

CANCER AND THE ENVIRONMENT

What You Need to Know
What You Can Do

U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES

National Institutes
of Health

National Cancer Institute

National Institute of Environmental
Health Sciences

CANCER AND THE ENVIRONMENT

This booklet was created by scientists at the National Cancer Institute (NCI) and the National Institute of Environmental Health Sciences (NIEHS) in response to many public requests for information. The content has been guided by responses from a series of *focus groups** that were conducted prior to producing the booklet. People from local communities throughout the country participated in these groups.

NCI and NIEHS are 2 of the 27 institutes/centers that make up the National Institutes of Health (NIH), an agency of the Federal Government's Department of Health and Human Services supported by your tax dollars. NIH is the major supporter of medical research in universities and academic centers throughout the country. To date, 102 Nobel Prize winners have been supported by funds from NIH, more than any other scientific institution in the world. For details, go to the NIH Web site at <http://www.nih.gov>.

NCI was established by Congress in 1937 as the Federal Government's principal agency for *cancer* research and training. Research projects include a broad range of topics: the cellular events in the development of cancer; the role of infectious agents or other agents in the environment or workplace; the role of genetic and hormonal factors; the interactions between environmental agents and genetic factors in the development of cancer; improved imaging techniques and biomarkers in the blood or urine for the early detection of cancer; and the role of diet and other chemicals in preventing cancer. Additional activities include tracking cancer trends, coordinating studies to test new drugs, and supporting new drug and vaccine development. Since the passage of the National Cancer Act in 1971, which broadened NCI's responsibilities, the institute has built an extensive network that includes regional and community cancer centers, specialized cancer physicians, and cooperative groups of researchers throughout the country and abroad to test new prevention and treatment agents. NCI's mission also includes the collection and dissemination of health information, programs to promote the incorporation of state-of-the-art cancer treatments into care of cancer patients, and the continuing care of cancer patients and their families. For more information, go to NCI's Web site at <http://www.cancer.gov>.

NIEHS was established by Congress in 1966 for the purpose of reducing human illness caused by hazardous substances in the environment. The National Toxicology Program, which is headquartered at NIEHS, helps coordinate toxicology studies among Federal agencies and identifies substances that might cause cancer. NIEHS conducts and supports extensive biomedical research, disease prevention, and intervention programs, as well as training, education, and community outreach efforts. NIEHS is a leader in understanding the effect of environmental pollution on birth and developmental defects, sterility, Alzheimer's and other brain and nerve disorders, pulmonary diseases, poverty and health, and cancer. For more information, go to the NIEHS Web site at <http://www.niehs.nih.gov>.

*All terms in *bold italics* are defined in the glossary (see page 35).

The authors dedicate this publication to Dr. Susan Sieber Fabro (1942–2002), a scientist at NCI, who provided the leadership to make the booklet a reality.

TABLE OF CONTENTS

- 1** Introduction
- 1** What causes cancer?
- 4** The nature of cancer
- 7** What substances in the environment are known to cause or are likely to cause cancer in humans? Where are they found?
 - 7 Tobacco
 - 8 Diet/Weight/Physical Inactivity
 - 9 Alcoholic drinks
 - 9 Ultraviolet radiation
 - 9 Viruses and bacteria
 - 10 Ionizing radiation
 - 11 Pesticides
 - 11 Medical drugs
 - 12 Solvents
 - 13 Fibers, fine particles, and dust
 - 13 Dioxins
 - 14 Polycyclic aromatic hydrocarbons (PAHs)
 - 14 Metals
 - 16 Diesel exhaust particles
 - 16 Toxins from fungi
 - 17 Vinyl chloride
 - 17 Benzidine
- 17** What are some ways to reduce the risk of developing cancer or detect cancer at an early stage?
- 22** How do scientists identify cancer-causing substances?
- 25** How do scientists decide which substances to test in animals, human laboratory cells, or human population studies?
- 26** What factors do scientists consider in determining the risk associated with different cancer-causing substances?
- 28** How do public health officials set acceptable exposure levels for environmental chemicals?
- 29** How have cancer trends changed over the past few years?
- 33** Where can I go for more information?
- 38** Glossary
- 41** Index

INTRODUCTION

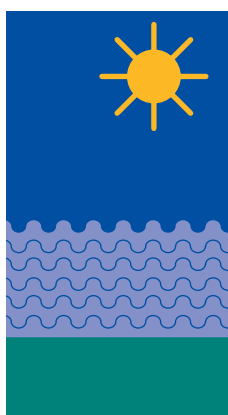
This booklet addresses concerns about the connection between **cancer*** and exposure to toxic substances in the environment. It contains information about which types of substances are either known to cause or likely to cause cancer, and what can be done to reduce exposures to them. It also explains how scientists discover which substances are likely to cause cancer. Although toxic substances may cause other health effects, cancer is the focus of this booklet.

At the end of the booklet, you will find information about the government agencies responsible for reducing exposures to harmful substances and where to go for more information. These agencies develop policies to limit our exposure to agents that can be hazardous to our health such as lead in gasoline and paint, **asbestos** in building insulation, **bacteria** in our water supplies, air pollutants, and **pesticides**. Some harmful exposures, however, result from personal choices or lifestyles.

The good news is that a large number of cancers can be prevented. It is estimated that as many as two-thirds of all cancer cases are linked to environmental causes. This number may even be higher. Many of these are linked to lifestyle factors that can be modified. For example, we know that one-third of all the cancer deaths in this country could be prevented by eliminating the use of tobacco products. In addition, about 25 to 30 percent of the cases of several major cancers are associated with obesity and physical inactivity.

WHAT CAUSES CANCER?

Cancer develops over several years and has many causes. Several factors both inside and outside the body contribute to the development of cancer. In this context, scientists refer to everything outside the body that interacts with humans as the “environment.”



Factors Outside the Body (Environmental Factors)

Exposure to a wide variety of natural and man-made substances in the environment accounts for at least two-thirds of all the cases of cancer in the United States. These environmental factors include lifestyle choices like cigarette smoking, excessive alcohol consumption, poor diet, lack of exercise, excessive sunlight exposure, and sexual behavior that increases exposure to certain **viruses** (see page 9). Other factors include exposure to certain medical drugs, hormones, radiation, viruses, bacteria, and environmental chemicals that may be present in the air, water, food, and workplace. The cancer risks associated with many environmental chemicals have been identified through studies of occupational groups that have higher exposures to these chemicals than the general population.

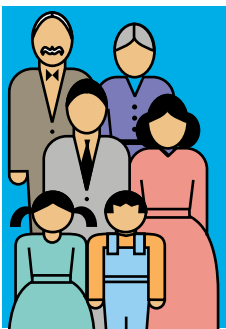
*All terms in **bold italics** are defined in the glossary (see page 38).

The importance of the environment can be seen in the differences in cancer rates throughout the world and the change in cancer rates when groups of people move from one country to another. For example, when Asians, who have low rates of prostate and breast cancer and high rates of stomach cancer in their native countries, immigrate to the United States, their prostate and breast cancer rates rise over time until they are nearly equal to or greater than the higher levels of these cancers in the United States. Likewise, their rates of stomach cancer fall, becoming nearly equal to the lower U.S. rates. Lifestyle factors such as diet, exercise, and being overweight are thought to play a major role in the trends for breast and prostate cancers, and infection with the *Helicobacter pylori* bacterium is an important risk factor for stomach cancer. Recently, the rapid rise in the rates of **colorectal** cancer in Japan and China suggests an environmental cause such as lifestyle factors.

Different environmental exposures are linked to specific kinds of cancer. For example, exposure to asbestos is linked primarily to lung cancer, whereas exposure to benzidine, a chemical found in certain dyes (see page 17), is associated with bladder cancer. In contrast, smoking is linked to cancers of the lung, bladder, mouth, colon, kidney, throat, voice box, esophagus, lip, stomach, cervix, liver, and pancreas.

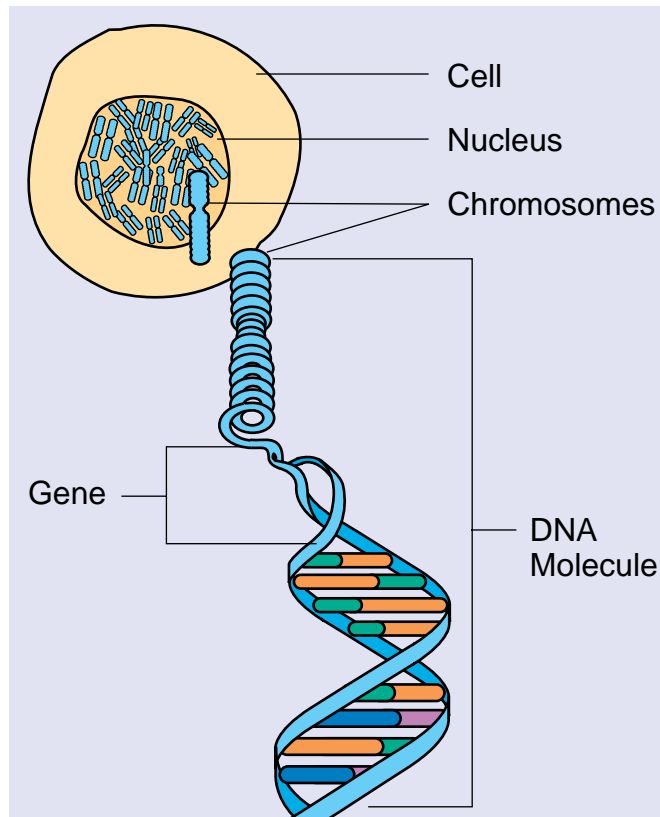
Factors Inside the Body

Certain factors inside the body make some people more likely to develop cancer than others. For instance, some people either inherit or acquire the following conditions: altered **genes** in the body's **cells**, abnormal hormone levels in the bloodstream, or a weakened immune system. Each of these factors may make an individual more **susceptible** to cancer.



One of the ways scientists know that genes play an important role in the development of cancer is from studying certain rare families where family members over several generations develop similar cancers. It appears that these families are passing on an altered gene that carries with it a high chance of getting cancer. Several genes that greatly increase a person's chance of developing certain cancers (e.g., colon, breast, and ovary) have been identified. Only a very small percentage of people in the general population have abnormal copies of these genes. Cancers caused by these genes, known as **familial cancers**, account for only two to five percent of all cancers.

Gene alterations may also contribute to individual differences in susceptibility to environmental **carcinogens** (cancer-causing substances). For instance, people differ in their ability to eliminate cancer-causing agents from their body to which they have been exposed, or to repair **DNA** damage that was caused by such agents. These gene alterations may also be passed on in families and account for higher rates of cancer in these families. Higher rates of cancer in families may also be related to shared environmental exposures like diet or exposure to carcinogens at work.



*Tightly coiled strands of DNA, which carry the instructions that allow cells to make **proteins**, are packaged in units called chromosomes. Subunits of DNA are known as genes.*

One of the main objectives of a growing field in cancer research called molecular **epidemiology** is to identify gene alterations that increase or decrease a person's chance of developing cancer after an environmental exposure.

PROTECTIVE FACTORS

Exposure to cancer-causing substances is only a part of what determines who will get cancer. For example, some people who smoke do not get lung cancer, and not all women who are infected with human papilloma virus (see page 9) develop cervical cancer. Scientists believe that there may be some protective genes, or other factors such as fruits and vegetables in the diet, that help prevent disease.

Interaction of Environmental Factors and Genes

Environmental factors such as viruses, sunlight, and chemicals interact with cells throughout our lives. Mechanisms to repair damage to our genes and healthy lifestyle choices (wearing protective clothing for sun exposure or not

smoking) help to protect us from harmful exposures. However, over time, substances in the environment may cause gene alterations, which accumulate inside our cells. While many alterations have no effect on a person's health, permanent changes in certain genes can lead to cancer.

The chance that an individual will develop cancer in response to a particular environmental agent depends on several interacting factors—how long and how often a person is exposed to a particular substance, his/her exposure to other agents, genetic factors, diet, lifestyle, health, age, and gender. For example, diet, alcohol consumption, and certain medications can affect the levels of chemicals in the body that break down cancer-causing substances.

Because of the complex interplay of many factors, it is not possible to predict whether a specific environmental exposure will cause a particular person to develop cancer. We know that certain genetic and environmental factors increase the risk of developing cancer, but we rarely know exactly which combination of factors is responsible for a person's specific cancer. This also means that we usually don't know why one person gets cancer and another does not.

INTERPLAY OF FACTORS

There are particular patterns of gene alterations and environmental exposures that make people both more susceptible or more resistant to cancer. One of the challenging areas of research today is trying to identify the unique combinations of these factors that explain why one person will develop cancer and another will not.

