Tropical Infections and Malaria

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Topic

- Malaria
- Leptospirosis
- Rickettioses
  - Scrub typhus
  - Murine typhus
- Melioidosis
- Enteric fever
Malaria

- Caused by *Plasmodium* protozoa transmitted by an infective female *Anopheles* mosquito

**Plasmodium Life Cycle**

**Erythrocytic stage:** *P. falciparum* - irregular cycle (about 48 h), *P. vivax* and *P. ovale* - 48 h, *P. malariae* - 72 h, *P. knowlesi* - 24 h
Morphology of *Plasmodium* spp.

<table>
<thead>
<tr>
<th>Rings</th>
<th>Trophozoites</th>
<th>Schizonts</th>
<th>Gametocytes</th>
</tr>
</thead>
</table>
| **P. falciparum** | | | | - Parasitized RBC = normal RBC
- RBCs contain immature trophozoites (ring form)
- Maurer’s dots
- 16-32 merozoites/schizont
- Parasitized RBC (young) > normal RBC
- Trophozoites → amoeboid form
- Schuffner’s dots
- 12-24 merozoites/schizont
- Hypnozoites in liver
- Parasitized RBC = normal RBC
- Trophozoites → amoeboid form
- RBCs contain all stages
- Trophozoites – band shape
- 6-12 merozoites/schizont, Rosette
- Parasitized RBC slightly > normal RBC
- Trophozoites → pigment spreads inside cytoplasm, band maybe seen (like *P. malariae*)
- RBCs contain all stages
- Multiple infection and high parasitemia (like *P. falciparum*)

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**Plasmodium falciparum**

- Normal size infected RBC
- Thin ring form
- Multiple infection
- Double chromatin ring
**Plasmodium vivax**

- Large infected RBC
- Amoeboid form

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**What you should know?**

- New species *P. knowlesi*: Malaysia, Indonesia, Philippines, Thailand (Yala, Krabi, Prachuab kirikhan, Chantaburi)
- *P. knowlesi* infection can be severe
- Erythrocytic stage of *P. knowlesi* = 24 h (shortest)
- Increase in prevalence of drug-resistant *P. falciparum*
- In Thailand: *P. vivax* 56.8%, *P. falciparum* 42.5%
- *P. vivax* infection can be severe (increased mortality)
Clinical Points

- *P. falciparum* infection incubation period = 1-2 weeks (up to 4 weeks) → antimalarial prophylaxis for 4 weeks upon return from an endemic area
- Incubation period of *P. malariae* about 4 weeks
- *P. vivax* and *P. ovale* may emerge weeks to months after the initial infection (hypnozoites)
- Treating the hypnozoite with a second agent (primaquine) is critical to prevent relapse
- When *P. vivax* and *P. ovale* are transmitted via blood, treatment with primaquine is not necessary, as it is the sporozoites that form hypnozoites in infected hepatocytes

Clinical Manifestations

- Flu-like symptoms: chills, headache, myalgia, and malaise, occur in a cyclic pattern
- Jaundice and anemia due to the lysis of the RBCs
- Lysis of infected and uninfected RBCs, suppression of hematopoiesis, and increased clearance of RBCs by the spleen leads to anemia and splenomegaly
Clinical Manifestations

- Plasmodia derive their energy solely from glucose (metabolize glucose 70 times faster than RBCs), causing hypoglycemia and lactic acidosis
- Thrombocytopenia in severe cases
- *P. falciparum* may induce renal failure, coma, and death

*P. falciparum*

- *P. falciparum* infect RBCs of all ages-high levels of parasitemia (>5% RBCs infected)
- *P. vivax* and *P. ovale* infect only young RBCs-lower level of parasitemia (usually < 2%)
- Sequestration is a specific property of *P. falciparum*
  - developed through its 48-hour life cycle
  - the organism demonstrates adherence properties
- Sequestration of parasites may contribute to mental-status changes and coma
Cytoadherence-rosetting-sequestration of infected and uninfected erythrocytes in the vital organs goes on uninhibited, it ultimately blocks blood flow, limits the local oxygen supply, hampers mitochondrial ATP synthesis, and stimulates cytokine production.

