Arthropod-borne viruses (Arboviruses) & rodent-borne viruses
(虫媒病毒 & 病毒性出血热)

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## Comparison of arthropod- and rodent-borne viruses

<table>
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<th>Viruses</th>
<th>arthropod-borne viruses</th>
<th>rodent-borne viruses</th>
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<td>Reservoir hosts</td>
<td>arthropods (e.g., mosquitoes, and ticks)</td>
<td>rodents (e.g., mice, rats, squirrels, and hamsters)</td>
</tr>
<tr>
<td>Transmitted by</td>
<td>bloodsucking arthropods from one vertebrate host to another</td>
<td>contact with body fluids or excretions of rodents</td>
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<td>Major diseases</td>
<td>yellow fever, dengue, Japanese B encephalitis, St. Louis encephalitis, western equine encephalitis, eastern equine encephalitis, Russian spring-summer encephalitis, West Nile fever, and sandfly fever</td>
<td>hantavirus infections, Lassa fever, South American hemorrhagic fevers, and African hemorrhagic fevers (Marburg and Ebola)</td>
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Part I
Arthropod-borne viruses (Arboviruses)

Overview

- General information of arbovirus
- Main properties of togaviruses (alphavirus)
- Chikungunya caused by alphavirus
- Main properties of flaviviruses
- Dengue fever caused by flavivirus
- Japanese B Encephalitis caused by flavivirus
Arboviruses

- Arboviruses spread by arthropod vectors, such as mosquitoes, ticks, and flies
- It has four families: togaviruses, flaviviruses, bunyaviruses and reoviruses
- The major arbovirus disease worldwide are yellow fever, dengue, Japanese B encephalitis, St. Louis encephalitis, Russian spring-summer encephalitis.
- Most illnesses caused by these viruses are mild fevers; some may cause severe encephalitis, and life-threatening hemorrhagic fever.
The influence of the Vectors

- Vectors and viruses tend to be clustered in the tropics and subtropics; many temperate zones have periodic epidemics.
- Arbovirus life cycles are closely tied to the ecology of the vectors.
- Infections show a peak incidence when the arthropod is actively feeding and reproducing (e.g., Dengue fever’s peak in Taiwan is Oct or Nov).
- Humans can serve as dead-end, accidental hosts or a maintenance reservoir.
- Controlling the vector controls the disease.
# Common Arboviruses

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<tr>
<th>Family</th>
<th>Genera</th>
<th>Species (of high economic/epidemiologic importance)</th>
<th>Vectors</th>
<th>Diseases caused</th>
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<td>mosquito</td>
<td>viral encephalitis, arthritis</td>
</tr>
<tr>
<td>Flaviviridae</td>
<td>Flavivirus</td>
<td>Japanese encephalitis virus, St. Louis encephalitis virus, West Nile virus</td>
<td>mosquito</td>
<td>viral encephalitis</td>
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<tr>
<td>Flaviviridae</td>
<td>Flavivirus</td>
<td>Dengue virus, Murray Valley encephalitis virus, Yellow fever virus</td>
<td>mosquito</td>
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<tr>
<td>Flaviviridae</td>
<td>Flavivirus</td>
<td>Louping ill virus, Powassan virus, Tick-borne encephalitis virus</td>
<td>tick (Ixodes spp.)</td>
<td>viral encephalitis</td>
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<tr>
<td>Bunyaviridae</td>
<td>Phlebovirus</td>
<td>Rift Valley fever virus</td>
<td>mosquito (Aedes spp., Culex spp.)</td>
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</tr>
<tr>
<td>Bunyaviridae</td>
<td>Phlebovirus</td>
<td>Pappataci fever, Toscana virus</td>
<td>Phlebotomus spp.</td>
<td>fever</td>
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<tr>
<td>Bunyaviridae</td>
<td>Orthobunyavirus</td>
<td>California encephalitis virus, La Crosse encephalitis</td>
<td>mosquito</td>
<td>viral encephalitis</td>
</tr>
<tr>
<td>Bunyaviridae</td>
<td>Nairovirus</td>
<td>Crimean–Congo hemorrhagic fever virus</td>
<td>tick</td>
<td>viral hemorrhagic fever</td>
</tr>
<tr>
<td>Bunyaviridae</td>
<td>Uukuvirus</td>
<td>Anopheles A, Anopheles B, Bakau, Crimean-Congo hemorrhagic fever, Kaisodi, Mapputta, Nairobi sheep disease, Phlebotomus fever, Turlock; 8 un-assigned viruses</td>
<td>tick</td>
<td>viral encephalitis, viral hemorrhagic fever</td>
</tr>
<tr>
<td>Reoviridae</td>
<td>Coltivirus</td>
<td>Colorado tick fever virus</td>
<td>tick</td>
<td>viral hemorrhagic fever</td>
</tr>
<tr>
<td>Reoviridae</td>
<td>Orbivirus</td>
<td>African horse sickness virus, Bluetongue disease virus, Epizootic hemorrhagic disease virus</td>
<td>Ceratopogonidae (Culicoides spp.)</td>
<td>viral encephalitis</td>
</tr>
</tbody>
</table>
Family: Togaviridae
Genus: Alphavirus
# Properties of Alphavirus

