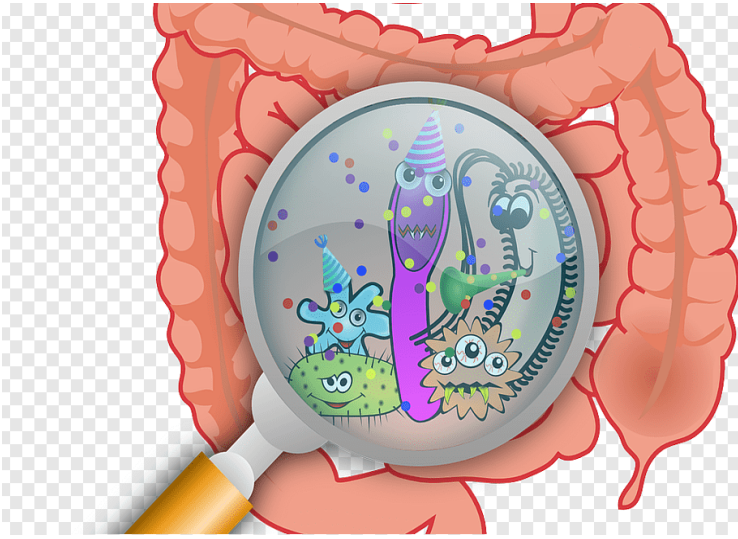
SALMONELLOSIS

Salmonellosis is an infectious disease caused by different nontyphoidal serotypes of Salmonella genus, which is characterized by various clinical manifestations in range from asymptomatic carrying to septic forms and mainly occurs in gastrointestinal tract



Salmonellosis, called *"the disease of civilization"*, is so widespread that at present no country in the world is faced with the question of their elimination, but they only talk about reducing the incidence rate and limiting the spread among the main sources of the pathogen.

Nontyphoidal salmonellae are one of the leading causes of bacterial diarrhea worldwide; they are estimated to cause approximately 153 million cases of gastroenteritis and 57,000 deaths globally each year.

Diseases are especially prevalent in developing areas, such as Southeast Asia, Africa, and South America.

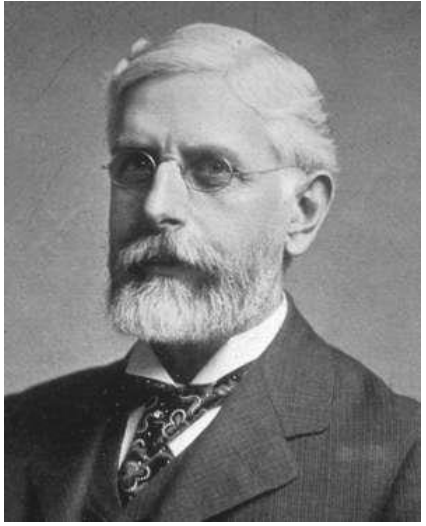
Salmonella is 1 of the 4 key global causes of diarrhoeal diseases.

Brief historical information.

For a long time, the disease was described as "meat poisoning." In 1885, American scientists D.E. Salmon and T. Smith found the causative agent in the organs of sick pigs, mistakenly considered it a swine plague , and named it B. Suipestifer .

Three years later, G. Gertner (1888) obtained the same microbe in the meat of a sick cow and in the spleen of a person who died after eating it, and called it B.enteritidis, and "meat poisoning" proved that the disease was of bacterial origin.

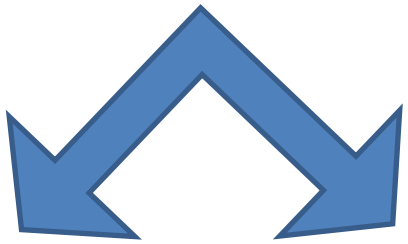
In 1934, the International Nomenclature named the bacterium salmonella in honor of the American scientist Daniel Elmer Salmon, who first described these bacteria (1885), and the disease caused by salmonella bacteria was named salmonellosis. In the following years, other bacteria belonging to this group were discovered.



D.E. Salmon

T. Smith

Diseases caused by salmonella in humans are divided into two groups:



I

anthroponotic infections with specific clinical and epidemiological features (typhoid fever and paratyphoid A, B, C)

II

the causative agent of "real" salmonellosis, which is pathogenic to both humans and animals. The term "salmonellosis" refers only to group II patients.

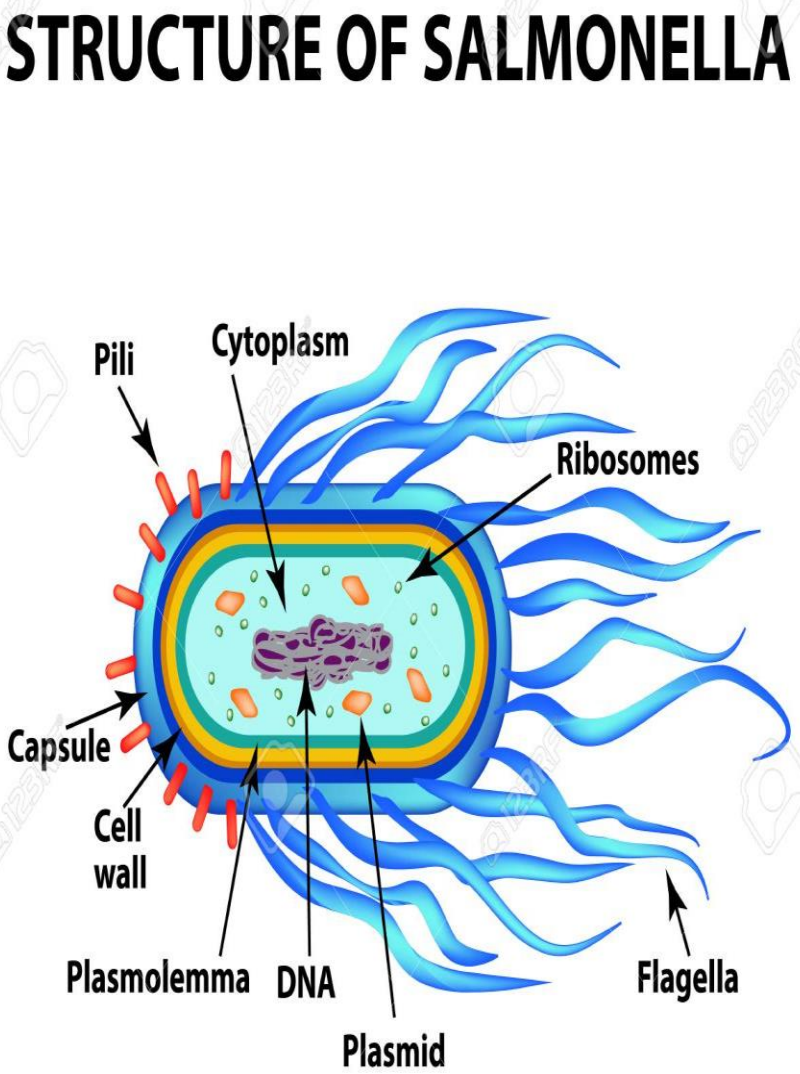
Typhoid fever and paratyphoid fever belong to an independent group of intestinal infections.

