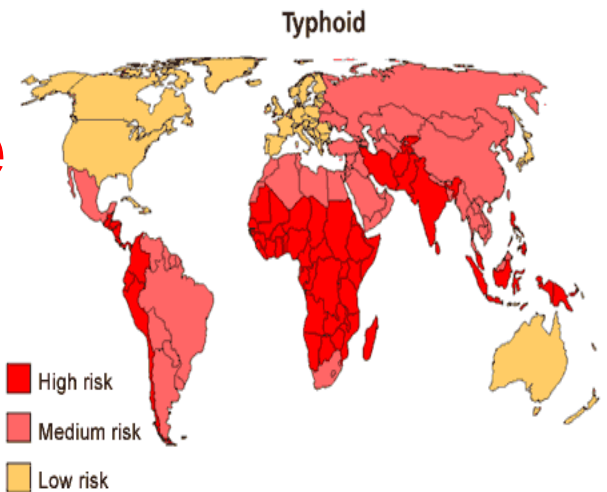


# TYPHOID FEVER



## Infectious Disease



**Presented by-**

**DR ANWAR AHMAD  
KGMU LUCKNOW UP**



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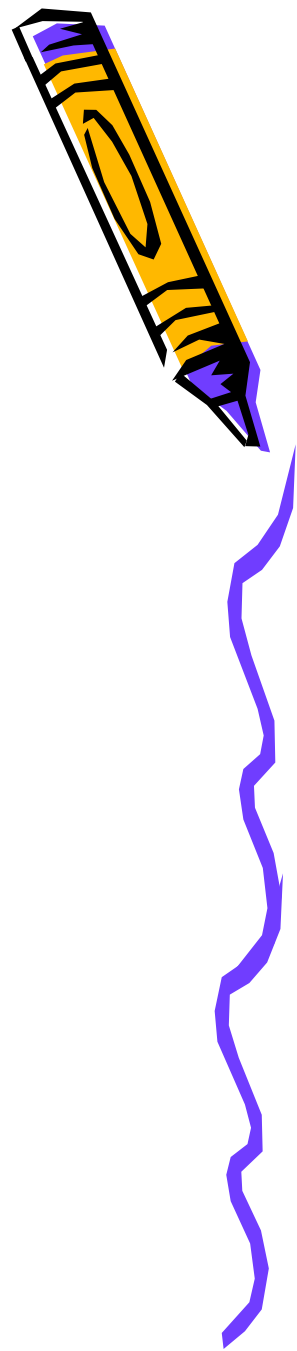
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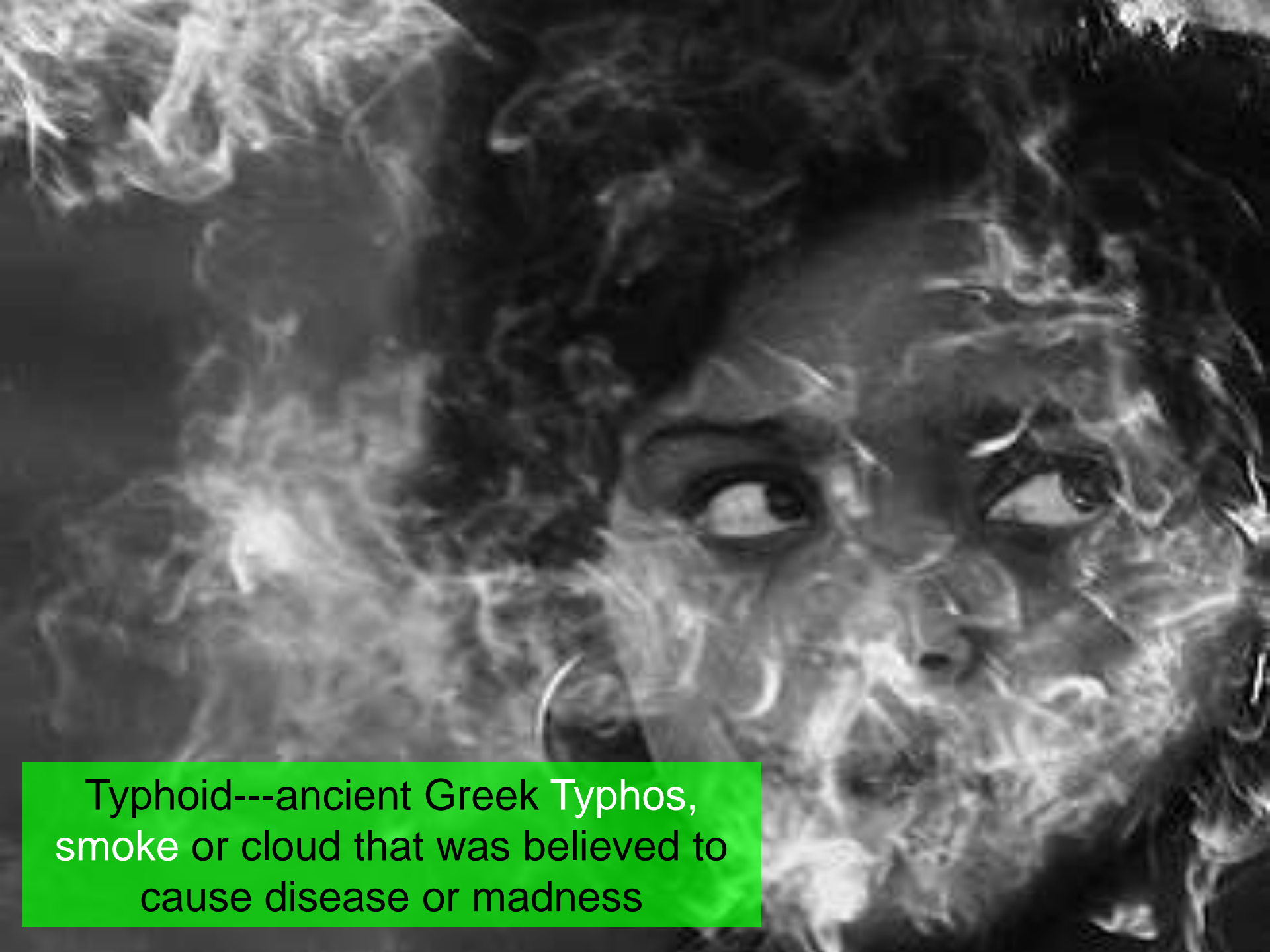
CONTROL OF TYPHOID FEVER





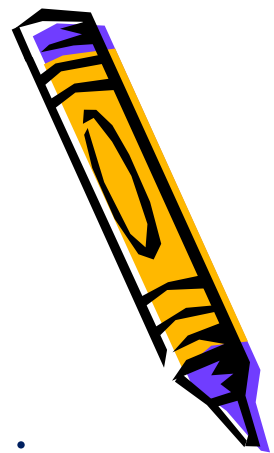
## International Classification of Disease Codes for Typhoid fever

Disease	ICD-9	ICD-10
Typhoid & paratyphoid fevers	002	A01
Typhoid fever	002.0	A01.0



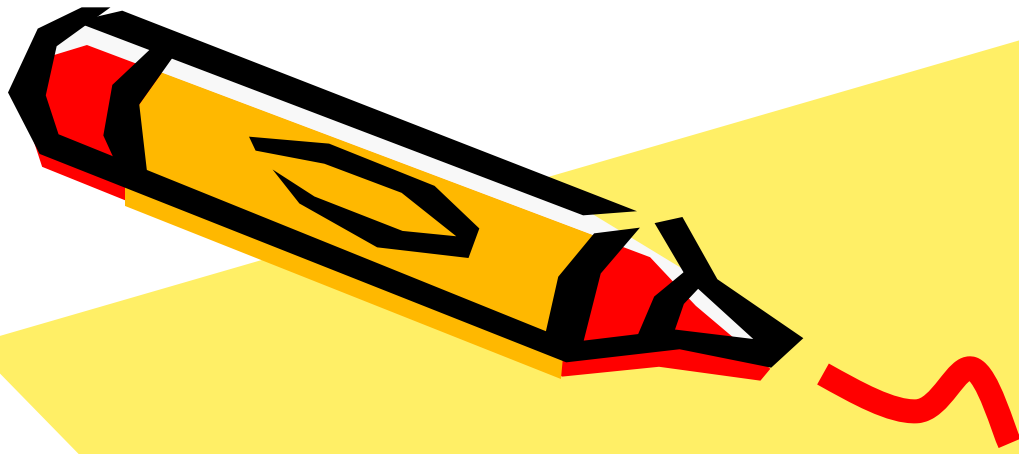
Typhoid---ancient Greek Typhos,  
smoke or cloud that was believed to  
cause disease or madness

# What is Typhoid Fever?



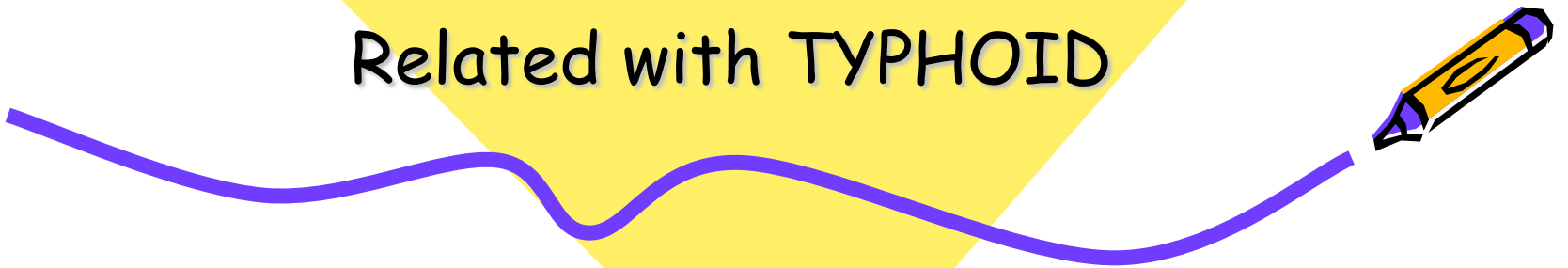
- Result of systemic infection caused by *S. typhi*.
- Clinically characterized by typical continuous fever for 3 to 4 weeks, relatively bradycardia with involvement of intestinal lymphoid tissues, reticulo-endothelial system & gall bladder.
- "Enteric fever" includes both typhoid and paratyphoid fever.
- May occur sporadically, epidemically or endemically. Found only in human.





