ATSDR
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY

Case Studies in Environmental Medicine

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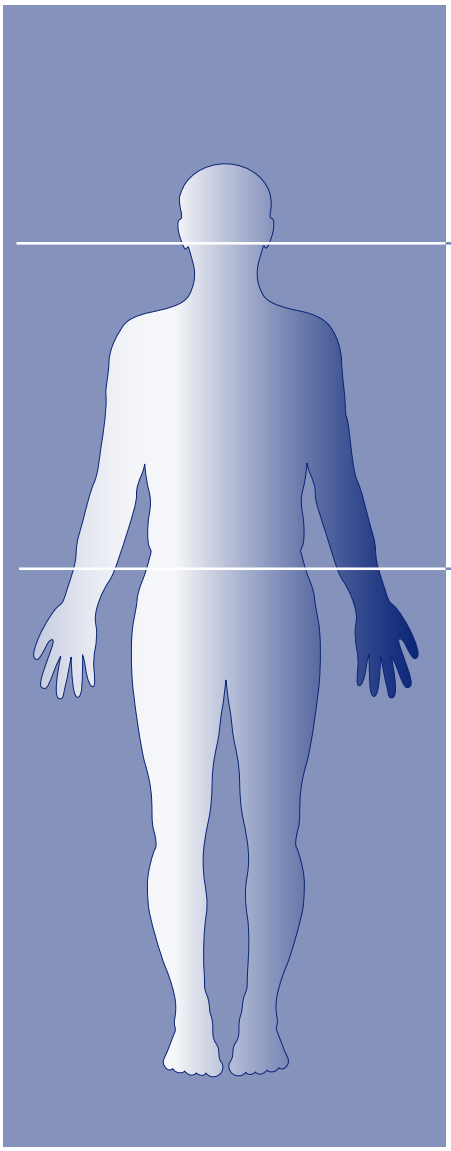

DISEASE CLUSTERS: AN OVERVIEW

Environmental Alert

- Busy clinicians are often expected to respond to patient inquiries about disease "cluster" events in their practices.
- Cluster events are groupings of a particular disorder or a class of disorders that appear unusually frequent in a place.

This monograph is one in a series of self-instructional publications designed to increase the primary care provider's knowledge of hazardous substances in the environment and to aid in the evaluation of potentially exposed patients. This course is also available on the ATSDR Web site, www.atsdr.cdc.gov/HEC/CSEM/. See page 3 for more information about continuing medical education credits, continuing nursing education units, continuing health education specialist credits, and continuing education units.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Agency for Toxic Substances and Disease Registry
Division of Health Education and Promotion

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Disclaimer

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Figures and Tables

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Final responsibility for the contents and views expressed in this monograph reside with ATSDR.

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Case Studies in Environmental Medicine (CSEM): Disease Clusters: An Overview

Goals and Objectives

The goals of this CSEM are to increase the knowledge of health care providers, especially pediatricians, of the special susceptibilities of children to hazardous substances in the environment and to aid in their evaluation of potentially exposed patients.

After completion of this educational activity, the reader should be able to define a disease cluster, describe the components of the public health department disease cluster investigation, and describe the physician's responsibility regarding disease clusters.

Accreditation

Continuing Medical Education (CME)

The Centers for Disease Control and Prevention (CDC) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. CDC designates this educational activity for a maximum of 1.5 hours in category 1 credit toward the American Medical Association (AMA) Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Continuing Nursing Education (CNE)

This activity for 1.6 contact hours is provided by CDC, which is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation.

Continuing Education Units (CEU)

CDC has been approved as an Authorized Provider of continuing education and training programs by the International Association for Continuing Education and Training and awards 0.1 continuing education units (CEUs).

Continuing Health Education Specialist (CHES)

CDC is a designated provider of continuing education contact hours (CECH) in health education by the National Commission for Health Education Credentialing, Inc. This program is a designated event for the CHES to receive 1.5 category 1 contact hours in health education.

Instructions

See page 4

The questionnaire and posttest must be completed and returned electronically, by fax, or by mail for eligibility to receive continuing education credit.

Instructions for Completing CSEM Online

1. Read this CSEM, *Disease Clusters: An Overview*; all answers are in the text.
2. Link to the MMWR/ATSDR Continuing Education General Information page (www.cdc.gov/atsdr/index.html).
3. Once you access this page, select the Continuing Education Opportunities link.
4. Once you access the MMWR/ATSDR site online system, select the electronic file and/or register and test for a particular ATSDR course.
   a. Under the heading "Register and Take Exam," click on the test type desired.
   b. If you have registered in this system before, please use the same login and password. This will ensure an accurate transcript.
   c. If you have not previously registered in this system, please provide the registration information requested. This allows accurate tracking for credit purposes. Please review the CDC Privacy Notice (www.cdc.gov/privacy.htm).
   d. Once you have logged in/registered, select the test and take the posttest.
5. Answer the questions presented. To receive continuing education credit, you must answer all of the questions. Some questions have more than one answer. Questions with more than one answer will instruct you to "indicate all that are true."
6. Complete the course evaluation and posttest no later than **September 29, 2005**.
7. You will be able to immediately print your continuing education certificate from your personal transcript.

Instructions for Completing CSEM On Paper

1. Read this CSEM, *Disease Clusters: An Overview*; all answers are in the text.
2. Complete the evaluation questionnaire and posttest, including your name, mailing address, phone number, and e-mail address, if available.
3. Circle your answers to the questions. To receive your continuing education credit, you must answer all of the questions.
4. Sign and date the posttest.
5. Return the evaluation questionnaire and posttest, no later than **September 1, 2005,** to CDC by mail or fax:

Mail
Continuing Education Coordinator
Division of Health Education and Promotion, ATSDR
1600 Clifton Road, NE (MS E-33)
Atlanta, GA 30333

or

Fax
404-498-0061
ATTN: Continuing Education Coordinator

6. You will receive an award certificate within 90 days of submitting your credit forms. No fees are charged for participating in this continuing education activity.

