



# Hantavirus: The next pandemic we are waiting for?

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# Brief Introduction

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- Hantaviruses, albeit reported more than 40 years ago, are now considered emerging viruses' because of their growing importance as human pathogens.
- In recent years an increasing number of infections and human-to-human transmission is creating a distressing situation.
- Hantaviruses are single-stranded RNA viruses (negative sense) capable of infecting species (shrews, moles and bats) including humans.
- The virion, comprising of genome encapsulated in glycol-ribonucleoprotein capsule, with an integral constituent enzyme RNA-dependent RNA-polymerase (RdRp).



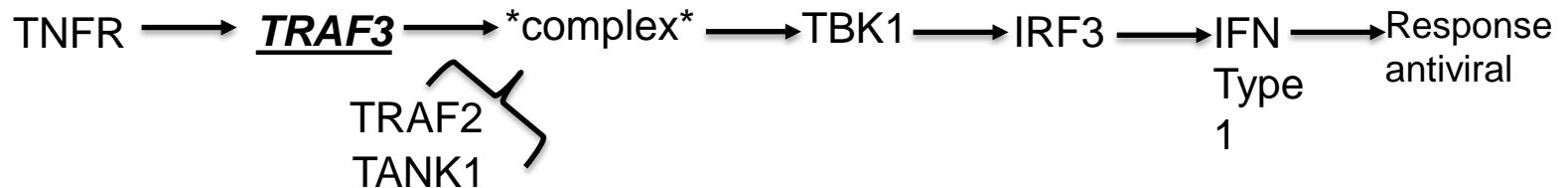
# The Biology of Hantaviruses

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- Three segments are called small (S), medium (M), and Large (L) based on their size.
  - 1) The viral polymerase is encoded in the L segment.
  - 2) Two viral surface glycoproteins (G1,G2 = Gn,Gc) is encoded in the M segment.
  - 3) Nucleocapside (N) protein is encode in the S element.
- The two different components of the S glycoprotein (four G1 spikes and four G2 spikes) encoded by the M segment may interact with the  $\beta$ -integrin and pave the way for the entry of Hantavirus to the host cell.

# The Biology of Hantaviruses

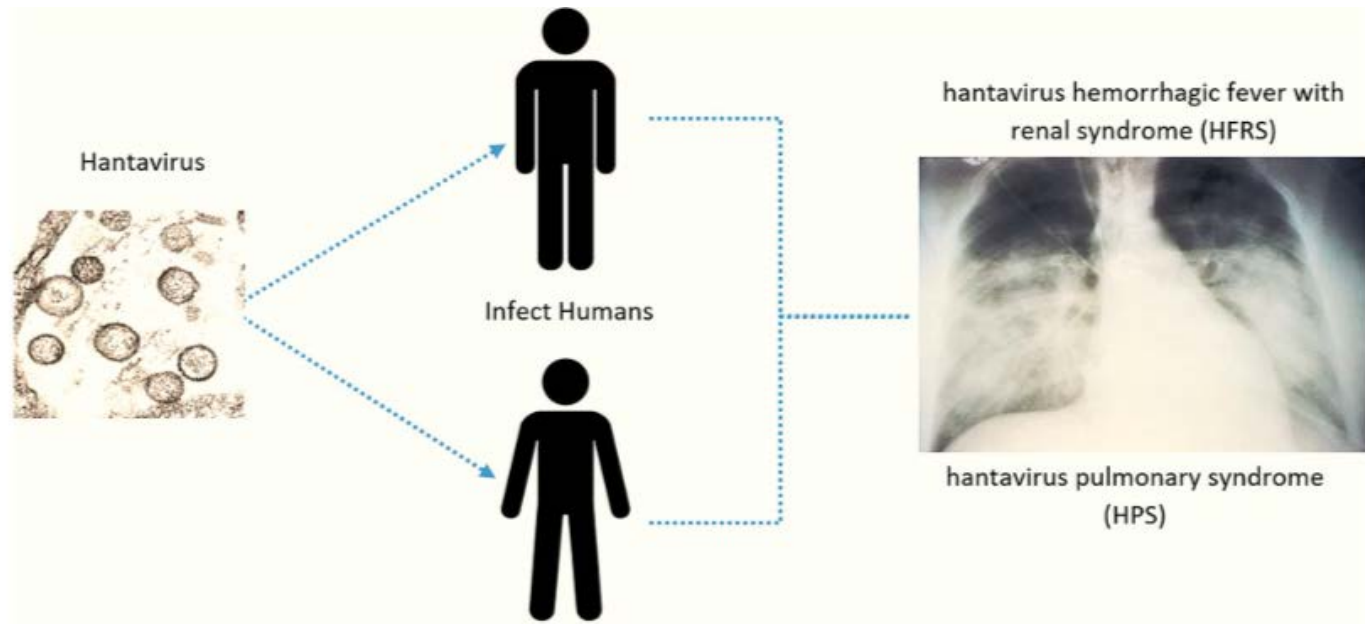
- To evade from the host response, the production of IFN- $\beta$  is inhibited by the *G1 portion of the S glycoprotein* of the Hantavirus by binding to **TRAF3** and preventing RIG-I/TBK1-directed IRF3 phosphorylation.