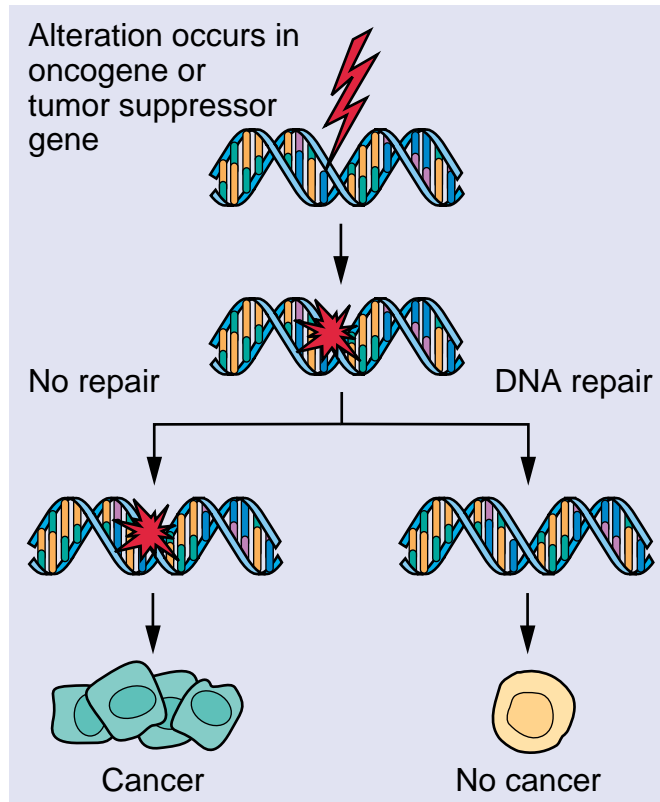
THE NATURE OF CANCER

There are more than 100 types of cancer. Cancer begins inside a cell, the basic building block of all living things. Normally, when the body needs more cells, older ones die off and younger cells divide to form new cells that take their place. When cancer develops, however, the orderly process of producing new cells breaks down. Cells continue to divide when new cells are not needed, and a growth or extra mass of cells called a **tumor** is formed. Over time, changes may take place in tumor cells that cause them to invade and interfere with the function of normal **tissues**.

It takes many years for the development of a tumor and even more years until detection of a tumor and its spread to other parts of the body. People exposed to carcinogens from smoking cigarettes, for example, generally do not develop detectable cancer for 20 to 30 years.

There is much evidence to suggest that permanent changes in our genes are responsible for tumor development. These can be inherited or acquired throughout one's lifetime. Scientists have identified more than 300 altered genes

that can play a role in tumor development. An alteration in growth-promoting genes, known as **oncogenes**, for example, can signal the cell to divide out of control, similar to having a gas pedal stuck to the floorboard. On the other hand, an alteration in **tumor suppressor genes**, which normally serve as brakes for dividing cells, will allow cells with damaged DNA to continue dividing, rather than repairing the DNA or eliminating the injured cells.



An alteration in growth-promoting genes, known as oncogenes, can signal the cell to divide out of control. An alteration in tumor suppressor genes will allow cells with damaged DNA to continue dividing, rather than repairing the DNA or eliminating the injured cells.

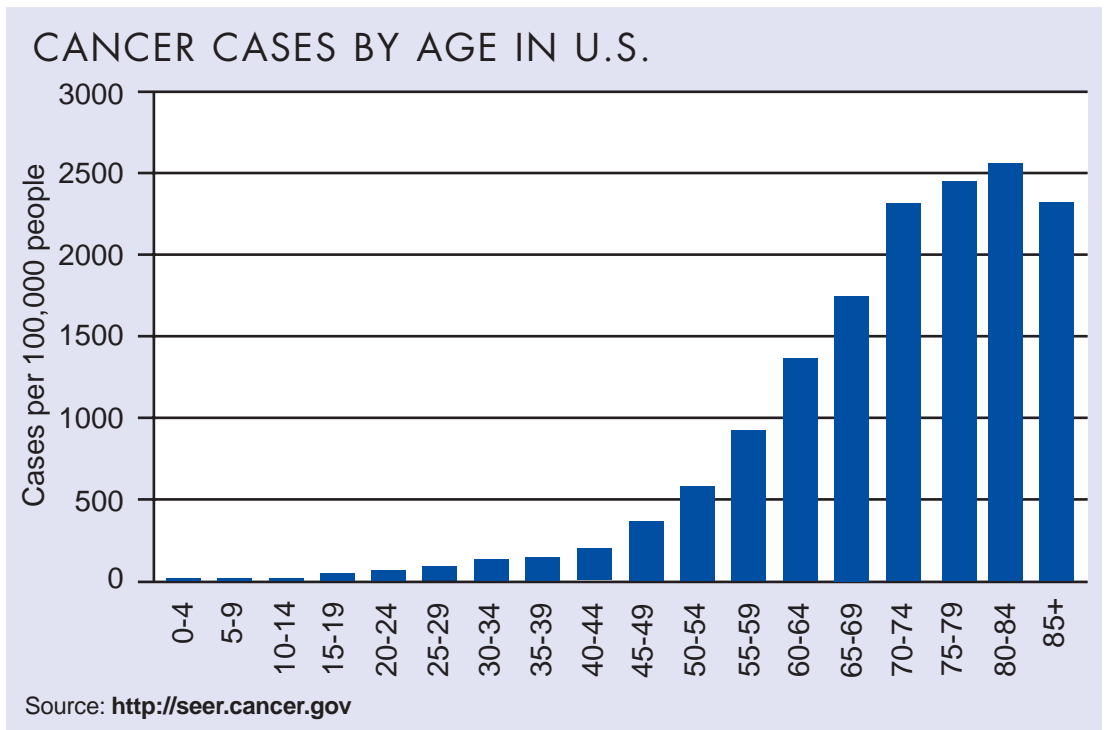
One explanation for the fact that cancer occurs more frequently in older people may be that, for a tumor to develop, a cell must acquire several gene alterations that accumulate as we age. As the graph on page 6 illustrates, less than 0.1 percent of the total number of cancer cases in the United States occur in people under the age of 15, whereas nearly 80 percent occur in people age 55 or older.

Types of Tumors

Tumors are classified as either benign or malignant. **Benign tumors** are not cancer and do not spread to other parts of the body.

A **malignant tumor** can metastasize—a process during which cancer cells escape from the tumor, enter the bloodstream or **lymphatic system**, and spread to nearby parts of the body and eventually to sites far away from the original tumor. Some benign tumors may, over time, become malignant tumors. The development of malignant tumors involves many steps taking place over several years. The earlier a tumor is detected, the less likely it will have spread to other parts of the body. In the past 25 years, enormous progress has been made in defining the molecular events that take place as a normal cell becomes malignant and the critical genes thought to be involved. See resources listed as “General Cancer Information” at the end of the booklet for more information.

Most cancers are named for the organ or type of cell in which they begin to grow, such as lung, stomach, breast, or colon cancer. Some of the names for other cancers, however, are less clear. **Melanoma** is a cancer of cells in the skin, eyes, and some other tissues, known as melanocytes, that make pigment. **Leukemias** are cancers of the blood cells, and **lymphomas** are cancers that develop in the lymphatic system. The most common cancers in the U.S are **carcinomas**. Carcinomas are cancers that develop in the tissue that lines the surfaces of certain organs, such as the lung, liver, skin, or breast. This tissue is called epithelial tissue. Cancers that develop in the epithelial tissue of specific organs are called carcinoma of the lung, or carcinoma of the breast, for example. Another group of cancers is **sarcomas**: these arise from cells in bone, cartilage, fat, connective tissue, and muscle.



WHAT SUBSTANCES IN THE ENVIRONMENT ARE KNOWN TO CAUSE OR ARE LIKELY TO CAUSE CANCER IN HUMANS? WHERE ARE THEY FOUND?

Every two years, scientists from a wide range of government agencies and educational institutions collaborate with scientists from the National Toxicology Program (NTP) in Research Triangle Park, NC, to publish the *Report on Carcinogens*. The report identifies substances that are either known to cause or suspected of causing cancer in humans and to which a significant number of people in the United States are exposed. It is the source for the agents listed in this booklet.

This booklet does not include all of the more than 200 agents listed in the *Report on Carcinogens*. The 50 or so discussed below are those for which there is a great deal of public interest:

■ Tobacco

Exposure to the carcinogens in tobacco products accounts for about one-third of all cancer deaths in the United States each year. Cigarette, cigar, and pipe smoking, chewing tobacco, snuff, and exposure to environmental tobacco smoke (ETS or secondhand smoke) are all linked to increased cancer risks. Cigarette, cigar, and pipe smoking have been associated with cancers of the lung, mouth, bladder, colon, kidney, throat, nasal cavity, voice box, esophagus, lip, stomach, cervix, liver, and pancreas, and with leukemia; smokeless tobacco has been linked to cancers of the mouth; and ETS has been implicated in lung cancer. Cigarette smoke contains more than 100 cancer-causing substances. The risk for cancers of the mouth, voice box, and esophagus is further increased among smokers who also drink more than two drinks/day.

The 10th *Report on Carcinogens*, published in December 2002, lists 228 substances that are either known to cause or suspected of causing cancer. It also describes where they are found and the scientific evidence that they cause cancer. The *Report* serves as a useful guide for the Federal agencies listed in the back of this booklet, which are responsible for establishing acceptable levels of exposure to chemical substances in the general environment, home, and workplace, and in food, water, and medical drugs. For this and future reports, visit the National Toxicology Program (NTP) Web site at **<http://ntp-server.niehs.nih.gov>**.

A longstanding international group known as the International Agency for Research on Cancer (IARC) also produces reports on known or suspected carcinogens, as well as occupations associated with cancer risk. Visit the IARC Web site: **<http://www.iarc.fr>**.

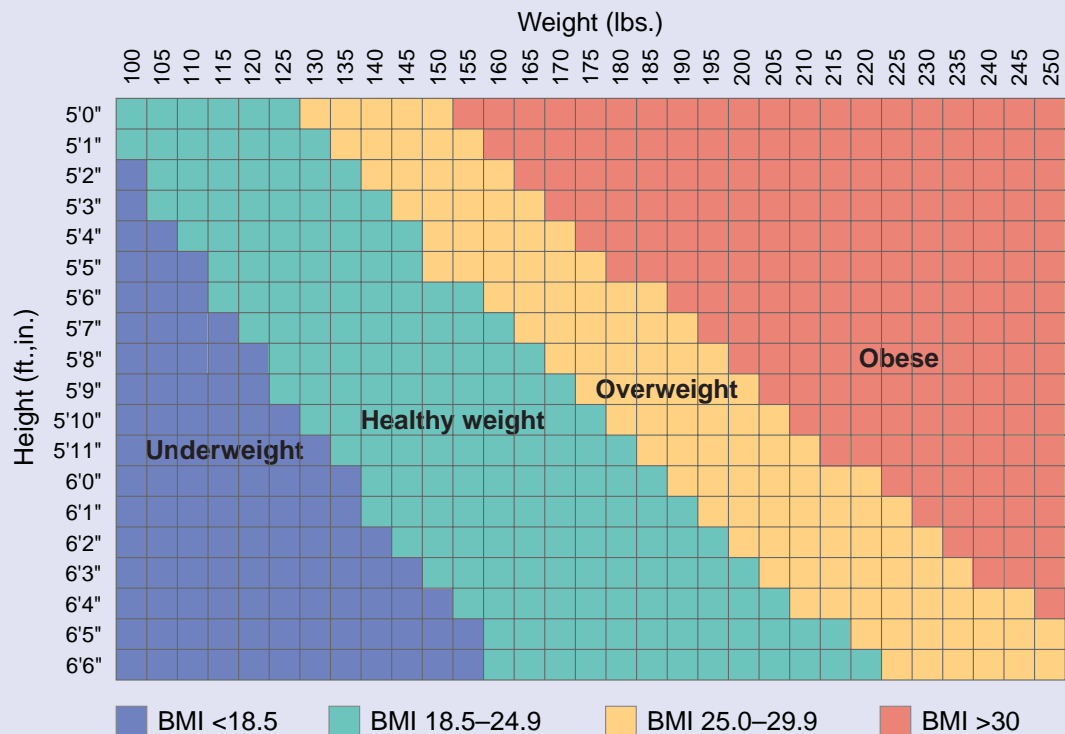
■ Diet/Weight/Physical Inactivity

Because there are few definite relationships between food and cancer, the *Report on Carcinogens* does not refer to the cancer-related effects of specific foods. However, several studies show that heavy consumption of red and preserved meats, salt-preserved foods, and salt probably increase the risk of colorectal and stomach cancers. There is also evidence that a diet rich in fruits and vegetables may decrease the risks of esophageal, stomach, and colorectal cancers.

Being overweight or obese appears to be one of the most important modifiable causes of cancer, after tobacco. Large population studies show a consistent association between obesity and certain kinds of cancer. The strongest links are with breast cancer in older women, and cancers of the **endometrium**, kidney, colon, and esophagus.

There is strong evidence that physical inactivity increases the risk for colon and breast cancer. The beneficial effect of exercise is greatest among very active people. Together, it is estimated that inactivity and obesity account for 25 to 30 percent of the cases of several major cancers—colon, breast (postmenopausal), endometrial, kidney, and cancer of the esophagus.

BODY MASS INDEX CHART, ADULTS 20 AND OVER



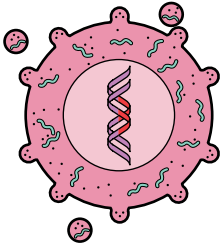
Body Mass Index (BMI) is a number that shows body weight adjusted for height. Based on their BMIs, adults 20 years and older fall into one of the four categories: underweight; healthy weight; overweight; and obese. Individuals in the overweight or obese category have a greater risk than those in the healthy weight category for many diseases, including certain cancers. To find which category you are in, locate your height and move across the chart to your weight.

■ Alcoholic drinks

Heavy drinkers (more than two drinks/day) have an increased risk of cancer, particularly among those who also smoke. Cancers associated with heavy drinking include cancers of the mouth, throat, voice box, liver, and esophagus. There is also some evidence linking alcohol and cancer of the breast.

■ Ultraviolet radiation

Ultraviolet (UV) radiation from the sun, sunlamps, or tanning beds causes premature aging of the skin and DNA damage that can lead to melanoma and other forms of skin cancer. The incidence of skin cancers is rapidly increasing.



