ARBOVIRUSES

Group of Viruses Containing Several Families of ARthropod-BOrne And Related Viruses

Dr Esam Ibraheem Azhar
Arthropod-borne Viruses

Arthropod-borne viruses (arboviruses) are viruses that can be transmitted to man by arthropod vectors.
ARBOVIRUS
Included Families

TRANSMITTED
By
MOSQUITOES
Or
TICKS

Togaviridae
Flaviviridae
Bunyaviridae
Reoviridae
**TOGAVIRIDAE**

**SIZE (nm):** 65  
**ENVELOPED:** Yes  
**CAPSID SYMM:** Icosahedral  
**NUCLEIC ACID:** RNA  
**CLASS:** IV  
**FORM:** ss+, 5’-CAP  
3’- polyA  
**SEG:** 1  
**GENES:** 7  
**KB:** 10 - 12  

**MEMBERS**

(Alphavirus) EEE, WEE, VEE, (Rubivirus) rubella, (Arterivirus), & (Pestivirus).
<table>
<thead>
<tr>
<th>GENERA</th>
<th>Characteristic Members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alphaviruses</td>
<td>Eastern equine encephalitis virus (EEE)</td>
</tr>
<tr>
<td></td>
<td>Venezuelan equine encephalitis virus (VEE)</td>
</tr>
<tr>
<td></td>
<td>Western equine encephalitis virus (WEE)</td>
</tr>
<tr>
<td>Rubivirus</td>
<td>Rubellavirus</td>
</tr>
</tbody>
</table>
Viruses are cytolytic.

Viruses establish systemic infection and viremia.

Viruses are good inducers of interferon, which can account for the influenza-like symptom of infection.
FLAVIVIRIDAE

SIZE (nm): 45
ENVELOPED: Yes
CAPSID SYMM: Icosahedral
NUCLEIC ACID: RNA
CLASS: IV
FORM: ss+, 5’-CAP
SEG: 1
GENES: 6 - 7
KB: 9.5 - 11

MEMBERS
Yellow-Fever, Dengue virus, HCV, West Nile virus
St. Louis Encephalitis (SLE), Japanese Encephalitis
<table>
<thead>
<tr>
<th>GENERA</th>
<th>Characteristic Members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flavivirus</td>
<td>Yellow fever virus</td>
</tr>
<tr>
<td></td>
<td>Dengue virus</td>
</tr>
<tr>
<td></td>
<td>West Nile virus</td>
</tr>
<tr>
<td></td>
<td>Japanese encephalitis virus</td>
</tr>
<tr>
<td></td>
<td>St. Louis encephalitis virus (SLE)</td>
</tr>
</tbody>
</table>
Viruses, except hepatitis C, are arboviruses.

Flaviviruses infect cells of the monocyte-macrophage lineage.

Non-neutralizing antibody can enhance flavivirus infection via Fc receptors on the macrophage.
BUNYAVIRIDAE

SIZE (nm): 100
ENVELOPED: Yes
CAPSID SYMM: Helix
NUCLEIC ACID: RNA
CLASS: V
FORM: ss- (ambisense)
SEG: 3
GENES: 6
KB: 12 - 13

MEMBERS
Rift Valley fever, CE
<table>
<thead>
<tr>
<th>GENERA</th>
<th>Characteristic Members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phlebovirus</td>
<td>Rift Valley fever virus</td>
</tr>
<tr>
<td>Bunyavirus</td>
<td>California encephalitis virus (CE)</td>
</tr>
<tr>
<td>Hantavirus</td>
<td></td>
</tr>
<tr>
<td>Nairovirus</td>
<td></td>
</tr>
<tr>
<td>Tospovirus</td>
<td></td>
</tr>
</tbody>
</table>
REOVIRIDAE

SIZE (nm): 60
ENVELOPED: No
CAPSID SYMM: Icosahedral
NUCLEIC ACID: RNA
CLASS: III
FORM: ds
SEG: 10
GENES: 10
KBP: 24

MEMBERS
Colorado tick fever, Rotavirus
<table>
<thead>
<tr>
<th>GENERA</th>
<th>Characteristic Members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coltivirus</td>
<td>Colorado tick fever virus</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Human Rotaviruses</td>
</tr>
</tbody>
</table>

Four Other Animal & Plant Genera
Transmission Cycles

• **Man - arthropod - man**
  – e.g. dengue, urban yellow fever.
  – Reservoir may be in either man or arthropod vector.
  – In the latter transovarial transmission may take place.

