Alimentary infections

ETIOLOGY

• bacterial, viral, parasitic (rare) or fungal (only in immunocompromised)

BACTERIAL DIARHHEAL DISEASES

Campylobacteriosis

etiology, epidemiology

•most frequent worldwide diarrheal infection

• hemorrrhagic enterocolitis – immunocompetent patients

• extraintestinal – immunocompromised

• G- rods, microaerophilic, special culture media, higer temperature (42C), Campylobacter jejuni, C. coli and others

• zoonosis – commensal in the intestine of wild and domestic animals, source – ingestion of contaminated food (e.g. chicken, pork

Campylobacteriosis

etiology, epidemiology

•most frequent worldwide diarrheal infection, incubation period – 2-7 days

• hemorrrhagic enterocolitis – immunocompetent patients

• extraintestinal – immunocompromised

• G- rods, microaerophilic, special culture media, higer temperature (42C), Campylobacter jejuni, C. coli and others

• zoonosis – commensal in the intestine of wild and domestic animals, source – ingestion of contaminated food (e.g. chicken, pork

pathogenesis: invasive, production of toxins, found – jejunum, ileum, colon

symptoms: from secretory diarrhea to severe illness, most common – hemorrhagic enterocolitis – mucus and blood, high fever, rarely extraintestinal – sepsis or localized (e.g. meningitis)

Campylobacteriosis

diagnosis: stool - culture, special media and atmosphere, PCR panel (including all GIT agens), **extraintestinal – blood culture** and other (CSF…)

treatment: mild or moderate cases – **rehydratation**, diet, adsorbent, probiotics, severe diarrhea and systemic inf. – macrolides, fluoroquinolones (systemic inf. – weeks depending on susceptibility)

Charcoal-based selective media (CSM)

- **Specimen** – **swab, stool and transport media**

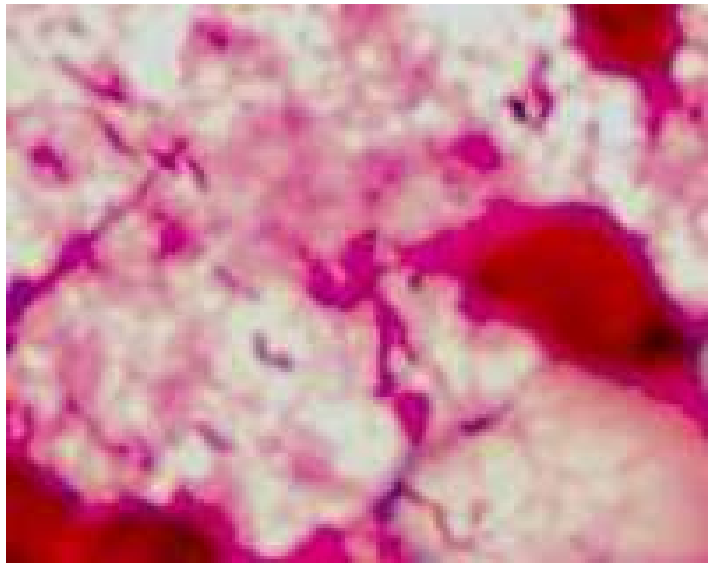
- e.g. Charcoal-based selective media (CSM) for isolation Campylobacter spp. from fecal specimes – small whitish or greyish colonies

- microaerophilic atmosphere at 42C, 48h

- microscopy – curved Gramnegative rods

- phenotypical identification – oxidase positive, mass spectrometry (MALDI)

- most significant *C. jejuni*



Microscopy of *Campylobacter* spp. (and also *Helicobacter pylori*) – curved Gramnegative rods, often as flying birds

Infection caused by Salmonella spp.

etiology, epidemiology

• Gram negative rods, Enterobacteriaceae, usually motile, hemorrrhagic enterocolitis – immunocompetent patients

Typhoid (enteric) fever –high fevere, abdominal pain, complications, high incidence – **developing countries**, incubation period – 5-24 days

• **Salmonella Typhi**

• source – contaminated water or food, rarely - person-to-person (ill, convalescent, carrier)

pathogenesis: across the intestinal mucosa – transient bacteremia, multiplication – lymph.nodes, ulcers – Payer pathes, complication-systemic inf

symptoms: untreated 4 weeks, fevere, headache, diarrhea – ½ patiens, could – constipation, intestinal perforation,…

Infection caused by Salmonella spp.

Diagnosis

- 1st week: **blood culture, later** could be positive – stool, urine
- 2nd week: Vidal´s reaction, O and H antibodies, Vi antibodies later

dif.dg: paratyphoid fever, malaria, others

Treatment: rehydrataion, supportive care, **antibiotics** – 10-14 days, fluoroquinolones, cotrimoxazol, ampicilin, chloramphenicol, developing countries – macrolides, cephalosporins of 3rd generation intravenously (systemic inf)

prevention: vacination is available

Infection caused by Salmonella spp.

