Viral infections of CNS

(CNS Block , Microbiology : 2020)

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***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

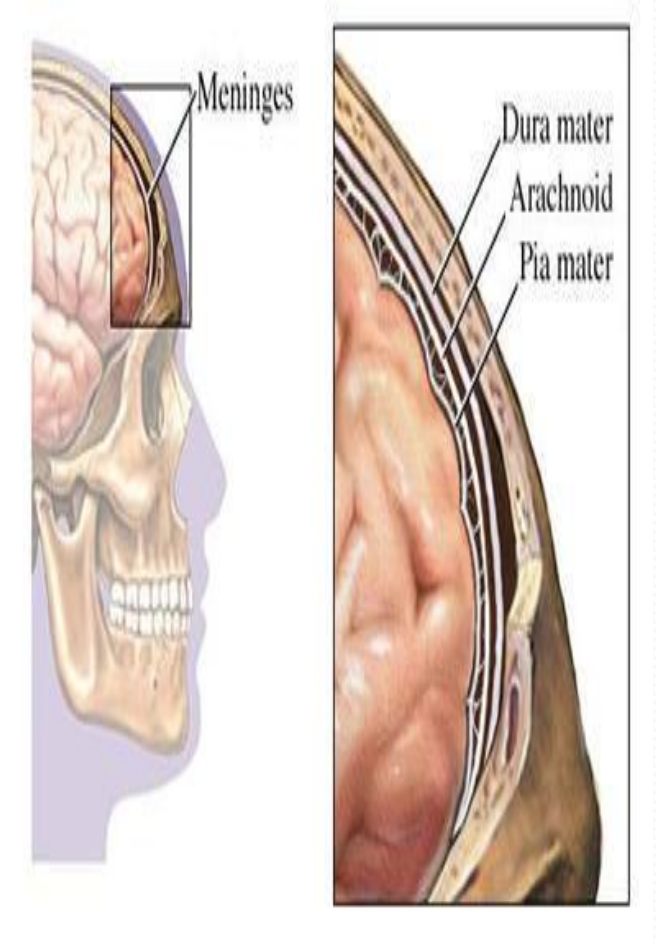
Meningitis

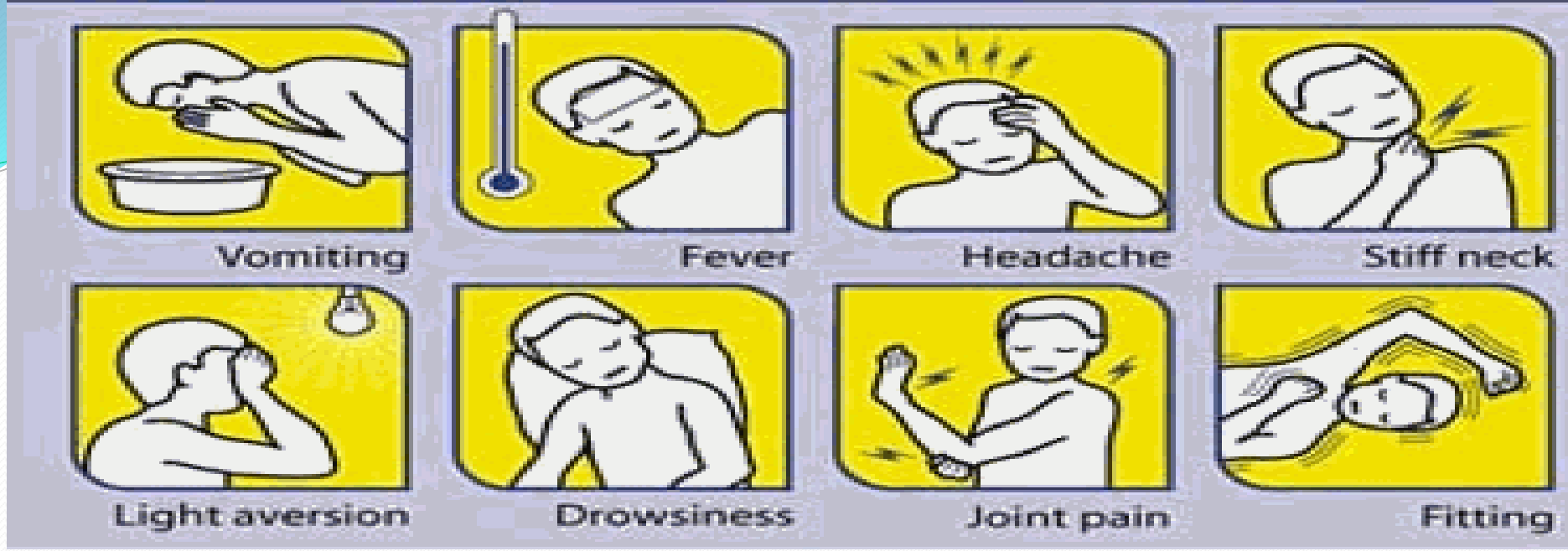
Caused by:

Infectious agents ;

- bacteria
- viruses
- fungi
- protozoa

Non-infectious agents.





