

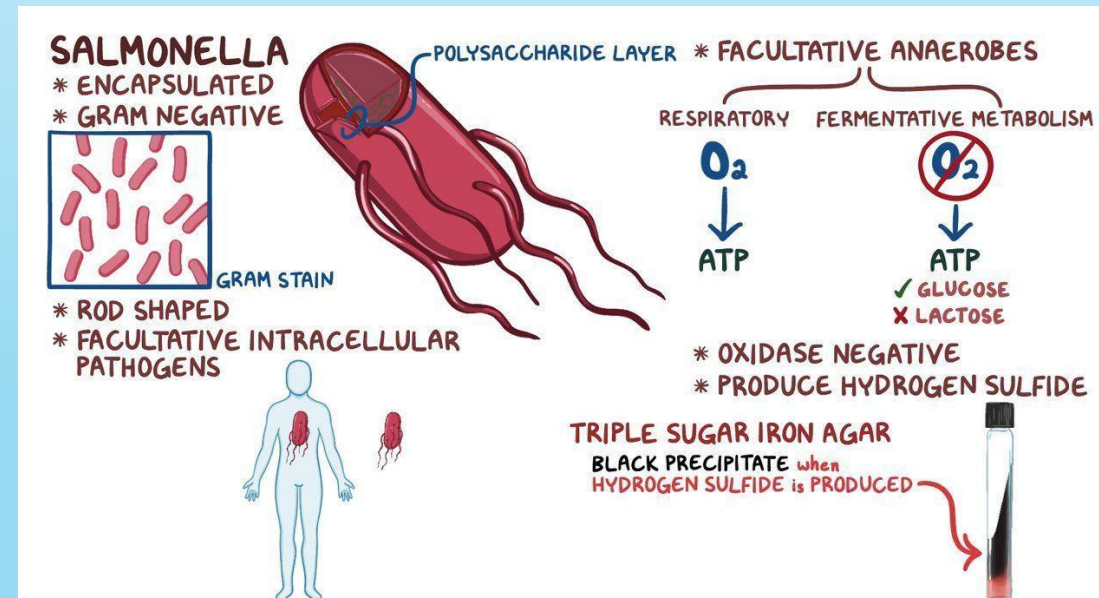
Typhoid

Dr. Ayesha Fatima
Pharm D
Assistant Professor
Dept of Pharmacy Practice

- Typhoid fever is also called "Enteric fever".
- Typhoid is an infectious communicable disease caused by various species of Salmonella, especially *Salmonella typhi* and *Salmonella paratyphi*. It is food and water borne disease.
- Typhoid continues to be a global health problem with an estimated 13 to 17 million cases worldwide resulting in 600,000 deaths per year.