**P. falciparum**

- End-organ diseases in patients with P falciparum infection
  - Central nervous system (CNS)
  - Lungs
  - Kidneys
- Other manifestations of *P. falciparum* infection include hypoglycemia, lactic acidosis, severe anemia, and multiorgan dysfunction due to hypoxia.
Severe Falciparum Malaria

### Clinical
- Impaired consciousness
- Prostration
- Multiple convulsions
- Deep breathing and respiratory distress
- Acute pulmonary edema and acute respiratory distress syndrome
- Circulatory collapse or shock
- Acute kidney injury
- Clinical jaundice plus evidence of other vital organ dysfunction
- Abnormal bleeding

### Laboratory
- Hypoglycemia (< 40 mg/dl)
- Metabolic acidosis
- Severe normocytic anaemia (hemoglobin < 5 g/dl)
- Hemoglobinuria
- Hyperlactataemia (lactate > 5 mmol/l)
- Renal impairment (Cr > 3 mg/dl)
- Pulmonary oedema (radiological)

Parasitemia ≥ 5% or schizontemia is associated with severity

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Severe Vivax Malaria

- Similar to those of severe *P. falciparum* malaria and can be fatal
- Severe anemia and respiratory distress occur at all ages
- Severe anaemia is particularly common in young children
Severe Knowlesi Malaria

- *P. knowlesi* replicates every 24 h, which can result in rapidly increasing parasite densities
- Severe disease and death in some individuals
- Severe disease are similar to severe falciparum malaria, with the exception of coma
- Patients with *P. malariae*-like infections (band form) and unusually high parasite densities (parasitemia > 0.5% by microscopy) should be managed as *P. knowlesi* infection
- Definitive diagnosis is made by PCR

Diagnosis

<table>
<thead>
<tr>
<th>Thick film</th>
<th>Thin film</th>
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<tbody>
<tr>
<td><img src="image1.png" alt="Thick film image" /></td>
<td><img src="image2.png" alt="Thin film image" /></td>
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</tbody>
</table>

- Number of parasites per 200 WBCs
- Number of parasites per 1000 RBCs
- Differentiate species
Rapid Diagnosis by ICT

- **pLDH**: Pf and non-Pf (produced by "live parasites")
- **PfHRP2** (histidine-rich protein 2): *P. falciparum* (detected in both "live and dead" parasites)
- Plasmodium aldolase: pan-malarial antigen (PMA) – used with *PfHRP2*

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Treatment of Uncomplicated Malaria

**P. falciparum**
- First-line drugs
  - Artesunate 4 mg/kg/day for 3 days + mefloquine 25 mg/kg in divided dose in 2-3 days
- Second-line drugs
  - Quinine 10 mg/kg + doxycycline 3 mg/kg OD or BID, or clindamycin 10 mg/kg/ bid 7 days
  - Artesunate 2 mg/kg/day + doxycycline 3 mg/kg OD or BID, or clindamycin 10 mg/kg/ bid 7 days

**Non-P. falciparum**
- Chloroquine 25 mg/kg in divided dose in 3 days
Treatment of Uncomplicated Malaria

- Pregnant woman
  - Use clindamycin
  - Second or third trimester use artesunate
  - Do not use doxycycline or primaquine (even single dose)
- Use ACT in malaria with unknown species
- Relapsed Pf malaria within 2 months- do not use mefloquine (use quinine+doxy/clinda or artesunate+doxy/clinda)

ACT = Artemisinin-combination therapy

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Treatment of Uncomplicated Malaria

