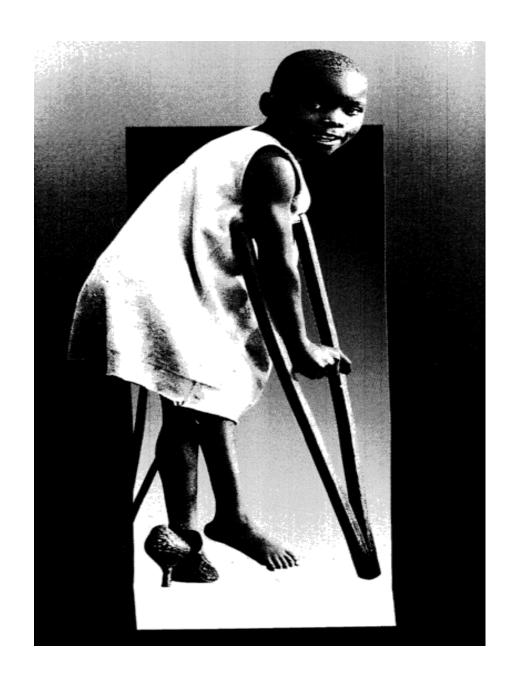


- Only **once** in human history have we witnessed the total eradication of dreaded disease, and that was smallpox more than two decades ago
- Now humanity stands on the brink of second triumph
 - -- a scourge that at one time killed or crippled half a million people a year, many of them children











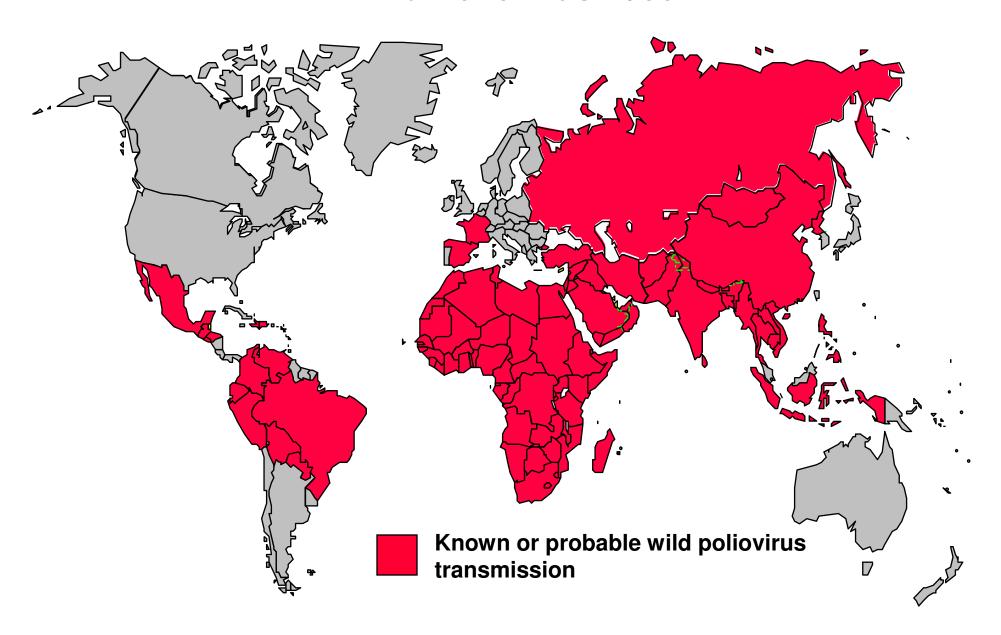


Poliomyelitis

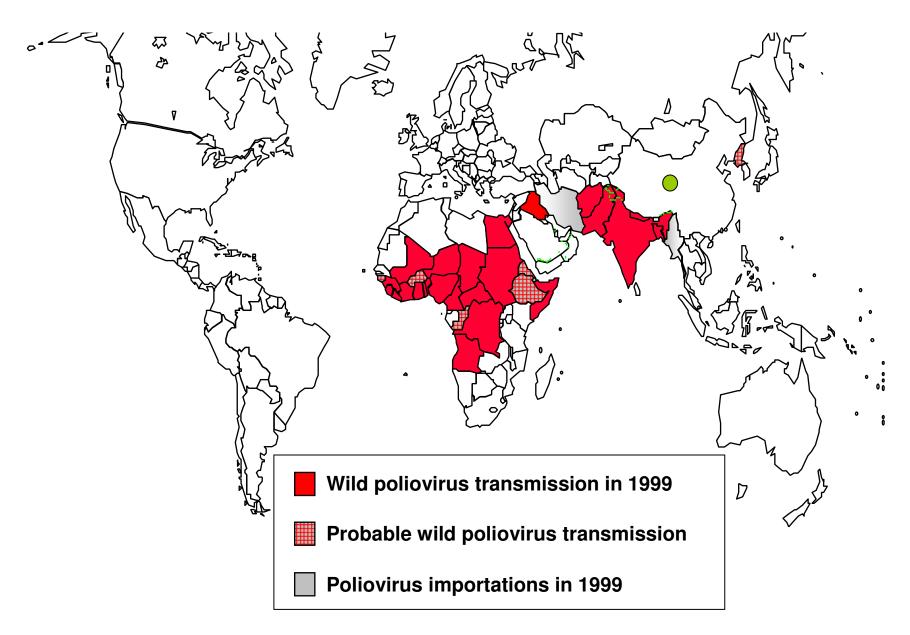
Composition of Term

- Polios = grey
- *Myelos* = marrow, spinal cord
- *Myelitis* = inflammation of spinal cord

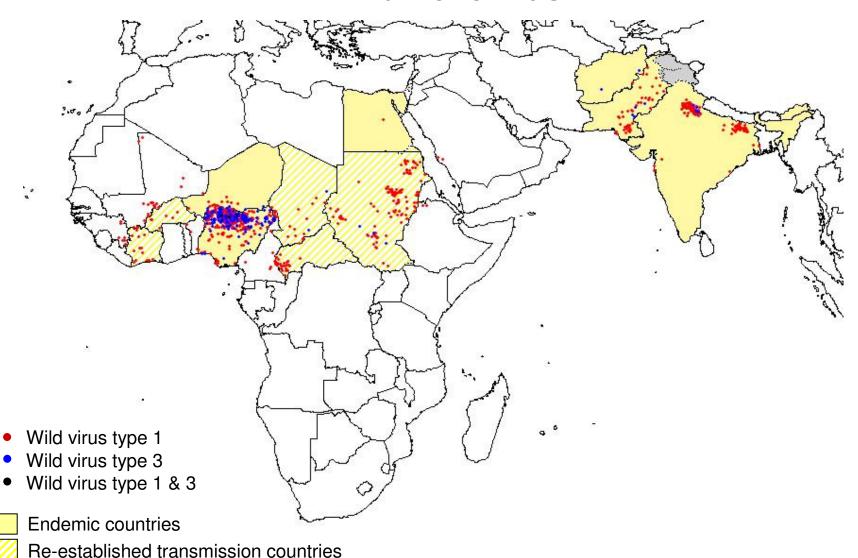
Wild Poliovirus 1988



Wild Poliovirus 1999



Wild Poliovirus*



Case or outbreak following importation

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

^{*}Excludes viruses detected from environmental surveillance and vaccine derived polio viruses.

