The Polio Virus

Getting to Know Your Old Enemy

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The Polio Virus

- Virus is smallest living thing that can reproduce itself
- Outer shell (capsid)
- Inner genetic material (RNA) and one protein
- Needs machinery in a cell to make more virus
- Only humans get polio

Did Cells Get Rid of ALL pv?

- PV is a “lytic” virus - destroys host cells
  - **Most pv eliminated by immune system to end acute infection**
- Stealth virus:
  - Persistent virus - cannot destroy host cell
- ***Some*** people have persistent polio virus - shown by many researchers
  - **Immune system plays a role in PPS**
  - **Helps to explain variation in symptoms**

Virus “Serotypes”

- *Serotype* - classify viruses, make vaccines
- Polio has 3 “serotypes”
- To find serotype of a virus:
  - infect “clean animal” with virus
  - collect serum - has antibody to this virus
  - add another virus to the serum
    - if SAME serotype it’s no longer infective
    - if it’s a DIFFERENT serotype, it can infective

Serotypes of Polio Virus
often called “strains” or “types”

- Each strain has many substrains
  - Sabin collected many to make vaccine
  - Most substrains have been lost

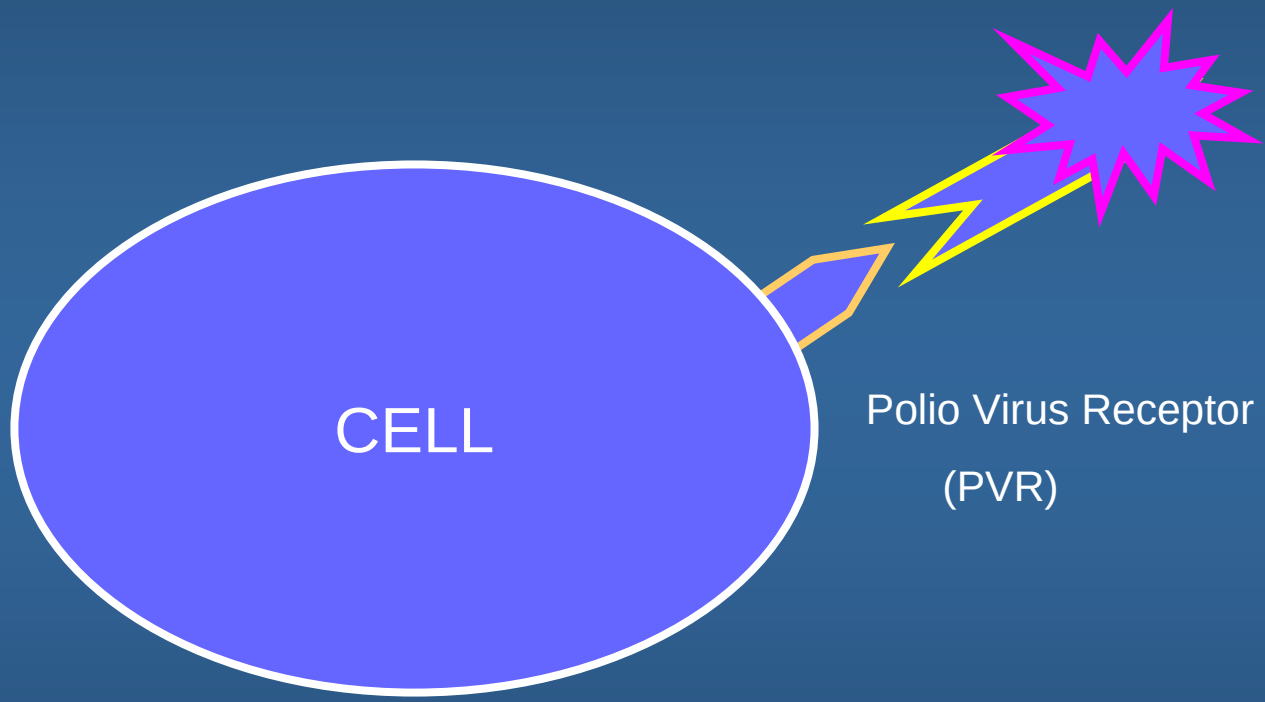
- **Strain 1:** Mahoney, Brunhilde, MEF2, Frederick
- **Strain 2:** Lansing, MEF1, Wilfred, YSK
- **Strain 3:** Leon (others have been lost)

Differences between pv strains:

- Structural differences are small
  - 85% to 95% identical at the molecular level
- BUT - large differences in infectivity, symptoms of acute illness and tendency to result in paralytic polio

- PV1 - produced most severe paralysis
  - **Most common during epidemics**
  - **Responsible for most paralytic polio cases**
- PV2 - meningitis, paralysis
  - **Often resulted in a coma, milder paralysis**
- PV3 - severe paralysis
  - **Less common during epidemics**
  - **Produced isolated cases**

To understand how polio virus infects, we need to look at some basic virology

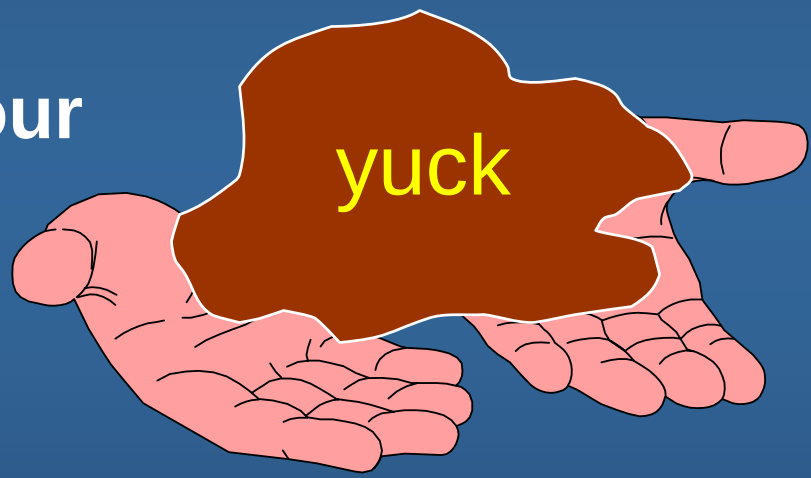


How does the virus get into the cells of your body ?

- **Virus attaches** to **receptor protein** on outside of cell
- **Enters** and hijacks the cell's own protein machinery to make 1000's of new viruses
- **Cell ruptures** and releases the virus to infect more cells

What happened when I was sick with polio?

- Picked up something with polio virus on it
- Put your hands in your mouth
- 2 - 3 weeks later you felt sick
- *NEXT ….*



The virus went to intestines

- Attached to receptors small intestine cells
  - entered the cells
- Made many copies of itself
  - killed many cells lining the intestine
- Have diarrhea or upset stomach
- Virus moved into blood stream - “viremia”
- Immune system starts to make antibodies to pv

- ALL polio infections reached this stage

Called sub-clinical or abortive polio!

Next ……..

The virus entered your nerves

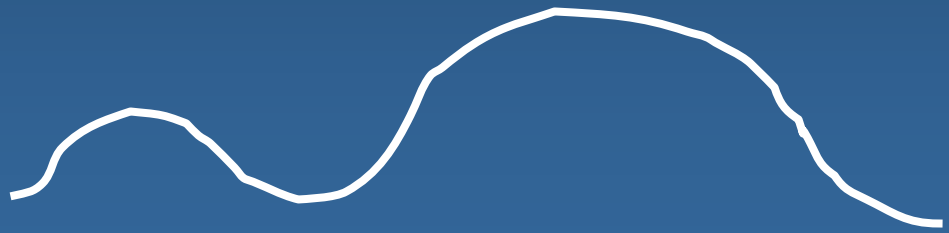
- To go from blood to the nerves, virus must cross the **blood/brain barrier**
- Usually at the brain stem area
- Produced signs of meningitis:
  - Headache, sensitivity to light, stiff neck
  - May have muscle cramps
- Called *Non-paralytic Polio*
- ***Then…….***

If infection continued you had:

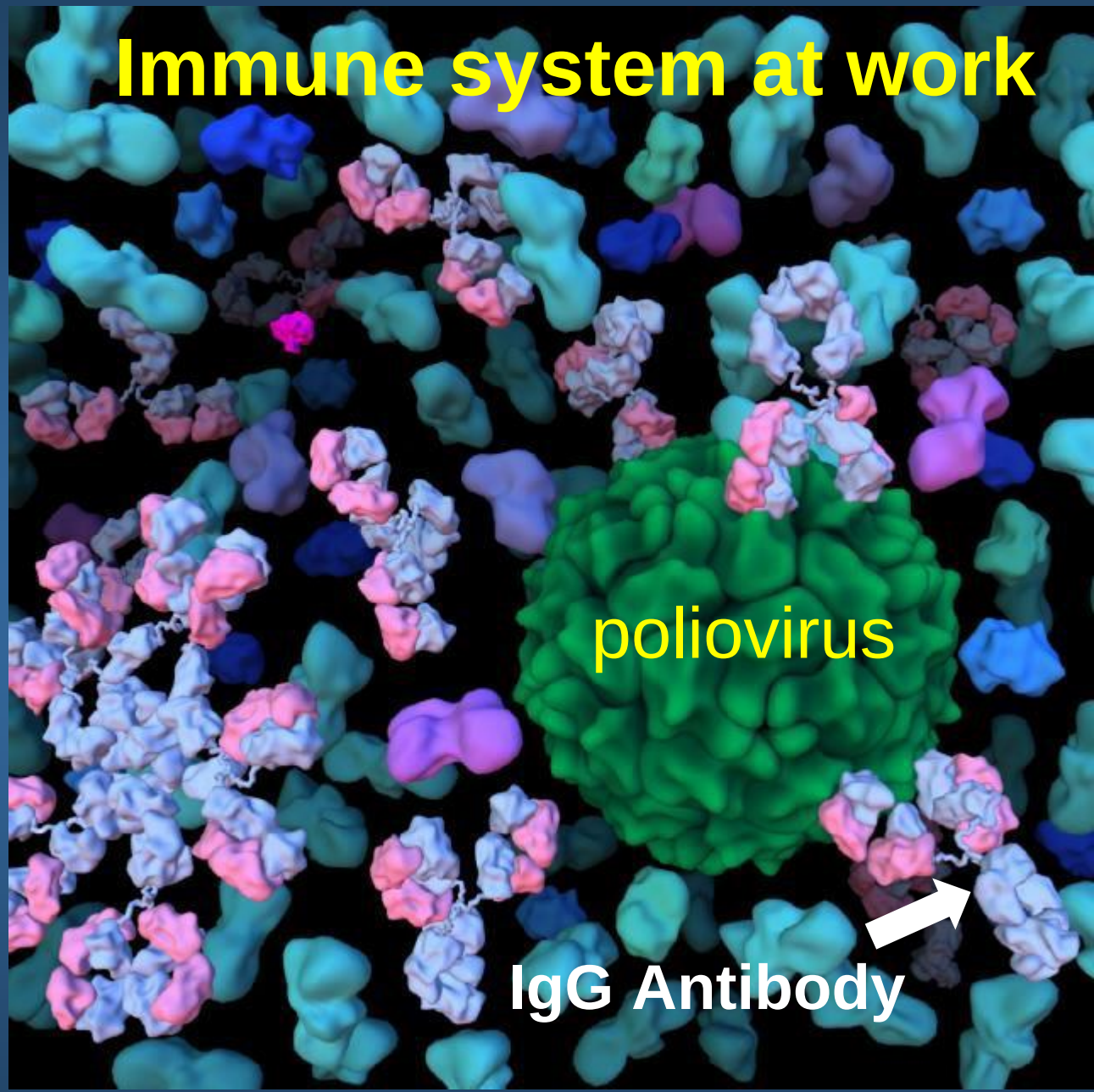
- ***PARALYTIC POLIO***
  - upset stomach, headache, light sensitive
  - stiff neck, cramps, constipated, incontinent
  - infected nerves resulted in muscle weakness
    - ~50% of nerves affected
  - nerve death resulting in paralysis
- **Progression stopped when immune system overcame the virus**

