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# A REVIEW ON THE DIAGNOSTIC ANALYSIS AND TREATMENT OF HANTAVIRUS INFECTION

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#### **ABSTRACT**

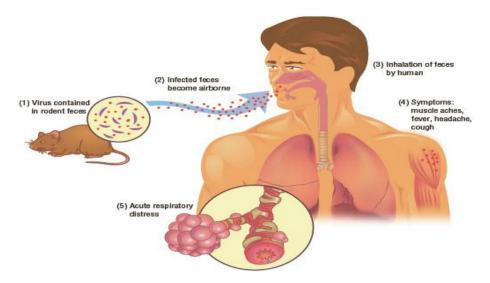
A case of infection with another Hantavirus has been reported by Search amid fear of Corona virus. It may take one to eight weeks to detect the infection according to the US centers for Disease Control. If a person is infected with Hanta virus, he has problems like pain, fever, cold, vomiting, and back pain. This causes trouble breathing and water filling in the lungs when the condition of the infected person worsens. Nine people died due to the Hanta virus in Patagonia in January 2019. According to various studies, the risk of Hanta virus spreading is higher in rural areas where woods, fields, and farms provide suitable habitat for the rodent hosting the virus. The Center for Disease Control learned from its studies that there are four species of mice that are the carriers of the hysteria. These are the most important fear mouse found in America. It is much smaller than common mice. So far for the treatment its vaccine has not been prepared nor is there any definitive treatment. Such patients need special care and are given oxygen therapy. The sooner the case gets caught, the better.

**KEYWORDS:** Hanta Virus, rodents, spread, antiviral, PCR.

### INTRODUCTION

Hantaviruses have gained worldwide attention after one individual died as a result of the Hantavirus in China's Yunnan province which causes fear among the people there. Hantavirus is rife on social media sites around the world. Under that stressful situation, knowledge of the Hantavirus is very important. This case is a frustrating one. Hantavirus is a genus of single-stranded, enveloped RNA viruses with a negative-sense. [1-3] Humans can become infected with Hantavirus after exposure to rodent urine, saliva, or feces. Taking some stresses by the patient cause potentially fatal illnesses in humans, such

as Reno virus fever with renal syndrome (HFRS), or Hantavirus pulmonary syndrome (HPS), also known as Hantavirus cardiopulmonary syndrome (HCPS). [4] At present, more than 21 Hantaviruses worldwide have been reported as causing disease in humans from proteinuria to pulmonary edema and frank hemorrhage diseases when transmitted from their rodent reservoirs. [5] Human Hantavirus infection was linked to nearly all has been related almost entirely too human contact with bite or scratch from infected rodent excreta, but human-to-human transmission to the Andes virus was recorded in South America in 2005 and 2019. [6]



### History of hantavirus

Some may call it a new virus but it doesn't. In a report, the United States National Center for Biotechnology Information (NCBI) writes that there are currently more than 21 species in the genus Hantavirus. In 1978, Korean haemologic fever, an infected agent near the Hunton River in South Korea, was isolated from small infected area rodents. The virus was named Hantan virus after the Hunton River. This initial discovery points to scientific approaches that were introduced after the Korean War (1951–1953), during which the United Nation (UN) troops had more than, 3,000 cases of hemorrhagic fever in Korea.<sup>[7]</sup>

### Biology and Epidemiology Morphology

Hantaviruses include one of five genera of the infection family Bunyaviridae. [8] They imitate in the cytoplasm of host cells furthermore, are made out of a circular lipid envelope; four viral proteins; and three single-abandoned, negative-detected RNA fragments assigned S (little), M (medium), and L (enormous) that are coding for the nucleocapsid protein (NP), the surface envelope glycoproteins G1 and G2, and the RNA-subordinate RNA polymerase, separately <sup>(9)</sup>. Extra minor open perusing outlines are available in the genomes of Hantaviruses, however to date, no comparing proteins were recognized. NP, the fundamental auxiliary protein, is complexed with the viral RNA genome sections that structure helical nucleocapsids.

