of treatments depend on the size, location, and type of cancer and the patient ŝ general health. Patients usually receive radiation therapy five days a week for five to eight weeks. Weekend rest breaks allow normal cells to recover.

Unlike surgery, radiation can destroy microscopic cancer cells that have moved into surrounding tissues. Radiation is also a safer option for older patients or those weakened from other diseases, who may not recover well from surgery. Oncologists may use radiation to shrink the tumor, making surgery feasible. For other tumors, radiation may be used following surgery. However, radiation does not always eliminate all tumor cells, and it cannot treat widespread metastases. Like surgery, radiation therapy may be used to relieve pain and discomfort, even when a cure is not likely.

C Chemotherapy

Chemotherapy uses powerful anticancer drugs that travel through the bloodstream, making it potentially useful for cancers that have spread. Oncologists use about 50 different chemotherapeutic

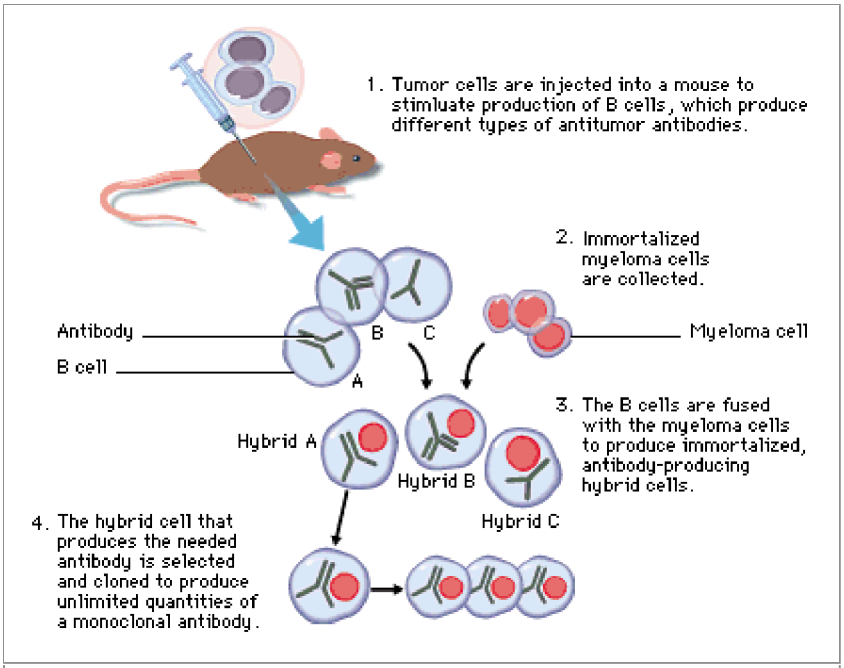
drugs to combat cancer, generally administering more than one drug at a time because these drugs are more powerful when combined. Taken orally or injected into the bloodstream, chemotherapeutic drugs interfere with cancer cells 'ability to make new DNA or divide properly. In some cases, the drugs cause programmed cell death. Many leukemias and lymphomas and cancer of the testicles are successfully treated with chemotherapy. Breast, lung, colorectal, and prostate cancer are not currently curable with chemotherapy alone, so chemotherapy is often used in combination with other therapies. In fact, the most common combination of cancer treatments is surgery or radiation therapy followed by chemotherapy.

Chemotherapy often causes severe side effects, particularly reduced resistance to infection, internal bleeding, diarrhea, nausea, vomiting, hair loss, and insufficient oxygen in the blood, known as anemia. Some tumors develop resistance to many drugs after exposure to just one drug, a condition called multidrug resistance. When this happens, there may be no drugs that are effective against the tumor.

