Kharkiv National Medical University
Department of Infectious Diseases

DIARRHEAL SYNDROME IN CLINIC OF INFECTIOUS DISEASES

D.Sc., Ass. Prof. Bondarenko A.V.

ANNUALLY

WHO

- 1,0 – 1,5 milliard of diarrhea cases are registered in the world
- 4 million persons die
- diarrheas of different etiology took the II place in the world after the cardiovascular system diseases as reason of rapid death (in first 2-3 d).

USA

- 76 million diarrhea cases, related to the use of the infected products
- 325 000 hospitalizations
- 5000 fatal outcomes
- 6 milliards $ of economic losses.

- **Diarrhea** is a change of normal characteristics of the faeces due to **increase in the excrement masses of water up to 85 - 95%**. Weight of excrements per day exceed 200 g (or 200 ml), that set conditions for increase of defecation frequency.
- An increase of frequency of defecating without the increase of water specific volume or episodes of fecal incontinence are not diarrhea.
- **Acute diarrhea** is considered, when its duration **does not exceed 14 days** and in anamnesis there is no information about similar episodes in the near past.

By pathogenesis:

I. **Motor** diarrhea – disturbances of intestinal motor activity .

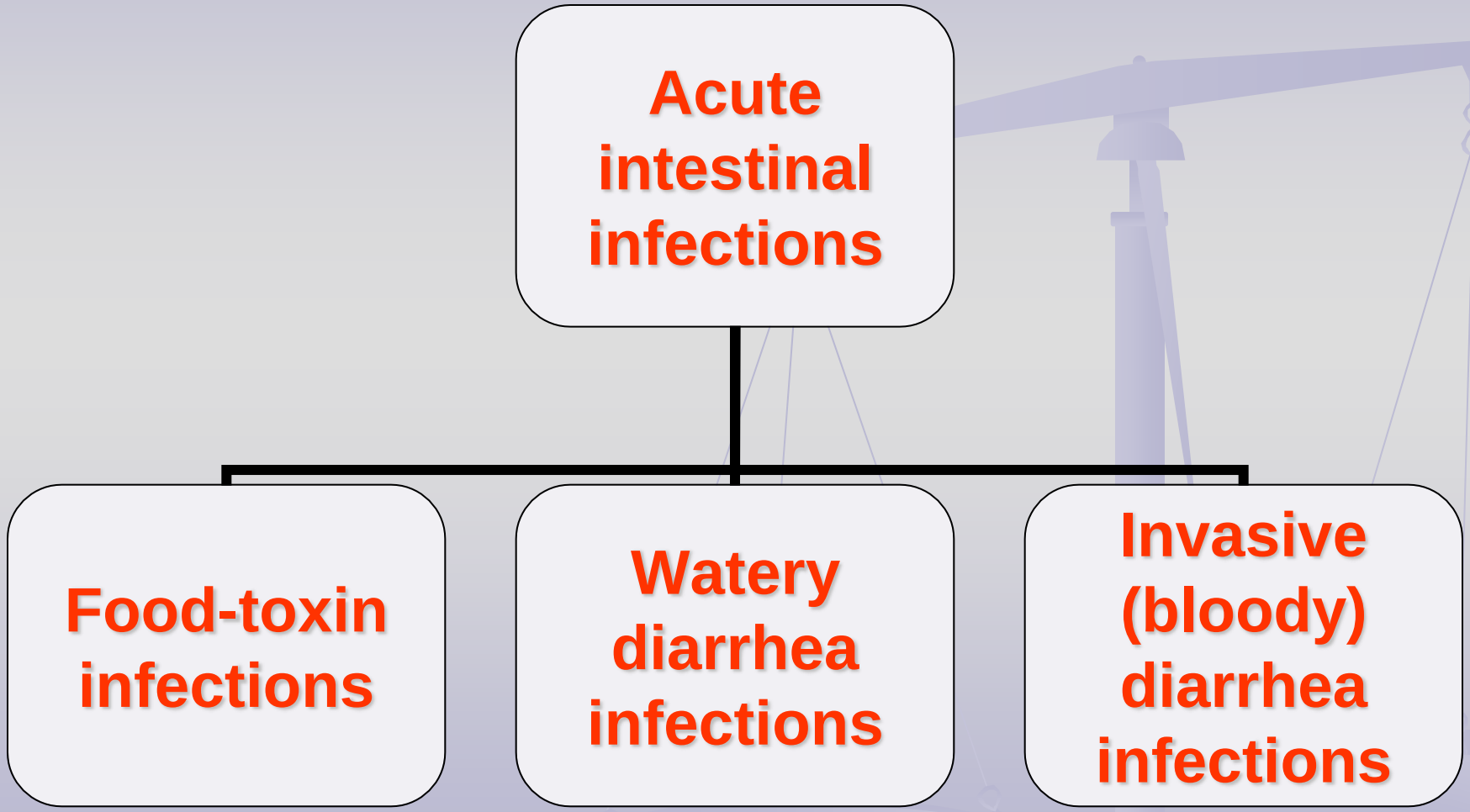
II. **Osmotic** diarrhea – disturbances of carbohydrates or peptides absorption and retention of water in thin intestine (osmolality > 290 mOsm/l).

