Arboviruses

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Arboviruses

- Arthropod-borne Viruses
- Affects vertebrate hosts
- Transmitted by Blood sucking arthropods
- Virus multiplies in vector but no disease
- Vector is infected for life
- Some are maintained by trans-ovarian transmission
Classification

- Most of the viruses are named after the disease / geographical area of 1\textsuperscript{st} isolation
- More than 450 viruses
- Nearly 100 human pathogens
Arbovirus families of importance to human diseases

- Togaviridae
  - Alphaviruses
- Flaviviridae
  - Flaviviruses
- Bunyaviridae
  - Bunyaviruses
  - Phleboviruses
  - Nairoviruses
  - Hantaviruses

Family **Reoviridae**
- Subfamily **Sedoreovirinae**
- Genus **Orbivirus**
- Genus **Seadornavirus**
- Subfamily **Spinareovirinae**
- Genus **Coltivirus**
Togaviridae

- Alphavirus
  - Chikungunya Virus
  - Eastern equine encephalitis Virus
  - Western EE Virus
  - Venezuelan EE Virus
  - Sindbis virus
Flaviviridae

- Flavivirus
  - Yellow fever Virus
  - Dengue Virus
  - Japanese Encephalitis Virus
  - West Nile encephalitis Virus
  - Kyasanur Forest Disease (KFD) Virus
  - Murray valley encephalitis Virus
  - Russian spring Summer encephalitis Virus
  - St.Louis encephalitis Virus
Bunyaviridae

- Bunyavirus
  - California Encephalitis Virus
  - Bunyamwera Virus
- Phlebovirus
  - Sandfly fever Virus
  - Rift valley Fever Virus
- Nairovirus
  - Crimean - Congo Hemorrhagic Fever Virus
- Hantavirus
  - Hantan Virus (Korean Hemorrhagic Fever Virus)
Transmission Cycles

- Man - arthropod - man
  - e.g. dengue, urban yellow fever.
  - Reservoir may be in either man or arthropod vector.
  - In latter transovarial transmission may take place.
- Animal - arthropod vector - man
  - e.g. Japanese encephalitis, EEE, WEE, Jungle yellow fever.
  - reservoir is in an animal.
  - virus is maintained in nature in a transmission cycle involving arthropod vector and animal. Man becomes infected incidentally.
- Both cycles may be seen with some arboviruses such as yellow fever.
Man-Arthropod-Man Cycle
Animal-Arthropod-Man Cycle
Vectors

- Mosquitoes
- Tick – *Ixodes spp*
- Sand fly
Examples of Arthropod Vectors

Aedes Aegyti

Culex Mosquito

Assorted Ticks

Phlebotmine Sandfly
**Arthropod Vectors**

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

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

**Sandflies**
Sicilian sandfly fever, Rift valley fever.
# Animal Reservoirs

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

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

- Fever and rash - usually a non-specific illness resembling a number of other viral illnesses such as influenza, rubella, and enterovirus infections.
- Encephalitis - e.g. EEE, WEE, St Louis encephalitis, Japanese encephalitis.
- Haemorrhagic fever - e.g. yellow fever, dengue, Crimean-Congo haemorrhagic fever.
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
DENGUE VIRUS

- Family: Flaviviridae
- +ve sense, ss, encapsulated RNA virus
- Contains 3 structural & 7 non-structural protein genes
Serotypes & Genotypes of DV

- DENV is very diverse
- 4 serotypes known: DV-1, DV-2, DV-3, DV-4
- Antigenic similarity but cross immunity lasts only a few months
- Distinct three to five genetic groups (genotypes) and lineages identified within each serotype
  - DV1: Genotype I, II, III
  - DV2: Genotype I, II, III, IV, V and sylvatic
  - DV3: Genotype I, II, III
  - DV4: Genotype I, II, III, IV, V
- Some circulating lineages within genotypes
Dengue Viruses

- Each serotype provides specific lifetime immunity, but poor cross-immunity.
- All serotypes can cause severe and fatal disease.
- Some genetic variants within each serotype appear to be more virulent or have greater epidemic potential.
Distribution of Dengue
GLOBAL SPREAD OF DENGUE

DENV Co-circulation. Cumulative number of DENV types reported by decade since 1943.

