UNIWERSYTET MEDYCZNY
IM. PIASTÓW ŚLĄSKICH WE WROCŁAWIU

Subject: Faculty Lectures of Virology

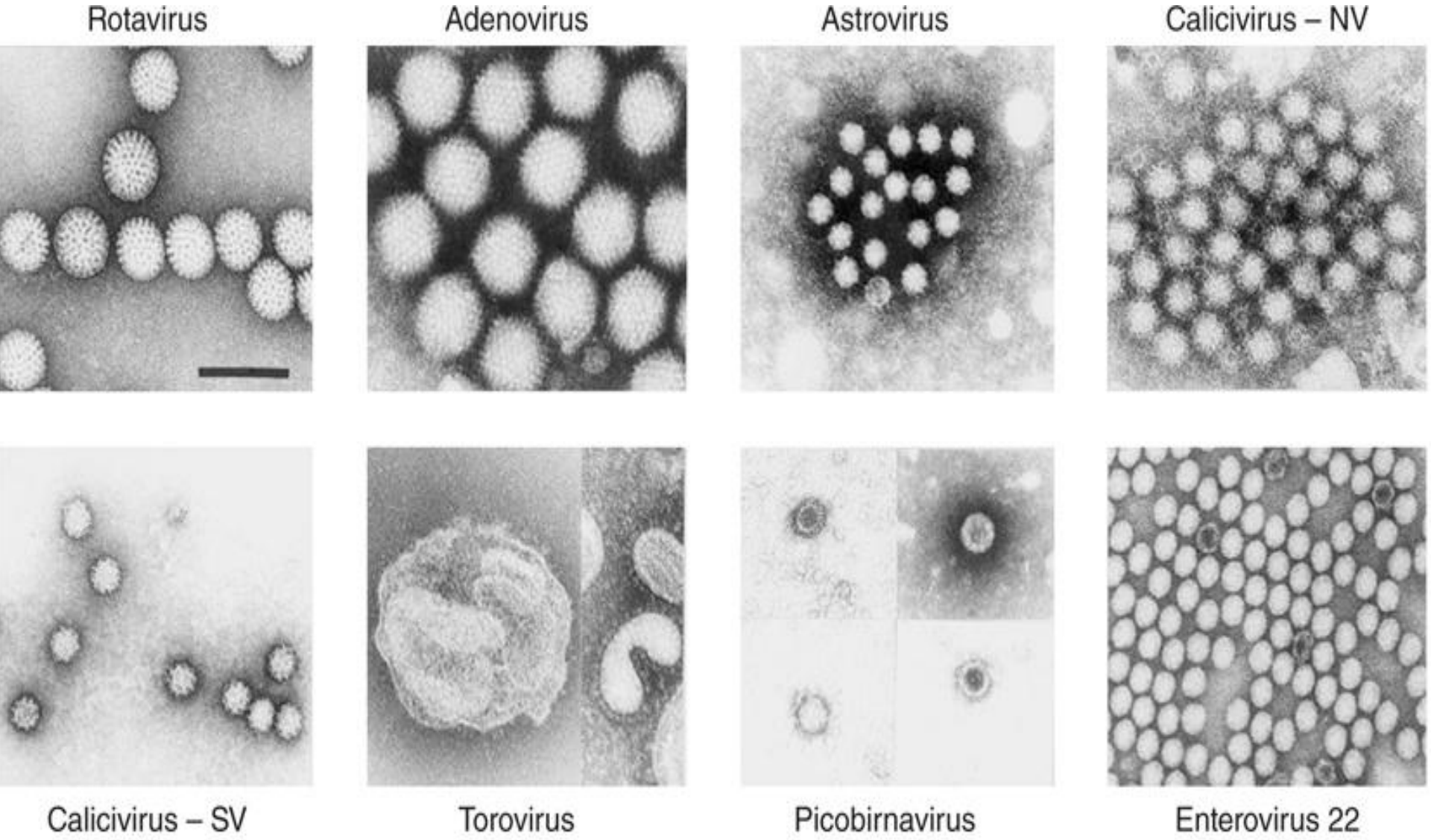
Topic: Viral gastrointestinal and urinary tract infections

Academic Year 2024/2025

Faculty: Medicine
Field of study: Virology
Level of study (uniform MA):
Form of study (full time):
Year of study: III

Academic title/professional title: professor
Name, last name of the lecturer: Beata Sobieszczańska
Position of person conducting classes: teacher
Wroclaw Medical University

Viruses are the most important etiologic causes responsible for approximately 70% of the episodes of acute gastroenteritis in children



Fuente: Dan L. Longo, Anthony S. Fauci, Dennis L. Kasper, Stephen L. Hauser, J. Larry Jameson, Joseph Loscalzo: *Harrison. Principios de Medicina Interna,* 18e: www.accessmedicina.com

General characteristics of viruses causing diarrheas

- RNA (except Adenoviruses)
- Non-enveloped (except Torovirus) – stable in the environment; resistant to drying
- Low infectious dose 10 – 100 viral particles
- Spread via fecal-oral route, direct and indirect contact
- Most often, viral GIT infections occur during winter and spring, but they are year-round in tropical areas