ETIOLOGY.

Salmonella **is an aerobic gram-negative bacillus** belonging to the ***Enterobacteriaceae family***, **that can grow readily on simple culture media.**

It is motile, and most strains do not ferment lactose. Members of the seven Salmonella subspecies can be serotyped into one of more than 2500 serotypes (serovars) according to antigenically diverse surface structures

Salmonella **species are non-spore-forming, predominantly motile enterobacteria with cell diameters between about 0.7 and 1.5 µm, lengths from 2 to 5 µm, and peritrichous flagella (all around the cell body).They are chemotrophs, obtaining their energy from oxidation and reduction reactions using organic sources. They are also facultative anaerobes, capable of generating ATP (Adenosine triphosphate) with oxygen ("aerobically") when it is available, or when oxygen is not available, using other electron acceptors or fermentation ("anaerobically").**



Salmonella secretes

exotoxins,

enterotoxins and

cytotoxins.

They have endotoxin.

♦Enterotoxins accelerate the secretion of fluid and minerals from the intestine.

♦ Cytotoxin destroys the membrane of enterocytes.

♦ Endotoxin mainly causes symptoms of intoxication.

Some Salmonella (S. enteritidis) have the ability to invade epithelial cells.

The antigenic structure of Salmonella is complex.

Salmonella has three main antigens:

- **0-somatic (thermostable)**
- **H-flagellated (thermolabile)**
- **K-surface (capsular)**

In addition, some Salmonella serotypes have been described other antigens:

Vi-antigen or "virulence" antigen (one of the components of the 0-antigen) and

M-antigen (mucous).

The antigenic structure is the basis of the International Serological Classification of Salmonella (Kaufman-White scheme).

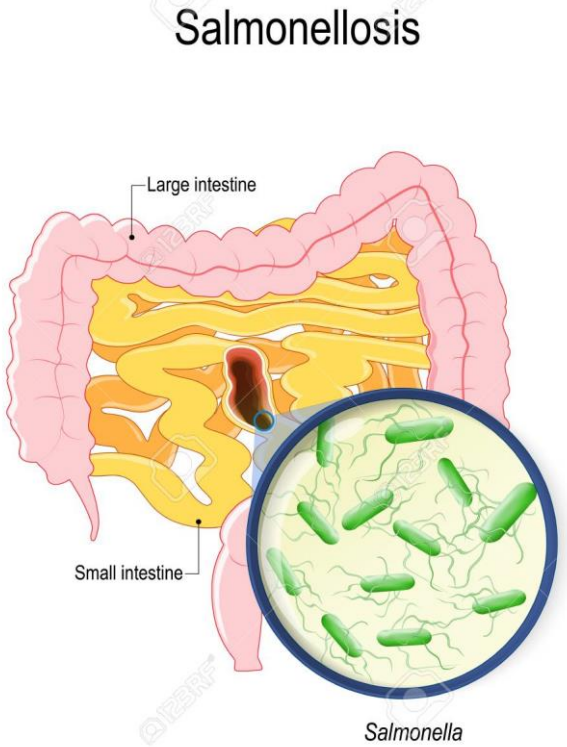
Differences in the structure of O-antigens made it possible to distinguish serological groups A, B, C, D, E, etc.

Based on differences in the structure of H-antigens, serological variants were established within each group.

ETIOLOGY.

Most of the cases of human salmonellosis are caused by

- ✔ ***S. typhimurium,***
- ✔ ***S. enteritidis,***
- ✔ ***S. panama,***
- ✔ ***S. anatum,***
- ✔ ***S. newport,***
- ✔ ***S. agona,***
- ✔ ***S. derby,***
- ✔ ***S. london,*** **etc.**



The serotype or serovar, is a classification of Salmonella into subspecies based on antigens that the organism presents. It is based on the Kauffman-White classification scheme that differentiates serological varieties from each other.

Serotypes are usually put into subspecies groups after the genus and species, with the serotypes/serovars capitalized, but not italicized: An example is *Salmonella enterica serovar Typhimurium.* More modern approaches for typing and subtyping Salmonella include DNA-based methods such as pulsed field gel electrophoresis,, multilocus sequence typing, and multiplex-PCR-based methods.

Salmonella can live in the environment for a long time:

in open water basins and drinking water –

11-120 days,

in sea water - 15-27 days,

in the soil - 1-9 months,

in room dust - 80-120 days (up to 18 months),

in sausage products

- 60-130 days,

in frozen meat - 6-13 months,

in eggs - up to 13 months,

in egg powder -

3- 9 months,

on frozen vegetables and fruits - from 2 weeks to 2.5 months.

In dairy and prepared meat products, Salmonella not only persist for up to 4 months, but also multiply without changing the organoleptic properties and appearance of the products.

Salmonella are resistant to salt, smoking and acids. To destroy bacteria, high-quality heat treatment is required. So, for the complete inactivation of Salmonella in a piece of meat weighing 400 g, it is necessary to cook it for at least 2.5 hours.

Salmonella is resistant to many antibacterial drugs, but is highly sensitive to common disinfectants.
The duration and sensitivity of drugs are not the same in different areas and vary from year to year.
While salmonella was highly sensitive to chloramphenicol, kanamycin, monomysin, ampicillin, and furazalidone in the 1970s, susceptibility to these drugs declined sharply in the 1980s.
In recent years, salmonella susceptibility to cephalosporins, nevigramones, aminoglycosides and erefuril.

EPIDEMIOLOGY

Salmonellosis occurs everywhere.
Sporadic cases and epidemic outbreaks are recorded. The incidence of salmonellosis in most countries tends to increase, especially in large cities with a centralized food supply system. The sources of infection are mainly many species of animals and birds, including agricultural and wild ones, in which salmonella serovars, dangerous to humans, often cause only carrier.In animals, a fecal-oral transmission mechanism is implemented, in birds, transovarial transmission of salmonella is also possible.

Salmonella **bacteria are widely distributed in domestic and wild animals. They are prevalent in food animals such as poultry, pigs, and cattle; and in pets, including cats, dogs, birds, and reptiles such as turtles.**

Salmonella **can pass through the entire food chain from animal feed, primary production, and all the way to households or food-service establishments and institutions.**

Salmonellosis in humans is generally contracted through the consumption of contaminated food of animal origin (mainly eggs, meat, poultry, and milk), although other foods, including green vegetables contaminated by manure, have been implicated in its transmission.

Person-to-person transmission can also occur through the faecal-oral route.

Human cases also occur where individuals have contact with infected animals, including pets. These infected animals often do not show signs of disease.