Spread of Dengue: India

1991

2010
Reasons for Dengue Expansion in the World

- Extensive vector infestation, with declining vector control
- unreliable water supply systems
- Increasing non-biodegradable containers and poor solid waste disposal
- Increased air travel
- Increasing population density in urban areas
VECTOR: MOSQUITO

- *Aedes aegypti*: commonest,
- *Aedes albopictus*
- white bands or scale patterns on legs and thorax
- lives in proximity to human habitations in urban areas
- Breeds mostly in man-made containers
- day-time feeder,
- peak biting periods: morning and dusk
- bites multiple people during each feeding period
- species are sensitive to environmental conditions such as temperature, precipitation and humidity.
Dengue Virus - Pathogenesis

1. Virus transmitted to human in mosquito saliva

2. Virus replicates in target organs

3. Virus infects white blood cells and lymphatic tissues

4. Virus released and circulates in blood
Dengue Virus – in Mosquito

5. Second mosquito ingests virus with blood

6. Virus replicates in mosquito mid gut and other organs, infects salivary glands

7. Virus replicates in salivary glands
Transmission of Dengue Virus by *Aedes aegypti*

- **Extrinsic incubation period**: 0-12 days
  - Mosquito feeds / acquires virus
  - Mosquito refeeds / transmits virus

- **Intrinsic incubation period**: 16-28 days

**Illness**
- Human #1
- Human #2

**Days**
- 0
- 5
- 8
- 12
- 16
- 20
- 24
- 28
Pathogenesis of DHF

- Infected Persons develop neutralizing antibodies to dengue virus of that same (homologous) serotype
- Subsequent infection with another serotype, the pre-existing heterologous antibodies form complexes but do not neutralize the new virus
- Leads to Antibody-dependent enhancement
- Infected monocytes release vasoactive mediators, resulting in
  - increased vascular permeability
  - hemorrhagic manifestations
Dengue Clinical Syndromes

- Undifferentiated fever
- Classic dengue fever (DF)
- Dengue hemorrhagic fever (DHF)
- Dengue shock syndrome (DSS)
Undifferentiated Fever

- May be the most common manifestation of dengue
Clinical Characteristics of Classical Dengue Fever

- Fever
- Headache (orbital)
- Muscle and joint pain
- Nausea/vomiting
- Rash
- Hemorrhagic manifestations
Hemorrhagic Manifestations of Dengue

- Skin hemorrhages, Petechiae, Purpura, Ecchymoses
- Gingival bleeding
- Nasal bleeding
- Gastro-intestinal bleeding, hematemesis, melena
- Hematuria
- Increased menstrual flow
Dengue Hemorrhagic Fever

4 Necessary Criteria:

- Fever, or recent history of acute fever
- Hemorrhagic manifestations
- Low platelet count (100,000/mm$^3$ or less)
- Objective evidence of “leaky capillaries:"
  - elevated hematocrit (20% or more over baseline)
  - low albumin
  - pleural or other effusions
Dengue Shock Syndrome

- 4 criteria for DHF
- Evidence of circulatory failure manifested indirectly by all of the following:
  - Rapid and weak pulse
  - Narrow pulse pressure OR hypotension for age
  - Cold, clammy skin and altered mental status
- Frank shock is direct evidence of circulatory failure
Danger Signs in Dengue Hemorrhagic Fever

- Abdominal pain - intense and sustained
- Persistent vomiting
- Abrupt change from fever to hypothermia, with sweating and prostration
- Restlessness
WHO Classification (Change from 1997 to 2009)

WHO Classification (Change from 1997 to 2009)

**CRITERIA FOR DENGE ± WARNING SIGNS**
- Probable dengue
  - Live in/ travel to dengue endemic area.
  - Fever and 2 of the following criteria:
    - Nausea, vomiting
    - Rash
    - Aches and pains
    - Tomiquet test positive
    - Leukopenia
    - Any warning sign
- Laboratory-confirmed dengue
  (Important when no sign of plasma leakage)

**Warning signs***
- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, restlessness
- Liver enlargement > 2cm
- Laboratory: Increase in HCT concurrent with rapid decrease in platelet count
* (requiring strict observation and medical intervention)

**CRITERIA FOR SEVERE DENGUE**
- Severe plasma leakage leading to:
  - Shock (DSS)
  - Fluid accumulation with respiratory distress
  - Severe bleeding as evaluated by clinician
- Severe organ involvement
  - Liver: AST or ALT > 1000
  - CNS: Impaired consciousness
  - Heart and other organs