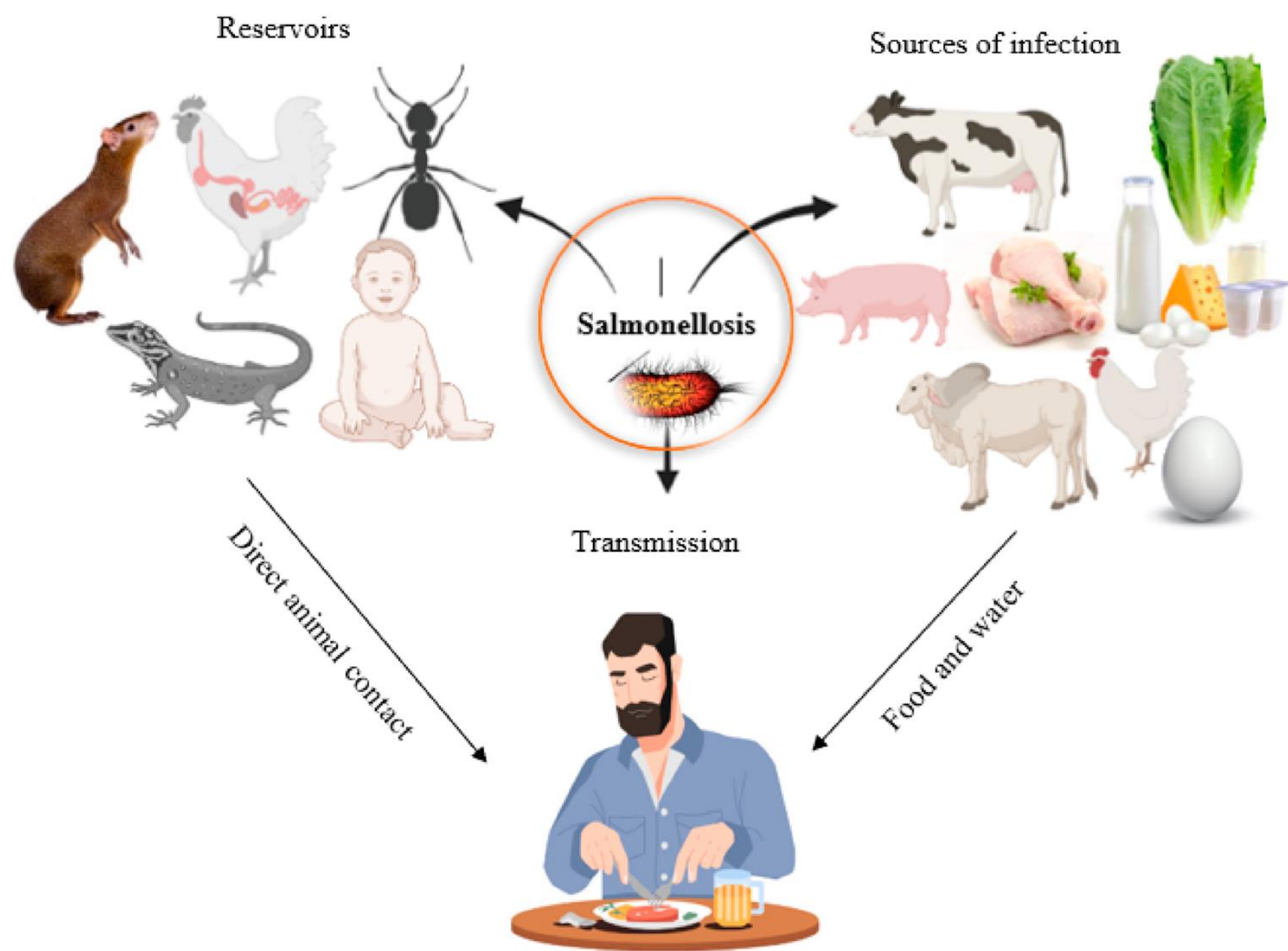
Causative Organism:

- Salmonella is a genus of Gram-negative bacilli bacteria that is the major cause of food-borne illness throughout the world. Today, there are more than 2500 known species of Salmonella.
- Species: *Salmonella typhi*, *Salmonella paratyphi*.
- Family: Enterobacteriaceae



