# **CANCER FACTS**

National Cancer Institute • National Institutes of Health Department of Health and Human Services

# **Cancer Clusters**

# **Key Points**

- Cancer clusters may be suspected when people report that several family members, friends, neighbors, or coworkers have been diagnosed with the same or related cancers (see Defining Disease Clusters section).
- Some amount of clustering may occur simply by chance (see Facts About Cancer Clusters section).
- Epidemiologists (scientists who study the frequency, distribution, causes, and control of diseases in populations) investigate suspected cancer clusters (see Facts About Cancer Clusters section).
- Concerned individuals may report a suspected cancer cluster to their local health department or state cancer registry (see Reporting Suspected Cancer Clusters section).
- Other resources may provide additional information about cancer clusters, cancer incidence and mortality, and environmental risk factors for cancer (see Resources section).

# **Defining Disease Clusters**

A disease cluster is the occurrence of a greater than expected number of cases of a particular disease within a group of people, a geographic area, or a period of time. Clusters of various diseases have concerned scientists for centuries. Some recent disease clusters include the initial cases of a rare type of pneumonia among homosexual men in the early 1980s that led to the identification of the human immunodeficiency virus (HIV) and acquired immunodeficiency



3.58 02/26/04 Page 1 syndrome (AIDS); the outbreak in 2003 of a respiratory illness, later identified as severe acute respiratory syndrome (SARS), caused by a previously unrecognized virus; and periodic outbreaks of food poisoning caused by eating food contaminated with bacteria.

Cancer clusters may be suspected when people report that several family members, friends, neighbors, or coworkers have been diagnosed with the same or related cancer(s). In the 1960s, one of the best known cancer clusters emerged, involving many cases of mesothelioma (a rare cancer of the lining of the chest and abdomen). Researchers traced the development of mesothelioma to exposure to asbestos, a fibrous mineral that was used heavily in shipbuilding during World War II and has also been used in manufacturing industrial and consumer products. Working with asbestos is the major risk factor for mesothelioma.

#### **Facts About Cancer**

Some concepts about cancer can be helpful when trying to understand suspected cancer clusters:

- Cancer is the uncontrolled growth and spread of abnormal cells anywhere in the body. However, cancer is not just one disease; it is actually an umbrella term for at least 100 different but related diseases.
- Each type of cancer has certain known and/or suspected risk factors associated with it.
- Cancer is not caused by injuries, nor is it contagious. It cannot be passed from one person to another like a cold or the flu virus.
- Cancer is almost always caused by a combination of factors that interact in ways which are not yet fully understood.
- Carcinogenesis (the process by which normal cells are transformed into cancer cells) involves a series of changes within cells that usually occur over many years. More than 10 years can go by between the exposure to a carcinogen (any substance that causes cancer) and a diagnosis of cancer. The long period of time

between the first cellular abnormality and the clinical recognition that cancer is present often makes it difficult to pinpoint the cause of the cancer.

- Cancer is more likely to occur as people get older; because people are living longer, more cases of cancer can be expected in the future. This increased longevity may create the impression that cancer is becoming much more common, even though an increase in the number of cases of cancer is partly related to the aging of the population.
- Some racial and ethnic groups have higher rates of cancer than other racial and ethnic groups. Such differences may be due to multiple factors, such as late stage of disease at diagnosis, barriers to health care access, history of other diseases, biologic and genetic differences, health behaviors, and other risk factors.
- More than 17 million new cases of cancer have been diagnosed since 1990.

# **Facts About Cancer Clusters**

Reported disease clusters of any kind, including suspected cancer clusters, are investigated by epidemiologists (scientists who study the frequency, distribution, causes, and control of diseases in populations). Epidemiologists use their knowledge of diseases, environmental science, lifestyle factors, and biostatistics to try to determine whether a suspected cluster represents a true excess of cancer cases.

Epidemiologists have identified certain circumstances that may lead them to suspect a potential common source or cause of cancer among people thought to be part of a cancer cluster. A suspected cancer cluster is more likely to be a true cluster, rather than a coincidence, if it involves:

- A large number of cases of a specific type of cancer, rather than several different types;
- A rare type of cancer, rather than common types; or
- An increased number of cases of a certain type of cancer in an age group that is not usually affected by that type of cancer.

Before epidemiologists can accurately assess a suspected cancer cluster, they must determine whether the type of cancer involved is a primary (original) cancer or a cancer that has spread from another organ (metastasis). This is important to know because scientists consider only the primary cancer when they investigate a possible cancer cluster. Epidemiologists also try to establish whether the suspected exposure has the potential to cause the reported cancer, based on what is known about that cancer's likely causes and what is known about the cancer-causing potential of the exposure.

