Viral infections of CNS

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OBJECTIVES

- Understand the different acute viral infections of the CNS. (Meningitis, paralysis and encephalitis).
- Differentiate between the clinical presentation and cerebrospinal fluid finding in the viral meningitis (aseptic meningitis) and bacterial meningitis (septic meningitis).
- Understand the common viruses causing aseptic meningitis and encephalitis with regard to classification, structure, epidemiology pathogenesis, infections, clinical presentation, lab diagnosis and prevention.
- understand general information of arboviruses and giving some example of arboviruses causing CNS infection.

Virus neurological diseases:

- ***Acute viral infections of the CNS.***

  Meningitis, paralysis & encephalitis.

- ***Chronic virus neurological diseases.***

  SSPE, PML, C-J disease, tropical spastic paraparesis, HIV dementia.

- ***Neurological diseases precipitated by viral infections.***

  Reye's syndrome, Guillian-Barré syndrome.

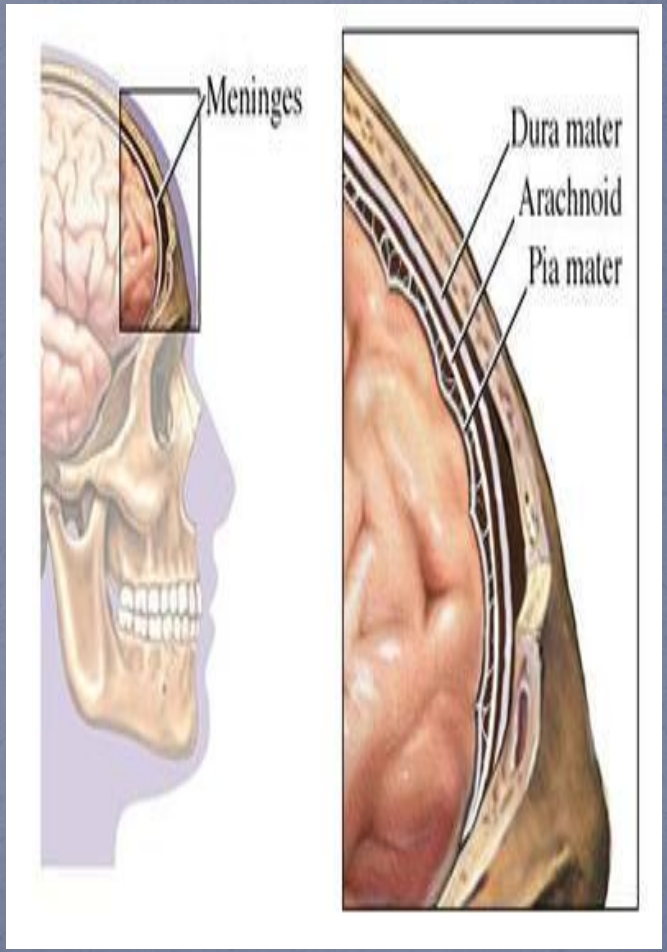
Meningitis

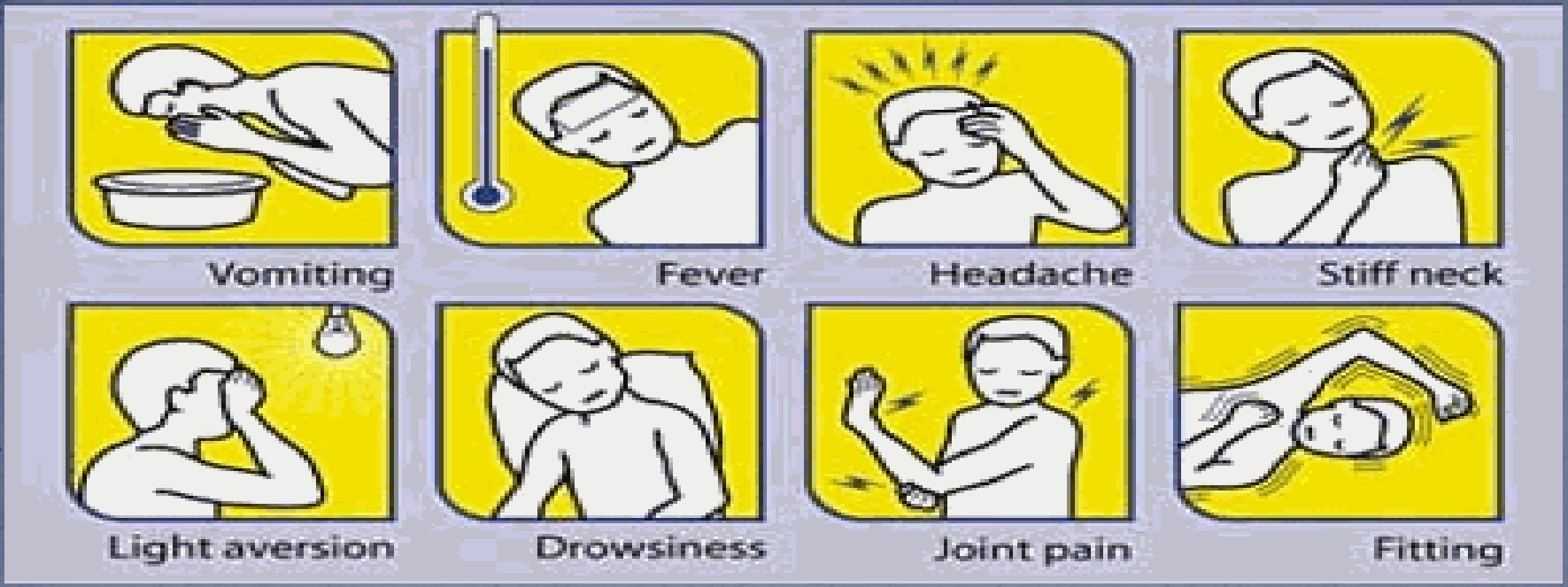
Caused by:

Infectious agents ;

- bacteria
- viruses
- fungi
- protozoa

Non-infectious agents.





