



# Dr. M.G.R

## EDUCATIONAL AND RESEARCH INSTITUTE

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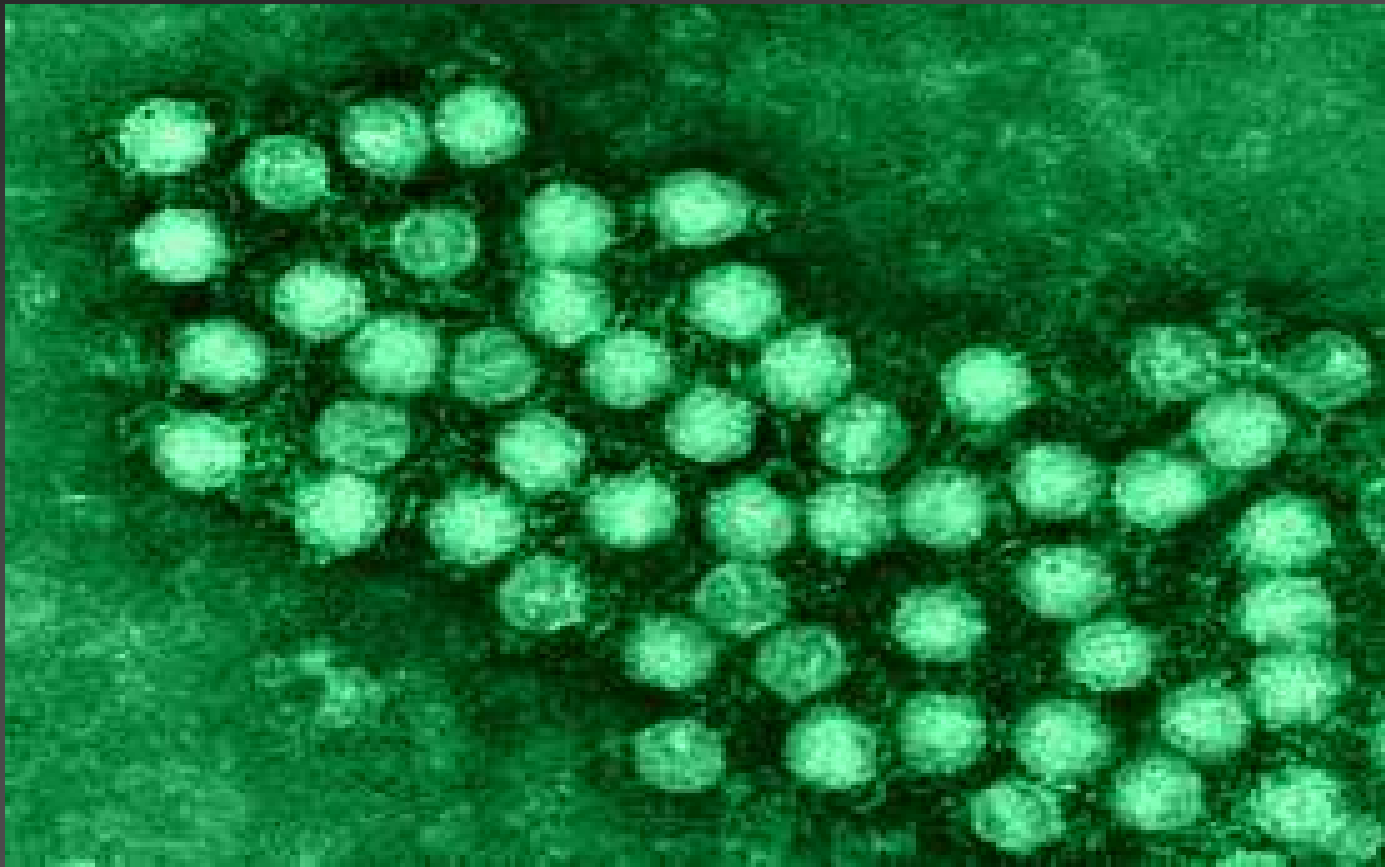
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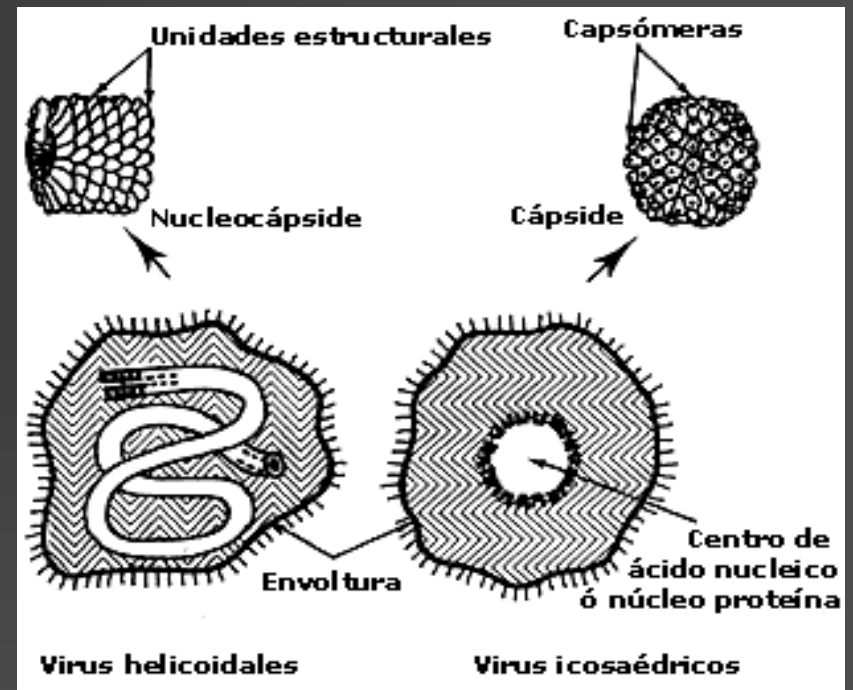


# PICORNA VIRUSES



# Characteristics

- Very small in size
- Icosohedral, non enveloped
- Single stranded RNA genome
- Resistant to fat solvents
- Susceptible to ionising radiation, formaldehyde and phenol