# FAMOUS HISTORICAL PERSONALITIES

Related with TYPHOID



# History



FIG. 6.  
**Antonius Musa**  
A Roman physician who achieved fame by treating the Emperor Augustus with cold baths when he fell ill with typhoid.

**Antonius Musa**, a Roman physician who achieved fame by treating the Emperor Augustus 2,000 year ago, with cold baths when he fell ill with typhoid.

**Thomas Willis** who is credited with the first description of typhoid fever in 1659.



FIG. 7.  
**Thomas Willis (1621-1675).**  
The first description of epidemic typhoid in 1659.





French physician **Pierre Charles Alexandre Louis** first proposed the name “**typhoid fever**”

**William Wood Gerhard** who was the first to differentiate clearly between typhus fever and typhoid in 1837.



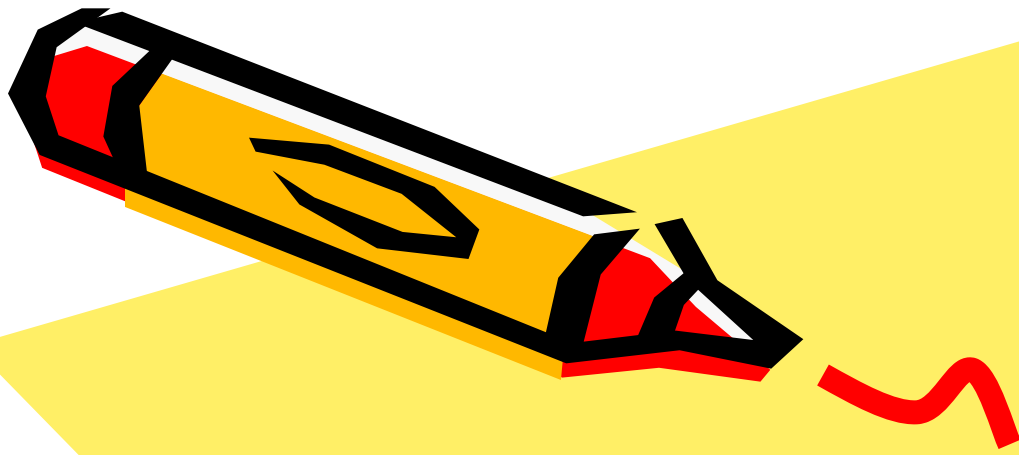




**Carl Joseph Eberth** who discovered the typhoid bacillus in 1880.

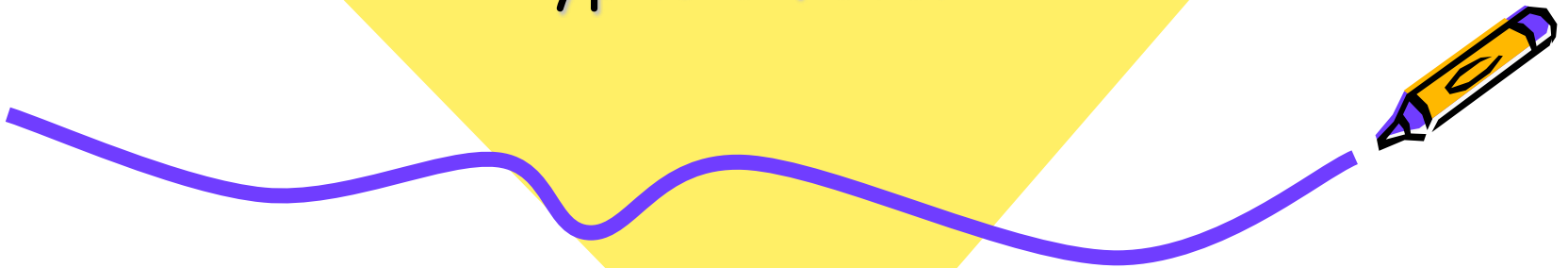
**Georges Widal** who described the 'Widal agglutination reaction' of the blood in 1896.



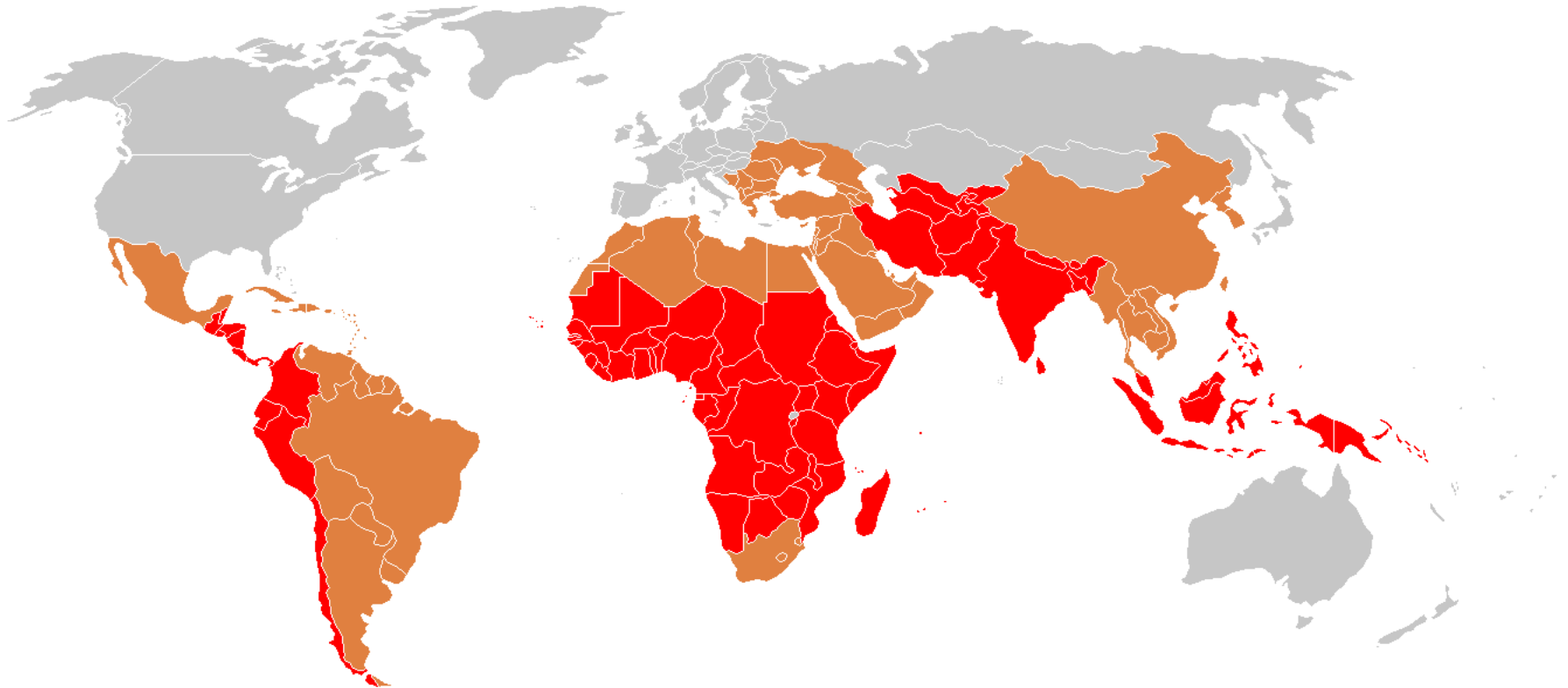


# PROBLEM STATEMENT

Typhoid fever



# Typhoid fever is prevalent in many regions in the world



- High endemicity (>100 cases per lac per year)
- Medium endemicity (10 cases per lac per year)
- Low endemicity (<10 cases per lac per year)