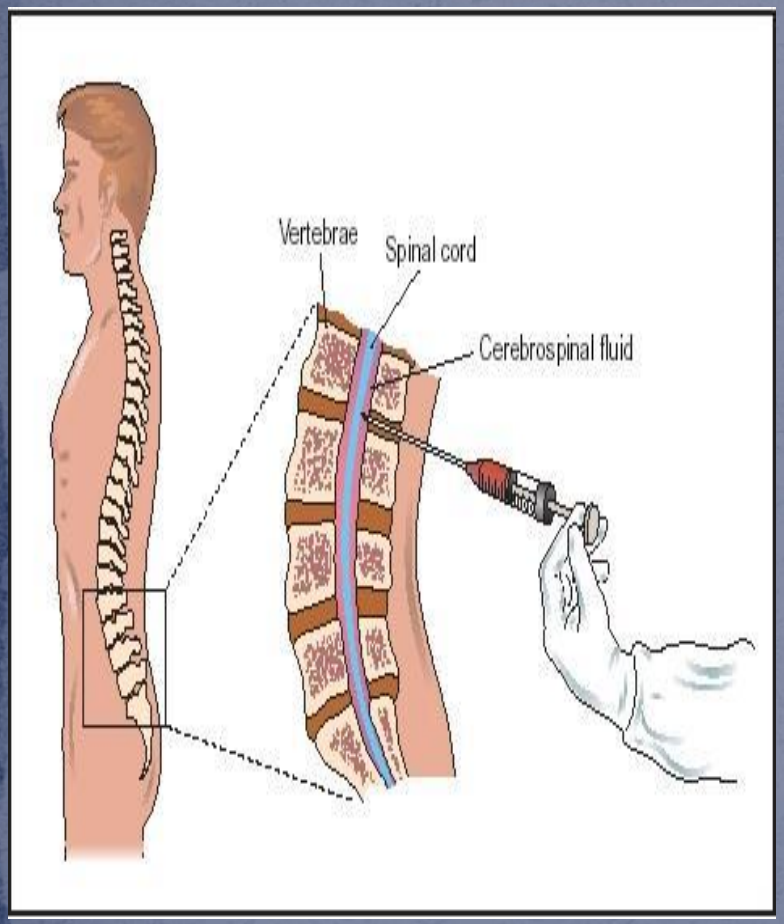
Viral Meningitis

- Aseptic meningitis
- Less severe
- Resolves without specific treatment within a week or two

Bacterial Meningitis

- Septic meningitis
- Quite severe and may result in
  a) brain damage
  b) hearing loss
  c) learning disability
- It would also causes death!

Cerebrospinal fluid (CSF) analysis ;



	Normal	Aseptic meningitis	Septic meningitis
Colour	Clear	Clear	Cloudy
Cells/mm^3	< 5	increase 100-1000 Lymphocytes	High/v. high 200-20,000 Neutrophils
Glucose mg/dl	45-85	Normal*	Low<45
Protein mg/dl	15-45	Normal/high 50-100	High>100
Causes		Viruses* , others	Bacteria

Viral Meningitis (Aseptic meningitis)

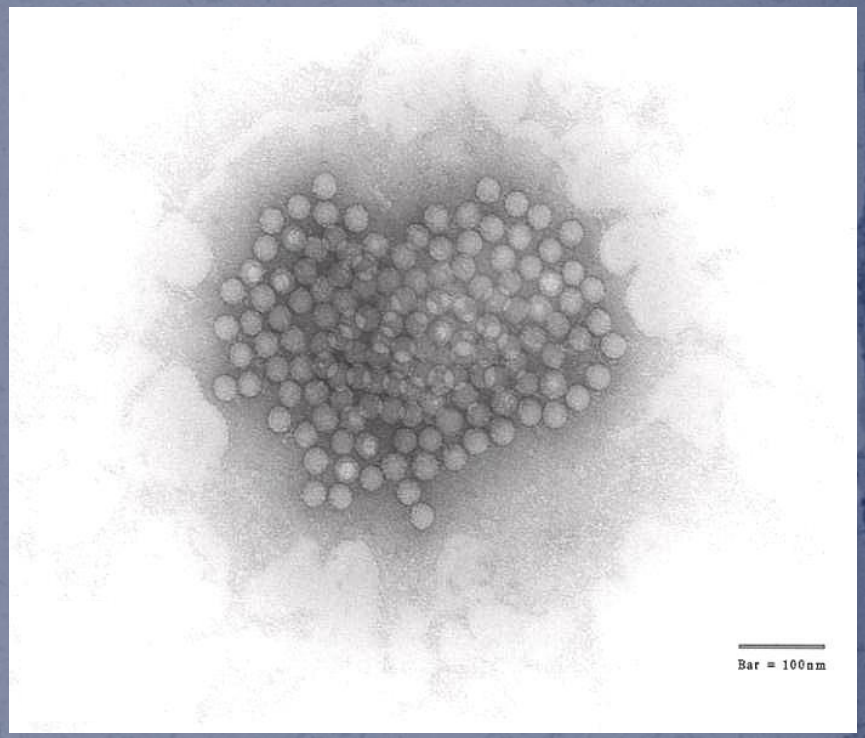
- Etiological Agents:
  - ***Enteroviruses***.**
  - Others:
    - Mumps virus.
    - Arboviruses.
    - Herpes viruses.
    - Human immunodeficiency virus.
    - Lymphocytic choriomeningitis virus.

Enteroviruses

- ***Picornaviridae***

Include;

- Poliovirus (1, 2&3 types)
- Coxsackieviruses (A&B)
- Echoviruses
- Enteroviruses (68-71)



