Typhoid caused by *Salmonella*

Introduction

- The genus *Salmonella is composed of* **motile bacteria** *that* conform to the definition of the **family *Enterobacteriaceae.***
- The genus *Salmonella is composed of* ***two species***,
  - ***Salmonella enterica and***
  - ***Salmonella bongori*** *(formerly subspecies* V).
- *Salmonella enterica has been subdivided into* six subspecies:

A. ***S. enterica subsp. enterica, designated subspecies* I**;

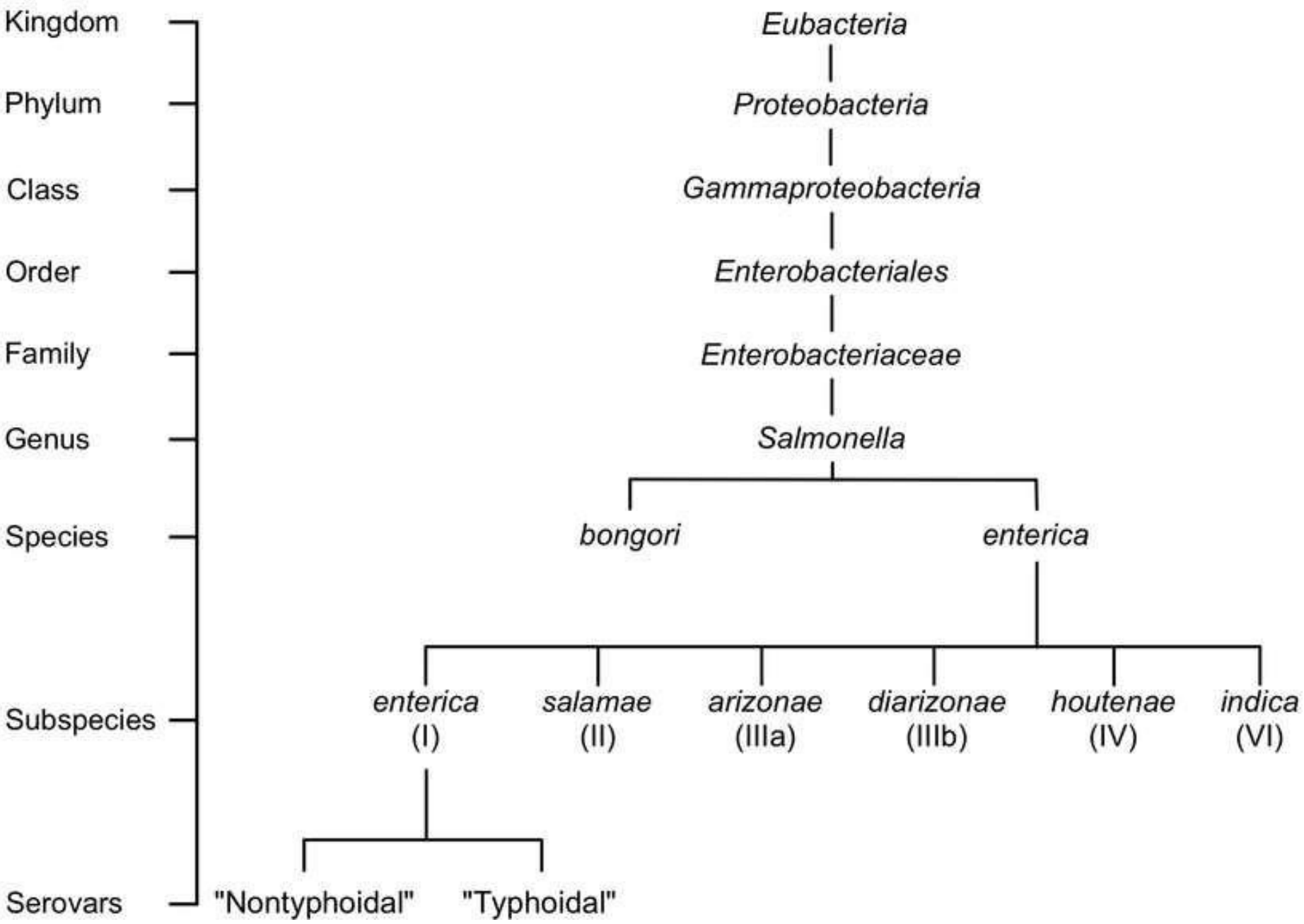
B. ***S. enterica subsp. salamae, subspecies II;***

C. ***S. enterica* subsp. *arizonae, subspecies IIIa;***

D. ***S. enterica subsp. diarizonae,* subspecies IIIb;**

E. ***S. enterica subsp. houtenae, subspecies IV;* and**

F. ***S. enterica subsp. indica, subspecies VI.***


Kingdom
Phylum
Class
Order
Family
Genus
Species
Subspecies
Serovars
Eubacteria
Proteobacteria
Gammaproteobacteria
Enterobacteriales
Enterobacteriaceae
Salmonella
bongori
enterica
enterica (I)
salamae (II)
arizonae (IIIa)
diarizonae (IIIb)
houtenae (IV)
indica (VI)
"Nontyphoidal"
"Typhoidal"

Introduction

- *The **type species** **is** **S. enterica subsp. enterica.***
- Subspecies I strains are **commonly isolated from humans and warm-blooded animals.**
- Subspecies II, IIIa, IIIb, IV, and VI strains and *S. bongori are usually isolated from coldblooded* animals and the environment.

❖ ***Salmonella Serotypes***

- Salmonella serotyping is a subtyping method based on the immunologic characterization of three surface structures:

❑ **O antigen**, which is the outermost portion of the **LPS layer** that covers the bacterial cell;

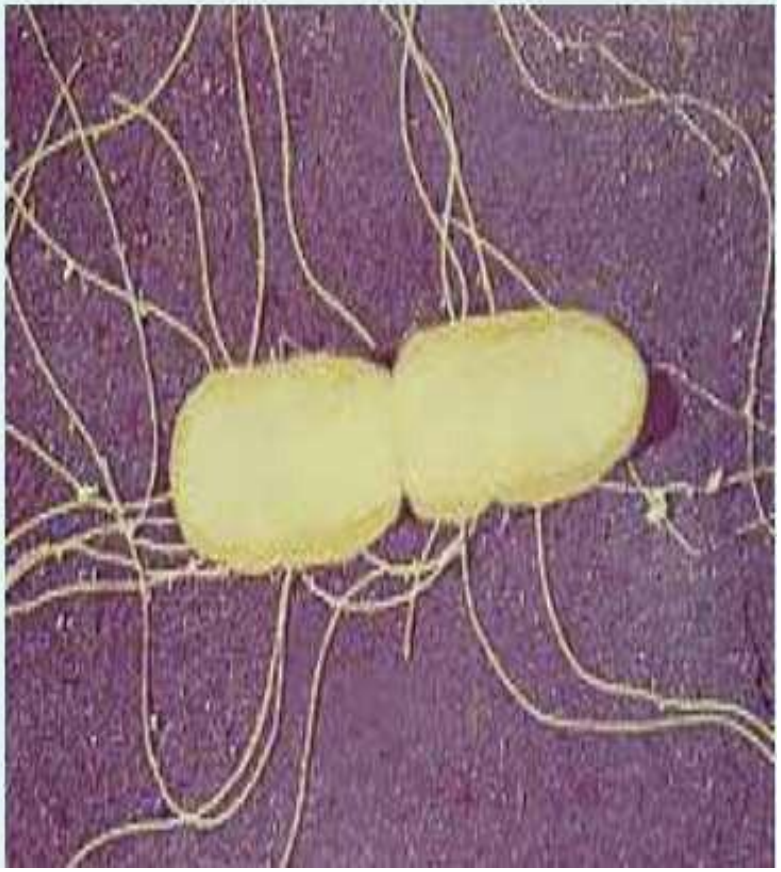
❑ **H antigen**, which is the **filament portion** of the bacterial flagella; and

❑ **Vi antigen**, which is a capsular polysaccharide present in specific serotypes.

