Viral infections of CNS

(CNS Block , Microbiology : 2016)

By: Dr.Malak M. El-Hazmi

***Virus neurological diseases*:**

- ***Acute viral infections of the CNS.***
- ***Chronic virus neurological diseases.***
- ***Neurological diseases precipitated by viral infections.***

OBJECTIVES;

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

➢ Aseptic meningitis , Paralysis &Encephalitis

➢;

- ✓ **Enteroviruses & polioviruses.**
- ✓ **Herpes simplex virus 1.**
- ✓ **Rabies virus.**
- ✓ **Arboviruses (West Nile virus).**

- ➢ structure
- ➢ Epidemiology
- ➢ Pathogenesis
- ➢ clinical presentations
- ➢ Lab diagnosis
- ➢ Treatment & prevention

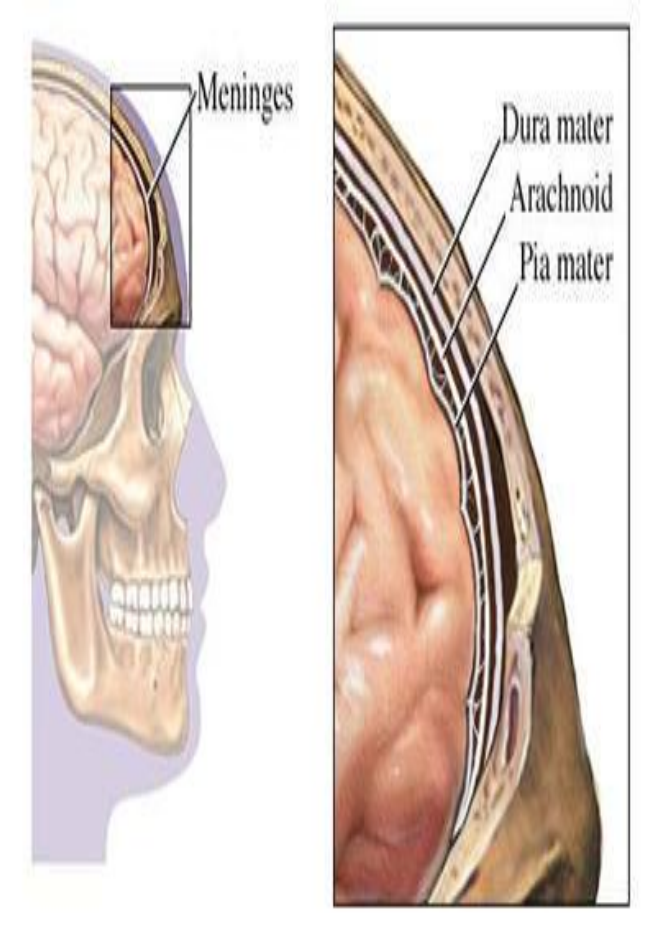
Meningitis

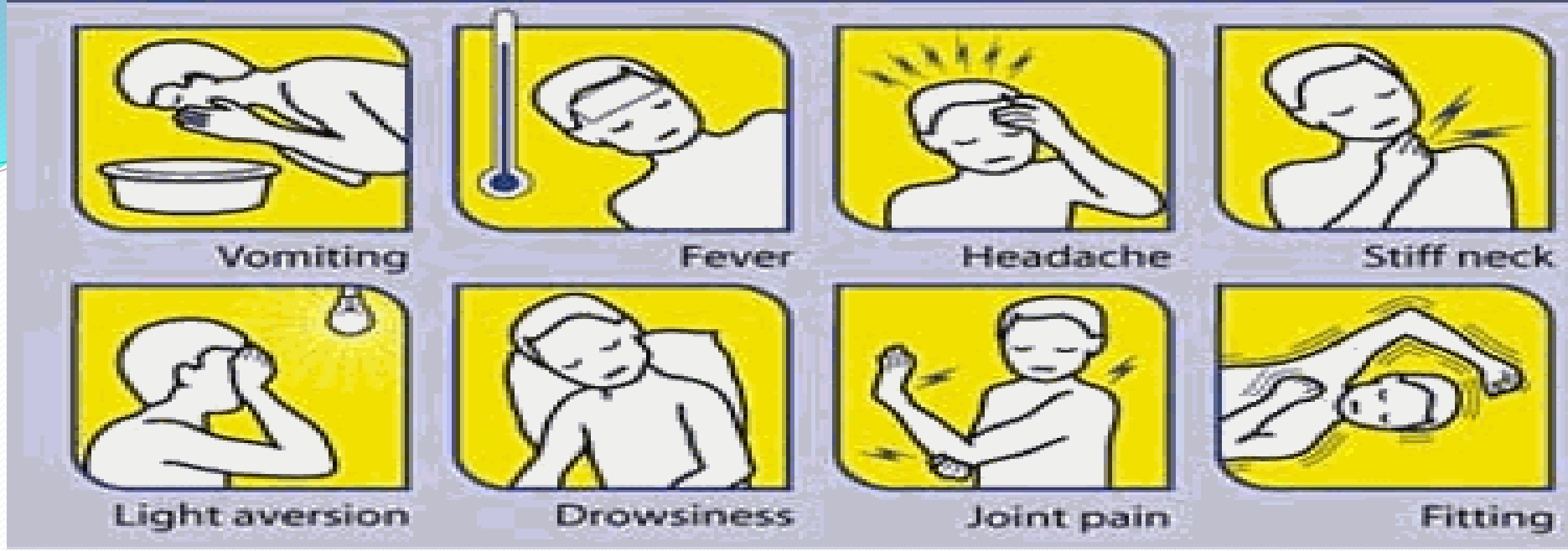
Caused by:

Infectious agents ;

- bacteria
- viruses
- fungi
- protozoa

Non-infectious agents.





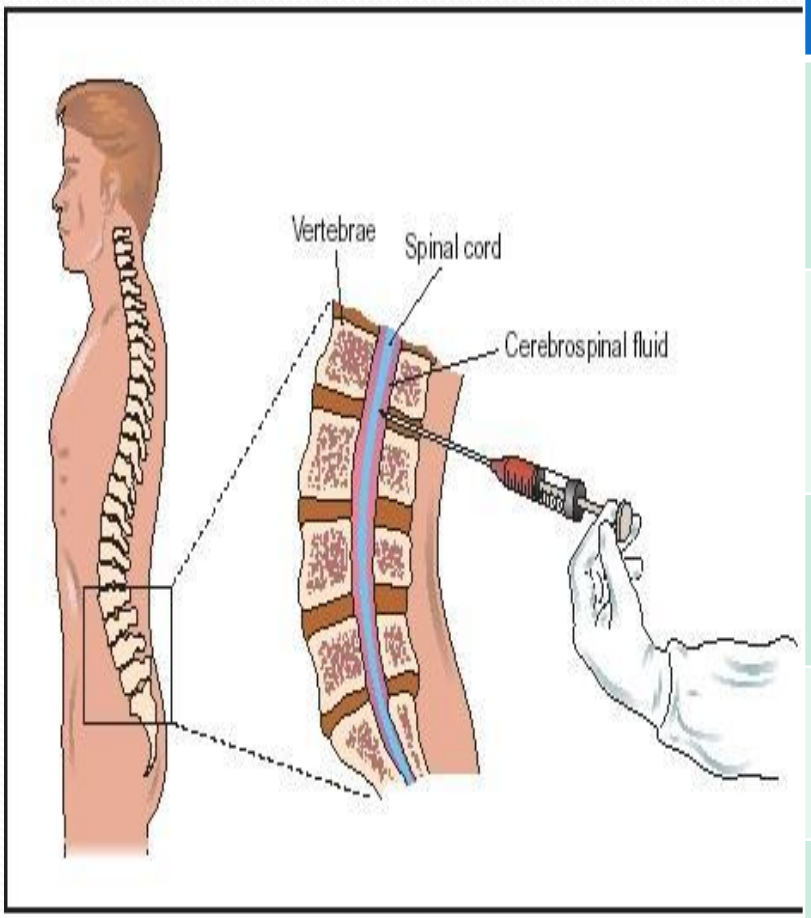
Viral Meningitis

- Aseptic meningitis
- Caused by virus.
- Less severe
- Resolves without specific treatment within a week or two

