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# Nevada Public Health: Hantavirus with Contributions by Drs. Stephen St. Jeor and T. Brian Callister

**By Chelsea Isom, Medical Student at UNSOM**

Disease with symptoms similar to the present day Hantavirus has been described in China since 1000 AD. It manifested in frightening ways, with conjunctival hemorrhages, petechial rashes, edema, cutaneous flushing, renal failure, and death. Even with high mortality and unknown cause, the disease was thought to be self-limiting and not spread by human contact. In the 1950s, this ancient disease probably reappeared in 3,200 American soldiers in Korea. Doctors described it as hemorrhagic fever with renal symptoms (HFRS). It would be over 25 years before its cause, Hantavirus, would become elucidated and found in the United States. The virus was named after the Hantaan River in Korea, the site of the 1950s outbreak, but when much later, it occurred in the United States, it became the "New World Hantavirus." This disease presented with pulmonary symptoms and not renal symptoms, and hence the name, Hantavirus Pulmonary Syndrome (HPS). By 2009, over 700 people were diagnosed in America. Nevada State Medical Association President Dr. Brian Callister documented Nevada's first case, and Dr. Stephen St. Jeor at the University of Nevada School of Medicine led the way with research. The following narrative tells the history of Hantavirus, reviews Callister's patients, and details St. Jeor's research.

In the 1950s, American soldiers stationed in Korea became ill with hemorrhagic renal syndrome with 20% mortality. Doctors recognized that all of the soldiers had the same disease, but efforts to identify its cause was unsuccessful. In 1978, Hantavirus was isolated from a striped field mouse, and doctors concluded that Hantavirus had caused HFRS in the American soldiers. A survey of rodents in the United States determined that different rodents were hosts to different strains of Hantavirus. The common rat carries Seoul Hantavirus, and the meadow vole carries Prospect Hill Hantavirus. The survey suggested that Hantavirus in the U.S. had evolved within separate rodent species. After these revelations, researchers reviewed patients in the Centers for Disease Control and Prevention's (CDC) database and found 3 patients in Boston with a mild hemorrhagic disease, and several patients on dialysis with antibodies to Hantavirus. This was just the beginning.

On May 14, 1993, the New Mexico Department of Health reported 3 unexplained deaths among previously healthy individuals. Two were engaged to be married to one another and died within days of each other. Later, the Indian Health Services identified 5 patients who died from acute respiratory failure in Four Corners where New Mexico, Arizona, Utah, and Colorado meet. Investigating agencies could not find the cause, similar to the situation that had occurred in Korea. However, within 8 weeks, 10 people died from acute pulmonary failure in Four Corners. All tests were negative,

but CDC scientists using a test developed by the U.S. Army found antibodies to the Hantavirus. Researchers also found the virus in mouse excrement, and Hantavirus nucleic acid sequences were then detected in a deer mouse in the home of the first deceased couple. The new world virus was named Four Corners where it was discovered, but local residents rejected the notoriety. The virus was subsequently renamed Hantavirus Sin Nombre, which translates to "Hantavirus Without Name." Once the infectious agent was discovered, CDC researchers took steps to determine risk factors and focused on patients in Four Corners with unexplained acute respiratory distress or pulmonary interstitial infiltrates.

Less than 3 months after the 1993 cases in Four Coroners, Nevada's Dr. Callister reported that two patients with Hantavirus in Nevada were treated by him, Chris Ward, D.O., and Hank Hayes, PA. The first Nevada patient in July 1993, was a 24 year-old housewife from Round Mountain, who presented in Tonopah with acute respiratory distress. She had a one week history of fever, myalgia, nausea, and malaise. When admitted, she had bilateral interstitial infiltrates consistent with Adult Respiratory Distress Syndrome (ARDS). In addition, she had antibodies to Hantavirus. Up until then, clinicians treated Hantavirus with intravenous fluid and **antiviral Ganciclovir**, but they had 90% mortality. On the other hand, Callister felt that this disease was secondary to an overactive immune response, and treated his patient with high flow oxygen, aggressive diuresis, and high dose corticosteroids.

One month later, a 51 year-old man from Tonopah developed fever, myalgia, nausea, and vomiting over 6 days. Within 12 hours after admission, he had rapidly progressing interstitial infiltrates, shortness of breath, and hypoxemia. He also had high levels of antibodies to Hantavirus. Once again, Dr. Callister treated the patient with oxygen, diuresis, and corticosteroids. Both patients fully recovered.

Dr. Callister related the following noteworthy facts about his patients: 1. Both were treated at Nye Regional Medical Center in Tonopah, even though physicians in Arizona and New Mexico criticized Callister for not referring them. Yet, both patients survived while referred patients had 90% mortality. 2. Both patients lived in absolutely filthy living conditions conductive to mice propagation. 3. A guiding principle for Callister's treatment was his opinion that adults with intact immune systems develop ARDS. For example, babies, elderly people, and immuno-compromised individuals rarely develop the syndrome suggesting that the life threatening complications of ARDS are indeed due to an over active immune response rather than viral toxemia. National guidelines now include corticosteroids as a treatment option.