Case Study

You are the senior partner in a busy suburban primary care practice. In the past 30 days, three of the physicians in your practice have come to you individually to discuss a case of concern. The cases are outlined below:

Case 1

The patient is a 40-year-old second-grade schoolteacher who came in for an annual checkup and breast exam. A mass was noted on her mammogram. The patient is scheduled for stereotactic biopsy. She expressed concerns that three other female teachers in her elementary school have been diagnosed with breast cancer in the 4 years that the school has been open. She is worried that working at the school might have caused all or some of these cases. The elementary school was built in an area that once housed several industrial facilities.

Case 2

The family practitioner in the group has a 35-year-old female primigravida in her 10th week of pregnancy with vaginal bleeding. The patient is concerned about the neighborhood where she has lived for 3 years. She recently learned in the past 4 years, six miscarriages in the first trimester have occurred in her neighborhood of 100 women.

Case 3

An 87-year-old grandmother of three who came in for her annual checkup had occult blood in her stool and is scheduled for a colonoscopy with biopsy. She mentioned that three of her neighbors from the active seniors club have been diagnosed with cancer in the past 2 years. She is concerned that living in her neighborhood is causing the cancer.

These patients' concerns and questions seem to have a common theme. You are planning the next physician education conference for the physicians in your practice and would like to discuss disease clusters and pertinent patient education points.

Busy clinicians are often expected to respond to patient inquiries about disease "cluster" events. Cluster events are groupings of a particular disorder or a class of disorders, such as potentially related cancers, that appear unusually frequent in a place. Such events pose challenges of interpretation that differ from clinical evaluation of individual patients. Accordingly, the goals of this monograph are to provide clinicians with a framework for discussion of disease clusters.

Pretest

1. *What is the definition of a disease cluster?*
2. *Who investigates disease clusters?*
3. *What happens in a disease cluster investigation?*
4. *What is the physician's overall responsibility?*
5. *Who is the first-line reporting contact?*
6. *What are the most important points to discuss with your patient regarding disease clusters and occurrence of disease?*

Definition of Disease Clusters

Unusual events such as clusters occur all the time, especially in large populations. From a statistical perspective, it is almost inevitable that some schools, church groups, friendship circles, and neighborhoods will be associated with clusters of chronic diseases. When first noticed, such clusters are often regarded as resulting from some specific, predictable process, rather than as events with independent causes that happened to have occurred by chance in one particular place (such as a coin toss).

A "cluster" is an unusual aggregation, real or perceived, of health events that are grouped together in time and space and that is reported to a public health department (CDC 1990). Several breakthroughs and triumphs in infectious disease control have resulted from the epidemiologic evaluation of clusters of cases.

Well-known examples of clusters include the epidemic of cholera in London in the 1850s (Snow 1965), the investigation of cases of pneumonia at the Bellevue-Stratford Hotel in Philadelphia in 1976 (Fraser et al. 1977), and the 1981 report that seven cases of *Pneumocystis carinii* pneumonia had occurred among young homosexual men in Los Angeles (CDC 1981).

Investigations of noninfectious disease clusters have also resulted in notable examples of breakthroughs linking a particular health effect to an exposure, such as angiosarcoma among vinyl chloride workers (Waxweiler et al. 1976), neurotoxicity and infertility in kepone workers (Cannon et al. 1978), dermatitis and skin cancer in persons wearing radioactively contaminated gold rings (Baptiste et al. 1984), adenocarcinoma of the vagina and maternal consumption of diethylstilbestrol (Herbst et al. 1971), and phocomelia and consumption of thalidomide (McBride 1961).

Disease clusters differ from sentinel events. Sentinel events are occurrences of unexpected diseases or disorders that are known to result from specific, recognized causes of likely relevance to the situation or setting (Joint Commission on Accreditation of Healthcare Organizations 2002). For example, the diagnosis of lead poisoning in a child (a sentinel event) should suggest the likelihood of environmental lead contamination that might affect other children. By contrast, disease clusters are occurrences of seemingly unexpected diseases for which no immediately apparent recognized cause exists.

Evaluating a Disease Cluster

The interface between the physician and the public health department is essential in recognizing and responding to disease cluster concerns. It is impractical for the busy clinician to perform epidemiologic and detailed fact-finding. The public health department has expertise in evaluating disease clusters.

It is essential to understand the components involved the public health department investigation of a disease cluster and the physician's role in the process. The primary role of the physician is confirming diagnosis, completing the exposure history when applicable, recognizing abnormal patterns of events, and reporting information to the appropriate public health department for investigation. Thus, the effective management of disease clusters is initiated after case reporting by an astute clinician who has completed the appropriate diagnostic tests and taken an exposure history (Schuman 1997) (Figure 1).

An exposure history is of particular importance if the patient's illness (a) occurs at an atypical age, (b) is unresponsive to treatment, or (c) is an acute condition where a direct link might exist between current exposure and disease (e.g., asthma, first-trimester miscarriages, or dermatologic conditions).