Paratyphoid fever A, B, C, similar to typhoid fever but milder

Etiology nad epidemiology: *Salmonella paratyphi* A, B, C

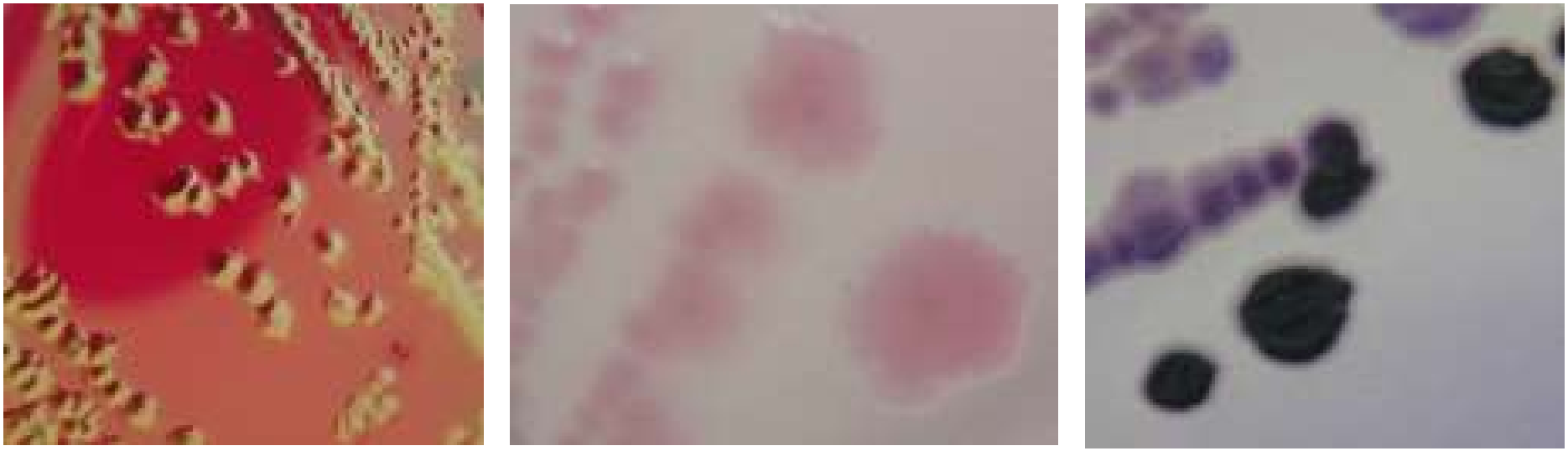
• source – **Paratyphoid fever** A, C only in humans, B zoonotic, source, transmission – water, food, rarely person-to-person contact, incubation period – 3-5 days

symptoms: Paratyphoid fever A – similar to typhoid, milder, Paratyphoid fever B – typhoid form and enterocolitis, Paratyphoid fever C – immunocompromised – pneumoina, sepsis with skin abscesses

