ENTEROVIRUSES
Poliovirus

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Dr. Sulaiman Mahmoud Bani Abdel-Rahman

MBBS, Mutah university

MSC Medical Microbiology – University of Manchester

PhD Medical Virology - University of Manchester

Picornaviridae Family

- **Characteristics**
  - Small, 20-30 nm, icosahedral particles.
  - Non-enveloped ss-RNA.
  - They replicate in the cytoplasm.
- **Classification**
  - Nine genera.
  - Only five cause human diseases:

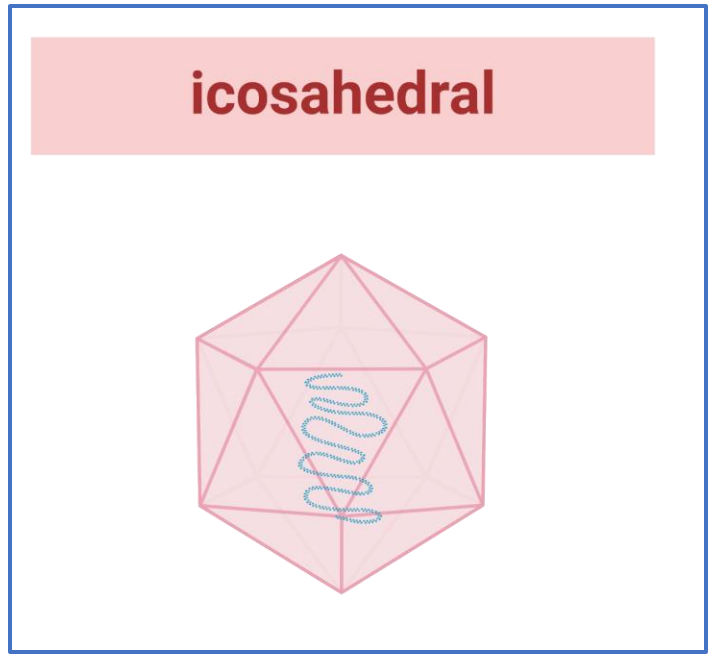
Genus *Enterovirus*	Polio, Coxsackie, Echo, & Enteroviruses	Human Pathogens
Genus *Rhinovirus*	Rhinoviruses	
Genus *Hepatovirus*	Hepatitis A virus	
Genus *Parechovirus*	Human Parechoviruses 1 & 2	
Genus *Kobuvirus*	Aichi virus	
Genus *Erbovirus*	Equine Rhinitis B viruses 1 & 2	
Genus *Cardiovirus*	EMCV, Theiler's viruses	
Genus *Aphthovirus*	FMDV	
Genus *Teschovirus*	Porcine teschoviruses 1-10	

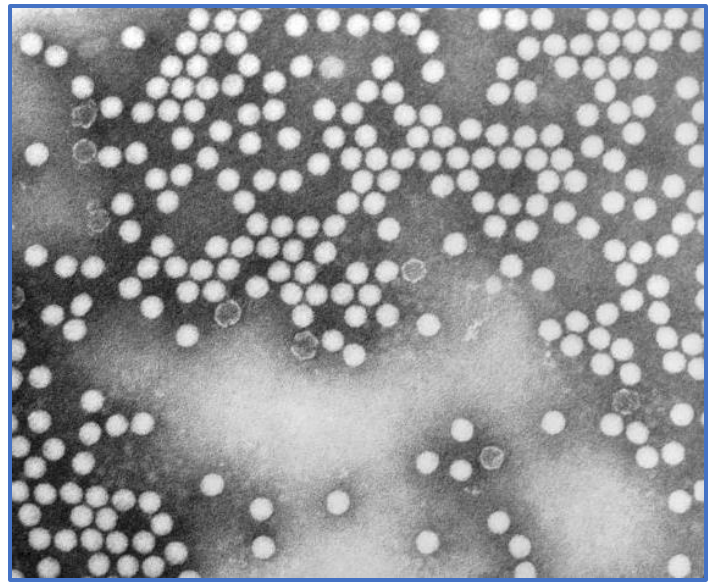
Introduction to Enteroviruses
Classification

