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A Review on an Overview of Hantavirus

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Abstract: ***Hantaviruses are rodent viruses that have been identified as etiologic agents of 2 diseases of humans: hemorrhagic fever with renal syndrome (HFRS) and hantavirus pulmonary syndrome (HPS). This article presents a concise review of hantavirus biology, the medical features of HFRS and HPS, and tests for the detection of hantavirus infections in humans. Hemorrhagic fever with renal syndrome is a disease found outside the Americas and denotes a group of clinically similar illnesses that vary in severity relative to the causative agent. Hantavirus pulmonary syndrome is associated with higher mortality than HFRS, was first recognized as a hantavirus disease in 1993, and occurs within the American continents. Recent genetic studies show that both Old and New World hantavirus species coevolved with specific rodent hosts. The list of distinct hantaviruses associated with HPS is growing. The burgeoning human population is causing disruption of natural habitats as more and more land is cleared for commercial and residential purposes. The Centre for Disease Control says that the virus is spread mainly from rodents. It goes on to say that infection with any of the hantavirus can cause hantavirus disease in people. Even when the world is trying to find a cure for the dreaded coronavirus pandemic, a report in Global Times said that a man from China's Yunnan province died from Hantavirus while on a bus to the Shandong province.***

Keywords: Hantavirus, microscopy, history, prevention, treatment

1. Introduction

Orthohanta virus is a genus of single-stranded, enveloped, negative-sense RNA viruses in the family Hantaviridae of the order Bunyavirales. Members of this genus may be called orthohanta viruses or simply hantaviruses. They normally cause infection in rodents, but do not cause disease in them. Humans may become infected with hantaviruses through contact with rodent urine, saliva, or feces. Some strains cause potentially fatal diseases in humans, such as hantavirus hemorrhagic fever with renal syndrome (HFRS), or hantavirus pulmonary syndrome (HPS), also known as hantavirus cardiopulmonary syndrome (HCPS), while others have not been associated with known human disease.HPS (HCPS) is a "rare respiratory illness associated with the inhalation of aerosolized rodent excreta (urine and feces) contaminated by hantavirus particles." Globally, emerging zoonotic pathogens remain a serious public health problem. In this regard, hantaviruses have attracted a lot of attention as novel pathogenic serotypes are frequently being reported. Hantaviruses belong to family Bunyaviridae and are hosted by small mammals. Humans get infected by either inhaling virus-contaminated aerosols or through contact with the animal droppings. Haemorrhagic fever with renal syndrome (HFRS) in Asia and Europe and hantavirus cardiopulmonary syndrome (HCPS) in the Americas are two important clinical syndromes associated with hantavirus infections. 'Hantavirus disease/fever' may be an inclusive terminology since pathogenesis and clinical features of these syndromes overlap.[1]

Family: Hantaviridae
Scientific name: Hantavirus
Class: Ellioviricetes
Order: Bunyavirales
Rank: Genus
Higher classification: Bunyaviridae

