

Neuroscience II

Lecture 3

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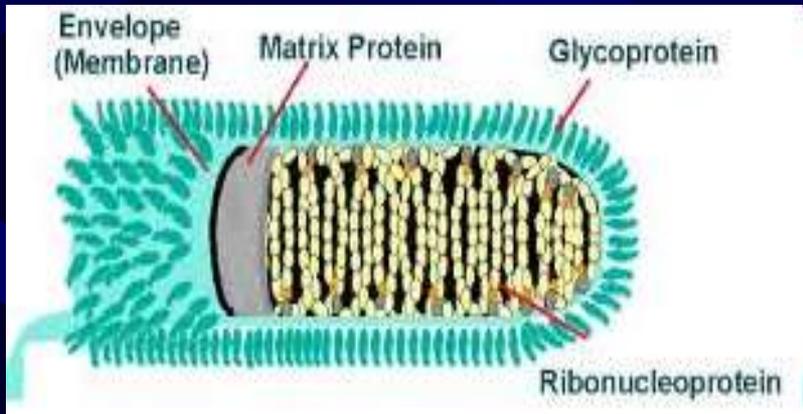
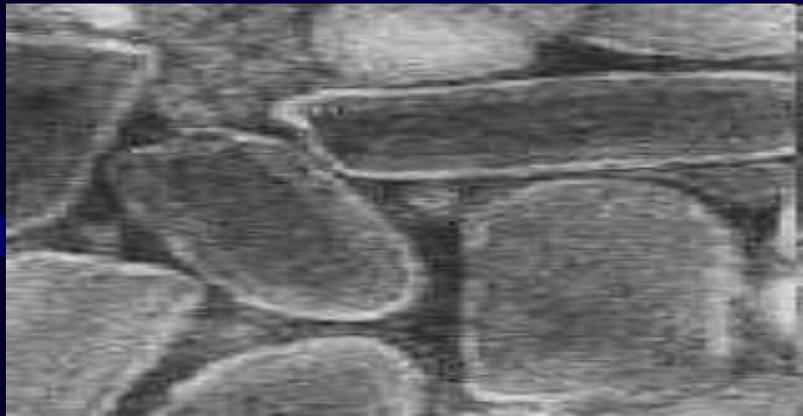
Faculty of Medicine/ Mutah University

Rabies

Main properties:

- Belongs to Rhabdo viruses family
- Single stranded negative sense RNA
- Has its own RNA-dependent RNA transcriptase
- Surrounded by a bullet shaped capsid and a lipoprotein envelop
- Single antigenic type
- It has a broad range of hosts, all mammals basically but also birds, reptiles.

Rabies Virus



Rabies

Life cycle:

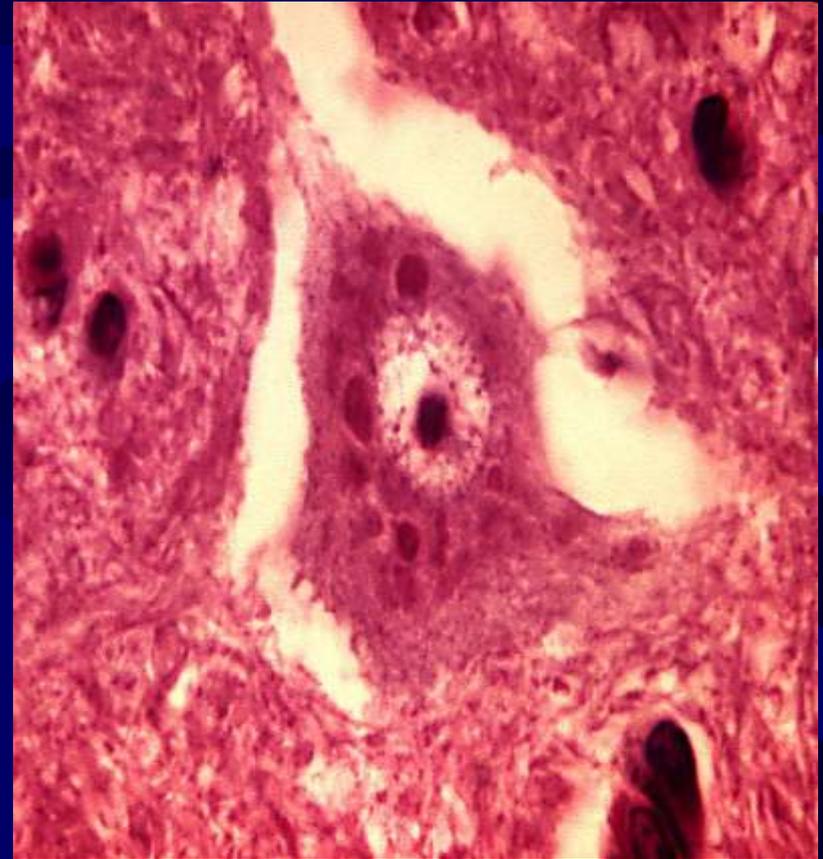
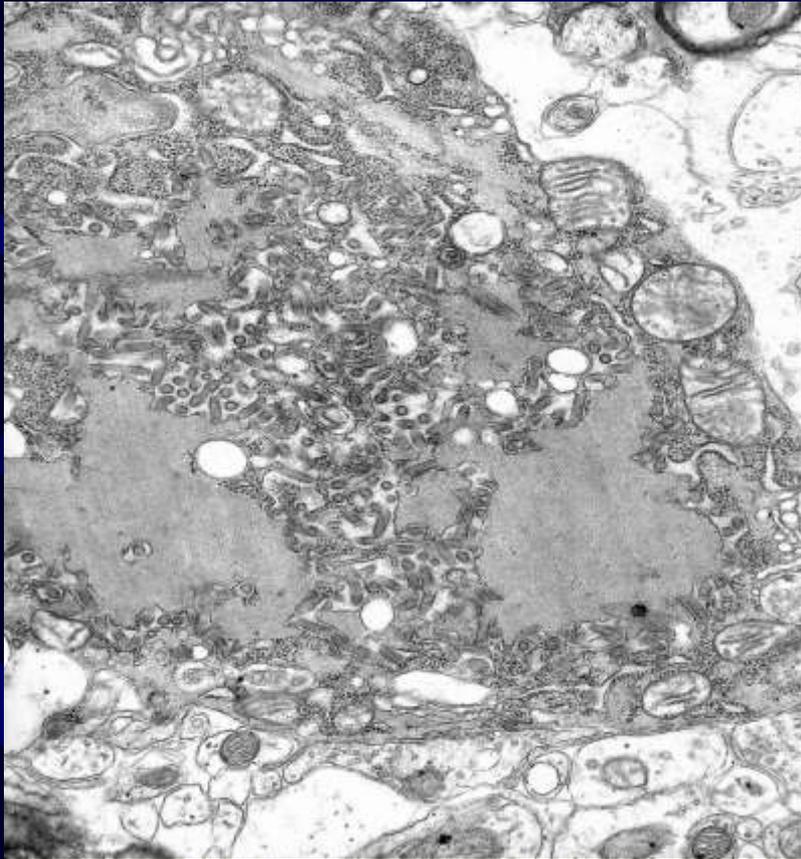
- Virus enters the muscular cell following the bite and replicate there > The viral RNA needs to be converted into a positive sense RNA > by the viral RNA transcriptase
- Viral RNA replication and protein synthesis > budding through the cell membrane
- Enters the neuron via acetylcholine receptors (could be wider) > Transported from the neurons to the CNS where it replicates in the brain (grey matter and brain stem, medulla)
- The virus migrates peripherally via autonomic nerves to salivary glands, conjunctiva, lactating glands, kidneys, hair..