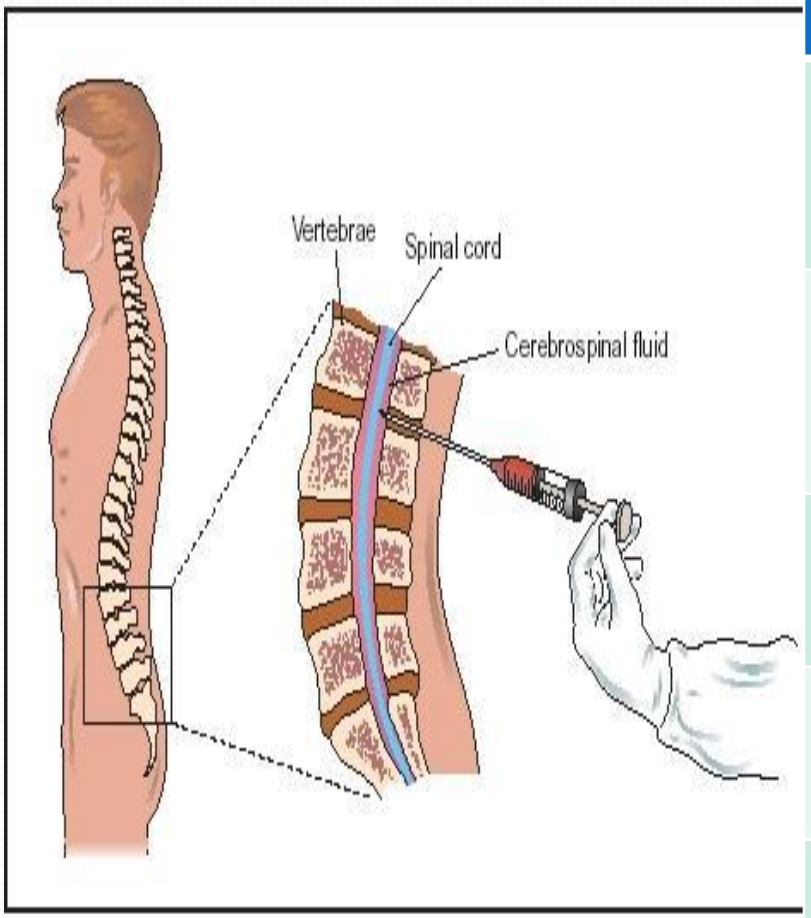
Viral Meningitis

- 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)

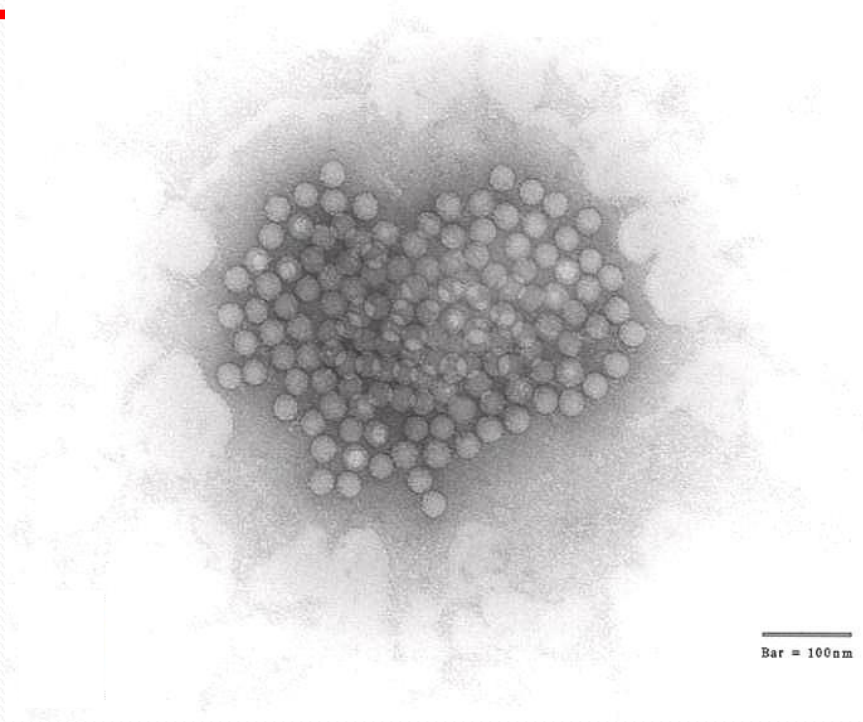
- Etiological Agents:
  - ***Enteroviruses*** .**
  - Other :
    - Mumps virus .
    - Arboviruses.
    - Herpes viruses.
    - Human Immunodeficiency Virus.
    - …..

Enteroviruses

- ***Picornaviridae***

Include ;

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



Nonenveloped , icosahedral , ss (+) RNA

Epidemiology

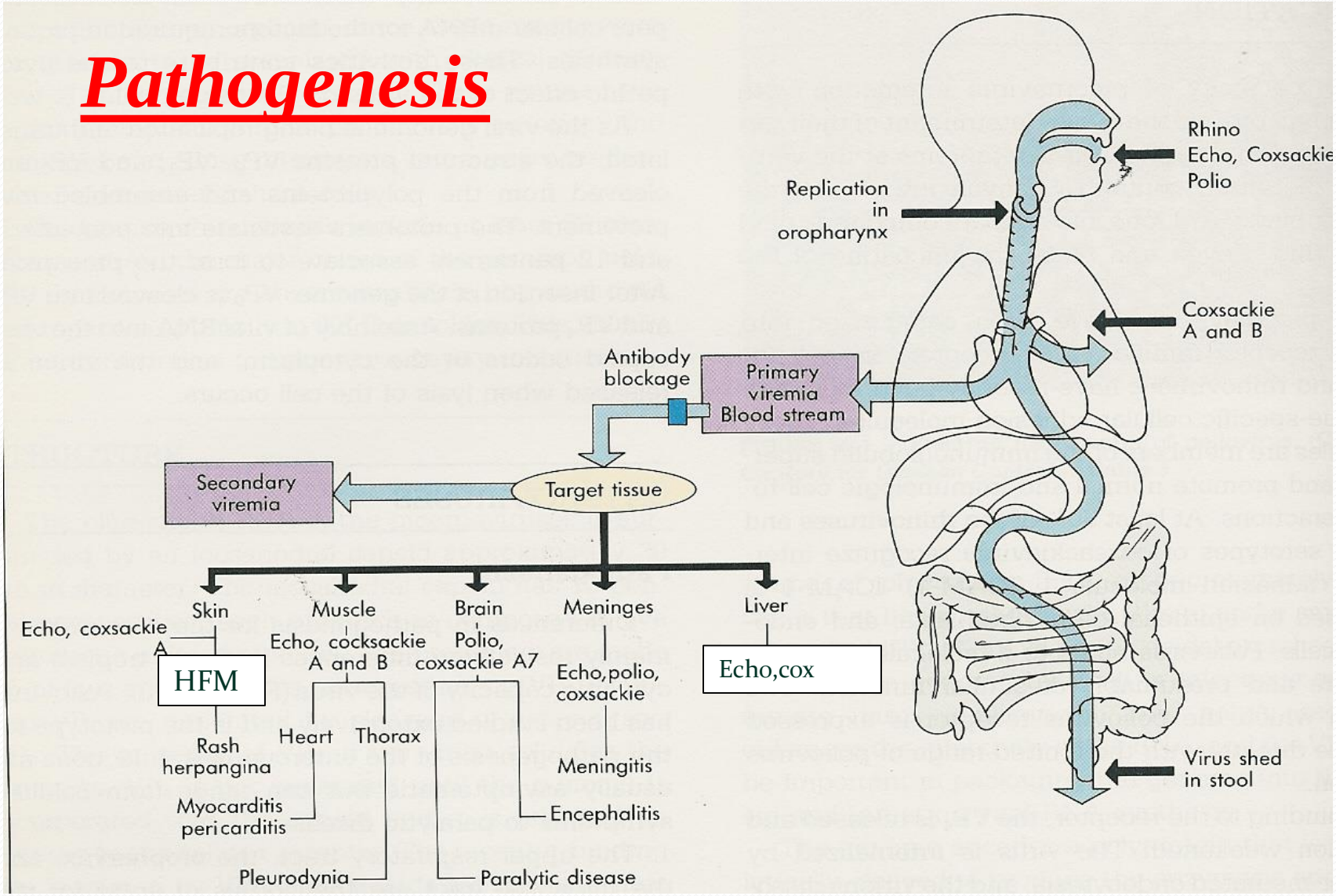
- Reservoir : Human
- Spread :
  - Fecal - oral route (mainly)
  - Inhalation of Infectious aerosols