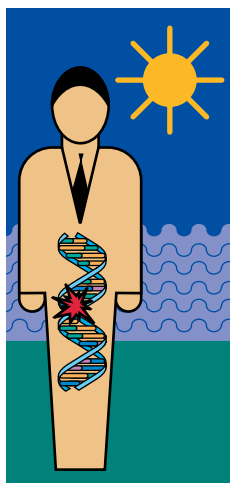
■ Viruses and bacteria

Infectious agents such as viruses and bacteria clearly contribute to the development of several types of cancer. A sexually transmitted virus called **human papillomavirus (HPV)** is the primary cause of cervical and **anal** cancer. Women who begin sexual intercourse at age 16 or younger or have many sexual partners have an increased risk of infection. Infection with HPV is increasingly common. However, even though infection with HPV is the primary cause of cervical cancer, most infections do not result in cancer.

Hepatitis B (HBV) and **hepatitis C (HCV)** viral infections are major causes of liver cancer. In Asia and Africa, HBV is usually acquired in childhood and it carries a high risk of liver cancer. HBV infection is less common in the United States. Risk factors for HBV include occupational exposure to blood products, injection drug use, and high-risk sexual behavior (unprotected sex with multiple partners). A vaccine is available to prevent infection with HBV. The rising incidence of liver cancer in the United States is thought to be due to HCV. The strongest risk factor for HCV infection is injection drug use, but sexual transmission is also possible. People who received a blood transfusion prior to 1989 may also be infected with this virus. Currently, there is no vaccine for HCV.

Almost all adults are infected with **Epstein-Barr virus (EBV)**, which is linked to some types of lymphoma. EBV is the virus that causes mononucleosis. Another type of virus called **Kaposi's sarcoma-associated herpesvirus (KSHV)**, also known as **human herpesvirus 8 (HHV-8)**, is linked to a particular type of sarcoma called Kaposi's sarcoma. KSHV infection only occurs through close person-to-person contacts. In Mediterranean and African countries, KSHV infection in childhood is common. In the U.S., KSHV infection is most common in homosexual men. The risk of cancer for people infected with either KSHV or EBV is low, except for those whose immune systems are weakened, such as people infected with the human immunodeficiency virus (HIV), the virus that causes AIDS.

Infection with *Helicobacter pylori*, a bacterium, is widespread and is the primary cause of peptic ulcers and chronic gastritis (inflammation of the stomach). *H. pylori* contributes to the development of stomach cancer. Most *H. pylori* infections, however, result in neither symptoms nor cancer.



■ Ionizing radiation

Ionizing radiation is invisible, high-frequency radiation that can damage the DNA or genes inside the body.

Everyone is exposed to very small doses of ionizing radiation from **cosmic rays** (rays that enter the earth's atmosphere from outer space). Radiation from this source may account for a very small percentage (about 1 percent) of our total cancer risk.

Some homes have elevated levels of **radon**, a naturally occurring radioactive gas found at low levels in most soil. Radon is produced by the breakdown of uranium, which naturally releases low levels of ionizing radiation. Higher levels of radon can be found in certain types of rocky soil. The health effects of radon were first seen in the elevated levels of lung cancer found in underground uranium miners in the United States and around the world. Radon gas seeps into homes from the surrounding soil through cracks and other openings in the foundation. About 1 out of 20 homes has elevated levels of radon. Even though the cancer risks for radon exposure in the home are much lower than for radon-exposed miners, it is estimated that about 20,000 lung cancer deaths every year are caused by radon exposure in homes. There are various strategies for reducing residential radon exposure.

Another source of ionizing radiation is the radioactive substances released by atomic bombs or nuclear weapons known as "**fallout**." The doses of ionizing radiation received by the atomic bomb survivors in Japan resulted in increased risks of leukemia and cancers of the breast, thyroid, lung, stomach, and other organs. Radioactive substances were also released in the above-ground atomic bomb testing conducted by the U.S. Government in the late 1950s and early 1960s in Nevada. People exposed, especially as children, to one radioactive form of iodine, called Iodine-131 or I-131, which collects in the thyroid gland, may have an increased risk of thyroid disease, including thyroid cancer. For more information visit: <http://cancer.gov/i131>.

People are also exposed to ionizing radiation during certain **medical procedures**. Some patients who receive radiation to treat cancer or other conditions may be at increased cancer risk. For example, persons treated with radiation in childhood to treat acne, ringworm, and other head and neck conditions have been shown to be at increased risk for thyroid cancer and other tumors of the head and neck. **X-rays** used to diagnose or screen for a disease are also forms of ionizing radiation. The dose of radiation from procedures used to diagnose or screen for a disease is much lower than the dose received to treat a disease. Most studies on the long-term effects of

exposure to radiation used to diagnose or screen for cancers or other diseases have not shown an elevated cancer risk, but it is possible that there is a small risk associated with this exposure. One exception is children whose mothers received diagnostic X-rays during pregnancy. These children were found to have increased risks of childhood leukemia and other types of cancer, which led to the current ban on diagnostic X-rays in pregnant women. Several other studies of women who received small weekly X-ray doses to the chest over extended periods to monitor treatment for tuberculosis showed a radiation-related increased risk of breast cancer.



■ Pesticides

Of the nearly 900 active ingredients in registered pesticides in the United States, about 20 have been found to be carcinogenic in animals, although not all have been tested. In the United States, a number of pesticides have been banned or their use has been restricted. These include **ethylene oxide, amitrole, some chlorophenoxy herbicides, DDT, dimethylhydrazine, hexachlorobenzene, hexamethylphosphoramide, chlordecone, lead acetate, lindane, mirex, nitrofen, and toxaphene**. Studies of people with high exposures to pesticides, such as farmers, pesticide applicators, crop duster pilots, and manufacturers, have found high rates of blood and lymphatic system cancers, cancers of the lip, stomach, lung, brain, and prostate, as well as melanoma and other skin cancers. So far, human studies do not allow researchers to sort out exactly which pesticides are linked to which cancers. Therefore, most of these pesticides are still listed in the *Report on Carcinogens* as likely to be cancer-causing, rather than as known carcinogens. For more information, visit: <http://www.aghealth.org>.

■ Medical drugs

Some drugs used to treat cancer (e.g., **cyclophosphamide, chlorambucil, melphalan**) have been shown to increase the occurrence of second cancers, including leukemia. Others that are used as immunosuppressants, such as **cyclosporin** and **azathioprine** for patients having organ transplants, also are associated with increased cancer risks, especially lymphoma. However, the Food and Drug Administration has determined that the life-saving benefits of these drugs outweigh the additional cancer risks years later. It is recommended that people weigh the risks and benefits concerning the use of a drug with the help of a physician or other health care specialist. Some medicines have been linked to reduced risk of cancer. For example, some studies find a reduced risk of colon cancer in persons who regularly take aspirin or other nonsteroidal anti-inflammatory medicines. Evidence for protection of other cancers such as breast cancer or prostate cancer is inconsistent.

Estrogens used to treat symptoms of menopause and other gynecological conditions have been shown to increase the incidence of endometrial cancer. In addition, some studies have shown an increased risk of breast cancer with estrogen use, but a reduced risk of colon cancer. **Progesterone**, another

hormone now taken in combination with estrogen for hormone replacement therapy in older women, helps to protect against the increased endometrial cancer risk with estrogen alone. However, increased risks of breast cancer, heart disease, stroke, and blood clots have recently been shown to be associated with the use of estrogen plus progestin, a synthetic form of progesterone. Long-term users of combination oral contraceptives have substantially reduced risks of endometrial and ovarian cancers, but may experience increases in early-onset breast cancers and liver cancer. The amount of estrogen and progesterone in oral contraceptives is substantially less than in previous years, which means that the risk of the current formulations is likely to be less than those used in the past.

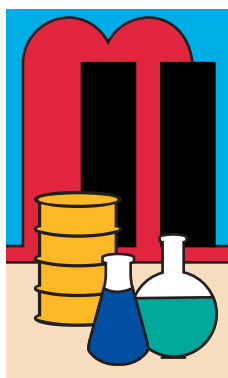
Increased risks of endometrial cancer as well as increased risks of stroke and blood clots are also associated with **tamoxifen** use. Tamoxifen is a synthetic hormone used to prevent the recurrence of breast cancer after breast cancer surgery. It is also used to prevent breast cancer in women at high risk for the disease because of family history or other factors. Again, it is recommended that people weigh the risks and benefits concerning the use of a drug with the help of a physician or other health care specialist.

Diethylstilbestrol (DES) is a synthetic form of estrogen prescribed to pregnant women from the early 1940s to 1971. It was found that their daughters who were exposed to DES before birth have an increased chance of developing a rare type of cervical and vaginal cancer. In addition, women who took DES during pregnancy may have a slightly higher risk for developing breast cancer. Based on these findings, DES is no longer prescribed, and its use as a cattle feed additive has been banned.

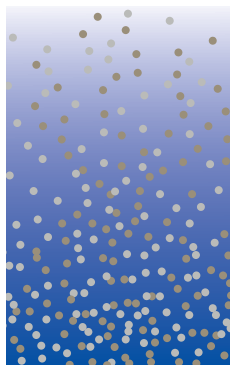
■ Solvents

Several solvents used in paint thinners, paint and grease removers, and in the dry cleaning industry are known or suspected of being cancer-causing in animal studies. These include **benzene**, **carbon tetrachloride**, **chloroform**, **dichloromethane (methylene chloride)**, **tetrachloroethylene**, and **trichloroethylene**. Human studies are suggestive, but not conclusive, except for benzene. Therefore, with the exception of benzene, these substances are listed as likely to be cancer-causing in humans.

Benzene is known to cause leukemia in humans. It has widespread use as a solvent in the chemical and drug industries and as a gasoline component. After 1997, its use as an ingredient in pesticides was banned. Workers employed in the petrochemical industry, pharmaceutical industry, leather industry, rubber industry, gas stations, and in the transportation industry are exposed to benzene. Inhaling contaminated air is the primary method of exposure. Because benzene is present in gasoline, air contamination occurs around gas stations and in congested areas with automobile exhaust. It is also present in cigarette smoke. It is estimated that half of the exposure to



benzene in the United States is from cigarette smoking. About half of the U.S. population is exposed to benzene from industrial sources, and virtually everyone in the country is exposed to benzene in gasoline.



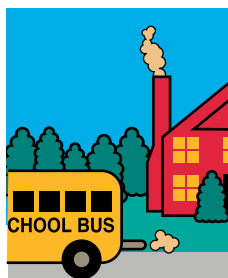
■ **Fibers, fine particles, and dust**

Exposures to various **fibers, fine particles, and dust** occur in several industrial settings and are associated with increased cancer risks. Exposure can also occur in nonindustrial settings. **Asbestos** fibers and all commercial forms of asbestos are human carcinogens. Increased rates of mesothelioma, a rare cancer of the lining of the lung and abdominal cavity, and cancer of the lung have been consistently observed in a variety of occupations involving asbestos exposure. Asbestos exposures account for the largest percent of occupational cancer, with the greatest risks among workers who smoke. Asbestos fibers are released into the environment from the use and deterioration of more than 5,000 asbestos products, including roofing, thermal, and electrical insulation; cement pipe and sheet; flooring; gaskets; plastics; and textile and paper products. Workers in asbestos insulation, brake maintenance and repair, and building demolition jobs are exposed to high levels of asbestos. The entire population may have been exposed to some degree because asbestos has been so widely used. Because the use of asbestos has been greatly restricted in the United States, exposure to the general population has decreased. Nonetheless, workers employed in construction trades, electricians, and carpenters can still experience high levels of asbestos exposures through renovations, repairs, and demolitions. **Ceramic fibers** are now used as insulation materials and are a replacement for asbestos. Because they can withstand high temperatures, they are used to line furnaces and kilns. These fibers cause lung cancer in experimental animals. **Silica dusts** are associated with an excess risk of lung cancer in humans and are found in industrial and occupational settings such as coal mines, mills, granite quarrying and processing, crushed stone and related industries, and sandblasting operations. **Wood dust**, associated with cancers of the nasal cavities and sinuses, is a known carcinogen for unprotected workers who are exposed regularly from sanding operations and furniture manufacturing.

■ **Dioxins**

Dioxins are unwanted byproducts of chemical processes that contain chlorine and hydrocarbons (substances that contain both hydrogen and carbon). There are at least 100 different kinds of dioxins. They are not intentionally manufactured by industry. They are produced by paper and pulp bleaching; incineration of municipal, toxic, and hospital wastes; certain electrical fires; and **smelters** (plants where metal is extracted from ores). They are also found as a contaminant in some insecticides, herbicides, and wood preservatives. Dioxins are widespread environmental contaminants. They accumulate in fats and break down slowly. A particular dioxin that is likely to

be carcinogenic to humans is called **TCDD** (2,3,7,8-tetrachlorodibenzo-*p*-dioxin). TCDD is highly carcinogenic in animals, and, in highly exposed workers, increased overall cancer death rates have been reported. Fortunately, modifications of industrial processes such as bleaching and incineration have resulted in reduced dioxin emissions and have lowered dioxin levels in people. The general population is exposed to low levels of TCDD primarily from eating dairy products, fish, and meat, including poultry.



■ Polycyclic aromatic hydrocarbons (PAHs)

A number of studies show increased incidence of cancer (lung, skin, and urinary cancers) in humans exposed to mixtures of polycyclic aromatic hydrocarbons (PAHs). The primary source of PAHs is from burning carbon-containing compounds. PAHs in air are produced by burning wood and fuel for homes. They are also contained in gasoline and diesel exhaust, soot, **coke**, cigar and cigarette smoke, and charcoal-broiled foods. In addition, they are the byproducts of open fires, waste incinerators, coal gasification, and coke oven emissions. Foods that contain small amounts of PAHs include smoked, barbecued, or charcoal-broiled foods, roasted coffees, and sausages.