III. **Secretory** diarrhea - stimulation by the toxins of water and salts secretion in intestine.

- **Exudative** diarrhea – transudation of proteins, loss of enzymes and immunoglobulins (high fecal WBC).

- The number of **diagnostic pitfalls** registered in patients with acute intestinal infections is great (**up to 15%**) and remains stable during many years.
- The **level of death rate** depends on quality of medical care, timeliness and adequacy of treatment in every case.
- Early clinical diagnostics, determining the volume of the first aid and further tactic of treatment, is of a large value.
- **Diagnostics** on the early stage must carry not etiologic, but **syndromal** character.

Pathogenetic groups



Food-toxin infections

group of **acute polyetiologic** diseases, arising from the ingestion of the **foodstuffs contaminated by bacteria** followed by an accumulation of their **exotoxins**, and characterized by a **short-time course**, **disturbances of digestive tract**, syndrome of **general intoxication** and **water-electrolytic abnormalities**.

- «**Food poisoning**» - is a disease arising from ingesting of natural toxins (inedible mushrooms and berries, germinating grain etc.).
- «**Food intoxication**» - is a disease arising from ingesting of chemical toxins (arsenic, sublimate, pesticides etc.).

Causative agents

opportunistic bacteria, capable of exotoxin production out of macroorganism (in foodstuffs)

- Cocci (*Staphylococcus* spp., *Streptococcus* spp.);
- Opportunistic enterobacteria (*Citrobacter*, *Proteus*, *Klebsiella*, *Providencia* etc.);
- Enterotoxigenic *Escherichia* spp. (ETEC);
- Spore anaerobes (*Clostridia perfringens*);
- Spore aerodes (*Bacillus cereus*);
- Pseudomonadaceae (*Pseudomonas spp.*);
- Halophilic vibrios (*Vibrio parahaemoliticus*)

- Opportunistic bacteria are widespread in nature. Revealed in water, soil, surrounding objects and even in air.
- **Mechanism of infection:**

  fecal-oral
- **Route of transmission:** alimentary
- **Factor of transmission:** foodstuffs
- **Seasonality** is not present, a peak of morbidity is on a summer period.

- A **favorable environment** for reproduction of bacteria are meat, fish products, dairy products, creams, vegetable salads.
- Dishes, exposed to insufficient heat treatment, are **especially dangerous** (creams, soufflé, stuffed and jellied fish, black pudding etc.).
- Majority of bacteria does not change **organoleptic properties** of foodstuffs.

Source of infection

- **Sick man**, and also carriers, excreting bacteria in an environment (acute intestinal infections, acute respiratory infections, pyoderma, furunculosis, panaritium etc.);
- **Sick animals** (mastitis, sepsis)
- Direct **human to human transmission** is absent.

General signs

- **Group character** of disease at persons, ingested the same dish not more, than **72 hours** prior to appearance of the first clinical symptoms;
- Factor of transmission - **foodstuffs**;
- **Acute onset** and **short-time course** (not more than 3 days);
- The first symptoms of disease (general toxic and gastrointestinal) are caused by the **action of toxins**.

- development of **acute gastritis or gastroenteritis** with frequent vomiting and diarrhea resulted in dehydration;
- **abdominal pain** are nonintensive and transient;
- **fever** and displays of intoxication are more frequently expressed unsharply and brief;
- **inflammatory changes** in blood are absent in most of the cases.

Staphylococcus

- Especially **short-termed.**
- **Removing of toxin** results in the disappearance of all displays of illness.
- General toxicosis can attain the degree of **ITS**, while a **diarrheal syndrome** (due to staphylococcal alpha-toxin) can be very moderate or even **absent**.
- Leading displays of gastrointestinal syndrome are a abdominal pain, nausea, vomiting.
- Expressed hypovolemia is rarely and caused mainly by the abundant repeated vomiting.
- Circulatory disorders are the result of general toxicosis, but not hypovolemia.

Gastric lavage

- Only in the **first hours** with the purpose of removing of toxins and restriction to their absorption.
- Carry out by **2-3% solution of sodium hydrocarbonate**, or **0,1% potassium permanganate**, at their absence – by the boiled water.
- **Not less than 3 l** of solutions of 18-20°C.
- Is conducted till moving of clean waters.

Contraindications

- myocardial infarction
- ischemic heart disease
- essential hypertension with high BP
- atherosclerosis with the affection of cerebrum vessels
- gastric or duodenum ulcer disease

- The main mechanisms of **enterosorbents** action are the removing of toxins and toxic metabolites from gastrointestinal tract through the **adsorption, absorption, ion exchange and complex forming mechanisms**.
- Classified as carbonic, silicon containing, natural organic and combined.
- Carbonic and silicon containing adsorbents have the porous structure.
- Other enterosorbents realize their adsorptive properties through their surface interactions.

Watery diarrhea infections

Viruses	**Rota-, entero-, adeno-, corona-, astro-, reo-**
Bacteria	**enterotoxigenic *E. Coli* (ETEC) O_6,O_9,O_{20},O_{25}, enteropathogenic *E. Coli* (EPEC) O_{111}:H_2,O_{119}:H_6,O_{142}:H_6,O_{55}:K_{59}, *V.cholerae* O_1 и O_{139}**

Large volume, no blood and WBCs.
No symptoms of systemic infection.
With viruses and ETEC, the stool C+S usually grows normal flora only.