- *P. falciparum*
  - Primaquine 0.25-0.5 mg/kg (15-30 mg) once
- *P. vivax*
  - Primaquine
    - 0.25 mg/kg (15 mg) OD for 14 day (if do not check for G-6-PD) → also used for *P. ovale*
    - 0.5 mg/kg (30 mg) OD for 14 day (if no G-6-PD deficiency)
    - 0.75 mg/kg (45 mg) weekly for 8 weeks (if mild G-6-PD deficiency)
  - Chloroquine
    - 5 mg/kg (300 mg) weekly suppressive therapy for PV and PO in pregnant women until postpartum then use primaquine
Treatment of Severe Malaria

First-line drugs
- Artesunate IV
  - 2.4 mg/kg IV PUSH at 0, 12, and 24 h Day 1 then 2.4 mg/kg once a day, if improved
  - Change to oral ACT for 3 days

Second-line drugs
- Quinine IV
  - Loading 20 mg/kg IV DRIP > 4 h then 10 mg/kg IV DRIP in 2-4 h q 8 h, if improved
  - Change to oral ACT for 3 days or
  - Change to quinine+doxy/clinda or artesunate+doxy/clinda for 7 days

• Doxycycline can be given once daily, starts when the patient has recovered sufficiently
• Mefloquine should be avoided due to risk of neuropsychiatric complications in the patient presented initially with impaired consciousness

A 18 years old male, no underlying disease
What is the diagnosis?

- A. Infective endocarditis
- B. Leptospirosis
- C. Dengue hemorrhagic fever
- D. Gram-negative sepsis with DIC
- E. Scrub typhus

Leptospirosis

- Zoonosis caused by spirochetes of the genus *Leptospira*
- First described by Adolf Weil in 1886 – ‘an acute infectious disease with enlargement of spleen, jaundice and nephritis’
- Risk factors
  - Occupational hazard (30-50%)
    - Miners, sewer workers, farmers, vets, rice field workers, soldiers
  - Recreational exposures
    - Water sports, canoeing, white water rafting
Etiology

• Of 20 *Leptospira* species, 9 were pathogenic
  - *Leptospira interrogans* → classic weil disease
  - More than 250 serovar
  - Pretibial erythematous rash – *L. interrogans* serovar Autumnalis
  - Gastrointestinal symptoms – *L. interrogans* serovar Grippotyphosa
  - Jaundice - 83% of patients with *L. interrogans* serovar Icterohaemorrhagiae and 30% with *L. interrogans* serovar Pomona
  - Aseptic meningitis - *L. interrogans* serovar Pomona or *L. interrogans* serovar Canicola

Leptospirosis

• Reservoir: 160 mammals, most important-rodent esp. rat (shed in urine)
• Transmission: skin contact with water, soil
• Incubation period: 2-26 days (average 10 days)
Clinical Manifestations

- Subclinical infection 40-70%
- Symptomatic cases – 90% mild or anicteric form
  - Acute febrile illness with a biphasic course (leptospiremic and immune phases) - good prognosis
  - Nonspecific signs and symptoms (flu-like)
    - Abrupt onset of fever, rigors, myalgias, and headache in 75-100%
    - Non-productive cough in 25 to 35%
    - Nausea, vomiting, and diarrhea in 50%
    - Conjunctival suffusion in 55%
    - Muscle tenderness, splenomegaly, lymphadenopathy, pharyngitis, hepatomegaly, muscle rigidity, abnormal respiratory auscultation, or skin rash in 7 to 40%
    - Aseptic meningitis seen in 25-50%

- Severe or icteric leptospirosis (Weil disease) – 10%
  - Mortality rate of 10%
  - Biphasic course may be indistinguishable
  - Fever, jaundice, renal failure (nonoliguric with hypokalemia), and hemorrhage
  - Other organ systems
    - Pulmonary system - pulmonary hemorrhage, ARDS
    - Cardiac system - myocarditis
    - Central nervous system - meningitis, meningoencephalitis
    - Uveitis
    - Rhabdomyolysis
Four broad clinical categories

