Viral infections of CNS

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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.

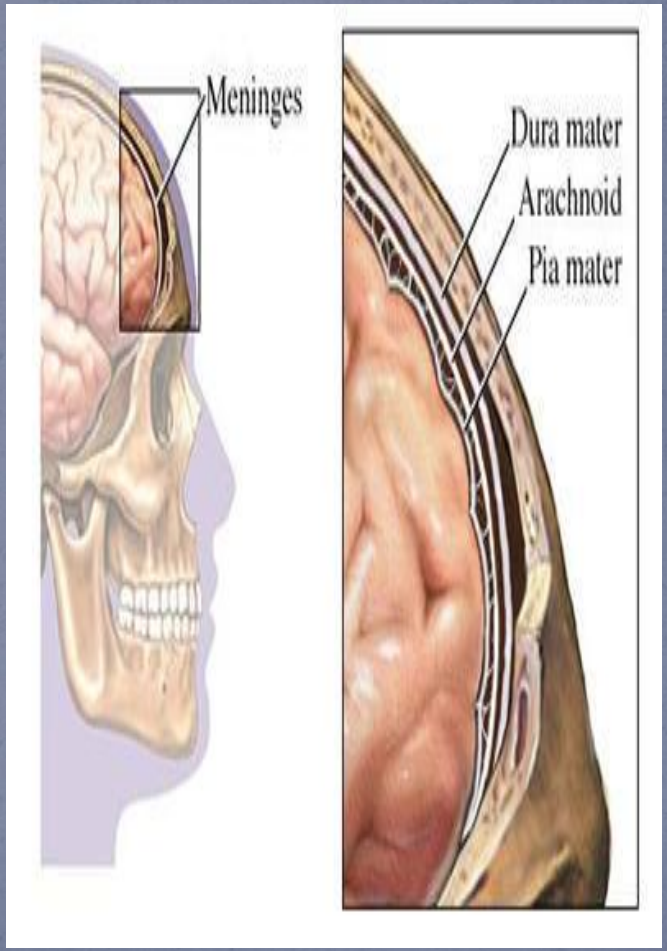
Meningitis

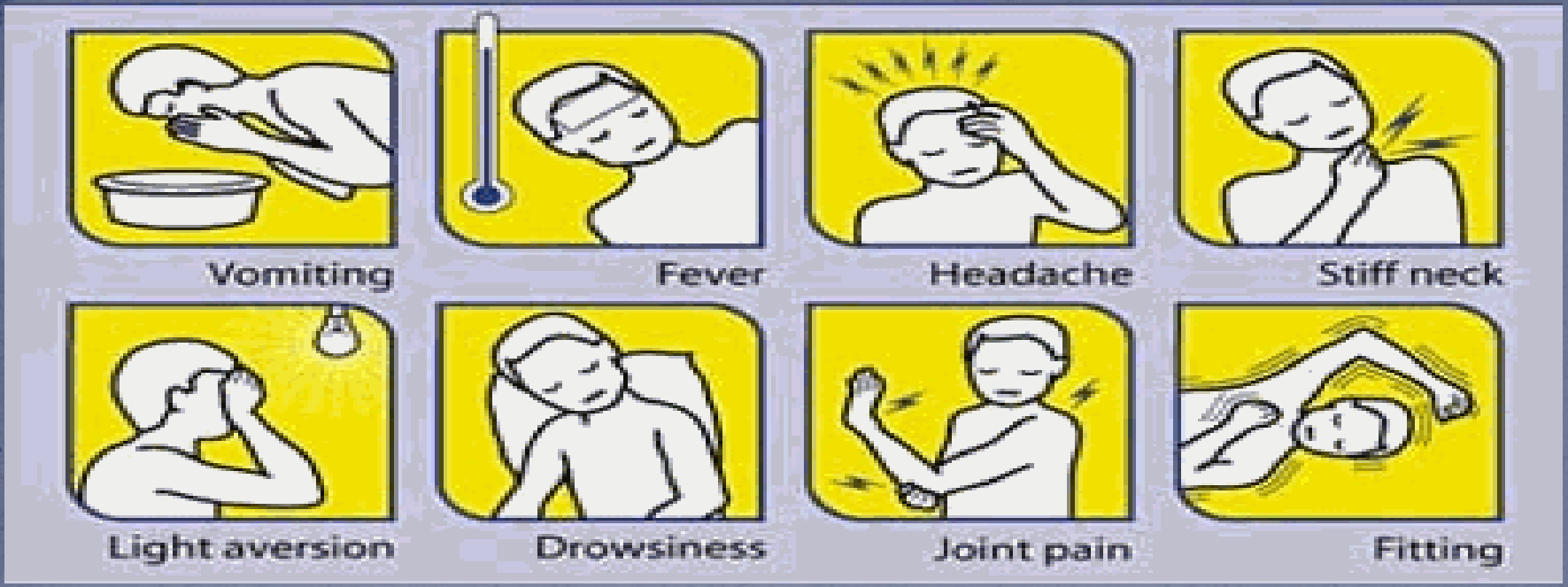
Caused by:

Infectious agents ;

- bacteria
- viruses
- fungi
- protozoa

Non-infectious agents.





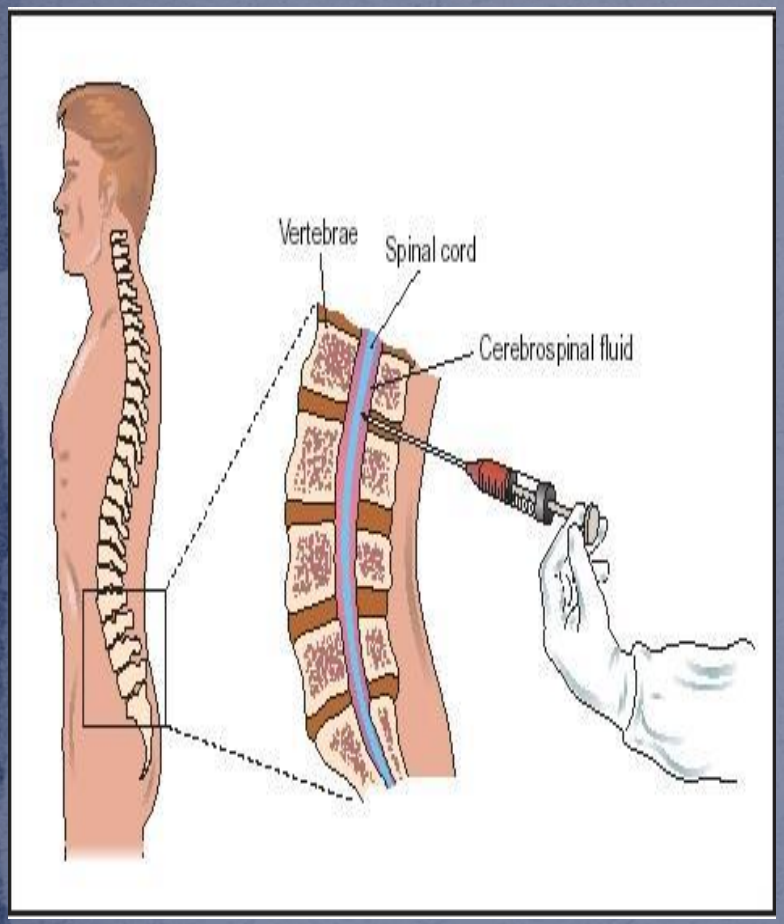
Viral Meningitis

- 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 cause 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)