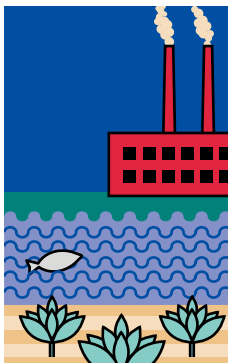
■ Metals

Arsenic compounds are associated with many forms of skin, lung, bladder, kidney, and liver cancers, particularly when high levels are consumed in drinking water. In addition, occupational exposure to inhaled arsenic, especially in mining and copper smelting, has been consistently associated with an increased risk of lung cancer. Arsenic is also used in wood preservatives, glass, herbicides, **insecticides** (ant killers), and pesticides, and it is a general environmental contaminant of air, food, and water.

Beryllium compounds are known to cause lung cancer based primarily on studies of workers in beryllium production facilities. These compounds are used as metals for aerospace and defense industries; for electrical components, X-ray tubes, nuclear weapons, aircraft brakes, rocket fuel additives, light aircraft construction, and the manufacture of ceramics; and as an additive to glass and plastics, dental applications, and golf clubs. Industry is also increasingly using beryllium for fiber optics and cellular network communication systems. Workers can be exposed through jobs related to the above activities, as well as through recycling of computers, cell phones, and other high-tech products. Outside of these industries, beryllium exposure occurs primarily through the burning of coal and fuel oil. The general population can be exposed to trace amounts of beryllium by inhaling air and consuming food contaminated with beryllium residues. Small concentrations have been reported in drinking water, food, and tobacco.

Studies of groups of workers show that **cadmium metal** and **cadmium compounds** are associated with an increased risk of lung cancer. Workers with the highest exposures are those involved in removing zinc and lead from minerals, producing cadmium powders, welding cadmium-coated steel, and

METAL	CANCERS	PRESENT IN	HUMAN CARCINOGEN?	WORKERS EXPOSED
Arsenic	Skin, lung, bladder, kidney, liver	Wood preservatives, glass, pesticides	Yes	Smelting of ores containing arsenic, pesticide application, and wood preservation
Beryllium	Lung	Nuclear weapons, rocket fuel, ceramics, glass, plastic, fiber optic products	Yes	Beryllium ore miners and alloy makers, phosphor manufacturers, ceramic workers, missile technicians, nuclear reactor workers, electric and electronic equipment workers, and jewelers
Cadmium	Lung	Metal coatings, plastic products, batteries, fungicides	Yes	Smelting of zinc and lead ores, producing, processing and handling cadmium powders, welding or remelting of cadmium-coated steel, and working with solders that contain cadmium
Chromium	Lung	Automotive parts, floor covering, paper, cement, asphalt roofing; anti-corrosive metal plating	Yes	Stainless steel production and welding, chromate production, chrome plating, ferrochrome alloys, chrome pigment, and tanning industries
Lead	Kidney, brain	Cotton dyes, metal coating, drier in paints, varnishes, and pigment inks, certain plastics, specialty glass	Probable carcinogen	Construction work that involves welding, cutting, brazing, or blasting on lead paint surfaces; most smelter workers, including lead smelters where lead is recovered from batteries; radiator repair shops
Nickel	Nasal cavity, lung	Steel, dental fillings, copper and brass, permanent magnets, storage batteries, glazes	Nickel metal: Probable carcinogen Nickel compounds: Yes	Battery makers, ceramic makers, electroplaters, enamellers, glass workers, jewelers, metal workers, nickel mine workers, refiners and smelters, paint-related workers and welders



working with solders that contain cadmium. Cadmium metal is primarily used to coat metals to prevent corrosion. Other uses are in plastic and synthetic products, in batteries, as stabilizers for polyvinyl chloride, and in **fungicides**. The industrial processes involved in making these products release cadmium into the air, surface water, ground water, and topsoil where it can be taken up by both land and water plants and, in turn, transferred to animals. Contaminated topsoil that allows uptake into tobacco plants may be indirectly responsible for the greatest nonoccupational human exposure to cadmium—smoking. Food is the main source of human exposure to cadmium for nonsmokers.



Some **chromium compounds** are known to cause lung cancer. The steel industry is the major consumer of chromium. It is used for protection against corrosion of metal accessories, including automotive parts, as well as for electroplating, layering one metal over another. Electroplating converts chromium 6, the carcinogenic form, to a noncarcinogenic form of chromium. This means that workers who handle chromium 6 are at greater risk than the general population. Other uses include nuclear and high-temperature research; the textile and leather-tanning industry; pigments for floor covering products, paper, cement, and asphalt roofing; and creating an emerald color in colored glass. Chromium is widely distributed in the air, water, soil, and food, and the entire population is probably exposed to some of these compounds. The highest exposure occurs in occupations related to stainless steel production, welding, chrome plating, and leather tanning. Typical levels in most fresh foods are low.

Lead acetate and **lead phosphate** are likely to be human carcinogens based on the evidence of kidney and brain tumors in animal studies. Lead acetate is used in cotton dyes; as a coating for metals; as a drier in paints, varnishes, and pigment inks; as a colorant in certain permanent hair dyes (progressive dyes); in explosives; and in washes to treat poison ivy. Lead phosphate is used as a stabilizer in certain plastics and specialty glass. Primary exposures are through skin contact, eating, and inhaling.

Nickel and **nickel compounds** are associated with several kinds of cancers in rats and mice. Studies in human populations link nickel exposure to cancers of the nasal cavity, lung, and possibly the larynx (voice box). Nickel is used in steel, dental fillings, copper and brass, permanent magnets, storage batteries, and glazes. Because nickel is present in the air, water, soil, food, and consumer products in the United States, we are exposed through eating, breathing, and skin contact.

■ Diesel exhaust particles

The particles in diesel exhaust are suspected of being carcinogens because of the elevated lung cancer rates found in occupational groups exposed to diesel exhaust, such as railroad workers, mine workers, bus garage workers, trucking company workers, car mechanics, and people who work around diesel generators. Cancer risks from lower exposures in day-to-day living are not known.

■ Toxins from fungi

Aflatoxins are cancer-causing substances produced by certain types of fungi growing on food. Grains and peanuts are the most common foods on which these fungi grow. Meat, eggs, and milk from animals that eat aflatoxin-contaminated feed are other sources of exposure. Agricultural workers are potentially at risk if they inhale contaminated airborne grain dust. Exposure to high levels of aflatoxins increases the risk of liver cancer. Peanuts are screened for aflatoxin in most countries, including the United States, before

processing. The risk of aflatoxin exposure is higher in developing countries where there is no screening for the fungus.

■ Vinyl chloride

Vinyl chloride, a colorless gas, is a human carcinogen associated with lung cancers and angiosarcomas (blood vessel tumors) of the liver and brain. It is used almost exclusively in the United States by the plastics industry in manufacturing many consumer products, including containers, wrapping film, electrical insulation, water and drain pipes, hosing, flooring, windows, and credit cards. Human exposure can occur primarily in workers in the plastic industry, not by using the end products such as vinyl siding or hosing. The major source of releases of vinyl chloride into the environment is believed to be from the plastics industries. People living near a plastics plant are exposed by breathing contaminated air, but the exposure of the general population away from the plant is essentially zero.



■ Benzidine

Benzidine was one of the first chemicals recognized as being associated with increased cancer risk in humans. As early as 1921, increased cases of bladder cancer were reported to be associated with benzidine, a compound used in the production of more than 250 benzidine-based dyes for textiles, paper, and leather products. Human exposure to either benzidine or **benzidine-based dyes** is now known to be carcinogenic. The dyes break down into benzidine once inside the body. In most cases, dyes that metabolize to benzidine are hazards only in the vicinity of dye and pigment plants where wastes may escape or be discharged.

WHAT ARE SOME WAYS TO REDUCE THE RISK OF DEVELOPING CANCER OR DETECT CANCER AT AN EARLY STAGE?

At least two-thirds of the cases of cancer are caused by environmental factors. Many of these cancers are linked to lifestyle factors that can be modified, such as cigarette smoking, excessive alcohol consumption, poor diet, physical inactivity, and being overweight or obese. For example, one-third of all the cancer deaths in this country could be prevented by eliminating the use of tobacco products. After tobacco, being overweight or obese appears to be the most important preventable cause of cancer.

In addition to lifestyle choices, precautions can be taken in the home and workplace to reduce exposure to other harmful exposures. Here are some rules you can follow to reduce your risk of developing cancer:

■ Don't smoke cigarettes, pipes, or cigars. Don't chew tobacco or dip snuff. Avoid smoke-filled rooms. The use of tobacco products is linked to many cancers.

■ Lose weight if you are overweight. Obesity is strongly linked to breast cancer in older women and cancers of the endometrium, kidney, colon, and esophagus.

■ Exercise regularly, at least 30 minutes per day for most days of the week. There is strong evidence that exercise by itself reduces the risk of colon and breast cancer. Risk is decreased the most among very active people.

■ Avoid high-calorie, high-fat food. The chief causes of obesity are a lack of physical activity and eating too much high-calorie food.

■ Avoid consuming large amounts of red and preserved meats, salt, and salt-preserved foods. These may increase the risk of colorectal and stomach cancers.

■ Eat a daily diet that includes a variety of foods from plant sources, such as fresh fruits, vegetables, whole grains, and whole grain breads and cereals. Fruits and vegetables contain substances (e.g., antioxidants) that help defend against toxic agents and disease.

■ Drink alcohol in moderation, if at all, especially if you smoke. (One or two alcoholic drinks a day is considered moderate.) Heavy drinking is linked to cancers of the mouth, throat, esophagus, voice box, liver, and breast.

■ Avoid too much sunlight, particularly if you are fair skinned, by avoiding sun exposure at midday (10 a.m.–4 p.m., when sun exposure is strongest), wearing protective clothing, and using sunscreen. Many of the more than one million skin cancers diagnosed every year can be prevented by protection from the sun's rays. Avoid tanning beds and other artificial sun or UV exposure.

■ Avoid viral or bacterial infections:

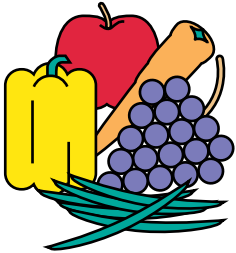
—Do not engage in unprotected or otherwise unsafe sexual intercourse that may result in HIV, HPV, hepatitis B, or hepatitis C infection.

—Do not use recreational injection drugs, such as heroin or cocaine, that may result in HIV, hepatitis B, or hepatitis C infection.

—Get vaccinated against hepatitis B infection, an easy and safe procedure if you are 18 years of age or younger. Also, get vaccinated if you are over 18 and at risk of infection. At-risk people include health care workers, IV drug users, and homosexual men. Currently, there is no vaccine for hepatitis C. (For vaccination information, visit: www.cdc.gov.)

—Seek medical attention for chronic stomach problems because they might be caused by *H. pylori* infection, which can be treated.

■ Seek medical attention and adhere to recommended treatments if you have HIV or hepatitis C infection. These infections increase your risk of developing certain cancers.



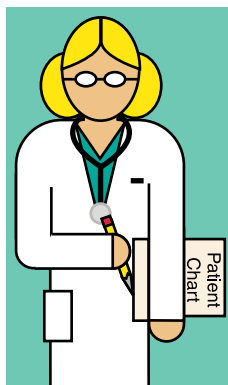
- Because repeated exposure to diagnostic X-rays could be harmful, talk to your doctor about the need for each X-ray and the use of shields to protect other parts of the body.
- Check your home for high levels of radon. Radon levels in a home can be greatly reduced by a professionally installed ventilation system in the basement. (For more information, visit the Environmental Protection Agency Web site: www.epa.gov/iaq/radon.)
- Avoid contact with pesticides. Exposure to pesticides comes largely through the skin. If contact occurs, wash up quickly.
- Make sure the room is well ventilated when working with solvents. Work outside, if possible, or open the windows.
- If you work in an environment with high exposures to fine particles, fibers, or dusts, wear the appropriate protective mask over your nose and mouth and make sure it fits properly and does not obstruct your view.
- Use good work practices when handling chemicals in the home or workplace. Wear proper personal protective equipment, keep protective equipment well maintained, clean spills immediately, keep work surfaces as free of dust and chemicals as possible, and use wet cleaning methods to avoid generating dust.



- Be aware that certain occupations are known to be associated with high cancer risks. Some of these include painters, furniture makers, workers in the iron, steel, coal, and rubber industries, and workers involved in boot and shoe manufacture or repair. (For more information, visit: <http://ehp.niehs.nih.gov/roc/tenth/append/appa.pdf> or call the National Institute for Occupational Safety and Health toll-free number, 1-800-356-4674.)
- Inquire at your workplace about Material Safety Data Sheets (MSDSs). A MSDS is a document that manufacturers of chemical products are required to develop for any product that contains hazardous substances. The MSDS contains information on the toxicity of a substance, whether it is considered to be cancer-causing, the recommended exposure levels of the ingredients in the product, and appropriate precautions to take or appropriate recommended personal protective equipment to wear. Employers are required to make the MSDSs accessible to employees and to inform/train employees about the information. (For information about possible workplace issues, visit the National Institute for Occupational Safety and Health Web site at www.cdc.gov/niosh/topics/chemical-safety or call the toll-free number, 1-800-356-4674.)
- Make sure your employer has put in place appropriate engineering controls such as local exhaust ventilation.

Detecting Cancers at an Early Stage

Sometimes exposures to toxic substances cannot be avoided. Certain diagnostic procedures will not reduce the exposure to substances in the environment but may detect cancers at an early stage before they spread to other parts of the body.



- Tell your health care provider about the chemicals you use at work or at home. With this information, your health care provider can perform appropriate medical screening tests for early detection of cancer.

- Ask your physician if there are increased cancer risks associated with your family or personal medical history or medical drugs you are taking. Appropriate screening procedures may be advised.

- Get a screening test on a regular basis for these cancers:

- Breast*: A mammogram, an X-ray of the breast, is the best method of finding breast cancer before symptoms appear. Several organizations recommend mammography screening every one to two years after age 40. Women at higher than average risk of breast cancer should seek expert advice about screening before age 40 and about the frequency of screening.