The mechanism of transmission of the pathogen is fecal-oral,
route of transmission is predominantly food.
This is usually observed with improper cooking, when infected products, mainly meat (minced meat, products from it, jelly, meat salads, boiled sausages), were in conditions favorable for the reproduction of Salmonella. Infection of meat occurs endogenously (during the life of the animal during its illness), as well as exogenously, during transportation, processing, storage. Often, food contamination occurs due to improper cooking, cooking on contaminated tables and using infected utensils.
In recent years, there has been a significant increase in the incidence of salmonellosis associated with the spread of the pathogen (S.enteritidis) through poultry meat and eggs.

Salmonellosis occurs throughout the year, with the highest incidence in summer and autumn,
due to poor storage conditions.

Pathogenesis

Portal of entry for infection is the gastrointestinal tract.

The development of the infectious process depends:

- **from the transmission mechanism (food, contact, etc.),**
- **from the infectious dose of the pathogen,**
- **the degree of its pathogenicity,**
- **from the state of immunology protection of macroorganisms,**
- **age of patients and so on..**

In some cases, in the manifestation of the disease is noted:

- **severe endotoxic shock,**
- **occurrence of toxicosis with excitosis**
- **generalization of the infectious process (septic forms)**
- **or clinical picture of acute intestinal infection with increased bacteremia (typhoid-like forms) arises,**

in other cases it is *erased,*
***subclinical* form,**
or *bacterial carrier*.

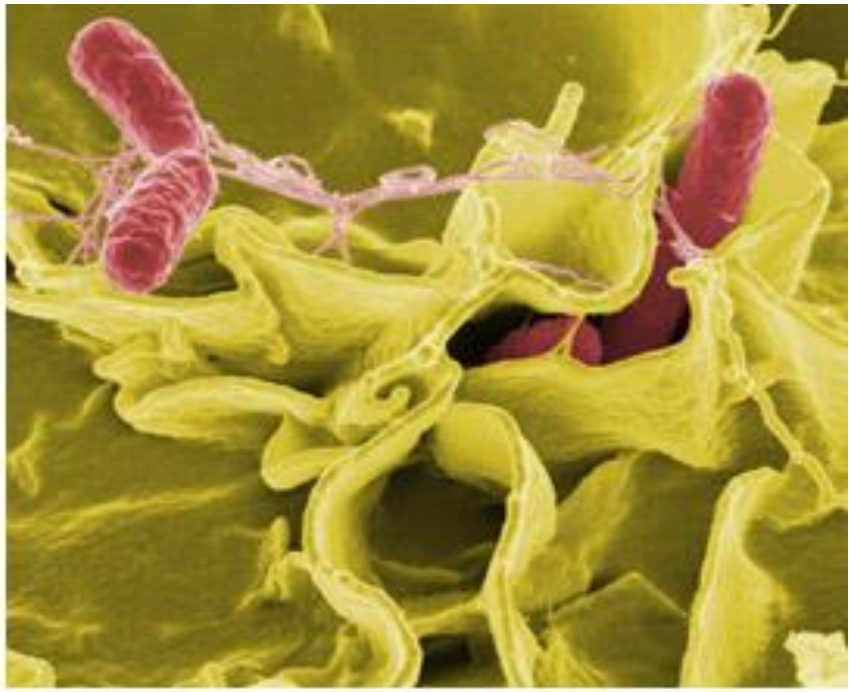
However, regardless of the form of the disease, the main pathological process develops in the gastrointestinal tract, especially in the small intestine.

Pathogenic salmonellae ingested in food survive passage through the gastric acid barrier and invade the mucosa of the small and large intestine and produce toxins.

Invasion of epithelial cells stimulates the release of proinflammatory cytokines which induce an inflammatory reaction.

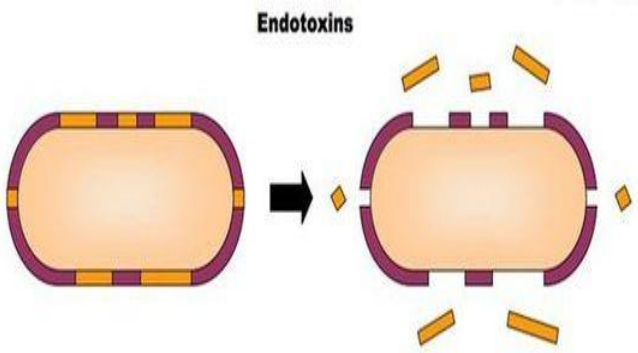
The acute inflammatory response causes diarrhea and may lead to ulceration and destruction of the mucosa.

The bacteria can disseminate from the intestines to cause systemic disease.



Color-enhanced scanning electron micrograph showing *Salmonella typhimurium* (red) invading cultured human cells

Main factors of pathogenicity are cholera-like enterotoxin and the lypopolysaccharyde endotoxin. Endotoxin may induce multiple effects in human organism: fever, microcirculation failure, even septic shock in complicated cases. The enterotoxin activates the adenylatecyclase of enterocytes, which leads to increase of cyclic AMF (adenosinemonophosphate) in cells. As a result normal transport of Na+ and Cl- ions through cell membrane of enterocyte is blocked increasing their concentration in lumen of the intestine. Because of the created osmotic gradient liquid leaves enterocytes and the watery diarrhea starts. In complicated cases failure of liquid-ion balance because of the loss of water amounts may result in decrease of blood volume, arterial blood pressure and hypovolemic shock. Disseminated intravascular coagulation can occur as a consequence of endotoxin influence on hemostasis and hypovolemia



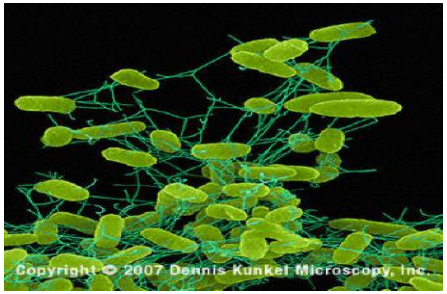
Thus, both

- **toxic and**
- **infectious factors**

are involved in the pathogenesis of the disease.

Bacteremia occurs in all forms of salmonellosis.

The bacteria enter the body in large quantities



in the upper parts of the digestive system (stomach, small intestine)

as a result of their destruction, many endotoxins are released

they are absorbed into the bloodstream and cause toxic syndrome ("toxemia phase");

during this period, the initial clinical signs of the disease appear.

When the disintegration intensity of bacteria is weak

and

if the development of non-specific protective factors of the gastrointestinal tract is incomplete (premature infants, newborns, debilitated and c.),

Salmonella passes

to small intestine

then to the large intestine

and there the first hearth of the pathological process emerges

(«enteral phase»).