WHO Estimate

Infected roughly **21.6**  
**million** people each  
year



WHO Estimate

Kills 216000-  
600000 people  
each year



WHO Estimate

62% of these occurring in  
Asia and 35% in  
Africa

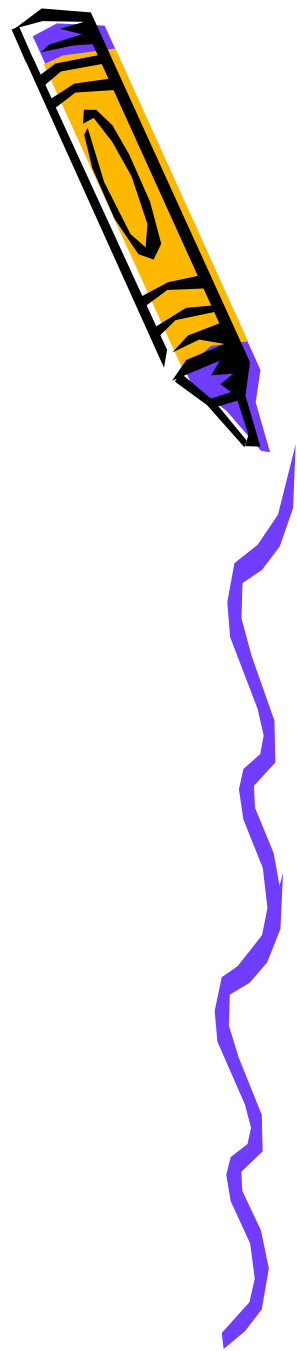
# India

- World largest outbreak of typhoid in **SANGLI** on December 1975 to February 1976. This disease is endemic in India
- **1992** : 3,52,980 cases with 735 deaths
- **1993** : 3,57,452 cases and 888 deaths
- **1994** : 2,78,451 cases and 304 deaths
- **2011** : 1.06million cases & 346 deaths
- **Prevalence**- 88 cases/lac population
- Case fatality rate due to typhoid has been varying between **1.1% to 2.5 %** in last few years.
- In south-East Asia 50% or more of the strains of bacteria has MDR



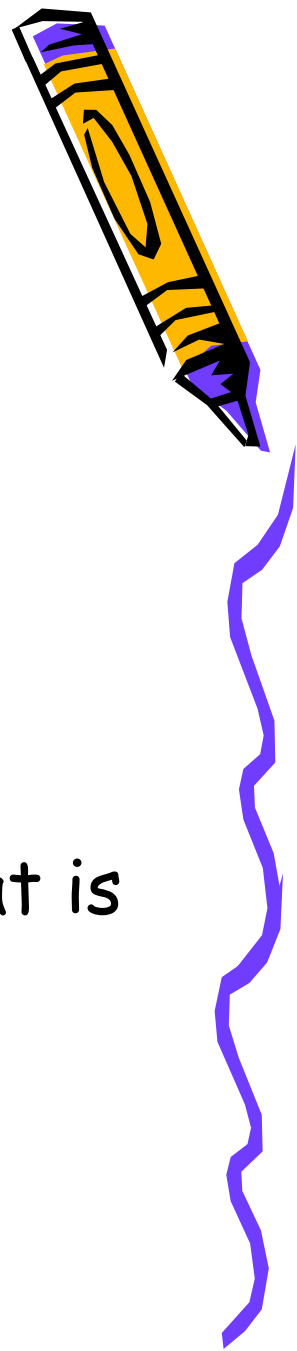
# EPIDEMIOLOGICAL DETERMINANTS

1. Agent factors
2. Host factors
3. Environmental & social factors
4. Incubation period
5. Mode of transmission



# 1- AGENT FACTORS

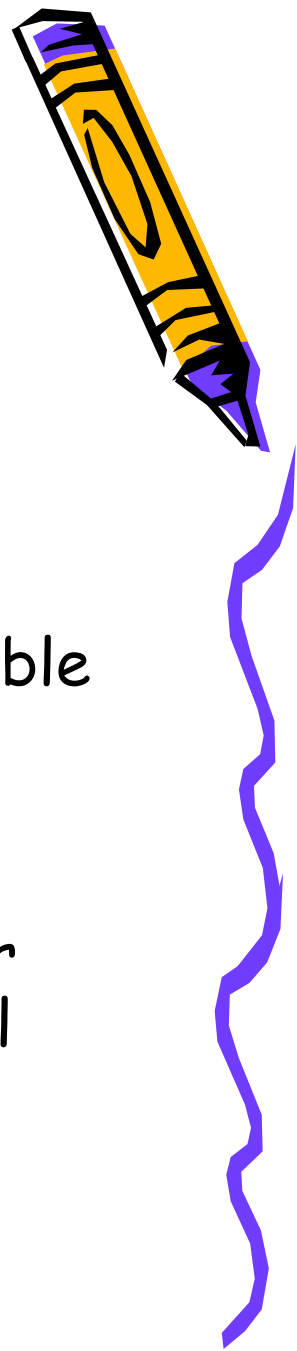
## a- Host



- Typhoid Fever mainly caused by the bacterium *Salmonella typhi* from the family Enterobacteriaceae.
- S. para A&b are relatively infrequent.
- *S. typhi* is a gram-negative, facultative aerobic, non spore forming bacteria that is motile due to its peritrichous flagella.
- The bacteria grows best at 37 C.



# *Antigenic structure of Salmonella*

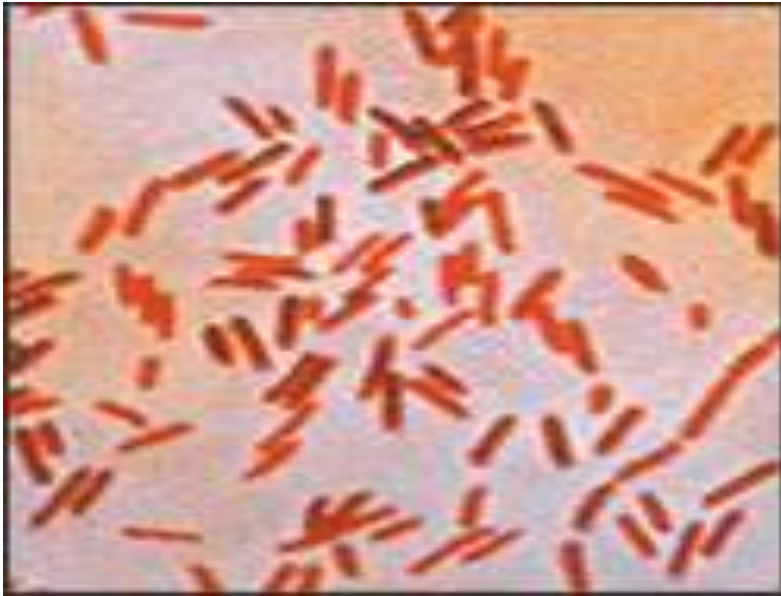


Two sets of antigens

Detection by serotyping

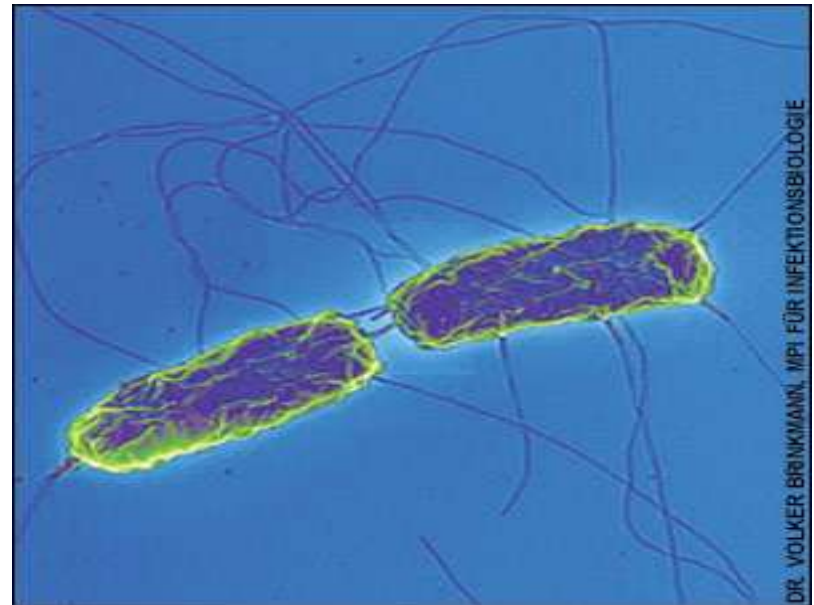
- **1 Somatic or O Antigens** contain long chain polysaccharides ( LPS ) comprises of heat stable polysaccharide commonly.
- **2 Flagellar or H Antigens** are strongly immunogenic and induces antibody formation rapidly and in high titers following infection or immunization. The flagellar antigen is of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





Color pink therefore  
Gram-negative

With peritrichous  
flagella



## **b- Reservoir of infection**

human is the only reservoir

### **1. Cases**

- A case is infectious as long as bacilli appears in stools or urine.
- Case may be missed, mild or severe.

### **2. Carriers**

- Temporary/incubatory- excrete bacilli for 6 to 8 weeks
- Chronic- excrete bacilli for more than a year, organism persist in gall bladder/biliary tract.  
e.g. “Typhoid Marry” real name Mary Mallon

Mary Mallon  
(wearing glasses)  
photographed  
with  
bacteriologist  
Emma Sherman  
on North Brother  
Island in 1931 or  
1932, over 15  
years after she  
had been  
quarantined there  
permanently.





- Mary Mallon was a cook in Oyster Bay, New York in early 1900s.
- Gave rise to more than 1300 cases in her life time.
- She died of pneumonia after 26 years in quarantine.



