Slide 1

Viral Hemorrhagic Fever

Slide 2

What is Viral Hemorrhagic Fever?

- Severe multisystem syndrome
- Damage to overall vascular system
- Symptoms often accompanied by hemorrhage
  - Rarely life threatening in itself
  - Includes conjunctivitis, petechia, echymosis

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Viral hemorrhagic fever (VHF) refers to a group of illnesses caused by several distinct families of viruses that effect humans and non-human primates. VHF is a severe multi-system syndrome characterized by diffuse vascular damage. Bleeding often occurs and depending on the virus may or may not be life threatening. Some VHF's cause mild disease while others may cause severe symptoms and death.

Slide 3

Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Humans
- Disease in Animals
- Prevention and Control

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In today's presentation we will cover information regarding the organisms that causes viral hemorrhagic fevers and their epidemiology. We will also talk about the history of the diseases, how transmission occurs, species that are affected (including animals, if applicable), and clinical and necropsy signs observed. Finally, we will address prevention and control measures for viral hemorrhagic fevers.

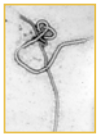
Slide 4

The Organisms

Slide 5

Viral Hemorrhagic Fever

- Viruses of four distinct families
  - Arenaviruses
  - Filoviruses
  - Bunyaviruses
  - Flaviviruses
- RNA viruses
  - Enveloped in lipid coating
- Survival dependent on an animal or insect host, for the natural reservoir



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VHF viruses are members of four distinct families: arenaviruses, filoviruses, bunyaviruses and flaviviruses. They are all RNA viruses that are enveloped in a lipid coating. The survival of these viruses is dependant on their natural reservoir, which in most cases is an animal or an insect host. Image: Ebola virus, from CDC.

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Classification

Arenaviridae	Bunyaviridae	Filoviridae	Flaviviridae
Junin	Crimean-Congo H.F.	Ebola	Kyasanur Forest Disease
Machupo	Hantavirus	Marburg	Omsk H.F.
Sabia	Rift Valley fever		Yellow Fever
Guanarito			Dengue
Lassa			

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The Arenaviridae family contains the following viruses: Junin, Machupo, Sabia, Guanarito, and Lassa. The Bunyaviridae include: Crimean-Congo hemorrhagic fever, Hantavirus, and Rift Valley fever. Marburg and Ebola are the two viruses within the Filoviridae family. The Flaviridae family includes: Kyasanur Forest Disease, Omsk hemorrhagic fever, Yellow fever and Dengue. Several of these virus families contain many more viruses but for the purposes of this presentation, only the viruses causing hemorrhagic fever will be discussed.

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Arenaviridae

Junin virus
Machupo virus
Guanarito virus
Lassa virus
Sabia virus

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Slide 8

Arenaviridae History

- First isolated in 1933
- 1958: Junin virus - Argentina
  - First to cause hemorrhagic fever
  - Argentine hemorrhagic fever
- 1963: Machupo virus – Bolivia
  - Bolivian hemorrhagic fever
- 1969: Lassa virus – Nigeria
  - Lassa fever

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The first arenavirus was isolated in 1933 during an outbreak of St. Louis Encephalitis virus. In 1958, the Junin virus was isolated in the plains of Argentina in agricultural workers. It was the first arenavirus found to cause hemorrhagic fever. Others soon followed including Machupo virus in Bolivia in 1963 and Lassa virus in Nigeria in 1969. Since 1956, a new arenavirus has been discovered every one to three years, but not all cause hemorrhagic fever.

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Arenaviridae Transmission

- Virus transmission and amplification occurs in rodents
- Shed virus through urine, feces, and other excreta
- Human infection
  - Contact with excreta
  - Contaminated materials
  - Aerosol transmission
- Person-to-person transmission

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New and Old World rats and mice are chronically infected with arenaviruses. The virus is vertically transmitted from host to offspring with most viruses in this family. Transmission among adult rodents may also occur through bites and other wounds. Rodents shed the viruses into the environment through urine, fecal droppings, and other excreta. Humans can become infected when coming into contact with rodent excreta or contaminated materials such as contact through abraded skin or ingestion of contaminated food. Inhalation of rodent excreta may also result in disease. Person to person transmission has also been documented in healthcare settings through close contact with infected individuals and contact with infected blood and medical equipment.