Chikungunya

- The name is derived from the Makonde word meaning "bends up" in reference to the stooped posture developed as a result of the arthritic symptoms of the disease.

- Chikungunya is a relatively rare form of viral fever (non-fatal viral illness) caused by alphavirus through mosquitoes.
Epidemiology of Chikungunya

- Chikungunya was first described in Tanzania, Africa in 1952.
- An outbreak of chikungunya was discovered in 1999 in Port Klang in Malaysia, affecting 27 people.
- A big outbreak was recorded in 2005 on the French island of Réunion in the Indian Ocean. More than 250,000 (1/3) residents were infected by the virus, resulting in about 220 deaths (~0.1%).
Symptoms

- Fever can reach 39 °C (102.2 °F).
- Headache, and slight photophobia.
- Maculopapular rash in trunk or limbs
- Arthritis affecting multiple joints
- Neurological complications
Diagnosis

The diagnostic tests include: detection of antigens/antibodies or viral RNA in the blood samples

- Enzyme linked immunosorbent assay (ELISA) for antibodies or antigens
- Polymerase chain reaction (PCR) for viral RNA
Treatment

- There are no specific therapeutics for Chikungunya.
- Arthritis-like symptoms cannot be relieved by aspirin.
- Chloroquine phosphate (250 mg/day) in clinical trial has given promising results, and may be used in the future.
- Anti-inflammatory agents may be used to combat the arthritis associated with Chikungunya virus.
Prevention

- There is no vaccine available.
- Preventing mosquitoes is the main strategy of prevention:
  * Eliminating stagnant water at home, schools and workplace to avoid breeding of mosquitoes.
  * Using insect repellents over exposed parts of the body.
  * Using mosquito screens or nets in rooms.
  * Wearing the long sleeved clothes for protection against mosquitoes.
  * Taking chemical or biological measures against mosquitoes
Family: Flaviviridae
Genus: Flaviviruses
# The main properties of Flaviviruses

<table>
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<th>Taxonomic Classification</th>
<th>Important Arbovirus and Rodent-Borne Virus Members</th>
<th>Virus Properties</th>
</tr>
</thead>
</table>
Transmission & Replication

- The virus infects the arthropod vectors (e.g., mosquitoes), replicating in the arthropod's gut.
- The virus then spreads to other organs and particularly the salivary glands.
- Once the virus is in the salivary glands, the infected arthropod vector is able to transmit the virus to a vertebrate host.
- The most successful hosts are monkeys, bats, birds and some domestic animals.
- Humans are usually dead-end hosts because the virus is unable to replicate to create a high enough titer to re-infect the vector.
The flavivirus lifecycle

