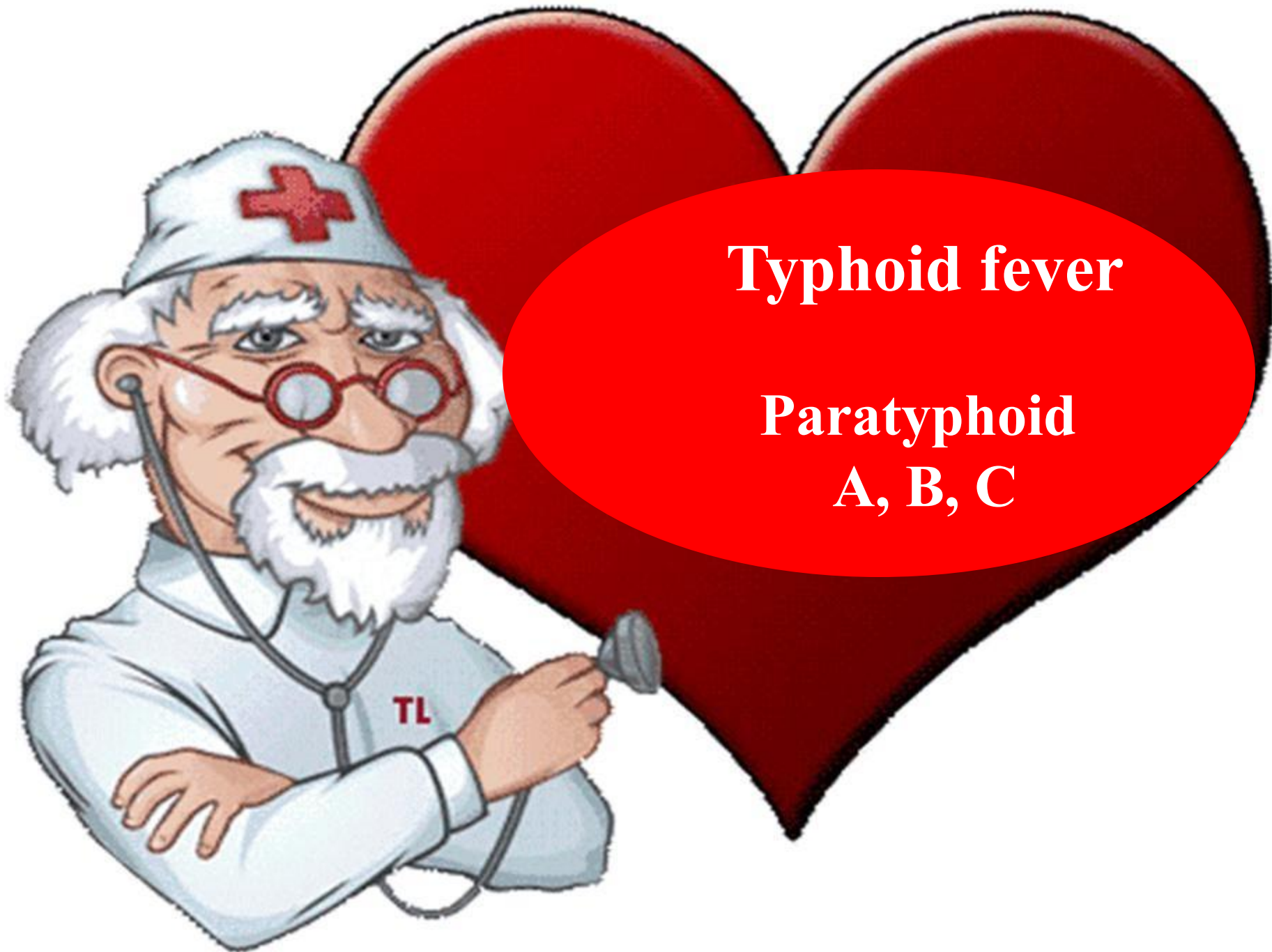


General characteristic of infectious diseases with fecal-oral mechanism of transmission

- specific localization of the **causative agent** in intestine (small or large, rectum, mesenterium)
- removing the agent with feces or vomiting mass
- can penetrate into a susceptible organism by next **ways of transmission** (**watery, alimentary, contact-household**)
- various **factors of transmission** (**foodstuff, water, hands, insects, toys, soil**)
- in intestine **causative agent** can be: in the lumen of intestine, intestinal epithelium, mucous membrane, lymphatic tissue of intestine
- causative agent can **constantly** be in intestine (cholera, dysentery, some helminthic invasion) or **temporarily**,
- penetration from intestine in blood and other tissue (ascariasis, amebiasis, strongyloidiasis, trichinosis, echinococcosis)

- **Morbidity of intestinal infection is the highest:**
 - in **warm and/or rainy period** of year
(in moderate climatic zones is more often registered during **summer or autumn**);
 - in countries with **low socio-economic level** of development;
 - among people of **risk-groups**:
 - 😊 - age - children and the elderly,
 - 😊 - chronic GIT-pathology - patients with gastritis, duodenitis, peptic ulcer, cholecystitis;
 - 😊 - profession - sanitary workers, plumbers, teachers, medical personal;
 - 😊 - occupation – fishermen, water-rescuers, veterinarians, animal trainers



Typhoid fever

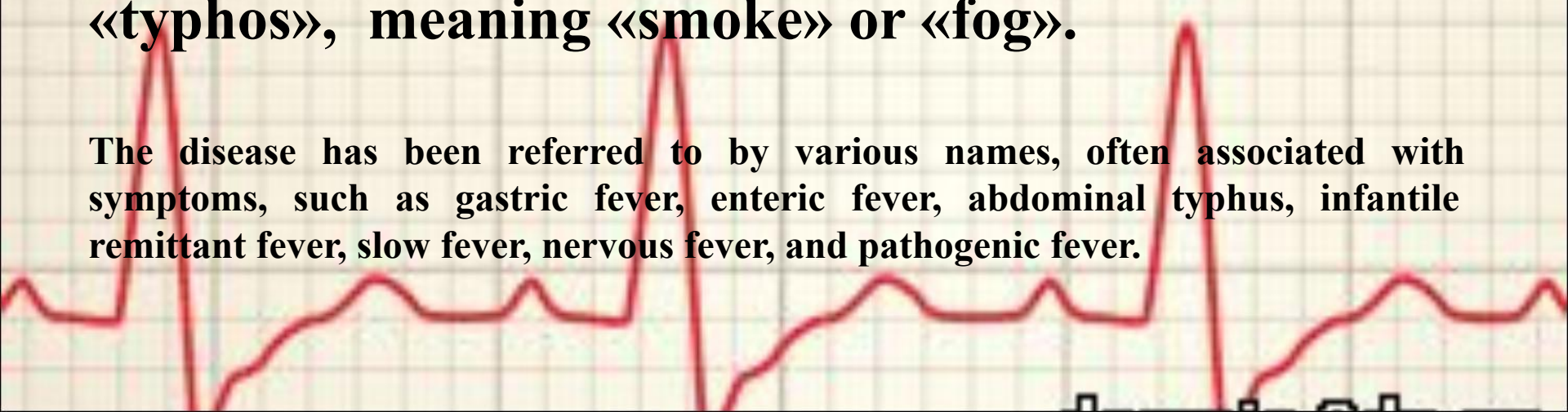
**Paratyphoid
A, B, C**

Definition

Typhoid fever – is an acute intestinal anthroponotic infection with fecal - oral mechanism of transmission caused by *S. typhi*, characterized by lesions of lymphatic apparatus of the small intestine and bacteremia, development of severe intoxication, hepatosplenomegaly and roseola rash.

The name of the disease came from the word «typhos», meaning «smoke» or «fog».

The disease has been referred to by various names, often associated with symptoms, such as gastric fever, enteric fever, abdominal typhus, infantile remittant fever, slow fever, nervous fever, and pathogenic fever.



History

★ The first data on typhoid fever obtained from the writings of the ancient historian Thucydides, who suffered this disease.

★ In 430 BC in Athens lost one-third of the population of Athens, including their leader Pericles.

★ Some historians believe that English colony of Jamestown, Virginia, died from typhoid. Typhoid fever killed more than 6000 settlers in the New World between 1607 and 1624.