- Cervix*: The Pap test or Pap smear is the most successful screening tool used to screen for cancer of the cervix. Cells are collected from the cervix and examined under a microscope to detect cancer or changes that may lead to cancer. Many doctors recommend yearly Pap tests. Less frequent screening is recommended by some organizations for women with at least three consecutive negative exams.

- Colon and Rectum*: A number of screening tests are used to find colon and rectal cancer. If a person has a family medical history of colorectal cancer or is over the age of 50, a doctor may suggest one or more of these tests: the fecal occult blood test checks for small amounts of blood in the stool; a sigmoidoscopy is the use of a lighted tube to examine the rectum and lower colon; a colonoscopy is performed to see the entire colon and rectum. With either a sigmoidoscopy or a colonoscopy, abnormal tissue can be removed and examined under a microscope.

Guidelines for the age and frequency of screening tests are constantly being revised as new information becomes available. To find out more, see the Web site: http://cancer.gov/cancer_information/testing.

■ Be alert for changes in your body. Cancer may cause a variety of symptoms. Here are some:

- Thickening or lump in any part of body
- Obvious change in a wart or mole
- A sore that does not heal
- Nagging cough or hoarseness
- Changes in bowel or bladder habits
- Indigestion or difficulty swallowing
- Unexplained changes in weight
- Unusual bleeding or discharge

These symptoms are NOT always caused by cancer. It is important to see a doctor about these or other physical changes that continue for some time. However, certain cancers have no obvious symptoms, so routine physical exams are recommended.

■ Stay informed and be proactive.

- Ask your doctor questions.
- If you suspect that you are exposed to a carcinogen in your work or home environment, try to find out more. Use the resources at the end of the booklet to contact the agencies responsible for protecting the environment.
- Get involved in activities aimed at reducing our exposure to cancer-causing substances. Government agencies, industries, health professionals, and individuals can all contribute to reducing the risks in the environment. For example, in order to control the obesity epidemic, efforts to increase physical activity and promote healthy eating are needed in many parts of society, including families, schools, day care centers, food companies, restaurants, work sites, health care systems, and departments of transportation and city-planning.

GOOD PLACES TO LOOK

For local environmental issues:

<http://www.cdc.gov/other.htm#states>

For workplace issues:

<http://www.cdc.gov/niosh/topics/chemical-safety>

For health effects of ingredients in common household products:

<http://householdproducts.nlm.nih.gov>

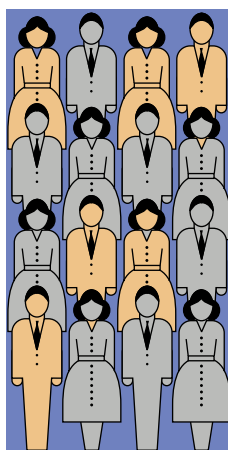
HOW DO SCIENTISTS IDENTIFY CANCER-CAUSING SUBSTANCES?

Over the last 30 years scientists have worked hard to identify substances in the home, workplace, and general environment that cause cancer. This is a challenging task because there are more than 100,000 chemicals commonly used by Americans in household cleaners, solvents, pesticides, food additives, lawn care, and other products. Every year, another 1,000 or so are introduced. Furthermore, these are single substances and do not take into account the mixtures and various combinations of commercial and consumer products that Americans are exposed to every day. In addition, many chemicals may be changed to different substances by the atmosphere, water, plants, and by incineration or combustion.

Adding to the complexity, scientists know that cancer-causing substances are sometimes created during the synthesis or combustion of other chemicals. Dioxin is an example of this kind of unwanted contaminant (see page 13).

Further complicating the problem is the fact that besides man-made chemicals, many natural products can also cause cancer. One example is aflatoxin, discussed on page 16.

Evidence for identifying cancer-causing substances comes from three sources: **human studies**, **animal studies**, and **laboratory experiments with human cells**. Evidence from each of these sources is important in helping public health officials make decisions about whether exposure to certain substances needs to be reduced or eliminated. The more information available, the more likely it is that they will be able to identify which substances are carcinogens.

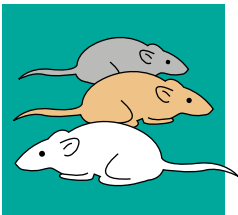


Human Studies

The most certain method of identifying cancer-causing substances is to observe whether they have caused cancer in people. Epidemiologists design studies that follow certain populations over time to observe whether a specific agent (e.g., arsenic or benzene) or exposure (e.g., sunlight or smoking) is likely to cause cancer. Environmental causes of cancer have frequently been first noticed in the workplace. This is because workers in certain occupations have higher exposures to particular chemicals and for longer periods of time than the general population. The International Agency for Research on Cancer (<http://www.iarc.fr>), an agency of the World Health Organization, classified certain occupations as associated with cancer-causing exposures because of the increased incidence of cancers in these settings. Some of these include painters, furniture makers, workers in the iron, steel, coal, and rubber industries, and workers involved in boot and shoe manufacture or repair. This knowledge has helped these industries and public health specialists develop processes and safety procedures designed to minimize worker exposure to cancer-causing substances. So the risk is less now than in previous years.

However, health agencies would fail in their responsibility to prevent cancer if they merely document workplace-related cancers, because they would find out about cancer risks only after many people developed symptoms of the disease, sometimes as long as 20 to 30 years after the exposure. Other epidemiology studies compare the exposure histories of people who have developed cancer to comparison groups of people who have not developed cancer at a particular point in time. Such studies allow researchers to look at a wide range of exposures that may have occurred in the past in a variety of settings, not just at those that occurred in a particular occupational setting. However, these studies may miss some important links between exposures and cancer. It is often difficult to determine what chemicals people were exposed to many years earlier, to what degree they were exposed, and which specific ones are harmful. But because we cannot test potential cancer-causing agents with people, observational epidemiological studies are the best source of data on real world exposures and often do provide important clues.

Other testing methods involving animals and laboratory experiments are also important. They allow scientists to anticipate potential cancer-causing exposures before they cause large numbers of human cancers.




Animal Studies

Mice or rats are most commonly used to test for cancer-causing substances because they are smaller, easier to handle, and more economical than larger animals. Also, they are generally similar to humans in their response to carcinogens. Most major forms of human cancer have been reproduced in such animals through exposure to chemical carcinogens. Because the lifetime of rodents is only two to three years, they generally provide information about the cancer-causing potential of test materials relatively quickly. Special strains of mice and rats have been developed to be particularly suitable for cancer testing. However, differences in animal and human digestive physiology complicate the relevance of diet studies in animals.

Laboratory Experiments

As part of an ongoing effort to reduce the use of animals in testing for cancer, researchers are using human cells grown in the laboratory. Cells exposed to potential carcinogens are monitored to see whether molecular changes characteristic of cancer cells develop. Besides reducing the use of animals, these kinds of studies can be done more quickly and economically and can be useful in evaluating whether to perform the studies in rats and mice. Results from laboratory experiments also provide clues to epidemiologists about which hypotheses to test in human population studies (e.g., human observational studies evaluating the effect of exposure to formaldehyde and methylene chloride were initiated because of data from laboratory and animal studies).

HOW WELL DO ANIMAL TESTS PREDICT WHETHER A SUBSTANCE CAN CAUSE CANCER IN HUMANS?

 f the approximately 200 agents known to cause cancer in humans, nearly all have also been shown to cause cancer in rats or mice. On the other hand, we do not know how many of the several hundred other chemicals that cause cancer in animals are also human carcinogens. In some instances, positive tests with mice or rats were later confirmed by the occurrence of cancer in exposed humans. In other instances, studies in human populations have failed to confirm the positive tests in mice. Most importantly, however, for many chemicals suspected of causing cancer in humans, no human studies have yet been done, so we do not know for sure whether these chemicals do or do not cause cancer in humans.

Because it is generally true that materials that cause cancer in one type of animal are found to cause cancer in others, public health officials must heed the warnings provided by animal tests. Positive tests in animals are often used as a basis for reducing or eliminating human exposure to probable cancer-causing agents. For instance, regulatory controls to reduce human exposures were put in place when drinking water disinfectant byproducts and several solvents were shown to be carcinogenic in rats and mice.

In a few cases, the evidence from laboratory experiments, along with knowledge of the behavior of related compounds known to be carcinogenic, was strong enough to classify a chemical as a known or probable human carcinogen. For example, experiments using human cells were used to classify more than 200 benzidine-based dyes as human carcinogens. Benzidine had already been classified as a known human carcinogen and scientists suspected that any dye that released benzidine inside the human body would also be a human carcinogen. When human cells grown in the laboratory were exposed to a particular dye, they were able to test whether benzidine was released. Those that did were classified as human carcinogens.

In another example, one piece of data that led to the classification of ethylene oxide (used as a starting material in the production of other chemicals and as a disinfectant and sterilant) as a known human carcinogen was from laboratory experiments showing that it caused DNA damage in blood cells from exposed workers.

Although these kinds of studies reduce our reliance on animals in toxicology research, the testing of potential carcinogens in rodents remains an important part of cancer prevention strategies. However, all scientific data available for a potential carcinogen are important. The combination of human studies, animal studies, and laboratory experiments provides scientists with the most complete understanding of chemical risks of cancer.

WE OFTEN READ ABOUT MICE OR RATS BEING GIVEN DOSAGES MUCH HIGHER THAN THOSE TO WHICH HUMANS NORMALLY WOULD BE EXPOSED. ARE HIGH DOSES REALLY USED AND, IF SO, WHY?

Yes, high doses are often used to increase the ability of the tests to detect cancer-causing potential.

Large numbers of people are exposed to low doses of chemicals, but the total impact may not be small at all. For example, a carcinogen might cause one tumor in every 10,000 people exposed to it. But exposure of 230 million Americans would result in 23,000 cancers—a public health disaster. To detect such a low cancer rate, we would need tens of thousands of mice. This would cost approximately \$50 million for every chemical tested. Not only would this be expensive and very time-consuming, but it would use far too many animals.

However, using high dosages, any potential cancer-causing effects are more likely to be detected even in small groups of rodents because the cancer rate among the test animals is increased correspondingly. If 20 or 30 of our test group of 50 mice developed cancers at much higher doses while the group not receiving the chemical had only a few cancers, we could conclude that the chemical was capable of causing cancer. When high doses do not cause cancer in animals, we also have greater assurance that the chemical will not cause cancer in people.

HOW DO SCIENTISTS DECIDE WHICH SUBSTANCES TO TEST IN ANIMALS, HUMAN LABORATORY CELLS, OR HUMAN POPULATION STUDIES?

Strategies for Testing in Animals or Human Laboratory Cells

Because resources are limited, scientists must decide which substances out of thousands of candidates should be selected for testing in animals or human cells. The tests are costly and time-consuming. For example, determining whether a chemical causes cancer in rats or mice can cost several million dollars and take several years to complete. Three factors generally guide the decision to test a substance:

- **The number of people exposed.** We want to test those chemicals that affect a large number of people or those for which the exposure levels have been unusually high. Pesticides, for example, fit both categories: they potentially affect a large number of people because of trace amounts on foods and their use in or around the home, and exposure levels are high in farming-related occupations.

■ **Previous data.** This could be a report that a chemical causes alterations in human DNA in laboratory cells, or a report that people exposed to a particular chemical in the workplace or at a specific geographical location are getting cancer at higher rates than expected. This kind of information provides important clues for decisions about animal testing. Before testing in animals was done, dioxins and polycyclic aromatic hydrocarbons were first suspected to be carcinogenic based on studies on human and animal cells.



■ **Public concern.** Chromium and some pesticides are examples of chemicals that were first brought to the attention of public health officials by a group of concerned citizens. The National Toxicology Program has a Web site available to the public to suggest agents suspected of causing cancer: <http://ntp-server.niehs.nih.gov>; click on “How to Nominate Compounds.”

Strategies for Carrying Out Large Population Studies

Similar considerations guide epidemiologists as to whether to begin large population studies. Some of these factors include:

- Data from animal studies suggesting a cancer-exposure link (e.g., vinyl chloride) or a related agent, which raises suspicion (e.g., acrylonitrile was studied because of its structural similarity to vinyl chloride)
- Suggestive results from other epidemiologic studies (large population studies)
- Biological mechanisms of an exposure that suggest a possible link to cancer
- Pockets of cancer that cluster in a particular town or place or unusual case reports
- Cancer trends—rates that change over time or with location
- Changes in cancer rates within a population upon migration to new area
- Introduction of a new exposure or technology for which epidemiologic data are needed, or an unusual exposure pattern that needs evaluation.

WHAT FACTORS DO SCIENTISTS CONSIDER IN DETERMINING THE RISK ASSOCIATED WITH DIFFERENT CANCER-CAUSING SUBSTANCES?

Exposures to some substances are associated with high risks for getting cancer, while exposures to other substances carry very little risk. It is important to know that just being exposed to a chemical agent does not mean that you will get cancer. Risk assessment is the term used to determine the relationship between exposure to a substance and the likelihood of developing disease from that exposure. Risk assessment is a critical tool used by public health agencies in making decisions about whether exposure to

certain substances needs to be reduced or eliminated. Three factors are important to consider in risk assessment:



■ **Potency:** Potency is a measure of the capacity of a given amount of the substance to cause cancer. In some cases, exposures to small amounts are sufficient, whereas for others much higher exposures are needed. One potent carcinogen is the solvent benzene, which increases the risk for leukemia from small amounts in the air. Others, like DDT and chloroform, require higher exposures to increase the cancer risk by the same amount.