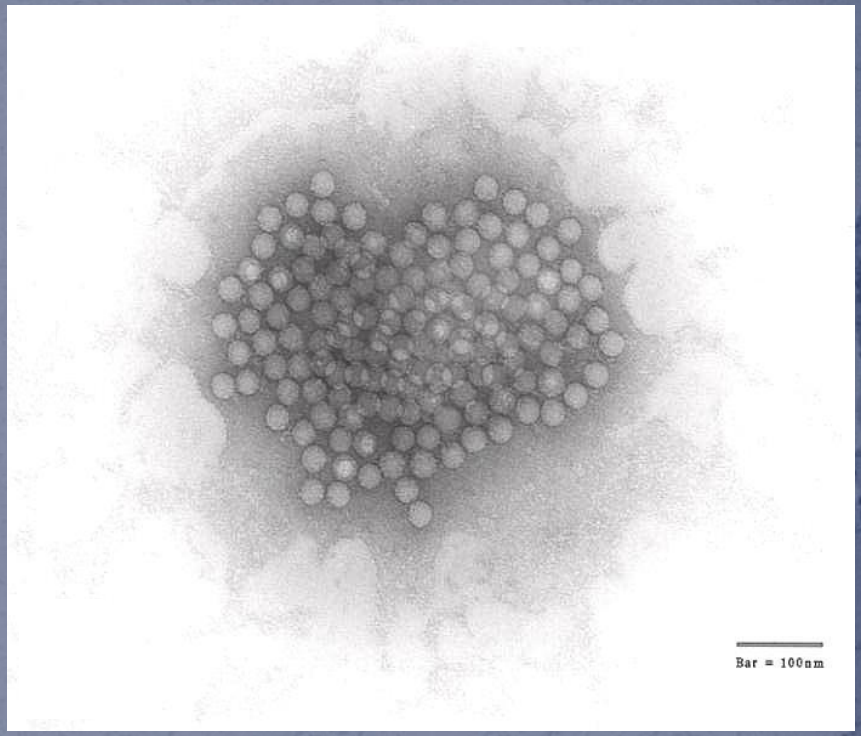
- Etiological Agents:
  - ***Enteroviruses***.**
  - Others:
    - Arboviruses.
    - Herpes viruses.
    - Mumps virus.
    - Human immunodeficiency virus.
    - Lymphocytic choriomeningitis virus.

Enteroviruses

- ***Picornaviridae***

Include;