Characteristics of Acute Polio Infection

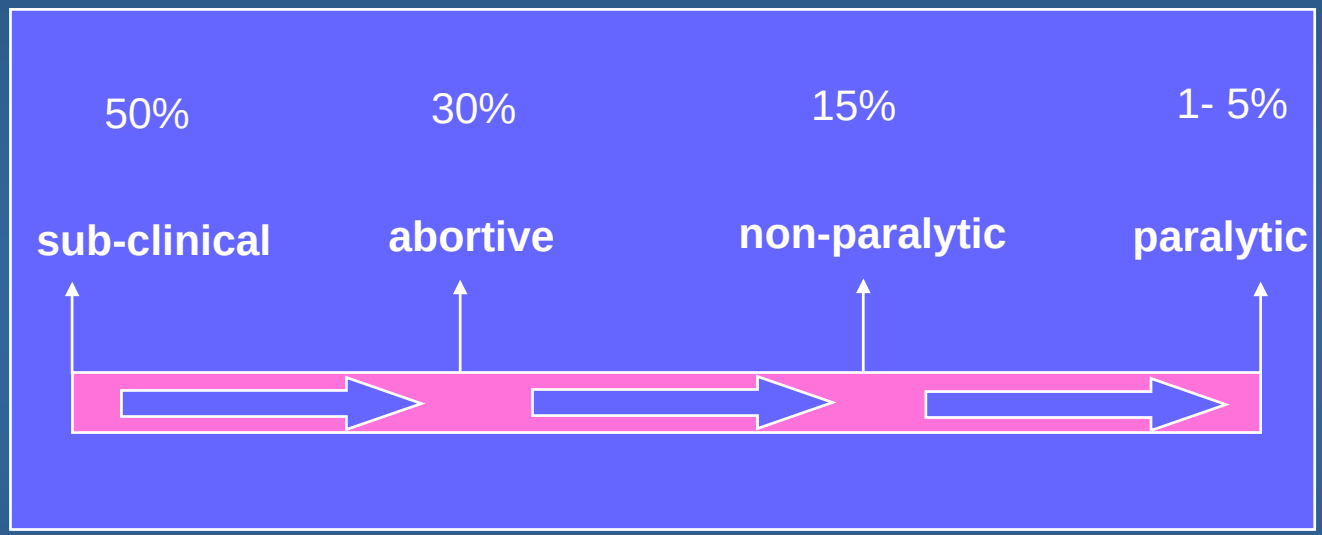
- Biphasic illness - 37%



- Sudden onset illness - 82%


Immune system at work
poliovirus
IgG Antibody

Abortive, Non-paralytic, Paralytic Polio



The category of polio depended upon how far your symptoms progressed.

Why Didn't Everybody Get Paralytic Polio ?

- **Only 1 to 5% got paralytic polio**
- **What happened to the other 95%?**
  - Lighter 'dose' of virus
  - Fewer receptors on intestinal cells
  - Faster immune response
  - Fewer receptors on neurons
  - Milder strain of polio virus

Bulbar or Spinal?
Both are forms of paralytic polio

- Bulbar Polio
  - Damage was mainly in the brain stem, facial area, neck and chest
  - Often resulted in swallowing and breathing problems
- Spinal Polio
  - Damage was mainly in the lumbar area, back, hips, legs, feet
  - Damage to arms and shoulders sometimes related to bulbar polio

Paralytic/non-paralytic: Due to differences in the virus?

Initial Case	Non-paralytic Subsequent cases	Paralytic Subsequent cases
Non-paralytic	77.5%	22.5%
Paralytic	21.3%	78.7%

Non-paralytic cases conferred protection against paralytic polio

Polio virus targets

Only ***some*** tissues are infected

- Brain - specific areas of the brain stem (not the cognitive areas of the cortex)
  - Hypothalamus, reticular activating center
- Anterior horn motor neurons in the spine
  - cervical and lumbar area, less often in thoracic area
- Sympathetic nervous system
  - governs response to cold, heat, blood pressure
- Nerves of eyes
  - taste nerves and nerves to ear sometimes affected

Neurovirulence

- Refers to the ability of the virus to kill neurons
  - Greater neurovirulence = more dead nerve cells
  - Lesser neurovirulence = more surviving nerve cells
- 50% or more neurons must be killed to detect muscle weakness

