



MEDICAL UNIVERSITY – PLEVEN
FACULTY OF MEDICINE
**DEPARTMENT OF INFECTIOUS DISEASES, EPIDEMIOLOGY,
PARASITOLOGY AND TROPICAL MEDICINE**

Lecture № 2

GASTROINTESTINAL INFECTIONS

TYPHOID FEVER
SALMONELLOSIS
SHIGELOSIS
COLIENTERITIS
CHOLERA
BOTULISM

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Typhoid fever – definition

- **Acute infectious disease with:**
 - ❖ **damage of the lymphoid structure of small intestine,**
 - ❖ **bacteremia,**
 - ❖ **cyclic course,**
 - ❖ **high and continuous fever,**
 - ❖ **marked intoxication,**
 - ❖ **hepatosplenomegaly,**
 - ❖ **typhoid status,**
 - ❖ **rash – rose colored spots,**
 - ❖ **frequent complications.**

Typhoid fever – introduction

- **Typhoid fever**, also known as **Typhoid**, is a common worldwide bacterial disease, transmitted by the ingestion of food or water contaminated with the feces of an infected person, which contain the bacterium *Salmonella enterica*, serovar Typhi.
- The name of "typhoid" comes from the neuropsychiatric symptoms common to typhoid and typhus (from Greek τῦφος, "stupor").

Typhoid fever – history

- The disease is known since ancient centuries.
- Hypocrite and Galen described disease similar to typhoid fever in soldiers during wars.
- The term “typhus” (smock) was given from Hypocrite because the changes in the consciousness.
- Typhoid fever was described as separate diseases during 18th century.
- The causative agent was discovered by Egbert during 1880.
- The serodiagnosis was discovered by Widal and Gruber (1896).

Typhoid fever – etiology

Salmonella typhi

This illustration depicts a three-dimensional (3D) computer-generated image of Salmonella serotype Typhi bacteria.

Source: CDC; March 26, 2014

Agent – **Salmonella enterica, serovar typhi**:

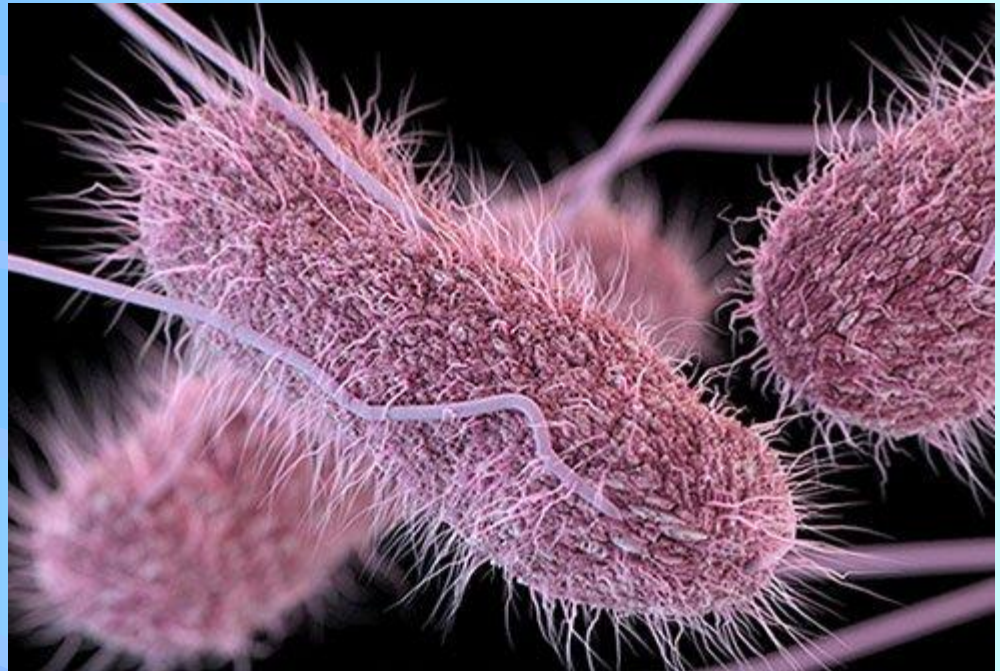
- ❖ Member of family Enterobacteriaceae.

- ❖ **Gram-negative** short bacillus that is motile due to its peritrichous flagella. Facultative anaerobe.

- ❖ The bacterium grows best at 37°C – human body temperature and on media containing bile.

- ❖ Resistant in the environment.

- ❖ Posses O (somatic), H (of the peritriches) and Vi (responsible for the virulence) antigens.

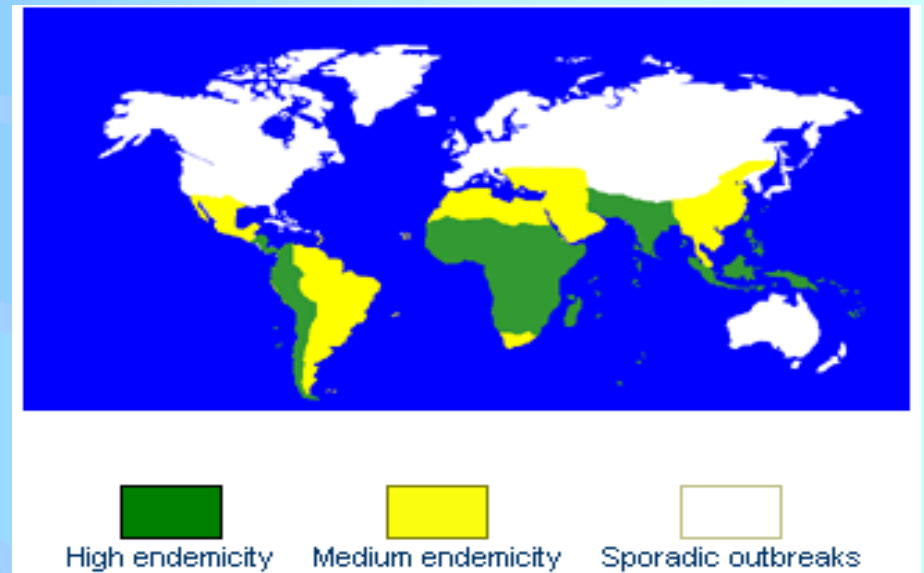


Typhoid fever – epidemiology

- **Antroponosis.**
- **Source of infection – only human** – patient or carrier (health, reconvalescent or chronic).
- **The agent is shared by feces, urine, saliva, sputum, vomit and breast milk.**
- A part of patients (up to 11%) becomes carriers from 1 to 30 years.
- **Rout of transmission – fecal-oral by direct contact, or fecally-contaminated food or water.**
- **Susceptibility** – to 40% of population, but in children, malnutrition and higher infective dose, it is higher.
- **Distribution – over the world**, depending of standard of life and hygiene.
- **Higher incidence during the summer and autumn.**
- Most often appears sporadically but contact, alimentary and water epidemics are possible.

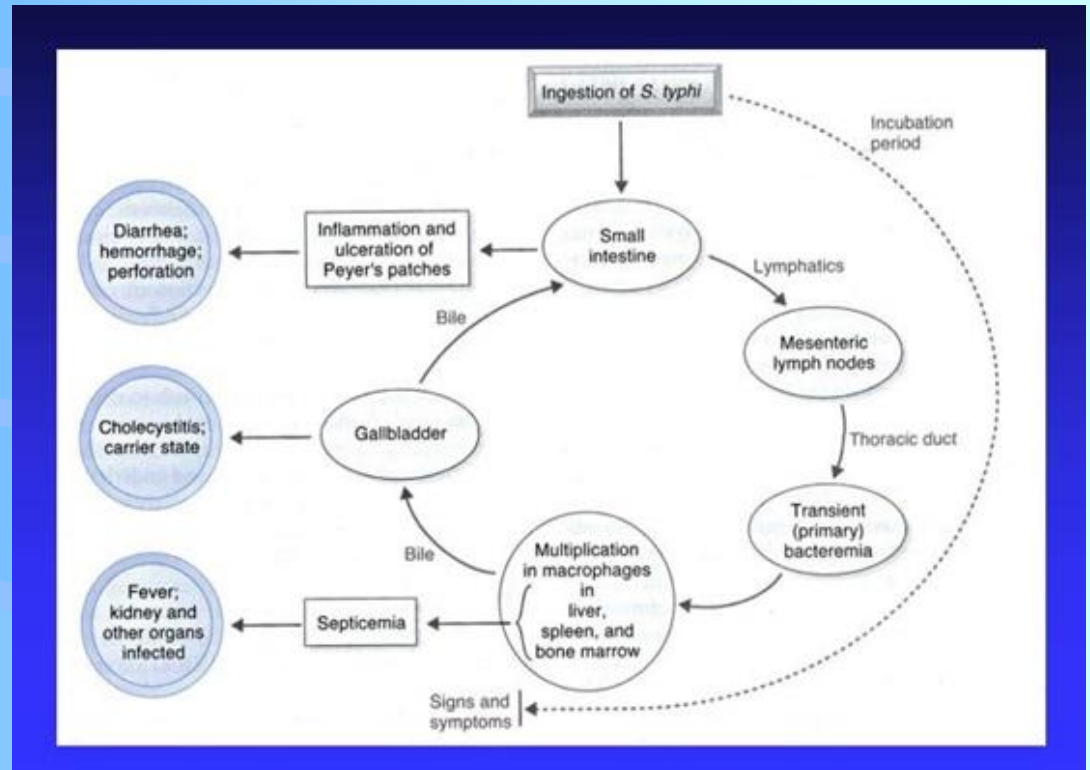
Typhoid fever – epidemiology

- **Annually 13 – 17 millions of cases with 600 000 deaths.**
- Endemic disease for India, Southern Asia, Africa, Latin and Central America.

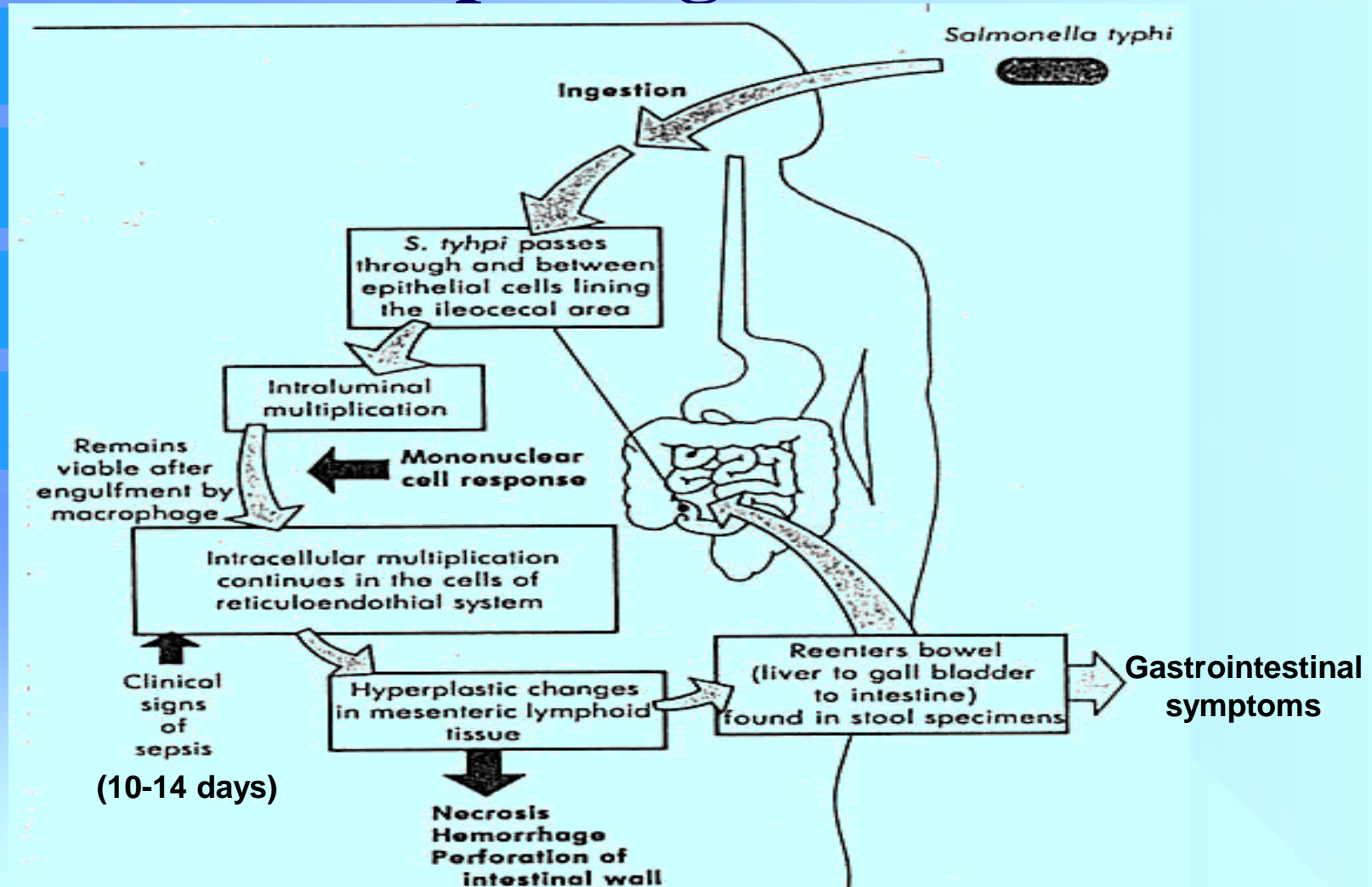


Typhoid fever – pathogenesis

- S. typhi pass through intestinal epithelial cells in ileocecal region, infect the regional lymphatic system, invade the bloodstream, and infect other parts of the reticuloendothelial system.
- Organisms are phagocytosed by macrophages and monocytes, but survive, multiply and are transported to the liver, spleen, and bone marrow where they continue to replicate.
- Second week: organisms reenter bloodstream and cause prolonged bacteremia; biliary tree and other organs are infected; gradually increasing fever likely from endotoxemia.
- Second to third week: bacteria colonize gallbladder, reinfect intestinal tract with diarrheal symptoms and possible necrosis of the Peyer's patches.