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



Nonenveloped , icosahedral , ss (+) RNA

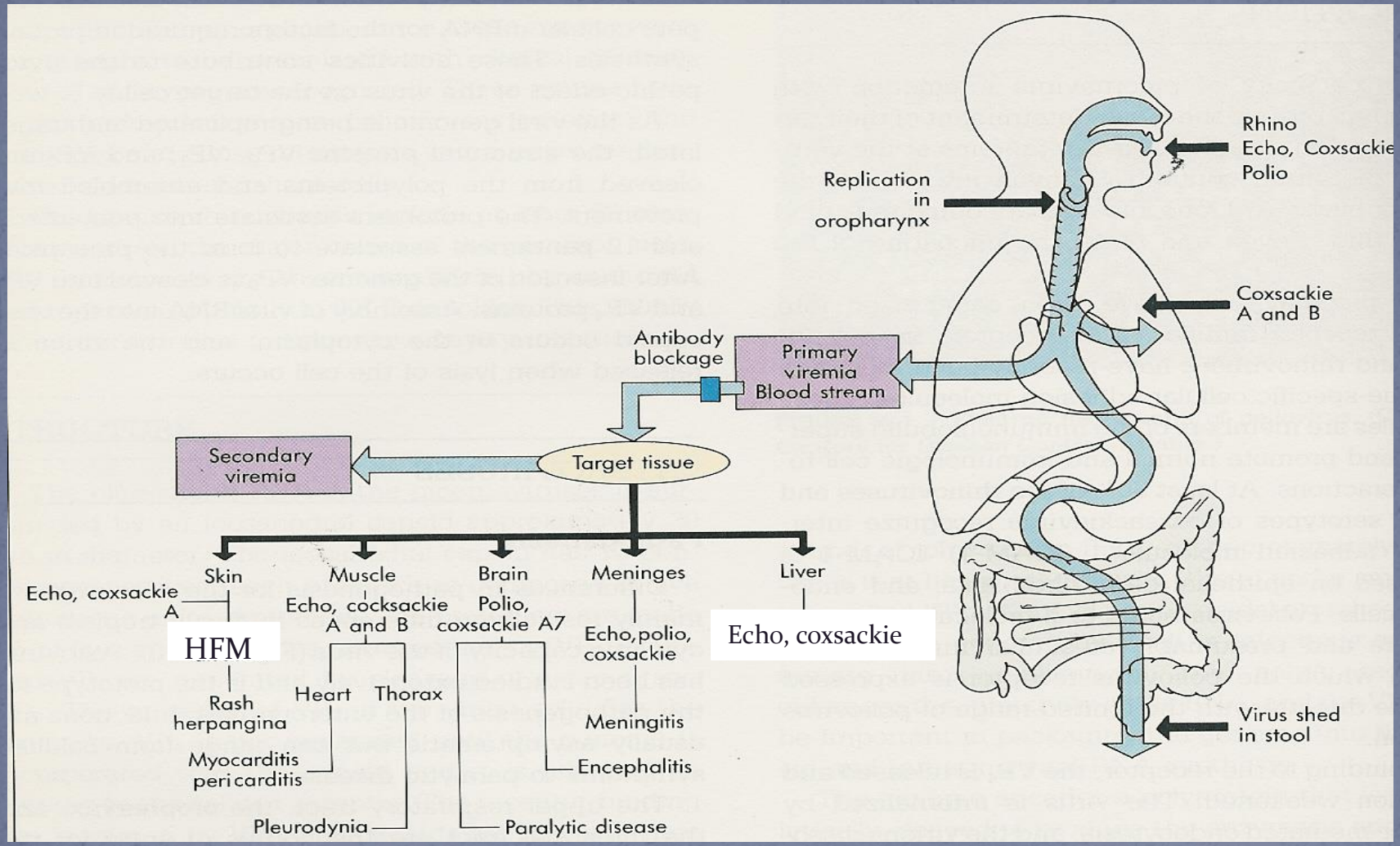
Epidemiology

- 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

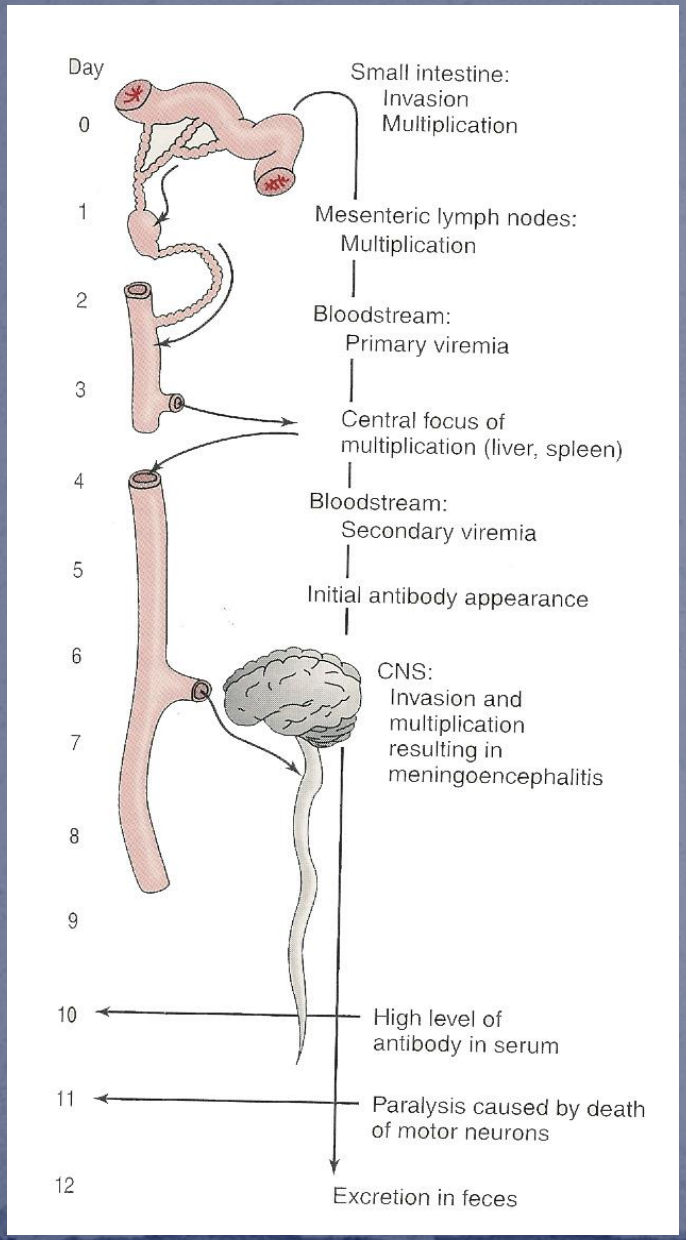
Exanthems

3-Acute hemorrhagic conjunctivitis

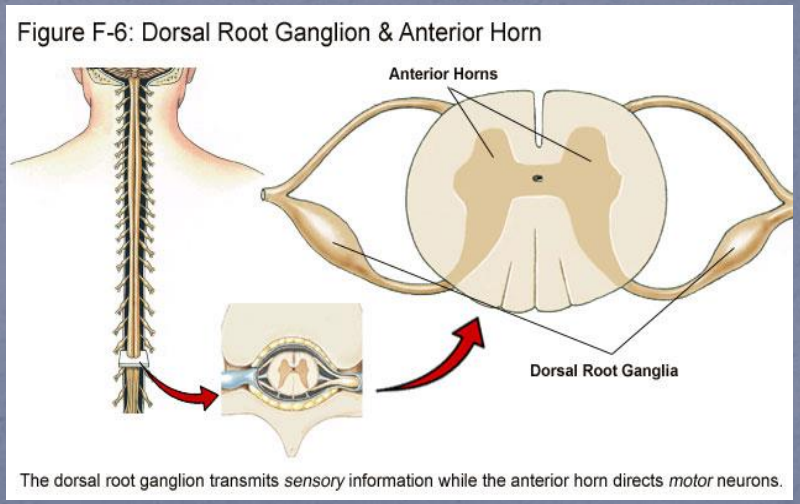
4-Respiratory tract infections.