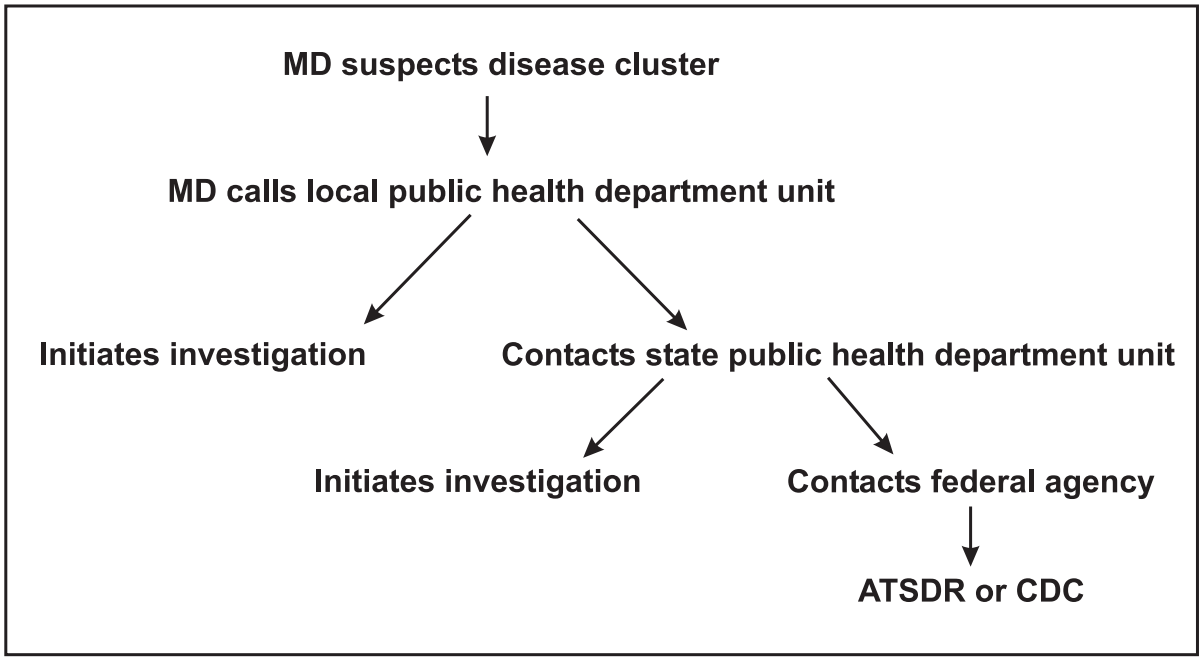

Figure 1. Effective Management of Disease Clusters
ATSDR, Agency for Toxic Substances and Disease Registry; CDC, Centers for Disease Control and Prevention; MD, medical doctor.

The clinician must also keep in mind that many organ systems are affected by toxic exposure (Table 1). Exposure and effects can be acute or chronic. The latency period from exposure to manifestation of disease can vary, ranging from immediate to delayed (hours or days) to prolonged (decades). The exposure history is covered in detail in *Case Studies in Environmental Medicine: Taking an Exposure History* (ATSDR 2001). The exposure history form is included in Appendix A of this case study.

The public health department's role in the disease cluster investigation involves

- collecting accurate case information,
- conducting active surveillance through local surveys or use of health data registries,
- conducting environmental or occupational exposure assessments when warranted,
- ensuring that appropriate public and health professional communication and education occurs (specifically related to the existence of a disease cluster and any associated factors), and

Table 1. Organs/Systems Often Affected by Toxic Exposure

Organ/System	Exposure Risks
Respiratory	**Asbestos**, **radon**, cigarette smoke, glues
Dermatologic	**Dioxin**, nickel, **arsenic**, **mercury**, cement (**chromium**), **polychlorinated biphenyls (PCBs)**, glues, rubber cement
Liver	**Carbon tetrachloride**, **methylene chloride**, **vinyl chloride**
Kidney	**Cadmium, lead, mercury, chlorinated hydrocarbon solvents**
Cardiovascular	Carbon monoxide, noise, tobacco smoke, physical stress, carbon disulfide, **nitrates, methylene chloride**
Reproductive	**Methylmercury**, carbon monoxide, **lead**, ethylene oxide
Hematologic	**Arsenic**, **benzene**, **nitrates**, **radiation**
Neuropsychologic	**Tetrachloroethylene**, **mercury**, **arsenic**, **toluene**, **lead**, **methanol**, noise, **vinyl chloride**

These substances are examples of toxicants that might affect organ systems; this is not an all-inclusive list. **Bold type** indicates that the substance is covered in one of the *Case Studies in Environmental Medicine*.

- initiating timely and effective actions to mitigate factors associated with the disease cluster.

An initial goal of the public health unit's evaluation should be to decide whether the cluster is "unusual" (i.e., whether an unexpectedly increased incidence of disease really exists) and, if so, whether some plausible biologic hypothesis can explain that unexpected disease rate. The public health department can perform the following cluster evaluation components (Figure 2):

- Establish a case definition.
- Confirm the suspected cases.
- Define a "population denominator" measured in person-years and search for additional numerator cases within that population. Draw conclusions about the "unusualness" of the cases.
- Review the literature for risk factors and exposure hypotheses.
- Perform an exposure assessment.
- Generate biologically plausible hypotheses.

Case definition and **person-years** are defined on pages 10 and 11, respectively.

