Lecture outline: **POLIO AND OTHER ENTERO-VIRUSES** 18.2.2016

Prof. N.P. Sunil-Chandra, Professor of Microbiology, Faculty of Medicine, University of Kelaniya

POLIO AND OTHER ENTERO-VIRUSES

INTRODUCTION

●These are small non-enveloped isometric viruses that multiply in the gut mucosa and are transmitted from person to person by the faecal-oral route (ingestion disease). They are spread throughout the body via the blood stream. Most infections occur during childhood, and they are usually transient but produce lifelong immunity.

●Clinical syndromes are generally mild, but occasional infections may cause serious disease e.g. paralytic poliomyelitis, meningitis, or myocarditis. There is a high degree of serological cross reactivity between the 72 members.

CLASSIFICATION

●Viruses belong to the family *Picornaviridae (pico*=SMALL - RNA viruses)
●**Enteroviruses:**
●Polio 1, 2, 3
●Coxsackie A 1-24
●Coxsackie B 1-6
●ECHO 1-34
●Entero 68-71
●Entero 72 (Hepatitis A)
●**Rhino viruses:** > 120 serotypes
●**Other animal viruses:** e.g. Foot & Mouth Disease virus

Poliovirus

●Poliovirus has been well studied and is a good example of an enterovirus.
●**Virus:** small (30nm) and stable; an icosahedral capsid enclosing a positive-sense, single-stranded RNA genome. Relatively resistant to extremes of pH and temperature, and to lipid solvents and detergents.
●**Types:** 3 types can be distinguished by antigenic properties.

CLINICAL

●***Source:*** Only known source is infected man
●***Incubation:*** After ingestion of the virus, there is local multiplication in the oropharynx and associated lymph nodes. Local multiplication also takes place in the gut mucosa and regional lymph nodes. Thereafter a viraemia follows, and the patient may experience a fever about a week after exposure.

Poliomyelitis Pathogenesis

Entry into mouth. Replication in pharynx, GI tract, local lymph nodes

Thereafter, a **viraemia** follows, and the patient may experience a fever about a week after exposure.

Hematologic spread to regional lymph nodes & central nervous system

Viral spread along nerve fibers

Destruction of motor neurons

Illness:

Infection may be clinically inapparent or range in severity from a non-paralytic fever to aseptic meningitis or paralysis

●Most infections are asymptomatic, although in some there is a minor transient febrile illness.

●Occasionally (between 1/100 and 1/1000 of cases) the viraemia may lead to CNS involvement and paralysis due to permanent damage to the anterior horn motor neurones of the spinal cord.

●The patient may experience degrees of headache, fever, meningism, aseptic meningitis and muscle pains, and finally muscle paralysis, usually asymmetrical.

●Paralysis develops more frequently in adults, and may be precipitated by muscle trauma (injections, exercise), tonsillectomy, pregnancy and steroid drug administration.

Proportion of inapparent to paralytic infection - in children = 1000:1

- in adults = 75: 1

●The spinal cord may be damaged in a progressive manner from distal to more central - some cases may progress to involve the medulla and brainstem *(bulbar paralysis)* with consequent respiratory paralysis and death, or life on a respirator.

●Virus is produced and released into the gut (and throat initially) and can be isolated from the throat or stools for some weeks following the incubation period. No true long term carrier status occurs.

●The host's antibody response begins soon after the viraemia. Good solid lifelong immunity results to the specific strain of poliovirus, but subsequent infection with other strains may still occur.

Outcome of infection:
Asymotomatic - 90%
Miner non CNS illness – 7%
Aseptic meningitis 2%
Paralytic poliomyelitis 1%

DIAGNOSIS
(1) *Demonstration of the virus*
Virus may be recovered from faeces (also throat swabs), by inoculation of cell cultures and recognition of *cytopathic effects* with confirmation by *neutralisation of infectivity* with specific antisera.

●Vaccine strains may be recovered and need to be differentiated from wild strains by molecular nucleic acid techniques (PCR).

●Multiple specimens over several days improves chances of recovery of the virus.

(2) *Serology*:
Most cases of poliomyelitis that come to medical attention present with paralysis, i.e. quite late in the pathogenesis, and antibodies have already been formed.