(i) a mild, influenza-like illness  
(ii) Weil's syndrome characterized by jaundice, renal failure, haemorrhage and myocarditis with arrhythmias  
(iii) meningitis/meningoencephalitis  
(iv) pulmonary haemorrhage with respiratory failure

Laboratory findings

- Peripheral leukocytosis with left shift or normal white counts, anemia, thrombocytopenia  
- Elevated CK  
- Transaminases are elevated less often and less significantly (usually < 200 U/L)  
- Jaundice and bilirubinemia disproportional to hepatocellular damage is common  
- Alkaline phosphatase levels may be elevated 10-fold  
- Proteinuria, leukocytes, erythrocytes, hyaline casts, and granular casts may be present in the urinary sediment
Clinical Course

Anicteric leptospirosis

(Icteric leptospirosis

(Incubation period 2-20 days)

Leptospiremic phase

3-7 days

Immune phase

0-30 days

Leptospiremic phase

3-7 days

Immune phase

0-30 days

Associated symptoms

Myalgia

Headache

Nausea, vomiting

Abdominal pain

 Conjunctival suffusion

Meningitis

Uveitis

Rash

Jaundice

Hemorrhage

Acute renal failure

Myocarditis

Hemorrhagic pneumonitis

Meningoencephalitis

Hypotension

Leptospires present in

Blood

CSF

Urine

Blood

CSF

Urine

Siriluck Anunnatsiri (with permission)
Differential Diagnosis

- Malaria
- Rickettsial diseases
- Dengue infection
- Salmonella infection
- Acute viral illnesses
- Huntavirus hemorrhagic fever
- Bacterial sepsis

Diagnosis

- Culture (blood, urine, CSF, tissue) – difficult and impractical
- Antibody detection (IgG, IgM)
  - Microscopic agglutination test (MAT) – considered reference standard but NOT perfect (only in reference laboratory), ELISA, IFA, Lateral flow
  - Need 4-fold rising for diagnosis
  - Single cutoff titer varies (for IFA $\geq 1:400$)
- PCR
Treatment

- **Mild leptospirosis**
  - Doxycycline, ampicillin, or amoxicillin

- **Severe leptospirosis**
  - Intravenous penicillin G - drug of choice
  - Third-generation cephalosporins: cefotaxime and ceftriaxone

A 42 years old farmer
Fever with headache for 10 days
Myalgia
The diagnosis is.......

**Scrub typhus**
**Rickettsioses**

- **Spotted fever group (15 rickettsioses)**
  - Rocky Mountain spotted fever (RMSF) caused by *Rickettsia rickettsii*
  - Rickettsialpox caused by *Rickettsia akari*
- **Typhus group**
  - Epidemic (louse-borne) typhus caused by *Rickettsia prowazekii*
  - Endemic (murine) typhus caused by *Rickettsia typhi*
- **Scrub typhus group**
  - Caused by *Orientia tsutsugamushi*

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**Clinical Characteristics**

- Caused by *O. tsutsugamushi*, a gram-negative coccobacillus
- Chigger bite (often painless and unnoticed)
- Incubation period of 6-20 days (average 10 days)
- Headaches, shaking chills, myalgias, rash, splenomegaly, lymphadenopathy, conjunctival injection, fever, anorexia, and general apathy
Clinical Characteristics

- Small, painless, gradually enlarging papule, which leads to an area of central necrosis and is followed by eschar formation (30-50%)
  - At axilla, perineum, groin, under breast line

Eschars

- Scrub typhus
- Ecthyma granulomatosum
- Cutaneous anthrax
- Plague
- Hobo spider poison
Severe Scrub Typhus

- Pneumonitis, ARDS
- Encephalitis, aseptic meningitis
- Rarely, acute renal failure, shock, and disseminated intravascular coagulation (DIC)
- Cardiac involvement is often minor and rare, but can cause fatal myocarditis
### Laboratory Findings