- Family: Picornaviridae
- Enteroviruses Include:
  - Polioviruses (3 serotypes)
  - Coxsackie A viruses (over 20 serotypes)
  - Coxsackie B viruses (6 serotypes)
  - Echoviruses (31 serotypes)
  - Other Enterovirus types (e.g., Enterovirus 68–71)

Introduction to Enteroviruses
Basic Characteristics

- Small, non-enveloped viruses (20-30 nm)
- Single-stranded RNA viruses (positive polarity)
- Icosahedral symmetry
- Stable in acidic pH
- Replicate in cytoplasm
- Commonly transmitted via the fecal–oral route
- They shed in stool
- They cause neurological and non-neurological diseases

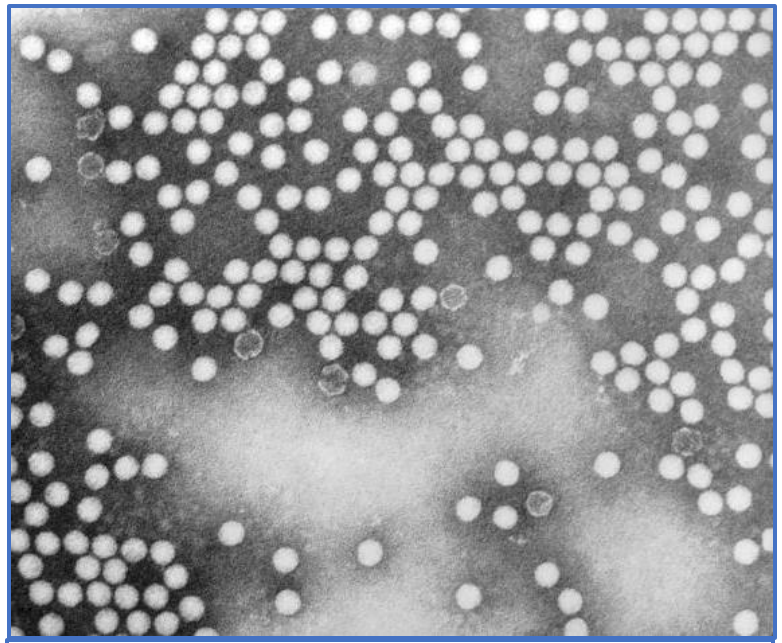




VIRUS	SEROTYPES	CLINICAL DISEASES
Polioviruses	3 types	Asymptomatic infection, viral meningitis, paralytic disease, poliomyelitis
Coxsackie A viruses	23 types (A1-A22, A24)	Viral meningitis plus, rash, ARD, myocarditis, orchitis
Coxsackie B viruses	6 types (B1-B6)	Viral meningitis, but no orchitis
Echoviruses	32 types	Viral meningitis, with orchitis
Other Enteroviruses	4 types(68-71)	Viral meningitis

Poliovirus Introduction

- **Structure:**
  - Small (25–30 nm), non-enveloped, icosahedral capsid
- **Genomic Material:**
  - Single-stranded, positive-sense RNA
- **Stability:**
  - Resistant to acidic pH, enabling survival in the gastrointestinal tract
- **Replication:**
  - Occurs in the cytoplasm of host cells



A transmission electron microscopic (TEM) image depicting numerous, round, poliovirus virions, which measure approximately 30 nm in diameter and exhibit icosahedral symmetry

Poliovirus Transmission

Following the beginning of infection, poliovirus multiplies in the intestine and is shed in feces. Transmission is typically person-to-person but can also result from ingestion of contaminated food and/or water.

