



University of Jordan  
Faculty of Medicine



Medical Committee  
The University of Jordan

Introduction to  
**Microbiology**

Title :

**GI viruses**

Professor:

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# : 35

Slides

Handout

Sheet

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groups/Doctor2018  
<http://medstudygroup.weebly.com>

We will continue about RNA viruses :

## **Respiratory Syncytial Virus (RSV)** continuation from last lecture:

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- It is a ssRNA enveloped virus, causes a sizable epidemic each year, present worldwide
- Peak incidence: 2-5 months age .
- It causes acute bronchiolitis and broncho-pneumonia in infants, especially in the first 2 years of life.
- Re-infection throughout life is common but the infection or the symptoms will be mild .
- It has a short incubation period : (2-7)days .

### **Manifestations**

#### **Slide #37/38/39**

- It causes **cough** and **rhinorrhea**(runny nose).
- 50 % of primary infections spread to LRT (Lower Respiratory Tract), so as a complication the infant might have **pneumonia** (we already mentioned it causes pneumonia)
- **Obstruction** by mucus & epithelium (enlarged due to the infection) occurs, and it causes **hyperinflation** in the chest.
- \*\*\* The most common cause of severe LRT infection in infants .
- It also can cause **croup**, (as we said : the main causative agent of croup is para-influenza virus especially type 1 ).

**# Note** about the para-influenza virus “ as we said “ :

- *It has 4 serotypes (1,2,3,4) .*
- *The most common are 1 and 3 .*
- *Type one is the main responsible for croup, which is acute laryngo-tracheo-bronchitis.*
- *Type three is responsible for LRT infection .*

#### **- Back to the RSV :**

- In older children and adults, the infection and the symptoms are much milder, because of previous infection during infancy

## Infants at Risk of Severe Infection

### Slide #40

- Those who have pre-existing conditions in the lung or the heart or are immunocompromised .

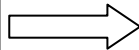
## Culturing and Diagnosis

### Slide #41/42

As we said it is mostly prevalent in the **winter** months, so you should :

- 1- Take history from the parents of the infant
- 2- Do a physical examination .
- 3- Then do a chest X-ray, and you may find :

*You shouldn't be concerned with them, we will take them in the clinical years*



- Hyperinflation .
- Peri-bronchial thickening .
- Increased interstitial markings .

- You should take a nasal wash or a broncho-alveolar lavage (**lavage means a washout**) from the patient and then inoculate it into a cell culture, then we can observe **multinucleated giant cells**

– Respiratory **Syncytial** Virus's name is derived from it forming Syncytia = multinucleated cells

- Another way to diagnose it is by **serology** .

## Treatment

### Sildes #43

- You should clear the airways by suction and give good amount of **oxygen** by a mask like a nasal mask

- In cases of severe infection, patients may benefit from **ribavirin** (antiviral drug ) .

- There is **no** vaccine available for RSV.

- RSV immunoglobulin can be used to protect infants at risk of severe RSV disease (those who have a pre-existing condition as we mentioned).

## Common Cold Viruses

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### **Slide #44**

- It is a term referring to **Rhinoviruses** and **Coronaviruses**.
- Common colds account for one-third to one-half of all acute respiratory infections in humans.
- Common cold means causing infection in the URT (Upper Respiratory Tract) .
- Rhinoviruses are responsible for 30-50% of common colds.
- Coronaviruses causes about 10-30% and the rest are due to adenoviruses, enteroviruses, RSV, influenza, and parainfluenza viruses, which may cause symptoms indistinguishable to those of rhinoviruses and coronaviruses.

### **1) RHINOVIRUSES**

#### **Slide#45/46/47**

- The optimal temp. for their growth is 33 degree and this is the temp. at the naso-pharyngeal region, so it causes infection in the URT and replicate there .
- It causes about 50 % of the URT infections .
- We always say that when having URT infection we will have, fluor( influenza ) as the Dr. said, however, Rhinoviruses cause infections more than the Influenza viruses (about 50 % of the URT infections is caused by Rhinovirus ).
- Rhinoviruses are the most important cause of :
  - \*The common cold
  - \* The upper respiratory infection (URI).
- more than100 serotypes have been discovered .
- It belongs to the **Picornaviridea** family, that has three genera (plural of genus) one of them is the Rhinovirus that has 100 serotypes.
- A ssRNA, icosahedral symmetric, non enveloped-Ether resistant virus .