- The primary target of the host immune system is the N protein which is a small and highly conserved protein among the hantaviruses.
- The role important of the *N protein* is protect the genetic material of the virus and interact with the host (Human) MxA(p78).
- Induction of the type I IFN against the viruses is the primary function of the MxA.

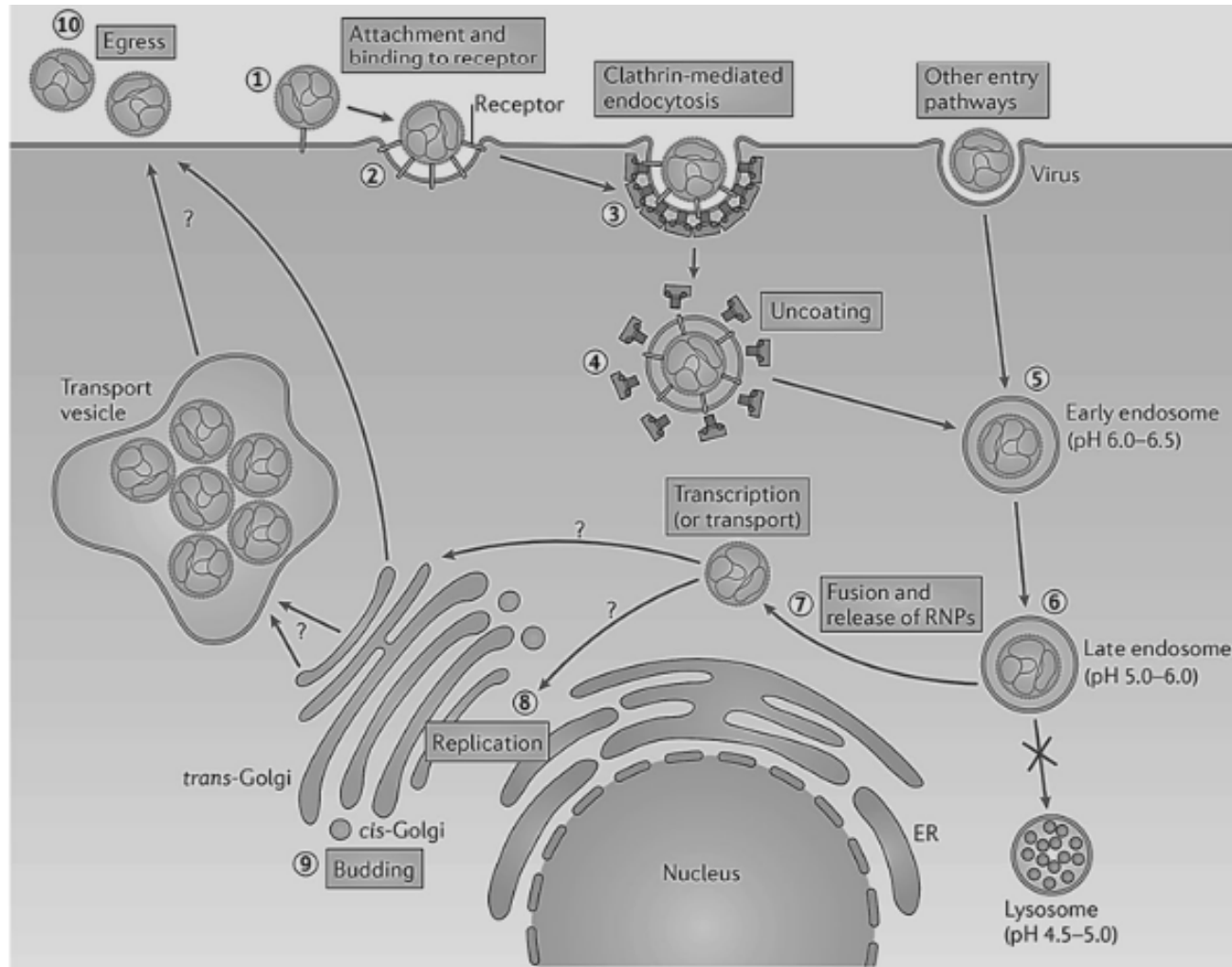
# The Pathogenesis & Immunology of Hantaviruses