  (Crowded, Poor hygiene & Sanitation)

- Age : children > adults
- Seasonal distribution:

  summer & fall

Pathogenesis



Enteroviral infections

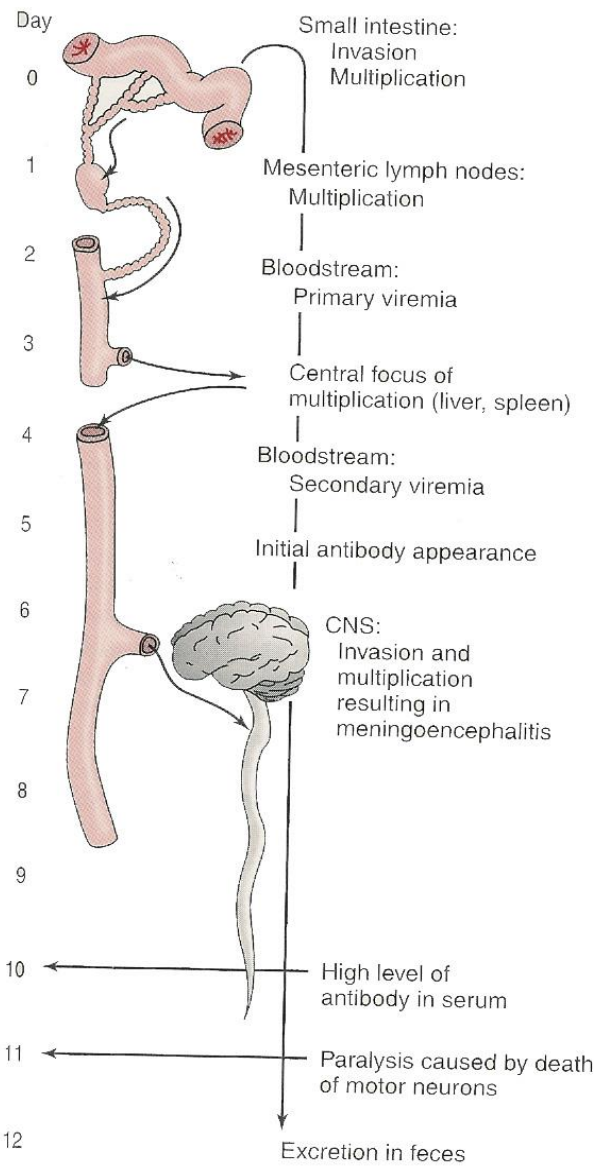
- Asymptomatic Infections*
- Diseases;

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

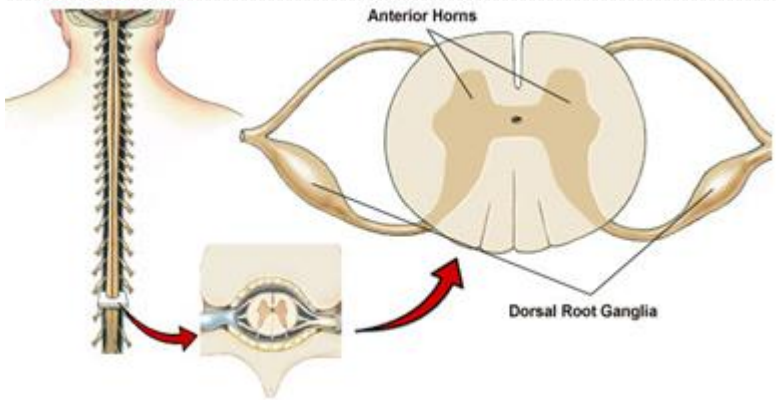
NON-Neurologic Diseases ;

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

Pathogenesis of polio:

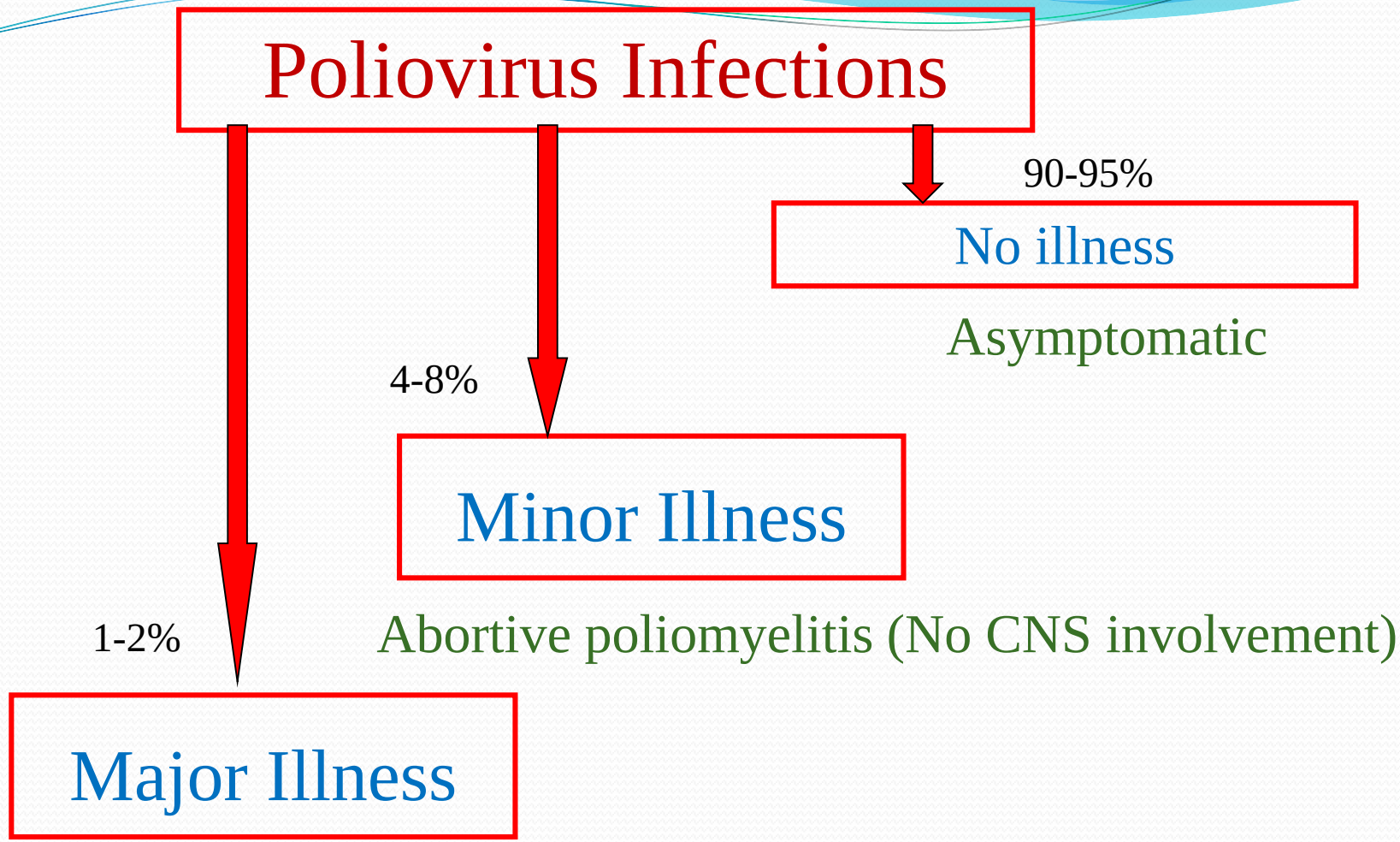


- Pathway to CNS by:
  - Blood
  - Peripheral nerves
- Causing destruction of motor neurons of AHCs
- Rarely affects brain stem (bulber poliomyelitis)



- **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
Transmission to others	No	Yes
Affords 2^{o} protection by spread to others	No	Yes
Reverts to virulance	No	Yes (rarely)
Causes disease in the immun ⇩ed	No	Yes

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

The battle against polio

The infectious viral disease remains endemic only in two countries

- **WHO declared Africa polio-free on August 25, four years after the last cases in Nigeria**

*cases in 2020 as of Aug 18

Source: WHO/EndPolioPakistan/GlobalPolioEradicationInitiative

AFP

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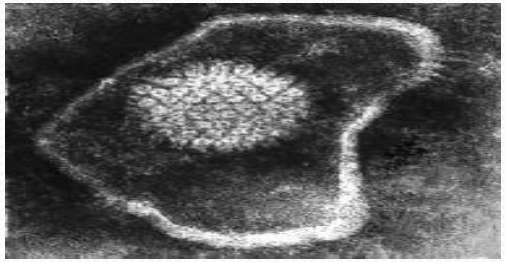
Viral Encephalitis

