**ENTERIC FEVER**

**Bacterial food-borne infections**
- Enterica
- Food poisoning
- Cholera
- Brucellosis
- Diarrheal diseases

**Causative agent:** Salmonella Typhi

- **3 antigens**
  - O: Somatic
  - H: flagellar
  - Vi: Virulence

**Salmonella paratyphi**
- S. Paratyphi A (frequent)
- S. Paratyphi B (most common)
- S. Paratyphi C (rare)

**PUBLIC HEALTH SIGNIFICANCE**
1. Worldwide distribution.
2. Endemic in Egypt
3. Sporadic cases throughout the year
4. Outbreaks may occur during summer months.
5. Resistant strains to chloramphenicol & other antibiotics have become prevalent in several areas of the world

**RESISTANCE OF ORGANISM**
- Survive for weeks in water, milk products, shellfish.
- Resist low temperature (ice cream).
- Destroyed by heat, pasteurization of milk and disinfectants (Phenol).

**RESERVOIRS**

<table>
<thead>
<tr>
<th>Human</th>
<th>Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>Carriers</td>
</tr>
<tr>
<td>Typical/ atypical</td>
<td>all types of carriers. May follow acute illness or mild/ subclinical infections</td>
</tr>
<tr>
<td>Rarely domestic farm animals for paratyphoid</td>
<td></td>
</tr>
</tbody>
</table>

**Exit**
- Stool and urine.

**Modes of transmission**
1. Ingestion of food (vegetables, fish & shellfish)/ water contaminated by
   - Handling: feces/urine of cases and carriers (Food Handlers)
   - Vector: flies-cockroaches
   - Dust: food exposed to contaminated dust
2. Direct hand to mouth infection.

**Incubation period**
- Typhoid fever: 1-3 weeks.
- Paratyphoid fever: 1-10 days.

**Period of communicability**
- As long as bacilli appear in excreta.
- From the last few days if IP up to convalescence.
- Variable in typhoid & 1-2 w for paratyphoid.
  - 10% of patients discharge bacilli for 1-2 months after onset of symptoms.
  - 5% become permanent carriers.

**Cases are classified as one of the following especially during outbreaks**

1. **suspected case**: meets clinical criteria (2 major & 1 minor)
   - Major
     - fever> 2d not reaching baseline
     - headache
     - abdominal discomfort
   - Minor
     - Non productive cough
     - relative bradycardia
     - Often reported by public health authorities for further investigation.

2. **Probable case**: suspected case with positive supportive lab consistent with the diagnosis

3. **Confirmed case**:
   - Lab-confirmed (isolation of organism from clinical specimen)
   - Epidemiologically linked confirmed case (exposed to point source of infection)
## SUSCEPTIBILITY & RESISTANCE

### [A] Host factors

- **Age**: all ages are susceptible. In endemic areas: (5 - 50 years) occur early in life.
- **Sex**: more among males. Carrier rate is more among females.
- **Medical causes**: Gastric achlorhydria & HIV infection increases susceptibility.

### Immunity acquired through:

1. Natural acquired immunity (Repeated subclinical infection/ Clinical attacks usually gives lasting immunity).
2. Artificial acquired immunity (Active immunization).

### Recurrent attacks:

- Exposure to heavy dose of infection, with declining acquired immunity by time.
- Giving chemotherapy very early in disease resulting in inadequate immune response.

### [C] Social factors

↑ the risk of infection:

1. Lack of:
   - safe drinking water
   - personal hygiene
   - food sanitation
2. Open air defecation
3. Illiteracy
   - Health ignorance.