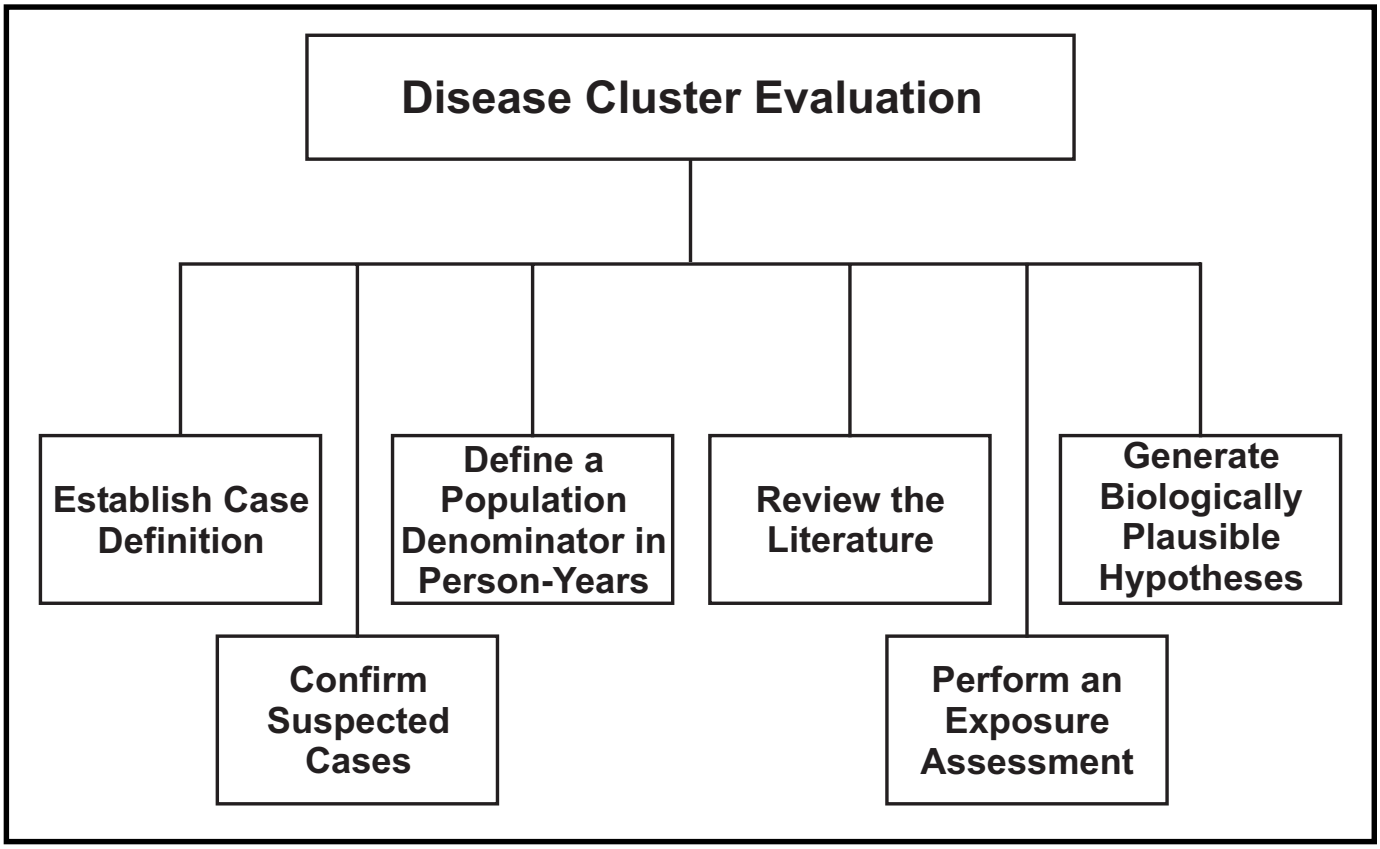

Figure 2. Components of a Disease Cluster Evaluation

Case Definition

Case definition has two applications:

- for epidemiologic surveillance studies relating to the prevalence of the disease.
- for diagnostic purposes using applicable diagnostic features, causes, and pathophysiology.

The **case definition** is based on that which is most unusual about the disease cluster under investigation. The choice of a case definition depends on the information at hand. Often, several differing case definitions exist that might be selected in light of what is initially known about a presumed cluster.

Case definitions can be narrow or expanded. A narrow case definition focuses on the most unusual or most coherent group of diseases reported to affect the population of concern. An expanded case definition would likely include a larger number of diseases that were each likely to be related to one another by a common cause. For example, if the public health department were evaluating a possible cluster of an apparently infectious disease that resembled measles, they might choose either a narrow case definition (such as children with fever, cough, and morbilliform rash) or an expanded case definition (such as all people with fever). In the case of the teacher with breast cancer, evaluation of what seems unusual (the breast cancer cases) is most appropriate.

Narrow definitions tend to exclude some cases that might be related to the cluster. By contrast, **expanded** definitions often decrease the possibility of finding an explanation for the cluster. It is more difficult to hypothesize a unique cause for a variety of less-related diseases than for a single disease or a homogeneous group of diseases.

Case definitions can group together diseases that might share common causes: for example, the childhood cancer cases in Toms River Township, New Jersey, with drinking water exposure, exposure to ionizing radiation, or exposure to cigarette smoke. A case definition that encompassed all of the outcomes known to be highly associated with those exposures could be a rational choice in some cluster settings (when the cause of a disease outbreak is known in advance, the disease outbreak is more properly called a **sentinel event**, not a cluster). As a general rule, expanded case definitions generally work best when consistent scientific information exists about the presumed causal exposure (as for cigarettes or radiation).

Case Confirmation

Once a case definition has been selected, it is then necessary to confirm that those "cases" that defined the "cluster" really exist. It is essential to confirm that all cases share some clearly defined set of symptoms, physical findings, radiographic findings, and/or laboratory findings. The

relevant importance of each type of information might vary depending on the specific disease of concern, but the need for case confirmation remains constant. The public health department's role is to determine and validate that the reported cases actually meet the case definition.

Many apparent clusters disappear at this stage of the cluster evaluation. In some cases, it might be discovered that an apparent cluster is actually an assortment of unrelated diseases and disease processes. For example, a "brain cancer cluster" might actually be found to include patients with metastases from distant sites, patients with nonneoplastic infiltrative diseases, and even patients who have suffered strokes. Other clusters might eventually be found to represent nothing but a random pattern of incorrectly reported laboratory results or clinical findings, or might reflect coding problems in hospital discharge summaries.

Define the Population Denominator

Once an acceptable case definition exists and the reported cases have been confirmed, the public health department will determine whether the suspected cluster is actually "unusual." This determination calls for an explicit comparison between the number of cases actually observed and the number that would have been expected under normal conditions. The numerator cases (e.g., four teachers with breast cancers) must ultimately be compared to some denominator population (e.g., expected number of teachers diagnosed with breast cancer in such an elementary school population). To make such comparisons, it is necessary to first define the population at risk and then determine the number of cases normally expected in that population. The public health epidemiologist undertakes the task of defining the population at risk.

All clusters appear unusual when first discerned; yet most are due to chance. Accordingly, it is necessary to restrain the natural tendency to jump to causal conclusions. Among the most important initial concerns are considerations of biologic plausibility. One aspect of such considerations is to thoughtfully define the nature of the cluster; another is to determine the scientific support for the obvious hypotheses.

Review the Literature

If the cluster is "unusual," then it is appropriate to consider possible causes for that cluster. The public health department would conduct a thorough search of the relevant literature. The objective of this literature

Person-years are the most frequently used measure of person-time. Person-time is the sum of individual units of time that persons in the study population have been exposed to the condition of interest. This measurement is used as a denominator in person-time incidence and mortality rates.