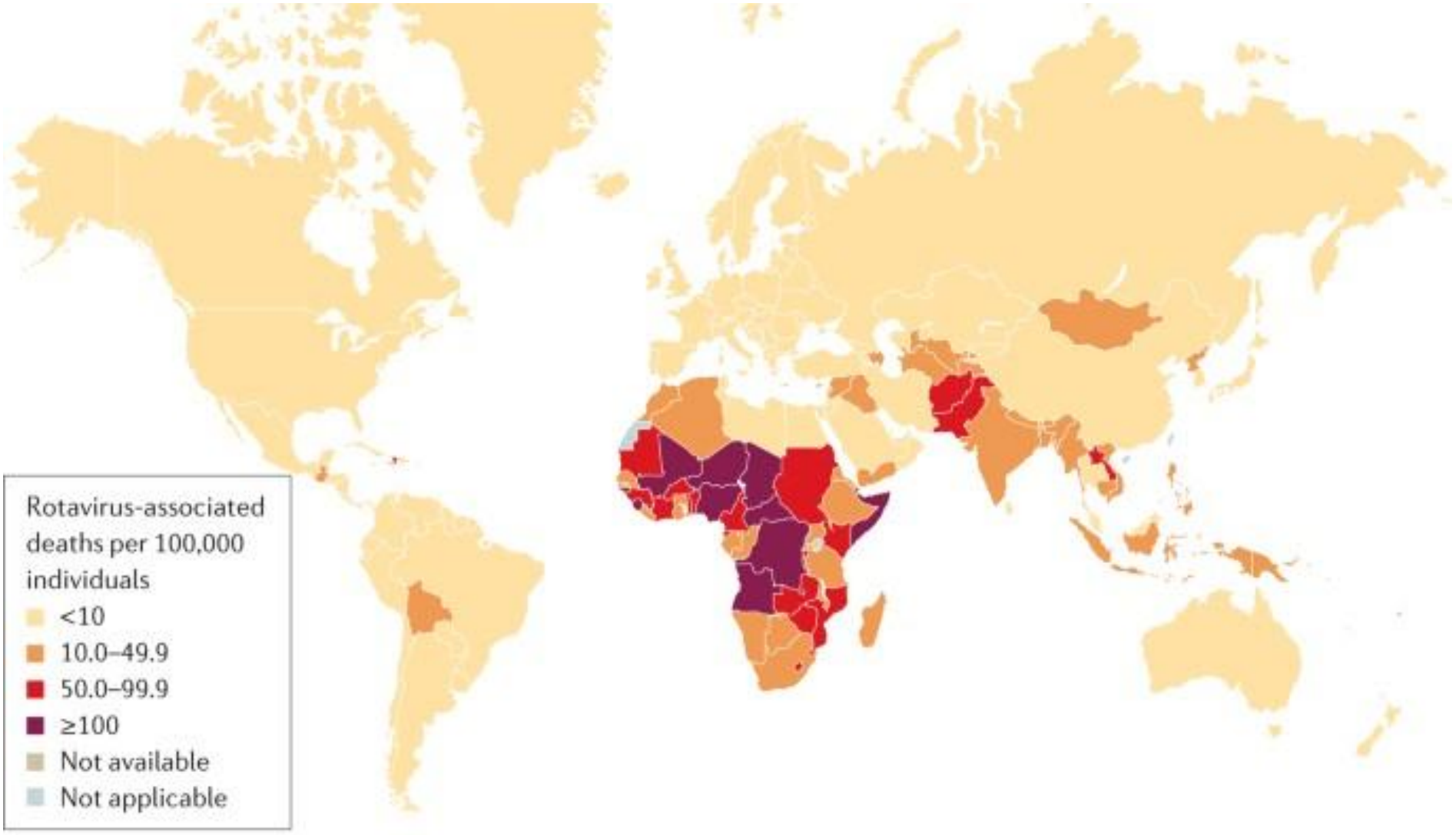
Rotavirus

Accounts for 50% - 80% of all cases of viral gastroenteritis

Most common cause of severe viral diarrhea

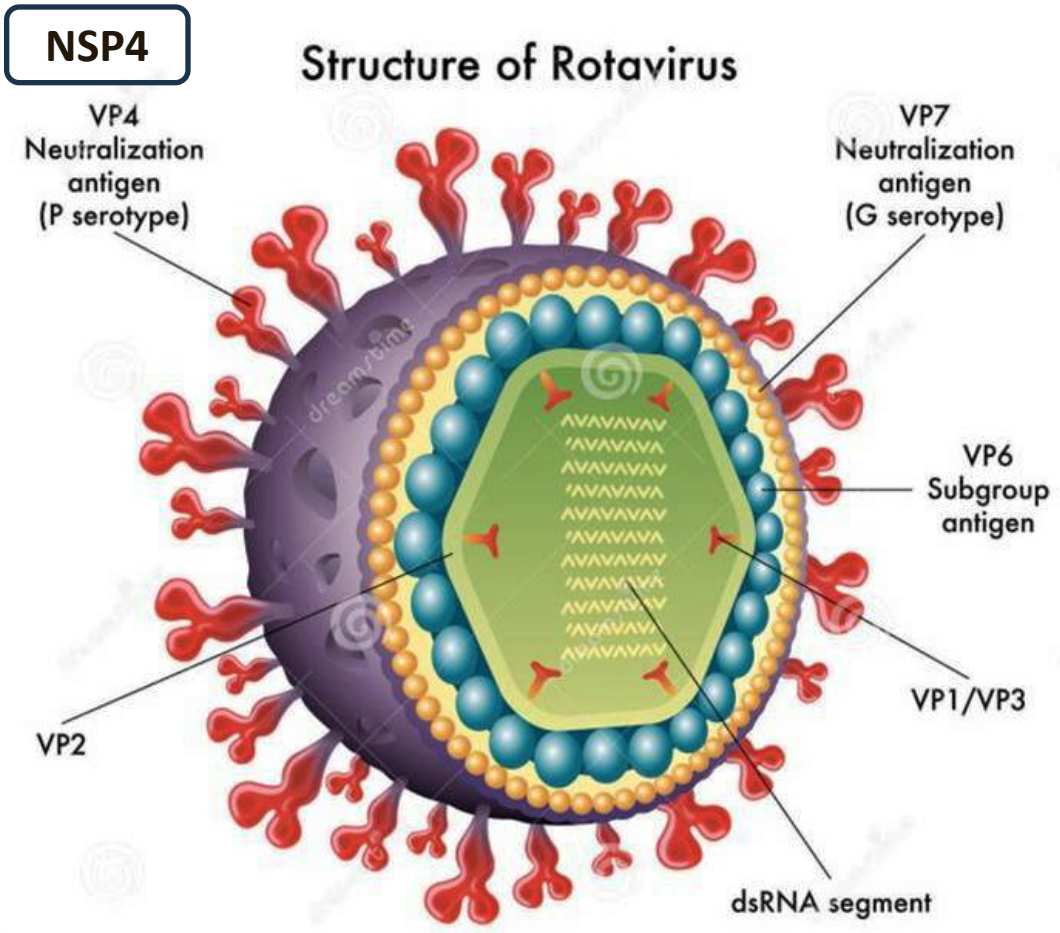
Causes the death of about 600,000 children worldwide annually

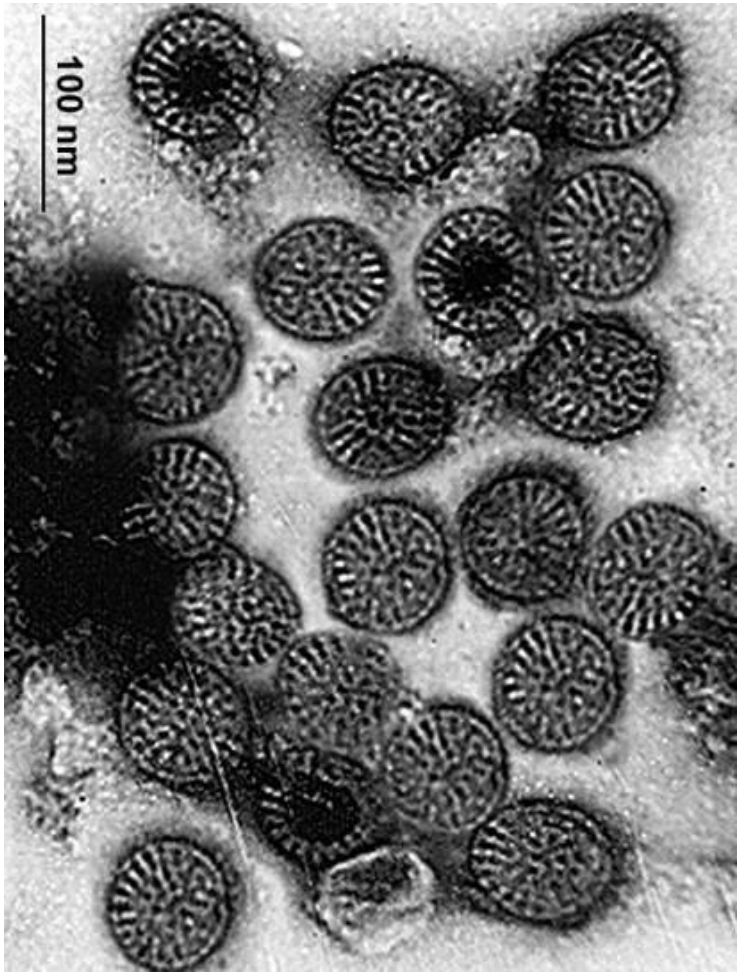
Rotavirus-associated mortality in children <5 years of age