■ **Type of Exposure:** Public health agencies classify substances as known or suspected human carcinogens based on evidence of cancer from at least one type of exposure, such as:

- Workplace exposures—either high short-term or long-term exposures
- Continuous low-level exposure or occasional exposure to carcinogens in air, food, water, drugs, or consumer products
- Single, acute exposures following industrial accidents or similar incidents

■ **Dose Response:** It is important to know whether the cancer risk increases as the exposure levels increase. This is known as a dose-response trend. Some dose-response trends are linear, which is often considered strong evidence for cancer risk. For example, if 10 units of a substance causes cancer in 1 out of 1,000 people, then 1 unit of exposure would cause cancer in 1 out of 10,000 people. In a linear dose response, the risk would continue to decrease as the exposure decreased all the way to zero. This means that a tiny risk of cancer is predicted for any exposure, no matter how small.

However, for some carcinogens, there may be an exposure level below which there is no detectable increase in risk. This type of dose response is sometimes called ***threshold dose response***.

Some exposures cause cancer only among susceptible individuals. Factors such as age, gender, general health, state of the immune system, smoking history, diet, childhood exposures, and patterns of genetic alterations may play a role in susceptibility. A chemical may be harmless unless a person has one or more factors that allow the chemical to be changed in the body to a more hazardous form. Risk assessment involves understanding the interactions of many susceptibility factors.

ACCEPTABLE RISK LEVELS

The risk level considered acceptable by regulatory agencies for a linear dose response ranges from 1 cancer in every million people exposed to 1 in every 1,000 people exposed. Acceptable risks are generally higher for exposure in the workplace than in the general environment. For example, allowable air levels of benzene in the workplace are approximately 40 times higher than allowed in the general environment.

HOW DO PUBLIC HEALTH OFFICIALS SET ACCEPTABLE EXPOSURE LEVELS FOR ENVIRONMENTAL CHEMICALS?

Linear Dose Response

One of the first considerations by regulatory agencies such as the Environmental Protection Agency, Food and Drug Administration, and Occupational Safety and Health Administration is to determine whether a carcinogen exhibits linear or threshold-like dose-response behavior. Even though government scientists conduct rigorous scientific reviews to evaluate everything that is known about a cancer-causing substance, there is frequently not enough information to distinguish between these two kinds of dose responses. Unless there is compelling evidence for a threshold-like mechanism, agencies assume, to protect the public health, that the dose response is linear. This means that they assume that any exposure, no matter how small, would have some risk.

Threshold-Like Dose Response

In the case of carcinogens exhibiting threshold-like dose responses, other factors such as age, gender, genetic makeup, and diet are taken into consideration. For example, the potentially greater health effects on children of pesticide residues on food are taken into consideration when setting acceptable exposure levels of pesticides. Moreover, if the cancer testing is done in rats and mice, scientists consider the possibility that people are more sensitive than rats or mice to the cancer-causing effects of a particular chemical. These factors can result in setting acceptable levels of exposure as much as 1,000 times below the level that causes a substantial increase in cancer in rodents. This approach gives more confidence that the acceptable level of exposure set by a regulatory agency will indeed protect the public health.

Risks Versus Benefits

Another factor adding to the difficulty of regulating the exposure to environmental chemicals is that many substances that may cause cancer in people also have some benefits.



Pharmaceuticals represent the best example of when benefit/risk analyses are routinely conducted. In the case of cancer chemotherapy drugs, we know that while they may be effective in treating or preventing cancer, they also may increase the risk of second cancers developing years after the treatment. However, since cancer is often immediately life-threatening, the benefits usually outweigh the risks. Tamoxifen, for example, which is effective in preventing the recurrence of breast cancer in many women, also increases the risk of uterine cancer, blood clots, and strokes. The benefits and risks were rigorously analyzed by the Food and Drug Administration, the National Cancer Institute, and the World Health Organization, and they all concluded that the benefits of tamoxifen for women who have had breast cancer or for a relatively small

number of women who are at high risk of developing breast cancer strongly outweigh the serious risks associated with the drug.

Another example is pesticides. The use of pesticides has increased crop yields and has significantly benefited agricultural production. Yet there is concern over potential health effects of pesticide residues on foods consumed by humans. These potential risks are reduced by setting maximum residue levels on fruits, vegetables, and other produce and by using pesticides that are not carcinogenic.

Uncertainty and Public Debate

Public health officials are in the best position to accurately identify carcinogens when evidence is available from all levels—human, animal, and laboratory, but this is seldom the case. Therefore, they often have to exercise scientific judgment and make decisions in the face of uncertainty. In these circumstances, public health agencies operate under the principle that public health protection is paramount. These decisions are debated in open public forums involving scientists from diverse disciplines, and interested members of industry, environmental groups, and the public.

Public health agencies attempt to convey this uncertainty by placing the substances in categories depending on the strength of the evidence. The categories used by the U.S. Department of Health and Human Services' (DHHS) *Report on Carcinogens* are “known to be” and “reasonably anticipated to be” human carcinogens.

PROTECTION OF PUBLIC HEALTH

In the face of uncertainty, public health agencies operate under the principle that protection of public health is paramount. This means that acceptable levels of exposure are set as much as 1,000 times below the level that causes a substantial increase of cancer in laboratory animals.

HOW HAVE CANCER TRENDS CHANGED OVER THE PAST FEW YEARS?

The yearly rate of new cancer cases increased between 1975 and 1992, as the graph on page 30 shows. There is some evidence of a decline after 1992 followed by stable rates since 1995. In this graph, scientists use the term **incidence** to describe the number of people that develop cancer out of 100,000 people within a certain period of time.

Increases in incidence rates are sometimes difficult to interpret. An increase in the number of new cases of cancer may result from exposure to a harmful substance in the environment. But increasing incidence may also reflect

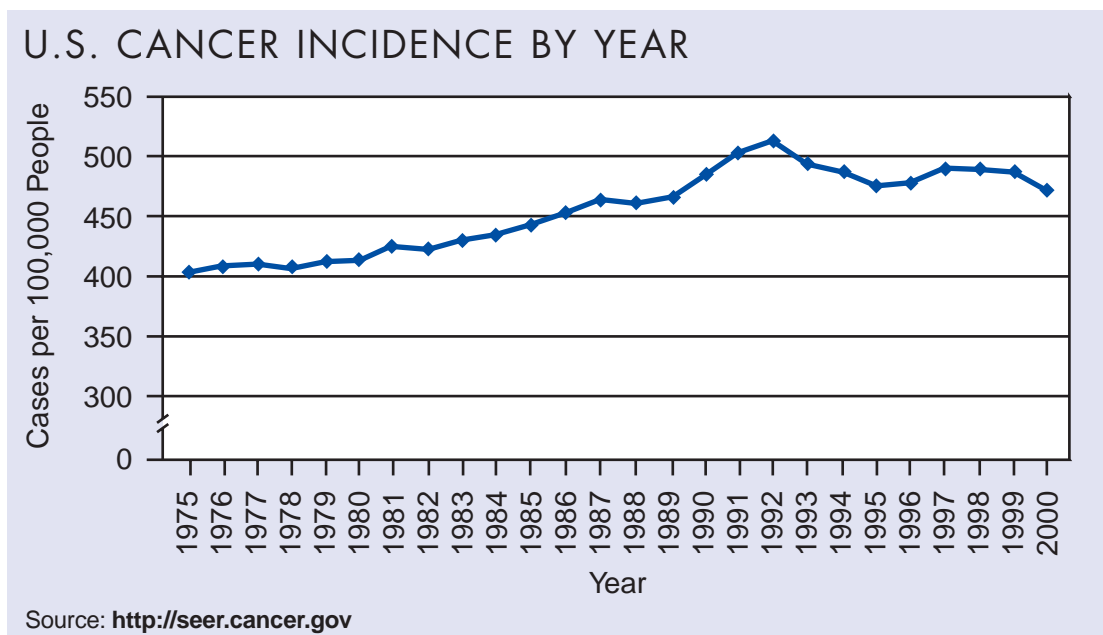
changes in clinical practice in hospitals or doctors' offices, which result in more cases being found—perhaps even some cases that would never produce symptoms of the disease. Decreases in incidence, on the other hand, are probably due to a decreased exposure to harmful substances, or to early detection and removal of precancerous growths.

For cancer deaths, the graph on page 31 shows that the rates increased steadily from 1975 to 1990, stabilized between 1990 to 1994, then declined on average 1.4 percent per year from 1994 to 1998. Since 1998, the rates again stabilized. In this graph, **mortality** is the number of cancer deaths that occur out of 100,000 within a certain period of time.

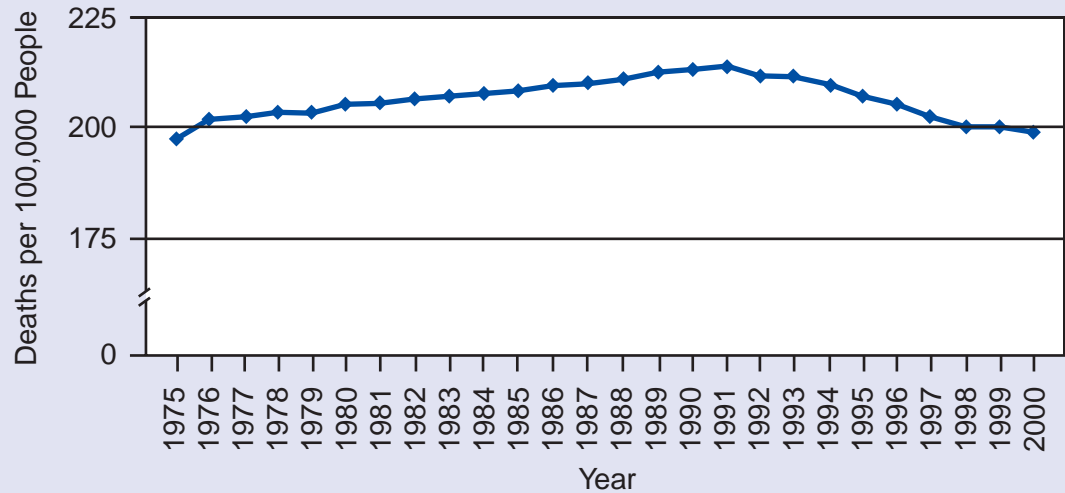
This is very good news because decreases in mortality are the best measure of progress against cancer. Mortality rates would be expected to decrease with a reduction in risk factors (stopping smoking and less exposure to certain pesticides, organic solvents, and asbestos fibers), successful early screening efforts (mammography, Pap test, and fecal occult blood test), or better treatments.

Changing Rates for Specific Cancers

The incidence and mortality rates for some cancers have been declining. These include testicular, childhood, cervical, stomach, throat, and cancers of the mouth (lip, tongue, gums). For example, in the last 25 years, mortality rates for childhood cancer (ages 1–14) and cervical cancer have nearly halved. Improvements in treatment are thought to account for the reduction in childhood cancer deaths, while increased screening (Pap smears) accounts for the decrease in cervical cancer rates. The incidence and mortality from



U.S. CANCER MORTALITY BY YEAR



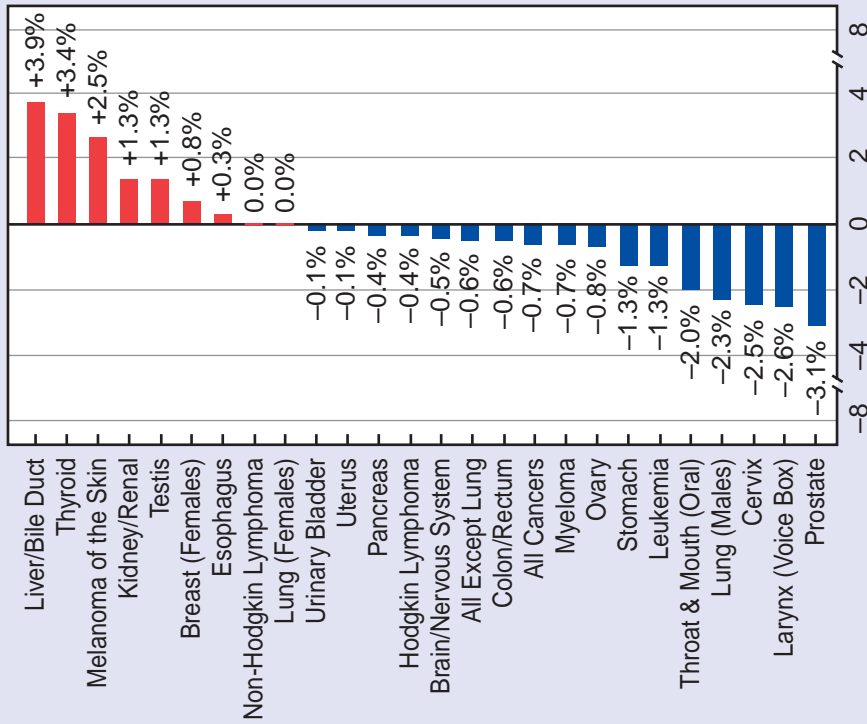
stomach and colon cancer and cancers of the mouth and throat have also decreased over this time period.

On the other hand, the incidence and mortality rates for certain cancers are not improving. From 1973 to 1999, the incidence rates for cancers of the breast, lung (in females), bladder, prostate, kidney, liver, esophagus, and brain increased, as did non-Hodgkin's lymphoma and melanomas of the skin. The larger percentage increase in lung cancer incidence rates for women compared to men reflects the fact that women began smoking later in the century than men—few women smoked before the 1960s. Death rates for melanomas of the skin, non-Hodgkin's lymphoma, and liver, kidney, lung, and brain cancers have also increased over the 26-year period.