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

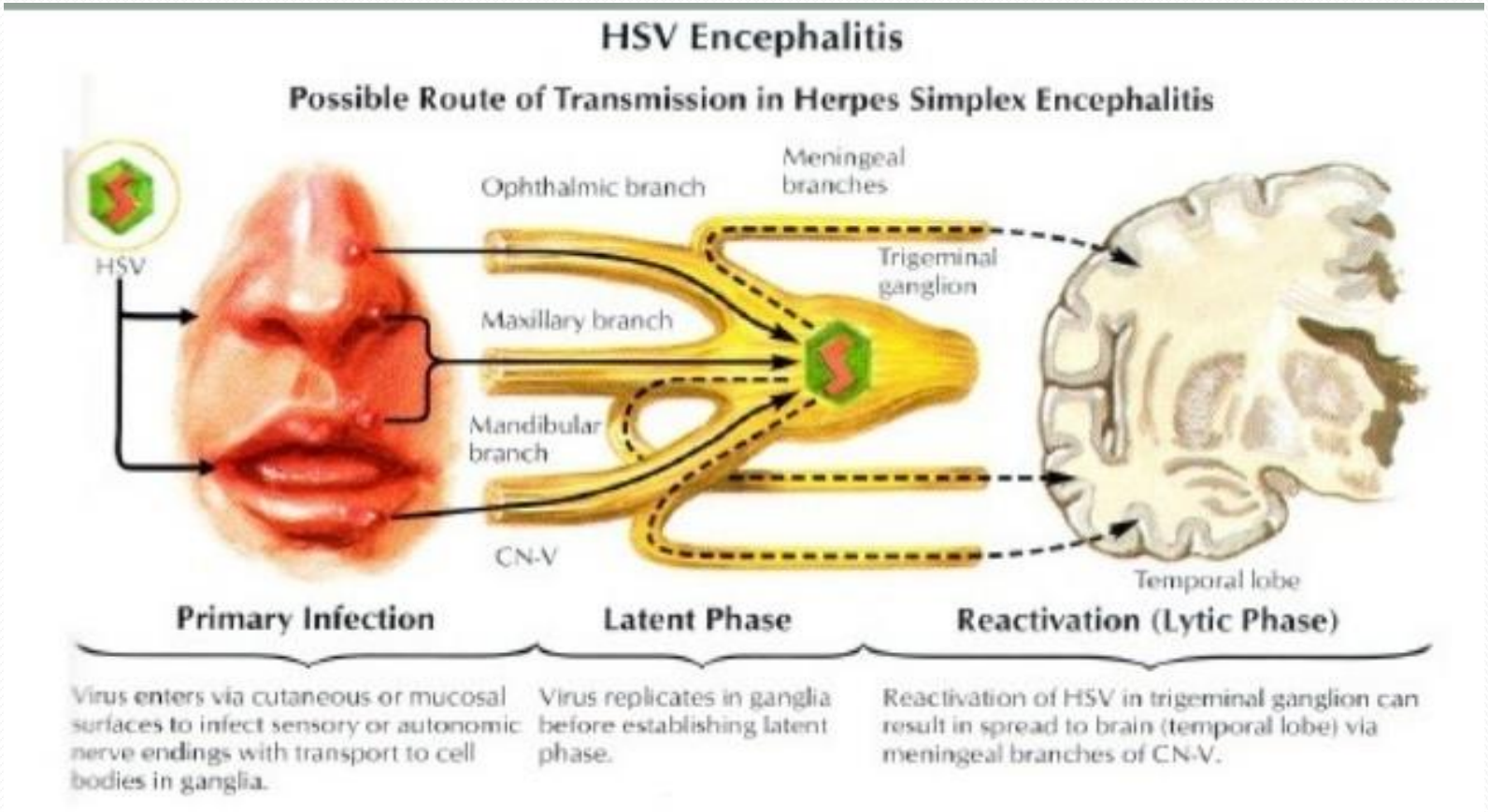
- Others

Herpes Simplex Encephalitis

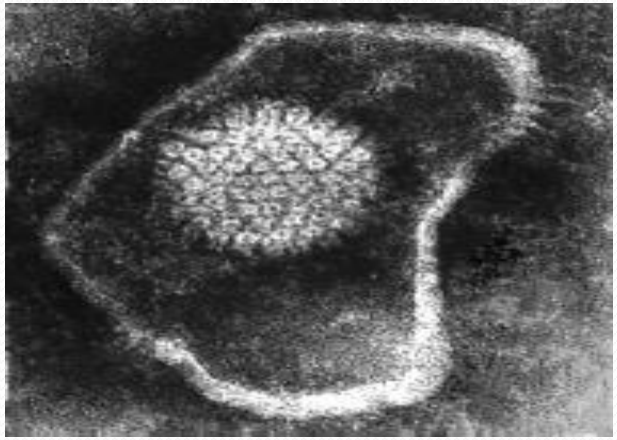


- Caused by;
  - Herpes simplex virus -1(HSV-1)

dsDNA , Enveloped , Icosahedral Virus



Herpes Simplex Encephalitis



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

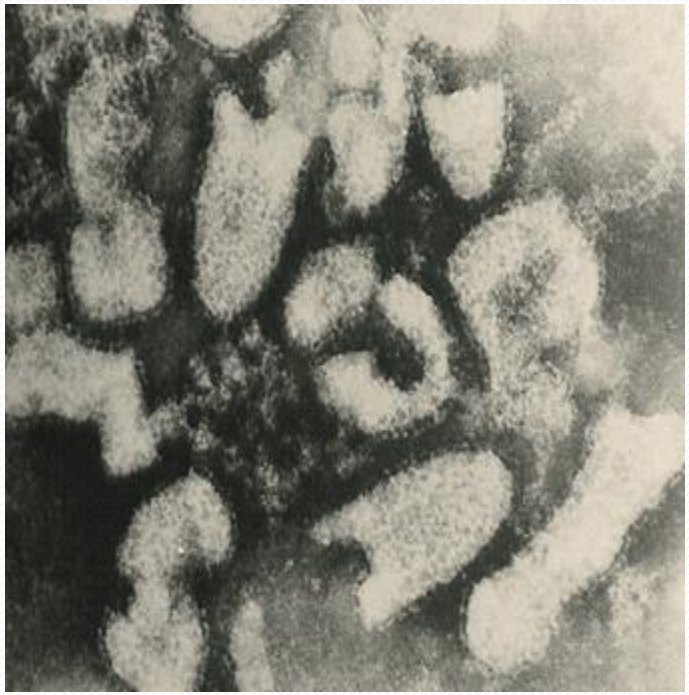
    dsDNA , Enveloped , Icosahedral Virus

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

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

  Acyclovir.

Rabies encephalitis



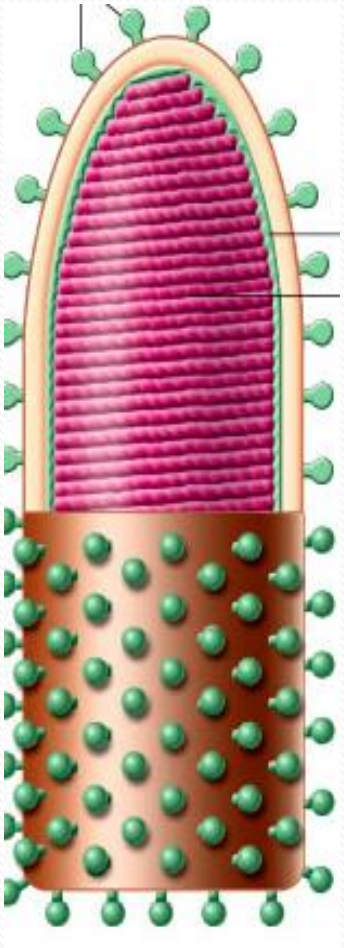
Rabies virus ;

Rhabdoviridae.

s.s (-)RNA genome,

Helical nucleocapsid,

Enveloped virus.