Nature Reviews | Disease Primers

Rotavirus





Latin ‘rota’ = wheel; Rotavirus name – wheel-like appearance under electron microscopy

Rotavirus – Reoviridae family

- dsRNA, icosahedral capsid, non-enveloped
- Stable in the environment for many months (susceptible to 96% ethanol, formalin)

- Divided into groups A through H
- Human pathogens: group A (most common), B (outbreaks in China), and C (worldwide) – isolated from humans and animals

- Reservoir – humans (infected subjects)
- Temporal pattern: fall and winter (temperate areas)
- Transmission: fecal-oral route (close person-to-person contact, fomites)

Hand washing and sanitation does not work due to resistant nature of the virus

Rotavirus

Rotavirus is highly communicable

- Infected persons shed large quantities of virus (ca. 10^{12} virions/1 gram) in their stool (2 days before the onset of diarrhea for up to 10 days after onset of symptoms)

- Causes disease in all age groups but most severe symptoms in neonates and young children
- Asymptomatic or mild infections are common in adults and older children
- Symptomatic infections are again common in people over 60 years of age
- Up to 30% mortality rate in malnourished children

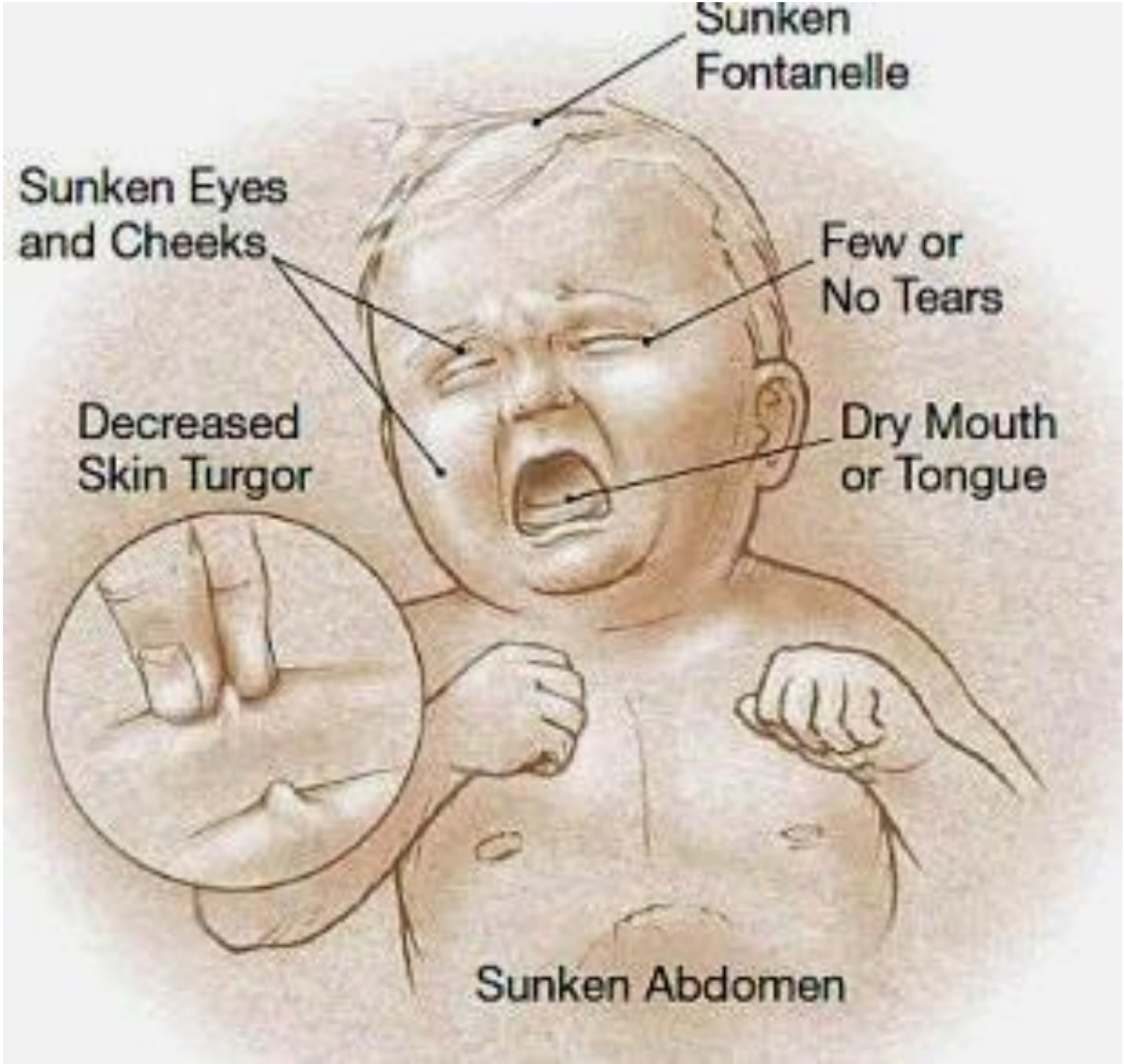
Rotavirus – clinical feature

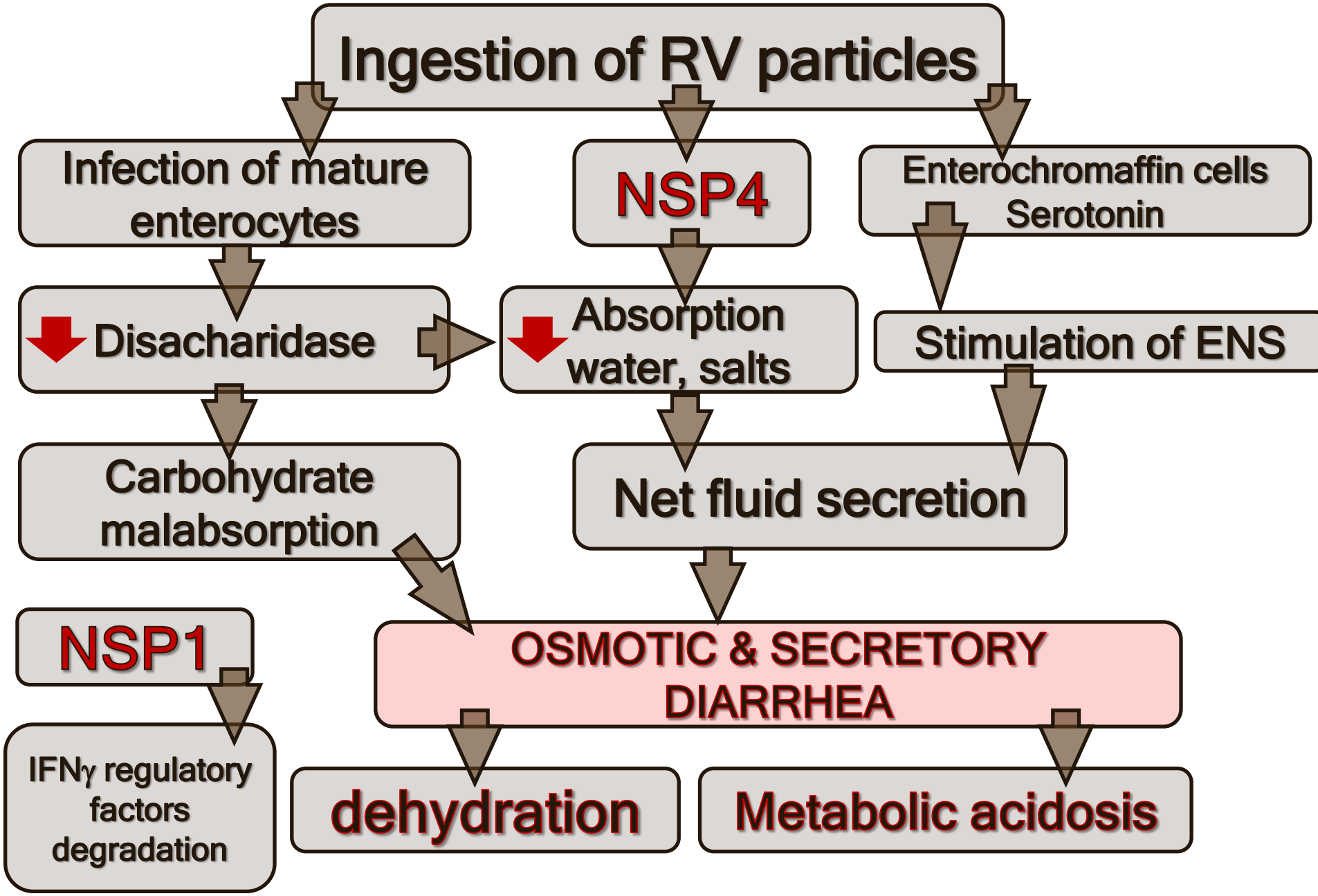
Uncomplicated cases

- Insidious onset
- Prodrome symptoms: fever (moderate grade), vomiting precedes diarrhea
- Watery diarrhea (lasts 3 to 7 days)
- Mild or moderate dehydration

Respiratory symptoms (cough, coryza) are pretty common

Viremia in malnourished or immunocompromised children


Sunken
Fontanelle
Sunken Eyes
and Cheeks
Few or
No Tears
Decreased
Skin Turgor
Dry Mouth
or Tongue
Sunken Abdomen


Ingestion of RV particles
Infection of mature enterocytes
NSP4
Enterochromaffin cells Serotonin
Disacharidase
Absorption water, salts
Stimulation of ENS
Carbohydrate malabsorption
Net fluid secretion
NSP1
OSMOTIC & SECRETORY DIARRHEA
IFNγ regulatory factors degradation
dehydration
Metabolic acidosis

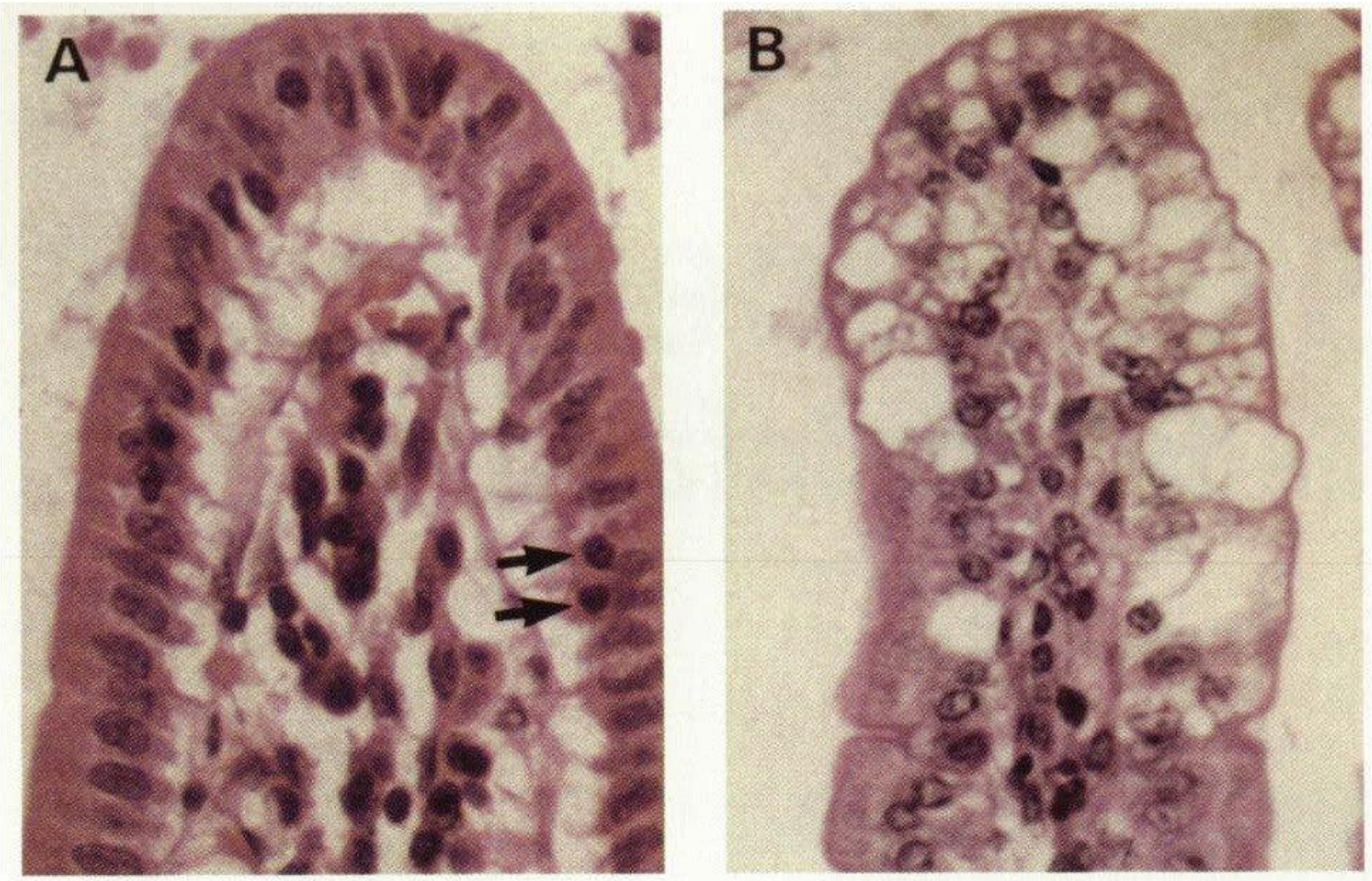


Figure 1. (A) Normal intestinal villus with intact epithelial layer. (B) Marked disruption and vacuolization of villous epithelial cells during rotavirus infection.

Rotavirus – clinical case

A previously healthy 2.5-year-old girl presented to the hospital following two febrile seizures. She has a 2-day history of diarrhea due to Rotavirus gastroenteritis (confirmed by lab test).