★ During the American Civil War 81 360 Union soldiers died of typhoid or dysentery, more than died of battle wounds.



★ The most notorious carrier of typhoid fever was Mary Mallon, also known as Typhoid Mary.

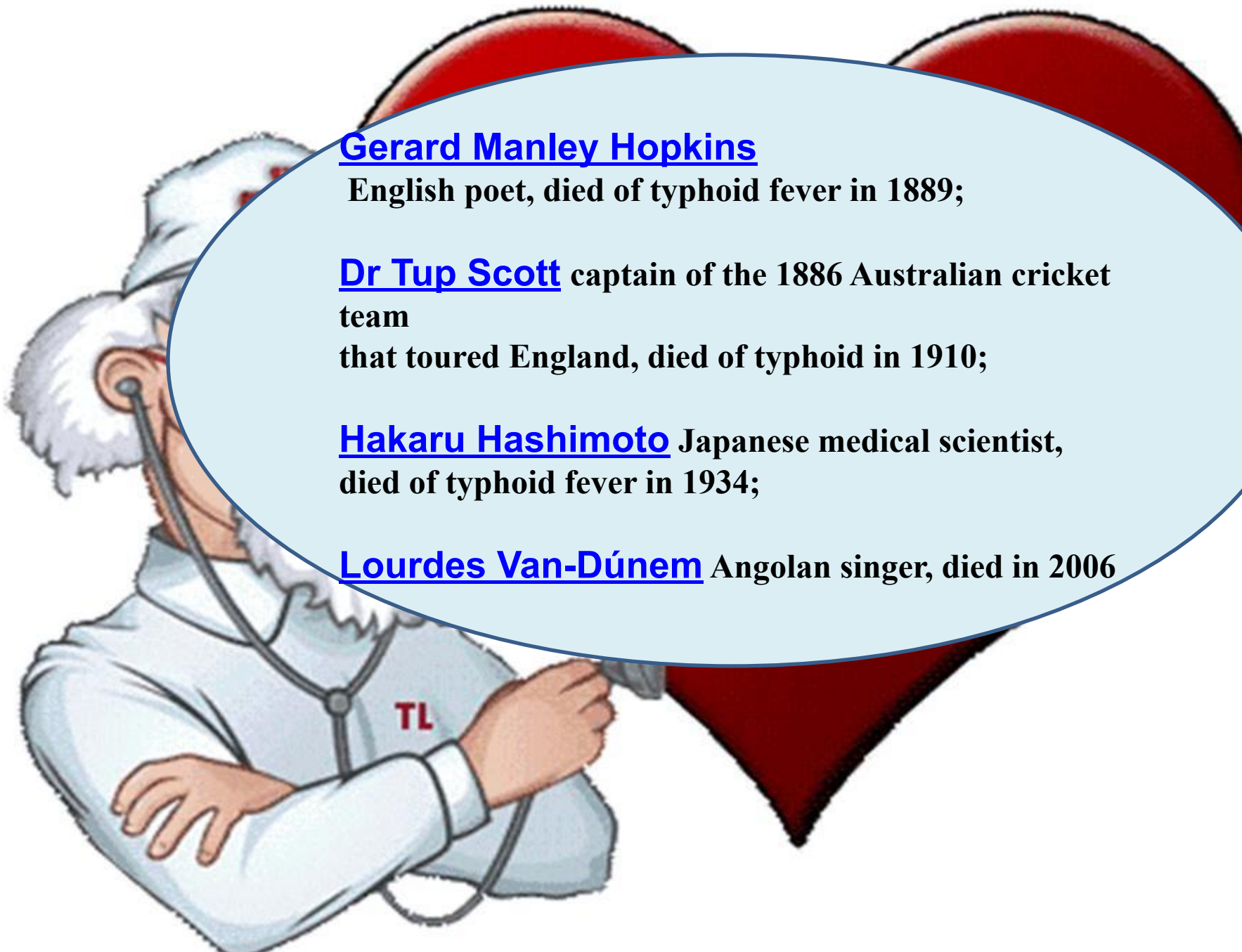
★ In 1907, she became the first carrier in the United States to be identified and traced. She was a cook in New York who is closely associated with 53 cases and 3 deaths.

★ Public health authorities told Mary to give up working as a cook or have her gall bladder removed, as she had a chronic infection that kept her active as a carrier of the disease.

★ Mary quit her job, but returned later under a false name. She was detained and quarantined after another typhoid outbreak.

She died of pneumonia after 26 years in quarantine.





Gerard Manley Hopkins

English poet, died of typhoid fever in 1889;

Dr Tup Scott captain of the 1886 Australian cricket team

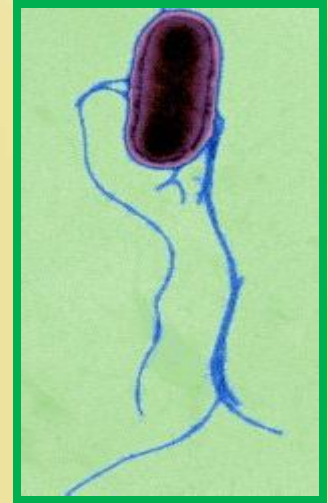
that toured England, died of typhoid in 1910;

Hakaru Hashimoto Japanese medical scientist, died of typhoid fever in 1934;

Lourdes Van-Dúnem Angolan singer, died in 2006

Causative Agent

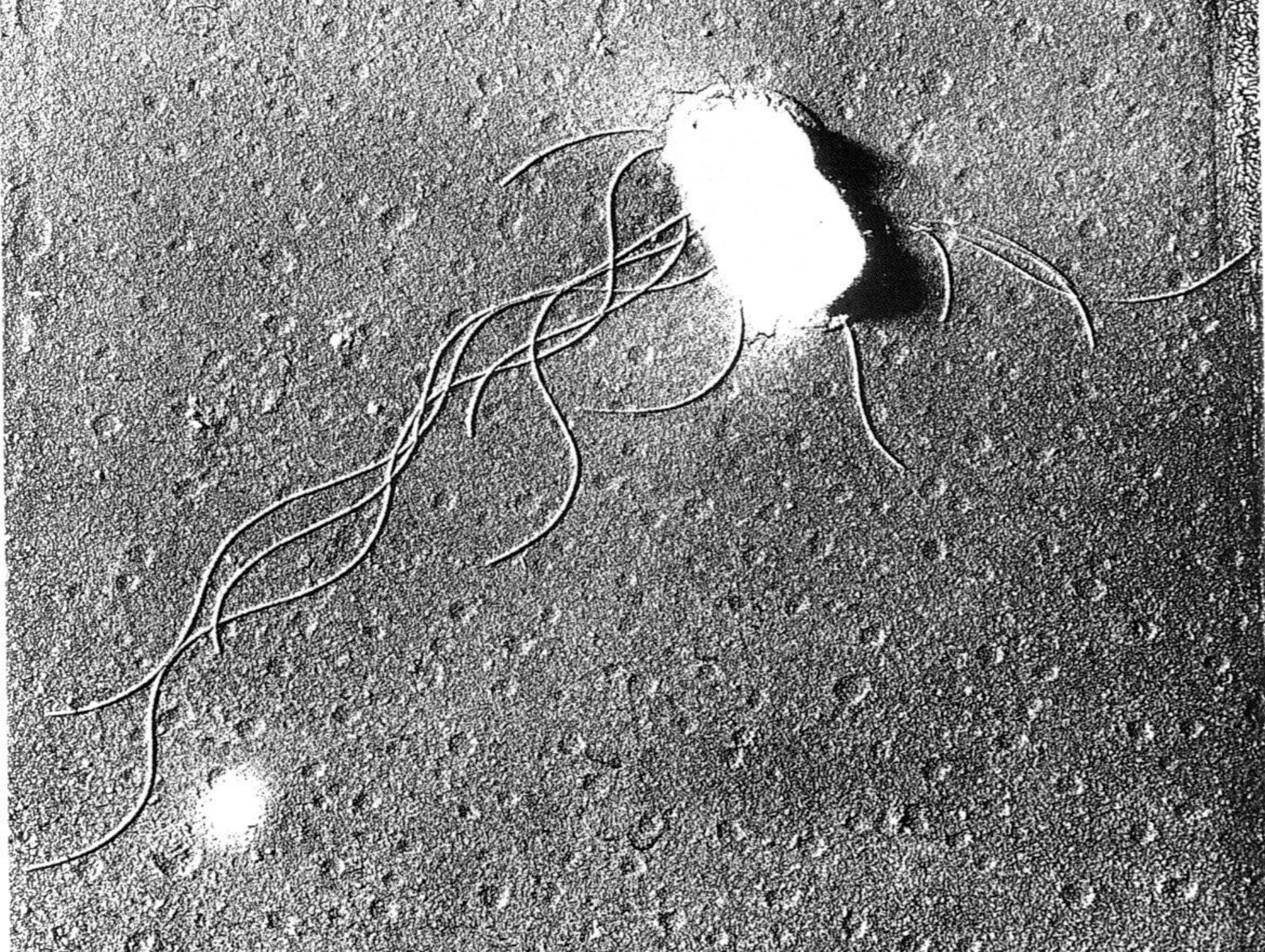
- ❑ Bacterium *Salmonella typhi*, also known as *Salmonella enterica* serotype typhi (D), parasitizing in the intestine and blood;
- ❑ gram-negative enteric bacillus belongs to the family of Enterobacteriaceae;
- ❑ motile due to peritrichous flagella;
- ❑ facultative anaerobe that is susceptible to various antibiotics;
- ❑ spores and capsules do not form; stable in the environment;
- ❑ grows best at 37°C on ordinary medium, especially with the addition of bile;
- ❑ releases endotoxin after destruction;



