

Viral Diarrhea

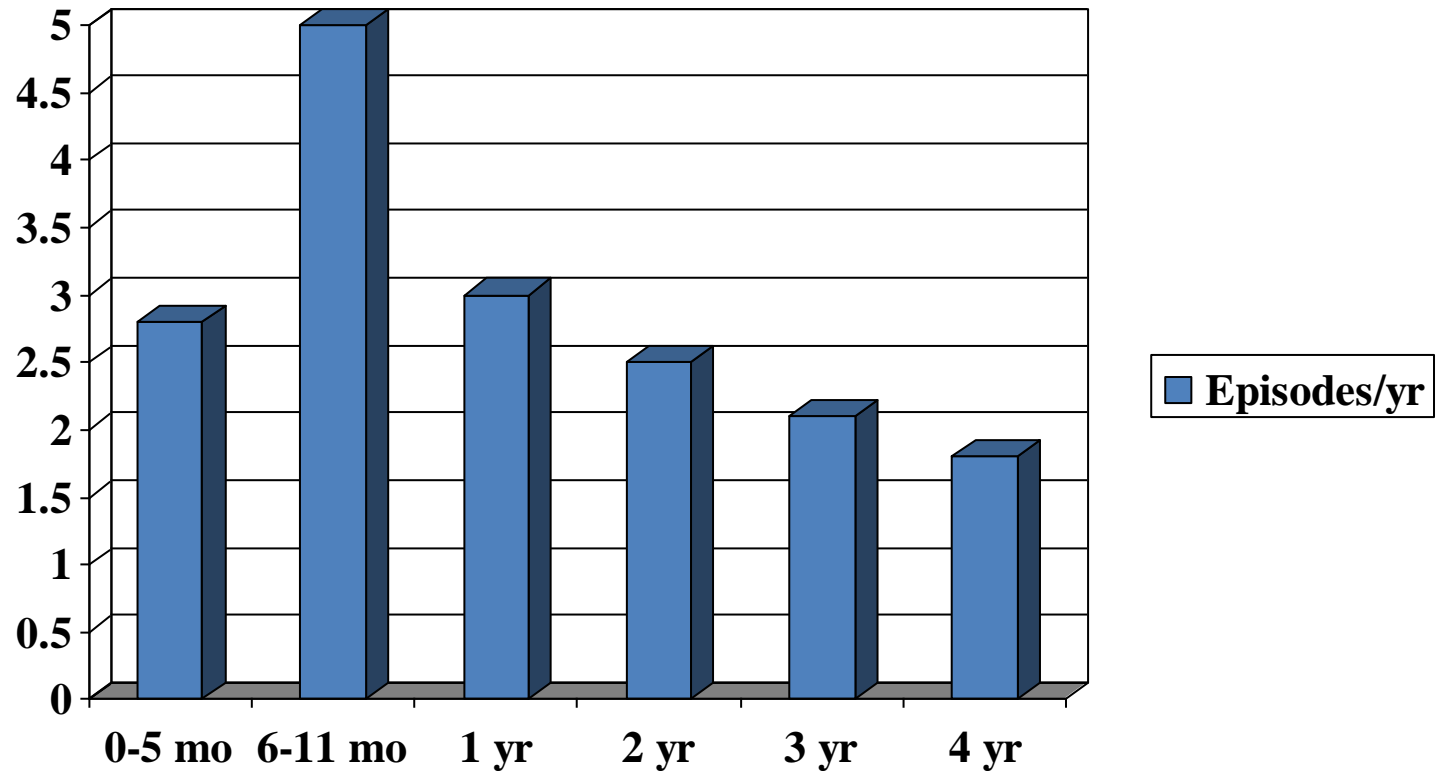
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Division of Gastroenterology, Hepatology,
and Nutrition

Virus Types

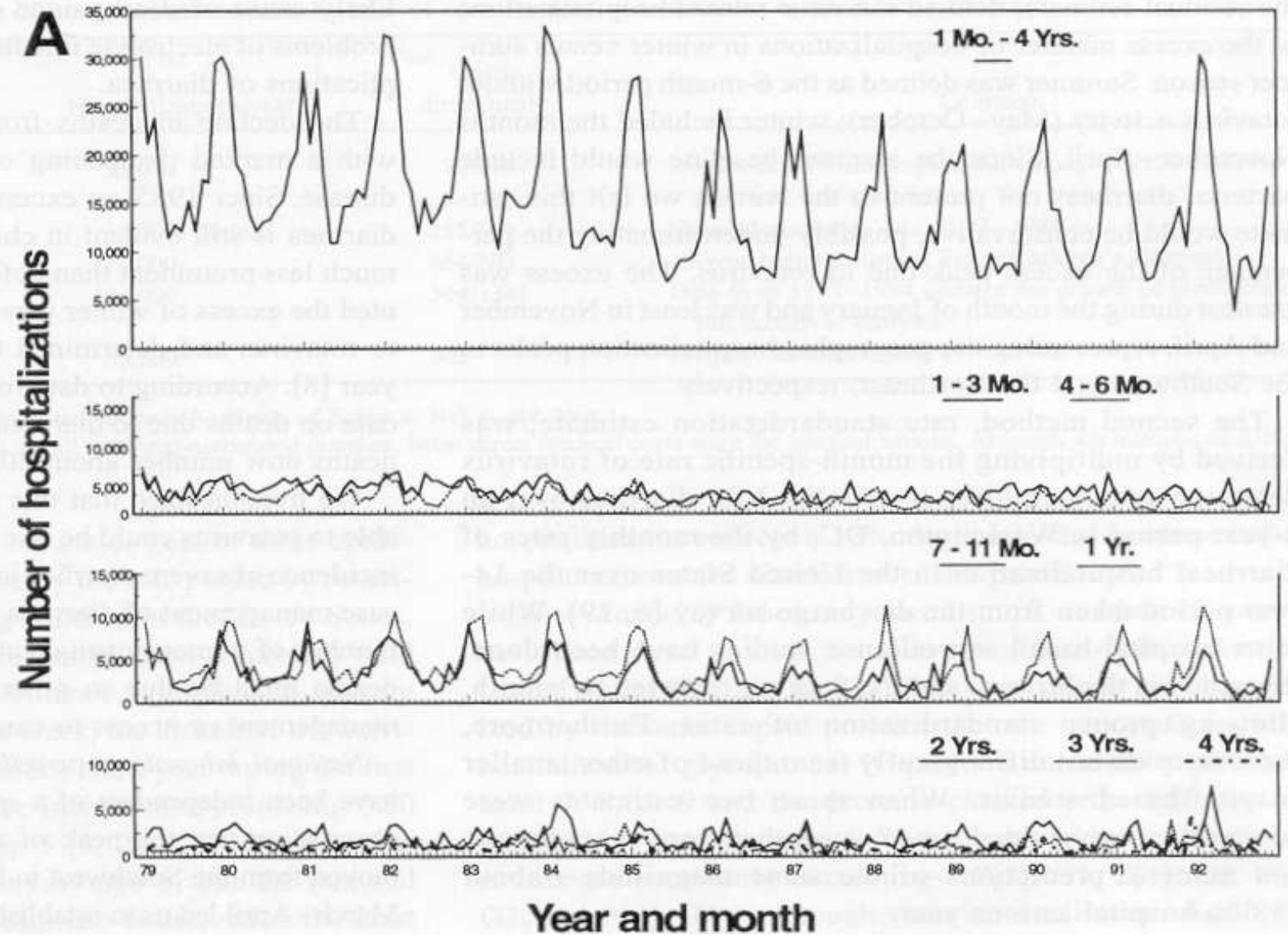
- **Viral gastroenteritis**
 - Rotavirus
 - Caliciviruses (Norovirus)
 - Adenovirus
 - Astrovirus
 - Others (Enterovirus, Torovirus, coronavirus, pestivirus)
- **Viral colitis**
 - Cytomegalovirus