Rabies

Pathology:

- Nerve cell degeneration
- Eosinophilic Intracytoplasmic inclusion bodies (Negri's bodies)

Negri's bodies



Rabies

Transmission:

Through non intact skin

- Bites of rabid animals (bats, cats, dogs, racoons, foxes, skunks)
- Abrasion or scratches on skin

Also

- Mucous membrane exposed to saliva from licks
- Inhalation of bats secretions



Rabies transmission



Rabies

- **Incubation period:**

1 week – 5 year (1 week – 3 months on average)

- **Risk** of developing rabies after a bite: 5-80%.

- Depends upon....

- Severity of exposure
- Location of the bite
- The biting animal

- **Bites on head and neck have shorter incubation time (as short as 15 days) because of rich peripheral nerve supply

Rabies

Two clinical patterns:

Dumb (paralytic) and Furious (encephalitis)

- **Non-specific symptoms:**

Bite site pain numbness, Fever, headache, dry throat, cough, insomnia

1. Dumb:

- symmetrical ascending paralysis
- 1/3 of cases
- May develop into encephalitis in 2-3 weeks > coma and death

Rabies

3. Furious:

- Encephalitis (delirium, convulsions, coma and death)
- Hydro and aerophobia
- In 2/3 cases
- Death usually in 1 week
- **Prognosis:**
 - ✓ Once symptoms occur: fatal in 3-10 days

Rabies

Diagnosis:

Samples:

- Hair follicle
- Brain and salivary glands
- Serum, CSF

Tools:

- Serology: ELISA detection of antibodies detection
- Histology (post mortem)
- Reverse transcription – PCR

- Also animal observation for 10-14 days

Rabies / treatment

- No effective treatment exists.
- Post exposure Prophylaxis
 - 1. Wound care:**
 - immediate thorough washing with soap and water and povidine-iodine
 - Doxycycline to cover for anaerobic bacteria

Rabies

2. Passive immunity:

- Anti rabies immunoglobulin
- 20 IU/kg
- Half at wound area and half I.M (gluteal muscle)
- As soon as possible

3. Active immunisation:

- Killed virus
- I.M in deltoid muscle
- 5 doses at 0, 3, 7, 14 and 30 days

Prevention:

- Vaccination of animals and those who work with animals
- Inhibit animals smuggling

RABIES BE CAREFUL



Arboviral Encephalitis

- Arboviruses are *arthropod-borne viruses*
 - Viruses are transmitted between hosts by blood-sucking arthropods (ex. mosquitoes)
- Mosquito-borne arboviruses cause various types of arboviral encephalitis
- As zoonotic diseases they rarely affect humans
- Signs/Symptoms
 - Arboviruses usually cause mild, coldlike symptoms
 - Arboviruses that cross the blood-brain barrier can cause encephalitis with symptoms similar to meningitis

