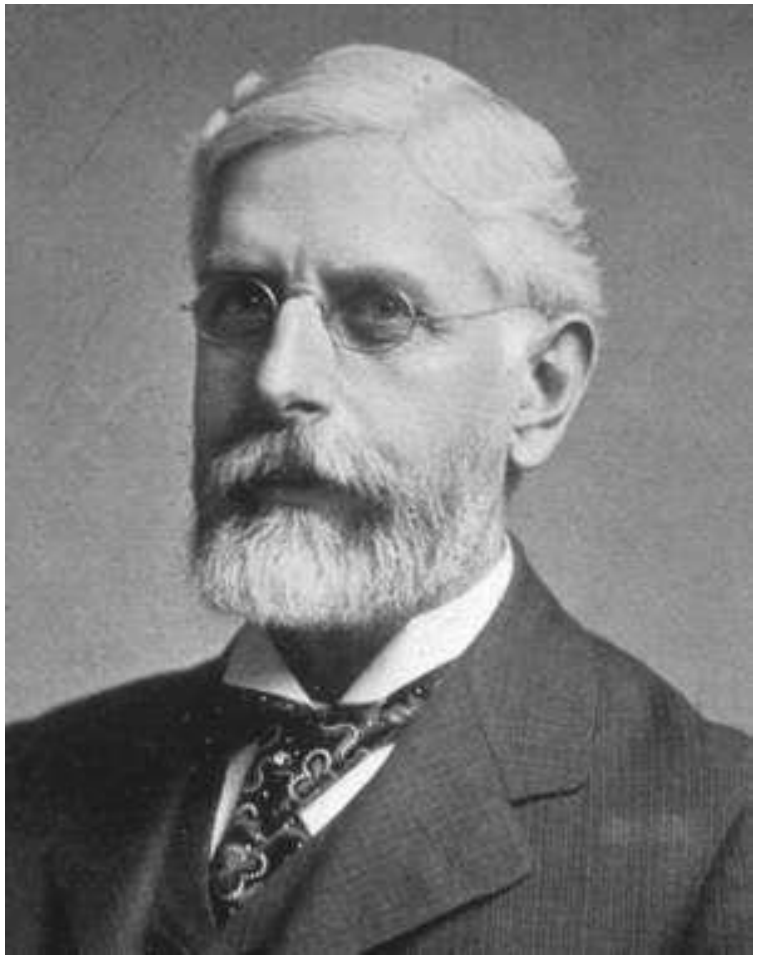
Typhoid Fever & Paratyphoid Fevers A, B, and C

Daniel Salmon



Taxonomy of typhoid & paratyphoid

family *Enterobacteriaceae*

genus *Salmonella*

Salmonella nomenclature is complicated. Initially each Salmonella species was named according to clinical considerations. Later, molecular findings led to the hypothesis that most serovars of Salmonella belongs to one species, S.enterica. But as this now formalized nomenclature is not in harmony with the traditional usage familiar to specialists in microbiology and infectologists, the ***traditional nomenclature is common:***

Typhoid fever, or commonly just typhoid is caused by

Salmonella typhi (*Salmonella enterica* serovar *Typhi*).

Paratyphoid fevers (paratyphoid) or enteric fevers are a group of enteric illnesses caused by three serovars of *Salmonellae*:

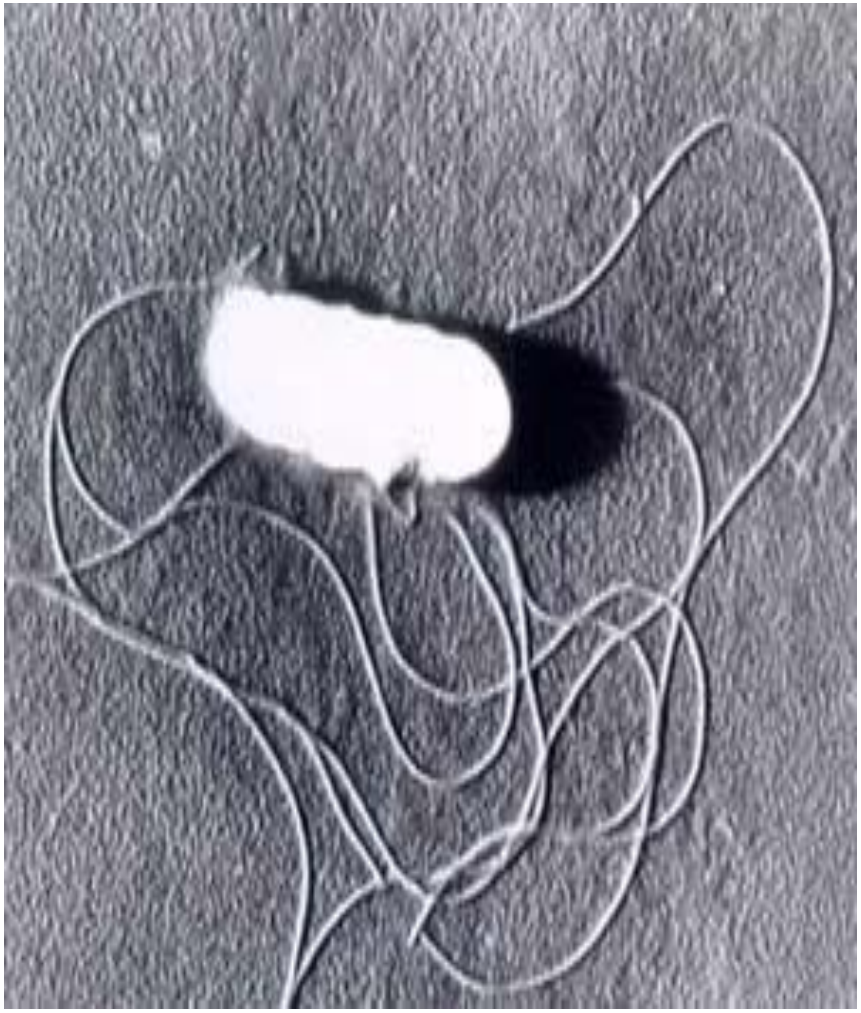
Salmonella paratyphi A,

S.paratyphi B (or *S.schottmuelleri*)

S.paratyphi C (*S.hirschfeldii*).

***Salmonella* typhi** (Salmonella enterica serovar Typhi)

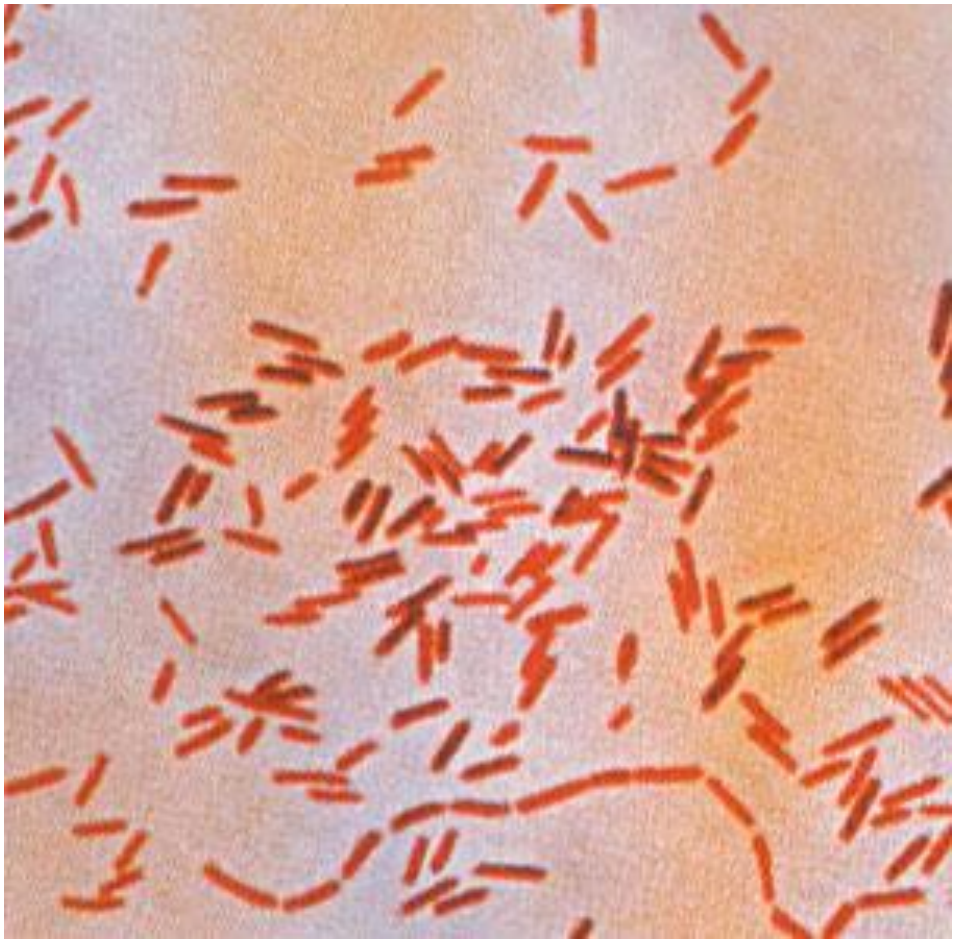
- ***Salmonella*** is a genus of rod-shaped, Gram-negative, non-spore forming, motile enterobacteria and flagella which project in all directions (i.e. peritrichous).



Salmonella typhi

- **They are chemoorganotrophs, obtaining their energy from oxidation and reduction reactions using organic sources and are facultative anaerobes; produce hydrogen sulfide.**
- **Most isolates exist in two phases; phase I is the motile phase and phase II the non-motile phase.**