Neurovirulence of polio virus varied from year to year and place to place

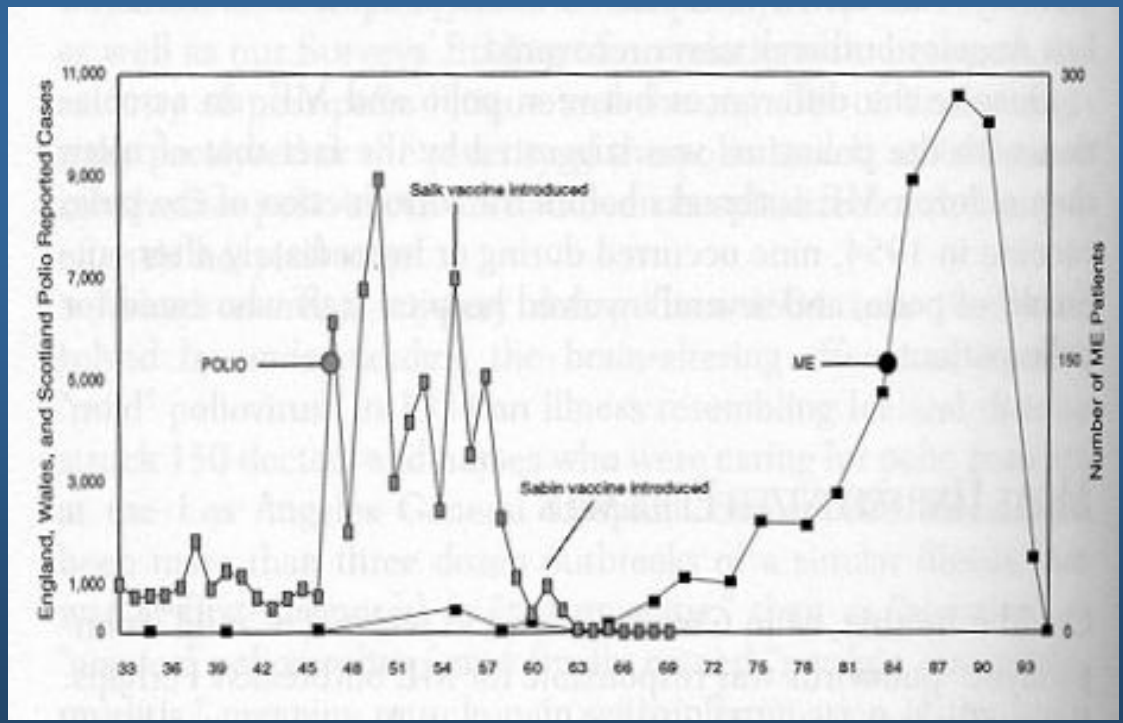
- NYC 1951 epidemic: 6.8 paralytic cases per100,000 people and a mortality rate of 3.6%
- NYC 1949 epidemic: 31 paralytic cases per 100,000 people and a mortality rate of 7.3%

Viruses closely related to polio

- Many viruses are closely related to polio and can cause paralysis, etc.
  - **Coxsackie A7, A9, B1, B2, B3, B4, B5, B6**
  - **Echo Virus 9, 70 and 71**
  - **European encephalitis virus**
- Some implicated in chronic fatigue
- Others cause cardiomyopathy
- No immunization to these viruses

Viruses Fill Empty Niche

- Immunization allows other viruses to replace polio



Polio Epidemics

- **Dramatic appearance in Europe and US about 100 years ago**
- **“Disease of better hygiene standards”**
  - **only partially true**
  - **early US epidemics, children under 1 year were more affected than those 1- 4 yrs old**
- **Epidemics occurred about every 4 to 6 years and usually lasted 1 to 2 years**