Magnitude of the Problem

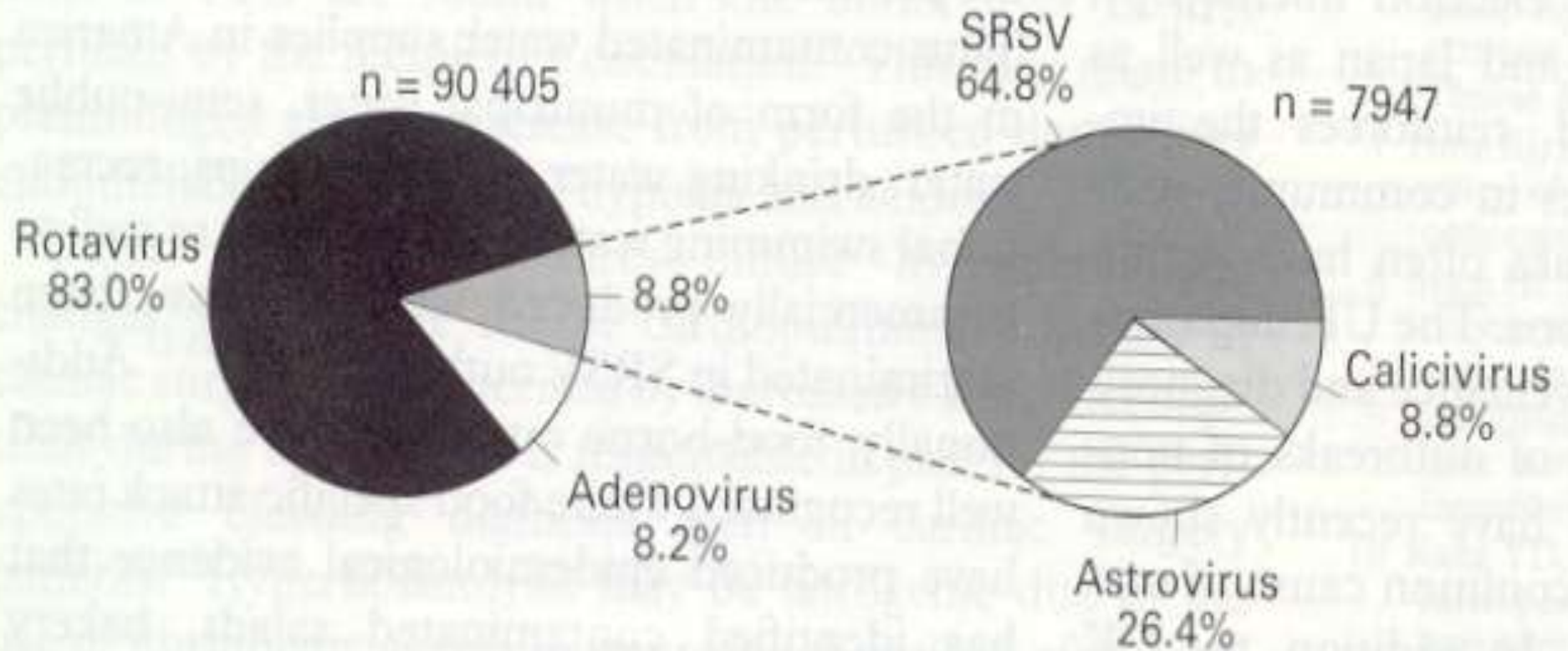


Magnitude of the Problem

- Developing countries
 - 2.6 episodes/child/year in children < 5
 - 700 million episodes/year
 - 3-5 million deaths/year
- United States
 - Approx 400,000 physician visits, 200,000 hospitalizations/year in children < 5
 - Mortality rare

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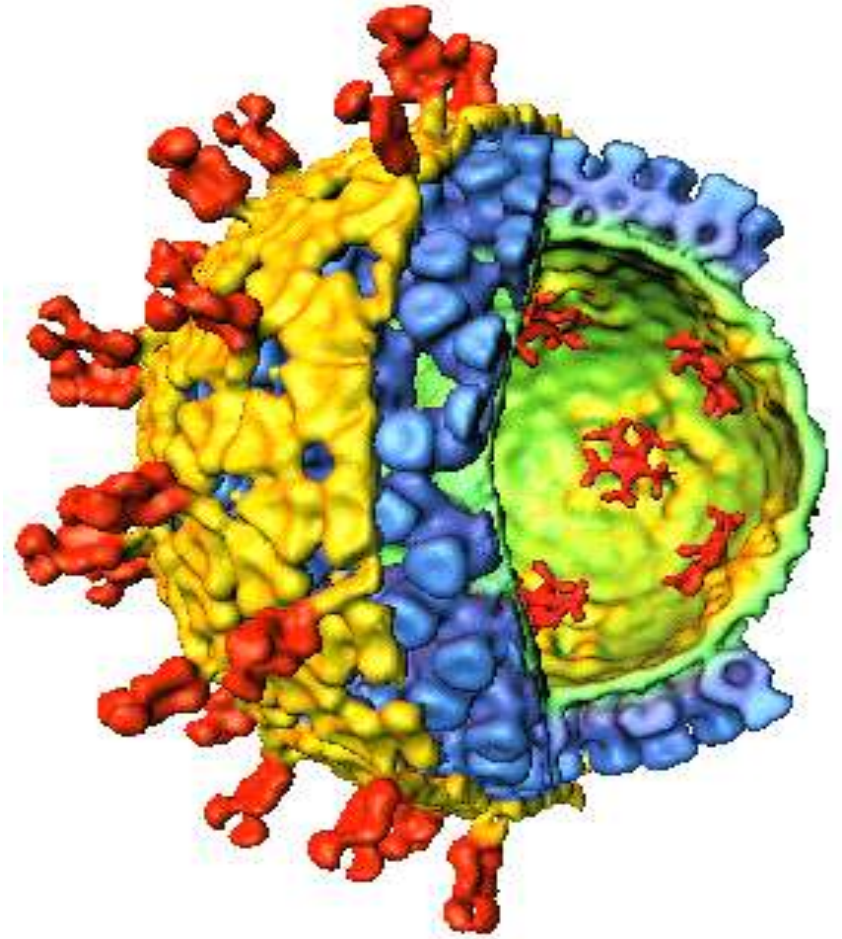
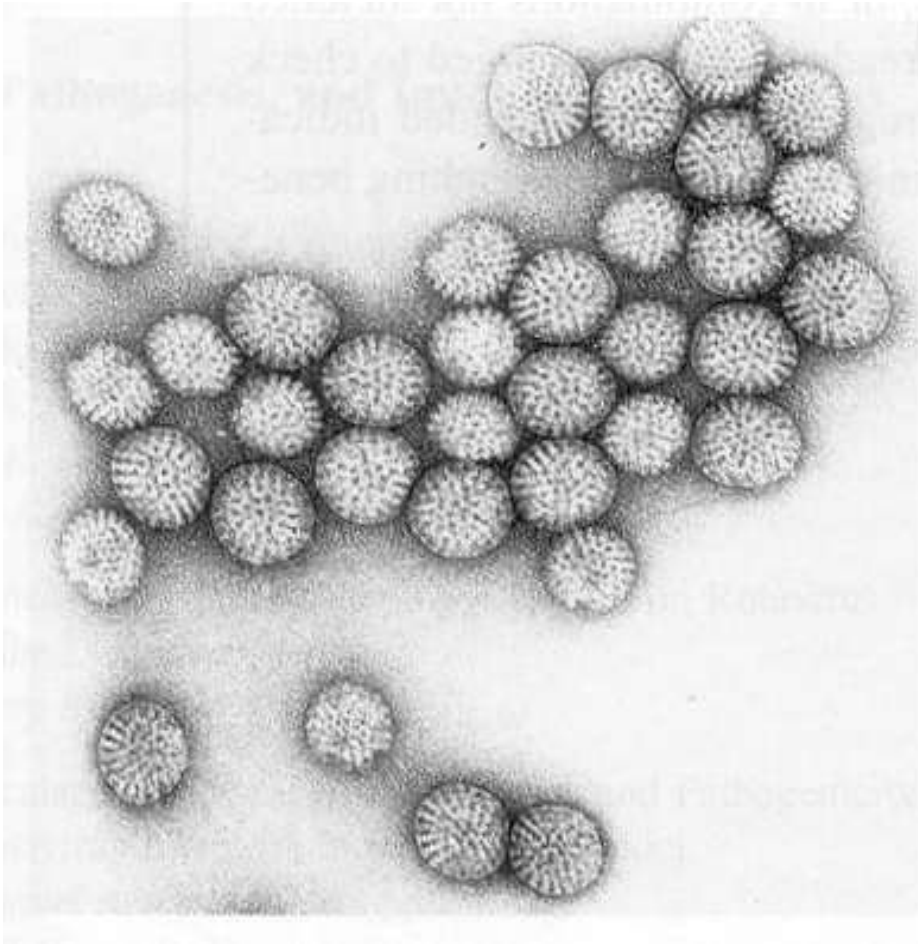
Viral Gastroenteritis in Children