- Serotyping of *Salmonella is commonly performed to facilitate* **surveillance for *Salmonella infection and to aid in the recognition* of outbreaks.**

Morphology of Salmonella

- Gram negative bacilli
- 1-3 / 0.5 microns,
- Motile by peritrichous flagella



Cultural Characters

- Aerobic / Facultatively anaerobic
- Grows on simple media – Nutrient agar,
- Temp 15 – 41°c / 37° c
- Colonies appear as large 2 -3 mm, circular, low convex,
- On MacConkey medium appear

  Colorless (NLF)

Selective Medium - Wilson Blair Bismuth sulphide medium. Produce Jet black colonies

H_2S produced by Salmonella typhi

Antigenic structure of Salmonella

- Two sets of antigens
- Detection by serotyping
- **1 *Somatic or 0 Antigens*** contain long chain polysaccharides (LPS) comprises of heat stable polysaccharide commonly.
- ***2 Flagellar or H Antigens*** are strongly immunogenic and induces antibody formation rapidly and in high titers following infection or immunization. The flagellar antigen is of a dual nature, occurring in one of the two phases.

Salmonella
Antigenic Structure

- H – Flegellar antigens
- O – Somatic antigen,
- Vi – Surface antigen in some species only
- H antigens also called flegellar antigens, heat labile protein,
- Boiling destroys antigenicity
- When mixed with Antiserum produces agglutination and fluffy clumps are produced
- H antigens are strongly immunogenic Induces antibodies rapidly,

Antigens – Salmonella (cont)

- O Antigens

- Forms integral part of Cell wall,
- Like Endotoxin
- 0 Antigens unaffected by boiling.
- When mixed with antiserum produce chalky clumps are formed, take more time reaction, at high temp 50° – 55° c
- O antigens are less immunogenic. than H antigens

Antigen (Vi) – Salmonella (contd)

- Vi antigens
- Many strains in S.typhi covers the O antigens- prevents agglutination.
- Resembles like K antigens
- Destroyed after boiling at 60° c / 1 hour.
- Vi a polysaccharide
- Acts as virulence factor, protects the bacilli against Phagocytosis and activity of Complement
- Poorly immunogenic
- Low titer of antibodies are produced, Not diagnostic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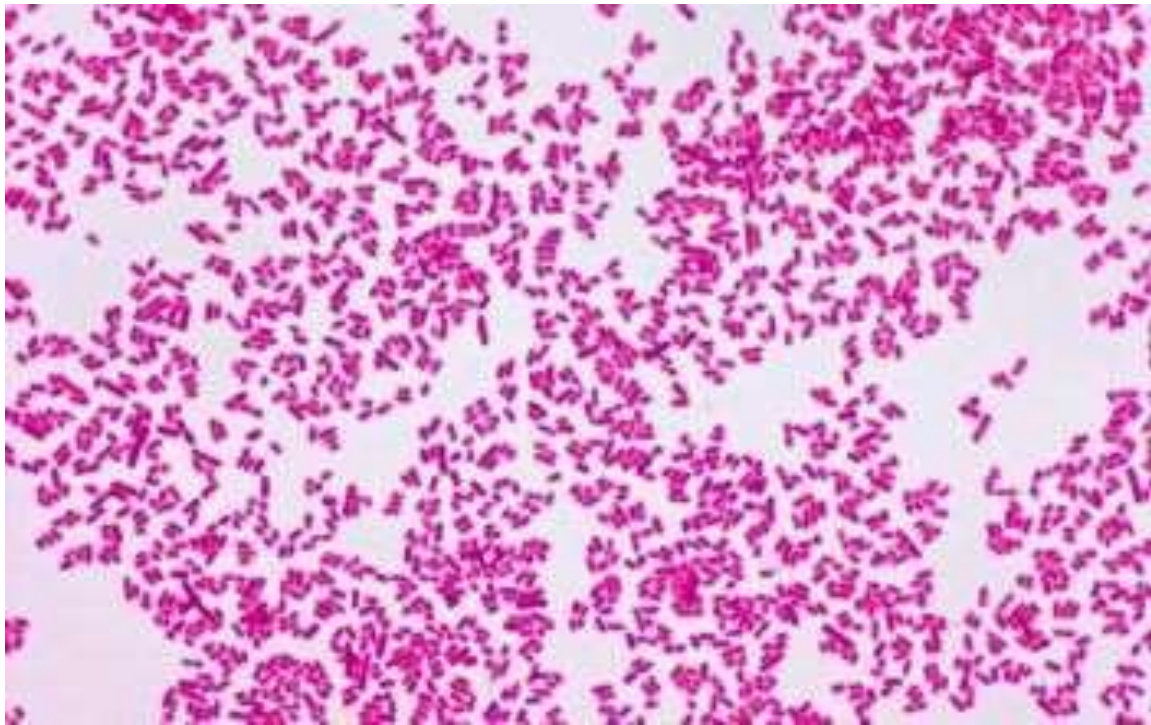


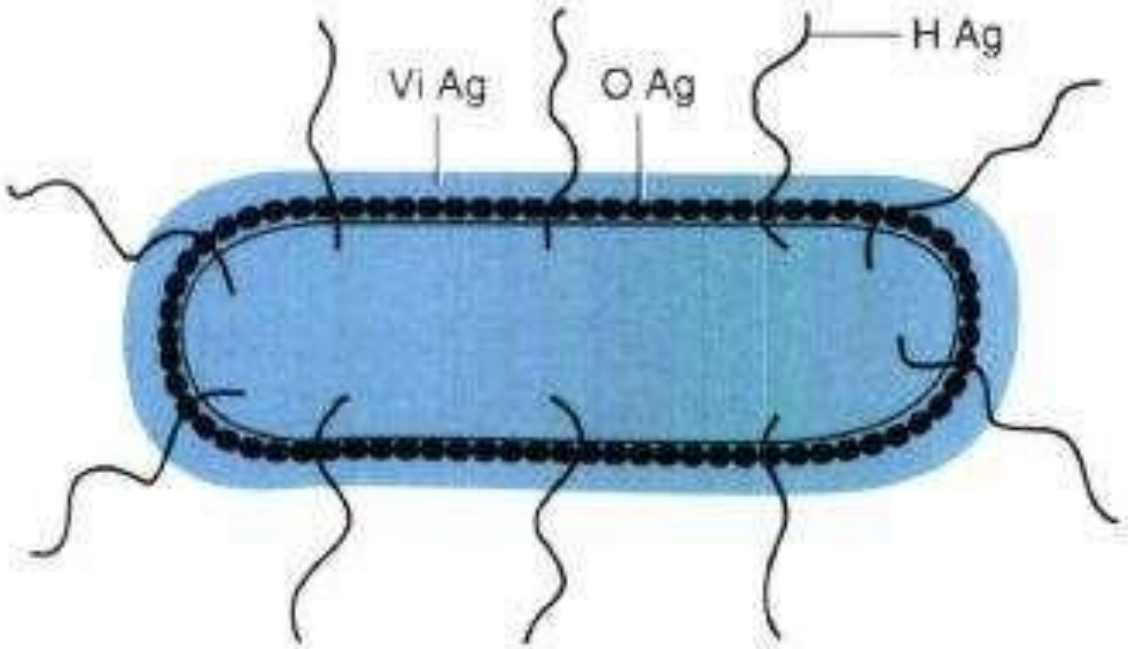


FIGURE 20-8 ■ The antigenic structures of salmonellae used in serologic typing.

Pathogenesis and Immunity

- After ingestion and passage through the stomach, salmonellae attach to the mucosa of the **small intestine and** invade into the **M (microfold) cells located in Peyer** patches, as well as into enterocytes.

- The bacteria remain in endocytic vacuoles, where they replicate. The bacteria can also be transported across the cytoplasm and released into the blood or lymphatic circulation.

- Regulation of the attachment, engulfment, and replication is controlled primarily by two large clusters of genes **(pathogenicity island I and II) on the bacterial chromosome.**

- **Pathogenicity** island I encodes **salmonella-secreted invasion proteins (Ssps) and a type III secretion system that injects** the proteins into the host cell.