After Dr. Callister's experience, by December 1994, there were 108 patients with HPS, and over one half were from Four Corners. Most of these illnesses appeared in spring/early summer, which suggested environmental/ seasonal factors. Researchers did not know whether this was a new disease or reemergence of an old disease. It turns out the second hypothesis is true.

In 1994, Dr. Stephen St. Jeor at the School of Medicine became interested in Sin Nombre Hantavirus. He learned about the virus from a friend, Dr. Stuart Nichole, who was in the special pathogen branch of the CDC. Dr. Nichole and colleagues discovered the virus in a deer mouse. St. Jeor and Nichole received a grant to determine virus transmission and investigate a possible vaccine. St. Jeor found the virus in 40% of deer mice in Nevada. He also found that workers at Truckee Meadows Community College in Reno had a terrarium of deer mice in their lunchroom. Approximately 20% of the mice harbored Hantavirus; however, not one worker had the virus antibody despite the fact that a ventilation fan blew across the terrarium into the lunchroom. Even more interesting, the deer mice had been together for several months, but they did not have close to a 100% infection rate as might be expected in animals living together in a cage.

In a closer-to-home tragedy, in the early 1990s, two faculty members in the College of Agriculture at UNR contracted HPS; one recovered but sadly the other died. When one looks at the difference in transmission statistics in the United States, the presence of Hantavirus in at-risk-individuals (forest workers and mammalogists) is very low compared to the carrier rate of the virus in deer mice. However, at-risk-individuals in Europe have a much higher infection rate than U.S workers adding to the mystery in differences in spread and immunity. Initially, evidence of the virus was found in salivary glands and kidneys of the rodents, but it could not be grown in the laboratory. Later, CDC scientists were able to isolate Hantavirus from deer mice but not from humans.

Dr. St. Jeor's study of the New World Hantavirus stretched from Reno's San Rafael Park to an Argentinean ski resort, Baraloche, where the strain is known as the Andes Hantavirus. It is the only Hantavirus that is proven to pass from human to human. St. Jeor is trying to discover why the virus only occasionally affects humans and to determine how the virus is spread between rodents. In the U.S., the total number of reported cases is approximately 400, the number of cases in South America is over 1,000, and worldwide there are about 100,000 cases per year. Dr. St. Jeor is also working on the

development of a vaccine, but because of the small number of human cases, pharmaceutical companies consider it to be financially impractical.

On another level, researchers questioned why the 1993 Hantavirus had reemerged in greater numbers than in previous years. They desired to determine factors that would predict future outbreaks. It was discovered that rain enhanced food supply producing an increase in deer mice. In 1997, there was a significant early rainfall, suggesting to scientists the possibility of a Hantavirus outbreak. The department of health warned Four Corners authorities about the increased risk. Despite these warnings, the number of patients increased from 6 in 1995-97 to 33 in 1998, which supported the precipitation theory.

The Sin Nombre strain of Hantavirus is present in the United States, and while it may not be widely reported in the news, it is still taking lives. In 2010, five children from Four Corners developed HPS and one died. All 5 lived or played in areas near deer mice. The Sin Nombre virus is in Nevada, but if it will ever cause a large number of infections like the Old World HHRS strain is uncertain. One thing is clear, to prevent this disease one needs to avoid areas where rodent's droppings are present or can be aerosolized.

The HPS virus-carrying deer mouse is brown, unlike the common gray colored house mouse found in homes throughout the world. On the other hand, there are other rodents that carry Hantaviruses associated with human infections, such as the Prospect Hill virus that is found in meadow voles throughout the world. The best advice is to avoid contact with all mice and voles.

**Dr. Brian Callister** finished his residency at UCLA, and Nye Regional Medical Center recruited him with financial aid from the Rural Nevada Health Service Corps to locate to Tonopah. He knew Tonopah from re-fueling stops in the small airplane when he flew as a child with his surgeon father. During 4 years of practice in Tonopah, he cared for the patients with Hantavirus and also became friends with physicians from Reno. When he decided to move to Reno, it was because of his relationships and respect for those Reno physicians, some of whom had flown into Tonopah regularly to see patients for him.

**Dr. Stephen St. Joer**, when a graduate student at the University of Utah, studied mechanisms by which arthropod-born encephalitis viruses, after being dormant, reappear in the spring. This research was instrumental in stimulating his interest in viruses found in nature. He worked with human herpes viruses for 30 years, both at the Pennsylvania State University's Hershey Medical Center and later at the University of Nevada School of Medicine, where he was working when the outbreak of Hantaviruses in Four Corners renewed his interest in the spread of viruses. When his colleague, Stuart Nichol, who had worked at UNR's College of Agriculture and the School of Medicine, moved to the CDC, St. Jeor remained friends with him. They later agreed to jointly study the new Hantavirus, which reignited Dr. St. Jeor's interest in the survival of viruses in nature.

