

RNA NON-ENVELOPED Picornaviruses

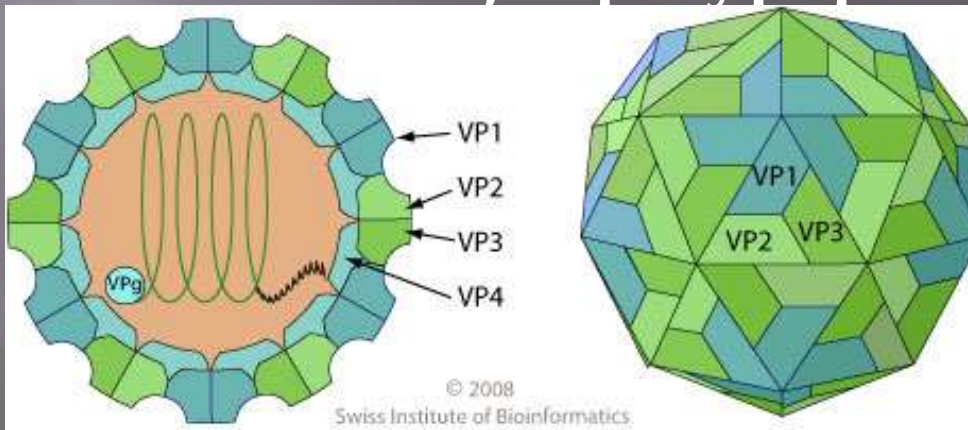
Dr. Mohammed J. M. Shallal

Picornaviruses

Represents a very large virus family with respect to the number of members, but one of the smallest in terms of virion size and genetic complexity.

Properties of Picornaviruses

- ▣ They are small non-enveloped viruses
- ▣ Icosahedral nucleocapsid.
- ▣ Genome: Single-stranded RNA, linear, positive-sense, infectious when purified
- ▣ Proteins: Four major polypeptides (VP1-4)



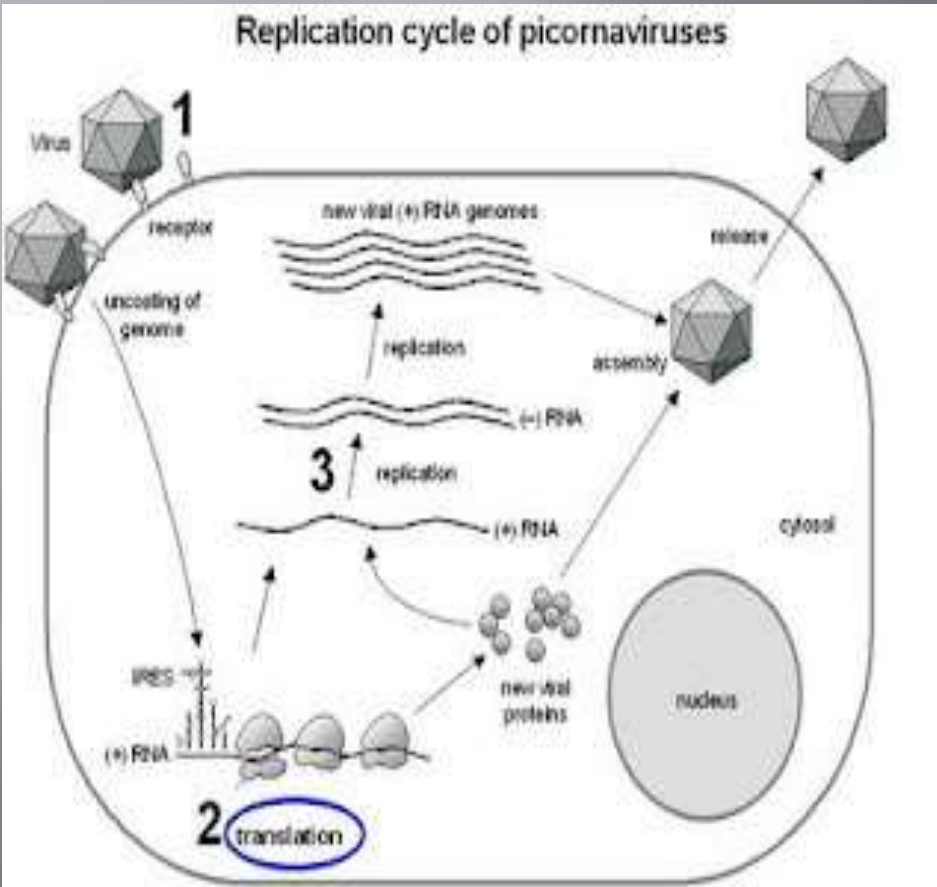
Properties of Picornaviruses

- ▣ Replicate in the cytoplasm of the cell.
- ▣ They are not inactivated by lipid solvent, such as ether, **because they do not have envelope.**
- ▣ family includes three medically important genera; **enteroviruses, rhinoviruses and *Hepatovirus* (hepatitis A virus).**

ENTEROVIRUSES:	- RHINOVIRUS
Major groups Polioviruses types 1-3. Coxsackieviruses A & B. Echoviruses.	100 serotype
Infect the enteric tract	Found in the nose and throat
Replicate at 37°C	Replicate at 33°C
Stable at acid pH 3-5, so survive at gastric acid	Acid labile

Picornavirus Replication

- occurs in the cytoplasm of cells.