An hour after arrival to the hospital she experienced two more seizures. The fourth and final seizure developed into status epilepticus so she was treated with intravenous diazepam.

As the seizure gradually ended ECG monitor showed a brief period of ventricular fibrillation followed by asystole. Immediate resuscitation attempts were unsuccessful. Rotavirus antigen was detected in CSF and in endocardium, and myocardium. The autopsy revealed brain edema.

Rotavirus – vaccines, diagnosis

RotTeq (RV5) and Rotarix (RV1) – both oral, contain live attenuated rotaviruses

Vaccine efficacy

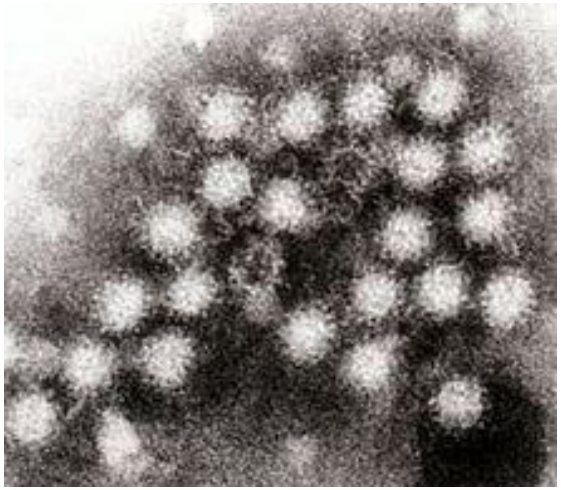
- any rotavirus gastroenteritis: 74% - 87%
- severe gastroenteritis: 85% - 98%

Both vaccines significantly reduce rotavirus-related hospitalization

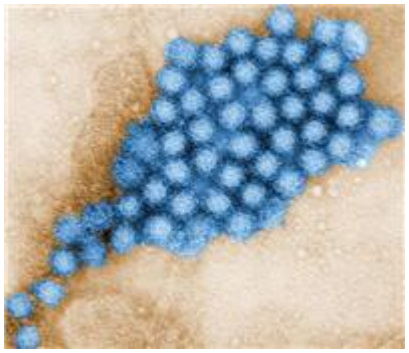
BUT – contraindicated in immunosuppressed children (SCID-severe combined immunodeficiency)

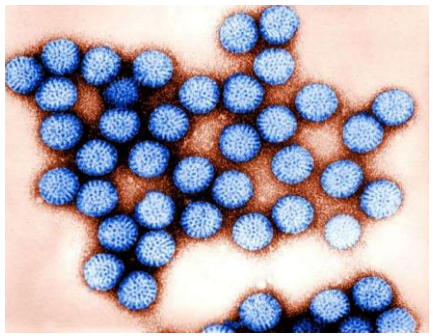
Diagnosis – detection of rotaviruses in stool specimens (ELISA assays, agglutination tests)

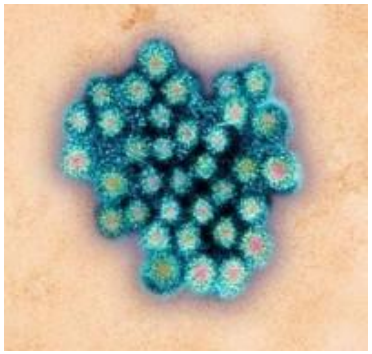
Noroviruses

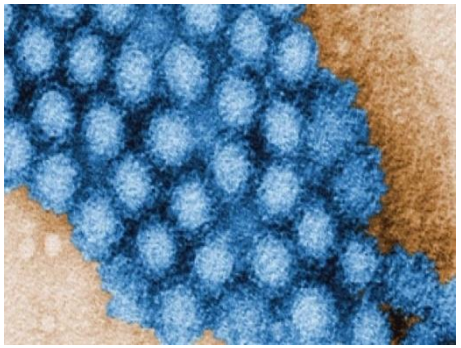


- Family: Caliciviruses
- (+) ssRNA, non-enveloped
- Norovirus (Norwalk-like virus)
- Divided into five groups: GI – GV
- Strains infecting humans: GI, GII and GIV
- Interspecies transmission of Noroviruses has not been documented









Norovirus

- Reservoir: humans
- Transmission: person-to-person, food-borne, water-borne
- Norovirus is highly contagious
- Affects people of all ages, even several times during life
- Gastroenteritis with prominent vomiting ‘winter vomiting disease’

How You Get Norovirus From People or Surfaces

Norovirus spreads when a person gets poop or vomit from an infected person in their mouth.

PROVIDING CARE

SHAKING HANDS

TOUCHING YOUR MOUTH

CHANGING DIAPERS

TOUCHING CONTAMINATED SURFACES

YOU BECOME ILL WITH NOROVIRUS

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

For more information, visit www.cdc.gov/norovirus

CS258219-B

Noroviruses are the predominant cause of gastroenteritis outbreaks worldwide

Outbreaks occur throughout the year although there is a seasonal pattern of increased activity during the winter months

In developing countries Norovirus causes 200,000 deaths in young children annually

Norovirus

- Symptoms: nausea, diarrhea, vomiting, stomach cramps
- Symptoms last 24-48 h (but may persist for several days, weeks, month or even years in immunocompromised and transplant patients)
- Patients remain contagious for 2-5 days after infection (but virus may be secreted up to 2 weeks following infection)
- Up to 30% of Norovirus infections are asymptomatic (but virus shedding occurs)

Norovirus

- Fever and body aches might be associated with the infection ('stomach flu')
- Life-threatening infections in the young and elderly, and persons with weakened immune system
- Necrotizing colitis in neonates, chronic diarrhea in immunocompromised patients and irritable bowel syndrome (IBS)
- There is no long lasting immunity after infection (strain-specific immunity)

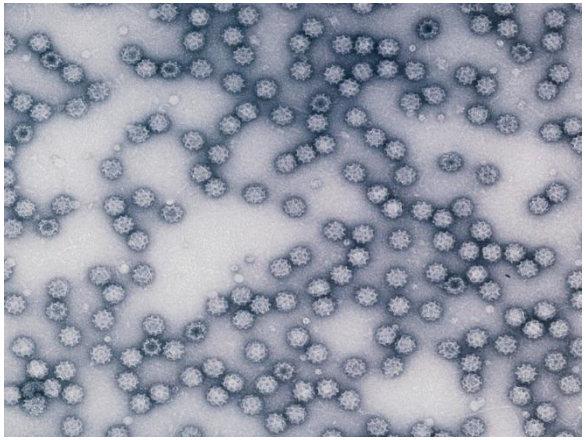
Norovirus

- Treatment: nonspecific – oral or intravenous fluid therapy
- No vaccine available

Diagnosis

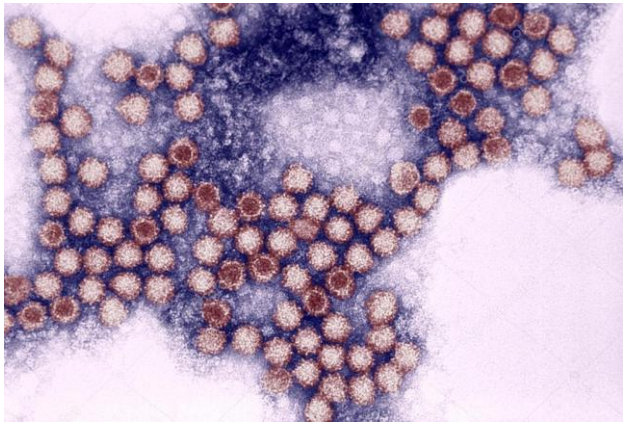
- Detection of viral antigens (EIA assays) or nucleic acid (molecular biology tests)

Sapovirus



- Family: Caliciviruses
- (+) ssRNA, non-enveloped
- Sapovirus (Sapporo-like virus)
- Highly diverse genetically and antigenically
- Similar to Noroviruses
- Responsible for 2.2% - 12.7% cases of gastroenteritis
- Highly infectious and easy to spread in settings where people have close contact with each other, such as schools, childcare centers, long-term care facilities, hotels, schools etc.