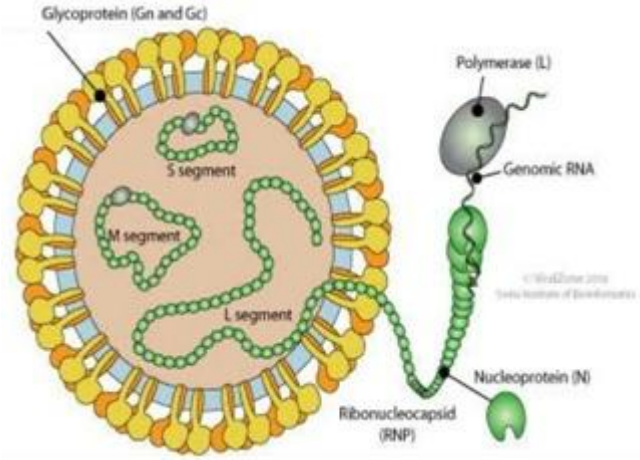

Figure 1: Orthohantavirus

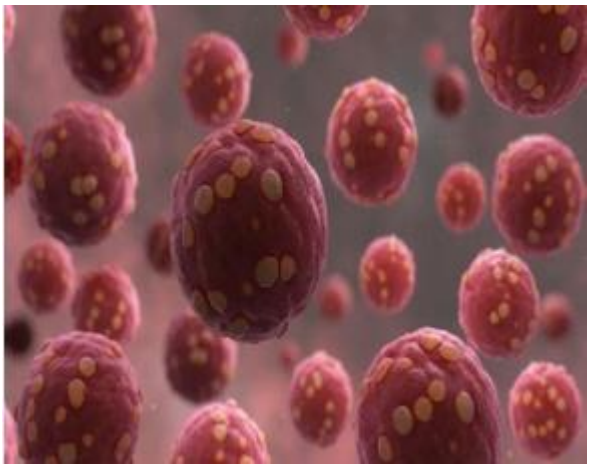

Figure 2: Hantavirus Scientific Animation (3D Model)

Microscopy

Genome:-Like other members of Bunyavirales, orthohantaviruses are enveloped viruses with a genome that consists of three single-stranded, negative-sense RNA segments designated S (small), M (medium), and L (large). The S RNA encodes the nucleocapsid (N) protein. The M RNA encodes a polyproteint hat is cotranslationally cleaved

to yield the envelope glycoproteins Gn (formerly G1) and Gc (formerly G2).The L RNA encodes the L protein, which functions as the viral transcriptase/replicase. Within virions, the genomic RNAs of hantaviruses are thought to complex with the N protein to form helical nucleocapsids, the RNA component of which circularizes due to sequence complementarity between the 5' and 3' terminal sequences of genomic segments. As with other Bunyavirales, each of the three segments has a consensus 3'-terminal nucleotide sequence (AUCAUCAUC), which is complementary to the 5'-terminase sequence and is distinct from those of the other four genera in the family. These sequences appear to form panhandle structure which seem likely to play a role in replication and encapsidation facilitated by binding with the viral nucleocapsid (N) protein. The large segment is 6530–6550 nucleotides (nt) in length, the medium is 3613–3707 nt in length and the small is 1696–2083 nt in length. No nonstructural proteins are known, unlike the other genera in this family. At the 5' and 3' of each segment are short noncoding sequences: the noncoding segment in all sequences at the 5' end is 37–51 nt. The 3' noncoding regions differ: L segment 38–43 nt; M segment 168–229 nt; and S segment 370–730 nt. The 3' end of the S segment is conserved between the genera suggesting a functional role.

Virions:-Hantavirus virions are about 120–160 nanometers (nm) in diameter. The lipid bilayer of the viral envelope is about 5 nm thick and is embedded with viral surface proteins to which sugar residues are attached. These glycoproteins, known as Gn and Gc, are encoded by the M segment of the viral genome. They tend to associate (heterodimerize) with each other and have both an interior tail and an exterior domain that extends to about 6 nm beyond the envelope surface. Inside the envelope are the nucleocapsids. These are composed of many copies of the nucleocapsid protein N, which interact with the three segments of the viral genome to form helical structures. The virally encoded RNA polymerase is also found in the interior. By mass, the virion is greater than 50% protein, 20–30% lipid and 2–7% carbohydrate. The density of the virions is 1.18 gram per cubic centimeter. These features are common to all members of the Hantaviridae family.[1][2]

