Week 13. The Four Corners outbreak of Hantavirus. Visit http://www.cdc.gov/ncidod/diseases/hanta/hps/noframes/outbreak.htm#Outbreak to see the article with pictures & links, or just read the article below:

Tracking a Mystery Disease: 
The Detailed Story of Hantavirus Pulmonary Syndrome

The "First" Outbreak

In May 1993, an outbreak of an unexplained pulmonary illness occurred in the southwestern United States, in an area shared by Arizona, New Mexico, Colorado and Utah known as "The Four Corners." A young, physically fit Navajo man suffering from shortness of breath was rushed to a hospital in New Mexico and died very rapidly.

While reviewing the results of the case, medical personnel discovered that the young man's fiancee had died a few days before after showing similar symptoms, a piece of information that proved key to discovering the disease. As Dr. James Cheek of the Indian Health Service (IHS) noted, "I think if it hadn't been for that initial pair of people that became sick within a week of each other, we never would have discovered the illness at all."

An investigation combing the entire Four Corners region was launched by the New Mexico Office of Medical Investigations (OMI) to find any other people who had a similar case history. Within a few hours, Dr. Bruce Tempest of IHS, working with OMI, had located five young, healthy people who had all died after acute respiratory failure.

A series of laboratory tests had failed to identify any of the deaths as caused by a known disease, such as bubonic plague. At this point, the CDC Special Pathogens Branch was notified. CDC, the state health departments of New Mexico, Colorado and Utah, the Indian Health Service, the Navajo Nation, and the University of New Mexico all joined together to confront the outbreak.

During the next few weeks, as additional cases of the disease were reported in the Four Corners area, physicians and other scientific experts worked intensively to narrow down the list of possible causes. The particular mixture of symptoms and clinical findings pointed researchers away from possible causes, such as exposure to a herbicide or a new type of influenza, and toward some type of virus. Samples of tissue from patients who had gotten the disease were sent to CDC for exhaustive analysis. Virologists at CDC used several tests, including new methods to pinpoint virus genes at the molecular level, and were able to link the pulmonary syndrome with a virus, in particular a previously unknown type of hantavirus.

Researchers Launch Investigations to Pin Down the Carrier of the New Virus

Researchers knew that all other known hantaviruses were transmitted to people by rodents, such as mice and rats. Therefore, an important part of their mission was to trap as many different species of rodents living in the Four Corners region as possible to find the particular type of rodent that carried the virus. From June through mid-August of 1993, all types of rodents were trapped inside and outside homes where people who had hantavirus pulmonary syndrome had lived, as well as in piñon groves and summer sheep camps where they had worked. Additional rodents were trapped for comparison in and around nearby households as well. Taking a calculated risk, researchers decided not to wear protective clothing or masks during the trapping process. "We didn't want to go in wearing respirators, scaring...everybody," John Sarisky, an Indian Health Service environmental disease specialist said. However, when the almost 1,700 rodents trapped were dissected to prepare samples for analysis at CDC, protective clothing and respirators were worn.

Photo: Protective gear, such as gloves, gown, and respirator, were worn during activities that required dissection.
Among rodents trapped, the deer mouse (*Peromyscus maniculatus*) was found to be the main host to a previously unknown type of hantavirus. Since the deer mouse often lives near people in rural and semi-rural areas—in barns and outbuildings, woodpiles, and inside people's homes—researchers suspected that the deer mouse might be transmitting the virus to humans. About 30% of the deer mice tested showed evidence of infection with hantavirus. Tests also showed that several other types of rodents were infected, although in lesser numbers.

The next step was to pin down the connection between the infected deer mice and households where people who had gotten the disease lived. Therefore, investigators launched a case-control investigation. They compared "case" households, where people who had gotten the disease lived, with nearby "control" households. Control households were similar to those where the case-patients lived, except for one factor: no one in the control households had gotten the disease.

The results? First, investigators trapped more rodents in case households than in control households, so more rodents may have been living in close contact with people in case households. Second, people in case households were more likely than those in control households to do cleaning around the house or to plant in or hand-plow soil outdoors in fields or gardens. However, it was unclear if the risk for contracting HPS was due to performing these tasks, or with entering closed-up rooms or closets to get tools needed for these tasks.

In November 1993, the specific hantavirus that caused the Four Corners outbreak was isolated. The Special Pathogens Branch at CDC used tissue from a deer mouse that had been trapped near the New Mexico home of a person who had gotten the disease and grew the virus from it in the laboratory. Shortly afterwards and independently, the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) also grew the virus, from a person in New Mexico who had gotten the disease as well as from a mouse trapped in California.

The new virus was called Muerto Canyon virus—later changed to Sin Nombre virus (SNV)—and the new disease caused by the virus was named hantavirus pulmonary syndrome, or HPS.

The isolation of the virus in a matter of months was remarkable. This success was based on close cooperation of all the agencies and individuals involved in investigating the outbreak, years of basic research on other hantaviruses that had been conducted at CDC and USAMRIID, and on the continuing development of modern molecular virologic tests. To put the rapid isolation of the Sin Nombre virus in perspective, it took several decades for the first hantavirus discovered, the Hantaan virus, to be isolated.