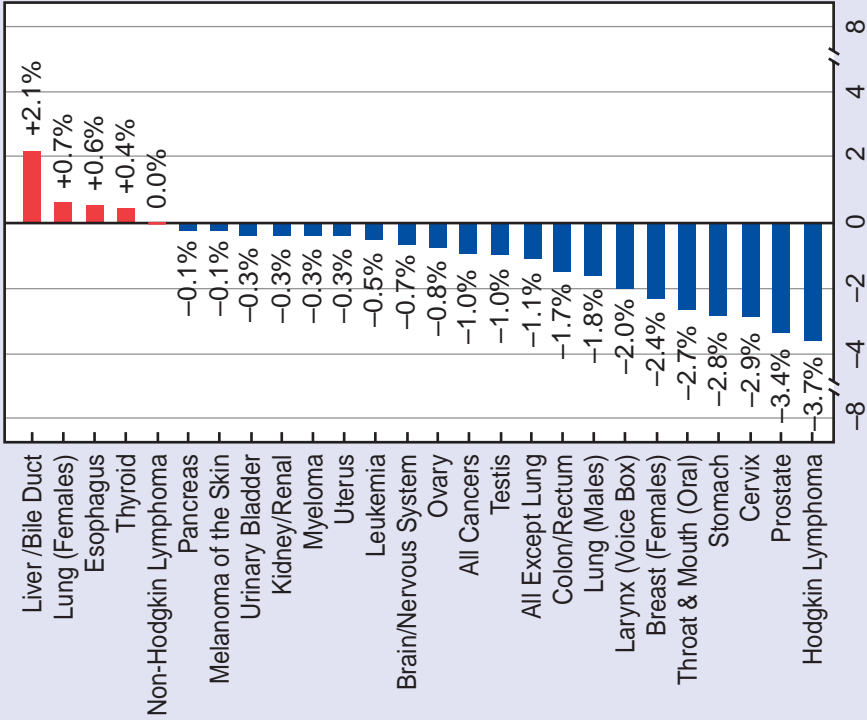
The more recent trends from 1992–2000 are shown in the graph on page 32. Today, for women, over half of the new cancer cases and deaths are due to breast, lung, and colon/rectal cancers. For men, more than half of the new cancer cases and deaths are from prostate, lung, and colon/rectal cancers. Scientists are eager to understand why these trends are occurring, in order to develop effective strategies for preventing cancers.

U.S. TRENDS IN RATES OF NEW CANCERS AND CANCER DEATHS: 1992–2000

Rates of New Cancers: Annual Percent Change



Rates of Cancer Deaths: Annual Percent Change



How to read these charts: The charts show the percentage changes in cancer rates for several cancers from 1992–2000. The chart on the left shows the percentage changes in the rates of new cancer cases, and the one on the right shows the changes in the rates of cancer deaths. Cancer rates in blue have decreased over this time, while those in red have increased. For example, the incidence rates of liver, thyroid, and melanoma cancers had the greatest percentage increase; the death rates for liver cancer, lung cancer in women, and esophageal cancers showed the largest increase. However, both the incidence and mortality rates for prostate and lung cancers (males) have decreased.

Source: SEER (<http://seer.cancer.gov>) and NCHS (www.cdc.gov/nchs).

WHERE CAN I GO FOR MORE INFORMATION?

The resources listed below are available to answer your questions and help you stay informed about our changing environment with its associated health risks.

Federal Government Agencies That Regulate Exposures to Carcinogens

There are several Federal agencies that are charged with establishing permissible levels of exposure to chemical substances in the general environment, home, and workplace, and in food, water, and pharmaceuticals. These include the Consumer Product Safety Commission (CPSC), Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), the Occupational Safety and Health Administration (OSHA), and the U.S. Department of Agriculture (USDA). In addition, the Agency for Toxic Substances and Disease Registry (ATSDR) has broad jurisdiction over hazardous waste issues.

■ **Consumer Product Safety Commission (CPSC):** <http://www.cpsc.gov>
CPSC is an independent Federal regulatory agency responsible for reducing the risk of injuries and deaths associated with consumer products. The consumer hotline is 1-800-638-2772 or the toll-free TTY number is 1-800-638-8270.

■ **Environmental Protection Agency (EPA):** <http://www.epa.gov> EPA is a government regulatory agency charged with protecting human health and safeguarding the natural environment.

—One-stop source for environmental information where you live:

<http://www.epa.gov/enviro>

—Learn about the environmental resources available in your community:

<http://www.epa.gov/epahome/comm.htm>

—EPA National Pesticide Information Center: <http://npic.orst.edu>.
1-800-858-7378

—EPA Superfund Hotline for hazardous waste: 1-800-775-5037 or 703-413-0223. The toll-free TTY number is 1-800-553-7672.

—General information about identifying and cleaning up hazardous waste sites: <http://www.epa.gov/superfund/about.htm>

—A list of hazardous waste sites:

<http://www.epa.gov/superfund/sites/index/htm>

—A list of common contaminants in hazardous waste sites and their health effects:

<http://www.epa.gov/superfund/programs/er/hazsubs/sources/htm>

—For more information about radon in your home, visit the EPA radon Web site: <http://www.epa.gov/iaq/radon> or the National Radon Information line: **1-800-SOS-RADON (1-800-767-7236)**

■ **Food and Drug Administration (FDA):** <http://www.fda.gov> FDA helps safe and effective products reach the market in a timely way and monitors the products for safety after they are in use.

—The National Center for Toxicological Research: <http://www.fda.gov/nctr>

—FDA Information: www.cfsan.fda.gov or 1-888-463-6332

■ **Occupational Safety and Health Administration (OSHA):** <http://www.osha.gov> OSHA is a Federal regulatory agency under the U.S. Department of Labor whose mission is to prevent work-related injuries, illnesses, and deaths. To report accidents, unsafe working conditions, or safety and health violations: 1-800-321-6742. OSHA also has a toll-free TTY number: 1-877-889-5627. Office of Communications: 202-693-1999. Individuals can also contact their local area offices.

■ **United States Department of Agriculture (USDA):** <http://www.usda.gov/services.html> The USDA has several agencies and programs related to agricultural products including food safety inspection, animal and plant inspection service, nutrition programs, and agricultural research programs.

■ **Agency for Toxic Substances and Disease Registry (ATSDR):** <http://www.atsdr.cdc.gov> ATSDR is an agency of the U.S. Department of Health and Human Services (DHHS) and is the principal Federal agency involved with hazardous waste issues and has fact sheets on various chemicals/agents. ATSDR Information Center: 1-888-422-8737

In many cases, more than one agency has the regulatory authority for a specific chemical, depending on its use and potential for human exposure. For example, pesticides are regulated by the EPA, FDA, USDA, and OSHA.

Other Federal Agencies

Other Federal agencies such as the NIEHS, NCI, and Centers for Disease Control (which includes the National Institute for Occupational Safety and Health and the National Center for Environmental Health) are charged with generating scientific information that helps regulatory agencies make sound regulatory decisions.

■ **National Institute of Environmental Health Sciences (NIEHS):** www.niehs.nih.gov NIEHS was established to reduce human illness caused by unhealthy substances in the environment. Today, NIEHS supports extensive biomedical research, prevention, and intervention programs, as well as training, education, and community outreach efforts.

—NIEHS Office of Communications for public inquiries: 1-919-541-3345. National Toxicology Program (NTP): <http://ntp-server.niehs.nih.gov> The NTP is an interagency program that coordinates toxicology research and testing activities within the U.S. Department of Health and Human Services. The NTP evaluates agents of public health concern by developing and applying tools of modern toxicology and molecular biology and publishes the biennial *Report on Carcinogens*. To contact the NTP Office of Liaison and Scientific Review: 919-541-0530 (phone); 919-541-0295 (fax); liaison@starbase.niehs.nih.gov (e-mail).

■ **National Cancer Institute (NCI):** <http://www.cancer.gov> NCI coordinates the National Cancer Program, which conducts and supports cancer research, training, and health information dissemination throughout the country.

—Fact Sheets available on: <http://cis.nci.nih.gov/fact>

—NCI Publications. NCI's on-line ordering service:
<https://cissecure.nci.nih.gov/ncipubs>

—Press Releases are available on NCI's main Web site at
<http://newscenter.cancer.gov> Press Office: 1-301-496-6641.

—NCI's SEER Program is the most authoritative source of information on cancer incidence and survival in the United States.
<http://seer.cancer.gov>

—For geographic patterns of rates of cancer death from 1950–1994 for over 40 cancers: <http://www3.cancer.gov/atlasplus>

—NCI's toll-free Cancer Information Service for information about cancer and to request publications: 1-800-4-CANCER (1-800-422-6237). The toll-free TTY number is 1-800-332-8615.

■ **Centers for Disease Control and Prevention (CDC):** <http://www.cdc.gov> CDC is an agency of DHHS that promotes health and quality of life by preventing and controlling disease, injury, and disability. Components of the CDC include:

—National Institute for Occupational Safety and Health (NIOSH):
<http://www.cdc.gov/niosh> A Federal agency responsible for conducting research and making recommendations for the prevention of work-related disease and injury. 1-800-356-4674

—National Center for Environmental Health (NCEH) Health Line:
<http://www.cdc.gov/nceh> 1-888-232-6789

—National Report on Human Exposure to Environmental Chemicals:
www.cdc.gov/nceh/dls/report 1-866-670-6052

—GIS (geographic information systems) and public health Web site:
<http://www.cdc.gov/nchs/gis.htm>

- National Center for Health Statistics (NCHS): <http://www.cdc.gov/nchs>
NCHS collects data to monitor the nation's health.
- CDC public inquiries: 1-800-311-3435
- National Program of Cancer Registries: www.cdc.gov/cancer/npcr Funds statewide cancer registries in 45 states, the District of Columbia, and several territories, and serves as a valuable resource for citizens concerned about a possible increased occurrence of cancer in their communities.
- The National Breast and Cervical Cancer Early Detection Program: www.cdc.gov/cancer/nbccedp/index.htm Provides free screening exams to poor, uninsured women in all 50 states.
- Office of Smoking and Health: www.cdc.gov/tobacco/mission.htm
- Division of Cancer Prevention and Control: www.cdc.gov/cancer
- State health departments: <http://www.cdc.gov/other.htm#states>
- Public health laboratories:
http://www.aphl.org/Public_Health_Labs/index.cfm

State Government Agencies

State government agencies also play a key role in establishing allowable exposure levels. The organizations dealing with environmental health issues vary widely among different states, but they usually include a Department of Health, a Department of the Environment, and an Occupational Health Department. For example, in North Carolina, there is a Department of Environment and Natural Resources and a Department of Health and Human Services. In addition, most county health offices can direct you to the appropriate state officials for obtaining information about local emissions of chemicals and exposure prevention rules and guidelines. State and local health departments: <http://www.cdc.gov/other.htm#states>

Cancer Statistics

Resources describing the trends over the past several years in new cases of cancer diagnosed or deaths due to cancer are listed below:

- NCI's SEER Program is the most authoritative source of information on cancer incidence and survival in the United States:
<http://seer.cancer.gov>
- National Center for Health Statistics (NCHS): This branch of the CDC collects national statistics to monitor the nation's health:
<http://www.cdc.gov/nchs> 301-458-4800

- National Program of Cancer Registries, which funds statewide cancer registries in 45 states, the District of Columbia, and several territories, serves as a valuable resource for citizens concerned about a possible increased occurrence of cancer in their communities:
www.cdc.gov/cancer/npcr
- For geographic patterns of rates of cancer death from 1950–1994 for over 40 cancers: **<http://www3.cancer.gov/atlasplus>**

General Cancer Information

- NCI's on-line library of cancer information:
http://cancer.gov/cancer_information/cancer_literature
- The National Library of Medicine, the world's largest medical library:
<http://www.nlm.nih.gov>

Other Resources

- The National Library of Medicine has compiled a list of the ingredients in common household products and their health effects:
<http://householdproducts.nlm.nih.gov>
- **International Agency for Research on Cancer (IARC):** **<http://www.iarc.fr>**
IARC is part of the World Health Organization and its mission is to coordinate and conduct research on the causes of human cancer. IARC publishes a series of reports that focuses on the cancer risks associated with particular kinds of agents such as industrial chemicals, viruses, and ionizing radiation.
- **World Health Organization's** document: "Diet, nutrition and the prevention of chronic diseases":
http://www.who.int/hpr/nph/docs/who_fao_expert_report.pdf
- **American Cancer Society's** nutrition and diet guidelines:
http://www.cancer.org/eprise/main/docroot/PED/ped_3_1x_ACS_Guidelines?sitearea=PED
- **Mine Safety and Health Administration (MSHA):** **<http://www.msha.gov>** An agency of the Department of Labor, MSHA's mission is to protect the health and safety of the miner.

General Health Information

- **National Institutes of Health (NIH):** **<http://www.nih.gov/health>** A single access point for consumer health resources at the NIH, the DHHS agency responsible for biomedical research. Public inquiries: 301-496-4000
- **Healthfinder:** **<http://www.healthfinder.gov>** A Web site created by DHHS to help consumers quickly find health and human services information.
- **Medline:** **<http://www.nlm.nih.gov>** The world's most extensive collection of published medical information, coordinated by the National Library of Medicine.

GLOSSARY

Anal cancer: Cancer that begins in the anus, the opening at the end of the large intestine where the waste from the body's digestive system passes out of the body.

Asbestos: Hard, nonflammable fibers used for insulating buildings.

Bacteria: Made of a single cell, bacteria are the simplest organisms found in nature. Bacterial infections can often be treated with antibiotics.

Benign tumor: Not cancerous; tumor does not invade nearby tissue or spread to other parts of the body.

Cancer: Diseases in which abnormal cells divide without control. Cancer cells can invade nearby tissues and can spread through the bloodstream and lymphatic system to other parts of the body.

Carcinogen: A substance that causes cancer.

Carcinoma: A cancerous growth made up of epithelial cells; cells from tissues that form the covering around organs, such as lung, liver, or breast, or the lining of blood vessels.