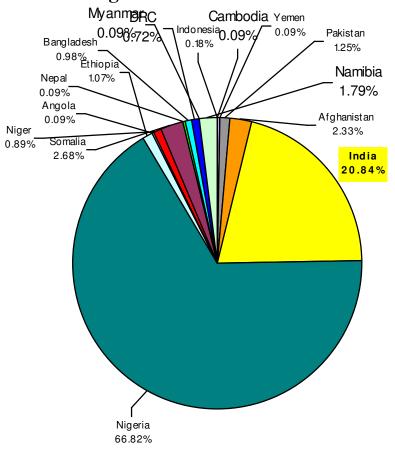
[©] WHO 2005. All rights reserved

Wild Poliovirus 2000 – 2006*

	Wild virus confirmed cases								
	Total								
Country or territory	2000	2001	2002	2003	2004°	2005	2006	% WPV(2006)	
Indonesia	0	0	0	0	0	303	2	0.18	
Yemen	0	0	0	0	0	478	1	0.18	
Pakistan	199	119	90	103	53	28	14	1.25	
Afghanistan	27	11	10	8	4	9	26	2.33	
India	265	268	1600	225	134	66	233	20.84	
Nigeria	28	56	202	355	782	802	747	66.82	
Eritrea	0	0	0	0	0	1	/ = /	00.02	
Ethiopia	3	1	0	0	1	22	12	1.07	
Angola	55	1	0	0	0	10	1	0.09	
Namibia*	0	0	0	0	0	0	20	1.79	
Sudan	4	1	0	0	127	27			
Niger	2	6	3	40	25	10	10	0.89	
Mali	0	0	0	0	19	3		0.00	
Cameroun	0	0	0	2	13	1			
Saudi Arabia	0	0	0	0	2	0			
Guinea	0	0	0	0	7	0			
Chad	4	0	0	25	24	2			
CAR	3	0	0	1	30	0	1		
Burkina Faso	0	0	1	11	9	0	1		
Côte d'Ivoire	1	0	0	1	17	0			
Benin	1	0	0	2	6	0			
Egypt	4	5	7	1	1	0			
Botswana	0	0	0	0	1	0			
Ghana	1	0	0	8	0	0	·		
Togo	0	0	0	1	0	0			
Lebanon	0	0	0	1	0	0			
Somalia	46	7	3	0	0	185	30	2.68	
Zambia	0	3	2	0	0	0			
Algeria	0	1	0	0	0	0			
Georgia	0	1	0	0	0	0			
Bulgaria	0	2	0	0	0	0			
Mauritania	0	1	0	0	0	0			
DRC	28	0	0	0	0	0	8	0.72	
Iran	3	0	0	0	0	0			
Cape Verde	12	0	0	0	0	0			
Congo	22	0	0	0	0	0			
Nepal	4	0	0	0	0	4	1	0.09	
Bangladesh	1	0	0	0	0	0	11	0.98	
Myanmar	2	0	0	0	0	0	1	0.09	
Iraq	4	0	0	0	0	0			
West Bank & Gaza Strip	0	0	0	0	0	0			
Cambodia	0	0	0	0	0	1	1	0.09	
Total	719	483	1918	784	1255	1952	1118		
No. of countries	23	15	9	15	18	16	16		
No. of endemic countries	20	10	7	6	6	6	6		
Countries highlighted in vellow are	ourrently or	domio							

Countries highlighted in pale yellow are considered to have active transmission of an imported virus.

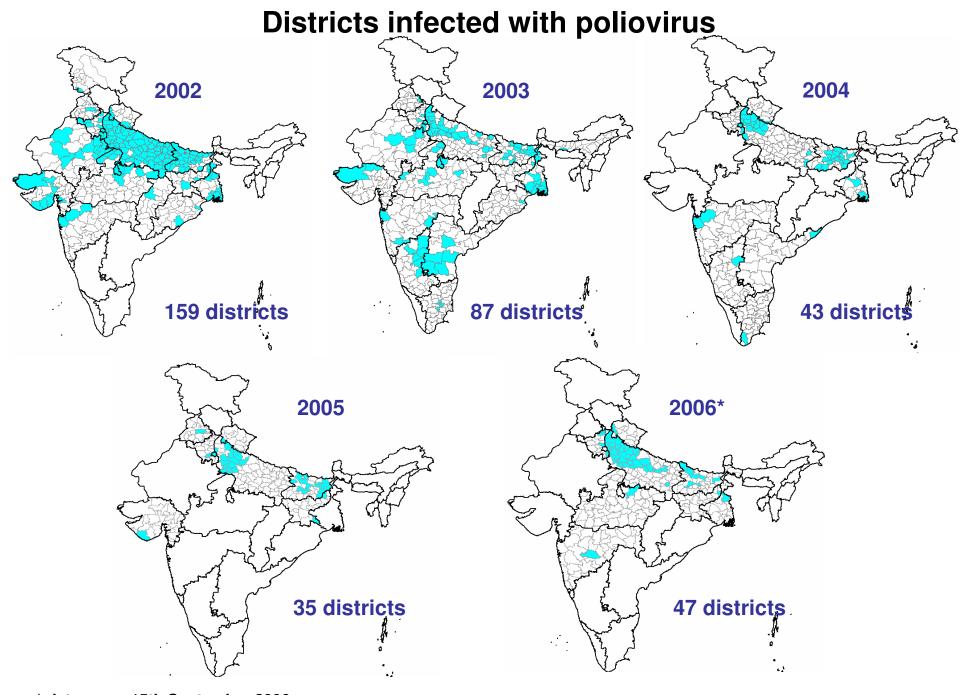
Percentage of Global Wild Polio Virus Case



N=1118

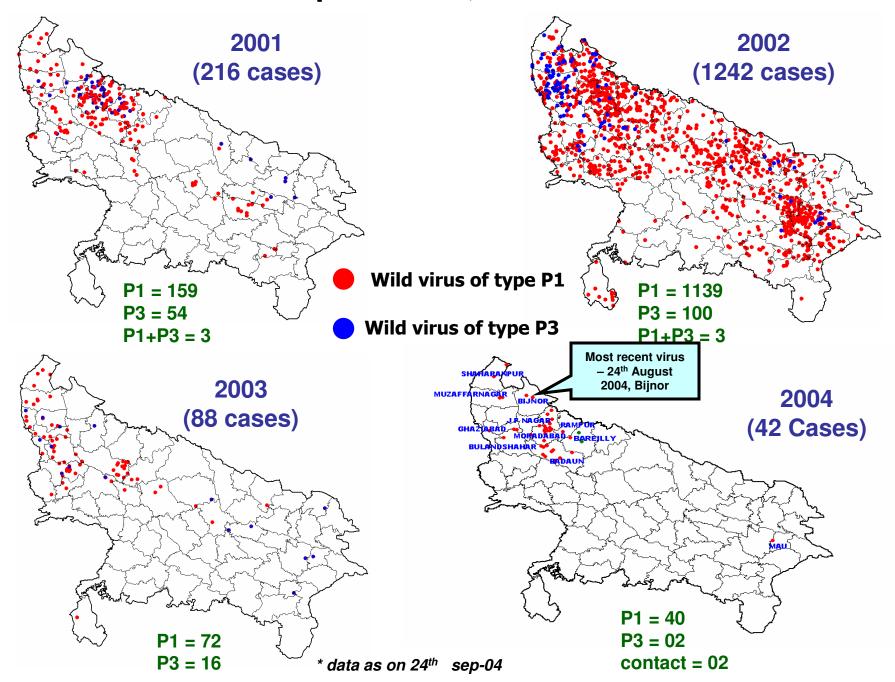
Location of poliovirus, India, 2002 - 2006 2002 2003 2004 1600 cases in 225 cases in 134 cases in 159 districts 43 districts 87 districts 2006* 2005 66 cases in 297 cases in 35 districts 47 districts

