

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 cancer(s) (see Defining Disease 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).
- Some amount of clustering may occur simply by chance (see Facts About Cancer Clusters section).
- A suspected cancer cluster may be reported to a state or 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 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 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 (something that may increase the chance of developing a disease) 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 flu virus.
- Cancer is almost always caused by a combination of factors that interact in ways that 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, which makes it difficult to pinpoint the cause of that 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 life expectancy may create the impression that cancer is becoming much more common, even though an increase in the number of cases of cancer is related in large part to the growing number of elderly people in 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.
- Cancer, in general, is common. 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 one or more of the following factors:

- A large number of cases of one type of cancer, rather than several different types.
- A rare type of cancer, rather than common types.
- 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 assess a suspected cancer cluster accurately, they must determine whether the type of cancer involved is a primary (original) cancer or a cancer that has metastasized (spread from another organ). 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 about the cancer-causing potential of the exposure.

After developing a case definition (the guidelines that determine whether the cases being investigated are related to the cluster), epidemiologists must identify the time period of concern and the population at risk. They then calculate the expected number of cases and compare that number with the observed number of cases. Epidemiologists must show that the number of cancer cases that 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.

Epidemiologists must also determine if the cancer cases could have occurred by chance. They often test for "statistical significance," which is a mathematical measure of the difference between groups. The difference is said to be statistically significant if it is greater than what would be expected to happen by chance alone. In common practice, a statistically significant finding means that the probability that the observed number of cases could have happened by chance alone is 5 percent or less. For instance, if one examines the number of cancer cases in 100 neighborhoods, and cancer cases are occurring by chance alone, one should expect to find about five neighborhoods with a statistically significant elevation in the number of cancer cases. In other words, some amount of clustering within the same family or neighborhood may occur simply by chance.

Accurately defining the group of people who should be considered "at risk" is important when investigating a possible cancer cluster. One of the greatest problems in defining clusters is the tendency to expand 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 geographic area and then determine if the number of cancers is excessive, creates many "clusters" that are not real.

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, an error in the calculation of the expected number of cancer cases, or differences in the case definition between observed and expected cases. Moreover, because people change where they live from time to time, it can be difficult for epidemiologists to identify previous exposures and find the medical 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 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 thought 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. Genetic factors are inherited, that is, passed from parents to children. However, establishing a genetic-environmental interaction (significant and valid evidence that a specific genetic factor leads to an increased chance that a particular environmental exposure will result in cancer) requires studies of large populations over long periods of time. Researchers are just beginning to learn about the roles genetics 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 genetic alterations that increase the risk of cancer are present at birth in the genes of all cells in the body, including reproductive cells. These changes, which are called germline mutations, can be passed from parent to child. This type of alteration is known as an inherited susceptibility; most cancers are not due to an inherited susceptibility.
- Most cancers result from genetic changes that occur after birth during one's lifetime. Genetic changes can occur in any cell that divides. These genetic changes are called somatic alterations.
- Familial cancer clusters (cancer that occurs in families more often than would be expected by chance) 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 necessarily mean that the individual will be diagnosed with the cancer; it means the chance of developing cancer increases if other factors that promote the development of cancer are present or are encountered later.

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.
- Hazardous substances are often found in higher levels in the workplace than in the general environment. For this reason, some workers may have greater and longer exposures to such substances than the general population. Findings of higher than expected numbers of cancer cases among workers in particular occupations or industries provide important leads regarding causes of cancer among the general public. In fact, occupational studies (studies of specific groups of workers) have identified many specific cancer-causing substances and have provided the motivation to find ways to reduce or eliminate exposures in the workplace and elsewhere.

Reporting Suspected Cancer Clusters

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

- Information about the potential cluster: type(s) of cancer, number of cases, suspected exposure(s), and geographic area/time period of concern.
- Information about each person with cancer in the potential cluster: name, address, telephone number, gender, race, age, occupation(s), as well as 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.

Most 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, epidemiologists will take the following steps to investigate a possible cancer cluster:

- Attempt to verify the reported cases 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 to determine if there is a higher than expected number of cases.
- 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.