D Hormone Therapy

Some types of cancer, such as breast and prostate cancer, depend on sex hormones to grow. Hormone therapy prevents cancer cells from receiving or using the hormones they need. Hormone therapy may include surgery to remove organs in the endocrine system that make hormones. In other cases, hormone therapy relies on drugs to stop hormone production or change the way hormones work. Antiestrogen drugs, such as tamoxifen and raloxifene, given to women with breast cancer block estrogen and inhibit its ability to stimulate cell growth. Sometimes called designer estrogens, these drugs cause only mild side effects because treatment is limited to tissues affected by hormones. Androgen blockers are given to men with prostate cancer to block the production of testosterone and other male hormones that may contribute to cancer growth.

E Immunotherapy



Producing Monoclonal Antibodies

In the creation of a monoclonal antibody, a normal B cell (a type of lymphocyte, or white blood cell) is united with a myeloma cell (a type of cancer). This union results in the formation of hybridomas (hybrid cells) that have the cancer cell s trait of dividing endlessly and the B cell s ability to produce a specific type of antibody. Monoclonal antibodies are designed to target specific molecules in the body. They have a variety of uses from pregnancy testing to treating certain cancers.

Immunotherapy, also called biologic therapy, uses the body s own immune system to fight cancer cells or protect the body from side effects. Immunotherapy relies on antibodies, naturally occurring proteins dedicated to defending the body against invasion by foreign substances. In one kind of immunotherapy, antibodies are used to attack tumor cells directly, while in another approach, antibodies are used to deliver toxic agents, such as radioactive substances or drugs, that selectively target and harm cancer cells. Monoclonal antibodies are laboratory-produced antibodies used to fight many diseases, including cancer. One of the newest treatments for breast cancer is a monoclonal antibody called Herceptin, which targets cancer cells that overproduce HER-2, the protein implicated in about one-third of all breast cancers.

Other forms of immunotherapy include the use of interferon, a naturally and synthetically produced protein that fights disease-causing agents in the body, particularly viruses. Interferons slow the growth of tumor cells in some patients, and they stimulate the immune system to attack cancerous cells. Another therapy, interleukin-2, is a naturally occurring immune system chemical that stimulates a type of immune cell that attacks cancer cells. Colony stimulating factors help regulate the production of white blood cells, enabling the body to better combat the disease.

VII PREVENTION

Scientists estimate that more than 60 percent of cancer deaths in the United States are preventable through lifestyle changes. Although there is no certain way to avoid all cancers, reducing individual risk factors significantly decreases the likelihood of contracting many forms of this devastating disease.

A Lifestyle Changes

Woodfin Camp and Associates, Inc./Alon Reininger

Walking for Exercise

Studies show that people who exercise regularly have lower rates of cancer than the general population. Moderate activity for just 30 minutes a day enhances the immune system, shortens the time food takes to move through the intestines, and improves body composition and hormone levels. Even relatively mild activities such as daily walks can provide significant health benefits.

The ACS estimates that smoking causes nearly 30 percent of all cancer deaths in the United States—that is, approximately 166,000 cancer deaths each year. All cancer deaths caused by tobacco smoking could be prevented completely by not smoking and not using smokeless tobacco. For those who already smoke, quitting will reduce the risk of developing cancer. Studies show that after about ten years of not smoking, a past smoker ŝ risk lowers to about the level of those who have never smoked.

After quitting smoking, eating a healthy diet is the best way to lower the risk of cancer. Certain foods have been found to protect against cancer. Among these foods are broccoli, cauliflower, cabbage, tomatoes, soy products, and foods high in vitamins A, C, and E. In addition, green and possibly black teas contain compounds that protect the body from carcinogens. These foods contain substances called antioxidants that block the action of free radicals. Other chemicals in fruits and vegetables are thought to block the cell growth promoting effects of steroid hormones, protecting against cancers of the breast and prostate.

To lower cancer risk, diets should include little or no red meat. Other foods to avoid or consume in moderation include sugar, saturated fat from animal products, and salt. Added fats and oils should come from vegetables, such as olives or corn, rather than from animal sources. Carbohydrates should come from whole grains, such as brown rice and whole wheat bread, rather than from processed foods, such as white rice and white bread.

