LECTURE 11. ***Lect. Dr. Ahmed Yaseen Abed***

Enteric viruses (Polio Virus, Rota virus and Rio)

Characteristic properties:

- Small, non-enveloped viruses

-**Multiply** in the **gut mucosa**

-Transmitted from **person to person by the fecal-oral route** (ingestion disease),
- 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

-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)

1.Enteroviruses:

- Polio 1, 2, 3
- Coxsackie A 1-24
- Coxsackie B 1-6
- ECHO 1-34
- Entero 68-71
- Entero 72 (Hepatitis A)

2.Rhino viruses: > 120 serotypes
3.Other animal viruses: e.g., Foot & Mouth Disease virus

POLIOVIRUS AND POLIOMYELITIS

General Characters: -

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. (There are three serotypes poliovirus **type-l** is most common and it causes most epidemics,

poliovirus **type-2** is usually associated with epidemics. Poliovirus **type-3** occasionally causes epidemics)

CLINICAL FEATURES: -

Source: Only known source is infected man.

Incubation: After ingestion of the virus, there is local multiplication in the oropharynx and associated lymph nodes, the gut mucosa and regional lymph nodes. Thereafter a viraemia follows, and the patient may experience a fever about a week after exposure.

Illness: **-**

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

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

3. The patient may experience degrees of headache, fever**,** meningism, aseptic meningitis, muscle pains, **and finally muscle paralysis**, usually asymmetrical.
4. **Paralysis** develops more frequently in adults.

5. The spinal cord may be damaged in a progressive manner from distal to more central with consequent respiratory paralysis and death, or life on a respirator.

6. 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.
7. No true long term carrier status occurs.

8. The host's antibody response begins soon after the viraemia.

9. Good solid lifelong immunity results to the specific strain of poliovirus, **but** subsequent infection with other strains may still occur.

Laboratory Diagnosis: -

(1) Demonstration of the virus: -

a. Virus may be recovered from faeces (also throat swabs), by inoculation of cell cultures and recognition of cytopathic effects with confirmation by neutralization of infectivity with specific antisera.

b. 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 (Host immune response):

a. Most cases of poliomyelitis present with paralysis, i.e., quite late in the pathogenesis, and antibodies have already been formed.

b. antibodies are not usually helpful in providing a positive diagnosis of poliomyelitis.
c. detection of specific IgM has not been applied to polio diagnosis.
d. antibodies are traditionally tested by micro-neutralization 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.

Polio Vaccines: -

(1) Live attenuated virus (SABIN) (1963).
2) Killed whole virus (SALK) (1957).
Polio is controlled (eliminated) by: -
(1) Education
(2) Vaccination
(3) Surveillance

ENTEROVIRUSES - OTHER THAN POLIOVIRUS

Coxsackie, Echo, Entero 68-72: -

Virus structure, Epidemiology, Pathogenesis of all the enteroviruses is remarkably similar.

Most infections are **silent**. Viraemia may lead to involvement of secondary 'target organs' and clinical symptoms and signs related to those organs. 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.

VIRAL GASTEROENTERITIS

Pediatric diarrhea remains one of the major causes of death in young children. The main factors for high incidence and mortality are unsafe water or inadequate sanitation**.**

The immediate causes are often of an infectious nature (bacteria, parasites, viruses). A number of different viruses cause diarrhea, of which the most important is the family of Rotaviruses.

1. Rotaviruses have been estimated to cause **30-50%** of all cases of severe diarrheal disease in man.

2. Some strains of adenovirus have also been associated with diarrheal disease.
3. A group of "small round viruses have been linked by genetic techniques as closely related to the **"Norwalk"** agent.

Astroviruses, Coronaviruses, Toroviruses are also associated with gastroenteritis in humans.