- Pathogenicity island II contains genes that allow the bacteria to evade the host's immune response and a second type III secretion system for this function

PATHOPHYSIOLOGY

Ingest contaminated food

↓

Ingested bacilli invade small intestinal mucosa

↓

Taken up by macrophage & transported to regional lymph node

↓

S.typhi multiply in the intestinal lymphoid tissue

↓

Intact with enterocytes & M cells(ileal Peyer's pathches) during the 1-3 week of incubation period (Diarrhoea)

↓

End of incubation period, bacilli enter bloodstream(Bacteraemia phase)

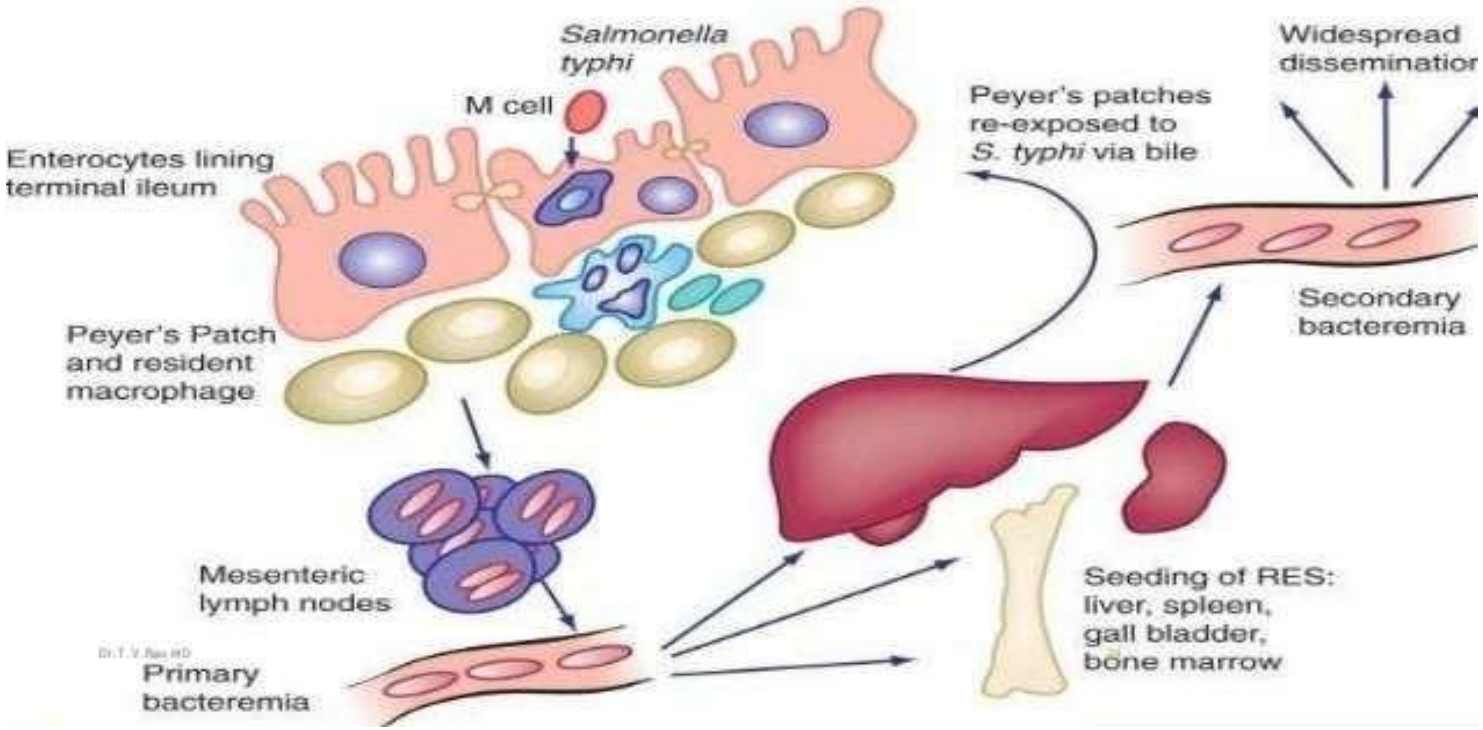
↓ (onset of typhoid fever)

Bacteria invade the gallbladder, biliary system and lymphatic tissue of the bowel and multiply in high number

↓

Then pass into the intestinal tract (stool)

Pathogenesis of typhoid fever



Epidemiology

- *Salmonella can colonize virtually all animals, including* poultry, reptiles, livestock, rodents, domestic animals, birds, and humans.
- **Animal-to-animal spread** and the use of *Salmonella-contaminated animal feeds maintain an* **animal reservoir.**
- **Serotypes such as *Salmonella Typhi* and *Salmonella Paratyphi are highly adapted to humans* and do not cause disease in nonhuman hosts.**
- In addition, in contrast with other *Salmonella serotypes, strains that are highly* adapted to humans (i.e., *Salmonella Typhi, Salmonella* Paratyphi) can **survive in the gallbladder and establish chronic carriage.**

Epidemiology

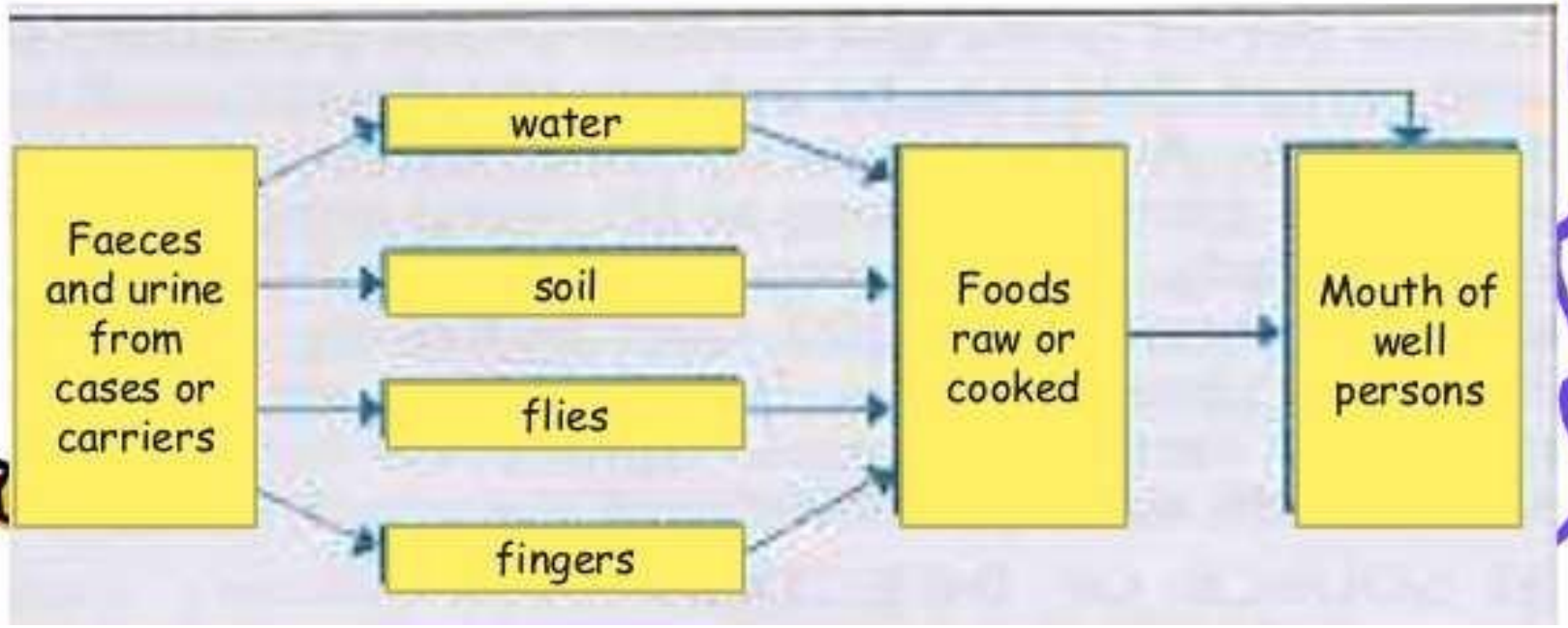
- **Most infections result from the ingestion of contaminated food products and, in children, from direct fecal-oral spread.**
- **The incidence of disease is greatest in children younger than 5 years and adults older than 60 years who are infected during the summer and autumn months, when contaminated foods are consumed at outdoor social gatherings.**
- **The most common sources of human infections are poultry, eggs, dairy products, and foods prepared on contaminated work surfaces (e.g., cutting boards where uncooked poultry was prepared).**
- ***Salmonella* Typhi infections occur when food or water contaminated by infected food handlers is ingested. There is no animal reservoir.**
- **It is estimated that 21 million *Salmonella Typhi* infections and 200,000 deaths occur each year worldwide.**