Nonenveloped , icosahedral , ss (+) RNA

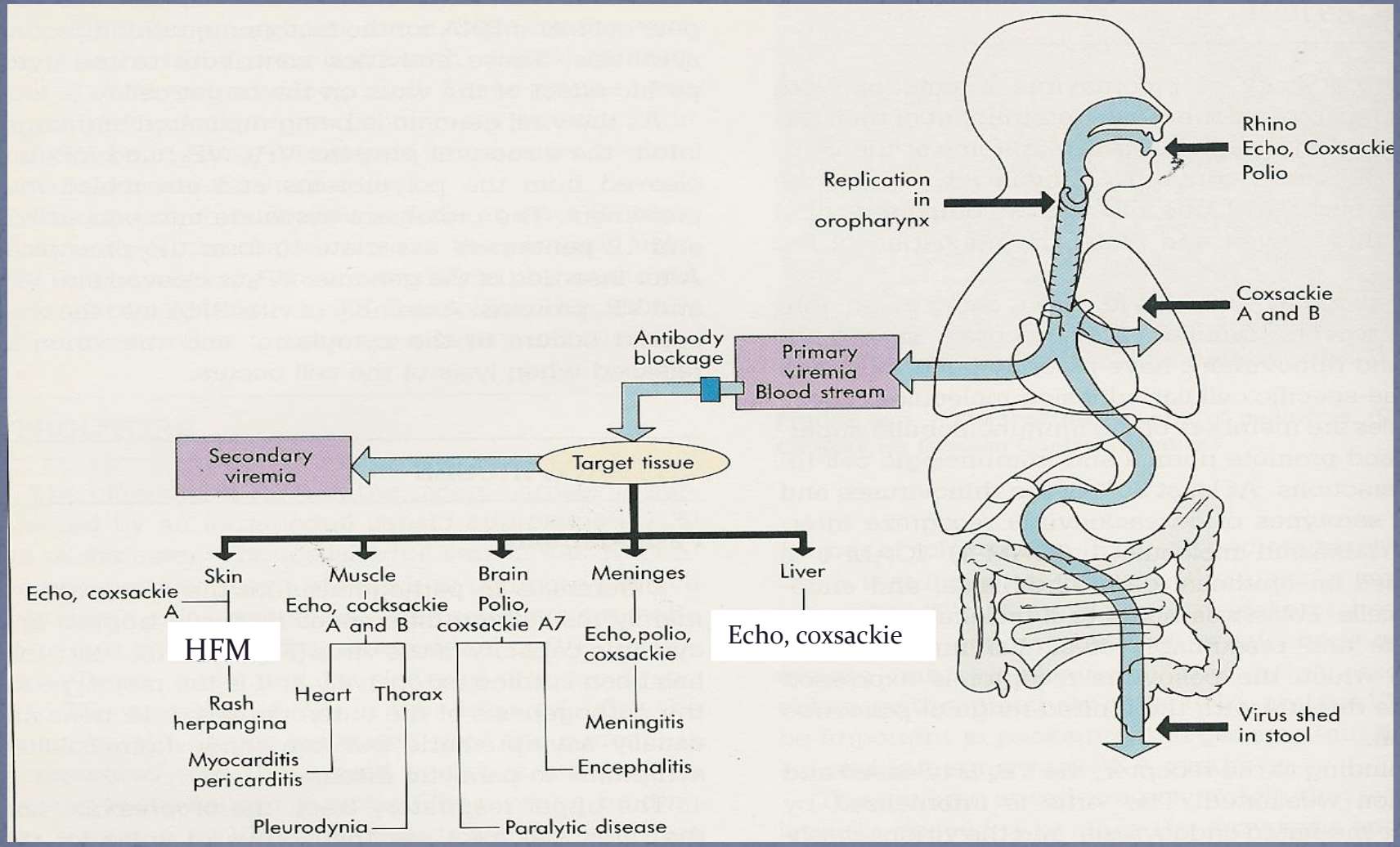
Epidemiology

- Reservoir: humans
- Spread:
  - Fecal - oral route (mainly)
  - Inhalation of infectious aerosols

  (Crowded, Poor hygiene & Sanitation)

- Age: children > adults
- Seasonal distribution: summer & fall

Pathogenesis



Enteroviral infections

- Asymptomatic Infections*
- Diseases;

Neurologic Diseases	Poliovirus Types 1-3	GPA COX. Types 1-24	GPB COX. Types 1-6	Echovirus Types 1-34	Enterovirus Types 68-71
Aseptic meningitis	1-3	Many	1-6	Many	71
Paralysis	1-3	7,9	2-5	2,4,6,9,11,30	70,71
Encephalitis		2,5-7,9	1-5	2,6,9,19	70,71

2-Cardiac and muscular;

Pleurodynia (epidemic myalgia)

Myocarditis, pericarditis

3- Skin and mucosa infections;

Herpangina

Hand-foot-and-mouth disease

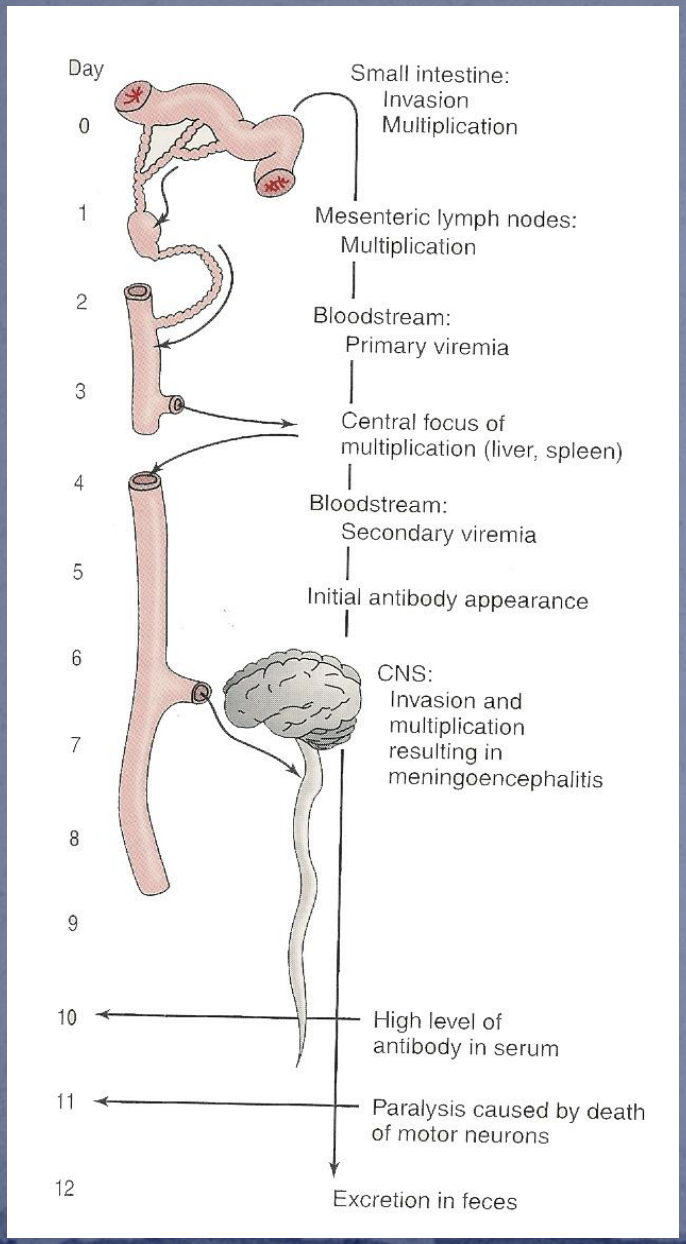
Exanthems

3-Acute hemorrhagic conjunctivitis

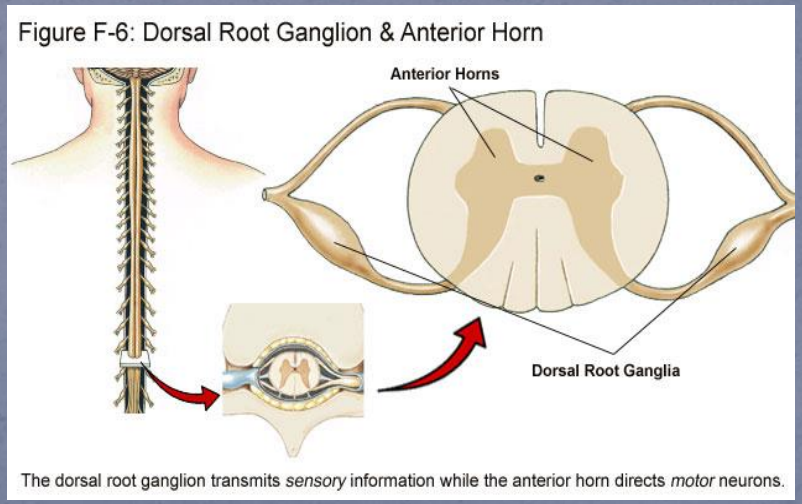
4-Respiratory tract infections.