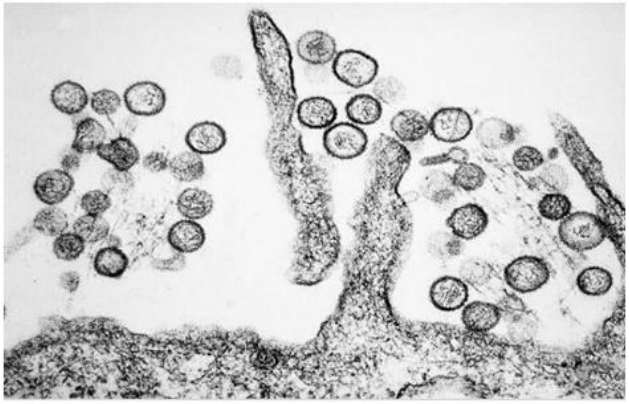

Figure 3: Electron microscope image of hantavirus

Life cycle: Entry into host cells is thought to occur by attachment of virions to cellular receptors and subsequent endocytosis. Nucleocapsids are introduced into the cytoplasm by pH-dependent fusion of the virion with the endosomal membrane. After the release of the nucleocapsids into cytoplasm, the complexes are targeted to the ER–Golgi Intermediate compartments (ERGIC) through microtubular-associated movement resulting in the formation of viral factories at ERGIC.[citation needed]These factories then facilitate transcription and subsequent translation of the viral proteins. Transcription of viral genes must be initiated by association of the L protein with the three nucleocapsid species. In addition to transcriptase and replicase functions, the viral L protein is also thought to have an endonuclease activity that cleaves cellular messenger RNAs (mRNAs) for the production of capped primers used to initiate transcription of viral mRNAs. As a result of this cap snatching, the mRNAs of hantaviruses are capped and contain nontemplated 5'-terminal extensions. The G1 (or Gn) and G2 (Gc) glycoproteins form hetero-oligomers and are then transported from the endoplasmic reticulumto the Golgi complex, where glycosylation is completed. The L protein produces nascent genomes byreplication via a positive-sense RNA intermediate. Hantavirus virions are believed to assemble by association of nucleocapsids with glycoproteins embedded in the membranes of the Golgi, followed by budding into the Golgi cisternae. Nascent virions are then transported in secretory vesicles to the plasma membrane and released by exocytosis.

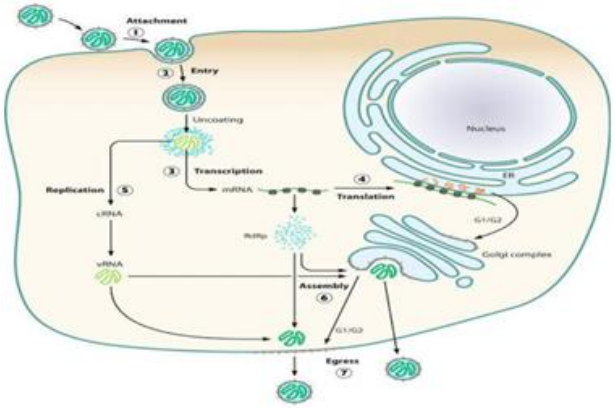

Figure 4: Life cycle of hantavirus

Facts About Hantaviruses
What You Need To Know To Prevent the Disease Hantavirus Pulmonary Syndrome (HPS).

What are hantaviruses?
Hantaviruses are a group of viruses that may be carried by some rodents. Some hantaviruses can cause a rare but deadly disease called hantavirus pulmonary syndrome. The disease is called HPS for short**.**

What animals can give people hantavirus?
Only some kinds of mice and rats can give people hantaviruses that can cause HPS. In North America, they are the deer mouse, the white-footed mouse, the rice rat, and the cotton rat. However, not every deer mouse, white-footed mouse, rice rat, or cotton rat carries a hantavirus. Other rodents, such as house mice, roof rats, and Norway rats, have never been known to give people HPS. Since it is hard to tell if a mouse or a rat carries a hantavirus, it is best to avoid all mice and rats and to safely clean up any rodent urine, droppings, or nests in your home. Dogs and cats cannot give people hantavirus infections.

