1 Poliovirus

Family: *Picornaviridae*

'Pico' - Something small

Single-stranded, positive-sense RNA genome

Genome: *Enterovirus*

Transmits through the intestine

Fecal-oral (or respiratory) transmission

Examples: Poliovirus, Enterovirus D68, Rhinovirus

1.1 Picornaviruses

~8 kb genome

Viral genome is 'infectious'

RNA is both mRNA and viral genome

Protein shell instead of lipid envelope (membrane)

Very stable

Host species: Humans and other mammals

3 poliovirus 'serotypes' are all variants that infect people

Disease: Paralysis (non-polio and polio-type), 'summer cold', meningitis, diarrhea

Picornaviruses replicate in close association with lipid membranes of host cells

Viral RNA replication machinery associated with membranes

1.2 Proteins

Picornaviruses make many individual proteins by breaking up (cleaving) a large 'polyprotein' with a virally-encoded protease

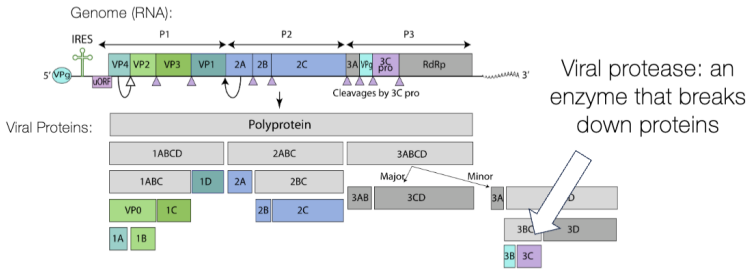

Figure 1: Picornavirus replication

Protease makes a good target for antibodies

1.3 Poliovirus (The Disease)

Mostly sporadic infection until 1905 when it became an epidemic

Poliovirus is an *enterovirus*

Spreads via fecal-oral but can also spread to and infect motor neurons

1. Most infections are mild or asymptomatic
2. Central nervous system infection in 0.5-1% of cases resulting in paralysis of limbs (Poliomyelitis)

   30% of cases are permanent
3. 40% of those who recover suffer 'post-polio syndrome' 30-40 years later
4. 5-10% of those paralyzed die when breathing muscles become immobile

1.4 Poliovirus Replication

1. Ingested polio replicates in oropharyngeal and intestinal mucosa
2. Excreded in feces over a period of several weeks after infection
3. Reaches the blood through the lymph nodes
4. In some cases, can enter the central nervous system

   Cause of paralytic polio
5. through retrograde axonal transport

   Stage blocked by antibodies (maternal or vaccination)

1.4.1 Success as a Pathogen

1. Only found in humans but is able to infect virtually all people
2. No treatment once infected
3. HIGHLY contagious

   Very stable in the environment (protein shell) and secreted for weeks or longer
4. High number of asymptomatic infections

2 Protection Against Polio

1910-1950: Summer in N hemisphere was seen as the season for polio (Due to relative humidity)

Only prevention is avoiding contact or vaccination

→ Closures of pools, schools, and public places

2.1 Vaccine Development

2.1.1 HeLa Cells

Henrietta Lacks died in 1951 from an aggressive cervical cancer

Her cells were incredibly robust (immortal)

→ Played a key role in dewvelopment of polio vaccines and many other biomedical studies

2.1.2 Inactivated Poliovirus Vaccine (IPV)

'Salk' Vaccine available in 1955

Inactivated virus: Killed (no replication)

Made by formalin(formaldehyde)-inactivation of wild type virus

2.1.3 Attenuated Oral Poliovirus Vaccine (OPV)

'Sabin' Vaccine available in 1959

Attenuated Virus: Live virus (can replicate)

Just 2 mutations in serotypes 2 and 3 are sufficient for reversion to a virulent virus

Created through 'attenuation'

Attenuation seeks to isolate a virus that induces immunity, but not disease

Attenuating mutations reduce initial viremia (more type for immune system to respond)

1. 9 mutations for type 1 poliovirus
2. 3 for type 2
3. 5 for type 3

2.1.4 Reversion of Virulence

Polio virus acquires 2% nucleotiee divergence in the 5 days that it takes the virus to go from the mouth to the gut in one individual

OPV can mutate when it replicates and revert to a viruelent form known as vaccine-derived poliovirus (VDPV)

OPV is no longer used in countries that have eradicated polio

Causes Vaccine-Associated Paralytic Poliomyelitis (VAPP)

2.2 Comparing the Vaccines

'Salk' Inactivated Polio Vaccine

Advantages:

1. No viral spread from vaccine

2. No risk of vaccine-related poliomyelitis
3. Induces serum antibodies that protect against infection of the CNS

Disadvantages:

1. Does not protect against infection of the intestine
2. Vaccinated people can still be infected (but won't get poliomyelitis)
3. Does not stop spread
4. Needs to be injected (trained personnel)
5. Cost (5x that of OPV plus cost of needles and trained health care worker)

'Sabin' Oral Polio Vaccine

Advantages:

1. Easy to administer without training (oral liquid)
2. Cheap: Sabin assigned his rights to the vaccine strains over to the WHO which greatly helped with low-cost availability
3. Replication in intestine induces mucosal immunity and prevents new infections
4. Virus is shed ('contact immunity')

Disadvantages:

1. Virus is shed: infection of immunocompromised hosts or naïve populations
2. But OPV can replicate in a vaccinee which means the virus can mutate
3. Reversion to wild-type in gut: non-attenuated strain can infect other people

2.3 Poliovirus Eradication

Reasons for vaccine success:

1. No animal reservoir
2. Two effective vaccines
3. Little antigenic variation
4. Cheap and easy to deliver OPV

Polio remains epidemic only in Pakistan and Afghanistan

VDPV in New York

Travel can lead to transmission into countries which have 'eradicated' polio

IPV does not replicate → virus can still replicate and spread

New attenuated poliovirus vaccine may not revert to virulence