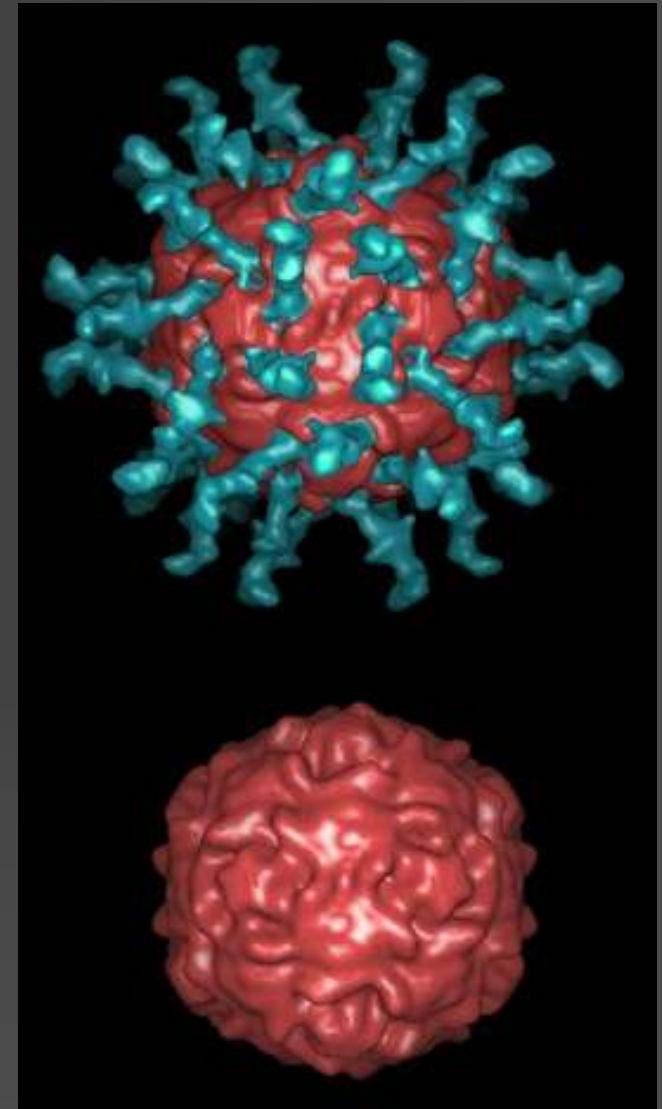


# Classification of Picorna viruses

- Aphtho viruses
- Cardio viruses
- Rhino viruses
- Entero viruses – Polio viruses 1-3
  - Coxsackie viruses A 1-24
  - Coxsackie viruses B 1-6
  - Echo viruses 1-34
  - Entero viruses 68-72

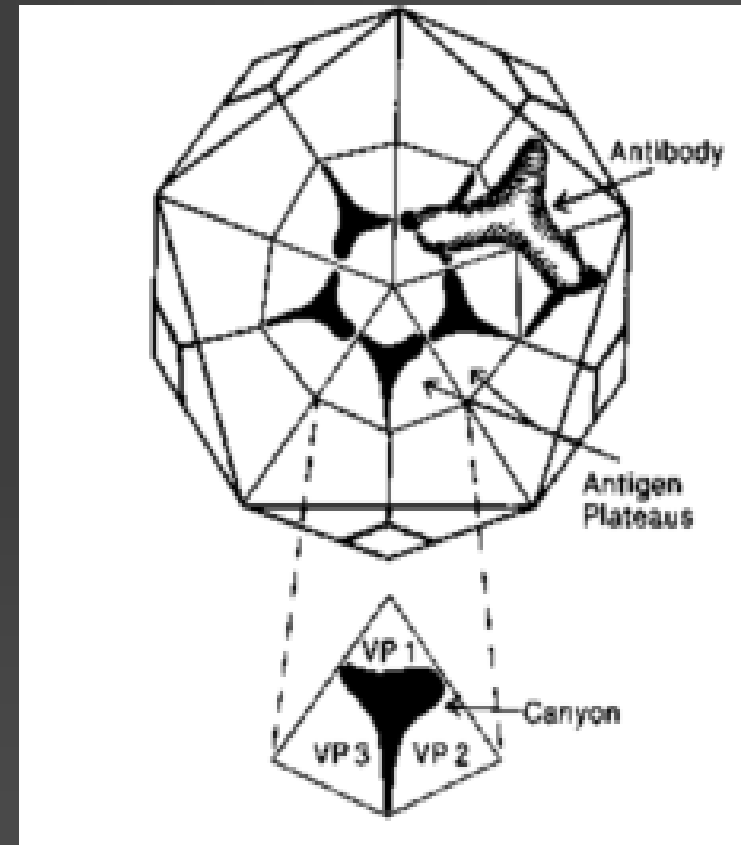
# Biology of Enteroviruses

- RNA genome of natural & attenuated polio & non polio enteroviruses sequenced
- 3' poly(A) nucleotide region confers infectivity
- Host cell susceptibility is determined by specific membrane receptors (glycoprotein)
- Rapid multiplication mapped in infected cells
  - Penetration,uncoating,
  - Release of RNA -10 mts
  - RNA synthesis - 30 mts
  - Progeny RNA - 2.5 hrs



# Biology of Enteroviruses ( Contd)

- Structural proteins VP1, VP2, VP3, VP4 make up the capsid shell
- VP1 has exposed epitopes inducing protective neutralising antibodies
- VP 2 and VP 3 partially exposed and antigenic
- Host protein and RNA synthesis severely compromised in 3 hrs.



