Viral Hemorrhagic Fevers (VHFs)

- Zoonoses caused by several different viruses.
- Geographically restricted, mostly to Africa.
- Occur in rural settings or in health-care facilities.
- Lassa fever is widespread in West Africa.
- Mortality overall may be low, as 80% are asymptomatic, but in hospitalized cases mortality averages 15%.
- Ebola outbreaks 1/Year in Congo, Uganda, Sudan.
- VHFs have extended into Europe, with an outbreak of Congo–Crimean hemorrhagic fever in Turkey & even mini epidemics in Iraq.
- All except Ebola & Marburg, have mild self-limiting forms.

Clinical Features

- All have similar non-specific presentations with fever, malaise, body pains, sore throat and headache.
- O/E: conjunctivitis, throat injection, an erythematous or petechial rash, hemorrhage, lymphadenopathy, bradycardia.
- Endothelial dysfunction with capillary leak & platelet dysfunction cause Bleeding
- Hypovolemic shock & ARDS may.
- In Lassa fever; joint and abdominal pain are prominent.
- A macular blanching rash may be present but bleeding is unusual, occurring in only 20% of hospitalized patients.
- Encephalopathy may develop & deafness affects 30% of survivors.
- **The clue:**
  - Travel to an outbreak area
  - Activity in a rural environment contact with sick individuals or animals within 21 days
  - Insect bites
  - Hospital visits
  - Attendance at ritual funerals (Ebola virus infection).
  - Fever within 21 days of leaving an endemic area
  - Presenting with hemorrhage or organ failure.
  - For Lassa fever retrosternal pain, pharyngitis, proteinuria has a positive predictive value of 80% in West Africa.

Investigations

- **Non-specific:** leucopenia, thrombocytopenia, proteinuria.
- In Lassa fever (AST) > 150 U/L associated with 50% mortality.

Management

- Patients at high risk of VHF or if infection is confirmed, must be transferred to a center with the appropriate biosafety & have an initial blood sample tested to exclude malaria.
- If this is negative, relevant specimens (blood, throat swab, urine and pleural fluid (if available) are collected and sent to an appropriate reference laboratory for nucleic acid detection (PCR), virus isolation & serology.
- In addition to general supportive measures, ribavirin is given IV (100 mg/kg, then 25 mg/kg daily for 3 days & 12.5 mg/kg daily for 4 days) when Lassa fever or South American hemorrhagic fevers are suspected.
### Viral Hemorrhagic Fevers

<table>
<thead>
<tr>
<th>Disease</th>
<th>Reservoir</th>
<th>Transmission</th>
<th>Incubation period</th>
<th>Geography</th>
<th>Mortality rate</th>
<th>Clinical features of severe disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lassa fever</strong></td>
<td>Multimammate rats (Mastomys natalensis)</td>
<td>Urine from rat Body fluids from patients</td>
<td>6-21 days</td>
<td>West Africa</td>
<td>15%</td>
<td>Hemorrhage, shock, encephalopathy, ARDS (responds to ribavirin) Deafness in survivors</td>
</tr>
<tr>
<td><strong>Ebola fever</strong></td>
<td>Undefined (?bats)</td>
<td>Body fluids from patients Handling infected primates</td>
<td>2-21 days</td>
<td>Central Africa Outbreaks as far north as Sudan</td>
<td>25-90%</td>
<td>Hemorrhage, hepatic and renal failure</td>
</tr>
<tr>
<td><strong>Marburg fever</strong></td>
<td>Undefined</td>
<td>Body fluids from patients Handling infected primates</td>
<td>3-9 days</td>
<td>Central Africa Outbreak in Angola</td>
<td>25-90%</td>
<td>Hemorrhage, diarrhea, encephalopathy, orchitis</td>
</tr>
<tr>
<td><strong>Yellow fever</strong></td>
<td>Monkeys</td>
<td>Mosquitos</td>
<td>3-6 days</td>
<td>Tropical Africa, South and Central America</td>
<td>~ 15%</td>
<td>Hepatic failure, renal failure, hemorrhage</td>
</tr>
<tr>
<td><strong>Dengue</strong></td>
<td>Humans</td>
<td>Aedes aegypti</td>
<td>2-7 days</td>
<td>Tropical and subtropical coasts; Asia, Africa, Americas</td>
<td>&lt; 10%&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Hemorrhage, shock</td>
</tr>
<tr>
<td><strong>Crimean-Congo hemorrhagic fever</strong></td>
<td>Small vertebrates Domestic and wild animals</td>
<td>Ixodes tick Body fluids</td>
<td>1-3 days up to 9 days 3-6 days up to 13 days</td>
<td>Africa, Asia, Eastern Europe</td>
<td>30%</td>
<td>Encephalopathy, hemorrhage, hepatic or renal failure, ARDS</td>
</tr>
<tr>
<td><strong>Rift Valley fever</strong></td>
<td>Domestic livestock</td>
<td>Contact with animals, mosquitos or other insect bites</td>
<td>2-6 days</td>
<td>Africa, Arabian peninsular</td>
<td>1%</td>
<td>Hemorrhage, blindness, meningoencephalitis (complications only in a minority)</td>
</tr>
<tr>
<td><strong>Kysanur fever</strong></td>
<td>Monkeys</td>
<td>Ticks</td>
<td>3-8 days</td>
<td>Kamataka State, India</td>
<td>5-10%</td>
<td>Hemorrhage, pulmonary edema, neurological features Iridokeratitis in survivors</td>
</tr>
<tr>
<td><strong>Bolivian and Argentinian hemorrhagic fever (Junin and Machupo viruses)</strong></td>
<td>Rodents (Calomys spp.)</td>
<td>Urine, aerosols Body fluids from case (rare)</td>
<td>5-19 days (3-6 days for parenteral)</td>
<td>South America</td>
<td>15-30%</td>
<td>Hemorrhage, shock, cerebellar signs (may respond to ribavirin)</td>
</tr>
<tr>
<td><strong>Hemorrhagic fever with renal syndrome (Hantaan fever)</strong></td>
<td>Rodents</td>
<td>Aerosols from feces</td>
<td>5-42 days (typically 14 days)</td>
<td>Northern Asia, northern Europe, Baikans</td>
<td>5%</td>
<td>Acute renal impairment, cerebrovascular accidents, pulmonary edema, shock (hepatic failure and hemorrhagic features only in some variants)</td>
</tr>
</tbody>
</table>

<sup>1</sup> All potentially have circulatory failure  
<sup>2</sup> Mortality of uncomplicated and hemorrhagic dengue fever, respectively

### Multiple Choice Questions:

1) VHF never occurs in Iraq. (F)
2) Congo-Crimean VHF is the type that occurs in Iraq. (T)
3) Suspected or confirmed case of VHF is usually managed in usual hospital wards. (F)
4) Malaria should be excluded first in a case of suspected VHF. (T)
5) Any patient presenting with fever or bleeding within 21 of leaving an endemic like Africa should be suspected of having VHF. (T)
6) The cause of bleeding in VHF is endothelial& platelet dysfunctions. (T)
7) Antivirals are essential in all types of VHF. (F)
8) Ebola & Marburg VHF have the highest mortality rates. (T)
9) Congo-Crimean VHF is the only type transmitted by ticks. (F)
10) All VHF types have high mortality rates. (F)