diagnosis: blood, stool, urine, pus cultivation

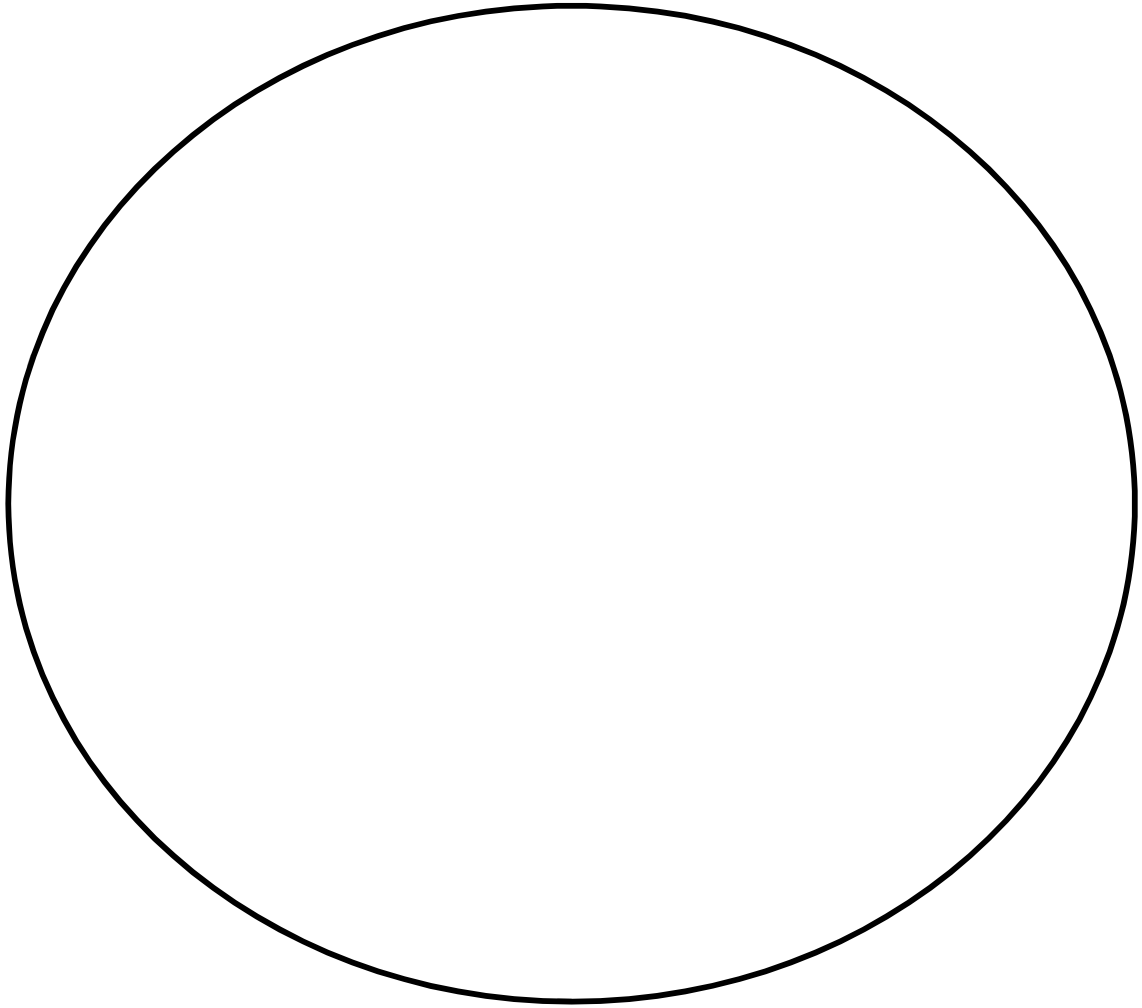
treatment: the same as in typhoid fever

prevention: vaccination is not available



A B C

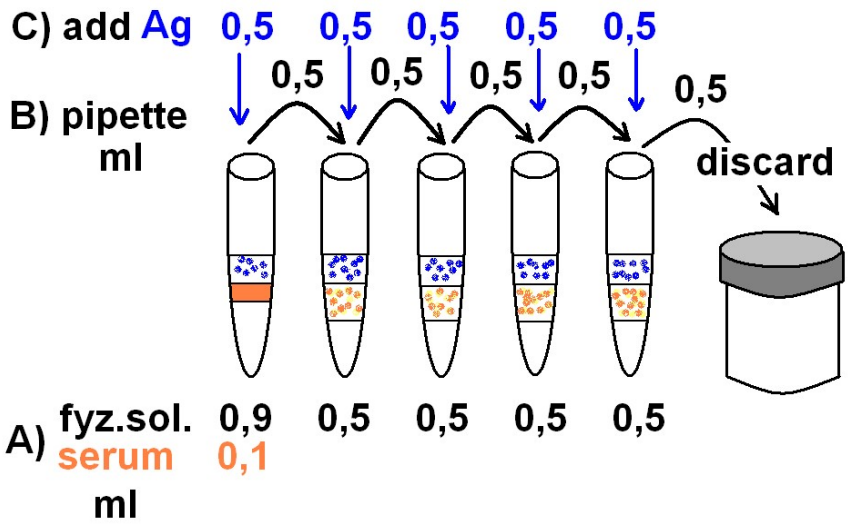
Lactose positive (dark, red) colonies (A) groving on Endo agar differentiate coliforms (e.g. *E. coli*, *Klebsiella* spp., *Citrobacter* spp.) from transparent lactose negative colonies (B) of enteric pathogen from family *Enterobacteriaceae* (*Salmonella* spp., *Shigella* spp., *Yersinia* spp.). Production of hydrogen sulfide is typical for almost of *Salmonella* spp.(black colonies in C) but rarely also in other eneterobacteria can be detected (e.g. *Citrobacter* spp.)

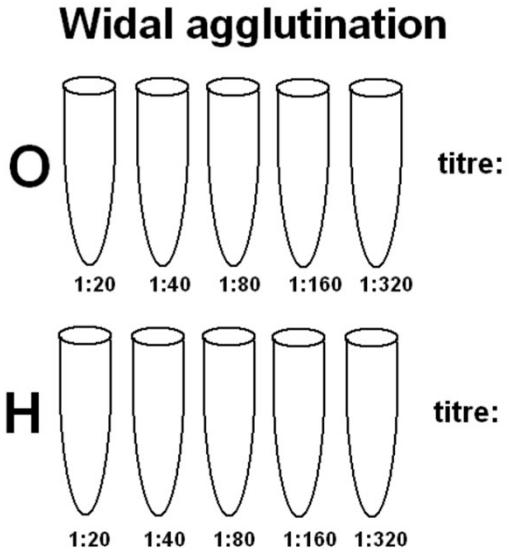


MICROSCOPY: Stain colonies of an enterobacterial species growing on culture media. After drying, fixing and gram-staining draw the morphology of the object that you could see in your microscope.

A B C D

All enterobacteria ferment glucose with production of gas (B) and can grow under mineral oil (C) what differentiates them from nonfermenters (e.g. *Pseudomomas* spp., *Acinetobacter* spp., *Burkholderia* spp.) which dont produce gas form glucose (A) and can only oxidase gluse without mineral oil (D)





INTERPRET THE RESULT OF SEROLOGICAL ANALYSIS OF A PATIENT WITH SUSPECTED ENETERIC FEVER. Dilute the serum of a patient geometrically, add the H and O Ag (following steps A, B and C indicated in the schema below), incubate overnight at 37°C and 45°C, respectively. Observe the positive reaction and determine the specific antibody titer

Bacillary dysentery (Shigellosis)

etiology, epidemiology

•Disease of „dirty hands“

• G- rods, Enterobactariaceae, ***Shigella dysenteriae, S. boydii, S. flexneri, S. sonnei***

• only human infection (hundres annually in the Czech Republic), usually small outbreaks

pathogenesis: invasive, production of toxin (**Shigatoxin** – similar to verotoxin, found – colon)

symptoms: hemorrhagic enterocolitis – mucuc and blood, high fever, rarely extraintestinal – sepsis caused by *Shigella dysenteriae* has been reported

diagnosis: repeatedly stool cultures, PCR

treatment: cotrimoxazol, quinolones, azithromycin

Escherichia coli associated diarrhea

• 5 groups, different mechanisms, G- rods, Enterobacteriaceae, source of inf – contaminated water, food, salads…

Enterotoxigenic E. coli (ETEC): major cause of traveller´s diarrhea and infants and children in developing countries

etiology, epidemiology: serotypes – e.g. O6, O8, O25, inf.dose – high (10/8 bacteria)

• **pathogenesis:** colonize small intestine, heat-stable amd heat-labile toxin inducing intestinal secretion

symptoms: low fever, vomiting, abdominal cramps, watery diarrheae 3-5 days

diagnosis: stool culture

treatment: rehydratation, severe - cotrimoxazol, fluoroquinolones

prevention: bottled water, well cooked meal

Escherichia coli associated diarrhea

Enterotoinvasive E. coli (EIEC): cause of „coli dysenteria“

etiology, epidemiology: serotypes – e.g. O28, O29, O32, inf.dose – high (10/8 bacteria)

- **pathogenesis:** invading intestinal epithelial cells, ulceration, hemorrhage in the colon
- **symptoms:** inflammatory bloody diarrhea
- **diagnosis:** stool culture
- **treatment:** rehydratation, antibiotic can be used - cotrimoxazol, ampicilin

Escherichia coli associated diarrhea

Shiga toxin producing E. coli (STEC), verotoxin producing E. coli (VTEC), enterohemorrhagic E. coli (EHEC): food-borne epidemics, ruminants – source of VTEC infections, severe complications – HUS, incub.period – 1-8 days

etiology, epidemiology: serotypes – STEC e.g. O26, O103, EHEC O157:H7, O104:H4

pathogenesis: STEC – Shiga and verotoxin- irreversible cessation of protein synthesis and cell death, HUS – toxin acts on vascular endothelial cells – endothelial damage and plate thrombi

symptoms: inflammatory bloody diarrhea, HUS – mortality 5%

diagnosis: stool culture, PCR

treatment: rehydratation, antibiotic are not recommended – incease risk of HUS development