**SEVERE DENGUE**
- 1. Severe plasma leakage
- 2. Severe haemorrhage
- 3. Severe organ impairment
Viral Risk Factors for DHF Pathogenesis

- Virus strain (genotype)
  - Epidemic potential: viremia level, infectivity
- Virus serotype
  - DHF risk is greatest for DEN-2, followed by DEN-3, DEN-4 and DEN-1
Figure 3. Reported and estimated DF/ DHF and dengue-2 infections during the 1997 DHF Cuban epidemic.21
Temperature, Virus Positivity and Anti-Dengue IgM, by Fever Day

Adapted from Figure 1 in Vaughn et al., J Infect Dis, 1997; 176:322-30.
Petechiae
Pleural Effusion Index

\[ PEI = \frac{A}{B} \times 100 \]
Tourniquet Test

- Inflate blood pressure cuff to a point midway between systolic and diastolic pressure for 5 minutes
- Positive test: 20 or more petechiae per 1 inch² (6.25 cm²)
Laboratory Diagnosis - Dengue

- Virus isolation
  - Mosquito cell line C6/36
  - Mosquito inoculation
- IgM ELISA test for serologic diagnosis
Virus Isolation:
Mosquito Inoculation
Treatment

- No specific antiviral therapy available
- Fluid management
- Rest
- paracetamol (avoid aspirin and non-steroidal anti-inflammatory drugs)
- Monitor blood pressure, hematocrit, platelet count, level of consciousness
Dengue Vaccine?

- No licensed vaccine at present
- Effective vaccine must be tetravalent
- Field testing of an attenuated tetravalent vaccine currently underway
- Effective, safe and affordable vaccine will not be available in the immediate future
Yellow Fever
The United States Army Yellow Fever Commission
(1900 - 1901)

U.S. Military Orders Establishing the Yellow Fever Commission - May 14, 1900
4th Commission - Yellow Fever - US coast & Caribbean
Distribution and incidence

- Occurs only in South America and Africa
- Resurgence has occurred in last 20 years in West Africa
- Epidemics also occur in urban areas - transmission human to human - through - *Ae. Aegypti* mosquito
Transmission and epidemiology

- *Ae. Aegypti* is found in forest
- Primates (monkeys) serve as viral reservoir
- Spread to humans through Mosquito bite
  - Forest areas --- Monkeys to Man
  - Urban areas ---- Man to Man
  - No direct Man to Man transmission.
Pathogenesis

- Incubation period is about 3-6 days.
- Virus replicates in lymph nodes, then spreads to bone marrow, liver and spleen
- Extensive liver damage
- Platelet dysfunction - Thrombocytopenia
- Hemorrhages throughout body…especially GI, pleura, brain
Clinical Manifestations

- Usually self-limited illness, but may be fatal in up to 50% of cases
- Manifested by myalgia, malaise, lethargy, prostration, fever, vomiting, and dehydration
- Often has an initial symptomatic period, followed by remission, then severe exacerbation
Clinical Manifestations

- Jaundice
- Petechial rashes, epistaxis, purpuric hemorrhages
- Progresses to renal failure, liver failure, encephalopathy and coma
- Death within 7-10 days after onset
Treatment

- No specific therapy
- Supportive of fluid and electrolyte balance
- Life-saving measures
Diagnosis

- Virus isolation (Not recommended)
- IgM Antibody detection - ELISA
Prevention and Control

- Live attenuated YF vaccine is 95% effective within 10 days of inoculation
- Reimmunization required every 10 years for travelers
Japanese Encephalitis
Japanese Encephalitis

- First discovered and originally restricted to Japan
- Large scale epidemics occur in China, India and other parts of Asia
- Flavivirus, transmitted by culex mosquitoes
- Virus is maintained in nature in a transmission cycle involving mosquitoes, birds and pigs
- Most human infections are subclinical: the unapparent 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 20 km, all local control measures usually fail
- An effective vaccine is available
Japanese Encephalitis

- Leading cause of viral encephalitis in Asia.
- 50,000 cases in Asia per year
- 15,000 deaths/year (5-35% case fatality rate)
- First recognized in India in 1955
- North Arcot district of Tamil Nadu.
- Since 1972 JE has spread to newer areas
- West Bengal, Uttar Pradesh, Assam, Manipur, Bihar, Andhra Pradesh, Pondicherry, Karnataka, Goa, Kerala and Maharashtra.
Japanese Encephalitis Virus