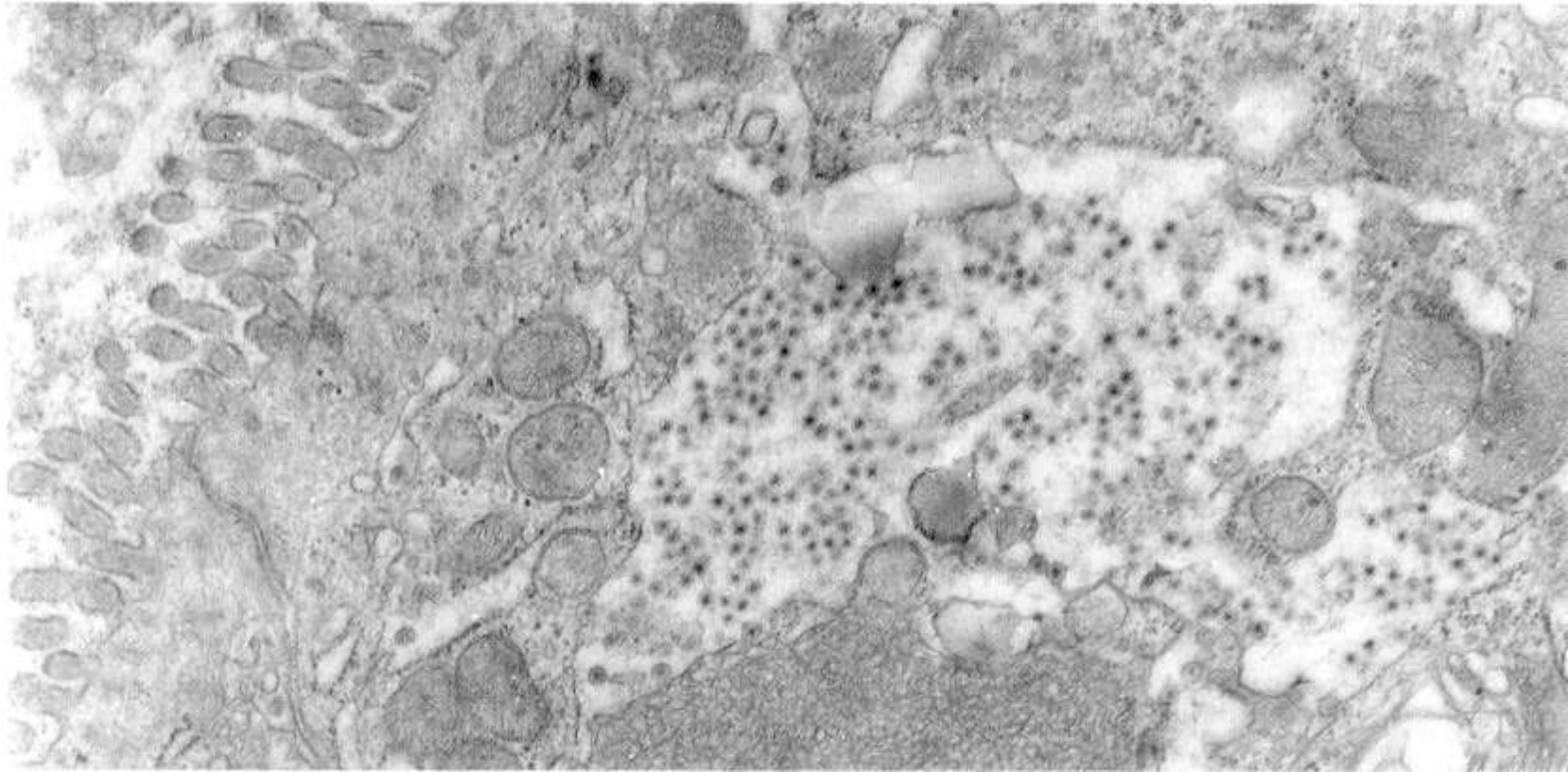
Rotavirus

- Discovered in 1973
- Worldwide distribution
- All children exposed by age 4-5
- Double stranded RNA virus
- Several groups (A-E vs G-P)
- Most common cause of viral diarrhea