Escherichia coli associated diarrhea

Enteropathogenic E. coli (EPEC): life-threating, infants less then 1 year

etiology, epidemiology: serotypes – e.g. O44, O55, O111,

pathogenesis: adherence to epithelial cells - alteration

•**symptoms:** watery diarrhea

•**diagnosis:** stool culture

treatment: rehydratation, antibiotic can be used - cotrimoxazol

Enteroaggregative E. coli (EPEC): persistent diarrhea, children developing countries

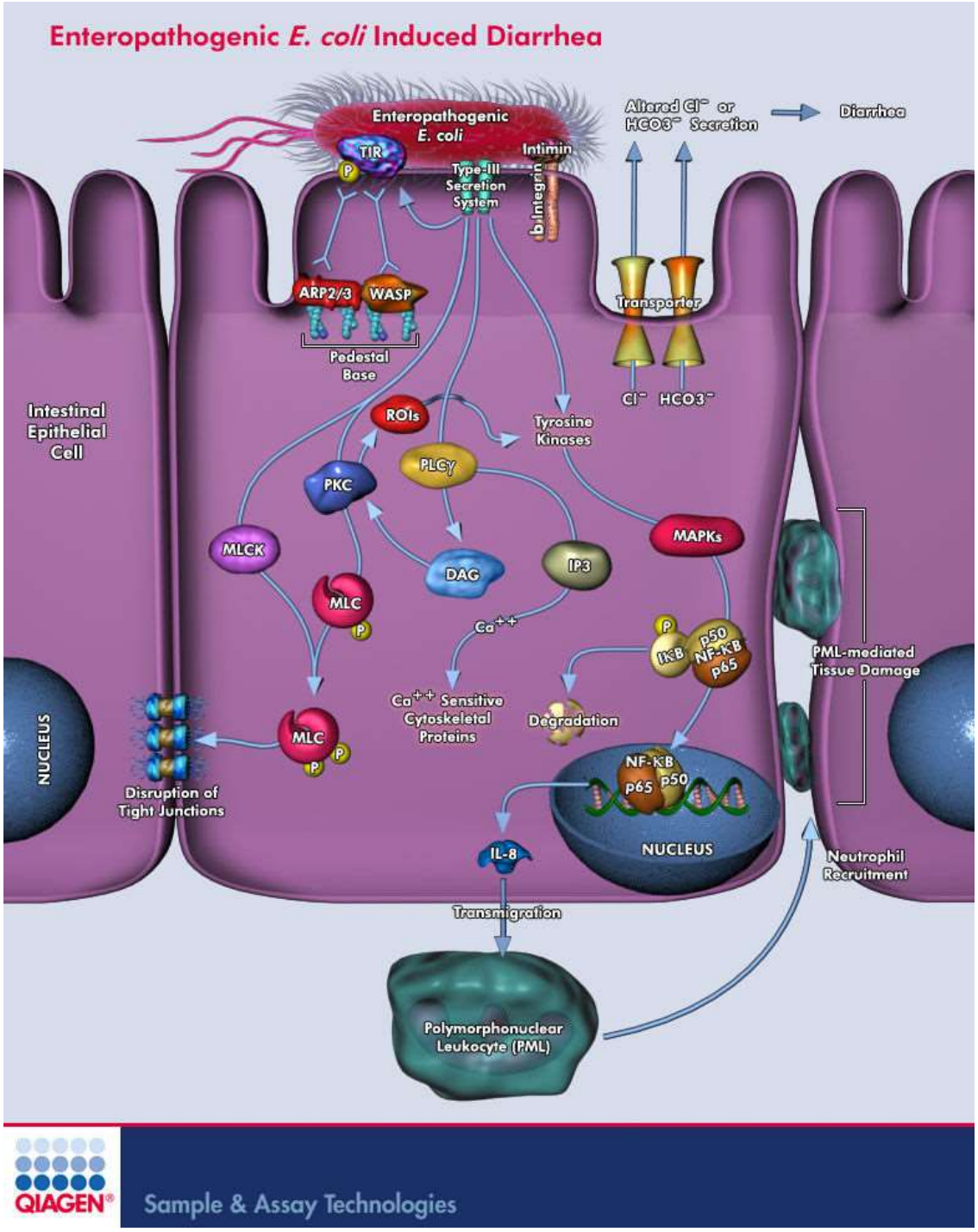
etiology, epidemiology: serotypes – e.g. O3, O6, O11