5-Others

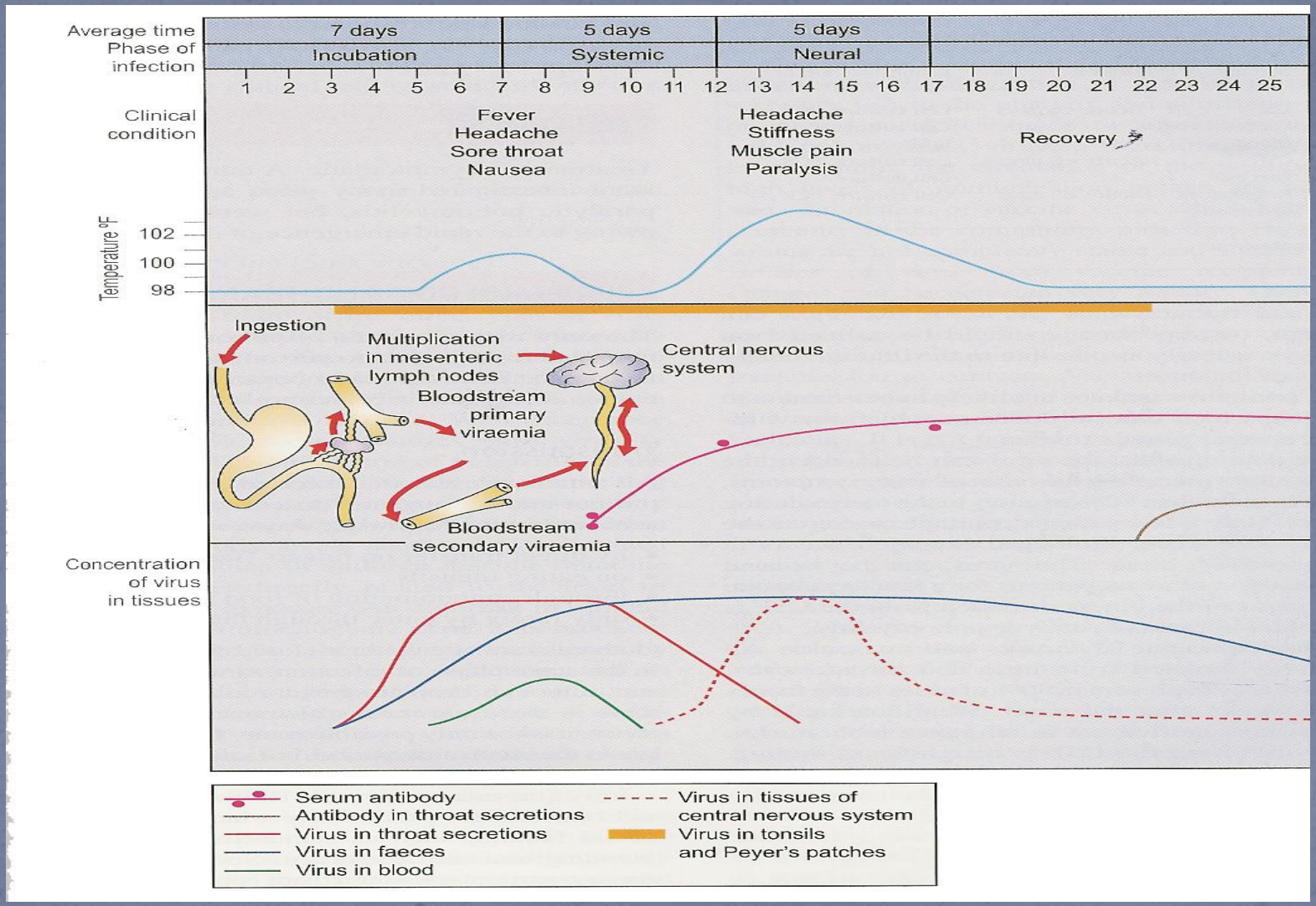
Pathogenesis of polio:



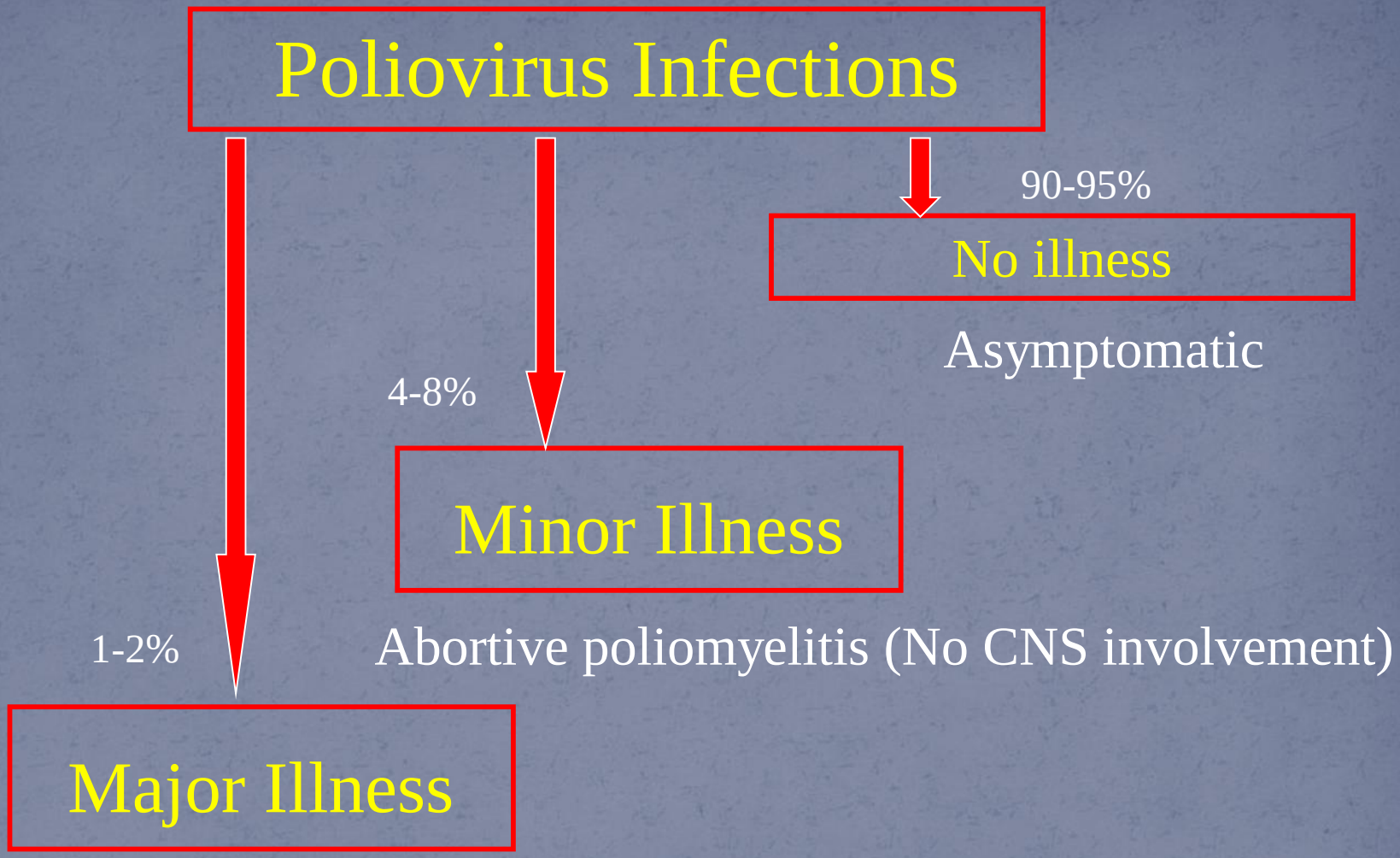
- Pathway to CNS by:
  - Blood
  - Peripheral nerves
- Causing destruction of motor neurons
- Rarely affects brain stem (bulbar poliomyelitis)