## Pathogenesis

### **Slide #48**

- In contrast to enteroviruses, rhinoviruses are **unable** to replicate in the gastrointestinal tract.
- Rhinoviruses grow best at 33 C, which may partly account for their predilection (liking) for the cooler environment of the nasal mucosa.
- Most viral replication occurs in the **nose**, and the severity of the symptoms correlates with the quantity (titer) of virus in nasal secretions. Meaning, the amount of the virus that started the infection, or entered into the nasal mucosa and replicated there correlates with the severity of the symptoms
  - Also the immune interfering action will increase the secretion of kinins especially **bradykinins**; their release account for the symptoms that we see, such as sore throat, rhinorrhea
- The receptor for rhinovirus is the glycoprotein "**Inter-Cellular Adhesion Molecule 1 (ICAM-1)**".

## Epidemiology

### **Slides #49**

The transmission of the virus :

- 1- Aerosols
- 2- DIRECT Contact (the Dr. didn't mention the indirect contact though it was written in the slides ) .

## Clinical symptoms

### **Slide #50**

URIs caused by rhinoviruses usually begin with **sneezing**, shortly followed by **rhinorrhea**.

- The rhinorrhea increases and is then accompanied by symptoms of nasal obstruction.
- Mild **sore throat** occurs along with **headache**, **malaise** (general discomfort) and the "**chills**" (rigors).
- The illness peaks in **three** to four days or longer.

\*\*\*As we said bradykinins play an important role in the symptoms that appear during the infection

### **Laboratory Diagnosis**

#### **Slide #51**

- We take a nasal washing, inoculate it into a cell culture, and observe the growth of the virus in the cell culture
- Cytopathic effect (CPE), is marked by **rounding** of the cell. There is **no** multinucleated giantcells.
- The virus can also be detected by ELISA.

### **Prevention and Treatment**

#### **Slide #52**

- **No** antiviral drug has been proved useful.
- **No** vaccine, the many serotypes pose a major problem for the development of vaccines.
- Hand Hygiene is the most potent method of prevention and control.

## **2) CORONAVIRUS**

***slide ( 53-58)***

#### **Slide #54**

- Is one of the coronaviridea genera .

### **The Characteristics**

#### **Slide #55**

- SS linear non segmented, +ve sense RNA.
- The largest among RNA viruses in the terms of genome .
- Enveloped virus; it acquires it's envelope from the ER (Endoplasmic Reticulum) and the Golgi **not** from the plasma membrane.
- The number of serotypes is not known but there are 2 serotypes that were studied which

are **OC43** and **229E** .

### **Slide #56**

The family coronaviridae is composed of **two** genera:

- Genus Coronaviruses
- Genus Torovirus: – Associated with gastroenteritis.

## **Genus Coronaviruses**

### **Slide #57**

- Genus Coronaviruses are difficult to isolate in cell culture .
- So infections with this virus are rarely diagnosed in clinical practice .
- Based on serologic studies, coronaviruses cause respiratory tract infections and pneumonia in humans.
- And due to their tropism to epithelial cells, they may cause gastroenteritis however **most of the time they are associated with URT infection.**

## **Genetic evolution**

### **Slide #58**

The Coronavirus shows a high frequency of:

- **Deletion** mutations
- High frequency of **recombination** during replication which is unusual for an RNA virus with an un-segmented genome.
- These high frequencies, mutate the virus (modify it) to be more virulent, or produce more virulent strains of the Coronaviruses.
- Recently we heard about an epidemic or even **apandemic** (more than epidemic) spread of Coronaviruses infection .
- The last case that caused death due to Coronaviruses infection was for a Jordanian woman living in U.A.E few weeks ago .
  
- To summarize, in the last couple of years the Coronaviruses infections have increased as a result of the high frequency of the deletion mutations and recombination;new more

virulent strains are appearing

Coronaviruses are also associated with **SARS**.

- **SARS**: Severe Acute Respiratory Syndrome, caused by modified Coronavirus.

- Associated with a virulent strain.

- Associated with lower respiratory tract infection.

- The progress of the infection (illness) is very rapid, and the patient's condition deteriorate quickly leading to respiratory failure and death.

### **Clinical picture and epidemiology**

#### **Slide #59**

- Upper respiratory infections are similar to "colds".

- 15-30% of respiratory illness in adults.