1. First, the virion attaches to a specific receptor in the plasma membrane. The receptors for **poliovirus** and **human rhinovirus** are members of the **immunoglobulin gene superfamily**, **echoviruses** recognize a member of the **integrin adhesion superfamily**.

2. Receptor binding triggers a conformational change in the virion which results in release of the viral RNA into the cell cytosol.

3. The infecting viral RNA is translated into a polyprotein (**coat proteins** and **essential replication proteins**).

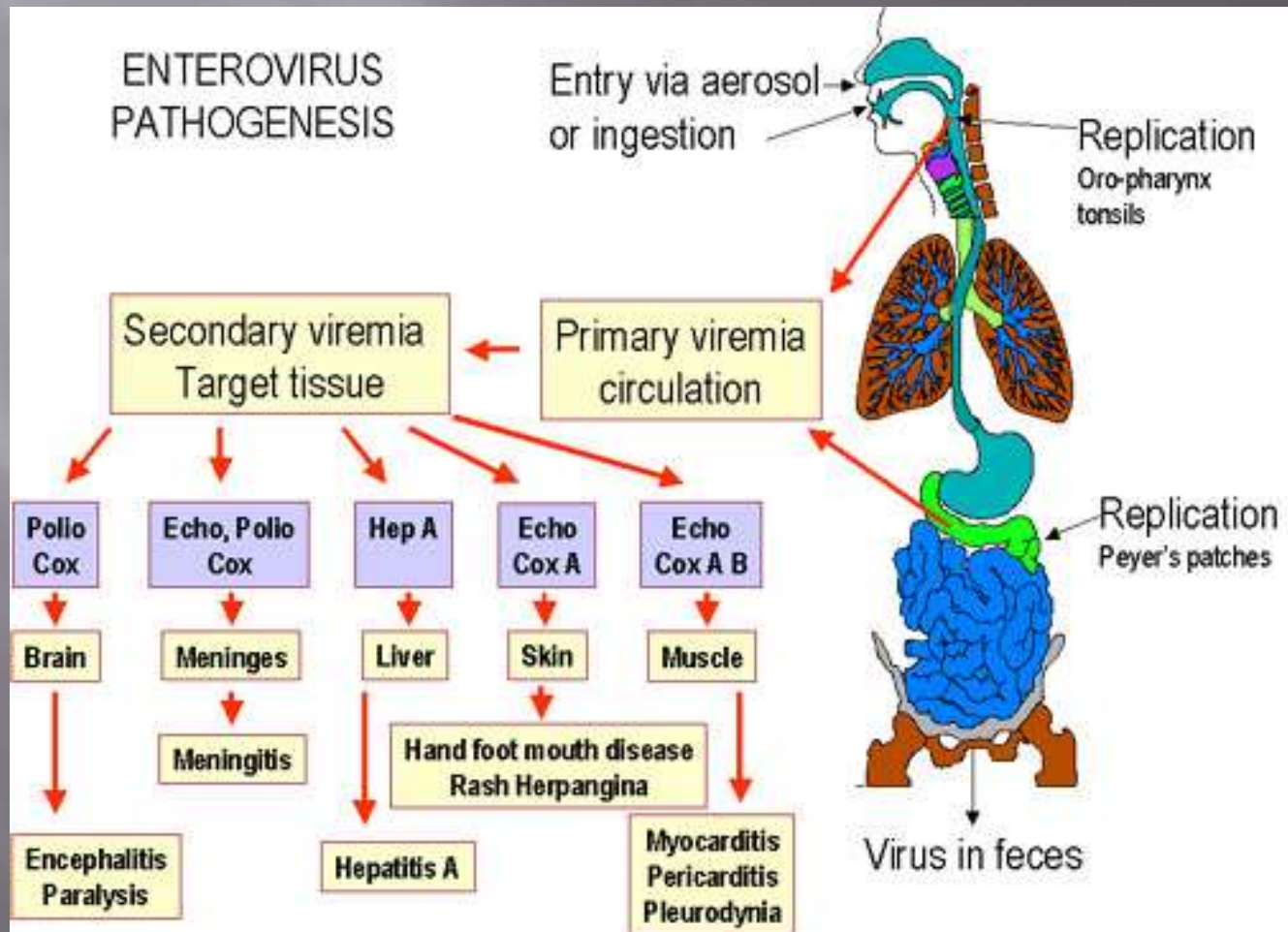
4. The mature virus particles are released when the host cell disintegrates

A. ENTEROVIRUSES

Polioviruses types 1-3

Coxsackieviruses A & B

Echoviruses



1. Poliovirus

▣ POLIOMYELITIS

is an acute infectious disease that in its serious form affects the central nervous system. **The destruction of motor neurons in the spinal cord results in flaccid paralysis.** But, most infections are subclinical

There are three antigenic (serologic) types based on different antigenic determinants on the outer capsid proteins. **Because there is little cross reaction, protection from disease requires the presence of antibody against each of the three types.**



Pathogenesis

The mouth is the portal of entry of the virus, and primary multiplication takes place in the oropharynx or intestine. The virus is regularly present in the throat and in the stools before onset of illness.

One week after infection the virus continues to be excreted in the stools for several weeks even though high antibody levels are present in the blood. The central nervous system may then be invaded by way of the circulating blood.