Transmission of Encephalitis Arboviruses

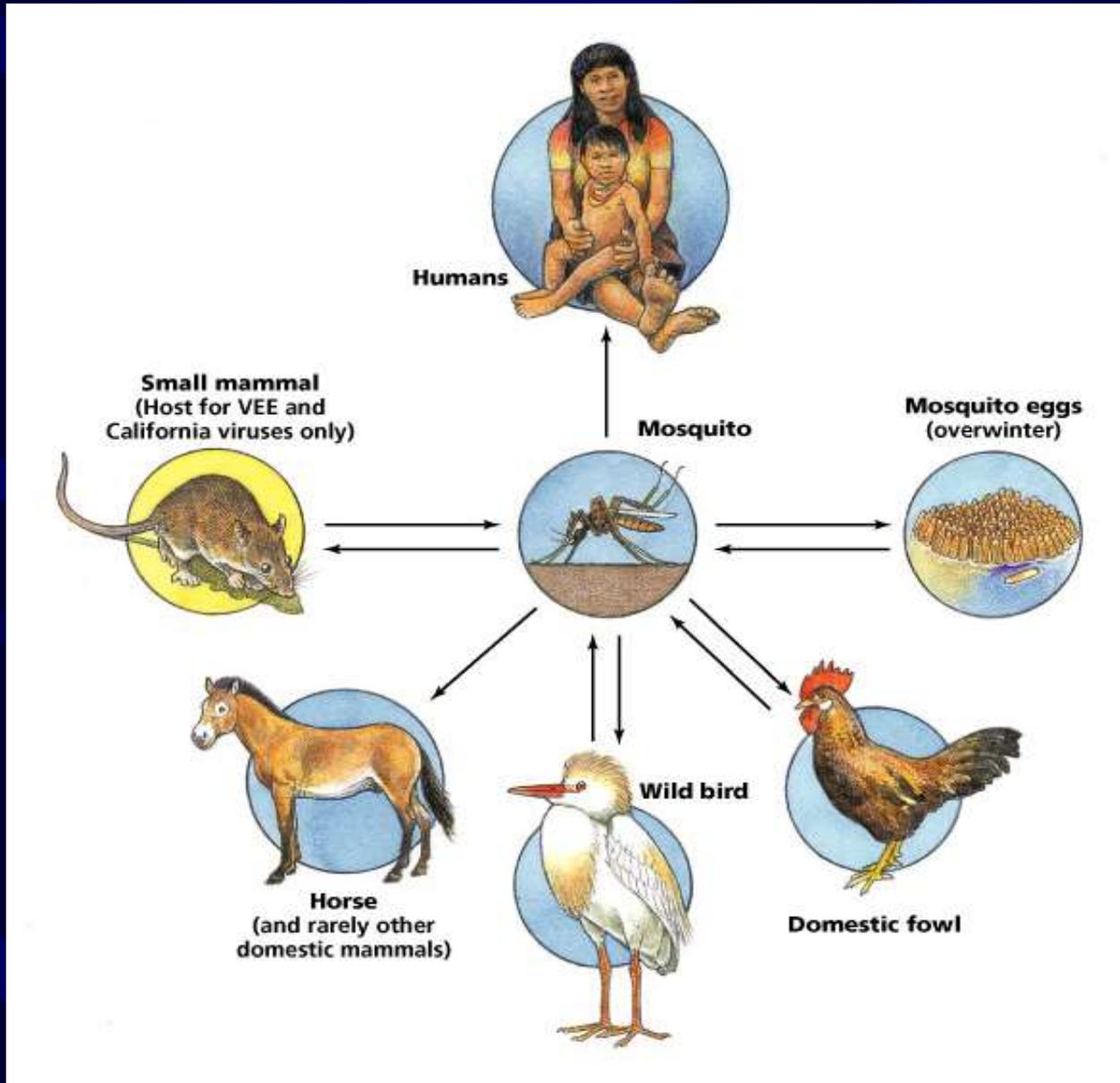


Figure 20.15

Arboviruses

- Arboviruses that can affect the nervous system :
- Alphaviruses (Togaviruses):
 1. Eastern equine encephalitis (EEE)
 2. Western equine encephalitis (WEE)
 3. Venezuelan equine encephalitis (VEE)

Arboviruses

- **Flaviviruses:**

1. Japanese encephalitis
2. St Louis encephalitis
3. West Nile virus
4. Dengue virus
5. Tick-borne encephalitis

- **Bunyaviruses:**

- Rift valley virus

- **Reoviruses:**

- Colorado tick fever

Arboviruses

- **Vectors:**

Mosquitoes, ticks and sand flies mainly.

- **Mosquitoes:**

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

- **Ticks:**

various tick-borne encephalities (including Flaviviruses).

- **Sandflies:**

Sicilian sandfly fever, Rift valley fever.