5-Others

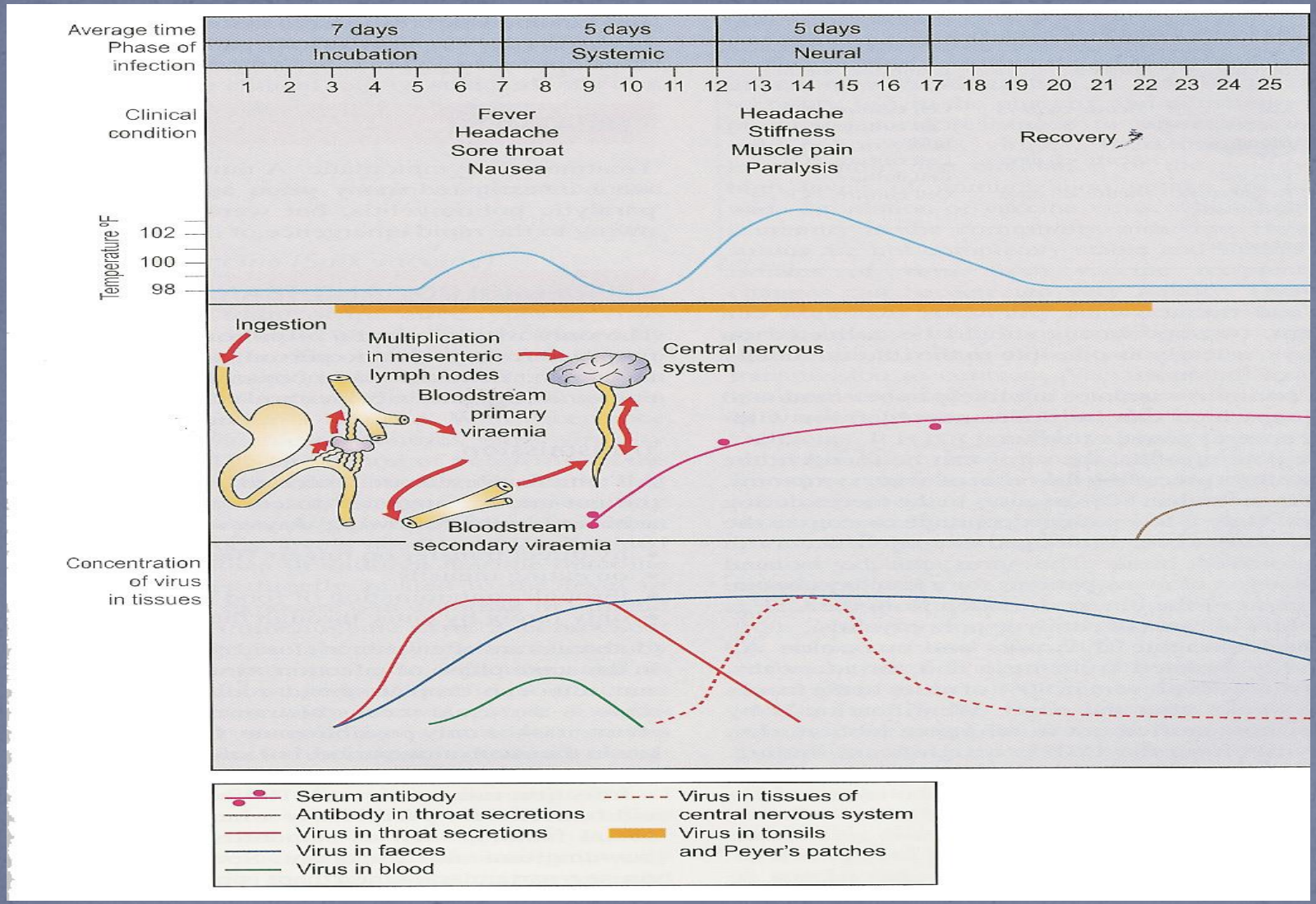
Pathogenesis of polio:



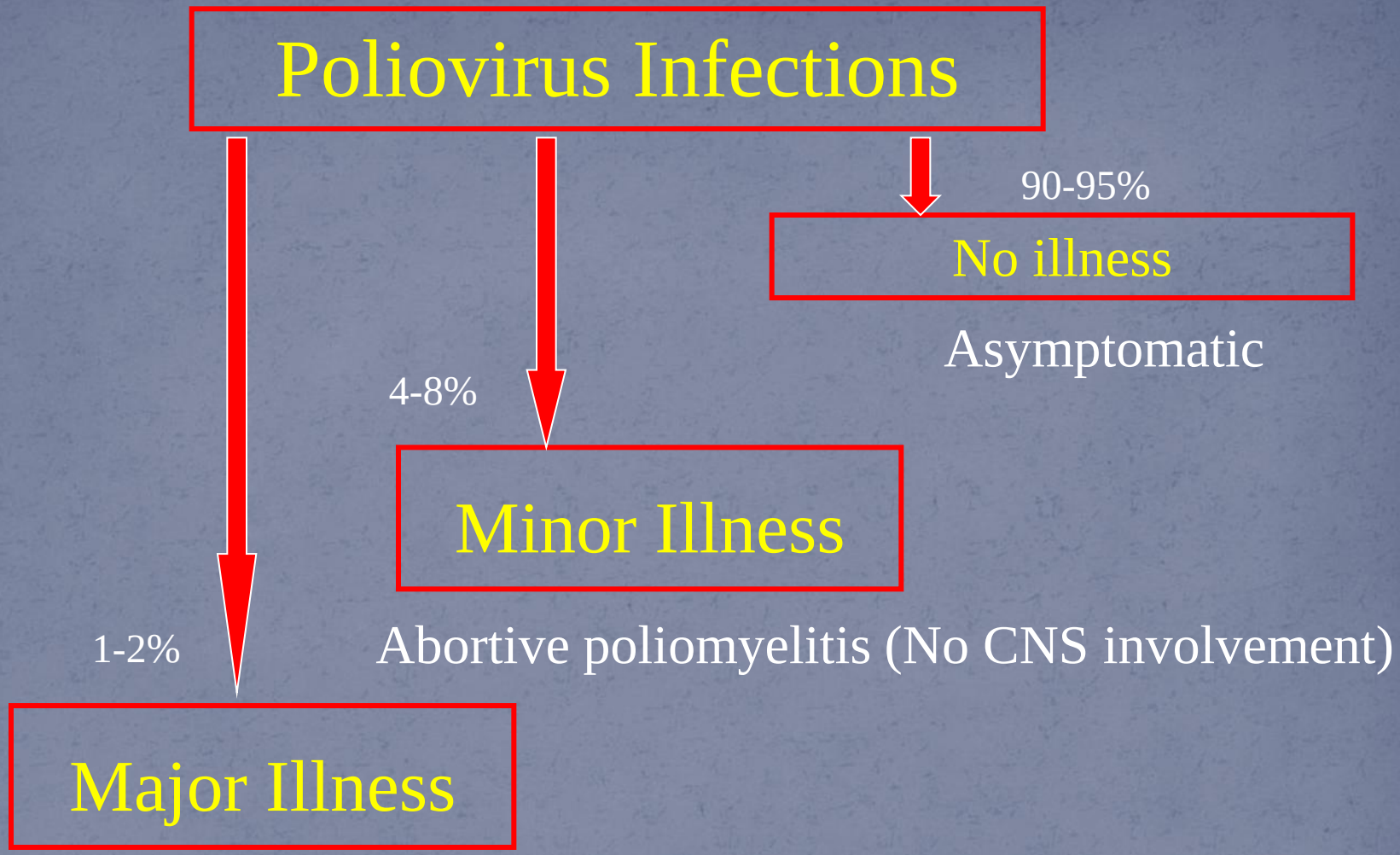
- Pathway to CNS by:
  - Blood
  - Peripheral nerves
- Causing destruction of motor neurons
- Rarely affects brain stem (bulbar poliomyelitis)



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 immuned	No	Yes
Requires refrigeration	No	Yes
Duration of immunity	Shorter	Longer