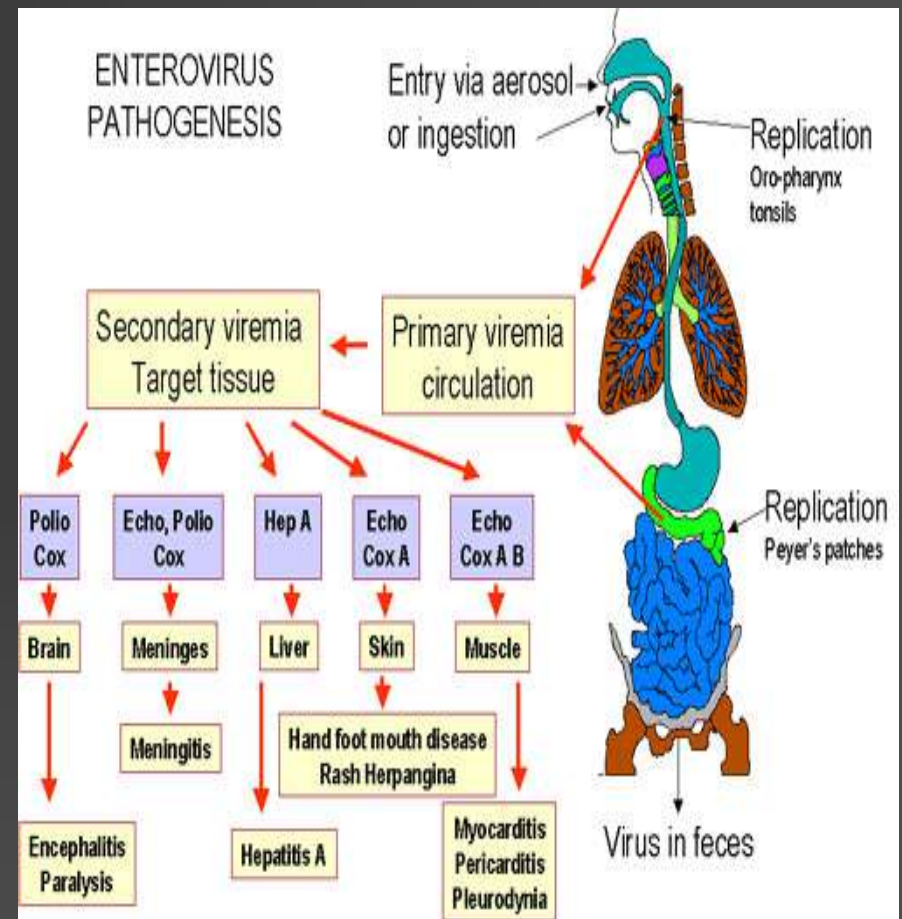
# Immunity and immune response

- Immunity is type specific – antibodies prevent virus implantation in GIT and dissemination to target organs
- Circulating antibodies prevent infection so passive immunity is possible
- Secretory Ig A, Ig M & Ig G produced.
- Antibodies secreted in colostrum and breast milk



# Epidemiology of Enteroviruses

- Distributed world wide –Endemic and epidemic behaviour
- Infections more common in children <15 yrs of low socioeconomic status
- All serotypes can exist simultaneously but one predominates
- Virus clustering common
- Transmission –Viral shedding from GIT
  - Faeco oral
  - Respiratory secretions
  - Fomites, fingers
  - Polio
  - Coxsackie
  - Enteroviruses





# Lab diagnosis of Enteroviral infections

- **Virus isolation** in cell culture – Gold standard .
- **Specimens** – CSF ,tissue ,blood, TW, stool.
- Multiple site sampling during acute phase increases recovery .
- **Cell lines** – Primary monkey kidney, human embryonic fibroblast, human rhabdomyosarcoma .
- Serotype identified by antiserum pools .
- **Antigen detection** – CIE ,ELISA PCR .
- **Antibody detection** –  
Microneutralisation (IgM assays) .  
Cross reactivity is a limiting factor .



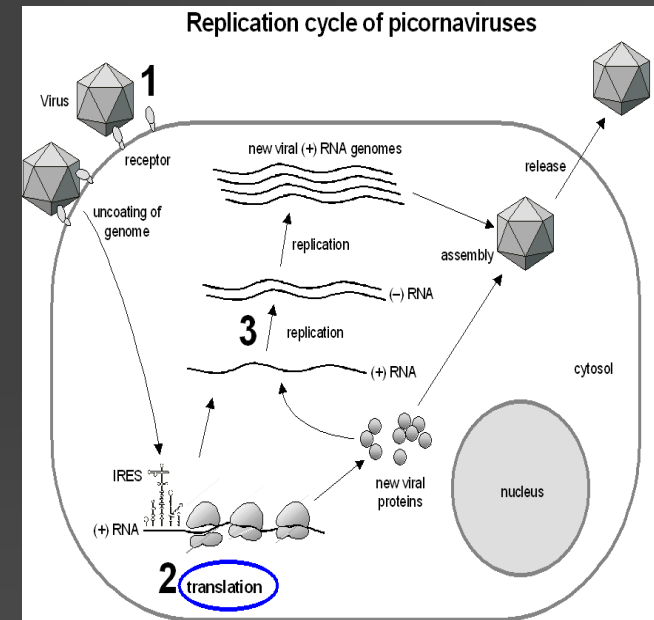
# History of poliovirus

- John Paul – First detailed record of poliomyelitis.
- 1840 – Sporadic cases documented .
- 1890 – Outbreaks in USA & Europe .
- 1909 – Landsteiner & Popper – Exp. transfer to animals.
- 1939 – Armstrong -Growth of virus in rodents .
- 1948 – Dalldorf -Coxsackie virus .
- 1949 – Weller ,Robbins-Viral growth in non neural cells .
- 1953 – Salk -Killed polio vaccine .
- 1962 – **Sabin** -Live attenuated vaccine



# Properties of polio virus

- Spherical ,27 nm diameter.
- ss RNA (Positive sense) .
- 4 virion proteins – VP1, VP2 , VP3 ,VP4 .
- Resistant to low pH & proteolytic enzymes.
- Resistant to 70% alcohol, 5% lysol ,ether & bile .
- Sensitive to 0.3% formaldehyde & chlorine.
- Survives refrigeration and freezing .

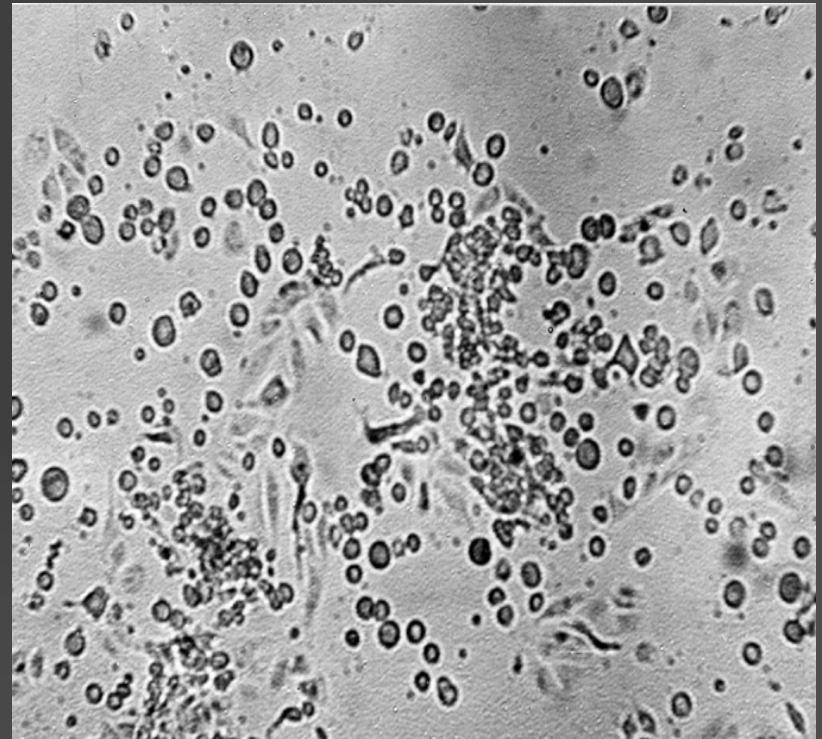


# Polio virus – Antigenic properties

- Types 1, 2 & 3 by neutralisation .
- ‘C’ antigen – Heated or coreless .
- ‘D’ antigen – Dense or native .
- Infection confers type specific life long immunity to disease but little or no immunity to infection or disease caused by heterologous serotype .
- Anti ‘D’ antibodies protective .
- Anti ‘C’ antibodies are non neutralising .