Immunity

In salmonellosis, as in other acute bacterial intestinal infections immunity occurs

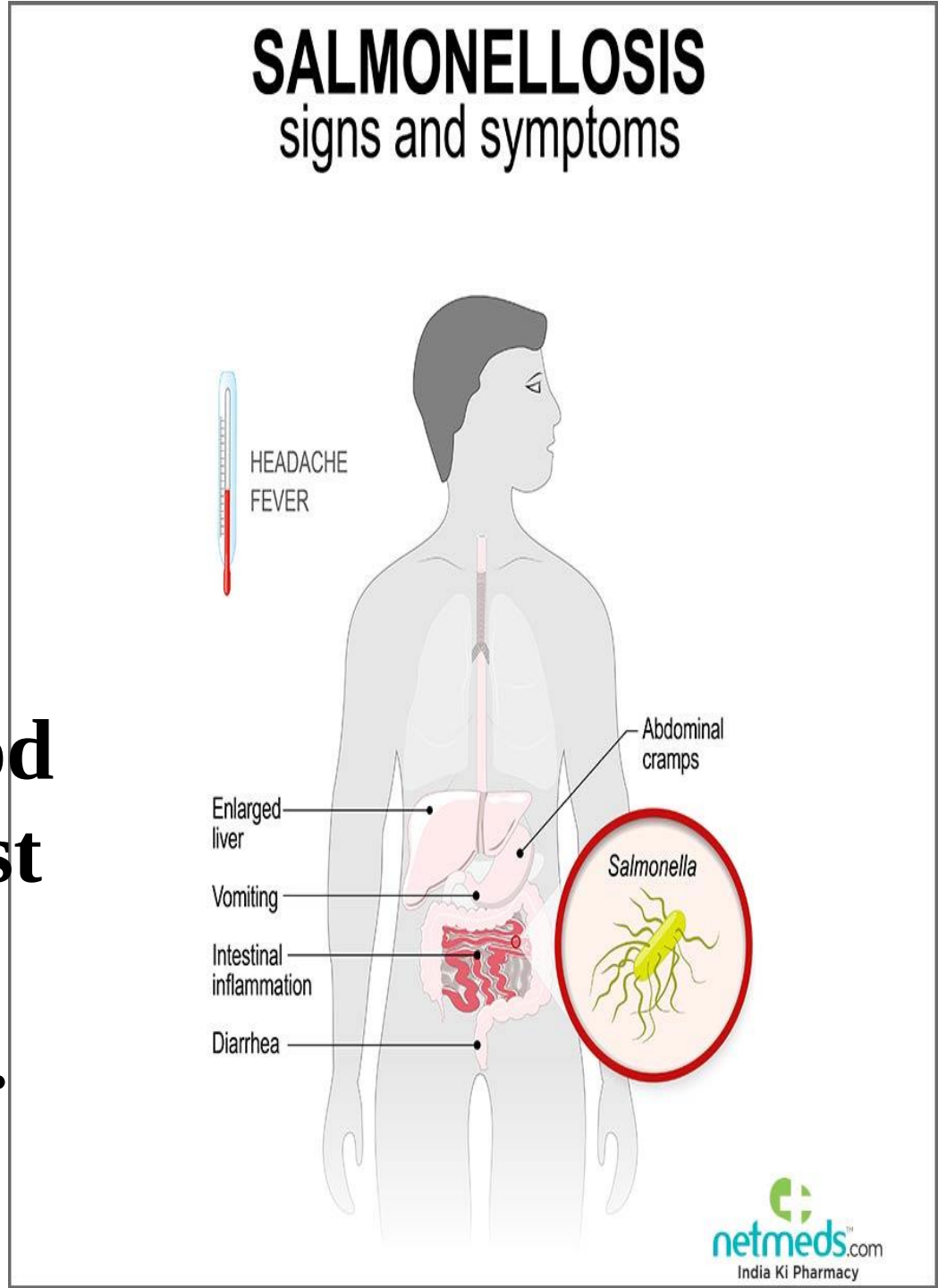
antibacterial,

typospecific

short-term (about 5-6 months)

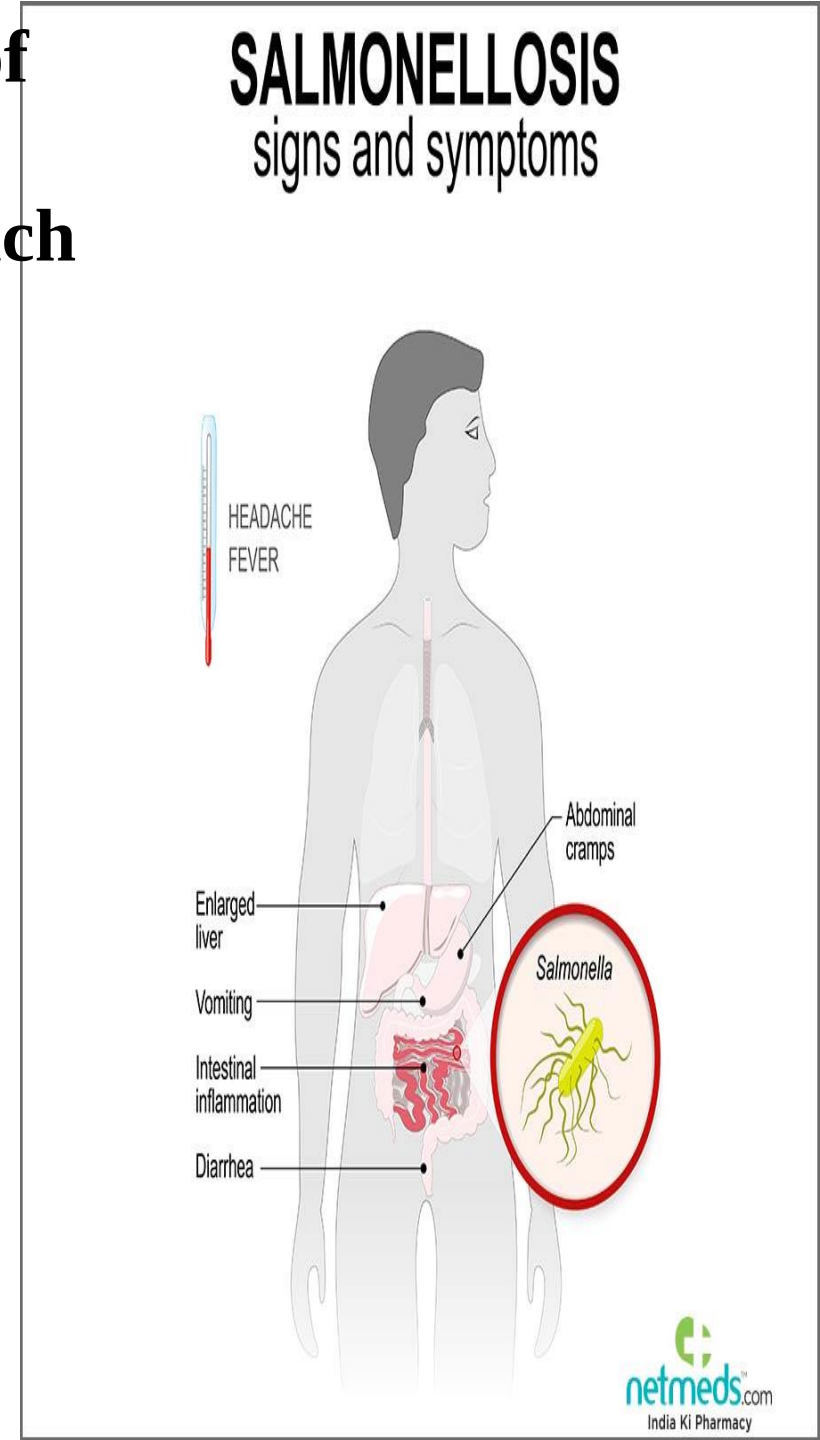
CLINICAL FEATURES

The incubation period depending on the host and the inoculum is generally 6-72 hours.