Hantavirus pulmonary syndrome (HPS) is found in North, Central and South America.It is an often fatal pulmonary disease. In the United States, the causative agent is the Sin Nombre virus carried by deer mice. Prodromal symptoms include flu-like symptoms such as fever, cough, muscle pain, headache, and lethargy. It is characterized by a sudden onset of shortness of breath with rapidly evolving pulmonary edema that is often fatal despite intervention with mechanical ventilation and potent diuretics. The fatality rate is 36%. Hantavirus pulmonary syndrome was first recognized during the 1993 outbreak in the Four Corners region of the southwestern United States. It was identified by Dr. Bruce Tempest. It was originally called "Four Corners disease, " but the name was changed to "Sin Nombre virus" after complaints by Native Americans that the name "Four Corners" stigmatized the region. It has since been identified throughout the United States. Rodent control in and around the home remains the primary prevention strategy.[9]

Who can get HPS?
Any man, woman, or child who is around mice or rats that carry harmful hantaviruses can get HPS. You do not have to already be sick to be at risk for HPS. Healthy people have become ill with HPS. While HPS is a very rare disease, cases have occurred in all regions of the United States except for Alaska and Hawaii.

These are some of the mice and rats that can carry hantaviruses in the United States.

Figure 5: Cotton Rat

Figure 6: Deer Mice

How do people get HPS?
People get HPS when they breath in hantaviruses. This can happen when rodent urine and droppings that contain a hantavirus are stirred up into the air. People can also become infected when they touch mouse or rat urine, droppings, or nesting materials that contain the virus and then touch their eyes, nose, or mouth. They can also get HPS from a mouse or rat bite.

Here are some activities that can put people at risk for HPS:
- Improperly cleaning up mouse and rat urine, droppings, and nests.
- Cleaning a shed or cabin that has been closed for some tim.
- Working in areas where mice and rats may live (such as barns).

In the United States, there has never been a case in which a person with HPS has given the disease to another person.

What are the symptoms of HPS?
If people get HPS, they will feel sick 1 to 5 weeks after they were around mice or rats that carried a hantavirus. At first people with HPS will have:
- Fever
- Severe muscle aches
- Fatigue

After a few days they will have a hard time breathing. Sometimes people will have headaches, dizziness, chills, nausea, vomiting, diarrhea, and stomach pain. Usually, people do not have a runny nose, sore throat, or a rash.

How can HPS be prevented?
- Keep mice and rats out of your home.
- Clean up mouse and rat urine, droppings, and nesting materials with adisinfectant or a mixture of bleach and water.

Transmission:-
Hantavirus is spread when virus-containing particles from rodent urine, droppings, or saliva are stirred into the air. It is important to avoid actions that raise dust, such as sweeping or vacuuming. Infection occurs when you breathe in virus particles. The viruses that cause hantavirus hemorrhagic fever have not been shown to transfer from person to person, except for Andes virus. For other species of hantavirus, aerosolized rodent excreta or rodent bites are the only known routes of transmission to humans. Similar negative-stranded RNA viruses, such as Marburg and Ebolahemorrhagic fevers, can be transmitted by contact with infected blood and body fluids, and are known to spread to healthcare workers in African hospitals, but do not transfer readily in a modern hospital setting with the appropriate precautions. Transmission through fomites (inanimate objects exposed to infection) has not been demonstrated in hantavirus disease in either the hemorrhagic or pulmonary form.

Where Hantavirus is Found
Cases of human hantavirus infection occur sporadically, usually in rural areas where forests, fields, and farms offer suitable habitat for the virus's rodent hosts. Areas around the home or work where rodents may live (for example, houses,

barns, outbuildings, and sheds) are potential sites where people may be exposed to the virus. In the US and Canada, the Sin Nombre hantavirus is responsible for the majority of cases of hantavirus infection. The host of the Sin Nombre virus is the deer mouse (Peromyscusmaniculatus), present throughout the western and central US and Canada. Several other hantaviruses are capable of causing hantavirus infection in the US. The New York hantavirus, carried by the white-footed mouse, is associated with HPS cases in the northeastern US. The Black Creek hantavirus, carried by the cotton rat, is found in the southeastern US. Cases of HPS havebeen confirmed elsewhere in the Americas, including Canada, Argentina, Bolivia, Brazil, Chile, Panama, Paraguay, and Uruguay.[3]