#### Host range

The fundamental normal supply of Hantaviruses is murid rodents (request Rodentia; family Muridae; subfamilies Murinae, Arvicolinae, and Sigmodontinae). Infection and host share a substantial stretch of co-advancement defined in a contaminated rodent of any hantavirus associated sickness. [10-11] Originally, one rat animal species was thought to be the dominant host for one Hantavirus animal species, but late an ever-increasing number of studies show that there could be different rats for single infection species and different infections in a

single host animal species.<sup>[12-14]</sup> Similarly, various studies have documented Hantavirus diseases to be present in non-rodent species of mammals, for example in dairy cattle, moose, feline, hound, etc. whether these creatures are inadvertently infected or talk to usual supplies has not yet been addressed.<sup>[15]</sup> The spread of single Hantavirus species is related to the geographic expansion of their hosts and the phylogenetically related Hantavirus genotypes of the corresponding geographic Zone.<sup>[16-17]</sup>

Humans have no position with the typical host spectrum of Hantaviruses, and diseases happens involuntarily by contamination involving, for example, Urine, dung or salivation, aerosolized rat discharges. Individuals living or working in close contact with infected rodents are at increased risk of diseases, and studies usually indicate high degree of seropositive people in meetings such as contrasted and control subjects: [18-19]

### Old World and New world hantaviruses

The Hantavirus variety is usually composed of two simple gatherings: Old World and New World hantaviruses. HFRS in human is caused by pathogenic Old World hantaviruses that contain Amur infection, Seoul infection, and HTNV, the most epidemiologically significant pathogens, with mortality rates of up to 15% in Asia, just like Dobrava infection (DOBV), Tula infection (TULV), and Puumala infection (PUUV) in Europe; the latter is the principle hantavirus species in Europe and act on Nephropathia epidemica (NE), a mellow HFRS type, with death rate of 0.1%. [20] HFRS affected about 200,000 peoples in Asia mainly per year. In 2004, 235 cases were registered in Germany according to an ongoing epidemiological announcement by the Robert-Koch Institute. The big pathogenic New World Hantavirus(Sin Nombre infection) was discovered in the United States districts of four corners in the mid1990s. [21] Several extra pathogenic New World Hantaviruses have been recognized and identified since. New World Hantaviruses are the causative operator of approximately 300 cases of HPS in North and South America per year,

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with lethality levels as high as half. Contamination with human Hantavirus are likely to occur unintentionally and men talk of an impasse for the Hantavirus lifecycle. [22-23] Infection particles usually don't switch from contaminated to uninfected individuals. One special case

in Argentina is the Andes Hantavirus strain sout which accounted for sporadic individual to individual transmission from. This finding uncovers Hantaviruses 'traumatic threat potential for human wellbeing.

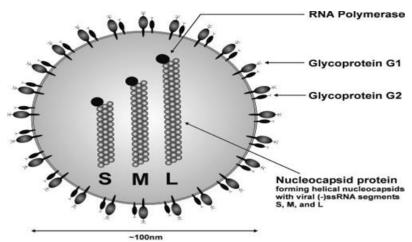


Fig: Morphology of a Hantavirus. The (-)ssRNA segments S (small), M (medium), and L (large) are encoded for the nucleocapsid protein, the glycoproteins G1 and G2, and the RNA-dependent RNA polymerase.

### How is it spread?

This is a category of viruses transmitted by rodents, especially rats and squirrels. This virus is known as New World Hanta virus in America, [26] and as Old World Hantavirus in Europe and Asia. This is the cause of the disease named Hanterus pulmonary ultra. There are many types of hanteras that spread out from different rodent artifacts. virus Carriers are human when they're exposed to rat urine, feces and saliva.