Bacterial Meningitis

- Caused by bacteria
- 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)

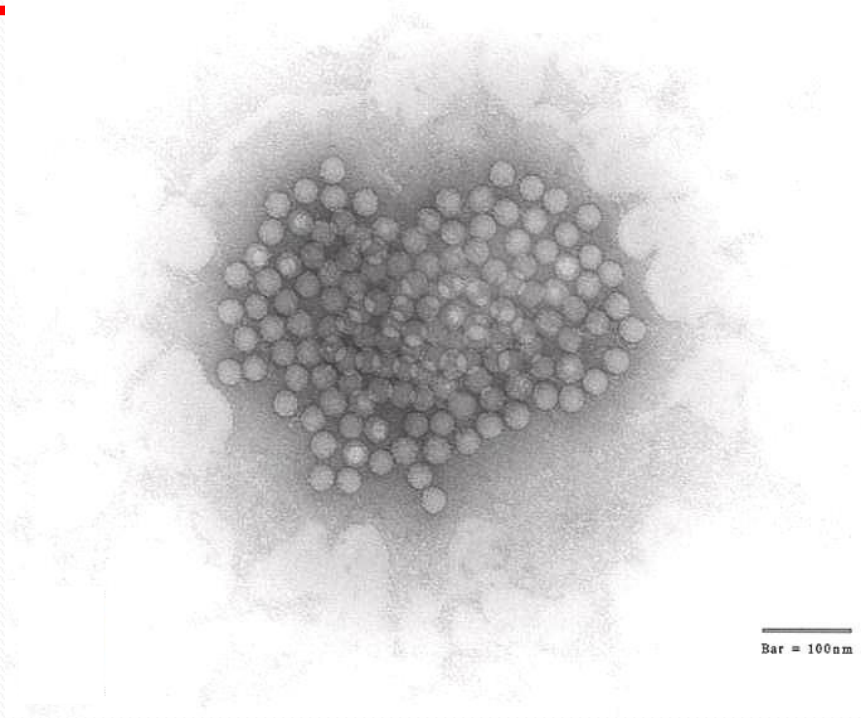
- Etiological Agents:
  - ***Enteroviruses*** .**
  - Other :
    - Mumps virus .
    - Arboviruses.
    - Herpes viruses.
    - Human Immunodeficiency Virus.
    - …..

Enteroviruses

- ***Picornaviridae***

Include ;

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



Nonenveloped , icosahedral , ss (+) RNA

Epidemiology

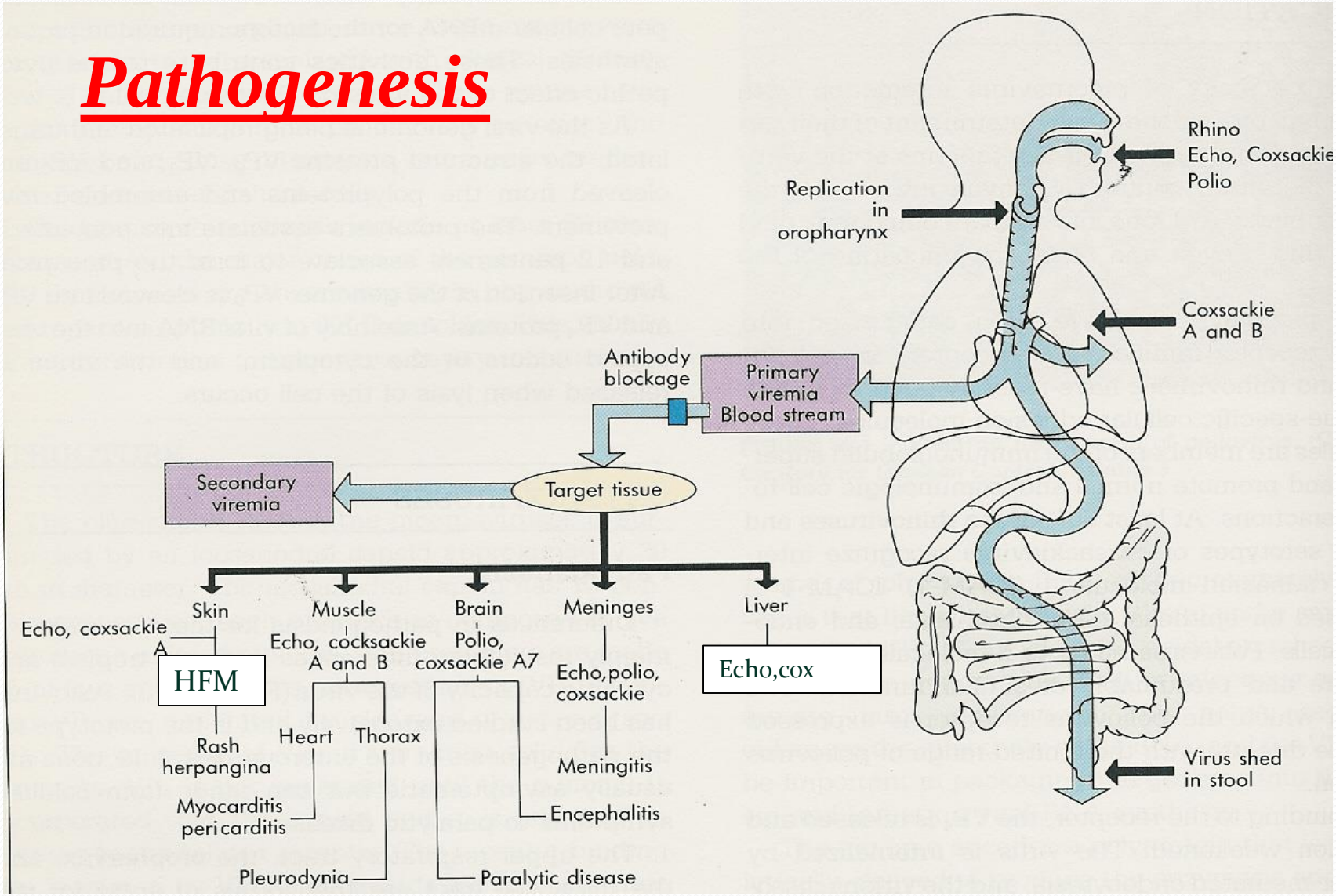
- Reservoir : Human
- Spread :
  - Fecal - oral route (mainly)
  - Inhalation of Infectious aerosols

  (Crowded, Poor hygiene & Sanitation)