- Antibodies appear early in childhood and are found in 90% in adults.

- CORONAVIRUSES may be associated with gastroenteritis.

# The end of RNA viruses 1



# Viruses that cause Gastroenteritis

- Viruses that cause Gastroenteritis are:
  - 1) Rotavirus (dsRNA)
  - 2) Toroviruses (ssRNA)
  - 3) Adenoviruses (dsDNA)
  - 4) Caliciviruses (ssRNA) : - Genus: Norovirus - Species: Norwalk viruses
  - 5) Astroviruses (ssRNA)

- **Comparison between these viruses:**

→ all are related to **Gastroenteritis**

→ they are **all RNA viruses except the adenovirus (dsDNA)**

→ the most imp. thing is that all of them are **naked viruses** [which might help them tolerate the **high acidity of the stomach** and the **sterilizing effect of the bile** more than enveloped viruses]

→ all of them have **short incubational periods** (1-3 days) ; the Norwalk viruses have even a shorter incubational period of about (6-12 hours).

→ **Site of infection :**

- **Rotavirus**: in the duodenum & jejunum
- **Caliciviruses (Norwalk)**: in the jejunum
- **Adenoviruses**: in the small intestine
- **Astroviruses**: in the small intestine

→ **Symptoms**: they all cause the same symptoms.

- It starts with vomiting followed by diarrhea.
- In the **Calici/Adeno/Astro**-virus → milder symptoms than the

**Rotavirus. why ?**

- because in the Rotavirus infection the **vomiting** might last for 1-3 days and the **diarrhea** for 4-8 days [start with vomiting and after 2-3 days diarrhea begins]

- In the Rotavirus infection the diarrhea starts as watery brown color diarrhea, after a while it becomes whitish (watery) diarrhea[a watery inconsistency diarrhea doesn't have any pigments]

There is a Japanese term for this shift which is "Hakori"

P.S. Hakori: the shift in severe cases. (changing in color from brown to watery diarrhea)

→ **Immunity**: not much is known about immunity for these viruses.

But we know that:

- Rotavirus produces humoral immunity [antibody production]So there is:

- 1) **Serum** immunity
- 2) **IgA** immunity [secretions in the intestine since the viruses act there ]
- 3) **IgG**

→ **Age group they infect:**

- **Rotavirus infection**: in infants (4-5 months - 2 years)\*
- **Caliciviruses infection**: in adults (mainly) & children (13-15 years)
- **Adenoviruses infection**:in children & adults
- **Astroviruses infection**:in children & adults

**\* Why Rotavirus can't infect infants before (4 or 5 months) ?**

- because of the breast milk which contains:

1) IgA

2) mucin glycoproteins [which confer protection against Rotavirus infection].

- Also there is another theory that talks about cross protection (immunity) during pregnancy for the fetus.

→ **Seasonality:**

- **Rotavirus infection:** mainly in winter

- Other viral infections: could be seen all the year  
[seen mainly in winter months]

→ **Spread of infection:**

- Q : How can the infections be transmitted ?

ans: all of them are transmitted by fecal-oral route.

- **Calicivirus:** spread by contamination of drinking water, sea food or vegetables.

[seen mainly in cruise ships, hospitals & schools - crowded places]

→ **Mortality rate:**

- They all are acute viral infections (illnesses)

- Might resolve in (2-7 days) [Rotavirus is the longest duration]

- The main threat for the infected patient especially infants is dehydration, so if we keep good hydration

of the infected patient → there is no harm and the infection might resolve completely without any complications, in a short period of time.

→ **Spread of infection:** (endemic or pandemic ..etc) ???

-They are spread worldwide. (all of them)

→ **Specific treatment :**

- There is **NO** specific antiviral treatment for any of them
- However, we have a vaccine for rotavirus, which will become a part of the national vaccination program soon (the decision have been already taken but not effective yet)
- We **DON'T** have vaccines for other viruses.

→ **Management of these diseases :**

- Good **hydration** is the most important thing in such infections.

→ **Culture growth :**

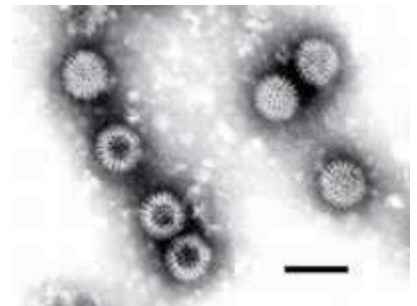
- None of them could be grown in culture. Why?? We'll mention the reason later.