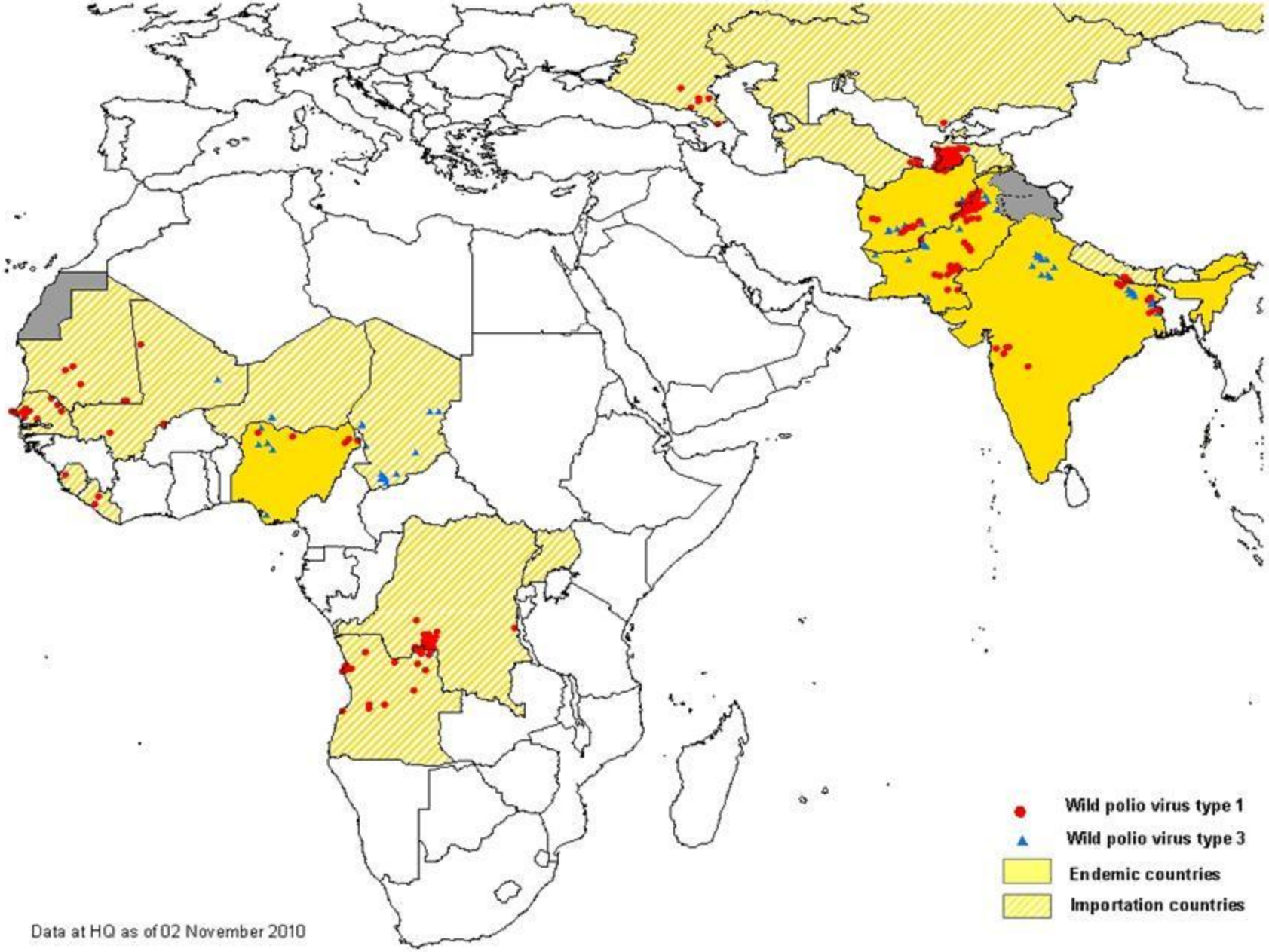
Poliovirus Vaccine

- Adverse reactions;
  - local reactions (IPV)
  - Vaccine -Associated Paralytic Poliomyelitis (OPV)
    adult, low immuned
- 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

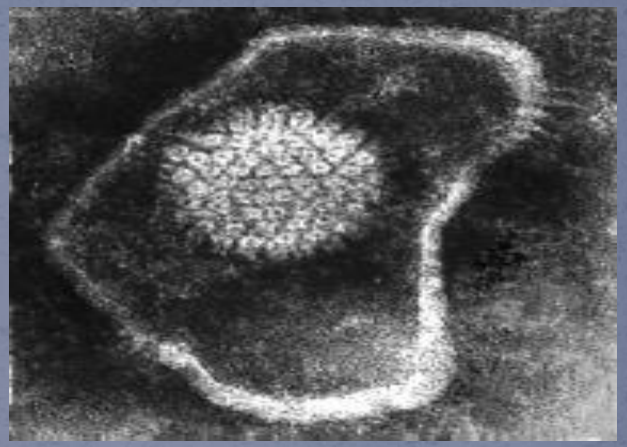
Wild Poliovirus*, 2010



Viral Encephalitis

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

HSV encephalitis



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

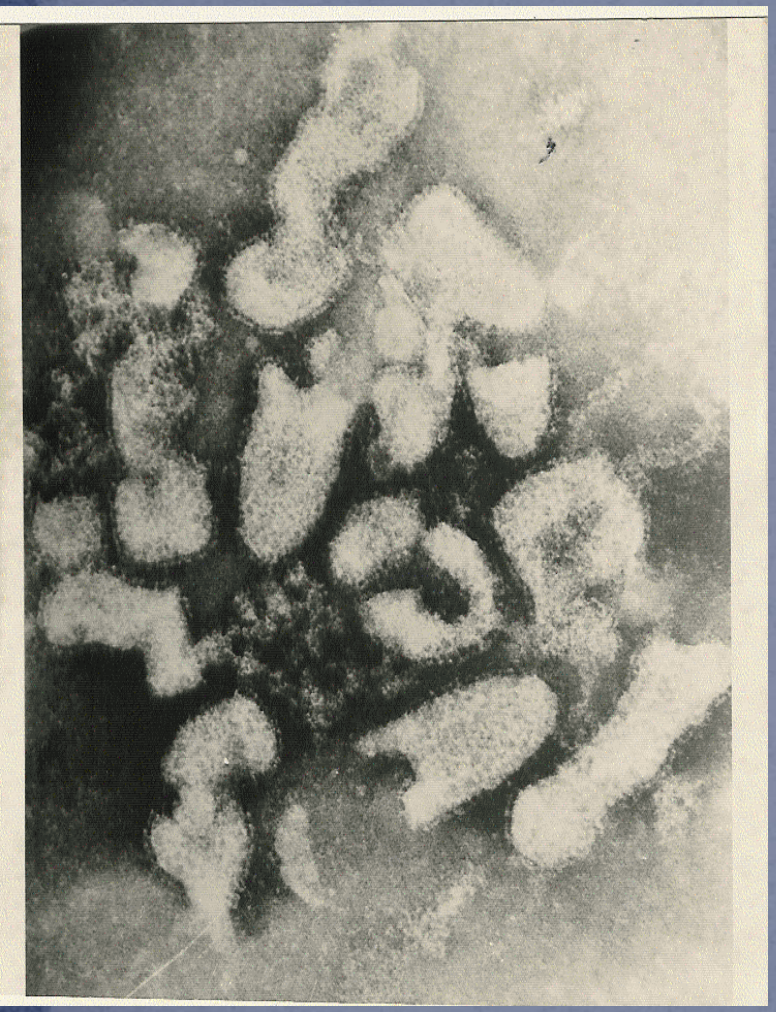
  dsDNA , Enveloped , Icosahedral Virus

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

    ---detection of HSV-1 DNA by PCR.
- Treatment:

  Acyclovir.

Rabies encephalitis



Bullet shaped virus

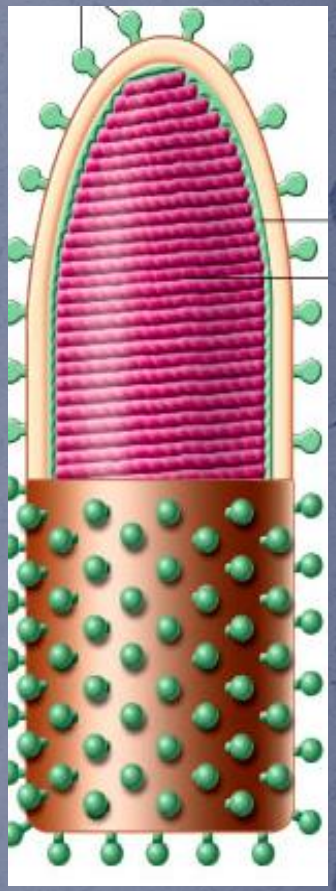
Rabies virus;

Rhabdoviridae.

ss (-)RNA genome,

Helical nucleocapsid,

Enveloped virus.



Epidemiology;

Reservoir;

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

Transmission;

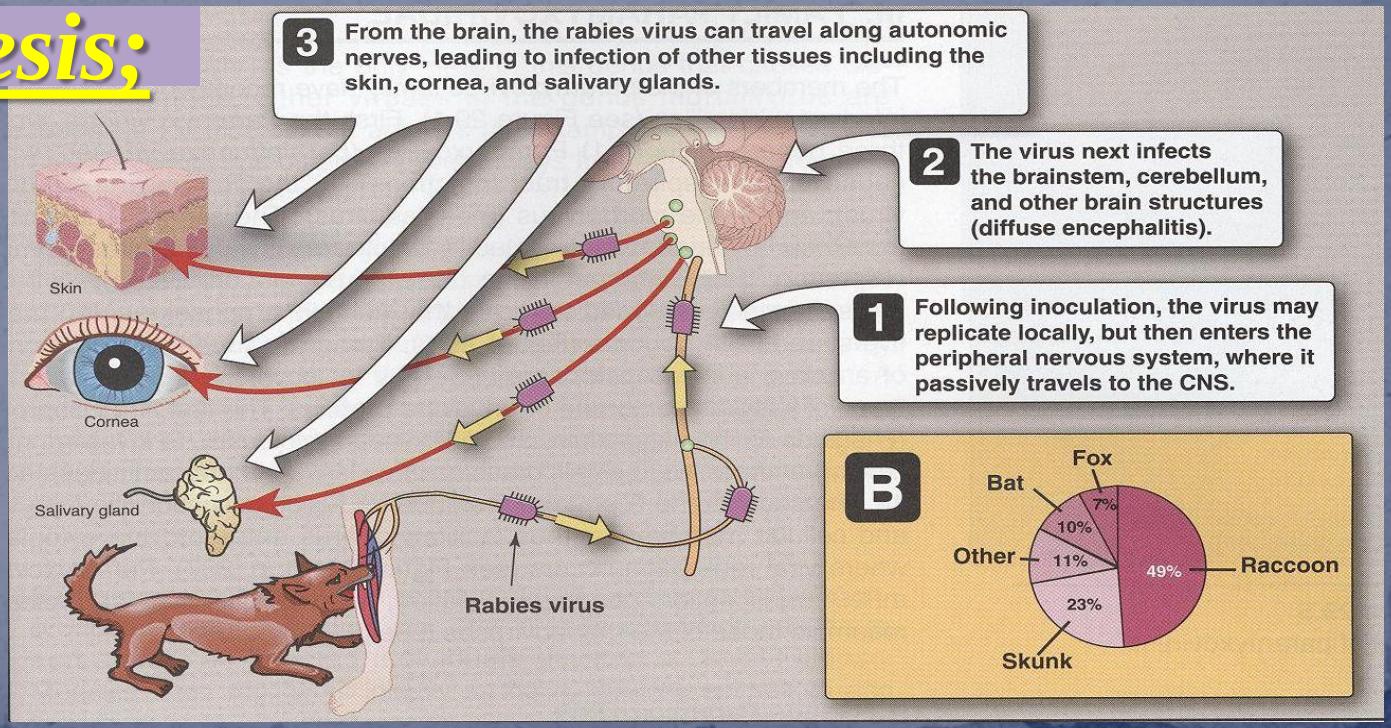
❖Common route

- 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

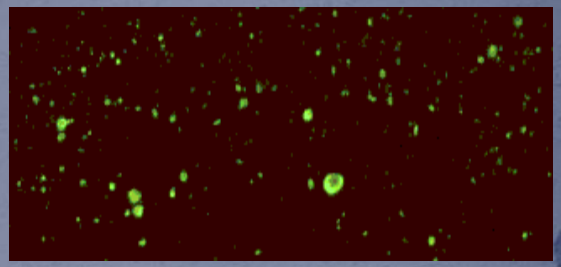
Nervous , lacrimation , salivation,
hydrophobia, convulsion , coma & death.

