Sentinel Health Events of Environmental Contamination: A Consensus Statement

Carl Shy, Ray Greenberg, and Deborah Winn

The Agency for Toxic Substances and Disease Registry (ATSDR) has specific interest in surveillance methods as part of its studies of health effects potentially associated with environmental contamination sites (1,2). An earlier ATSDR-sponsored conference, held 30 October–1 November 1989 in Asheville, North Carolina, laid much of the groundwork for considering a specific listing of health events as candidates for this sentinel application (3). This report is the product of a sequel conference charged to review the available scientific literature, assimilate relevant experiences, and produce a framework for a listing of sentinel health events (SHEs) for use in monitoring health around sites of environmental contamination. This consensus panel was convened 18–19 May 1992 at the University of North Carolina, Chapel Hill, to identify SHEs that could serve as indicators of environmental contamination.

Early in the conference there were several presentations building upon Rustein's original supposition regarding SHEs (4). Recent other works relating to the use of sentinel events in public health surveillance were also discussed (5–9). Two days of deliberations followed. Presented here are the consensus statements and recommendations that resulted from this endeavor.

Listing of SHEs for Environmental Contamination, by Type

Type I. The following acute conditions are regarded as SHEs in the form of the definition by Rustein (I): 1) poisonings, especially due to pesticides, metals, or other agents that might be found in waste streams, in disposal sites, or other accessible locations. Children are especially vulnerable to this hazard. Lead and carbon monoxide poisoning are SHEs. Cholinesterase inhibition would also be classified under poisoning; 2) selected cancers that are specific for known physical or chemical agents. In general, cancers are poor SHEs because of their long latencies. Some cancers whose biology is sufficiently well studied may be considered SHEs, e.g., mesothelioma, clear cell cancer of the vagina, and angiosarcoma of the liver; 3) precocious puberty or thelarche. Many pesticides, industrial chemicals, and food additives have estrogenic activity. Precocious puberty is so rare that an inquiry into possible sources of estrogen exposure is warranted; 4) methemoglobinemia is a classic poisoning. It was included from the previous panel's work (4); 5) toxic neuropathy. Elicitation of an unusual exposure to a toxic agent is required to make a diagnosis of toxic neuropathy; i.e., with Minimata disease, the case definition includes exposure to methylmercury.

Type II. Unusual health patterns (e.g., statistically significant excess cases or space-time patterns) in incidence of the following conditions, identified via general surveillance, may represent SHEs in a population perspective. That is to say, the population's experience forms a sentinel pattern, and the pattern represents the event. 1) Bladder cancer. Bladder cancer is one of the human cancers with a strong association with chemical exposures. The occurrence of bladder cancer in a person without other risk factors, such as smoking or occupational exposures, or at a young age, should at least be considered for investigation. Bladder cancer in a human and a companion animal should also be similarly considered. Bladder cancer occurring in genetically unrelated individuals of any age living at the same place may warrant investigation.

2) Lung cancer in nonsmokers. Multiple suspicious events (three or more cases in a “space-time cluster”) should be investigated.

3) Primary liver cancer in nondrinkers. The liver is an extremely plausible site for environmentally related cancer; thus, occurrence of liver cancer in a person without cirrhosis or a history of exposure to hepatitis B should be investigated.

4) Rare cancers with some evidence to suggest possible hazardous environmental exposure. A few rare cancers that may be considered as type II SHEs are haldomyosarcoma, myelogenous leukemia, acute leukemia in children, and acute glucocorticoid leukemia in adults. Multiple occurrences of these events raise suspicions about potential environmental hazards. The occurrence of cancer and potentially biologically related conditions, such as aplastic anemia, may be sentinels.

5) Asthma in children. There may be low-risk groups of children, such as those who have no allergies, live in nonsmoking households, etc., in whom the occurrence of wheezing could be a SHE; however, the specificity of the event, even if identified, would be low. 6) New diseases. The panel encourages attention to the possible environmental etiology of new diseases. Examples are eosinophilia myalgia syndrome, toxic oil syndrome, Yusho/Yucheng, Kawasaki disease, and Minimata disease.

Some laboratory measures were discussed as possible sentinel findings or biologic markers of hazardous environmental exposures: 7) PCBs and PBBS, persistent pesticides, other trace industrial chemicals. There are a variety of xenobiotics (PCBs, dioxins, dibenzofurans, DDT, termiocides) that can be measured in human or animal tissues. Abnormal levels of these compounds are not established, and levels are dependent on the analytical method used. At this time it is unlikely that these findings can serve as sentinels. As methods are developed for large-scale applications and distributions in populations become known, these measurements may begin to serve as SHEs.