*Thin-section electron micrograph of Sin Nombre virus isolate, a causative agent of hantavirus pulmonary syndrome (HPS). From the 1993 outbreak of HPS in the southwestern United States. Electron micrograph.*

**HPS Not Really a New Disease**

As part of the effort to locate the source of the virus, researchers located and examined stored samples of lung tissue from people who had died of unexplained lung disease. Some of these samples showed evidence of previous infection with Sin Nombre virus—indicating that the disease had existed before the "first" known outbreak—it simply had not been recognized!

Other early cases of HPS have been discovered by examining samples of tissue belonging to people who had died of unexplained adult respiratory distress syndrome. By this method, the earliest known case of HPS that has been confirmed has been the case of a 38-year-old Utah man in 1959.

Interestingly, while HPS was not known to the epidemiologic and medical communities, there is evidence that it was recognized elsewhere. The Navajo Indians, a number of whom contracted HPS during the 1993 outbreak, recognize a similar disease in their medical traditions, and actually associate its occurrence with mice. As
strikingly, Navajo medical beliefs concur with public health recommendations for preventing the disease.

**Why Did the Outbreak Occur in the Four Corners Area?**

But why this sudden cluster of cases? The key answer to this question is that, during this period, there were suddenly many more mice than usual. The Four Corners area had been in a drought for several years. Then, in early 1993, heavy snows and rainfall helped drought-stricken plants and animals to revive and grow in larger-than-usual numbers. The area's deer mice had plenty to eat, and as a result they reproduced so rapidly that there were ten times more mice in May 1993 than there had been in May of 1992. With so many mice, it was more likely that mice and humans would come into contact with one another, and thus more likely that the hantavirus carried by the mice would be transmitted to humans.

**Person-to-Person Spread of HPS Decided Unlikely**

"Although person-to-person spread [of HPS] has not been documented with any of the other known hantaviruses, we were concerned [during this outbreak] because we were dealing with a new agent," said Charles Vitek, a CDC medical investigator.

Researchers and clinicians investigating the ongoing outbreak were not the only groups concerned about the disease. Shortly after the first few HPS patients died and it became clear that a new disease was affecting people in the area, and that no one knew how it was transmitted, the news media began extensive reporting on the outbreak. Widespread concern among the public ensued.

Unfortunately, the first victims of the outbreak were Navajo. News reports focused on this fact, and the misperception grew that the unknown disease was somehow linked to Navajos. As a consequence, Navajos found themselves at the center of intense media attention and the objects of the some people's fears.

By later in the summer of 1993, the media frenzy had quieted somewhat, and the source of the disease was pinpointed. Researchers determined that, like other hantaviruses, the virus that causes HPS is not transmitted from person to person the way other infections, such as the common cold, may be. The exception to this is an outbreak of HPS in Argentina in 1996. Evidence from this outbreak suggests that strains of hantaviruses in South America may be transmissible from person to person.

To date, no cases of HPS have been reported in the United States in which the virus was transmitted from one person to another. In fact, in a study of health care workers who were exposed to either patients or specimens infected with related types of hantaviruses (which cause a different disease in humans), none of the workers showed evidence of infection or illness.

**HPS Since the First Outbreak**

After the initial outbreak, the medical community nationwide was asked to report any cases of illness with symptoms similar to those of HPS that could not be explained by any other cause. As a result, additional cases have been reported.

Since 1993, researchers have discovered that there is not just one hantavirus that causes HPS, but several. In June 1993, a Louisiana bridge inspector who had not traveled to the Four Corners area developed HPS. An investigation was begun. The patient's tissues were tested for the presence of antibodies to hantavirus. The results led to the discovery of another hantavirus, named Bayou virus, which was linked to a carrier, the rice rat (*Oryzomys palustris*). In late 1993, a 33-year-old Florida man came down with HPS symptoms; he later recovered. This person also had not traveled to the Four Corners area. A similar investigation revealed yet another hantavirus, named the Black Creek Canal virus, and its carrier, the cotton rat (*Sigmodon hispidus*). Another case occurred in New York. This time, the Sin Nombre-like virus was named New York-1, and the white-footed mouse, *Peromyscus leucopus,*
was implicated as the carrier.

More recently, cases of HPS stemming from related hantaviruses have been documented in Argentina, Brazil, Canada, Chile, Paraguay, and Uruguay, making HPS a pan-hemispheric disease.

**References**

Information for this page was developed using the CDC video *Preventing Hantavirus Disease* and resource articles listed in the bibliography.

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Special Pathogens Branch  
Division of Viral and Rickettsial Diseases  
National Center for Infectious Diseases  
Centers for Disease Control and Prevention  
U.S. Department of Health and Human Services

**Questions.**

1. In May 1993, two healthy young people died within a few days of each other of an unknown pulmonary disease. What was their relationship to one another?

2. Rodents, suspected to be carriers of the new hantavirus, were collected from “case” and “control” households. Case & control households were matched and considered similar except for what one factor?

3. In retrospect, Hantavirus pulmonary syndrome existed before 1993, but was not recognized. In what year was the earliest confirmed case?

4. Why was there an outbreak of HPS in 1993 in the Four Corners area?

5. Is the *Sin nombre* hantavirus the only hantavirus found in the U.S.?