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Arenaviridae Epidemiology

- Africa
  - Lassa
- South America
  - Junin, Machupo, Guanarito, and Sabia
- Contact with rodent excreta
- Case fatality: 5 – 35%
- Explosive nosicomial outbreaks with Lassa and Machupo

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Arenaviruses are found worldwide; however the viruses responsible for causing hemorrhagic fever are restricted to two continents. Lassa virus is endemic to the region of West Africa while Junin, Machupo, Guanarito, and Sabia viruses are all found in South America. The later are grouped together as the Latin American hemorrhagic fevers. Humans who have frequent contact with rodent excreta have an increase risk of developing an infection with an arenavirus. Who is exposed depends on the type of rodent carrying the virus. Agricultural and domestic exposure are the most common. Case fatality for arenaviruses ranges from 5 -35%. Lassa and Machupo can cause explosive hospital-acquired outbreaks.

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Arenaviridae in Humans

- Incubation period
  - 10–14 days
- Fever and malaise
  - 2–4 days
- Hemorrhagic stage
  - Hemorrhage, leukopenia, thrombocytopenia
  - Neurologic signs

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The incubation period for arenaviruses is typically between 10 – 14 days. Disease onset begins with a fever and general malaise for 2 - 4 days. Most patients with Lassa fever will recover following this stage; however, those infected with the Latin American hemorrhagic fevers typical progress to more severe symptoms. The hemorrhagic stage of the disease quickly follows and leads to hemorrhaging, neurologic signs, leukopenia and thrombocytopenia.

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Bunyaviridae

Rift Valley Fever virus
Crimean-Congo Hemorrhagic Fever virus
Hantavirus

Slide 13

Bunyaviridae History

- 1930: Rift Valley Fever – Egypt
  - Epizootic in sheep
- 1940s: CCHF - Crimean peninsula
  - Hemorrhagic fever in agricultural workers
- 1951: Hantavirus – Korea
  - Hemorrhagic fever in UN troops
- 5 genera with over 350 viruses

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RVF virus was first isolated in 1930 from an infected newborn lamb, as part of investigation of a large epizootic of disease causing abortion and high mortality in sheep in Egypt. Crimean-Congo Hemorrhagic Fever virus was first recognized in the Crimean peninsula located in southeastern Europe on the northern coast of the Black Sea in the mid-1940s, when a large outbreak of severe hemorrhagic fever among agricultural workers was identified. The outbreak included more than 200 cases and a case fatality of about 10%. The discovery of hantaviruses traces back to 1951 to 1953 when United Nations troops were deployed during the border conflict between North and South Korea. More than 3,000 cases of an acute febrile illness were seen among the troops, about one third of which exhibited hemorrhagic manifestations, and an overall mortality of 5% to 10% was seen. The family now consists of five genera which contain 350 viruses that are significant human, animal, and plant pathogens.

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Bunyaviridae Transmission

- Arthropod vector
  - Exception – Hantaviruses
- RVF – *Aedes* mosquito
- CCHF – Ixodid tick
- Hantavirus – Rodents
- Less common
  - Aerosol
  - Exposure to infected animal tissue

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Most Bunyaviruses except for Hantaviruses utilize an arthropod vector to transmit the virus from host to host. In some cases the virus may be transmitted from adult arthropods to their offspring. Humans are generally dead end hosts for the viruses and the cycle is maintained by wild or domestic animals. Crimean-Congo Hemorrhagic Fever virus is transmitted by ixodid ticks and domestic and wild animals such as hares, hedgehogs, sheep, etc. serve as amplifying and reservoir hosts. In contrast, Rift Valley Fever virus is transmitted by *Aedes* mosquitoes resulting in large epizootics in livestock. Humans are incidentally infected when bitten by infected mosquitoes or when coming into contact with infected animal tissues. The viruses is believed to be maintained by transovarial transmission between the mosquito and its offspring. Hantaviruses cycle in rodent hosts and humans become infected by coming into contact with rodent urine. Aerosolization of viruses and exposure to infected animal tissues are also two lesson common modes of transmission for some Bunyaviruses.