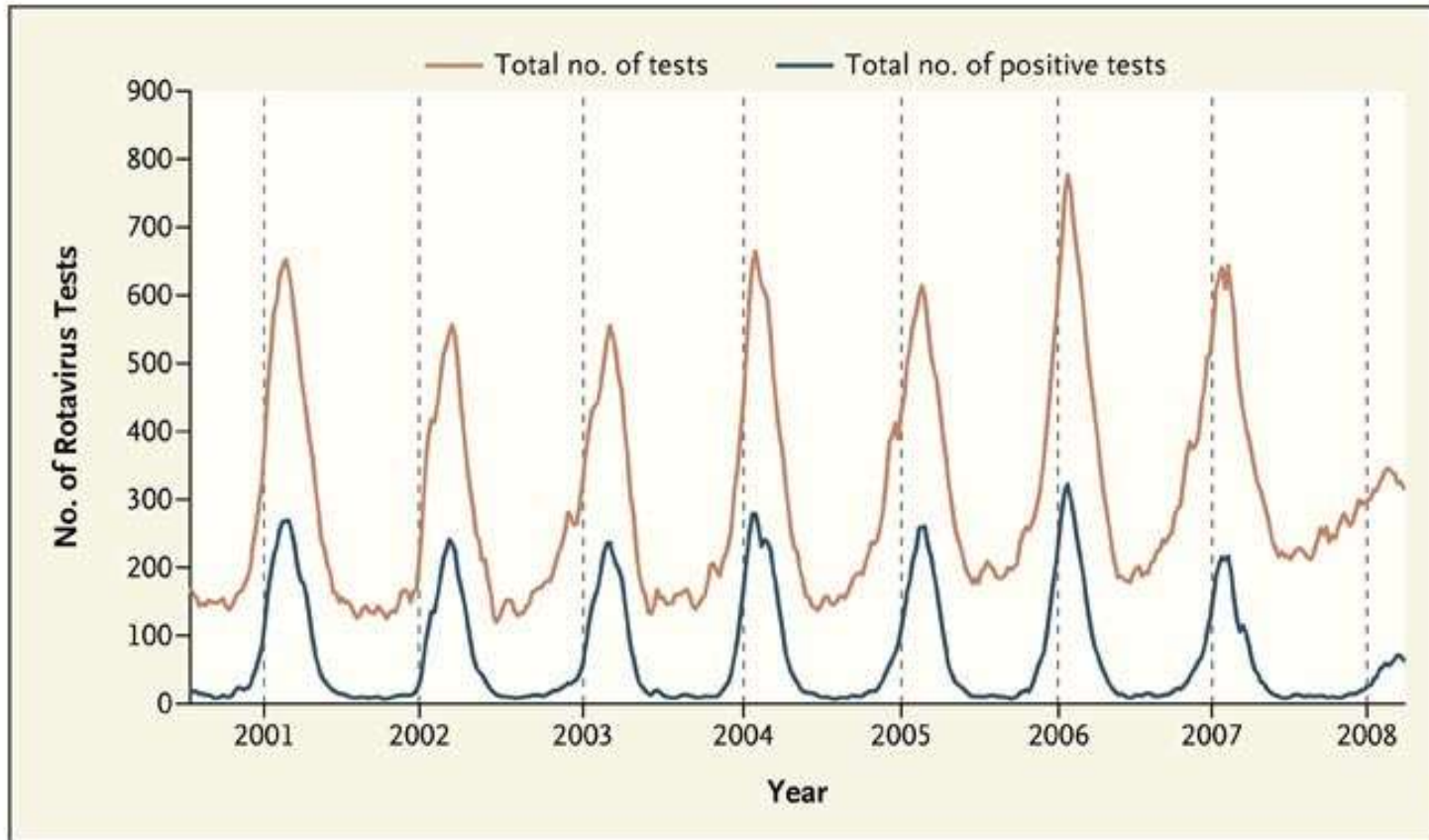
Rotavirus



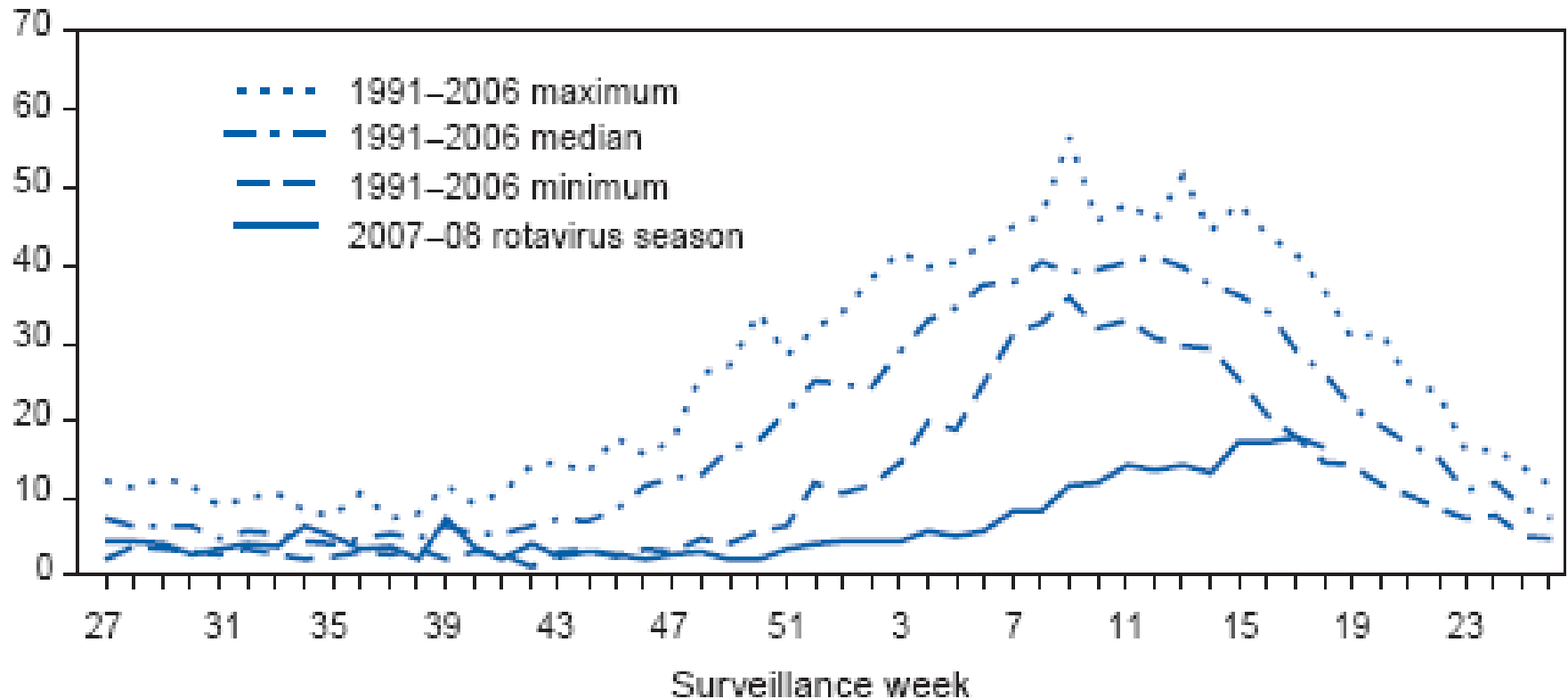
Rotavirus



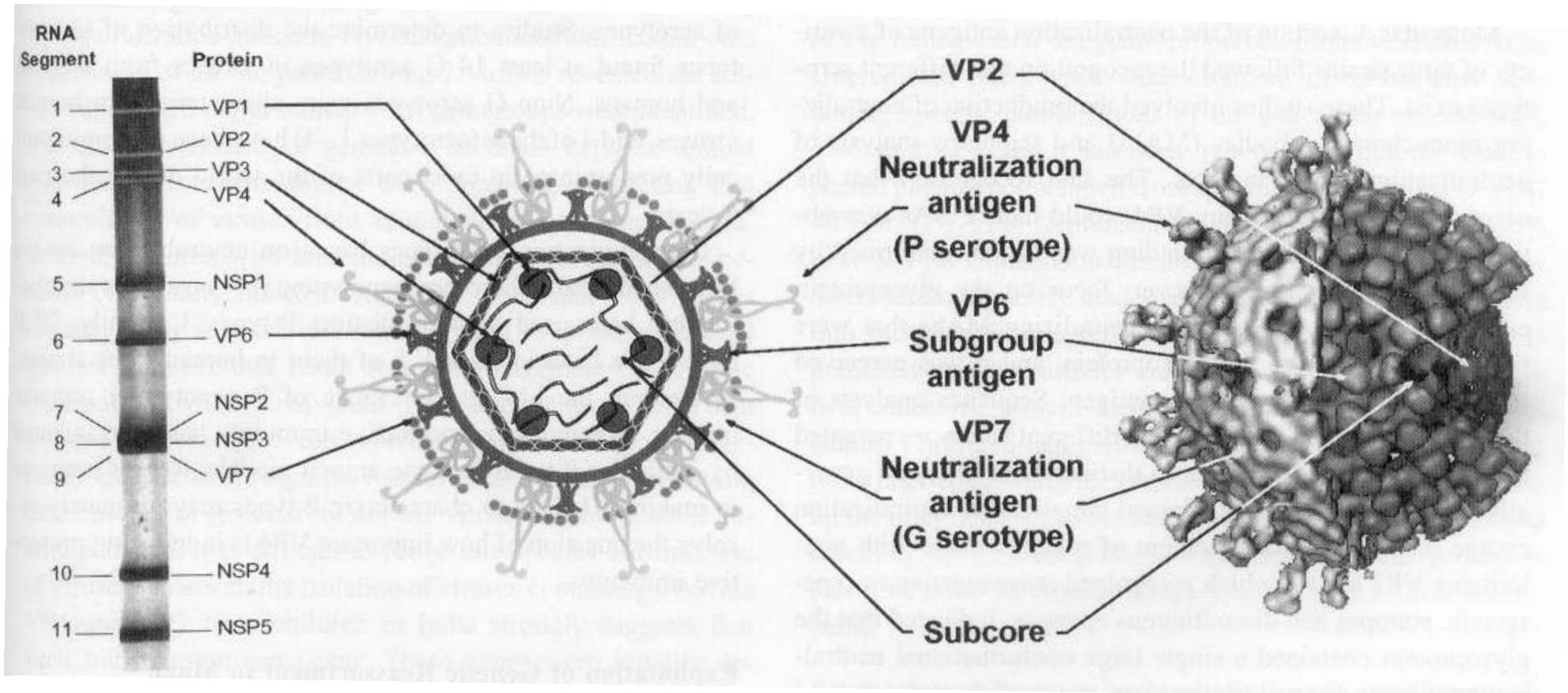
Rotavirus



Percentage of Rotavirus tests with positive results from US



Rotavirus structure

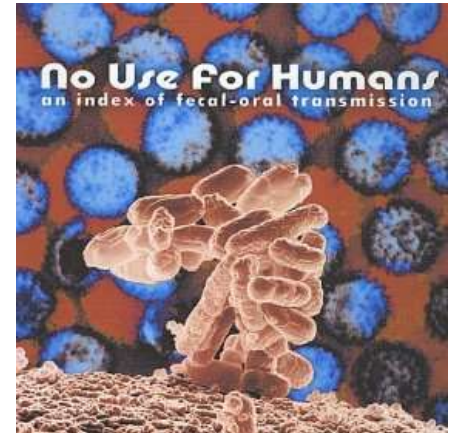


Most common serotypes G1, G2, G3, G4, P1(8)

Transmission of Rotavirus

Fecal-oral

- Usual kid stuff
- Contaminated water supplies
- Poor hygiene
- Food
- Fomites



Including hits like dysentery of the bloody flux and rotavirus

Rotavirus: Clinical Syndromes

- Childhood gastroenteritis
 - Endemic in tropics
 - Winter in temperate zone
- Outbreaks
 - Day care centers
 - Hospitals
- Immunocompromised adults

How does Rotavirus cause diarrhea?

- Injures intestinal epithelium
 - Malabsorption
- Increases secretion by epithelium

Diarrhea Classification

- Pathophysiology
 - Osmotic
 - Secretory
 - Exudation
 - Abnormal motility
- Duration
 - Acute (< 6 weeks)
 - Chronic (> 6 weeks)

Daily intake and endogenous secretions are efficiently absorbed by the gastrointestinal tract



Oral intake 2000

Salivary Glands 1500

Stomach 2500

Bile 500

Pancreas 1500

Intestine 1000

9000

Total presented to intestine

- 8800

Absorbed

Stool 200

Net Balance $2000 - 200 = 1800$

Endogenous Secretions 7000

% Absorbed $\frac{8800}{9000} = 98\%$



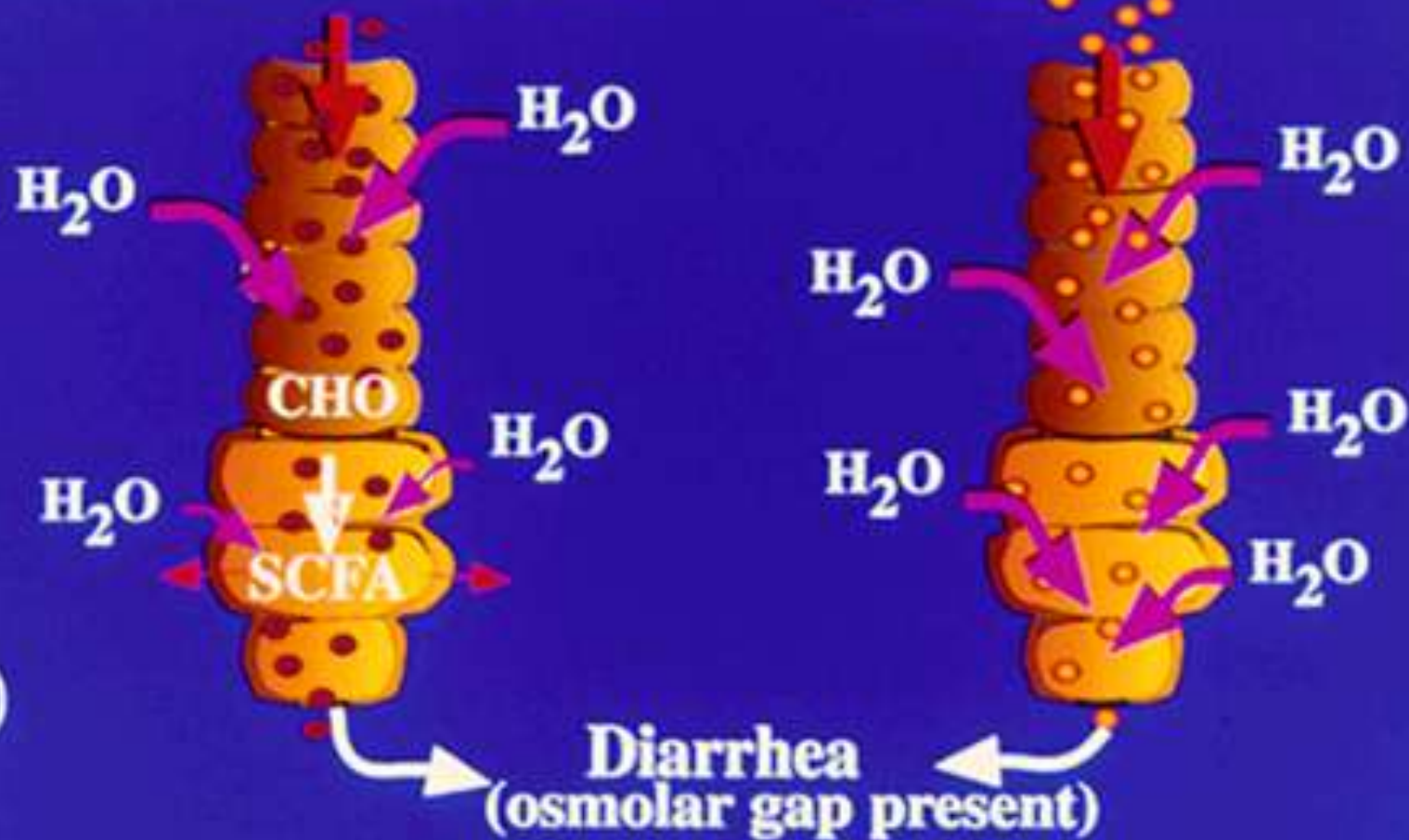
Osmotic diarrhea is caused by the presence of poorly absorbed luminal osmols