# ROTAVIRUS

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**Slide#3**

- The rotavirus can't be missed under microscope because of its wheel-shaped appearance with radiating spikes.
- This shape comes from its structure which contains **two** Icosahedral capsids (an outer capsid and an inner one).
- Family Reoviridae
- Genus Rotavirus



**Slide#4**

- It's a Non-enveloped virus (naked)
- Double stranded (ds) RNA in **11 segments** . We have previously talked about another segmented virus which is the influenza virus which has 8 segments (influenza virus type C has 7).
- The capsid is cleaved by **trypsin** to form ISVP
- **ISVP** : [intermediate/infective sub-viral particle].

## **Slide#5-7**

- **We have two main proteins which are included in the viral replication process:**
  - 1- **VP4:** is a glycoprotein or a spike and it has a function in attachment.
  - 2- **VP7:** is the outer capsid which has a role in attachment and fusion.
- The rotavirus itself is non infectious. It could start or initiate growth but it's not a complete growth(actually, all GI viruses are growing partially and that's why we couldn't culture them as we mentioned before).

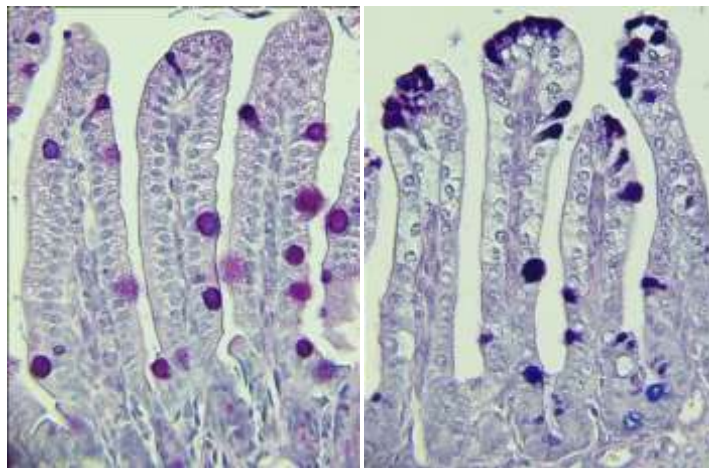
That's because it needs to be cleaved by **proteases** which are present in the GI tract. These proteases cleave VP7 (the outer capsid) ,and after that cleave the VP4 (a spike) finally giving us the ISVP which is the infectious form of the virus.
- **So, unless it is converted to ISVP, the rotavirus is non infectious (can't start the infection).**
- **NSP4 :** a rotavirus protein that works as an **enterotoxin** and has a role in the pathogenesis of the virus infection. So, the severe symptoms seen with rotavirus infection are associated with NSP4.
- They (virologists) think about it (NSP4) as a causative agent that is associated with the severity of the infection.
- And this is one of the things that makes rotavirus infection more severe than other viral infections.
- As we said before they are acute and lytic viral infections.
- The cell destruction seen with rotavirus is more **significant** than other viruses and it takes two to eight weeks for the GI cells (mucus & epithelium) in order to go back to their original situation and get recovered(in other viral infections this process may take maximally two weeks).

**The rotavirus infection is more severe than other viral infections and the destructed cells with it need more time for recovery.**
- **Targeted host cells** - mature enterocytes lining the tips of intestinal villi.
- Intermediate/infective sub-viral particle (ISVP) produced through proteolysis.
- Enter host cell by receptor-mediated **endocytosis**.
- Virus replicates in the host cell cytoplasm

### **Slide#8-9**

- **You could identify these signs with rotavirus infection:**

- Mature enterocytes lining the tips of intestinal villi are affected
- It leads to Villous **atrophy** and **blunting**
- Death of the mature enterocytes
- Infiltration of lamina propria with mononuclear cells
- Repopulation of the villous tips with **immature** secretory cells ("even the secretory cells are replaced").