Typhoid fever – pathogenesis



Typhoid fever – ulcers



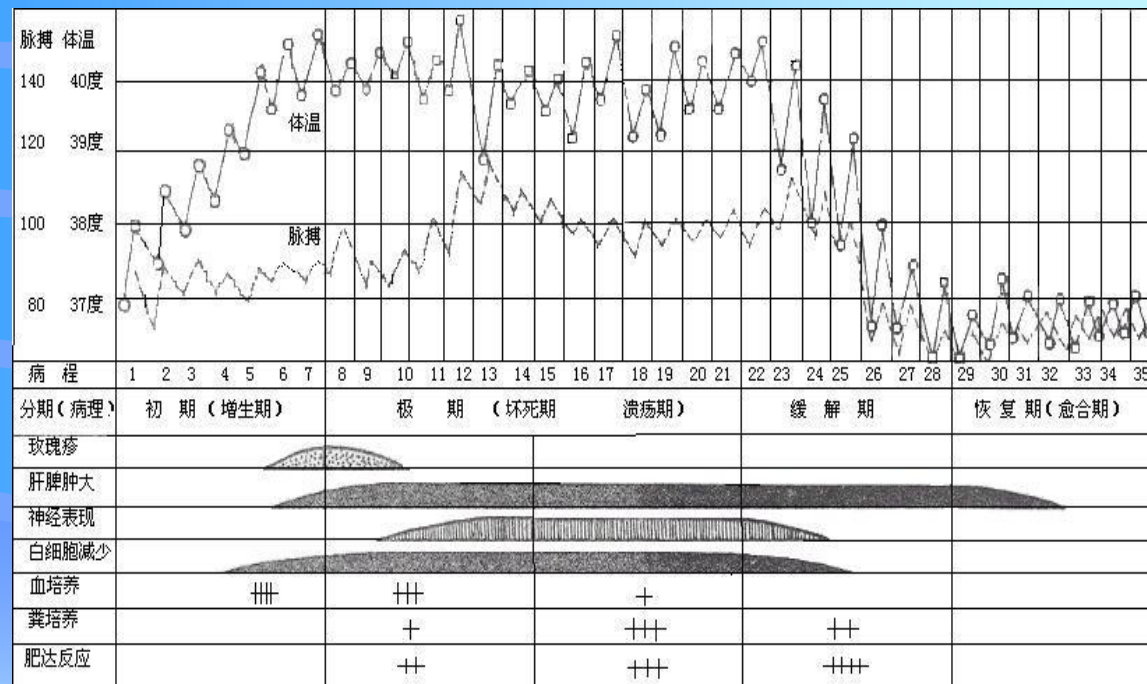
Typhoid fever – clinical features

1. **Incubation period – 9 to 14 days** (minimal 3 days, maximal 21 days).
2. **Initial period – to 1 week:**
 - ❖ **Gradual onset** with gradually increasing of temperature, headache, dizziness, disorders in sleeping.
 - ❖ Pains in the abdomen, lumbar region, joints.
 - ❖ Loss of appetite.
 - ❖ Pale face, dry lips, hollow-eyed-cheeked.
 - ❖ The tongue is whitely coated with red margins.
 - ❖ The throat – hyperemic or ulcerated on the tonsils.
 - ❖ To the end of first week – bronchitis, relative bradycardia, hepatosplenomegaly appear.
 - ❖ The abdomen is bloated with discomfort in lower region.

Typhoid fever – clinical features

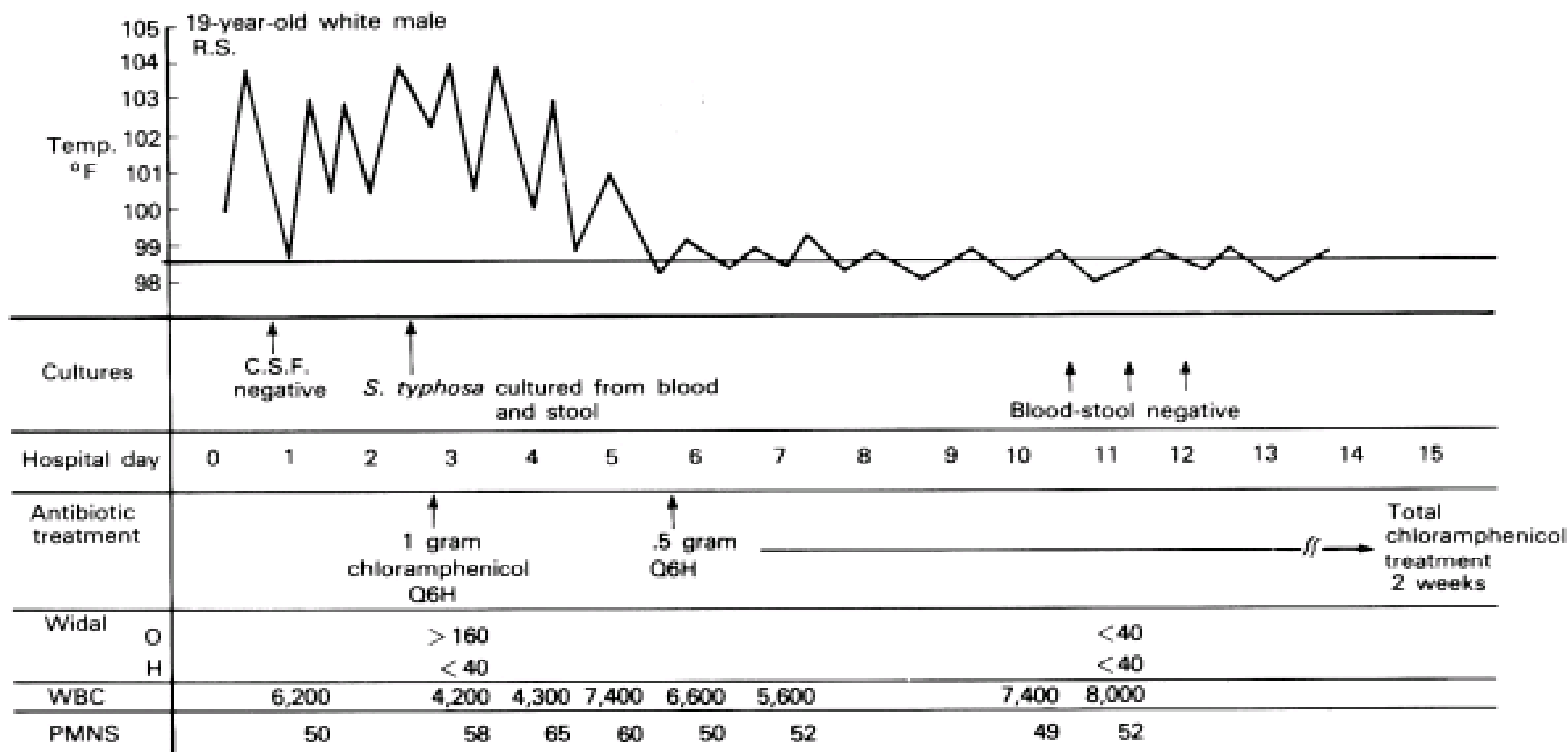
3. **Second and third week** – common complications or lethal outcome.
 - ❖ The intoxication is most severe.
 - ❖ Maximal temperature – up to 40-41 degrees of Centigrade within 1-2 weeks.
 - ❖ The patient is pale, confused, desoriented, with strong headache (**typhoid status**). It is possible appearing of meningoencephalitis, delir, stupor, comma.
 - ❖ On 8-11-th day rash appears – few number of rose colored spots on the abdomen, chest, axils. It is visible 3-4 days and disappears without marks.
4. **Fourth week** – intensity of symptoms decreases and patient recovers.

Typhoid fever – continuous fever



Events in a typical case of typhoid fever

CHART 23. — Course of typhoid fever of a previously immunized American patient in Vietnam



Source: Records of patients treated by Lt. Col. Kenneth W. Hedlund, MC, 85th Evacuation Hospital, Vietnam.

Typical rash – rose colored spots



Typhoid fever – clinical features

- ❖ Abdominal symptoms – variable: anorexia, nausea, vomiting, brownish coated tongue, spontaneous abdominal pains or palpatory abdominal tenderness, constipation, more rarely diarrhea – feces is as “pea-soup”. The diarrhea is common in children or immunocompromised.
- ❖ Hepatosplenomegaly with increased aminotransferases, in some cases moderate jaundice.
- ❖ Cardiovascular disorders – relative bradycardia, hypotension.
- ❖ Pulmonary disorders – pneumonia, pleural effusions.
- ❖ Urinary tract – oliguria, in sediment (+) albumin, bacteria, casts.

Typhoid fever – laboratory parameters

- Blood picture:
 - ❖ In the initial days – leucocytosis.
 - ❖ After the third day – leucopenia with relative lymphopenia, left shift, lympho- and monocytosis, lack of eosinophils, thrombocytopenia and anemia.
 - ❖ Gradually increased erythrocytes sedimentation rate (ECR)
- Increased aminotransphrases.
- Urine – (+) albumin, casts, bacteria.

Typhoid fever – clinical forms

- Abortive (rudimentary) – typical onset but to 5-6-th day temperature suddenly decreases and the patient recovers.
- Mild
- Moderate
- Severe – marked intoxication, typhoid status, continuous (3-4 weeks) high temperature (up to 40-41 degrees of Centigrade), pulmonary disorders, cardiovascular failure, hemorrhagic rash.
- Modern typhoid fever – acute onset, maximal temperature reaches within 3-4 days and in followed 2 weeks is intermittent. Jaundice and bronchitis are frequent but typhoid status is rare. Appearing of complications is early.
- Typhoid fever in children (especially immunized) – acute onset with symptoms of inflammation of upper respiratory tract, gastroenteritis, dehydration with dyselectrolytemia. The rash appears earlier.
- Typhoid fever in elder patients – severe course with low-grade fever, but severe typhoid status, rash and often pulmonary disorders.

Typhoid fever – complications

- Intestinal bleeding and perforation of ulcers to peritonitis.
- Myocarditis.
- Cholecystitis, pancreatitis, liver and spleen abscesses.
- Osteomyelitis.
- Acute renal failure.
- Thrombophlebitis.
- Gram-negative septic shock with multiorgan dysfunctions.
- Rhabdomyolysis.
- Otitis, parotitis.
- Pneumonia.
- Meningitis, meningoencephalitis, brain abscess.
- Mono- and polyneuritis.

Relapses and recidives – in up to 20% of cases.

Carriage – 3 to 11% of cases. More often in women and in patients with gallbladder diseases or gastrointestinal neoplasm.

Mortality rate – up to 1%.