Pathology

Poliovirus can spread along axons of peripheral nerves to the central nervous system, where it continues to progress along the fibers of the lower motor neurons to increasingly involve the spinal cord or the brain. Poliovirus invades certain types of nerve cells, and in the process of its intracellular multiplication it may damage or completely destroy these cells

Clinical Findings

When an individual susceptible to infection is exposed to the virus, the response ranges from inapparent infection without symptoms, to a mild febrile illness, to severe and permanent paralysis.

The incubation period is usually 7-14 days

1-Mild Disease: This is the most common form of disease characterized by fever, malaise, drowsiness, headache, nausea, vomiting, Recovery occurs in a few days.

2-Nonparalytic Poliomyelitis (Aseptic Meningitis): In addition to the symptoms and signs listed in (1), the patient with the nonparalytic form has **stiffness and pain in the back and neck**. The disease lasts 2–10 days, and recovery is rapid and complete.

3-Paralytic Poliomyelitis: The predominating complaint is flaccid paralysis **resulting from lower motor neuron damage**. Maximal recovery usually occurs within 6 months, with residual paralysis lasting longer.

4-Progressive Postpoliomyelitis Muscle Atrophy

Laboratory Diagnosis

1. The virus may be recovered from throat swabs taken soon after onset of illness and from rectal swabs or stool samples collected over long periods.
2. An isolated virus is identified and typed by neutralization with specific antiserum.
3. Virus can also be identified by RT -PCR assays

2. Coxsackieviruses

Transmission & Epidemiology:

Coxsackieviruses can be transmitted by fecal-oral route, but respiratory aerosols also play a role.

Pathogenesis & Pathology:

Virus has been recovered from the blood in the early stages of natural infection in humans. Virus is also found in the throat for a few days early in the infection and in the stools for up to 5–6 weeks. Virus distribution is similar to that of the other enteroviruses.

Clinical Findings

Group A Specific Diseases:

- A. Herpangina : fever, sore throat, and tender vesicles in oropharynx.
- Hand-foot-mouth Disease: vesicular rash on the hands and feet and ulceration in the mouth.

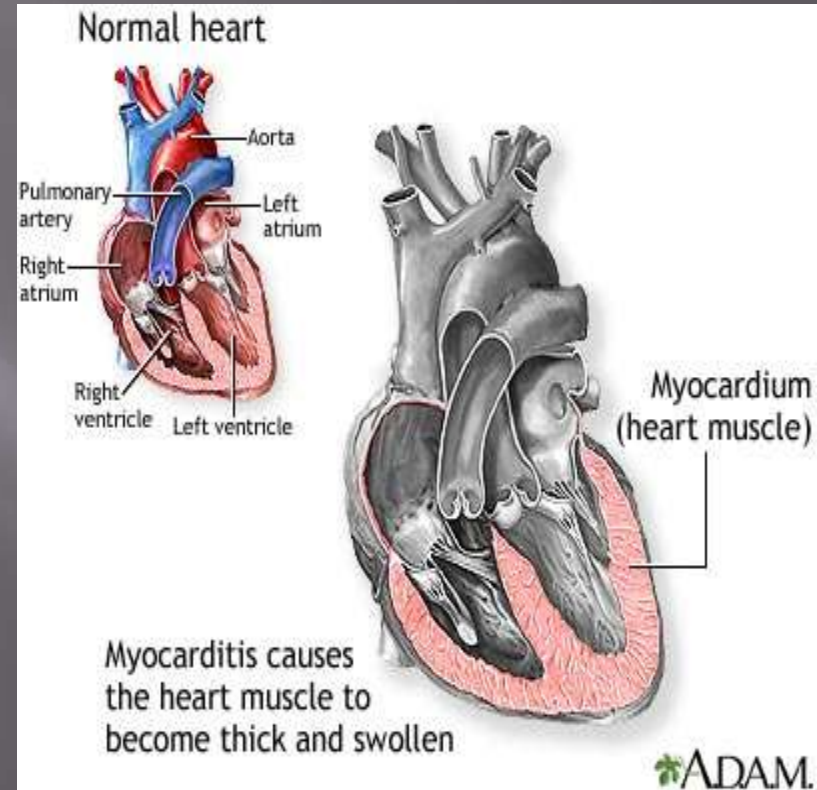


B. Group B Specific Diseases:

- **Pleurodynia:** fever and severe pleuritic chest pain
- Myocarditis and pericarditis
- **Diabetes:** suspected to have a role in juvenile diabetes in humans.