- Family: Flaviviridae
- Enveloped virus
- Spherical
- Size 40-50 nm in diameter
Reservoir host - JEV

- Wading Birds
  - Carries the virus
  - Viremia
  - No clinical disease
Amplifier host

- Pig (Swine)
  - Breeding and slaughter of Pigs - located adjacent to populated areas
  - Susceptible pig population, crowded conditions, Paddy field and proximity to mosquito populations - amplify virus
Mosquitoes (Culex tritaeniorhynchus, C. Vishnui)

- Breeds in rice fields
- Good rainfall encourage breeding
- Highest prevalence during monsoon season
- Highest biting activity from dusk to midnight
- Prefers to feed on pigs
Conducive conditions for Transmission
Transmission Cycles

Wading Birds → Mosquitoes → Pigs → Mosquitoes → Maintenance Cycle

Amplifying Cycle
Japanese Encephalitis - Pathogenesis

- Arboviral disease transmitted by mosquitoes
- Only 1/300 to 1/1000 infections are symptomatic
- Symptomatic illness ranges from mild to severe
  - Mild cases resolve within 2 weeks
  - 50% are severe with progressive neurologic impairment, stupor and coma leading to death or permanent neurologic damage
JE - Pathogenesis

- Primary multiplication of Virus occurs probably in fibroblasts
- Virus then reaches regional lymph nodes.
- A brief period of viremia 2 – 3 days
- In some individuals, virus invades CNS
- Usually gray matter of brain is involved
- Lesions are seen in thalamus, substantia nigra, cerebral cortex, cerebellum, Ammon’s horn and anterior horn of spinal cord.
JE - Clinical Manifestations

- **Prodromal stage:** 2-3 days
  - high-grade fever, headache & malaise.

- **Acute Encephalitis Stage:** Lasts for usually 3-4 days or longer
  - Focal asymmetric neurological deficits.
  - Fever, headache, vomiting and meningeal irritation
  - Seizures and/or other abnormal movements
  - Asymmetrical spontaneous eye movements or Doll's eye movements
  - Cranial nerve palsies
  - Mortality in JE is very high
  - Recovery from severe encephalitis may result in neurological deficits or sequelae.
Laboratory Diagnosis- JE

- **Serological tests**
  - Haemaglutination Inhibition (HI Test)
  - IgM capture ELISA
  - Neutralization test

- **Virus isolations & propagation**
  - Tissue culture
  - Infant mouse inoculation
  - Mosquito inoculations

- **Antigen detections:**
  - Immunofluorescence Test
  - Antigen capture ELISA

Specimen: CSF
Blood Ac and Con
Laboratory Diagnosis - JE

- **Specimen:** Blood / CSF
- **Virus isolation**
  - Mosquito cell line C6/36
  - Mosquito inoculation
- **IgM ELISA** test for serologic diagnosis (Sensitive after 5-7 days)
JEV Isolation

Mosquito

Infant mouse
JE vaccine

- Live, attenuated SA 14-14-2 vaccine Inactivated
- Presentation • 5-dose or single dose vial,
  - Lyophilized powder requiring reconstitution with supplied diluent
  - Single dose given
  - 0.5 mL dose given by subcutaneous injection
- Boosters • Boosters are unlikely to be required: as with most live, attenuated vaccines, it is thought one dose will provide lifelong protection.
- Studies have already documented ongoing protection from a single dose for a minimum of five years in a JE-endemic area.
JE Vaccine

- Killed JE Vaccine, Nakayama strain
- Mouse brain derived vaccine
- 60 – 80 % seroconversion
- Administration • 0.5 mL dose given by subcutaneous injection. • 1 mL dose (0.5 mL for children <3 years)
- Two doses given at an interval of 1-4 weeks
- Boosters required every year
- Manufactured by Central Research Institute, Kasauli, Stopped recently
- Not used commonly any more
- Need to produce better and cost effective vaccine for mass immunization.
Vector- Mosquito - Control
Vector Control Methods: Chemical Control

- Larvicides may be used to kill immature aquatic stages
- Fumigation not very effective against adult mosquitoes
- Mosquitoes may have resistance to commercial aerosol sprays
Vector Control Methods:
Biological and Environmental Control