- The Hantavirus reservoir infection hosts are not affected (probably due to immunosuppression of the host), but in humans, it is causing hemorrhagic fevers, including the “hemorrhagic fever with renal syndrome” (HFRS) and “hantavirus cardiopulmonary syndromes” (HCPS).



# The Pathogenesis & Immunology of Hantaviruses

- The schematic representation of viral attachment and multiplication within the host cell.





# The Pathogenesis & Immunology of Hantaviruses

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- Pathologically these syndromes are described as aggravated immune reactions, with amplification in the permeability (vascular trickle) of the endothelial cells in the capillaries.
- Like typical viral infections, hantavirus infection is characterized by high fever, body aches and nausea in renal infection Proteinuria, hematuria and nephritis.
- The *HFRS* follows five distinct phases which are febrile, hypotensive, oliguric, polyuric and convalescent.
- A sudden onset of respiratory failure due to pulmonary oedema and cardiogenic shock, myalgia, cough and diarrhoea is frequently associated with *HCPS*.





# The Pathogenesis & Immunology of Hantaviruses

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- The adaptive immunity obtained against hantaviruses by the hosts lasts the entire life, and hence there is no relapse of the infection in the lifetime after the primary infection.
- The inflammatory symptoms developed in the infection is due to the Cytokines like interleukin-1 (IL-1) IL-6 and tumor necrosis factor (TNF). The raised levels of IL-6 are reported to be associated with thrombocytopenia and renal failure.





# Epidemiological perspective

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- More than 1,500 cases of HCPS have been documented caused by 15 genetically distinct strains of hantaviruses in the Americas, all correlated with sigmodontine rodents.
- The reported hantavirus cases in countries including; Germany (2017) 1,713, Canada 109 (with estimated death rate 29%), and the United States 728 cases.
- Approximately 1,50,000 HFRS cases are estimated to occur worldwide annually.
- Over the past ten years, 112,177 HFRS cases while 1,116 deaths are reported in China among which 84.16% are from the only nine provinces.
- China is reported to contribute 40–50% to the worldwide cases.