- **Transmission Route:**
  - Fecal–oral pathway (contaminated water, food, and contact)
  - Respiratory droplets (rare)
  - Conjunctival contact (rare)
- **Primary Replication Sites:**
  - Gut and oropharynx
- **Shedding:**
  - Virus excretion in stool, contributing to widespread transmission
- **Incubation time**
  - 7–14 days

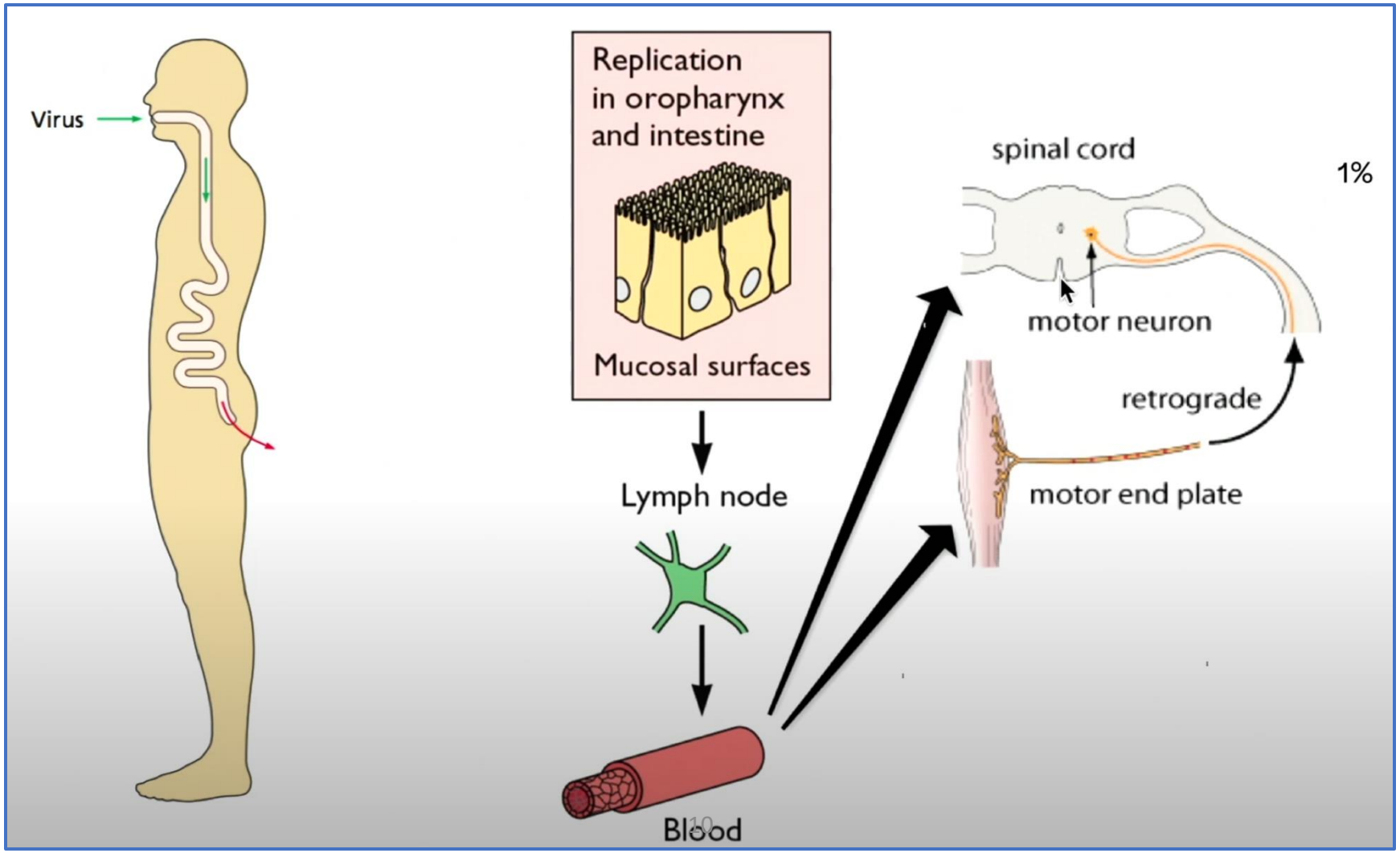
Poliovirus
Clinically relevant species

- Poliomyelitis is caused by 3 serotypes of poliovirus:
  - Wild type 1 (most common and most virulent)
  - Wild types 2 and 3 (considered eradicated)