- **Biological control**
  - Largely experimental
  - Use of Guppy fish in water collection to eat larvae
  - Introduction of sterile (transgenetic) males

- **Environmental control**
  - Elimination of larval habitats
  - Most likely method to be effective in the long term
KYASANUR FOREST DISEASE (KFD)

- March 1955 – forest - Shimoga district, Karnataka State
- Heavy mortality in languor and bonnet monkeys
- The mortality in monkeys followed by high incidence of acute prostrating febrile illness among the villagers
- 10 -15% fatality
- Virus isolated from Monkeys, man and ticks.
- Yearly 40 -1000 cases
KFD

- Similar to Russian Spring Summer encephalitis virus
- Member of family Flaviviridae.
- Enveloped
- Spherical particles
- Size 45 nm in diameter.
- Neurotropic Virus
KFD – Clinical features

- Incubation Period 2-7 days
- Sudden onset - chills, frontal headache high fever (40°C).
- Continuous fever for 12 days or longer
- Severe myalgia, cough, diarrhea, vomiting and photophobia.
- Prolonged Convalescent Period
- Can relapse after 1 to 2 week of afebrile period.
- The second phase lasts for 2-12 days
- Neck stiffness, mental disturbance, giddiness
Vectors

• **Ticks**
  • *Isolated from 16 species of ticks*
  • *Major vector: Haemaphysalis spinigera*

Highly anthropophilic tick
Bites the people who trespass forest
Vertebrate Hosts

- Langur monkey (*Presbytis entellus*)
- Bonnet monkey (*Macaca radiata*)
- Small rodents
- Neutralising antibodies found in a number of animals and birds – But not major reservoir
- Human – Accidental host – Dead end
Shimog a forest
Vaccine - KFD

- Formalin inactivated Chick Embryo tissue culture Vaccine
- Developed by NIV
- About 70% Seroconversion - neutralizing antibodies
Biosafety Concerns

- During investigations, over 100 laboratory persons got infected
- KFD virus is ranked as Risk group 4 pathogen
- **Needs Bio Safety Level-4 laboratory**
West Nile Virus
West Nile virus

- Closely Related to Japanese Encephalitis virus
- Neurotropic Virus
- Usually Causes Asymptomatic infection
- But can cause severe Encephalitis
- Indegenous to Africa, Asia, Europe, Australia
- Recently introduced to USA (1999)
- Recent Out break of West Nile Virus Encephalitis in USA New York city—More than 142 cases and 18 deaths
The Organism

• Flaviviridae
  • *Flavivirus*
    • Single-stranded RNA virus

• 2 genetic lineages
  • Linage 1
    • 3 clades (1a, 1b, 1c)

• Infects humans, birds, mosquitoes, horses, and other mammals
Transmission Cycle
Mosquito – Bird – Mosquito cycle

- Reservoir Hosts
  - Birds – Ravens, Crows

- Vectors
  - Mosquito – Culex spp

- Man, Horse etc. – Accidental hosts
West Nile Virus - Distribution
Incidental hosts

Vectors

Humans, horses, and other animals

Amplifying hosts

Birds

Culex spp., Aedes spp., Ochlerotatus spp.
Human Transmission

- Direct contact
  - Infected birds, tissues
- Laboratory acquired
- Blood transfusions
  - Screening implemented in 2003
- Organ transplants
- Transplacental transmission
- Breast feeding
Disease in Humans

- Incubation: 2 to 14 days
- Many WNV infections asymptomatic
- Two forms of disease
  - **West Nile fever**
    - Most common form, Resembles influenza
  - **West Nile neuroinvasive disease**
    - Occurs rarely
    - Can be severe and life-threatening
    - Three syndromes
      - Encephalitis
      - Meningitis
      - Acute flaccid paralysis
    - Persistent neurological dysfunction may occur
Diagnosis in Humans

- Serology
  - Serum or CSF
  - IgM capture ELISA
    - Cross reactions possible
  - Plaque neutralization test
- Detection of virus, antigen, or nucleic acids
  - RT-PCR
  - Immunohistochemistry
Prevention and Control

- No vaccine available
- Vector - Mosquito Control
Chikungunya
Asian Distribution
States reporting Chikungunya in India

Chikungunya

- CHIKV: arthropod-borne alphavirus
- Causes an acute febrile illness
- Vector: *Aedes* species
- First recognized as a human pathogen during the 1950s in Africa
- It has become endemic in south and central India
- First outbreak in 1952 on the Makonde Plateau
- Border between Tanganyika and Mozambique
- First published report is from Africa in 1955 by Marion Robinson and W.H.R. Lumsden
- Recent large epidemic occurred in Malaysia in 1999
- Significant urban outbreaks of chikungunya fever in India: from 1963 through 1973
- Epidemic resurgence of CHIKV in India: during 2005-06 after a gap of 32 years
What is this virus?

