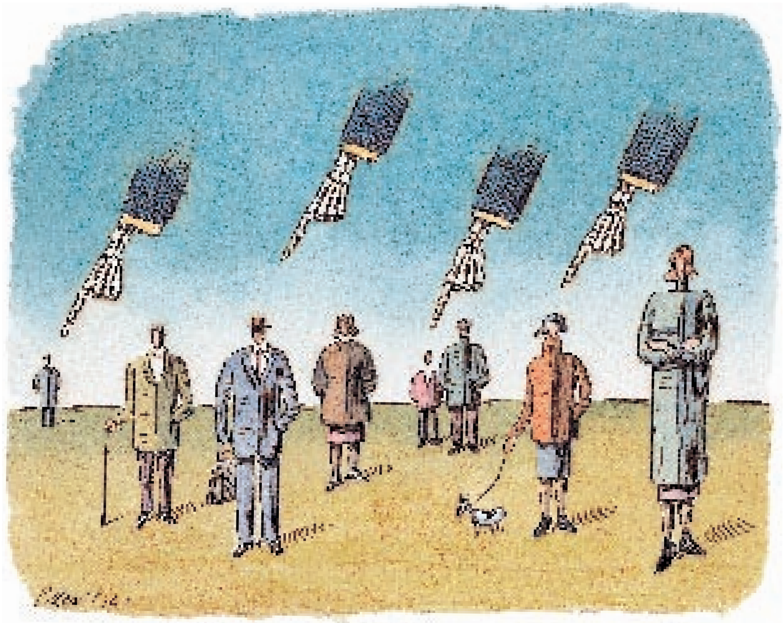
MEDICAL DISPATCH

THE CANCER-CLUSTER MYTH

When a dozen people in a neighborhood develop tumors, it can't be coincidence. Or can it?

BY ATUL GAWANDE



PETER TILL

Is it something in the water? During the past two decades, reports of cancer clusters—communities in which there seems to be an unusual number of cancers—have soared. The place names and the suspects vary, but the basic story is nearly always the same. The Central Valley farming town of McFarland, California, came to national attention in the eighties after a woman whose child was found to have cancer learned of four other children with cancer in just a few blocks around her home. Soon doctors identified six more cases in the town, which had a population of sixty-four hundred. The childhood-cancer rate proved to be four times as high as expected. Suspicion fell on groundwater wells that had been contaminated by pesticides, and lawsuits were filed against six chemical companies.

In 1990, in Los Alamos, New Mexico, a local artist learned of seven cases of brain cancer among residents of a small section of the town's Western Area. How could seven cases of brain cancer in one neighborhood be merely a coincidence? "I think there is something seriously wrong with the Western Area," the artist, Tyler Mercier, told the *Times*. "The neighborhood may be contaminated." In fact, the Los Alamos National Laboratory, which was the birthplace of the atomic bomb, had once dumped millions of gallons of radioactive and toxic waste in the surrounding desert, without providing any solid documentation about precisely what was dumped or where. In San Ramon, California, a cluster of brain cancers was discovered at a high-school class reunion. On Long Island, federal, state, and local officials are currently spending twenty-one million dollars to try to find out why towns like West Islip and Levittown have elevated rates of breast cancer.

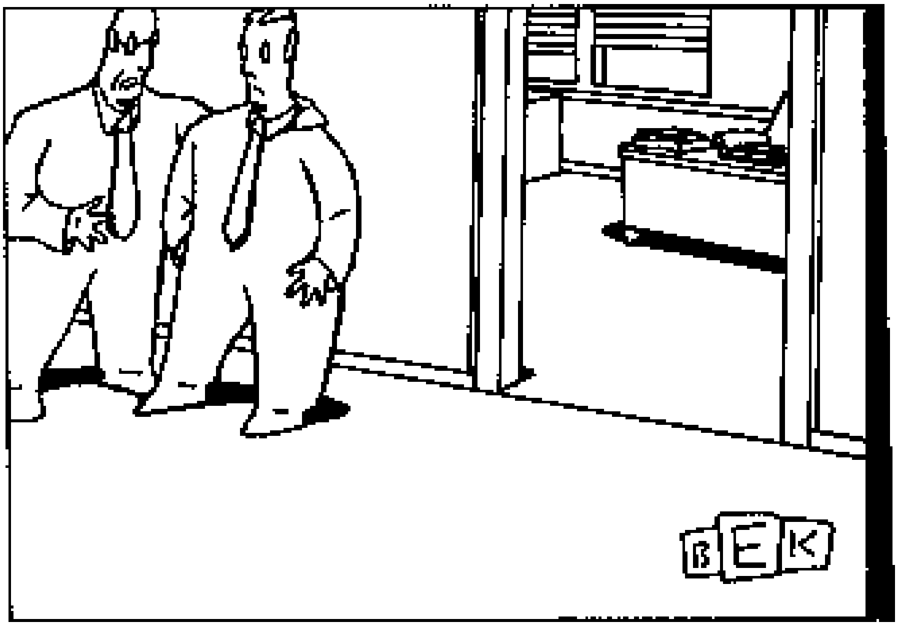
I myself live in a cancer cluster. A resident in my town—Newton, Massachusetts—became suspicious of a decades-old dump next to an elementary school after her son developed cancer. She went from door to door and turned up forty-two cases of cancer within a few blocks of her home. The cluster is being investigated by the state health department.

