Fact or Fiction?

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Clusters

Cancer clusters are the stuff of headlines and protest parades.[1] It's one of the tools the media and concerned folks use to bring our attention to some potentially harmful scare, such as electromagnetic fields or hazardous waste sites. What's a cluster? As Fumento[2] points out: "Strictly speaking, a cluster is simply an elevated incidence of disease or other problem in a given population." Some clusters are genuine, but most are found by a process attributed to the mythical Texas Sharpshooter: fire a gun at the wall and draw the target around the bullet hole.[1]

Let's put this on a personal level to better explain clusters. Assume you were recently diagnosed with cancer. You start looking around your neighborhood and realize that five out of six of your nearest neighbors have at least one person in their house with cancer. You ask the question: Isn't this more than the expected number of cases for my neighborhood? You then look out your front window and see the power pole on the street and connect this with a report you vaguely remember hearing about electromagnetic fields and cancer. You are well on you way to convincing yourself that you are part of a cancer cluster.

Clusters are a wonderful tool for crusaders seeking to indict something as a cause of disease. Tell someone that a given office building or city block has had twice the cancer or heart attack victims as the expected rate, and they quickly assume that something is wrong in that building or on that block. For example, a study of a Woburn, MA, site associated a cluster of 20 childhood leukemia cases with the site. The fact that it didn't matter that none of the contaminants at the site causes leukemia shows the power of a cluster.[3] Ames and Gold [4,5] in their HERP Index, which is also called the "peanut butter chart"[6] because it used a sandwich made from all-natural peanut butter as the standard with which to assess risks, reported the following to be more carcinogenic than a glass of tap water from the Woburn wells found to contain trichloroethylene: a glass of herb tea; one raw, nonpoisonous mushroom; one can of diet soda; one cup of coffee; one glass of wine or one beer. More detail on the HERP Index can be found in the March 1998 issue of this column.[7]

Another example is an "epidemic" of male breast cancer among telephone linemen in New York state. A close look at the data revealed that although a relative risk of 6.5:1 was obtained, there were only two cases that were recorded. Furthermore, the two people involved weren't even linemen, but phone company office workers. Yet, on the basis of these two cases, some scientists and many media outlets concluded incorrectly that there was a serious problem.[8] Mathematicians generally characterize clusters as statistical anomalies, such as a coin toss that turns up heads 70 times out of 100.

Now let's look at cancer. One out of every three people in the U.S. will develop cancer sometime during their lifetimes. This is called the background risk or "natural" rate of cancer, and it's ours by virtue of our birth. If you analyze cancer rates by geographic region of state or county or city or neighborhood, you will likely find that some areas will have a cancer rate of exactly 1 in 3. However, most areas will have cancer rates that are greater or less than 1 in 3.[3] Orient[9] reports that some clusters don't have a common cause; they just happen. It's not necessarily abnormal for a neighborhood to have a higher-than-average incidence of a particular disease, just as it's normal for some students to have a higher-than-average score on a test.

According to R.R. Neutra[10,11] of the California Department of Health Services, probability theory suggests that 17 percent of the 29,000 towns or census tracts in the U.S. will have at least one of the 80 recognized types of cancer elevated in any given decade, producing 4,930 chance clusters. He also points out that the relative risk of an environmentally caused cancer cluster in a neighborhood would often need to be above eight to achieve statistical significance. In other words, you would need to find eight times what you would expect. Think about this the next time you read a headline that says: "Study at Z Plant Shows Link Between EMF and Brain Cancer," or "Women Working with Y Chemical Have Three Times Usual Miscarriage Rate."

This shows that most cancer clusters happen by chance, and it's largely for this reason that health officials are usually reluctant to investigate reports of localized excesses in cancer incidence. As an example, the Center for Disease Control and Prevention gave up routinely investigating cancer clusters in 1990 because of the intensive resources required for the little information that was obtained.[11]

It should be noted, however, that on some occasions cancer clusters have proven fruitful. Typically, these have been occupational or medical clusters and not neighborhood clusters. In one case, lung cancer among packaging industry workers revealed that polyvinyl chlorides were the cause, and in another, vaginal cancer in young women identified diethylstilbestrol as

the cause.[12]

The important point in both these cases, which were industry-related, was that the prevalence of the disease was rare and suddenly increased in frequency. Neutra[10] reported that only one carcinogen has been discovered as the result of a neighborhood cluster. Death certificates showed 20 mesothelioma deaths (which is uniquely associated with fibrous minerals) in four years in a Turkish village with a population of 800. This represents a relative risk of 9,000—far higher than the value of 8 or more recommended by Neutra[10] for further study. Investigation revealed that the culprit was the mineral erionite, which was found in plentiful supply in the soil and building materials of the village.