- Binds to cells via viral E proteins;
- Enters cells via endocytosis;
- Fuses with endosomal membranes under low pH;
- Releases viral genome into the cytoplasm;
- Replicates in cytoplasm;
- Assembles in cytoplasmic reticulum (ER);
- Buds into Golgi;
- Release mature virions out of cell.
Generalized transmission cycle of tick-borne flaviviruses

- Virus is passed to succeeding tick stages during moulting (transstadial transmission), as well as transovarially to progeny of adult ticks.
- Both male and female ticks are involved in transmission.
- Tick-borne encephalitis virus may be transmitted to uninfected ticks cofeeding on a vertebrate host without the requirement for active viremic infection of the host.
Flavivirus Encephalitis

- Inflammation of the BRAIN due to flavivirus infection. Humans show an age-dependent susceptibility: Infants and the elderly being most susceptible.

- Clinical findings: incubation period: 4-21 days
  - Symptoms:
    a. A sudden onset of headache, chills, fever (lasting 4-10 days), vomiting, generalized pain;
    b. 24-48 hours later, develops marked drowsiness, mental confusion, tremors or coma in severe cases.
  - Sequelae is mild to severe, including mental deterioration, personality changes
Dengue Virus

- Dengue virus is transmitted from certain species of mosquitoes
- There are four Serotypes (Dengue 1-4)
- Three manifestations:
  1. Dengue Fever
  2. Dengue Hemorrhagic Fever
  3. Dengue Shock Syndrome
- Leads to death in 5% of cases
- More dangerous if infected second time by different serotype, particularly Dengue 2 → Dengue 1 (mediated by antibodies)
- It is very hard to create vaccine
- Global warming may be a cause of the increased epidemic of dengue fever

Aedes aegypti and Aedes albopictus
Global epidemiology of Dengue fever

- About 2.5 billion people, or 40% of the world’s population, are living in areas where there is a risk of dengue transmission.
- Dengue is endemic in at least 100 countries in Asia, the Pacific, the Africa, Americas, and the Caribbean.
- WHO estimates that there are 50 to 100 million new infections per year, including 500,000 dengue hemorrhagic fever (DHF) cases and 22,000 deaths, mostly among children.

http://www.cdc.gov/dengue/epidemiology/index.html
How does Dengue spread in human body?

1. Mosquitoes transmit dengue virus to human dendritic cells

2. Dengue virus moves to areas with high WBC count (liver, spleen, lymph nodes, bone marrow, and glands)

3. Dengue virus enters WBCs & lymphatic tissue

4. It goes to blood circulation
Dengue Clinical Presentations

About 80% of patients have no symptom or only have mild symptoms such as an uncomplicated fever.

Clinical Characteristics of Dengue Fever

- Fever
- Headache
- Muscle and joint pain
- Vomiting
- Rash (similar to the measles rash)
- Hemorrhagic manifestations
One of the most significant symptoms of dengue hemorrhagic fever is purpura
Laboratory diagnosis

1. Antibody Detection
2. Genomic Sequencing
3. Viral Isolation & Characterization
Antibody detection

- Most common methods
  1. Hemagglutinin inhibition test (HI test)
  2. ELISA for IgM: early diagnostic tool
  3. ELISA for IgG: > 4X increase from acute to convalescence
Genomic sequencing

- RT-PCR method
- Quicker, more accurate, and more reliable
- May not distinguish among serotypes
- Beware of false-positives due to contamination

http://animal.intron.co.kr/Image/RT-pcr.gif
Viral isolation & characterization

- Cell culture (mammals & mosquitoes)
- Indirect immunofluorescence
  - Useful to study basic virology, epidemiology, and pathogenesis
  - Impractical for rapid diagnosis
Prevention

- No vaccine is available;
- Education;
- Since mosquito is the vector, using mosquito nets and repellents can reduce dengue transmission
Japanese B Encephalitis Virus

A member of flaviviruses
Single serotype, 5 genotypes based on E protein
Globalization of Japanese B Encephalitis
Transmission cycle of Japanese B encephalitis

- Mosquitoes transmit the viruses among pigs, bats, water birds and humans
- Pigs are the main contributors in the transmission cycle, because these animals often stay close to humans.
- Humans are a dead-end host because of low viremia, preventing the human-to-human transmission.