### [B] Environmental factors

1. **Season**: sporadic throughout year ↑ during late summer & early autumn.
2. **Water**: Survives for 7 days in clean water not survive long in contaminated water.
3. **Ice**: freezing does not destroy bacilli.
4. **Milk**: bacilli grow rapidly in milk w/o altering its taste/ appearance.
5. **Soil**: Persists up to 70 days (2 months) in soil irrigated with sewage.
6. **Flies**: Mechanical transmission (carry bacilli from feces to food remain viable for 20 days on surface of fly)

### CLINICAL PICTURE

#### I. Classic untreated cases

**Prodromal (invasion) stage: 1 week**

- **Fever** *(step ladder rise)*
  - Gradual onset sustained fever is usually higher in the evening.
- **Pulse**: bradycardia (slow relative to fever).

**Constitutional manifestation**:

- malaise & headache
- body aches
- anorexia
- sore throat & cough.
- Rash appears on 6th day.

**Advance stage: 2 weeks**

- Continued high fever.
- Worse physical & mental condition.
- Abdominal distension with diarrhea or constipation.

**Complications (advance stage)**

1. Ulceration of payers' patches
2. Intestinal hemorrhage: 2nd or 3rd week.
3. Intestinal perforation: 3rd week.
4. Cholecystitis, meningitis osteomyelitis thrombophlebitis
5. Bronchitis and pneumonia.

**Decline stage/ convalescence: 4th week**

- Uncomplicated cases gradually improves - Temperature ↓ -Abdominal manifestations disappear with satisfactory general condition.

**Relapse**

- in 10% of untreated cases
- It occurs 1-2 weeks after return of temperature to normal.

#### II. Treated cases

- Chemotherapy rapidly controls disease and shortens its duration.
- Incidence of complication is low.
- Relapse (20% of cases) with improper chemotherapy especially when stopped once convalescence starts.

**Case Fatality rate of typhoid**

- 10% in untreated cases & 1% in treated cases.

*Paratyphoid fever* presents a similar clinical picture, but tends to be milder with lower case fatality rate.
## TYPES OF CARRIER

<table>
<thead>
<tr>
<th>Relation to case</th>
<th>Period of carrier state</th>
<th>According to Foci of infection</th>
<th>Flow of the organism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubatory carrier</td>
<td>Temporare carrier (10% discharge organism for 1-2 months).</td>
<td>✓ Fecal carrier (more common) organism is in Gall bladder, Peyer's patches of SI excreted in urine</td>
<td>Continous or intermittent</td>
</tr>
<tr>
<td>Convalescent carrier</td>
<td>chronic carriers (3-5% convalescent carriers for 1 yr/more)</td>
<td>✓ Urinary carrier: (more dangerous) organism is in kidney</td>
<td></td>
</tr>
<tr>
<td>Healthy carrier: acquire subclinical infection from polluted environment (water) and transmit it for about 2 weeks.</td>
<td>Previous cholecystitis, biliary tract abnormalities &amp; urinary schistosomiasis favor chronic carrier state. Even carrier may be permanent carrier</td>
<td></td>
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</tbody>
</table>

### Typhoid Mary

(September 23, 1869 – November 11, 1938), better known as Typhoid Mary, was the first person in the US identified as an asymptomatic carrier of the pathogen associated with typhoid fever.

- Infected 1300 contacts throughout her life

### Detection of carriers

- Vi agglutination test: persistence of Vi antibody or rising of its titer. Present in 80% of chronic carriers.
- Isolation of typhoid bacilli from urine, stool or duodenal contents.
- Conclusive evidence of the carrier state.
- Intermittent excretion (three consecutive negative results are necessary before excluding carrier state).

### Laboratory diagnosis:

1st week: blood cultures. Positive blood culture is conclusive but not exclusive 75% +ve
2nd & 3rd week: Widal test & stool & urine cultures.
Bone marrow culture: the best bacteriologic confirmation (90-95%) even in patients received antibiotics.

### Widal test (low sensitivity – low specificity)

- “O” antibodies (1/80): recent infection.
- “H” antibodies (1/80): remote infection or immunization.
- Rising of titer is diagnostic (4 fold or greater rise).