Epidemiology

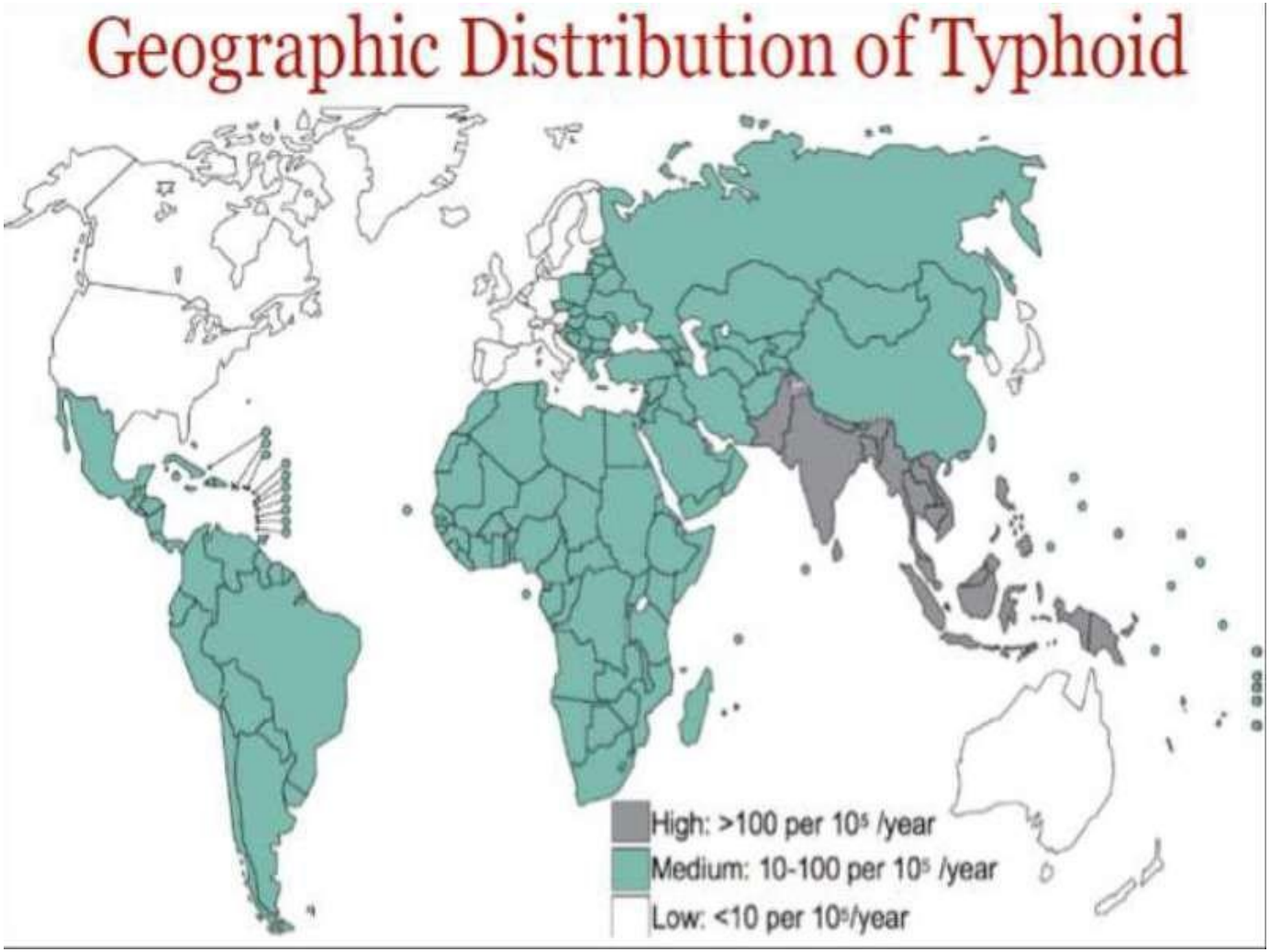
- **The infectious dose for *Salmonella Typhi infections* is low**, so person-to-person spread is common.
- In contrast, a large inoculum (e.g., 10^6 to 10^8 bacteria) is required for symptomatic disease to develop with most other *Salmonella serotypes.*
- *The organisms can multiply to this* high density if contaminated food products are improperly stored (e.g., left at room temperature).
- The infectious dose is lower for people at high risk for disease because of age, immunosuppression or underlying disease (leukemia, lymphoma, sickle cell disease), or reduced gastric acidity.

5- MODE OF TRANSMISSION

The disease is transmitted by "faeco-oral route" or "urine-oral routes" either directly through hands soiled with faeces or urine of cases or carriers or indirectly by ingestion of contaminated water, milk, food, or through flies. Contaminated ice, ice-creams, and milk products are a rich source of infection.



Geographic Distribution of Typhoid



Clinical Diseases

- The following four forms of *Salmonella infection exist:* gastroenteritis, septicemia, enteric fever, and asymptomatic colonization.

❖ ***Gastroenteritis-***

- Gastroenteritis is the **most common form of salmonellosis** in the United States.
- Symptoms generally **appear 6 to 48 hours** after the consumption of contaminated food or water, with the initial presentation consisting of **nausea, vomiting, and nonbloody diarrhea.**
- **Fever, abdominal cramps, myalgias, and headache** are common.
- Colonic involvement can be demonstrated in the acute form of the disease.
- Symptoms can persist from **2 to 7 days** before spontaneous resolution.

Clinical Diseases

❖ ***Septicemia***

- All *Salmonella species can cause bacteremia, although* infections with *Salmonella Typhi*, *Salmonella Paratyphi*, and *Salmonella Choleraesuis more commonly lead to a* bacteremic phase.

- The risk for *Salmonella bacteremia is* higher in **pediatric and geriatric patients and in immunocompromised patients (HIV infections, sickle-cell disease, congenital immunodeficiencies**).

- The clinical presentation of *Salmonella bacteremia is like that of* other gram-negative bacteremias; however, localized suppurative infections (e.g., **osteomyelitis, endocarditis, arthritis**) can occur in as many as 10% of patients.

Clinical Diseases

❖ ***Enteric Fever***

- *Salmonella Typhi produces a febrile illness called* ***typhoid*** **fever.**
- **A milder form of this disease, referred to as paratyphoid fever, is produced by**
  - ***Salmonella Paratyphi A,***
  - *Salmonella Paratyphi* B), and
  - *Salmonella* Paratyphi C).
- The bacteria responsible for enteric fever pass through the cells lining the intestines and are engulfed by macrophages. They replicate after being transported to the liver, spleen, and bone marrow.

Clinical Diseases

- Ten to 14 days after ingestion of the bacteria, patients experience
  - **gradually increasing fever, with**
  - **nonspecific complaints of headache, myalgias, malaise, and anorexia.**
  - These symptoms persist for 1 week or longer and are followed by
  - gastrointestinal symptoms. This cycle corresponds to an initial bacteremic phase that is followed by colonization of the gallbladder and then reinfection of the intestines.
- Enteric fever is a serious clinical disease and must be suspected in febrile patients who have recently traveled to developing countries where disease is endemic.

Clinical Diseases

- *Enteric fever is a misnomer, in that* ***the hallmark features of*** **this disease—fever and abdominal pain—are variable.**
- Although fever is documented at presentation in >75% of cases, abdominal pain is reported in only 30–40%.
- Thus a high index of suspicion for this potentially fatal systemic illness is necessary when a person presents with fever and a history of recent travel to a developing country.
- **The incubation period for *S.Typhi averages 10–14 days* but ranges from 3 to 21 days,** with the duration likely reflecting the inoculum size and the host's health and immune status.
- The **most prominent symptom is prolonged fever (38.8°–40.5°C; 101.8°–104.9°F), which can continue for up to 4 weeks if untreated.**
- *S. Paratyphi A is* thought to cause milder disease than *S.Typhi, with predominantly* gastrointestinal symptoms.