- Age : children > adults
- Seasonal distribution:

  summer & fall

Pathogenesis



Enteroviral infections

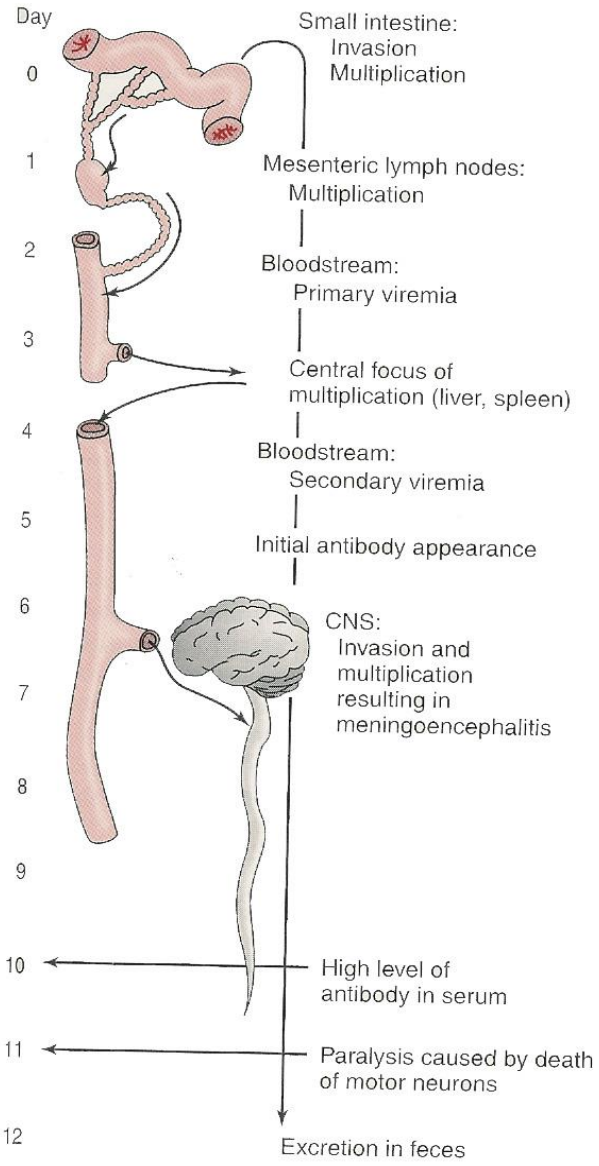
- Asymptomatic Infections*
- Diseases;

Neurologic Diseases	Poliovirus Types 1-3	GP A COX. Types 1-24	GP B 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

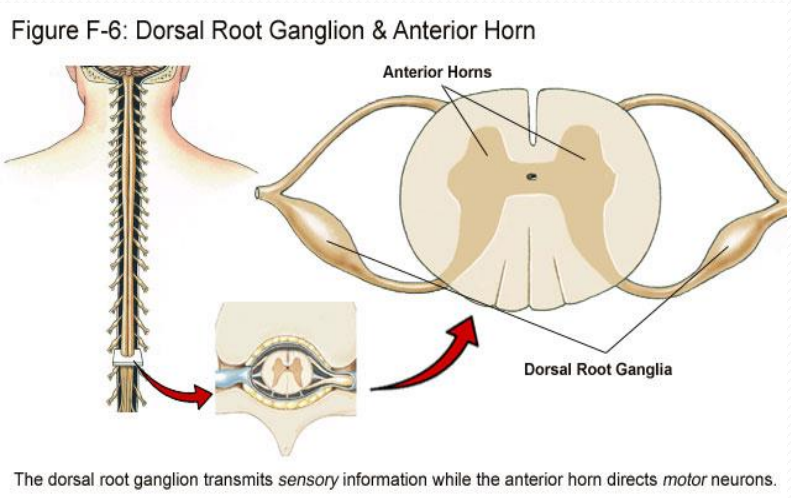
NON-Neurologic Diseases ;

Respiratory tract infections.
Skin and mucosa infections;
Cardiac infections
Acute hemorrhagic conjunctivitis
Others

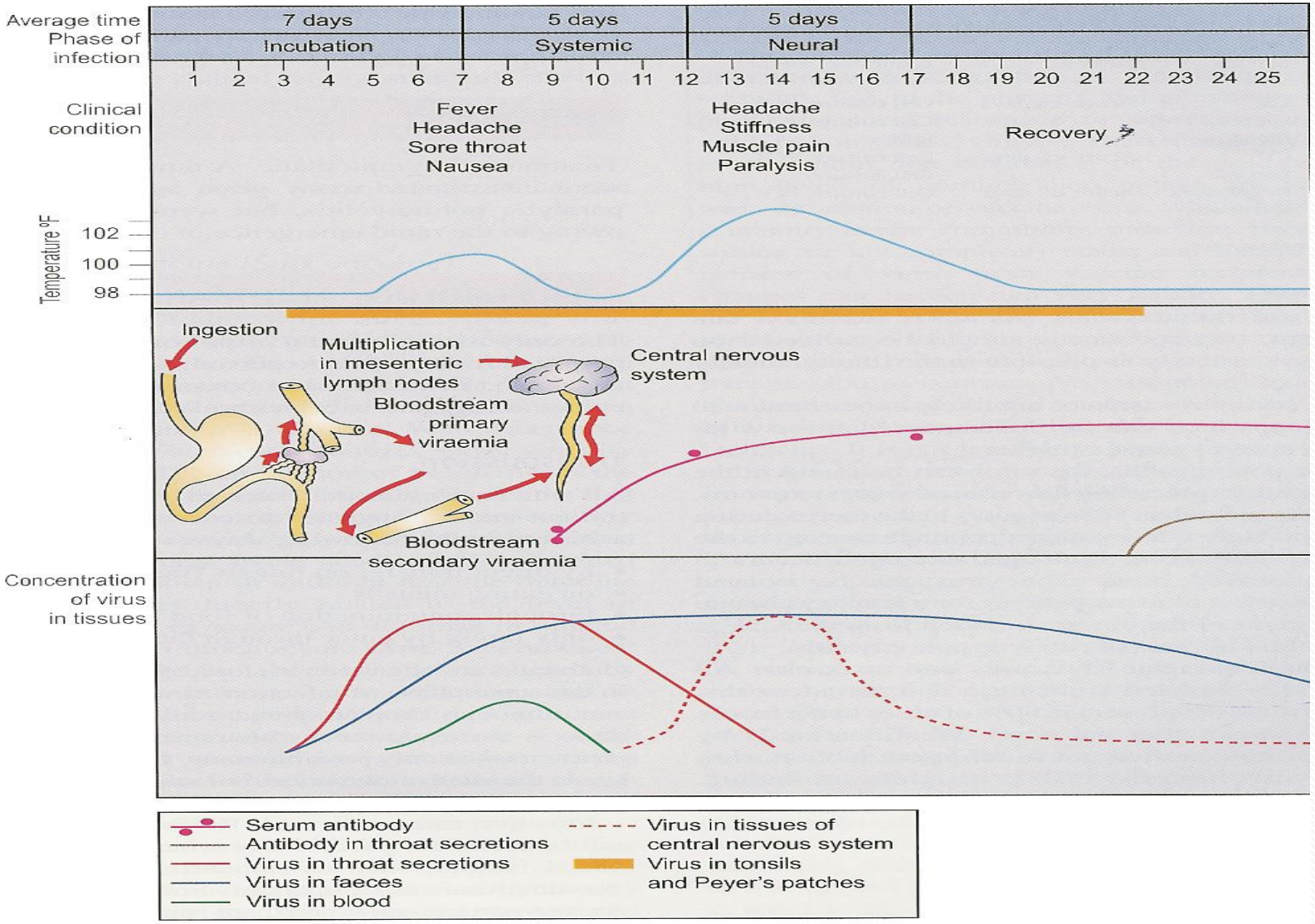
Pathogenesis of polio:



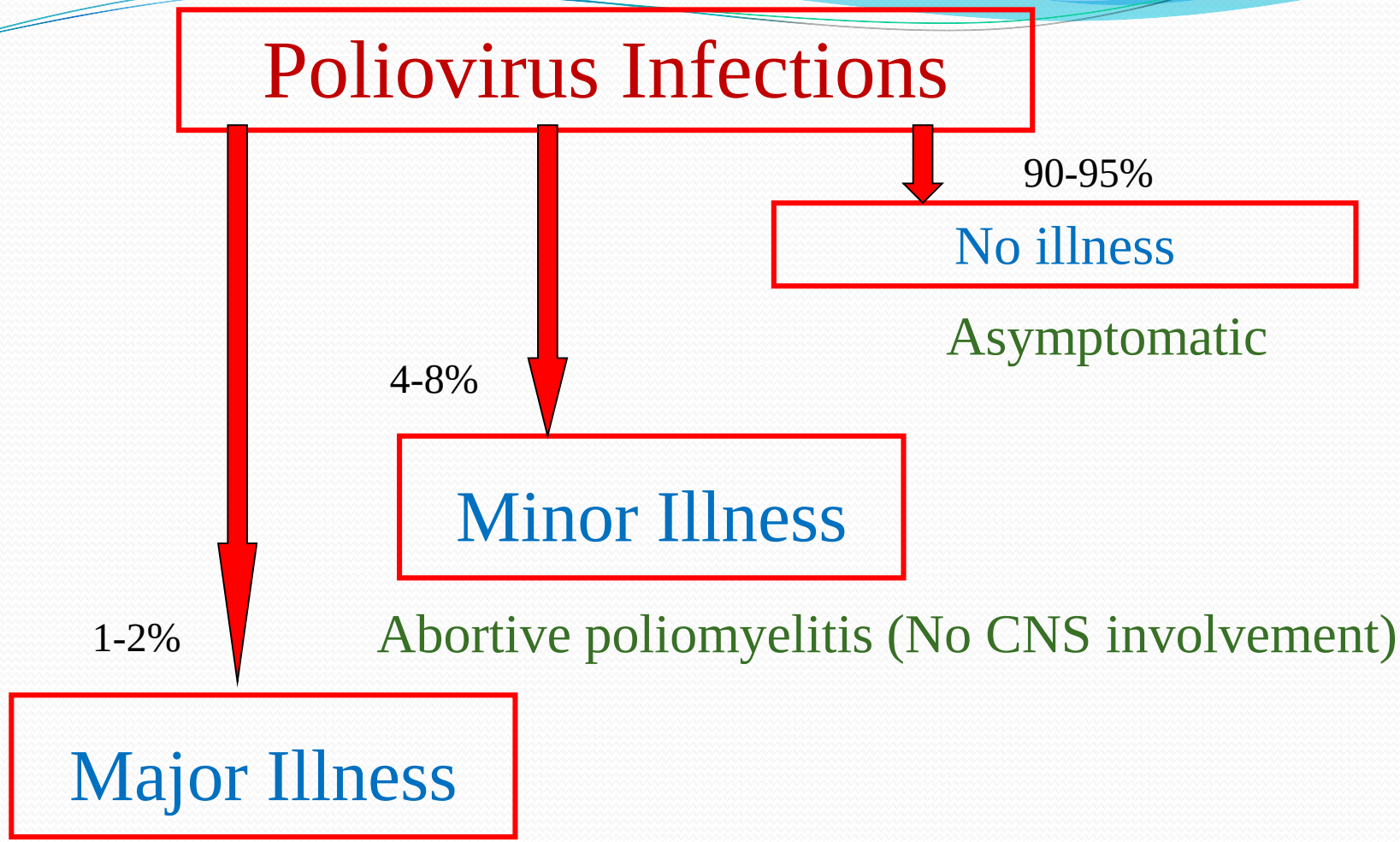
- Pathway to CNS by:
  - Blood
  - Peripheral nerves
- Causing destruction of motor neurons of AHCs
- Rarely affects brain stem (bulber poliomyelitis)



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 cell cultures

    All EVs grown except some strains of Cox A viruses
  - Observe for CPE
  - Identify the type

  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

- Rx:
  - No antiviral Rx

- Prevention:
  - Sanitation & Hygienic measures
  - Poliovirus vaccines

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

b- Live-attenuated polio vaccine (OPV)
(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
Interrupts transmission	No	Yes
Affords 2º protection by spread to others	No	Yes
Reverts to virulance	No	Yes (rarely)
Causes disease in the immun ed	No	Yes
Co-infection with other EVs may impair immunization	No	Yes
Requires refrigeration	No	Yes
Duration of immunity	Shorter	Longer

Poliovirus Vaccine

- Adverse reactions ;
  - local reactions (IPV)
  - Vaccine -Associated Paralytic Poliomyelitis (OPV)

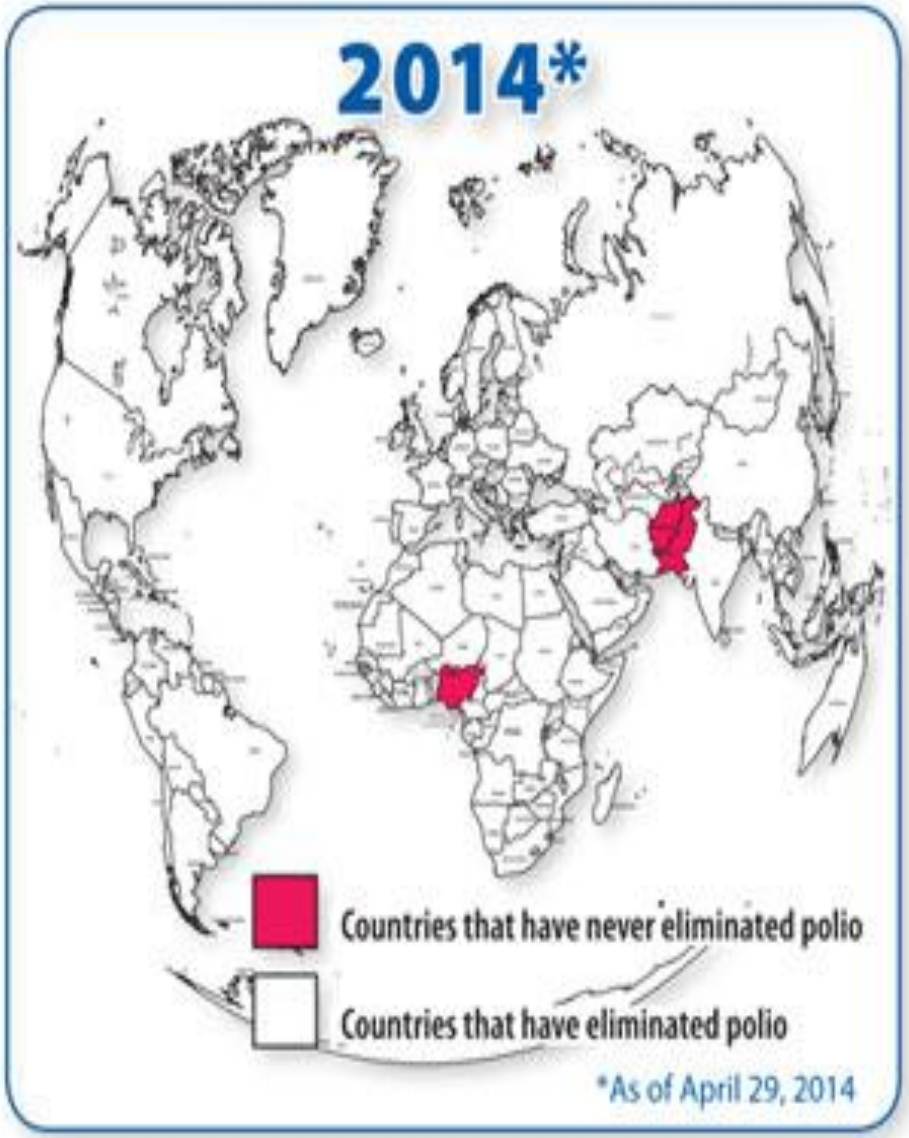
    adult , immuno↓ed
- 4 doses of PV; 2, 4 , 6-18 ms