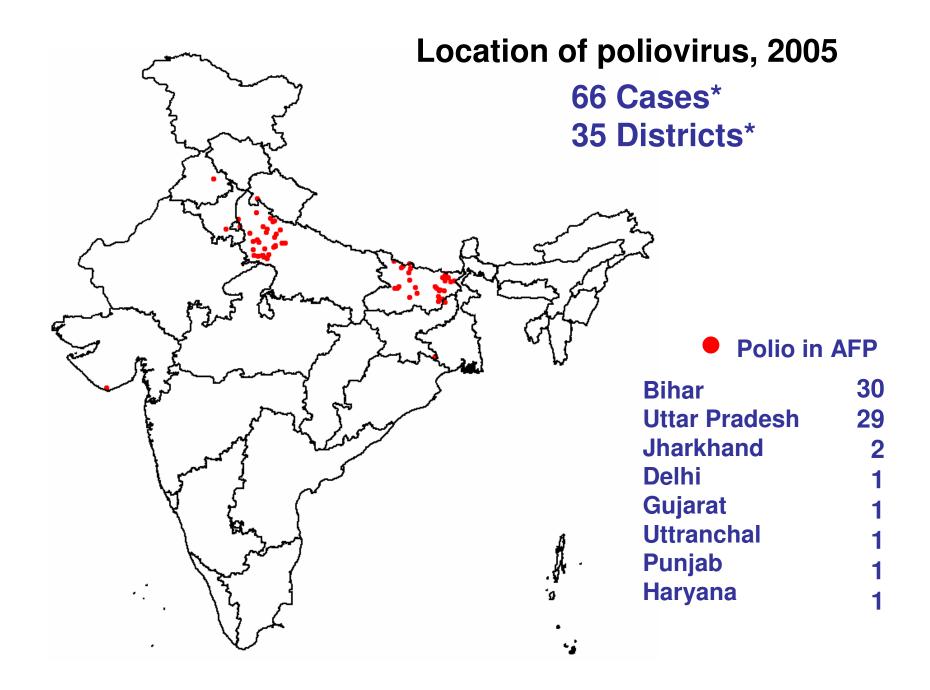
^{*} data as on 15th September 2006

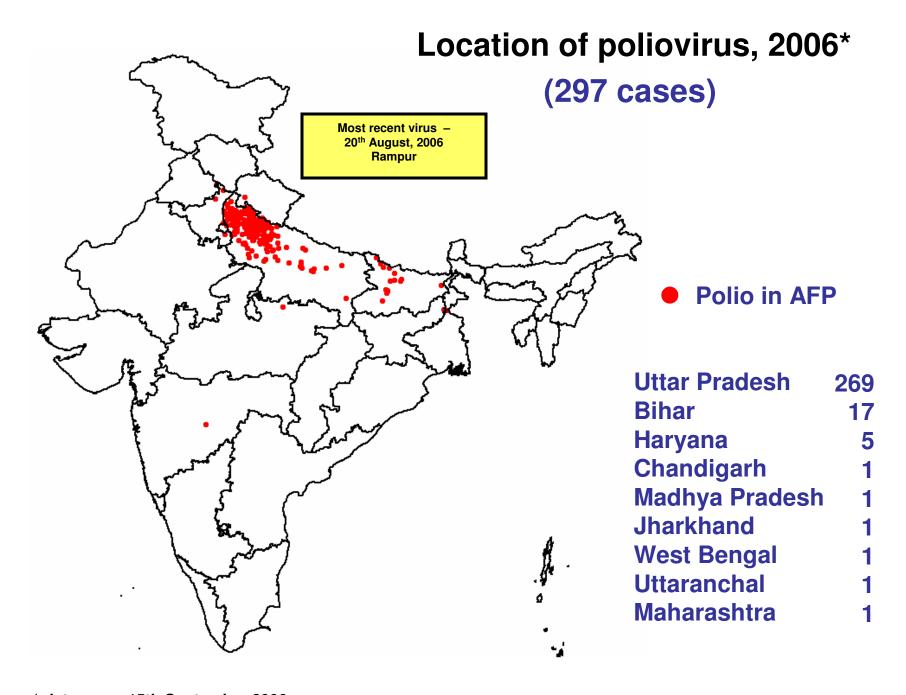


^{*} data as on 15th September 2006

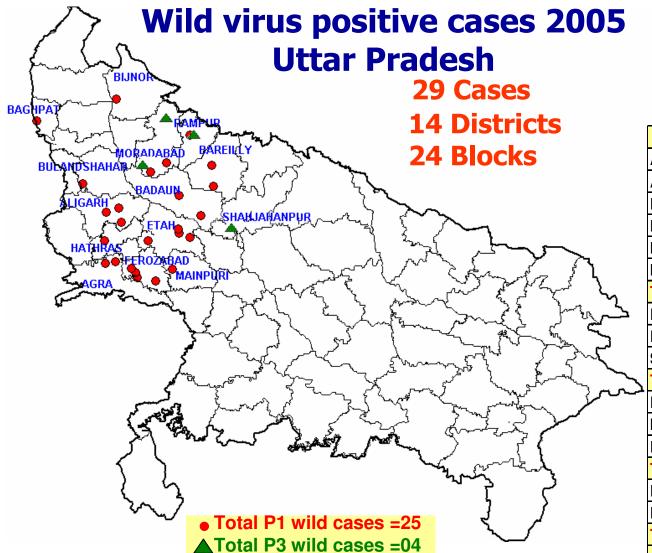
Location of poliovirus, Uttar Pradesh





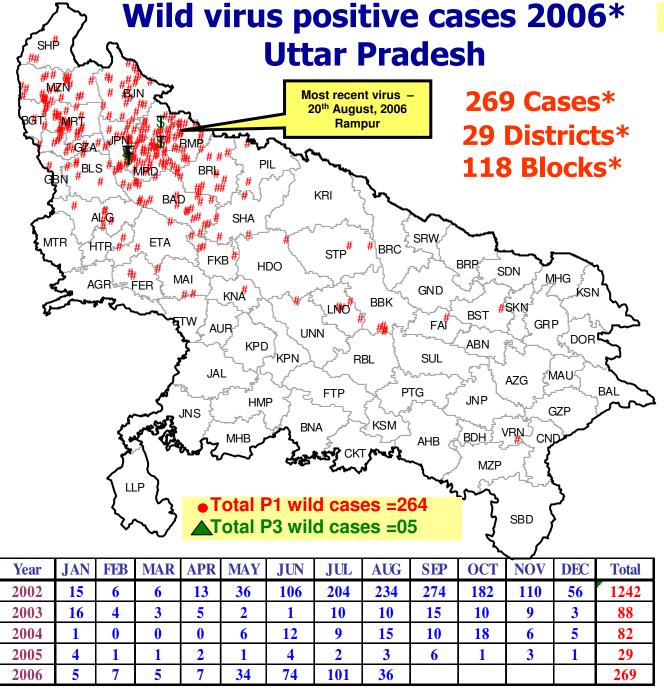


^{*} data as on 15th September 2006



District	P1W	P3W	Total
AGRA	2	0	2
ALIGARH	3	0	3
ETAH	4	0	4
FEROZABAD	4	0	4
HATHRAS	1	0	1
MAINPURI	1	0	1
Total Agra div.	15	0	15
BADAUN	2	0	2
BAREILLY	2	0	2
SHAHJAHANPUR	0	1	1
Total Bareilly div	4	1	5
BIJNOR	1	0	1
MORADABAD	2	2	4
RAMPUR	1	1	2
Total Moradabad di	4	3	7
BAGPAT	1	0	1
BULANDSHAHAR	1	0	1
Total Meerut div	2	0	2
Total: UP	25	4	29

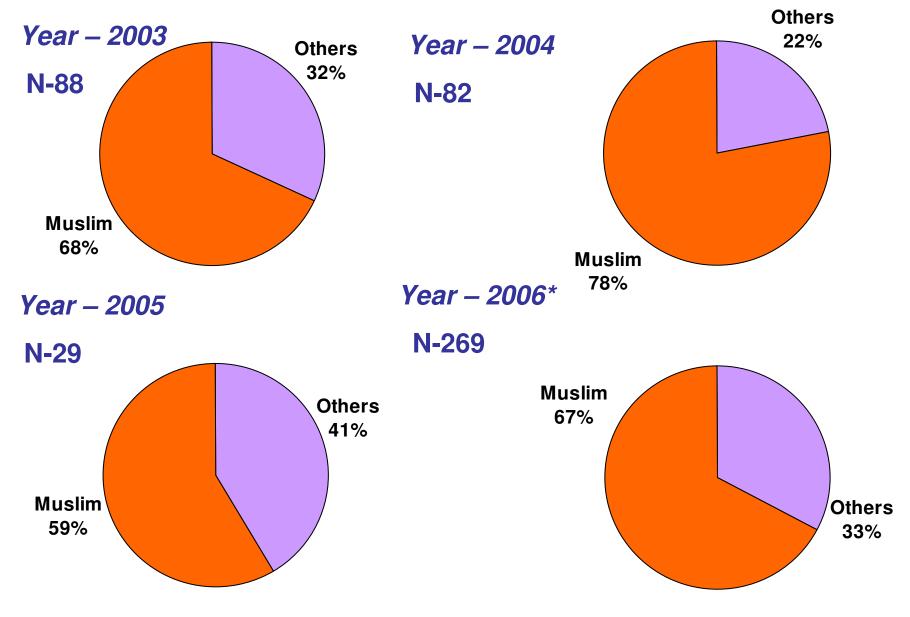
Year	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	Total
2002	15	6	6	13	36	106	204	234	274	182	110	56	1242
2003	16	4	3	5	2	1	10	10	15	10	9	3	88
2004	1	0	0	0	6	12	9	15	10	18	6	5	82
2005	4	1	1	2	1	4	2	3	6	1	3	1	29



* data as on 15th Sept 2006

District	P1W	P3W	WPV
ALIGARH	6	0	6
FEROZABAD	2	0	2
MAINPURI	3	0	3
ETAH	2	0	2
HATHRAS	1	0	1
Tot. Agra div.	14	0	14
MORADABAD	51	5	56
J P NAGAR	19	0	19
RAMPUR	21	0	21
BIJNOR	23	0	23
Tot. Moradabad div	114	5	119
BAGPAT	2	0	2
BULANDSHAHAR	6	0	6
G.B. NAGAR	1	0	1
GHAZIABAD	11	0	11
MEERUT	24	0	24
Tot. Meerut div	44	0	44
MUZAFFARNAGAR	25	0	25
SHAHARANPUR	3	0	3
Tot. Shaharanpur div	28	0	28
SITAPUR	2	0	2
LUCKNOW	4	0	4
HARDOI	2	0	2
Tot. Lucknow div	8	0	8
FARRUKHABAD	4	0	4
KANNAUJ	1	0	1
Tot. Kanpur div	5	0	5
BADAUN	24	0	24
BAREILLY	13	0	13
PILBHIT	3	0	3
SHAHJAHANPUR	4	0	4
Tot. Bareilly div	44	0	44
FAIZABAD	1	0	1
BARABANKI	4	0	4
Tot. Faizabad Div	5	0	5
VARANASI	1	0	1
Tot. Varanasi Div	1	0	1
BASTI Tab Basti Bio	1	0	1
Tot. Basti Div	1	0	1
Total: UP	264	5	269