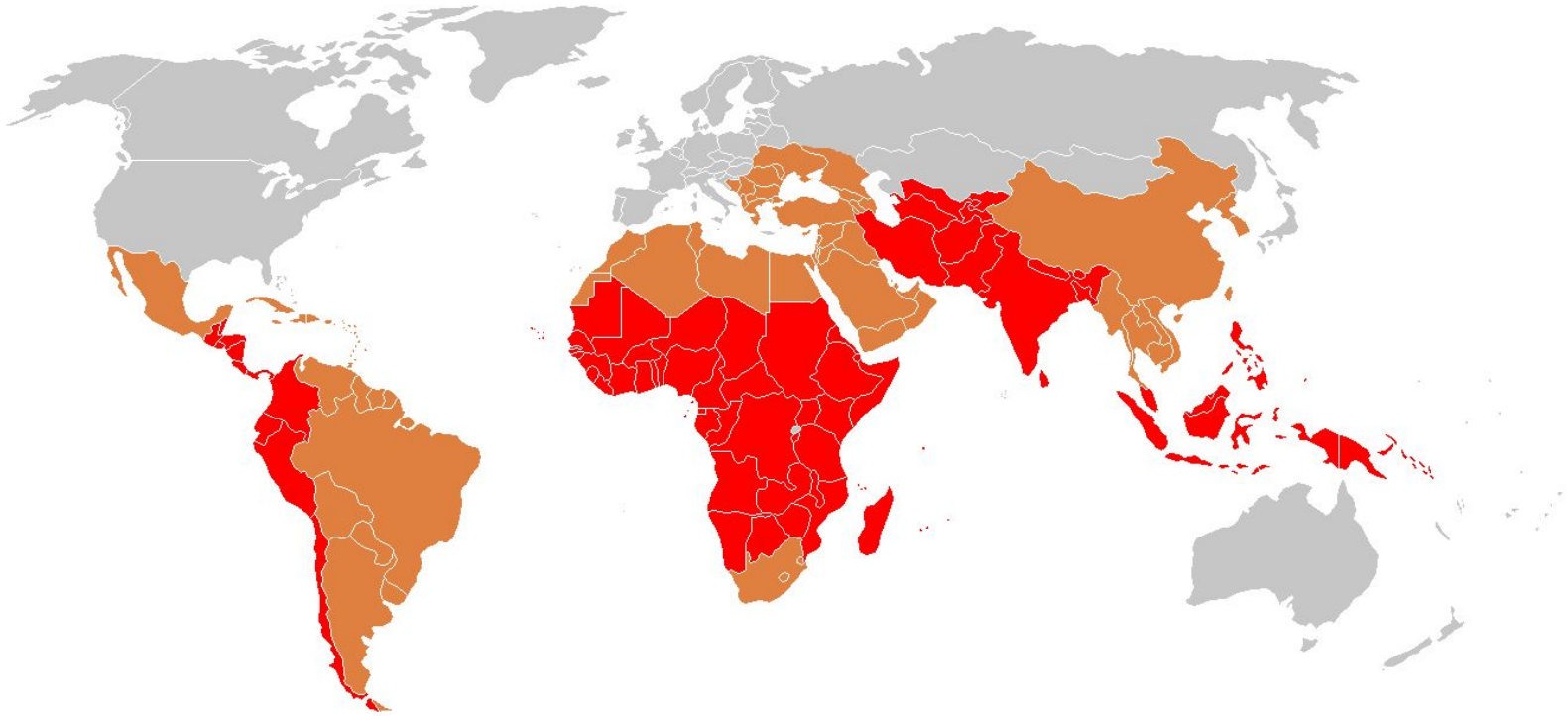
Salmonella typhi, the agent of typhoid fever. Gram stain



Typhoid

- **Typhoid**,is a common worldwide illness, transmitted by the ingestion of food or person.
- Typhoid transmission is only from human to human.
- Typhoid can only spread in environments where human feces or urine are able to come into contact with food or drinking water.