CARBOHYDRATES

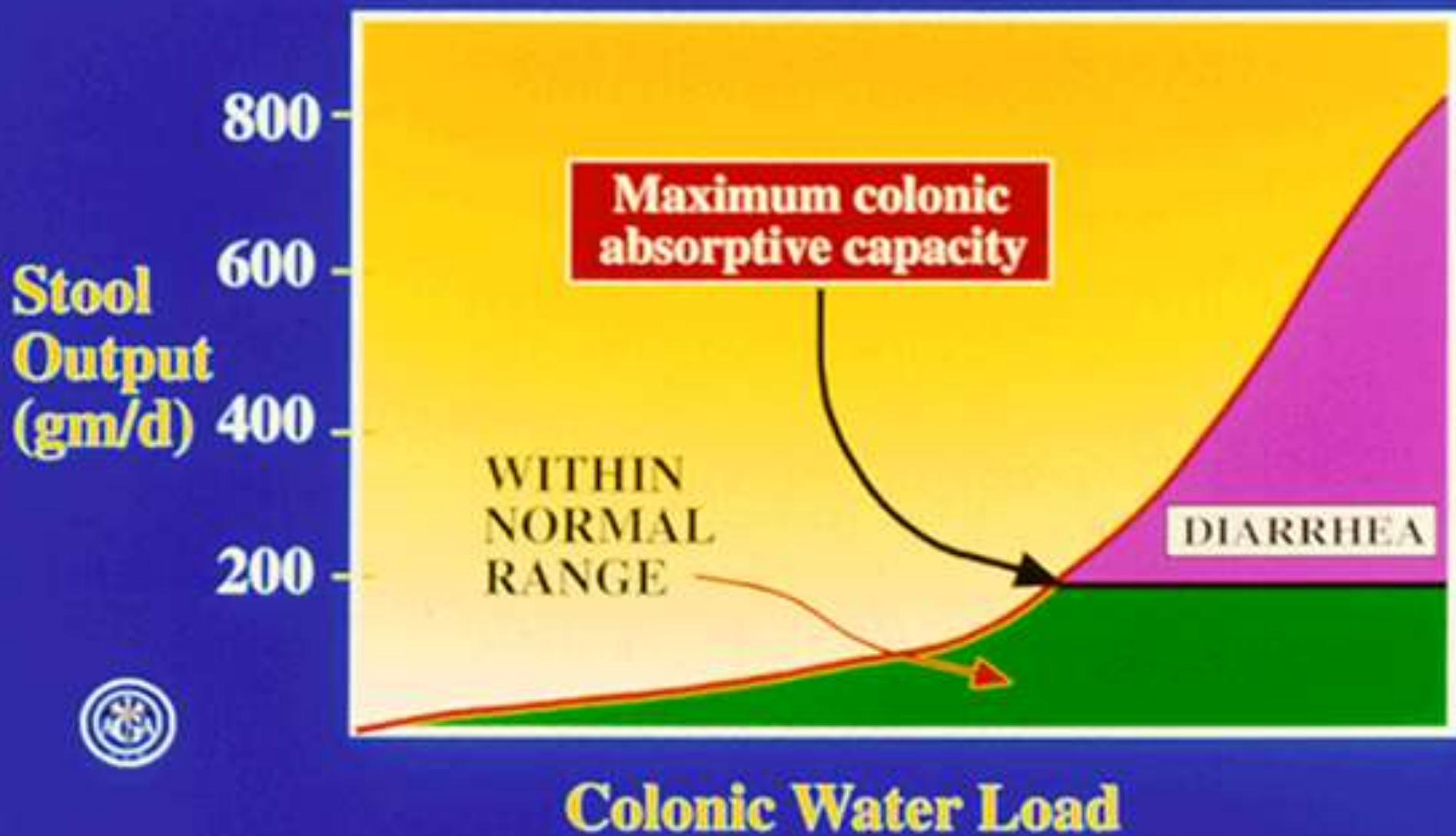
Lactose (lactase deficiency)
Sorbitol (chewing gum)

MINERALS

Na Sulfate Lavage Solutions
Mg Citrate



Diarrhea occurs when colonic water load exceeds absorptive capacity



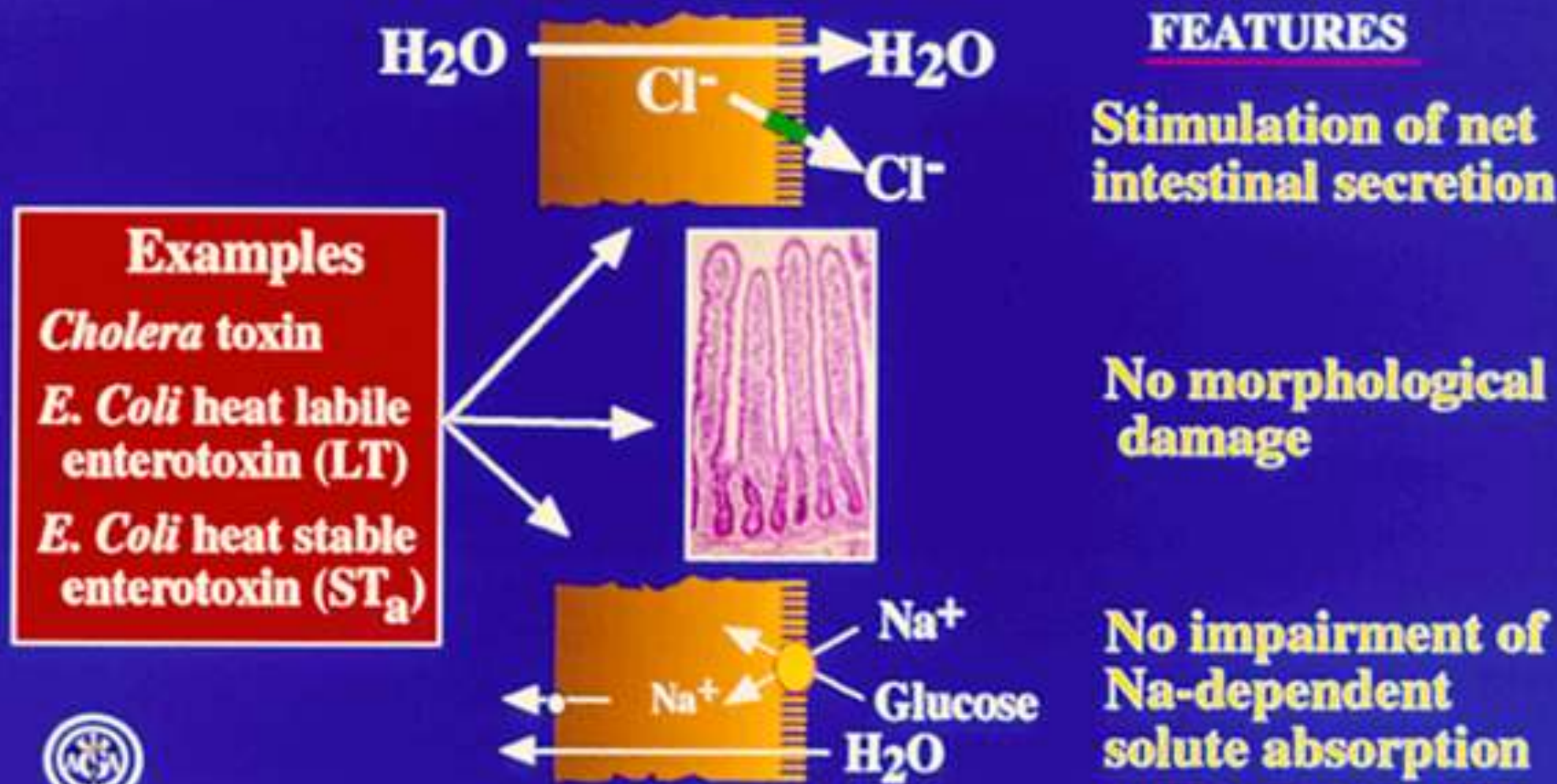
Osmotic diarrhea

- Def: Increased amounts of poorly absorbed, osmotically active solutes in gut lumen
- Interferes with reabsorption of water
- Solutes are ingested
 - magnesium
 - sorbitol
 - malabsorption of food (mucosal injury, lactase deficiency)

Secretory diarrhea

- Excess secretion of electrolytes, fluid across mucosa
- May also have decrease in absorption
- Watery, high-volume diarrhea with dehydration
- Enterotoxins: Cholera, E. coli, food poisoning, Rotavirus, Norovirus

Bacterial enterotoxins causing secretory diarrhea have several characteristic features