Clinical Diseases

- Symptoms reported on initial medical evaluation included
- **headache (80%),**
- **chills (35–45%),**
- **cough (30%),**
- **sweating (20–25%),**
- **myalgias (20%),**
- **malaise (10%), and**
- **arthralgia (2–4%).**
- **Gastrointestinal symptoms included**
- **anorexia (55%),**
- **abdominal pain (30–40%),**
- **nausea (18–24%),**
- **vomiting (18%), and**
- **diarrhea (22–28%)** more commonly than **constipation (13–16%).**

Clinical Diseases

- Physical findings included
  - coated tongue (51–56%),
  - splenomegaly (5–6%), and
  - abdominal tenderness (4–5%).
- Early physical findings of enteric fever include
  - rash (“rose spots”),
  - hepatosplenomegaly (3–6%),
  - epistaxis, and
  - relative bradycardia at the peak of high fever.

Clinical Diseases

- Rose spots **make up a faint, salmon-colored, blanching,** maculopapular rash located primarily on the trunk and chest.
- The rash is evident in ~30% of patients at the end of the first week and resolves without a trace after 2–5 days.
- Patients can have two or three crops of lesions, and *Salmonella can be cultured from punch biopsies of* these lesions.
- The faintness of the rash makes it difficult to detect in highly pigmented patients.

Clinical Diseases

❖ **Complications of Enteric Fever-**

1. Gastrointestinal bleeding
2. Intestinal perforation (usually of terminal ileum
3. Encephalopathy accompanied by hemodynamic shock
4. Hepatitis
5. Cholecystitis
6. Pneumonia (may be due to secondary infection with other organisms such as *Streptococcus pneumoniae)*
7. Myocarditis
8. Acute kidney injury, nephritis

Clinical Diseases

- Complications of Enteric fever-

1. Deep-seated abscess (e.g., spleen, large joint, bone)
2. Anemia
3. Meningitis
4. Neurological disturbance (cerebellar ataxia)
5. Miscarriage
6. Psychiatric disturbance
7. Disseminated intravascular coagulation
8. Chronic carriage (fecal or urinary carriage for 1 yr)
9. Carcinoma of gallbladder

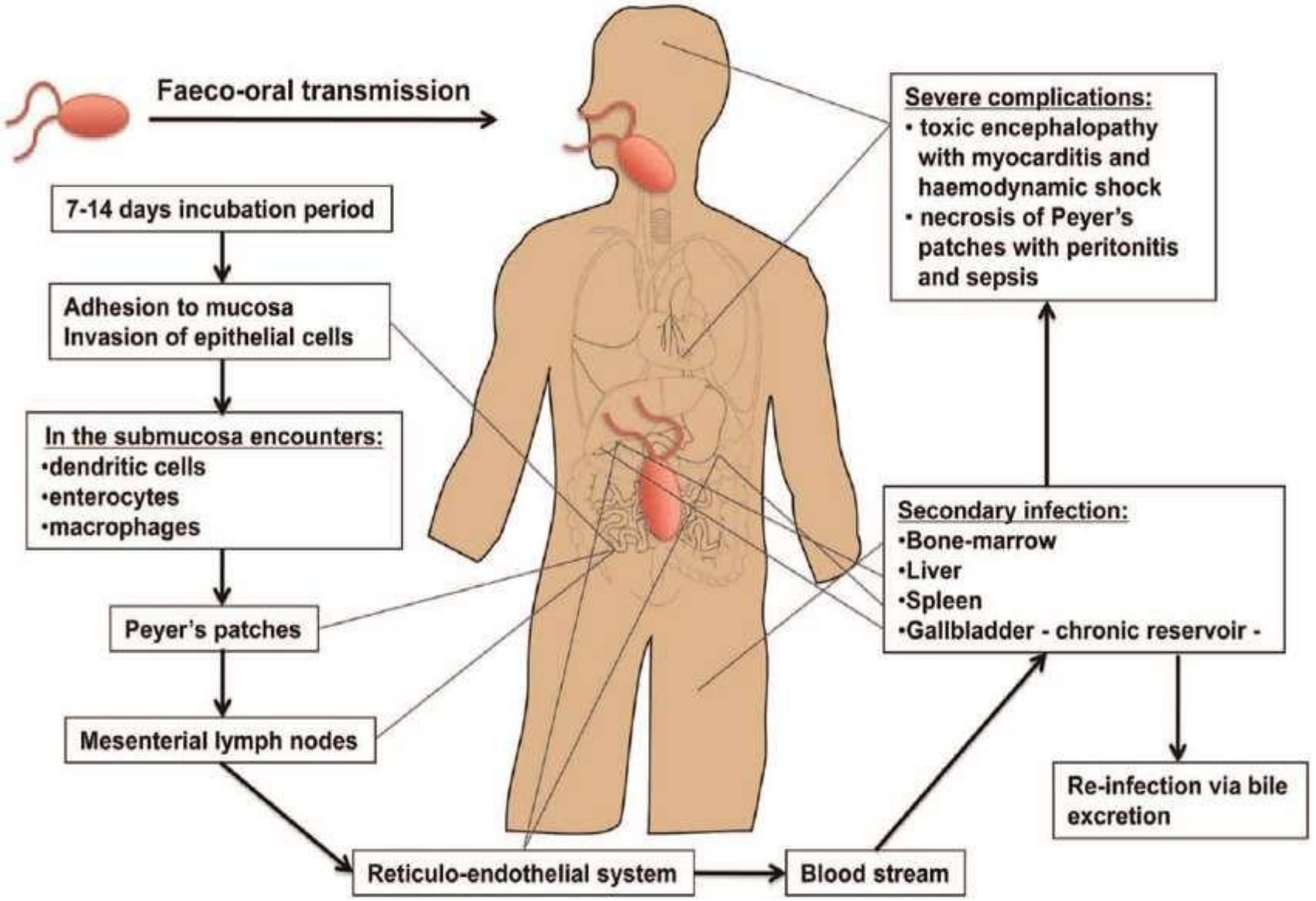
Clinical Diseases

❖ ***Asymptomatic Colonization***

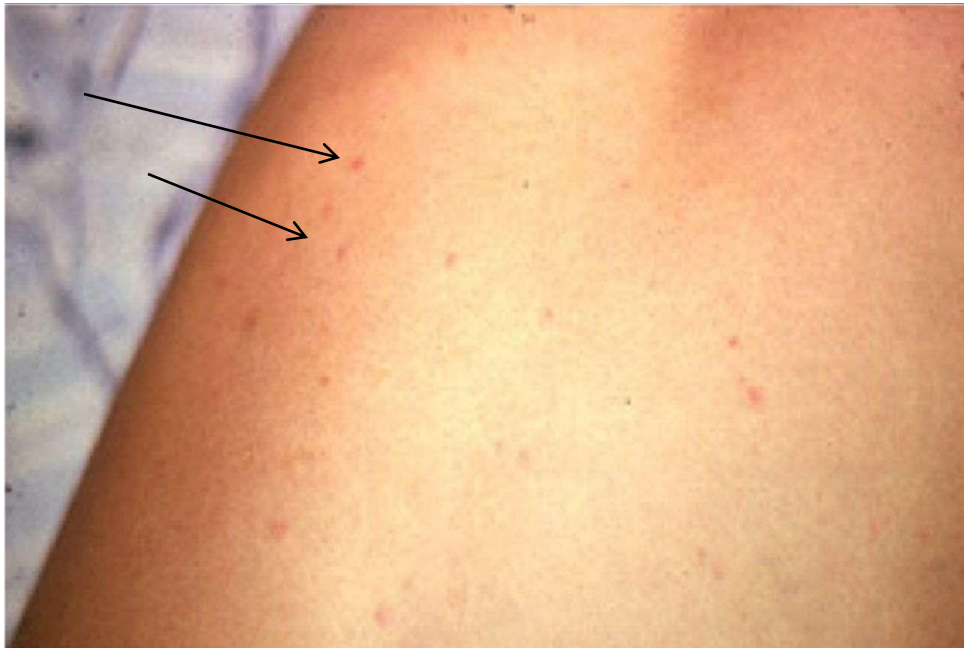
- The strains of *Salmonella responsible for causing typhoid* and paratyphoid fevers are maintained by human colonization.