●Antibodies are not usually helpful in providing a positive diagnosis of poliomyelitis, but do give the immune status of an individual (does/does not need further vaccination).

●Detection of specific IgM has not been applied to polio diagnosis. Antibodies are traditionally tested by micro-neutralisation of infectivity *in vitro* using antisera to known virus strains

●CSF: Polio virus is never found in the CSF but antibodies here mean either CNS infection or a leak from blood antibodies

EPIDEMIOLOGY

Reservoir: Human

Transmission: Fecal-oral & Oral-oral possible

Communicability: 7-10 days before & after *(most infectious)* the onset of symptoms
Virus present in stool up to 6 weeks or longer

Source: Only known source is infected human

Incubation: ranges from 3-21 days

●**Before the introduction of a vaccine, (< 1960)**, polio was endemic in the tropics, with rapid circulation in young children (poor hygiene facilitates faecal-oral spread) with minimal paralysis (? protective effect of residual maternal antibody).

●This ensured high "herd immunity" without epidemics.

●In temperate regions, polio showed peaks in summer/autumn. As conditions of hygiene improved, viral spread was hindered and the age of primary exposure rose.

●Primary infection in adulthood resulted in a much higher incidence of paralytic disease. These tendencies rose to a climax in Scandinavian countries just before the vaccine era ,when they experienced devastating epidemics of paralytic poliomyelitis

POLIO VACCINES

●(1) Live attenuated virus (SABIN)(1963)
●Strains of poliovirus 1, 2 and 3 which have been attenuated by passage in unnatural conditions to lose neurovirulence.

●3 live strains mixed, given as oral drops (easy administration).

●Given on 3 occasions plus boosters (one strain may interfere with uptake of another, hence must be given repeatedly to ensure immunity to all 3 types).

●Wild enteroviruses coincidentally present in the gut may also interfere, especially in the tropics.

●Live vaccination mimics natural infection with good immunity including IgA in the gut. This vaccine is used in RSA, USA and most other countries. It is very important to maintain 'cold chain' when storing and distributing vaccine as it may lose potency.

(2) Killed whole virus (SALK)(1957)

●Polio 1, 2 and 3 grown in cell cultures, mixed, killed with formalin.
3 injections at 3 to 6 months of age; later boosters.
Much antigen is required which makes the vaccine expensive.
Effective when coverage is good (nearly 100% immunity in people regularly vaccinated).
Still used in some countries (Netherlands, Scandinavia) in 1990's.

Inactivated Polio Vaccine	Oral polio vaccine
• Contains 3 serotypes of vaccine virus • Grown on monkey kidney (Vero) cells • Inactivated with formaldehyde • Contains 2-phenoxyethanol, neomycin, streptomycin and polymyxin B • Highly effective in producing immunity to poliovirus • >90% immune after 2 doses • >99% immune after 3 doses • Duration of immunity not known with certainty	●Strains of poliovirus 1, 2 and 3 which have been attenuated by passage in unnatural conditions to lose neurovirulence. ●3 live strains mixed, given as oral drops (easy administration). • Given on 3 occasions plus boosters (one strain may interfere with uptake of another, hence must be given repeatedly to ensure immunity to all 3 types). • Highly effective in producing immunity to poliovirus • 50% immune after 1 dose • >95% immune after 3 doses • Immunity probably lifelong

Polio Eradication

- Last case in United States in 1979
- Western Hemisphere certified polio free in 1994
- Last isolate of type 2 poliovirus in India in October 1999
- Global eradication goal

Polio is controlled (?eliminated) by:
(1) Education
(2) Vaccination
(3) Surveillance

●Refer: EPI of Sri Lanka

ENTEROVIRUSES - OTHER THAN POLIO
i.e. Coxsackie, Echo, Entero 68-72

●**Virus structure, Epidemiology, Pathogenesis** of all the enteroviruses are remarkably similar and follow the pattern described for polio.

●Most infections are silent. Viraemia may lead to degrees of involvement of secondary 'target organs' and clinical symptoms and signs related to those organs. For example, meningitis seen is aseptic meningitis caused by coxsackie or echo viruses (which can often easily be isolated from the CSF, in contrast to polio). Viral meningitis resolves spontaneously without treatment but bacterial meningitis is a medical emergency requiring treatment.

