# Hantavirus Pulmonary Syndrome

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**KEYWORDS**

• Hantavirus • Pneumonia • Viral pneumonia
• Acute respiratory failure • Hemorrhagic fever

Hantavirus pulmonary syndrome (HPS), a disease now known to have been present for centuries, if not millennia, in the Americas was discovered only 16 years ago in the southwestern United States.[1] Two young long-distance runners who lived together in the New Mexican desert fell victim in early May, 1993, to what seemed to be a rapidly progressive pulmonary infection, and both of them died within days. The unusual circumstance of two highly fit individuals succumbing in this manner, especially in the spring, led health officials to investigate the cause and initiate surveillance for other, similar cases. It soon became evident that they were in the midst of an outbreak of a seriously deadly infectious agent and that the syndrome was one that had not been previously described by the medical community.

The causative agent for the illness was soon (<6 weeks after the index cases were identified) determined to be an unidentified North American member of the *Hantavirus* genus. The clinical syndrome caused by this agent, ultimately named *Sin Nombre virus* (SNV), came to be called the *hantavirus pulmonary syndrome*. This designation distinguished it from previously described hantaviral illnesses, which were characterized as hemorrhagic fever with renal syndrome (HFRS). Early in the course of events it became evident that cardiac function, and respiratory function, are markedly impaired by infection with this virus. For that reason, some authors have adopted the moniker *Hantavirus cardiopulmonary syndrome*. Although that name certainly has logic, the Centers for Disease Control and Prevention (CDC) continue to refer to the illness as HPS, as does this article.

## HANTAVIRUSES

The hantaviruses are an enveloped genus of the family Bunyaviridae. Virions are spherical and encapsulated by a bilayered phospholipid membrane. The composition of each virion is greater than 50% protein, 20% to 30% lipid, and 2% to 7% carbohydrate,

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making them easily disrupted with heat, detergents, organic solvents, and hypochlorite solutions.[2] Diameters range from 71 to 200 nm, with an average of approximately 100 nm.[3] The genome consists of three single-stranded, negative-sense RNA segments: long (L), medium (M), and short (S). Each of the segments encodes only one protein. The S segment codes for the nucleocapsid protein (N protein), the M segment codes for the viral envelope glycoproteins (two proteins, G1 and G2), and the L segment codes for viral transcriptase.[4] The 3′ terminal and 5′ terminal end are complementary sequences, resulting in the RNA strand forming "pan-handle" structures that seem to be important in viral transcription and replication.[5] Each segment also has short noncoding regions, the function of which is yet to be elucidated. **Fig. 1** shows a schematic of SNV based on CDC electron micrographs.[6]

Hantaviruses principally target vascular endothelial cells, but also infect alveolar macrophages and follicular dendritic cells. Renal tubular epithelium can also be a site for infection. Cell entry of hantaviruses is mediated by binding to β3 integrins.[7] Sin Nombre and New York viruses enter human cells by way of αvβ3 and αIIbβ3

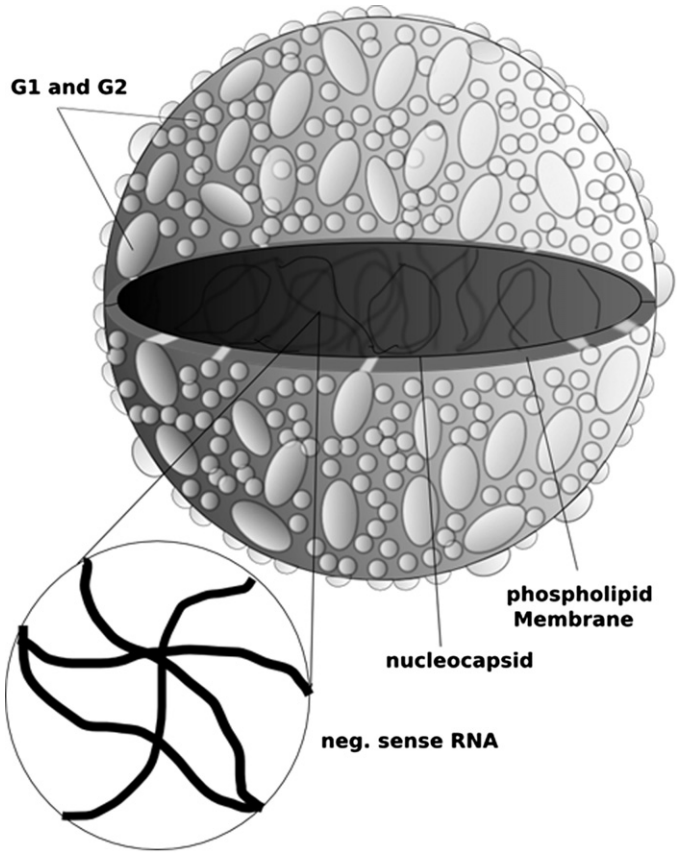


**Fig. 1.** Schematic diagram of Sin Nombre virus, based on Centers for Disease Control and Prevention electron micrographs. Structures are not drawn to scale. *G1* and *G2* represent glycoproteins that mediate attachment of virions to human cells by way of β3 integrins. The virus consists of a phospholipid bilayer envelope surrounding a nucleocapsid protein. Three strands of negative sense RNA constitute the viral genome. (*Courtesy of* N. Simpson, Fairway, KS.)