With this approach, each subject contributes only as many years of observation to the population at risk as he or she is actually observed; if the subject leaves after 2 years, he or she contributes 2 person-years. This method can be used to measure incidence over extended and variable time periods.

review is to determine what is already known or hypothesized about the cluster. Have similar clusters been observed and, if so, how common are they? Have other individuals expressed concerns or documented associations with any environmental exposures? Have previously investigated clusters of the same or similar diseases yielded insights that might be useful for understanding the cluster concerns you? What is already well accepted about the causes of first-trimester miscarriages?

Exposure Assessment

After determining that the number of confirmed disease cases is in excess of what is expected and reviewing the literature to identify potential causes, the public health department will evaluate how exposures might have occurred. The public health department conducts an exposure assessment, which obtains basic information about the proposed exposure sources. For example, the public health department might investigate the following questions:

- What chemicals, physical hazards, or biologic hazards are present?
- What are the biologic effects of these chemicals or hazards? Have any been associated in reputable scientific literature with the disease(s) of concern?
- Are there known or potential pathways by which these chemicals or hazards might have impacted the population at risk? What were the likely doses that resulted from such exposures?

In many cases, patient concerns focus on an exposure "source"—such as a landfill, dump, or manufacturing facility—rather than on one or more specific exposures that might have occurred.

Develop Biologically Plausible Hypotheses

On completion of the exposure assessment, the public health department will decide whether the available information is sufficient to generate a biologically plausible hypothesis to explain the cluster.

To generate a biologically plausible hypothesis, the public health department conducts structured interviews with each affected individual. By means of standardized, structured questionnaires, each patient is asked about medical history, family history, work history, hobbies and

other activities, lifestyle, historical exposures, and risks of exposures. Some cluster investigations also delve into acquaintanceship patterns. The interview results are carefully reviewed in an effort to find patterns suggesting possible similarities linking the affected cases that can form the basis of exposure hypotheses. Once common factors are identified among the cases, a comparison of the affected individuals to randomly selected groups of others from the denominator population can then test the significance of such patterns.

Biologic plausibility might also depend on whether there is evidence of shared exposure to a chemical capable of causing the disease of concern, whether the exposures had been of sufficient magnitude to cause adverse effects, and whether all affected individuals had been exposed. Additionally, the temporal relationship between exposure and effect should be evaluated in terms of what information is known. Many diseases such as cancers develop only after a delay (or latency period) lasting years or, more often, decades. (Latency period is the duration of time from first exposure to first symptoms or signs of a disease.) For that reason, it would not be biologically plausible to link very recent exposure to the onset of cancer.

Clinicians in communities affected by disease clusters have an important role in understanding and translating the science of cluster investigations and an equally important role in reporting possible disease clusters to the local public health units in their practice communities.

The physician's responsibility is to

- Suspect a cluster of disease based on clinical observation.
- Complete an exposure history.
- Confirm case(s) through accurate clinical and laboratory diagnosis.
- Act as a sentinel in reporting cases to the local public health department.
- Educate patients about occurrence of disease.

The first line for contact is the public health department. The public health department can initiate

- active surveillance,
- exposure assessments, and
- development of local registries.

Risk Communication: Sample Patient Education Scenario

Doctor: Your mammogram illustrates two abnormal areas that I would like to explore further by performing a biopsy. The biopsy will show whether the tissue is malignant or benign.

Patient: Four teachers at my school have been diagnosed with breast cancer in the past 4 years that the school has been open.

Doctor: Ms. Jones, cancer develops over a long period of time—decades—and it is important to know the family history. A percentage of cancer cases are inherited and recent research has identified changes (mutations) in two genes that greatly increase the risk for breast cancer.

Patient: So are you saying it is unlikely that the school is the cause of my cancer?

Doctor: First, I am not diagnosing you with cancer at this time. You have two abnormal areas that need to be biopsied so that we can determine whether the tissue is cancerous or not.

Patient: What about the school?

Doctor: It is highly unlikely that the school would be the cause because the school has only been open for 4 years. The latency period for cancer can be decades.

Patient: I understand. When do you want to schedule the biopsy?

The most important points to discuss during patient education are

- The current problem and the next appropriate diagnostic step.
- Specific factors related to the occurrence of the particular disease (e.g., latency period for cancer, significance of family history, and other confounding factors).
- Whether it is likely or unlikely that the patient's perceived exposure might be responsible for the problem: If it is likely, discuss your role and responsibility.

Following are specific clinical points based on the case study scenarios.

In **case scenario 1**, the possibility would be unlikely that the breast cancer was caused by exposures in the school, which has only been open for 4 years. Successful cluster investigations most often involve a high occurrence of uncommon diseases.

In **case scenario 2**, the possibility would be unlikely that the miscarriages are caused by the neighborhood. Spontaneous abortion occurs in 10%–14% of pregnancies in women. Statistically, it would be expected that spontaneous abortion would occur in 10–14 of 100 women. Recurrent spontaneous abortions (defined as the

loss of three or more consecutive pregnancies) occur in about 3%–4% of these women. Most spontaneous abortions occur because of abnormalities in the fetus (Matorras et al. 1998).

In **case scenario 3,** the possibility would be unlikely that the cancers are directly related to living in the neighborhood. The latency period for cancer can be decades. Additionally, several confounding factors including smoking, family history of cancer (particularly breast cancer), and potential workplace exposures must be explored in the medical history, family history, and exposure history before attempting to consider that the cancer rates in this neighborhood are related to a neighborhood exposure.

Most cluster associations result from coincidence and chance, but that does not mean that clusters are not useful sources of information. Numerous instances exist where reports of a disease cluster led to recognition of a new disease-causing agent or environment. Some examples from the occupational medicine literature include the associations of vinyl chloride monomer with angiosarcoma of the liver, dibromochloropropane with male infertility, and bis-chloromethyl ether with small-cell lung cancer in young men. Table 2 shows a list of other examples, such as human disease caused by toxicants, organisms, and dusts.