- **Chronic colonization for more than 1 year after** symptomatic disease develops in 1% to 5% of patients, the gallbladder being the reservoir in most patients.

- Chronic colonization with other species of *Salmonella* occurs in less than 1% of patients and does not represent an important source of human infection.


Faeco-oral transmission
7-14 days incubation period
Adhesion to mucosa
Invasion of epithelial cells
In the submucosa encounters:
•dendritic cells
•enterocytes
•macrophages
Peyer's patches
Mesenterial lymph nodes
Reticulo-endothelial system
Blood stream
Severe complications:
• toxic encephalopathy with myocarditis and haemodynamic shock
• necrosis of Peyer's patches with peritonitis and sepsis
Secondary infection:
•Bone-marrow
•Liver
•Spleen
•Gallbladder - chronic reservoir -
Re-infection via bile excretion

Rose Spot



Laboratory diagnosis of Enteric Fever

- Diagnostic tests are needed for the diagnosis of-

  - invasive *Salmonella* infections,
  - for the detection of convalescent and chronic fecal carriage of typhoidal *Salmonella*,
  - *and to estimate the burden of* disease for public health assessment.

- It may be important to be able to detect both *Salmonella serovar Typhi and Salmonella serovar Paratyphi A infections, as they cannot be distinguished* from each other clinically.

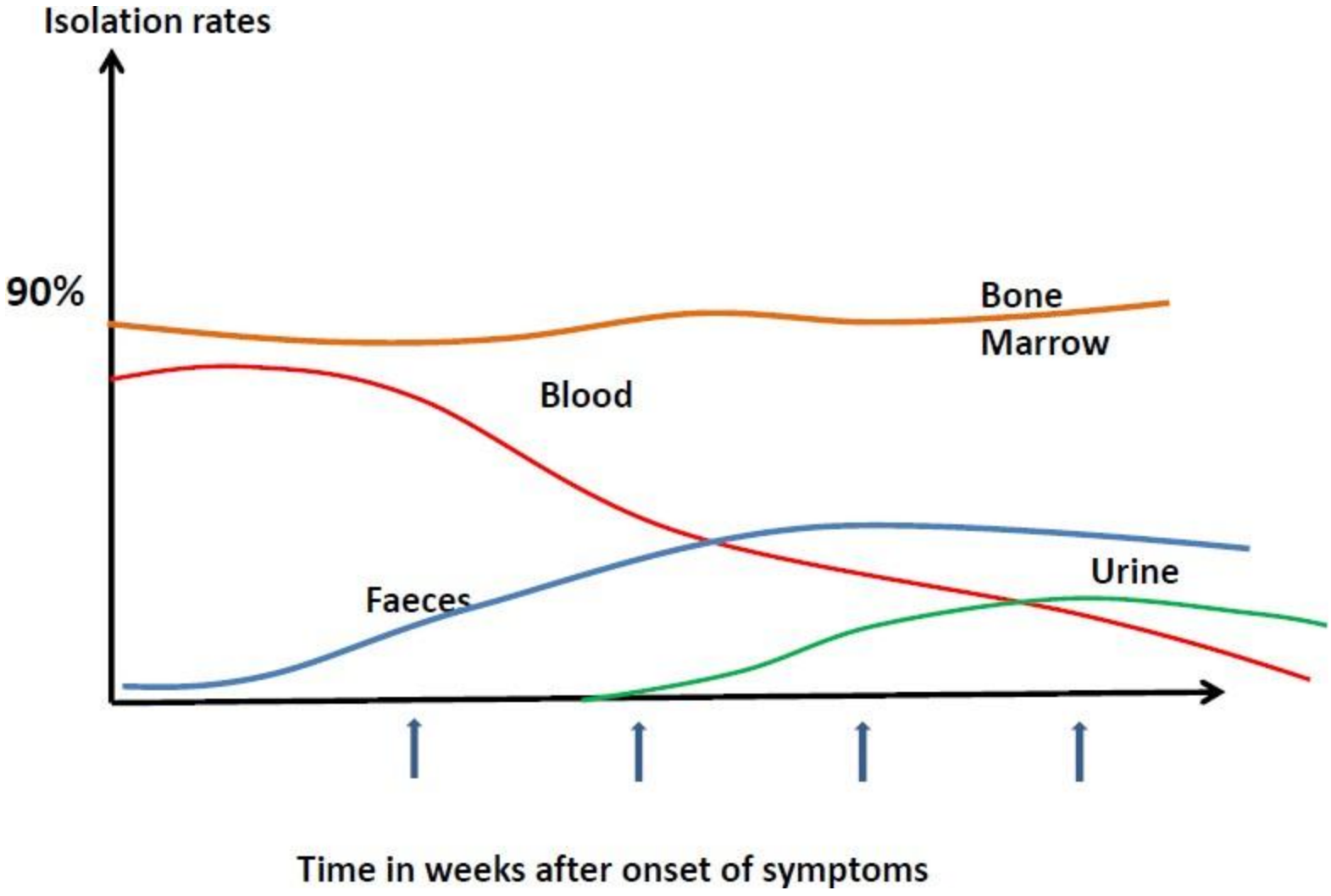
- Microbial culture is the mainstay of diagnosis.

- Antibody and antigen detection and nucleic acid amplification tests have limitations, as described below.

Laboratory diagnosis of Enteric Fever

- The test of choice depends on the duration of disease-

Duration of disease	Specimen	Positivity (%)
1st week	Blood culture	90
2nd week	Blood Culture Feaces culture Widal test	75 50 Low titre
3rd week	Widal test Blood culture Feaces culture	80-100 60 80


Isolation rates
90%
Bone
Marrow
Blood
Faeces
Urine
Time in weeks after onset of symptoms

Laboratory diagnosis of Enteric Fever

- The definitive diagnosis of enteric fever relies on the isolation of *Salmonella enterica from normally sterile clinical samples*, *usually* blood and bone marrow.
- Culture confirms the diagnosis and provides an isolate for antimicrobial susceptibility testing, epidemiologic typing, and molecular characterization.
- **Blood culture-**
- Blood cultures are positive in approx. 90% of cases in the first week of fever, 75% in the second week and 60% in the third week.
- Positivity rates decline thereafter and blood cultures remain positive in 25% cases till the subsidence of pyrexia.

Laboratory diagnosis of Enteric Fever

- 10 mL of blood is collected under aspectic conditions into blood culture bottles(Glucose and Taurocholate broth).
- Before transferring the blood into blood culture bottles, caps of these bottles should be thoroughly cleansed with spirit. Blood should be transferred through a hole in a cap by inserting the needle, thus avoiding contamination from external environment.
- The dilution ratio is 1: 10 for blood culture(5 mL blood in 50 mL blood culture bottles.)
- The blood culture bottles are incubated at 37^0 C.

Laboratory diagnosis of Enteric Fever

- In areas of endemicity where antimicrobials are frequently taken before evaluation, the yield from blood culture can be as low as 40%, and in this setting, **bone marrow aspirate culture is usually considered the reference standard method, with a sensitivity of 80%.**

- The optimum period for detecting organisms circulating in the bloodstream is considered to be in the first or second week of the illness, although cultures can still remain positive in the third week in the absence of antimicrobial exposure.

- It is possible that if a sufficiently large volume of blood is taken for culture using modern media and systems, blood culture may be as sensitive as bone marrow culture.

- **Rose spot culture has been reported to be positive in 70% of patients**, although in practice rose spots are rarely present.

- Cerebrospinal fluid culture is usually positive only in very young children

Laboratory diagnosis of Enteric Fever

- Blood culture bottles are sub-cultured in Blood and MacConkey agar and pale lactose non-fermenting colonis are selected for Biochemical and serological identification.

❖ **Clot Culture-**

- It is an alternative to blood culture. 5 mL of blood is withdrawn aseptically into a sterile container and allowed to clot.