■ C. Diseases Caused by both Groups:

- Aseptic meningitis.
- Upper respiratory tract infections with or without rash



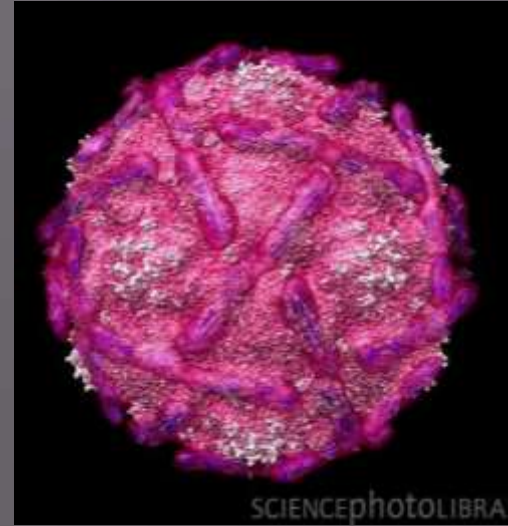
Lab. Diagnosis:

- Isolation of the virus in cell culture
- Rise in Ab titer
- Reverse transcription-PCR tests can be broadly reactive (**detect many serotypes**) or more specific. Such assays have advantages over cell culture methods

Treatment and Prevention:

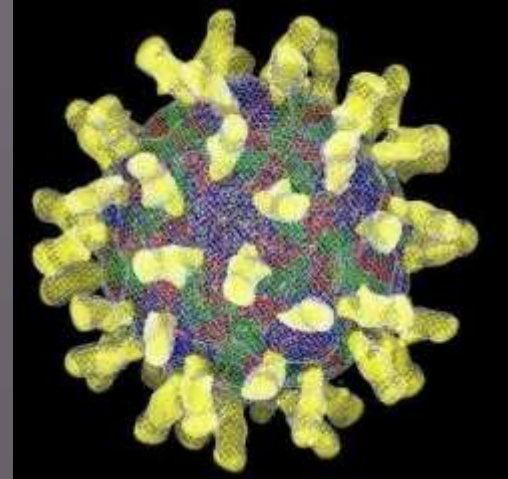
- ▣ No antiviral therapy or vaccine

3. ECHOVIRUSES:



- ▣ Disease: viruses cause variety of diseases such as aseptic meningitis, upper respiratory infection, febrile illness with or without rash, infantile diarrhea, and hemorrhagic conjunctivitis.
- ▣ They are transmitted by fecal-oral route.
- ▣ They are one of the leading cause of aseptic (viral) meningitis

B. RHINOVIRUSES



Disease: **The main cause of common cold**

Important Properties:

- More than 100 serotypes.
- Replicate better at 33 degree C than in 37.
- Acid-labile, killed by gastric acid.
- ▣ Replication: the cell surface receptor for rhinoviruses is **ICAM-1**.

Transmission a & Epidemiology:

- ▣ there are two modes of transmission
 - Direct from person to person via aerosols of respiratory droplets.
 - Indirect in which respiratory droplets are deposited on the hands or on a surface then transported via fingers to nose or eyes.

Clinical Findings:

- After an incubation period of 2-4 days, sneezing, nasal discharge, sore throat, cough, and headache are common.
- The illness lasts about 1 week.

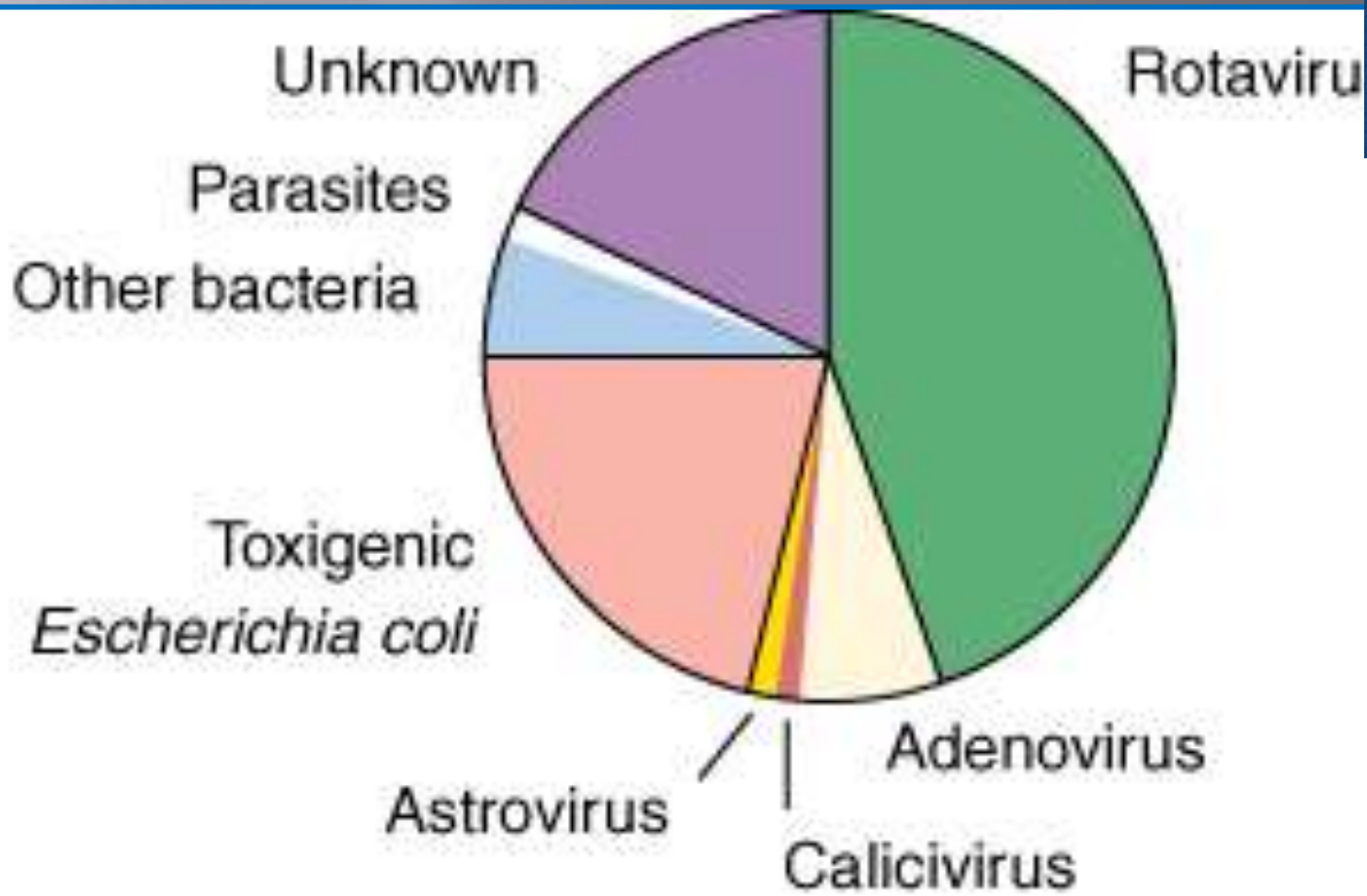
Treatment & Prevention:

- No specific antiviral therapy
- ▣ Vaccines appear impractical because of large number of serotypes.

RNA NON-ENVELOPED VIRUSES

Reoviruses

- ▣ Reoviruses are medium-sized viruses with a double-stranded, segmented RNA genome. The family includes human rotaviruses, the **most important cause of infantile gastroenteritis around the world**
- ▣ Acute gastroenteritis is a very common disease with significant public health impact. In developing countries it is estimated to cause as many as 1.5 million deaths of preschool children annually

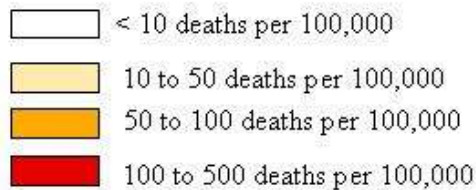
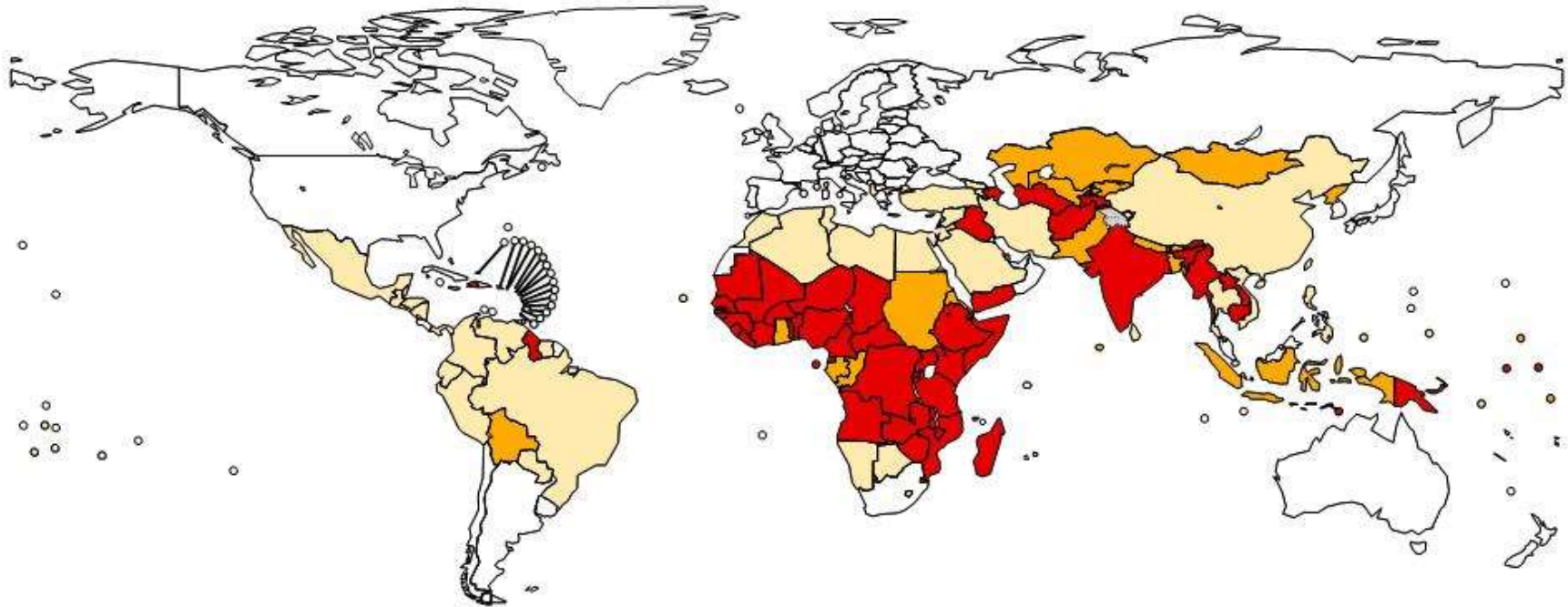


B

Developing countries

An estimate of the role of etiologic agents in severe diarrheal illnesses requiring hospitalization of infants and young children

Under-5 mortality rate due to rotavirus disease per 100,000 population (<5 years of age)



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.