Typhoid fever – diagnosis

- **Clinico-epidemiological.**
- **Microbiological** – isolation of agent on media:
 - ❖ blood culture – positive during the first week in more than 80% of cases;
 - ❖ Culture of bone marrow aspirate – more informative (performs when the hemoculture is negative);
 - ❖ Urine culture – during the 2-3rd week;
 - ❖ Bile culture;
 - ❖ Material derived from rose spot by skin biopsy.
- ❖ **Serological – Widal' test (positive to 6-8th days)**, Reaction of passive hemagglutination (RPHA), ELISA, immunofluorescent agglutination (IFA), PCR.

Typhoid fever – management and treatment

- *The aims of management are to eliminate the infection with antibiotics, to restore fluid and nutritional deficits, and to monitor the patient for dangerous complications.*
- **Obligate hospitalization; bed rest** to 6-7th day after normalizing of the temperature; **diet** – easy for utilization, with enough vitamins, liquid, with less cellulose – **especially during the 2-3rd weeks because of danger of intestinal perforation.**

Typhoid fever – management and treatment

- Fluoroquinolones – optimal for the treatment of typhoid fever!
- ❖ Relatively inexpensive, well tolerated and more rapidly and reliably effective than the former first-line drugs, viz. chloramphenicol, ampicillin, amoxicillin and trimethoprim-sulfamethoxazole.
- ❖ Attain excellent tissue penetration, kill *S. typhi* in its intracellular stationary stage in monocytes/macrophages and achieve higher active drug levels in the gall bladder than other drugs.
- ❖ Rapid therapeutic response, i.e. clearance of fever and symptoms in three to five days, and very low rates of post-treatment carriage.

Typhoid fever – etiological treatment

Table 1. Treatment of uncomplicated typhoid fever

Susceptibility	First-line oral drug			Second-line oral drug		
	Antibiotic	Daily dose (mg/kg)	Days	Antibiotic	Daily dose (mg/kg)	Days
Fully susceptible	Fluoroquinolone (e.g. ofloxacin)	15	5-7 [↑]	Chloramphenicol Amoxicillin Trimethoprim-sulfamethoxazole	50-75 75-100 8 (trimethoprim)-40 (sulfamethoxazole)	14 20 14
Multidrug-resistant	Fluoroquinolone	15	5-7	Azithromycin Third-generation cephalosporin	8-10 20	7 7-14
Quinolone-resistant	Azithromycin or Fluoroquinolone	8-10 20	7 10-14	Third-generation cephalosporin	20	7-14

Typhoid fever – etiological treatment

Table 2. Treatment of severe typhoid fever

Susceptibility	First-line oral drug			Second-line oral drug		
	Antibiotic	Daily dose (mg/kg)	Days	Antibiotic	Daily dose (mg/kg)	Days
Fully susceptible	Fluoroquinolone (e.g. ofloxacin)	15	10-14	Chloramphenicol Ampicillin Trimethoprim- sulfamethoxazole	100 100 8 (trimethoprim)- 40(sulfamethoxazole)	14-21 10-14 10-14
Multidrug-resistant	Fluoroquinolone	15	10-14	Ceftriaxone or Cefotaxime	60 80	10-14
Quinolone-resistant	Ceftriaxone or Cefotaxime	60 80	10-14	Fluoroquinolone	20	10-14

Typhoid fever – supportive treatment

- **Restoration of fluid-electrolytes dysbalance**
- **Corticosteroids** – Dexamethasone for CNS complications – should be immediately be treated with high-dose intravenous dexamethasone in addition to antimicrobials:
 - ❖ Initial dose of 3 mg/kg by slow i.v. infusion over 30 minutes
 - ❖ 1 mg/kg 6 hourly for 2 days.
 - ❖ Mortality can be reduced by some 80-90% in these high-risk patients.
- **Bioproducts** – Human albumin
- **Vitamins**
- **Immunotherapy** – Immunovenin and trimethoprim-sulfamethoxazole (in convalescent period to prevent relapse and recidive).

Typhoid fever – prevention

- **Specific:**
 - ❖ The injectable vaccine, (typhim –vi) contains purified Vi polysaccharide antigen derived from S.typhi strain ty 21, given as single subcutaneous or intramuscular injection
 - ❖ A live oral vaccine (typhoral) is a stable mutant of S.typhi strain Ty 21a lacking the enzyme UDP Galactose -4-epimerase. One capsule given orally taken before food, with glass of water or milk, on 1, 3, 5 days **(three doses)**. No antibiotics should be taken during the period of administration of vaccine.
 - ❖ **Vaccination can reduce risk of disease for travelers in endemic areas!**
- **Non specific** – active surveillance upon sanitary requirements in production of food products; preparation and cooking of foods; water supply.
- **Observation of convalescents to 1 year. Especially attention to epidemiologically risk groups!!!**

Salmonellosis – definition

- **Acute gastrointestinal infectious diseases, caused by Salmonella, with course of food born infections, more rare as sepsis or no intestinal visceral localizations.**

Salmonellosis – etiology

Causative agents – bacteria
belonging to genus
Salmonella,
family Enterobacteraceae.

Classification and Taxonomy of Salmonella (Confused)

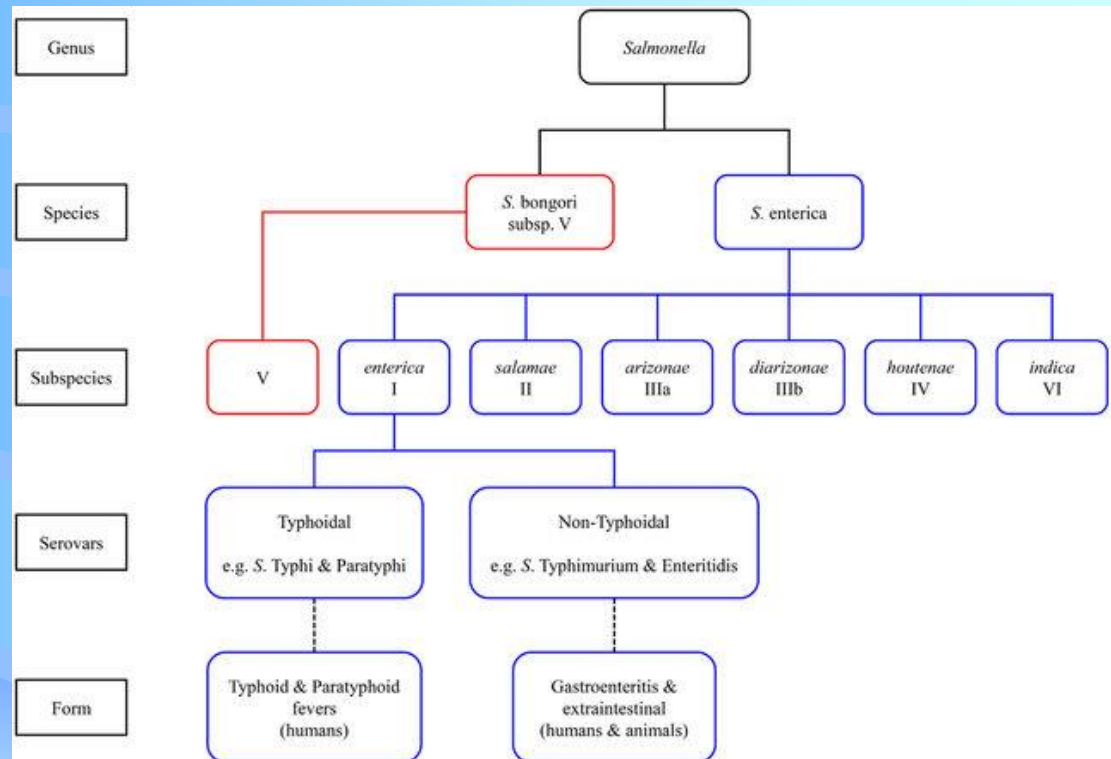
Formally, there are only
two species within this
genus: *S. bongori* and
S. enterica (formerly called
S. choleraesuis), which are
divided into

six subspecies:

I – *enterica*, II – *salamae*,
IIIa – *arizonae*, IIIb –
diarizonae, IV – *houtenae*,
V – *bongori*, VI – *indica*.

Classification of Salmonella species and subspecies

(Created by M. Martins)



Salmonellosis – etiology

- ❖ **Gram-negative** short rods that is motile due to peritrichious flagella. Facultative anaerobes.
- ❖ They grow on differentiating media.
- ❖ Resistant in the environmental.
- ❖ Possesses O (somatic), H (peritrichial) and Vi (responsible for the virulence) antigens.

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

Credit: Rocky Mountain Laboratories, NIAID, NIH

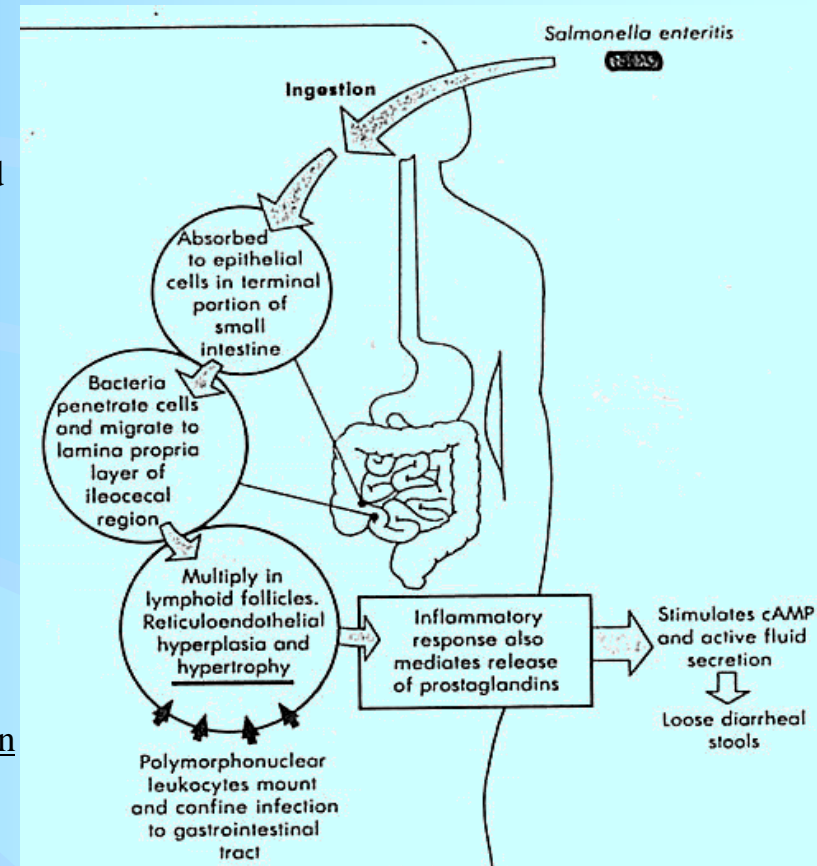


Salmonellosis – epidemiology

- **Zooanthroponosis.**
- Sources of infection – domestic and wild animals, birds and human (case or carrier).
- **Route of transmission – fecal-oral by direct contact, or fecally-contaminated food or water.**
- Most often – after consumption of eggs, meat, fish, milk and meat products that are primarily contaminated from animals or in process of cooking.
- Possible contamination by direct contact person-to-person with patient or carrier.
- Possible aerosol mechanism of contamination.
- Nosocomial infections are often especially in wards for neonates.
- All individuals are susceptible but most often children (especially neonates); more common in warm months.
- Sporadically or often as outbreaks in restaurants, fast-food places, hospitals, kindergartens, military groups.
- The incidence increases in recent years including developed countries.

Salmonellosis – pathogenesis

- After ingestion salmonella enter into the stomach where they are destroyed and release endotoxin, that provokes gastritis and intoxication.
- The survived salmonella reach to the small intestine where they attach to the epithelial cells (enterocytes) and by bacterially induced phagocytosis enter into the cells. By this mode they avoid destroying by polymorph nuclear cells.
- Transcellularly (cell by cell) they reach subepithelial layer – lamina propria, where they penetrate into the macrophages where they multiply and by them reach to the reticuloendothelial system. Some bacteria reach to the polymorph nuclear cells that destroy them and big amount of endotoxin releases.
- When the gut barrier penetrate, bacteria reach to the regional lymph nodes and the blood. **Bacteriemia in salmonellosis is common, but transient and early. Only in generalized (septic) forms of disease it is massive and continuous.**
- The major pathogenic factor is endotoxin. It activates the prostaglandin synthesis in enterocytes. The prostaglandins stimulate adenylatcyclase. This leads to increased secretion of cyclic adenosine-mono-phosphate (c-AMP), that stimulates abnormal secretion of water and electrolytes in intestinal lumen. In result – diarrhea, dehydration, demineralization, metabolic acidosis, in severe cases hypovolemic shock appear.
- The endotoxin activates cytokines, that lead to fever, increased vascular permeability, supression of phosphorilation, increased intensity of intracellular anaerobic glycolysis, microcirculatory and clothing disorders.