In addition, epidemiologists must show that the number of cancer cases which have occurred is significantly greater than the expected number of cases, given the age, gender, and racial distribution of the group of people at risk of developing the disease. They must also determine if the cancer cases could have occurred by chance. Epidemiologists often test for "statistical significance," which is a measure of the likelihood that the observed association could simply have been due to chance. In common practice, a statistically significant finding means that there is a 5 percent or less chance that the observed number of cases could have happened by chance. For instance, if one examines the number of cancer cases in 100 neighborhoods, and cancer cases are occurring randomly, one should expect to find about five neighborhoods with statistically significant elevations. In other words, some amount of clustering within the same family or neighborhood may occur simply by chance.

Another difficulty epidemiologists face when investigating a possible cancer cluster is accurately defining the group of people who should be considered "at risk." One of the greatest pitfalls of defining clusters is the tendency to extend the geographic borders of the cluster to include additional cases of the suspected disease as they are discovered. The tendency to define the borders of a cluster on the basis of where known cases are located, rather than to first define the population and then determine if the number of cancers is excessive, creates many "clusters" that are not genuine.

Epidemiologists must also consider that a confirmed cancer cluster may not be the result of any single, external cause or hazard. A cancer cluster could be the result of chance, miscalculation of the expected number of cancer cases, or differences in the case definition (the criteria that determine whether or not the cases being investigated are related to the cluster) between observed cases and expected cases. Moreover, because people change residence from time to time, it can be difficult for epidemiologists to identify previous exposures and find the records that are needed to determine the kind of cancer a person had—or if it was cancer at all.

Because a variety of factors often work together to create the appearance of a cluster where nothing abnormal is occurring, most reports of suspected cancer clusters are not shown to be true clusters. Many reported clusters do not include enough cases for epidemiologists to arrive at any conclusions. Sometimes, even when a suspected cluster has enough cases for study, a greater than expected number of cases (a true statistical excess) cannot be demonstrated. Other times, epidemiologists find a true excess of cases, but they cannot find an explanation for it. For example, a suspected carcinogen may cause cancer only under certain circumstances, making its impact difficult to detect.

#### **Genetics and Environment**

Because most cancers are likely to be caused by a combination of factors related to genetics and environment (including behavior and lifestyle), studies of suspected cancer clusters usually focus on these two issues. However, establishing significant and valid evidence that a specific genetic factor leads to an increased chance that a specific environmental exposure will result in cancer (called a gene-environment interaction) requires studies of large populations over

long periods of time. Researchers are just beginning to learn about the roles heredity and

environmental exposures play in carcinogenesis. Some of their discoveries are outlined below:

#### **Genetics**

- All cancers develop because of genetic alterations of one kind or another. An alteration is a change or mutation in the physical structure of a gene that interferes with the gene's normal functions.
- Some alterations that increase the risk of cancer are present at birth in the genes of all cells in the body, including reproductive cells. These alterations, which are called germline alterations, can be passed from parent to child. This type of alteration is known as an inherited susceptibility and is uncommon as a cause of cancer.
- Most cancers are <u>not</u> due to an inherited susceptibility but result from genetic changes that occur during one's lifetime within the cells of a particular organ. These genetic changes are called somatic alterations.
- Familial cancer clusters (multiple cases among relatives) have been reported for many types of cancer. Because cancer is a common disease, it is not unusual for several cases to occur within a family.
- Familial cancer clusters are sometimes linked to inherited susceptibility, but environmental factors and chance may also be involved.
- Having an inherited susceptibility for a type of cancer does not guarantee that the cancer will occur; it means there is an increased chance of developing cancer if other factors that promote the development of cancer are present or later develop.

#### Environment

- The term *environment* includes not only air, water, and soil, but also substances and conditions in the home and workplace. It also includes diet; the use of tobacco, alcohol, or drugs; exposure to chemicals; and exposure to sunlight and other forms of radiation.
- People are exposed to a variety of environmental factors for varying lengths of time, and these factors interact in ways that are still not fully understood. Further, individuals have varying levels of susceptibility to these factors.

• Because some workers may have greater and more prolonged exposures to hazardous chemicals that are found widely at lower levels in the general environment, positive findings from studies in the workplace provide important leads regarding causes of cancer in other settings. In fact, occupational studies have identified many specific chemical carcinogens and have provided direction for prevention activities to reduce or eliminate cancer-causing exposures in the workplace and elsewhere.

#### **Reporting Suspected Cancer Clusters**

Concerned individuals may report a suspected cancer cluster to their state or local health department. State and local health departments use established criteria to investigate reports of cancer clusters. When a suspected cancer cluster is first reported, the health department gathers information about the suspected cluster and gives the inquirer general information about cancer clusters. Although health departments may use different processes, most follow a basic procedure in which increasingly specific information is obtained and analyzed in stages. Health departments are likely to request the following:

- Information about the potential cluster: type(s) of cancer, number of cases, suspected exposure(s), and suspected geographic area/time period.
- Information about each person with cancer in the potential cluster: name, address, telephone number, gender, race, age, occupation(s), and area(s) lived in/length of time.
- Information about each case of cancer: type of cancer, date of diagnosis, age at diagnosis, possible causes, metastatic sites, and physician contact.