# This virus spreads in three ways<sup>[27]</sup>

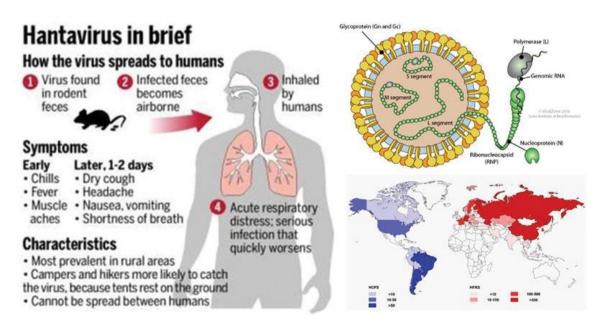
**First:** if the rat carrying the virus bites a human, even though these case are uncommon.

**Second:** The rat comes into contact with the feces or urine or saliva present at some place or item, and gives its nose and mouth softness.

**Third:** If a human eats something that has feces or semen on rats.

# Signs and Symptoms<sup>[28]</sup>

Symptoms like high fever, headache, body ache, abdominal pain, vomiting, and diarrhea indicate infection. The severity of infection rises Within 4 to 10 days, and there is trouble breathing, as water starts to fill the lung. Death can also happen if symptoms continue, similar symptoms were seen in pre-death patient in China. It can take between one to eight weeks to detect the infection.



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# Diagnosis of hantavirus by serological assay. [29-31]

Serological tests are considered a positive result for evidence of any virus. This involves evidence of viral antigen in the tissue, or the existence in blood or tissue of amplified viral RNA sequences.

Tests were developed based on unique viral antigens from SNVs and are now widely used for routine diagnosis of Hantavirus infection. The CDC uses an enzyme-linked immune sorbent assay (ELISA) connected to the enzyme to detect IgM antibodies to SNVs and to diagnose acute infection with other Hantaviruses. Only the serological test is conducted in some state health laboratories

#### Isolation

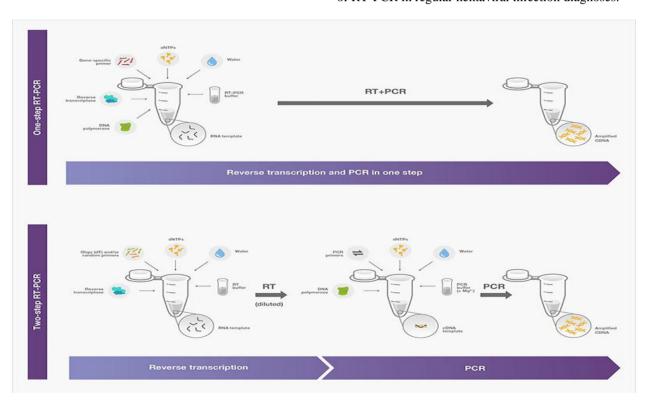
Hantavirus re difficult to isolate from infected human hence virus isolation for diagnostic purpose is not a consideration.

#### **Immunohistochemistry (IHC)**

The IHC test can be used to detect formalin-fixed tissue Hantavirus antigen with various monoclonal and polyclonal antibodies, and has been shown to be an effective method for confirming of hanta viral infection in the laboratory. The IHC plays an important role in the diagnosis of HPS in patients whose serum sample and frozen tissue cannot be used for clinical trials and in retrospective assessment of disease distribution in a given geographic region. [32]

# Polymerase chain reaction $(PCR)^{[33-35]}$

Reverse transcriptase-PCR (RT-PCR) can be used for the identification of homoviral RNA in freshly frozen lung tissue, blood clots, or nucleated blood cells. RT-PCR is therefore very flat to cross-contamination and should be treated as an experimental technique. In the United States, variation in viruses hinders the use and sensitivity of RT-PCR in regular hentaviral infection diagnoses.