Pathogenesis of Polio:



Immunity: IgA & IgG = Lifelong type-specific immunity



1- Nonparalytic poliomyelitis (Aseptic meningitis)

2- Paralytic poliomyelitis: (Flaccid paralysis)

Lab Diagnosis of Enteroviruses

- **Virus isolation*:**
  - Samples: Stool (best), rectal, throat swabs & CSF
  - Inoculate in MKC & HDF

  All EVs grown except some strains of Cox A viruses
  - Observe for CPE
  - Identify the type by Neutralization Test
- CSF in aseptic meningitis; lymphocytosis

  Glucose level N to slightly ↓ , Protein level N or slightly ↑

  Isolation rate is variable

  *EV RNA detected in CSF by RT-PCR**
- **Serology** (limited value)

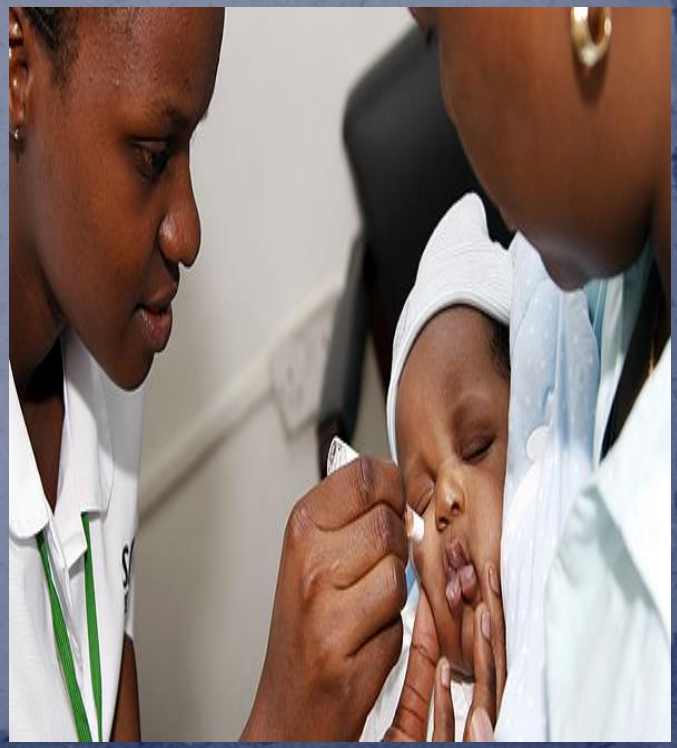
Management

- Treatment:
  - No antiviral therapy

- Prevention:
  - Sanitation & Hygienic measures
  - Poliovirus vaccines

  a- Inactivated polio vaccine (IPV) for adults. (Salk, Killed) (S/C or IM)

  b- Live-attenuated polio vaccine (OPV) for children. (Sabin, oral)



Important Features of Polio Vaccines

Attribute	Killed (IPV)	Live (OPV)
3 types (trivalent)	Yes	Yes
Prevents disease	Yes	Yes
Induces humoral IgG	Yes	Yes
Route of administration	Injection	Oral
Induces intestinal IgA	No	Yes
Affords 2^{o} protection by spread to others	No	Yes
Reverts to virulance	No	Yes (rarely)
Causes disease in the low immune	No	Yes
Duration of immunity	Shorter	Longer

Poliovirus Vaccine

- Adverse reactions;
  - local reactions (IPV)
  - Vaccine-Associated Paralytic Poliomyelitis (OPV)
    adult, low immune
- 4 doses of PV; 2, 4 , 6-18 ms & 4 - 6 yrs
- Pediarix contains IPV, DTaP & HB vaccines.

Polio Vaccination of Adults

- Indications:
  - Travelers to polio-endemic countries
  - Health care workers
- IPV

1988

- 350,000 cases
- 125 endemic countries
- World Health Assembly voted to eradicate polio

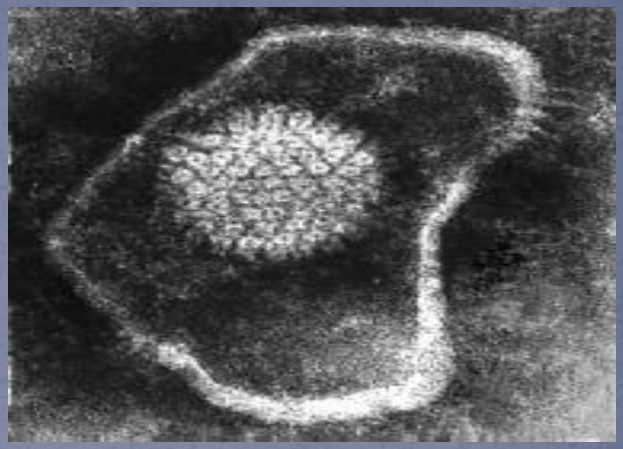
2016

- 34 cases reported*
- 3 endemic countries

Viral Encephalitis

- Etiological Agents:
  - Enteroviruses
  - Herpes viruses.
  - Rabies virus
  - Arboviruses.
  - Others

HSV encephalitis



- Caused by:
  - Herpes simplex virus -1(HSV-1)

  dsDNA , Enveloped , Icosahedral Virus

- C/F:
  - Fever, headache, vomiting, seizures & altered mental status.
  - High mortality rate
- Diagnosis:
  - Magnetic resonance imaging (MRI)

  (temporal lesion)

  - CSF---Lymph, glucose-N & Protein- ⬆
    ---detection of HSV-1 DNA by PCR.
- Treatment:

  Acyclovir.

Rabies encephalitis

Bullet shaped virus

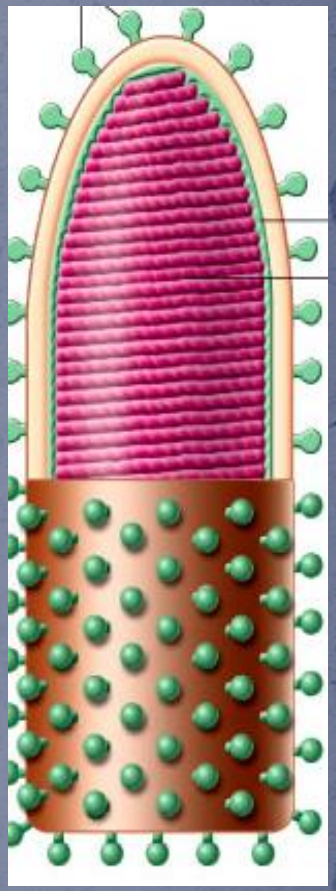
Rabies virus;

Rhabdoviridae.

ss (-)RNA genome,

Helical nucleocapsid,

Enveloped virus.



