Probing Disease Clusters: Easier to Spot Than Prove

By GINA KOLATA

THE trouble began when Bobbie Gallagher noticed that her 2-year-old daughter was behaving strangely, obsessively spinning and scrupulously setting her toys in rows. Alanna Gallagher turned out to have autism, a rare neurological disorder of unknown cause.

So did Alanna's little brother. So did about 40 other children who lived in the Gallaghers' town of Brick, N.J., near the seashore.

The parents in Brick were alarmed. On average, 1 child in 500 is autistic; in the town, the figure is about three times that.

But what does it mean? Does Brick have toxic chemicals in the water, pollutants in the air?

The problem, scientists say, may be impossible to resolve. It was yet another instance of a phenomenon that makes many statisticians shudder. It was a disease cluster — the Boy Who Cried Wolf of epidemiology.

Every time a disease cluster turns up, communities worry, scientists scramble for a cause and, as in the new movie based on Jonathan Harr's 1995 book, "A Civil Action" (Random House), about a leukemia cluster in Woburn, Mass., lawyers start suing. Yet over and over again, despite years — sometimes decades — of efforts to link the disease with a cause, scientists usually come up empty handed.

It can sound paradoxical. Here are unusual numbers of people with a disease. Toxic chemicals are everywhere, and many of them cause cancers and other diseases in laboratory animals. Why should it be so hard to find a cause?

Some disease clusters have been successfully linked to toxins: Coal miners got black lung disease; asbestos workers got mesothelioma. Workers cleaning containers where polyvinyl chloride was synthesized, breathing in fumes, got cancer of the blood vessels of the liver until machines replaced them.

But these examples of proven cause and effect are the rare exceptions, statisticians say. And they have two things in common: The chemical exposure was enormous, and the disease was extraordinarily rare.

Most disease clusters are very different. Autism, breast cancer and leukemia are fairly common. And even when there does seem to be an unusually high incidence of a disease, the search for a chemical basis usually turns up minute amounts of toxic substances that also are found in other places where there are no clusters. In other words, linking the suspect chemicals to the disease can be very hard. It can also be difficult to know if a cluster is anything more than a chance occurrence. And chance is hard to ignore.

Clusters will naturally appear even when events occur at random, said Dr. Persi Diaconis, a statistician at Stanford University. "There was a famous example of this when bombs were hitting London during World War II," he said. "People were sure they were targeting individual places and they made up the most elaborate scenarios" to explain how the bomb targets were selected. But in the end, when the pattern was analyzed, the bombing turned out to be random.

ANOTHER problem is how to draw the boundaries of a cluster.

Dr. James Robins, a statistician at Harvard University's School of Public Health, said it is a natural tendency to draw boundaries around groups of events to make clusters happen. If there are three children with cancer on a single block, you may draw your circle around the block — making that a cluster — rather than around the town as a whole, which may show no cluster.

Say you do find a cluster. Unless you identify, say, black lung or mesothelioma, statisticians say, the next question is: How can you decide if the cluster was caused by blind random clumpings of cases, with no environmental cause, or by a toxin in the environment?

Why would only one town have a disease cluster, some experts ask, while other places with the same pollutants in the air or water do not? One possibility might be an unidentified chemical in a mix of pollutants that is unique to the town. But that, of course, raises questions of how to find it.

Finally, there is the indirect exposure problem. If there is no direct link between chemicals and a disease, the tendency is to look for other exposures. Could the fathers, for example, have had their sperm affected when they were growing up? Or could the mothers have been exposed to chemicals during pregnancy? Some statisticians say that if people look hard enough and slice the data enough ways and an association will emerge. What it means is another question.

Others are optimistic. Suzanne Condon, the director of the bureau of environmental health assessment at the Massachusetts Department of Public Health, said that in an unpublished study her department found that in the Woburn case, women who drank water from certain wells when they were pregnant were more likely to have children who developed leukemia. "We believe this sheds a lot of light on what happened in Woburn," she said. W. R. Grace, which was accused along with Beatrice Foods of dumping chemicals in a way that allowed them to reach the water supply, paid $8 million into a settlement fund. Both companies agreed to finance an expensive cleanup plan.

The Massachusetts' health department, however, warned on its Web page, "Findings should be interpreted with caution due to the limitations of conducting statistical analyses on small populations."

THAT may not be what people want to hear, statisticians concede. "People — and I, too — find it hard to accept that it is just random chance that brought this horrible consequence," said Dr. David Freedman, a statistician at the University of California at Berkeley.

Some statisticians ask whether it is worthwhile to keep pouring money and effort into searches for clusters and searches to explain them.

"The question is, at what point do you say we've see too many like this?" Dr. Robins asked. "Huge amounts of money" have gone to study disease clusters where the suspected cause was tiny amounts of chemicals, he added, and so far, "nothing has come of it."