- Early lymphopenia with late lymphocytosis
- Thrombocytopenia is also seen
- Elevated transaminase levels (2-3 x UNL) may be present in 75-95% of patients
- Hypoalbuminemia occurs in about 50% of cases
- Hyperbilirubinemia is rare

### Diagnosis and Treatment

- Indirect immunoperoxidase test (IPO) and immunofluorescent assay (IFA)
- An infection is confirmed by a 4-fold increase in antibody titers between acute and convalescent serum specimens
- A single high titer ≥ 1:400 with classic clinical features is considered a probable case
- Treatment: Doxycycline, azithromycin for 7 days
Murine Typhus

- Caused by the bacteria *Rickettsia typhi*
- Transmitted by rat fleas
- These fleas are not affected by the infection
- Human infection occurs because of flea-fecal contamination of the bites on human skin.

Clinical Characteristics

- Headache, fever, muscle pain, joint pain, nausea and vomiting
- MP rash 40-50% - about six days after the onset
- Neurological signs 45% - confusion, stupor, seizures or imbalance
- Symptoms may resemble those of measles or rubella

Investigation and treatment

- Same as scrub typhus
A woman with severe murine typhus and ARDS

5 days after treatment

A man post liver transplantation

- CMV viral load < 20 copies/mL
- Serum gallactomanan: negative
- Serum cryptococcus Ag: negative

Bronchoscopy
**A man post liver transplantation**

<table>
<thead>
<tr>
<th>Lab</th>
<th>18/6/56</th>
<th>23/6/56</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/dL)/Hct (%)</td>
<td>12.1/35.1</td>
<td>9.6/28.1</td>
</tr>
<tr>
<td>WBC (/mm³)</td>
<td>6,140</td>
<td>3,130</td>
</tr>
<tr>
<td>N (%)</td>
<td>92.5</td>
<td>62</td>
</tr>
<tr>
<td>L (%)</td>
<td>5</td>
<td>27.8</td>
</tr>
<tr>
<td>M (%)</td>
<td>2.3</td>
<td>8.9</td>
</tr>
<tr>
<td>E (%)</td>
<td>0</td>
<td>0.3</td>
</tr>
<tr>
<td>B (%)</td>
<td>0.2</td>
<td>1</td>
</tr>
<tr>
<td>Platelets (/mm³)</td>
<td>56,000</td>
<td>93,000</td>
</tr>
<tr>
<td>BUN/Cr (mg/dL)</td>
<td>14.6/1.42</td>
<td>28.1/2.22</td>
</tr>
<tr>
<td>TB/DB (mg/dL)</td>
<td>0.5/0.31</td>
<td>0.9/0.8</td>
</tr>
<tr>
<td>AST/ALT (mg/dL)</td>
<td>55/38</td>
<td>1,545/488</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>96</td>
<td>616</td>
</tr>
<tr>
<td>Alb/Glob (mg/dL)</td>
<td>2.6/2.5</td>
<td>2.1/3.1</td>
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**Date**

<table>
<thead>
<tr>
<th>IFA (IgG+M)</th>
<th>Leptospira spp.</th>
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<tbody>
<tr>
<td>IgG</td>
<td>&lt;1:50</td>
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<tr>
<td>IgM</td>
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**IFA (IgG+M) O. tsutsugamushi**

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<thead>
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<tr>
<td>IgM</td>
<td>&lt;1:50</td>
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**IFA (IgG+M) R. typhi**

<table>
<thead>
<tr>
<th>IFA (IgG+M)</th>
<th>R. typhi</th>
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<tbody>
<tr>
<td>IgG</td>
<td>1:800</td>
</tr>
<tr>
<td>IgM</td>
<td>1:800</td>
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</tbody>
</table>