Status of WPV Cases by Community – Uttar Pradesh 2003-2006*



*Data as on 15th Sept, 2006

Prevalence

- Lameness (of leg) Surveys –
 number of cases
- Rough Prevalence = cases x 1.25 (includes all other sites)
- Prevalence of all cases = RP x
 1.33 (to account for attrition)

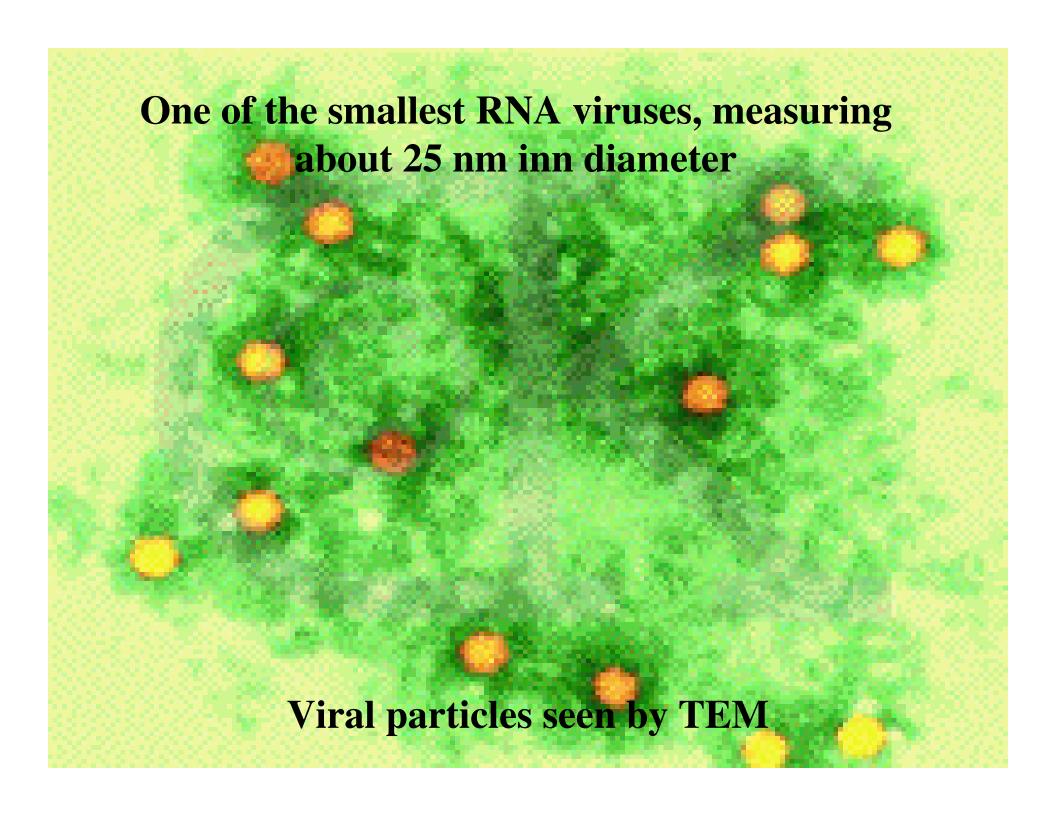
The Agent

Classification of Poliovirus

- Family Picornaviridae
- Genera
 - 1. Enteroviruses
 - (a) Poliovirus
 - (b) Non-Polio Enteroviruses or NPEV Coxsackie, Echo
 - 2. Rhinoviruses Influenza virus
 - 3. Aphthoviruses
 - 4. Cardioviruses

The Polio virus

- Single strand of positive sense RNA
- Stable at Acid pH, not affected by lipid solvents
- Looses infectivity in 30 minutes at 56°C
- Period of Communicability 7-10 days before
 & after the onset