Clusters provide opportunities and impetus for developing new hypotheses about previously unsuspected exposure-outcome relationships. Some of these new hypotheses lead to better understanding of disease causation. Disease clusters help us to identify previously unrecognized hazards.

Table 2. Examples* of Community Clusters Leading to the Identification of New Exposure-Disease Relationships

Population	Year	Exposure	Outcomes
Rural dwellers	1928	Castor bean dust	Asthma
Harbor dwellers	1989	Soybean dust	Asthma
Children and adults	1979, 1989	Polychlorinated biphenyls	Developmental, central nervous system, lipid disorders
Homosexual males	1981	Human immunodeficiency virus (HIV)	*Pneumocystis carinii* opportunistic infection
Drug users symptoms	1983	N-methyl-4-phenyl-1,2,5,6-tetrahydropyridine	Parkinson-like
Health food consumers	1989	L-tryptophan (contaminated)	Eosinophilia-myalgia
Fish handlers and estuarine visitors	1995	*Pfiesteria piscicida*	Memory disturbance
Dieters	1997	Fenfluramine-Phentermine	Valvular heart disease

*More examples of clusters, and many more of sentinel events, are available.

Web Resources

Association of Occupational and Environmental Clinics (AOEC) at www.aoec.org or 202-347-4976.

Agency for Toxic Substances and Disease Registry (ATSDR). For general information, contact www.atsdr.cdc.gov or toll-free (1-888-42-ATSDR or 1-888-422-8737). The ATSDR Emergency Response 24-hour hotline number is 404-498-0120.

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National Institute for Occupational Safety and Health (NIOSH) at www.cdc.gov/niosh or toll-free (1-800-35-NIOSH or 1-800-356-4674).

National Research Council (NRC) at www.nationalacademies.org/nrc/.

Occupational Safety and Health Administration (OSHA) at www.osha.gov or emergency toll-free 1-800-321-OSHA (1-800-321-6742).

Pediatric Environmental Health Specialty Units (PEHSUs) at www.aoec.org/pesu.htm or 202-347-4976 (AOEC office).

State and local health departments, toxicologists, and industrial hygienists.

U.S. Environmental Protection Agency (EPA) at www.epa.gov.

Suggested Reading List

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*Waxweiler RJ, Stringer W, Wagoner JK, Jones J, Falk H, Carter C. 1976. Neoplastic risk among workers exposed to vinyl chloride. Ann N Y Acad Sci 271:40–8.

Answers to Pretest Questions

1. The term "cluster" is an unusual aggregation, real or perceived, of health events that are grouped together in time and space and that are reported to a public health unit.

2. The public health department investigates disease clusters. The public health department's role in the disease cluster investigation involves the following:

- collecting accurate case information,
- conducting active surveillance through local surveys or by using health data registries,
- conducting environmental or occupational exposure assessments when warranted,
- ensuring that appropriate public and health professional communication and education is occurring specifically related to the existence of a disease cluster and any associated factors, and
- initiating timely and effective actions to mitigate factors associated with the disease cluster.

3. The steps involved in a disease cluster investigation are (1) establish a case definition; (2) confirm the suspected cases; (3) define a "population denominator" measured in person-years, search for additional numerator cases within that population, and draw conclusions about the "unusualness" of the cases; (4) review the literature for risk factors and exposure hypotheses; (5) perform an exposure assessment; and (6) generate biologically plausible hypotheses.

4. The physician's overall responsibility is to suspect a cluster of disease on the basis of clinical observation, complete an exposure history, confirm cases through accurate clinical and laboratory diagnosis, act as a sentinel in reporting cases to the local public health unit, and educate patients about occurrence of disease.

5. The first line for contact is usually the public health department.

6. Following are the most important education points:

- The current problem and the next appropriate diagnostic step.
- Specific factors related to the occurrence of the particular disease (e.g., latency period for cancer, significance of family history, and other confounding factors).
- Whether it is likely or unlikely that the patient's perceived exposure might be responsible for the problem; if it is likely, discuss your role and responsibility.

Case Studies in Environmental Medicine:

Disease Clusters: An Overview

Evaluation Questionnaire and Posttest, Course Number SS3096

Course Goal: To increase the primary care provider's knowledge of hazardous substances in the environment and to aid in the evaluation of potentially exposed patients.

Objectives

- Define a disease cluster.
- Describe the components of the public health department disease cluster investigation.
- Describe the physician's responsibility regarding disease clusters.

Tell Us About Yourself

Please carefully read the questions. Provide answers on the answer sheet (page 25). Your credit will be awarded based on the type of credit you select.

1. What type of continuing education credit do you wish to receive?
****Nurses should request CNE, not CEU. See note on page 24.**

A. CME (for physicians)
B. CME (for non-attending)
C. CNE (continuing nursing education)
D. CEU (continuing education units)
E. [Not used]
F. [Not used]
G. [Not used]
H. None of the above
I. CHES (certified health education specialist)

2. Are you a...

A. Nurse
B. Pharmacist
C. Physician
D. Veterinarian
E. None of the above

3. What is your highest level of education?

A. High school or equivalent
B. Associate, 2-year degree
C. Bachelor's degree
D. Master's degree
E. Doctorate
F. Other

4. Which of the following best describes your current occupation?

A. Environmental Health Professional
B. Epidemiologist
C. Health Educator
D. Laboratorian
E. Physician Assistant
F. Industrial Hygienist
G. Sanitarian
H. Toxicologist
I. Other patient care provider
J. Student
K. None of the above

5. Which of the following best describes your current work setting?

A. Academic (public and private)
B. Private health care organization
C. Public health organization
D. Environmental health organization
E. Non-profit organization
F. Other work setting

6. Which of the following best describes the organization in which you work?

A. Federal government
B. State government
C. County government
D. Local government
E. Non-governmental agency
F. Other type of organization

Tell Us About the Course

7. How did you obtain this course?

A. Downloaded or printed from Web site
B. Shared materials with colleague(s)
C. By mail from ATSDR
D. Not applicable

8. How did you first learn about this course?

A. State publication (or other state-sponsored communication)
B. *MMWR*
C. ATSDR Internet site or homepage
D. PHTN source (PHTN Web site, e-mail announcement)