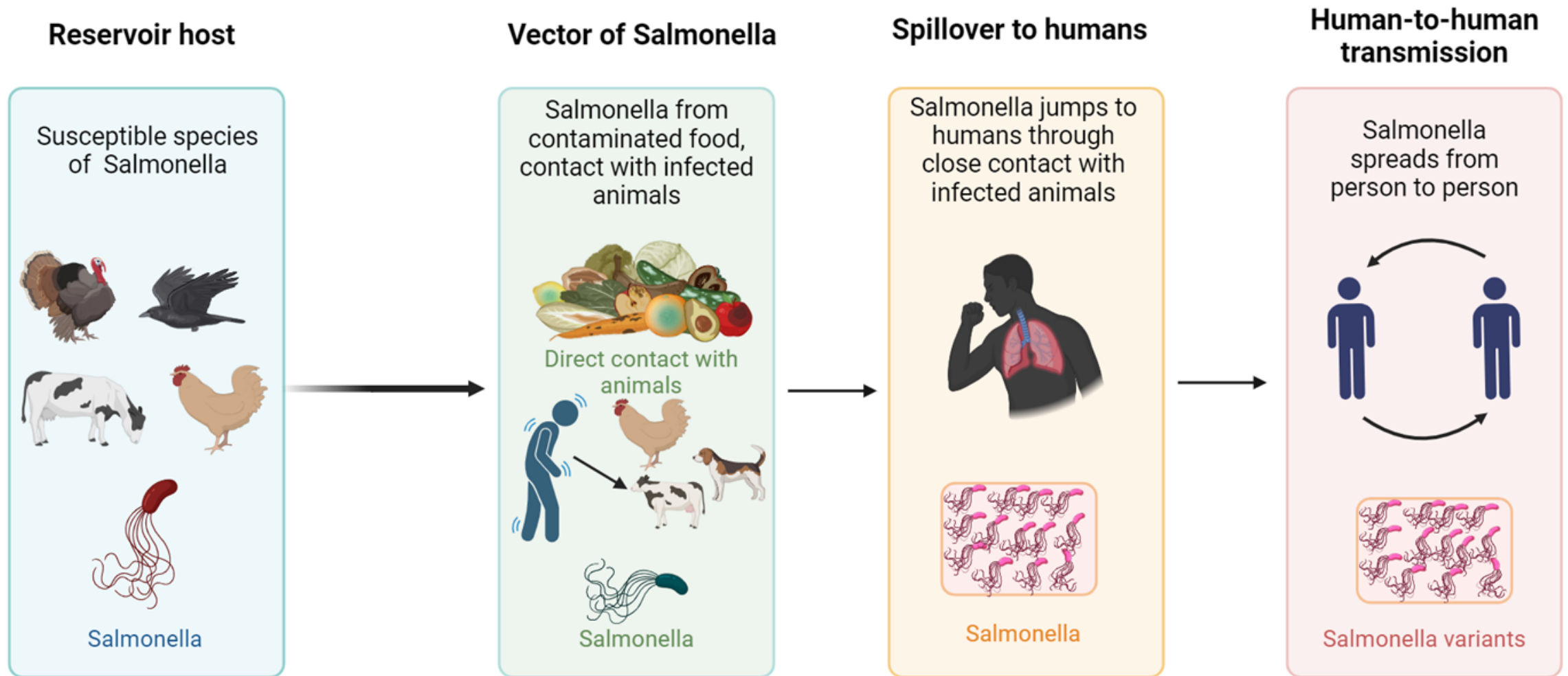
Mode of transfer:

- Organisms usually enter the body through contaminated food or water.
- Infection commonly occurs via the faecal-oral route.
- Contaminated faeces are a major source of transmission.
- Consumption of contaminated beef and chicken, especially when inadequately washed or undercooked, increases risk.
- Flies and cockroaches act as mechanical vectors, spreading the organisms to food and water.
- Poor sanitation and improper food handling facilitate transmission.



Fecal–oral transmission, eating raw or undercooked meat, poultry, and eggs or egg products or by drinking unpasteurized milk

Zoonotic transmission of Salmonella



Pathogenesis

- The incubation period varies from 5-14 days.
- The typhoid bacilli, which are ingested through contaminated food or water, are usually resistant to the gastric acid, following which they move to the intestine.
- They rapidly penetrate the mucosal epithelium and reach the lamina propria.
- The macrophages ingest the bacilli but do not generally kill them.
- Some bacilli remain within macrophages of the small intestinal lymphoid tissue.
- Other typhoid bacilli are drained into mesenteric lymph nodes, where there is further multiplication and invasion of the lymphoid follicles and Peyer's patches (several lymph nodes near the junction of the ileum and colon) of the small intestine.
- Following this, the bacilli invade the bloodstream.
- The bacilli disseminate throughout the body and colonize in the reticuloendothelial tissues, like the liver, spleen, lymph nodes, and bone marrow.

Ingestion of Bacilli (Contaminated Food/Water)