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Bunyaviridae Epidemiology

- RVF - Africa and Arabian Peninsula
  - 1% case fatality rate
- CCHF - Africa, Eastern Europe, Asia
  - 30% case fatality rate
- Hantavirus - North and South America, Eastern Europe, and Eastern Asia
  - 1-50% case fatality rate

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Bunyaviruses are found worldwide but each virus is usually isolated to a local region. RVF is found primarily in sub-Saharan Africa and was recently isolated in Saudi Arabia and Yemen in 2000. The case fatality rate in humans is generally around 1%. CCHF is found in most of sub-Saharan Africa, eastern Europe and Asia. The case fatality rate is 30% and nosicomial outbreaks have been documented through exposure to infected blood products. Hantaviruses are divided into two groups based on location: Old World Viruses are found in eastern Europe and eastern Asia while New World viruses are found in North and South America. Depending on the virus, case fatality rate can vary between 1 and 50%.

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Bunyaviridae Humans

- RVF
  - Incubation period – 2-5 days
  - 0.5% - Hemorrhagic Fever
- CCHF
  - Incubation period – 3-7 days
  - Hemorrhagic Fever - 3–6 days following clinical signs
- Hantavirus
  - Incubation period – 7–21 days
  - HPS and HFRS

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Most humans suffering from Rift Valley Fever will experience flu-like symptoms and recover with no complications after an incubation period of 2-5 days. In 0.5% of cases, hemorrhagic fever will develop following the initial febrile stage. Another 0.5% of cases will develop retinitis or encephalitis 1 to 4 weeks following infection. Most human infections will occur one to two weeks following the appearance of abortion or disease in livestock. In contrast to RVF, most humans infected with CCHF will develop hemorrhagic fever. The incubation for the disease is 3-7 days and most patients will develop hemorrhagic fever 3 to 6 days following the onset of flu-like symptoms. Hantaviruses generally cause one of two clinical presentations: HFRS, Hemorrhagic Fever with Renal Syndrome generally caused by Old World Hantaviruses or HPS, Hantavirus Pulmonary Syndrome generally caused by New World Hantaviruses. Incubation period is 7 to 21 days followed by a clinical phase of 3-5 days. Severity of illness is dependent on the virus.

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Bunyaviridae Animals

- RVF
  - Abortion – 100%
  - Mortality rate
    - >90% in young
    - 5-60% in older animals
- CCHF
  - Unapparent infection in livestock
- Hantaviruses
  - Unapparent infection in rodents

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Rift Valley Fever causes severe disease in livestock animals. Abortion rates can reach 100%. Mortality rates in animals less than 2 weeks of age can be greater than 90% with most animals succumbing to disease within 24 – 36 hours from the onset of fever. Older animals also suffer from a less severe febrile illness with mortality rates ranging from 5 – 60%. In contrast, CCHF virus causes an unapparent or subclinical disease in most livestock species and is maintained in the herds through the bite of a tick. Rodents are persistently infected with Hantaviruses but show no clinical signs. The virus is transmitted from rodent to rodent through biting, scratching, and possible aersolization of rodent urine.

Note: For more information of Hantaviruses and Rift Valley Fever, please see those disease specific PowerPoint presentations.

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Filoviridae

Marburg virus
Ebola virus

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Filoviridae History

- 1967: Marburg virus
  - European laboratory workers
- 1976: Ebola virus
  - Ebola Zaire
  - Ebola Sudan
- 1989 and 1992: Ebola Reston
  - USA and Italy
  - Imported macaques from Philippines
- 1994: Ebola Côte d'Ivoire

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Marburg virus was first isolated in 1967 from several cases of hemorrhagic fever in European laboratory workers in Germany and former Yugoslavia working with tissues and blood from African green monkeys imported from Uganda. Ebola virus was first reported simultaneously in Zaire and Sudan in 1976 when two distinct subtypes were isolated in two hemorrhagic fever epidemics. Both subypes later named Zaire and Sudan caused severe disease and mortality rates greater than 50%. A third subtype of Ebola (Reston) was later found in macaques imported from the Philippines into the US in 1989 and Italy in 1992. Four humans were asymptomatically infected and recovered without any signs of hemorrhagic fever. In 1994, a fourth subtype of Ebola was isolated from a animal worker in Côte d'Ivoire who had preformed a necropsy on an infected chimpanzee. Scattered outbreaks have occurred periodically with latest being an outbreak of Ebola in the Republic of the Congo in 2003.