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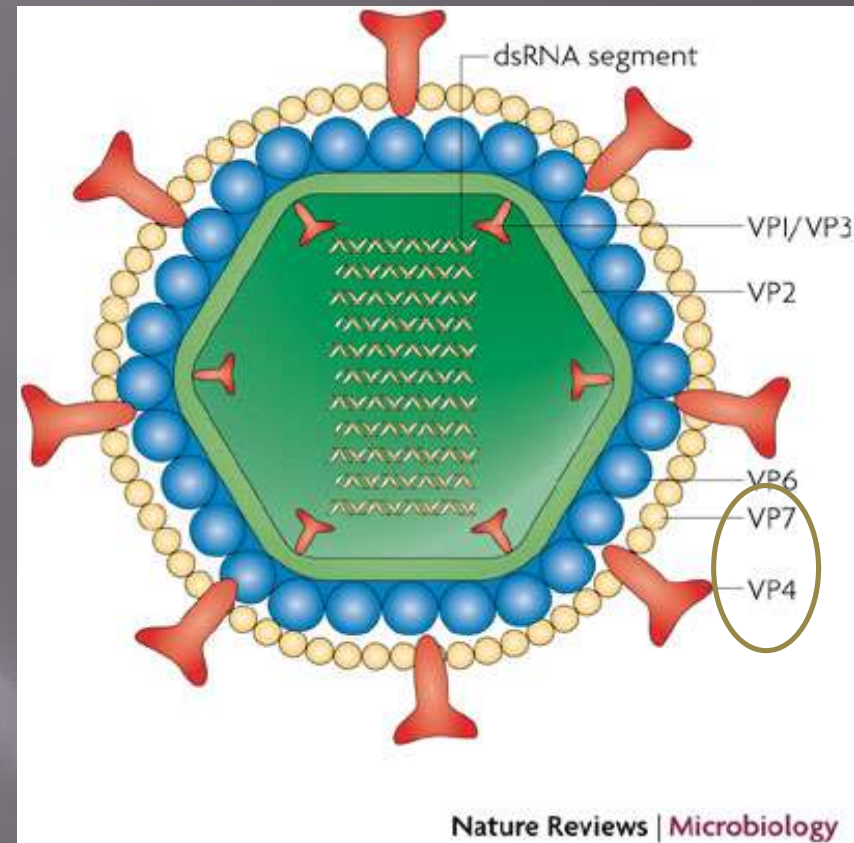
Rotaviruses

- **Important properties:**
- **They are composed of:**
 - **Segmented double-stranded RNA genome**
 - **Double-layered icosahedral capsid without envelope.**
 - **RNA-dependent RNA polymerase.**
 - **Rotaviruses have been classified into five species (A–E)**
 - **Group A rotaviruses are the most frequent human pathogens**

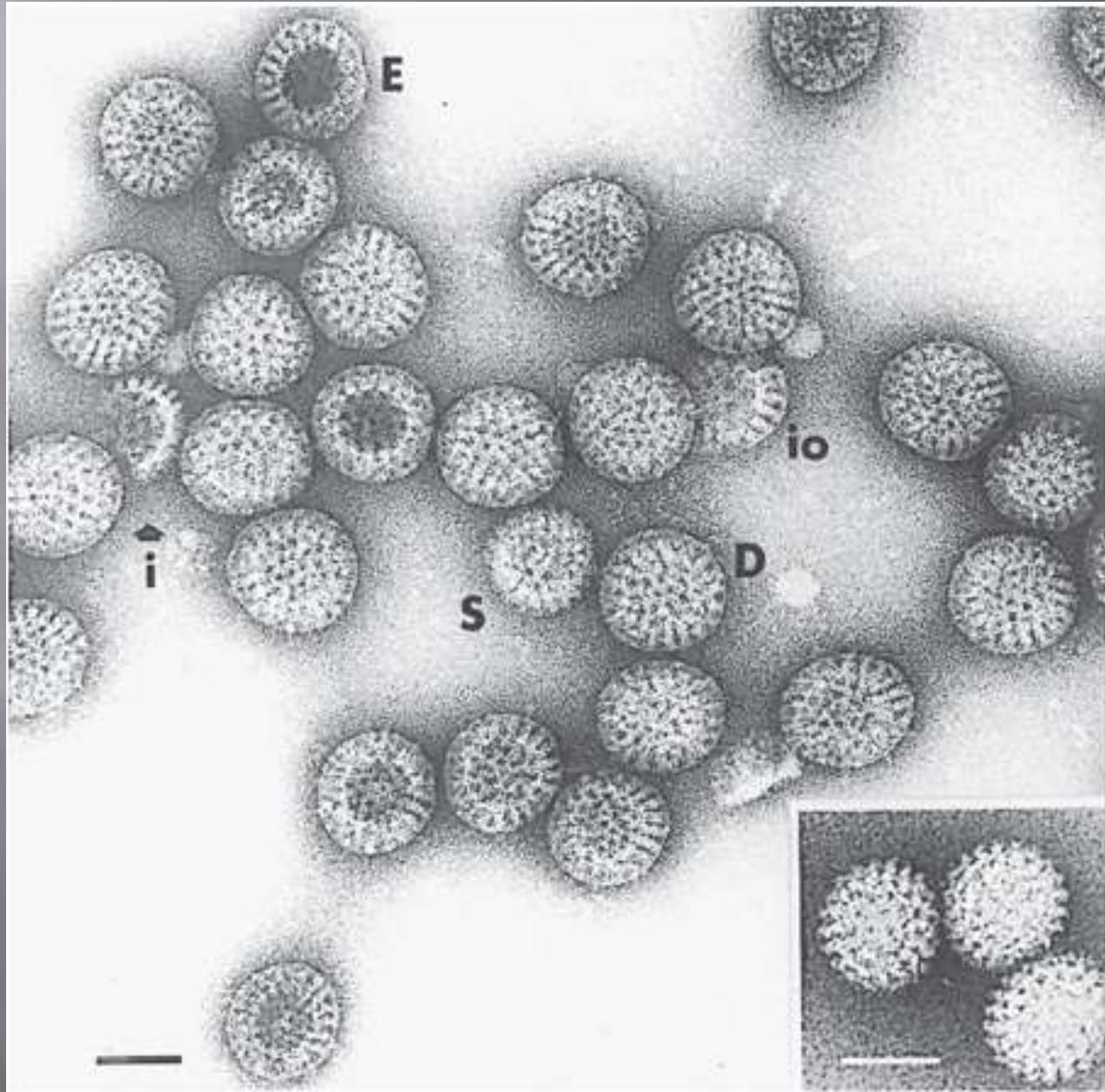
Outer capsid proteins VP4 and VP7 carry epitopes important in neutralizing activity, with VP7 glycoprotein being the predominant antigen.