Resistance to Gastric Acid Entry into Intestine



Penetration of Mucosal Epithelium to Lamina Propria



Macrophage Ingestion Some Bacilli Remain in Intestinal Lymphoid



Drainage to Mesenteric Lymph Nodes Multiplication/Invasion

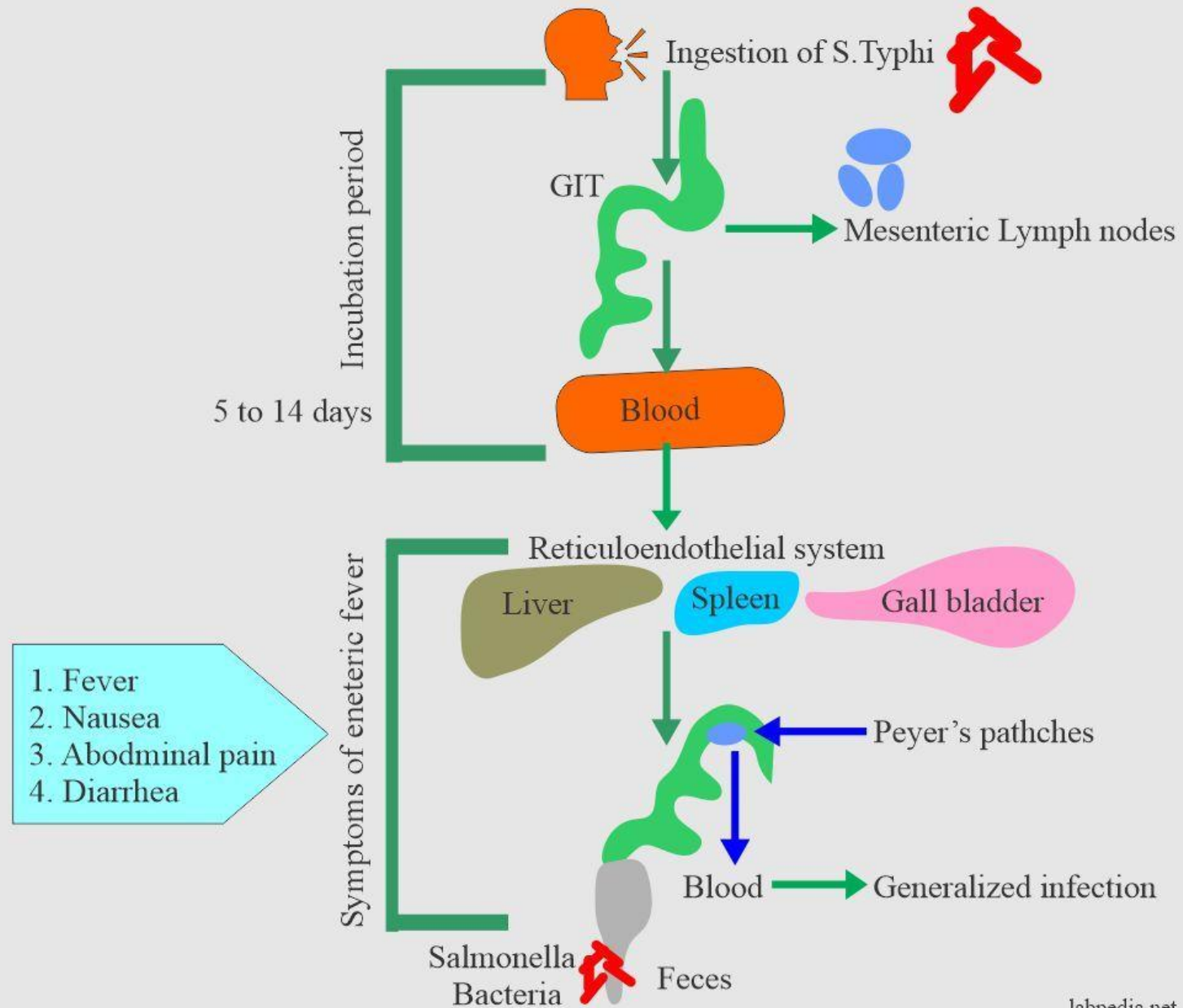


Bacilli Invade Bloodstream (Bacteremia)



Dissemination & Colonization in Reticuloendothelial

Enteric Fever Pathogenesis



Pathology of Enteric fever

① First week

Bacteremia

③

Third week

1. Ulceration of the peyer's patches
2. Intestinal bleeding
3. Intestinal ulceration

Chronic stage ④

1. Colonization in the gallbladder
2. Chronic carrier state
3. Chronic infection may involve the joints, bones, meninges and other sites