pathogenesis: adherence to epithelial cells - alteration

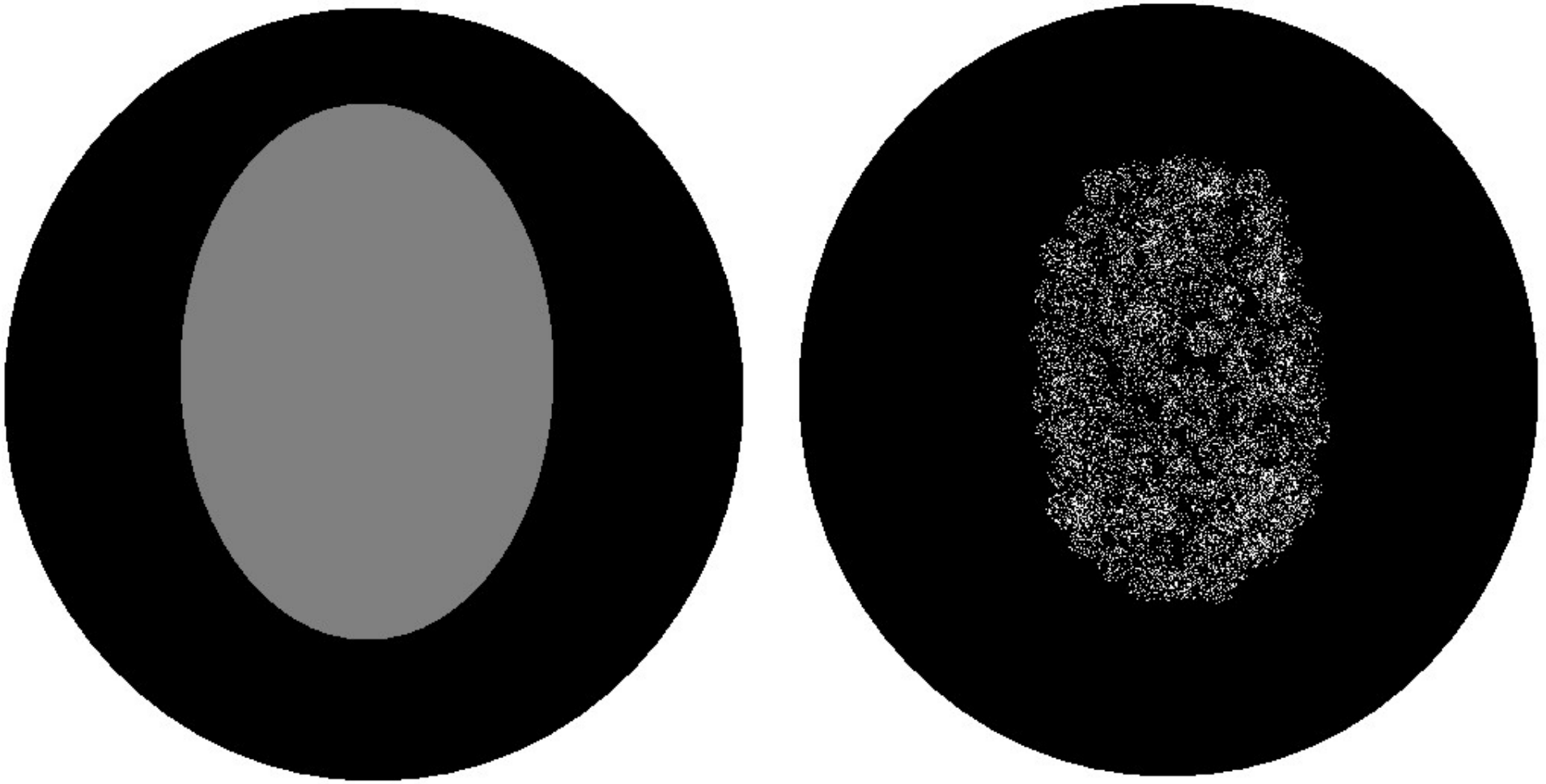
• **symptoms:** watery diarrhea more than 14 days

• **diagnosis:** stool culture

treatment: rehydratation



Enteroadhesiveness step and production of a toxin identical to Shigella toxin. A plasmid is involved in the attachment of enteropathogenic E. coli to intestinal mucosa which results in a pathognomonic histopathologic lesion visualized by electron microscopy. The lesion involves dissolution of enterocyte microvilli by the bacteria, effacement of the enterocyte outer membrane, and formation of a pedestal around the bacterium at point of contact with the outer membrane of the enterocyte.



A B

SEROTYPING (REVERSE AGGLUTINATION) OF ENTEROPATOGENIC E.COLI O55. Mix the culture of *E.coli* of an infant with antiserum against O55 serotype. Positive agglutination apperar in case the analysed strains is of the O55 serotype. Draw the reaction. Negative (A) a positive O55 serotype (B)

Yersiniosis

etiology, epidemiology

• infrequent diarrhea (hundreds annually - CR), rarely severe extraintestinal forms

• G- rods, *Yersinia enterocolitica* (*Y. pseudotuberculosis*)

• zoonosis – ingestion of contaminated food and water

• **pathogenesis:** invasive, production of endotoxin, enterotoxin, mucosal ulceration

• **symptoms: hemorrhagic enterocolitis** –high fever, bloody diarrhea, **, pseudoappendicitis**

• **diagnosis: cultivated** from stool**, PCR,** specifiec antibodies – especially usefull for dg of pseudoappendicitis

• **treatment:** rehydratation, usually selflimited, severe – cotrimoxazol, fluoroqiunolones