There can be such clinical forms of salmonellosis:

- **Gastrointestinal (localised), which can occur in**
  - **gastritic,**
  - **gastroenteritic,**
  - **gastroenterocolitic and**
  - **enterocolitic variants;**
- **Generalised forms:**
  - **typhoid-like and**
  - **septic variants;**
- **Carrying of salmonella:**
  - **acute,**
  - **chronic and**
  - **transient;**
- **Subclinical forms**



Depending on the severity of the disease, the degree of development of toxicosis and intestinal symptoms, there are:

- **mild form**
- **moderate**
- **severe**

Along the course, the disease can be:

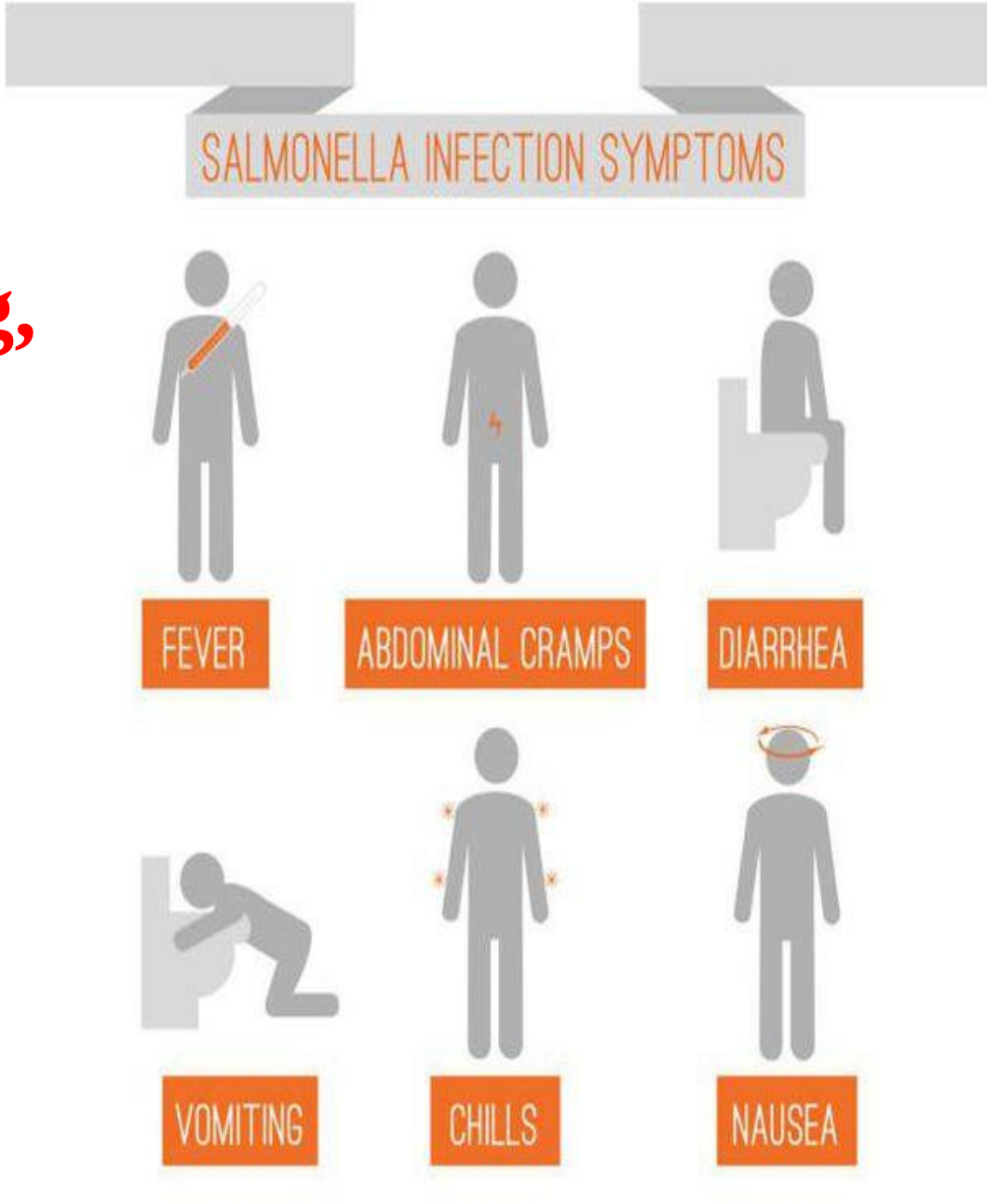
- **acute (up to 1 month),**
- **prolonged (up to 3 months)**
- **chronic (more than 3 months)**

By the nature of the flow

- **smooth, without complications**
- **with complications and**
- **recurrent forms**

In cases of relapse and exacerbation, super- or reinfection (shigellosis, rotavirus or opportunistic infections) should be ruled out first.

Fever (38° to 39°C), abdominal cramping, nausea, vomiting, and chills frequently are reported. Headache, myalgias, and other systemic symptoms also may occur.



***The gastrointestinal form* is the most common.**

This disease starts

- ***acute,***
- ***temperature (in severe forms up to 39 ° C and above),***
- ***weakness,***
- ***headache,***
- ***chills,***
- ***nausea,***
- ***vomiting,***
- ***pain in the epigastric and umbilical regions,***
- ***later the disorder of a chair joins***

Changes in the gastrointestinal tract are most pronounced by the end of the first and on the second and third days from the onset of the disease, their duration depends on the severity of the disease.

Diarrhea is usually self-limited, typically lasting for 3 to 7 days.

Diarrhea that persists for more than 10 days should suggest another diagnosis. If fever is present, it usually resolves within 48 to 72 hours. Occasionally, patients require hospitalization because of dehydration, and death occurs infrequently.

Extraintestinal focal infections develop in approximately 5% to 10% of persons with Salmonella bacteremia (cardiorespiratory system, nervous system, bones, joints, hepatobiliary area).

Gastroenteric variant

the most common. The sickness begins acutely, with symptoms of intoxication:

- **temperature,**
- **headache,**
- **Chills**
- **feelings of aching muscles,**
- **cramping pain in the abdomen.**
- **Nausea, vomiting, diarrhea.**
- **Paleness of the skin is noted, in more severe cases - cyanosis.**

Tongue dry, coated. The abdomen is swollen, painful on palpation in all departments, more in the epi- and mesogastrium, peristalsis is increased. Muffled heart sounds, tachycardia, blood pressure reduced. Decreased urine output. Seizures are possible.