Poliovirus
Epidemiology

- Poliovirus has been eradicated in most countries because of extensive vaccination efforts.
- Endemic countries include:
  - Pakistan
  - Afghanistan

Poliovirus
Pathophysiology



Poliovirus
Pathophysiology - 1

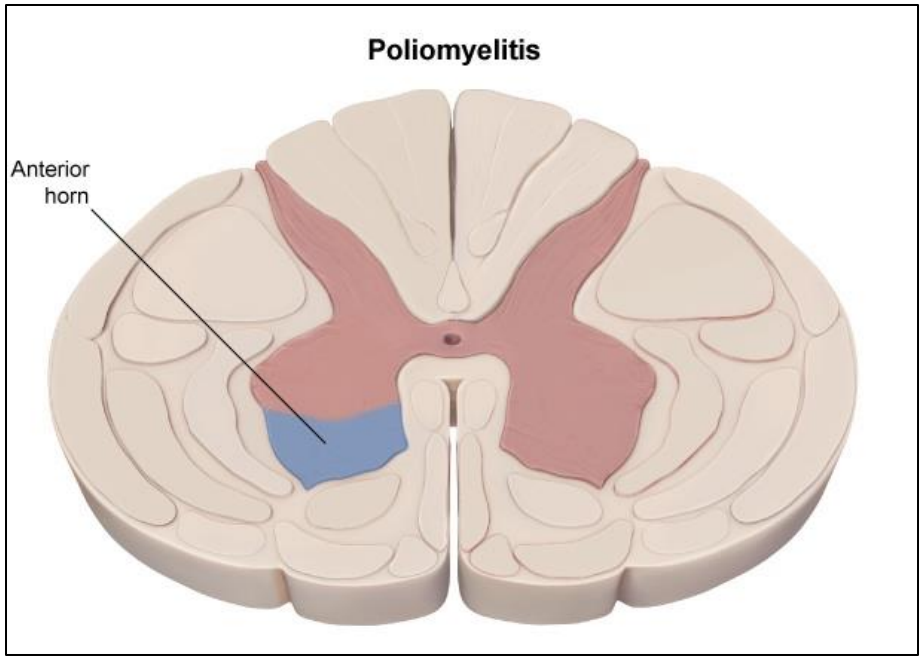
- The infection begins when the virus is ingested, its primary areas of multiplication are the throat and small intestine. This accounts for the initial sore throat and nausea.
- **Multiply locally:** They multiply in intestinal epithelial cells, submucosal lymphoid tissues, tonsils and Peyer's patches
- **Receptor:** Viral entry into the host cells is mediated by binding to CD155 receptors present on the host cell surface

Poliovirus
Pathophysiology - 2

- **Spread to CNS/spinal cord:**
  - **Hematogenous spread (most common):** Virus spreads to the regional lymph nodes and spills over to the bloodstream (primary viremia). After further multiplying in the reticuloendothelial system, the virus enters the bloodstream again, causing secondary viremia. Then it is carried to the spinal cord and brain
  - **Neural spread:** Virus may also spread directly through nerves. This occurs especially following tonsillectomy where the virus may spread via glossopharyngeal nerve present in the tonsillar fossa.

Poliovirus
Pathophysiology - 3

- **Site of action:** The final target site for poliovirus is the motor nerve ending, i.e. anterior horn cells of the spinal cord which leads to muscle weakness and flaccid paralysis
- **Neuron degeneration:** Virus-infected neurons undergo degeneration.



Poliovirus
Clinical features

- Most of infections with poliovirus are asymptomatic.
- Clinical infections, which typically present with flu-like symptoms, occur in a small percentage of cases.
- Less than 1% of infected individuals develop paralysis.
- Could result in
  - Poliomyelitis **without** CNS involvement (abortive poliomyelitis)
  - Poliomyelitis **with** CNS involvement
    - Nonparalytic poliomyelitis: aseptic meningitic form
    - Paralytic poliomyelitis

Poliovirus
Clinical features

The manifestations may range from asymptomatic stage to the most severe paralytic stage.