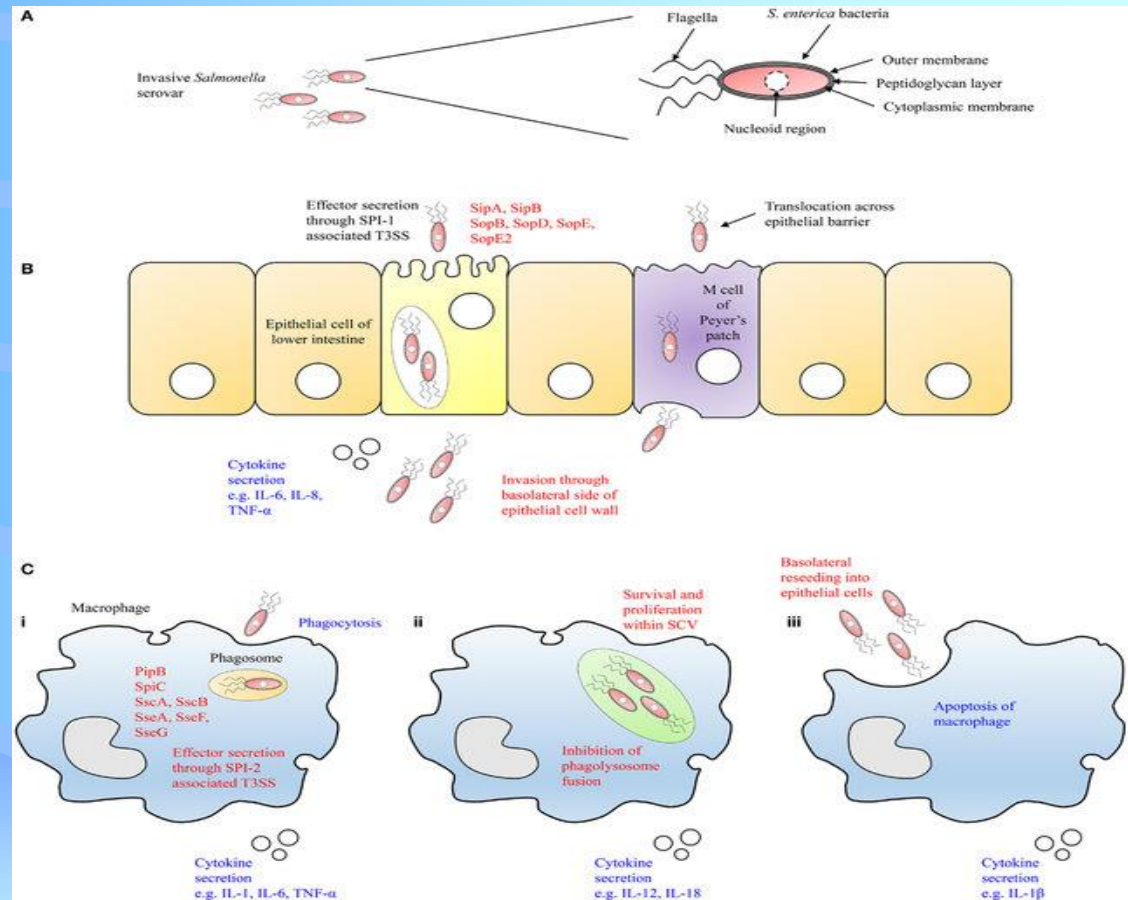
Salmonellosis – pathogenesis

- A) *The complex membrane structure of Salmonella allows it to survive until reaching the epithelial cell wall of the host in the lower intestine.*
- B) *Salmonella then translocate across M cells of Peyer's patches or actively invade epithelial cells by the secretion of effector proteins through the SPI-1 encoded T3SS-1.*
- C) (i) *After crossing the epithelial barrier, Salmonella are engulfed by proximal macrophages that will secrete effector proteins into the cytosol of the cell via the SPI-2 encoded T3SS-2 and prevent fusion of the phagosome with the lysosome.*
 (ii) *Within the SCV, Salmonella will proliferate resulting in cytokine secretion by the macrophage.*
 (iii) *Finally, the macrophage will undergo apoptosis, and Salmonella will escape the cell to basolaterally reinvade epithelial cells or other phagocytic cells of the host innate immune system.*

Schematic illustration of the infection of epithelial cells of the lower intestine and macrophages by Salmonella is shown.

Source: [D. Hurley](#), [M. P. McCusker](#), [S. Fanning](#) and [M. Martins](#).

Salmonella–host interactions – modulation of the host innate immune system.
 Front. Immunol., 07 October 2014



Salmonellosis – clinical forms – criteria

- **Mode of contamination:**
 - ❖ Alimentary toxiiinfection – ingestion of both bacteria and endotoxin – short incubation period, fulminant course with severe intoxication with marked nausea and vomiting (gastritis, gastroenteritis); enterocolitis are rare.
 - ❖ Salmonella infection – most often person-to-person. Longer incubation period, gradual onset, more slowly increasing of intensity of symptoms, with prevalent diarrhea than vomiting. That is enterocolitis.
- **Localization:**
 - ❖ Localized gastrointestinal forms – gastritis, enteritis, gastroenteritis, enterocolitis (most common in infants), colitis and gastroenterocolitis.
 - ❖ Generalized: septic – high and continuous fever, severe intoxication, hepatosplenomegaly, jaundice, damage of kidneys, hemorrhagic syndrome, positive hemo- and uroculture. Septicopiemic – metastatic foci in other organs (arthritis, meningitis, pleuritis etc.)
 - ❖ Extraabdominal localizations – abscess in brain, spleen, soft tissues, lung; thyreoiditis, parotitis, osteomyelitis, pyelonephritis, epiglottitis etc.
 - ❖ Superinfection – salmonellosis in immunocompromised (diabetes, collagenosis, neoplasma, AIDS).
- **Severity** – mild, moderate and severe.

Salmonellosis – clinical manifestations of localized forms

- **Incubation period** – 6-48 hours in salmonella toxoinfection and 2-8 days in salmonella infection.
- **Acute onset** – adynamia, headache, myalgia, arthralgia.
- **Nausea, vomiting, epigastral pain, periumbilical pain or in ileocaecal region.**
- **Diarrhea** – increased number of defecations of liquid yellowish-greenish feces with admixtures of mucus (in infants possible and blood).
- **Dehydration** – hypovolemia, hypoelectrolytemia. There are 3 grades of dehydration.

Salmonellosis – laboratory parameters

- Leucocytosis (to extremely increased number of leucocytes in generalized forms) with left shift, increased percent of polymorph nuclear cells.
- Hemoconcentration – increased hematocrit and hemoglobin.
- Decreased levels of electrolytes.
- Metabolic acidosis.
- Increased nitrogen parameters (blood urea nitrogen, creatinine).
- Hypoproteinemia.

Salmonellosis – complications

- In infants – paralytic ileus, neurotoxicosis, myocarditis, toxic hepatitis.
- In elder – acute renal failure, shock (hypovolemic, endotoxic, mixed), thrombophlebitis.
- Secondary bacterial infections – otitis, pneumonia etc.
- Prognosis – good in localized forms (mortality rate up to 2%); **serious in generalized forms (mortality rate up to 50%).**

Salmonellosis – diagnosis

- Clinical and epidemiological – group of cases in same time, consumption of suspicious food, acute onset with marked intoxication, diarrhea – liquid greenish feces with mucus, fast dehydration.
- Microbiological – culture of feces, urine, vomit, parts of food, blood, cerebrospinal fluid etc.

Salmonellosis – differential diagnosis

- Other gastrointestinal infections –
 - shigellosis,
 - enteritis with viral etiology,
 - coli enteritis,
 - like-cholera form of salmonellosis,
 - cholera.
- Acute illnesses
with non infectious etiology –
 - acute appendicitis,
 - ileus,
 - mesenteric thrombosis,
 - invagination,
 - chronic ulcero-haemorrhagic colitis,
 - Chroon-disease,
 - neoplasmas of the gut;
 - posterior myocardial infarction,
 - perforation of stomach or duodenal ulcer;
 - food poisoning with staphylococcal etiology,
 - alimentary mistakes e. o.

Salmonellosis – management and treatment

- Ambulatory treatment in mild forms without epidemiological risk; hospitalization of severe cases or that with epidemiological risk.
- **Diet.**
- **Etiologic treatment** – only in gastrointestinal, septic and extraabdominal forms; **in severe forms. Antibiotic of choice** – ciprofloxacin, in infants – cephalosporin 3rd generation, aminoglycosides – amikacin (**no gentamycin – high resistance!!!**) **Alternative** – cephalosporin 1st and 2nd generation, Nalidix acid, trimethoprim-sulfamethoxazole.
- **Supportive treatment** – rehydration, corticoids in severe forms, management of complications – gut palsy, acute renal failure, cardiac disorders, hypovolemic shock.
- **Symptomatic treatment** – antidiarrhoica.
- **There are not specific prophylaxis.**

Shigellosis – definition

- **Acute infectious disease with fecal-oral route of transmission that are caused by bacteria, belonging to genus *Shigella*, with manifested intoxication and colitis.**

Shigellosis – etiology

Causative agents –

43 serotypes in 4 subgroups

– Shigella dysenteriae,

S. flexneri, S. boydii, S. sonnei.

- ❖ Belong to family Enterobacteriaceae
- ❖ Gram-negative no motile rods, facultative anaerobes.
- ❖ They grow on simple media.
- ❖ Resistant in the environmental.
- ❖ Possesses O, but some serotypes and K antigens.
- ❖ Shigella dysenteriae produces exotoxin.

S. flexneri, a bacteria associated with shigellosis.

Source: Trivedi MK, Branton A, Trivedi D, Nayak G, Shettigar H, et al. (2015) Antibigram Pattern of Shigella flexneri: Effect of BioField Treatment. Air Water Borne Diseases 3: 122.
doi:10.4172/2167-7719.1000122



Table 1. Virulence factors of Shigella and their mechanisms of action

VIRULENCE FACTORS	MECHANISM OF ACTION
Invasion plasmid antigen	Mediated attachment to, and penetration of, mucosal epithelial cells Mediate escape from phagocytic vesicles
Intercellular spread proteins	Mediated attachment to cytoskeleton proteins, facilitate transfer of bacteria to adjacent cells through membrane proteins
Shiga toxin – heat labile, produced by <i>S. dysenteriae</i>	Inactivates 60S ribosomal subunit of mammalian cell ribosomes, thus inhibiting protein synthesis

Shigellosis – epidemiology

- **Anthroponosis – source of infection – case or carrier.**
- **Fecal-oral route of transmission by direct contact, or fecally-contaminated food or water.**
- Factors for transmission – contaminated fingers, foods, water, flies.
- All individuals are susceptible (contagious index up to 30%) but most often children (especially 2 to 6 years old).
- More common in warm months.
- Sporadically or often as outbreaks or epidemics.
- Nosocomial infections are common.
- Facilitating factors – pureness, bed hygiene.