The risk of cancer of the esophagus increases with heavy alcohol consumption, and many studies suggest that consuming alcoholic beverages increases the risk of breast cancer as well. Studies show that limiting intake to two drinks a day for men, and one drink per day for women, reduces cancer risk.

Photo Researchers, Inc./Charles D. Winters

Sources of Dietary Fiber

Vegetables, fruits, grains, and legumes constitute a rich source of dietary fiber. Composed of the indigestible cell walls of plant material, fiber acts like a scouring pad to cleanse and flush the digestive tract. Researchers claim it helps eliminate cancer-causing chemicals and may decrease the amount of cholesterol in the blood stream.

Low levels of physical activity have been implicated in colon cancer. Moderate activity for 30 minutes a day enhances the immune system, shortens the time food takes to move through the intestines, and alters body composition and hormone levels. Researchers are studying how these effects might lower cancer risk. Physical activity also helps avoid obesity, which is associated with an increased risk for cancers of the colon and rectum, prostate, breast, endometrium, and kidney. By maintaining a healthy weight through regular physical activity and a healthy diet, individuals can substantially lower their risk for these cancers.

Protecting the skin from the sun's rays could prevent about 80 percent of all skin cancers. When in the sun for prolonged periods, always wear sunscreen with a sun protection factor (SPF) of 15 or greater, particularly if you have fair skin or freckles. Skin needs protection every day, not just on sunny days. The Skin Cancer Foundation also recommends that people avoid the sun at its peak (from 10 AM to 4 PM), seek shade, and cover up with clothing and a brimmed hat.

People also can help prevent cancer by practicing safe sex or abstaining from sex. The human papilloma virus (HPV) linked to cervical cancer is the most common cancer-causing virus in the United States. Minimizing the number of sexual partners, using condoms, or practicing sexual abstinence reduces risk of infection with HPV. Infection with the human immunodeficiency virus (HIV), also sexually transmitted, greatly increases an individual's risk for cancers of the immune and lymphatic system, such as Kaposi's sarcoma. Infection with the hepatitis B virus (HBV) is the predominant cause of liver cancer in the United States. HBV is transmitted from person to person through unprotected sexual intercourse with an infected person, or through the sharing of infected needles or other sharp instruments that break the skin. Vaccination against hepatitis B reduces the spread of this virus, which

leads to reduced incidence of liver cancer.

B Screening and Early Detection

Photo Researchers, Inc./CNRI/Science Source

Double-Contrast Barium X Ray of the Large Intestine

Detecting cancer in its early stages significantly improves a patient ŝ chances for survival. The American Cancer Society recommends that symptom-free patients undergo a number of regular screening tests. One such test, a double-contrast barium enema, is used to detect colorectal cancer. Barium, an X-ray opaque material or contrast medium, makes intestinal tumors and other defects stand out as dark spots against the brighter healthy intestinal tissue in X rays. The American Cancer Society recommends people over age 50 have a double-contrast barium enema every 5 to 10 years.

The next best thing to lifestyle changes is early detection to prevent cancer from becoming life threatening. Detecting a tumor while it is still in an early stage is the best predictor of long-term survival. For this reason, the ACS recommends a number of screening tests for people who do not have symptoms. A cancer-related checkup is recommended every three years for people aged 20 to 40 and every year for people over age 40. For more information about other screening tests, see the table on Cancer Screening Recommendations.

In addition to regular cancer check ups, advanced technologies may help detect certain cancers. Scientists have developed tests for the presence of certain genetic mutations. People who test positive for these genetic mutations may take preventive measures such as more frequent cancer screening examinations and dietary modification to reduce their risk. Women who test positive for a mutated breast cancer gene, such as BRCA1 or BRCA2, may choose to have a mastectomy even when no cancer is present. This eliminates most breast tissue before cancer has a chance to form.