VIRAL DIARRHEAS

- **Source of infection:** humans sick or carriers
- **Mechanism of infection:** fecal-oral
- **Route of transmission:** watery, alimentary, contact
- **Incubation period: 1-5 days**

Rotavirus gastroenteritis

- acute anthroponotic disease with a fecal-oral mechanism of transmission, characterized by the affection of mucous membranes of thin intestine and oropharynx
- 30-80% cases in Europe, 20-40% - in the developing countries
- 800 000 of children die annually
- Family: Reoviridae, Genus: Rotavirus,

  Species: A, B, C, D, E, F, G
- RNA-containing virus
- Seasonality: winter

- onset is **acute**;
- severity is mainly **mild**;
- excrements are **abundant watery** with a strong smell, sometimes muddy-whitish, 5–10 one time per days depending on weight. The loud **rumbling** is characteristic in abdomen;
- **Abdominal pain** quite often is intensive, with primary localization in an epigastrium and paraumbilical area, increase before defecation

- **abdomen is swollen** from the first days of illness;
- diarrhea combines with development of **general intoxication** (weakness, pains in muscles, headache, dizziness, chilling), increase of temperature (within the 38 °C). More high fever is characteristic for a enterovirus infection;
- combination of diarrhea with the **signs of respiratory tract affection** (rhinitis, pharyngitis, hyperemia and granulosis of mucous membrane of oropharynx);
- **inflammatory changes** in blood absent

Supplement Facts

serving size: 1 capsule

	amount per serving
Full Strength Pancreatin†	500mg*
providing:	
Protease	111,500 USP units*
Amylase	122,500 USP units*
Lipase	17,750 USP units*

* Daily Value not established

Other Ingredients: Gelatin Capsule, Calcium Carbonate, Silicated Cellulose, and Ascorbyl Palmitate.

†Lactose Free

CHOLERA

- acute anthroponotic infectious disease with fecal-oral mechanism of transmission caused by an enterotoxin of *V. cholerae* O1 or O139 characterized by profound, rapidly progressive dehydration and demineralization due to watery diarrhea and vomiting.
- belong to the group of quarantine infections, which are submitted to "international medicosanitary regulations".

V. cholerae

actively motile, facultatively anaerobic, short (0.2-0.4×1.5-4.0μm), slightly curved, non-sporing gram-negative rods, one or two polar flagella, endotoxin (LPS), O- and H- antigens

>140 serogroups

O1

biotypes

cholerae (classical)

eltor (hemolysin, resistance to polymyxin B)

O139 Bengal (polysaccharide capsule)

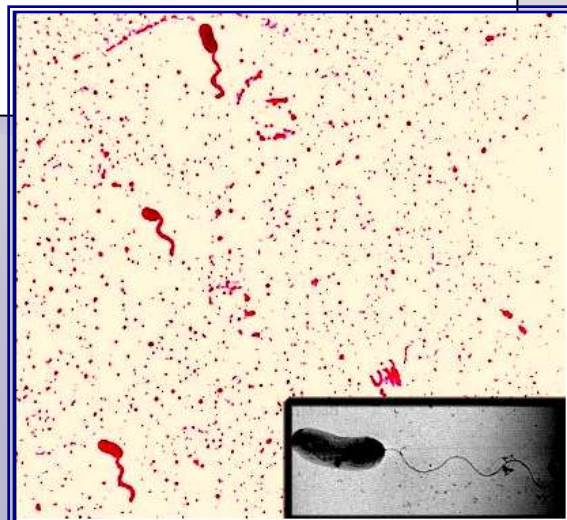
non-O1 non-O139 NAG or NCV (don't possess enterotoxin genetic element and genes for the toxin-coregulated pilus)

serotypes

Ogawa (AB)

Hikojima (ABC)

Inaba (AC)



- Killed by heating at 55° for 15 min.
- In moist soil persists for 6-10 days at 20-28°.
- In faeces remains viable for up to 5 days,
- in potable water (salinity 0.01 - 0.1 %) > 24 h, in brackish, estuarine or sea water (salinity 2%, pH 7.0-8.5, 25°) - 40 months.
- Eltor vibrios survive longer in water and in foodstuffs.

- Production of enterotoxin (**choleragenoid**).
  - 5 B-subunits of enterotoxin attach to GM1 ganglioside receptors on the surfaces of the epithelial cells.
  - Single A-subunit is transported into enterocytes and **activates the adenylate cyclase** and affects an **increase** in **the level** of intracellular cyclic **adenosinemonophosphate** (AMP).
  - Activation of phospholipase and prostaglandins.
  - Inhibition of phosphodiesterase.
  - **Change in the intestinal ion transport** (irreversible hypersecretion of chloride, bicarbonate and water in the crypt cells and the inhibition of normal sodium absorption in the villous cells).
- Rapid outpouring of isotonic body fluid (**profound dehydration**).