Epidemiology;

Reservoir;

- Major;
  Raccoons, Foxes, Wolves & Bats.
- Imp; cats & dogs

Transmission;

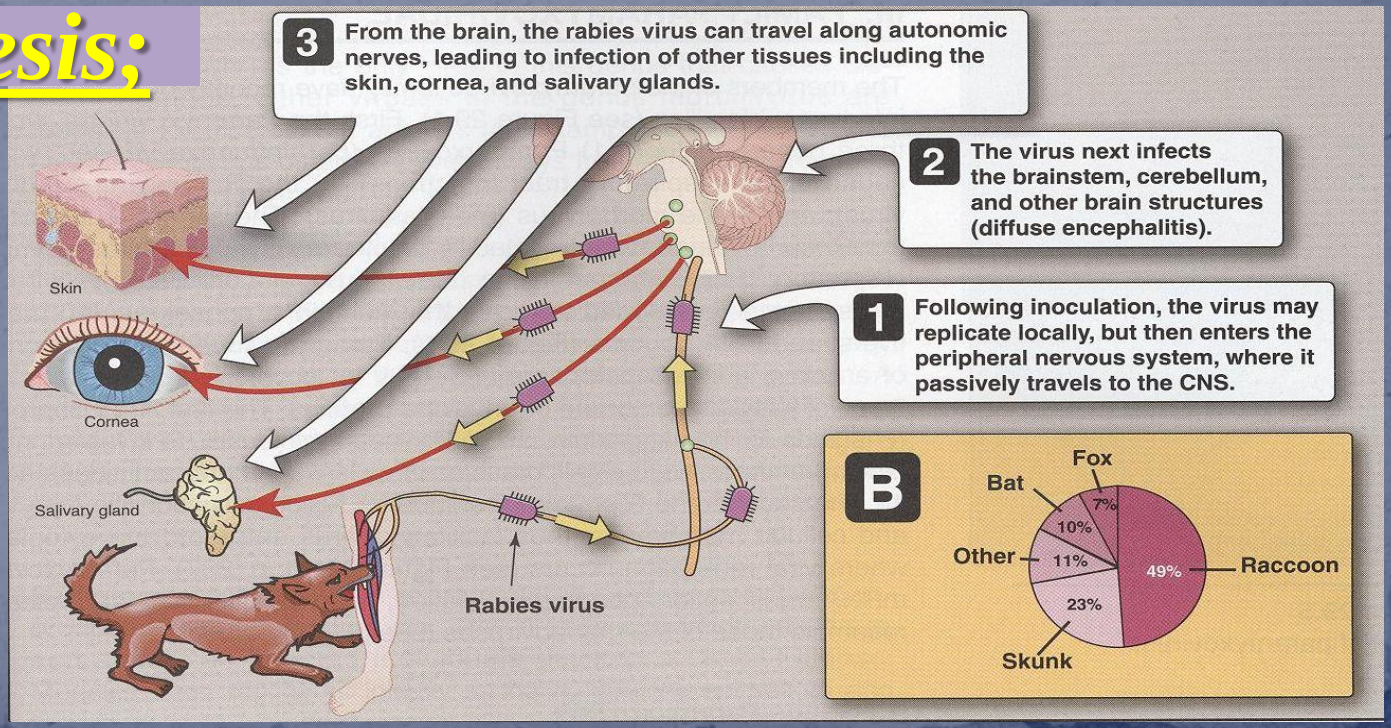
❖Common route

- Bite of a rabid animal

❖Uncommon route

- Inhalation while in a bat-infested cave
- Corneal transplant

Pathogenesis;



Rabies; A fatal acute encephalitis

- zoonotic disease .
- 4 phase :

1-The incubation period: 1-3 m

2-The prodromal phase:

Fever, Headache, Malaise, Anorexia, Nausea & Vomiting.
Abnormal sensation around the wound.

3-Neurological phase ;

1- Encephalitis

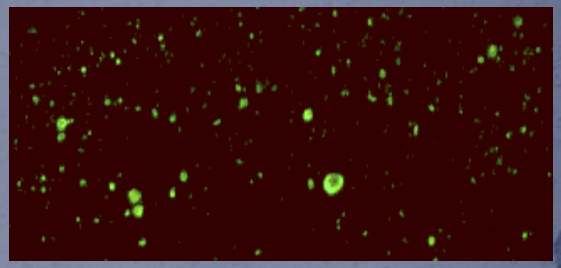
Nervous , lacrimation , salivation,
hydrophobia, convulsion , coma & death.

2-Paralytic illness; Ascending , Death, associated with Bat bite.

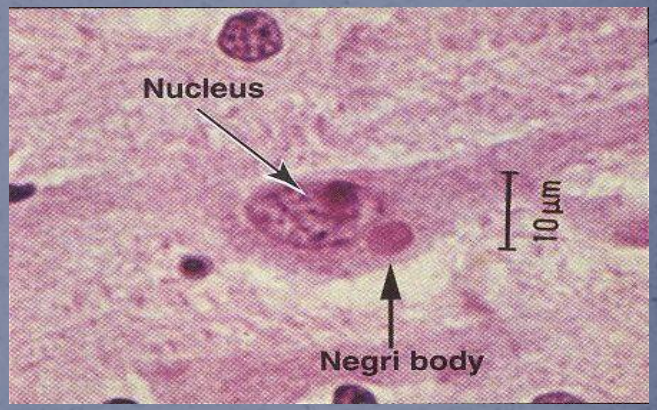
4- Recovery; Extremely rare

Laboratory Diagnosis

- PCR; R. RNA in saliva
- Rapid virus antigen detection (IF)
  Neck skin biopsy
  Corneal impressions
  Brain tissue
- Histopathology
  neuronal brain cells
  intracytoplasmic inclusions
  (Negri bodies)
- Virus cultivation



Rabid brain stained with
Fluorescent anti-rabies antibody



Negri bodies are diagnostic of rabies.

Prevention

❖***Control measures*** against canine rabies include;

- Stray animals control.
- Vaccination of domestic animals.

- ***Pre-exposure prophylaxis*** (Vaccine)

  Persons at increased risk of rabies

  e.g. vets, animal handlers etc.