The ability to determine a person's genetic risk for cancer years or even decades before it develops

has raised a number of ethical, social, and psychological implications. Several government committees have published guidelines to prevent discrimination in hiring or firing employees who have had a genetic test or have tested positive for a particular cancer-causing gene. Families with high risk for cancer are also affected by the psychological implications of knowing which family members are at risk and which are not. In some cases, tests are available to identify people at risk for certain cancers, such as inherited forms of breast or colon cancers, but surefire preventive or treatment measures for these cancers have not been developed yet. While some people would prefer to know their risk for disease so they can make appropriate lifestyle changes, others prefer not to be hampered by this knowledge when no treatment exists for the problem.

VIII CANCER RESEARCH

Sixty percent of people diagnosed with cancer now survive more than five years. Between 1990 and 1995 cancer incidence and death rates dropped for the first time in 20 years. In 1998 the ACS, the NCI, and the Centers for Disease Control and Prevention (CDC) confirmed that cancer rates are still on the decline. In the past 40 years, the death rate from cancer in children has dropped 62 percent. These improved cancer statistics are due in part to behavioral and lifestyle changes, but equal credit goes to the advances in cancer research that have taken place in the last three decades.

A Clinical Trials

Clinical trials are research studies that use human patients to determine if a new treatment is effective. Medical and ethical panels overseen by the Food and Drug Administration (FDA) carefully review the research methods and ethics of a clinical trial before the trial begins, then monitor the trial throughout its four main phases. Phase I of a clinical trial studies a small number of patients to determine the best dosage and delivery method of a new drug treatment. Patients who participate in a Phase I trial usually have advanced cancer and would not be helped by other known treatments. Phase II, conducted with a different group of patients, determines how well the treatment actually works in different types of cancer. Phase III compares the effectiveness of the new treatment in one set of patients to another set of patients who receive the best currently available drug treatment. In Phase IV studies, the treatment becomes part of the standard treatment regimen, but it is tested for how effective it is when combined with other treatments.

Researchers continually study and find new ways to treat cancer. Studies in an area of research called antimetastasis focus on halting tumor cells from spreading and invading new tissues. Other researchers study how to stop a tumor from developing its own blood supply, a process called antiangiogenesis. Two antiangiogenesis drugs, called angiostatin and endostatin, stop the growth of blood vessels and have been quite successful in treating tumors in mice. These two drugs are currently in clinical trials in humans.

Several drugs that block oncogene signals are in clinical trials. Researchers are also introducing genes into immune cells that will specifically recognize and kill cancer cells. Other research is investigating the introduction of a normal gene into a tumor cell to increase the tumor's sensitivity to chemotherapeutic drugs.

A growing field of cancer prevention research is chemoprevention, or the use of natural or synthetic compounds to decrease the number of mutations that may lead to cancer. Chemoprevention research seeks to identify those compounds that reduce risk and use them in pills or food additives as a prevention measure for those who are at high risk for cancer. More than two dozen chemopreventive compounds are currently being studied for how well they work in humans.

B Basic Research

Rainbow/Dan McCoy

New Tools in Cancer Research

Using a Silicon Graphics workstation and goggles designed to view three-dimensional images, a scientist examines images of enzymes used in the treatment of cancer. The 3-D technology creates the illusion for the scientist of being inside the images, enabling him to better observe the enzymes.

Scientists who conduct basic research on the causes of cancer focus on the fundamental genetic mutations that underlie cancer. One goal seeks to identify all of the mutations present in a patient's tumor, enabling better prediction of the tumor's future behavior. Developing technologies use a tiny glass chip the size of a computer chip to compare DNA in tumor cells to DNA in healthy cells. This new diagnostic tool will someday help physicians to tailor the treatment of individual patients according to their tumors 'genetic makeup.

Since cancer is uncontrolled cell division, research into the genetic mechanisms that control normal cell division also holds promise. A better understanding of the normal function of a mutated gene may provide better insight into what goes wrong in tumor cells. This may lead to better treatments designed to combat specifically the effects of the mutation.

Contributed By:

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