②

Second week

1. Wide spread reticuloendothelial involvement
2. Foci of necrosis in liver
3. Splenomegaly

Necrosis

Pathology of Enteric fever

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③

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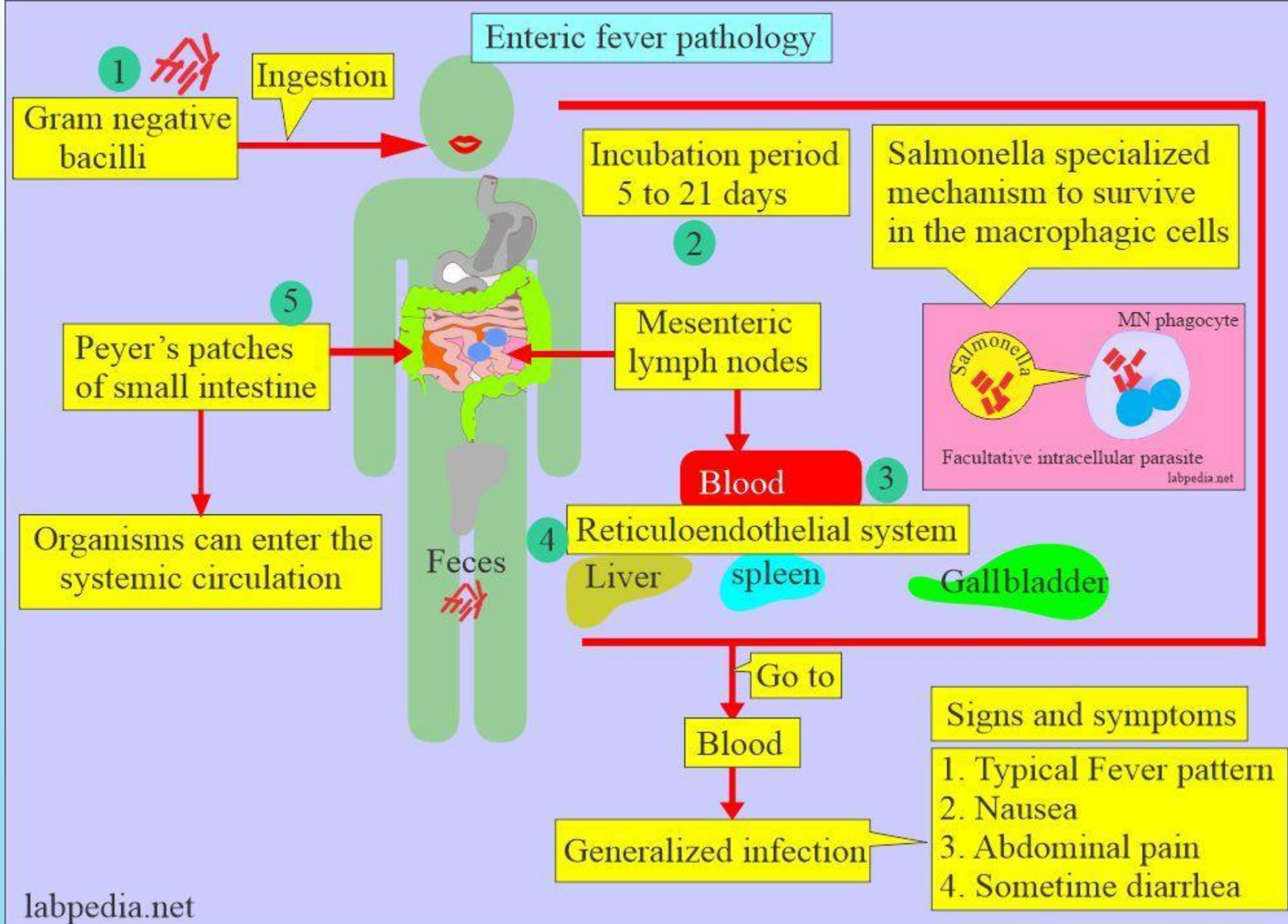
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Necrosis



Clinical Manifestations

Uncomplicated Enteric Fever

1. Prolonged high fever (103–104 °F).
2. Bowel disturbances:
 1. Constipation in adults.
 2. Diarrhoea in children and HIV patients.
3. Headache.
4. Malaise and anorexia.
5. Early-stage cough.
6. Rose spots (exanthem) on chest, abdomen, and back in up to 25% of patients.

Severe / Complicated Enteric Fever

1. Melena (blood in stool).
2. Intestinal perforation.
3. Peritonitis.
4. Abdominal discomfort.
5. Hypotension.
6. Marked abdominal tenderness.
7. Rising white blood cell count.