Epidemiology of Poliovirus

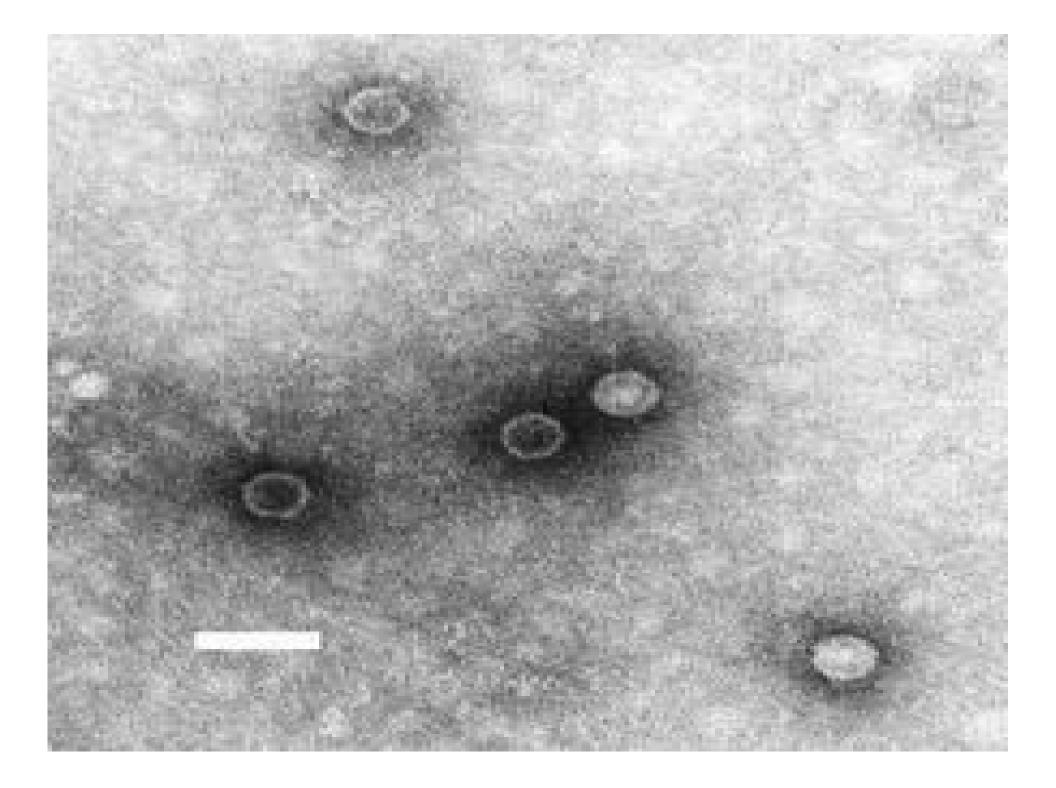


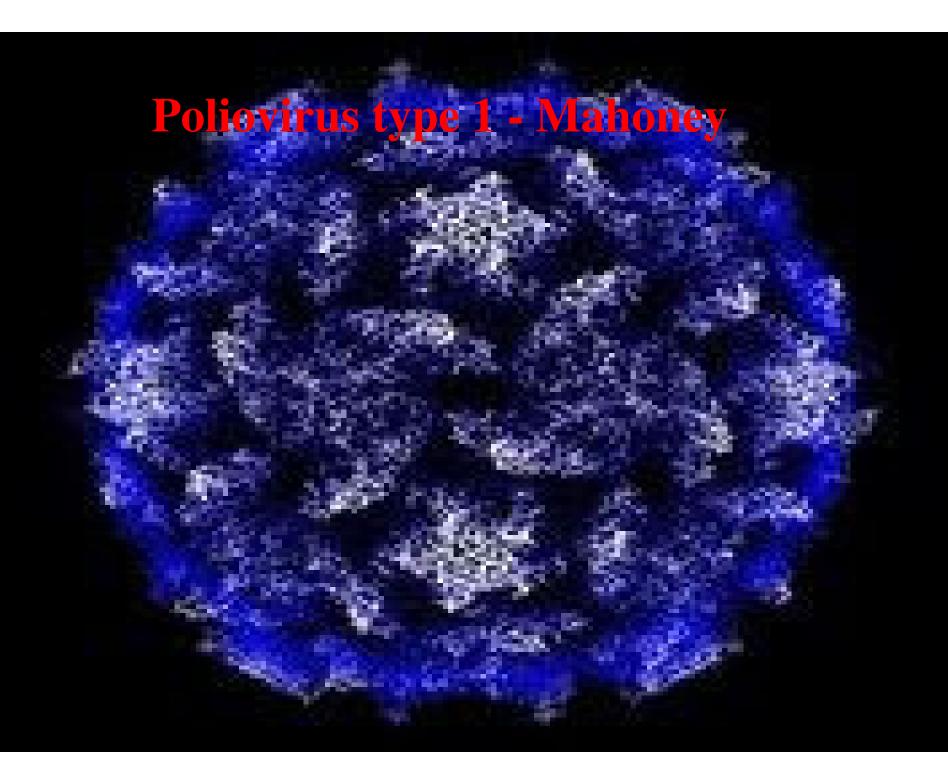
• 3 types

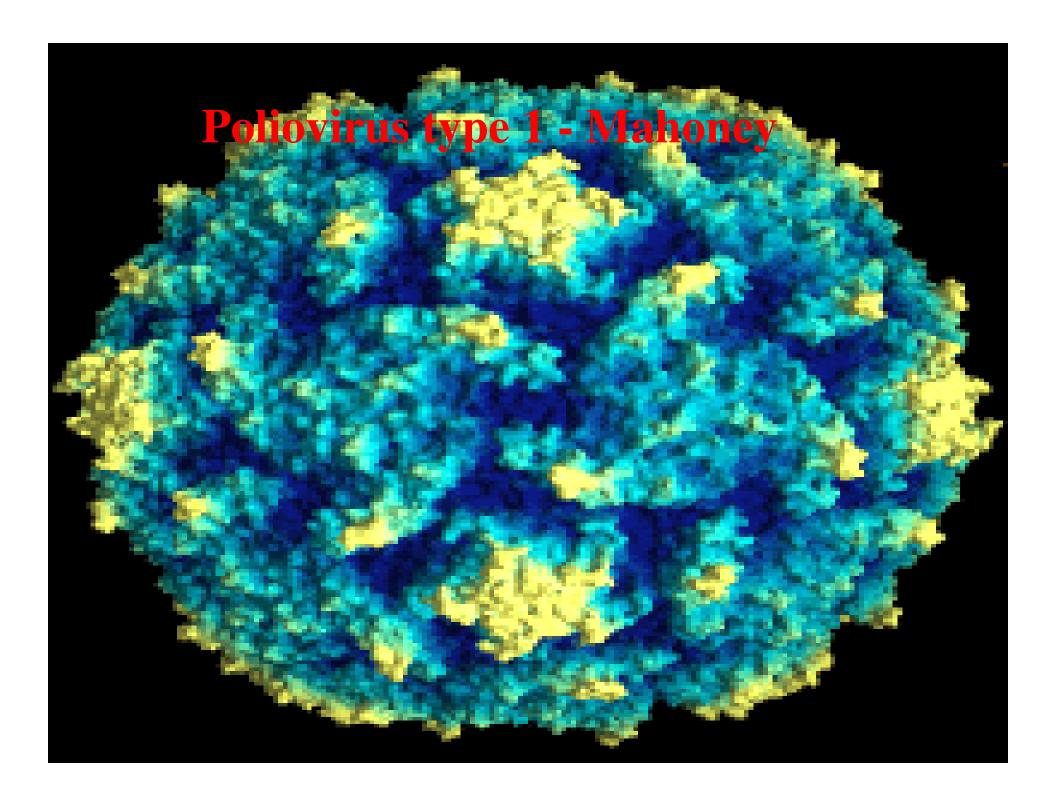
Type 1 (Brunhilde/Mahoney): mostly causes outbreaks Type 2 (Lansing): easiest to eradicate Type 3 (Leon): often last to be eradicated

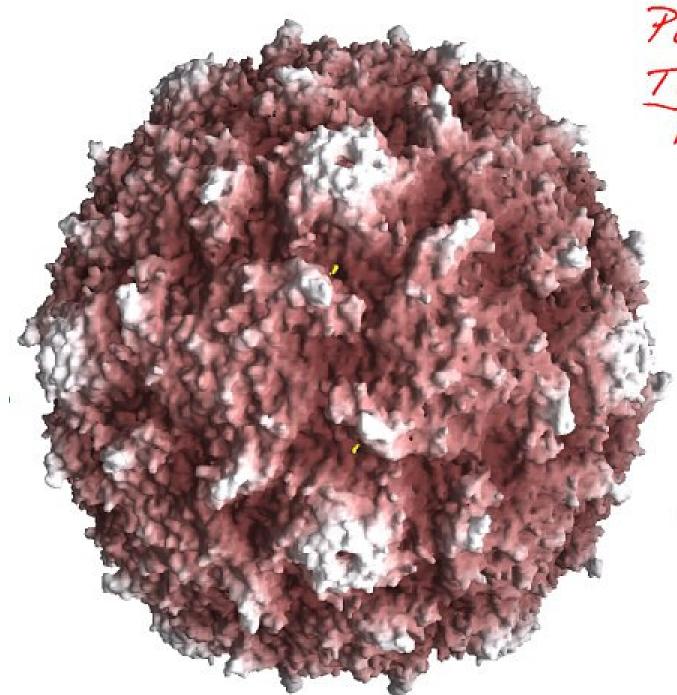
- Highly contagious (usually infects 100% of all susceptibles)
- Occurs worldwide and is seasonal
- Inapparent to apparent infection ratio = 200-1000:1

100nm









Poliovirus
Type 2
Lansing

Xray Structure determination:

K.N.LENTZ, A.D.SMITH, S.C.GEISLER, S.COX, P.BUONTEMPO, A.SKELTON, J.DEMARTINO,E.ROZHON, J.SCHWARTZ, V.GIRIJAVALLABHAN, J.O'CONNELL,E.ARNOLD (1997)