Enteric pathogens cause diarrhea by several different mechanisms

1. Stimulation of net fluid and electrolyte secretion



3. Mucosal destruction and increased permeability



2. Increased propulsive muscle contractions



4. Nutrient malabsorption

CHO malabsorption CHO



Rotavirus Clinical Syndromes

- Asymptomatic carriers
- Diarrheal illness
 - 2-3 day incubation period
 - Diarrhea (high volume, watery), vomiting, fever
 - 3-7 days
 - high infectivity
- Complications
 - dehydration
 - chronic diarrhea
 - dissemination
 - NEC (necrotizing enterocolitis)

Diagnosis of rotavirus

- Electron microscopy
 - Small intestine
 - Stool
- Antigen in stool
 - **commercial ELISA**
 - research PCR, nucleic acid probes

Therapy for rotavirus

- Rehydration
 - ORT
 - Intravenous
- Probiotics
 - lactobacillus GG
- Bismuth
- Other anti-diarrheals (Imodium)

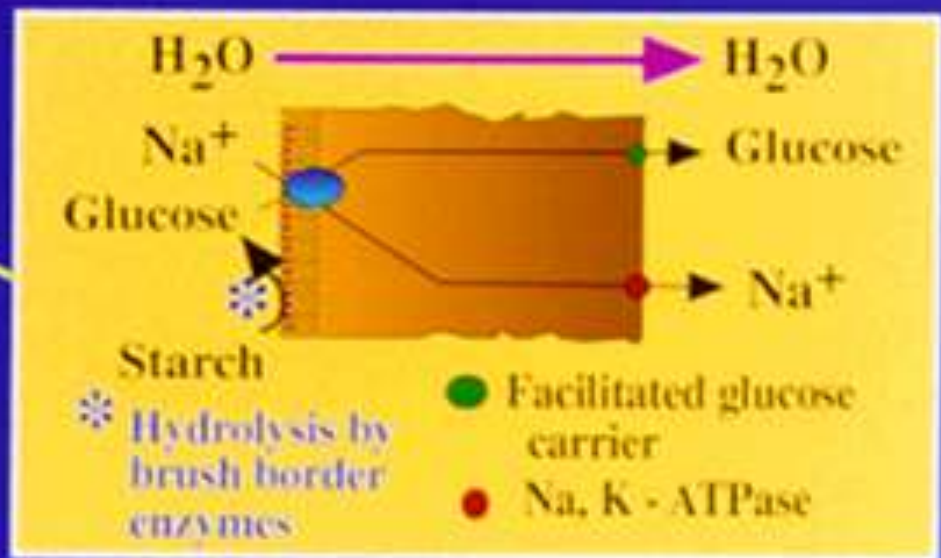
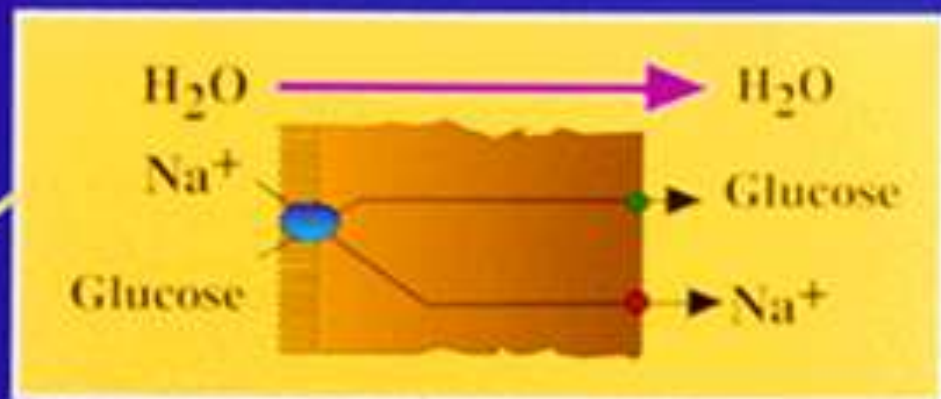
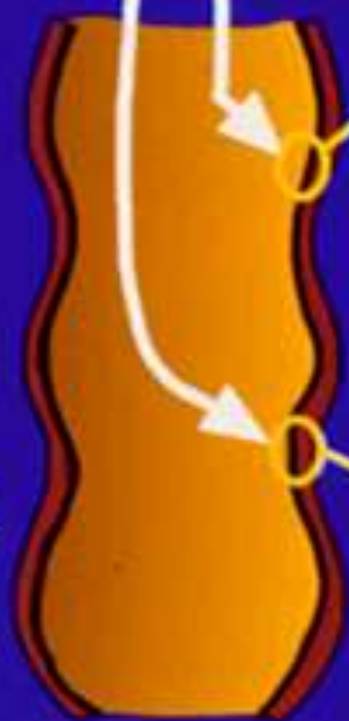
Oral rehydration solutions

<u>Components</u>	<u>WHO</u>	<u>Ricelyte®</u>	<u>Pedialyte®</u>
Na (mEq/L)	90	50	45
K (mEq/L)	20	25	20
Cl (mEq/L)	80	45	35
Citrate (mEq/L)	30	34	30
Glucose (g/L)	20	30	25

Glucose and starch based oral replacement solutions (ORS) promote absorption of sodium and water

ORS (glucose)
ORS (starch)

- Secretion is unaffected



Oral rehydration solutions can correct metabolic abnormalities resulting from severe diarrhea

Plasma Values	Untreated	Treated
Na (mEq/L)	141	142
Cl (mEq/L)	107	106
K (mEq/L)	4.5	3.6
HCO₃ (mEq/L)	9	21
Arterial pH	7.21	7.43
Plasma specific gravity	1.05	1.026
Stool output (liters/day)	7.5	8.0



Prevention of Rotavirus

- Natural immunity 50-80% protective (sIgA)
- Vaccination
 - Monovalent (G1P8) attenuated human: Rotarix[®]
 - 85% efficacy (G1P8 most common)
 - Oral dose at 2 and 4 months of age
 - Pentavalent reassortant rotavirus: Rotateq[®]
 - 95-98% efficacy against most common serotypes G1, G2, G3, G4, P1(8)
 - Oral dose at 2,4,6 months of age
- Universal infant immunization is recommended

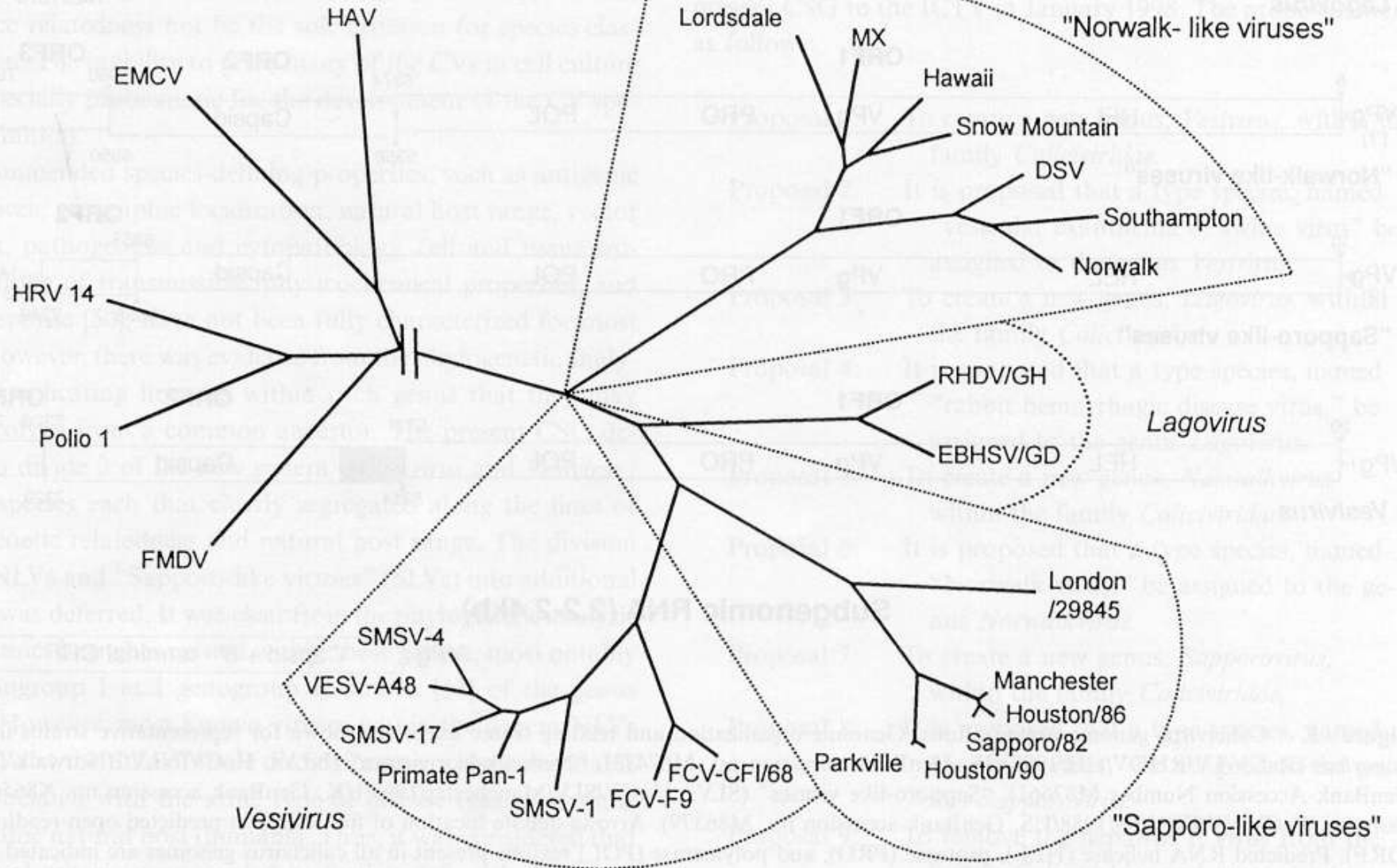
Calicivirus

- Norovirus: Norwalk virus and “Norwalk-like”
- Sapovirus: “Sapporo-like” viruses
- Vesivirus
- Lagovirus
- All single stranded RNA viruses