The bowel movements are initially fecal in nature, but quickly become watery, frothy, offensive, sometimes with a greenish tint, and have the appearance of "swamp mud".

Gastroenterocolitic variant

the clinical picture is the same, but already on the 2-3rd day of illness, the volume of stool decreases.

An admixture of mucus, sometimes blood, appears in them.

On palpation of the abdomen, infiltration and tenderness of the sigmoid colon are noted.

In some cases, a colitis variant of the disease is possible, which is difficult to distinguish from shigellosis.

Typhoid-like variant

of the generalized form of salmonellosis, the disease usually begins acutely. In most patients, the onset and course of the disease is similar to typhoid fever and paratyphoid fever A and B. However, in some patients, the first symptoms of the disease may be intestinal disorders in combination with fever and general intoxication, but after 1-2 days intestinal dysfunction disappears, and the temperature body remains high, symptoms of general intoxication increase. The fever is more often undulating or remittent, but may be of a constant type. Patients are lethargic, apathetic. In some patients on the 2nd-3rd a day a herpetic rash appears, and from the 6-7th day - a roseolous rash with a predominant localization on the skin of the abdomen. There is relative bradycardia, lowering blood pressure, muffled heart sounds. Abdomen swollen. By the end of the 1st week of the disease, an increase in the liver and spleen appears. Duration of fever 1-3 weeks.

Relapses are rare

The most severe variant of the generalized form of salmonellosis is the septic form.

The disease begins acutely, in the first days it has a typhoid-like course. In the future, the condition of patients worsens. Body temperature becomes abnormal - with large daily swings, repeated chills and profuse sweating. The disease proceeds, as a rule, severe, poorly amenable to antibiotic therapy. The formation of secondary septic foci in various organs is characteristic, as a result of which the clinical manifestations of this variant of salmonellosis are very diverse, and its diagnosis is difficult.

With this form of the disease, osteomyelitis and arthritis often develop.

Septic endocarditis, aortitis with subsequent development of aortic aneurysm are sometimes observed. Relatively often there are cholecystocholangitis, tonsillitis, cervical purulent lymphadenitis, meningitis (the latter is usually in children). Rarely, purulent foci of other localizations form, for example, liver abscess, infection of an ovarian cyst,

mastoiditis,

abscess of the gluteal region.

Mild form

subfebrile body temperature, single vomiting, loose watery stools up to 5 times a day,
the duration of diarrhea is 1-3 days, the loss of fluid is not more than 3% of body weight.

Moderate form

the temperature rises to 38-9 ° C, the duration of fever is up to 4 days, repeated vomiting, stools up to 10 times a day, the duration of diarrhea is up to 7 days; tachycardia, a decrease in blood pressure are noted, dehydration of the I-II degree, fluid loss up to 6% of body weight may develop.

Severe form

there is a high fever (above 39 ° C), which lasts 5 or more days. Vomiting is usually repeated, observed for several days; stools more than 10 times a day, copious, watery, fetid, greenish in color, may be mixed with mucus. Diarrhea lasts up to 7 days or more. In such patients, there is an increase in the liver and spleen, icterus of the skin and sclera is possible. Dryness and cyanosis of the skin, aphonia, tachycardia, a significant decrease in blood pressure, convulsions are often observed, which is due to a violation of the water-salt metabolism (dehydration II-III degree). Fluid loss reaches 7-10% of body weight. Changes in the kidneys are revealed: oliguria, albuminuria, erythrocytes and casts in the urine, the content of residual nitrogen increases. Acute renal failure may develop. Due to thickening of the blood, the level of hemoglobin and erythrocytes increases, a pronounced intoxication syndrome leads to leukocytosis with a shift of the leukocyte formula to the left.

Complications.

Gastrointestinal form

- **Vascular collapse, Hypovolemic shock, Acute cardiovascular failure**
- **Acute renal failure**

Septic complications:

- **Purulent arthritis**
- **Osteomyelitis**
- **Endocarditis**
- **Meningitis**
- **Peritonitis**
- **Appendicitis**

Diagnosis

Diagnosis of salmonellosis is made on the basis of clinical, epidemiological and laboratory data.

Infection with nontyphoidal Salmonella most often results in self-limited acute gastroenteritis that is indistinguishable from that caused by many other enteric bacterial pathogens.

Freshly passed stool is the preferred specimen for isolation of nontyphoidal Salmonella species.

Since stool carriage of Salmonella may be prolonged, the interpretation of positive results merits caution, and the diagnosis should be established only when accompanied by clinical findings that are typical of infection.

Clinical diagnostics

Characterized by

- **an acute onset with fever,**
- **nausea,**
- **vomiting,**
- **diarrhea**
- **pain in the stomach**
- **characteristic type of stool.**

Epidemiological diagnostics

Eating food prepared and stored in violation of sanitary standards, eating raw eggs, group outbreaks.

In megacities, the identification of group cases of the disease is very difficult if a product contaminated with Salmonella is sold through a distribution network or public catering establishments.