_Culex genus_
Pathogenesis and clinical profiles of Japanese B encephalitis

- JEV (Japanese encephalitis virus) enters the blood and crosses the blood-brain barrier.
- Blood monocytes/macrophages and peripheral lymphoid tissues and spleen are involved.
- Cerebro-spinal fluid is affected.
- Astrocytes and microglia are activated, leading to inflammation.
- Neuronal death occurs, followed by apoptosis/necrosis.
- Clinical outcome or death results.
Clinical Features

- Incubation period is about 5 to 15 days
- Only 1 in 300 infections develop into encephalitis, rest asymptomatic
- Course of disease - 3 stages:
  a) Prodromal stage: Fever and headache (1-6 days).
  b) Acute encephalitic stage: Fever, 38 to 40.7°C, nuchal rigidity, focal CNS signs & altered sensorium.
  c) Late stage: Temperature & ESR touch normal level, neurological signs become stationary
- Immune responses: Infection induces lifelong immunity.
Diagnosis

Laboratory Tests

- RT-PCR: Specific and sensitive. – Early diagnosis
- Antibodies
  - JE-specific IgM in serum or cerebrospinal fluid (CSF): appear <4 days post infection, >90% positive. *Early diagnosis
  - JE-specific IgG (ELISA): titers in convalescence > 4X acute infection. * Diagnosis
  - HI antibodies: appear>5 days, cross-reactive to other flavivirus. * useful tool for surveillance

- Virus or antigen
  - Virus isolation: CSF sample, brain
    * Identification and diagnosis
  - Viral antigen in serum or CSF: ELISA
    * Early diagnosis
Treatment

- There is no specific treatment for Japanese encephalitis
- Since there is no transmission from person to person, patients do not need to be isolated.
- Supportive treatment with assistance given for feeding and breathing as required:
  - Fluid management
  - Control of raised intracranial pressure by use of mannitol
  - Anticonvulsants
  - Head elevation
  - Invasive monitoring
  - Controlled ventilation
Prevention & control

- Housing animals (pigs) in-doors in screened stabling, providing protection from mosquitoes;
- If possible, vaccinate pigs and horses;
- Mosquito nets and repellents should be used;
- Vaccination of humans where the vaccine is available.
<table>
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<tr>
<th>Vaccine Type</th>
<th>Strain &amp; Substrate</th>
<th>Producer</th>
<th>Licensure &amp; distribution</th>
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<tr>
<td>Inactivated</td>
<td>Nakayama Mouse Brain</td>
<td>Biken (Japan); Green Cross (South Korea); CRI (India); Vabiotech (Vietnam); GPO (Thailand)</td>
<td>International</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Local &amp; Region</td>
</tr>
<tr>
<td></td>
<td>Beijing 1 Mouse Brain</td>
<td>Kaketsuken; Biken; Kitasota (Japan)</td>
<td>Production stopped; Bulk storage</td>
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<tr>
<td></td>
<td>P3 PHK or Vero</td>
<td>Multiple (China)</td>
<td>Domestic</td>
</tr>
<tr>
<td>Live, Attenuated</td>
<td>SA14-14-2 PHK</td>
<td>Chengdu; Wuhan; Lanzhou (China)</td>
<td>China; India, Nepal, South Korea, Sri Lanka</td>
</tr>
</tbody>
</table>
Questions?

- How are flaviviruses transmitted and what is the main disease caused by the flavivirus infection?
- What methods can be used for laboratory diagnosis of dengue virus infection?
Overview

- Properties of viruses causing VHF
- Epidemiology of VHF
- **Bunyaviruses**: Hemorrhagic fever with renal syndrome (HFRS) and Hantavirus pulmonary syndrome (HPS)
- **Filoviruses**: Ebola hemorrhagic fever (EHF)
- **Arenaviruses**: Lassa fever
What are VHF s?