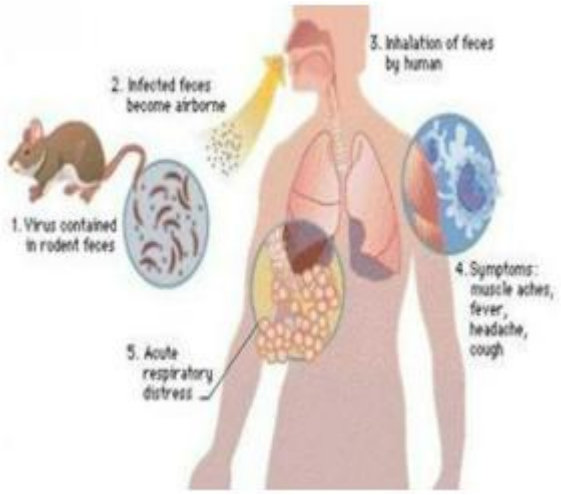

Figure 7: Huntavirus pulmonary Syndrome

Sign and symptoms

Due to the small number of HPS cases, the "incubation time" is not positively known. However, on the basis of limited information, it appears that symptoms may develop between 1 and 8 weeks after exposure to fresh urine, droppings, or saliva of infected rodents.

Early Symptoms

Early symptoms include fatigue, fever and muscle aches, especially in the large muscle groups—thighs, hips, back, and sometimes shoulders. These symptoms are universal. There may also be headaches, dizziness, chills, and abdominal problems, such as nausea, vomiting, diarrhea, and abdominal pain. About half of all HPS patients experience these symptoms.

Late Symptoms

Four to 10 days after the initial phase of illness, the late symptoms of HPS appear. These include coughing and shortness of breath, with the sensation of, as one survivor put it, a "…tight band around my chest and a pillow over my face" as the lungs fill with fluid.

Prevention

According to the CDC, the best prevention against contracting hantavirus is to eliminate or minimize contact with rodents in the home, workplace, or campsite. As the virus can be transmitted by rodent saliva, excretions, and bites, control of rats and mice in areas frequented by humans is key for disease prevention. General prevention can be accomplished by disposing of rodent nests, sealing any cracks and holes in homes where mice or rats could enter, setting traps, or laying down poisons or using natural predators such as cats in the home.

The duration that hantaviruses remain infectious in the environment varies based on factors such as the rodent's diet, temperature, humidity, and whether indoors or outdoors. The viruses have been demonstrated to remain active for two to three days at normal room temperature, while ultraviolet rays in direct sunlight kills them within a few hours. However, rodent droppings or urine of indeterminate age should always be treated as infectious. Eliminate or minimize contact with rodents in your home, workplace, or campsite. If rodents don't find that where you are is a good place for them to be, then you're less likely to come into contact with them. Seal up holes and gaps in your home or garage. Place traps in and around your home to decrease rodent infestation. Clean up any easy-to-get food. Recent research results show that many people who became ill with HPS developed the disease after having been in frequent contact with rodents and/or their droppings around a home or a workplace. On the other hand, many people who became ill reported that they had not seen rodents or rodent droppings at all. Therefore, if you live in an area where the carrier rodents are known to live, try to keep your home, vacation place, workplace, or campsite clean.[8]

Vaccine

Hantavirus vaccine is a vaccine that protects in humans against hantavirus infections causing hantavirus hemorrhagic fever with renal syndrome (HFRS) or hantavirus pulmonary syndrome (HPS). The vaccine is considered important as acute hantavirus infections are responsible for significant morbidity and mortality worldwide. It is estimated that about 1.5 million cases and 46, 000 deaths occurred in China from 1950 to 2007. The number of cases is estimated at 32, 000 in Finland from 2005 to 2010 and 90, 000 in Russia from 1996 to 2006.