Incidence of Typhoid fever



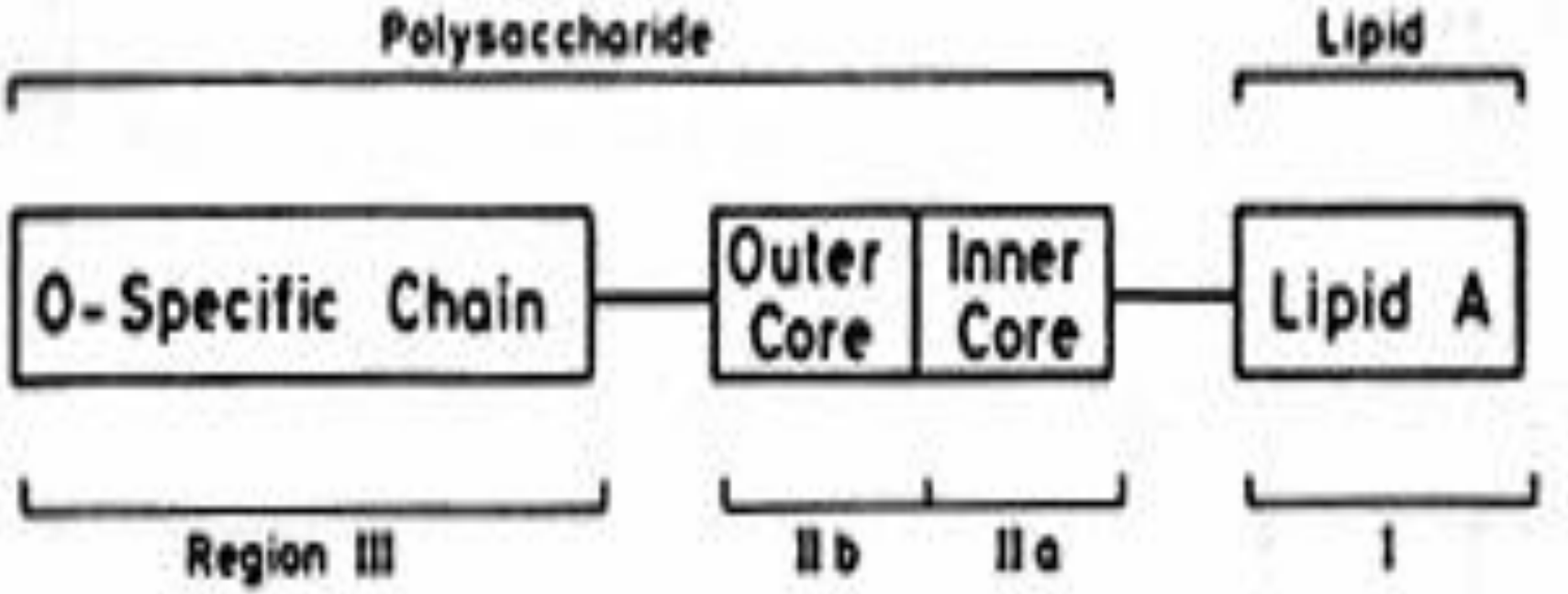
Virulence factors of *Salmonella typhi*

1) Endotoxin (LPS)

2) Adhesins - fimbria

3) Antiphagocytic factor – Vi antigen

Structural components of the outer membrane of Gram-negative bacteria (LPS).

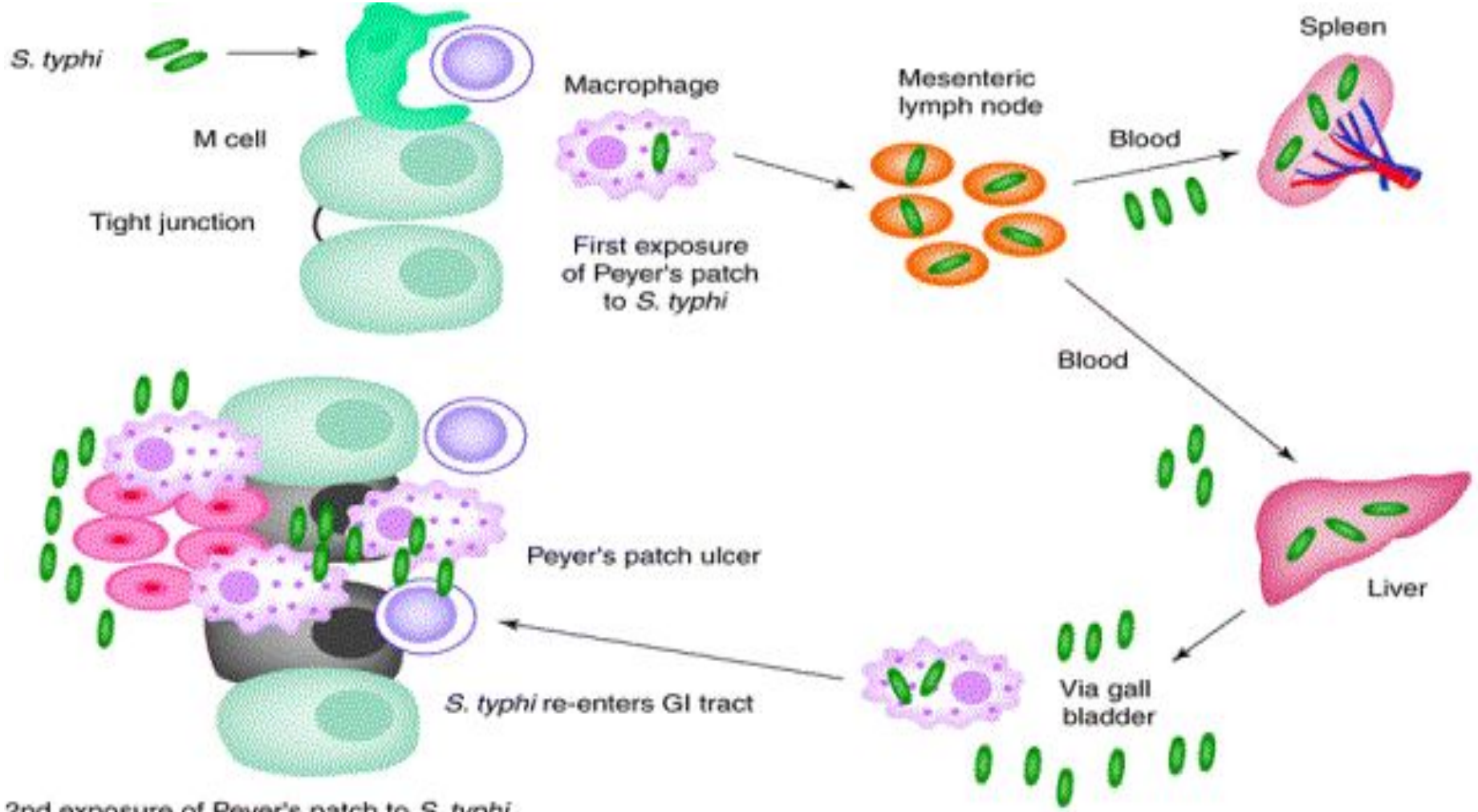


Significance of LPS

LPS released into the bloodstream by lysing Gram-negative bacteria is first bound by certain plasma proteins identified as **LPS-binding proteins**. The LPS-binding protein complex interacts with CD14 receptors on monocytes and macrophages and other types of receptors on endothelial cells. Endotoxins evoke fever, activate the serum complement, kinin, and clotting systems, depress myocardial function, and alter lymphocyte function. Circulating endotoxin may be responsible in part for many of the manifestations of septic shock that can occur in systemic infections.

