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CENTER FOR DISEASE PREVENTION & EPIDEMIOLOGY • OREGON HEALTH DIVISION

CANCER CLUSTERS: COMMON CAUSE OR CHANCE?

Many people have seen the recent movie, *Erin Brockovich*, in which environmental contamination of the water supply by an irresponsible industrial corporation resulted in residents of a small community being afflicted by a number of ailments, including cancer. That followed last year's movie, *A Civil Action*, in which criminal industrial waste dumping left an area contaminated with carcinogens that were apparently responsible for a cluster of childhood cancers. If the public was not attuned to identifying cancer clusters before, with Love Canal, it certainly is now.

The Oregon Health Division has for years received occasional inquiries about suspected cancer clusters. The majority of subsequent investigations do not yield a common etiology because most cancer clusters occur by chance and are otherwise unrelated. This week's *CD Summary* informs readers about how we respond to a suspected cancer cluster, and the experience of others investigating such reports.

RESPONSE TO A SUSPECTED CLUSTER

The purpose in investigating a cancer cluster is to evaluate the plausibility of an environmental, occupational, iatrogenic, or other preventable exposure associated with an increased risk of cancer. Reports of apparent clusters of cancer come from both concerned citizens who may hear about several cases of cancer (often they themselves or family members have cancer and they hear about other cases in the community) and from astute physicians who notice an unusual number of cases of a specific cancer among their patients.

Since 1996, the Oregon State Cancer Registry (OSCaR) at the Health Division has been collecting data on new cancers diagnosed in the state. Information recorded in OSCaR includes: cancer site, histologic type,and stage at diagnosis. In addition, demographic information on the patient, including age, race, sex and place of residence, is collected. These data are useful in determining whether or not an apparent cluster exists. Were a cancer cluster to be documented, additional investigation would need to be conducted into possible causes and common exposures among the patients.

STEPS TO INVESTIGATING A CANCER CLUSTER

Step 1: The initial report

Regardless of who makes the initial report, we need to gather (and document) more information regarding: the number of cases; the population group or area involved; the time period over which cases occurred and the suspected cause.

The Health Division has developed an "Initial Cancer Inquiry Report Form" (hey, we're the government and we love forms!) to collect some of this additional information. We ask that one form be filled out on each of the patients involved in the cluster. The form includes the patient's name, age, sex, race, address, and how long they have lived in the community, as well as information about the type of cancer, date of diagnosis, name of physician, family history, smoking history, employment history, etc.

A copy of the form is available on our web site: *www.ohd.hr.state.or.us/oscar/docs/review.pdf*.

It is common for reports, especially from the public, to be based on combinations of diseases that are very unlikely to be etiologically related. Initial reports also may include cancers in individuals who recently moved into the area from some other location (e.g., out of state), and/or may not include some cases that would logically be included in any cluster based on a geographic location. The purpose of the initial investigation is to settle on whether a plausible excess of cases of cancer can be defined by location, by time period, and by cancer type. Frequently the process of filling out the forms leads the reporting person to the conclusion that there really is no cluster.

Step 2: Establish a case definition

It is important to establish a case definition by which suspect cases can definitely be included in or excluded from the cluster. The elements of a case definition include: (1) what (the cancer type); (2) where (neighborhood, community, county); (3) when (the time period during which cases occurred); (4) who (a particular age group, such as children; employees at a particular worksite, etc).

Step 3: Verify the reported cases

For there to be a true cluster, all suspected cases must fit with the established case definition. Once we get the initial report forms, we can check the OSCaR database for the accuracy of the information. The OSCaR database is used to confirm: the diagnosis, age, sex, address of patient, the date of diagnosis; and the treating physician. If the cases are recent, they may not have been reported to OSCaR. In this case, physicians may be contacted by OSCaR staff trying to establish the nature of a suspected cluster, to verify diagnoses or diagnosis dates, to verify patient addresses, or to discuss the need for a patient contact.