• **Animal - arthropod vector - man**
  – e.g. Japanese encephalitis, EEE, WEE, jungle yellow fever.
  – The reservoir is in an animal.
  – The virus is maintained in nature in a transmission cycle involving the arthropod vector and animal. Man becomes infected incidentally.

• **Both cycles may be seen with some arboviruses such as yellow fever.**
Man-Arthropod-man Cycle
Urban Cycle
Animal-Arthropod-Man Cycle
Jungle Cycle
Arthropod Vectors

**Mosquitoes**
Japanese encephalitis, dengue, yellow fever, St. Louis encephalitis, EEE, WEE, VEE, Rift valley fever etc.

**Ticks**
Crimean-Congo haemorrhagic fever, various tick-borne encephalitides etc.

**Sandflies**
Sandfly fever.
Examples of Arthropod Vectors

Aedes Aegyti

Assorted Ticks

Culex Mosquito

Phlebotmine Sandfly
Animal Reservoirs

In many cases, the actual reservoir is not known. The following animals are implicated as reservoirs:

<table>
<thead>
<tr>
<th>Animal</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birds</td>
<td>Japanese encephalitis, St Louis encephalitis, EEE, WEE</td>
</tr>
<tr>
<td>Pigs</td>
<td>Japanese encephalitis</td>
</tr>
<tr>
<td>Monkeys</td>
<td>Yellow Fever</td>
</tr>
<tr>
<td>Rodents</td>
<td>VEE, Russian Spring-Summer encephalitis</td>
</tr>
</tbody>
</table>
Diseases Caused

- **Fever and rash** - this is usually a non-specific illness resembling a number of other viral illnesses such as influenza, rubella, and enterovirus infections. The patients may go on to develop encephalitis or haemorrhagic fever.

- **Encephalitis** - e.g. EEE, WEE, St Louis encephalitis, Japanese encephalitis.

- **Haemorrhagic fever** - e.g. yellow fever, dengue, Crimean-Congo haemorrhagic fever.
**ARBOVIRUS INFECTIONS**

<table>
<thead>
<tr>
<th>GENERA</th>
<th>Characteristic Members</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>INFECTIONS</td>
</tr>
<tr>
<td></td>
<td>Encephalitis</td>
</tr>
<tr>
<td></td>
<td>Rash fevers</td>
</tr>
<tr>
<td></td>
<td>Hemorrhagic fevers</td>
</tr>
</tbody>
</table>

**DETAILS OF INFECTION**
1. Virus introduced into bloodstream
2. Viremia produced

**EARLY SYMPTOMS**
- Fever, chills, aching
- Rapid onset
ENCEPHALITIS

TARGET ORGANS
Central Nervous System

DISEASES
St. Louis encephalitis
Eastern equine encephalitis
Western equine encephalitis
Venezuelan equine encephalitis
California encephalitis

- St. Louis encephalitis
- Rocio and St. Louis (Brazil)
- West Nile virus
- Japanese encephalitis
- West Nile and Japanese encephalitis
- Japanese and Murray Valley encephalitis
- Murray Valley and Kunjin
Most Frequently Reported Encephalitis in USA

- **California serogroup/La Crosse encephalitis (Bunyavirus family)**
  Recent cases have been predominantly in the Eastern US. Reservoir is small mammals, transmitted by mosquitos. Children more often develop symptoms than adults. Fatality and morbidity low.

- **St. Louis encephalitis (Flavivirus family)**
  Elderly are most severely affected. The case fatality rate (CFR) varies from 3-25%. Reservoir is birds. Transmitted by mosquitos. Can have an urban cycle as well.
- **Eastern equine encephalitis (Alphavirus genus of Togavirus family)**  
  Reservoir is birds. Transmitted by mosquitos. Horse is a dead end host. Children more likely to have severe clinical symptoms than adults.