- Five serotypes are responsible for the majority of human disease.

Transmission and epidemiology:
The rotavirus transmitted by the fecal-oral route.



EM picture of Rota Virus



Pathogenesis

Rotaviruses infect cells in the villi of the small intestine

They multiply in the cytoplasm of enterocytes and damage their transport mechanisms.

One of the rotavirus proteins, NSP4, is a viral enterotoxin and induces secretion by triggering a signal transduction pathway.

Damaged cells may slough into the lumen of the intestine and release large quantities of virus, which appear in the stool.

Viral excretion usually lasts 2–12 days in otherwise healthy patients but may be prolonged in those with poor nutrition.

Diarrhea caused by rotaviruses may be due to impaired sodium and glucose absorption as damaged cells on villi are replaced by non-absorbing immature crypt cells. It may take 3–8 weeks for normal function to be restored



Rotavirus

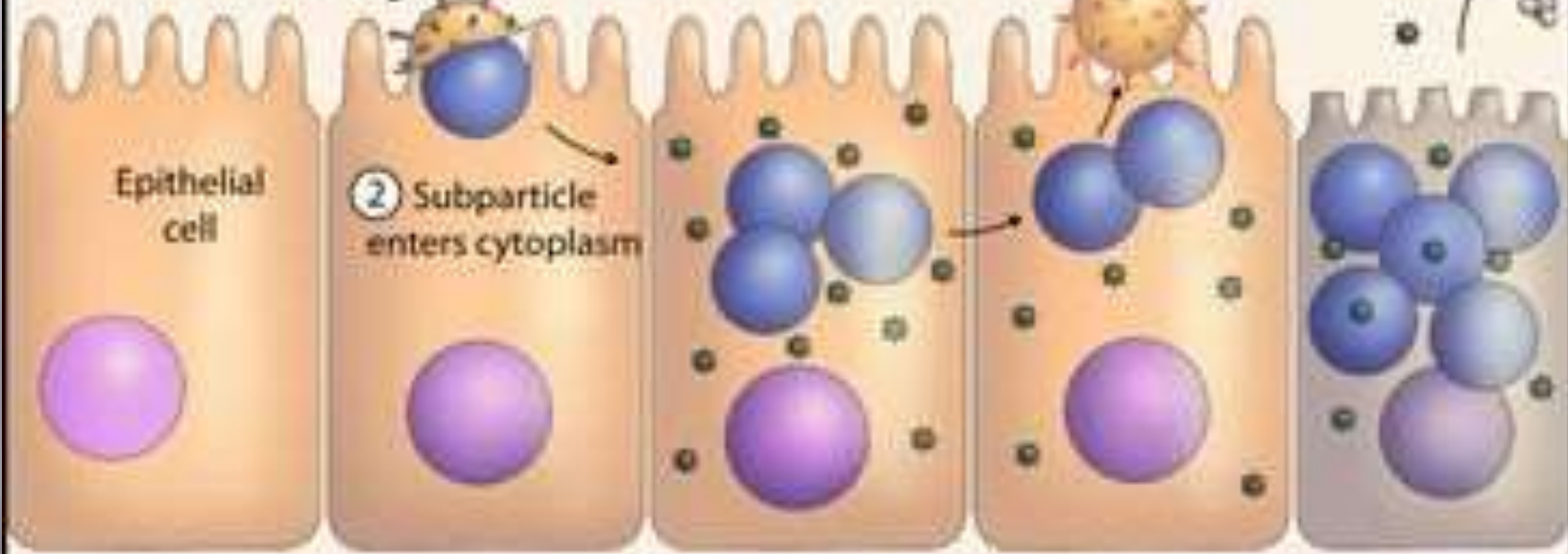


VP4

① VP4 spikes attach to lining and outer shell is shed

④ New virus leaves infected cells to invade healthy ones

⑤ Epithelial cells die and fluids exit the body



② Subparticle enters cytoplasm

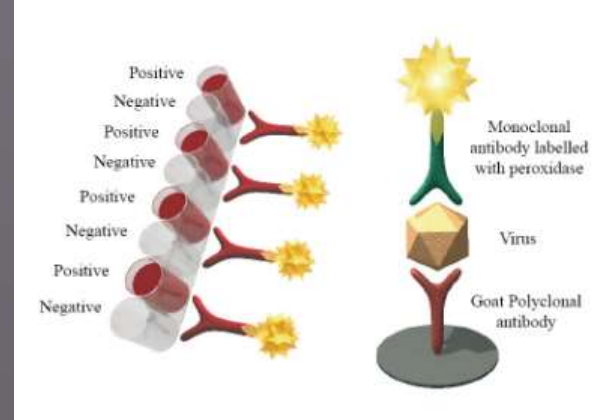
③ Virus multiplies and produces toxin

Clinical Findings

- ▣ Rotaviruses cause the major portion of diarrheal illness in infants and children worldwide but not in adults.
- ▣ The incubation period is 1-3 days.
- ▣ Typical symptoms include **watery diarrhea, fever, abdominal pain, and vomiting, leading to dehydration.**
- ▣ In infants and children, severe loss of electrolytes and fluids may be fatal unless treated

▣ Laboratory diagnosis

- ▣ 1. Virus in stool is demonstrated by enzyme immunoassays (EIAs)
- ▣ 2. Serologic tests can be used to detect an antibody titer rise, particularly ELISA.
- ▣ 3. Genotyping of rotavirus nucleic acid from stool specimens by the polymerase chain reaction is the most sensitive detection method.



▣ Epidemiology

- ▣ Rotaviruses are the single most important worldwide cause of gastroenteritis in young children.
- ▣ up to 50% of hospitalized children throughout the world are caused by rotaviruses.
- ▣ Rotavirus infections usually predominate during the **winter** season.
- ▣ Symptomatic infections are most common in children between ages **6 months and 2 years**

Treatment & Control

- ▣ is supportive, to correct the loss of water and electrolytes that may lead to dehydration, acidosis, shock, and death.
- ▣ replacement of fluids and restoration of electrolyte balance either intravenously or orally, as feasible.
