

# Rotavirus

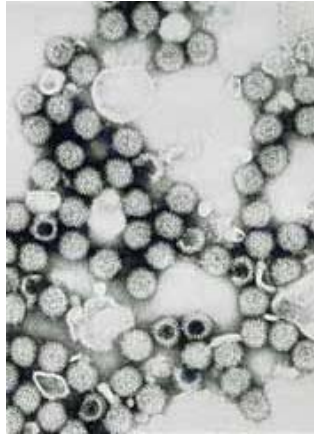
Viral diarrhea and vaccine  
development

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# Rotaviruses

- First discovered in 1973
  - Detected by EM
- Major etiologic agents of diarrhea in infants and young children
- In developing countries, most frequently detected pathogen in children under the age of 2

[www.niaid.nih.gov/.../discovery/graphics/rotavirus.jpg](http://www.niaid.nih.gov/.../discovery/graphics/rotavirus.jpg)



## Transmission of rotaviruses

- Fecal/oral route
- Respiratory route has been implicated
- Poor hygiene, over-crowding
- Common nosocomial infection

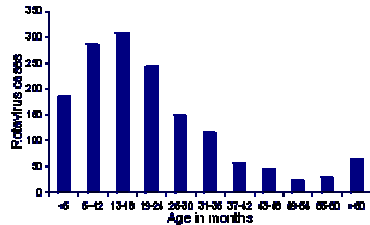
## Transmission of rotaviruses

- Efficient
- Large number of shed particles
- Resistance to physical inactivation
  - Environmental contamination

## Clinical features

- Most common in children 2 months to 3 years old
- Diarrhea - 98% frequency
- Vomiting – 87%
- Fever – 84%
- Abdominal pain
- Malnutrition increases severity of symptoms
- Symptoms associated with severe volume depletion

[www.health.gov.au/pubhlth/  
cdi/cdi2407/cdi2407e.htm](http://www.health.gov.au/pubhlth/cdi/cdi2407/cdi2407e.htm)



## Adult Rotavirus infections

- Reinfections are common
- Usually minimal or no clinical manifestations
- Epidemics can occur
  - Nursing homes, military personnel, travelers
- Most adult infections are acquired from a sick infant

## Complications

- Dehydration
- Very young children – intussusception of the small bowel
- Aspiration of vomitus

## Diagnosis

- Laboratory diagnosis is usually not needed for self-limited infections
- ELISA
- Culture
- EM
- Latex agglutination

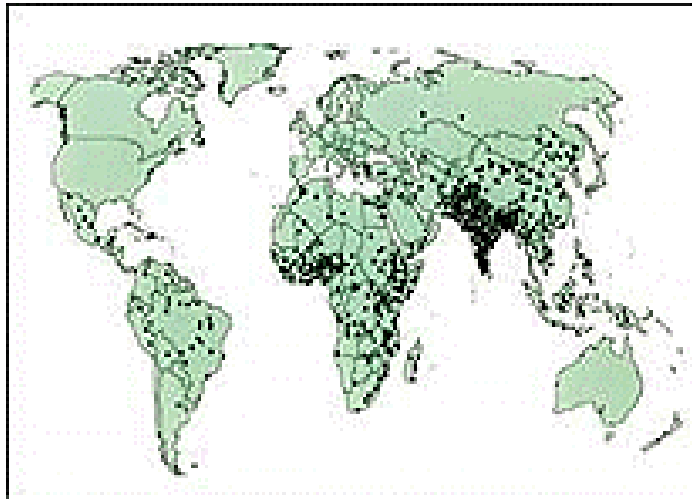
## Rotavirus infections in the U.S.

- 4 of 5 children will have rotavirus infections before the age of 5
- Large economic impact
- 100,000 hospitalizations annually, 250 deaths
- Second most common disease, 16% of illnesses (Cleveland family study)

## Rotavirus – U.S.

- High morbidity/low mortality rate
  - Replacement of fluids and electrolytes

## Global distribution of annual rotavirus deaths ([www.vaccinealliance.org/newsletter](http://www.vaccinealliance.org/newsletter))



## Classification of rotaviruses

- Grouped into serogroups and then serotypes
- 7 antigenically different sero-groups – A-G

## Group A rotaviruses

- Cause most human disease
  - Further subdivided into subgroups
- Principal etiologic agent of severe gastroenteritis in infants and young children
- Responsible for 1 billion cases of severe diarrhea
- Major cause of mortality among the young