- **West Nile encephalitis (Flavivirus)**  
  - Those over 50 years of age are most severely affected.  
  - The case fatality rate is approximately 10%. Reservoir is birds.  
  - Transmitted by mosquitos.  
  - Possible that ribavirin may be active against West Nile virus.
Less Commonly Reported Encephalitis in USA

- **Western equine encephalitis (Alphavirus genus of Togavirus family)**
  - Reservoir is birds.
  - Transmitted by mosquitos.
  - Horse is a dead end host.
  - Children are more likely to have severe clinical symptoms that adults.

- **Venezuelan equine encephalitis (Alphavirus genus of Togavirus family)**
  - This virus is predominantly problem in central and South America, but it is periodically a problem in the southern US (Texas, Florida).
  - Its reservoir is small mammals and horses.
Japanese Encephalitis

- First discovered and originally restricted to Japan. Now large scale epidemics occur in China, India and other parts of Asia.
- Flavivirus, transmitted by Culex mosquitoes.
- The virus is maintained in nature in a transmission cycle involving mosquitoes, birds and pigs.
- Most human infections are sub-clinical: the in apparent to clinical cases is 300:1
- In clinical cases, a life-threatening encephalitis occurs.
- The disease is usually diagnosed by serology. No specific therapy is available.
- Since Culex has a flight range of 20km, all local control measures will fail. An effective vaccine is available.
RASH FEVERS

TARGET ORGANS

Skin, muscles & joints

DISEASES

Dengue
Rift Valley
Colorado Tick Fever
HEMORRHAGIC FEVERS

TARGET ORGANS
- Skin
- Other specific organs (liver)

DISEASES
- Yellow Fever
- Dengue
Yellow Fever (1)

- Flavivirus, mainly found in West Africa and S America
- Yellow fever occurs in 2 major forms: urban and jungle yellow fever. Man may become incidentally infected on venturing into jungle areas.
- The urban form is transmitted between humans by the Aedes aegypti mosquito
- Classically Yellow Fever presents with chills, fever, and headache. Generalized myalgias and GI complaints.
- Some patients may experience an asymptomatic infection or a mild undifferentiated febrile illness.
Yellow Fever (2)

- After a period of 3 to 4 days, the more severely ill patients with a classical YF course will develop bradycardia (Faget's sign), jaundice, and haemorrhagic manifestations.
- 50% of patients with YF will develop fatal disease characterized by severe haemorrhagic manifestations, and hypotension.
- Diagnosis is usually made by serology
- There is no specific antiviral treatment
- An effective live attenuated vaccine is available against yellow fever and is used for persons living in or traveling to endemic areas.
Dengue (1)

- Dengue is the biggest arbovirus problem in the world today with over 2 million cases per year. Dengue is found in SE Asia, Africa and the Caribbean and S America.

- Flavivirus, 4 serotypes, transmitted by Aedes mosquitoes which reside in water-filled containers.

- Human infections arise from a human-mosquitoes-human cycle

- Classically, dengue presents with a high fever, lymphadenopathy, myalgia, bone and joint pains, headache, and a maculopapular rash.

- Severe cases may present with haemorrhagic fever and shock with a mortality of 5-10%. (Dengue haemorrhagic fever or Dengue shock syndrome.)
Dengue (2)

- Dengue haemorrhagic fever and shock syndrome appear most often in patients previously infected by a different serotype of dengue.
- Diagnosis is made by serology.
- No specific antiviral therapy is available.
- Prevention of dengue in endemic areas depends on mosquito eradication. The population should remove all containers from their premises which may serve as vessels for egg deposition.
- A live attenuated vaccine is being tried in Thailand with encouraging results.
Dengue Hemorrhagic Fever (DHF)

- DHF is a potentially deadly complication of dengue fever.
- It appears to be an immunopathological consequence of the infection of a person with a virus of one serotype who has developed immunity to another serotype, although the mechanism is not really understood.
- It is more severe in children in whom the presence of maternal antibody may result in DHF even from a first infection with Dengue virus.
- There are four serotypes of dengue virus and multiple serotypes circulate in Asia, Africa and the Americas.
World Distribution of Dengue - 2000

Areas infested with *Aedes aegypti*

Areas with *Aedes aegypti* and dengue epidemic activity

CDC
A large subcutaneous haemorrhage on the upper arm of a patient with dengue haemorrhagic fever.
Rift Valley Fever (1)