Bullet shaped virus

Pathogenesis;

Epidemiology;

Reservoir;

- Major;

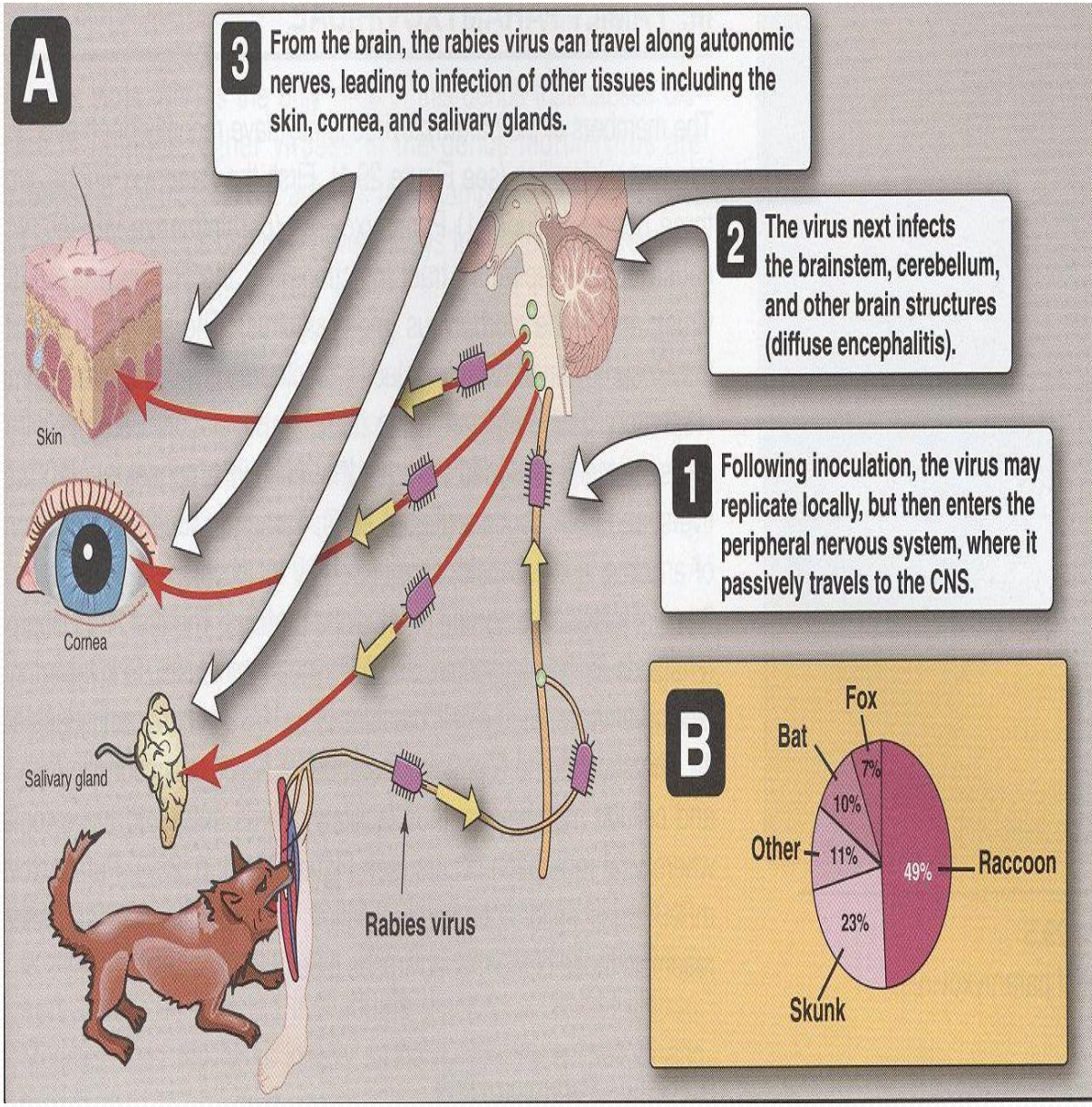
  Raccoons , Foxes, Wolves & bats.
- Imp ; cats & dogs

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 ,

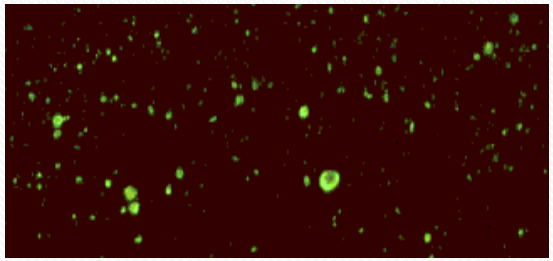
Convulsion ,coma & death .

2-Paralytic illness ; Ascending , Death , Bat.

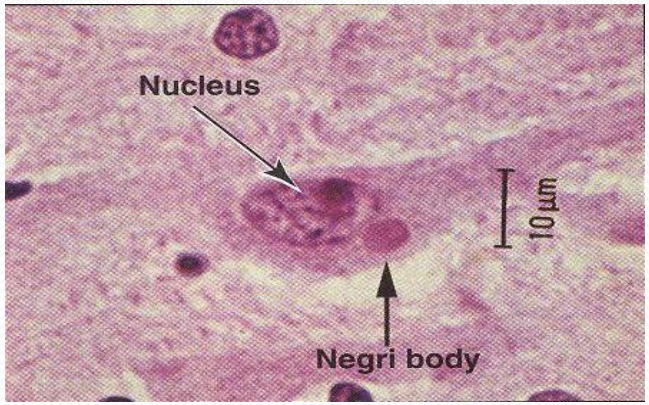
4- Recovery; Extremely rare

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 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