CLASSIFICATION OF CHOLERA

- V. cholerae O1 biotype cholerae
- V. cholerae O1 biotype eltor
- V. cholerae O139 Bengal

Clinical forms (by Rudnev G.P.):

- Typical:
  - "Enteritis" (Mild)
  - "Gastroenteritis" (Moderate)
  - Algid (Severe): Reactive and Asphyctic phase
- Atypical:
  - Effaced
  - Fulminant
  - Cholera Sicca
  - Cholera Typhoid
- Vibriocarrier (subclinical)

Dehydration degree (by Pokrovskiy V.I.):

- I losses of fluid up to 3% of normal body weight
- II losses of 4 to 6%
- III losses of 7 to 9%
- IV losses of above 10%

- Clinical case/infection ratio with the classical biotype – 1:6; with infection due to eltor biotype – 1:50.
- **INCUBATION PERIOD**: 12 hours – 6 days (24-72h)
- **PRODROMAL PERIOD** (15-17% cases):

  (abdominal discomfort, loss of appetite and mild diarrhoea)

I DEGREE OF DEHYDRATION (50-60% cases):

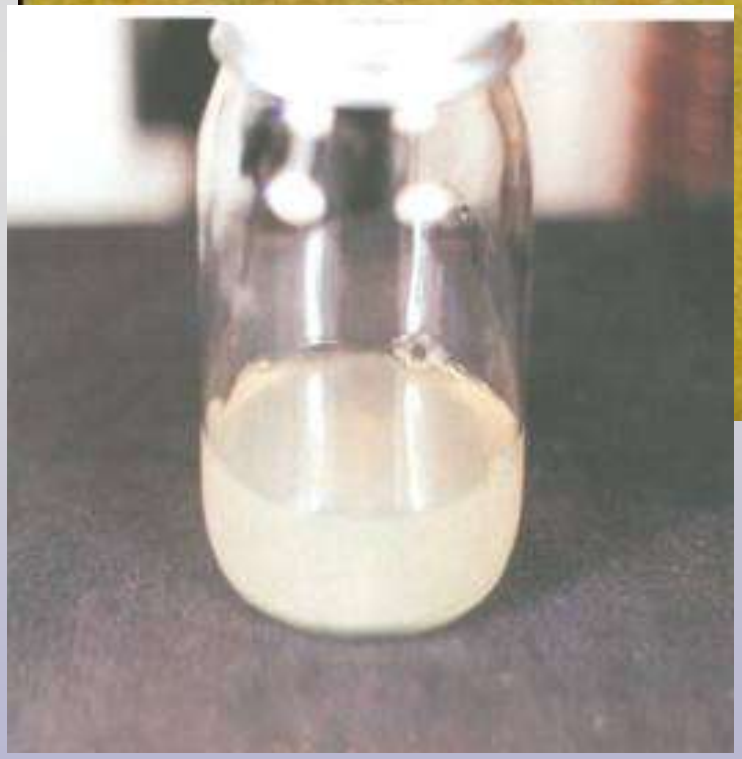
- Moderate thirst; dryness of mucous membranes;
- diarrhea is not abundant (pappy or watery) 3-10 times daily from several hours up to 1-2 days;
- labile pulse; rumbling in abdomen; meteorism.

II DEGREE OF DEHYDRATION (18-23% cases):

- Thirst; husky voice; fatigue; pale and dry skin and mucous membranes; slightly reduced turgor of tissues; cramps of a sural muscles, muscles of hands and feet; muscle weakness;
- circulatory disturbances (tachycardia, moderate arterial hypotonia, acrocyanosis, extremities coldness, oliguria);
- diarrhea is abundant (watery, no blood, and a somewhat sweet, inoffensive, fishy odor) 10-20 times daily up to 3-4 days;
- fountain vomiting 5-10 times daily without nausea.

III DEGREE OF DEHYDRATION (15-20% cases):

- Expressed circulatory disturbances (general cyanosis, cold extremities, BP declining (hypotonia or collapse), weak or thready pulse, tachycardia, muffled heart sounds, oliguria or anuria); skin turgor is sharply decreased; wrinkled ("washerwoman") skin; tonic convulsions of separate muscles groups; face gaunt; dry scleras; glassy sunken eyes; aphonia; hypopyrexia (35,5-35oC).
- Stool is more than 10 times daily, abundant ("rice-water" - nonbilious, gray, slightly cloudy fluid with flecks of mucus).
- Recurring abundant fountain vomiting.
- Blood concentration is moderate (density of plasma, viscosity of a blood and hematocrit are on a upper bound of norm or moderately enlarged).
- Erythrocytosis, hypokalemia and hypochloremia.
- Moderate compensator hypernatremia.



IV DEGREE OF DEHYDRATION (8-15% cases):

- All signs of dehydration are expressed maximum.
- Algid – hypopyrexia (34-35°C); boxer posture; prostration; face gaunt; total cyanosis, cyanosis round the eyes ("dark glasses"); "washerwoman hands"; tonic cramps; hiccup; no obtainable blood pressure (collapse, decompensate hypovolemic shock);
- pulse is absent; dyspnea; anuria.
- Defecation and vomiting are discontinued.
- Blood concentration is marked
- (relative density of plasma is up to 9,2;
- hematocrit is 65-70%, viscosity of a blood – 0,5-1,0).
- Potassium, sodium and chlorine level in plasma is considerably reduced.
- Decompensate metabolic acidosis and respiratory alkalosis. Coma. Asphyxia.