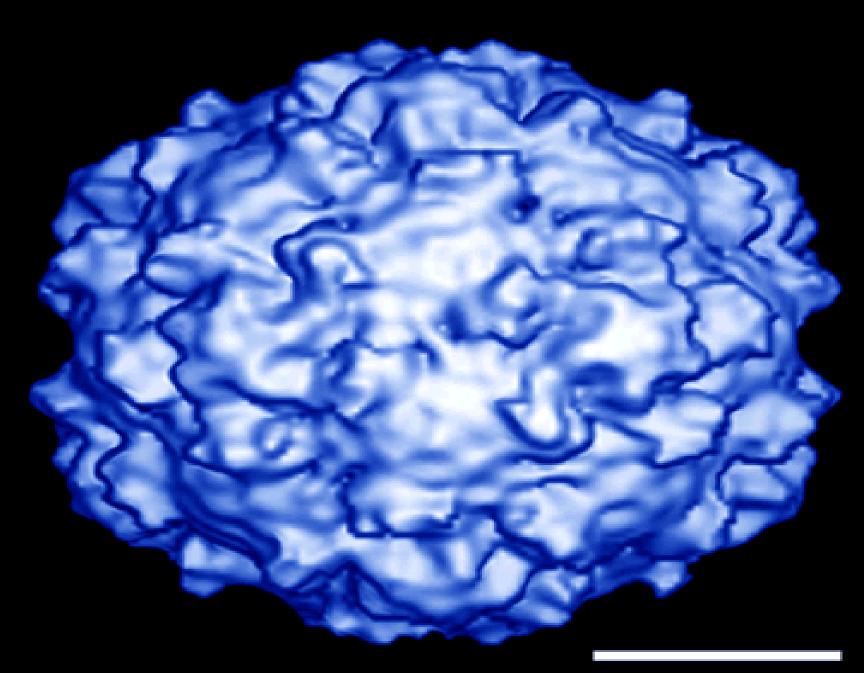
Structure (London) 5, 961-978

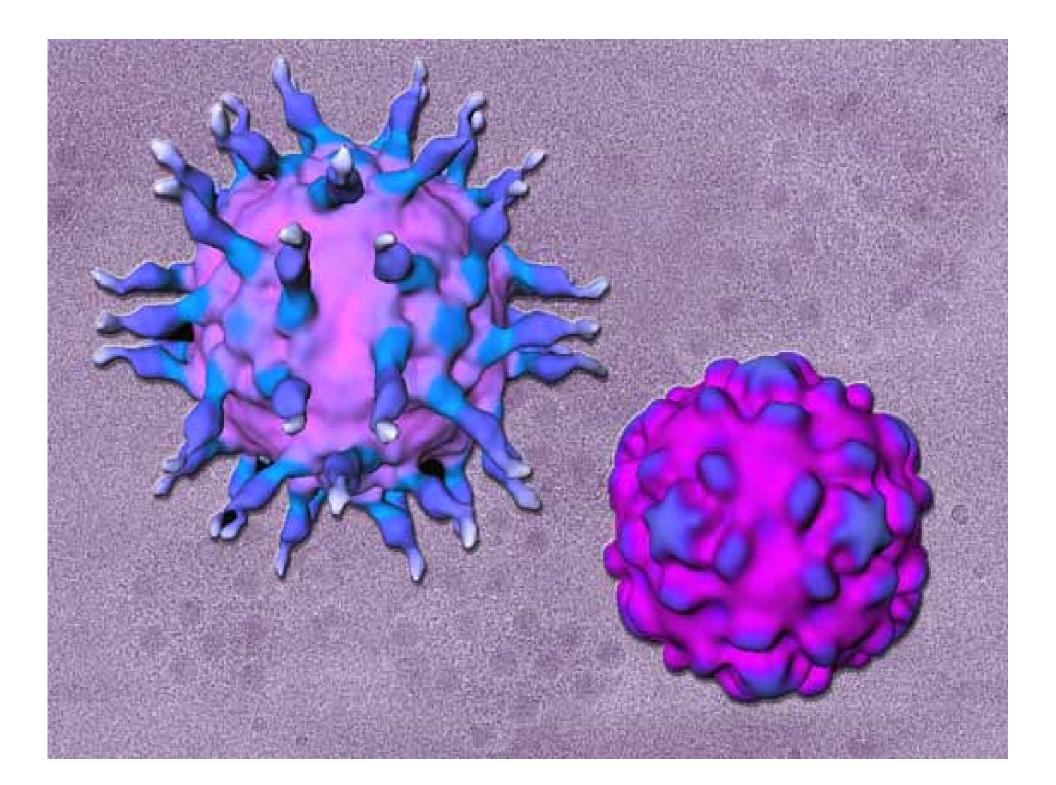
STRUCTURE OF POLIOMRUS TYPE 2
LANSING COMPLEXED WITH
ANTIMIRAL AGENT SCH48973:
COMPARISON OF THE
STRUCTURAL AND BIOLOGICAL
PROPERTIES OF THREE POLIOMRUS
SEROTYPES

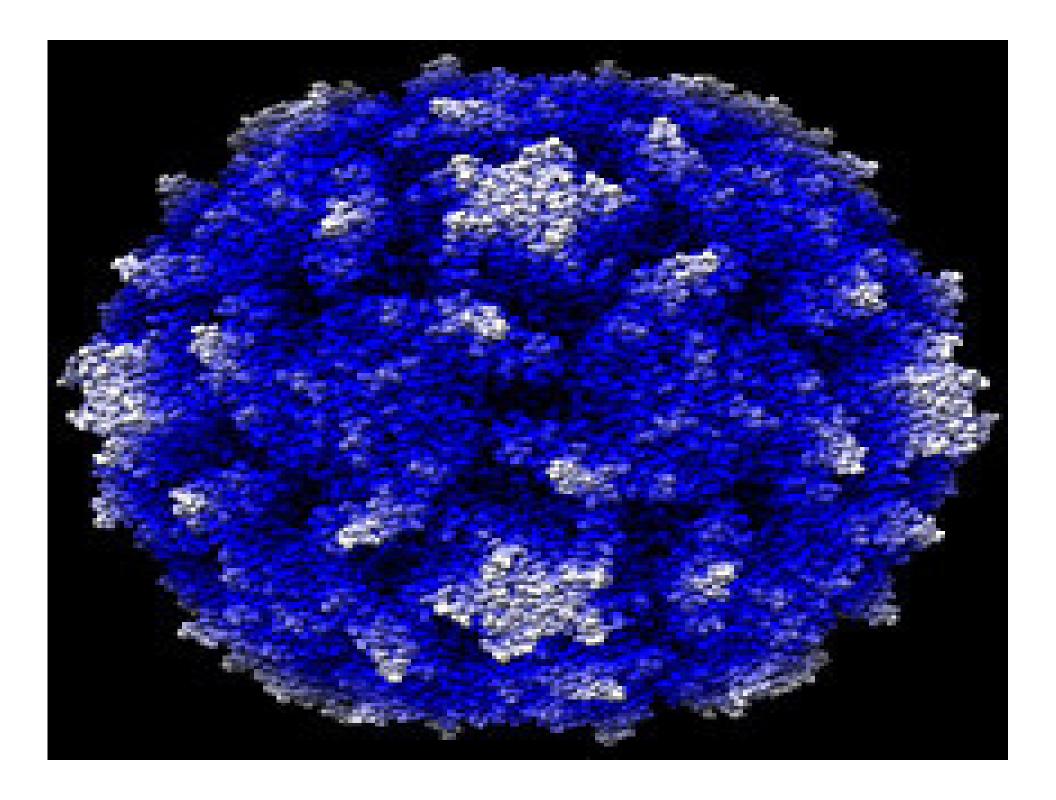
(PDB ENTRY: 1EAH)

Radial Depth Cue Rendering with grasp (A. NICHOLLS) on Silicon Graphics:

J-Y. SGRO







- ➤ Polioviruses: Are human enteroviruses that exist as three well defined serotypes, which infect cells via a specific receptor [PVR: CD 155]
- ➤ Wild polioviruses: field isolates and reference strains of polioviruses known to have circulated persistently in the community.
- ➤ Oral poliovirus vaccine strains: attenuated polioviruses approved for use in oral vaccines by national control authorities.
- > Vaccine derived polioviruses: mutated progeny of approved poliovirus vaccine strain.

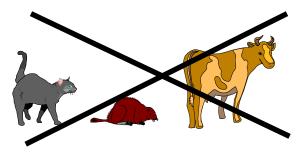
Epidemiology of Poliovirus

Reservoir

infects only humans



• no animal reservoir



- does not survive long in environment
- no long term carrier state
- Survival outside human very brief

The Host

- **Age** most vulnerable 6 months to 3 years
- Sex 3 males:1female
- **Risk Factors** Fatigue, trauma, IM injections, tonsillectomy, alum containing DPT
- **Immunity** No cross immunity, by natural/immunization

Immunity

Active

- through immunization / natural infection
- immunity believed to be lifelong
- immunity to one type not protective against infection with other types
- two types of immunity: intestinal and humoral

Passive

 infants born to mothers with high antibody protected for first several weeks

The Environment



- Rate of inactivation of this virus varies with immediate environment. *Infectivity decreases by 90%*
 - In soil every 20 days in winter.
 - every 1.5 days in summer.
 - In water at ambient temperature
 - » sewage water every 26 days.
 - » freshwater every 5.5 days.
 - » sea water every 2.5 days.
- It can survive at –
 Freezing temperature for many years,
 Under refrigeration for many months,
 At room temperature for many days.
- Rate of inactivation slows by presence of org matter.

Place and time

• Place

occurrence, not randomly distributed

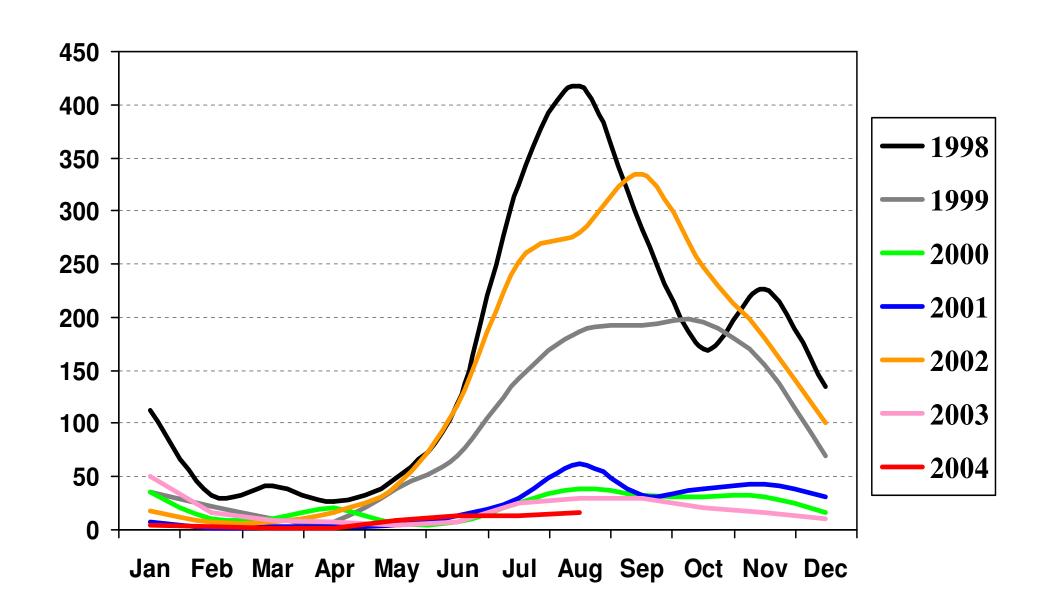
• Incidence highest in -

- low immunization coverage
- poor sanitation
- crowded conditions
- urban slums

• Time - seasonal

- rainy season in warm climate countries
- summer / early autumn in temperate climate countries