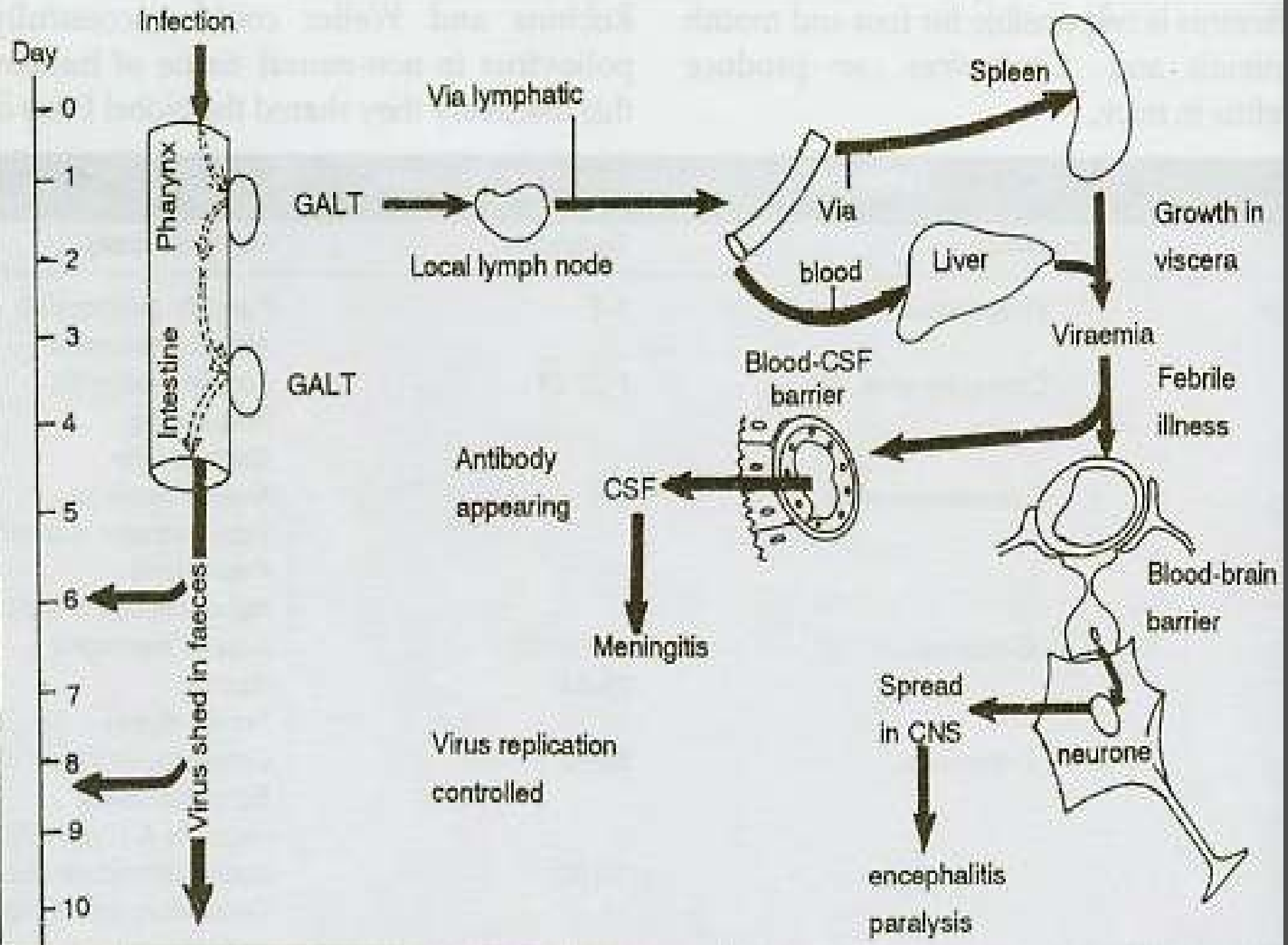
# Host range & virulence

- Human beings –natural hosts and primary reservoirs .
- Natural virus > 10 million fold neurovirulent.
- Paralysis production in humans requires much higher dose of virus than animals .
- Infectivity is maximal for human gut .
- Vaccine strains are less neurovirulent ,temp sensitive & exhibit subtle antigenic differences .
- **CPE in cell lines** –rounding up, pyknosis, refractility, eosinophilic intranuclear inclusions, plaque formations .



# Pathogenesis of polio

- Implantation & replication in gut and GALT .
- Viremia following spread to deep lymph nodes .
- **Minor viremia** –subclinical abortive illness .
- **Major viremia** –spread to spinal cord and brain.
- Spread to CNS also from muscle across peripheral nerves .
- **Pathology** –Motor and autonomic neurons .
- **Sites** –Gray matter of AHC ,Motor nuclei of pons & medulla .
- Clinical features depend on severity of lesions .
- **Fatal cases** –Brain stem & cranial nerves involved .
- Virus detectable in CNS till 1 week after onset of paralysis .





# Clinical features

- Inc. period- 9 to 12 days (5 – 35).
- Virus detectable in faeces before onset of illness.
- Most infections inapparent; abortive infections produce self limiting symptoms; non paralytic type produce meningeal signs.
- **Spinal paralytic poliomyelitis** occurs 1-3 days after minor illness. Characterised by intense muscle pain, meningeal symptoms and palsy .
- **Bulbar paralytic poliomyelitis** involves medulla and cranial nerves .
- **Polio encephalitis** characterised by seizures & spastic paralysis .

# Complications of Poliomyelitis

- Airway obstruction & respiratory failure.
- Myocarditis.
- GI bleed ,paralytic ileus ,gastric dilatation.
- UTI due to prolonged bed rest .