1. **Inapparent infection:** Following infection, the majority (91-96%) of cases are asymptomatic
2. **Abortive infection (without CNS involvement):**
   - About 5% of patients develop minor symptoms such as fever, malaise, sore throat, anorexia, myalgia, and headache for 1–3 days
   - Complete recovery without complications or transition to poliomyelitis

Poliovirus
Clinical features

3. Nonparalytic poliomyelitis

- Poliomyelitis with CNS involvement - presented as aseptic meningitis
- Fever, neck stiffness, headache, vomiting, muscle pain
- No paresis

Poliovirus
Clinical features

Tripod sign

4. Paralytic poliomyelitis

- The least common form (<1%) among all the stages
- Poliomyelitis with CNS involvement
- It is characterized by descending asymmetric acute flaccid paralysis (AFP)
- Proximal muscles are affected earlier than the distal muscles; paralysis starts at hip → proceeds towards extremities; which leads to the characteristic tripod sign (child sits with flexed hip, both arms are extended towards the back for support)

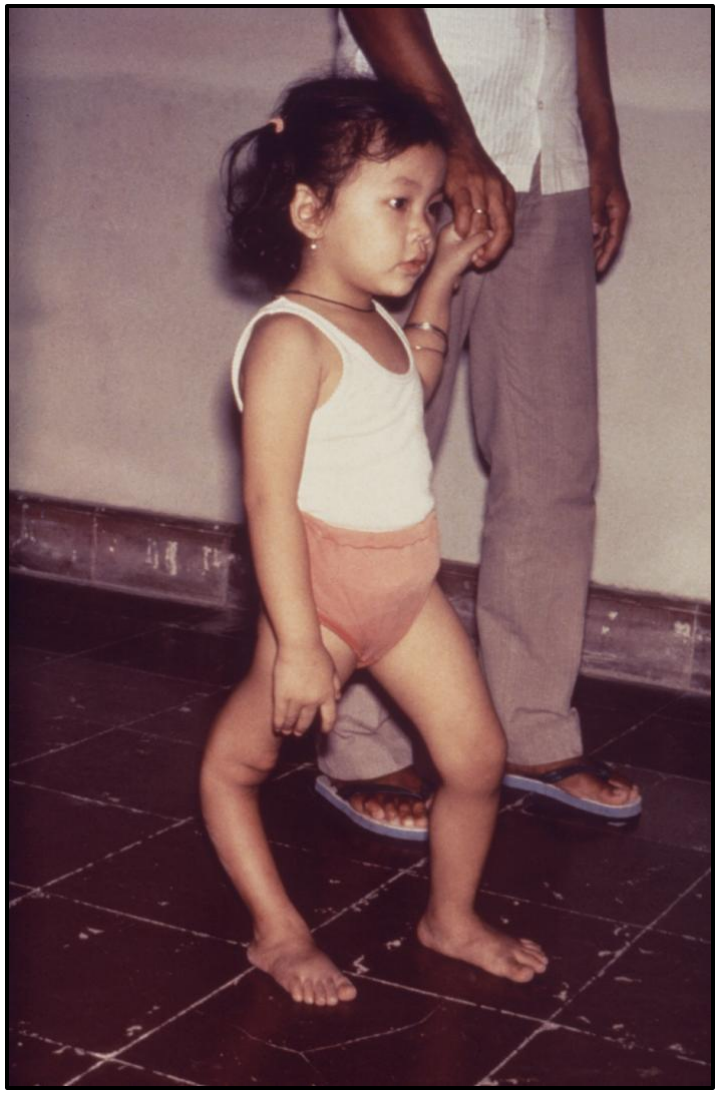
Poliovirus
Clinical features

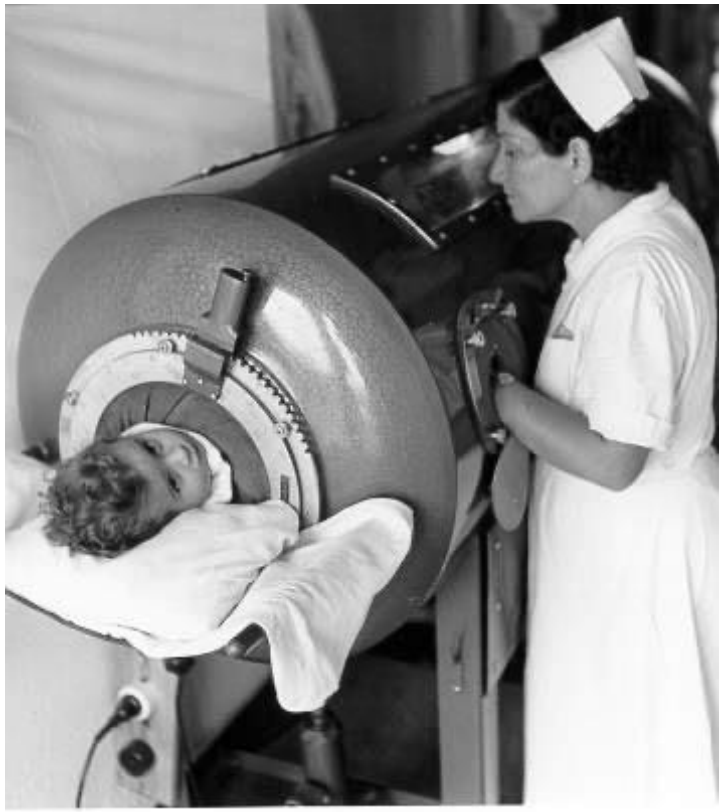
4. Paralytic poliomyelitis (cont.)

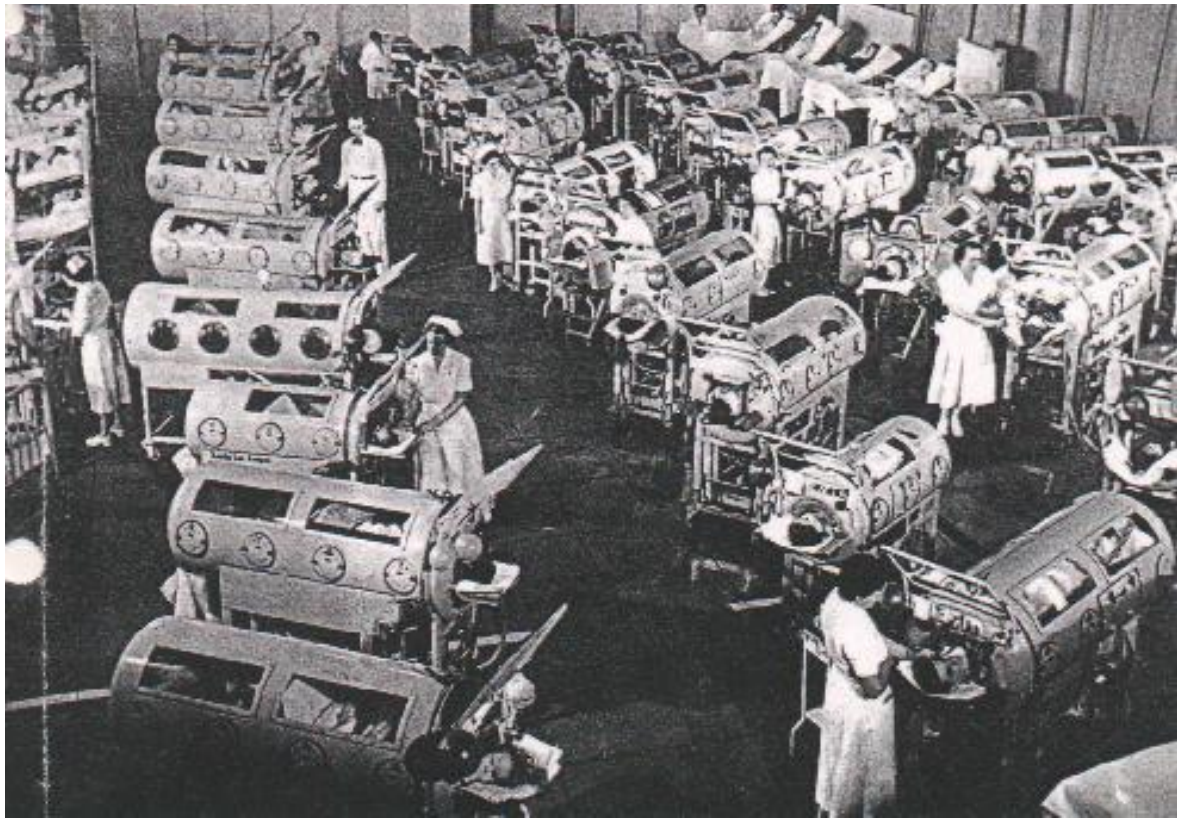
- **Sites involved** can be spinal, bulbospinal and bulbar. Accordingly, the nature of paralysis varies (e.g. respiratory insufficiency or dysphagia are common in bulbar involvement)
  - Bulbar form with brain stem involvement (rare): damage to the cerebral or autonomic nerve centers (cranial nerves and respiratory center) → central respiratory paralysis
- **Biphasic course:** In children, the disease progression is typically biphasic; aseptic meningitis occurs first → recovery → return of fever with paralytic features 1-2 days later
- Muscle atrophy