●Enteroviruses may be found in the gut of healthy as well as sick children; the association with any illness may be purely co-incidental.

CLINICAL SYNDROMES of *Enteroviruses*
(Refer to pictures of clinical manifestations)
Polio 1, 2, 3
Coxsackie A 1-24
Coxsackie B 1-6
ECHO 1-34
Entero 68-71
Entero 72 (Hepatitis A)

Common virus associated with the clinical syndrome (<u>in bold letters</u>)
Less commonly associated virus (not bold)

●ASYMPTOMATIC
All enteroviruses

●PARALYSIS - permanent
●**Polio 1, 2, 3**
Coxsackie A7

●PARALYSIS - temporary
Coxsackie B1-6

●MENINGITIS (aseptic)
Echo, Coxsackie A and B
Polio, Entero 71

●ENCEPHALITIS
Entero 71
Polio, Echo

●<u>RASH</u>
- *macular*
Many enteroviruses

- *vesicular* - (e.g. 'Hand Foot Mouth')
Coxsackie A

●
●SUMMER FEBRILE ILLNESS
Many enteroviruses

●VESICULAR PHARYNGITIS *('Herpangina')*
Coxsackie A

●MYOCARDITIS
Coxsackie B

●EPIDEMIC MYALGIA *('Bornholm')*
Coxsackie B

●UPPER RESPIRATORY INFECTION *(cold)*
Echo, Coxsackie A

●PANCREATITIS
Coxsackie B

●GASTRO-ENTERITIS
Many enteroviusess

●CONJUNCTIVITIS *(Haemorrhagic)*
Entero 70

●HEPATITIS
Entero 72 (hepatitis A virus)

Coxsackie Viruses

What are Coxsackie Viruses?

- A group of enteroviruses that are associated with a variety of diseases, including meningitis, myocarditis, and pericarditis, and primarily affect children during the summer months.

When Was Coxsackie virus Discovered?

- Discovered in Coxsackie, New York
- First investigated in 1948
- Found in town of close to 9,000 people (2000 census)

What Are Signs and Symptoms Coxsackie virus infection?

- About half the time there are no symptoms
- Sudden high fevers (101 to 104 degrees Fahrenheit)
- Abdominal discomfort
- Nausea
- Sore throat
- Sore muscles

More Signs and Symptoms

- Can cause several different patterns of symptoms that affect different body parts
    - Hand, Foot, and Mouth Disease
    - Herpangina
    - Pleurodynia
    - Hemorrhagic Conjunctivitis

Hand, Foot, and Mouth Disease

- Type of Coxsackie Virus syndrome
- Causes painful red blisters on:
    - Throat
    - Tongue
    - Gums and Cheeks
    - Palms of hands
    - Soles of Feet

Herpangina

- Infection of the Throat
- Causes red-ringed blisters
- Cause ulcers on the tonsils
- Causes ulcers on the roof of mouth and tongue

Pleurodynia

- Also called Bornholm disease
- Causes painful spasms in the muscles of the chest and upper abdomen
- Males: may have pain in the testicles

Hemorrhagic Conjunctivitis

- Infection that affects the whites of eyes
- Starts as eye pain
- Followed by red, watery eyes
- Causes eye swelling and light sensitivity
- Blurry vision may occur

What Are Some Facts About This Virus?

- Can also cause meningitis
- Can cause encephalitis
- Can cause myocarditis
- Can cause hepatitis
- Can cause Cyanosis
    - Turns skin, lips, and nails a bluish color
    - Lack of oxygen

Is Coxsackie Contagious?

- VERY contagious
- Passed on by:
    - Unwashed hands
    - Surfaced contaminated by feces
    - Sneezes or coughs

Can You Prevent Coxsackie?

- No vaccine
- Toys should be sterilized regularly
- Wash hands
    - Particularly after using the toilet
    - What is The Incubation and Duration Time?

Incubation time:

- 2-10 days
- Duration time:
- Varies depending upon type
- Fevers usually last 3 to 4 days

Treatment

- Medications may be prescribed to make the child feel more comfortable
- Viruses cannot be treated with antibiotics
- Complications
- Child may become dehydrated
- Causes by mouth sores (makes it hard to eat and drink)
- IV fluids may be necessary