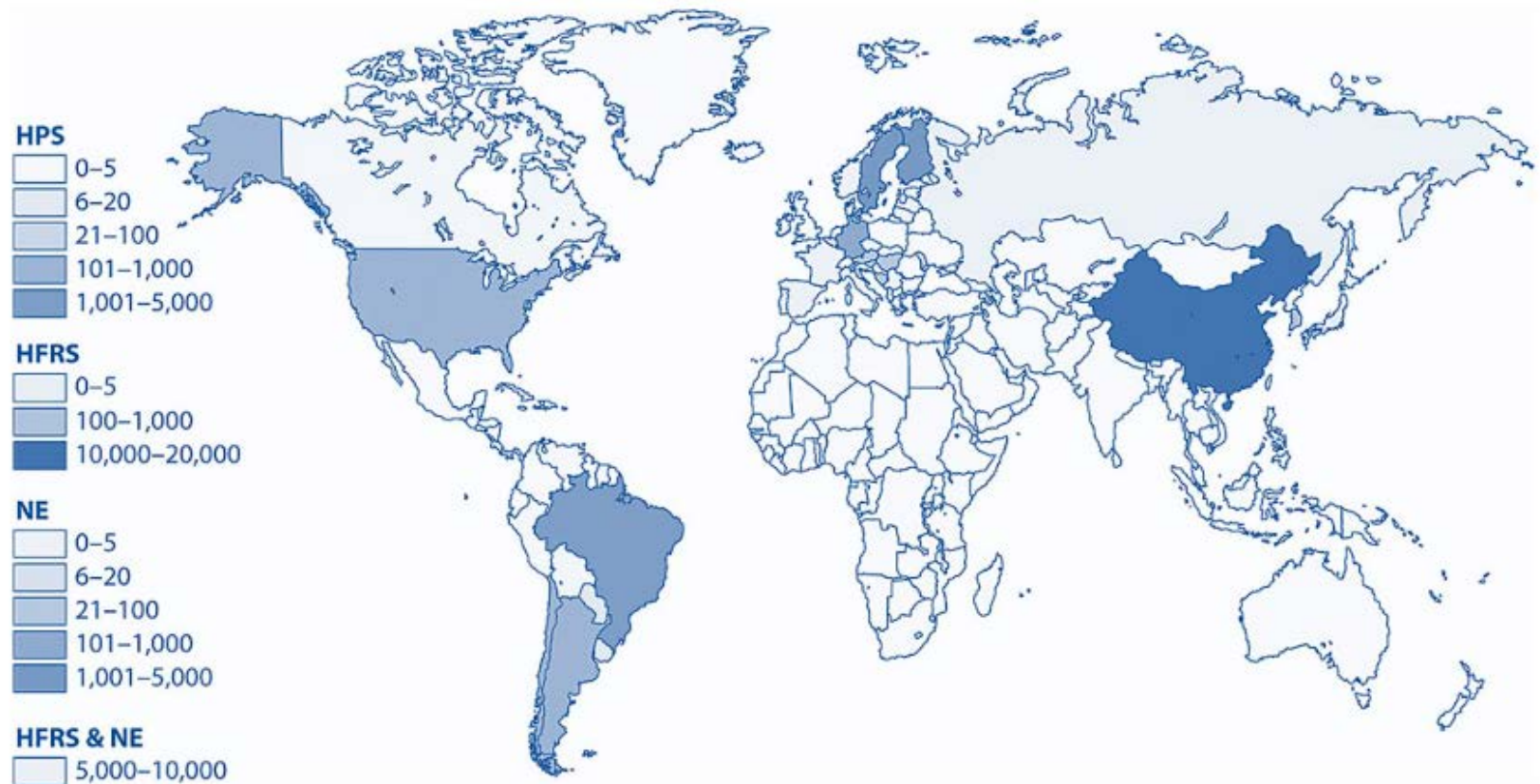


# Epidemiological perspective

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- Six hundred twenty-four cases of HCPS were registered in the United States during the period 1993–2013.
- In Europe, more than 3,000 HFRS cases are diagnosed per year (*PUUV* and *DOBV*).
- 100–200 HCPS cases are registered annually in Argentina.
- Before 2013, Brazil reported 1,600 cases of HCPS.
- The most impenetrable scenario is the human-to-human transmission, reported in 2005 and 2019, having the tendency to cause another global pandemic of more lethal virus compared to the corona virus (because of its high death rate of 50%).

# Epidemiological perspective



**Fig. 2** Geographical illustration and per year country wise incidences reported by Douglas Goodin, Kansas State University[37]

# Future perspective & policy recommendation

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- The Asian population is protected from the severity of recent coronavirus due to the advantage of Bacillus Calmette–Guérin (BCG) vaccination. So, looking into the same nature of diseases, the practice of BCG vaccination throughout the world should be exercised to develop the immune response against such attacks.
- The most important point is to exercise the practice of drug repurposing and other therapeutic agents at first hand. Discovering new drugs or other therapeutic molecules such as vaccines takes a longer time.
- Data-sharing platform should be provided where all the researchers should share and make available all the necessary information such as genomics, proteomics, host-factors, and other epigenetics information.



# Conclusion

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- This article is a systematic review on the hantavirus, addressing topics like its biology and pathophysiology.
- The article exposes the emerging need to further investigate this pathogen.

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