  & 4 - 6 yrs
- Combination vaccine ; IPV, DTaP ,Hib & HB vaccines

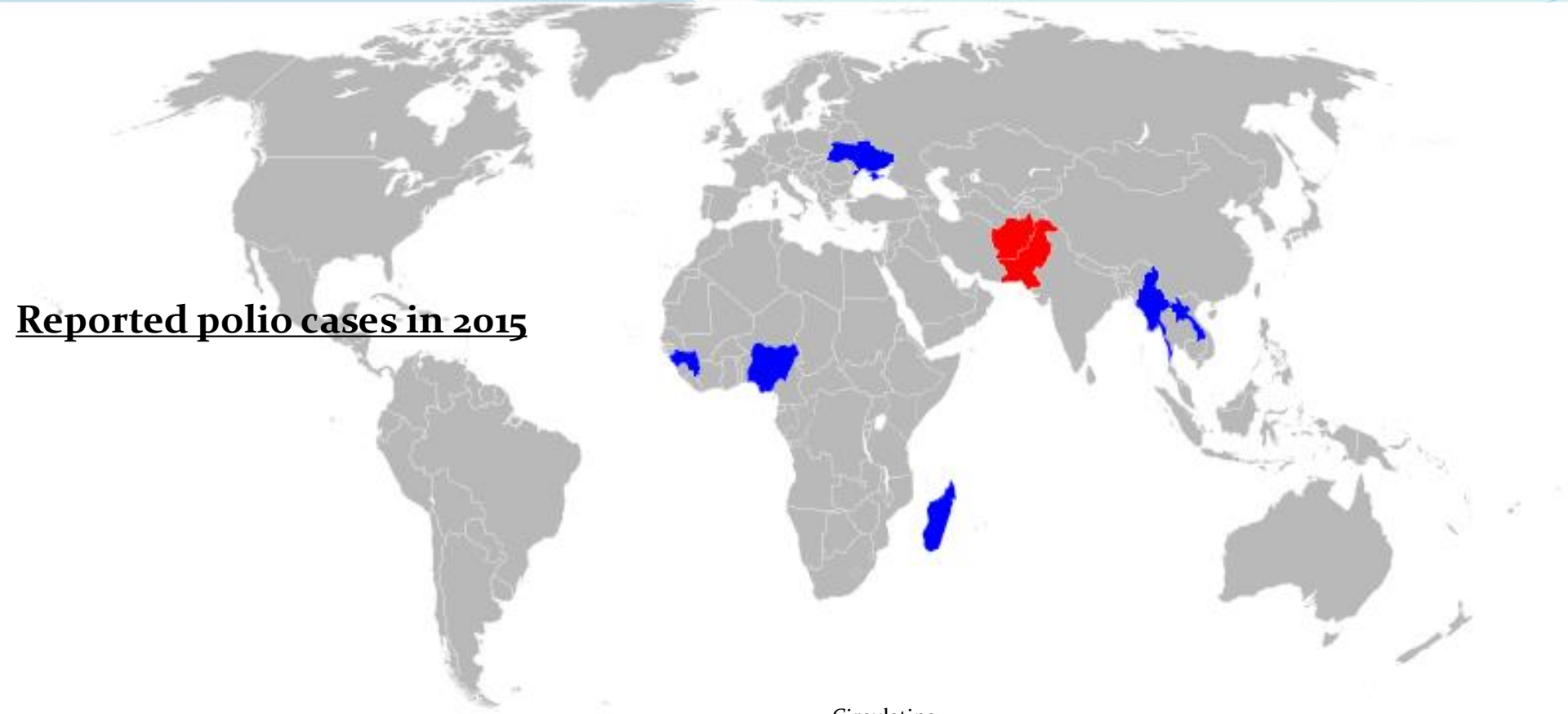
Polio Vaccination of Adults

- Indications:
  - Travelers to polio-endemic countries
  - HCW
- IPV


1988
Countries that have never eliminated polio
Countries that have eliminated polio


2014*
Countries that have never eliminated polio
Countries that have eliminated polio
*As of April 29, 2014

Reported polio cases in 2015



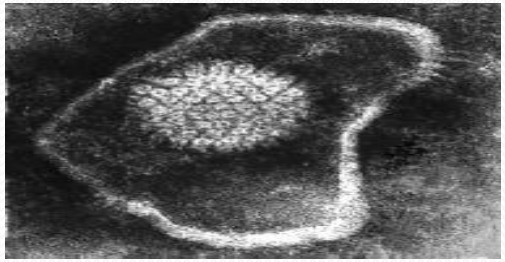
Country	Wild cases	Circulating vaccine-derived cases	Transmission status
Pakistan	54	2	endemic
Afghanistan	20	0	endemic
Madagascar	0	10	circulating vaccine-derived only
Laos	0	6	circulating vaccine-derived only
Guinea	0	4	circulating vaccine-derived only
Myanmar	0	2	circulating vaccine-derived only
Ukraine	0	2	circulating vaccine-derived only
Nigeria	0	1	circulating vaccine-derived only
Total	71	27	

Viral Encephalitis

- Enteroviruses
- Herpes viruses.
- Rabies virus
- Arboviruses.