LABORATORY ABNORMALITIES:

- Mild neutrophilic leukocytosis
- Elevated hematocrit
- Elevated plasma protein
- Increased plasma and whole-blood specific gravity
- Decreased plasma bicarbonate (<15 mmol/l)
- Low arterial pH (about 7.2)
- Normal plasma sodium
- Slightly increased plasma chloride
- Moderately elevated plasma potassium
- Elevated levels of blood urea nitrogen and creatinine

DIAGNOSTIC TESTS:

- Dark-field microscopy
- Method of immobilization and microagglutination
- Method of macroagglutination
- Reaction of neutralization
- Culture test (bile-salt agar, glycerine-taurocholate-teliurite agar, thiosulphate-citrate-bile-salt-sucrose (TCBS) agar, Carey-Blair transport medium, alkaline-peptone water-enrichment medium or Monsur's medium).
- ELISA
- Monoclonal antibody diagnostic
- Polymerase chain reaction

Oral Rehydration Solutions

	NaCl	$NaHCO_3$	KCl	sodium citrate	glucose	starch
ORS, WHO	3,5		1,5	2,9	20,0	
Regidrone	3,5		2,5	2,9	10,0	
Glucosolan	3,5	2,5	1,5		20,0	
ORS II generation	3,5		1,5	2,9		50,0

An ORS packet is dissolved in 1 L of tap water

Intravenous Rehydration Solutions

Trisolum

- Sodium Chloride 5 g
- Potassium Chloride 1 g
- Sodium Hydrocarbonate 4 g
- Water for injections 1 L

Disolum

- Sodium Acetate 2 g
- Sodium Chloride 6 g
- Water for injections 1 L

Quartasolum

- Sodium Chloride 4.75g
- Potassium Chloride 1.5g
- Sodium Acetate 2.6 g
- Sodium Hydrocarbonate 1 g
- Water for injections 1 L

Total volume of replacement solutions over a period of 2 days therapy – 36 litres

- Although antimotility agents (e.g., Imodium*, Lomotil*) can effectively relieve diarrhea and cramps, they may prolong the time it takes the body to rid itself of the toxin.
- Antimotility medications should be avoided by persons with high fevers or bloody diarrhea, and should be discontinued if diarrhea symptoms persist more than 48 hours.

INVASIVE DIARRHEA INFECTIONS

Bacteria	*Salmonella* spp., *Shigella* spp., *Yersinia* spp., *Campylobacter* spp., *Proteus* spp., Enteroaggregative *E. coli* (EAggEC) - O_{104}:H_4, Enteroinvasive *E.coli* (EIEC) - O_{124},O_{144},O_{151}, Enterohemorrhagic *E.coli* (EHEC) - O_{157}:H_7 , *Pseudomonas* spp., *C. difficile*, *C. perfringens* type C
Protozoa	*Entamoeba histolytica, Balantidium coli, Giardia lamblia*

Cause histologic damage
Symptoms of colitis +/-
Contains many WBCs, +/- blood

Salmonellosis

- acute anthropozoonotic infectious disease, caused by different serotypes of **Salmonella enterica**, characterized by the primary affection of gastrointestinal tract and manifested more frequently in gastrointestinal, rarer generalized forms.

- Family: Enterobacteriaceae,
- Genus: Salmonella, Species: enterica,
- Serotypes: > 2200
- Gram (-) rods, nonspore-forming, mobile
- Antigens: O - somatic, H - flagellate and K -superficial (capsule).
- Factors of pathogenicity: endotoxin (LPS), enterotoxin, at the row of strains - exotoxin

- Temperatures of growth (from +**6 to +46°**C) and pH (from **4,1 to 9,0**).
- **Protractedly saved in an external environment**: 5 month in water, in a room dust and soil - 18 month, in meat from 2 to 4 months, in the frozen - 6 month, in milk - to 20 days, in cheeses - to 1 year, in beer - up to 2 months.
- In some products (milk, meat products) able to multiply.

- **Mechanism of transmission**: fecal-oral.
- **Routes of transmission:** alimentary, watery and contact.
- **Sources of infection:** home, wild animals and birds. Fish, shellfishes etc., humans.
- **Hospital salmonellosis**.