Pathogenesis of typhoid & paratyphoid

- **The bacteria then perforate through the intestinal wall and are phagocytosed by macrophages. Alters its structure allow them to exist within the macrophage. This renders them resistant to damage by PMN's, complement and the immune response. The organism is then spread via the lymphatics while inside the macrophages.**


S. typhi
M cell
Tight junction
Macrophage
First exposure of Peyer's patch to S. typhi
Mesenteric lymph node
Blood
Spleen
Blood
Liver
Via gall bladder
S. typhi re-enters GI tract
Peyer's patch ulcer
2nd exposure of Peyer's patch to S. typhi
Key:
Peyer's patch
Salmonella typhi
Macrophage
Lymph node
Red blood cells
Necrotic Peyer's patch
T cells

The bacteria perforate through the intestinal wall

Typhoid, symptoms

- **The incubation period is usually 7-14 days.**
- **Typhoid fever is characterized by a slowly progressive as high as 40 °C (104 °F), profuse sweating, gastroenteritis, and nonbloody diarrhea. Less commonly a rash of flat, rose-colored spots may appear.**

Rose-colored spots

Typhoid, symptoms

- Untreated typhoid fever is divided into four stages, each lasting one week.
- In the first week, there is a slowly rising temperature with relative bradycardia
- malaise, headache and cough.

Typhoid, symptoms

- In the second week of the infection, the patient lies prostrated with high fever in plateau around 40 °C (104 °F) and bradycardia. Delirium is frequent.
- This delirium gives to typhoid the nickname of "nervous fever".
- The spleen and liver are enlarged (hepatosplenomegaly) and tender and there is elevation of liver transaminases.

Typhoid fever”s complications

- In the third week of typhoid fever a number of complications can occur:
- 1. Intestinal hemorrhage
- 2. Intestinal perforation in distal ileum
- 3. Metastatic abscesses, cholecystitis, endocarditis and osteitis
- By the end of third week the fever has started reducing (defervescence). This carries on into the fourth and final week.

Diagnosis

- ***Clinical specimen during first week of disease is blood***
- 1. Blood culture are positive in approximately 90% of case during the first week of fever.
- Blood is collected by vein puncture and inoculated into a culture containing 50-100 ml 0.5% bile broth. Bile is a selective medium for the Salmonella
- The main method of diagnosis is bacteriological method during the first week of typhoid fever.

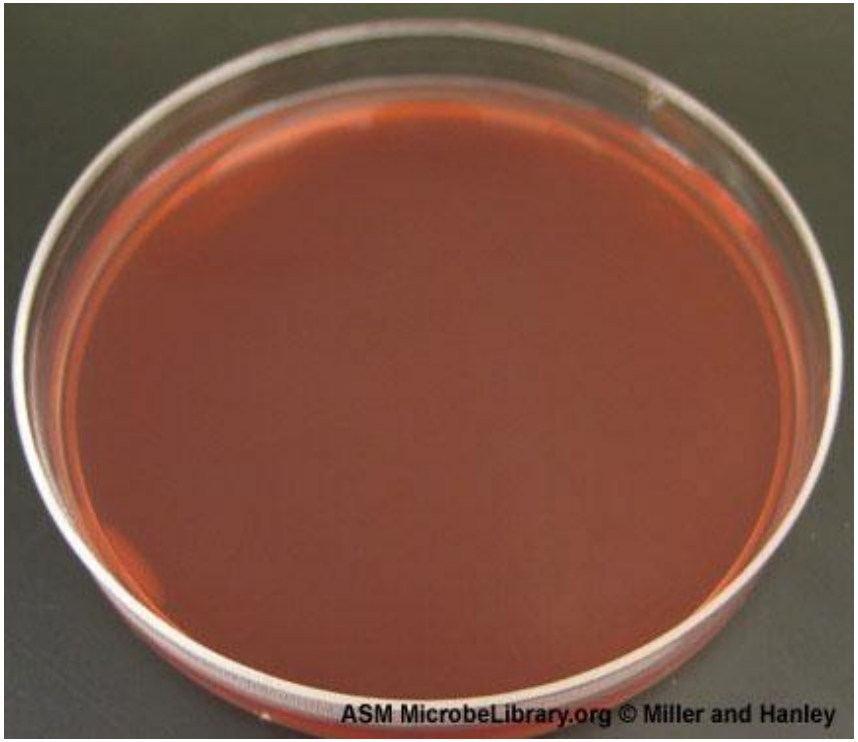
Bacteriological method (culture) for typhoid & paratyphoid

- **Preliminary stage.** Inoculation of 10 ml of patient's blood in the Rappoport's medium (contains bile broth).
- **1 stage**: Inoculation of the culture from the Rapport's medium on Endo or MacConkey's media for obtaining the isolated colonies.
- **2 stage**: Study of cultural properties of colonies & staining of particular colonies by Gram method. Inoculation of *lac* – colony (pale nonlactose fermenting colony) on Ressel's or Kligler's media (prick into agar slope and stroke on the slant surface). Inoculation of suspension from that colony in API-20E system.