# Factors predisposing to CNS involvement

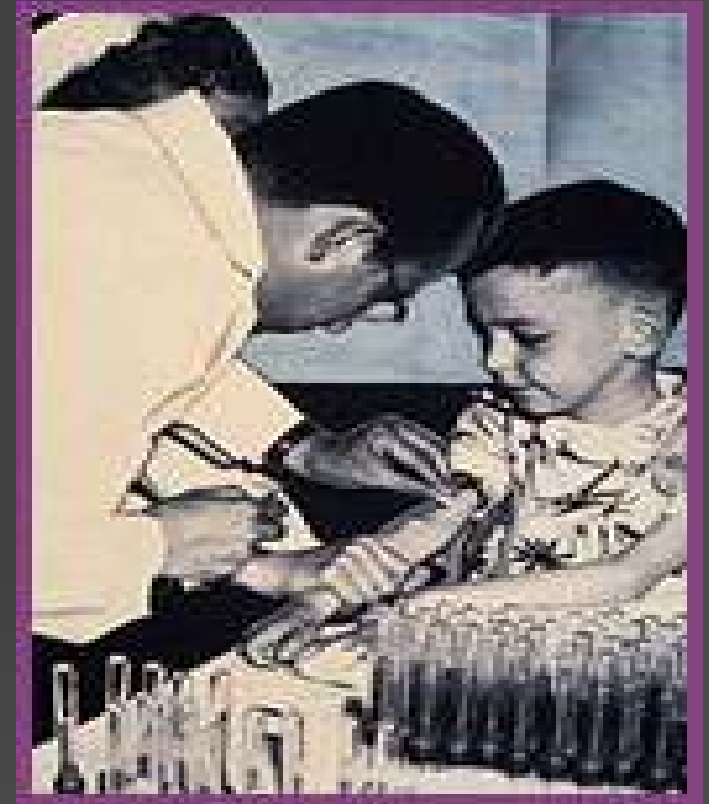
- Elderly age.
- Pregnancy.
- Trauma.
- Tonsillectomy.
- Stress and fatigue.
- Inoculations.
- Absence of antibody against polio virus.
- Gene on chromosome 19.

# Lab diagnosis of poliomyelitis

- **Isolation**- From throat secretions in first week of illness; from faeces for several weeks.
- Rarely isolated from CSF.
- **Specimen**- Appropriate processing (Centrifugation, Ether & antibiotic treatment).
- **Tissue culture inoculation**- PMK, RD .
- **Cytopathic effects** in 2-3 days .
- **Identification** by neutralisation with pooled specific sera .
- Virus isolation should always be interpreted with clinical findings.
- **Serodiagnosis**- Rise in antibody by NT and CFT.
- Antibodies appear with onset of paralysis.
- CF 'C' antibodies appear and disappear early .

# Prophylaxis of polio

- **Passive immunization**- gamma globulin in high risk cases only.  
Eg- Pregnancy.
- **Active immunization- Salk vaccine.**
  - Injectable formalin inactivated polio viruses 1,2,3 grown in monkey kidney cells.
  - Safe ,80-90% protective efficacy.
  - 3 doses 5-6 weeks apart.
  - Booster doses 3-5 years.  
(? Every year)
  - Enhanced potency vaccine from human diploid cell line.



# Sabin vaccine

- Live attenuated by repeated passage in rats
- No neurovirulence but set up intestinal infection
- Have stable genetic character and produce adequate immune response
- Wild strains differ from vaccine strains by growth at 40° C, poor growth in PMK, tolerance to low levels of bicarbonate and inactivation by specific antisera



# Oral polio vaccine in India

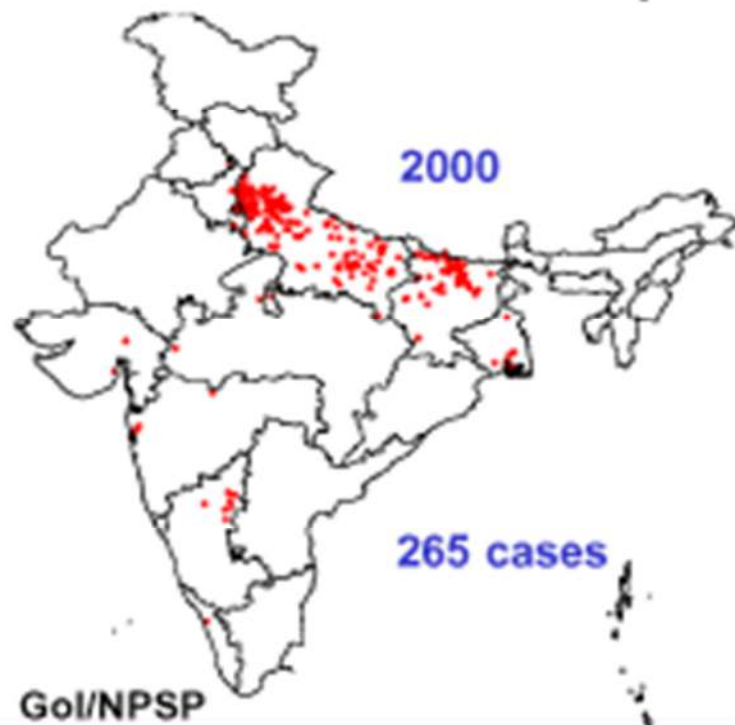
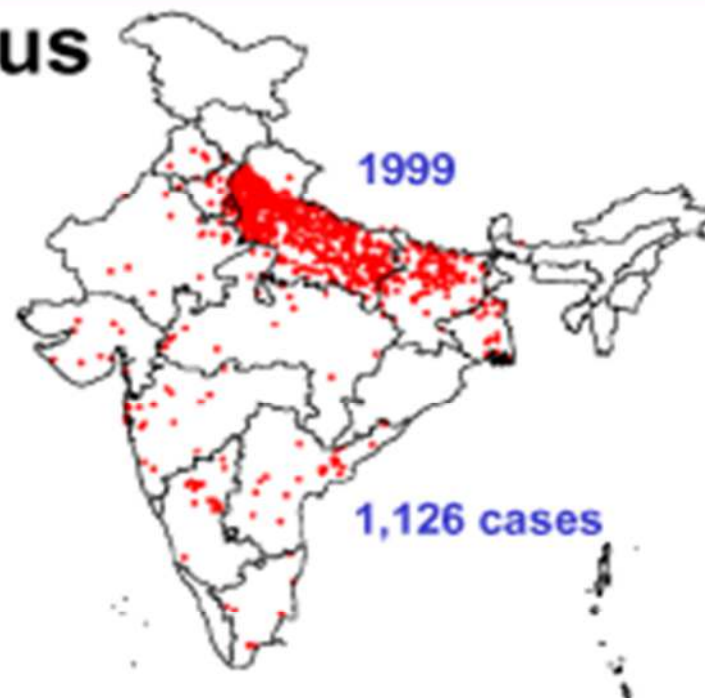
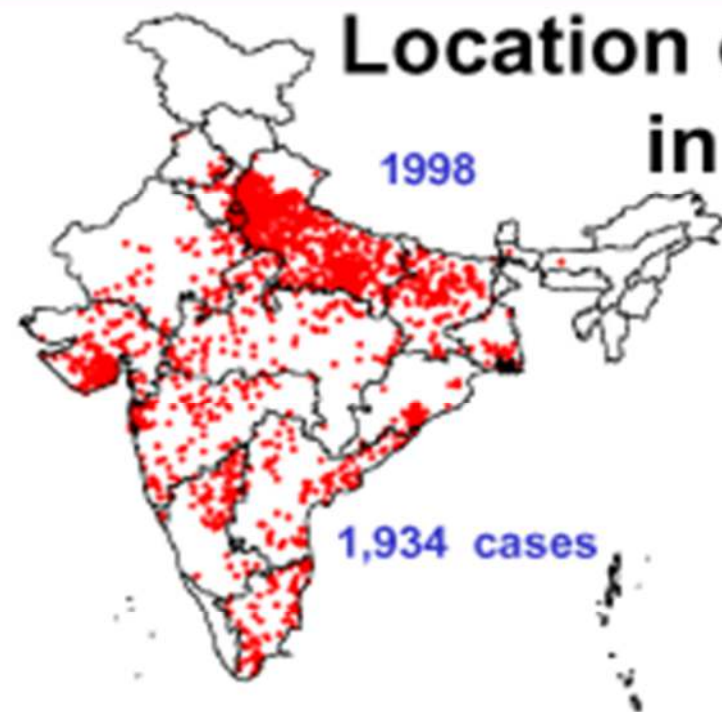
- Administered orally in monovalent or trivalent form
- Three doses 6 to 8 weeks apart ( 0.5 ml)
- Has 10 L type1 virus , 2 L type2 , 3 L type3 virus
- Stabilised by Mgcl<sub>2</sub>, stored at 4-8° C for 4 months and –20° C for 2 yrs
- Cannot be administered to immunosuppressed
- 90-100 % seroconversion with single dose
- Induces herd immunity
- Reasons for failure in tropical countries
  - Intestinal carriage of enteroviruses
  - Intestinal hypermotility due to diarrhoea
  - Neutralisation of strain by Ab in breast milk
  - Inhibitor substances in saliva