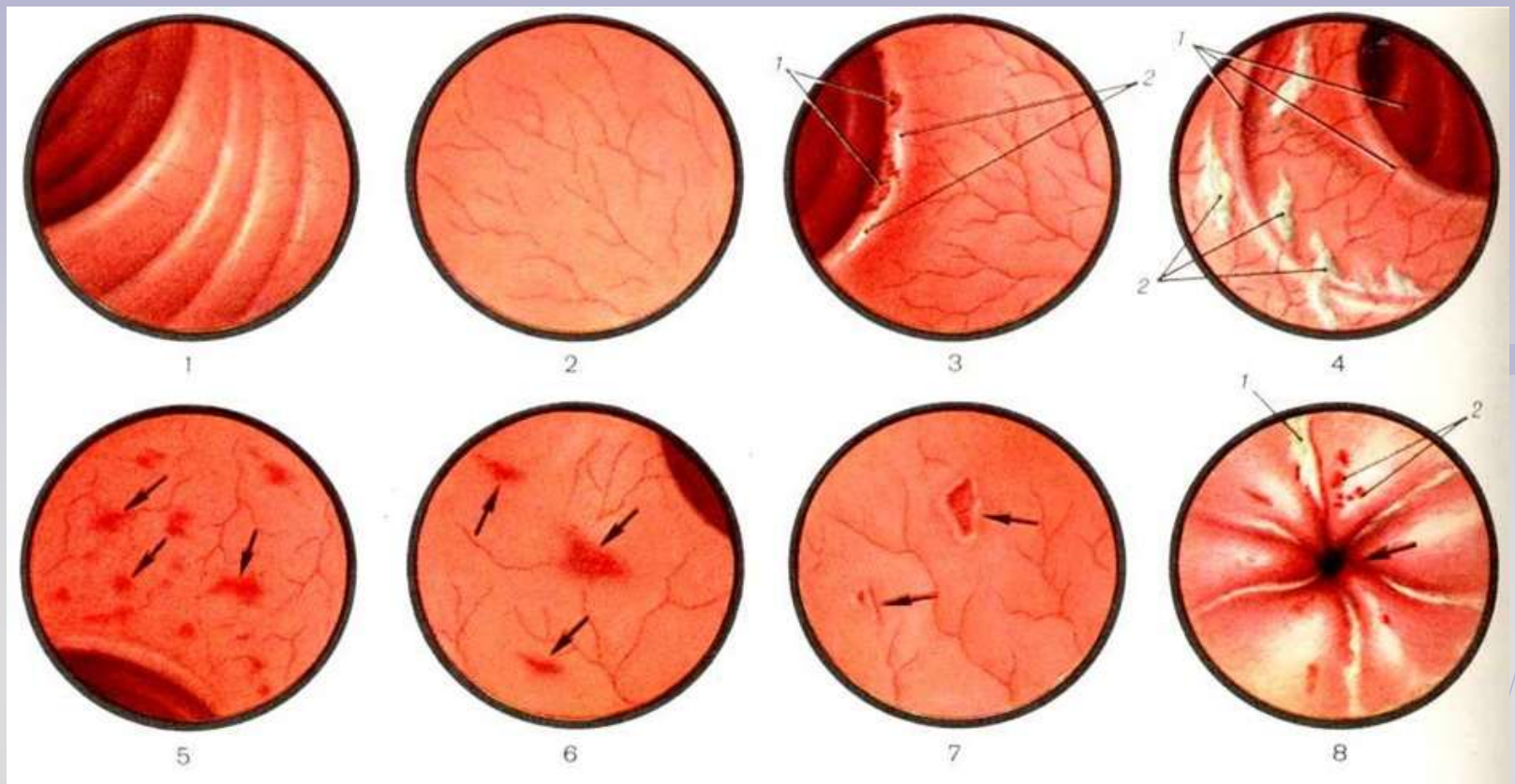
- Acute onset with stormy manifestation of **gastroenteritis** (gastroenterocolitis) with a high fever and expressed displays of intoxication;
- Repeated (frequent) vomiting;
- Excrements are abundant, liquid, often of greenish color;
- **Signs of dehydration**;
- Absence or weak expressed signs of distal colitis;
- Signs of acute vascular insufficiency (infectious toxic, dehydration or mixed types of shock);
- At generalized forms development of typhoid or septicopyemic variants;
- Inflammatory changes in blood of different degree of expression;

Shigellosis

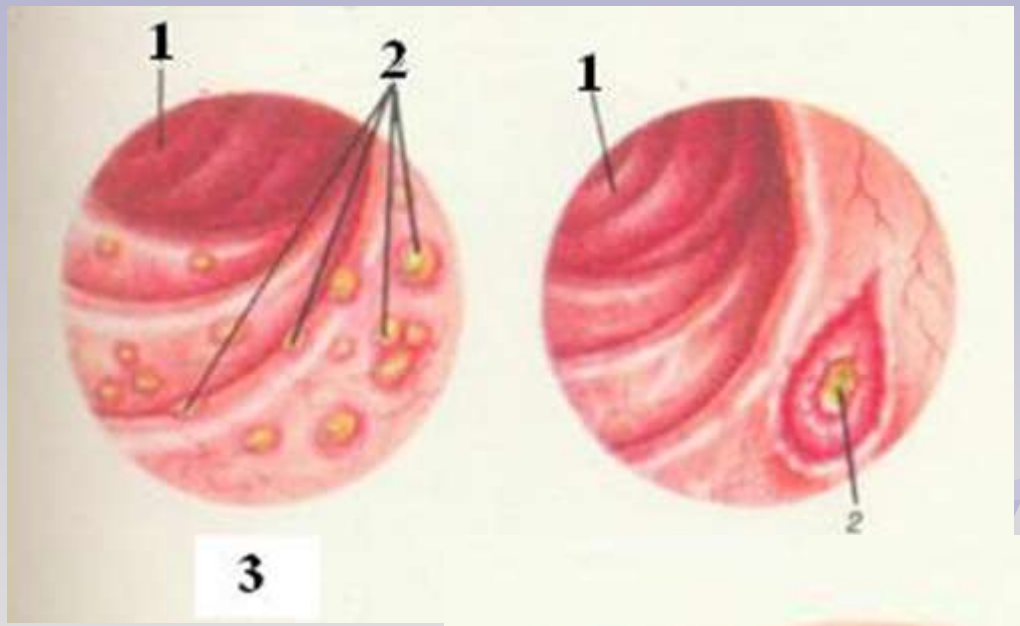
- Acute antroponotic infectious disease, characterized by intoxication and affection of colon mucous membranes with formation of colitis (hemorrhagic colitis).