## Other Rotaviruses

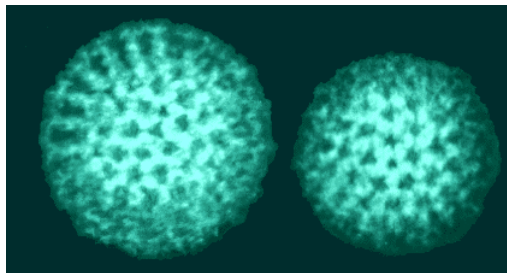
- Group B
  - Adult diarrhea
- Group C
  - Primarily veterinary pathogens
- Groups D, E, F, G
  - Only known to infect animals



## Viral structure

- Mature virion
  - Rota – wheel
  - Triple layered virions
- Non-enveloped, with 3 structural layers
- Two capsids surround the RNA genome
  - 11 double stranded RNA segments

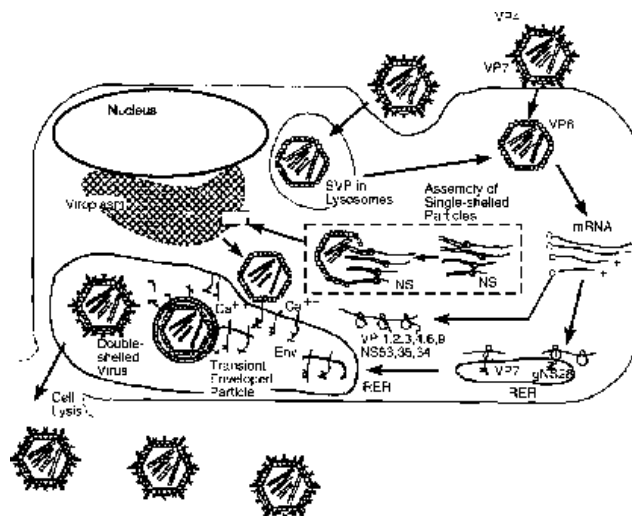
## Rotavirus particles



# Rotavirus life cycle

- Attachment
  - VP7
    - Major component of outer capsid
  - VP4
    - hemagglutinin
- Entry – involves VP4
- Transcription/translation
- maturation

[condor.bcm.tmc.edu/ Molvir/estes1.gif](http://condor.bcm.tmc.edu/Molvir/estes1.gif)



## Rotavirus

- Following replication
  - Shedding of mature particles into the intestinal lumen after cell lysis

## Rotavirus diarrhea

- Malabsorption
- Secretory diarrhea
  - NSP4 – enterotoxin
    - Enteric nervous system
    - Inflammatory responses
    - Calcium mobilization

## Pathophysiology

- Incubation period
  - 24-72 hours
- Viral replication
  - Replication in columnar epithelial cells of intestinal villi
- Denudation, shortening, and widening of the villi

## Treatment

- Prevention of dehydration
  - Oral rehydration is effective

## Resistance to recurrent disease

- The presence of antibodies to rotavirus in the lumen of the small intestine
  - Primary determinant

## Epidemiology of Rotavirus infections

- Epidemics during cold months
- Infants protected 2-3 months from severe disease due to transplacental acquisition of maternal antibodies
- Over 3 years of age – infections are mild or asymptomatic with acquired in the family setting

## Inactivation of Rotavirus

- Relatively resistant to a wide range of chemical disinfectants
  - Particularly dried virus on porous surfaces
- Resistant to temperature variation
- Inactivation
  - 95% ethanol
  - Careful handwashing

## Rotavirus vaccine

- Rhesus rotavirus tetravalent vaccine
  - Serotypes 1, 2, 3, 4 for VP7
  - Reassortant strains
  - Protective against 80% of the cases of severe diarrhea, 100% of the dehydration cases
  - Rotashield
    - Was recommended at 2, 4 and 6 months of age
    - Risk of intussusception – 1 in 12,274 infants

## Intussusception

- Blockage of the bowel
- Death is rare with prompt treatment
- In the U.S., intussusception affects 70 of 100,000 infants yearly
- Seen in infants between 3 and 9 months

## Other candidate vaccines

- Oral vaccine from Merck, based on bovine-human reassortant strains
- Oral vaccine from Glaxo, based on single, weakened human strain