- Causative agent is an RNA – VIRUS
- Class – Arbo Virus (Arthropod Borne)
- Family – Togaviridae
- Genus – Alpha Virus
- Species – Chikungunya Virus
- Similar to Semliki Forest Viruses (SFV) in Africa and Asia.
Transmission

- Reservoir – Non-human primates in Africa
- No animal reservoir is found in India
- Maintained in nature by man – mosquito – man cycle
- Vector – Aedes aegypti, Ae. albapticus mosquito
- Same vector as for Dengue and Yellow fevers
- Vehicle of transmission – None
- No known mode - other than mosquito bite
- Incubation Period – 2 days to 12 days
Notable Outbreaks

- 1963 to 1965 - An epidemic was reported in Calcutta – 4.37% of the people were later found to be seropositive
- 1973 – An epidemic 37.53% in Barsi - Sholapur district
- 2006 – Present epidemic after 33 years is the largest
- 9,06,360 or more cases in Andhra Pradesh
- 5,43,286 cases from Karnataka; 66,109 from B’lore
- Maharashtra 2,02,114 cases; Gujarat 2,500 cases
- Tamil Nadu 49,567 cases; Orissa 4,904 cases,
- Madhya Pradesh 43,784 and Pune 138 cases
Distribution in India

- The disease is common with periodic epidemics
- Sporadic outbreaks described in Madras and Vellore
- Cases were reported in Chennai, Pondicherry, Vellore
- Vizag in 1964; Rajahmundry, Kakinada, Nagpur in 1965
- The last epidemic in India was in 1973
- From Yavat village (Pune) in 2000
- 2.9% in the Andaman & Nicobar Islands are seropositive
- Infected mosquitoes seen in Pune, Maharastra State
Most Recent Epidemics

• Epidemic of CHIKV occurred in Malaysia – 1999
• French island of Réunion in the Indian Ocean - 2005
• Epidemic was recorded in Mauritius – 2005
• Madagascar, Mayotte and Seychelles – 2005
• Hong Kong and Malaysia early 2006
• Present indian epidemic is the largest -from Dec ’05
• Maximum # of cases from Andhra Pradesh so far
Symptoms

- Sudden onset of fever, chills
- Headache, nausea, vomiting, abdominal pain
- Joint pain with or without swelling,
- Low back pain and rash
- Very similar to those of Dengue but
- Unlike in Dengue, no hemorrhagic / shock syndrome
Clinical Features

- Incubation period is 2-12 d; usually 3-7 days
- Viremia last for 5 days (infective period)
- Silent CHIKV – inapparent infections in children
- Flu-like symptoms, Severe headache and chills
- High grade fever (40°C or 104°F),
- Arthralgia or arthritis – lasting several weeks
- Conjunctival suffusion and mild photophobia
- Nausea, vomiting, abd. pain, severe weakness
The Arthralgia

- The small joints of the lower and upper limbs
- Migratory poly arthralgia – not much effusions
- Larger joints may also be affected (knee, ankle)
- Pain worse in the morning – less by evening
- Joints may be swollen & painful to the touch
- Some patients have incapacitating joint pains
- Arthritis may last for weeks or months.
Kun gunyala

The Contorted Posture
Rare Clinical Features

- A petechial or maculo papular rash usually involving the limbs may occur.
- Hemorrhage is rare
- Nasal blotchy erythema, freckle-like pigmentation over centro-facial area,
- Flagellate pigmentation on face and extremities
- Lichenoid eruption and hyper pigmentation in exposed areas
Rare Clinical Features

- Multiple aphthous-like ulcers over scrotum, crural areas and axilla
- Unilateral or bilateral lymphoedema of the limbs
- Lymphadenopathy not common
- Multiple ecchymotic spots in children
- Vesiculo-bullous lesions in infants and
- Sub-ungual hemorrhages
- Severe menigo-encephalitis – rare; may be fatal
Who are at greater risk?