- This virus is able to cause severe disease in domestic animals and man.
- The disease is found in all parts of Africa, where epidemics have occurred from time to time with significant morbidity and mortality.
- It was originally isolated in Kenya during an epizootic of fatal hepatic necrosis and abortion in sheep.
- Rift valley fever virus extended into Egypt in 1977 causing a widespread epidemic with at least 600 deaths. The virus subsequently disappeared from Egypt.
- The virus is thought to transmitted mainly by mosquitoes although it can be transmitted by Sandflies. Aerosol transmission had also been documented where man had become infected after coming into contact with animal carcasses.
Rift Valley Fever (2)

• Most infections are symptomatic and usually present as a mild non-specific febrile illness, a small proportion (~1%) develop haemorrhagic fever, retinal vasculitis and encephalitis.

• Treatment is supportive, although ribavirin, interferon and passive immunization have been shown to be useful in animal models. Certain ribavirin should be considered as part of the management.

• A formalin-inactivated cell culture vaccine is available and is thought to be effective and safe, although it is very expensive and thus its use should be confined to susceptible laboratory and veterinary workers.
<table>
<thead>
<tr>
<th>DISEASE</th>
<th>Colorado Tick Fever</th>
</tr>
</thead>
<tbody>
<tr>
<td>REOVIRUS</td>
<td></td>
</tr>
<tr>
<td>TRANSMISSION</td>
<td>Tick bite</td>
</tr>
<tr>
<td>SYMPTOMS</td>
<td>Like other rash fevers: Fever, headache, myalgia, rash Not severe</td>
</tr>
</tbody>
</table>
Colorado tick fever (Reovirus family)

- This occurs in the Rocky Mountain States.
- It is a mild disease resulting in fever, headache, myalgia and often rash.
- The virus is transmitted by ticks.
- In diagnosis, the physician must consider the much more serious Rocky Mountain spotted fever (rickettsial disease) which may have similar initial symptoms and should be treated promptly.
Diagnosis

- **Serology** - usually used to make a diagnosis of arbovirus infections.

- **Culture** - a number of cell lines may be used, including mosquito cell lines. However, it is rarely carried out since many of the pathogens are group 3 or 4 pathogens.

- **Direct detection tests** - e.g. detection of antigen and nucleic acids are available but again there are safety issues.
Prevention

• **Surveillance** - of disease and vector populations

• **Control of vector** - pesticides, elimination of breeding grounds

• **Personal protection** - screening of houses, bed nets, insect repellants

• **Vaccination** - available for a number of Arboviral infections e.g. Yellow fever, Japanese encephalitis, Russian tick-borne encephalitis
Viral Zoonosis
Definition

- Zoonosis are diseases of vertebrate animals that can be transmitted to man: either directly or indirectly through an insect vector.

- When an insect vector is involved, the disease is also known as an Arboviral disease.

- However, not all Arboviral diseases are zoonosis: where the transmission cycle takes place exclusively between insect vector and human e.g. dengue and urban yellow fever.

- Examples of viral zoonosis that can be transmitted to man directly include rabies, hantaviruses, Lassa and Ebola fevers.
RHABDOVIRIDAE

SIZE (nm): 175 x 75
ENVELOPED: Yes
CAPSID SYMM: Helix
NUCLEIC ACID: RNA
CLASS: V
FORM: ss-
SEG: 1
GENES: 5 - 6
KB: 11-12

MEMBERS
Rabies, VSV
Rabies Virus

Structure of rabies virus (Source: CDC)

Rabies virus particles
<table>
<thead>
<tr>
<th>GENERA</th>
<th>Characteristic Members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lyssavirus</td>
<td>Rabies virus</td>
</tr>
<tr>
<td>Vesiculovirus</td>
<td>Vesicular stomatitis virus (VSV)</td>
</tr>
<tr>
<td>Ephemeroovirus</td>
<td>Bovine ephemeral virus</td>
</tr>
<tr>
<td>plant-infecting</td>
<td></td>
</tr>
<tr>
<td>Rhabdoviruses</td>
<td></td>
</tr>
</tbody>
</table>
Epidemiology

Rabies is a zoonosis which is prevalent in wildlife. The main animals involved differs from continent to continent.