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. In addition, links to state and selected local health department Web sites can be found at <http://www.cdc.gov/nceh/clusters/statelocal.htm> on the Internet.
- 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, gender, 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. Contact information for state cancer registries can also be found at <http://apps.nccd.cdc.gov/cancercontacts/npcr/contacts.asp> on the Internet.

- The **Centers for Disease Control and Prevention's (CDC) National Center for Environmental Health (NCEH)** cancer clusters Web site provides links to cancer cluster resources, answers to frequently asked questions, and an online inquiry form. NCEH can 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
4770 Buford Highway
Atlanta, GA 30341
Telephone: 1-800-232-4636 (1-888-CDC-INFO) (toll-free)
E-mail : cdcinfo@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 can be contacted at:

Address: Hazard Evaluation 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 **Agency for Toxic Substances and Disease Registry (ATSDR)**, an agency of the U.S. Department of Health and Human Services (DHHS), conducts public health assessments of waste sites, performs health consultations concerning specific hazardous substances, maintains health surveillance and registries, responds to emergency releases of hazardous substances, and provides education and training concerning hazardous substances. Contact information for ATSDR regional offices can be found at http://www.atsdr.cdc.gov/DRO/dro_contact.html on the Internet. The ATSDR can be contacted at:

Telephone: 1-800-232-4636 (1-800-CDC-INFO)
TTY: 1-888-232-6348
Internet Web site: <http://www.atsdr.cdc.gov>

- The **National Institute of Environmental Health Sciences (NIEHS)**, a part of the National Institutes of Health (NIH), studies how environmental exposures, genetic susceptibility, and age interact to affect an individual's health. The NIEHS can be contacted at:

Address: The National Institute of Environmental Health Sciences
Post Office Box 12233
Research Triangle Park, NC 27709
Telephone: 919-541-3345
Internet Web site: <http://www.niehs.nih.gov>

- The **Occupational Safety and Health Administration's (OSHA) Office of Occupational Medicine** performs workplace-related case evaluations and cluster investigations, including medical record review, employee interviews, and medical screening activities. OSHA can be contacted at:

Address: Office of Occupational Medicine
Occupational Safety and Health Administration
U.S. Department of Labor
Room N3457
200 Constitution Avenue, NW.
Washington, DC 20210
Telephone: 202-693-2323
Internet Web site: <http://www.osha.gov/dts/oom/index.html>

- The **Where You Live** Web page, which is managed by the U.S. Environmental Protection Agency (EPA), allows users to enter a ZIP Code and choose from four databases to retrieve environmental information about a community or to locate a regional office. This resource is available at <http://www.epa.gov/epahome/whereyoulive.htm> on the Internet.
- The **National Cancer Institute (NCI)**, another component of the NIH, has the **Cancer Mortality Maps and Graphs** Web site, which provides interactive maps, graphs, text, tables, and figures showing geographic patterns and time trends of cancer death rates for the time period 1950-94 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 and Graphs Web site can be accessed at <http://www3.cancer.gov/atlasplus/> on the Internet.

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Related NCI materials and Web pages:

- National Cancer Institute Fact Sheet 6.7, *Cancer: Questions and Answers* (<http://www.cancer.gov/cancertopics/factsheet/Sites-Types/general>)
- *Cancer and the Environment: What You Need To Know, What You Can Do* (<http://www.cancer.gov/newscenter/Cancer-and-the-Environment>)
- *What You Need To Know About™ Cancer* (<http://www.cancer.gov/cancertopics/wyntk/cancer>)

How can we help?

We offer comprehensive research-based information for patients and their families, health professionals, cancer researchers, advocates, and the public.

- **Call** NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237)
- **Visit** us at <http://www.cancer.gov> or <http://www.cancer.gov/espanol>
- **Chat** using LiveHelp, NCI's instant messaging service, at <http://www.cancer.gov/livehelp>
- **E-mail** us at cancergovstaff@mail.nih.gov
- **Order** publications at <http://www.cancer.gov/publications> or by calling 1-800-4-CANCER
- **Get help** with quitting smoking at 1-877-44U-QUIT (1-877-448-7848)

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