# Epidemiology of polio virus

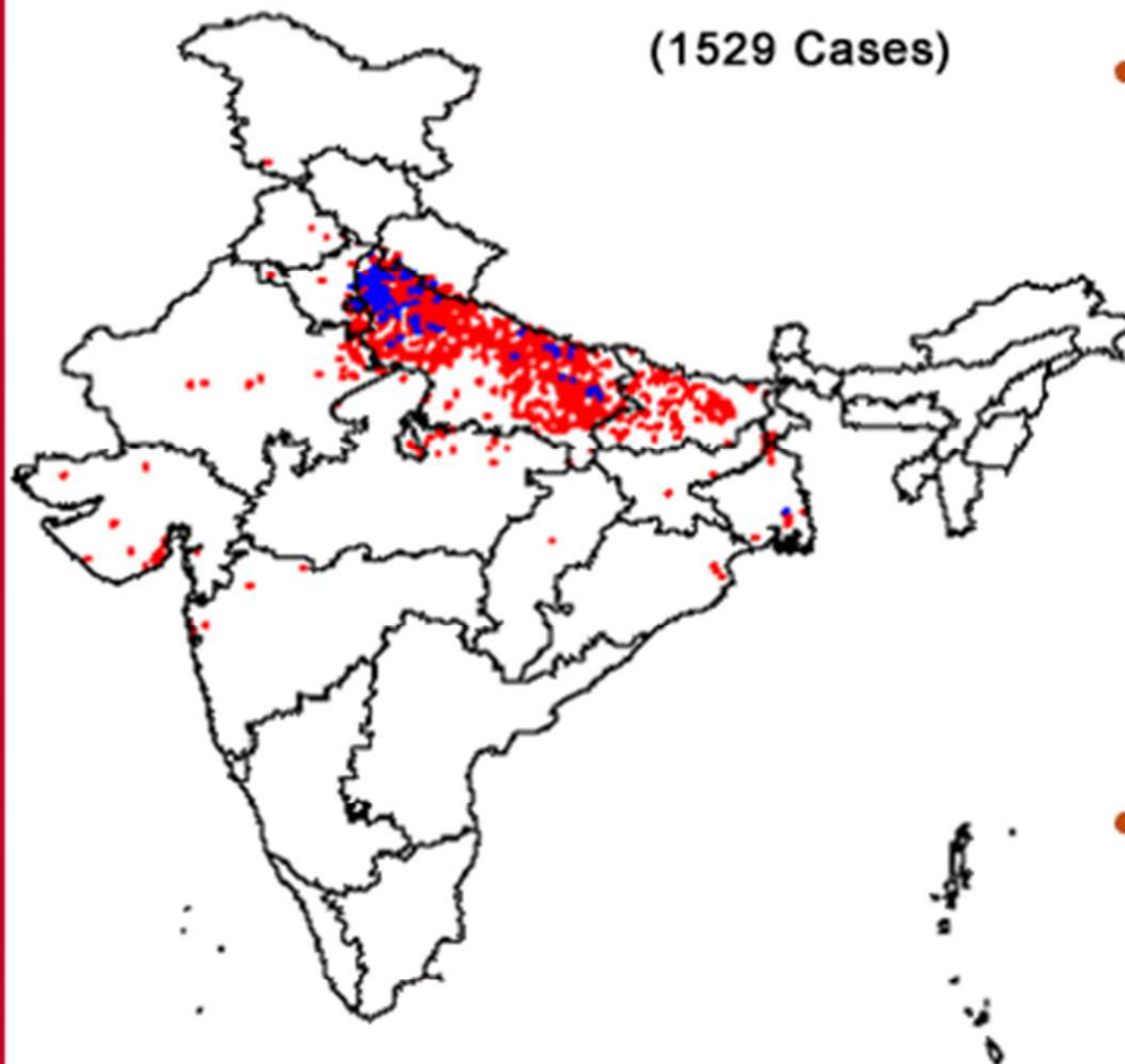
- Exclusive human disease
- Symptomless carrier state 1:1000
- Faecal shedding lasts for weeks to months
- Sewage main source of infection
- Droplet infection from throat also occur
- Outbreaks of infection depends on virulence of strain
- Most epidemics caused by type 1
- In India ,paralysis occurs with type 2
- Immunity is type specific but cross protection is seen
- Incidence directly related to living conditions