8) Adducts. Adducts of DNA or hemoglobin are done on a research basis in a number of laboratories. Public health authorities are unlikely to be the recipients of such information on a regular basis. For the immediate future, such information will be gathered only in the context of a specific research study.

Data Sources for Monitoring SHEs

The panel identified a number of data sources already in operation that could be used for monitoring health conditions potentially related to environmental exposures. The extent that type I SHEs would be represented among such health condition is simply a matter of defining the type I SHEs to be considered. These sources of data for general surveillance, as well as SHE monitoring (of either type), include death certificates, cancer registries, hospital/outpatient records, laboratory data (10), birth defects registries (11), poisoning centers, and animal necropy data bases (12). These sources were considered to have the best potential use in identifying sentinel health events associated with environmental exposure. The strengths, limitations, and applications of these sources were discussed by the panel in a context with the manner by which health events could come to the attention of an alert health care provider (13,14). The United States has sometimes been criticized for having a medical care delivery system that impedes public health surveillance and detection of SHEs. This is because no unique universal identifiers exist, thus records about health events are fragmented across the health care delivery system, and record linkage studies are difficult to undertake. The alert provider is usually the person who detects type I SHEs. In infectious disease outbreaks (e.g., pneumocystis pneumonia), the role of the alert clinician is well

Address correspondence to T.E. Aldrich, Central Cancer Registry, PO Box 29538, Raleigh, NC 27619-0538 USA.

Appreciation is extended to Jeffrey Lybarger and Gene Lengerich for their contributions as speakers at this conference. Consensus conference and statement funded by Agency for Toxic Substances and Disease Registry, grant no. R13/ATR49613-01.
demonstrated. The alert practitioner also often is the primary identifier of type II problems; for example, in Puerto Rico enlarged breasts in offspring of factory workers exposed to hormones (12). Such reports as these come from practitioners and from the general public. Public health agencies must begin to be more responsive with investigating type I SHEs and should deliberately search for type II SHEs by systematically examining the available databases.

**Dissemination of SHE Technology**

Modifying data systems to look for SHEs will require resources, as well as a reorientation in thinking by many public health workers (15). In public health the emphasis is on common, preventable diseases, and most epidemiologists and public health workers are not taught to look for rare, improbable events. Public health funding is not currently available for examining rare events or the associated occurrence pattern. Technology is making processing and examining large quantities of data faster and more routine. However, even with easy to use, sophisticated, and efficient computer systems, systematic examination for rare and unusual events will still take material resources.

It is expected that the primary health care provider, whether nurse, physician, dentist, veterinarian, or other, will be the primary identifier of SHEs. SHEs should be brought to the attention of county health departments, state health departments, or the federal government through the state health departments. Clinical practitioners could be apprized of these candidate sentinel events and explanations of what represents an unusual health event pattern in the same ways that the original occupational modes of SHEs were publicized (e.g., publication in medical journals, continuing medical education courses).

Particular committees of the American Academy of Pediatrics and of the American Medical Association concern themselves with the environment and could provide leadership for the use of SHE reasoning. National Institute of Health-funded centers for environmental health train medical residents and offer courses through which information regarding SHE surveillance may be distributed.

**Discussion**

The alert health care provider will frequently be the first and most critical element in detecting SHEs, especially type I. This is particularly true because obtaining morbidity data with high coverage in the United States through existing data sources is limited. These providers need to be educated about their role in detecting SHEs.

It is difficult to find examples of SHEs detected through analysis of a database. However, most investigations rely on a partnership between the practitioner and a public health agency. The practitioner may identify the first indication of a problem, but the agency is needed to evaluate, confirm, and determine the scope of the problem. For example, with the problem of vitamin D in Massachusetts, three cases were found, but the public health agency identified more cases and did investigative work (14). Public health agencies should play a greater role in the study of type I SHEs and should search for type II SHEs by examining available databases. When local public health agencies receive reports about type I SHE occurrences, they should be evaluated by familiar methods of confirming diagnosis, comparing rates, etc. (15).