Poliovirus
Paralytic poliomyelitis

- A young girl with a deformity of the right lower extremity as a consequence of paralysis from paralytic poliovirus infection







It is theorized that the Roman Emperor Claudius was stricken as a child, and this caused him to walk with a limp for the rest of his life.

An Egyptian stele thought to represent a person with polio.

Poliovirus
Postpolio syndrome

A recrudescence (تجدد) of paralysis and muscle wasting has been observed in individuals, usually decades (20-40 years) after the episode of paralytic poliomyelitis.

Poliovirus
Diagnosis

- Diagnosis is based on clinical presentation and supported by the diagnostic workup.
- **Lumbar puncture:**
  - Often done in the setting of aseptic meningitis. Findings include:
    - Moderate pleocytosis, ↑ Protein, Normal glucose
- **Specific testing:**
  - Viral culture
    - Viral isolation in stool: gold standard
    - Can also be performed with throat secretions/swabs
  - PCR
  - Serology

Poliovirus Management

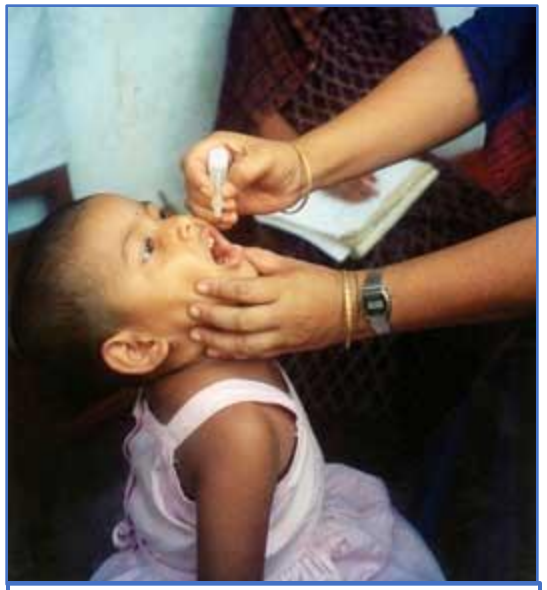
- There is no effective antiviral therapy for poliomyelitis. Management is supportive.
  - Close hemodynamic monitoring for patients with bulbar involvement
  - Mechanical ventilation for respiratory failure or airway protection (Poliomyelitis with bulbar involvement can cause autonomic dysfunction.)
  - Analgesics for pain
  - Splints to prevent deformities