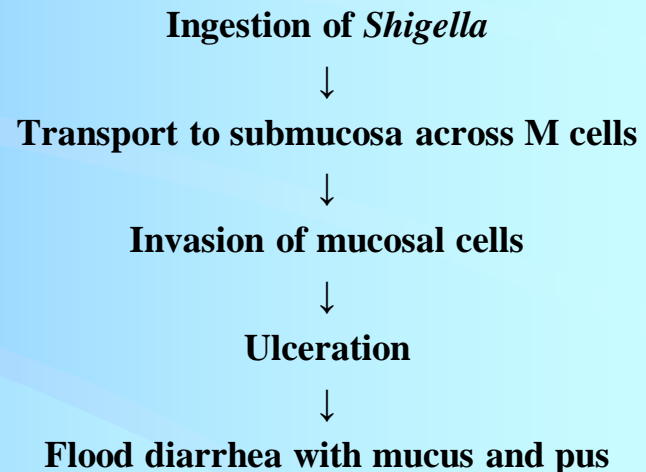
Shigellosis – pathogenesis

- **Shigella are the most virulent intestinal pathogens.**
- Minimal infective dose – 100 bacterial cells; *Shigella dysenteriae* – 10.
- Portal of entry – oral cavity.
- After ingestion through the stomach they reach to distal small intestine where invade intestinal mucosa and penetrate cell by cell.
- **Bacteremia is casuistic.**
- **Toxins are the most important factor for virulence.**

Shigellosis – pathogenesis

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Pathogenesis is as follows:

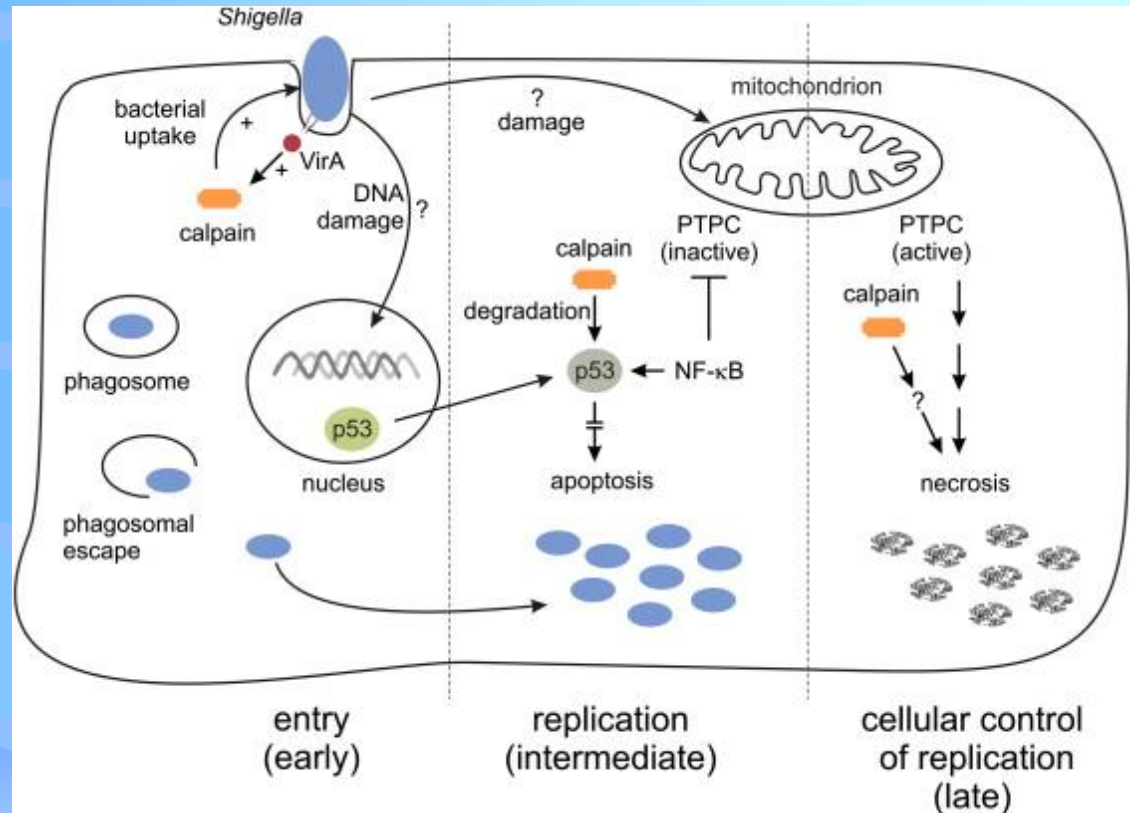


Shigellosis – pathogenesis

Upon contact with epithelial cells, *Shigella* injects via its type III secretion system several proteins that trigger the uptake of the bacteria. Bacterial VirA activates calpain that supports the uptake of *Shigella*. Uptake is accompanied by massive DNA damage followed by the upregulation of p53. Under these conditions, p53 would activate apoptotic cell death to destroy the damaged cell. VirA-activated calpain, however, degrades p53 and thus keeps the cell alive to allow replication of *Shigella* in the cytosol of the host cell for some time. NF- κ B is activated in *Shigella*-infected cells and may play a dual role: in the presence of p53 it supports apoptosis, but since p53 is degraded, NF- κ B transiently protects the mitochondria from severe damage that would lead to the breakdown of the membrane potential by the opening of the permeability transition pore complex (PTPC). Ultimately, sustained calpain activity and PTPC opening lead to the host cell undergoing a necrotic type of cell death that limits the replication of *Shigella*.

Figure 2. VirA-Activated Calpain Controls *Shigella* Entry and Host Cell Survival.

Source: Cell Host & Microbe 2012 11, 219-221 DOI: (10.1016/j.chom.2012.02.004)



Shigellosis – clinical features

- Incubation period – 2-3 (1-7) days.
- Uncommon prodromal period – headache, adynamia, loss of appetite, low grade fever.
- **Most common is acute onset with fever, weakness, abdominal cramps; in children seizures and changes in consciousness are possible.**

Shigellosis – clinical features

- **Period of manifested clinical symptoms:**
 - ❖ **Intoxication**
 - ❖ **Diarrhea** – in the onset (enteric phase) feces is liquid in big amount, but colitis appears – small amount of feces with admixtures of blood and mucus. Common is so called “dysenteric sputum” – mix of blood, mucus and pus without fecal material.
 - ❖ **Abdominal pains** – colic and cramps in left lower region before defecation. In the following hours tenesmes appear (false posives for defecation).
 - ❖ **Dehydration is not marked.**
- Short convalescent period.

Shigellosis – clinical forms

- Typical

- ❖ Mild

- ❖ Moderate

- ❖ Severe

- Atypical

- ❖ Abortive

- ❖ Hypertoxic – serious prognosis.

- Chronic – uncommon.

Shigellosis – complications

- In infants – intestinal palsy or ileus, intestinal invagination, perforation, prolapsed rectum, toxicosis and neurotoxicosis, hemolytic-uremic syndrome (hemolytic anemia, uremia, thrombocytopenic purpura).
- In adults – acute renal failure, paralytic ileus, shock (toxic and hypovolemic), perforation of gut.

Shigellosis – diagnosis

- Clinical and epidemiological.
- Microbiological – culture of feces on selective and differentiated media.
- Serologic – without significance for practice.

Shigellosis – differential diagnosis

- **Salmonellosis** – their “like-shigellosis” form – the abdominal pain is without character of tenesmus, the stools are with bad smell and without blood’s admixture.
- **Colenteritis**, caused by EHEC – the general toxic and nervous symptoms, the fast dehydration are leading.
- **Cholera** – it is without abdominal pain. The dehydration is massive and leading to hypovolemic shock.
- **Amebiasis** – gradual onset, stool is like “raspberry jelly”. Often has been occurred hepatosplenomegaly.
- **Other parasitosis** – balantidiasis, lamblasis – the admixtures from blood in feces are seldom.
- **Other non-infectious illness with hemolytic syndrome** – chronic ulcerohemorrhagic colitis, intestinal invaginations, mesenterial thrombosis, neoplasms of the colon etc.
- **Most responsible is differential diagnosis between shigellosis in the children and invagination.**

Shigellosis – management and treatment

- **Bed rest** – in acute stage and at severe course; ambulatory in mild forms and without epidemiological risk; hospitalization – at severe course and with epidemiological risk.
- **Diet.**
- **Etiologic treatment:** first line – ciprofloxacin, in infants – cephalosporins third generation, aminoglycosides (amikacin). Alternative – cephalosporins first and second generation, Nalidixic acid, trimethoprim-sulfamethoxazole. Course of treatment 5-7 days.
- **Supportive treatment** – rehydration, detoxification, management of complications – intestinal paralysis, acute renal failure, cardiac disorders, hypovolemic shock.
- **Symptomatic drugs.**
- Convalescents working in risk fields need of observation to 3 months. Specific prophylaxis not exists.

Escherichia coli infections – definition

- Although most strains of E. coli are commensals of the intestinal tract, some have acquired virulence factors that have placed them among the leading causes of diarrhoea, particularly in the developing world.
- **Acute intestinal infectious diseases prevalently in infants that are caused by enteropathogenic Escherichia coli (EPEC), with enteritis or enterocolitis, marked intoxication and unbalance of fluids and electrolytes.**

Escherichia coli infections – etiology

- Causative agents – **Escherichia coli**
 - ❖ Belong to family Enterobacteriaceae
 - ❖ Gram-negative motile peritrichial rods.
 - ❖ They grow on simple media.
 - ❖ Resistant in the environmental.
 - ❖ Some strains form capsule.
 - ❖ Possesses O, H and K antigens.

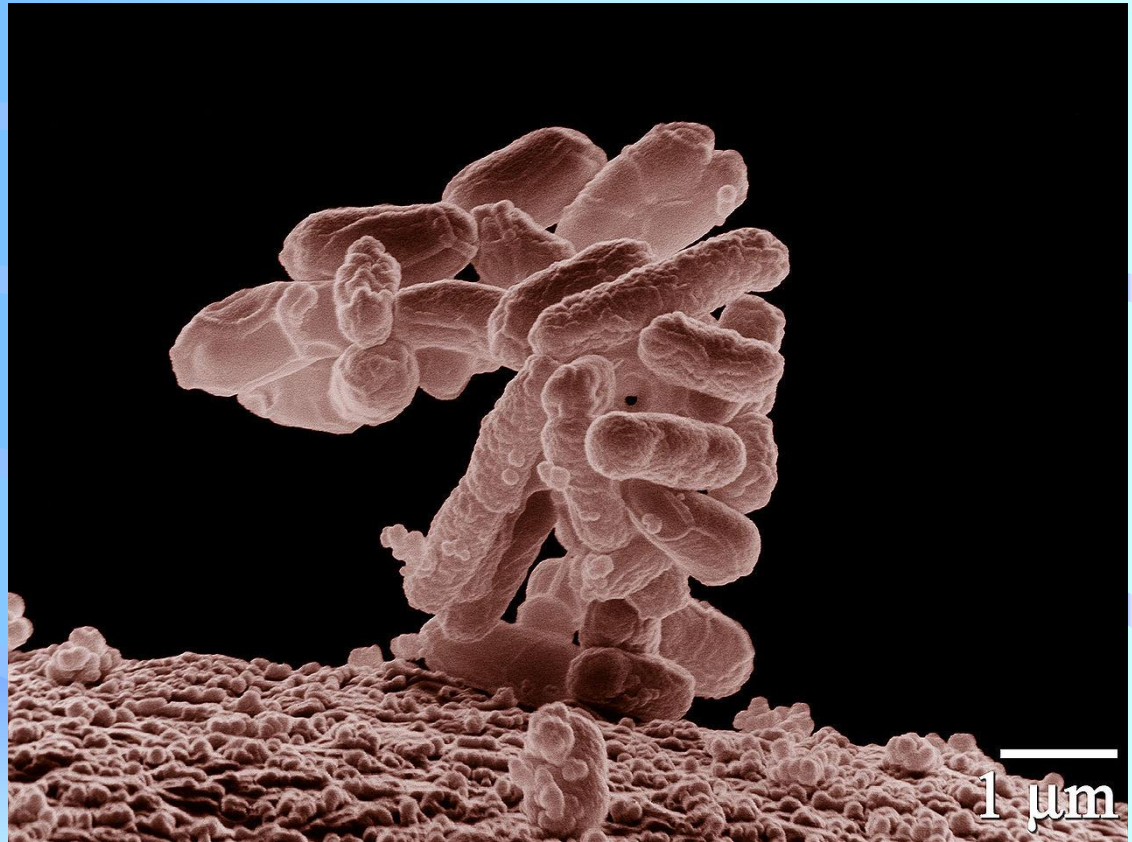
Escherichia coli infections – etiology

Low-temperature electron micrograph of a cluster of E. coli bacteria, magnified 10,000 times. Each individual bacterium is oblong shaped.

Source: Photo by Eric Erbe, digital colorization by Christopher Pooley, both of USDA ([United States Department of Agriculture](#)), ARS, EMU. - ARS Image Gallery Image Number **K11077-1**

Causative agents – **Escherichia coli**

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Escherichia coli – determinants of pathogenicity

- **Adhesion factors.** Many pathogenic strains of *E. coli* develop the ability to colonize the epithelial lining of the gastrointestinal and urinary tract.
- **Enterotoxins** are implicated in many gastrointestinal disorders caused by pathogenic strains of *E. coli*.
- The enterotoxigenic strains of *E. coli* (ETEC) produce two types of enterotoxins:
- **Heat-labile toxins** (LT-I and LY-II are closely related to cholera toxin both structurally and functionally. These toxins, which are plasmid-coded, stimulate intestinal guanylate cyclase.
- **Heat-stable toxins** (ST) bind to cellular guanylate cyclase and caused an increase in the intracellular levels of cyclic guanosine monophosphate (cGMP), which in turn deregulates ion transporters and causes effects similar to those of LT. The genes coding for LT, ST and adhesion factors are carried by plasmids.
- Enterohemorrhagic (verotoxin-producing) *E. coli* (EHEC, VTEC). The most virulent uropathogenic strains of *E. coli* produce **hemolysin**, which have general cytotoxic properties.
- **Antiphagocytic capsule.** The K₁ strain of *E. coli*, which is involved in 80% of cases of neonatal meningitis, has an antiphagocytic capsule. The K₁ sialic acid homopolymer capsule, which does not activate complement (and therefore, does not induce opsonization), seems to be antigenically cross-reactive with the human adhesion molecule N-CAM. Newborns and infants are tolerant to N-CAM, which may explain their lack of reactivity against the K capsule determinants.