## Dr. Oscar Johnstone's Widow's Chloroform Death

**By Anton P. Sohn, M.D.**

In the spring 2011 issue of *Greasewood Tablettes,* we commented on Dr. O. P. Johnstone's brief career in pathology in Reno. The article stated he was born in Missouri, but a later history noted he was born in Iowa in 1871. After graduating in 1905 from Rush Medical College, he instructed at Columbia University, practiced in Pittsburgh, and was an instructor at the Denver College of Medicine. In 1909, Dr. Oscar Percy Johnstone came to Reno to be one of Nevada's first pathologists and was in charge of the State Hygienic Laboratory. He resigned after five years to associate with Dr. W. L. Samuels in a clinic at the Masonic Temple.

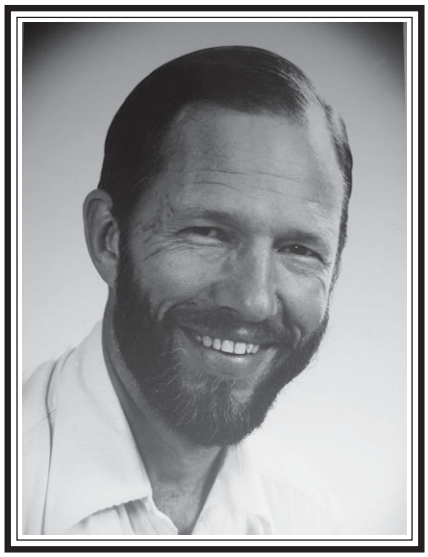
At 1:00 PM, November 9, 1916, Dr. Johnstone was found dead sitting in his office chair. An office attendant, Miss Ada Hussman, had noticed him two hours earlier sitting in the exact same position and thought him to be asleep. Doctors S. K. Morrison and Mullins did the autopsy and assigned the cause of death to be atheromatous degeneration of the arteries of the heart. Johnstone was considered to be one of the leading authorities "on the West Coast in bacteriology and pathological diagnosis." (NSJ, Nov. 10, 1916) He was a member of the Nevada State Board of Health and was vice-president of the Washoe County Medical Society.

Two weeks after Dr. Johnstone's death his widow, Bertha Shryock Johnstone, administered chloroform to kill herself and their three children, Eric—six years, Thorwald—four years, and William—less than six

## Remembering Prominent Faculty Member Dr. John N. Chappel

**By Robert Daugherty, M.D.**

Dr. John Chappel died on March 9, 2011, at home of Parkinson's Disease associated with Lewy Body Disease. John was born in 1931 in Canada and graduated with an M.D. from the University of Alberta. He later earned a Masters of Public Health from Harvard and did a residency in psychiatry at the University of Chicago. He came to University of Nevada School of Medicine (UNSOM) in 1974 and served with distinction until he retired in 2009.



*Dr. John Chappel 1931 - 2011*

**Bob Daugherty,** Emeritus Dean, UNSOM—I will always remember that John, as chair of the Dean's search committee when I interviewed, was very gracious and kind. He was the very first physician in Nevada to become interested in aiding physicians who experienced personal problems with alcohol and drug abuse. Dr. Chappel was a tremendous asset to his community, his church, and our university. The following comments made to me tell of his success, inspiration, and influence.

**Bud Baldwin**, Professor Emeritus, UNSOM—I think first and foremost of his integrity. He was his own man, strong within, quiet, subtle sense of whimsical and insightful humor, utterly and thoroughly knowledgeable, compassionate, clinically competent, steady as a rock….

**Grant Miller,** Professor Emeritus, UNSOM—There were a number of VA patients who I felt were abusing the system and that troubled me. Since I didn't enjoy feeling this way, I went to John and he simply said: "Trust until you have reason to distrust." This simple and supportive statement stuck with me and is a good way to live.

**Ira Pauley,** Emeritus Psychiatry Chair, UNSOM—He was a major reason why I accepted the chair of the department. John was most interested in his teaching role, which centered on his interest in alcoholism and substance abuse. As a result, we now have a generation of Nevada physicians who have the appropriate attitude and concern for the multitude of patients they see with these all too common medical problems.

**Richard Pugh,** Former CEO, NSMA—The positive results of his intervention treatment for physicians in Reno and throughout the state are legend.

**Darlene Galleron,** Former CEO, WCMS—Dr. Chappel was an inspiration to physicians who experienced impairment in their practices and private lives. He was the leader in forming the WCMS committee to treat impaired physicians.

**Jerry May,** Professor Emeritus, UNSOM—John possessed a rather unique and delightful personal quality. He had the ability to blend together elements in his life to become an outstanding physician, psychiatrist, teacher, and clinician. He was highly respected for his understanding and helping those with substance abuse.

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