- ❑ *Salmonella typhus* possesses 3 main antigenic factors:

1. - O, or somatic antigen,
2. - Vi, or encapsulated antigen,
3. - H, or flagellar antigen





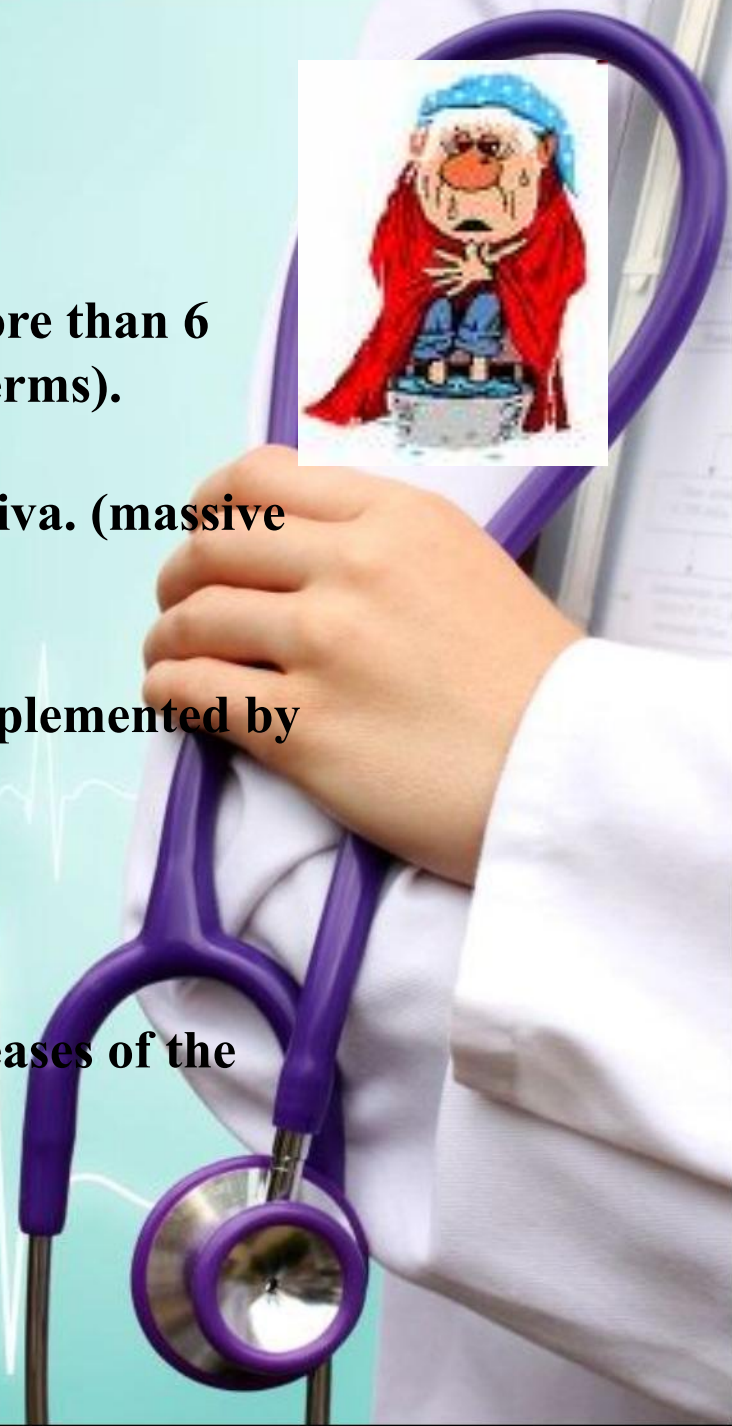
Epidemiology

Source of infection: - bacilli- carrier:

- the acute - releases within 3 months, chronic – more than 6 months (the most dangerous in epidemiological terms).
- patient discharges bacteria with feces, urine, saliva. (massive discharging starts from the 7th day of illness).

Mechanism of transmission: – fecal-oral implemented by
– water, – food, – contact-household ways.

- Sensitivity:** - children, young people, elderly,
- 54% of typhoid fever cases involved males;
 - patients with immunodeficiency and chronic diseases of the gastrointestinal tract;
- After the disease develops persistent immunity.
Characterized by seasonality (summer, autumn).



- Typhoid fever occurs worldwide, primarily in developing nations whose sanitary conditions are poor.
- Typhoid fever is endemic in Asia, Africa, Latin America, the Caribbean, and Oceania, but 80% of cases come from Bangladesh, China, India, Indonesia, Laos, Nepal, Pakistan, or Vietnam.
- Within those countries, typhoid fever is most common in underdeveloped areas.
- Typhoid fever infects roughly 21.6 million people (incidence of 3.6 per 1,000 population) and kills an estimated 200,000 people every year



Regions of earth with high risk infection by typhoid fever.

Annually in the world **are ill** 20 million persons from which 800.000 **died**.

Typhoid fever



Pathogenesis

1-st phase Penetration

- Development of the disease depends on intake of necessary infectious dose ($10^7 - 10^9$) and condition of protective barriers.

**Incubation (14-17 days).
1-st week of contact with
the agent. Clinic no.**

2-nd phase Primary regional infection

- Penetration into mucosa of the small intestine,
- accumulation in the solitary follicles,
- formation of primary foci of inflammation,
- multiplication in mesenteric lymph. nodes,
- development of lymphadenitis and lymphangitis.

**Incubation.
2-nd week of contact with
the agent. Clinic no.**

**3-d phase
Bacteremia
and
toxemia**

- Upon reaching a sufficient number Salmonella enters the blood via the thoracic duct and dies due to action of the bactericidal properties of blood releasing endotoxin.

**Initial period
(1-st week of
disease).
Development of
intoxication
syndrome
(nonspecific
symptom).**

**4-th phase
Parenchymal
diffusion**

- With the blood flow Salmonella penetrates into the parenchymal target organs (liver, spleen, bone marrow and skin), forming secondary foci of inflammation (granulomas)

**Climax period
(2-3-d week of the
disease).
Appearance of the
typical
pathognomonic
syndromes of illness
(hepatosplenomegaly,
pancytopenia, rash).**

5-th phase
**Excretory-
allergic**



- Elimination of the pathogen and immune complexes through the kidneys, bile duct and intestine.
- The remaining bacteria are embedded in sensitized lymph. follicles, causing hyperergic inflammation with necrosis.



Climax period
(3-4-th week of the
disease).
Pathognomonic
symptoms persist.