**A 45-year-old female**

- with poorly controlled type 2 DM presented with a 1-week fever and right upper quadrant abdominal pain. She lives in Ubonratchathani and had a history of chronic intermittent abdominal dyscomfort for a year. CT abdomen showed multiple ring enhancing lesions at the liver and gall stones. Needle aspiration of liver abscess was performed and Gram's stain showed gram-negative rod with bipolar staining, gram-positive cocci and gram-positive bacilli. Melioidosis titer was positive with titer 1:64. What is the diagnosis?
- A. Pyogenic liver abscess
- B. Melioidosis
- C. Primary bacteremic liver abscess
- D. Liver metastasis
- E. *Fasciola hepatica* infestation
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  - A. Pyogenic liver abscess
  - B. Melioidosis
  - C. Primary bacteremic liver abscess
  - D. Liver metastasis
  - E. Fasciola hepatica infestation
Melioidosis

- Caused by a gram-negative bacterium *Burkholderia pseudomallei*
- Category B bioterrorism

Risk factors

- Incubation 1-21 days (average 9 days), longest 62 yr.
- 75 to 81% rainy season
- Incidence peaks between age 40 and 60 years
- 80% of patients have one or more risk factors
  - Diabetes (23 to 60%)
  - Heavy alcohol use (12 to 39%)
  - Chronic pulmonary disease (12 to 27%)
  - Chronic renal disease (10 to 27%)
  - Thalassemia (7%)
  - Glucocorticoid therapy (<5%)
  - Cancer (in 5%)
**Clinical Classification**

- Disseminated septicemic melioidosis
- Non-disseminated septicemic melioidosis
- Multifocal localized melioidosis
- Localized melioidosis
- Probable melioidosis
- Subclinical melioidosis

**Clinical Manifestations**

## Clinical Manifestations

- Pneumonia (51%)
- Genitourinary infection (14%)
- Skin infection (13%)
- Bacteremia without evident focus (11%)
- Septic arthritis or osteomyelitis (4%)
- Neurologic involvement (3%)
- Internal-organ abscesses and secondary foci in the lungs, joints, or both - common

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## Clinical Manifestations

- Acute fulminant septic illness to a chronic infection (symptoms for >2 months for 11% of cases)
- May mimic cancer or tuberculosis – the great imitator
- Over half of patients have bacteremia on presentation, and septic shock develops in approximately one fifth
Clinical Manifestations

- Suppurative parotitis 40% in children in Thailand and Cambodia (extremely rare in Australia)
- Prostatic melioidosis - 20% of male (in Australia)
- Neurologic melioidosis
  - Brain-stem encephalitis w/wo cranial-nerve palsies (esp. CN VII)
  - Myelitis with peripheral motor weakness
- Recurrent melioidosis occurs 1 in 16 patients, often in the first year
  - About 25% reinfection
  - 75% relapse
- Mortality 40%

A 45 years old female, DM
A middle-age man with diabetes
Diagnosis

- Culture is a must
- Serologic testing alone is inadequate for confirming the diagnosis, especially in endemic regions (> 50% positive)
- Empirical therapy for melioidosis should not be continued if *B. pseudomallei* is not detected in adequate cultures of specimens obtained before therapy
- Molecular identification – PCR, sequencing is useful

Treatment

Initial intensive therapy (10-14 days)
- Ceftazidime 50 mg/kg of body weight (up to 2 g), every 6-8 hr
- Meropenem 25 mg/kg (up to 1 g), every 8 hr
- Imipenem 25 mg/kg (up to 1 g), every 6 hr

Oral eradication therapy (3-6 months)
- TMP-SMX - based on body weight
  - > 60 kg: TMP/SMX DS 2 tabs q 12 hr
  - 40-60 kg: TMP/SMX SS 3 tabs q 12 hr
  - < 40 kg, adult: TMP/SMX SS 2 tabs q 12 hr
  - < 40 kg, child: 8 mg of TMP/kg and 40 mg of SMX/kg, every 12 hr