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

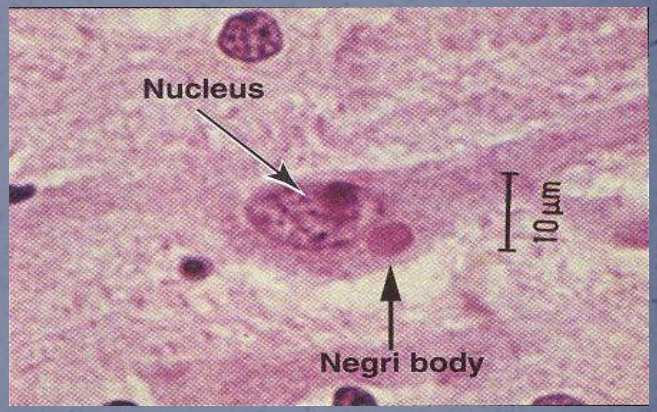
4- Recovery; Extremely rare

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

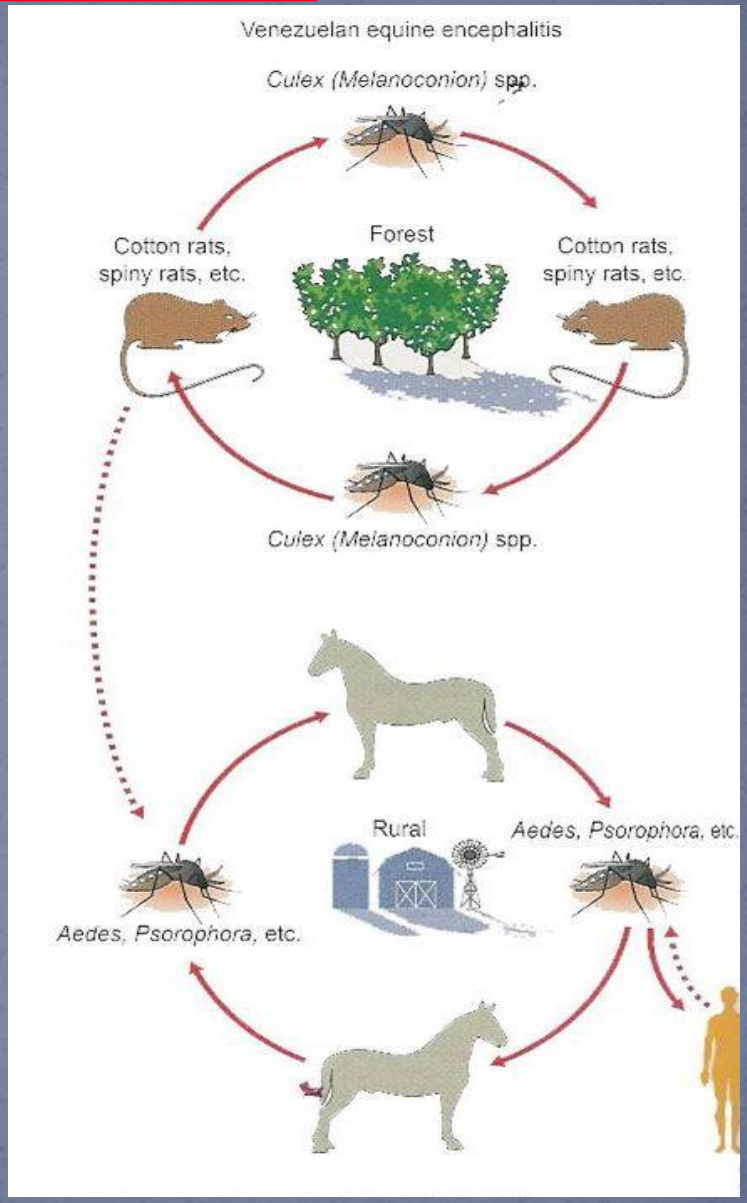
Vector: Mosquito, Tick & Sandfly

Transmission: bite of infected vector

❖ Infections

- Asymptomatic Infections*
- Diseases

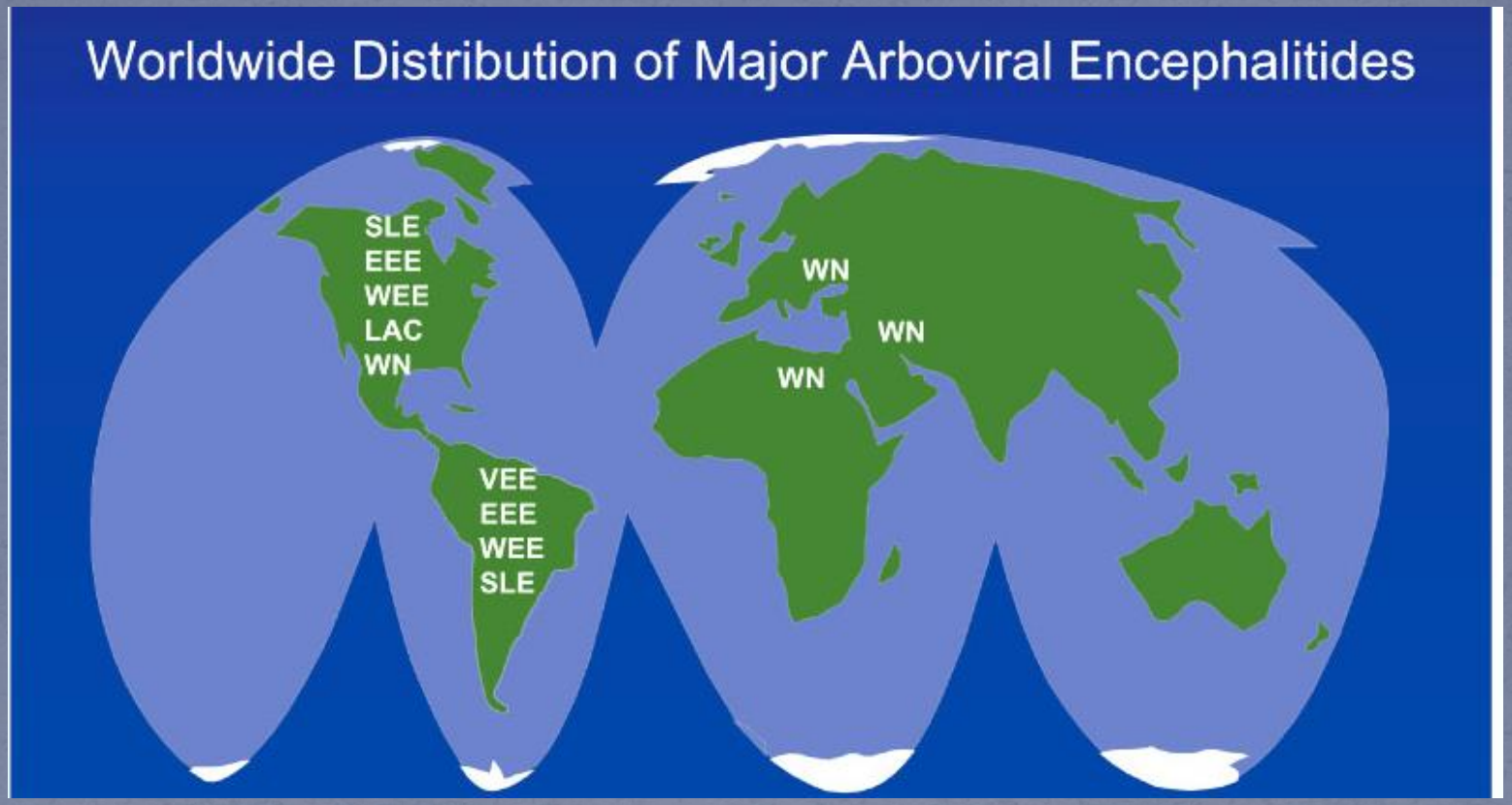
1) Fever, Rash & Arthralgia
2) Hemorrhagic fever ± hepatitis
3) CNS disease (meningitis & encephalitis)