# Focus reduction neutralization test<sup>[36-38]</sup>

While the exams mentioned above are used to assess whether a patient has been infected with Hantavirus, none of the tests will ascertain which Hantavirus was responsible for the diseases due to the fact that there is a big humoral cross-response between Hantavirus antibodies. The particular tainting Hantavirus can be distinguished by center decrease balance test (FRNT), which is the best quality level for Hantavirus testing. FRNT can recognize and gauge killing antibodies by contrasting serum titers and the pertinent Hantaviruses and despite the fact that it recognizes Hantaviruses with serum from tentatively tainted rodents; it was less

explicit when serum from intense stage patients was tried. Since FRNT requires cell culture, it must be led under BSL-3. The measure is likewise tedious and work escalated.

### **Treatment of hantavirus infection**

There is no specific treatment for Hantavirus- affected individuals. The patient affected needs to be handled properly. Patient will continue therapy with the correct broad spectrum antibiotics only after confirmation of the virus infection. Patients may include antipyretics and analgesia if appropriate, along with treatment and early state of diseases.

# Take-home Message for Care Providers:

- · Rapid transfer to ICU
- · Careful monitoring
- · Fluid balance
- · Electrolyte balance
- Blood pressure

When there is a strong sensation of respiratory infection, patients should be moved immediately transferred to an emergency department or intensive care unit (ICU) for close observation and treatment. Because of respiratory blockage ICU diagnosis patients with fulminate diseases have low prognosis. Management of ICU should include careful examination, monitoring and adjustment of volume status and cardiac function, including inotropic and vasopressor help if appropriate. Given the potential leakage, Fluids should be handled carefully. If the patient become hypoxic, supplemental oxygen should be given. Intubation and mechanical ventilation equipment and material and supplies should be readily available, as it can be precipitous to induce respiratory failure.

# Virus like Particles (VLP) Vaccines [39-42]

Past research has shown that, when analyzed by electron microscopy, S and M or merely M communicated quality items gather in infection like particles (VLP) that look like Hantavirus virions. In China, with an end goal of eliminating security concern with the inactivated whole infection antibody, successions of the film bound types of invulnerable invigorating particles CD40 ligand (CD40L) and granulocyte macrophage settlement animating variable (GM-CSF) were consolidated into vectors alongside HTNV S and M parts, and in vitro VLPs were made. Upgraded HTNV-explicit counter acting agent and killing immunizer were seen in VLPinoculated mice, despite decreasing viral burden in organs after testing altogether. The drawn out defensive viability of the HTNV CD40 GM-CSF VLPs was expected to adopt 2 dosages and a half -year HTNV challenge after high killing immune response titers in mice were incubated.

# Antiviral medicine<sup>[43]</sup>

Intravenous ribavirin, a guanosine derivative, has not been shown to be compelling to treat Hantavirus contamination despite its impact on a related disease, renal hemorrhagic fever (HFRS), caused by old world Hantaviruses. Controlled prelaminar showed a decline in the off risk of causality being treated with ribavirin for HFRS patients. Nonetheless, following ribavirin's in

high degree of suspicion of Virul infection

- immediately transferred to an emergency department
- monitoring and adjustment of volume status and cardiac function

vitro action against SNV, neither an open-name preliminary led during the 1993 flare-up nor an endeavored fake drug controlled preliminary exhibited clinical benefit for HPS. Ribavirin is not approved for HPS care and is not eligible under any existing research convention for this use.

