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Typhoid and paratyphoid

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Introduction

Typhoid fever is a systemic disease contracted by ingestion of contaminated food or water. It is caused by the bacterium *Salmonella enterica* serovar Typhi, which is a pathogen only of humans. The illness may be mild or severe.

Paratyphoid is a clinically similar illness (though often less severe), caused by *Salmonella enterica* serovar Paratyphi A, B or C.

These conditions are sometimes referred to collectively as enteric fever.

Epidemiology

Global epidemiology

Typhoid and paratyphoid mainly affect low income regions of the world, where sanitation and clean water are lacking. The World Health Organization (WHO) estimates that 16 to 33 million cases of typhoid fever occur each year, with 500,000 to 600,000 deaths (a case fatality rate of between 1.5 and 3.8%) [1]. There are no WHO estimates of the annual incidence of paratyphoid; however, a study in 2004 estimated that 5.4 million cases of paratyphoid occur each year [2].

The majority of typhoid occurs in Asia, Africa, and Latin America where frequent outbreaks are reported. Outbreaks have also been reported in eastern Europe and central Asia [3], and since 2004 small scale outbreaks have occurred in Kyrgyzstan, the Ukraine and Russia [4].

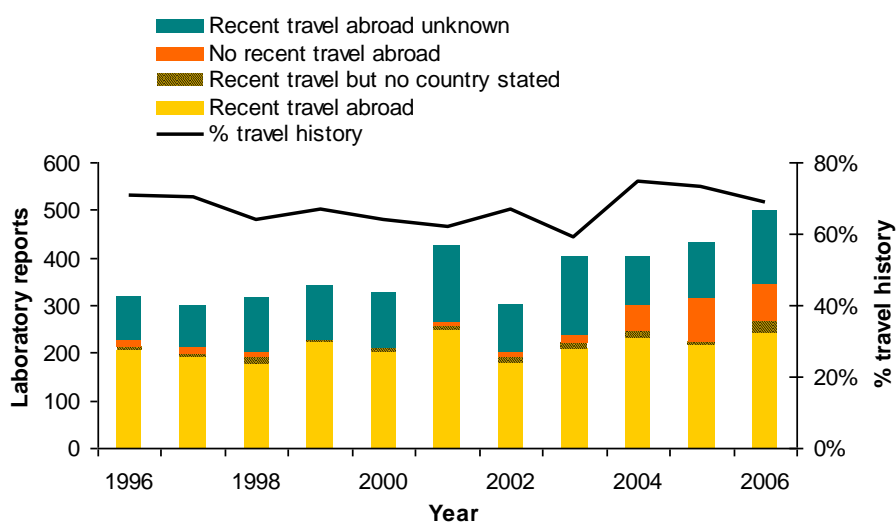
Typhoid and paratyphoid in travellers from England, Wales, and Northern Ireland

In the UK, typhoid and paratyphoid usually occur in travellers who have visited or are arriving from endemic areas. Occasionally cases occur following transmission from a returned traveller (usually within family or household settings), or rarely, from chronic carriers.

In 2006, there were 497 cases of enteric fever (232 typhoid, 258 paratyphoid A, and seven paratyphoid B) reported in England, Wales, and Northern Ireland through routine surveillance. This was the highest number reported in ten years after an average annual increase of 6% since 1996 [figure 1]. In 2006, 54% of cases were reported as being associated with recent foreign travel, however, travel history is not always complete. Because of the need to improve surveillance in order to identify risk groups and target preventive action, the Travel and

Migrant Health Section of the HPA Centre for Infections piloted an enhanced surveillance for enteric fever from 1 May 2006 to 30 April 2008 [5].

Figure 1. Laboratory reports of enteric fever by travel history, England, Wales, and Northern Ireland: 1996 – 2006



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Four hundred and fifty seven laboratory confirmed cases of enteric fever were reported during the period of enhanced surveillance and 406 surveillance forms were returned (89% return rate). There were 226 cases of typhoid, 224 paratyphoid A, and seven paratyphoid B.

Travel history was available for 98% (399/406) of cases, of which 294 cases had travelled abroad from the UK (travel-associated cases). The Indian sub-continent (ISC) was the most visited region of the world for enteric fever cases [table 1.].