Between 75 and 80 percent of reports of suspected cancer clusters are resolved at this initial contact because concerned individuals realize that what seemed like a cancer cluster is not a true cluster. If further evaluation is needed, the health department will take the following steps to investigate a possible cancer cluster:

- Attempt to verify the reported diagnoses by contacting patients and relatives and obtaining medical records.
- Compare the number of cases in the suspected cancer cluster with information in census data and cancer registries.
- Review the scientific literature to establish whether the reported cancer(s) has been linked to the suspected exposure.
- Work with Federal agencies, if necessary, to gather additional information to help decide whether to conduct a comprehensive epidemiological study.

Most state health departments report that fewer than 5 percent of cancer cluster investigations are

determined to require a comprehensive study.

#### Resources

The following resources may provide additional information about cancer clusters, cancer

incidence (the number of new cases) and mortality (the number of deaths), and environmental

risk factors for cancer:

- Local and state health departments are listed under such headings as "health department" and "public health commission" in the Blue Pages of Government Listings in telephone books.
- State cancer registries collect data on cancer incidence and mortality. The data in these registries can be used to compare expected cancer rates in certain categories, such as geographic area, age, or racial group, with rates reported in a suspected cancer cluster to determine whether there is a true excess of cases. State cancer registries are listed under such headings as "health department" and "public health commission" in the Blue Pages of Government Listings in telephone books.
- The **National Institute of Environmental Health Sciences (NIEHS)** studies how environmental exposures, genetic susceptibility, and age interact to affect an individual's health. The NIEHS may be contacted at:

Address:Post Office Box 12233<br/>Research Triangle Park, NC 27709Telephone:919–541–3345Internet Web site:http://www.niehs.nih.gov

• The Centers for Disease Control and Prevention's (CDC) National Center for Environmental Health (NCEH) cancer cluster Web site provides links to cancer cluster resources, answers to frequently asked questions, and an online inquiry form. NCEH's cancer cluster Web site also provides contact information for state and local health departments, and state cancer registries. NCEH also manages the CDC/ Agency for Toxic Substances and Disease Registry (ATSDR) Cancer Cluster Public Inquiry Triage System, which includes triaging, answering, tracking, and reporting on cancer cluster inquiries. The system provides inquirers with accurate, consistent, and timely responses to cancer cluster inquiries. NCEH may be contacted at:

Address:	Division of Environmental Hazards and Health Effects
	National Center for Environmental Health
	Centers for Disease Control and Prevention
	Re: Cancer Clusters
	Mail Stop F–52
	4700 Buford Hwy
	Atlanta, GA 30341
Telephone:	1-888-232-6789 (toll-free) or 770-488-3400
E-mail:	ehheinq@cdc.gov
Internet Web site:	http://www.cdc.gov/nceh/clusters/

• The CDC's National Institute for Occupational Safety and Health (NIOSH) conducts research and makes recommendations for the prevention of work-related disease and injury. Information about possible workplace cancer clusters and how they are evaluated is available on NIOSH's Occupational Cancer Web page at http://www.cdc.gov/niosh/topics/cancer/ on the Internet. NIOSH's Health Hazard Evaluation (HHE) Program investigates potentially hazardous working conditions, including suspected cancer clusters, when employers, authorized employee representatives, or employees request it. The HHE Program may be contacted at:

Address:	Hazard Evaluations and Technical Assistance Branch
	NIOSH
	Mail Stop R–9
	4676 Columbia Parkway
	Cincinnati, OH 45226
Telephone:	1-800-356-4674 (1-800-35-NIOSH) (toll-free)
Internet Web site:	http://www.cdc.gov/niosh/hhe

• The NCI's Cancer Mortality Maps & Graphs Web site provides interactive maps, graphs, text, tables, and figures showing geographic patterns and time trends of cancer death rates for the time period 1950–1994 for more than 40 cancers. It also

provides interactive mortality charts and graphs, customizable mortality maps, and links to related domestic and international Web sites, including a link to the online publication of NCI's *Atlas of Cancer Mortality in the United States: 1950–94*. The NCI's Cancer Mortality Maps & Graphs Web site can be accessed at http://www3.cancer.gov/atlasplus/new.html on the Internet.

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# **Related Resources**

#### Publications (available at http://www.cancer.gov/publications)

- Cancer and the Environment: What You Need To Know, What You Can Do
- Cancer Facts 6.7, Cancer: Questions and Answers
- What You Need To Know About<sup>TM</sup> Cancer

# National Cancer Institute (NCI) Resources

#### **Cancer Information Service (toll-free)**

Telephone: 1–800–4–CANCER (1–800–422–6237) TTY: 1–800–332–8615

#### Online

NCI's Web site: http://www.cancer.gov *LiveHelp*, NCI's live online assistance: https://cissecure.nci.nih.gov/livehelp/welcome.asp

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