3 stage: ***Identification*** staining properties (smear, stained by Gram method); cultural properties; biochemical properties on differential--diagnostic system API-20E; serological identification (with O- & H-antiserums); phage typing; susceptibility for antibiotics by disc method.

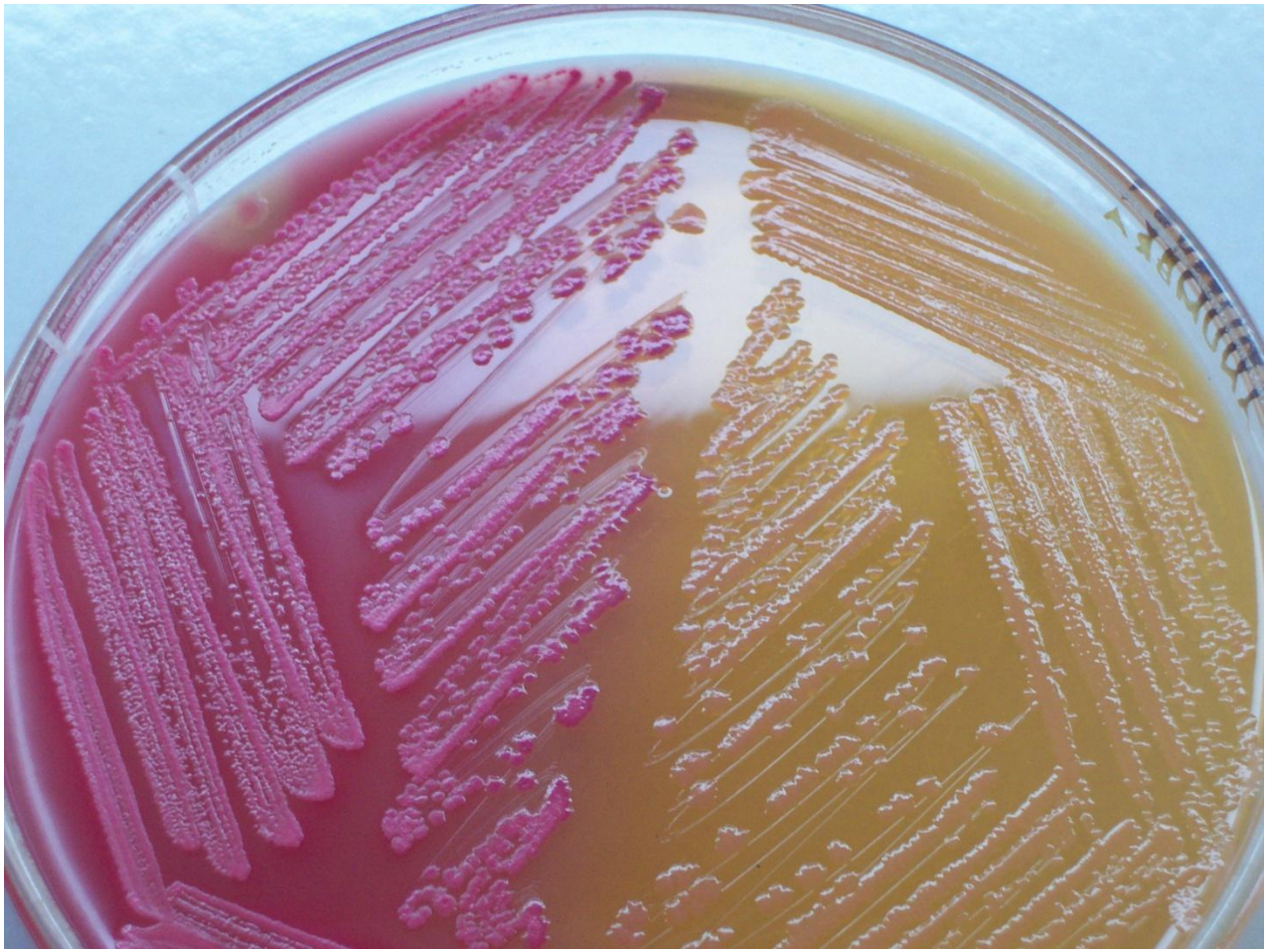
Blood culture

Nonlactose fermenting colonies



Growth on MacConkey or Endo agar

lac+ lac-



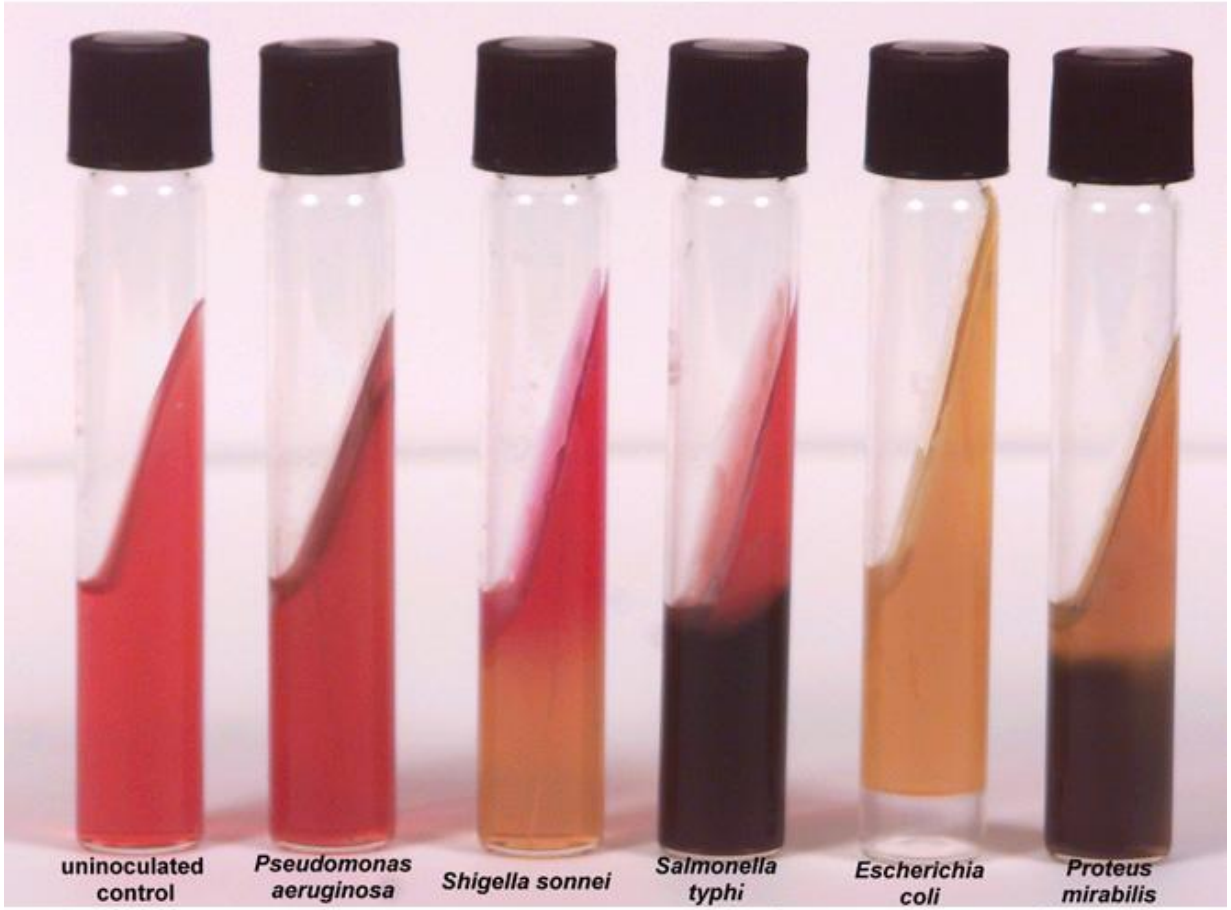
Salmonella typhi

- Salmonella will be motile, ferment glucose, mannitol and maltose but not lactose or sucrose.
- S.typhy will be anaerogenic, while paratyphoid will form acid and gas from sugar.

Kligler agar

- The Kligler's iron agarThe Kligler's iron agar is a test tube that contains agarThe Kligler's iron agar is a test tube that contains agar, a pH-sensitive dye (phenol redThe Kligler's iron agar is a test tube that contains agar, a pH-sensitive dye (phenol red), 1% lactoseThe Kligler's iron agar is a test tube that contains agar, a pH-sensitive dye (phenol red), 1% lactose, 0.1% glucoseThe Kligler's iron agar is a test tube that contains agar, a pH-sensitive dye (phenol red), 1% lactose, 0.1% glucose, as well as sodium thiosulfateThe Kligler's iron agar is a test tube that contains agar, a pH-sensitive dye (phenol red), 1% lactose, 0.1% glucose, as well as sodium thiosulfate and ferrous sulfateThe Kligler's iron agar is a test

Kligler agar



Diagnosis from the third week of typhoid

Clinical specimen

- **Stool cultures - isolation from feces can be successful from the 3-rd week of disease.**
- **Fecal samples are placed directly on MacConkey or Endo agar, Wilson-Blair medium S.typhi form large black colonies, with metalic sheen.**
- **Urine culture – are positive only in the 2-3 weeks and only 25% of cases.**
- **Bone marrow culture is positive in most cases even when blood culture are negative.**
- The main method of diagnosis is bacteriological method during the third week of typhoid fever: the same principle as for the first week but without preliminary stage because the number of typhoid bacilli is enough for inoculation on solid media (**on Endo or MacConkey's media**).