- A group of illnesses that are caused by several distinct families of viruses
- A severe multisystem syndrome (multiple organ systems in the body are affected)
- Vascular system damaged
- Body’s ability to regulate itself is impaired.
- Many cause severe and life-threatening diseases
- Classified as biosafety level four (BSL4) pathogens.
VHF: Viruses

- Enveloped, single stranded RNA viruses
- Similar syndromes, but different pathogenesis & treatments
- Persistent in nature: rodents, bats, mosquitoes
- Geographically restricted by hosts
- Potential infectious hazards from laboratory aerosols
Viral hemorrhagic fever (VHF)

- Acute infection:
  
  fever, progression to prostration

- Small vessel involvement:
  
  increased permeability, cellular damage

- Multisystem compromise (varies with pathogen)

- Hemorrhage may be small in volume
  
  (indicates small vessel involvement)

- Poor prognosis associated with:
  
  shock, encephalitis, extensive hemorrhage
VHF: Viruses

- Bunyaviruses
  - Hemorrhagic fever with renal syndrome (HFRS)
  - Hantanvirus pulmonary syndrome (HPS)
  - Rift Valley fever (RVF)
  - Crimean Congo Hemorrhagic fever (CCHF)

- Filoviruses
  - Ebola Hemorrhagic fever (EHF)
  - Marburg virus

- Arenaviruses
  - Lassa fever “New World Arenaviruses”
Bunyaviruses

Hemorrhagic fever with renal syndrome (HFRS)

- HFRS is a group of clinically similar illnesses caused by hantaviruses from the family Bunyaviridae.
- HFRS includes diseases such as Korean hemorrhagic fever, and epidemic hemorrhagic fever.
- The viruses that cause HFRS include Hantaan, Dobrava, Saaremaa, Seoul, and Puumala.
HFRS is found throughout the world

- Hantan virus is widely distributed in eastern Asia, particularly in China, Russia, and Korea.
- Puumala virus is found in Scandinavia, western Europe, and western Russia.
- Dobrava virus is found primarily in the Balkans, and Seoul virus is found worldwide. Saaremaa is found in central Europe and Scandinavia.
- In the Americas, hantaviruses cause a different disease known as hantavirus pulmonary syndrome (HPS).
During the Korean War, several thousand UN soldiers became ill with "Korean haemorrhagic fever" (now called HFRS).

The virus isolated from the Hantan River area in South Korea was named hantavirus.
Hantaviruses

- In 1993, an outbreak of Hantavirus pulmonary syndrome (HPS) occurred in the Four Corners region in the southwestern United States.
- 2/3 (20 out of 30 persons) with acute hantavirus-associated respiratory disease died in a few days.
- The viral cause of the disease was found only weeks later and was called the Sin Nombre virus (SNV, “Sin Nombre” means "nameless virus" in Spanish).

Transmission of hantaviruses

- Hantaviruses are carried and transmitted by rodents.
- People can become infected with these viruses and develop HFRS after exposure to the secretions of the infected rodents.
- Transmission may also occur when infected urine or these other materials are directly introduced into broken skin or onto the mucous membranes of the eyes, nose, or mouth.
- Individuals who work with live rodents can be exposed to hantaviruses through rodent bites from infected animals.
- Human-to-human may occur, but is extremely rare.

Apodemus agrarius
黑线姬鼠
The lifecycle of hantavirus

1. Attaches to host cell via interactions between viral glycoprotein and cellular receptors;
2. Enters into cells through receptor-mediated endocytosis, Releases viral genomes via uncoating;
3. Transcripts viral RNA using host-derived primers
4. Translate L, M, and S mRNAs into viral proteins in ER;
5. Viral RNA replicates and assembly with the N protein;
6. Assemble viral components in the Golgi apparatus;
7. Release the new virions.
Symptoms of HFRS