Monthly incidence of wild polio cases 1998-2004



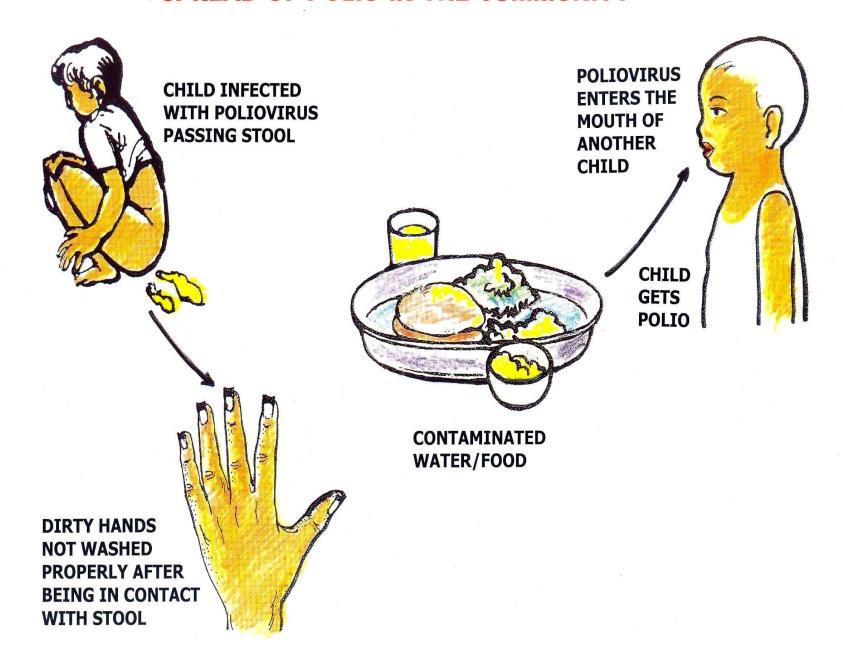
Transmission

- Rapid widespread transmission to non-immune children
- Clusters of susceptibles needed to maintain circulation
- Silent transmission >99% of cases are sub clinical
- Highly communicable
 - One infected individual will infect all non-immune persons in a household
- Faeco-oral route predominates

Virus Excretion

- Virus intermittently excreted for 6-8 weeks after infection
- Most heavy excretion
 - just prior to paralysis onset
 - up to first two weeks
 - dramatically tapers off after 4 weeks

SPREAD OF POLIO IN THE COMMUNITY



Incubation period

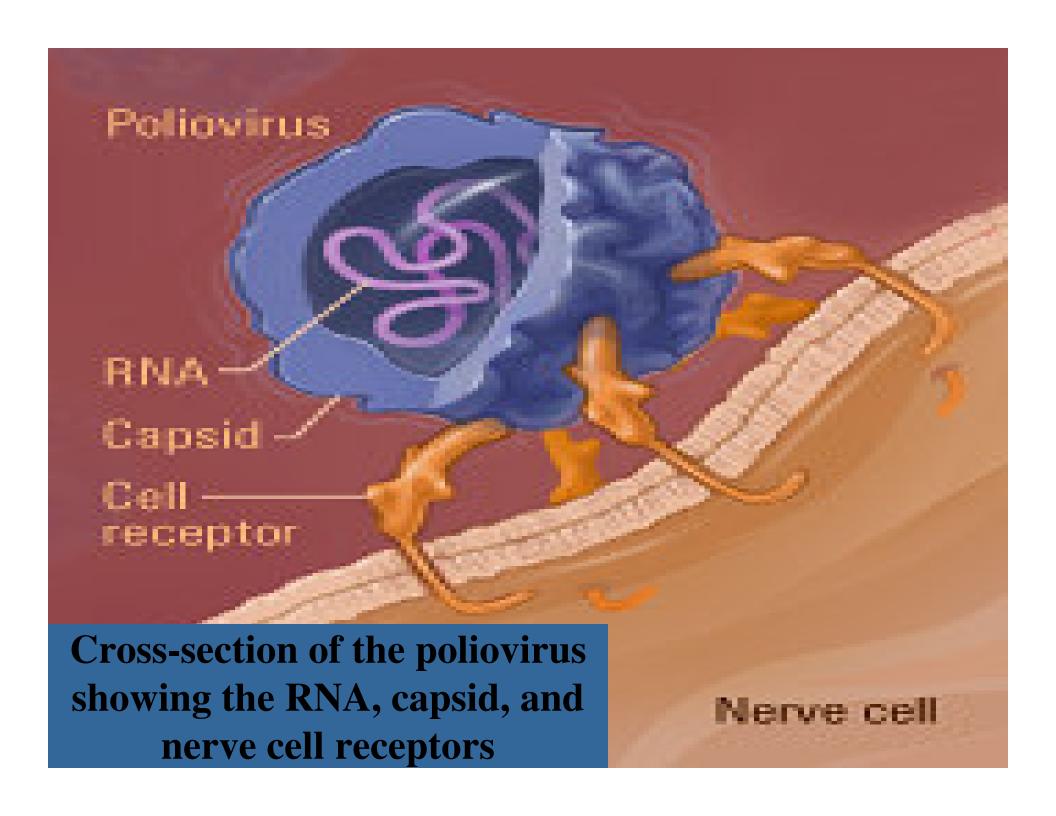
Short incubation period

usually 7-14 days,

but may be a short as 4 days (range 3-35 days)

Pathogenesis

- Virus enters oral cavity
- Local replication in tissues expressing receptor (tonsils, intestinal M cells, Peyer patches of ileum, and lymph nodes)
- Viremia with hematologic spread to CNS
- Retrograde spread along neurons to spinal cord
- Motor neurons destroyed by viral replication
- Paralysis extent depends on proportion of motor neurons lost



Life Cycle of a Poliovirus

A poliovirus approaches a nerve cell via the bloodstream.

2 Nerve cell receptors attach to the virus.

3 The capsid (protein shell) of the virus breaks to release its RNA

(genetic material) into the cell.

receptor

nerve cell

(host)