Epidemics 1885-1916

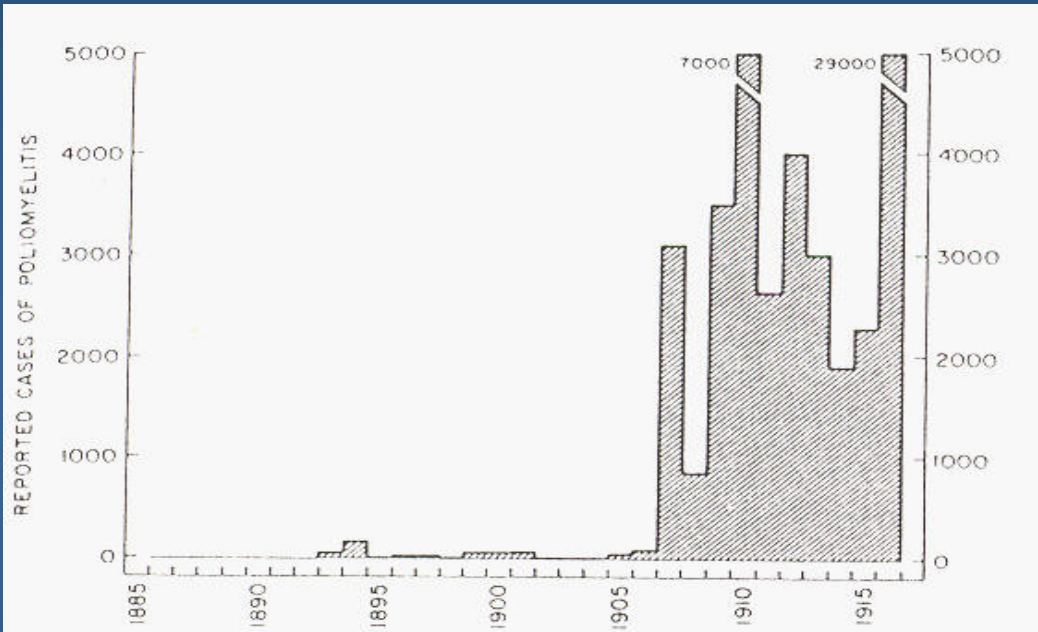


FIGURE 1. The appearance of epidemic poliomyelitis in the United States, 1885–1916. Based on reported cases (mainly paralytic) during an era when reporting was estimated at about 50 per cent.

First major epidemic in US was in 1907

Why polio epidemics appeared is not understood

- **Evidence points to changes in the polio virus itself as one cause of polio epidemics!**

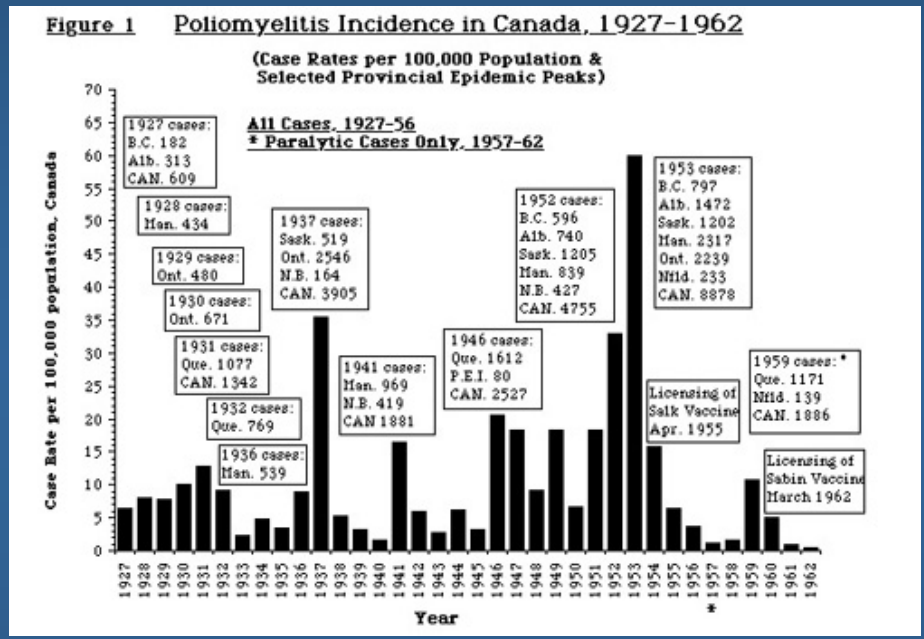
Polio Virus Mutates

- Mutated PV called a “variant”
- All polio infections produced variants
- Changes in neurovirulence occur often
  - **PV1: Mahoney strain and Frederick strain**
- Variants can change paralytic rate
  - **1 in 10,000 cases to 5 in 100 or greater**

PV2 mutated to give: Cincinnati “Flu”