*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

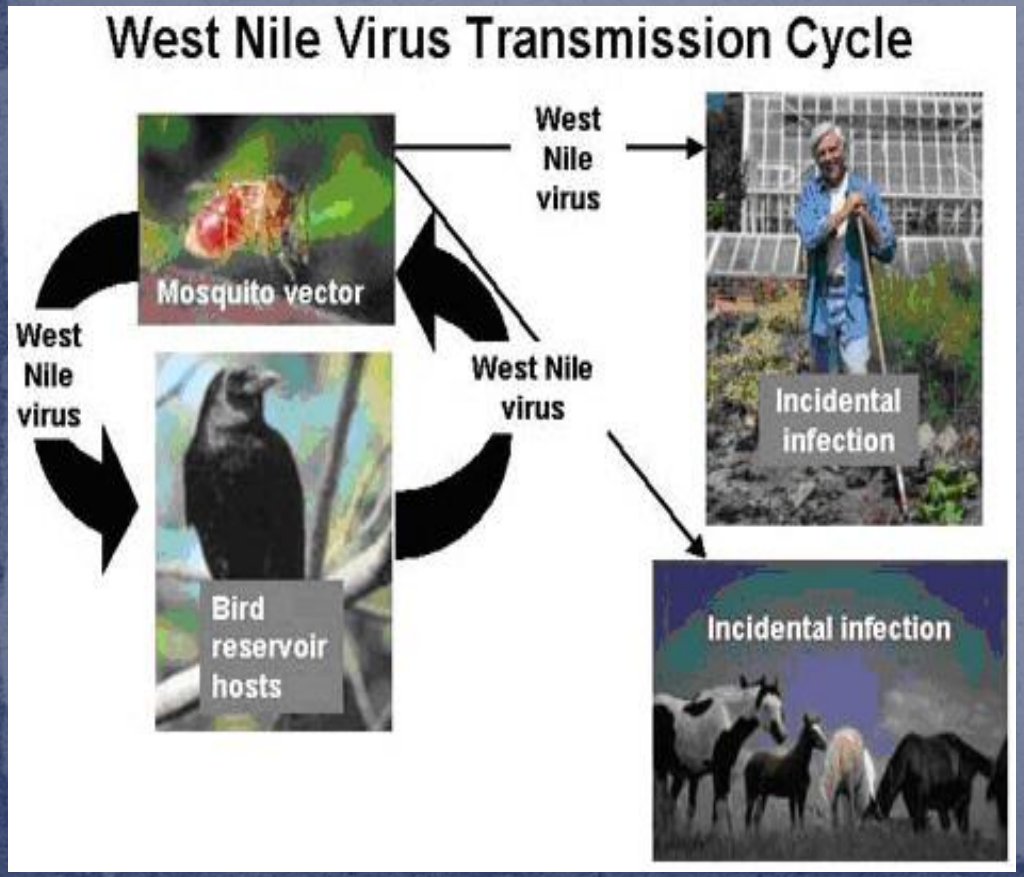
Arboviral encephalitis is prevalent worldwide

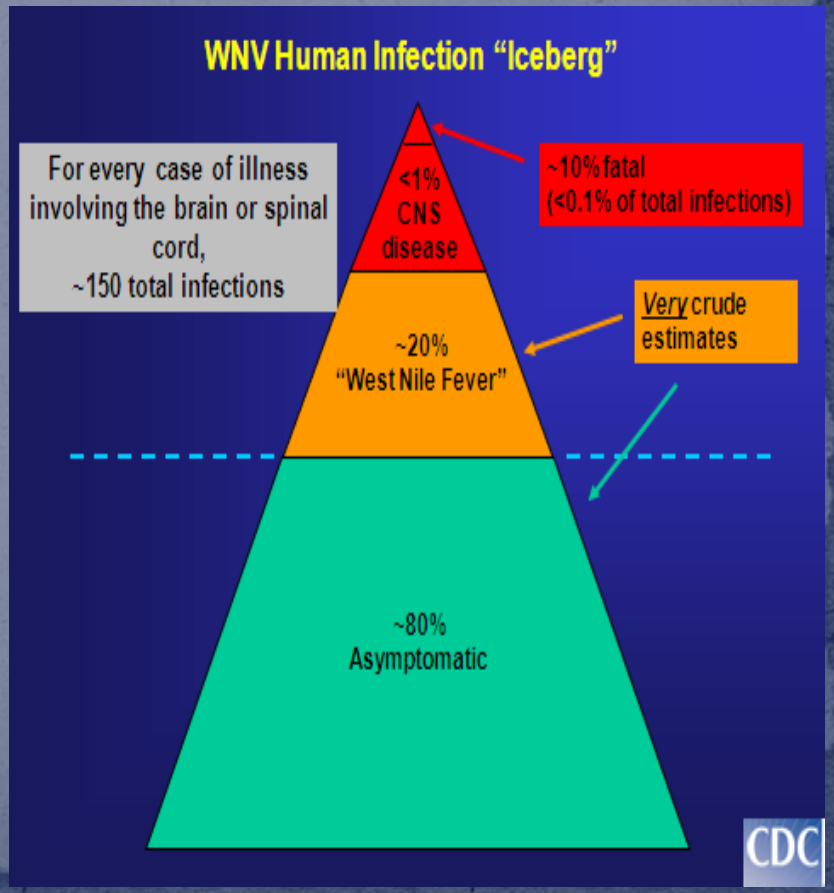


EEE: Eastern equine encephalitis
LAC: LaCrosse encephalitis
SLE: St. Louis encephalitis
WEE: Western equine encephalitis
WN: West Nile encephalitis
VEE: Venezuelan equine encephalitis

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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