The first hantavirus vaccine was developed in 1990 initially for use against Hantaan River virus which causes one of the most severe forms of HFRS. It is estimated that about two million doses of rodent brain or cell-culture derived vaccine are given in China every year. The wide use of this vaccine may be partly responsible for a significant decrease in the number of HFRS cases in China to less than 20, 000 by 2007.Other hantaviruses for which the vaccine is used include Seoul (SEOV) virus. However the vaccine is thought not to be effective against European hantaviruses including Puumala (PUUV) and Dobrava-Belgrade (DOBV) viruses. The pharmaceutical trade name for the vaccine is Hantavax. As of 2012 no hantavirus vaccine have been approved for use in Europe or USA. A phase 2 study on a human HTNV/PUUV DNA hantavirus vaccine is ongoing. In addition to Hantavax three more vaccine candidates have been studied in I–II stage clinical trials. They include a recombinant vaccine and vaccines derived from HTNV and PUUV viruses. However, their prospects are unclear.

Figure 8: Seal up the hole inside & outside of the home to keep rodents out}

Figure 9: Trap rodents around the home to help reduce the population

Pathology:- Immunohistochemistry analysis has shown that viral antigens are distributed primarily within the endothelium of capillaries throughout various tissues from patients with HPS. Marked accumulations of hantaviral antigens are seen in the pulmonary microvasculature and in follicular dendritic cells within the lymphoid follicles of spleen and lymph nodes. Hantaviral nucleic acids can also be localized to endothelial and inflammatory cells in tissues from HPS cases by using in situ hybridization. Electron micrographic studies confirm the infection of endothelial cells and macrophages in the lungs of HPS patients. Typical hantaviral inclusions are seen frequently in pulmonary endothelial cells, and their identity can be confirmed by immunolabeling. In the heart, endothelial staining is mainly in the capillaries of the myocardium and varies from focal immunostaining insome cases to diffuse and extensive staining in others. Occasionally, staining of endothelial cells lining the endocardium is observed. Functional impairment of vascular endothelium is central to the pathogenesis of HPS. However, thepathogenesis of HPS is complex, and a myocardial depressant may contribute significantly to the mortality of this disease. It is unclear how the shock syndrome relates to factors such as viral distribution and immunologic and pharmacological mediators of capillary permeability. There appears to be compartmentalization of a selective immune response in the lungs of HPS patients in combination with extremely high levels of viral antigens in the pulmonary vasculature. This feature suggests that the mechanism of inflammatory cell recruitment in the lungs of HPS patients may result from specific attraction and adherence of a selective population of inflammatory cells to an activated pulmonary microvascular endothelium.

The pathogenesis of hantavirus infections is unclear as there is a lack of animal models to describe it (rats and mice do not seem to acquire severe disease). While the primary site of viral replication in the body is not known, in HFRS the main effect is in the blood vessels while in HPS most symptoms are associated with the lungs. In HFRS, there are increased vascular permeability and decreased blood pressure due to endothelial dysfunction and the most dramatic damage is seen in the kidneys, whereas in HPS, the lungs, spleen, and gall bladder are most affected. Early symptoms of HPS tend to present similarly to the flu (muscle aches, fever and fatigue) and usually appear around 2 to 3 weeks after exposure. Later stages of the disease (about 4 to 10 days after symptoms start) include difficulty breathing, shortness of breath and coughing.

Epidemiology:- Hantavirus infections have been reported from all continents except Australia. Regions especially affected by hemorrhagic fever with renal syndrome include China, the Korean Peninsula, Russia (Hantaan, Puumala and Seoul viruses), and northern and western Europe (Puumala and Dobrava virus). Regions with the highest incidences of hantavirus pulmonary syndrome include Argentina, Chile, Brazil, the United States, Canada, and Panama.

Africa:- In 2010, a novel hantavirus, Sangassouvirus was isolated in Africa which causes hemorrhagic fever with renal syndrome.

Asia:- In China, Hong Kong, the Korean Peninsula and Russia, hemorrhagic fever with renal syndrome is caused by Hantaan, Puumala and Seoul viruses.