— symptom —

6-th phase
Immunological



- Production of specific antibodies,
- Normalization of microcirculation and restore organ functions.

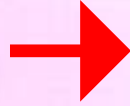


The period of
convalescence
(5-th week – early
convalescence,
6-th – late
convalescence).
Gradual
disappearance of
the syndromes.

Morphology

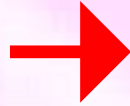
Penetration

**Primary
regional
infection**



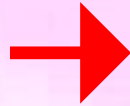
Hyperplasia of the solitary lymph follicles in the mucosa of the small intestine.

**Bacteremia
and toxemia**



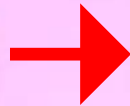
Cerebrum-like swelling of lymphoid structures of the small intestine.

**Parenchymal
diffusion**



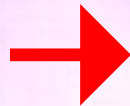
Formation of ulcers. In the center of the follicles are formed necrosis with green, gray, or yellow surface covered with fibrin.

**Excretory-
allergic**

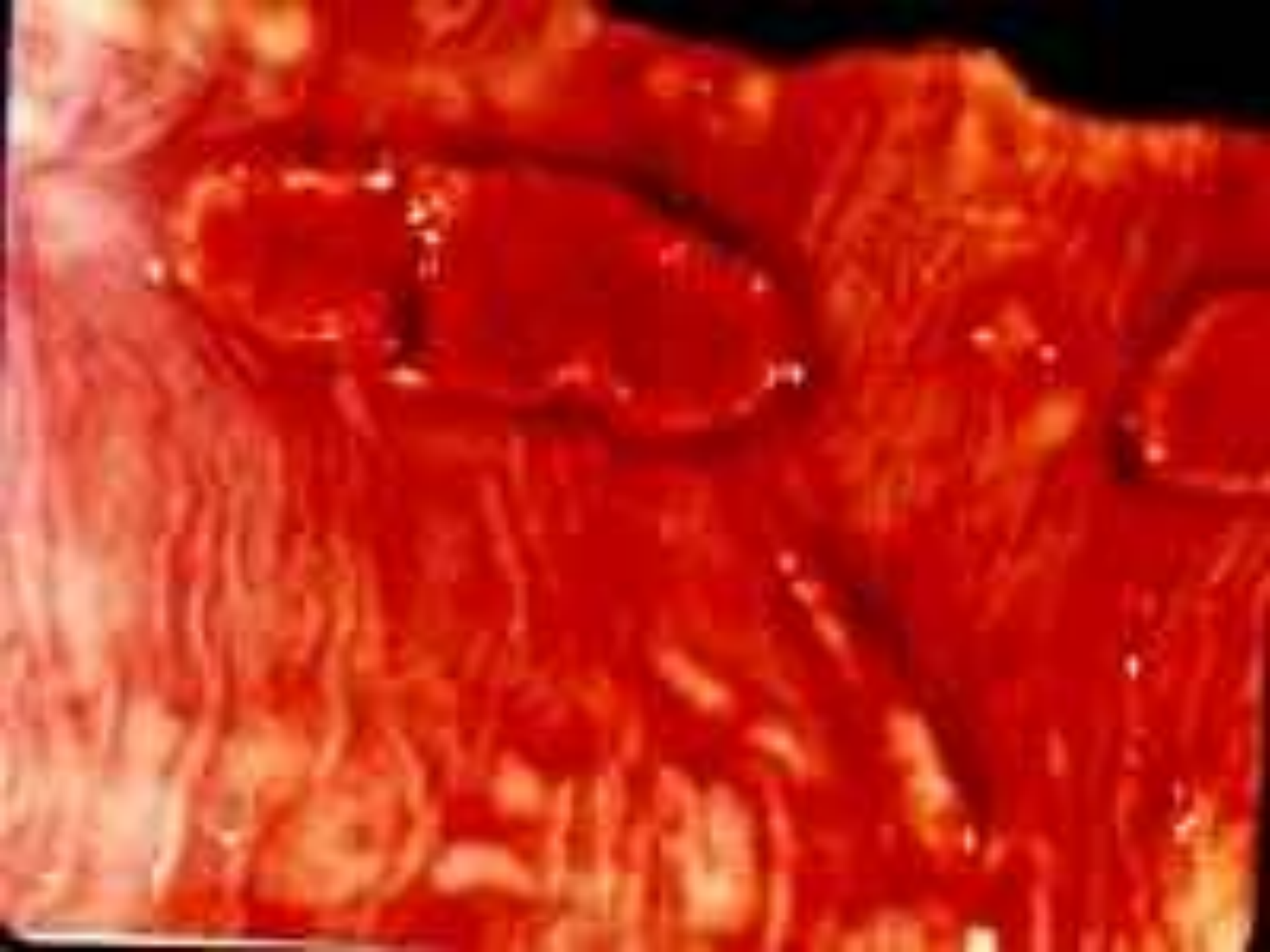


**Stage of “dirty” ulcers
(deep layers covered by fibrin)**

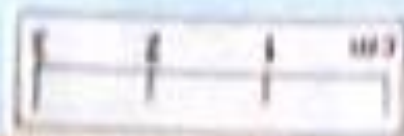
Immunological



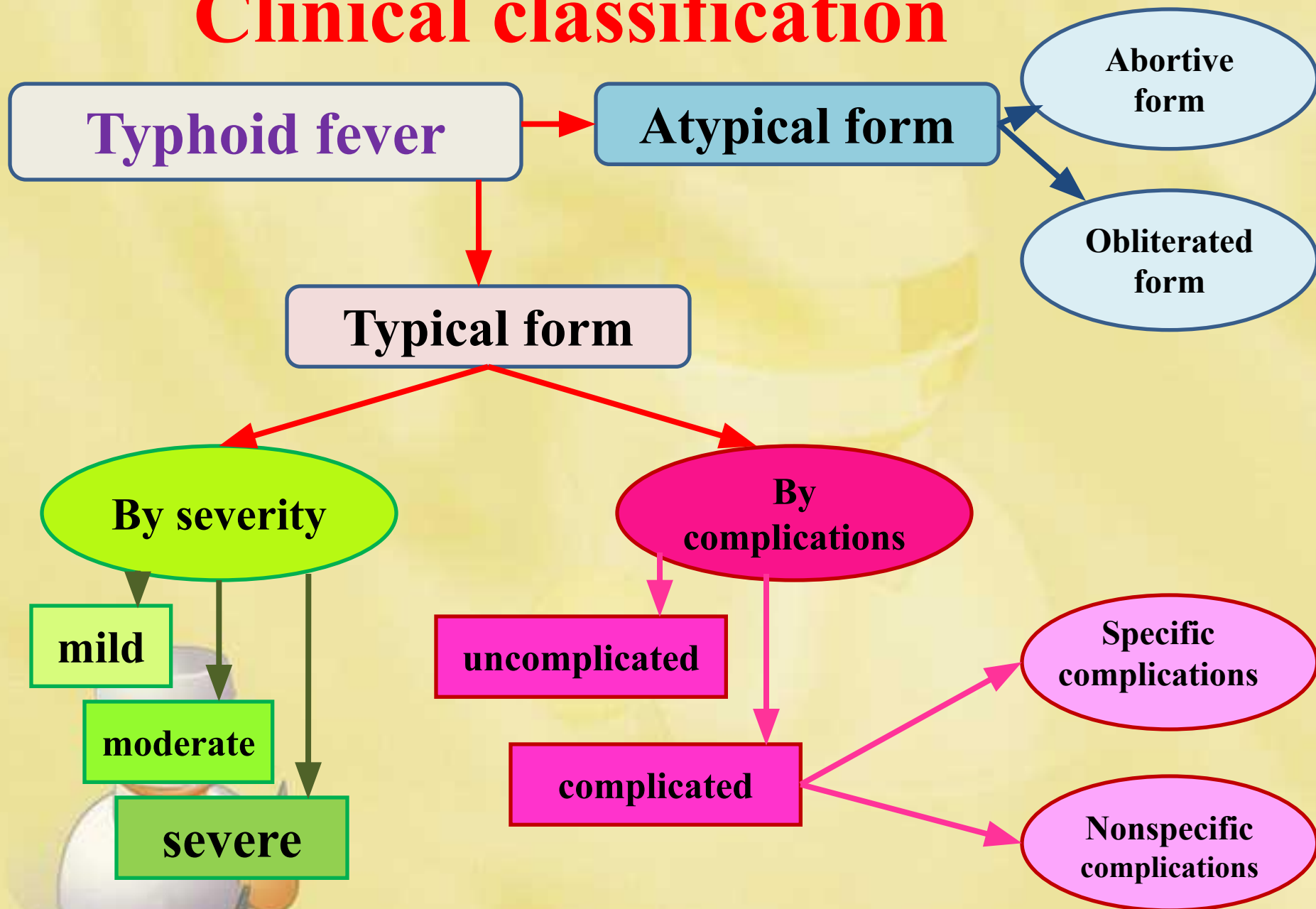
Period of “clean” ulcers, purification of fibrin. Healing of ulcers without scarring, deformation, but the pigmentation is gray-black in color.