- **Family:** Enterobacteriaceae
- **Genus:** Shigella
- **Serogroups: A.** S. disenteriae; **B.** S. flexneri; **C.** S. boydii; **D.** S. sonnei
- Gram (-) rods, nonspore-forming, not mobile
- **Antigens:** O – somatic and K -superficial.
- **Factors of pathogenicity:** endotoxin (LPS), enterotoxin, neurotoxin


Shigella on EMB
Shigella on MacConkey
Shigella on ENDO
Shigella on Hektoen
Shigella on SS agar



P. 3. erosive proctosigmoiditis: erosions (1) mucus (2)
P. 4. catarrhal-mucous proctosigmoiditis: hyperaemia (1) mucus (2)
P. 5. catarrhal-haemorrhagic proctosigmoiditis: hemorrhages
P. 6. erosive proctosigmoiditis: erosions
P. 7. ulcerative proctosigmoiditis: ulcers
P. 8. erosive sigmoiditis: pus (1) erosions (2)



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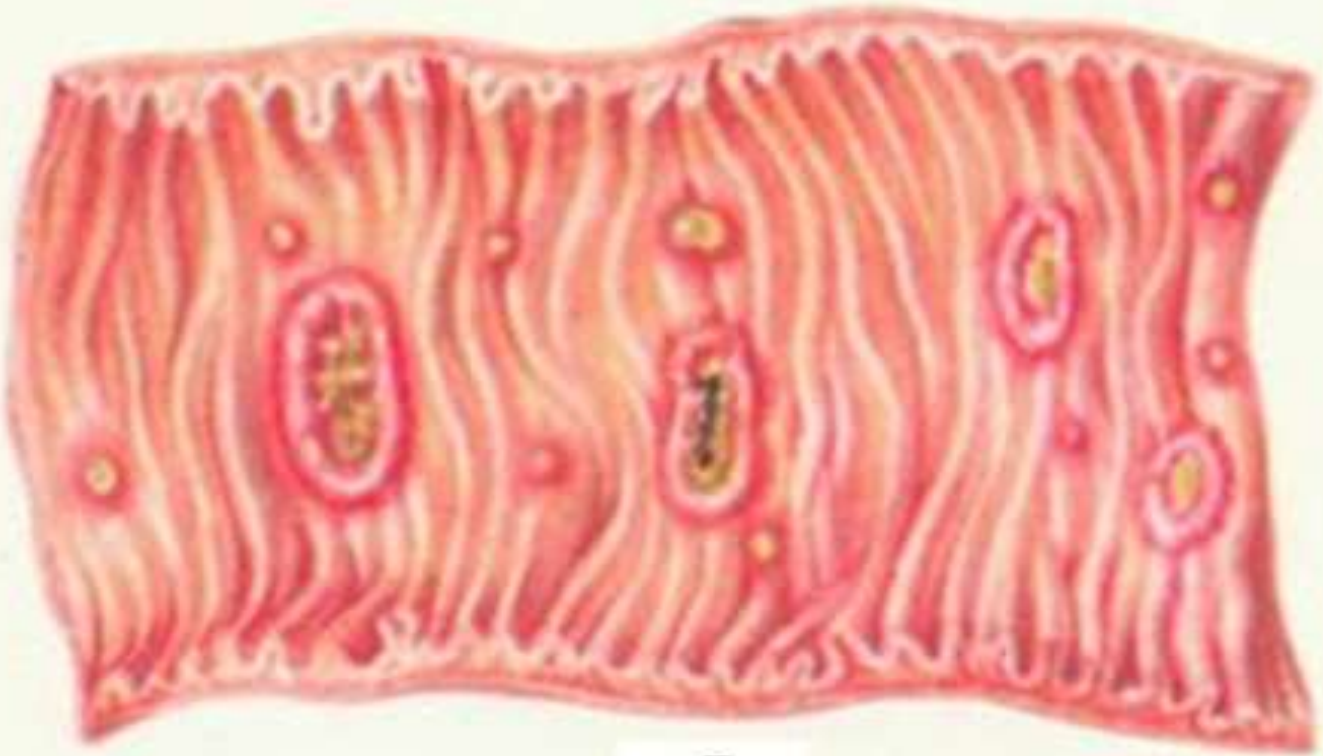

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Antibiotic therapy lost its effectiveness of the followings factors:

- viral etiology of most infectious diarrhea cases (60% and more);
- leading role of toxic factors at food toxicoinfections;
- natural resistance of opportunistic bacteria to most antibacterial preparations;
- rapid obtaining of resistance (by R-plasmids and other factors) to antibiotics and antiseptics;
- forming of dysbiosis;
- development of the secondary immunodeficiency states;
- presence of side effects;
- development of lactase deficiency;
- decline of repair processes in the cells
- possibility of development of antibiotic-associated diarrhea (*C. difficile* infection) etc.

