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
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
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)

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
Rotavirus

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

Rotavirus diarrhea

• Maladsorption
• 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