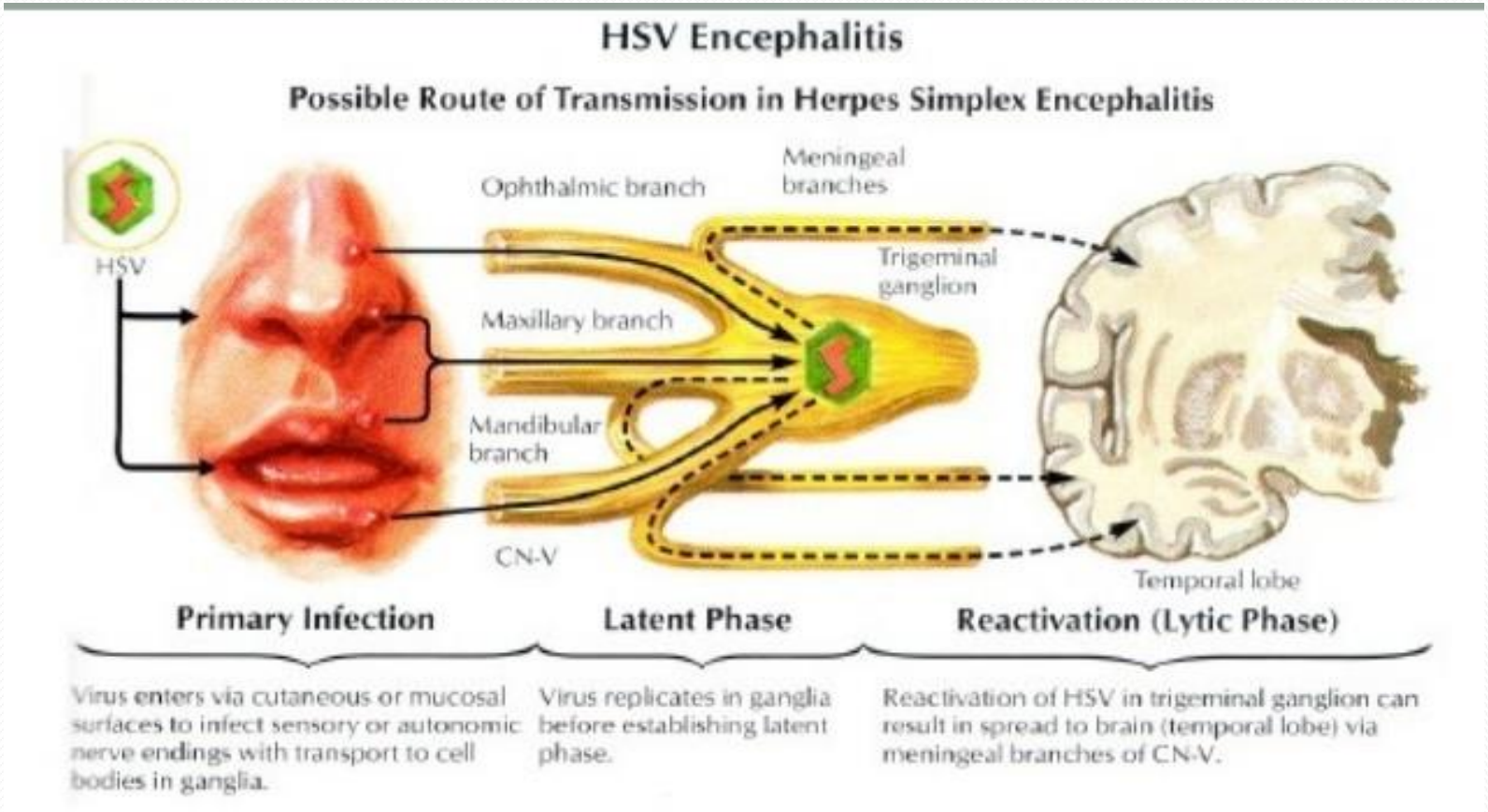
- Others

Herpes Simplex Encephalitis

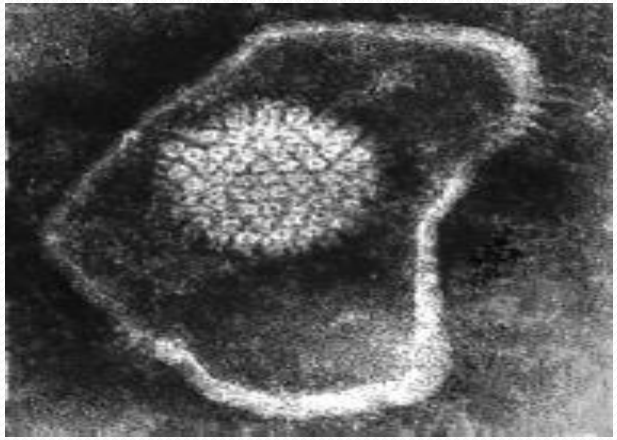


- Caused by;
  - Herpes simplex virus -1(HSV-1)

dsDNA , Enveloped , Icosahedral Virus



Herpes Simplex Encephalitis



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

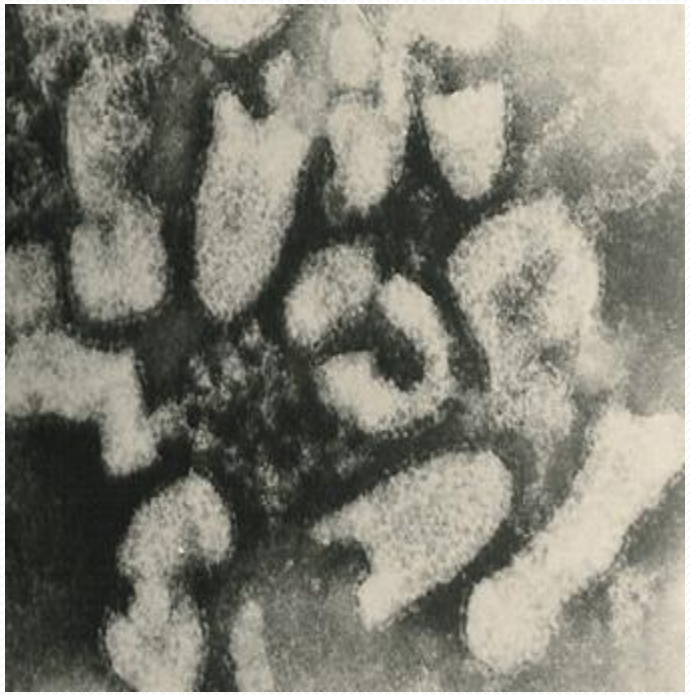
    dsDNA , Enveloped , Icosahedral Virus

- C/F;
  - F,H,V ,Seizures & altered mental status.
  - High mortality rate
- Dx;
  - MRI
  - CSF---Lymph, glucose-N & Protain- ⇑

    ---detection of HSV-1 DNA by PCR.
- Rx;

  Acyclovir.

Rabies encephalitis



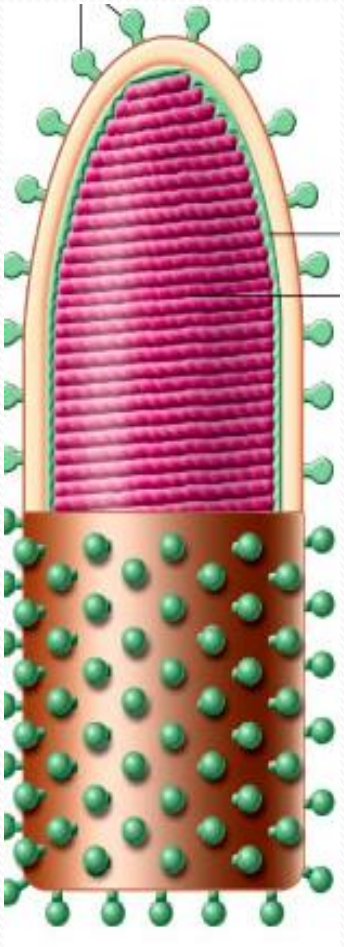
Rabies virus ;

Rhabdoviridae.

s.s (-)RNA genome,

Helical nucleocapsid,

Enveloped virus.