capsid

polio RNA

4 Polio RNA moves toward a ribosome, the cell's protein assembly station.

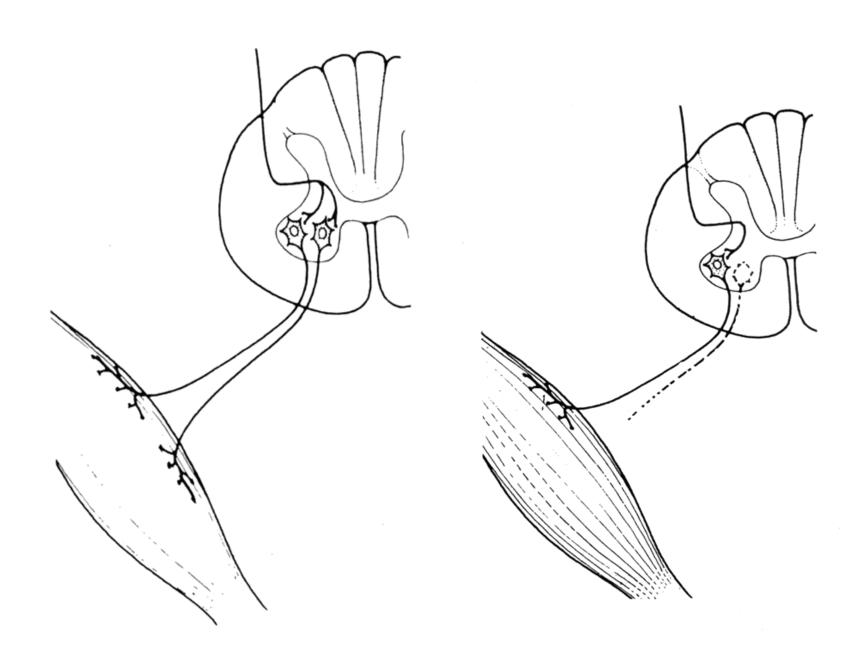
ribosome

5 Polio RNA takes over the ribosome and forces it to make more polio RNA and more capsids.

RNA replication

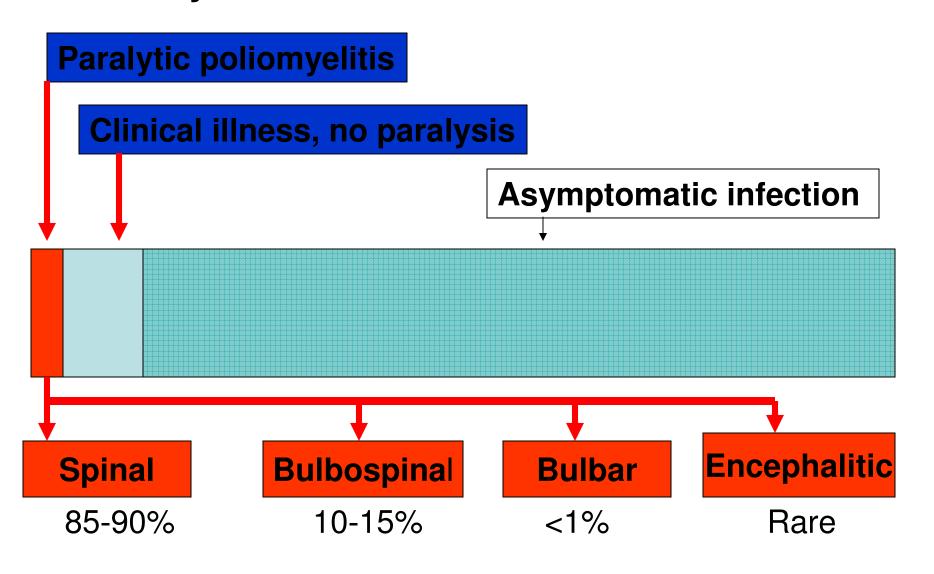
> The new polio capsids and new polio RNA unite to form more polioviruses.

7 The host cell swells and bursts, releasing thousands of new viruses back into the bloodstream.



Clinical Outcome of Poliovirus Infections

Paralysis is unusual manifestation of infection



Clinical aspects

- A. Inapparent (asymptomatic) in 90-95%
- **B. Abortive** in 4-8%: non-specific symptoms
 - low grade fever
 - malaise
 - sore throat
 - Anorexia, nausea, vomiting
 - Unlocalized abdominal pain, constipation
 - recovery rapid and complete
 - no paralysis
 - indistinguishable from other mild viral infections

C. Non paralytic

- Symptoms similar to abortive
- Headache nausea vomiting more intense
- Stiffness and soreness of muscles in neck trunk & limbs
- **D. Paralytic Poliomyelitis** in 0.5% of infections
- symptoms in 2 phases minor and major CNS phase
- sometimes separated by several days without symptoms

• Minor phase – indistinguishable with abortive polio

Major phase

- -muscle pain, spasms
- -return of fever
- -rapid onset of flaccid paralysis
- -progression usually complete within 72 hours
- -sensation remains normal
- -reflexes (DTRs) diminished
- asymmetric paralysis (legs>arms)
- -proximal more than distal
- -residual flaccid paralysis at 60 days

Clinical aspects

- Rarely "bulbar polio"
 - affects motor neurons of cranial nerves
 - may develop
 - respiratory insufficiency
 - difficulty in swallowing, eating and speaking
 - risk of death high
- Very rarely poliovirus may cause meningitis or encephalitis
 - clinically indistinguishable from other causes

Prognosis

Among children who are paralyzed by polio:

- 30% make a full recovery
- 30% are left with mild paralysis
- 30% have medium to severe paralysis
- 10% die

Distinguishing Clinical aspects....

- asymmetric flaccid paralysis (GBS)
- proximal > distal
- rapid progression to paralysis 2-3 days
- deep tendon reflexes diminished or absent (UMN Paralysis)
- fever at onset, muscle pain
- preservation of sensory nerve function (Transverse Myelitis)
- residual paralysis after 60 days

Differential Diagnosis

- AIDP (Acute Infectious Demyelinating Polyneuropathy) or Gullian-Barre Syndrome of Infectious Polyneuropathy
- Traumatic Neuritis
- Transverse Myelitis
- Post-dipthehric Polyneuritis
- Hemiparesis/Hemiplegia
- Transient Paralysis Unproven hypokalemia
- Poisonings

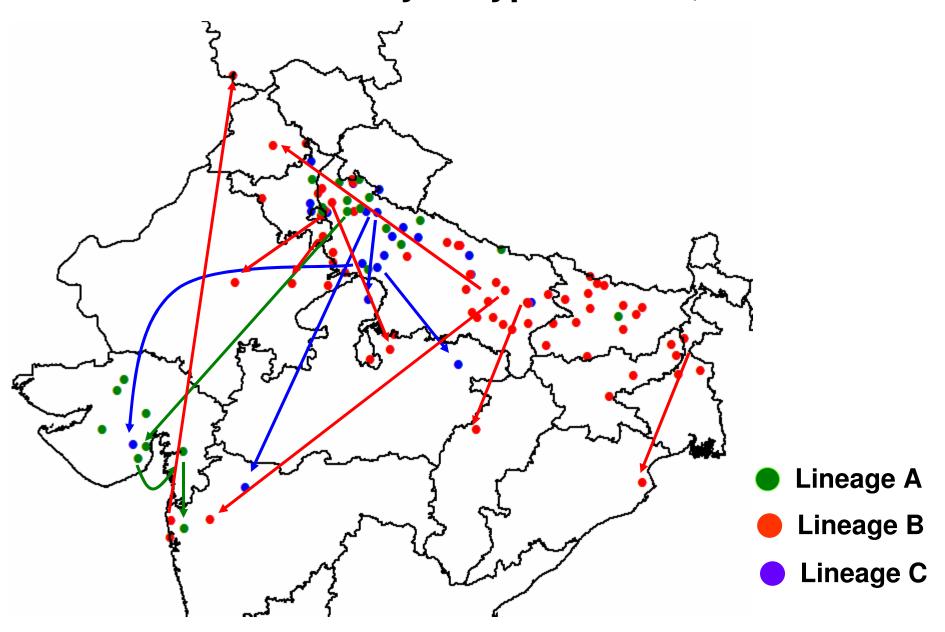
Differential Diagnosis

Signs & Symptoms	Polio	GBS	Transverse Myelitis	Traumatic Neuritis
Fever Onset	High, always present	Not Common	Rare	Common
Flaccidity	Acute, asymmetrical, proximal	Acute, asymmetrical, distal	Acute, symmetrical, both lower limbs	Acute, asymmetric limbs
M. Tone	Diminished	Diminished	Diminished in LL	Diminished
DTRs	Decreased or absent	Absent	Absent in LL early, hyper-reflexia later	Decreased or absent
Sensation	Severe Myalgia & backache, NO sensory changes	Cramps, tingling, hypoanesthesia	Anesthesia	Pain in gluteal region
Cranial Nerve	Only in Bulbar and Bulbospinal	Often	Absent	Absent
Bladder dysfunction	Absent	Transient	Present	Never
NCV	Abnormal – AHC disease	Abnormal - demyelination	Normal/abnormal	Abnormal in affected nerve
EMG	Abnormal	Normal	Normal	Normal

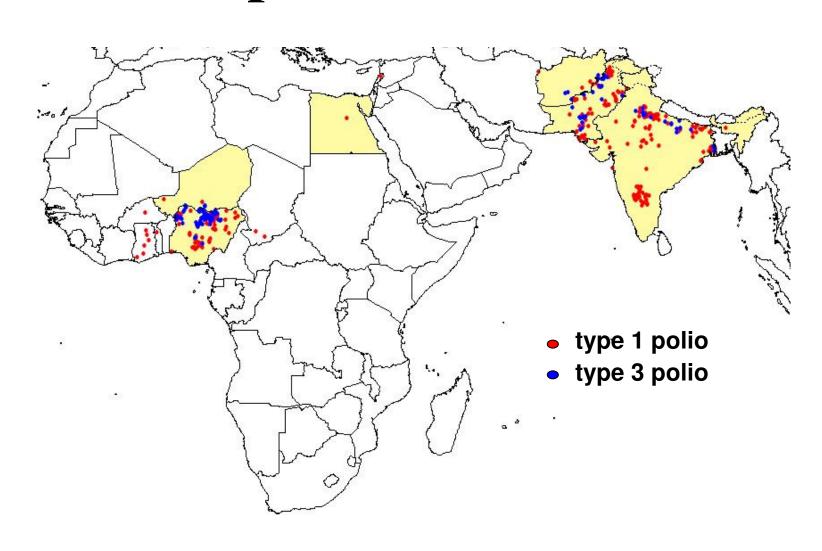
Molecular Epidemiology - Tracking the virus

- Possible through genetic mapping & matching
- Origin of virus determined
- Identification of persistent reservoirs
- Detecting gaps in AFP surveillance
- Detect importations
- When and where and was the transmission of various lineages interrupted

Biodiversity of type P1 wild, 2002



Importations - 2003



P1 poliovirus

Genetic lineages over the years