No doubt, one reason for the veritable cluster of cancer clusters in recent years is the widespread attention that cases like those in McFarland and Los Alamos received, and the ensuing increase in public awareness and concern. Another reason, though, is the way in which states have responded to that concern: they've made available to the public data on potential toxic sites, along with information from "cancer registries" about local cancer rates. The result has been to make it easier for people to find worrisome patterns, and, more and more, they've done so. In the late eighties, public-health departments were receiving between thirteen hundred and sixteen hundred reports of feared cancer clusters, or "cluster alarms," each year. Last year, in Massachusetts alone, the state health department responded to between three thousand and four thousand cluster alarms. Under public pressure, state and federal agencies throughout the country are engaging in "cancer mapping" to find clusters that nobody has yet reported.

A community that is afflicted with an unusual number of cancers quite naturally looks for a cause in the environment—in the ground, the water, the air. And correlations are sometimes found: the cluster may arise after, say, contamination of the water supply by a possible carcinogen. The problem is that when scientists have tried to confirm such causes, they haven't been able to. Raymond Richard Neutra, California's chief environmental health investigator and an expert on cancer clusters, points out that among hundreds of exhaustive, published investigations of residential clusters in the United States, not one has convincingly identified an underlying environmental cause. Abroad, in only a handful of cases has a neighborhood cancer cluster been shown to arise from an environmental cause. And only one of these cases ended with the discovery of an unrecognized carcinogen. It was in a Turkish village called Karain, where twenty-five cases of mesothelioma, a rare form of lung cancer, cropped up among fewer than eight hundred villagers. (Scientists traced the cancer to a mineral called erionite, which is abundant in the soil there.) Given the exceedingly poor success rate of such investigations, epidemiologists tend to be skeptical about their worth.

WHEN public-health investigators fail to turn up any explanation for the appearance of a cancer cluster, communities can find it frustrating, even suspicious. After all, these investigators are highly efficient in tracking down the causes of other kinds of disease clusters. "Outbreak" stories usually start the same way: someone has an intuition that there are just too many people coming down with some illness and asks the health department to investigate. With outbreaks, though, such intuitions are vindicated in case after case. Consider the cluster of American Legionnaires who came down with an unusual lung disease in Philadelphia in 1976; the startling number of limb deformities among children born to Japanese women in the sixties; and the appearance of rare *Pneumocystis carinii* pneumonia in five young homosexual men in Los Angeles in 1981. All these clusters prompted what are called "hot-pursuit investigations" by public-health authorities, and all resulted in the definitive identification of a cause: namely, *Legionella* pneumonitis, or Legionnaires' disease; mercury poisoning from contaminated fish; and H.I.V. infection. In fact, successful hot-pursuit investigations of disease clusters take place almost every day. A typical recent issue of the Centers for Disease Control's *Morbidity and Mortality Weekly Report* described a cluster of 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, whose suppliers fished the same tributaries of the Mississippi River.

What's more, for centuries scientists have succeeded in tracking down the causes of clusters of cancer that aren't residential. In 1775, the surgeon Percivall Pott discovered a cluster of scrotal-cancer cases among London chimney sweeps. It was common practice then for young boys to do their job naked, the better to slither down chimneys, and so high concentrations of carcinogenic coal dust would accumulate in the ridges of their scrota. Pott's chimney sweeps proved to be a classic example of



"Sometimes it's important to stop whatever break you're taking and just do the work."