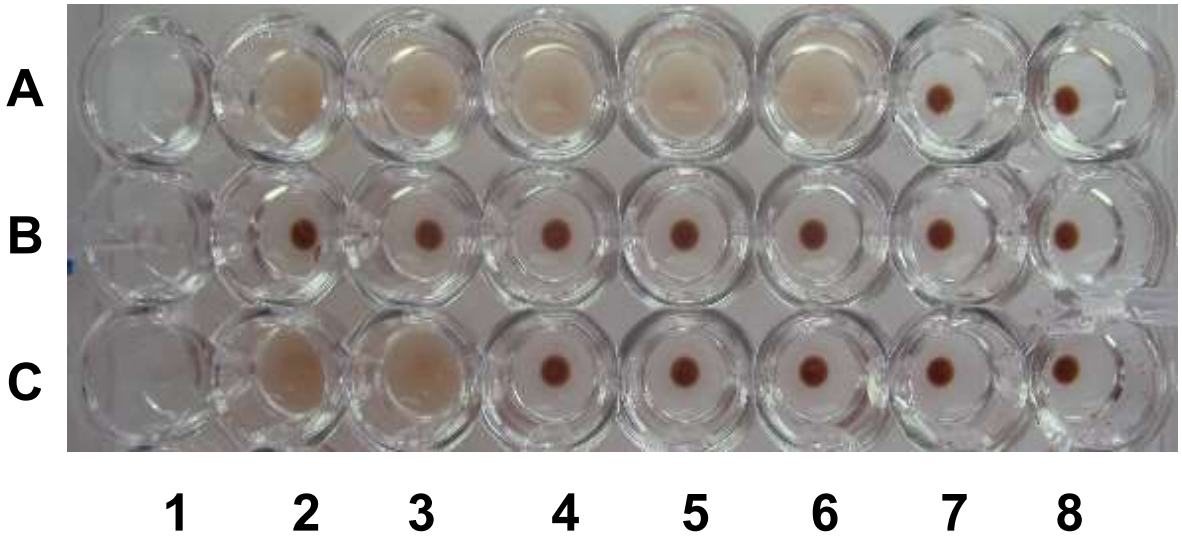


Fig.7. Hemagglutination assay with specific somatic antigens of *Yersinia enterocolitica* (serotype O3, enteric pathogen). Erythrocytes are senzitized with purified Ag of *Y. enterocolitica*. The sensitized erythrocytes agglutinate if specific Ab are presented in patient sera. Patients´ sera (A1, B1,C1) are diluted geometrically from dilution 1:10. Patient A has titre of specific Ab 1:160, patient B negative, patient C has titre 1:20.

Cholera

Epidemic diarrheal disease

etiology, epidemiology

• **G- curved rods,** Vibrio cholerae, serogroups O1 and non-O1, different serotypes, El Tor last 7 pandemics

• source – contaminated water, food, incub.period – 1-5 days, high infectious dose

• **pathogenesis: cholera enterotoxin** promotes secretion of fluids and electrolytes

• **symptoms:** depend on biotype, El Tor – high mortality, abrupt onset of watery diarrhea, vomiting, dehydratation, sunked eyes, dry mucous membranes, hypovolemic shock, renal failure

• **diagnosis: stool** - special **culture** media, **PCR**

• **treatment: rehydratation,** antibiotics – secondary role, **doxycyclin,** fluorochinolones, azithromycin, cotrimoxazol

•**prevention:** oral vaccine

Clostridium difficile associated diarrhea (CDAD)

Antibiotic-associated colitis

etiology, epidemiology

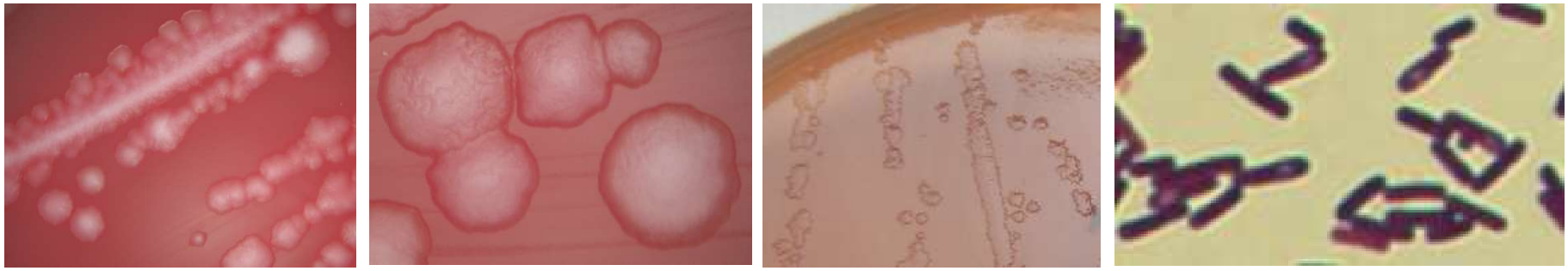
• G+ anaerobic spore-forming rods in 1978 indetified as causative pathogen (earliest cases attributed largely to clindamycin, today also fluoroquinolones, broad-spectrum penicillins and cephalosporins), other risk factors – hospitalization, advenced age, gastric acid suppresion, resistant to alcohol desinfectants, fecal-oral route

• **pathogenesis:** Once spores are in the colon they convert to vegetative, toxin-producing cells and become susceptible to antibiotics. Produce 2 potent A and B exotoxins that mediate colitis and diarrhea

• **symptoms:** watery diarrhea 10-15 times daily (ranging form asymptomatic to severe fulminant disease with toxic megacolon), cramping, white count 15000, **pseudomembranous colitis** – in addition – pseudomembranes, relapse or reinfection can occur (10-25%), **fulminant colitis** – fever, diffuse paint in lower abdominal quadrant, diarrhea, white count 40 000, complication – toxic megacolon

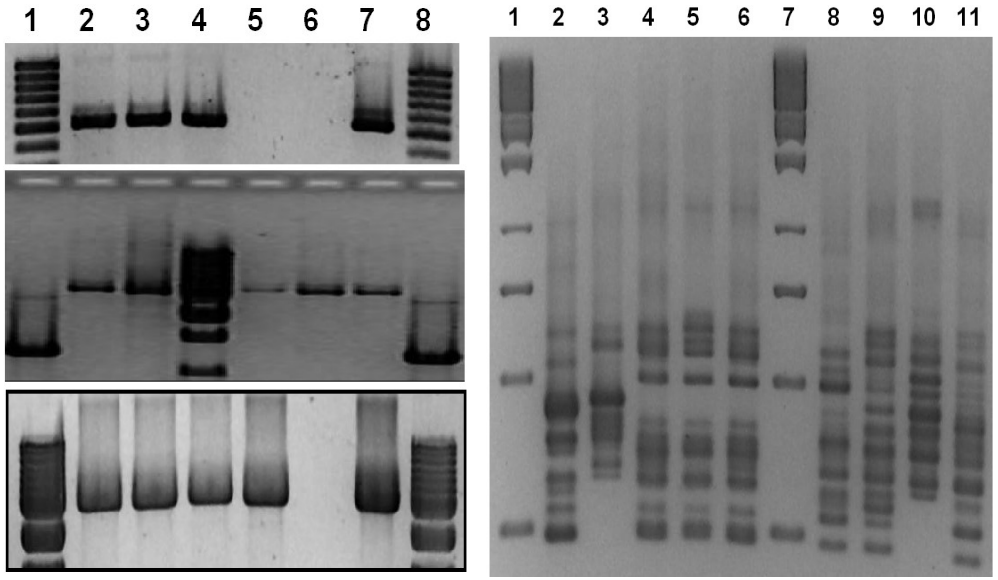
Clostridium difficile associated diarrhea (CDAD)