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Filoviridae Transmission

- Reservoir is UNKNOWN
  - Bats implicated with Marburg
- Intimate contact
- Nosicomial transmission
  - Reuse of needles and syringes
  - Exposure to infectious tissues, excretions, and hospital wastes
- Aerosol transmission
  - Primates

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The reservoir for filoviruses is still unknown. Bats have been implicated for Marburg virus, but no evidence of Ebola viruses have been found in over 3000 species of animals tested in the areas of human outbreaks. Intimate person-to-person contact is the main means of transmission of filoviruses for humans. Nosicomial transmission has been a major problem in outbreaks in Africa through the reuse of needles and syringes and exposure to infected tissues, fluids, and hospital materials. Aerosol transmission has been observed in primates but does not seem to be a major means in humans.

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Filoviridae Epidemiology

- Marburg – Africa
  - Case fatality – 23-33%
- Ebola - Sudan, Zaire and Côte d'Ivoire – Africa
  - Case fatality – 53-88%
- Ebola – Reston – Philippines
- Pattern of disease is UNKOWN

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Marburg and Ebola subtypes Sudan, Zaire, and Côte d'Ivoire appear to be found only in Africa and all three Ebola subtypes have only been isolated from human cases in Africa. The case fatality rate for Marburg ranges from 23-33% and 53-88% for Ebola with the highest rates found in Ebola Zaire. The presence of Ebola Reston in macaques from the Philippines marked the first time a filovirus was found in Asia. The pattern of disease of humans in nature is relatively unknown except for major epidemics.

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Filoviridae Humans

- Most severe hemorrhagic fever
- Incubation period: 4–10 days
- Abrupt onset
  - Fever, chills, malaise, and myalgia
- Hemorrhage and DIC
- Death around day 7–11
- Painful recovery

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Filoviruses cause the most severe hemorrhagic fever in humans. The incubation period for both Marburg and Ebola is generally 4 to 10 days followed by abrupt onset of fever, chills, malaise, and myalgia. The patient rapidly deteriorates and progresses to multisystem failure. Bleeding from mucosal membranes, venipucture sites and the gastrointestinal organs occurs followed by DIC. Death or clinical improvement usually occurs around day 7 to 11. Survivors of the hemorrhagic fever are often plagued with arthralgia, uveitis, psychosocial disturbances, and orchitis for weeks following the initial fever.

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Filoviridae Animals

- Hemorrhagic fever
  - Same clinical course as humans
- Ebola Reston
  - High primate mortality - ~82%

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Filoviruses cause severe hemorrhagic fever in non-human primates. The signs and symptoms found are identical to humans. The only major difference is Ebola Reston has a high mortality in primates (~82%) while it does not seem to be pathogenic to humans.

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Flaviviridae

Dengue virus
Yellow Fever virus
Omsk Hemorrhagic Fever virus
Kyassnur Forest Disease virus

Flaviviruses can cause an array of clinical manifestations. For the purposes of this presentation, we will concentrate on those causing hemorrhagic fever.

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Flaviviridae History

- 1648 : Yellow Fever described
- 17th–20th century
  - Yellow Fever and Dengue outbreaks
- 1927: Yellow Fever virus isolated
- 1943: Dengue virus isolated
- 1947
  - Omsk Hemorrhagic Fever virus isolated
- 1957: Kyasanur Forest virus isolated

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Yellow Fever was first described in 1648 in Yucatan. It later caused huge outbreaks in tropical Americas in 17th, 18th, 19th, and 20th century. The French failed to complete the Panama Canal because their work force was decimated by Yellow Fever. Yellow Fever virus was first flavivirus isolated in 1927 and the first virus to be proved to be transmitted by an arthropod vector. Dengue virus which was also found to be transmitted by an arthropod was isolated in 1943. Major outbreaks of dengue with hemorrhagic fever have occurred in Australia in 1897, Greece in 1928, and Formosa 1931. Since the cessation of the use of DDT to control mosquito vectors, dengue has now spread to most of the tropical regions of the world. Omsk hemorrhagic fever virus was first isolated in 1947 from the blood of a patient with hemorrhagic fever during an epidemic in Omsk and Novosibirsk Oblasts of the former Soviet Union. Kyasanur Forest virus was isolated from a sick monkey in the Kyasanur Forest in India in 1957. Since its recognition 400 to 500 cases a year have been reported.