# Location of polio virus in India



# Wild Polio Virus in 2002

(1529 Cases)



## ● P1 Wild (1423 cases)\*\*

Uttar Pradesh  
Bihar  
West Bengal  
Haryana  
Rajasthan  
Gujarat  
Delhi  
Madhya Pradesh  
Jharkhand  
Uttaranchal  
Maharashtra  
Orissa  
Punjab  
Chandigarh  
Chattisgarh  
Jammu & Kashmir

## ● P3 Wild (109 cases)\*\*

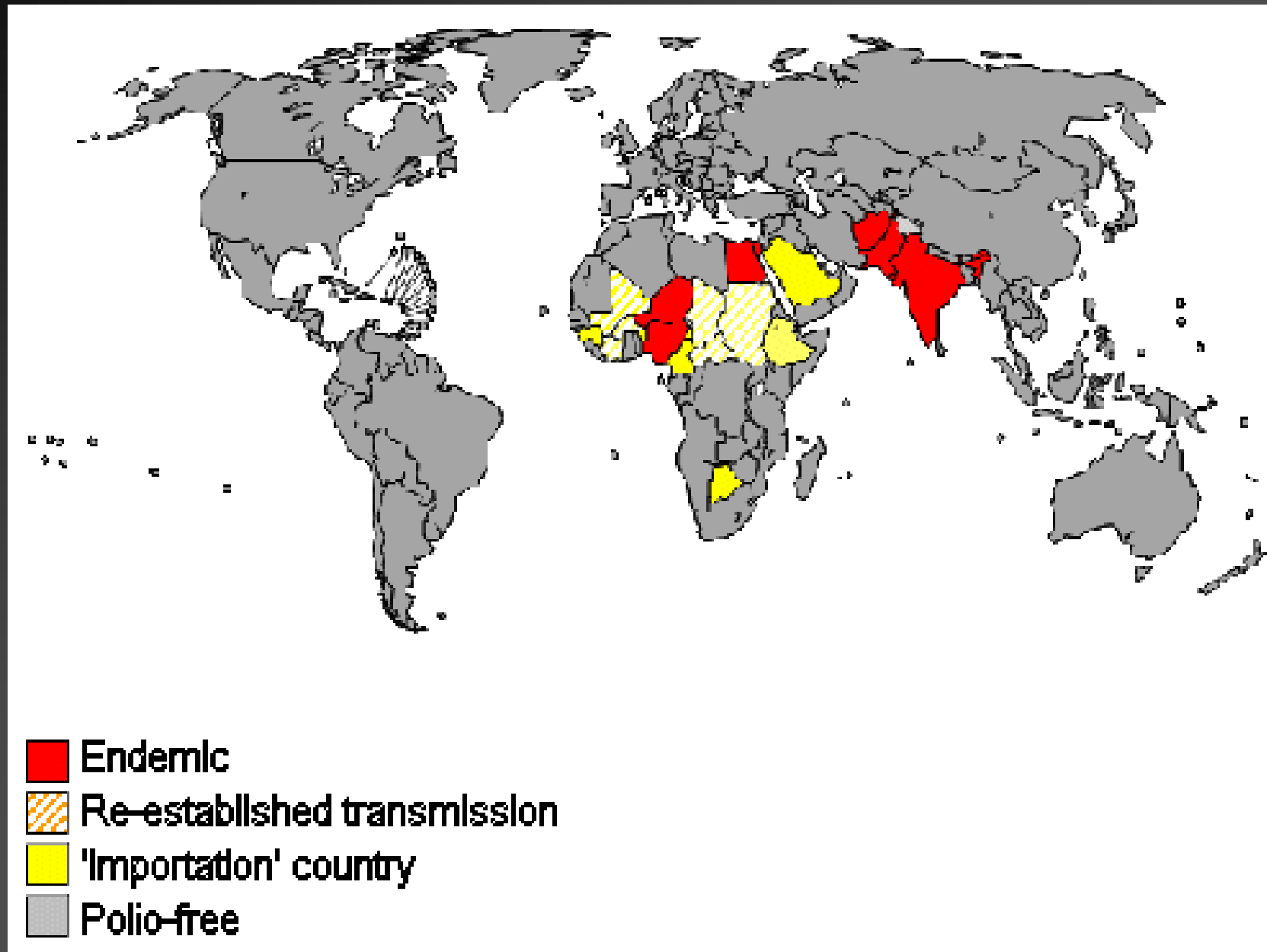
Uttar Pradesh  
Delhi  
Uttaranchal  
Haryana  
West Bengal

\*\* number includes 3 cases of P1 wild and P3 wild mixture  
GOL/NPSP ● data as on 18th January 2003