REOVIRUSES

General Features and Disease: -

-A group of viruses which have a wide host range, including vertebrates, invertebrates, plants, protists and fungi.
-They lack lipid envelopes and package their segmented genome within multilayered capsids.
-Reoviruses can affect the gastrointestinal system (such as rotaviruses) and respiratory tract
-The name "reo-" is an acronym for "respiratory enteric orphan" viruses.
-The term "orphan virus" refers to the fact that some of these viruses have been observed not associated with any known disease. Even though viruses in the family Reoviridae have more recently been identified with various diseases, the original name is still used -Reovirus infections occur often in humans, but most cases are mild or subclinical. Rotaviruses, however, can cause severe diarrhea and intestinal distress in children, and laboratory studies in mice have implicated orthoreoviruses in the expression of coeliac disease in pre-disposed individuals.
The virus can be readily detected in feces, and may also be recovered from pharyngeal or nasal secretions, urine, cerebrospinal fluid, and blood.
-Despite the ease of finding reoviruses in clinical specimens, their role in human disease or treatment is still uncertain.
-Some viruses of this family, such as phytoreoviruses and oryzaviruses, infect plants. Most of the plant-infecting reoviruses are transmitted between plants by insect vectors. The viruses replicate in both the plant and the insect, generally causing disease in the plant, but little or **no harm** to the infected **insect**.

ROTAVIRUSES - (REO virus family)

General Characters: -

Particles are 70 nm round, non-enveloped, double shelled, enclosing a genome of 11 segments of double stranded RNA. The virus is **hardy** and may **even survive in sewage,** despite stringent treatment. Human rotavirus has proved

difficult to culture in vitro, **but** the serologically related monkey and calf rotaviruses grow easily in cell culture.

Clinical Features: -

Essentially an **ingestion** disease **(faecal-oral route).** Incubation is short: **1 to 3** days. Illness: Sudden onset watery diarrhea, with or without vomiting. May last **up to 6 days** (or longer if **immunocompromised**). The disease is self-limiting. Complications: Dehydration may result, this can be severe and life threatening in young children.

Laboratory Diagnosis: -

Detection of virus **in stools** (peaks at day 3 or 4 of diarrhea):-

1.Latex agglutination.
2.Elisa.
3.Electron Microscopy (labour intensive, relatively insensitive).
4.Electrophoresis of RNA segments.
5.Antibody can be detected but is not clinically useful.

Prevention: -

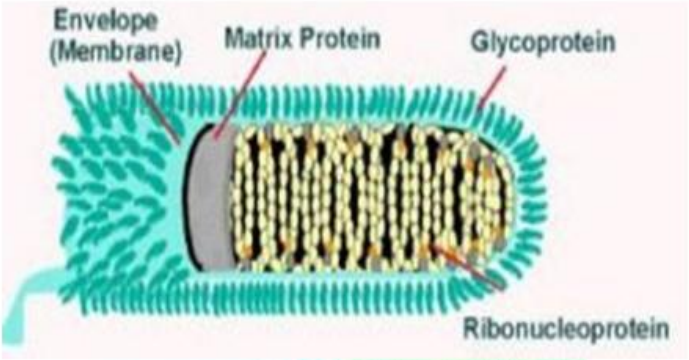
Improved hygiene, education**, clean water**, specific **- breast feeding** helps to provide passive immunity in the newborn (from maternal antibodies), oral rehydration, **development of a vaccine** for Rota virus infection. The prevention of severe dehydration is the main aim, rather than totally preventing infection

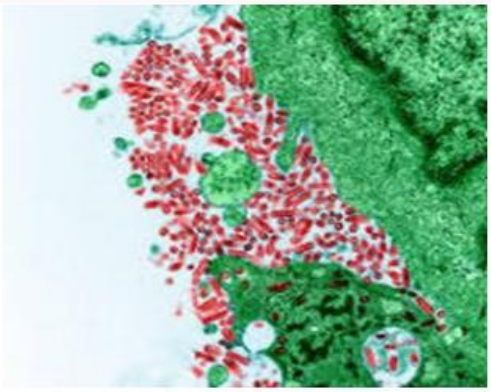
LECTURE-12 ***Lect. Dr. Ahmed Yaseen Abed***

-Rabies virus

Classification and General Characters: -

- Member of the Lyssavirus of the Rhabdoviridae.
- **ssRNA** enveloped virus, helical symmetry.
- Infectivity destroyed by lipid solvents.
- 6-7 nm spike projections are present on the envelope.
- Characteristic bullet-shaped appearance.
- virion 130-240nm.
- **-ve** stranded **RNA** codes for **5** proteins.
- Members of the family Rhabdoviridae exceeding wide range of hosts including vertebrates, invertebrates, and plants.
- Rabies virus has been adapted to growth in a wide variety of primary and continuous cell systems.
- The virus is grown in **human diploid cells** for the purpose of producing a **vaccine.** It has also been adapted to growth in avian embryos