## c- Source of infection

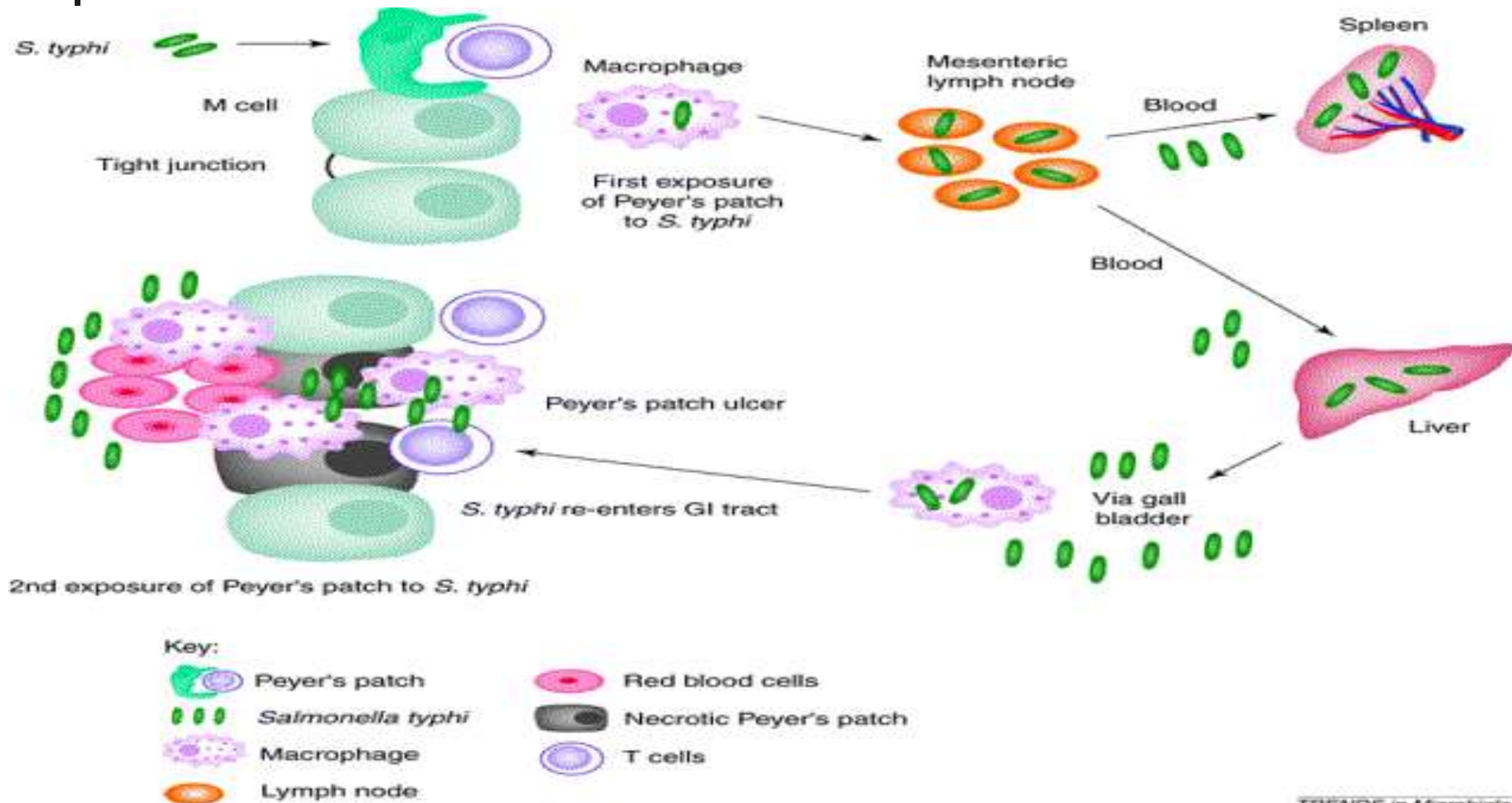
### Primary sources

- Faeces & urine of cases and carriers.
- Faecal carriers are more frequent than urinary carriers.

### Secondary sources

- Contaminated
  - Water
  - Food
  - Fingers
  - Flies

# How does the bacteria cause disease ?



**Ingestion of contaminated food or water**



*Salmonella* bacteria

**Invade small intestine and enter the bloodstream**



**Carried by white blood cells in the liver, spleen, and bone marrow**



**Multiply and reenter the bloodstream**



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



**Then pass into the intestinal tract and can be identified for diagnosis in cultures from the stool tested in the laboratory**

## **2- HOST FACTORS**

(a) **Age**- occur at any age but highest incidence in 5-19 yrs age group.

(b) **Sex**- cases more in Males than Female  
carrier rate is more in females

(c) **Immunity**- antibody may be stimulated by infection or immunization. Antibody against (O) antigen is higher in patient with the disease and antibody against (H) antigen is higher in immunized person. S.Typhi is intracellular organism so cell mediated immunity plays a major role in combating the infection.

### **3- ENVIRONMENTAL & SOCIAL FACTORS**

- ❑ Typhoid fever regarded as “Index of general sanitation” in any country.
- ❑ Increase incidence in July-September.
- ❑ Outside human body bacilli found in-
  - water- 2 to 7 days but not multiply
  - soil irrigated with sewage- 35 to 70 days
  - ice & icecream- over a month
  - food- multiply & survive for sometime
  - milk- grow rapidly without altering its taste
- ❑ Vegetables grow in sewage plant.
- ❑ Pollution of drinking water supplies.
- ❑ Open area defecation & urination.
- ❑ Low personal hygiene.
- ❑ Health ignorance.

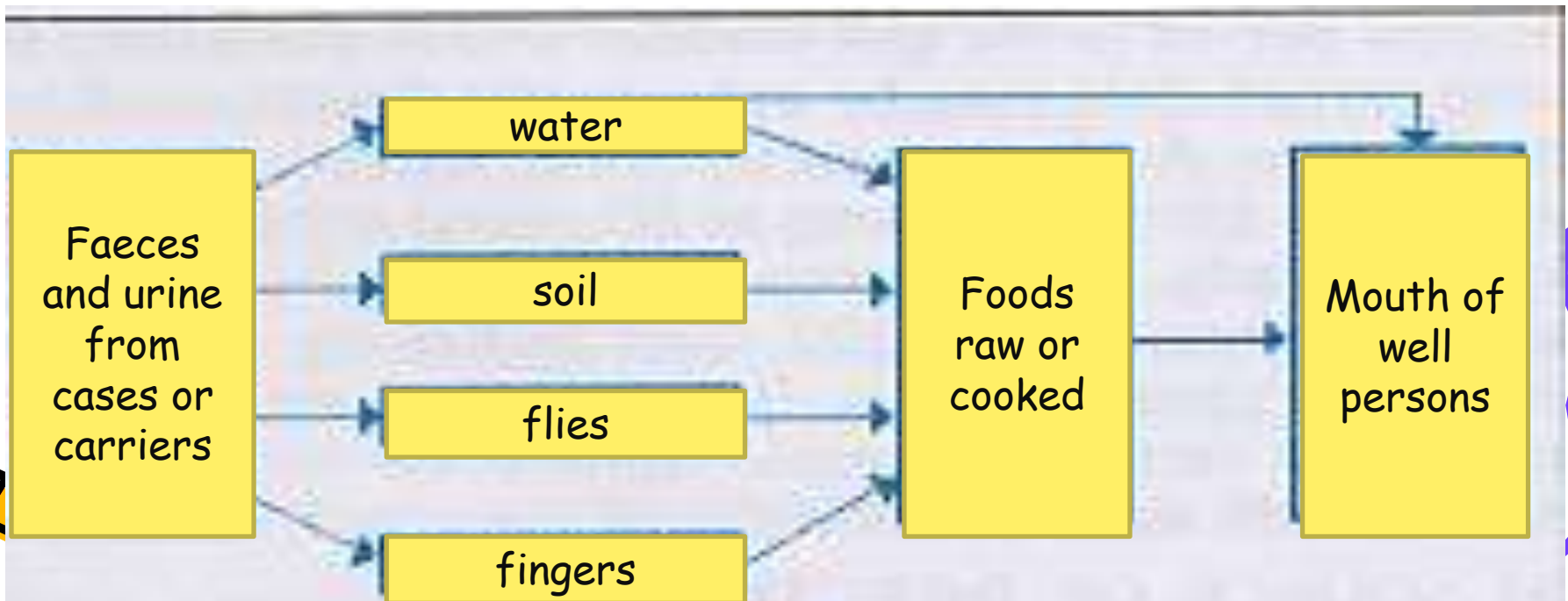
## 4- INCUBATION PERIOD

Usually 10-14 days but it may be as short as 3 days or as long as 21 days depending upon the dose of the bacilli ingested.