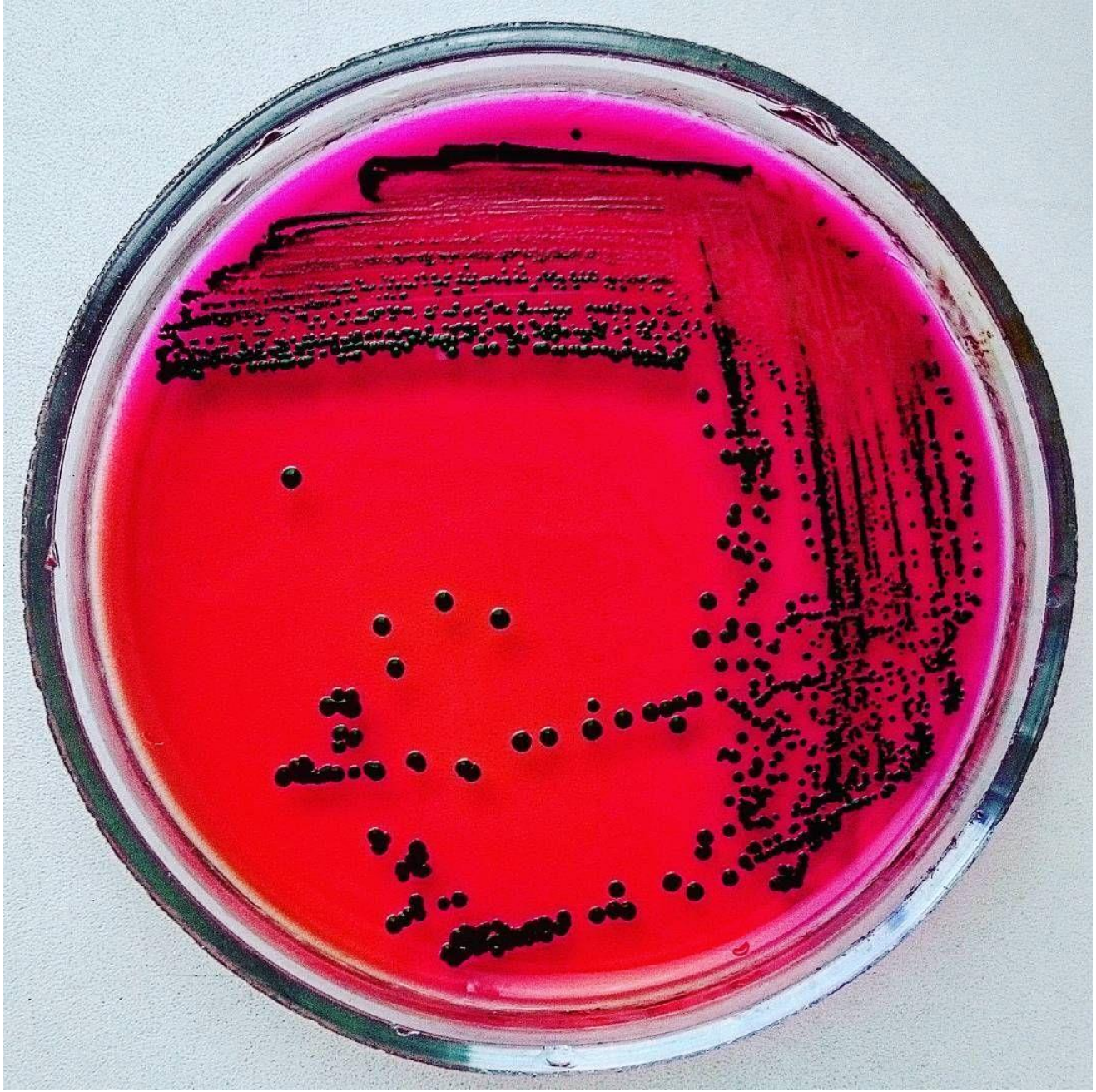
Without confirmation of the diagnosis by laboratory tests, the differential diagnosis of salmonellosis with FP is very difficult.

Laboratory diagnostics

- ✓ **A detailed general clinical blood test (leukocytosis with a shift of the leukocyte to the left - stab, an increase in ESR, in severe cases - erythrocytosis);**
- ✓ **general clinical analysis of urine (oliguria, albuminuria, erythrocyturia, cylindruria, increased density);**
- ✓ **biochemical blood test (increased hepatic transaminases, acute phase indicators);**
- ✓ **coprological method (fat, starch grains, mucus, muscle fibers);**

Laboratory diagnostics

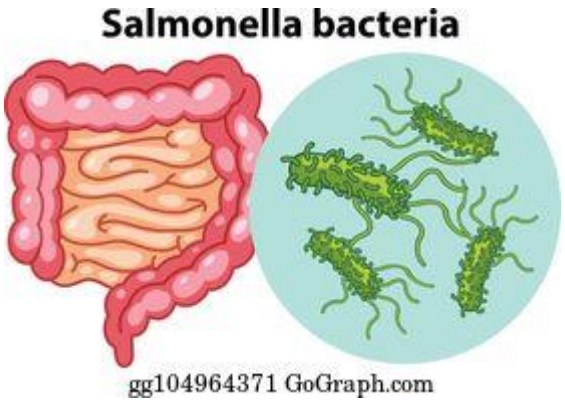
Bacteriological analysis of feces (one or two times), vomit masses, blood, urine, bile, gastric lavage, remnants of suspicious products. (results in 3-4 days)

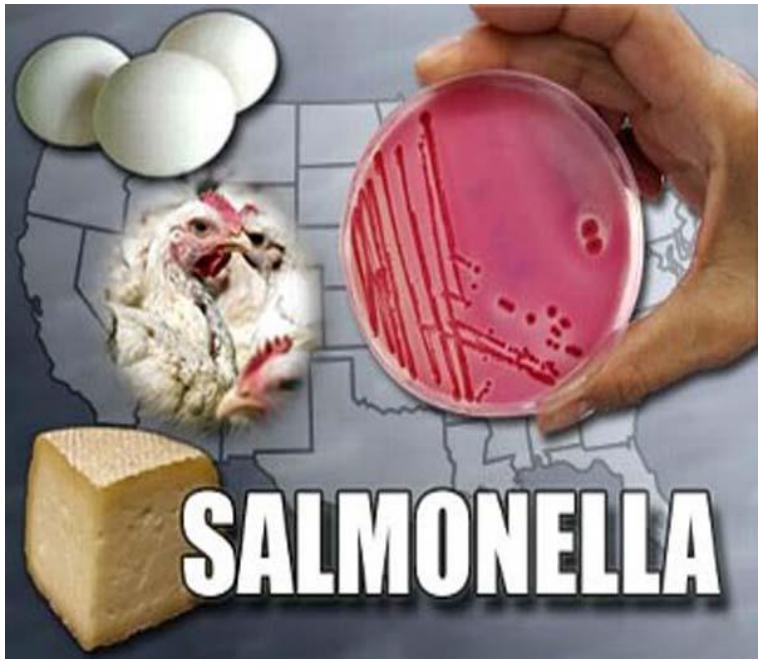


Salmonella Enteritidis

Salmonella antigens can be detected in blood and urine using ELISA and Indirect hemagglutination reaction (IHAR).
For retrospective diagnosis, the determination of specific antibodies (IHAR and ELISA) is used.
Examine paired sera taken at intervals of 5-7 days.
An increase in titers four times or more is of diagnostic value.
In generalized forms, bacteriological examination of blood and the detection of fragments of the pathogen genome by molecular genetic PCR are important.

The final diagnosis is based on the results of laboratory tests (detection of salmonella in the stool or the presence of a diagnostic titer of specific antibodies in the blood).





Differential diagnosis:

Typhoid fever
Paratyphoid
Campylobacter infections,
Escherichia coli infections,
Shigellosis,
Vibrio infections,
Yersinia enterocolitica.
Plague,
Food poisoning,
Botulism,
Poisoning by heavy metal salts,
Appendicitis, etc.

Based on clinical and epidemiological data, salmonellosis can only be roughly distinguished from these diseases.

Treatment

Salmonella gastroenteritis is usually a self-limited disease, and therapy primarily should be directed to the replacement of fluid and electrolyte losses.

Patients with a severe course or those who are prone to developing complications are hospitalized,
in other cases, patients receive treatment at home.

The main prescriptions for treatment:

- Lavage of the gastrointestinal tract;
- Diet therapy;
- Etiotropic therapy
- Pathogenetic therapy;

Correction of violations of normal intestinal microflora

Gastric lavage is a mandatory procedure if the patient has a history of nausea, vomiting. It does not matter how much time has passed since the onset of the disease, because pathogenic microorganisms (including salmonella) can persist for a long time in the folds of the mucous membrane of the digestive tract. For gastric lavage use:

0.5% solution of sodium bicarbonate, 0.1% potassium permanganate, it is possible to use boiled water.