Diagnosis: 3 or more loose stool per day for at least 2 days, some patients – ileus, endoscopy – pseudomembranes in the colon, CT imaging – thickening of colonic wall
laboratory dg – enzyme immunoassay (EIA) of toxin A and B, cytotoxicity assay, somatic **antigen - glutamate dehydrogenase (GDH)** production assay, **PCR** – identification and **the toxin A, B** gene detection
Treatment: cessation of the on-going antibiotic therapy, fluid and electrolytes replacement, alternative therapies – probiotics, intavenous immunoglobulins, **non-severe CDAD**: oral **metronidazole or vancomycin**, **severe CDAD**: also the antibiotics, supportice care, surgery (colectomy, ileostomy) if the patient´s status fails to improve, if distension and dimintution of diarrhea – toxic megacolon is suspected



A B C D

Colonies of C. difficile growing on Schaedler agar (A) and their details (B), colonies growing on yolk egg agar (C) and subterminal spores (D) could be seen.



Detection genes of binary and A and B toxin of *C. difficile* (left, from the top to the below). However they virulent factors could be used also as species specific markers. B. identification of *C. difficile* on subspecies level by ribotyping

VIRAL DIARHHEAL DISEASES

Rotaviral gastroenteritis

Most common cause of severe acute diarrhea in children worldwide

etiology, epidemiology

•RNA viruses, humand diseases – serogroups A, B, C

• very low inf.dose (10 viral particles) – highly contagious inf.- fecal-oral route of transmission - contaminated food but also person-to-person contact

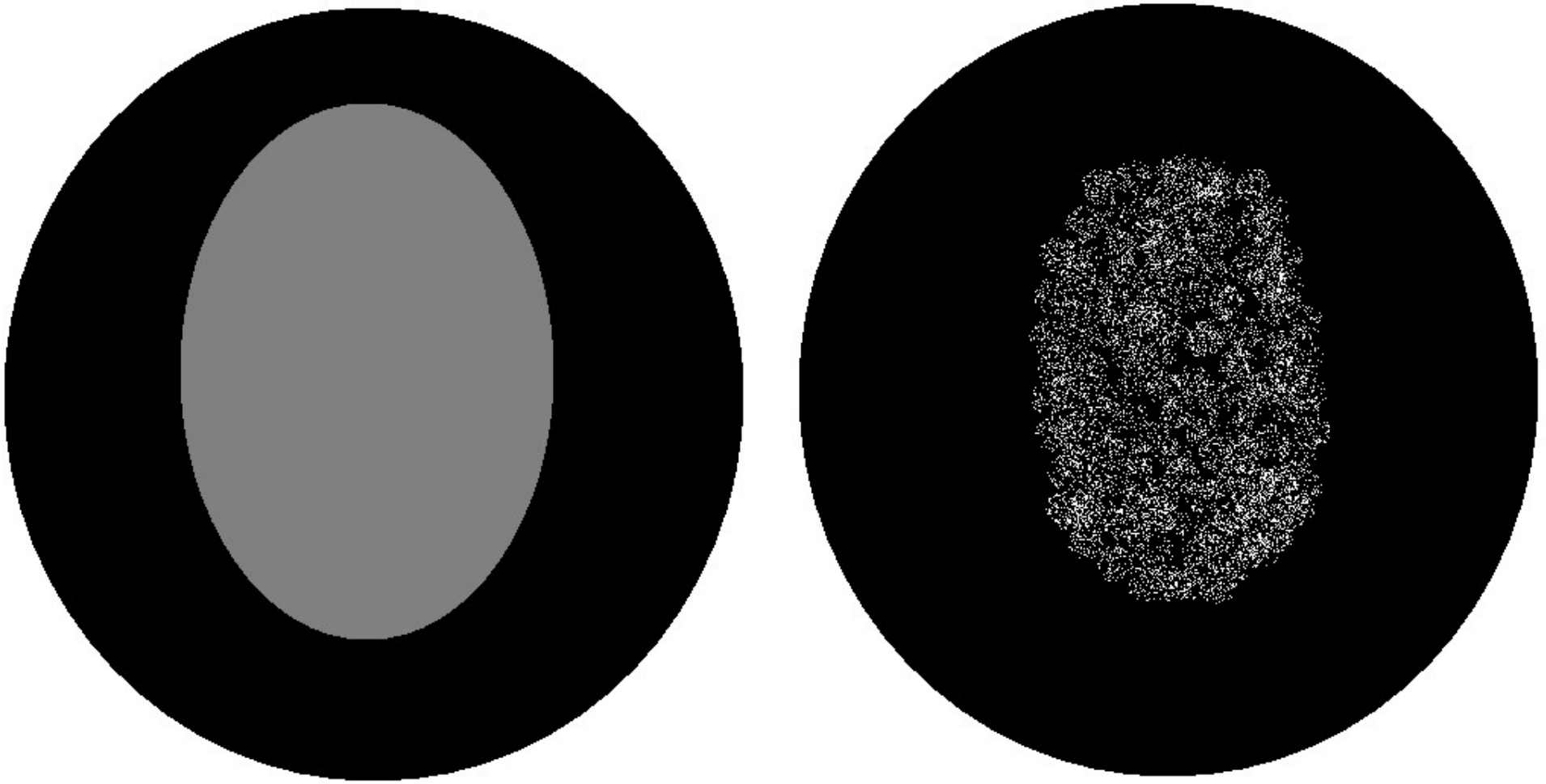
• **pathogenesis** – complex still not well understood, damge of intestinal mucosa, lactose malabsorption

• **symptomatology** – febrile gastroenteritis, start with fever and vomiting, tens of watery green stools, can be accompanied by respiratory symptoms