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an "occupational" cluster. Scientists have also been successful in investigating so-called "medical" clusters. In the late nineteen-sixties, for example, the pathologist Arthur Herbst was surprised to come across eight women between the ages of fifteen and twenty-two who had clear-cell adenocarcinoma, a type of cervical cancer that had never been seen in women so young. In 1971, he published a study linking the cases to an anti-miscarriage drug called diethylstilbestrol, or DES, which the mothers of these women had taken during pregnancy. Subsequent studies confirmed the link with DES, which was taken by some five million pregnant women between 1938 and 1971. The investigation of medical and occupational cancer clusters has led to the discovery of dozens of carcinogens, including asbestos, vinyl chloride, and certain artificial dyes.

So why don't hot-pursuit investigations of neighborhood cancer clusters yield such successes? For one thing, many clusters fall apart simply because they violate basic rules of cancer behavior. Cancer develops when a cell starts multiplying out of control, and the process by which this happens isn't straightforward. A carcinogen doesn't just flip some cancer switch to "on." Cells have a variety of genes that keep them functioning normally, and it takes an almost chance combination of successive mutations in these genes—multiple "hits," as cancer biologists put it—to make a cell cancerous rather than simply killing it. A carcinogen provides one hit. Other hits may come from a genetic defect, a further environmental exposure, a spontaneous mutation. Even when people have been subjected to a heavy dose of a carcinogen and many cells have been damaged, they will not all get cancer. (For example, DES causes clear-cell adenocarcinoma in only one out of a thousand women exposed to it in utero.) As a rule, it takes a long time before a cell receives enough hits to produce the cancer, and so, unlike infections or acute toxic reactions, the effect of a carcinogen in a community won't be seen for years. Besides, in a mobile society like ours, cancer victims who seem to be clustered may not all have lived in an area long enough for their cancers to have a common cause.

To produce a cancer cluster, a carcinogen has to hit a great many cells in a great many people. A brief, low-level exposure to a carcinogen is unlikely to do the job. Raymond Richard Neutra has calculated that for a carcinogen to produce a sevenfold increase in the occurrence of a cancer (a rate of increase not considered particularly high by epidemiologists) a population would have to be exposed to seventy per cent of the maximum tolerated dose in the course of a full year, or the equivalent. "This kind of exposure is credible as part of chemotherapy or in some work settings," he wrote in a 1990 paper, "but it must be very rare for most neighborhood and school settings." For that reason, investigations of occupational cancer clusters have been vastly more successful than investigations of residential cancer clusters.

Matters are further complicated by the fact that cancer isn't one disease. What turns a breast cell into breast cancer isn't what turns a white blood cell into leukemia: the precise combination of hits varies. Yet some clusters lump together people with tumors that have entirely different biologies and are unlikely to have the same cause. The cluster in McFarland, for example, involved eleven children with nine kinds of cancer. Some of the brain-cancer cases in the Los Alamos cluster were really cancers of other organs which had metastasized to the brain.

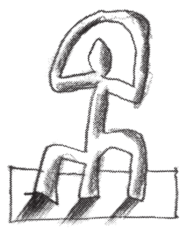
If true neighborhood clusters—that is, local clusters arising from a common environmental cause—are so rare, why do we see so many? In a sense, we're programmed to: nearly all of them are the result of almost irresistible errors in perception. In a pioneering article published in 1971, the cognitive psychologists Daniel Kahneman and Amos Tversky identified a systematic error in human judgment which they called the Belief in the Law of Small Numbers. People assume that the pattern of a large population will be replicated in all its subsets. But clusters will occur simply through chance. After seeing a long sequence of red on the roulette wheel, people find it hard to resist the idea that black is "due"—or else they start to wonder whether the wheel is rigged. We assume that a sequence of R-R-R-R-R-R is somehow less random than, say, R-R-B-R-B-B. But the two sequences are equally likely. (Casinos make a lot of money from the Belief in the Law of Small Numbers.) Truly random patterns often don't appear random to us. The statistician William Feller studied one classic example. During the Germans' intensive bombing of South London in the Second World War, a few areas were hit several times and others were not hit at all. The places that were not hit seemed to have been deliberately spared, and, Kahneman says, people became convinced that those places were where the Germans had their spies. When Feller analyzed the statistics of the bomb hits, however, he found that the distribution matched a random pattern.

Daniel Kahneman himself was involved in a similar case. “During the Yom Kippur War, in 1973, I was approached by people in the Israeli Air Force,” he told me. “They had two squads that had left base, and when the squads came back one had lost four planes and the other had lost none. They wanted to investigate for all kinds of differences between the squadrons, like whether pilots in one squadron had seen their wives more than in the other. I told them to stop wasting their time.” A difference of four lost planes could easily have occurred by chance. Yet Kahneman knew that if Air Force officials investigated they would inevitably find some measurable differences between the squadrons and feel compelled to act on them.