#### **CONCLUSION**

This study tells us how the Hantavirus spread and can be prevented by bearing in mind the following issues, such as Endeavor should be done in advance by thinking about the disease of hantavirus and people should be treated normally at the contamination well. 1) Keep mice and believers in your house. 2) Minimize rodent activity inside your office or campground. 3) Clean the mouse and the rodent feces, scrape droppings and dispose of a disinfectant agent or a combination of water and dye. Three significant techniques exist for the etiologic analysis of Hantavirus diseases: i) Serology: This is the decision-making method for the study of Hantavirus diseases. The discovery of IgG or IgM antibodies to Hantavirus using ELISA is the most widely used technique in the finding as most HPS cases display IgM antibodies during the extreme ailmenttime and remain recognizable for 6-8 months. During or shortly after the presence of IgM antibodies, the presence of clear IgG can occur and they can remain at substantial levels for a while. ii) Viral antigen detection: Immunohistochemistry is an incredible technique for viral antigen detection in tissues, particularly in deadly cases where there is no other form of test.iii) Molecular recognition: The use of RT-PCR allow for the presence of viral RNA in whole blood, clumps or tissue in the first 10 days of the diseases. Likewise, the technique is helpful in identifying viral RNA in tainted rodent tissues. For Hantavirus, the use of antivirals and vaccines are useful in the treatment of hantavirus infection.

### REFERENCE

 Amaral CD, Costa GB, de Souza WM, Alves PA, Borges IA, Tolardo AL, Romeiro MF, Drumond BP, Abrahão JS, Kroon EG, Paglia AP, Figueiredo LTM and de Souza Trindade G: Silent Orthohantavirus

- Circulation Among Humans and Small Mammals from Central Minas Gerais, Brazil. Ecohealth, 2018; 15(3): 577-589.
- Kuenzli AB, Marschall J, Schefold JC, Schafer M, Engler OB, Ackermann-Gäumann R, Reineke DC, Suter-Riniker F and Staehelin C: Hantavirus Cardiopulmonary Syndrome Due to Imported Andes Hantavirus Infection in Switzerland: A Multidisciplinary Challenge, Two Cases and a Literature Review. Clin. Infect. Dis, 2018; 13, 67(11): 1788-1795.
- Shipley LC, Taylor ST, Grimsley C, Stoffer K and Goldstein J: Rats! Hantavirus: A Case Report of a Suspected Case in Eastern Tennessee. Perm J, 2018; 19, 22: 17-222.
- 4. Linderholm M and F. Elgh: Clinical characteristics of Hantavirus infections on the Eurasian continent. Curr. Top. Microbiol. Immunol, 2001; 256: 135–151.
- Lednicky JA: Hantavirus: a short review. Arch Pathol Lab Med, 127: 30-35.
- 6. Avšič-Županc T, Saksida A and Korva M: Hantavirus infections. Clin Microbiol Infect, 2019; 21S: e6–16. 10.1111/1469-0691.12291.
- 7. Chandy S and Mathai D: Globally emerging Hantaviruses: An overview. Indian J Med Microbiol, 2017; 35(2): 165-175.
- 8. Schmaljohn CS and Dalrymple JM: Analysis of Hantaan virus RNA: Evidence of a new genus of Bunyaviridae. *Virology*, 1983; 131: 482–491.
- 9. Plyusnin A, Vapalahti O and Vaheri A: Hantaviruses: Genome structure, expression and evolution. *J Gen Virol*, 1996; 77: 2677–2687.
- 10. Maes P, Clement J, Gavrilovskaya I and Van Ranst M: Hantaviruses: Immunology, treatment, and prevention. *Viral Immunol*, 2004; 17: 481–497.
- 11. Ulrich R, Hjelle B, Pitra Cand Kruger DH: Emerging viruses: The case 'hantavirus.' *Intervirology*, 2002; 45: 318–327.
- 12. Nemirov K, Henttonen H, Vaheri A and Plyusnin A: Phylogenetic evidence for host switching in the evolution of hantaviruses carried by Apodemus mice. *Virus Res*, 2002; 90: 207–215.
- 13. Scharninghausen JJ, Faulde M and Cavaljuga S: Hantavirus host/virus interactions within Southeast Europe. *Bosn JBasic Med Sci*, 2004; 4: 13–18.
- Weidmann M, Schmidt P, Vackova M, Krivanec K, Munclinger P and Hufert FT: Identification of genetic evidence for Dobrava virus spillover in rodents by nested reverse transcription (RT)-PCR and TaqMan RT-PCR. *J Clin Microbiol*, 2005; 43: 808–812.
- 15. Zeier M, Handermann M, Bahr U, Rensch B, Muller S, Kehm R, Muranyi W and Darai G: New ecological aspects of Hantavirus infection. A change of a paradigm and a challenge of prevention—A review. *Virus Genes*, 2005; 30: 157–180.
- 16. Plyusnin A and Morzunov SP: Virus evolution and genetic diversity of Hantaviruses and their rodent