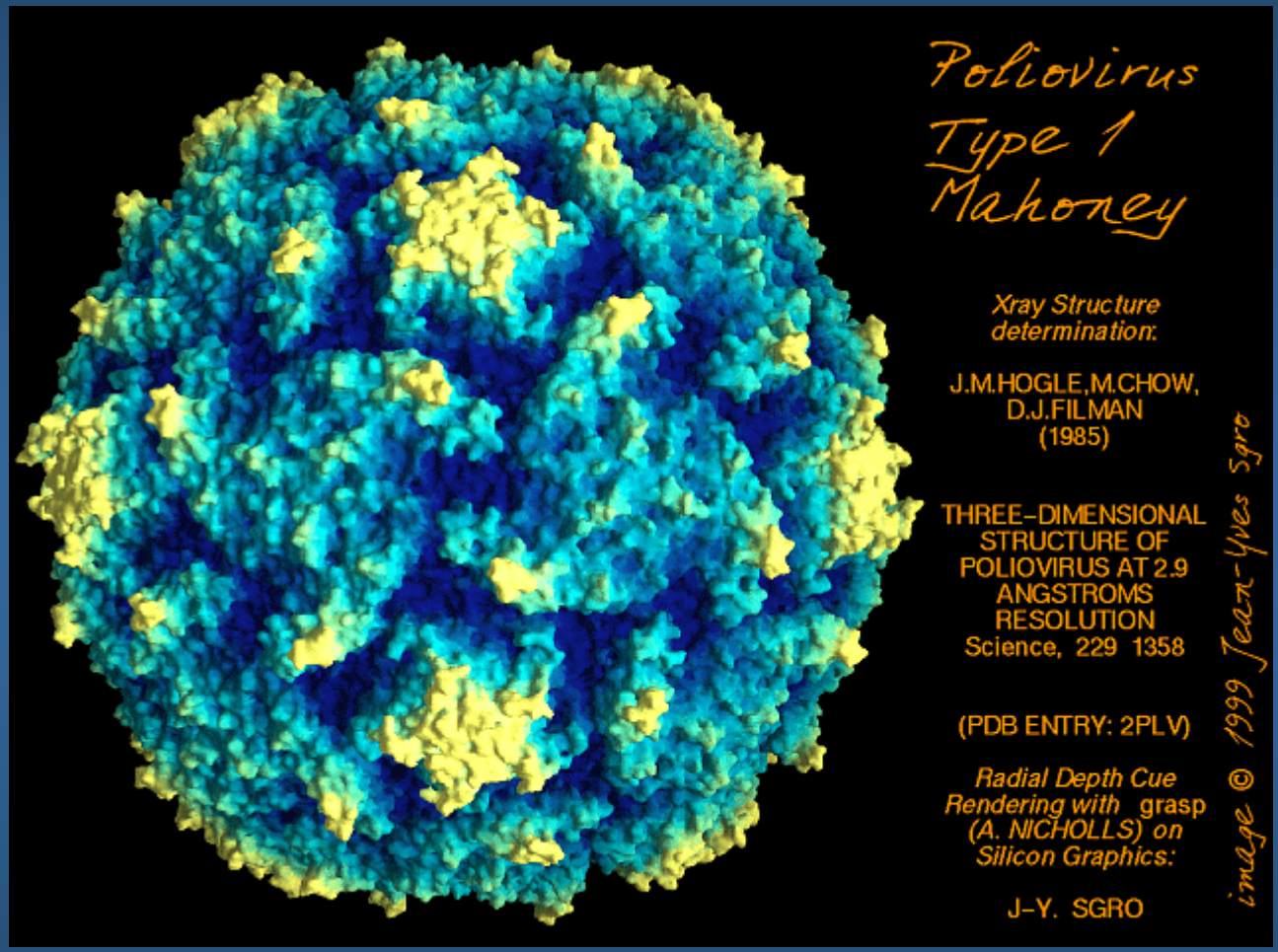
- **1949 - fever, sore throat, abdominal pain, brief stiff neck - 10,000+ cases in 4 weeks**
  - **often biphasic illness**
  - **complete recovery**
- **Samples inoculated into monkeys**
  - **developed paralytic polio**
- **Children developed antibodies to pv2 and some resistance to the other two strains of polio virus**

Annual Incidence of Polio in Canada between 1927 and 1962



Is there any correlation between the year of the acute polio illness and PPS symptoms?

We Don't Know !


Poliovirus
Type 1
Mahoney
Xray Structure
determination:
J.M.HOGLE,M.CHOW,
D.J.FILMAN
(1985)
THREE-DIMENSIONAL
STRUCTURE OF
POLIOVIRUS AT 2.9
ANGSTROMS
RESOLUTION
Science, 229 1358
(PDB ENTRY: 2PLV)
Radial Depth Cue
Rendering with grasp
(A. NICHOLLS) on
Silicon Graphics:
J-Y. SGRO
image © 1999 Jean-Yves Sgro

Did I Have Polio?

- Diagnosis without lasting paralysis was uncertain
  - People told, no history of polio - no PPS!
- Is there a test?
- Antibody Titer Test
  - **If you're immunized - will have Abs to all 3 pv**
  - **If you had polio, Ab level to the infecting pv will be higher**

Conclusions

- Polio virus is among the best understood viruses in the world
- Much remains to be learned about the polio virus
- The relationship of the acute infection to PPS remains unclear but may be related to:
  - **immune system activation**
  - **persistent polio virus in the body**
  - **type and amount of neuronal damage**
  - **the infecting substrain of virus**