Clinical classification



Clinical characteristics

1. Incubation – (14-17 days) - asymptomatic;

2. Initial period – (1 week) – nonspecific syndroms:

- ♥ - General intoxication;
- ♥ - Cardio-vascular syndrome;
- ♥ - Respiratory syndrome;
- ♥ - Gastrointestinal syndrome;

3. Climax period – (2-3 weeks) – typical syndroms:

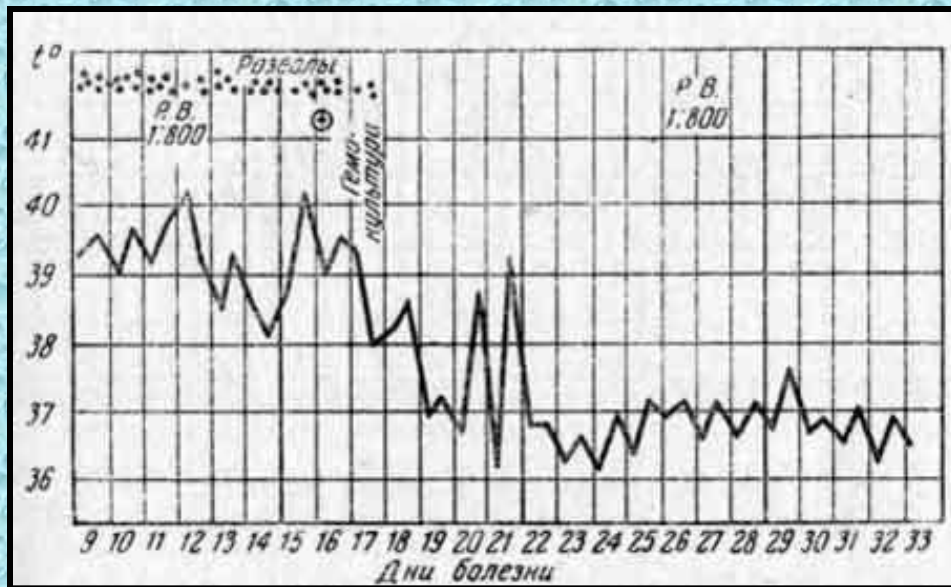
- ♥ - Hepatosplenomegaly;
- ♥ - Roseola rash;
- ♥ - Status typhosus;
- nonspecific syndroms:
- ♥ - General intoxication;
- ♥ - Cardio-vascular syndrome;
- ♥ - Respiratory syndrome;
- ♥ - Abdominal syndrom;

4. Convalescence period – (2-3 weeks) – asthenovegetative syndrom

Incubation period lasts from 7 to 25 days, an average of 9-14 days. When the water route of infection - up to 1 month. Clinical picture no.

Initial period characterized by:

1. Intoxication syndrome with acute (peak within 2-3 days) or gradual beginning:

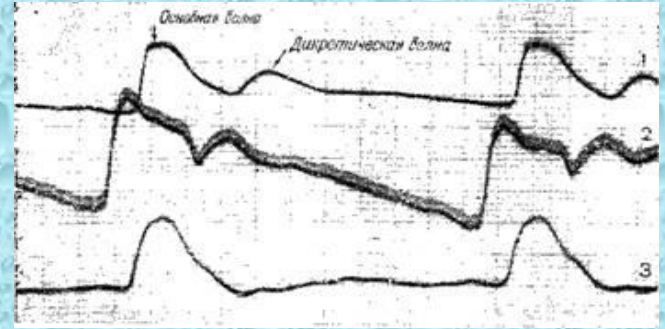
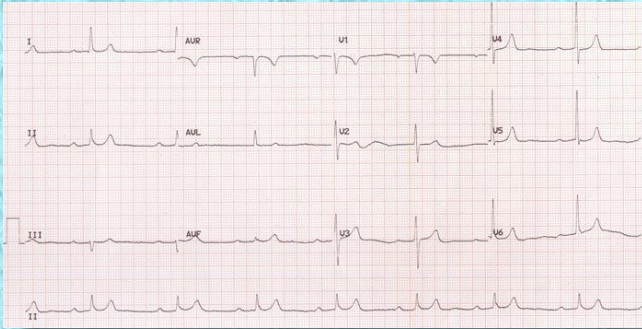


- sleep disturbance;
- pale face and skin;

- fatigue, weakness, chills;
- headache, apathy;
- temperature rises gradually to 38-39 °C (by the 5-7-th day of illness);



2. **Cardio-vascular syndrome:** - relative bradycardia and puls dicrotia;
- decrease of blood pressure;



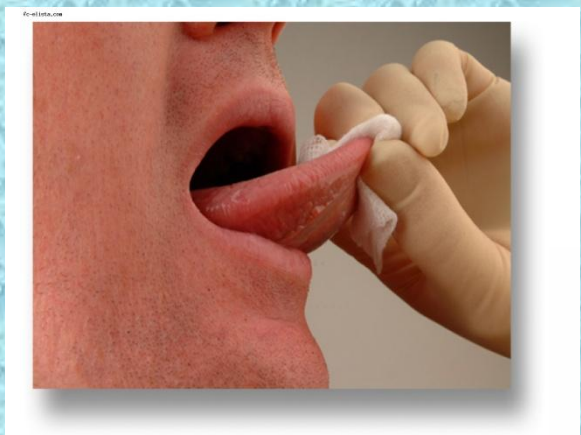
3. **Respiratory syndrome:**

- hard breathing,
- diffuse dry rales (as bronchitis),
- coughing;



4. **Gastroenteric syndrome :**

- loss of appetite or anorexia;
- tongue is thickened, covered with gray – white fur and imprints of teeth;
- the mucous membrane of oropharynx is hyperemic, tonsils can be increased;



- meteorism, abdomen distended, rumbling, painful along the small intestine at palpation (ileitis);

- at percussion – is a shortening of sound in the right iliac area

- (“+” **Padalka – sign** due to hyperplasia of the mesenteric lymph. nodes),

- within 2-4 days of disease may be seen **diarrhea** (stool is stinking with a sour smell, up to 2 – 4 t/day, foamy, liquid, greenish like pea soup.

- **enlargement of the spleen and liver** (at the end of 1st week),



Climax period

(begins with the appearance of the rash on the 2-d week of the disease and lasts an average of 2-3 weeks)

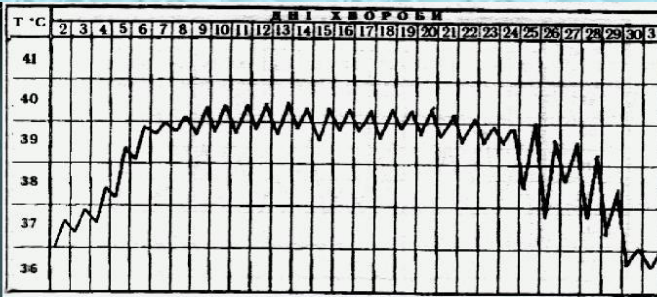
1.Intoxication syndrome:

- headache is the most expressed, not relieved by drugs;
- insomnia, drowsiness;
- chills, weakness;
- photophobia;
- status typhosus - delayed mental reactions, sometimes prostration, stupor condition and coma, tremor of fingers, chin and tongue;
- apathy, adynamia;
- temperature is febrile or hectic (39-40°C), increases every day for 1-2°C during the week and lasts for about 2 weeks.