- ***Post-exposure prophylaxis***
  - Wound treatment
  - Passive immunization;

    human anti-rabies immunoglobulin applied around the wound & IM.
  - Active immunization;

    Human Diploid Cell Vaccine (HDCV)**

    5 - 6 doses

Arthropod –borne Viruses

Arboviruses > 500 Vs

Epidemiology:

Reservoir: Wild birds & Mammals

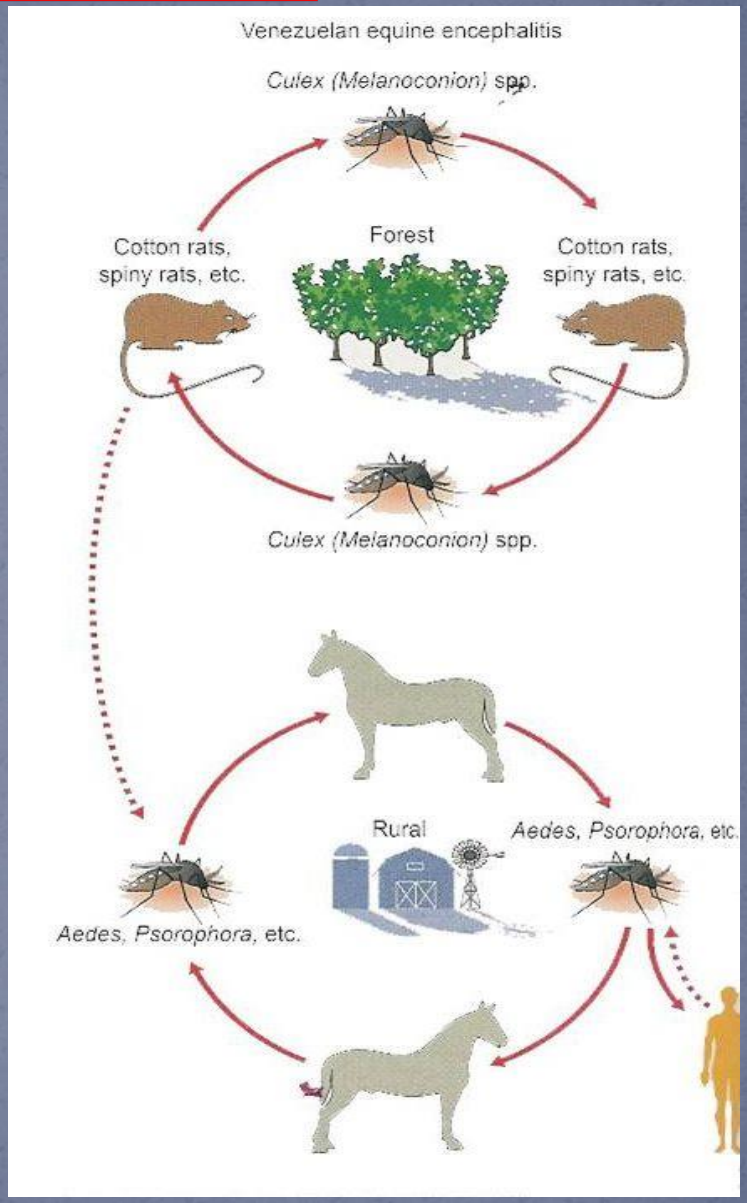
Vector: Mosquito, Tick & Sandfly

Transmission: bite of infected vector

Infections

- Asymptomatic Infections*
- Diseases

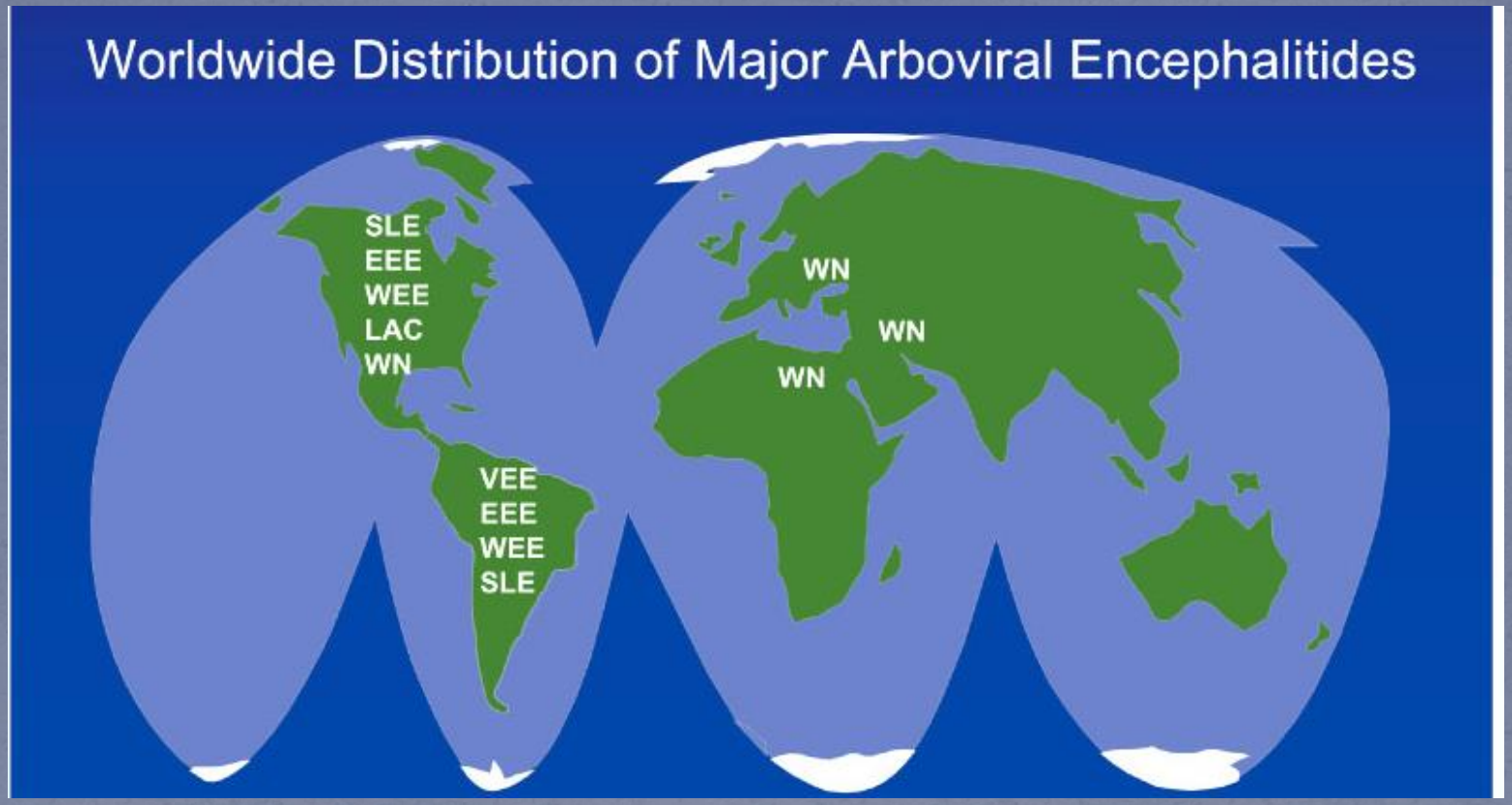
1) Fever, Rash & Arthralgia
2) Hemorrhagic fever ± hepatitis
3) CNS disease (meningitis & encephalitis)



