

1. **Title**
Fact sheet on typhoid and paratyphoid fever

2. **Infectious Agents**
Typhoid and paratyphoid fevers, also known as the enteric fevers, are caused by members of the genus *Salmonella*. Typhoid fever is caused by *Salmonella typhi*, and paratyphoid fever by *Salmonella paratyphi* A, B, or C. Nomenclature of the genus *Salmonella* is controversial, and it has been proposed that these organisms should be classified as serotypes of *Salmonella enterica* (e.g. *Salmonella enterica* serovar Typhi), but the traditional classification is used in this document for simplicity.

3. **Geographical Distribution of Disease**
Typhoid and paratyphoid fevers have a worldwide distribution. The annual worldwide incidence is estimated at 17 million cases, with 600,000 deaths. Endemic disease is seen in communities with poor sanitation or poor personal hygiene. Typhoid fever is estimated to be around 10 times more common than paratyphoid fever, but paratyphoid fever caused by *S.paratyphi A* is commoner than typhoid in some regions of China and India.

4. **Pathogenesis**
After ingestion of contaminated food or water, *S.typhi/paratyphi* bacilli reach the small intestine, penetrate the mucosa, and then remain viable within the macrophages which ingest them. The bacilli reach the bloodstream via the lymphatic system, and are then disseminated to the organs of the reticuloendothelial system within the first 24 hours of infection. After the incubation period (3 days – 1 month, usually 8-14 days) which is affected by the infective dose, the clinical syndrome appears.

5. **Clinical Features**
The spectrum of disease varies from a mild illness with low grade fever, malaise, and slight dry cough to a severe clinical picture with abdominal discomfort and multiple complications. The disease is characterized by prolonged fever, constipation or diarrhea, headache malaise and anorexia. Leucopenia with a relative lymphocytosis is commonly seen. Splenomegaly is typical. There may be “rose spots” on the thorax or abdomen of up to 25% of patients. Paratyphoid fever has similar clinical features to typhoid fever, but is generally milder, and has a lower mortality rate. Depending on the setting, up to 10% of typhoid fever cases have severe disease, with complications such as intestinal perforation, CNS involvement, haemorrhages, hepatitis, myocarditis, pneumonia, DIC, thrombocytopenia, or HUS. Relapses are reported to occur in 10-20% of cases around a week after stopping antibiotic therapy, but the relapse rates may now be lower with newer fluoroquinolone therapy. Around 1-5% of typhoid cases become chronic carriers, harbouring *S.typhi* in the gallbladder.

6. **Epidemiology and Transmission**
The reservoir for both typhoid and paratyphoid is humans, occasionally being domestic animals for paratyphoid. The disease is acquired by the ingestion of food or water contaminated by the faeces or urine of a case or carrier. Important food vehicles include shellfish from contaminated waters, raw fruits, vegetables fertilized by night soil, and contaminated milk products.

7. **Diagnosis**
 - a) Culture – *S.typhi* or *S.paratyphi* can be grown from blood in around 80% of cases in the early stages of illness. Bone marrow is the “gold standard” for cultural diagnosis, and can

enhance the diagnostic yield from blood cultures. The organism may also be found in stool in a smaller proportion of patients. Biosafety Level 3 laboratory practices and procedures are recommended for activities likely to generate aerosols or for activities involving production quantities of organisms.

b) Serological – The traditional Widal test has moderate sensitivity and specificity, and may be negative in up to 30% of culture proven cases. It may be used as an adjunct to culture methods. Newer diagnostic serological tests (e.g.IDL Tubex test, Typhidot test, IgM dipstick test) have been reported to give improved sensitivity and specificity in initial evaluations, but are not yet widely utilized.

c) Antimicrobial susceptibility testing – Testing is typically undertaken for ampicillin, chloramphenicol, co-trimoxazole, fluoroquinolones (ciprofloxacin, ofloxacin) or 3rd generation cephalosporins (ceftriaxone, cefotaxime). Laboratories are recommended to also test for resistance to nalidixic acid, which is associated with poorer response to fluoroquinolone therapy, even when susceptibility tests for the fluoroquinolones suggest they are susceptible.

8. Treatment

Treatment regimens for uncomplicated and severe typhoid fever are given below. The drugs of choice in adults are the fluoroquinolones (ciprofloxacin, ofloxacin). Alternatives are 3rd generation cephalosporins, chloramphenicol, co-trimoxazole, or azithromycin. Fluoroquinolones are not recommended in children or pregnant women, although fluoroquinolones may be considered for the treatment of multidrug-resistant disease in children if other agents are unavailable.

Treatment of uncomplicated typhoid fever (WHO)						
Susceptibility	Optimal therapy			Alternative effective drugs		
	Antibiotic	Daily dose mg/kg	Days	Antibiotic	Daily dose mg/kg	Days
Fully sensitive	Fluoroquinolone e.g. ciprofloxacin or ofloxacin	15	5-7 ^a	Chloramphenicol Amoxicillin TMP-SMX	50-75 75-100 8-40	14-21 14 14
Multidrug resistance	Fluoroquinolone or cefixime	15 15-20	5-7 7-14	Azithromycin Cefixime	8-10 15-20	7 7-14
Quinolone resistance ^b	Azithromycin or ceftriaxone	8-10 75	7 10-14	Cefixime	20	7-14

^a Three day courses are also effective and are particularly so in epidemic containment.

^b The optimum treatment for quinolone resistant typhoid fever has not been determined. Azithromycin, 3rd generation cephalosporins, or a 10-14 day course of high dose fluoroquinolones, is effective.

Treatment of severe typhoid fever (WHO)						
Susceptibility	Optimal parenteral drug			Alternative effective parenteral drug		
	Antibiotic	Daily dose mg/kg	Days	Antibiotic	Daily dose mg/kg	Days
Fully sensitive	Fluoroquinolone e.g. ciprofloxacin or ofloxacin	15	10-14	Chloramphenicol Amoxicillin TMP-SMX	100 100 8-40	14-21 14 14
Multidrug resistance	Fluoroquinolone	15	10-14	Ceftriaxone or cefotaxime	60 80	10-14
Quinolone resistance	Ceftriaxone or cefotaxime	60 80	10-14	Fluoroquinolone	20	7-14

9. The Hong Kong Situation

There were 67 cases of typhoid fever and 21 cases of paratyphoid fever reported in Hong Kong in 2002. Of 119 enteric fever notifications evaluated from 2000, 16(13.4%) were imported cases.

10. Prevention and Infection Control

a) Preventive measures – ensuring safe water supply, food hygiene, adequate sanitation, and health promotion for the above.

b) Vaccination – there are two vaccines which are currently used for the prevention of typhoid i) the Vi polysaccharide vaccine, and ii) the live oral Ty21a vaccine. They are used in travelers and regions where the disease is highly endemic, and in laboratory workers.

c) Hospital infection control – Patients should be nursed with Standard Precautions: handwashing; gloves for contact with blood, excretions, secretions, and contaminated items; eye protection and gown for splashes of blood, secretions and excretions. Consider Contact Precautions (single room, gowns and gloves for patient contact) for patients with diarrhoea.

11. Notification

Both typhoid and paratyphoid fevers are notifiable diseases and should be reported to the DH and HAHO by the standard mechanism.

12. Reference

- i) World Health Organization. Background document: the diagnosis, treatment and prevention of typhoid fever. WHO/V&B/03.07, 2003.
- ii) Chin J (ed.). Control of Communicable Diseases Manual, 17th edition. American Public Health Association, 2000.