<table>
<thead>
<tr>
<th>O titre</th>
<th>H titre</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Low</td>
<td>Recent vaccination infection or</td>
</tr>
<tr>
<td>Low</td>
<td>High</td>
<td>Past infection or old vaccination</td>
</tr>
</tbody>
</table>

### Sero-diagnosis of typhoid

- Widal test
- Tubex test: Detect IgM 09 within few minutes
- Typhidot test: Detect IgM & IgG within 3 hours
- PCR: highly sensitive & specific (16hrs).

### Differential diagnosis:

- Brucellosis.
- T.B.
- Malaria.

### Factors influencing antibody titer:

1. Recent TAB vaccination.
2. Repeated subclinical infection.
3. Early stage of disease (2nd week).
5. Individual variation (Anamnestic reaction).
## General Prevention

1. **Environmental sanitation:**
   - Safe water supply.
   - Sanitary waste disposal.
   - Fly control.
   - Food – milk sanitation
2. Examination of food handlers
3. Strict measures for food preparation, processing or handling (10 golden rules of WHO).

## Specific prevention

(1) **killed vaccines:**
   - **Dose:** 2 doses of 0.5 and 1 ml
   - **Mode:** S.C 4 weeks apart.
   - **A booster dose every 2 years.**
   - **Side effects:**
     - local redness & tenderness
     - low fever and headache.
   - **Moderate preventive value.**

(2) **Oral live vaccine: Typhoral vaccine**
   - **Enteric coated capsules of lyophilized vaccine.**
   - **Given to adults and children > 6 yrs of age.**
   - **4 doses, 2 days apart, one hour before meal with water.**
   - **Protection: two weeks after taking the last capsule for 3 years.**
   - **Revaccination (three doses) every 3 years.**

(3) **Purified Vi capsular polysaccharide antigen:**
   - **Contain Vi antigen in 0.5 ml**
   - **80% protection.**

(4) **Combination of HAV & typhoid injectable vaccine**

## CONTROL

### Cases
1. Early case finding.
2. Notification to local health office
3. Isolation at home (if sanitary)/ hospital.
4. Disinfection Concurrent & terminal.
5. Specific treatment: chloramphenicol, amoxicillin, quinolone or third generation cephalosporins.
6. Release after 3 negative cultures of stools and urine 24 hours apart.

### Carriers
- Recognize & diagnose especially among food handlers- pre-employment exam.
- Exam of food handlers by vi agglutination test if positive repeat stool & urine culture
- Carriers should be excluded from handling food.
- Ttt till 3 negative successive samples.
- Chronic gall bladder carriers: cholecystectomy
- And surgical management of UB lesions.

### Contacts
- Enlistment: age, sex, vaccination Hx
- Surveillance for 2 weeks from the date of last exposure.
- Investigation for contacts and source of infection
- Active immunization (low value).
- Food handlers are excluded from work & bacteriologically examined until proved not to be carriers.

### Community (Epidemic) measures:
1. Environmental measures:
   - Selective elimination of suspected food
   - Super-chlorination of water
   - Control of flies
   - Review the integrity of waste & sewage system
2. Health education of the public.
3. Vaccination of population at risk.
4. Epidemiologic study to trace the sources and channels of infection

## Review questions:
1. Discuss host, environmental and social factors responsible for endemicity of typhoid in Egypt.
2. Discuss role of carrier in spread of enterica
3. Enumerate laboratory diagnosis of typhoid and its epidemiological significance
4. Discuss specific prevention of typhoid
5. Enumerate steps taken to investigate and control outbreak of typhoid in a military camp

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<table>
<thead>
<tr>
<th>TYPE</th>
<th>TAB vaccine</th>
<th>TABC vaccine</th>
<th>Typhoid vaccine</th>
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<tbody>
<tr>
<td>heat-killed, phenol preserved</td>
<td>1ml contain 1000 million S. typhi &amp; 750 million S. Paratyphi A,B</td>
<td>Paratyphi C is added in endemic areas.</td>
<td>1ml contain 1000 million S. typhi only.</td>
</tr>
</tbody>
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