## 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.



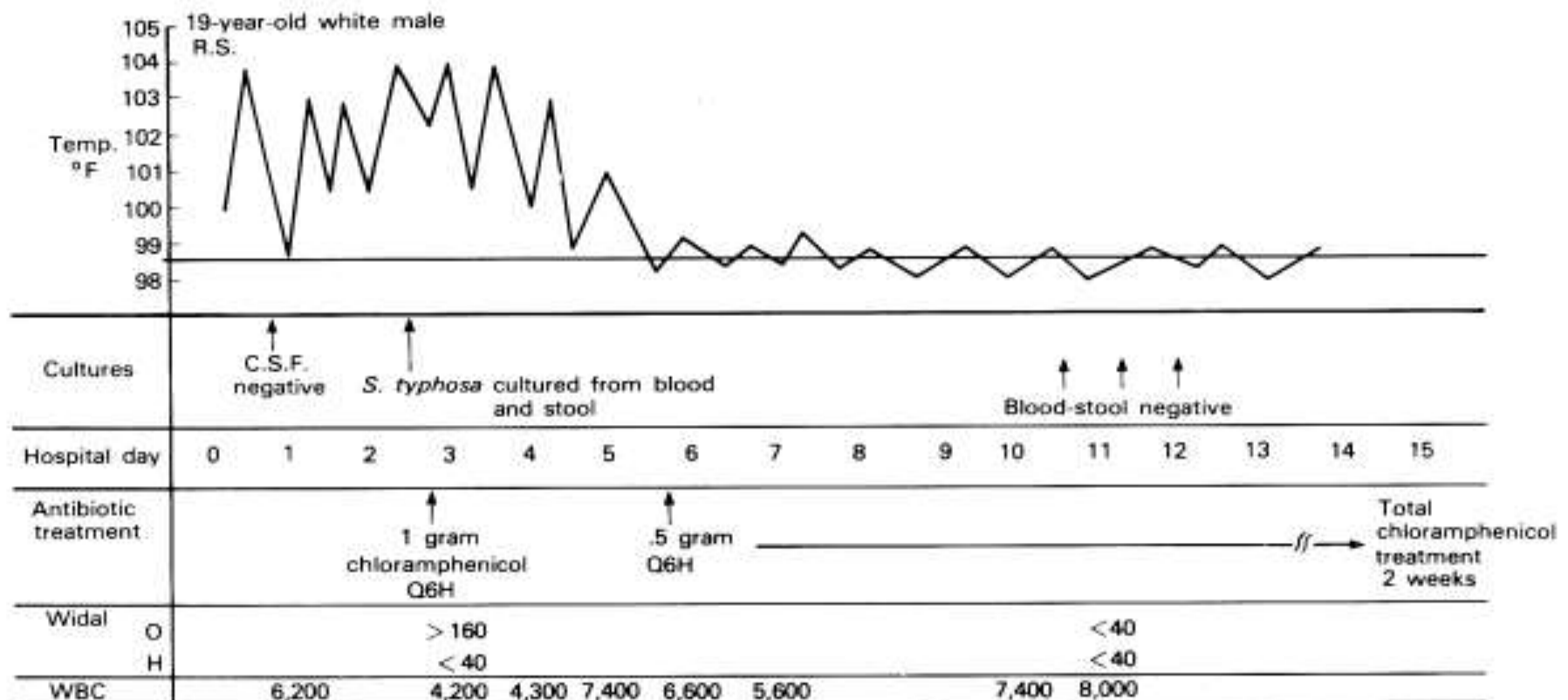


# CLINICAL FEATURES

- **First week:** malaise, headache, cough & sore throat in prodromal stage. The disease classically presents with step-ladder fashion rise in temperature ( $40 - 41^{\circ}\text{C}$ ) over 4 to 5 days, accompanied by headache, vague abdominal pain, and constipation or pea soup Diarrhoea.
- **Second week:** Between the 7th -10th day of illness, mild hepatosplenomegally occurs in majority of patients. Relative bradycardia may occur and rose-spots may be seen.
- **Third week:** The patient will appear in the "typhoid state" which is a state of prolonged apathy, toxemia, delirium, disorientation and/or coma. Diarrhoea will then become apparent. If left untreated by this time, there is a high risk (5-10%) of intestinal hemorrhage and perforation.
- **Rare complications:**  
Hepatitis, Pneumonia, Thrombophlebitis, Myocarditis, Cholecystitis, Nephritis, Osteomyelitis, and Psychosis.  
2-5% patients may become Gall-bladder carriers