*ArboVs associated with CNS disease:

Virus	Vector	Reservoir	Distribution
Eastern equine encephalitis EEEV	Mosquito	Birds	America
Western equine encephalitis WEEV	Mosquito	Birds	America
Venezuelan equine encephalitis VEEV	Mosquito	Rodent	America
Japanese encephalitis V	Mosquito	Birds, Pigs	Orient
Murray Valley encephalitis V	Mosquito	Birds	Australia
West Nile V	Mosquito	Birds	Europe, Africa Middle East Asia, America

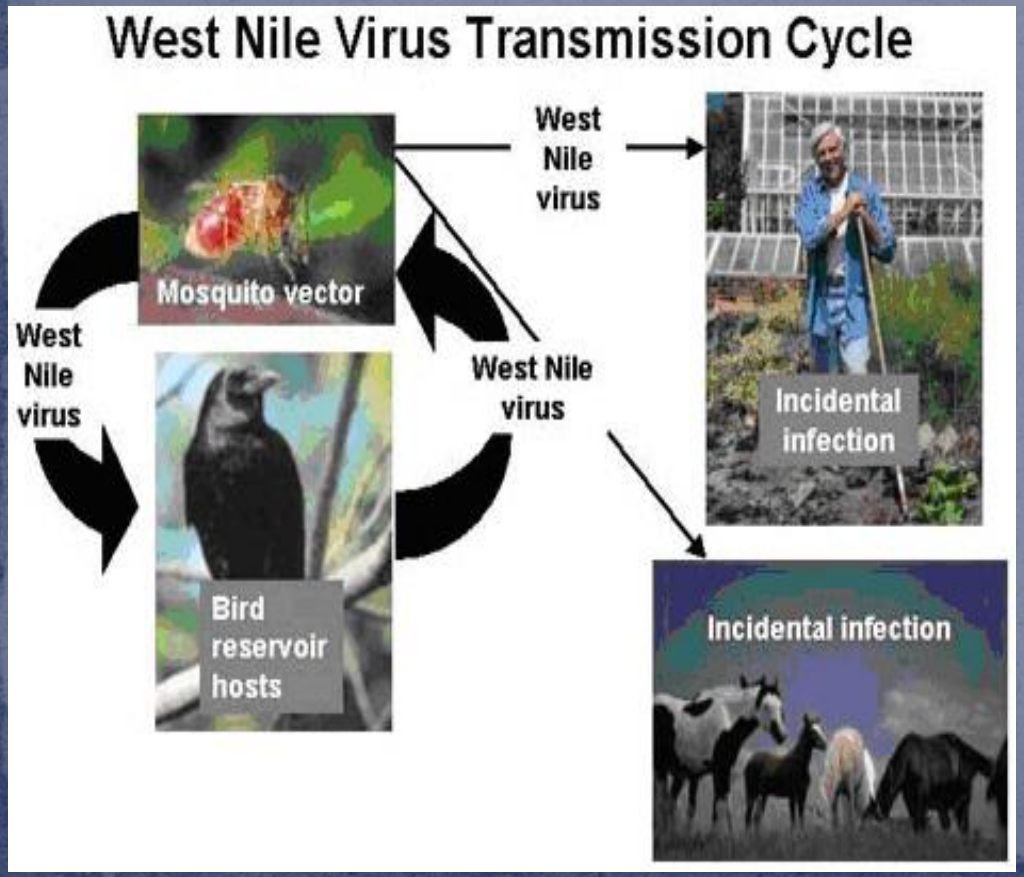
Arboviral encephalitis is prevalent worldwide

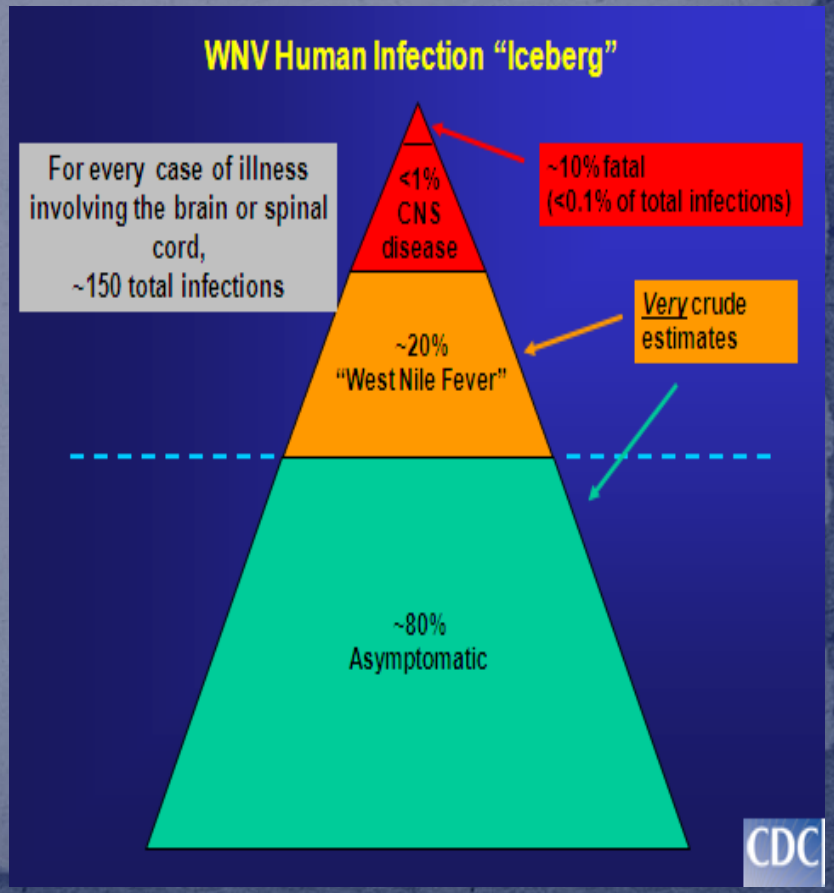


EEE: Eastern equine encephalitis
LAC: LaCrosse encephalitis
SLE: St. Louis encephalitis
WEE: Western equine encephalitis
WN: West Nile encephalitis
VEE: Venezuelan equine encephalitis

West Nile virus

- Flaviviridae (enveloped +ssRNA)
- Febrile illness → ***meningitis***, encephalitis.





Diagnosis:

- Reference Lab
- Lab Methods:

A. Isolation (Gold standard)

Samples: blood, CSF, Viscera.

Cell culture → CPE

→ Identify by IF

B - IgM -AB* - ELISA, IF: (most used)

C - Arbovirus RNA by RT-PCR.

Prevention

1. ***Vector Control:***
   - Elimination of vector breading sites
   - using insecticides
   - Avoidance contact with vectors (repellants, net)
2. ***Vaccines:***

Tick-borne encephalitis vaccine

Japanese encephalitis vaccine

Reference books

&the relevant page numbers

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