- Pregnant women
- Elderly people
- Newborns
- Women in general
- Diabetics
- Immuno-compromised patients
- Patients with severe chronic illnesses
Laboratory Diagnosis

1. Four fold or more rise of HI Antibody
2. IgM capture ELISA using MAbs
3. Indirect Immuno Flourescence Test (I IFT)
   - On infected cells from tissues
4. Virus Isolation – Infant Swiss Albino mice
   - Vero BHK-21 cell lines are used
5. Nucleic acid amplification by PCR & RT PCR
Laboratory Diagnosis

- IgM capture ELISA – Good serological test
- Not commercially available
- NIV – Pune, NICD – Delhi only
- Positive after 5-10 days & lasts up to 6 months
- HI Antibody appears on day 3 or 4
- RT – PCR confirmatory – before the 5th day
Crimean Congo hemorrhagic fever
Crimean Congo hemorrhagic fever

- Clinical entity in 1944-1945 in Crimea during World War II
- CCHF virus circulates in an enzootic tick-vertebrate-tick cycle
- Vector: *Hyalomma spp.* ticks
- A CCHF outbreak was reported in Gujarat in 2011
- characterized by a zoonotic origin and a person-to-person spread in hospital setting
- further spread of the disease curtailed by:
  - High index of clinical suspicion,
  - early laboratory diagnosis
  - containment measures
CCHF

- During December 2010, NIV, Pune detected Crimean-Congo hemorrhagic fever virus specific IgG antibodies in livestock serum samples from Gujarat and Rajasthan.
- During January 2011 Crimean-Congo hemorrhagic fever virus was confirmed in a nosocomial outbreak, in Ahmadabad.
- Retrospective investigation of suspected human samples confirmed that the virus was present in Gujarat state, earlier to this outbreak.
- Case fatality rate ranging from 5 to 80%.
- Presence of hemagglutination inhibition antibodies have been detected in animal sera from Jammu and Kashmir, the western border districts, southern regions and Maharashtra.
- Antibodies were observed during and after the outbreak in human beings, ticks and domestic animals (buffalo, cattle, goat and sheep) from Gujarat.
- 2012, this virus was again reported in human beings and animals.
Phylogenetic analysis showed that all the four isolates of 2011, as well as the S segment from specimen of 2010 and 2012 were highly conserved and clustered together in the Asian/Middle East genotype IV.

S segment of South-Asia 2 type was closest to a Tajikistan strain TADJ/HU8966 of 1990.

Biosafety level 3 laboratories required for diagnosis
CCHF: geographic distribution

North limit for the geographic distribution of genus *Haemaphysalis* ticks

- **CCHF viral isolation**
- **Country at risk** (serological evidence + vector)
- **Country with low risk** (presence of vector only)
Hanta Virus
History

- Haemorrhagic Fever with Renal Syndrome (HFRS: later renamed hantavirus disease) first came to the attention during the Korean war when over 3000 UN troops were afflicted.
- described by the Chinese 1000 years earlier.
- In 1974, the causative virus 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.
Hantaviruses

- Forms a separate genus in the Bunyavirus family.
- Family: *Bunyaviridae*, genus: *Hantavirus*
- 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.
- Most widely distributed zoonotic rodent-borne viruses
- Causes 2 clinical syndromes:
  - haemorrhagic fever with renal syndrome (HFRS) in Asia
  - hantavirus pulmonary syndrome (HPS) in Americas
Hantavirus
• Thottapalayam virus: first hantavirus isolated from an insectivores in 1964 in Vellore, South India.
• Serological investigation of patients with pyrexic illness revealed presence of anti-hantavirus IgM antibodies in 14.7% of them.
• Sero-positivity of hantavirus infections in general population is about 4%
• People who live and work in close proximity with rodents have a greater risk of acquiring hantavirus infections
• Molecular and serological evidence of hantavirus infections in rodents and man documented in India
Diagnosis

- **Serological diagnosis** - IF, HAI, SRH, ELISAs have been developed.
- **Direct detection of antigen** - 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 of great use in diagnosing hantavirus pulmonary syndrome.
- **Virus isolation** - isolation of virus from urine early in hantavirus disease. Isolation of virus from blood is less consistent.
- **Immunohistochemistry** - useful in diagnosing HPS.
Be Prepared
Be Aware
Be Ready