# Events in a Typical typhoid Fever

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



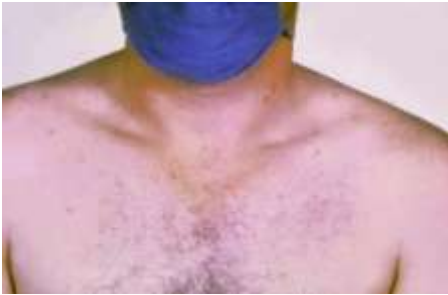
## Rose spots

Pink papule 2-3mm on trunk, fade on pressure

Disappears in 3-4 days



# SIGNS & SYMPTOMS



**Rose spots**



**Aches and pains**



**High fever**



**Diarrhoea**



**Chest congestion**



**Typhoid Meningitis**

# GENERAL COMPLICATIONS



BOIL



TONSILLITIS



DEHYDRATION

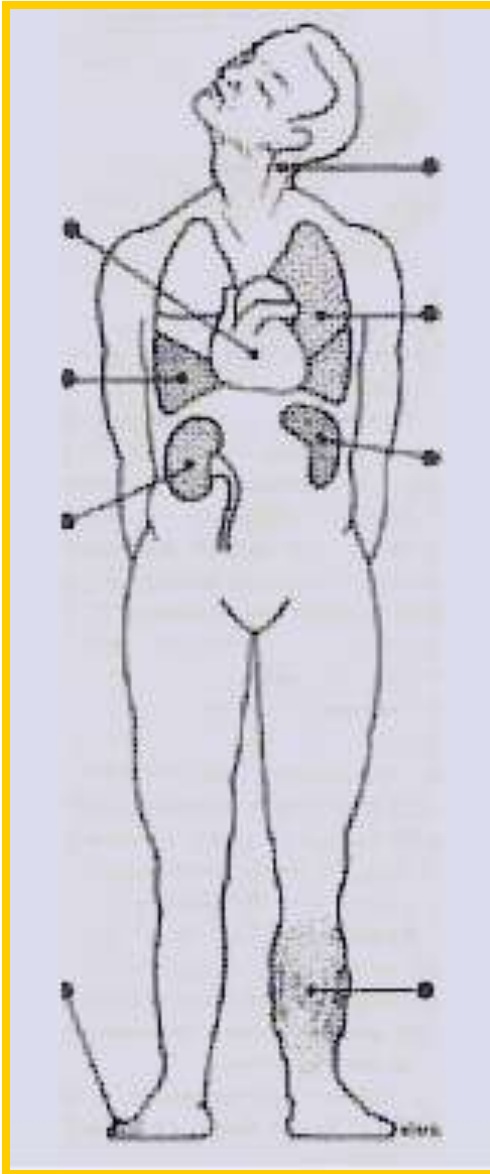
# MEDICAL COMPLICATIONS

TOXIC  
MYOCARDITIS

TYPHOID  
LOBAR PNEUMONIA

TYPHOID  
NEPHRITIS

PERIPHERAL  
NEURITIS



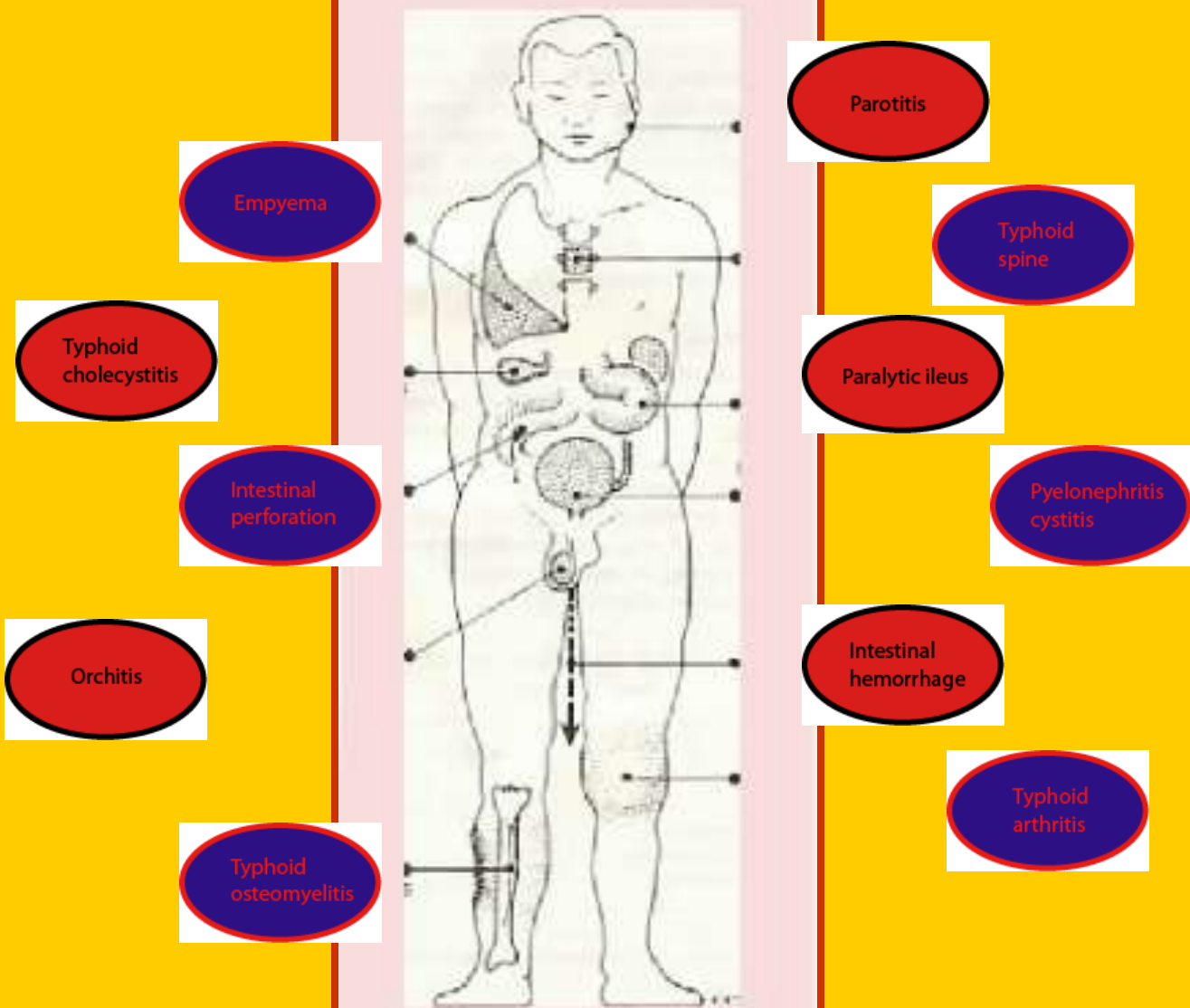
MENINGITIS

SEVERE  
BRONCHITIS

HEMOLYTIC  
ANEMIA

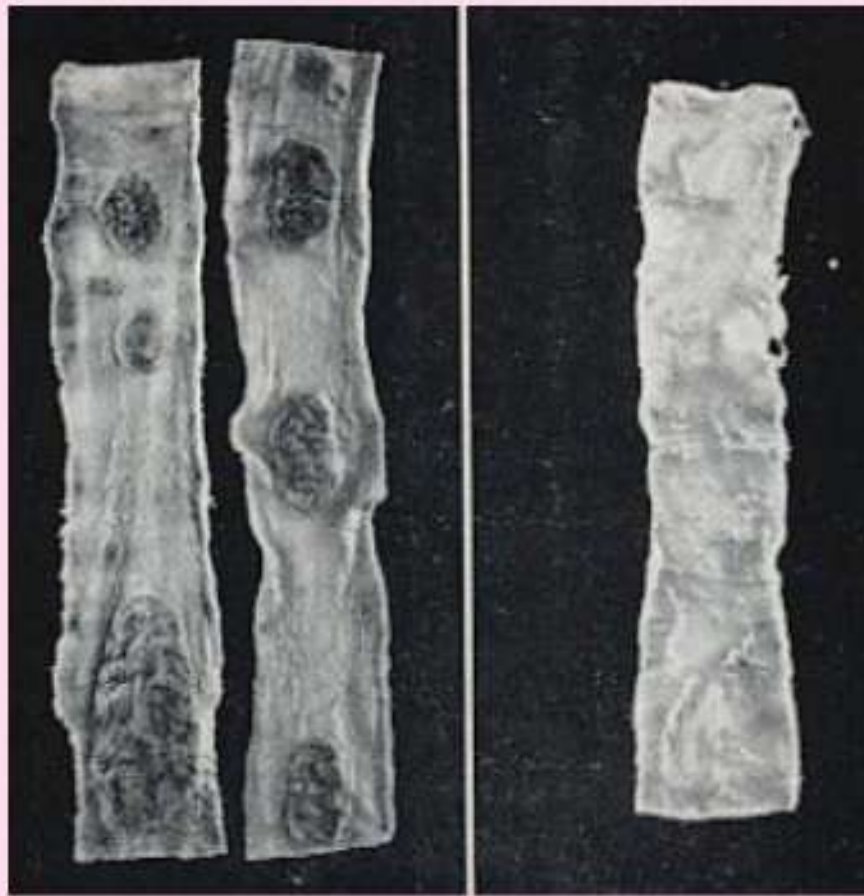
VENOUS  
THROMBOSIS

# MAJOR SURGICAL COMPLICATIONS

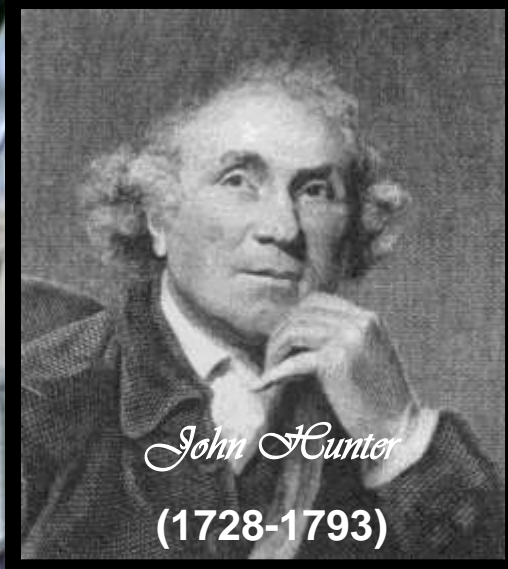




# S P E C I M E N S



TERMINAL ILEUM (JOHN HUNTER'S SPECIMENS)  
LT: ENLARGED PEYER'S PATCHES  
RT: THINLED OUT AREAS READY TO PERFORATE



# Hemorrhage

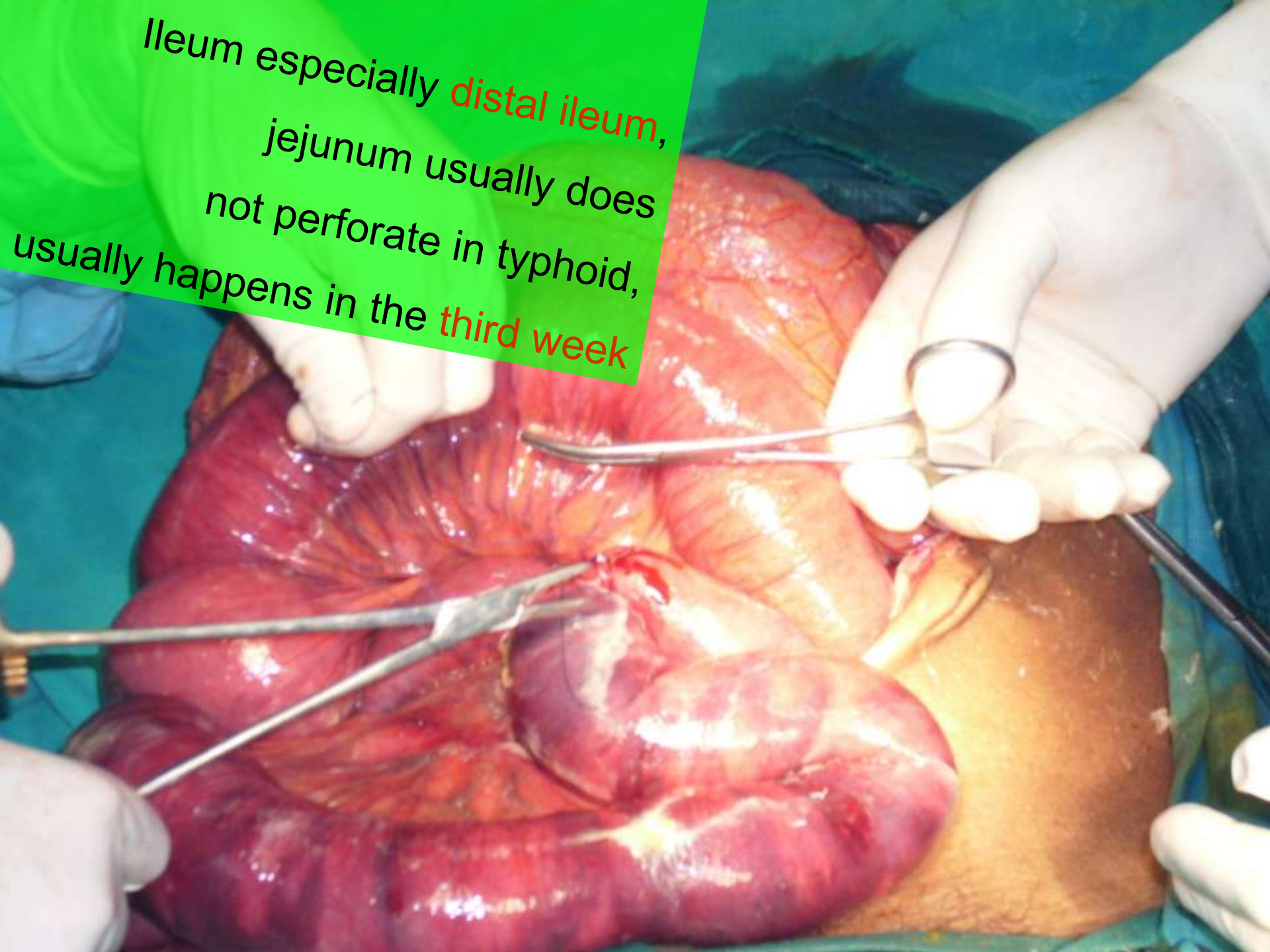
## presentation



Intestinal bleeding is often marked by a sudden drop in blood pressure and shock, followed by the appearance of blood in stool



Ileum especially **distal ileum**,  
jejunum usually does  
not perforate in typhoid,  
usually happens in the **third week**



**PATIENT**

**PERFORATION**



**PATIENT WITH INTESTINAL PERFORATION  
SHOWING RAPID DETERIORATION OF GENERAL  
CONDITION AT AN EARLY STAGS OF  
PERFORATION**