Arboviruses

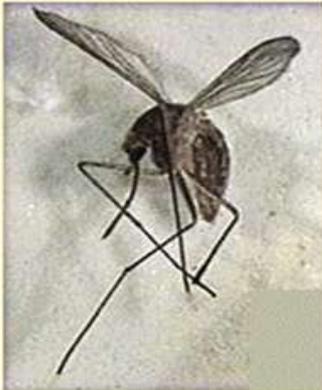
Examples of Arthropod Vectors



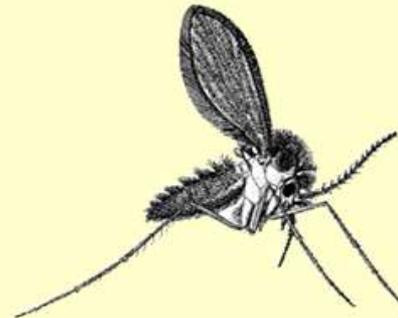
Aedes Aegypti



Assorted Ticks



Culex Mosquito



Phlebotomine Sandfly

Arboviruses /Animal reservoirs

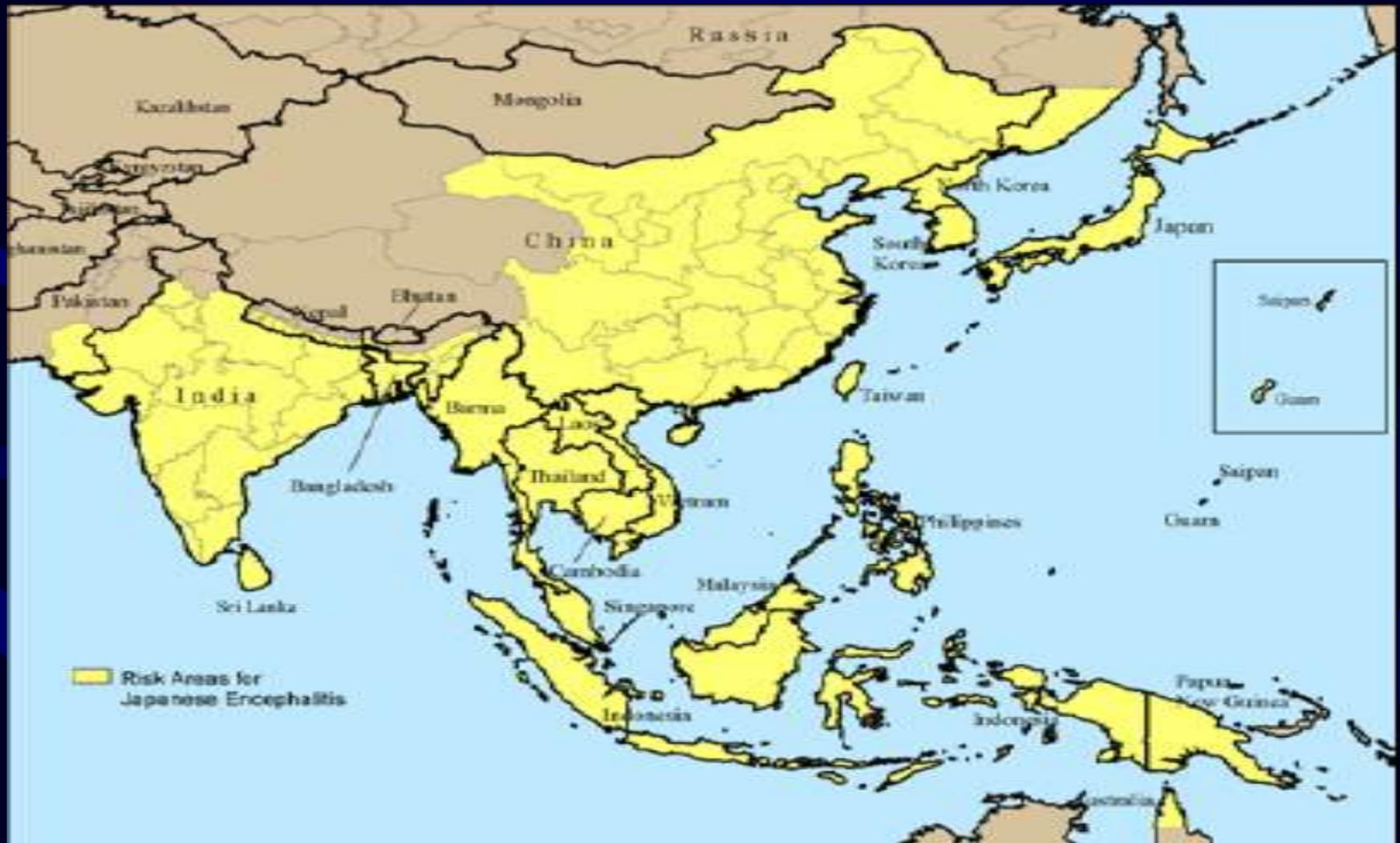
In many cases, the actual reservoir is usually not precisely known. However, The following animals are examples of known reservoirs