In comparing the scientific and service components of the public health response to an acute cluster with a cancer cluster, Neutra used the interesting case of the Eleven Blue Men.[10,13] In 1944, 11 very ill or unconscious derelicts were found in a neighborhood of New York City. All of them had an unusual sky-blue color. The diagnosis on the first man to arrive was cyanosis, which results from an insufficient supply of oxygen in the blood. The doctor postulated that this was a case of carbon monoxide poisoning. Within a few hours, 10 more blue men were brought in, and all were rigid, cyanotic, and in a state of shock. This caused the medical investigators to look elsewhere for the cause. Turns out the derelicts were the victims of a type of poisoning so rare that only 10 previous outbreaks of it had been recorded in the medical literature. They had contracted methemoglobinemia, which is caused by ingestion of sodium nitrite.

Investigation implicated a certain restaurant and its use of salt. It was discovered that one of the restaurant's salt shakers contained sodium nitrite instead of sodium chloride. The victims had eaten oatmeal that had been flavored with sodium nitrite instead of salt. The proportion of nitrite in each batch of oatmeal was considerably higher than 1:5,000. After cooking, it was estimated to contain about 1:80, since cooking destroyed the rest. Note how much higher this is than the one part per 5,000 allowed when sodium nitrite is used for preventing the growth of deadly botulism agents.[14] Cooking safely destroys this amount, but not enough is destroyed when the initial concentration of sodium nitrite is one *to* 5,000 instead of one *in* 5,000.

Now, the question is: How is this case different from the procedures used for investigating a cancer cluster? First, there was no question of the legitimacy of the complaint. All 11 men were sky-blue in color, and how many sky-blue people have you ever seen? Contrast this with how many people you know who have cancer.

Another cluster involved six patients who developed muscle pain after eating fried fish. Investigation by health authorities identified the condition as Haff disease, which is caused by a toxin sometimes present in buffalo fish. Four of the cases were traced to a single Louisiana wholesaler.[15]

As Neutra[10] points out, "With cancer clusters, things are usually much less clear-cut, and an experienced public health worker finds that a majority of calls can be legitimately handled with verbal or written explanations about the epidemiology of cancer." Second, cancer has a long and indefinite incubation period. In the case of the 11 blue men or infectious disease, the relevant exposure has occurred in the very recent past. The same analysis applies to those who ate the buffalo fish. These exposures are easy to remember. With cancer, however, the exposure could have occurred many years ago, making it difficult to remember and reconstruct the details.

If neighborhood clusters are so rare, why do we see so many? One answer is that the media and concerned citizens bring them to our attention. Couple this with the fact that, as Gawande[15] points out, we're programmed to see clusters because people assume that the pattern of a large population will be replicated in all its subjects. This type of thinking has been called the "Belief in the Law of Small Numbers." It's just like assuming that, after seeing a long sequence of red on the roulette wheel, we feel that "black" is due. We assume that a sequence of R-R-R-R-R is somehow less random than, say, R-R-B-R-B. In actuality, the two sequences are equally likely.[15]

Conclusion

Although several known carcinogens have been discovered through occupational or medical clusters, only one neighborhood cancer cluster has ever been traced to an environmental cause.[11] So the next time you read or hear about a supposed neighborhood cancer cluster because of a power pole or chemical, pause and give thought to some of the statistics involved with cancer.

Unlike outbreaks of infectious disease, which can be linked to a well-defined recent exposure, a cluster of cancer cases might have its root in an exposure that occurred 10 to 20 years ago, or it might just be a statistical anomaly because of the high incidence of cancer in our world. P&SF

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