Type II SHEs may be detected through existing surveillance systems. New technologies have made traditionally time-consuming and laborious activities easier (e.g., mapping disease cases). ATSDR has recently produced a software package expressly to facilitate these types of statistical analyses (17). There are many innovative and existing uses of geographic information systems for health applications that may facilitate identification of type II SHEs. More innovations are likely to become available in the future. Research attention is needed for ways of setting priorities and handling reports of type II SHEs.

**References**

1. ATSDR. The feasibility and value of performing multisite epidemiologic studies for superfund sites. Atlanta, GA:Agency for Toxic Substances and Disease Registry, 1992.
2. ATSDR. Final report of the panel on the national disease registry. Atlanta, GA:Agency for Toxic Substances and Disease Registry, 1990.
3. Rothwell CJ, Hamilton CB, Leaverton PE. Identification of sentinel health events as indicators of environmental contamination. Environ Health Perspect 94:261–263(1991).
4. Rustein DD, Mullan RJ, Frazier TM, Halperin WE, Melius JM, Seino JP. Sentinel health events (occupational): a basis for physician recognition and public health surveillance. Am J Public Health 73(9):1054–1062(1983).
5. Schulte PA, Kaye WE. Exposure registries. Arch Environ Health 43(2):155–161(1988).
6. Mason TJ, Vogler WJ, Bladder cancer screening at the Dupont chambers works: a new initiative. J Occup Med 32(9):874–877(1990).
7. Griffith JD, Duncan RC, Riggan WB, Pellom AC. Cancer Mortality in U.S. counties with hazardous waste sites and ground water pollution. Arch Environ Health 44:69–74(1989).
8. Wagener DK, Buffle PA. Geographic distribution of deaths due to sentinel health event (occupational) causes. Am J Ind Med 16:355–372(1989).
9. Thacker SB, Berkelman RL. Public health surveillance in the United States. Epidemiol Rev 10:164–190(1988).
10. Harrell P, Woerlce CH, Mazlish N, Osorio A, Tolentino N, Keller J, Leinherr M, Howe H, Currier R, Coe E, Rabin R, Gerwel B, Stone R, O'Conner T, Gordon JE, Logue J, Pichette J, Perrott DA. Surveillance of elevated blood lead levels among adults—United States, 1992. Morbid Mortal Weekly Rep 41(17):285–90(1992).
11. Geshwind SA, Stolwijk AAJ, Bracken M, Frigereld E, Stark A, Olsen C, Melius J. Risk of congenital malformations associated with proximity to hazardous waste sites. Am J Epidemiol 135(11):1197–1207(1992).
12. Committee on animals as monitors of environmental hazards. Animals as sentinels of environmental hazards. Washington, DC:National Academy Press, 1991.
13. Harrington JM, Stein GF, Rivers RO, demorales AV. The occupational hazards of formulating contraceptives—a survey of plant employees. Arch Environ Health 33:12–15(1978).
14. Jacobus CH, Holick MF, Shaq Q, Chen TC, Holm JA, Kolodny JM, Fuleihan GE, Seely EW, Hypervitaminosis D associated with drinking milk. N Engl J Med 326(18):1173–1177(1992).
15. Aldrich TE, Leaverton PE. Sentinel event strategies in environmental health. Annu Rev Pub Health (14):205–217(1993).
16. Armenian HK. Case investigation in epidemiology. Am J Epidemiol 134(10):1067–1072(1991).
17. Aldrich TE, Drake JW. CLUSTER: users manual for software to assist with investigations of rare health events. Atlanta, GA:Agency for Toxic Substances and Disease Registry, 1993.

---

**Panelists**

**Don Austin**
Oregon Department of Health Services, Portland, Oregon

**Larry Glickman**
Purdue University, West Lafayette, Illinois

**Jack Griffith**
U.S. EPA, Research Triangle Park, North Carolina

**Hanna Assaf**
N.C. Division of Solid Waste Management, Raleigh, North Carolina

**Paul Leaverton**
University of South Florida, Tampa, Florida

**Tom Mason**
Fox Chase Cancer Center, Cheltenham, Pennsylvania

**Tom Sinks**
Centers for Disease Control, Atlanta, Georgia

**Ron Forthofer**
Longmont, Colorado

**Wendy Kaye**
Agency for Toxic Substances and Disease Registry, Atlanta, Georgia

**Charles Hamilton**
University of Tennessee, Knoxville, Tennessee

**Barry H. Margolin**
University of North Carolina, Chapel Hill, North Carolina

**Darlene Mesery**
University of Utah, Salt Lake City, Utah

**Walter Rogan**
NEHS, Research Triangle Park, North Carolina