- hosts. Curr TopMicrobiol Immunol, 2001; 256: 47–75
- 17. Plyusnin A: Genetics of hantaviruses: Implications to taxonomy. *Arch Virol*, 2002; 147: 665–682.
- Deutz A, Fuchs K, Schuller W, Nowotny N, Auer H, Aspock H, Stunzner D, Kerbl U, Klement C and Kofer J: Seroepidemiological studies of zoonotic infections in hunters in southeastern Austria— Prevalences, risk factors, and preventive methods. Berl Munch Tierarztl Wochenschr, 2003; 116: 306– 311
- Zoller L, Faulde M, Meisel H, Ruh B, Kimmig P, Schelling U, Zeier M, Kulzer P, Becker C and Roggendorf M: Seroprevalence of hantavirus antibodies in Germany as determined by a new recombinant enzyme immunoassay. *Eur J Clin Microbiol Infect Dis*, 1995; 14: 305–313.
- 20. Vapalahti O, Mustonen J, Lundkvist A, Henttonen H, Plyusnin A and Vaheri A: Hantavirus infections in Europe. *LancetInfect Dis*, 2003; 3: 653–661.
- 21. Hjelle B, Jenison S, Torrez-Martinez N, Yamada T, Nolte K, Zumwalt R, MacInnes K, and Myers G: A novel Hantavirus associated with an outbreak of fatal respiratory disease in the southwestern United States: Evolutionary relationships to known hantaviruses. *J Virol*, 1994; 68: 592–596.
- 22. Padula PJ, Edelstein A, Miguel SD, Lopez NM, Rossi CM and Rabinovich RD: Hantavirus pulmonary syndrome outbreak in Argentina: Molecular evidence for person-to-person transmission of Andes virus. *Virology*, 1998; 241: 323–330.
- 23. Pinna DM, Martinez VP, Bellomo CM, Lopez C and Padula P: New epidemiologic and molecular evidence of person to person transmission of Hantavirus Andes Sout. *Medicina (BAires)*, 2004; 64: 43–46.
- 24. Rodent-borne diseases". European Centre for Disease Prevention and Control. *Retrieved*, 2018; 06:04
- 25. Barros N, McDermott S, Wong AK and Turbett SE: "Case 12-2020: A 24-Year-Old Man with Fever, Cough, and Dyspnea". New England Journal of Medicine, 2020; 382(16): 1544–1553. doi:10.1056/NEJMcpc1916256.
- CDC Hantavirus Pulmonary Syndrome (HPS) -Hantavirus". Cdc.gov. 2013-02-06. Retrieved, 2013; 07: 07
- 27. American lung Association. Hantavirus Pulmonary Syndrome Symptoms and Diagnosis, 2020; 27: 02. Retrieved from Lung.org/covid19: https://www.lung.org.
- 28. Bayard V, Kitsutani PT and Barria EO: Outbreak of hantavirus pulmonary syndrome. Los Santos, Panama, 1999-2000. Emerg Infect Dis, 2004; 10(9): 1635-42.
- 29. Maes PE, Keyaerts J and Clement V: Detection of Puumala hantavirus antibody with ELISA using a recombinant truncated nucleocapsid protein