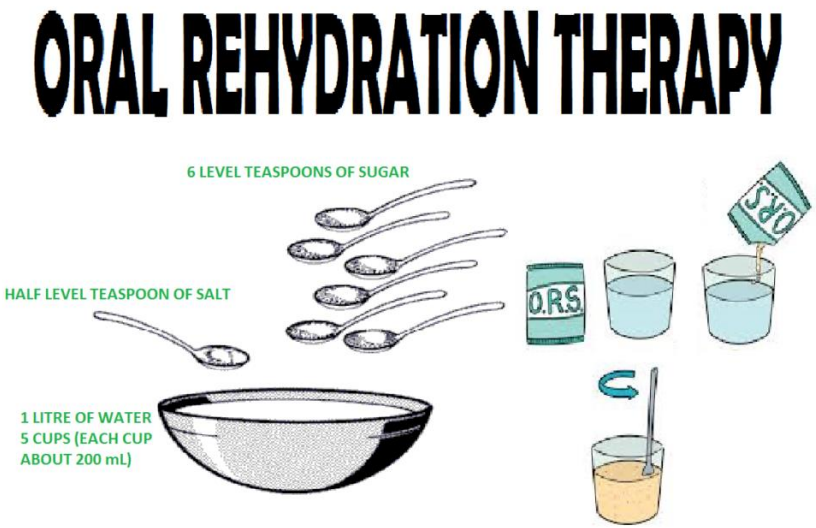
Gastric lavage continue until clean wash water is discharged, usually at least 3-5 liters of liquid, in some cases this requires up to 10 liters.

The main directions of pathogenetic therapy of salmonellosis are the following:

- **1) detoxication:**
- **2) normalization of water and electrolyte metabolism;**
- **3) fight against hypoxemia, hypoxia, metabolic acidosis;**
- **4) maintenance of hemodynamics at the physiological level, as well as the functions of the cardiovascular systems and kidneys.**

Oral rehydration therapy can be used to rehydrate 95% or more of patients with mild to moderate salmonellosis. Patients with severe dehydration require fluid therapy at the beginning of treatment, and then, after correcting the initial deficit, oral rehydration is performed. Oral rehydration therapy has many advantages over infusion therapy, and is well suited for widespread use.

Therefore, parenteral rehydration onon therapy is carried out in cases where, for some reason, oral rehydration cannot be performed, or it has proven to be ineffective



The volume of ORS solutions administered is determined by the degree dehydration and body weight of the patient.

Typically, in patients with acute intestinal infections with grade I dehydration, ORS solutions are used in volume of 30-40 ml / kg., and II-III degree in the volume of 40-70 ml / kg. for the first stage of rehydration.

More severe dehydration may require intravenous infusion therapy with isotonic polyionic solutions.

Detoxification therapy with colloidal solutions or 10% dextran solution is carried out only after the restoration of water and electrolyte homeostasis.
Signs of severe metabolic acidosis are an indication for intravenous sodium bicarbonate.

Treatment in severe cases consists of electrolyte replacement (to provide electrolytes such as sodium, potassium, and chloride ions that are lost in vomiting and diarrhea) and rehydration.

An indication to stop intravenous fluid administration is a combination of the following factors:

- **disappearance of vomiting,**
- **stabilization of hemodynamics,**
- **restoration of the excretory function of the kidneys.**

An important criterion for deciding whether to stop intravenous infusions is a significant predominance of the amount of urine excreted over the number of stools during the last 4 hours.

Routine antimicrobial therapy is not recommended for mild or moderate cases in healthy individuals.

This is because antimicrobials may not completely eliminate the bacteria and may select for resistant strains, which subsequently can lead to the drug becoming ineffective. However, health risk groups such as infants, the elderly, and immunocompromised patients may need to receive antimicrobial therapy. Antimicrobials are also administered if the infection spreads from the intestine to other body parts. Because of the global increase of antimicrobial resistance, treatment guidelines should be reviewed on a regular basis taking into account the resistance pattern of the bacteria based on the local surveillance system.

Salmonella antibiotic treatment regimens:

ciprofloxacin 500 mg per os twice daily × 5-7 days,

ceftriaxone 2g per day intramuscular/intravenous × 5-7 days.

Treatment may be prolonged for 14 days if deeply immunocompromised (or if relapsing disease).

Prevention.

The most cost-effective approach to the control of salmonellosis is attention to good personal hygiene and maintenance of timetemperature standards for food handling.

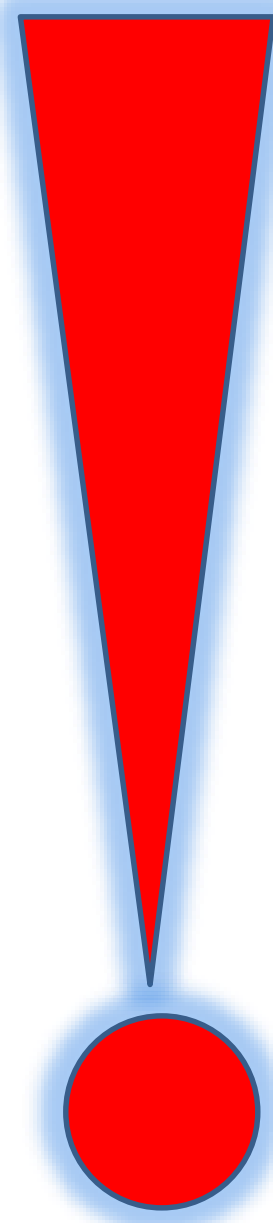
Prevention methods

Prevention requires control measures at all stages of the food chain, from agricultural production, to processing, manufacturing and preparation of foods in both commercial establishments and at home.

Preventive measures for *Salmonella* in the home are similar to those used against other foodborne bacterial diseases.

The contact between infants/young children and pet animals that may be carrying *Salmonella* (such as cats, dogs, and turtles) needs careful supervision.

National and regional surveillance systems on foodborne diseases are important means to know and follow the situation of these diseases and also to detect and respond to salmonellosis and other enteric infections in early stages, and thus to prevent them from further spreading.



Through cooking: **Cooking should be thorough enough to kill all bacteria. One of the great dangers in not thawing frozen food sufficiently. In addition, the Chief Medical Offices recommended in 1988 that raw eggs should be avoided and vulnerable groups such as the elderly, sick, babies and pregnant women should consume only eggs which have been cooked until the white and yolk are solid.**

Carriers:

Symptom less carriers of the disease can retain the organisms in the faeces for some time and present a problem in society. About 2-5 people per thousand of the general population are thought to be carriers. Known carriers and people who have suffered the disease are not allowed to work in the food industry until samples of their faeces have been shown to be clear of the pathogenic organisms.

There is no vaccine to prevent salmonellosis