- The serum is separated and used for Widal test.

- The clot is broken up with a sterile glass rod and added to bile broth containing streptokinase (100 units/ml.) which digests the clot and bacteria is released from the clot.

Laboratory diagnosis of Enteric Fever

❖ **Faeces Culture-**

- Salmonella is shed in the feaces throughout the diseaes and even in the convalescence.
- Hence, feacal culture may be helpful in patients and also in detection of carriers. It is also valuable during antibiotic therapy when blood cultures become negative.
- Successful culture depends on the use of Enrichment and Selective media.
- **Feacal samples are inoculated into one tube each of Selenite and Tetrathionate broth(Both enrichment media) and also plated directly MacConkey agar, DCA/ XLD and Wilson-Blair Media.**
- Salmonella appear as pale yellow colonies on MacConkey agar and DCA media. On W-B medium, S. typhi form large black colonies with metallic sheen whereas S. paratyphi A produces green colonies due to lack of H2S production.
- Enrichment broths are incubated for 6-8 hrs. before subculture to MacConkey and DCA agar and incubated overnight for 37^0C.

Laboratory diagnosis of Enteric Fever

❖ **Biochemical Identification of Isolates-**

Tests	S. typhi	S. Paratyphi
Catalase	+ve	+ve
Oxidase	-ve	-ve
Nitrate Reduction	+ve	+ve
Glucose	+ve (Acid only)	+ve(Acid and Gas)
Mannitol	+ve (Acid only)	+ve(Acid and Gas)
Lactose	-ve	-ve

Salmonella on XLD agar

Salmonella on MA

M331
S. Typhimurium
14028

Wilson-Blair Media

Laboratory diagnosis of Enteric Fever

❖ **Serological Identification of Isolates-**

- A loopful of the growth from a nutrient agar slop is emulsified in 2 different drops of saline,
- one acts a control (check for Autoagglutination), another is tested by Polyvalent O & H antisera.
- Positive agglutination confirms identification of salmonella genus.
- Further typing can be done in a **Reference lab. Like National Salmonella Reference Center , Kasauli.**

Laboratory diagnosis of Enteric Fever

❖ **Demonstration of Antibodies-**

Widal Test-

- It is an **agglutination test** for detection of **agglutinins (H and O)** present in patients with enteric fever. Antibodies start appearing at the **end of the 1st week and rise sharply at 3rd week.**

❑ **Procedure-**

- **Two types of tubes** are used for this test- **Dreyer's Tube (narrow tube with a conical bottom) and Felix tube (Short, round bottom)**.
- Equal vol. (0.4 ml) of **serial dilutions of serum (1:10 to 1:640)** and **H and O antigengs (for S. Typhi) and AH & BH antigens (for S. Paratyphi)** are mixed and incubated in a water bath at 37^0C for 4 hours and read after overnight refrigeration at 4^0C.
- **Control tubes** containing the antigen and normal saline are included to check for autoagglutination.

Laboratory diagnosis of Enteric Fever

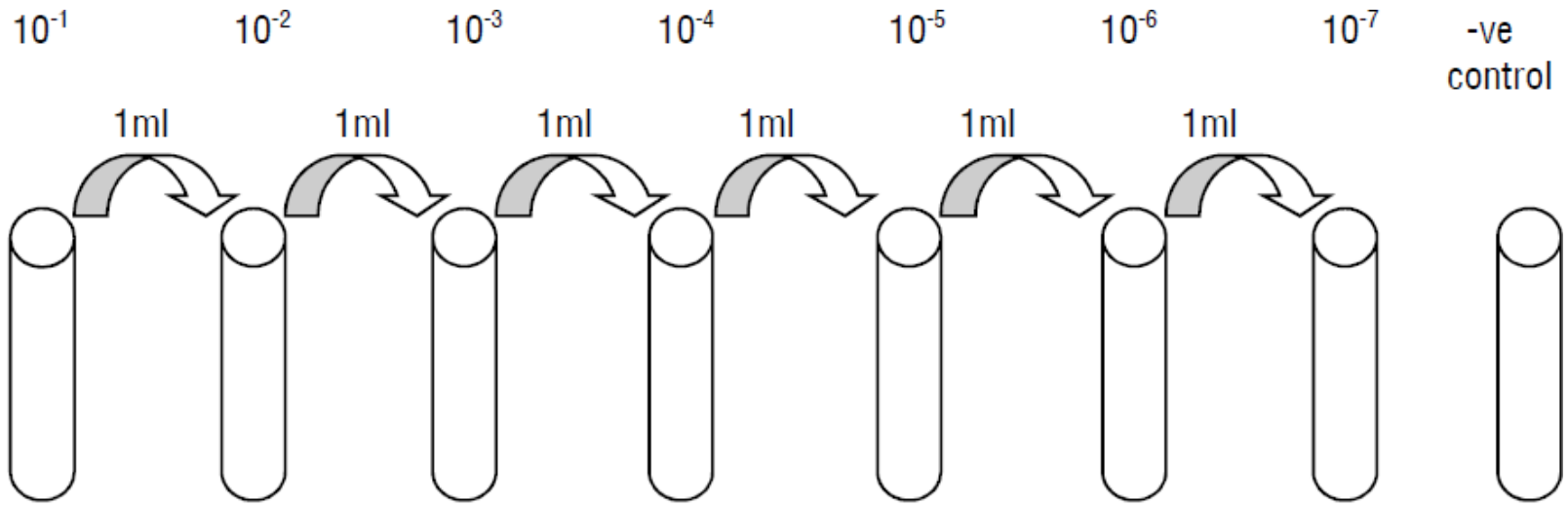
❖ **Interpretation of Widal Test-**

1. The test may be negative in early part of first week.
2. **Single test is usually of not much value**
3. **A rise in titer between two sera specimens is more meaningful than a single test.**
4. If the first sample is taken late in the disease, a rise in titer may not be demonstrable. Instead, there may be a fall in titer.
5. **Baseline titer of the population must be known before attaching significance to the titers.**
6. The antibody levels of healthy individuals in population of a given area give the baseline titer.
7. **A titer of 100 or more for O antigen is considered significant and a titer in excess of 200 for H antigens is considered significant generally.**