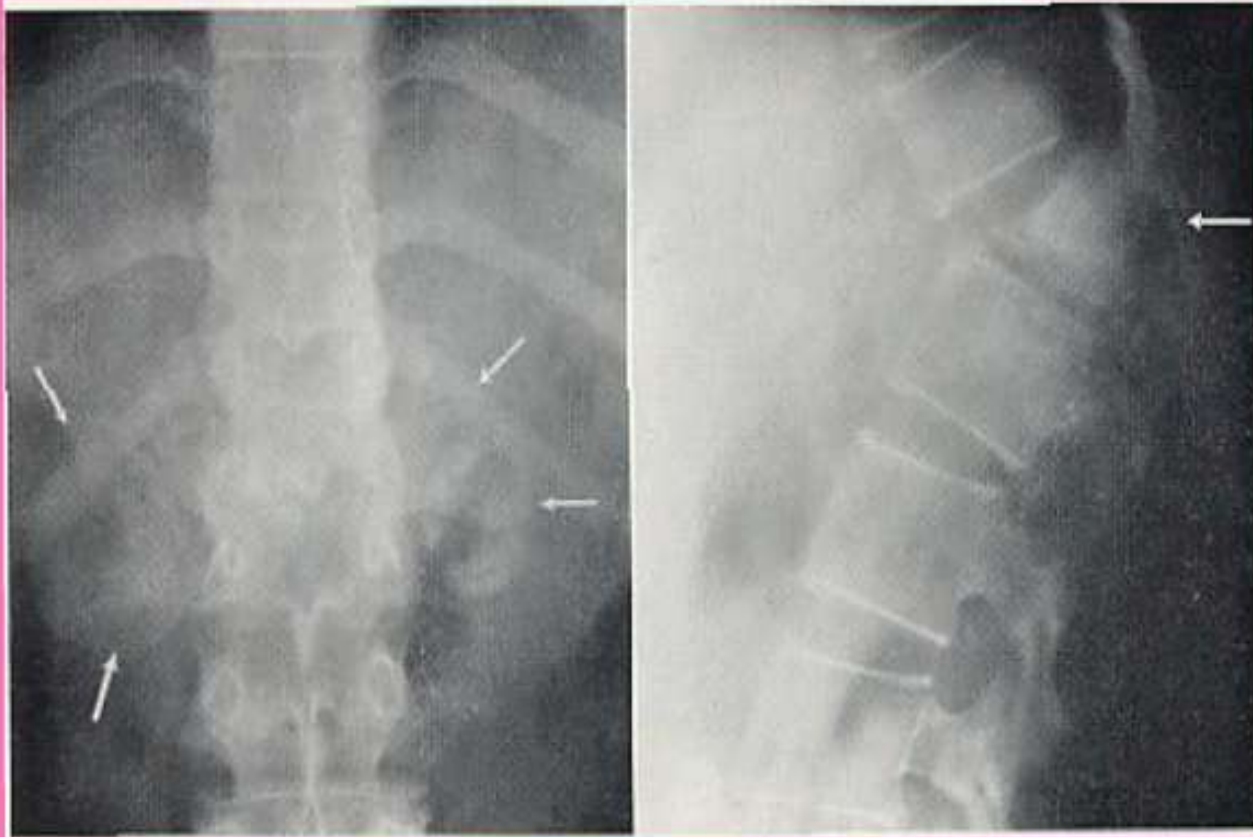
# MAJOR SURGICAL COMPLICATIONS



TYPHOIS OSTEOMYELITIS OF  
THE LOWER FEMUR WITH  
DISCHARGING SINUS

TYPHOID OSTEOMYELITIS  
OF THE LOWER FEMUR WITH  
ASSOCIATED FRACTURE





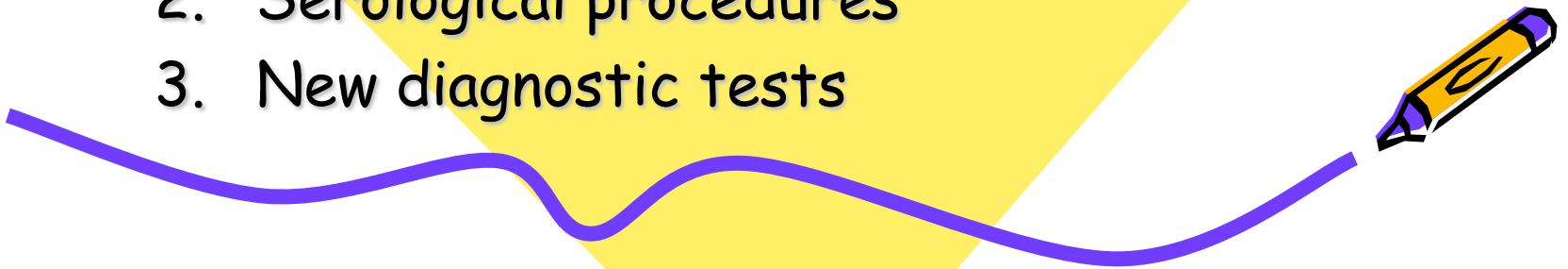
**TYPHOID SPINE (PRE-OPERATIVE)**  
X-RAY THORACIC & LUMBAR SPINE SHOWING COMPLETE  
COLLAPSE OF THE TWO VERTEBRAE & INTERVERTEBRAL  
DISC WITH PARTIALLY CALCIFIED ABSCESS

## MAJOR SURGICAL COMPLICATIONS



# LABORATORY DIAGNOSIS OF TYPHOID

1. Microbiological procedures
2. Serological procedures
3. New diagnostic tests



# **1- Microbiological procedure**

## **Blood Cultures**

- Bacteremia occurs early in the disease
- Blood Cultures are positive in

1<sup>st</sup> week in 90%

2<sup>nd</sup> week in 75%

3<sup>rd</sup> week in 60%

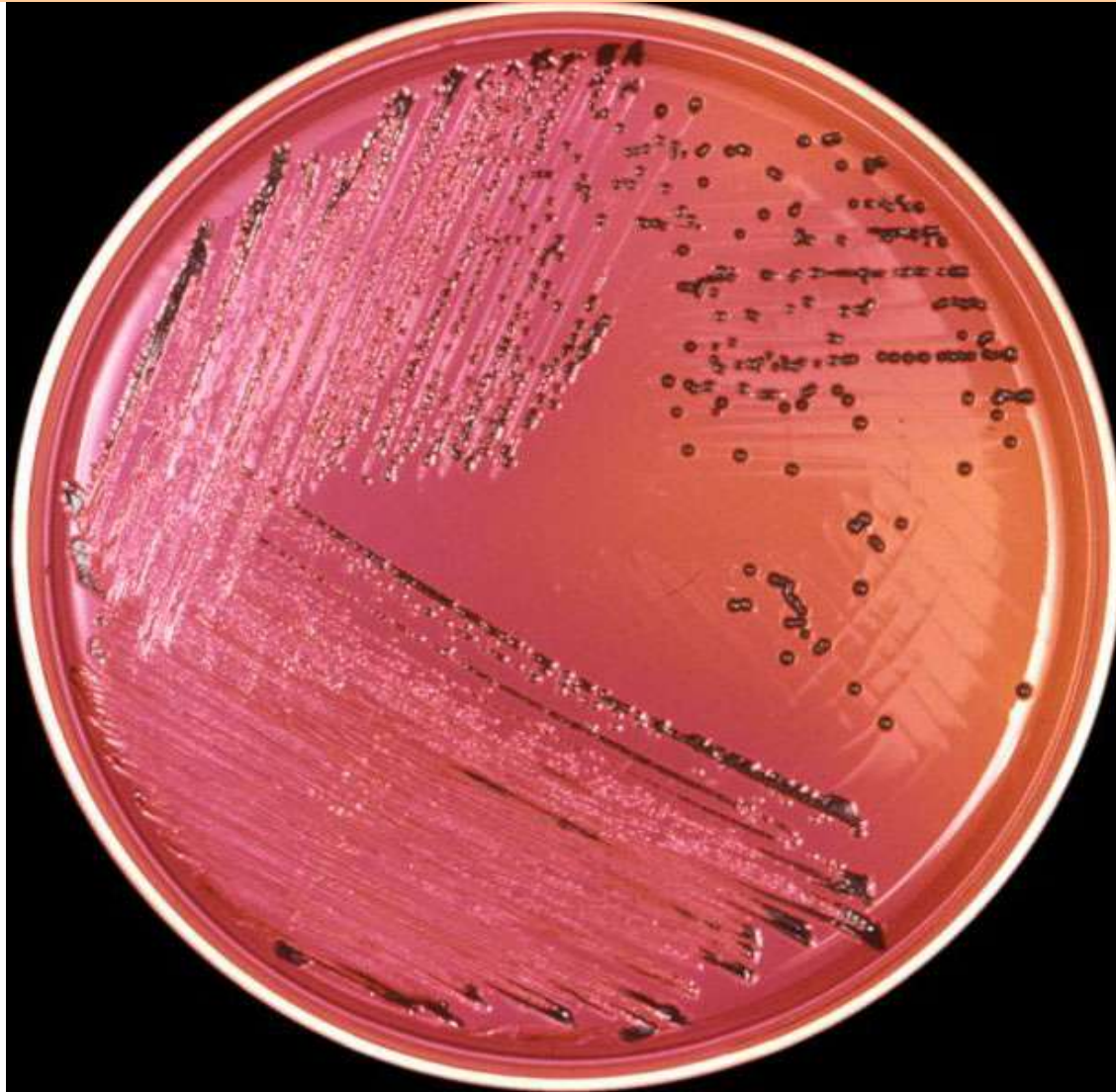
4<sup>th</sup> week and later in 25%





# Salmonella on Mac Conkey's agar





**Wilson and Blair bismuth sulphite medium jet black colony with a metallic sheen**

# 2- SEROLOGICAL PROCEDURE

## FELIX-WIDAL TEST

### Significant Titers helps in Diagnosis

- Serum agglutinins raise abruptly during the 2nd or 3rd week
- Following Titers of antibodies against the antigens are significant when single sample is tested
  - $O > 1 \text{ in } 160$
  - $H > 1 \text{ in } 320$
- Testing a paired sample (7-10 days) for raise of antibodies carries a greater significance

### Limitations of Widal test

Classically, a four-fold rise of antibody in paired sera Widal test is considered diagnostic of typhoid fever. However, paired sera are often difficult to obtain and specific chemotherapy has to be instituted on the basis of a single Widal test. Furthermore, in areas where fever due to infectious causes is a common occurrence the possibility exists that false positive reactions may occur as a result of non-typhoid

### 3- NEW DIAGNOSTIC TESTS

- **IDL Tubex** detects IgM09 antibodies with in few minutes
- **Typhidot** test that detects presence of IgM and IgG in one hour (sensitivity>95%, Specificity 75%)
- **Typhidot-M**, that detects IgM only (sensitivity 90% and specificity 93%)
- **Typhidot rapid** (sensitivity 85% and Specificity 99%) is a rapid 15 minute immunochromatographic test to detect IgM.
- **IgM dipstick test**



## *Diagnosis of Carriers*

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- Useful in public health purpose.
- Useful in screening food handlers, cooks, to detect carrier state
- Typhoid bacilli can be isolated from feces or from bile aspirates
- Detection of Vi agglutinins in the Blood can be determinant of carrier state.