Table 1. Countries of travel for travel-associated enteric fever cases by organism

Country of travel	Organism			Total
	S. Typhi	S. Paratyphi A	S. Paratyphi B	
India	57	89	-	146
Pakistan	37	59	-	96
Bangladesh	19	8	-	27
Nepal	1	-	-	1
India, Nepal	2	-	-	2
Bangladesh, Nepal	1	-	-	1
China	-	1	-	1
China (Hong Kong)	-	1	-	1
China (Tibet), Nepal, Thailand	-	1	-	1
Sri Lanka, Thailand	-	1	-	1
Thailand	-	-	1	1
Indonesia	1	1	-	2
Indonesia, Malaysia	-	1	-	1
Malaysia	1	-	-	1
Philippines	1	-	-	1
Far East	1	-	-	1
Morocco	-	-	1	1
Egypt	2	-	-	2
Turkey	-	1	-	1
Nigeria	2	-	-	2



Cameroon	1	-	-	1
Sierra Leone	1	-	-	1
Costa Rica, El Salvador, Guatemala	1	-	-	1
Country not stated	1	-	-	1
Total	129	163	2	294

The most common reason reported for travel for enteric fever cases was to visit friends and relatives (VFR) (86%, 252/294). Eighty-seven percent of VFR travellers (219/252) were of Indian, Pakistani, or Bangladeshi ethnicity and were both UK and non UK born.

The rate of infection with enteric fever in all travellers to India, Pakistan and Bangladesh was 17.3 per 100,000 visits compared to 0.05 per 100,000 visits to countries in the rest of the world. The rate of illness was higher in VFR travellers with highest rate in VFR travellers to Bangladesh (36.9 cases per 1000,000 visits). The highest number of both typhoid and paratyphoid cases were those who travelled to India (N=148). However, as there were more travellers to India, the rate of infection for India travellers was 14.2 per 100,000. VFR travellers were less likely to have sought pre-travel health advice and those who were UK born were more likely to seek pre-travel advice than those who were non UK born.

The full report on the enteric fever enhanced surveillance pilot is available from the [Health Protection Agency](#).

Risk for travellers

In endemic countries, risk-factors for contracting enteric fever include eating or drinking contaminated food or water, inadequate sanitation and sub-standard living conditions, poor personal hygiene, and close contact with those infected with *S. Typhi* or *Paratyphi*.

The risk of contracting typhoid fever is variable and depends on the country visited, but is highest (17.3 cases per 100,000 travellers) for travellers to the Indian sub-continent (India, Pakistan and Bangladesh) [5,6]. The risk of typhoid and paratyphoid fever in high income countries such as those in Europe, North America and Australasia is very low, less than 1 case per million visits.

Transmission

Transmission occurs following the ingestion of food or water that has been heavily contaminated (10^5 or more organisms may be required to cause illness) by the bacterium *S. Typhi* (typhoid) or *S. Paratyphi* (paratyphoid). *S. Typhi* can be passed in the faeces of persons who are acutely ill with typhoid fever or are chronic carriers. The bacteria can then enter the food chain and water supply if sanitation is inadequate. Direct faecal-oral transmission also occurs.

Ingestion of vegetables fertilized with human waste (night soil) and eaten raw, shellfish harvested from sewage-contaminated beds, and contaminated milk products can result in typhoid infection [7].

Signs and symptoms

Typhoid

Typhoid is a systemic disease that varies in severity, but nearly all patients experience fever and headache. Young children may experience a mild illness, but they can also suffer from severe disease.

The incubation period for typhoid fever is usually 7-14 days, but can be shorter or longer depending upon how many bacteria are ingested. Symptoms include low-grade fever (which typically becomes higher as the illness progresses), chills, headache, myalgia, malaise, anorexia and nausea. There can be abdominal discomfort and constipation, and diarrhoea can occur early in the course. Moderate enlargement of the liver and/or spleen occurs in about 50% of cases. In some cases, a macular rash (rose spots) consisting of pink lesions which fade on pressure under a glass, will appear on the trunk. The rash may be difficult to see in dark-skinned individuals.

Complications occur in 10-15% of all cases and are more likely in untreated cases or cases that present late in the course. Complications include intestinal haemorrhage and perforation, toxic myocarditis, pneumonia, seizures, typhoid encephalopathy, and meningitis (usually in young children).

The case fatality is usually less than 1% with prompt antibiotic therapy, but may be as high as 20% in untreated cases.

Following recovery, convalescing patients may continue to excrete *S. Typhi* in their faeces. Between 1-3% will become long-term carriers, continuing to excrete the organism for more than one year after the initial illness [8]. The carrier state is more common in women and those with biliary tract abnormality [7,8]. Chronic carriers require prolonged courses of antibiotics to clear the organism.

Paratyphoid fever

Paratyphoid is clinically similar but the disease may be more mild and of shorter duration [8].