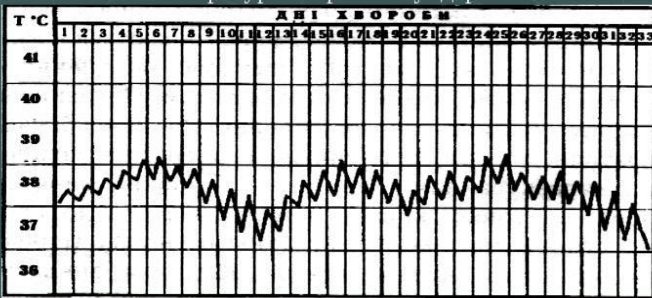




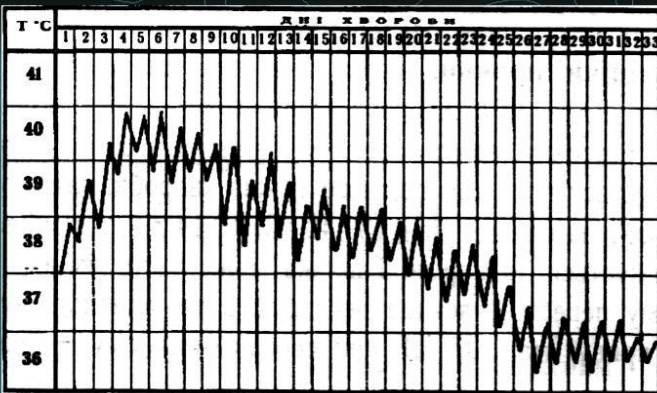
There are 3 possible types of the temperature curve in the clinic:



Температурная кривая Вундерлиха



Температурная кривая Боткина



Температурная кривая Кильдюшевского

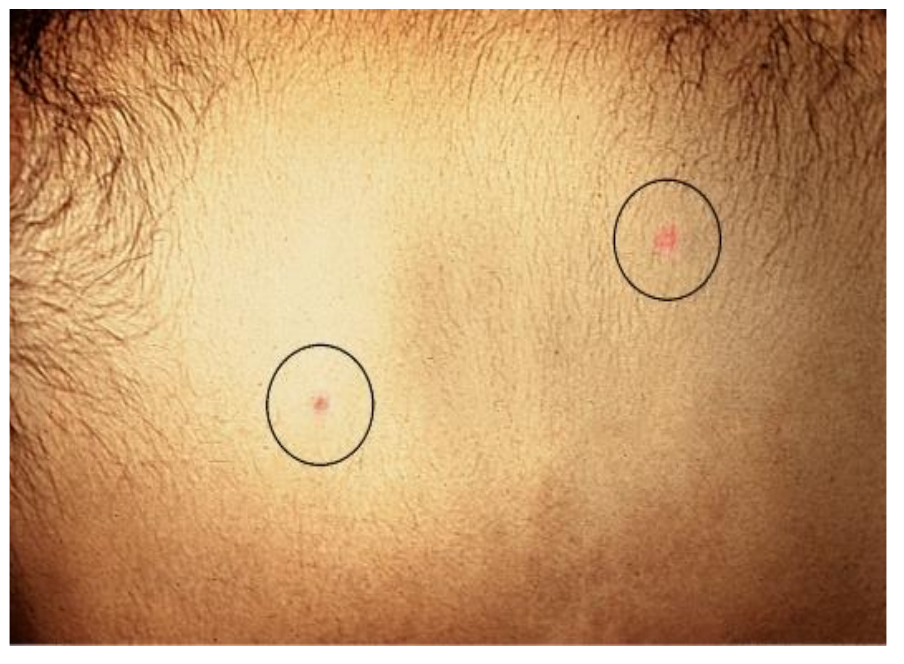
Wunderlich – trapezoidal – *f. continua* - daily fluctuations of temperature not more than 1°C, The 1-st phase (3-4 days) characterized by an increase of temperature. In the 2-d phase (1, 5-2-3 weeks) fever is continuous between morning and evening temperature marked a slight remission. The 3-d phase (amphibolitic) – is characterized by high ranges of the temperature curve. In the 4-th phase (5-8 days) and in the temperature is reduced.

Botkin – wave-like – *f. undulans* - with sequential alternating 3-4-days episodes of febrile and subfebrile temperature. Daily fluctuations of temperature within 0,5-1°C;

Kildushevsky – triangular - with a short (1 -2 days) stage of constantly high temperature and prolong (2-2,5 weeks) stage of decreasing;

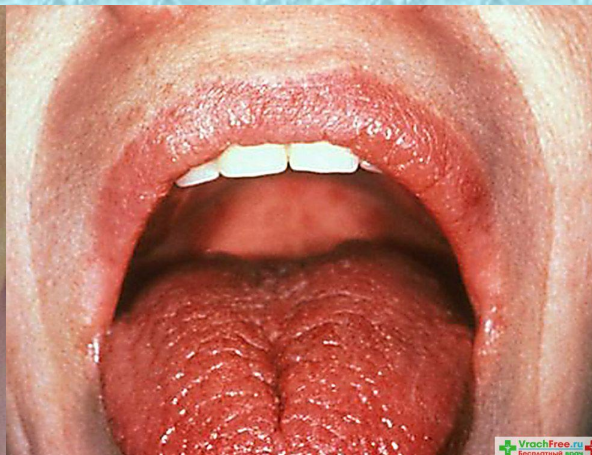
2. Rush (roseola-like):

Appearance	On the 8-10-th day of the disease
Localization	Skin of the abdomen and lower parts of the chest
Character	Monomorphic, consists of roseola
Intensity	Scanty (up to 6-15 elements)
Characteristic of elements	Roseola - pale pink round shaped spot with clear edges, in diameter of 3-6 mm, elevated above the skin and disappears when pressed
Duration	From 2 to 5 days, on average 3-4 days
Elimination	Without a trace, sometimes pigmentation but rarely
Frequency of rashes	Wave-like



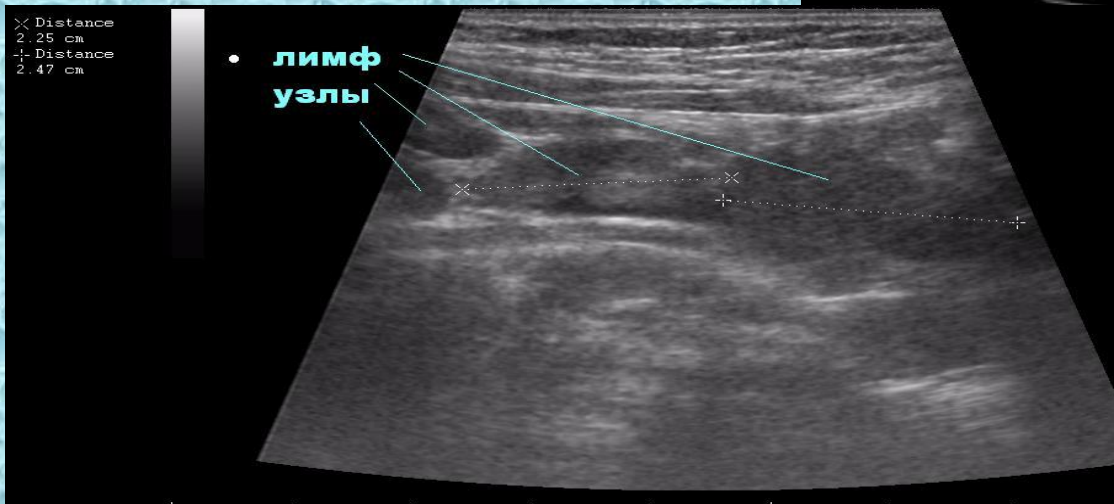
3. Gastrointestinal syndrome:

- anorexia;
- **pale skin**, dry lips and mucous membranes;
- tongue is dry enlarged with teeth prints, bright red, covered with brown fur (**fuliginous**);
- abdomen distended, rumbling, painful palpation;
- **“+” Padalka** and cross-Sternberg symptoms;
- Philippovich-symptom - icteric staining of the palms and feet – due to carotene skin hyperchromia (liver damage);
- **obstipation**;



4. Hepatosplenomegaly :

- liver is dough-like consistency, painful on palpation but has a smooth edge;
- spleen is enlarged and painful;
- clinic cholecystitis, pancreatitis, hepatitis.