E. Colleague
F. Other

9. What was the most important factor in your decision to obtain this course?
A. Content
B. Continuing education credit
C. Supervisor recommended
D. Previous participation in ATSDR training
E. Previous participation in CDC and PHTN training
F. Ability to take the course at my convenience
G. Other

10. How much time did you spend completing the course, evaluation, and posttest?
A. 1 to 1.5 hours
B. More than 1.5 hours but less than 2 hours
C. 2 to 2.5 hours
D. More than 2.5 hours but less than 3 hours
E. 3 hours or more

11. Please rate your level of knowledge before completing this course.
A. Great deal of knowledge about the content
B. Fair amount of knowledge about the content
C. Limited knowledge about the content
D. No prior knowledge about the content
E. No opinion

12. Please estimate your knowledge gain after completing this course.
A. Gained a great deal of knowledge about the content
B. Gained a fair amount of knowledge about the content
C. Gained a limited amount of knowledge about the content
D. Did not gain any knowledge about the content
E. No opinion

Please use the scale below to rate your level of agreement with the following statements (questions 13–21) about this course.
A. Agree
B. No opinion
C. Disagree
D. Not applicable

13. The objectives are relevant to the goal.

14. The tables and figures are an effective learning resource.

15. The content in this course was appropriate for my training needs.

16. **Participation in this course enhanced my professional effectiveness.**

17. **I will recommend this course to my colleagues.**

18. **Overall, this course enhanced my ability to understand the content.**

19. **I am confident I can define a disease cluster.**

20. **I am confident I can describe the components of the public health department disease cluster investigation.**

21. I am confident I can describe the physician's responsibility regarding disease clusters.

Posttest

If you wish to receive continuing education credit for this program, you must complete this posttest. Each question below contains five suggested answers, of which one or more is correct. **Circle all correct answers on the answer sheet.**

22. Disease clusters are best characterized by

A. absence of exposure hypotheses.
B. an unusual aggregation, real or perceived, of health events that are grouped together in time and space and that are reported to a public health unit.
C. community group.
D. proximity to waste sites.
E. awkward communications.

23. A component of a cluster investigation includes

A. creating a testable exposure hypothesis.
B. safeguarding public health funds.
C. performing an effective risk assessment.
D. ensuring that all stakeholders reach a compromise outcome.
E. closing the case.

24. Which of the following disease-exposure relationships was first characterized by cluster reports?

A. Angiosarcoma of the liver from vinyl chloride.
B. Adenocarcinoma of the vagina and maternal consumption of diethylstilbestrol.
C. Phocomelia and maternal consumption of thalidomide.
D. Neurotoxicity from chlordecone (kepone).
E. All of the above.

25. Which of the following conditions is most likely to describe a disease cluster with a clearly identifiable environmental cause?

A. Excess of a common disease in a large population.
B. Excess of a common disease in a small population.
C. Excess of a rare disease in a large population.
D. Excess of a rare disease in a small population.
E. Excess of several different common diseases in a large population.

26. The case definition can be

A. narrow.
B. expanded.

C. based on that which is most unusual about the disease cluster under investigation.
D. a choice that depends on the information at hand.
E. all of the above.

27. The federal agency that conducts evaluations of human health outcomes from toxic waste is the
A. U.S. Environmental Protection Agency.
B. Office of the Surgeon General.
C. Agency for Toxic Substances and Disease Registry.
D. National Institute for Occupational Safety and Health.
E. Bureau of Land Management.

28. The physician's overall responsibility includes
A. suspecting a cluster of disease based upon clinical observation.
B. completing an exposure history.
C. confirmation of case(s) through accurate clinical and laboratory diagnosis.
D. acting as a sentinel in reporting cases to the local public health unit.
E. all of the above.

29. The public health department initiates
A. active surveillance.
B. exposure assessments.
C. development of local registries.
D. all of the above.
E. none of the above.

Note to Nurses

CDC is accredited by the American Nurses Credentialing Center's (ANCC) Commission on Accreditation. ANCC credit is accepted by most State Boards of Nursing.

California nurses should write in "ANCC - Self-Study" for this course when applying for relicensure. A provider number is **not** needed.

Iowa nurses must be granted special approval from the Iowa Board of Nursing. Call 515-281-4823 or e-mail marmago@bon.state.ia.us to obtain the necessary application.

Case Studies in Environmental Medicine:

Disease Clusters: An Overview

Answer Sheet, Course Number SS3096

Instructions for submitting hard-copy answer sheet: Circle your answers. To receive your certificate, you must answer **all** questions. Mail or fax your completed answer sheet to

Fax: 404-498-0061, ATTN: Continuing Education Coordinator

Mail: Continuing Education Coordinator
Agency for Toxic Substances and Disease Registry
Division of Health Education and Promotion
1600 Clifton Road, NE (MS E-33)
Atlanta, GA 30333

Be sure to fill in your name and address on the back of this form.

Remember, you can access the case studies online at www.atsdr.cdc.gov/HEC/CSEM/ and complete the evaluation questionnaire and posttest online at www2.cdc.gov/atsdrce/.

Online access allows you to receive your certificate as soon as you complete the posttest.

1. A B C D E F G H I
2. A B C D E
3. A B C D E F G
4. A B C D E F G H I J K
5. A B C D E F
6. A B C D E F
7. A B C D
8. A B C D E F
9. A B C D E F G
10. A B C D E
11. A B C D E
12. A B C D E
13. A B C D
14. A B C D
15. A B C D
16. A B C D
17. A B C D
18. A B C D
19. A B C D
20. A B C D
21. A B C D
22. A B C D E
23. A B C D E
24. A B C D E
25. A B C D E
26. A B C D E
27. A B C D E
28. A B C D E
29. A B C D E

Name: E-mail (not required):

Address:

Zip code:

○ Check here to be placed on the list to pilot test new case studies

fold here first

Place Stamp Here

Continuing Education Coordinator

Agency for Toxic Substances and Disease Registry

Division of Health Education and Promotion

1600 Clifton Road, NE (MS E-33)

Atlanta, GA 30333

fold here second

Access the case studies online at www.atsdr.cdc.gov/HEC/CSEM/ and complete the evaluation questionnaire and posttest online at www2.cdc.gov/atsdrce/.