Human beings evidently have a deep-seated tendency to see meaning in the ordinary variations that are bound to appear in small samples. For example, most basketball players and fans believe that players have hot and cold streaks in shooting. In a paper entitled “The Hot Hand in Basketball,” Tversky and two colleagues painstakingly analyzed the shooting of individual players in more than eighty games played by the Philadelphia 76ers, the New Jersey Nets, and the New York Knicks during the 1980-81 season. It turned out that basketball players—even notorious “streak shooters”—have no more runs of hits or misses than would be expected by chance. Because of the human tendency to perceive clusters in random sequences, however, Tversky and his colleagues found that “no amount of exposure to such sequences will convince the player, the coach, or the fan that the sequences are in fact random. The more basketball one watches and plays, the more opportunities one has to observe what appears to be streak shooting.”

In epidemiology, the tendency to isolate clusters from their context is known as the Texas-sharpshooter fallacy. Like a Texas sharpshooter who shoots at the side of a barn and then draws a bull’s-eye around the bullet holes, we tend to notice cases first—four cancer patients on one street—and then define the population base around them. With rare conditions, such as Haff disease or mercury poisoning, even a small clutch of cases really would represent a dramatic excess, no matter how much Texas sharpshooting we did. But most cancers are common enough that noticeable residential clusters are bound to occur. Raymond Richard Neutra points out that, given a typical registry of eighty different cancers, you could expect twenty-seven hundred and fifty of California’s five thousand census tracts to have statistically significant but perfectly random elevations of cancer. So if you check to see whether your neighborhood has an elevated rate of a specific cancer, chances are better than even that it does—and it almost certainly won’t mean a thing. Even when you’ve established a correlation between a specific cancer and a potential carcinogen, scientists have hardly any way to distinguish the “true” cancer cluster that’s worth investigating from the crowd of cluster impostors.

One helpful tip-off is an extraordinarily high cancer rate. In Karain, Turkey, the incidence of mesothelioma was more than *seven thousand times* as high as expected. In even the most serious cluster alarms that public-health departments have received, however, the cancer rate has been nowhere near that high. (The lawyer Jan Schlichtmann, of “Civil Action” fame, is now representing victims of a cancer cluster in Dover Township, New Jersey, where the childhood-cancer rate is thirty per cent higher than expected.)



This isn’t to say that carcinogens in the local environment can’t raise cancer rates; it’s just that such increases disappear in all the background variation that occurs in small populations. In larger populations, it’s a different story. The 1986 Chernobyl disaster exposed hundreds of thousands of people to radiation; scientists were able to establish that it caused a more than one-hundred-fold increase in thyroid cancer among children years later. By contrast, investigating an isolated neighborhood cancer cluster is almost always a futile exercise. Investigators knock on doors, track down former residents, and check medical records. They sample air, soil, and water. Thousands, sometimes millions, of dollars are spent. And, with all those tests, correlations inevitably turn up. Yet, years later, in case after case, nothing definite is confirmed.

“The reality is that they’re an absolute, total, and complete waste of taxpayer dollars,” says Alan Bender, an epidemiologist with the Minnesota Department of Health, which investigated more than a thousand cancer clusters in the state between 1984 and 1995. The problem of perception and politics, however, remains. If you’re a public health official, try explaining why a dozen children with cancer in one neighborhood doesn’t warrant investigation. According to a national study, health departments have been able to reassure people by education in more than seventy per cent of cluster alarms. Somewhere between one and three per cent of alarms, however, result in expensive on-site investigations. And the cases that are investigated aren’t even the best-grounded ones: they are the cases pushed by the media, enraged citizens, or politicians. “Look, you can’t just kiss people off,” Bender says. In fact, Minnesota has built such an effective public-response apparatus that it has not needed to conduct a formal cluster investigation in three years.

Public-health departments aren’t lavishly funded, and scientists are reluctant to see money spent on something that has proved to be as unproductive as neighborhood cluster alarms or cancer mapping. Still, public confidence is poorly served by officials who respond to inquiries with a scientific brushoff and a layer of bureaucracy. To be part of a cancer cluster is a frightening thing, and it magnifies our ordinary response when cancer strikes: we want to hold something or someone responsible, even allocate blame. Health officials who understand the fear and anger can have impressive success, as the ones in Minnesota have shown. But there are times when you cannot maintain public trust without acting on public concerns. Science alone won’t put to rest questions like the one a McFarland mother posed to the Los Angeles *Times:* “How many more of our children must die before something is done?” ♦