Europe  fox, bats
Middle East  wolf, dog
Asia  dog
Africa  dog, mongoose, antelope
N America  foxes, raccoons, insectivorous bats
S America  dog, vampire bats
**DISEASE**

**Rabies**

**EARLY SYMPTOMS**
- Nausea
- Vomiting
- Pain at bite site
- Anxiety

**LATER SYMPTOMS**
- Spasms, confusion, inability to swallow, paralysis, death

**SEQUENCE OF INFECTION**

- Bite Subject
- Domesticated Animal
- Creature In The Wild
Laboratory Diagnosis

- **Histopathology** - Negri bodies.

- **Rapid virus antigen detection** - virus antigen detection by IF had become widely used. Corneal impressions or neck skin biopsy are taken. The Direct Fluorescent Antibody test (DFA) is commonly used.

- **Virus cultivation** - The most definitive means of diagnosis is by virus cultivation from saliva and infected tissue. Cell cultures may be used or more commonly, the specimen is inoculated intracerebrally into infant mice. Because of the difficulties involved, this is rarely offered by diagnostic laboratories.

- **Serology** - circulating antibodies appear slowly in the course of infection but they are usually present by the time of onset of clinical symptoms.
Diagnosis of Rabies

Negri Body in neuron cell  
(source: CDC)

Positive DFA test  
(Source: CDC)
Management and Prevention

- **Pre-exposure prophylaxis** - Inactivated rabies vaccine may be administered to persons at increased risk of being exposed to rabies e.g. vets, animal handlers, laboratory workers etc.

- **Post-exposure prophylaxis** - In cases of animal bites, dogs and cats in a rabies endemic area should be held for 10 days for observation. If signs develop, they should be killed and their tissue examined.

- Wild animals are not observed but if captured, the animal should be killed and examined. The essential components of post-exposure prophylaxis are the local treatment of wounds and active and passive immunization.

- Once rabies is established, there is nothing much that could be done except intensive supportive care. To date, only 2 persons with proven rabies have survived.
Post-exposure Prophylaxis

• **Passive immunization** - human rabies immunoglobulin around the area of the wound; to be supplemented with an i.m. dose to confer short term protection.

• **Active immunization** - the human diploid cell vaccine is the best preparation available. The vaccine is usually administered into the deltoid region, and 5 doses are usually given.

• There is convincing evidence that combined treatment with rabies immunoglobulin and active immunization is much more effective than active immunization alone. Equine rabies immunoglobulin (ERIG) is available in many countries and is considerably cheaper than HRIG.
Control of Rabies

• **Urban** - canine rabies accounts for more than 99% of all human rabies. Control measures against canine rabies include;
  – stray dog control.
  – Vaccination of dogs.
  – quarantine of imported animals.

• **Wildlife** - this is much more difficult to control than canine rabies. However, there are on-going trials in Europe where bait containing rabies vaccine is given to foxes. Success had been reported in Switzerland.
Viral Diseases In Which Reservoir Or Vector Is Unclear

<table>
<thead>
<tr>
<th>Family</th>
<th>Envelope</th>
<th>Symmetry</th>
<th>Genome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filoviridae</td>
<td>yes</td>
<td>helical</td>
<td>ssRNA negative sense</td>
</tr>
</tbody>
</table>

- **Ebola Virus**
- **Marburg virus**
<table>
<thead>
<tr>
<th>GENERA</th>
<th>Characteristic Members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filovirus</td>
<td>Ebola hemorrhagic fever virus</td>
</tr>
<tr>
<td></td>
<td>Marburg virus</td>
</tr>
</tbody>
</table>
Ebola and Marburg viruses cause hemorrhagic fevers and have a case-fatality rate which can be as high as 60-70% for certain strains of the viruses.

These viruses occur in Africa, but the natural reservoir is unknown.

They occasionally infect humans, but the means by which this occurs is usually not clear.

Patients have severe hemorrhages and there is a lot of virus present, so stringent barrier nursing techniques are needed to prevent further spread.