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Flaviviridae Transmission

- Arthropod vector
- Yellow Fever and Dengue viruses
  - *Aedes aegypti*
  - Sylvatic cycle
  - Urban cycle
- Kasanur Forest Virus
  - Ixodid tick
- Omsk Hemorrhagic Fever virus
  - Muskrat urine, feces, or blood

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Flaviruses utilize an arthropod vector to transmit disease. Yellow Fever is a zoonotic diseases that is maintained in non-human primates. The virus is passed from primate to primate through the bite of the mosquito. This is known as the sylvatic cycle. Humans contract the disease when bitten by an infected mosquito usually *Ae. aegypti* and the disease can then be epidemically spread from human to human by these mosquitoes. This cycle is known as the urban cycle. Dengue virus is maintained in the human population and is primarily transmitted in this manor. Kyasanur Forest virus is transmitted by an ixodid tick. The tick can pass the virus from adult to eggs and from one stage of development to another. The basic transmission cycle involves ixodid ticks and wild vertebrates, principally rodents and insect-eating animals. Humans become infected when bitten by an infected tick. The basic transmission cycle of the Omsk Hemorrhagic Fever virus is unknown. An ixodid tick are believed to transmit the viruses from rodent to rodent. Muskrats are epizootic hosts, and human infections occur by direct contact with their urine, feces, or blood.

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Flaviviridae Epidemiology

- Yellow Fever Virus – Africa and Americas
  - Case fatality rate – varies
- Dengue Virus – Asia, Africa, Australia, and Americas
  - Case fatality rate – 1-10%
- Kyasanur Forest virus – India
  - Case fatality rate – 3–5%
- Omsk Hemorrhagic Fever virus – Europe
  - Case fatlity rate – 0.5–3%

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Yellow Fever virus is found throughout sub-Sahran Africa and tropical South America but activity is intermittent and localized. The annual incidence is believe to be about 200,000 cases per year globally. Case fatality rate ranges greatly depending on the epidemic but may reach up to 50% in severe yellow fever cases. Dengue virus is found throughout the tropical Americas, Africa, Australia, and Asia. Cases of Dengue Hemorrhagic Fever (DHF) have been increasing as the distribution of *Ae. aegypti* increases following the collapse of mosquito control efforts. Case fatality rates for DHF is generally low 1-10% depending on available treatment. Kyasanur Forest virus is confined to Mysore State of India but spreading. Case fatality rate is 3 -5%. Omsk Hemorrhagic Fever virus is still isolated to the Omsk and Novosibirsk regions of the former Soviet Union. Case fatality is 0.5 – 3%.

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Flaviviridae Humans

- Yellow Fever
  - Incubation period – 3–6 days
  - Short remission
- Dengue Hemorrhagic Fever
  - Incubation period – 2–5 days
  - Infection with different serotype
- Kyasanur Forest Disease
- Omsk Hemorrhagic Fever
  - Lasting sequela

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Yellow Fever can cause a severe hemorrhagic fever. The incubation period in humans is 3 to 6 days. The clinical manifestations can range from mild to severe signs. Severe Yellow Fever begins abruptly with fever, chills, severe headache, lumbosacral pain, generalized myalgia, anorexia, nausea and vomiting, and minor gingival hemorrhages. A period of remission may occur for 24 hours followed by an increase in the severity of symptoms. Death usually occurs on day 7 – 10. Dengue virus will cause a mild flu-like illness upon first exposure. If the person is then infected by a different sero-type, dengue hemorrhagic fever can occur. The disease will begin like a normal infection of dengue virus with an incubation period of 2-5 days but will quickly progress to a hemorrhagic syndrome. Rapid shock ensues but can be reversed with appropriate treatment. Kyasanur Forest virus in humans is characterized by fever, headache, myalgia, cough, bradycardia, dehydration, hypotension, gastrointestinal symptoms, and hemorrhages. Recovery is generally uncomplicated with no lasting sequelae. Omsk Hemorrhagic Fever virus has a similar presentation to Kyasanur Forest virus however hearing loss, hair loss, neuropsychiatric complaints are commonly reported following recovery.