Poliovirus
Prognosis

- Patients with nonparalytic poliomyelitis make complete recoveries. For those with paralytic poliomyelitis:
  - 2 out of 3 patients will not regain full strength.
  - 30%–40% will develop postpoliomyelitis syndrome.
  - Mortality:
    - 4%–6%
    - 10%–20% in adults or bulbar disease

Poliovirus Prevention

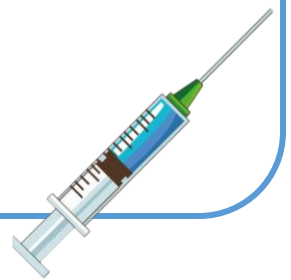
- There is no cure for polio; it can only be prevented. There are three different serotypes of the poliovirus: types 1, 2, and 3. Immunity must be provided for all three.
- There are 2 vaccines used:



A young girl receiving the oral poliovirus vaccine

Salk (inactivated poliovirus vaccine):

- Killed
- Given parenterally (injection)
- Forms only IgG antibodies, not IgA



Sabin (oral poliovirus vaccine):

- Live attenuated
- Creates IgG and IgA
- Not used in the United States
- Patients shed the virus → may be able to mutate and circulate

Poliovirus Vaccines

- **IPV**
  - IPV is much safer than oral polio vaccine (OPV), safer even in immunocompromised people
  - It does not cause vaccine-associated paralytic polio (VAPP)
  - It does not provide herd immunity: Being inactivated vaccine, it cannot spread by feco-oral route
  - It is not useful during epidemics; as there is no community protection.
  - It does not induce mucosal IgA production, hence, the local immunity is absent
  - It is relatively expensive than OPV

Poliovirus Vaccines

- **OPV**
  - **Herd immunity:** OPV strains being live, can shed in the feces and spread in the community by feco-oral route, hence, it can induce herd immunity. It can provide both individual and community protection
  - OPV is the vaccine of choice during epidemics
  - **Local immunity:** OPV induces mucosal IgA production, hence provides local or mucosal immunity
  - Cheaper than IPV
  - Easy to administer (given by oral route)
  - **Safety:** OPV is otherwise safe, but it is risky to give in immunocompromized people, during pregnancy, and in old age
  - OPV can cause vaccine-associated paralytic poliomyelitis (VAPP) and vaccine-derived polioviruses (VDPV) (described in next slides).

Vaccine-Associated Paralytic Poliomyelitis (VAPP) vs. Vaccine-Derived Poliovirus (VDPV)

- **Simple Comparison**
- **VAPP**: One person, directly from the vaccine, no spread to community
- **VDPV**: Many people, evolved vaccine virus, spreads through community

Feature	VAPP	VDPV
Definition	Paralysis caused directly by OPV vaccine strain with minimal genetic changes	Poliovirus strains derived from OPV that have genetically mutated during replication
Occurrence	Rare: ~1 case per 2.7 million OPV doses	Emerges in areas with low vaccination coverage
Timeframe	Occurs within 4-60 days after vaccination	Can circulate for months or years in community
Spread	Limited to vaccine recipient or immediate contacts	Can spread extensively in under-immunized populations
Genetic Changes	Minimal genetic changes from vaccine strain (<1%)	Substantial genetic divergence from vaccine strain (>1%)
Outbreak Potential	No person-to-person transmission beyond immediate contacts	Can cause outbreaks similar to wild poliovirus
Types	No subtypes	• cVDPV: Circulating (community spread) • iVDPV: Immunodeficiency-associated • aVDPV: Ambiguous source
Prevention	Prevented by using IPV instead of OPV	Prevented by maintaining high population immunity
Clinical Example	Child develops flaccid paralysis 2 weeks after receiving OPV	Unvaccinated children in community develop paralysis months after OPV campaigns ended
Public Health Response	Individual case management	Full outbreak response with mass vaccination

Thank You