Step 4: Additional case finding

In addition to verifying the cases that have been reported to us, it is important to identify whether or not there are additional cases, unknown to the reporting source, that may appropriately fit within the case definition. In identifying additional cluster-associated cases, we look for other cases of the same type of cancer, in the same age group, geographic location, and time period. If the suspected cluster is recent, we may call hospitals or oncologists in the same area to see if they have observed recent cases of the same type of cancer.

Step 5: Determine the expected number of cases

When all available cluster-associated cases are assembled, it must then be determined whether this cluster represents a true excess over the number of expected cases. To do this, we define the population from

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which the cases arose (e.g., all residents of one county, residents of a particular age group, etc.). We then compute how many cases of the cancer would be expected under "normal" rates. We base "normal" rates on the overall state rate, the rates in surrounding counties, or the rate in the county of interest during previous years.

Step 6: Observed versus expected

Once we have calculated the expected number of cases, we compare whether or not the observed number is greater than expected. We can perform statistical testing to determine whether there is a significant difference, or whether the difference is what would have been expected by chance.

PREVIOUS STUDIES

When clusters of cancer have been suspected in occupational settings, epidemiologic investigations have been rather fruitful.[1] Many of the known occupational carcinogens were identified through such investigations, including exposures to aniline dyes, radium paint, asbestos, bis (chlormethyl) ether, vinyl chloride, benzene, and others. In contrast, investigations of geographic clusters have been disappointingly unproductive.[2] This is in spite of the fact that dozens of geographic clusters have been identified which, in after-the-fact applications of statistical tests, have been found to be extremely unlikely to have occurred by chance. What accounts for this frustrating lack of results?

CANCER CLUSTER STATISTICS 101

A statistician once pointed out that rare things do occur, rarely, but when they do, they almost invariably get noticed. That only partially applies to cancer clusters, because they are not really rare. The simple math is that, given 18 age categories, 2 sexes, 80 types of cancer codes, and 5,000 census tracts, a "statistically significant" cluster will occur 2,750 times, strictly by chance. In other words, *some* type of cluster is expected more often than not, if only one looks hard enough. It is not fruitful, of course, to investigate chance clusters, and statistical tests are useless in identifying them. The Massachusetts Department of Health responded to between three and four thousand reported cancer clusters in a recent year. The Minnesota Department of Health investigated over 1,000 cancer clusters between 1984 and 1995. Other health departments have had similar experiences. No convincingly unequivocal environmental cause has been identified from what has been estimated nationally as billions of dollars of investigative efforts into community-based cancer clusters.

One of the problems is that we are all programmed to notice unusual occurrences. If the unusual event has serious health implications, it is of greater concern. Further, most of us believe that the pattern (or average) for a large number will be replicated with smaller numbers. If we know that out of 1000 coin flips, there should be close to 500 heads, we expect similar results with six coin flips, but out of the 64 possible combinations, exactly three heads only happens 20 times. The accompanying figure illustrates the placement of 20 randomly placed X's on a grid with 100 squares. There appear to be several clusters and an absence of X's in the center. Rows 8 and 9 have 35% of the X's while row 3 has none. Placement was random.

20 Random Numbers on a 10 x 10 Grid

\	1	2	3	4	5	6	7	8	9	10
1			X				X			X
2			X					X		
3										
4	X								X	
5		X								X
6			X							
7			X				X			
8					X		X			X
9		X		X		X			X	
10								X		

AN OSCAR FOR OSCaR?

Dealing with cluster investigations is a balance of science and public relations. On one hand, every cluster report must be taken seriously and pursued to the point where science and logic can determine that it would not be useful to pursue the matter further, and sometimes it takes considerable effort to reach that point. On the other hand, both the actual experience of states like Minnesota in conducting cancer cluster investigations, and an understanding of the laws of chance, teach us that the probability of identifying an addressable health hazard by this approach is very small. Even so, the next report could be the real one, and the successful identification of the cause of a cancer cluster is a professional coup and, (who knows?) may lead to a movie contract. For more information, contact OSCaR at 503/731-4858.

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