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Flaviviridae Animals

- Yellow Fever virus
  - Non-human primates – varying clinical signs
- Dengue virus
  - Non-human primates – No symptoms
- Kyasanur Forest Disease Virus
  - Livestock – No symptoms
- Omsk Hemorrhagic Fever Virus
  - Rodents – No symptoms

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Yellow Fever is maintained in non-human primates. Depending on species, yellow fever may be an unapparent infection or a severe hemorrhagic illness. Dengue has been isolated from several non-human primates in Africa but does not cause clinical signs. Livestock may develop a viremia with Kyasanur Forest Disease Virus but generally do not show clinical signs. Omsk Hemorrhagic Fever Virus is maintained in rodents but does not cause clinical signs.

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Disease in Humans

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Clinical Symptoms

- Differ slightly depending on virus
- Initial symptoms
  - Marked fever
  - Fatigue
  - Dizziness
  - Muscle aches
  - Exhaustion

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Specific signs and symptoms vary by the type of VHF, but initial signs and symptoms often include marked fever, fatigue, dizziness, muscle aches, loss of strength, and exhaustion.

Image: A Medical Officer at Lacor hospital in Gulu, Uganda examines a child suspected of being infected with the Ebola virus. (AP Photo/Sayyid Azim)

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Clinical Symptoms

- More severe
  - Bleeding under skin
    - Petechiae, echymoses, conjunctivitis
  - Bleeding in internal organs
  - Bleeding from orifices
  - Blood loss rarely cause of death

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More severe clinical symptoms include bleeding under the skin causing petechia, echymoses and conjunctivitis. Bleeding may also occur in internal organs and from orifices (like the eye, nose or mouth). Despite widespread bleeding, blood loss is rarely the cause of the death.

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Diagnosis

- Specimens must be sent to
  - CDC
  - U.S. Army Medical Research Institute of Infectious Disease (USAMRIID)
    - Serology
    - PCR
    - IHC
    - Viral isolation
    - Electron microscopy

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Clinical microbiology and public health laboratories are not currently equipped to make a rapid diagnosis of any of these viruses, and clinical specimens in an outbreak need to be sent to the CDC or the US Army Medical Research Institute of Infectious Diseases (USAMRIID) located in Frederick, Md. These are the only 2 level D laboratories in the Laboratory Response Network. These laboratories can conduct serology, PCR, immunohistochemistry, viral isolation and electron microscopy of VHFs.

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Treatment

- Supportive treatment
- Ribavirin
  - Not approved by FDA
  - Effective in some individuals
  - Arenaviridae and Bunyaviridae only
- Convalescent-phase plasma
  - Argentine HF, Bolivian HF and Ebola
- Strict isolation of affected patients is required
- Report to health authorities

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Patients infected with a VHF receive supportive therapy, with special attention paid to maintaining fluid and electrolyte balance, circulatory volume, blood pressure and treating for any complicating infections. There is no other established treatment. While there are no antiviral drugs approved by the U.S. Drug Administration (FDA) for treatment of VHF's. Ribavirin, has been effective in treating some individuals with Arenaviridae and Bunyaviridae but has not shown success against Filoviridae or Flaviviridae infections. Treatment with convalescent-phase plasma has been used with success in some patients with Junin, Machupo, and Ebola. If infection with a VHF is suspected it should be reported to health authorities immediately. Strict isolation of a patient is also required.

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Prevention and Control

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Prevention and Control

- Avoid contact with host species
  - Rodents
    - Control rodent populations
    - Discourage rodents from entering or living in human populations
    - Safe clean up of rodent nests and droppings
  - Insects
    - Use insect repellents
    - Proper clothing and bed nets
    - Window screens and other barriers to insects

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Prevention of VHFs is done by avoiding contact with the host species. Because many of the hosts that carry VHFs are rodents, prevention should involve rodent control methods. Steps for rodent prevention include the control of rodent populations, discouraging their entry into homes and safe clean up of nesting areas and droppings. For VHFs that are spread by arthropod vectors, prevention efforts should focus on community-wide insect and arthropod control. In addition, people are encouraged to use insect repellant, proper clothing, bed nets, window screens, and other insect barriers to avoid being bitten.