5. Cardio-vascular system:

- relative bradycardia; dicrotic pulse;
- hypotension;
- enlargement of the heart sizes;
- dull heart tones, systolic murmur at the apex of the heart (due to intoxication inhibition of the conducting system of myocardium).



6. Respiratory syndrome:

- hard breathing, diffuse dry rales;
- sometimes bronchial pneumonia.



During this period, there are specific complications caused by pathogenic action of bacteria and its toxin.

Often develop:

- **intestinal bleeding** – (1-2%) is observed on the 3-d week of illness (due to damage of the blood vessel at the bottom of the ulcer). Has diffuse or the capillary character;
- **perforative peritonitis** – (0,5-1,5%) develops in 2-4 weeks (due to perforation of ulcer in intestine);
- **infectious-toxic shock** – (0,5 – 0,7%) develops at the end of the initial period (due to the massive penetration of bacteria and their toxins in the blood).

Laboratory diagnostics

Specific studies (allow to confirm the diagnosis):

1. Bacteriologic analysis - the main method of laboratory diagnosis of typho-paratyphoid diseases, allows to select and determine the type of pathogen.



Bacteriological research is subjected to **blood** (52—78%), **urine** (0,7—2,1%), **feces** (11—19%) , **bile** and scraping of the **rash**, **bone marrow**, pus, sputum.

The time of selection of the material:

- 1-2-d week – the blood;
- 2-3-d week – the urine, stool;
- during the whole of the disease – the duodenal contents.



Blood should be taken from the first days of sickness and whole period of the fever in volume of 5-10ml on a nutrient medium containing a bile (Rappoport-medium).

The ratio between the **blood** and **nutrition** – **1:10** (because the blood has antibacterial properties destroys the microbe).

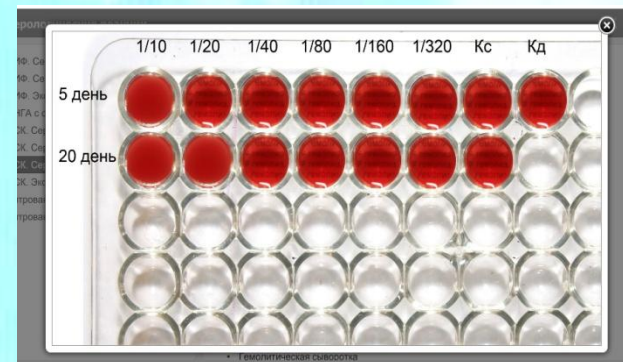


Stool-, bile-, urin-culture can be obtained on the nutrient medium called Ploskirev-medium.

2. Serological method (high-sensitivity):

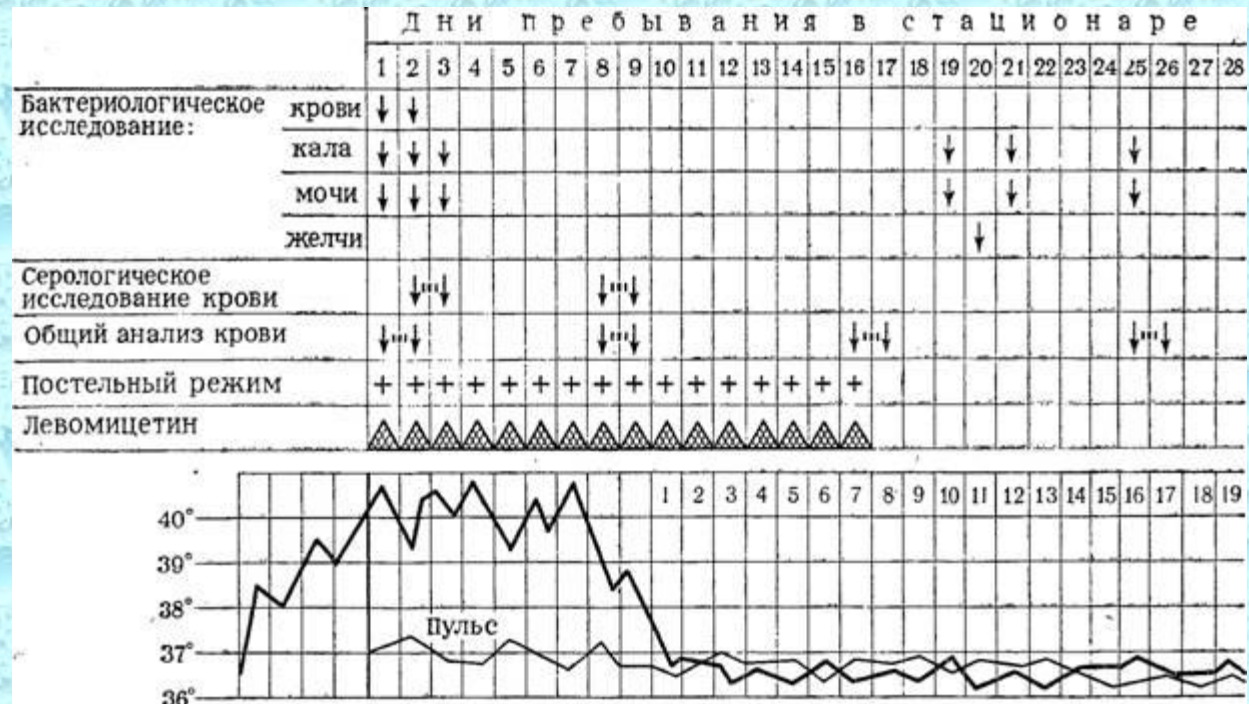
allow to detect specific antibodies in the blood or antigens in biosubstrate, should be performed by paired serums method; the diagnostic titer – increase of antibodies titer in 4 and more times.

- Vidal-test (*reaction of agglutination*) - detection of specific O – and H- antibodies-agglutinins in the blood of the patient using the appropriate antigens.
Positive results can be obtained with 8-9 days of illness (titer 1:200);
- RIHA (*reaction of indirect hemagglutination*) – with erythrocyte O - , H - and Vi-antigens;
- RIF (*reaction of immunofluorescence*), RIA;
- ELISA, PCR of different samples



Nonspecific diagnostic

- CBC:** the first 2-3 days of the disease is leukocytosis then leukopenia with a shift formula to the left (4-5-th day), uneosinophilia, thrombocytopenia, lymphocytosis, tendency to anemia, increased ESR;
- Urinalysis:** signs of “toxic kidney” (proteinuria, microhematuria, casts);
- Coprocytogram:** leukocytes (90 % from them monocytes);



Additional methods of diagnostics

1. Chest x-ray – to detect focal changes in lungs (pneumonia).
2. Radiography of the abdomen - if you suspect an intestinal perforation.
3. ECG, monitor heart activity - to diagnose myocarditis.
4. Spinal puncture - is performed when a positive meningeal signs, suspicion for the development of meningitis.
5. Ultrasound of the abdomen - helps to determine the size of the liver and spleen.



Diagnostic criteria for typhoid fever

- epidemiological **anamnesis** (contact with the sick person or carrier, using of unboiled water and contaminated food);
- **gradual onset** with a classic temperature curve;
- chills and sweating, hot dry **pale skin**;
- **bloating** (mainly in the classic version);
- tenderness on palpation of the abdomen and **positive Padalka-symptom**;
- presence of **watery stool** a yellowish or greenish color without pathological admixtures, transforming into **constipation**;
- tongue with **prints of teeth** on lateral surfaces;
- **enlarged liver and spleen**;
- symptoms of **intoxication** (headache, sleep disturbance and weakness);
- rash (roseola-like)** on the skin of the abdomen and thorax on the 8-9th day of illness;
- relative **bradycardia**.