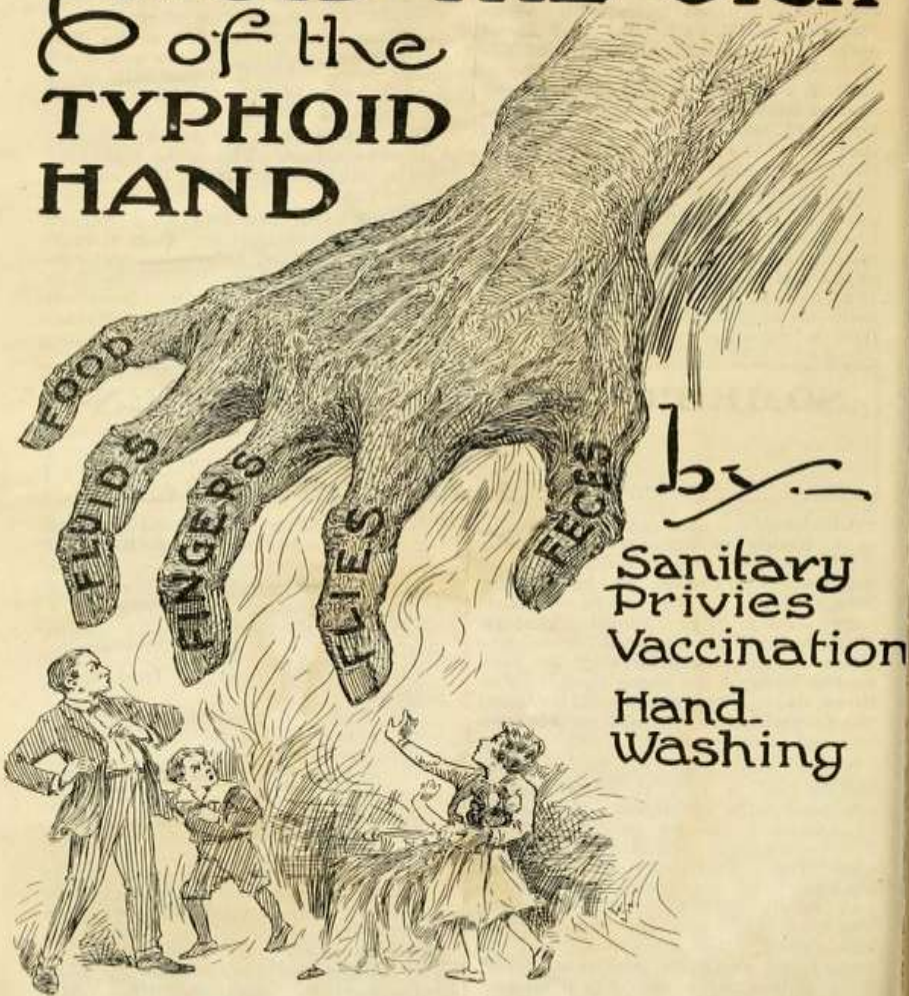
# Misdiagnosis

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- Paratyphoid fever- similar to typhoid fever but usually less severe.
- Paraenteric fever- a typhoid-like fever but not caused by Salmonella.
- Gastroenteritis- mild case of typhoid fever may be mistaken for gastroenteritis.
- Typhomalarial fever
- Brucellosis
- Tuberculosis
- Infective endocarditis
- Q fever
- Rickettsial infections
- Acute diarrhea (*type of Diarrhea*)
- Viral Hepatitis
- Lymphoma
- Adult Still's disease
- Malaria



# AVOID THE GRIP of the TYPHOID HAND



## CONTROL OF TYPHOID FEVER

1. Control of reservoirs-  
cases & carriers
2. Control of sanitation
3. immunization

# CASES

- I. Early diagnosis by culture of blood & stool
- II. Notification done where it is mandatory
- III. Isolation till 3 negative tests
- IV. Treatment by appropriate antibiotics
- V. Disinfection of stool & urine by 5% cresol for 2 hours and cloths by 2% chlorine
- VI. Follow-up examination of stool & urine at 3-4 months & at 12 months after discharge





# Management of typhoid fever:

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- **General:** Supportive care includes
  - Maintenance of adequate hydration.
  - Antipyretics.
  - Appropriate nutrition.
- **Specific:** Antimicrobial therapy is the mainstay treatment.
- Chloramphenicol, Ampicillin, Amoxicillin, Trimethoprim & Sulphamethoxazole, Fluroquinolones
- In case of quinolone resistance – **Azithromycin, 3rd generation cephalosporins (ceftriaxone)**

# Treatment of typhoid fever

	OPTIMAL THERAPY			ALTERNATIVE EFFECTIVE DRUGS		
Susceptibility	Antibiotic	Daily dose mg/kg	Days	Antibiotic	Daily dose mg/kg	Days
Fully sensitive	Fluoroquinilone Cipro/oflox	15	5-7	Chloramphenicol	50-75	14-21
				Amoxicillin	75-100	14
				TMP-SMX	8-40	14
Multidrug resistance	Fluoroquinilone Or Cefixime	15	5-7	Azithromycin Cefixime	8-10	7
		15-20	7-14		15-20	7-14
Quinolone resistance	Azithromycin Or Ceftriaxone	8-10 75	7 10-14	Cefixime	20	7-14

**UNCOMPLICATED**

CIPROFLOXACIN (PO)  
OFLOXACIN (PO)

**COMPLICATED**

CIPROFLOXACIN IV OR  
CEFTRIXONE IV

OCCATIONAL MDR-area

MDR-area

**UNCOMPLICATED**

CEFIXIME (PO)  
AZITHROMYCIN (PO)

**COMPLICATED**

CEFTRIXONE IV OR  
CEFOTAXIME IV OR  
AZTREONAM IV OR  
IMEPENE IV

**MEDICATION TREATMENT**

**WHO RECOMMENDATIONS**



---

## Diet

- Fluids and electrolytes should be monitored and replaced diligently.
- Oral nutrition with a soft digestible diet is preferable in the absence of abdominal distension or ileus.

## Activity

- No specific limitations on activity are indicated.
- Rest is helpful, but mobility should be maintained if tolerable.
- The patient should be encouraged to stay home from work until recovery.

# CARRIERS

- Identification by culture & serological examination.
- Treatment by intensive course of ampicillin/amoxicillin with probenecid for 6 weeks.
- Surgery like cholecystectomy if needed.
- Kept under surveillance.
- Health education.

## **2- CONTROL OF SANITATION**

- Protection & purification of drinking water supplies
- Improvement of basic sanitation
- Promotion of food hygiene





**Best prevention**

**Scrub them off your hands**

***Simple hand hygiene and washing can reduce several cases of Typhoid***





# 3- IMMUNIZATION

## Vaccination recommended to-

- 1- those live in endemic area
- 2- household contacts
- 3- Group at risk like school children and hospital staff etc.
- 4- those attending melas & yatras

## Three types of vaccines-

1. Injectable Typhoid vaccine  
(TYPHIM –Vi, TYPHIVAX)
2. The live oral vaccine (TYPHORAL)
3. TAB vaccine

## Injectable Typhim –Vi Vaccine

1. This single-dose injectable typhoid vaccine, from the bacterial capsule of *S. typhi* strain of Ty21a.
2. This vaccine is recommended for use in children over 2 years of age.
3. Sub-cutaneous or intramuscular injection
4. Efficacy : 64% -72%

# Typhoral Vaccine

1. This is a **live-attenuated-bacteria vaccine** manufactured from the **Ty21a** strain of **S. typhi**.
2. The efficacy rate of the oral typhoid vaccine ranges from **50-80%**
3. *Not* recommended for use in children younger than **6 years of age**.
4. The course consists of one capsule orally, taken an hour before food with a glass of water or milk (**1st day, 3<sup>rd</sup> day & 5<sup>th</sup> day**)
5. No antibiotic should be taken during this period
6. Immunity starts **2-3 weeks** after administration and lasts for **3 years**
7. A booster dose after **3 years**

# ***Facts of Vaccines for Typhoid***

Immunity lasts for 3 years

Need a booster

**Vaccines are not effective in  
prevention of Paratyphoid fevers**

**Ty21a**—Oral live attenuated vaccine

# REMEMBER

## Oral Typhoid Fever Vaccine

DAY

1



DAY 2  
SKIP

DAY

3



DAY 4  
SKIP

DAY

5



DAY 6  
SKIP

DAY

7



9/9

9/11

9/13

9/15

**Vivotif®**

Typhoid Vaccine Live Oral Ty21a

800-533-5899

Berna  
Products

Crucell Vaccines Inc.

>B-



**Vi-CPS — parenteral vaccine**



**THANK YOU**