Picornaviridae

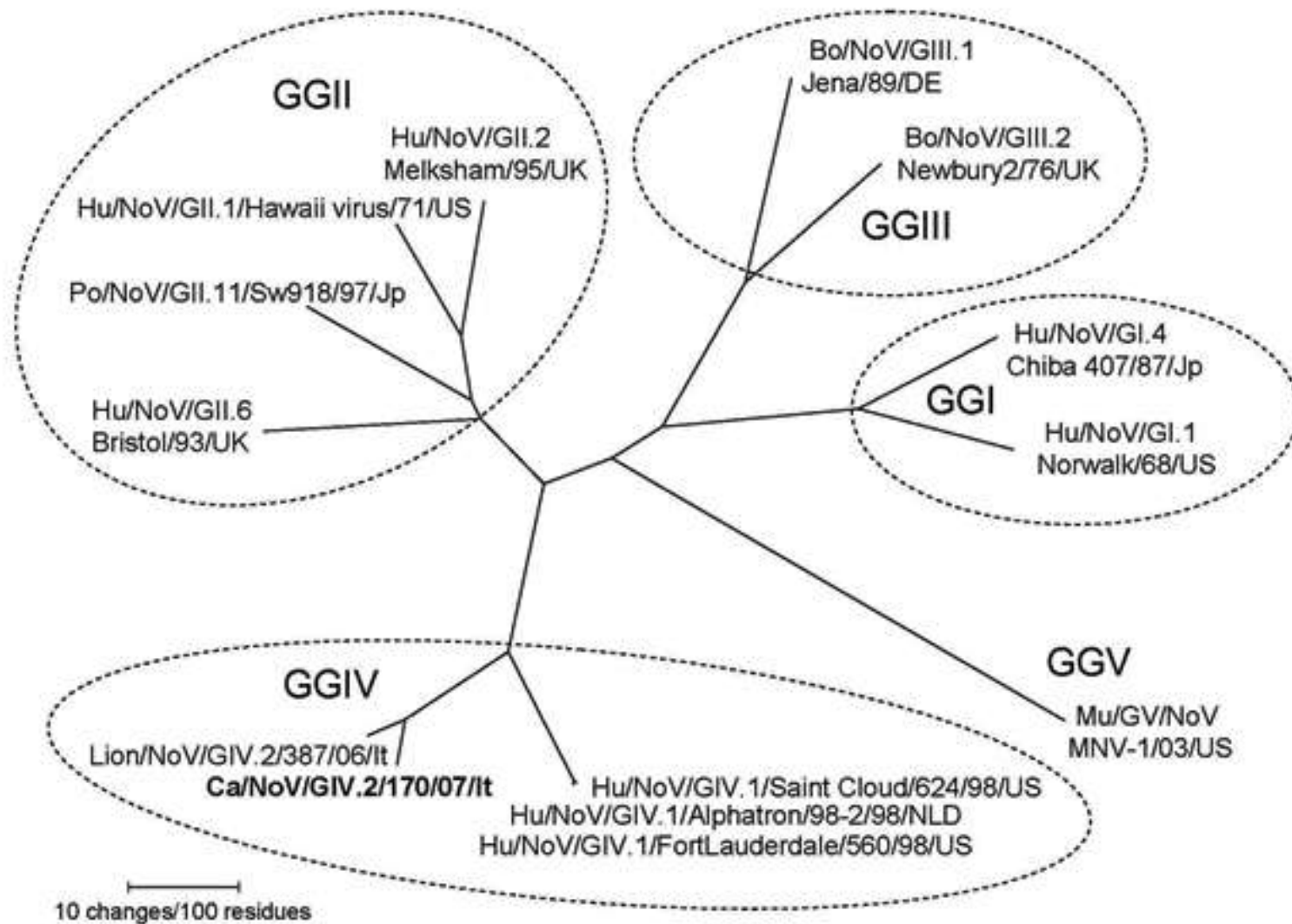
Caliciviridae

Norovirus or

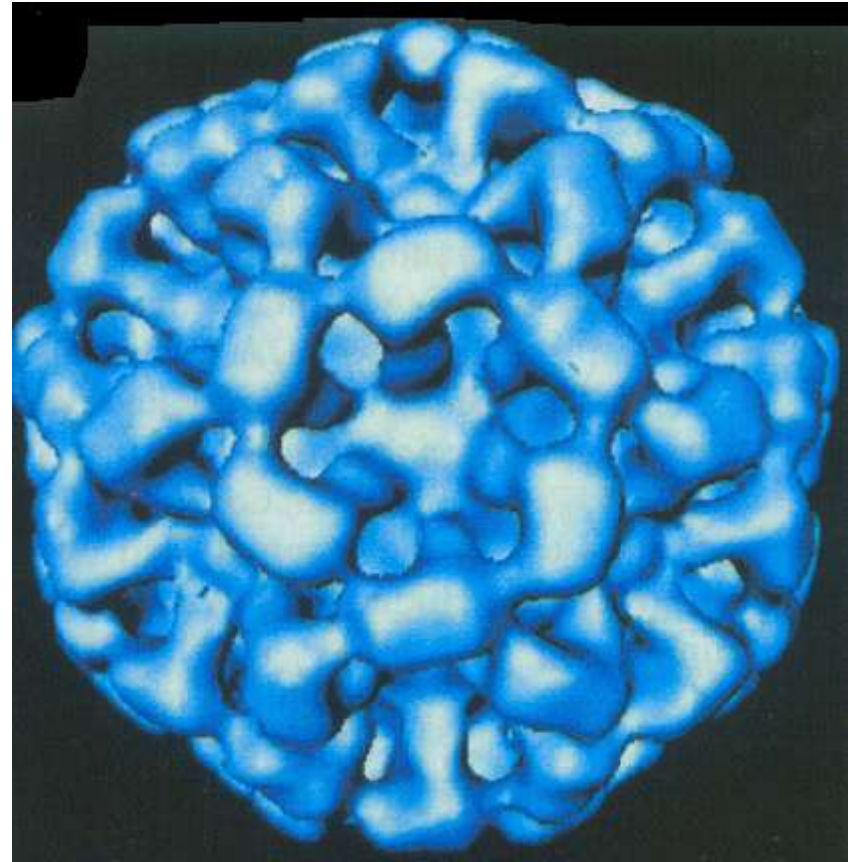
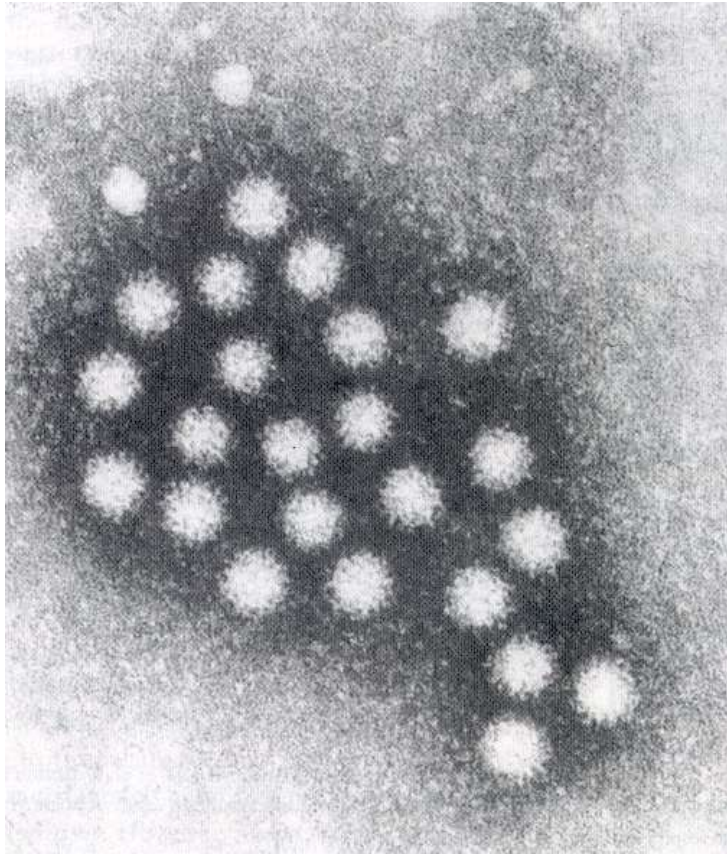