Escherichia coli infections – etiology

- Groups E. Coli:
 - ❖ Enteropathogenic (EPEC)
 - ❖ Enteroadherent E. coli (EAEC)
 - ❖ Enterotoxigenic E. coli (ETEC) – produce a cholera-like enterotoxin
 - ❖ Enteroinvasive E. coli (EIEC)
 - ❖ Enterohemorrhagic E. coli (EHEC)

Escherichia coli infections – pathogenesis (generally)

- Portal of entry – oral cavity. Agents penetrate through the stomach acidity and reach to the small intestine. In some cases they get over the barrier of intestinal mucosa, reach to the mesenterial lymph nodes and the blood and hematogenically spread to different organs where provoke secondary inflammation (sepsis).
- Endogenous activation of previously existing latent focus is possible.

Escherichia coli infections – pathogenesis (depending on group of E. coli)

Three main “virulence types” of pathogenic E. coli have been associated with gastrointestinal disease:

- Enterotoxigenic E. coli (**ETEC**) causes traveler diarrhea and other types of diarrhea in patients of all ages. The diarrhea usually is rapid in onset, profuse and self-limiting, but it can follow a more serious course in infants. The pathogenesis of diarrhea caused by ETEC strains has two main steps:
 - Intestinal colonization (mediated by CFA-I and CFA-II – capsule antigens – K antigens)
 - Hypersecretion of water and electrolytes caused by ST or LT enterotoxins, or both.
- Enteropathogenic E. coli (**EPEC**), which cause diarrhea affect mostly children and infants and frequently isolated in developing countries. The pathogenesis of diarrhea caused by EPEC strains is not completely understood, however it is known that EPEC strains adhere tightly to the surface of epithelial cells, destroying microvilli without overtly invading mucosal cells. The adherence properties seem to depend on a plasmid known as EPEC adherence factor.
- Enterohemorrhagic E. coli (**EHEC**) can cause common diarrhea, hemorrhagic colitis (a unique type of self-limiting, profuse, bloody diarrhea), and the hemolytic-uremic syndrome (acute renal failure, thrombocytopenia, and microangiopathic hemolytic anemia).
- Serotype O₁₅₇:H₇ is commonly involved in the most severe forms of disease and has been shown to produce a Shiga-like toxin, also designated as verotoxin or verocytotoxin because it is cytotoxic to *vero cells* in culture.

Rarer strains of pathogenic E. coli have been isolated from infants and children with diarrhea, including:

- 1) Enteroinvasive E. coli (**EIEC**), which resemble *Shigella* in their pathogenicity and general properties, but do not produce a Shiga-like toxin.
- 2) Enteroadherent E. coli (**EAEC**) produce a special type of fimbriae that may allow the bacteria to attach to the intestinal mucosa.

Escherichia coli infections – clinical features

- Incubation period – 3-7 (1-22 days).
- Acute onset with fever, loss of appetite, agitation, diarrhea, vomiting.
- Diarrhea – frequent defecations (up to 20 per day) with watery yellow or yellowish-greenish stool with mucus, rarely droops of blood. The abdomen is bloated.
- Marked intoxication – the children are flaccid, dehydrated, with loss of body weight.

Escherichia coli infections – clinical forms

- Mild
- Moderate
- Severe – with fever, intensive diarrhea and vomiting, progressing dehydration, bloated abdomen with flaccid peristalsis to intestinal paralysis and paralytic ileus.
- Colenteritis caused by ETEC – 70-80% of so called diarrhea of travelers.
- Colitis
- Sepsis
- Hemorrhagic-necrotic colitis.

Escherichia coli infections – complications

- Common, especially in infants – pneumonia, otitis, pyelonephritis, arthritis, secondary viral and bacterial infections, neurotoxicosis, ileus, toxic hepatitis.

Escherichia coli infections – diagnosis

- Clinical and epidemiological.
- Microbiological – culture of feces, more rare vomit, blood, urine, cerebrospinal fluid (CSF) on selective and differentiating media.
- Serologic – without significance for practice.

Escherichia coli infections – differential diagnosis

With other gastrointestinal infections as:

- salmonellosis,
- shigellosis,
- enterocolitis with viral etiology,
- cholera – more seldom.

Escherichia coli infections – management and treatment

- **Hospitalization.**
- **Diet.**
- **Etiologic treatment:** first line – ciprofloxacin, in infants – cephalosporins third generation, aminoglycosides (amikacin), trimethoprim-sulfamethoxazole, carbapenems.
- **Supportive treatment** – rehydration, decontamination, management of complications – intestinal paralysis, acute renal failure, hypovolemic shock.
- **Symptomatic drugs.**
- **Specific prophylaxis not exists.**
- **Non specific prophylaxis – strong control of preventive measures in risk wards and pediatric sectors. Attention to mothers and staff.**

Cholera – definition

- **Very dangerous infectious disease,**
with profuse diarrhea, progressive
dehydration, hypotension,
hypo electrolytemia tended to epidemic
and pandemic spreading.

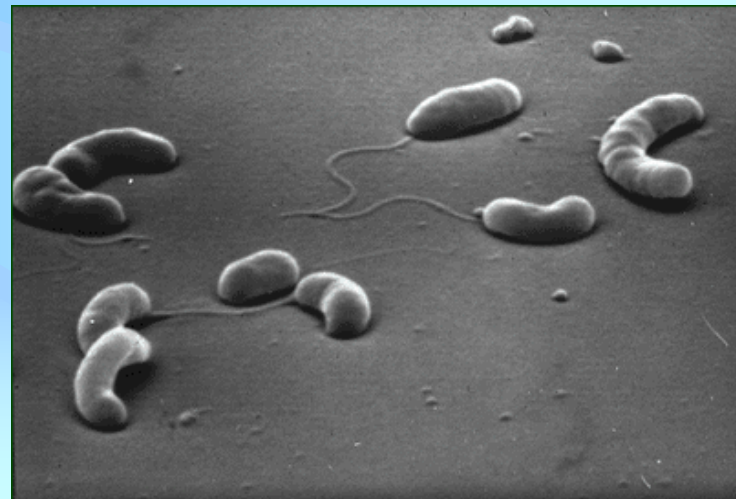
Cholera – historical data

- The disease is known in India and China since 2 000 years.
- It is endemic in Asia – Southwestern region, India and Bangladesh; since 1960 – endemic foci in Africa and Latin America.
- Since 1817 – 7 pandemics. The last is since 1961 in Indonesia, since 1971 in Africa and Europe and new wave in 1991 – spreading in Peru and other countries in Latin America.
- The causative agent has been discovered in 1854 by Italian scientist Filippo Pacini and rediscovered by Robert Koch in 1884.

Cholera – etiology

- *Vibrio cholerae*, called in 1965 *Vibrio cholerae* Pacini 1854.
- Gram-negative highly motile without producing of capsule or spores. View as comma with long flagella. Resistant in environmental especially in water and low temperatures.
- Posses 2 antigens – flagellar heat labile H antigen (non specific, same for all vibrios) and heat stable somatic O antigen – specific for each species.

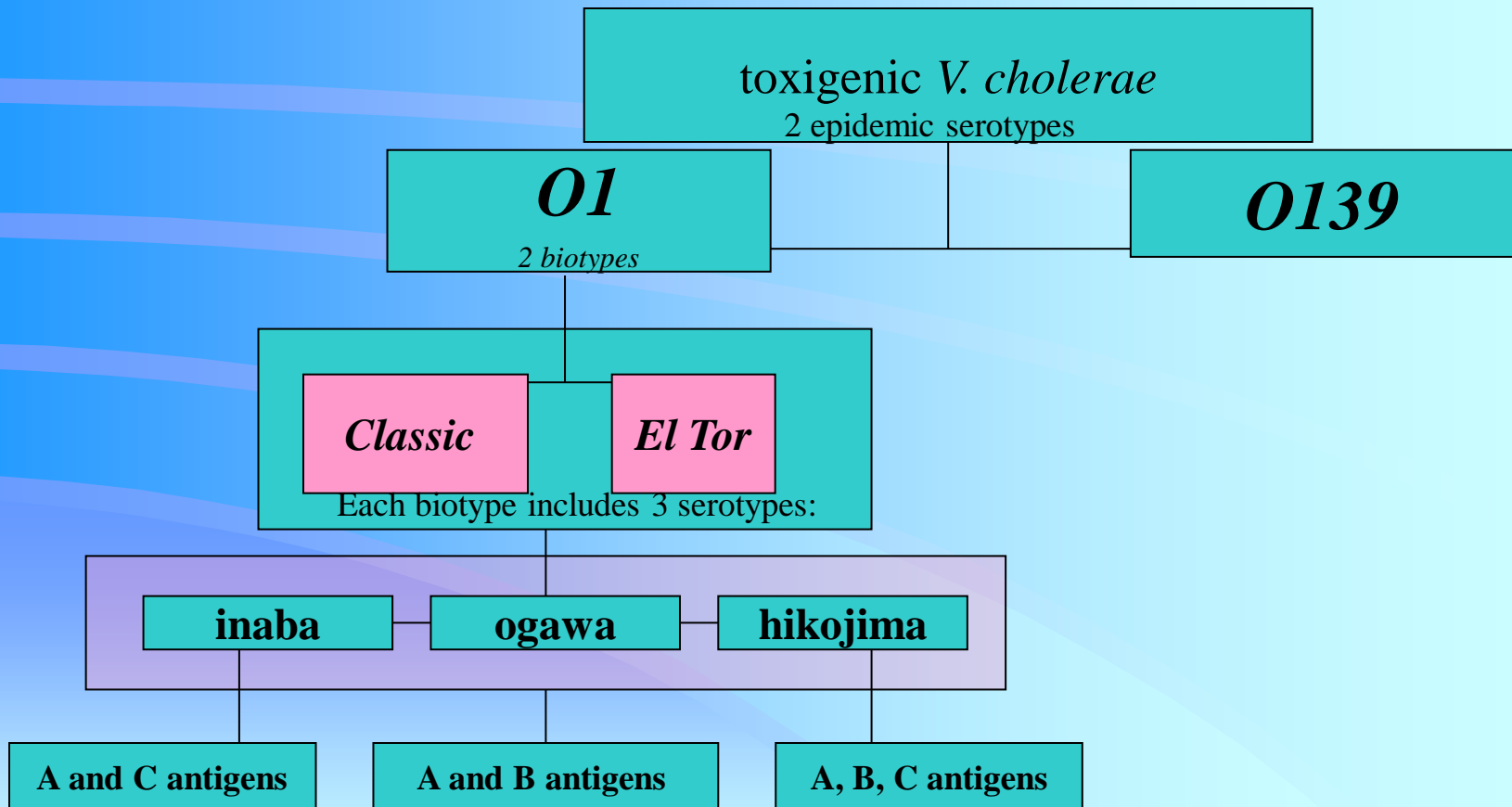
Vibrio cholerae



Cholera – etiology

- According to differences in O antigen there are **2 biotypes** (**classic and El Tor**) and **3 serotypes** (Inaba, Hikojima and Ogawa).
- **Inaba is the most virulent and causes epidemics**, followed by Hikojima.
- These two biotypes are from group O1 of genus Vibrio, in difference than Vibrio cholerae O139. El Tor and Vibrio cholerae O139 had caused the last seventh pandemy.
- Epidemiological and clinical features of diseases caused by O1 V. cholerae и V. cholerae O139 are same, but there are not cross immunity.

Classification of toxigenic Vibrio cholerae



Cholera – etiology

- V. Cholerae produces enterotoxin (holeragen) which is genetically encoded and is the major virulent factor. It is globular protein by two subunits A and B. B is responsible for attachment to the cell membranes but A posses toxic activity.
- The vibriions that are not agglutinated by O1 sera, are called NAG and cause cholera-like diseases. They cause gastroenteritis, hemocolitis and even sepsis.