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Prevention and Control

- Vaccine available for Yellow fever
- Experimental vaccines under study
  - Argentine HF, Rift Valley Fever, Hantavirus and Dengue HF
- If human case occurs
  - Decrease person-to-person transmission
  - Isolation of infected individuals

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The only established and licensed vaccine is for yellow fever. This live vaccine is safe and effective and gives immunity lasting 10 or more years. An experimental vaccine is under study for Junin virus which provides some cross protection to Machupo virus. Investigational vaccines are in the development phase for Rift Valley Fever, Hantavirus and Dengue. For VHF's that can be transmitted person-to-person including: the Arenaviridae, the Bunyaviridae (excluding Rift Valley Fever) and the Filoviridae, close physical contact with infected people and their body fluids should be avoided. One infection control technique is to isolate infected individuals to decrease person to person transmission.

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Prevention and Control

- Protective clothing
  - Disposable gowns, gloves, masks and shoe covers, protective eyewear when splashing might occur, or if patient is disoriented or uncooperative
- WHO and CDC developed manual
  - "Infection Control for Viral Hemorrhagic Fevers In the African Health Care Setting"

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Wearing protective clothing is also needed to reduce transmission between people. The World Health Organization (WHO), and CDC have developed practical, hospital-based guidelines, entitled "Infection Control for Viral Hemorrhagic Fevers In the African Health Care Setting." The manual can help health-care facilities recognize cases and prevent further hospital-based disease transmission using locally available materials and few financial resources.

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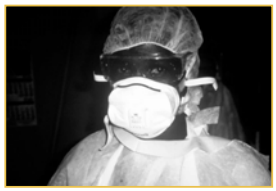

Protective equipment worn by a nurse during Ebola outbreak in Zaire, 1995

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Zairian nurse in full protective clothing prepares to enter the isolation ward during the Ebola VHF outbreak in Kikwit, Zaire, 1995.
Image from CDC.

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Prevention and Control

- Anyone suspected of having a VHF must use a chemical toilet
- Disinfect and dispose of instruments
  - Use a 0.5% solution of sodium hypochlorite (1:10 dilution of bleach)

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Other infection control recommendations include proper use, disinfection, and disposal of instruments and equipment used in treating or caring for patients with VHF, such as needles and thermometers. Place any disposable items, including linens, in a double plastic bag and saturate with 0.5% sodium hypo chlorite (1:10 dilution of bleach). Place sharps in the sharps container saturated with the 0.5% solution, wipe the containers with the 0.5% solution and send them to be incinerated.

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VHF Agents as Biological Weapons

- Outbreak of undifferentiated febrile illness 2-21 days following attack
  - Could include
    - Rash, hemorrhagic diathesis and shock
- Diagnosis could be delayed
  - Unfamiliarity
  - Lack of diagnostic tests
- Ribavirin treatment may be beneficial

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VHF agents could cause an outbreak of an undifferentiated febrile illness in 2 to 21 days. Other symptoms associated with VHFs could include rash, hemorrhagic diathesis, and shock. The mode of transmission and clinical course would vary depending on the specific pathogen. Diagnosis may be delayed due to clinicians' unfamiliarity with these diseases and lack of widely available diagnostic tests. Initiation of ribavirin therapy in the early phases of illness may be useful in treatment of some of these viruses, although extensive experience is lacking.

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VHF Agents as Biological Weapons

- Most are not stable in dry form
- Most have uncertain stability and effectiveness in aerosol form
  - Arenaviruses have tested effectiveness in aerosol form
- Marburg and Ebola have high case fatality rates
- Rift Valley is the most stable VHF in liquid or frozen state
- VHFs do pose a threat as aerosolized agents

Most VHF agents are not stable in the dry form and have uncertain stability and effectiveness in the aerosol form. All arenaviruses have been tested and are infectious in aerosols. Marburg has a high case-fatality rate. Rift Valley is the most stable of the VHF in liquid or frozen state. Most experts agree that aerosolized VHF do pose a threat as a biological weapon.

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Author: Jamie Snow, DVM, MPH

Co-authors: Radford Davis, DVM, MPH
Stacy Holzbauer, DVM