Stage 1 (1st Week)	End of 1st Week	Stage 2 (2nd Week)	Stage 3 (3rd Week)	Stage 4 (4th Week)
Slowly rising (stepladder-pattern) fever for 4–5 days Abdominal pain and myalgia Malaise Headache Constipation Relative bradycardia	Rose spots on upper abdomen and back Cough Splenomegaly Abdominal distension with tenderness Diarrhea	Progression of symptoms from the 1st week <u>End of 2nd Week</u> Delirium Development of complications Progression to coma and death if untreated	Patient becomes febrile, toxic, and anorexic Significant weight loss Typhoid state (apathy, confusion, psychosis) High risk of intestinal hemorrhage and perforation → may cause death	Recovery phase Fever, mental status, and abdominal distension gradually improve Intestinal and neurologic complications can still occur in untreated survivors Persistent weight loss and debilitating weakness lasting months Some survivors become asymptomatic <i>S. typhi</i> carriers and can transmit the bacteria indefinitely

Diagnosis

1. Culture-Based Diagnosis

- ✓ Diagnosis is commonly done using blood, urine, stool, or bone marrow cultures.
- ✓ Samples are placed on culture media that promote *Salmonella* growth.
- ✓ Cultures are incubated for 48–72 hours and examined microscopically.

Culture Media

- ✓ Blood samples:
 - ✓ Blood agar
 - ✓ MacConkey agar
- ✓ Stool/rectal swabs:
 - ✓ MacConkey agar
 - ✓ Salmonella–Shigella (SS) agar
 - ✓ Deoxycholate citrate agar (DCA)
- ✓ Additional Culture Points
 - ✓ Urine and stool cultures useful in 2nd & 3rd week.
- ✓ Bone marrow culture is:
 - ✓ 90% sensitive, even after 5 days of antibiotic therapy.
 - ✓ Often obtained from CSF, peritoneal fluid, mesenteric lymph nodes, resected intestine, gallbladder, pharynx, tonsils, abscess, or bone.
- ✓ Punch-biopsy culture of rose spots: ~63% sensitive.

2. Serological Diagnosis

Widal Test

- Most widely used serological test.
- Detects antibodies that agglutinate *Salmonella* antigens.
- Uses antigens:
 - *S. typhi* O antigen
 - *S. typhi* H antigen
 - *S. paratyphi* AH antigen
- Serum is mixed with antigens and incubated at 37°C overnight.
- Agglutination = Positive.
- **ELISA**
Detects **specific Salmonella antibodies/antigens.**
More sensitive than Widal.

Fluorescent Antibody Tests

Identify antigenic substances specific for *Salmonella typhi*.

3. Other Non-Specific Laboratory Findings

- ✓ Moderate anemia
- ✓ Elevated ESR
- ✓ Thrombocytopenia
- ✓ Lymphopenia
- ✓ Mild hyponatremia & hypokalemia
- ✓ Slightly elevated PT and aPTT
- ✓ Low fibrinogen
- ✓ Liver enzymes and bilirubin increased
2× normal
- ✓ ALT : LDH ratio

Ideal specimen for typhoid diagnosis

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graph TD; A[Ideal specimen for typhoid diagnosis] --> B[First week]; A --> C[Second week]; A --> D[Third week]; A --> E[Fourth week]; B --> F[Blood for culture]; C --> G[Serum for antibody detection]; D --> H[Stool]; E --> I[Urine];
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First week

Blood for
culture

Second week

Serum for
antibody detection

Third week

Stool

Fourth week

Urine

Treatment (Adopted from the WHO typhoid guidelines)

1. Supportive measures are essential in typhoid fever management, including:
 1. Oral rehydration
 2. Proper nutrition
 3. Use of antipyretics
2. More than 90% of patients can be managed at home if they have:
 1. Oral antibiotics
 2. Reliable caregiving
 3. Close medical follow-up for complications or poor response to therapy
3. Hospitalization and parenteral antibiotics are required for patients who have:
 1. Persistent vomiting
 2. Severe diarrhoea
 3. Abdominal distension

Susceptibility	Optimal therapy			Alternative effective drugs		
	Antibiotic	Daily dose (mg/kg)	Days	Antibiotic	Daily dose (mg/kg)	Days
Fully sensitive	Fluoroquinolone (E.g., Ofloxacin or Ciprofloxacin)	15	5-7	Chloramphenicol Amoxicillin *TMP-SMX	50-75 75-100 8-40	14-21 14 14
Multidrug resistance	Fluoroquinolone Cefixime	15 15-20	5-7 7-14	Azithromycin Cefixime	8-10 15-20	7 7-14
Quinolone resistance	Azithromycin Ceftriaxone	8-10 75	7 10-14	Cefixime	20	7-14

*TMP-SMX: Trimethoprim-Sulfamethoxazole

Fluoroquinolones

- Optimal treatment for typhoid fever in adults.
- Advantages:
 - Inexpensive and well-tolerated.
 - More reliable than older drugs (chloramphenicol, ampicillin, amoxicillin, TMP-SMX).
 - Excellent tissue penetration.
 - Effective against *S. typhi* in intracellular stationary phase (monocytes/macrophages).
 - Achieve higher active drug levels in the gall bladder.
- **Contraindications:**
 - Relatively contraindicated in children in some countries due to risk of articular damage.