Sapovirus



- Reservoir: humans
- Transmission: fecal-oral route
- Symptoms: vomiting and diarrhea for 2-3 days, nausea, abdominal pain, headache, malaise, myalgia, fever rare

Symptoms are usually self-limited

They cause disease in humans of all ages worldwide

Infections more frequent in children under 5 years of age

Treatment: preventing dehydration

The clinical symptoms of Norovirus and Sapovirus are indistinguishable without testing

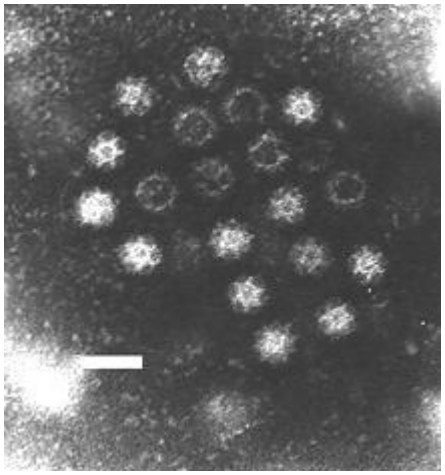
Torovirus of Coronaviridae family

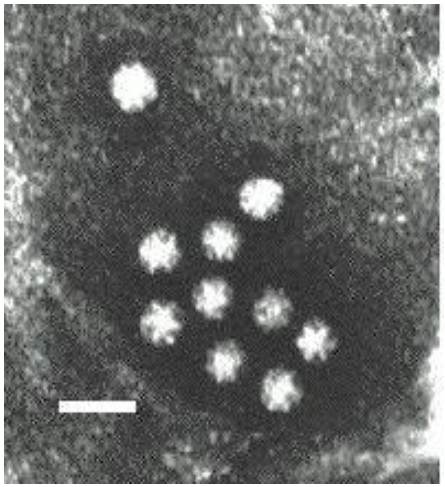
- (+) ssRNA, enveloped
- Reservoir: humans, animals (cattle, pigs, horses)
- Transmission: fecal-oral route
- Important cause of nosocomial diarrhea
- Symptoms: less vomiting but frequent blood diarrhea

Toroviruses more frequently infect immunocompromised and hospitalized

Astrovirus

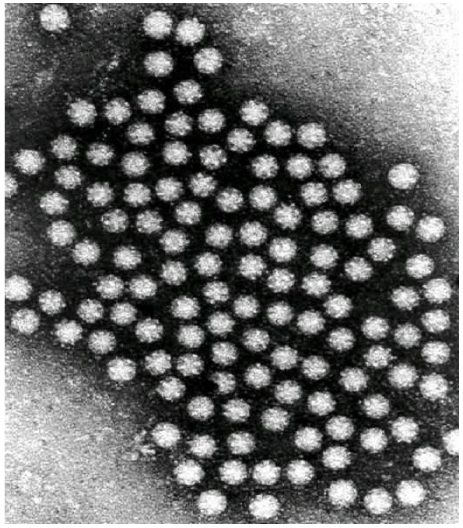
- Astroviridae family (+) ssRNA non-enveloped
- 8 distinct serotypes of human Astroviruses
- Serotype 1 detected most commonly
- Frequent cause of mild gastroenteritis in children under 2 to 5 years of age
- Causes self-limiting watery diarrhea
- Typically involved in sporadic cases of gastroenteritis, but outbreaks have also been described worldwide

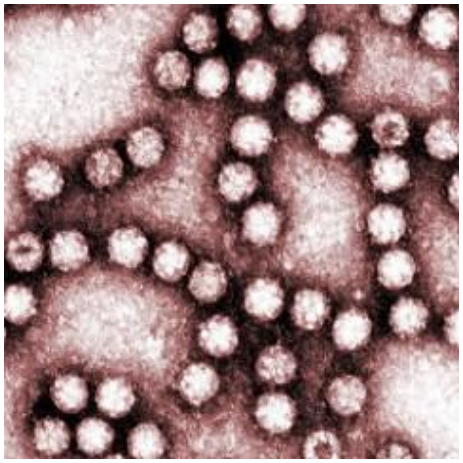


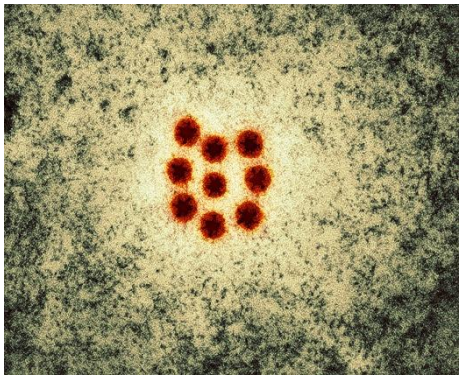


Astrovirus

- Transmitted person-to-person by fecal-oral route
- Infection is more pronounced in immunocompromised patients
- Asymptomatic shedding common in children and adults
- Seasonality: temperate climate – winter, tropical climate – rainy season

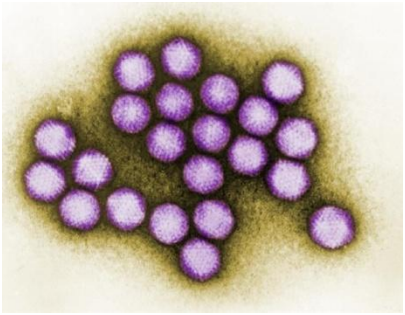


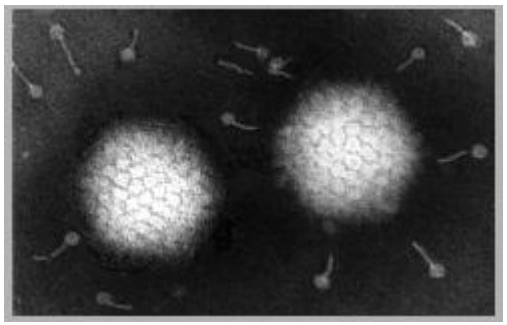




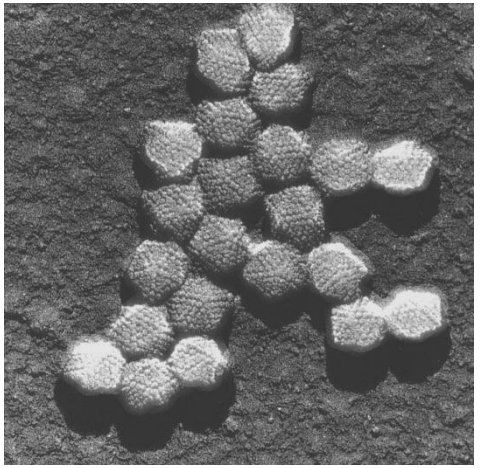
Adenovirus

- Adenoviridae family dsDNA
- Over 52 serotypes grouped into 6 species A to F
- Worldwide distributed
- Reservoir – humans
- Transmission: fecal-oral, respiratory, recreational water etc.
- Ubiquitous in the environment where contamination by human feces or sewage has occurred