- Initial symptoms begin suddenly (1 to 2 weeks after exposure to infectious material) and include intense headaches, back and abdominal pain, fever, chills.
- Individuals may have flushing of the face, inflammation or redness of the eyes, or a rash.
- Later symptoms can include low blood pressure, acute shock, vascular leakage, and acute kidney failure.
- The severity of the disease varies depending upon the virus causing the infection. Hantaan and Dobrava virus infections usually cause severe symptoms, while Seoul, Saaremaa, and Puumala virus infections are usually more moderate.
Diagnosis of HFRS

- Following laboratory tests are used to confirm a diagnosis of HFRS in patients with a clinical history compatible with the disease:
  * Serologic test results positive for hantavirus infection
  * Immunohistochemical staining and microscope examination for Hantavirus antigen in tissue
  * PCR for Hantavirus RNA sequences in blood or tissue.
Treatment of HFRS

- No specific therapeutics, but mainly supportive therapy.
- Careful management of the patient’s fluid (hydration) and electrolyte (e.g., sodium, potassium, chloride) levels, maintenance of correct oxygen and blood pressure levels, and appropriate treatment of any secondary infections.
- Dialysis may be required to correct severe fluid overload.
- Intravenous ribavirin may decrease illness and death associated with HFRS if used very early in the disease.
Prevention of HFRS

- There is no vaccine available.
- Rodent control is the primary strategy for preventing hantavirus infections.
- Individuals should avoid contact with rodent urine, droppings, saliva, and nesting materials.
Filoviruses

Ebola

极度恐慌 1995
Epidemiology

- Ebola Hemorrhagic Fever was first found in 1976.
- It struck two countries in that year:
  a. Sudan – in a town called N’zara
  b. Zaire, now known as the Democratic Republic of Congo
- In these two instances the mortality rate was between 50 –90%.
- Following those epidemics, Ebola hit Africa in many other instances the worst yet being in the year 2000 when it struck Uganda infecting more than 400 people.
1995 Zaire

- 315 cases were reported
- The case-fatality is 81%
- It was unrecognized 3 months
- 25% were health care workers
- Identified 2 “super-spreaders”
Ebola Virus

- Genome has 7 genes:
  - NP, VP35, VP40, GP, VP30, VP24, and L

- Glycoproteins (GP):
  - Fusion and Entry
    - Likely pH dependent
Fruit Bats Were Believed to Be Reservoir of Ebola Virus

- Antibodies against Ebola isolated from fruit bats
- Ebola gene sequences found in fruit bats’ livers and spleens
- Fruit bats do not show any symptoms
- More research needs to be done
Transmission of Ebola Virus

- **Direct contact**
  - Blood, secretions, organs
- **Unsterilized needles**
- **Handling of infected chimpanzees**
- **Airborne transmission**
  - Limited evidence of human-human
- **Incubation period**
  - 2 to 21 days
- **Contagiousness**
  - Not during early stages
  - As the illness progresses, bodily fluids represent an extreme biohazard
Symptoms of Ebola Virus

Initial Signs
- Fever (at least 102° F)
- Weakness & exhaustion
- Pain
  - Severe headache
  - Muscles & joints
  - Abdominal pain
- Sore throat
- Nausea
- Dizziness

Progressed Symptoms
- Vomiting
- Diarrhea
- Maculopapular rash
  - Spreads over the body (often hemorrhagic)
- Extensive bleeding
  - Red eyes
    - Hemorrhage of sclerotic arterioles
    - From mouth, nose, eyes, rectum & mucous membranes
- Other secondary symptoms
  - Hypotension
  - Organ damage
  - Internal and external bleeding
Diagnosis

Sample collection:
Blood, tissues, saliva and urine

Methods:
- ELISA for IgM
- ELISA for IgG
- ELISA for antigens
- PCR for viral RNA
A potential bioterrorism agent

- Ebola virus disease has fatality rates ranging from 50-90%.
- Death from Ebola virus disease is commonly due to multiple organ failure and hypovolemic shock.
- There is no cure or vaccine available
- Some countries have investigated the use of filoviruses for biological weapons
Prevention and Control