- expressed in Escherichia coli. Viral Immunol, 2004; 17(2): 315-321.
- Kruger DH, Figueiredo LTM, Songc JW and Klempa B: Hantaviruses – globally emerging pathogens. J Clin Virol 2014. Available from: http://dx.doi.org/10.1016/j. jcv.2014.08.033
- 31. Coons AH, Creech HJ and Jones RN: Immunological properties of an antibody containing a fluorescent group. Proc Soc Exp Biol Med, 1941; 47: 200-202.
- 32. Jonsson B, Figueiredo M and Vapalahti O: A global perspective on hanta virus ecology, epidemiology and disease. Clin Microbiol, 2010; 23: 412-441
- 33. Amada T, Yoshimatsu K, Yasuda SP, Shimizu K, Koma T, Hayashimoto N, Gamage CD, Nishio S, Takakura A and J Arikawa: Rapid, whole blood diagnostic test for detecting anti-hantavirus antibody in rats. J Virol Method, 2013; 193(1): 42-9
- 34. Noh JY, Cheong HJ, Song JY, Kim WJ, Ki-Joon S, Klein TA, Lee SH, Yanagihara R and Jin-Won S: Clinical and Molecular Epidemiological Features of Hemorrhagic Fever with Renal Syndrome in Korea over a 10-year Period. J Clin Virol, 2013; 58(1): 11-17.
- 35. Bharadwaj M, Botten J and Torrez-Martinez N: Rio Mamore virus: genetic characterization of a newly recognized hantavirus of the pygmy rice rat, Oligoryzomys microtis, from Bolivia. Am J Trop Med Hyg, 1997; 57(3): 368-374.
- 36. Chaofeng M, Zengguo W, Shen L, Yuan X, Rui W, Jing W, Muhammad N, Huaiyu T, Bing X, Jingjun W and Pengbo Y: Analysis of an Outbreak of Hemorrhagic Fever with Renal Syndrome in College Students in Xi'an, China. Viruses, 2014; 6: 507-15.
- 37. Lederer S, Lattwein E and Hanke M: Indirect Immunofluorescence Assay for the Simultaneous Detection of Antibodies against Clinically Important Old and New World Hantaviruses. PLoS Negl Trop Dis, 2013; 7(4): e2157. doi:10.1371/journal.pntd.0002157
- 38. Medina RA, Mirowsky-Garcia K, Hutt J and Hjelle B: Ribavirin, human convalescent plasma and antibeta3 integrin antibody inhibit infection by Sin Nombre virus in the deer mouse model. J Gen Virol, 2007; 88: 493–505.
- 39. Acuna R, Cifuentes-Munoz N, Marquez CL, Bulling M, Klingstrom J, Mancini R, Lozach PY and Tischler ND: Hantavirus gn and gc glycoproteins self-assemble into virus-like particles. J. Virol, 2014; 88: 2344–2348. Doi: 10.1128/JVI.03118-13.
- 40. Betenbaugh M, Yu M, Kuehl K, White J, Pennock D, Spik K and Schmaljohn C: Nucleocapsid- and virus-like particles assemble in cells infected with recombinant baculoviruses or vaccinia viruses expressing the M and the S segments of hantaan virus. Virus Res, 1995; 38: 111–124. doi: 10.1016/0168-1702(95)00053-S.
- 41. Ying Q, Ma T, Cheng L, Zhang X, Truax AD, Ma R, Liu Z, Lei Y, Zhang L and Ye W: Construction and immunological characterization of CD40L or

- GM-CSF incorporated hantaan virus like particle. Oncotarget, 2016; 7: 63488–63503. Doi:10.18632/oncotarget.11329.
- 42. Dong Y, Ma T, Zhang X, Ying Q, Han M, Zhang M, Yang R, Li Y, Wang F and Liu R: Incorporation of CD40 ligand or granulocyte-macrophage colony stimulating factor into hantaan virus (HTNV) virus-like particles significantly enhances the long-term immunity potency against HTNV infection. J. Med. Microbiol, 2019; 68: 480–492. Doi: 10.1099/imm.0.000897.
- 43. Hantavirus: "Canadian Lung Association". 26 November 2015. Archived from the original on 2 March 2011. Retrieved, 2018; 23.

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