Birds	Japanese encephalitis, St Louis encephalitis, EEE, WEE
Pigs	Japanese encephalitis
Monkeys	Yellow Fever
Rodents	VEE

Arboviruses / Japanese encephalitis

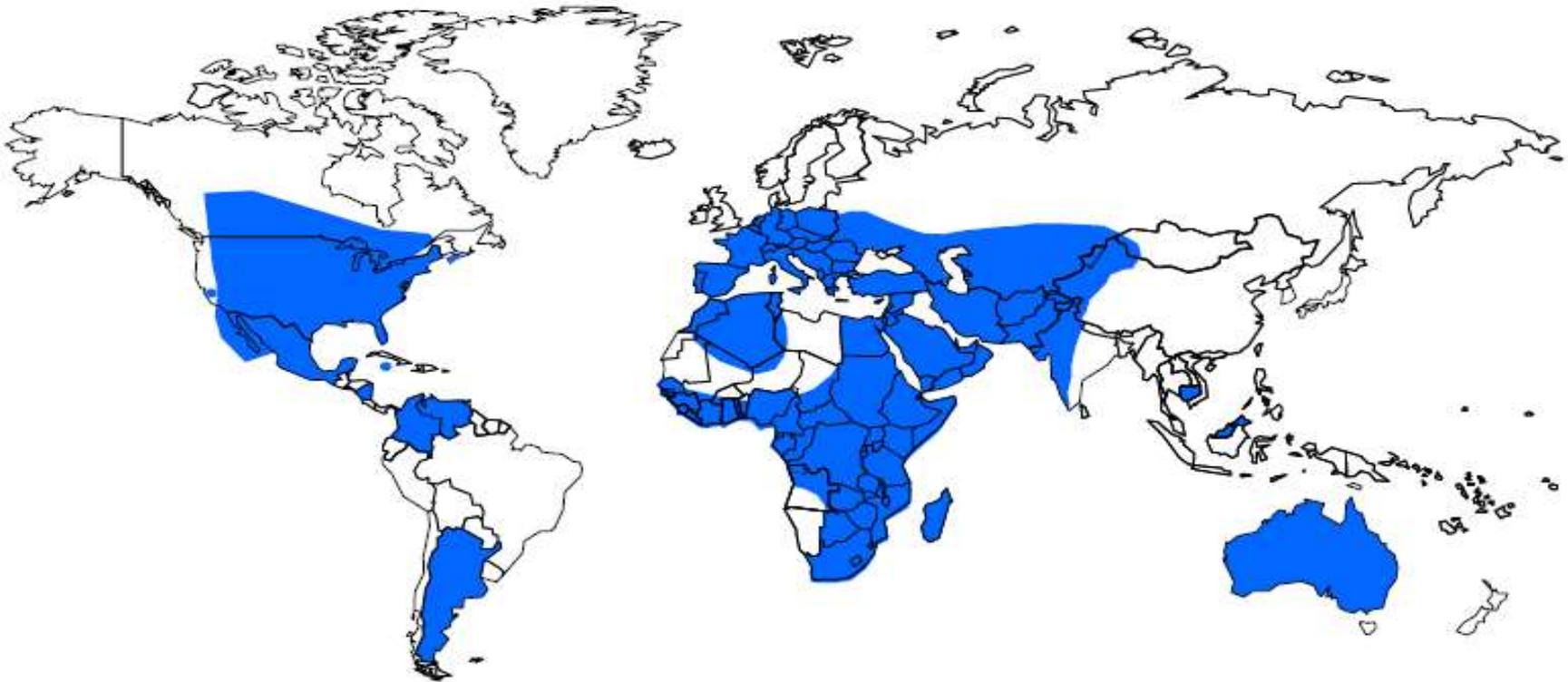
- In clinical cases, a life-threatening encephalitis can occur with complication
- Fatality rate : 30%; flaccid Paralysis (Parkinsonian syndrome) as a complication: 30%
- Vaccine: Yes (live attenuated and killed)