There have been a few cases where humans have been infected by apparently healthy laboratory monkeys.
## Viral Diseases Transmitted By Rodents

### ARBOVIRUSES - RODENT BORNE

<table>
<thead>
<tr>
<th>Family</th>
<th>Envelope</th>
<th>Symmetry</th>
<th>Genome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arenaviridae</td>
<td>yes</td>
<td>helical</td>
<td>ssRNA ambisense segmented</td>
</tr>
<tr>
<td>Bunyaviridae</td>
<td>yes</td>
<td>helical</td>
<td>ssRNA negative sense segmented</td>
</tr>
</tbody>
</table>
ARENAVIRIDAE

SIZE (nm): 100
ENVELOPED: Yes
CAPSID SYMM: Helix
NUCLEIC ACID: RNA
CLASS: V
FORM: ss-
(ambisense)
SEG: 2
GENES: 5
KB: 10 - 11

MEMBERS
Lassa fever, LCM
<table>
<thead>
<tr>
<th>GENERA</th>
<th>Characteristic Members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arenavirus</td>
<td>Lassa Fever virus</td>
</tr>
<tr>
<td></td>
<td>Lymphocytic Choriomeningitis virus (LCMV)</td>
</tr>
<tr>
<td></td>
<td>Tacaribe group</td>
</tr>
<tr>
<td>ARENAVIRUSES</td>
<td></td>
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<tr>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>DISEASE</td>
<td></td>
</tr>
<tr>
<td>Lassa Fever</td>
<td></td>
</tr>
<tr>
<td>(primarily Nigeria &amp; West Africa)</td>
<td></td>
</tr>
</tbody>
</table>

**TRANSMISSION**  
Rodent to man

**SYMPTOMS**  
Fever, headache, myalgia  
Rash of face & neck  
Mouth lesions, shock syndrome
<table>
<thead>
<tr>
<th>ARENAVIRUSES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DISEASE</strong></td>
</tr>
<tr>
<td>Bolivian HF</td>
</tr>
<tr>
<td>(South America)</td>
</tr>
<tr>
<td><strong>TRANSMISSION</strong></td>
</tr>
<tr>
<td>Rodent to man</td>
</tr>
<tr>
<td><strong>SYMPTOMS</strong></td>
</tr>
<tr>
<td>Fever, headache, myalgia</td>
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<td>Mouth lesions, shock syndrome</td>
</tr>
<tr>
<td>DISEASE</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>TRANSMISSION</td>
</tr>
<tr>
<td>SYMPTOMS</td>
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</tbody>
</table>
Junin and Macupo Viruses

- Junin and Macupo viruses are the causative agents of Argentine and Bolivian Haemorrhagic fever respectively.
- *Calomys musculinensis* and *C callosus* are the rodent vectors.
- The clinical presentations are similar to that of Lassa fever. Neurological signs are much more prominent than in Lassa fever.
- Unlike Lassa virus, no secondary human to human spread had been recorded.
- Hyperimmune serum and ribavirin had been shown to be effective in treatment.
Clinical Manifestations

- Incubation period of 3-5 days.
- Insidious onset of non-specific symptoms such as fever, malaise, myalgia and a sore throat.
- Typical patchy or ulcerative pharyngeal lesions may be seen.
- Severe cases may develop the following:
  - Myocarditis
  - Pneumonia
  - Encephalopathy
  - Haemorrhagic manifestations
  - Shock
- The reported mortality rate for hospitalized cases of Lassa fever is 25%. It carries a higher mortality in pregnant women.
Lassa fever virus is a Group 4 Pathogen. Laboratory diagnosis should only be carried out in specialized centers.

- **Detection of Virus Antigen** - the presence of viral antigen in sera can be detected by EIA.

- **Serology** - IgM is detected by EIA. Using a combination of antigen and IgM antibody tests, it was shown that virtually all Lassa virus infections can be diagnosed early.

- **Virus Isolation** - virus may be cultured from blood, urine and throat washings. Rarely carried out because of safety concerns.

- **RT-PCR** - being used experimentally.
Management and Prevention

- Good supportive care is essential.
- **Ribavirin** - had been shown to be effective against Lassa fever with a 2 to 3 fold decrease in mortality in high risk Lassa fever patients. Must be given early in the illness.
- **Hyperimmune serum** - the effects of hyperimmune serum is still uncertain although dramatic results have been reported in anecdotal case reports.
- Post-exposure Prophylaxis - There is no established safe prophylaxis. Various combinations of hyperimmune immunoglobulin and/or oral ribavirin may be used.
- There is no vaccine available, prevention of the disease depends on rodent control.
Dr. Azhar

**DISEASE**

Lymphocytic Choriomeningitis (LCM)