Cholera – epidemiology

- Anthroponosis.
- Source of infection – human – patient, convalescent or carrier.
- Vibrions shed by feces (1 ml stool contains ~ 10 billions vibrions) and less by vomits. They exist in sea water and in outflow of the rivers.
- Fecal-oral route of transmission – contaminated water, food, by direct contact.
- Sporadic, epidemic and pandemic disease.
- All individuals are susceptible. Infective dose – 1 billion vibrions. Even in epidemics the incidence is 15%.

Cholera – epidemiology



Cholera – pathogenesis

- V. Cholerae → stomach → proximal small intestine – colonise the mucosa → attach to the microvilli of the enterocytes and produce enterotoxin.
- B-subunit of enterotoxin binds to the receptors of enterocytes.
- A-subunit of enterotoxin penetrates through the cell membrane of enterocyte and activates adenylatcyclase on the internal surface of cell membrane → activates the system adenylatcyclase-cyclic adenosinemonophosphat (cAMP) → increasing of intracellular level of cAMP → activation of chloral channels → increased secretion of Cl⁻, followed by increased secretion of Na and passive transport of water in intestinal lumen → profuse secretion of electrolytes and water from enterocytes → the volum of secreted fluids in small intestine is times higher than resorbtive capacity of large intestine → profuse diarrhea and vomiting appear → dehydration, loss of electrolytes, metabolic acidosis, hypotension to shock, acute renal failure.
- Endotoxin reabsorbed in intestine endotoxin leads to damage in vesels, myocard, nervous system, liver, kidneys.

Cholera – clinical features

- Incubation period – 2-3 days (1 to 8 days).
- Prodroms are possible – low grade fever, mild weakness, dizziness.
- Acute onset with diarrhea – big amounts of watery stool, abdominal discomfort, heaviness in epigastrium; without pains, tenesms and pathological admixtures in feces.
- The feces soon lose the typical view and become in big volume pale fluid without smell, containing small particles – “rice water”. The number of defecations are 5-10 to uncountable per day. This is enteric phase – 1-2 days.

Cholera – clinical features

- In progressing of the disease appears vomiting – the vomit materials are similar to the fecal materials – this is gastroenteric phase.
- Dehydration observes – in 3 grades:
 - First grade – loss of body weight to 5% – without changes in consciousness, dry mucosa, marked thirst.
 - Second grade – loss of body weight to 10% – very dry mucosa, poor skin turgor, hollow-eyed-cheeked, dry cornea, tachycardia, hypotension, cramps of the muscles; the children cry without tears with silent voice; seizures are possible.

Cholera – clinical features

- Third degree of dehydration – **algid phase** – loss of body weight above 10% – hypovolemic shock – the diarrhea and vomiting decrease. “Hypocratic” face – deeply hollow-eyed-cheeked, lethargic appearance, generalized cyanosis, hypothermia – 34-35 degrees of Centigrade. Cold skin with poor turgor. Hollowed abdomen. Tachypnea. Extreme tachycardia, pulse is very soft or impossible to palpation. Blood pressure – to 0. Anuria, azotemia, severe metabolic acidosis appear.
- The algid phase follows by asphyxia – progressive dyspnea, cyanosis, somnolence and stupor to comma and death.



A child, lying on a cholera cot, showing typical signs of severe dehydration from cholera.

The patient has sunken eyes, lethargic appearance, and poor skin turgor, but within two hours was sitting up, alert, and eating normally.

Cholera – laboratory parameters

- Marked leucocytosis, left shift, increased percent of neutrophils, lack of eosinophils, monocytosis, relative lymphopenia.
- Normal platelet count.
- Increased hematocrite.
- Decreased level of Na, K, Cl and Ca.
- Metabolic acidosis and hypoxia.
- Increased lactate.
- Increased blood urea nitrogen and creatinine.

Cholera – clinical forms – criteria

- Phases of the disease – choleric enteritis, gastroenteritis, algid.
- Severity – mild, moderate, severe.
- Atypical forms:
 - ❖ Abortive – in 10-15%. в 10-15% от случаите.
 - ❖ Cholera siderans (fulminant form) – lethal outcome within some hours.
 - ❖ Cholera sicca – early intestinal paresis because of toxicosis and hypokaliemia, deposition of huge amount isotonic fluid in the intestine. Fulminant course with progressive dehydration, hypotension, oligo- to anuria, **lack of diarrhea!!!**

Cholera – clinical forms

- ❖ In children – fever, CNS-disorders (seizures, meningeal syndrome, comma). Mortality rate 20-30%.
- ❖ In elder – common cardiovascular disorders (presteral pain, tachypnea, cyanosis, hypotension); anuria, hypotermia, hallucinations, delirious, retrograde amnesia.

Cholera – complications

- Secondary pneumonia
- Otitis
- Pyelitis
- Thrombosis, embolism
- Parotitis
- Stomatitis
- Myocarditis
- Acute cholecystitis
- Choleric typhoid – superinfection with Salmonella with generalized septic course (protracted septic fever, hepatosplenomegaly).

Cholera – diagnosis

- Clinic-epidemiological.
- Microbiological – isolation of the causative agent in feces, vomited materials, bile by direct microscopy and culture.
- Serological – by reaction of agglutination and ELISA.



Vibrio species on TCBS agar

*Vibrio species can be selective recovered from stool by culture on thiosulfate-citrate-bile salts-sucrose (TCBS) agar. On this medium, V. parahaemolyticus usually produces a green colony and **V. cholera a yellow colony** (indicative of the fermentation of sucrose).*

Courtesy of Harriet Provine

Cholera – management and treatment

- Etiological – tetracycline (doxycyclin) 3 x 100 mg for 5 days; aminoglycosides (amikacin, gentamycin), quinolones (ciprofloxacin).
- Supportive – rehydration, correction of electrolytes dysbalance and acidosis.

Ward for cholera with typical beds



Botulism – definition

- **Acute life-threatening infectious disease with specific paralysis that are caused by exotoxin, produced by *Clostridium botulinum*.**

Botulism – etiology

Clostridium botulinum

Gram-positive peritrichious rod, spore forming, anaerobe.

It is not resistant in the environmental.

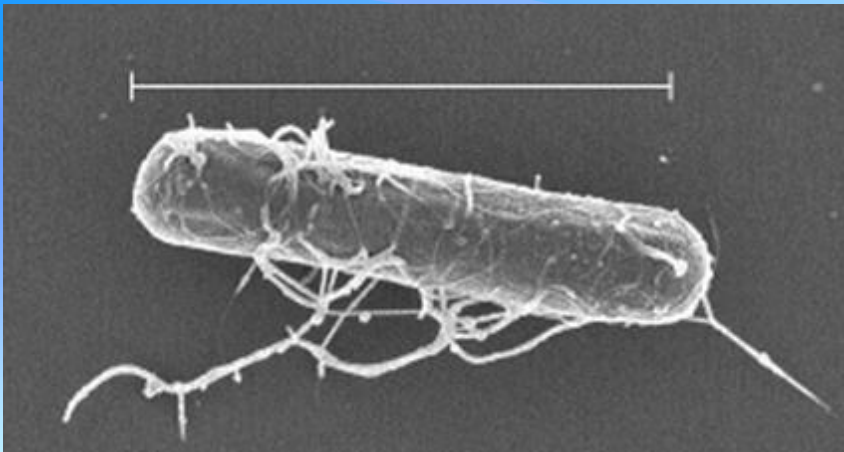
Eight serotypes exist.

Pathogenic for human are serotypes A, B and E, seldom F and G.

Scanning electron micrograph of Clostridium botulinum type C/D, strain BKT015925

Note the flagella, which are clearly visible in both images. The length of the scale bar is equivalent to 4 µm.

Source: Image: Hanna Skarin (SVA) and Leif Ljung (BMC).



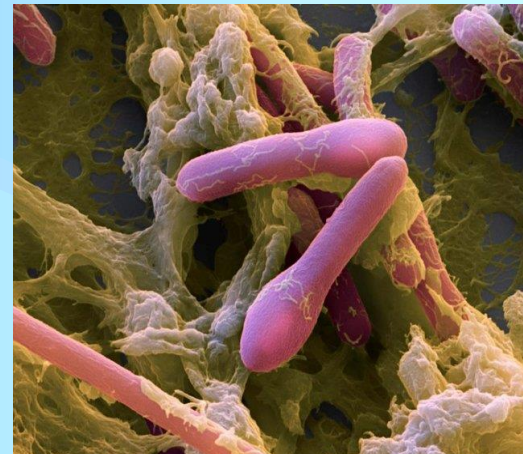
Produces heat labile exotoxin – the most potent biological poison.

The exotoxin contains neurotoxin and hemagglutinin.

The neurotoxin has double stranded structure – the one strain causes damages, but other is responsible for binding to the receptors and penetration into the cells.

Clostridium botulinum

Source: Coloured scanning electron micrograph of Clostridium botulinum bacteria (rod-shaped). The rods are 0.3-1.9 µm in width and 1.6-9.4 µm in length (Smith and Hobbs, 1974). Magnification: x13,300. Credit EYE OF SCIENCE/SCIENCE PHOTO LIBRARY.

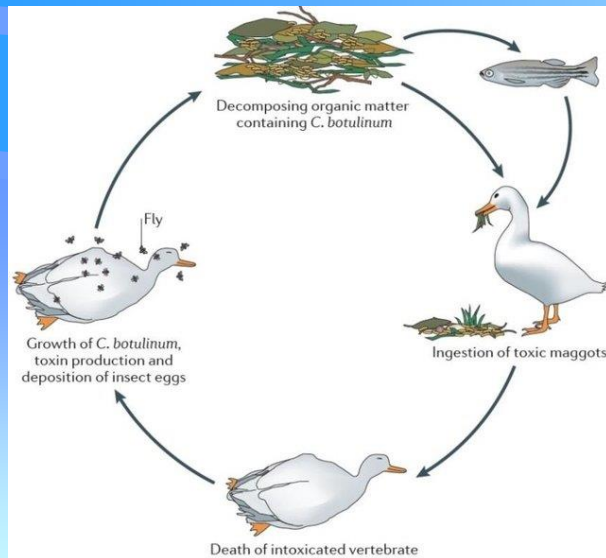


Botulism – epidemiology

- Major reservoir – heat blood animals, especially livestock, cattle, horses, swine etc. Less common fishes, swellfish. The animals eat spores with food, and spores in the stomach grow to vegetative forms that shed by animal feces transforms to spores that contaminate the soil, grass, vegetables, fruits. The spores are too resistant in the environmental.

The maggot cycle

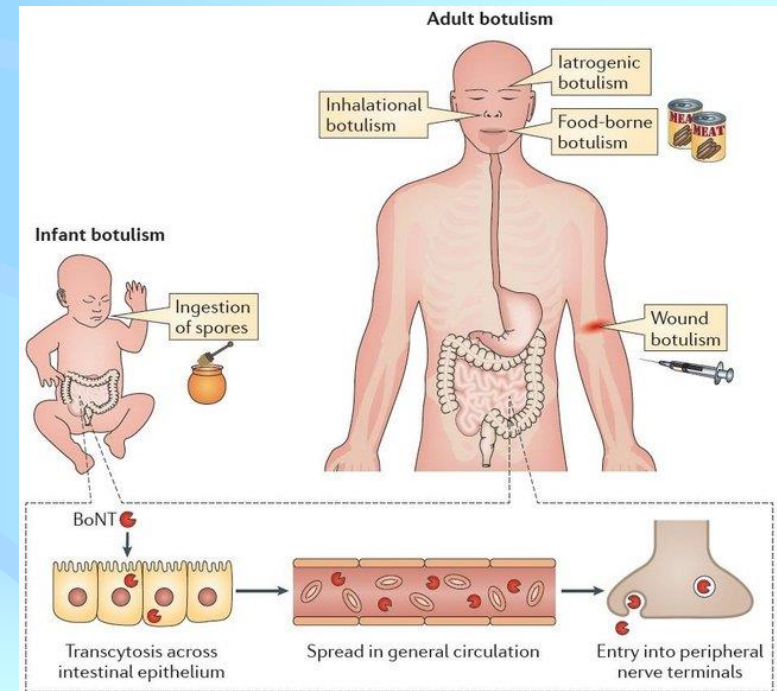
Source: Rossetto, O., Pirazzini, M., Montecucco, C., 2014. Botulinum neurotoxins: genetic, structural and mechanistic insights. Nat Rev Microbiol 12, 535-549.