Alternative Oral Therapies

- Ampicillin / Amoxicillin
 - Dose: 500 mg orally, 3–4 times daily.
 - Adding clavulanic acid to amoxicillin shows no added benefit.
- Trimethoprim–Sulfamethoxazole (TMP-SMX)
 - Adults: 160 mg TMP + 800 mg SMX, twice daily.
 - Children: 4 mg/kg TMP + 20 mg/kg SMX, for 14 days.

Treatment for Resistant Strains

Third-generation cephalosporins

Cefixime: 15–20 mg/kg/day

Adults: 100–200 mg, twice daily.

Azithromycin

Effective for uncomplicated typhoid in adults & children.

Dose: 500 mg (10 mg/kg) once daily for 7 days.

Severe / Complicated Typhoid Fever

- Requires intravenous antibiotics.
- IV Fluoroquinolones (preferred):
 - Ciprofloxacin or Ofloxacin: 15 mg/kg/day for 7–14 days.
- IV Cephalosporins:
 - Ceftriaxone: 50–75 mg/kg/day (Adults: 2–4 g/day), 1–2 doses.
 - Cefotaxime: 40–80 mg/kg/day (Adults: 2–4 g/day), 2–3 doses.
 - Cefoperazone: 50–100 mg/kg/day (Adults: 2–4 g/day), 2 doses.
- Parenteral fluoroquinolones are preferred in severe infections.
- Minimum duration of fluoroquinolone therapy in severe cases: 10 days.

Neurological Complications

- Mental status changes (delirium, stupor) → Evaluate for meningitis via CSF exam.
- If CSF normal and typhoid meningitis suspected:
 - Start high-dose corticosteroids:
 - Dexamethasone 3 mg/kg, slow IV infusion.
 - Continue appropriate antimicrobials.

Patient Education:

About the Disease

1. Typhoid is a communicable but curable disease caused by *Salmonella* bacteria.
2. The symptoms of typhoid include fever, abdominal pain, headache, uneasiness, vomiting, constipation in adults, and diarrhoea in children.
3. Typhoid infection commonly spreads through poor hygiene, improperly cooked food and meat, and contaminated drinking water.
4. A small number of patients may develop complications such as intestinal ulcers, infections of the heart or brain, or, rarely, multiple organ failure.

About the Medications

1. The patient should take all medications regularly exactly as prescribed by the doctor.
2. The patient should not skip doses or stop taking medicines after temporary relief.
3. If a dose is missed, it should be taken as soon as the patient remembers, but if the next dose is due soon, the missed dose should not be doubled.
4. If the patient experiences any adverse effects, they should contact the pharmacist or doctor immediately.

About Lifestyle Modifications

1. Patients with typhoid may pass the bacteria in their stools, which can contaminate their hands and surroundings.
2. They should avoid going to work or school until they are free of symptoms.
3. Patients should maintain good hygiene, including washing and drying their hands after using the toilet and before handling food.

Prevention of typhoid

1. Typhoid fever can be prevented by maintaining good personal hygiene, especially washing hands thoroughly with soap and clean water before eating and after using the toilet.
2. Drinking only safe, clean, and properly treated water helps prevent the spread of typhoid fever.
3. Eating well-cooked food and avoiding raw or street food from unhygienic places reduces the risk of infection.
4. Fruits and vegetables should be washed with clean water or peeled before eating to prevent contamination.
5. Proper sanitation practices, such as safe disposal of human waste, play a major role in preventing typhoid fever in the community.
6. Vaccination against typhoid is an effective preventive measure, especially for individuals living in or traveling to high-risk areas.
7. Avoiding close contact with infected individuals and maintaining clean surroundings help reduce the spread of the disease.