Laboratory diagnosis of Enteric Fever

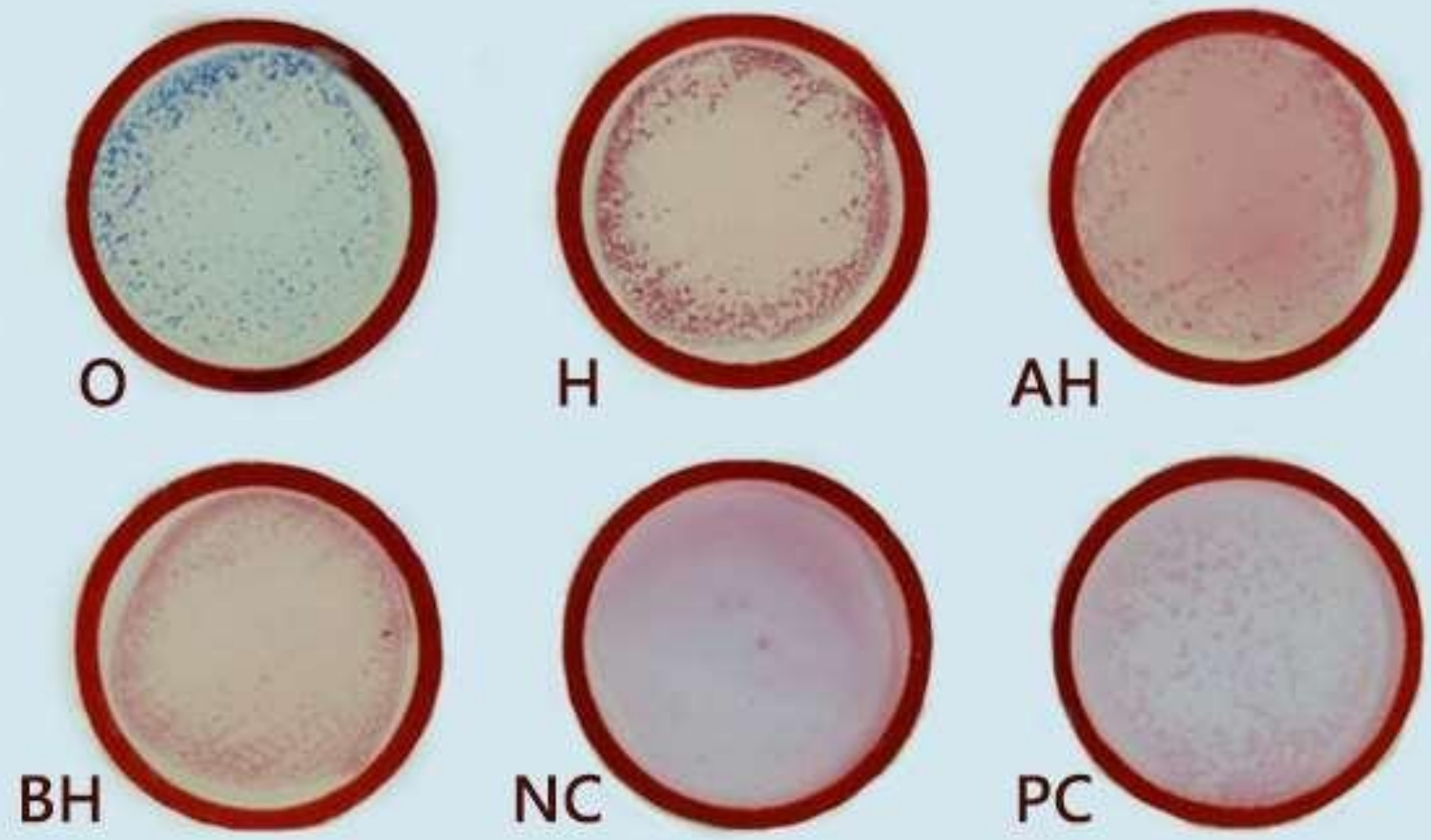
❖ **Interpretation of Widal Test-**

1. Patients already **treated with antibiotics** may not show any rise in titer, instead there may be fall in titer.
2. Patients treated with antibiotics in the early stages may not give positive results.
3. Patients who have **received vaccines** against Salmonella may give false positive reactions.
4. This can be differentiated from true infection by repeating the test after a week. True untreated infection results in rise in titer.
5. Those individuals with **past infections** may develop anti-Salmonella antibodies during an unrelated or closely related infection…. **"anamnestic response" …..differentiated from true infection by lack of any rise in titer on repetition after a week.**



Tube no	1	2	3	4	5	6	7	8
Saline-	1.9 ml	1 ml	1ml	1ml	1ml	1ml	1ml	1ml
Test Serum-	+ 0.1ml							
	1:20	**1:40**	**1:80**	**1:160**	**1:320**	**1:640**	**1:1280**	

Widal Test Report Analysis



Healthcheckup.com

Laboratory diagnosis of Enteric Fever

❖ **Other Serological Tests-**

1. ELISA
2. Reverse Passive Haemagglutination Test (RPHA)
3. The TyphiDot is a DOT enzyme immunoassay (Typhidott and Typhidot-Mt)
4. TUBEX (IDL Biotech, Sollentuna, Sweden) is a semiquantitative test that uses polystyrene particle agglutination to detect IgM antibodies to the O9 antigen.
5. *S. Typhi antigen can be detected in the urine of some typhoid patients by co-agglutination and ELISA*


TYPHIDOT Rapid IgM
TYPHIDOT RAPID
IgM
IgG
C
T
C
T


iDL Biotech
TUBEX® TF
RAPID TYPHOID DETECTION
CE


CALBIOTECH
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Laboratory diagnosis of Enteric Fever

❖ ***Molecular Diagnosis-***

- Targets for *Salmonella serovar Typhi* PCR-based assays have included
- **theHdflagellin gene *fliC-d,***
- **the Vi capsular gene *viaB,***
- ***the tyvelose epimerase gene (tyv)* (previously *rfbE),***
- ***the paratose synthase gene (prt) (previously rfbS),***
- ***groEL,***
- ***the 16sRNA gene ,***
- ***hilA*** *(a regulatory gene* in *Salmonella pathogenicity island 1 [SPI-1]), the gene encoding* the 50-kDa outer membrane protein ST50

- The food industry has used PCR technology for several decades and guidelines are published for quantitative detection of *Salmonella in food by PCR.*
- Studies using single or nested PCR primers for *fliC of S. Typhi have reported good results from PCR.*

TABLE 4 Characteristics of selected serologic tests used for the diagnosis of infection with *Salmonella* Typhi and *Salmonella* Paraty

Test	Test methodology	Reported characteristics[b]
Enterocheck-WB	Dipstick detecting anti-LPS IgM antibodies	Sensitivity, 89%; specificity, 97%
LifeAssay Test-it	Detects IgM antibodies against *Salmonella* Typhi LPS in an ICT LFA cassette format	Sensitivity, 59%; specificity, 98%
Mega *Salmonella*	ELISA detecting IgG and IgM antibodies against an undefined *Salmonella* Typhi antigen	Sensitivity, 91%; specificity, 49%
Multi-Test-Dip-S-Ticks	Dipstick detecting anti-LPS IgG and IgM	Sensitivity, 89%; specificity, 53%
PanBio	ELISA detecting anti-LPS IgG and IgM	Sensitivity, 78%; specificity, 80%
SD Bioline	ICT LFA cassette detecting IgG and IgM antibodies against an undefined *Salmonella* Typhi antigen	Sensitivity, 69%; specificity, 79%
Tubex TF	Detects antibody against *Salmonella* Typhi LPS with an inhibition assay format and a visual result readout	Sensitivity, 56–100%; specificity, 58–100%
Typhidot	Measures IgM and IgG antibodies against a 50-kDa outer membrane protein of *Salmonella* Typhi in an immunodot test format	Sensitivity, 67–98%; specificity, 58–100%
Typhidot M	Measures IgM antibodies, after removal of IgG antibodies, against a 50-kDa outer membrane protein of *Salmonella* Typhi in a dot blot format	Sensitivity, 47–98%; specificity, 65–93%
TyphiRapid IgM and IgG IgM (Combo)	Measures IgM antibodies, after removal of IgG antibodies, against a 50-kDa outer membrane protein of *Salmonella* Typhi in an ICT LFA[a] cassette format	Sensitivity, 89–100%; specificity, 85–89%
Widal test	Measures agglutinating antibodies against O and H antigens of *Salmonella* Typhi and *Salmonella* Paratyphi A; uses a tube or slide format	Very variable sensitivity and specificity; lack of standardized reagents

ANTIBIOTIC THERAPY FOR ENTERIC FEVER IN ADULTS

INDICATION	AGENT	DOSAGE (ROUTE)	DURATION, DAYS
Empirical Treatment			
	Ceftriaxone[a]	1–2 g/d (IV)	7–14
	Azithromycin	1 g/d (PO)	5
Fully Susceptible			
	Ciprofloxacin[b] (first line)	500 mg bid (PO) or 400 mg q12h (IV)	5–7
	Amoxicillin (second line)	1 g tid (PO) or 2 g q6h (IV)	14
	Chloramphenicol	25 mg/kg tid (PO or IV)	14–21
	Trimethoprim-sulfamethoxazole	160/800 mg bid (PO)	14
Multidrug-Resistant			
	Ciprofloxacin	500 mg bid (PO) or 400 mg q12h (IV)	5–7
	Ceftriaxone	2–3 g/d (IV)	7–14
	Azithromycin	1 g/d (PO)[c]	5
Nalidixic Acid–Resistant			
	Ceftriaxone	1–2 g/d (IV)	7–14
	Azithromycin	1 g/d (PO)	5
	High-dose ciprofloxacin	750 mg bid (PO) or 400 mg q8h (IV)	10–14

[a]Or another third-generation cephalosporin [e.g., cefotaxime, 2 g q8h (IV), or cefixime, 400 mg bid (PO)].
[b]Or ofloxacin, 400 mg bid (PO) for 2–5 days.
[c]Or 1 g on day 1 followed by 500 mg/d PO for 6 days.

THANK YOU