- Human infects by consumption of spores-contaminated foods. Other rare modes – after contamination of wounds (wound botulism), after consumption of contaminated honey (infant botulism), aerosolised (as biological weapon).

Human forms of botulism.

Intoxication due to consumption of food contaminated with botulism toxin is responsible for the majority of human botulism outbreaks. Toxicoinfection occurs in young children by ingestion of *C. botulinum* spores that will produce the toxin in-vivo. Wound botulism is mainly responsible for drug addict outbreaks.



Botulism – determinants of pathogenicity

- The toxin produced by *C. botulinum* is generically designated as botulin; however, the various strains of *C. botulinum* actually produce eight toxins (A, B, C_a, C_b, D, E, F, and G).
- These toxins are structurally homologous – an active (A) region and binding (B) region can be defined in all of them.
- Generally, a given strain produces only one toxin. Human pathogenic strains most frequently produce toxins A, B, and E.
- Toxin A through F are neurotoxins that interfere with neurotransmission at the peripheral cholinergic synapses by preventing the release of acetylcholine (Ach), causing flaccid paralysis.
- Toxin G is the only with which no disease is associated.
- Although the toxins are considered exotoxins, they are only released when the bacterium undergoes autolysis. Some require partial digestion by proteolytic enzymes to become active. In cultures the toxin first appears as a prototoxin, which is subsequently activated by a trypsin-like enzyme.

Botulism – pathogenesis

- Portal of entry – most often gastrointestinal tract.
- Exotoxin and pathogens → stomach – part of exotoxin is absorbed and caused mild reactive gastritis; the remainder exotoxin → in small intestine – resorption → because of neurotropism exotoxin localizes in cranial and spinal motor neurons, vegetative structures, in terminal myoneural synapses of cholinergic axons. It tightly binds with presynaptic clefts and suppress releasing of acetylcholine blocking transmission of neural impulses. Paralysis appears.
- The paralysis of chest muscles and diaphragm → suppressed breathing → cyanosis, tachypnea, pneumonia.
- Disorders of vegetative nerve functions → dryness in the mouth, retention of urine, constipation.

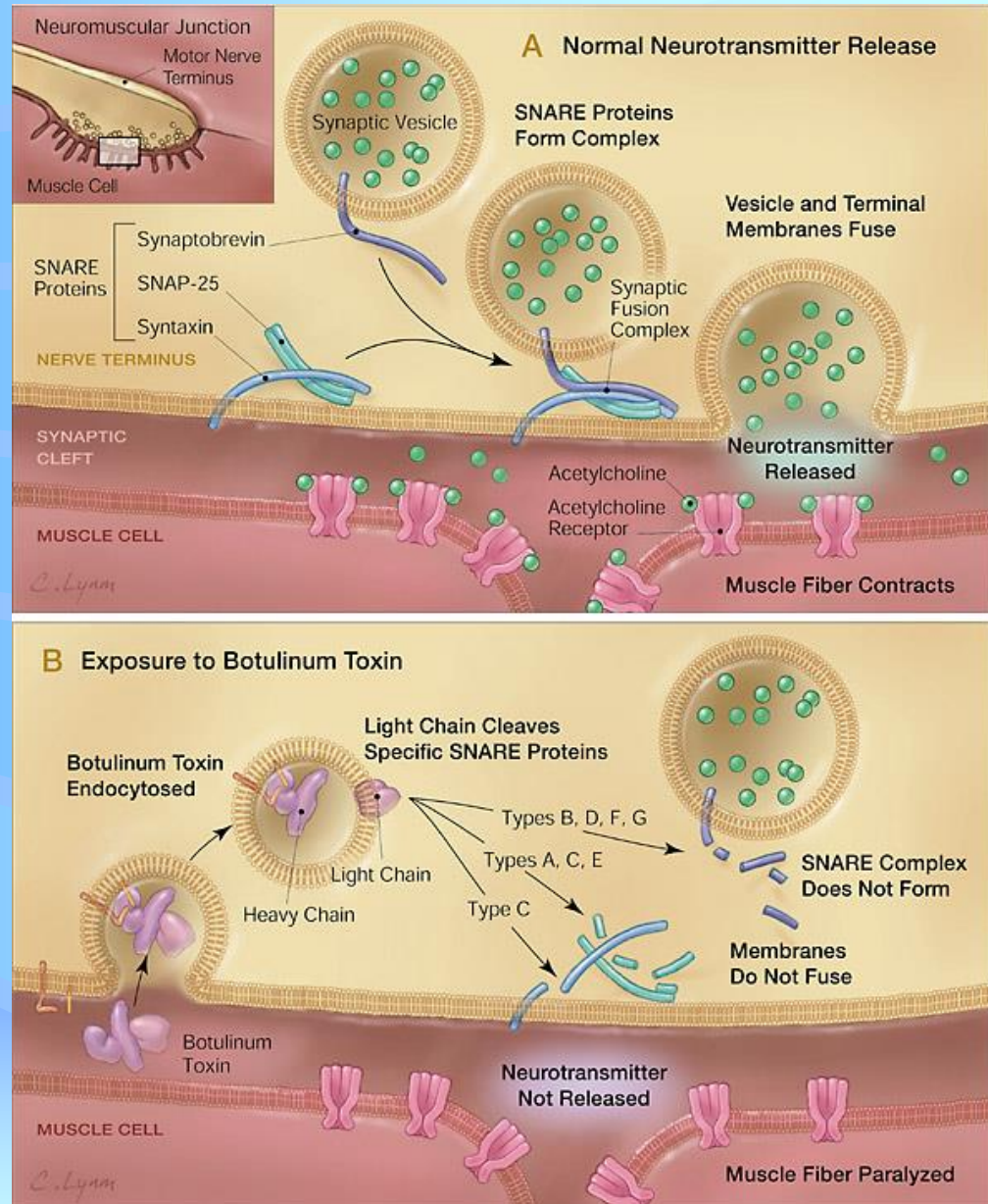
Botulism – pathogenesis

Normal neurotransmitter releasing (A) and blocked after exposure to botulinum toxin (B)

A. Release of acetylcholine at the neuromuscular junction is mediated by the assembly of a synaptic fusion complex that allows the membrane of the synaptic vesicle containing acetylcholine to fuse with the neuronal cell membrane. The synaptic fusion complex is a set of SNARE proteins, which include synaptobrevin, SNAP-25, and syntaxin. After membrane fusion, acetylcholine is released into the synaptic cleft and then bound by receptors on the muscle cell.

B. Botulinum toxin binds to the neuronal cell membrane at the nerve terminus and enters the neuron by endocytosis. The light chain of botulinum toxin cleaves specific sites on the SNARE proteins, preventing complete assembly of the synaptic fusion complex and thereby blocking acetylcholine release. Botulinum toxins types B, D, F, and G cleave synaptobrevin; types A, C, and E cleave SNAP-25; type C also cleaves syntaxin. Without acetylcholine release, the muscle is unable to contract.

SNARE, Soluble N-ethylmaleimide-sensitive-factor Attachment protein Receptor; SNAP-25, synaptosomal-associated protein of 25 kDa. From Arnon et al., 2001.

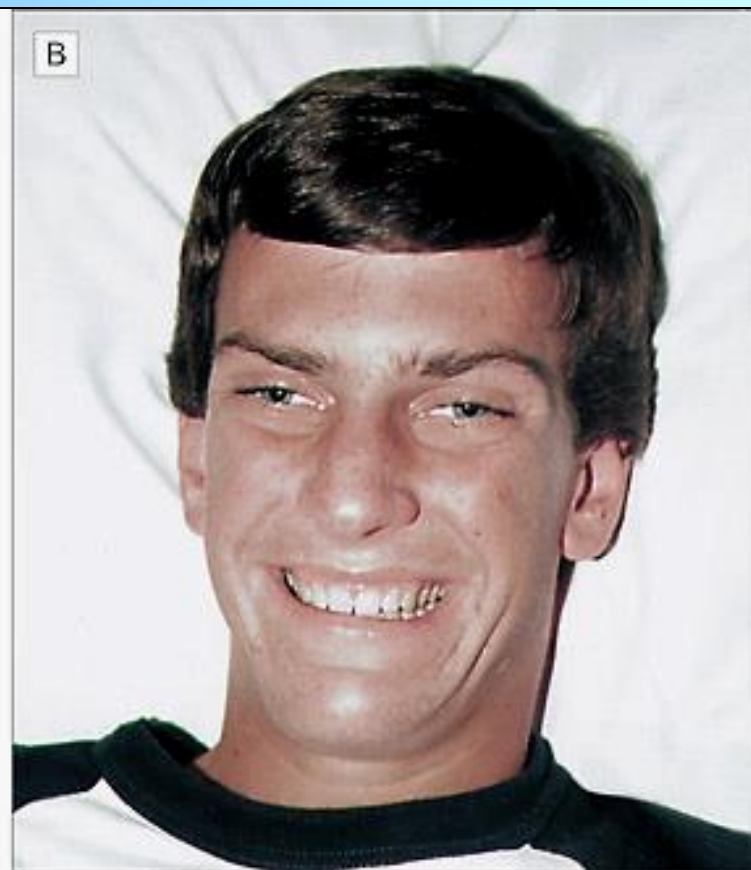


Botulism – clinical features

- Incubation period – 6-36 hours (seldom 8 days).
- Acute onset with acute abdominal pain, nausea, vomiting, short diarrhea, intoxication (headache, dizziness, weakness, dryness in the mouth, progressive weakness of the muscles, tachypnea, dyspnea etc.).
- **Syndrome of ophtalmoplegia** (some hours to 1-2 days after the onset) – blurred vision or diplopia, ptosis, difficult movements of eyes, midriasis with slow reaction to the light, anizocoria, divergent strabismus, dry conjunctiva.
- **Bulbar palsy** (hours after appearing of syndrome of ophtalmoplegia) – dysphonia to aphonia, difficulty in swallowing, the fluids come out the nostrils, in oral cavity saliva accumulate, the breathing is noisy.

Botulism – clinical features

- **Neurovegetative disorders** – dryness in the eyes and oral cavity, intestinal palsy with meteorism, decreased peristalsis and constipation to subileus, retention of urine.
- Increasing of intoxication – severe adynamia to prostration, pale face with poor appearance, dizziness, headache, anorexia etc.
- **Syndrome of total myoneuroplegia** (after 1-2 days) – appearance of flaccid, descendent, symetric paresis and paralysis. Inability to hold the head and shoulders, the arms – inability to move, intercostal muscles – increased frequency of breathing, the last – paralysis of the legs. Tachycardia with hypotension.
- Severe condition but afebrile, without sensory disorders, with suppressed reflexes, hypotonic muscles, without pathological reflexes.
- Slow recovery.



Botulism – clinical forms

- Mild – only ptosis and blurred vision; fast recovery.
- Moderate – all symptoms present but without paralysis of breathing and respiratory failure.
- Severe – short incubation period, fast evolution, within 2-3 days paralysis of breathing and possible death.
- Fulminant – sudden onset, within hours paralysis including and breath muscles; within 2-3 days – death because of acute respiratory failure.
- Wound botulism – when a wound contaminates by spores. Clinical manifestations are same as in classical botulism. Common in intravenous drug addicted .
- Infant botulism – when the feeding of infant is by bottle smeared with honey – “floppy baby syndrome” – high risk for death.

Botulism in infants



Risk factors for different forms of botulism



Botulism – diagnosis

- Clinical and epidemiological.
- Microbiological – inoculation of blood from patient to newborn white mice. Culture of vomit, feces and suspicious food.

Botulism – management and treatment

- Prompt hospitalization, lavage of the stomach, deep enema.
- Etiological treatment:
 - ❖ Penicillin, cephalosporins, tetracyclines, macrolides. **Aminoglycosides are contraindicated – increasing of paralysis!!!**
 - ❖ Botulin serum – up to 4-5 doses, containing to 10 000 antitoxic units (AU) type A and E and 5 000 AE type B.
- Supportive treatment – nivalin, prostigmin for improving of intestinal motility, aspiration by nasogastral sonde, enema, parenteral nutrition; in respiratory failure – intubation, mechanic ventilation; in retention of urine – catheter.

Botulism – prophylaxis

- Strong control to cooking and preparing of foods.
- High temperature in boiling!!!
- Suspicious foods needs by investigation!!!
- Person which is consumed suspicious food – injection of 1 dose hyperimmune botulin serum.

**THANK YOU FOR YOUR
ATTENTION !**