- Prevention of Ebola HF is difficult because the identity and location of the natural reservoir of Ebola virus are unknown.
- Isolation of Ebola HF patients from contact with unprotected persons.
- To avoid any person’s contact with the patient’s blood or secretions of any patient.
- Health-care providers must employ practical HF isolation precautions, barrier nursing techniques and infection-control measures.
- May take some antiviral drugs (e.g., ribavirin) for pre- or post-exposure prophylaxis.
Lab Safety Precautions

- Education about organism
- Sterile environments
- Protective clothing
- Proper disposal of waste products
- Limit contact with contaminated medical equipment

Laboratory safety: BSL-4
Current Research on Vaccines

- **Plasmids coding viral glycoprotein (GP)**
  * Vaccination of guinea pigs induced GP-specific immune responses
  * Vaccinated animals were protected from viral challenge
  * The protection was correlated with antibody titer and antigen-specific T-cell responses to GP.

- **Harmless-Ebola-like particles (eVLPs)**
  * These eVLPs were found to be immunogenic both in vitro and in vivo.
  * Mice were vaccinated with these eVLPs, and developed high titers of Ebola virus specific antibodies, including neutralizing antibodies.
  * All the mice in the study were protected from Ebola virus inoculation.
Arenaviridae

- Arenaviruses can be divided into two serogroups by geographical distribution.
  - "Old World" arenaviruses: found in the Eastern Hemisphere in places such as Europe, Asia, and Africa.
  - "New World" arenaviruses: found in the Western Hemisphere, such as Argentina, Bolivia, Venezuela, Brazil, and the United States.
Arenavirus Lassa

- Arenavirus Lassa can cause viral hemorrhagic fever
- Transmitted from rodents to humans
- Discovered in Nigeria, 1969
- Endemic in portions of West Africa
- Seasonal clustering: Late rainy and early dry season
- Affects all age groups and both sexes
Arenavirus Lassa

- Name derived from “arenosus” (Latin “sandy”) describing appearance of virions on examination by electron microscopy
- Enveloped virus, round or pleomorphic, 50-300 nm in diameter
- Single-stranded genome divided into 2 RNA segments: small (~3.4 kb) and large (~7.1 kb)
- 2 genes on each segment, arranged in unique “ambisense” orientation, encoding 5 proteins
- Inactivated by:
  * heating to 56°C
  * pH<5.5 or >8.5
  * UV/gamma irradiation
  * detergents
Epidemiology

- Endemic in areas of West Africa
- Estimated 300,000-500,000 infections and 5,000 deaths each year.
- Rodent-to-human transmission
- Secondary human-to-human transmission with the potential for outbreaks with high case-fatality
Transmission

- Rodent-to-human:
  - Inhalation of aerosolized virus
  - Ingestion of food or materials contaminated by infected rodent excreta
  - Catching and preparing rats as a food source

- Human-to-human:
  - Direct contact with blood, tissues, secretions or excretions of infected humans
  - Needle stick or cut
Pathogenesis

- Endothelial cell damage/capillary leak
- Platelet dysfunction (resulting in bleeding)
- Suppressed cardiac function
- Cytokines and other soluble mediators of shock and inflammation
Clinical Aspects

- Incubation period of 5-21 days
- Gradual onset of fever, headache, and other non-specific signs and symptoms
- A minority present with classic symptoms of bleeding, neck/facial swelling and shock
- Mortality 1-3% overall, 15-20% among hospital patients
- Particularly severe in pregnant women and their offspring
Diagnostics

- Clinical diagnosis often difficult
- ELISA (Enzyme-linked immunosorbent assays) for antigen, IgM, and IgG
- RT-PCR for viral RNA
- As research tools:
  - Virus isolation
  - Immunohistochemistry (for post-mortem diagnosis)
Treatment

- There is no specific treatment available
- Supportive measures
- Ribavirin: may be effective when started within the first 6 days of illness
Questions?

- Why is Ebola virus the most dangerous bioterrorism agent and how to prevent Ebola virus infection?
- How is Lassa virus transmitted and how to prevent its transmission?
Thanks!