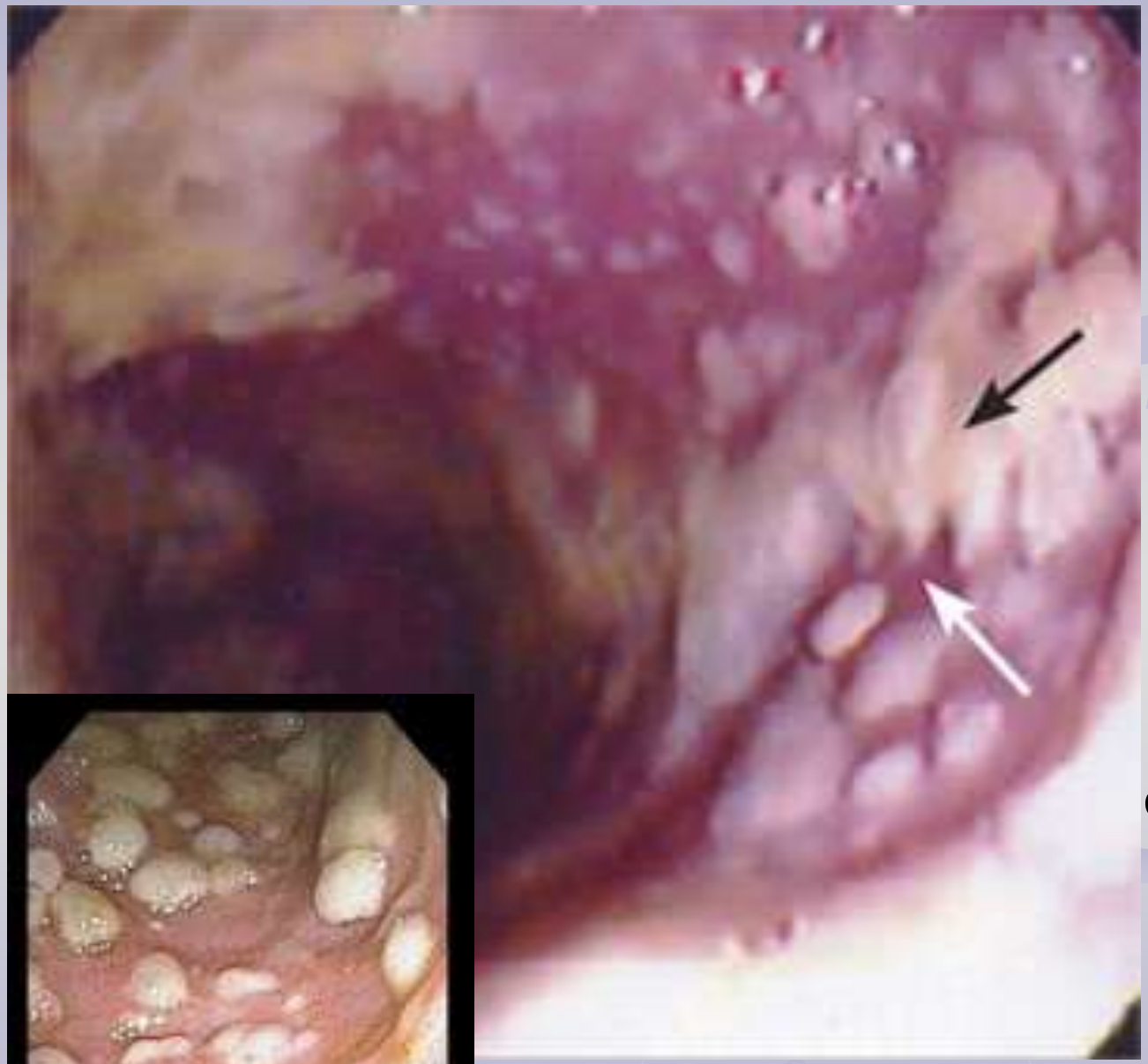
C. difficile - associated disease

Mild CDAD

- Non-bloody, watery diarrhea (5-10 watery stools a day)
- Low-grade fever
- Abdominal cramping
- Dehydration
- Nausea
- Loss of appetite

Pseudomembranous colitis (in addition to mild symptoms)

- Profuse watery diarrhea (greater than 10 watery stools a day)
- High fever (39-40°C)
- Blood in the stool
- Weight loss
- Severe abdominal pain and tenderness
- Death (6%-30% mortality rate)



Irregular yellow plaques of necrotic debris

Intervening edematous bowel mucosa

Criteria of etiotropic treatment

- generalized forms of disease;
- all forms and in all age-related groups of patients on amebiasis and cholera;
- severe course of invasion infections with a threat of generalization of process and development of septic shock (regardless of etiology and age of patient);
- moderate course of invasion infections with prevailing of distal colitis signs;
- invasion infections in children of the first two years of life;

- development of the second bacterial complications;
- exacerbation of concomitant diseases;
- immunodeficient state (including AIDS, splenectomy etc);
- aneurysm of aorta;
- artificial valves of heart and implants;
- warty endocarditis;
- Haemolytic anaemias;
- thalassemia.