Adenovirus



- Gastroenteritis:
- Ad40 (<20%) year-round
- Ad41 (40-80%) autumn
- Less common serotypes: 3,5,7,31

The second most common viral cause of gastroenteritis

- Most infections occur in children under 2 years
- Can cause occasional outbreaks
- Most people have antibodies against enteric adenoviruses by the age of ten

Adenovirus

- Incubation period: 8 – 10 days
- Symptoms: watery diarrhea, fever, vomiting – resolve within 1-2 weeks (protracted)
- Severe dehydration is rare
- Enteric adenoviruses have also been implicated in mesenteric lymphadenitis, adenitis and intussusception

- Diagnosis: molecular techniques and virus antigen detection

TABLE 1: TYPES OF ACUTE VIRAL GASTROENTERITIS[7]*

Virus	Incubation Period	Duration	Seasonality	Transmission
Rotavirus	1-3 days	5-7 days	Predominantly in winter and fall	Fecal-oral route and respiratory transmission
Norovirus	12-48 hours	1-4 days	Year-round, but especially in winter	Fecal-oral route, aerosolization, respiratory transmission, food, fomites, and water
Sapovirus	1-2 days	3-4 days	Year-round	Fecal-oral route
Astrovirus	4-5 days	5-6 days	Predominantly in winter	Fecal-oral route and water
Enteric adenovirus (40 and 41)	3-10 days	6-9 days	Predominantly in summer	Fecal-oral route

*This is not a comprehensive list.

Viruses are an uncommon cause of urinary tract infections (UTI) in immunocompetent hosts, but they are increasingly recognized as the cause of UTI, especially hemorrhagic cystitis (HC) in immunosuppressed patients

BK virus, adenoviruses (11 and 21), and CMV are predominant pathogens involved in HC after stem cells and solid organ transplantation

Adenovirus and BK virus infections typically occur during childhood and remain latent

Viruses causing urinary tract infections

- In the pediatric population, the species most commonly isolated is adenovirus type 11, which has a propensity for the urinary tract
- It reactivates with profound immunosuppression
- It is also the most common cause of hemorrhagic cystitis in the healthy children

Polyomaviruses

- BK, JC and SV40 - small non-enveloped dsDNA
- Humans are natural hosts
- Transmission not established (most probably respiratory route)
- Primary infections during childhood (60-100% seroprevalence): antibodies anti-BKV in >50% of children by the age of 3 and >90% by the age of 10
- Life-long latency mainly in kidneys parenchyma, renal pelvis, ureter, and bladder in immunocompetent individuals

Polyomaviruses

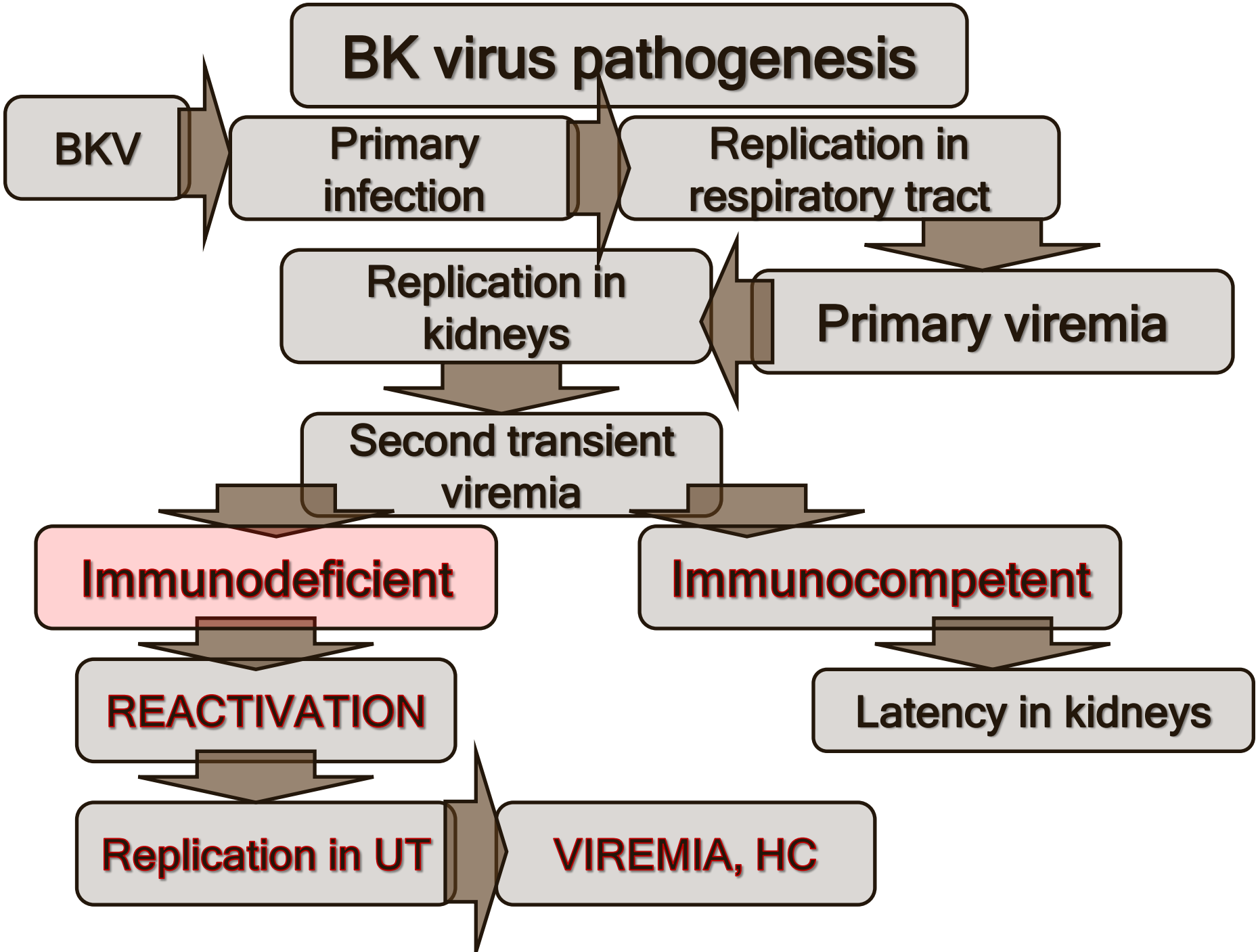
- Reactivation of infection and viruria: transplantation, pregnancy, diabetes, cancer, HIV infection
- BKV – problem in renal transplant recipients