Online access allows you to receive your certificate as soon as you complete the posttest.

tape or staple here

Appendix A: Exposure History Form

Part 1. Exposure Survey

Please circle the appropriate answer.

Name: _____ **Date:** _____

Birth date: _____ **Sex (circle one):** Male Female

1. Are you currently exposed to any of the following?

metals	no	yes
dust or fibers	no	yes
chemicals	no	yes
fumes	no	yes
radiation	no	yes
biologic agents	no	yes
loud noise, vibration, extreme heat or cold	no	yes

2. Have you been exposed to any of the above in the past? no yes

3. Do any household members have contact with metals, dust, fibers, chemicals, fumes, radiation, or biologic agents? no yes

If you answered *yes* to any of the items above, describe your exposure in detail—how you were exposed, to what you were exposed. If you need more space, please use a separate sheet of paper.

4. Do you know the names of the metals, dusts, fibers, chemicals, fumes, or radiation that you are/were exposed to? no yes →

5. Do you get the material on your skin or clothing? no yes

6. Are your work clothes laundered at home? no yes

7. Do you shower at work? no yes

8. Can you smell the chemical or material you are working with? no yes

9. Do you use protective equipment such as gloves, masks, respirator, or hearing protectors? no yes →

10. Have you been advised to use protective equipment? no yes

11. Have you been instructed in the use of protective equipment? no yes

If *yes*, list them below.

If *yes*, list the protective equipment used.

12. Do you wash your hands with solvents?		no	yes
13. Do you smoke at the workplace?		no	yes
At home?		no	yes
14. Are you exposed to secondhand tobacco smoke at the workplace?		no	yes
At home?		no	yes
15. Do you eat at the workplace?		no	yes
16. Do you know of any co-workers experiencing similar or unusual symptoms?		no	yes
17. Are family members experiencing similar or unusual symptoms?		no	yes
18. Has there been a change in the health or behavior of family pets?		no	yes
19. Do your symptoms seem to be aggravated by a specific activity?		no	yes
20. Do your symptoms get either worse or better	at work?	no	yes
	at home?	no	yes
	on weekends?	no	yes
	on vacation?	no	yes
21. Has anything about your job changed in recent months (such as duties, procedures, overtime)?		no	yes
22. Do you use any traditional or alternative medicines?		no	yes

If you answered *yes* to any of the questions, please explain.

Part 2. Work History

Name: _____

A. Occupational Profile

Birth date: _____ **Sex:** Male Female

The following questions refer to your current or most recent job:

Job title: _____ Describe this job: _____

Type of industry: _____

Name of employer: _____

Date job began: _____

Are you still working in this job? yes no

If *no*, when did this job end? _____

Fill in the table below listing all jobs you have worked including short-term, seasonal, part-time employment, and military service. Begin with your most recent job. Use additional paper if necessary.

Dates of Employment	Job Title and Description of Work	Exposures*	Protective Equipment

*List the chemicals, dusts, fibers, fumes, radiation, biologic agents (i.e., molds or viruses) and physical agents (i.e., extreme heat, cold, vibration, or noise) that you were exposed to at this job.

Have you ever worked at a job or hobby in which you came in contact with any of the following by breathing, touching, or ingesting (swallowing)? If *yes*, please check the box beside the name.

- ○ Acids
- ○ Alcohols (industrial)
- ○ Alkalies
- ○ Ammonia
- ○ Arsenic
- ○ Asbestos
- ○ Benzene
- ○ Beryllium
- ○ Cadmium
- ○ Carbon tetrachloride
- ○ Chlorinated naphthalenes
- ○ Chloroform
- ○ Chloroprene
- ○ Chromates
- ○ Coal dust
- ○ Dichlorobenzene
- ○ Ethylene dibromide
- ○ Ethylene dichloride
- ○ Fiberglass
- ○ Halothane
- ○ Isocyanates
- ○ Ketones
- ○ Lead
- ○ Mercury
- ○ Methylene chloride
- ○ Nickel
- ○ PBBs
- ○ PCBs
- ○ Perchloroethylene
- ○ Pesticides
- ○ Phenol
- ○ Phosgene
- ○ Radiation
- ○ Rock dust
- ○ Silica powder
- ○ Solvents
- ○ Styrene
- ○ Talc
- ○ Toluene
- ○ TDI or MDI
- ○ Trichloroethylene
- ○ Trinitrotoluene
- ○ Vinyl chloride
- ○ Welding fumes
- ○ X-rays
- ○ Other (specify)

B. Occupational Exposure Inventory

Please circle the appropriate answer.

1. Have you ever been off work for more than 1 day because of an illness related to work? no yes
2. Have you ever been advised to change jobs or work assignments because of any health problems or injuries? no yes
3. Has your work routine changed recently? no yes

Part 3. Environmental History

Please circle the appropriate answer.

1. Do you live next to or near an industrial plant, commercial business, dump site, or nonresidential property? no yes
2. Which of the following do you have in your home?
   Please circle those that apply.
   Air conditioner Air purifier Central heating (gas or oil?) Gas stove Electric stove
   Fireplace Wood stove Humidifier
3. Have you recently acquired new furniture or carpet, refinished furniture, or remodeled your home? no yes
4. Have you weatherized your home recently? no yes
5. Are pesticides or herbicides (bug or weed killers; flea and tick sprays, collars, powders, or shampoos) used in your home or garden, or on pets? no yes
6. Do you (or any household member) have a hobby or craft? no yes
7. Do you work on your car? no yes
8. Have you ever changed your residence because of a health problem? no yes
9. Does your drinking water come from a private well, city water supply, or grocery store?
10. Approximately what year was your home built?_____

If you answered *yes* to any of the questions, please explain.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
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