Arboviruses / Japanese encephalitis



Arboviruses / West Nile Virus (WNV)

- Mosquito-borne Flavivirus (*Culex species*), Ticks occasionally
- Human to human: Rarely via blood tx and organ transplants
- Wide geographic distribution



Arboviruses/WNV / Clinically

- Birds are the main host
 - I.P 3-15 days
 - Clinically can be:
 1. **Asymptomatic** (~ 80%)
 2. **WN fever** (~ 20%): resolution in a week.
 3. **Severe neurologic disease** (~ 1%)
 - Meningitis (~ 40% of WNND)
 - Fever, nuchal rigidity, CSF
 - Encephalitis (~ 60% of WN neurological diseases)
 - Alteration of mental status or focal neurologic findings
 - Acute flaccid paralysis
- Overall WN neurological diseases fatality rate ~ 10%

Arboviral Encephalitis

- Diagnosis made based on signs and symptoms and positive test for antibodies against specific arboviruses in the CSF
- Treatment is supportive
- Prevention involves limiting contact with mosquitoes
 - Use netting and insect repellants
 - Reduce mosquito numbers by eliminating stagnant water
- Vaccines for horses available against EEE, WEE, VEE, and WNV

Prions

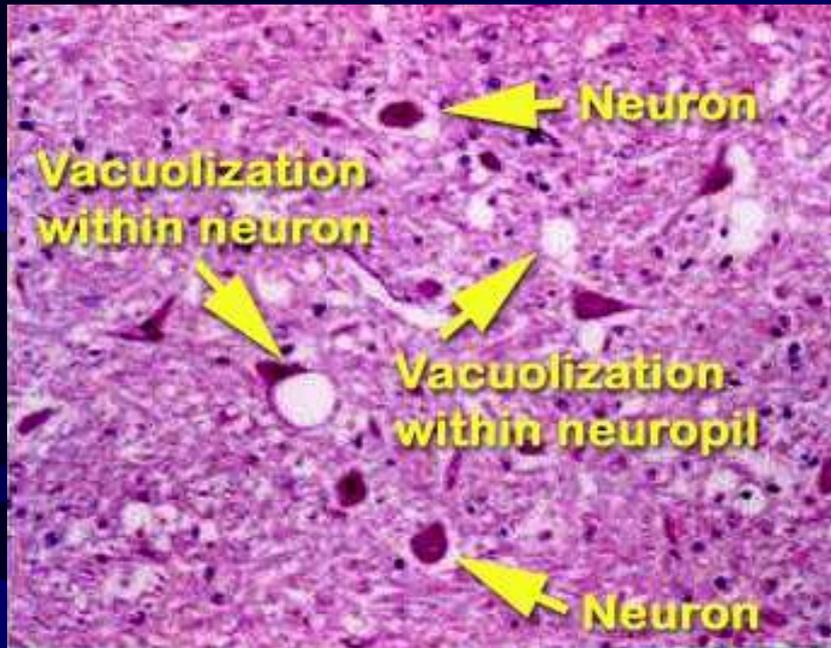
Main properties:

- Occurs in human and animals causing transmissible spongiform encephalopathies
- These proteins has no nucleic acid
- Highly resistant to heat and disinfectants
- Sensitive to hypochlorite, sodium hydroxide and phenols
- No immune response is generated to these proteins
- Caused by a mutant normal human protein $\text{PrP}^c > \text{PrP}^{\text{sc}}$

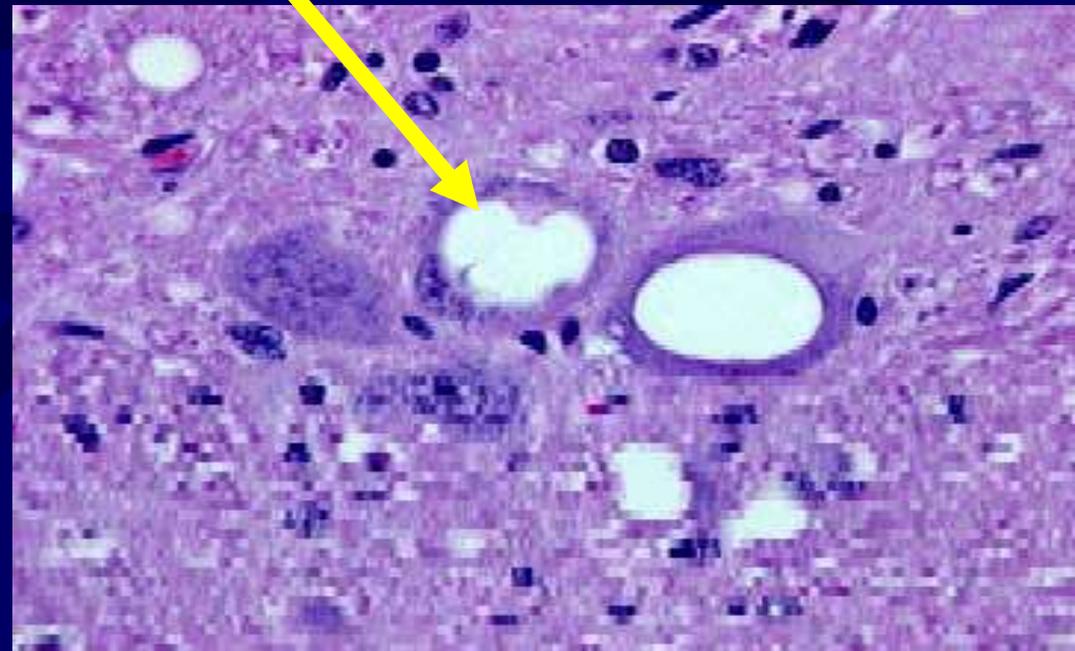
Prions

- First identified with “Spongiform encephalopathies”
- **Characteristics of infection:**
 - Loss of motor control
 - Dementia
 - Paralysis
 - Encephalitis
 - Widespread neuronal loss
- **Ways of infection:**
 - Infectious, Iatrogenic (including diet, after surgical procedures, corneal transplants etc.)
 - Hereditary (autosomal and dominant)

Brain Damage from Spongiform Encephalopathy



vacuole



Transmissible spongiform encephalopathies

- **Animals**
 - Bovine spongiform encephalopathy (BSE)
 - Scrapie in sheep and goats
 - Chronic wasting disease of deer, elk
- **Humans**
 - Kuru
 - Creutzfeldt-Jacob disease (CJD)
 - Fatal familial insomnia (FFI)
 - Gerstmann-Straussler syndrome (GSS)
- **TSEs are always fatal**

Prions

Diagnosis:

- clinically
- EEG
- Post-mortem

Treatment:

No specific treatment