**Location of  
poliovirus,  
2003  
(194 cases)**

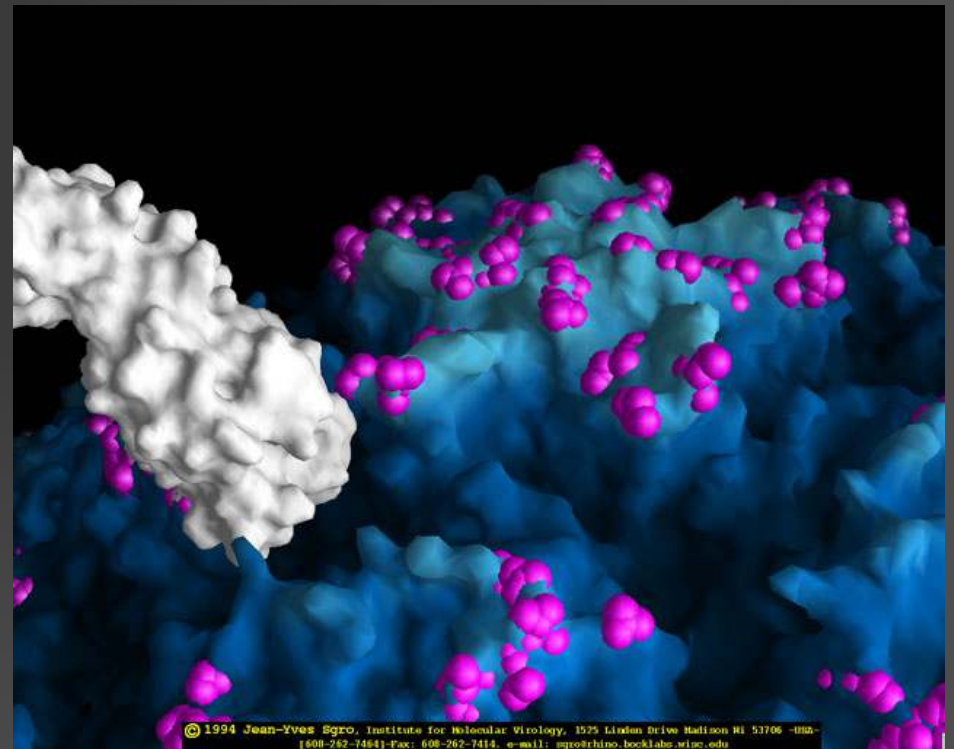


# Polio Global status 2004



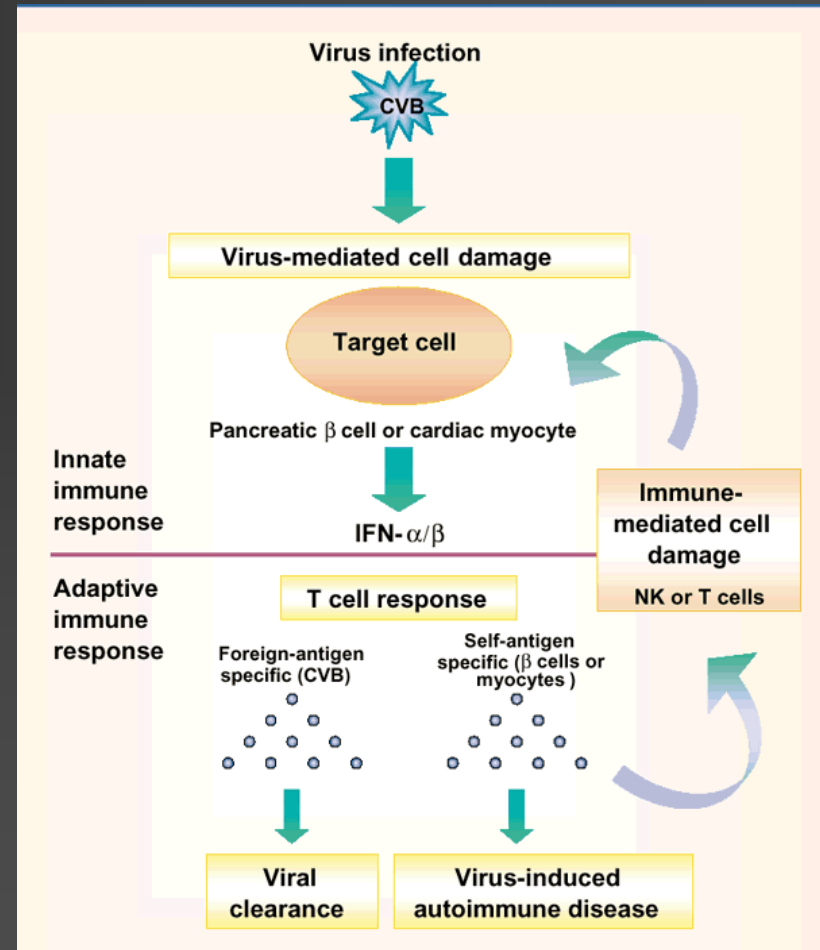
# Coxsackie viruses

- Classified as types A & B
- Type A cause flaccid paralysis and diffuse myositis in mice
- Type B cause spastic paralysis, focal myositis, hepatitis, myocarditis & pancreatitis in mice
- Isolation-Suckling mice and hamster; also in PMK and HeLa cells



# Coxsackie virus – clinical syndromes

- Herpangina
- Aseptic meningitis(A & B)
- Fever with rash ( A)
- Respiratory infections(A)
- Epidemic pleurodynia(B)
- Myocarditis,pericarditis(B)
- Juvenile diabetes(B4)
- Orchitis
- Transplacental & neonatal transmission



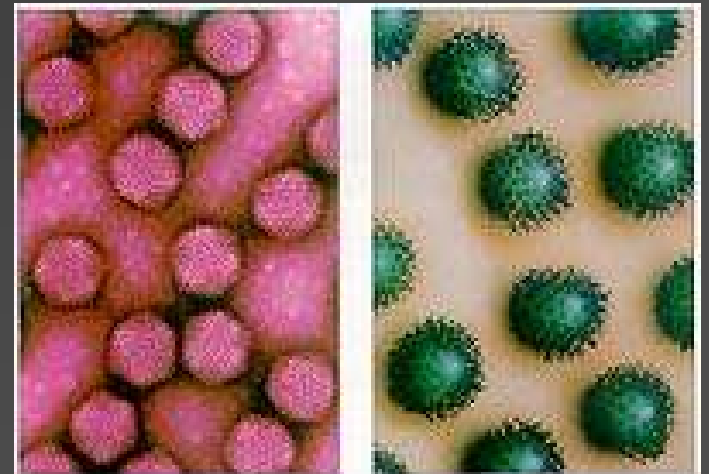


# Echo viruses

- Enteric Cytopathic Human Orphan Viruses
- Some agglutinate human RBC s
- Grow well in human & simian kidney cells with CPE
- Natural infection only in humans
- Clinical syndromes-Fever with rash,minor respiratory disease,gastroenteritis,hepatic necrosis
- Lab diagnosis by isolation from throat swab,stool,CSF; Identification with pooled antisera

# Rhino viruses

- Viruses of common cold
- Acid labile, heatstable
- Over 110 serotypes conferring type specific immunity
- Infection in humans, chimpanzees
- Infection by droplets, fomites, self inoculation, conjunctiva
- IP – 2 days
- Virus shedding short period



Cold Viruses

# New enteroviruses and human disease

- Serotype 68 - Pneumonia & bronchitis
- Serotype 69 - No known disease
- Serotype 70 – Haemorrhagic conjunctivitis
- Serotype 71 – Meningitis, Encephalitis
- Serotype 72 - Hepatitis A

Thank You!



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