0.2

0.1



Norovirus



Norovirus

- “winter vomiting disease” 1968, Norwalk OH
- Most common cause of nonbacterial gastroenteritis epidemics (40-50%)
- Explosive epidemics
 - camps, cruise ships, nursing homes, amusement parks, military facilities, hospitals
 - Several law firms do nothing but sue Cruise ship lines over norovirus outbreaks (www.noroblog.com)
- Food borne illness
 - raw shellfish

Food-borne illness

<u>Agent</u>	<u>1981-89</u>	<u>Present</u>
Norovirus	33%	45%
C. perfringens	14%	12%
Salmonella	11%	11%
Staph aureus	7%	3%
B cereus	7%	2%
Campylobacter	4%	3%
E Coli 0157	1%	4%

Shellfish-borne infections



<u>Agent</u>	<u>Before 1990</u>	<u>Present</u>
Norovirus	3%	52%
Vibrio	2%	37%
Unidentified	56%	7%
Salmonella	23%	0%
Hepatitis A	13%	< 1%

Norovirus: Clinical Features

- 24-48 hour incubation period
- vomiting prominent
- watery diarrhea 1-3 days
- affects all ages
 - antibodies in 60% of adults
- complications rare
 - immunocompromised

Norovirus

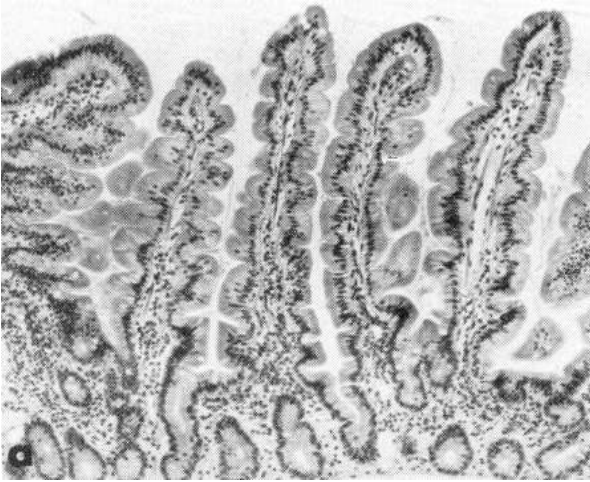
- Readily transmissible (median infectious dose only 18 viruses)
- Viral shedding at very high levels (7.7×10^{10} viruses/gm stool), persisting weeks after symptoms have resolved
- Over the past decade, most epidemics associated with emerging G II.A strain (“Farmington Hills” strain)

How does Norwalk virus cause diarrhea?

- Infection affects proximal small bowel
- Patchy mucosal injury with villous blunting
- Malabsorption (osmotic mechanism)
- Excess secretion likely but no enterotoxin identified
- Cause of vomiting unclear



Norwalk virus



Before ingestion



2 days



6 days

Diagnosis of Norwalk virus

- Clinical diagnosis (exclude rotavirus)
- Immune EM
- Serology of antibody response
- enzyme immunoassays
- RT-PCR
- oligonucleotide probes

Treatment of Norwalk virus

- Rehydration
- Supportive measures
 - bismuth
 - antidiarrheals (Lomotil, Immodium)

Other viruses causing gastroenteritis

- Astrovirus
 - children, outbreaks
- Adenovirus
 - children, prolonged course
- Torovirus
 - children, bovine pathogen
- Enterovirus

Cytomegalovirus

- Herpesvirus
- Immune competent
 - Mononucleosis-type syndrome
- Immunocompromised
 - retinitis
 - hepatitis
 - gastrointestinal involvement (colon)

The clinical presentation of diarrhea may be helpful in identifying the site of involvement

Small bowel and colonic

Large stool volume
Moderate increase in number
Minimal urgency
No tenesmus
Little mucus

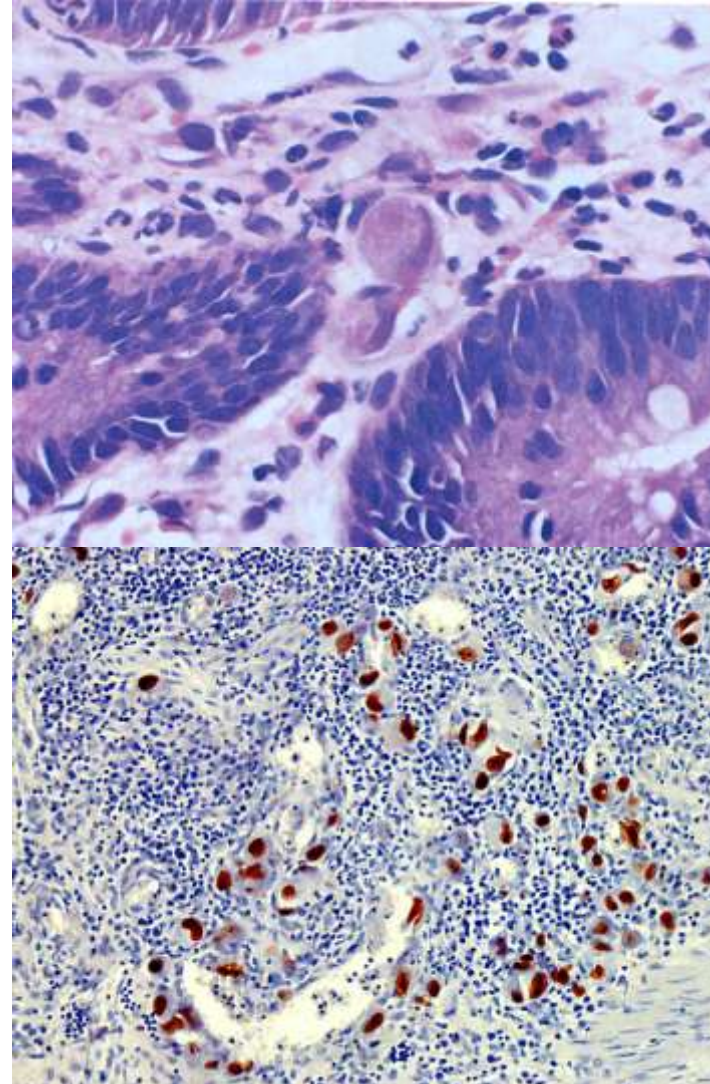
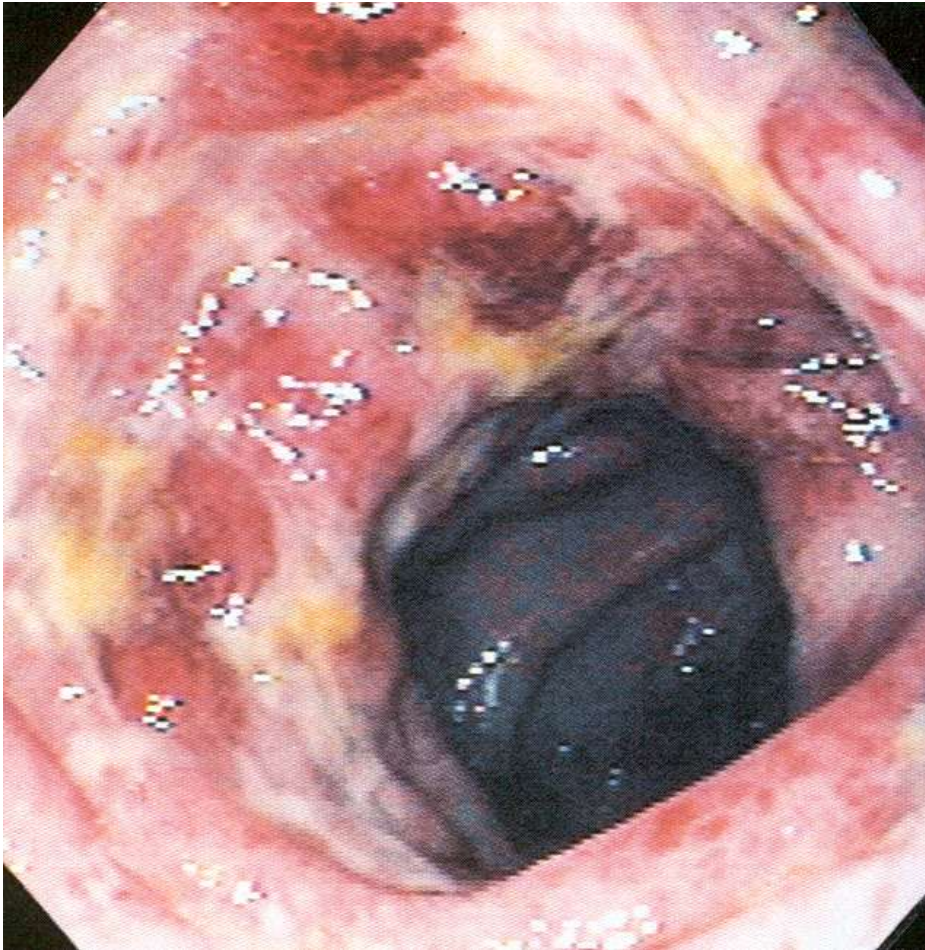


Recto-sigmoid

Small amount of stool
Frequency
Urgency
Tenesmus
Mucus
Blood



Cytomegalovirus colitis



Cytomegalovirus

- Diagnosis requires tissue biopsy
- Occurs in immuno-compromised patients
 - Chemotherapy
 - Steroids
 - HIV
 - Transplant
- Difficult to treat