Treatment

From its introduction in 1948, chloramphenicol was the drug of choice to treat typhoid [9], but in the early 1970s, chloramphenicol-resistant strains of *S. Typhi* began to emerge. Large outbreaks of resistant *S. Typhi* occurred in Mexico and India, and resistant *S. Typhi* became endemic in many countries of south and South East Asia [10]. Other antibiotics such as ampicillin and co-trimoxazole have been used to treat typhoid, but resistance to multiple antibiotics has developed since 1987 in endemic regions such as China, South East Asia and the Indian sub-continent [11]. In 1997, a large outbreak of multi-drug resistant typhoid was reported in Dushanbe, Tajikistan involving 8,901 cases and 95 deaths [12].

Drug-resistant strains have been seen in the UK in returned travellers. Of 692 samples taken from cases of typhoid fever imported into the UK between 2000 and 2003, 22% were multi-drug resistant and 39% were resistant to fluoroquinolone antibiotics (e.g. ciprofloxacin) [13]. In the pilot enhanced surveillance for enteric fever, more than two thirds of all cases had isolates of *S. Typhi* or *S. Paratyphi A* that exhibited reduced susceptibility to ciprofloxacin, representing an increase since 2001 [5].

Typhoid can be successfully treated with appropriate antibiotics. Treatment is usually with fluoroquinolones, cephalosporins [14], or azithromycin in cases that are resistant to fluoroquinolones [15]

Relapse will occur in less than 10% of patients treated with antibiotics. Relapse illness is usually milder and of shorter duration than the original illness. Those successfully treated with fluoroquinolones are less likely to suffer relapse or become chronic carriers.



Prevention

All travellers should exercise food and water hygiene precautions to prevent all types of enteric fever.

Typhoid

Vaccination is recommended for travellers whose planned activities put them at higher risk for typhoid in areas where sanitation and food hygiene are likely to be poor. This includes travellers visiting friends and relatives, young children, long-term travellers, and others exposed to poor sanitation. Vaccine is also recommended for laboratory workers who may have contact with the bacterium [16].

Vaccine recommendations for specific countries can be found on the NaTHNaC Country Information Pages: http://www.nathnac.org/ds/map_world.aspx

Paratyphoid

There is currently no vaccine available against paratyphoid.

Vaccine Information

Indications for use of vaccine

Typhoid vaccine is recommended for:

- Travellers visiting typhoid-endemic areas whose planned activities put them at higher risk including travellers visiting friends and relatives, young children, long-term travellers, and those exposed to conditions of poor sanitation
- Laboratory personnel who may handle *S. Typhi* in the course of their work [16]

Vaccine recommendations for specific countries can be found on the NaTHNaC Country Information Pages: http://www.nathnac.org/ds/map_world.aspx

Typhoid vaccine is not recommended for those who will have close contact with cases or those who are typhoid carriers [16].

Availability of vaccine

Vaccine	Manufacturer/distributor	Schedule	Length of protection	Age range
Typhim Vi	Sanofi Pasteur MSD	Single dose	3 years	Adults & children from 2 years of age
Typherix	GlaxoSmithKline UK	Single dose	3 years	Adults & children from 2 years of age
Vivotif	Crucell UK Ltd	3 capsules 1 st on day 1,	1 year	Adults and children from 6

		2 nd day 3, 3 rd day 5		years of age
Viatim (combined hepatitis A and typhoid vaccine)	Sanofi Pasteur MSD	Single dose of combined vaccine	<p><u>Component</u></p> <p><u>Typhoid</u> Revaccination with single dose purified polysaccharide typhoid vaccine every 3 years</p> <p><u>Hepatitis A</u> Booster dose of inactivated hepatitis A vaccine at 6-12 m</p>	Adults from 16 years of age
Hepatyrix	GlaxoSmithKline	Single dose of combined vaccine	<p><u>Component</u></p> <p><u>Typhoid</u> Revaccination with single dose purified polysaccharide typhoid vaccine every 3 years</p> <p><u>Hepatitis A</u> Booster dose of inactivated hepatitis A vaccine at 6-12 m</p>	From 15 years of age

Contraindications

- Hypersensitivity to any constituent of vaccine (both of the combined Hepatitis A/Typhoid contain traces of neomycin).
- Individuals who develop symptoms of hypersensitivity after vaccination should not receive further doses
- **Specific contraindications for Vivotif:** congenital or acquired immune deficiency, including patients receiving immunosuppressive or antimetabolic drugs
- Acute febrile illness or during an acute gastrointestinal illness
- Persons known to be hypersensitive to any component of the vaccine or the enteric-coated capsule

The Summary of Product Characteristics (SmPC) for the individual vaccine should be consulted for specific information relating to the product [17,18,19].

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Further reading

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