**The pictures here show the difference between the normal and infected cells and you could see the differences specially the secretory cell occupation.**

## **EPIDEMIOLOGY**

### **Slide #10**

- It's a major cause of diarrhea-associated hospitalizations and deaths
- Sero-prevalence studies show that antibody is present in most by age of 4yrs (90%)

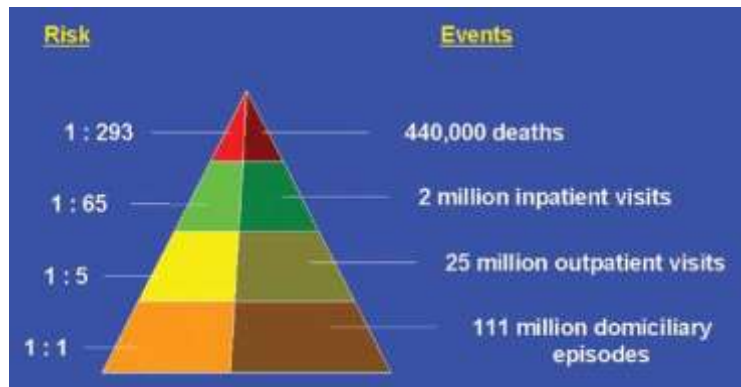
**This is a way also to compare between rotavirus and the Norwalk virus:**

1. In the rotavirus infection: in 3-4 years of age we have 90% of population with sero-conversion (antibodies against the rotavirus).
2. In the Norwalk virus : up to 50 years of age there is around 40-50% seroconversion.

**Sorotavirus infection is more spread than Norwalk virus.**

## Slides # 11

- we have 440 thousands deaths annually and most of them is due to dehydration (the Dr. read the numbers on the right side).



## Slides # 12

- Common age: children 4months - 2 years are most affected
- Asymptomatic infections are common, especially in adults or those who are **pre-exposed** to the virus previously.
- It's associated with nosocomial infections (Hospital-acquired infection)
- It can be associated with outbreaks.
- The disease is more severe in young and immuno-compromised patients.

## TRANSMISSION

### Slide#13

- Mainly person to person via **fecal-oral** route.
- Could be spread through **fomites**

## EPIDEMIOLOGY – spread

### Slide #14

- Contagious from before onset of diarrhea to a few days after end of diarrhea
- Large amounts of viral particles are shed in diarrheal stools 2-12 days

- **This is another difference between rotavirus infections and other viral infections that rotavirus infection shedding last longer than other viruses. (other virus shed only in 2-5 days).**

## **CLINICAL FEATURES**

### **Slide # 15**

#### **Clinical features :**

1. Fever, mostly low fever but can be high in 30% of cases (>39C).
2. Vomiting (1-3 days), nausea
3. Diarrhea (last 4-8 days).
4. May cause Dehydration which is the main contributor to mortality
5. Secondary **mal-absorption** (poor absorption) of lactose and fat, and **chronic diarrhea** are possible due to **loss and blunting of villi**.

## **DIAGNOSIS**

### **Slide# 16**

- **All these viral infections can be diagnosed by three methods :**
  1. ELISA
  2. PCR
  3. Electron microscopy.

## **TREATMENT AND PREVENTION**

### **Slide# 17**

#### **Treatment :**

**Supportive:** treatment of fever, Oral or IV **re-hydration:** to replace the lost water and electrolytes (most important thing).



## Prevention:

- Any viral infection that is transmitted through the fecal-oral route could be prevented by a good **hygiene**, especially by doctors in clinics, while examining patients, make sure you wash hands in between patients.

## Slide# 18

- We have two companies producing vaccines for it.
- It's a live attenuated vaccine named RotaTeq (Merck).
- This vaccine can be given **orally**.
- Given as three doses at 2,4,6 months of age.
- However the first dose can be given as early as 6-12 weeks of age. And the following dose should be 4-10 weeks apart. i.e : you could give the vaccine 2,4,6 months or you could give the first dose earlier in 6-12 weeks age and then wait for 4-10 weeks to give the two booster doses.
- Do not initiate series after 12 weeks of age.

We're so sorry for any mistakes ..

كل الأمنيات بالتوفيق والتميز إن شاء الله ^\_\*

"إن الأمة الخاملة صف من الأصفار. ماقيمة صف من الأصفار؟ ولكن إن بعث الله لها ((واحداً)) مؤمناً صادق الإيمان داعياً إلى الله خبيراً بأساليب هذه الدعوة، صار صف الأصفار مع الواحد كمئة مليون، والتاريخ مليء بالشواهد على ما أقول"

الشيخ / علي الطنطاوي

لا تستصغر نفسك إن كنت "واحد" .. ^\_ ^