Pathogenesis and Clinical Features: -

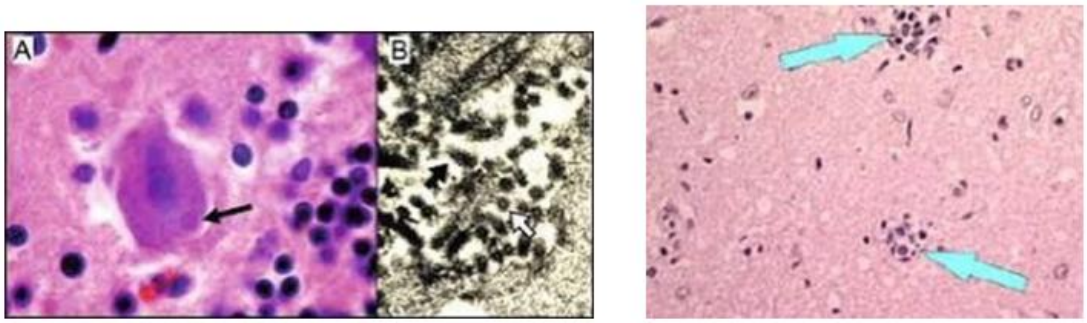
Human infection is usually caused by **the bite of dogs or other animals**, the virus is present in the **saliva** of the animals, the disease can also be caused by licks or aerosols.
Once bites take place the virus (in animal saliva) enter deep into the muscle and **start** multiplying in both muscle tissue and connective tissue **then** reaching nerves, nerve cells, and **finally** the **brain** producing **Negri bodies** as round or oval inclusions within the cytoplasm of nerve cells of infected human. Negri bodies act to concentrate viral proteins, cellular factors and nucleic acids to build a platform facilitating viral replication. They **might** also **prevent** the **activation** of host **innate immunity** and **restrain** the **access** of **viral machineries** to **cellular antiviral proteins**

Five general stages of rabies are recognized in humans:

1-**incubation period:** - usually **30 to 90 days** but ranging from as few as 5 days to longer than 2 years after initial exposure.
2-**Prodromal period**, which usually lasts from **2 to 10 days**, the symptoms are often nonspecific including fever, nausea, vomiting, headache, fatigue, sore throat, cough.

3-**Acute neurological period** (2 to 3 days, rarely up to 6 days).
4-**coma**.
5- **death**.
The incubation period is highly variable, ranging from 7 days to several years. It depends on several factors such as: -
1. Dose of inoculum
2. The severity of the wound
3. The length of the neural path **from** the wound to the brain, e.g., wounds on the face have a shorter incubation period than wounds in the leg.

Laboratory Diagnosis: -
The diagnosis of animal and human rabies can be made by several methods: -
(1) histopathology (**detection of Negri bodies**).
(2) virus cultivation.
(3) Serology (The most commonly used serological tests were the mouse infection neutralization test (MNT) or the rapid fluorescent focus inhibition test (RFFIT). These tests have now been largely replaced by **EIAs**. Serology had been reported to be the most useful method for the diagnosis of rabies.
(4) virus antigen detection in biopsy specimen from **corneal scrapings** or **skin from nape of neck.**
(5) intracerebral inoculation of suckling mice.
(6) Detection of viral N.A (**Nucleic Acid**) by **PCR**.
Although each of the first 3 methods have distinct advantages, none provide a rapid definitive diagnosis.



Negri bodies (Rabies)

PREVENTION AND TREATMENT:

• No specific treatment

• **Washing of wound** with **soap** and **water** for 10 to 15 minutes.
•contacting a healthcare provider to determine if **post-exposure prophylaxis is required.**

• **Vaccination**: **post-exposure** and also **pre-exposure for high-risk groups**, e.g.,
veterinarians and animal handlers. (Rabies vaccine is 100% effective if given early, and still has a chance of success if delivery is delayed).
•**Administration**, **post-exposure**, **of immunoglobulins** to non-vaccinated persons. Vaccination after exposure, post-exposure prophylaxis (PEP), is **highly successful** in **preventing** rabies. In unvaccinated humans, rabies is virtually always fatal after neurological symptoms have developed.