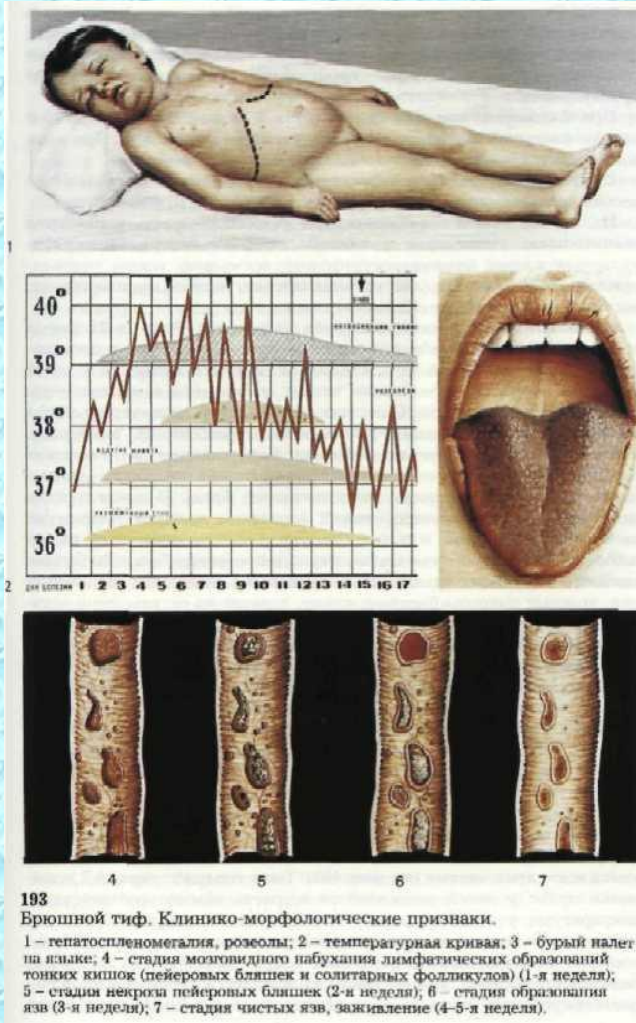
Complications

Specific:

- Intestinal bleeding - **1 - 2 %**
- Perforation of intestinal wall - **0,5 - 1,5 %**
- TISH - **0,5 - 0,7 %**
- Relapses (are more often in 2-3 weeks) - **7-9%**

Nonspecific:

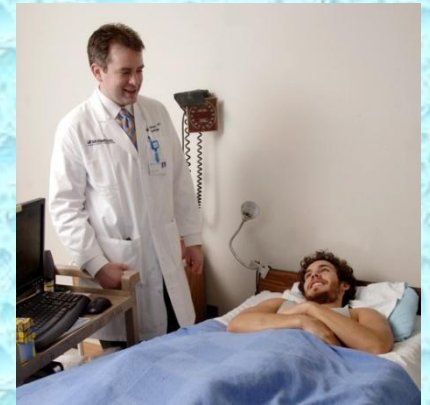
- pneumonia, osteomyelites, purulent arthritises,
- abscesses, pyelonephrites, endophthalmias,
- meningitises



Treatment

1. Bed rest regime (prevention of complications):

- strict bed regime - up to 6-7-th day of apyrexia;
- sitting position - from the 7-8-th day of apyrexia;
- allowed to walk - from the 10-11th day of normal body-temperature;



2. Diet №4 - the entire febrile period and up to 7-8-th day of apyrexia. Food must be mechanically and chemically sparing;



Allowed

Contraindicated

3. Specific therapy:

- antibiotics on the sensitivity of the microorganism (first choice);
- duration of a/b treatment – till 10-12-th days of normal body-temperature;
- gradual dose reduction.



Specific therapy

1. Chloramphenicol (first choice a/b):

- per os - in mild and moderate severity (without vomiting)
0,5-1,0 g × 4 t/d (daily dose - 2-4g);
- parenteral (i/m or i/v) – in severe cases and vomiting
1-2 g × 2 t/d (daily dose - 2-4g);

On the 2nd day of normalization of body temperature the dose is reduced gradually and should be given per os in **0,5 g × 4 t/d** 10 days of apyrexia.

2. Ampicillinum:

(effect is slower than of chloramphenicol, but relapse is less often)

- per os or parenteral (i/m) – **1-1,5 g × 4 t/d;**

3. Ciprofloxacin:

- per os - **0,5 g × 4 t/d;**

4. Trimethaprim – sulphamethoxazole:

- per os - **0,960 g × 2 t/d;**

5. Alternative remedies: ceftriaxone - **2 g/day**, ofloxacin - **0,8 g/day**, azitromicin - **0,25-0,5 g/day**, cefoxim - **0,4 g/day**.



For the treatment of a carrier:

- ampicillinum in a dose **40-50 mg/kg** per os 4 t/d within 4 - 6 weeks (efficiency 80 %).

Nonspecific (supporting) therapy:

- desintoxication therapy (PO or IV);
- sufficient hydration (PO or IV);
- hemostatic therapy (intestinal bleeding);
- glucocorticoids (TISH);
- antioxidants;
- antiferment drugs;
- probiotics, eubiotics.



Symptomatic therapy:

- analgetics, antipyretics, antiemetics;

Rules of discharging the patient out from the hospital:

Discharge the patient from the hospital is possible on 21-st day of normal temperature, but not before the 4-th week of illness.

1. Clinical recovery;
2. 2 negative copro- and urine-cultures (5, 10 day of normal temperature);
4. 1 negative bile-culture (12-14-th day of normal temperature)

Prophylaxis:

- immunity after **T.F.** is often intensive but the relapse appears in 20-25 %

The vaccines do **not form a complete protection**, but should be used:

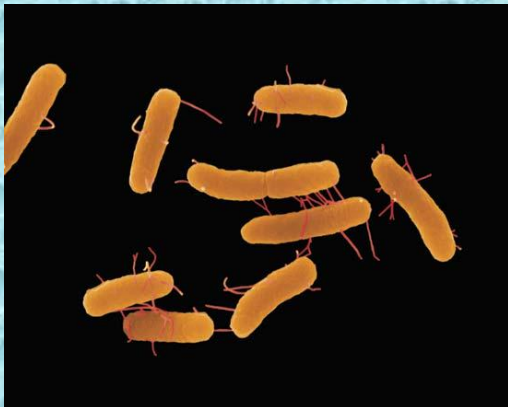
- at close family contact with patient or carrier;
- during outbreaks of **T.F.**
- before visiting the areas endemic on **T.F.**

Basic preventive measures:

- keeping of rules of personal hygiene;
- control of cooking and storage of nutrition;
- registration, treatment and discharge from work carriers of S.t;
- careful clearing of the drinking water;
- disinfection of the sewers;
- constant medical control for decreed risk groups in population

Paratyphoid A, B, C

Sign	Paratyphoid A	Paratyphoid B,C
General	Present O-; H-antigens, absent Vi-antigen	
Source of the infection	Antroponosis (patient, carrier)	Zooantroponosis (animals, domestic birds, patient, carrier)
Vidal-test	Negative may be seen “+” result seldom	Positive



Paratyphoid A, B, C

Symptoms	Paratyphoid A	Paratyphoid B, C
Incubation	Shorter than TF (about 8-19 days)	5-10 days
Beginning	Acute	Often sudden but may be acute
The first symptoms	Runny nose, cough, hyperemia of the face, injection of sclera, herpes	Chills, muscle pain, sweating, clinic of gastroenteritis
Temperature	Wave-like or remittent accompanied by chills and sweats	Wave-like, shorter than TF
Rash	Appears in the early stages (4-7 days of illness), polymorphic (consist of roseola, may be macula, papula, petechia), more plentiful than TF	Appears earlier (4-6-th day), plentiful, polymorphic basically roseola-like



Symptoms	Paratyphoid A	Paratyphoid B, C
Intoxication	Moderate, typhoid status is not developed	Moderate 3 -5 days
Hemogramm	Normocytosis, may be leukocytosis with lymphomonocytosis	Leukocytosis
Severity of clinic	Moderate	Different, depends on age and accompanied diseases More often is mild but may be moderate,
Complications	Intestinal bleeding, perforation, bronchopneumonia	Meningitis, meningoencephalitis, sepsis-like state
Relapses	Common	Rarely

Be calm and enjoy the life!