Treatment

- ≥ 4 weeks IV therapy may be necessary in patients with severe disease
- The addition of 8 mg of TMP and 40 mg of SMX per kg (up to 320 mg of TMP and 1600 mg of SMX) every 12 hours should be considered in neurologic, prostatic, bone, or joint melioidosis
- Second-line oral therapy
  - Amoxicillin–clavulanate or doxycycline
  - Amoxicillin–clavulanate 20 mg of amoxicillin and 5 mg of clavulanate per kg 3 times daily (high rate of relapse)

Enteric Fever

Salmonella infection

- Enteric fever
  - Typhoid fever: *Salmonella* Typhi
  - Paratyphoid fever: *Salmonella Paratyphi* A, B and C
- Invasive non-typhoidal salmonellosis
  - Bacteremia and/or focal infection associated with HIV disease or immunocompromised hosts
Etiology

- Transmitted by oral route, food
- Incubation period 7-14 days
- *Salmonella enterica* subspecies *enterica* serovar Typhi serotype Group D (*Salmonella Typhi*)
- *Salmonella* Paratyphi A
- *Salmonella* Paratyphi B
- *Salmonella* Paratyphi C

Clinical Manifestations

1st week of illness
- Fever, that starts low and increases daily (stepwise), as high as 39.4 or 40°C
- Headache, weakness and fatigue, dry cough, loss of appetite, abdominal pain, diarrhea or constipation, rash (rose spot-resolved in 2-5 days)
Clinical Manifestations

2nd week of illness
- Continuing high fever, either diarrhea or severe constipation, considerable weight loss, extremely distended abdomen
- Splenomegaly, relative bradycardia

3rd week of illness
- Febrile, more toxic and anorexic with significant weight loss
- Lung crackles, abdominal distension, foul, green-yellow, liquid diarrhea (pea soup diarrhea)
- Develop “typhoid state”: apathy, confusion, and psychosis
- Complication: bowel perforation and peritonitis, toxemia, myocarditis, or intestinal hemorrhage may cause death

4th week of illness
- Improvement may come slowly during the fourth week

Investigations

- Anemia, thrombocytopenia, leucopenia, relative lymphopenia
- Liver transaminase and serum bilirubin values usually rise to twice the reference range
- Diagnosis
  - Cultures from blood, stool, bone marrow
# Treatment

<table>
<thead>
<tr>
<th>Uncomplicated typhoid fever</th>
<th>Severe typhoid fever</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drugs</strong></td>
<td><strong>Dose (mg/day)</strong></td>
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<tr>
<td>Fully susceptible</td>
<td></td>
</tr>
<tr>
<td>First Line</td>
<td>Ciprofloxacin</td>
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<tr>
<td></td>
<td>Ofloxacin</td>
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<tr>
<td>Second line</td>
<td>Chloramphenicol</td>
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<tr>
<td></td>
<td>Amoxicillin</td>
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<td></td>
<td>Co-trimoxazole</td>
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<tr>
<td>MDR</td>
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</tr>
<tr>
<td>First Line</td>
<td>Ciprofloxacin</td>
</tr>
<tr>
<td></td>
<td>Ofloxacin</td>
</tr>
<tr>
<td>Second line</td>
<td>Cefixime</td>
</tr>
<tr>
<td></td>
<td>Azithromycin</td>
</tr>
<tr>
<td>Resistant to nalidixic acid or fluoroquinolones</td>
<td></td>
</tr>
<tr>
<td>First Line</td>
<td>Cefixime</td>
</tr>
<tr>
<td></td>
<td>Azithromycin</td>
</tr>
<tr>
<td>Second line</td>
<td>Ciprofloxacin</td>
</tr>
</tbody>
</table>


Thank you for your attention

GOOD LUCK IN YOUR BOARD EXAM !!!!!!!!