China:- In March 2020, a man from Yunnan tested positive for Hantavirus. He died while travelling to Shandong for work on a chartered bus. According to the Global Times reports, around 32 other people have been tested for the virus.

North America

Canada:- The primary cause of the disease in Canada is Sin Nombre virus-infected deer mice. Between 1989 and 2014, there were a total of 109 confirmed cases, with the death rate estimated at 29%.The virus exists in deer mice nationwide, but cases were concentrated in western Canada (British Columbia, Alberta, Saskatchewan and Manitoba) with only one case in eastern Canada. In Canada "[a]ll cases occurred in rural settings and approximately 70% of the cases have been associated with domestic and farming activities."

United States:- In the United States, minor cases of HPS include Sin Nombreorthohantavirus, New York orthohanta virus, Bayou orthohantavirus, and possibly Black Creek Canal orthohantavirus. As of January 2017, 728 cases of hantavirus had been reported in the United States cumulatively since 1995, across 36 states, not including cases with presumed exposure outside the United States. More than 96% of cases have occurred in states west of the Mississippi River. The top 10 states by number of cases reported (which differs slightly from a count ordered by the state of original exposure) were New Mexico (109), Colorado (104), Arizona (78), California (61), Washington

(50), Texas (45), Montana (43), Utah (38, Idaho (21), and Oregon (21); 36% of the total reported cases have resulted in death.

Australia:- As of 2005, there were no human infections reported in Australia, though rodents were found to carry antibodies.[5]

2. Diagnosis and treatment

Diagnosing HPS

Diagnosing HPS in an individual who has only been infected a few days is difficult, because early symptoms such as fever, muscle aches, and fatigue are easily confused with influenza. However, if the individual is experiencing fever and fatigue and has a history of potential rural rodent exposure, together with shortness of breath, would be strongly suggestive of HPS. If the individual is experiencing these symptoms they should see their physician immediately and mention their potential rodent exposure. Doctors diagnose hantavirus with several tests. Blood tests identify proteins (antibodies) associated with the virus. Blood tests can also reveal signs of the disease. These signs may include larger-than-normal white blood cells and an abnormally low amount of platelets (a substance that helps blood clot). Serology and virus detection are the best method of diagnosis for hantavuris.

Treatment

There is no specific treatment for hantavirus pulmonary syndrome. It is important the infection is diagnosed early so patients can receive supportive care including oxygen therapy, fluid replacement, and blood pressure medications. Kidney dialysis may be needed. There is no specific treatment, cure, or vaccine for hantavirus infection. However, we do know that if infected individuals are recognized early and receive medical care in an intensive care unit, they may do better. In intensive. care, patients are intubated and given oxygen therapy to help them through the period of severe respiratory distress. The earlier the patient is brought in to intensive care, the better. If a patient is experiencing full distress, it is less likely the treatment will be effective. Therefore, if you have been around rodents and have symptoms of fever, deep muscle aches, and severe shortness of breath, see your doctor immediately. Be sure to tell your doctor that you have been around rodents—this will alert your physician to look closely for any rodent-carried disease, such as HPS.

Ribavirin may be a drug for HPS and HFRS but its effectiveness remains unknown, still, spontaneous recovery is possible with supportive treatment. People with suspected hantavirus infection may be admitted to the hospital, given oxygen and mechanical ventilation support to help them breathe during the acute pulmonary stage with severe respiratory distress. Immunotherapy, administration of human neutralizing antibodies during acute phases of Hantavirus, has only been studied in mice, hamsters, and rats. There are no reports of controlled clinical trials.[7]

3. Conclusion

The results conclude that the Hantavirus is maintained within the rodent population, specifically the deer mouse. ... Hantavirus is not only deadly but may have a very simple reservoir. the patients died from Hantavirus spread from deer mice around or near their homes. Over the past few decades the understanding and recognition of hanta virus disease throughout the world has greatly expanded. serological testing is the preferable method for dignosis of hantavirus.

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