• **diagnosis** – detected from stool – latex agglutination, ELISA, immunochromatography, electron microscopy, PCR

• **treatment** – causative treatment is not available, cornestone – rehydratation, adsorbents, probiotics

• **prevention** – personal hygiene, disinfection, 2 perorally live vaccines for children

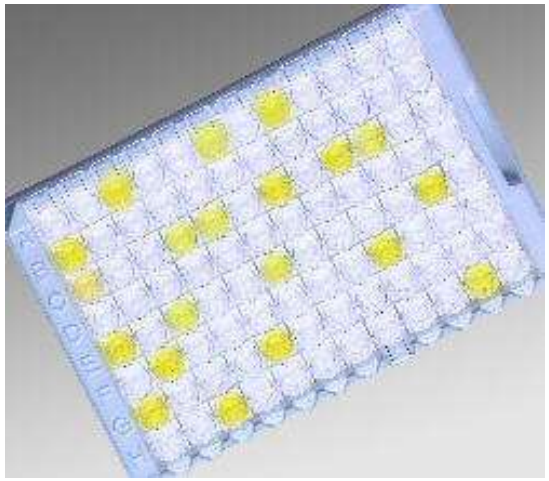


A B

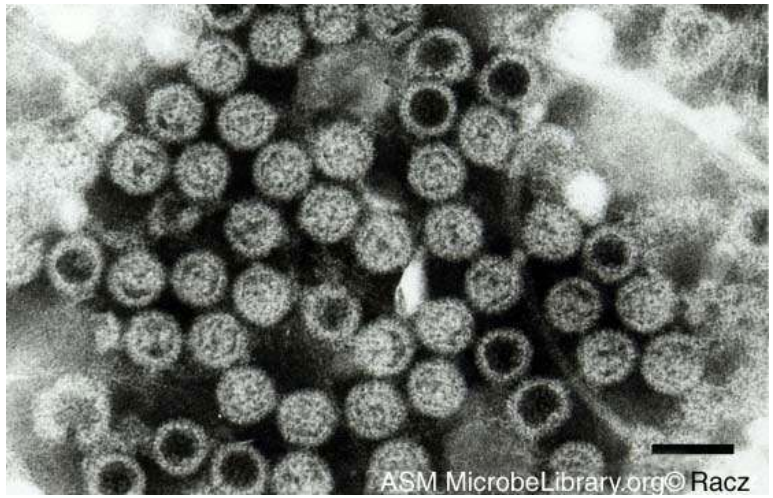
Latex agglutination for detection of rotaviruses in patient stool. A) Negative result. B) Positive result – latex coated immune serum react with rotaviral particles from patient sample

Other methods

EIA enzyme immunoanalysis



Electron microscopy



Immunochromatography test

Caliciviral gastroenteritis

Caliciviruses (5 genera, 2 genera ***Norovirus*** and ***Sapovirus***) common agents of diarrhea worldwide, Noroviruses – 90% of outbreaks of viral gastroenteritis

etiology, epidemiology

• RNA viruses, humand diseases – serogroups A, B, C

• **highly contagious** inf., very low inf. dose, incubation 18-72 h, Noroviruses (Norwalk, Norwalk-like) infect primarily older children and adults, Sapoviruses – affect smaller children rather than adults

• **pathogenesis** – **reversible histopathological lesions in jejunum**

• **symptomatology** – noroviral gastritis- „winter vomiting“, **selflimited,** sudden onset of low-grade fever, vomiting, watery blood diarrhea, 2-3 days duration, sapovirosis - milder

• **diagnosis** – short shedding of viruses, direct detection – electron microscopy, ELISA, PCR

• **treatment** – specific not available**, rehydratation**, supportive care, diet

• **prevention** – prevention of water contamination, vaccination is not available

Astroviral gastroenteritis

Astroviruses cause of a **mild gastroenteritis** in small children without necessity of hospitalization

etiology, epidemiology

• small RNA viruses (family *Astroviridae*) , genus Mamastrovirus – 8 serotypes

• worldwide spread, fecal-oral route, incubation 3-4 days, peak in winter

•**pathogenesis** – small intestine - villous shortening and inflammation in lamina propria, decreased disaccharides activity – osmotic diarrhea, lactose malabsobtion

• **symptomatology** – mild gastroenteritis, watery stool

• **diagnosis** – direct detection – electron microscopy, ELISA, PCR

• **treatment** – **self-limited,** supportive therapy – rehydratation, adsorbents, probiotics

Adenoviral gastroenteritis

Infection occurs usualy in small children, usually **milder and longer than in rotaviral infection**

etiology, epidemiology

• DNA viruses, subgroups A-F, 51 serotypes

• very low inf.dose (10 viral particles) – highly contagious inf.- fecal-oral route of transmission - contaminated food but also person-to-person contact

• **symptomatology** – manifests disease looks like rotaviral infection, but milder and longer (8-12 days)

• **diagnosis** – detected from stool – latex agglutination, ELISA, immunochromatography, electron microscopy, PCR

• **treatment** – causative treatment is not available, **cornestone – rehydratation,** adsorbents, probiotics

• **prevention** – personal hygiene, disinfection, 2 perorally live vaccines for children

Coronaviral gastroenteritis

Enteric coronaviruses cause acute gastroenteritis or hemorrhagic enterocolitis in infants less than 1 year old (a few outbreaks of necrotizing enterocolitis in newborns)

etiology, epidemiology

- largest RNA viruses, up to 220 nm (respiratory and enteric coronaviruses)
- fecal-oral route, without seasonal pattern, could be asymptomatic (in the tropics)
- **symptomatology** – fever, watery or bloody diarrhea, vomiting, abdominal cramps,
- **diagnosis** – detected from stool – electron microscopy, PCR
- **treatment** – causative treatment is not available, cornestone – rehydratation, adsorbents, probiotics

References

- Jiřina Hobstová, Head of Inf.Dis.Department, Motol, Infectious Diseases, Karolinum, 2012 (in English)