- After kidney transplantation:

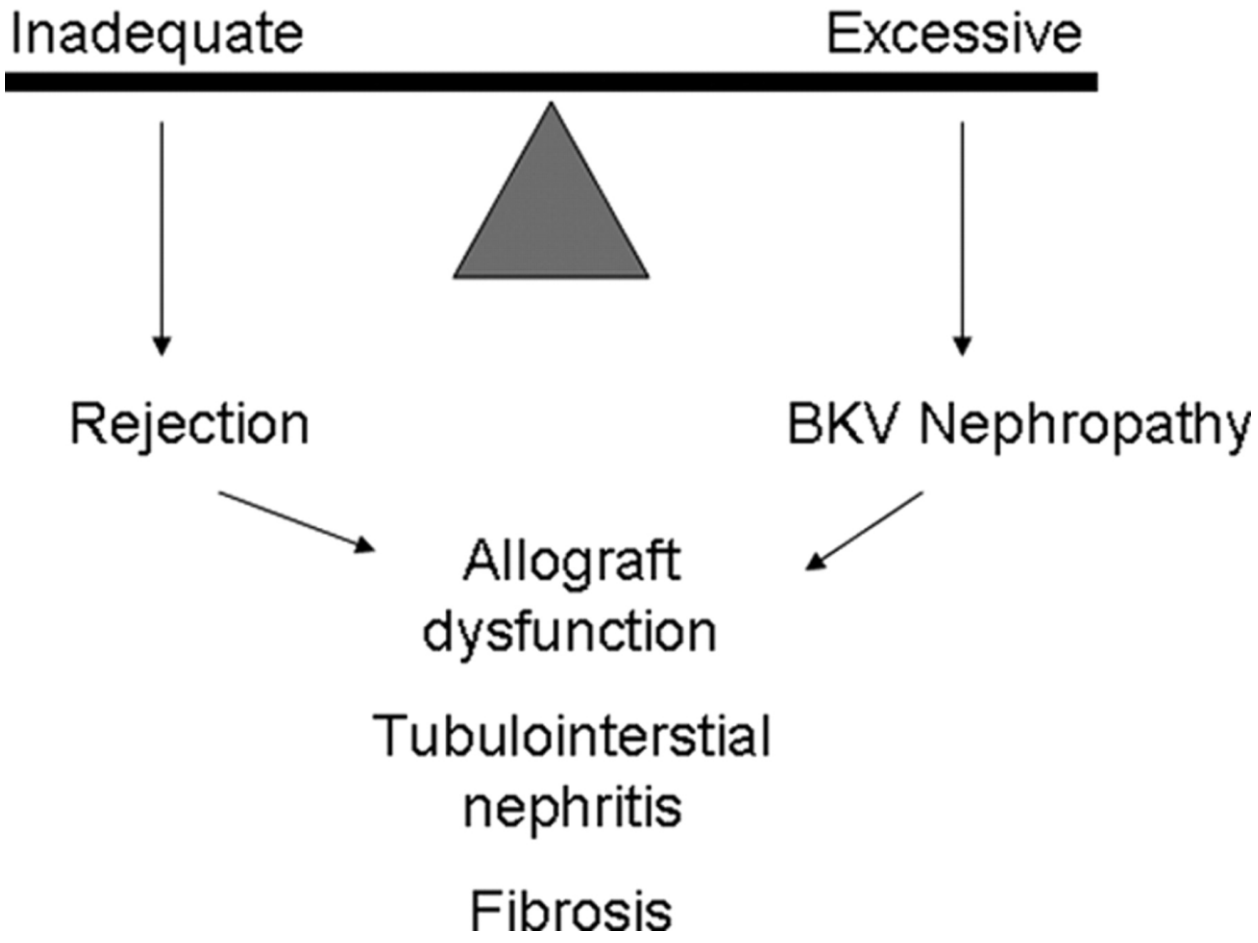
30-60% of recipients develop BKV viruria

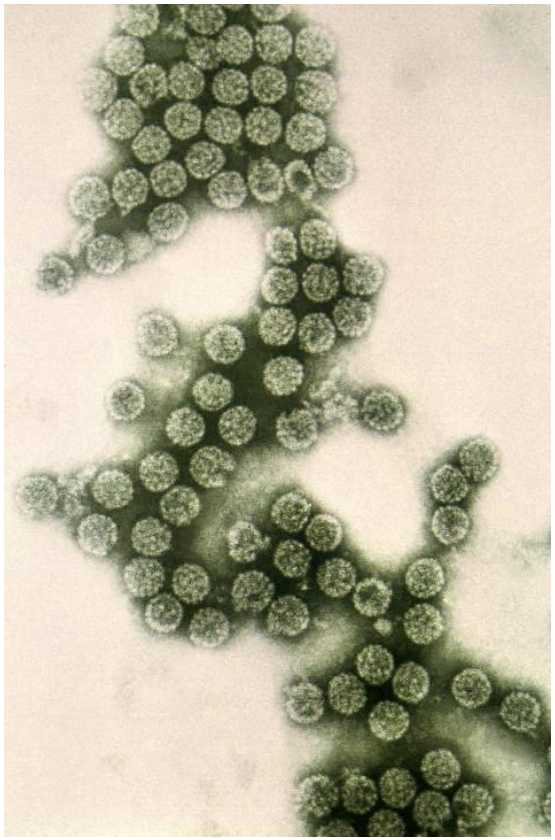
10-20% develop BKV viremia

5-10% develop nephropathy


BK virus pathogenesis
BKV
Primary infection
Replication in respiratory tract
Primary viremia
Replication in kidneys
Second transient viremia
Immunodeficient
Immunocompetent
REACTIVATION
Latency in kidneys
Replication in UT
VIREMIA, HC

Immune Suppression

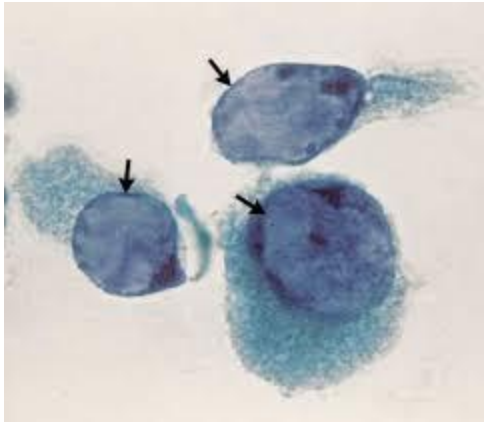




Polyomaviruses

- No specific treatment but…..
- Recent study indicated that cidofovir has in vitro anti-polyomavirus activity – however it is nephrotoxic but….
- Brincidofovir – lipid ester-conjugated pro-drug of cidofovir is not nephrotoxic and can be used to treat renal transplant recipients

DECOY cells



Answer questions

- What viruses are associated with UTI?
- What viral gastrointestinal tract infection can produce clinical systemic symptoms and even death of the patient?
- List the most common viruses causing gastroenteritis in humans.

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IM. PIASTÓW ŚLĄSKICH WE WROCŁAWIU

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