**ARENAVIRUS**

**TRANSMISSION**

Rodent to man

**EARLY SYMPTOMS**

Fever, headache, myalgia

**LATER SYMPTOMS**

Stiff neck, vomiting, severe headaches, disorientation

**MENINGES**

Membranes Enveloping The Brain and Spinal Cord
Hantaviruses

- Forms a separate genus in the Bunyavirus family.
- Unlike under Bunyaviridae, its transmission does not involve an arthropod vector.
- Enveloped ssRNA virus.
- Virions 98nm in diameter with a characteristic square grid-like structure.
- Genome consists of three RNA segments: L, M, and S.
History

• Haemorrhagic Fever with Renal Syndrome (HFRS: later renamed hantavirus disease) first came to the attention of the West during the Korean war when over 3000 UN troops were afflicted.

• It transpired that the disease was not new and had been described by the Chinese 1000 years earlier.

• In 1974, the causative was isolated from the Korean Stripped field mice and was called Hantaan virus.

• In 1995, a new disease entity called hantavirus pulmonary syndrome was described in the “four corners” region of the U.S.
Rodent Carriers of Hantaviruses

Stripped field mouse (*Apodemus agrarius*)

Bank vole (*Clethrionomys glareolus*)

Deer Mouse (*Peromyscus maniculatus*)

Rat (*Rattus*)
Hantavirus Pulmonary Syndrome (HPS)

- More than 250 cases of HPS have been reported throughout North and South America with a mortality rate of 50%.
- In common with classical HVD, HPS has a similar febrile phase.
- However, the damage to the capillaries occur predominantly in the lungs rather than the kidney.
- Shock and cardiac complications may lead to death.
- The majority of HPS cases are caused by the Sin Nombre virus. The other cases are associated with a variety of other hantaviruses e.g. New York and Black Creek Canal viruses.
Diagnosis

- **Serological diagnosis** - a variety of tests including IF, HAI, SRH, ELISAs have been developed for the diagnosis of HVD and HPS.

- **Direct detection of antigen** - this appears to be more sensitive than serology tests in the early diagnosis of the disease. The virus antigen can be demonstrated in the blood or urine.

- **RT-PCR** - found to be of great use in diagnosing hantavirus pulmonary syndrome.

- **Virus isolation** - isolation of the virus from urine is successful early in hantavirus disease. Isolation of the virus from the blood is less consistent. Sin Nombre virus has never been isolated from patients with HPS.

- **Immunohistochemistry** - useful in diagnosing HPS.
# Hantavirus Pulmonary Syndrome

## Common Laboratory Findings

<table>
<thead>
<tr>
<th>Hematology</th>
<th>Chemistry</th>
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<tbody>
<tr>
<td>Low platelet count</td>
<td>Low albumin</td>
</tr>
<tr>
<td>Atypical lymphocytes (immunoblasts)</td>
<td>Elevated LDH</td>
</tr>
<tr>
<td>Left shift on WBC differential</td>
<td>Elevated AST (SGOT)</td>
</tr>
<tr>
<td>Elevated hematocrit</td>
<td>Elevated ALT (SGPT)</td>
</tr>
<tr>
<td>Elevated WBC</td>
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Treatment and Prevention

- Treatment of HVD and HPS depends mainly on supportive measures.

- **Ribavirin** - reported to be useful if given early in the course of hantavirus disease. Its efficacy is uncertain in hantavirus pulmonary syndrome.

- **Vaccination** - an inactivated vaccine is being tried out in China. Other candidate vaccines are being prepared.

- **Rodent Control** - control measures should be aimed at reducing contact between humans and rodents.
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<tr>
<th>DISEASE</th>
<th>Korean HFRS (SE Asia)</th>
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<tr>
<td>TRANSMISSION</td>
<td>Rodent to man</td>
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<td>SYMPTOMS</td>
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**BUNYAVIRUS**

**DISEASE**

HFRS

(Europe and Asia)

**TRANSMISSION**

Rodent to man

**SYMPTOMS**

Fever, headache, myalgia

Rash of face & neck

Mouth lesions, shock syndrome
BUNYAVIRUS

DISEASE

Hantavirus pulmonary syndrome (HPS)
(N. and S. America)

TRANSMISSION

Rodent to man

SYMPTOMS

Fever, headache, pulmonary edema, shock syndrome