Cell: The basic unit of all living things. Organs are made up of millions of cells. Each cell contains several smaller components enclosed in a membrane.

Coke: Solid black material similar to charcoal that is left after burning coal. Coke is used as fuel and in making steel.

Colorectal cancer: Cancers that begin in either the colon or the rectum are called colorectal cancer. Together, the colon and rectum make up the large intestine, a long, muscular tube where the waste from the body's digestive system is stored until it passes out of the body through the anus. The colon makes up the first four to five feet of the large intestine and the rectum is the last four to five inches.

DNA: Deoxyribonucleic acid is the molecule inside the cell that carries genetic information and is passed on from one generation to the next.

Endometrium: Tissue lining the wall of a woman's uterus, the organ where a baby grows.

Epidemiology: The study of the patterns of diseases in human populations and the factors that influence the patterns.

Familial cancers: Cancers that occur frequently in certain cancer-prone families in which a mutated gene that is associated with a high risk of developing cancer is passed on from one generation to the next.

Focus group: A qualitative research technique in which an experienced moderator leads about 8–10 participants through a semi-structured discussion on a selected topic, allowing them to talk freely and spontaneously.

Fungicide: An agent that destroys fungi.

Gene: Pieces of DNA, or heredity units found inside cells passed from parent to offspring. Genes contain the information for making proteins.

Herbicide: An agent that destroys weeds.

Incidence: The number of people who develop a disease divided by the number of people at risk of developing the disease in a specific time period.

Insecticide: An agent that destroys insects.

Leukemia: A type of cancer that forms from cells in the blood and bone marrow, including leukocytes or white blood cells that help the body fight infections and other diseases.

Linear dose response: A type of response in which the cancer risk changes at the same rate as the exposure—if the exposure increases, the cancer risk increases at the same rate. A cancer risk is present at all levels of exposure, even very low ones.

Lymphatic system: The tissues and organs that produce, store, and carry white blood cells, which fight infection and other diseases. This system includes the bone marrow, spleen, thymus, and lymph nodes, and a network of thin tubes that carry lymph and white blood cells to all the tissues of the body.

Lymphoma: Cancer that arises in cells of the lymphatic system.

Malignant tumor: A cancerous growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body.

Melanoma: A malignant form of skin cancer that arises in melanocytes, the cells that produce pigment. Melanoma usually begins in a mole.

Mortality: The number of people who die from a disease divided by the number of people at risk of dying from the disease in a specific time period.

Oncogene: An altered gene that normally directs cell growth. An oncogene promotes uncontrolled growth of cancer. Alterations can be inherited, occur randomly, or be caused by an environmental exposure to carcinogens.

Pesticide: An agent used to destroy pests of any sort; the term includes fungicides, herbicides, and insecticides.

Proteins: Molecules in the cell that perform a wide variety of functions, such as protection (skin), support/movement (muscles), transportation (e.g., hemoglobin transports oxygen), and activation of the chemical reactions that sustain life (e.g., enzymes for digesting food).

Sarcoma: A cancer of the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.

Smelters: Plants where valuable metals are extracted from rocks or minerals.

Susceptible: A term used to describe someone who is more likely to develop a disease.

Threshold dose response: A type of response in which, at very low exposures, there appears to be no detectable increased risk of disease; there is a threshold below which no risk is detected.

Tissue: A group or layer of cells, such as the skin, that together performs specific functions.

Tumor: An abnormal mass of tissue that results from too much cell division. Tumors perform no useful body function. They may be either benign (not cancerous) or malignant (cancerous).

Tumor suppressor gene: A gene whose normal function is to prevent abnormal cells from dividing. Certain mutations in tumor suppressor genes lead to cancer.

Virus: Viruses are smaller than a single cell or bacteria and cannot reproduce outside a living organism.

INDEX

- A** aflatoxins 16, 17, 22
- age 4–6, 20, 27
- agricultural worker(s) 16
- AIDS 9
- air pollutants 1, 12, 14, 27
- alcohol, alcoholic drinks 1, 4, 7, 9, 17, 18
- amitrole 11
- antioxidant(s) 18
- arsenic 14, 15, 22
- asbestos 1, 2, 13, 15, 30
- azathioprine 11
- B** bacteria 1, 2, 9, 10, 18
 - Helicobacter pylori* 2, 10, 18
- benzene 12, 13, 22, 27
- benzidine 2, 17, 24
- beryllium compounds 14, 15
- blood clots 12, 28
- blood transfusion 9
- body mass index 8
- bone 6
- C** cadmium compounds 14, 15
- cadmium metal 14, 15
- cancer 2, 3, 6–18, 20, 28–31
 - cases by age 5, 6
 - causes 1–4, 7, 8, 10–12, 16, 17, 19, 21–23, 26–29
 - deaths 1, 7, 10, 14, 17, 30, 31
 - detectable 4, 27
 - early-stage localized 12, 20
 - exposure link 2, 7, 9, 11, 16–18, 23, 26
 - familial, family history of 2, 12, 20
 - nature of 4
 - occupational 1, 9, 13–16, 19, 22, 23, 25, 28
 - screening tests for 20, 29
 - second 11, 28
 - susceptibility to 2, 4, 27
 - symptoms of 11, 21, 23, 30
 - trends for 2, 29, 31
- cancer, types of 4, 15
 - anal 9
 - angiosarcomas 17
 - bladder/urinary tract 2, 7, 14, 15, 17, 31
 - blood cells 6
 - brain 11, 15, 17, 31
 - breast 2, 6, 8–12, 18, 20, 28, 29, 31
 - carcinoma(s) 6
 - cervical 2, 3, 7, 9, 12, 20, 30
 - childhood 9–11, 27, 30
 - colon and rectal (colorectal) 2, 6–8, 11, 18, 20, 31
 - endometrial 8, 11, 12, 18
 - esophageal 2, 7–9, 18, 31
 - eyes 6
 - head and neck 10
 - kidney 2, 7, 8, 14–16, 18, 31
 - laryngeal (voice box) 2, 7, 9, 16, 18, 30, 31
 - leukemia 6, 7, 10–12, 27
 - lip 2, 7, 11, 30
 - liver 2, 6, 7, 9, 12, 14–18, 31
 - lung 2, 3, 6, 7, 10, 11, 13–17, 31
 - lymphoma 6, 9, 11, 31
 - melanoma 6, 9, 11, 31
 - mesothelioma 13
 - mouth 2, 7, 9, 18, 19, 30, 31
 - nasal cavity and sinuses 7, 13, 15, 16
 - non-Hodgkin's lymphoma 31
 - ovarian 2, 12
 - pancreatic 2, 7
 - prostate 2, 11, 31
 - sarcomas 6, 9, 17
 - skin 6, 9, 11, 14, 15, 18, 31
 - stomach 2, 6–8, 10, 11, 30, 31
 - testicular 30
 - throat 2, 7, 9, 18, 30, 31
 - thyroid 10
 - tongue 30
 - uterine 28
 - vaginal 12
 - voice box (see laryngeal)
- carbon tetrachloride 12
- carcinogen(s) 2, 4, 7, 8, 10, 13–17, 21–29
 - environmental 2, 4, 7, 13, 14, 16, 17, 21, 22, 28, 29
 - human 7, 13, 15–17, 24, 27, 29
 - in food 2, 8, 27–29
- cartilage 6
- chemical(s) 1–4, 7, 12, 13, 17, 19, 20, 22–28
- chlorambucil 11
- chlordecone 11
- chlorine 13
- chloroform 12, 27
- chlorophenoxy herbicides 11
- chromium compounds 15, 16, 26
- chromosome(s) 3, 24
- colonoscopy 20
- connective tissue 6
- cyclophosphamide 11
- cyclosporin 11
- D** DDT 11, 27
- dichloromethane (methylene chloride) 12, 23
- diesel exhaust particles 14, 16
- diet, dietary factor(s) 1–4, 8, 17, 18, 23, 27, 28
- diethylstilbestrol (DES) 12
- dimethylhydrazine 11
- dioxin(s) 13, 14, 22, 26
- DNA 2, 3, 5, 9, 10, 26
- dose response 27, 28
- drug(s) 1, 7, 9, 11, 12, 18, 20, 27, 28, 29
- dust(s) 13, 16, 19
- E** early detection 20, 30
- employer requirements 19
- environment 1, 2, 4, 7, 13, 17, 19, 20–22, 27, 29
- environmental
 - causes/factors 1–4, 17, 22
 - contaminant(s) 13, 14
 - exposure 1–4, 7, 13, 14, 17, 22, 28
 - tobacco smoke (ETS) 7
- epidemiology 3, 23
- epithelial tissue 6
- Epstein-Barr virus (EBV) 9
- estrogen(s) 11, 12

- ethylene oxide 11, 24
- exercise 1, 2, 8, 18, 29
- exposure 1–4, 7, 9–30
 - acceptable levels of 7, 28, 29
 - biological mechanisms of 26
 - childhood 9–11, 27
 - occupational 1, 9, 13–16, 19, 23
 - reducing 1, 10, 14, 17, 19–22, 24, 27, 30
- F** fallout 10
- fecal occult blood test 20, 30
- fibers 13–15, 19, 30
- fine particles 13, 19
- food 1, 7, 8, 14–16, 18, 25, 27–29
 - high-calorie, high-fat 18
 - salt-preserved 8, 18
- fruit 3, 8, 18, 29
- fungicide(s) 15
- G** gastritis 10
- gender 4, 27, 28
- gene(s) 2–6, 10
 - abnormal copies of 2
 - alterations 2–5
 - growth-promoting 5
 - oncogenes 5
 - permanent changes in 4
 - protective 3
 - proto-oncogenes 5
 - tumor suppressor 5
- genetic factor(s) 4
- genetic makeup 28
- H** *Helicobacter pylori*: see bacteria 2, 10
- hepatitis B (HBV) and C (HCV) 9, 18
- herbicide(s) 11, 13, 14
- hexachlorobenzene 11
- hexamethylphosphoramide 11
- hormone(s) 1, 2, 11
- human herpesvirus 8, 9
- human immunodeficiency virus (HIV) 9, 18
- human papillomavirus (HPV) 3, 9
- hydrocarbon(s) 13, 14, 26
- I** immune system 2, 9, 27
- immunosuppressant(s) 11
- incidence 9, 11, 14, 22, 29–31
- infection(s) 2, 9, 10, 18
- insecticide(s) 13, 14
- iodine 131 (I-131) 10
- K** Kaposi's sarcoma-associated herpesvirus (KSHV) 9
- L** lead 1, 11, 14–16
- lifestyle 1–4, 17
- lindane 11
- lymphatic system 6, 11
- M** mammogram 20, 30
- melanocyte(s) 6
- melfalan 11
- metal(s) 14–16
- metastasis 6
- mirex 11
- molecular epidemiology 3
- mortality 30, 31
- N** nickel, nickel compounds 15, 16
- nitrofen 11
- O** obesity 1, 8, 17, 18
- occupational groups at risk 13, 15, 16, 19, 22, 25
- oncogene(s): see genes
- oral contraceptives 12
- overweight 2, 8, 17, 18
- P** Pap test 20, 30
- peptic ulcers 10
- pesticide(s) 1, 11, 12, 14, 19, 22, 25, 26, 28–30
- physical inactivity 1, 8, 17, 18
- polycyclic aromatic hydrocarbons (PAHs) 14, 26
- precancerous growths 30
- prevention 1, 12, 17, 18, 23, 24, 28, 31
- progesterone, progestin 11, 12
- proto-oncogene(s): see genes 5
- R** radiation 1, 9–11, 15
 - X-rays 10, 11, 19, 20
- radon 10, 19
- rate(s) 2, 11, 13, 14, 16, 25, 26, 29–31
 - death 14, 30, 31
 - incidence 2, 11, 13, 16, 25, 26, 29–31
- regulatory agencies 27, 28
- repair mechanisms 2, 3, 5
- Report on Carcinogens* 7, 8, 11, 29
- risk 1, 2, 4, 7–14, 16–24, 26–30
 - acceptable level of 27
 - benefit/risk analyses 11, 12, 26–29
 - factors 2, 9, 30
- S** secondhand smoke 7
- sexual behavior 1, 9, 18
- smelters 13, 15
- smoking 1–4, 7, 13, 15, 17, 22, 27, 30, 31
 - cigar 7, 14, 17
 - cigarette 1, 4, 7, 12–14, 17
 - pipe 7, 17
- solvents 12, 19, 22, 24, 27, 30
- stroke 12, 28
- sunlamp(s) 9
- sunlight 1, 3, 9, 18, 22
- sunscreen 18
- susceptibility 2, 27
- T** tamoxifen 12, 28
- tanning bed(s) 9, 18
- TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) 14
- tetrachloroethylene 12
- thyroid disease 10
- tobacco 1, 4, 7, 8, 14, 15, 17
 - chewing; snuff 7, 17
 - products 1, 7, 17
 - carcinogens in 4, 7
 - smokeless 7
- toxaphene 11
- toxicity 19
- toxins from fungi 16
- trichloroethylene 12
- tumor(s) 4–6, 10, 16, 17, 25
- tumor suppressor genes: see genes
- V** vaccination, vaccine 9, 18
- vegetable(s) 3, 8, 18, 29
- vinyl chloride 15, 17, 26
- virus(es) 1, 3, 9
- water, drinking 1, 14, 16, 17, 24, 27
- weight 2, 8, 17, 18, 21
- wood preservative(s) 13–15
- workplace 1, 7, 17, 19, 21–23, 26, 27
- X** X-rays, diagnostic, during pregnancy 10, 11, 19, 20
- Z** zinc 14, 15



**National Institute
of Environmental
Health Sciences**

NIH Publication No. 03-2039
Printed August 2003