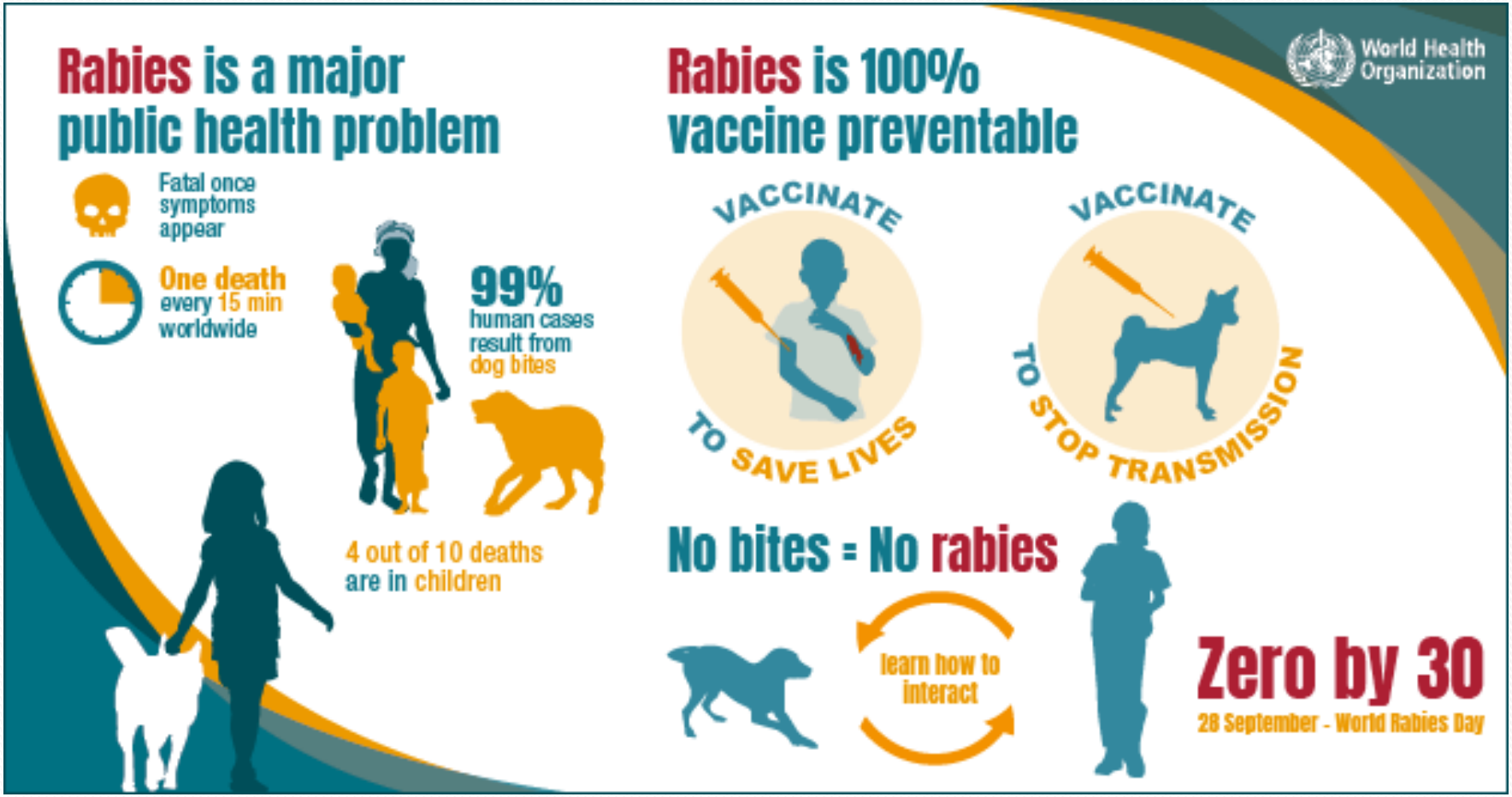
  e.g. vets, animal handlers etc.

- ***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


Rabies is a major public health problem
Fatal once symptoms appear
One death every 15 min worldwide
99% human cases result from dog bites
4 out of 10 deaths are in children
Rabies is 100% vaccine preventable
World Health Organization
VACCINATE TO SAVE LIVES
VACCINATE TO STOP TRANSMISSION
No bites = No rabies
learn how to interact
Zero by 30
28 September - World Rabies Day

Arthropod –borne Viruses

Arboviruses > 500 Vs

❖ Epidemiology:

Reservoir: Wild birds & Mammals

Vector: Mosquito, ticks& Sandfly

Transmission: bite of infected vector

❖ Infections

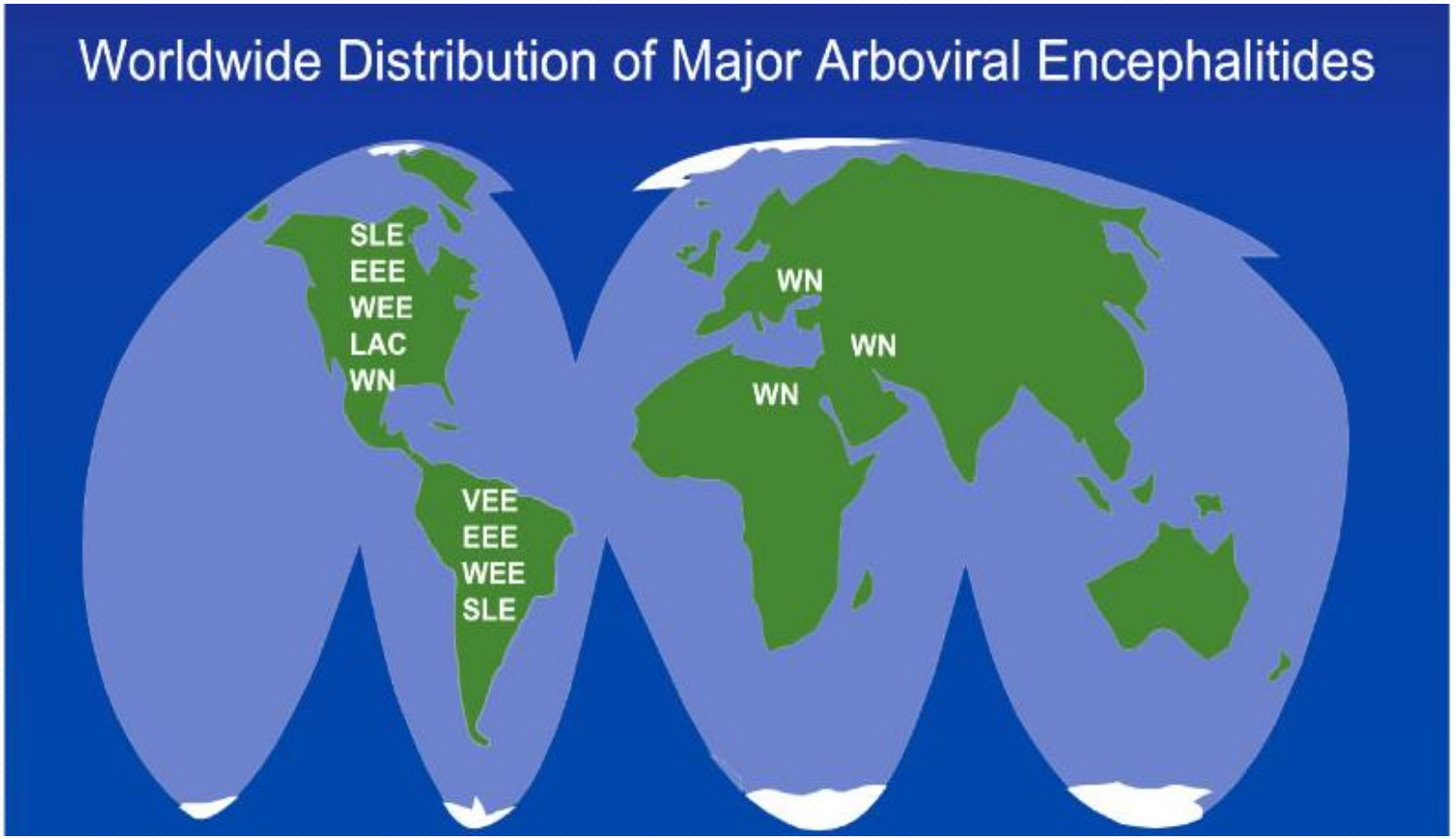
- Asymptomatic Infections*
- Diseases

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

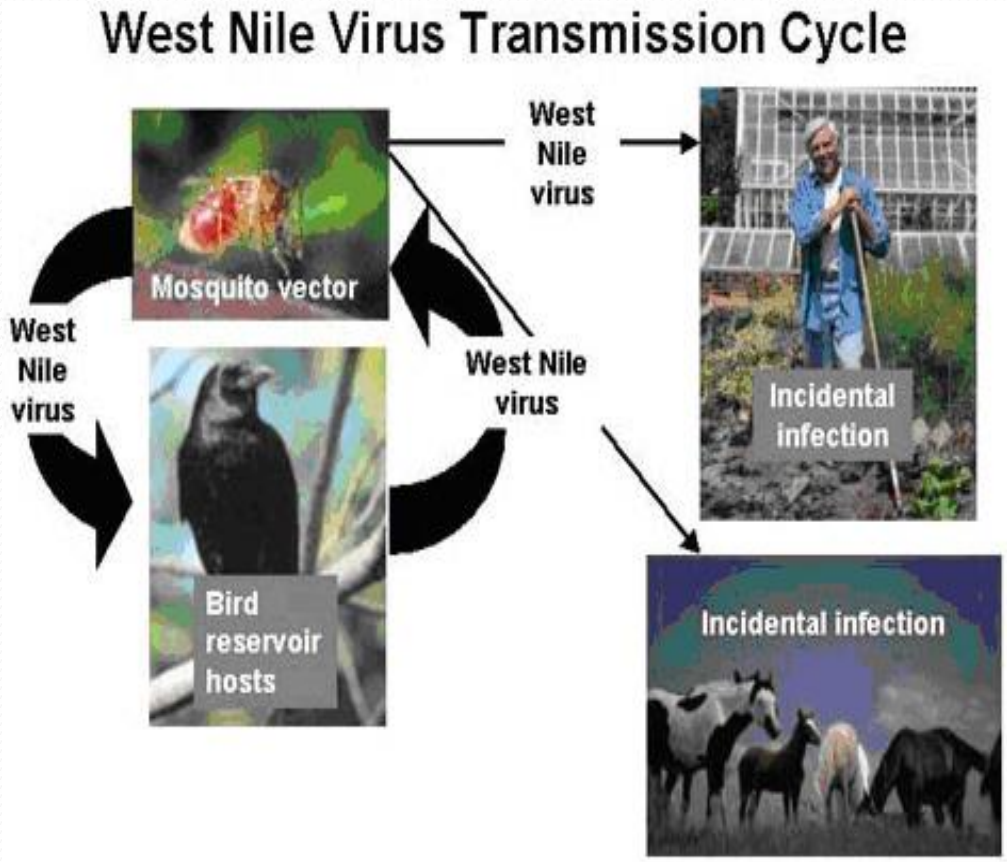
Worldwide Distribution of Major Arboviral Encephalitides

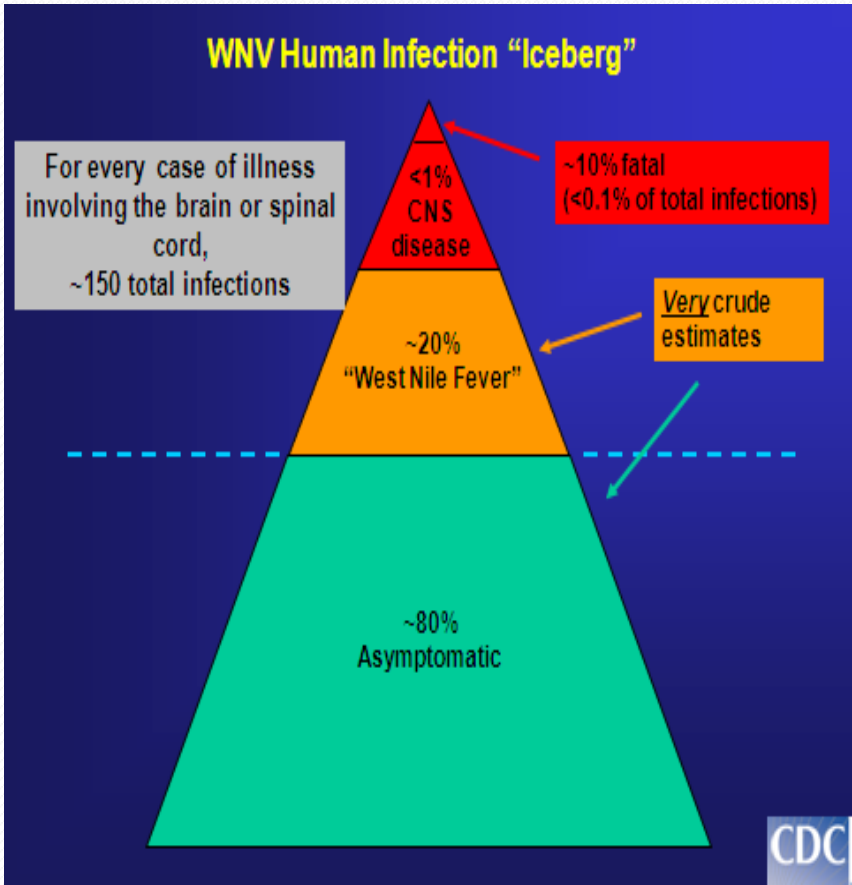


EEE: Eastern equine encephalitis
LAC: LaCrosse encephalitis
SLE: St. Louis encephalitis
WEE: Western equine encephalitis
WN: West Nile encephalitis
VEE: Venezuelan equine encephalitis

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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