- ▣ An oral live attenuated rotavirus vaccine (contains up to five strains of rotavirus) (withdrawn after 1 year).
- ▣ To children between the ages of 6 weeks and 32 weeks old.
- ▣ Side effects of vaccine such as **intussusception** (bowel blockages) as an uncommon but serious side effect associated with the vaccine.
- ▣ In 2006, an oral pentavalent human-bovine rotavirus vaccine) reassortant live-attenuated, oral vaccine (RotaTeq) has been developed **by Merck Research Co**, (not associated with intussusception). (VP4 protein from the human rotavirus parent strain and the outer capsid protein G6 from the bovine rotavirus parent strain.

Caliciviruses

- ▣ In addition to rotaviruses and adenoviruses, members of the family **Caliciviridae** are important agents of viral gastroenteritis in humans. The most significant member is Norwalk virus
- ▣ **Noroviruses (Norwalk virus)** are the most important cause of epidemic viral gastroenteritis in adults

Caliciviruses

Properties

- ▣ **Virion:** Non-enveloped, Icosahedral, Single-stranded RNA, linear, positive-sense, nonsegmented
- ▣ **Proteins:** capsid is composed of a single protein
- ▣ **Replication:** Cytoplasm

Noroviruses are major cause of nonbacterial epidemic gastroenteritis

- ▣ Human viruses are noncultivable

Astroviruses

- ▣ Astroviruses are about 28–30 nm in diameter and exhibit a distinctive star-like morphology in the electron microscope
- ▣ They contain single-stranded, positive-sense RNA
- ▣ Astroviruses cause diarrheal illness and may be shed in large quantities in feces.
- ▣ The viruses are transmitted by the fecal–oral route through contaminated food or water

Viruses cause GIT infections

- ▣ Overview on Viruses that cause GIT infections
- ▣ 1-Rota v.
- ▣ 2-Adeno v.
- ▣ 3-Coxsackie v.
- ▣ 4-Astrovirus
- ▣ 5-Norwalkvirus (Norovirus)
- ▣ 6-Echo v.

Overview on Viruses that cause Common cold

- ▣ rhinoviruses (over 100 types),
- ▣ coronaviruses,
- ▣ influenza viruses,
- ▣ parainfluenza viruses.
- ▣ respiratory syncytial virus
- ▣ Coxsackie viruses
- ▣ Echovirus

Overview on Viruses that cause lower respiratory tract infections

- ▣ Influenza,
- ▣ Parainfluenza,
- ▣ RSV (respiratory syncytial virus)
- ▣ Coronaviruses

Overview on Viruses that cause Genital tract and sexually transmitted Infections

- ▣ Localized genital lesion
- ▣ Vesicular or ulcerative genital lesions (HSV-2 or less commonly type 1 or VZV)
- ▣ Non-vesicular or non-ulcerative genital lesions
- ▣ Papilloma virus or genital warts
- ▣ Molluscum contagiosum
- ▣ Systemic infections that are sexually transmitted
- ▣ HIV, HBV, HDV, HCV

Thank You

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