Bullet shaped virus

Pathogenesis;

Epidemiology;

Reservoir;

- Major;

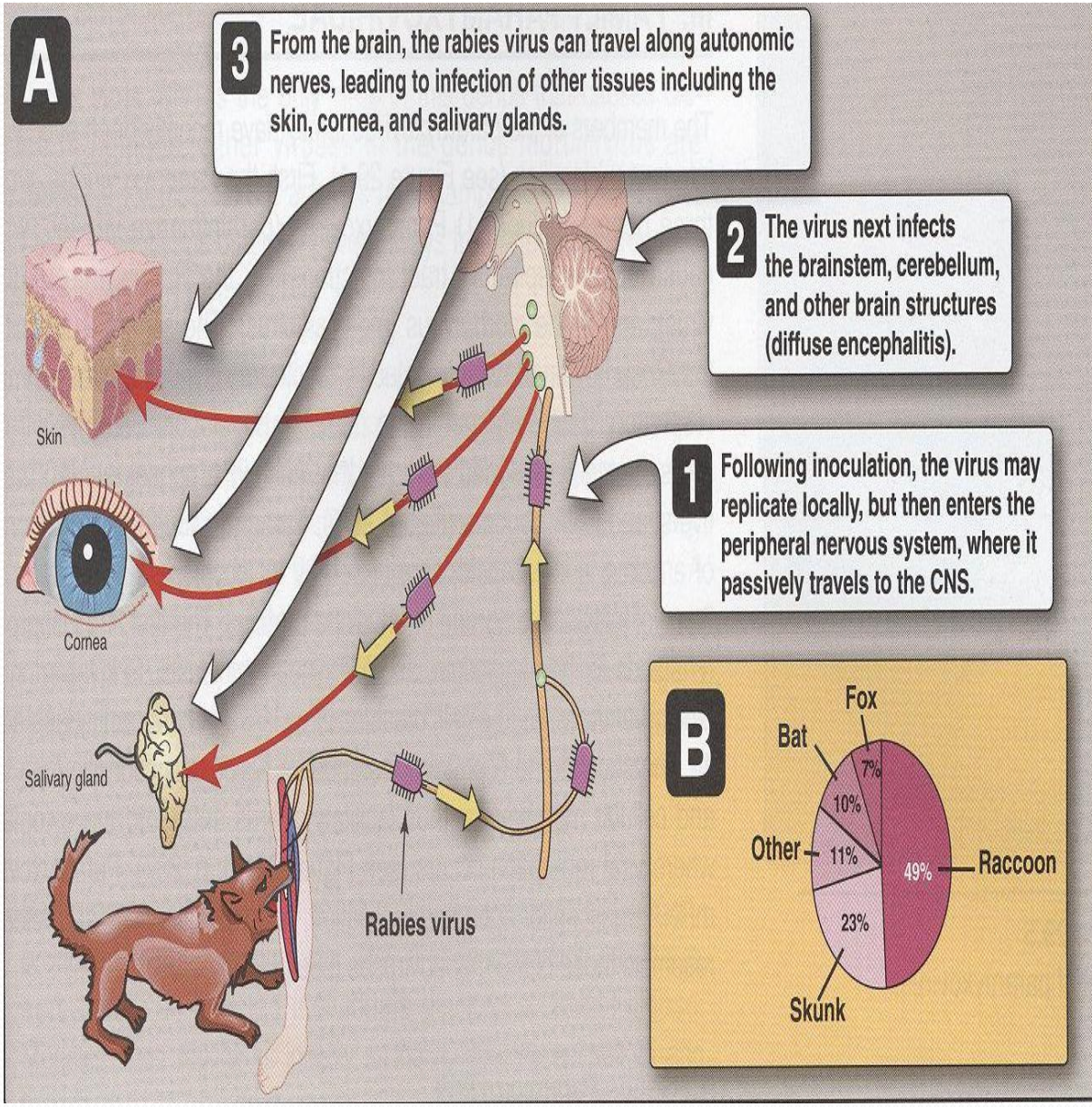
  Raccoons , Foxes, Wolves & bats.
- Imp ; cats & dogs

Transmission;

- ❖Common route
- ➢Bite of a rabid animal
- ❖Uncommon route
- ➢Inhalation

while in a bat infested cave

- ➢Corneal transplant



Rabies; A fatal acute encephalitis

- zoonotic disease .

1-The incubation period: 1-3 m > longer

2-The prodromal phase:

F, H , M , A, N &V.

Abnormal sensation around the wound.

3-Neurological phase ;

1- encephalitis

Nervous , Lacrimation , salivation,

Hydrophobia ,

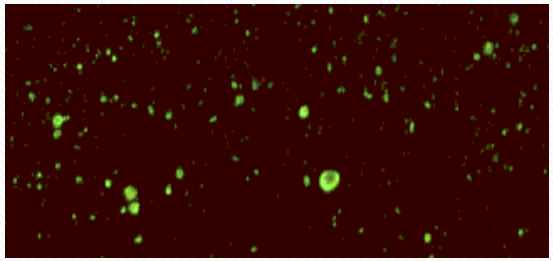
Convulsion ,coma & death .

2-Paralytic illness ; Ascending , Death , Bat.

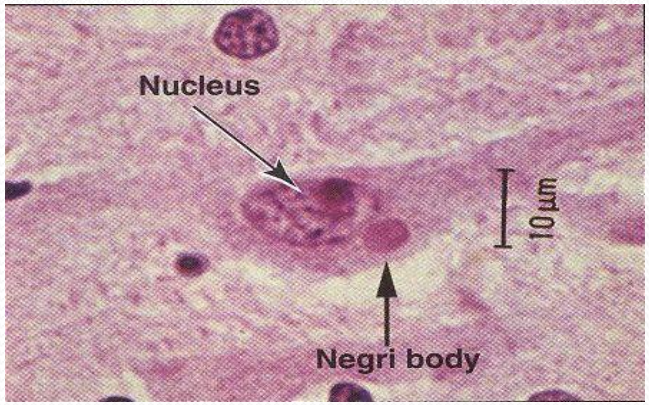
4- Recovery; Extremely rare

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
- serology



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 around the wound & I M.
  - Active immunization;

    Human Diploid Cell Vaccine (HDCV)**

    5 - 6 doses

Arthropod –borne Viruses

Arboviruses > 500 Vs

❖ Epidemiology:

Reservoir: Wild birds & Mammals

Vector: Mosquito, ticks& Sandfly

Transmission: bite of infected vector

❖ Infections

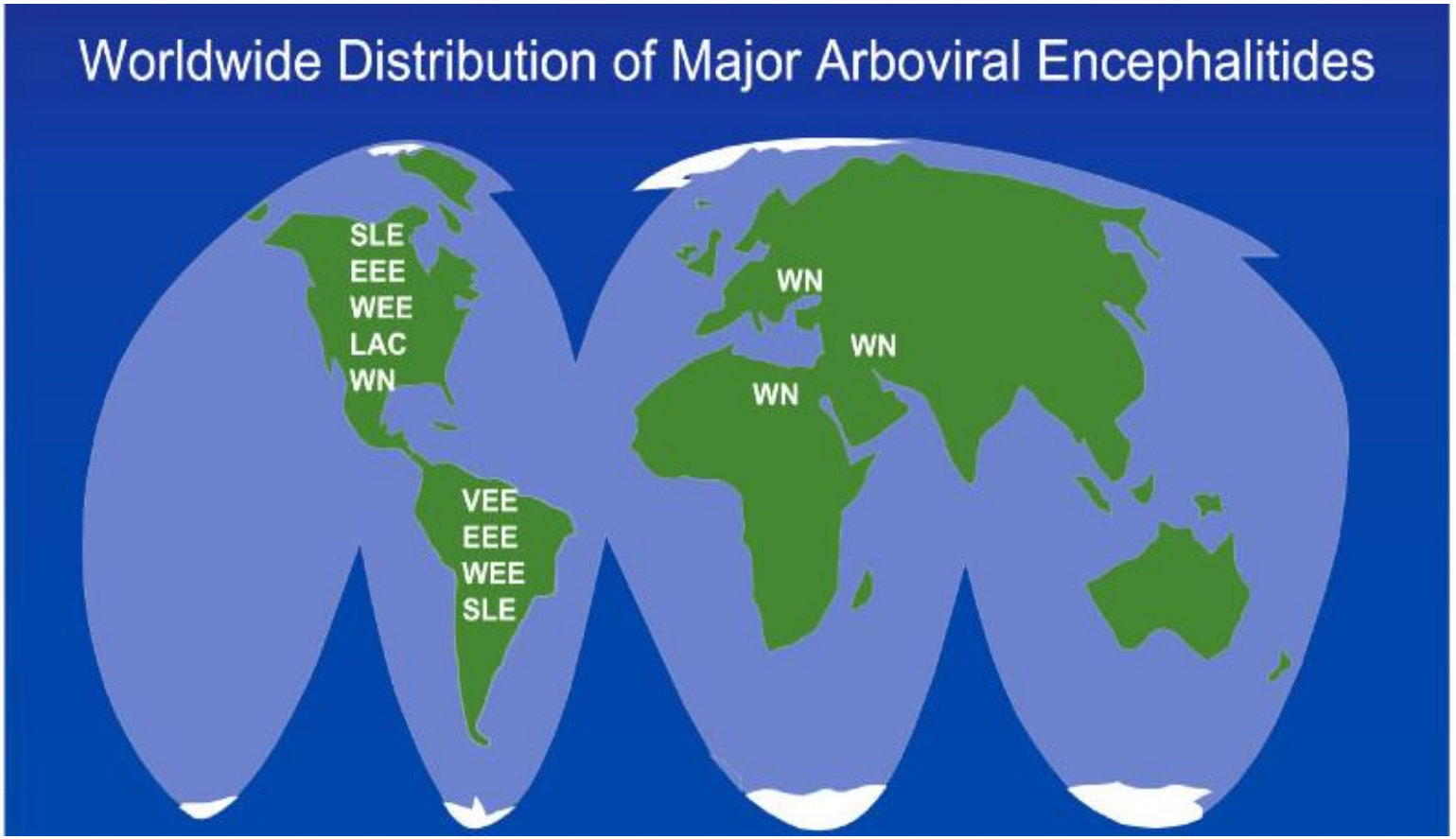
- Asymptomatic Infections*
- Diseases

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

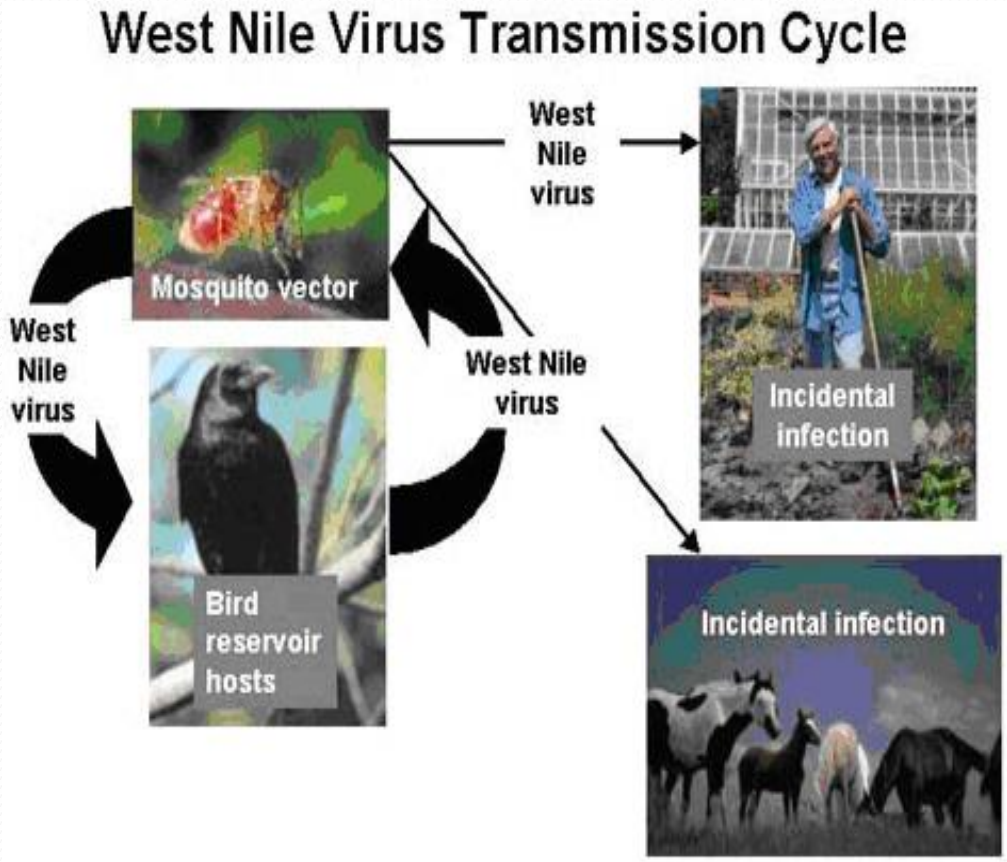
Worldwide Distribution of Major Arboviral Encephalitides

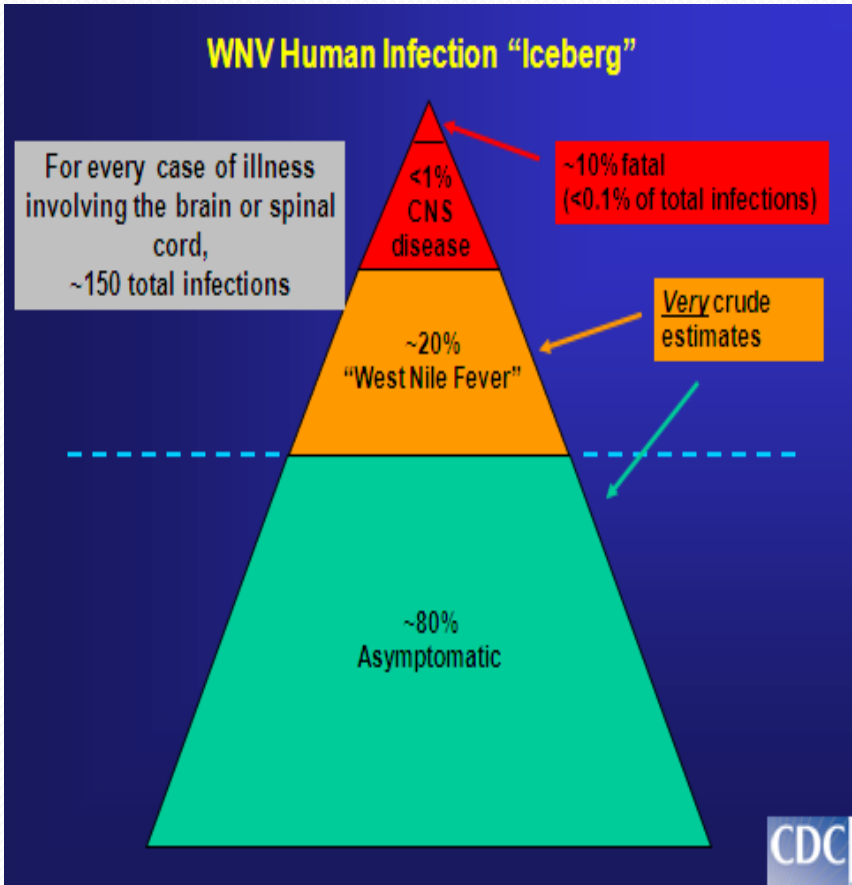


EEE: Eastern equine encephalitis
LAC: LaCrosse encephalitis
SLE: St. Louis encephalitis
WEE: Western equine encephalitis
WN: West Nile encephalitis
VEE: Venezuelan equine encephalitis

West Nile virus

- Flaviviridae
- Febrile illness → *meningitis* , encephalitis





Laboratory Diagnosis

A. Isolation (Gold standard)

(Reference Lab)

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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