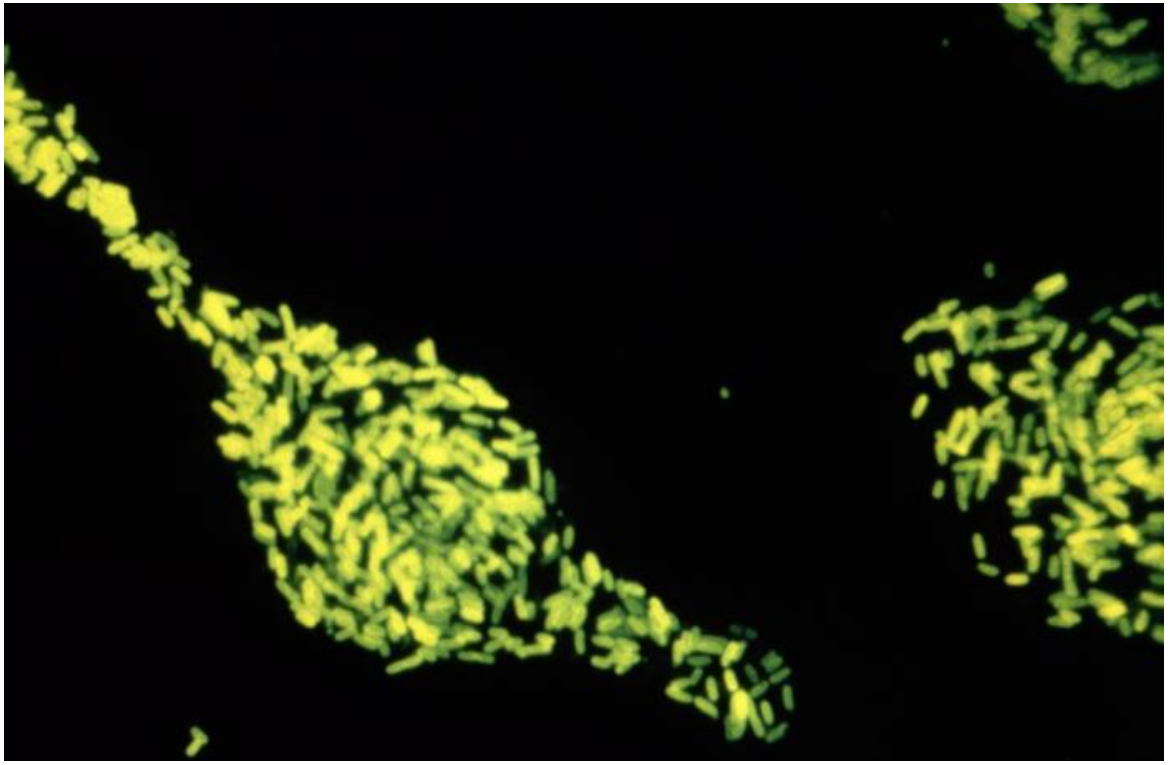
Kauffman and White classification

The **Kauffman and White classification** scheme is a classification system that permits serological varieties of the genus *Salmonella* to be differentiated from each other. This scheme differentiates isolates by determining which surface antigens to be differentiated from each other. This scheme differentiates isolates by determining which surface antigens are produced by the bacterium. First, the "O" antigen type is determined. "O" antigens are the polysaccharides to be differentiated from each other. This scheme differentiates isolates by determining which surface antigens are produced by the bacterium. First, the "O" antigen type is determined. "O" antigens are the polysaccharides associated with the lipopolysaccharide to be differentiated from each other. This scheme differentiates isolates by determining which surface antigens are produced by the bacterium. First, the "O" antigen type is determined. "O" antigens are the polysaccharides associated with the lipopolysaccharide of the bacterial outer membrane to be differentiated from each other. This scheme differentiates isolates by determining which surface antigens are produced by the bacterium. First, the "O" antigen type is

Serological Diagnosis of typhoid

Widal test Widal test (demonstration of salmonella antibodies Widal test (demonstration of salmonella antibodies against antigens Widal test (demonstration of salmonella antibodies against antigens O-somatic Widal test (demonstration of salmonella antibodies against antigens O-somatic and H-flagellar in tube agglutination) for typhoid and paratyphoid in the patient's sera from the second week of disease and later periods. Diagnostical titer is

Salmonella stained using the direct fluorescent-antibody technique.



Prevention

- Sanitation and hygiene are the critical measures
- Careful food preparation and washing of hands are crucial to preventing typhoid.

Specific prophylaxis of typhoid

There are two vaccines currently recommended by the WHO for the prevention of typhoid: these are the live, oral Ty21a vaccine (sold as *Vivotif Berna*) and the injectable Typhoid polysaccharide vaccine (sold as *Typhim Vi* by Sanofi Pasteur and *Typherix* by GlaxoSmithKline). Both are between rather weak vaccines. They have 50% to 80% protective efficiency and are recommended for travelers to areas where typhoid is endemic.

Paratyphoid fevers lack any specific prophylaxis.

Treatment of typhoid and paratyphoid

1.Oral rehydratation therapy.

2. Antibiotics are effective, such as Chloramphenicol, Cotrimoxazole , and Quinolones (ciprofloxacin).

3. Typhoid & paratyphoid A&B bacteriophages (administered orally)