



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

Typhoid and paratyphoid in the UK are most often associated with foreign travel. Occasionally indigenous transmission occurs after contact with a carrier or case, usually in family/household settings. In the ten years through 2005 there has been an average of 172 typhoid and 192 paratyphoid cases reported each year in England, Wales, and Northern Ireland [Figures 1 and 2]. Just over 60% of typhoid and paratyphoid cases are associated with recent travel, although travel history information is not always available and the number of travel-associated cases is likely to be higher [5].

Figure 1: Laboratory reports of *Salmonella* Typhi by travel history, England, Wales, and Northern Ireland: 1996 to 2005. [5]

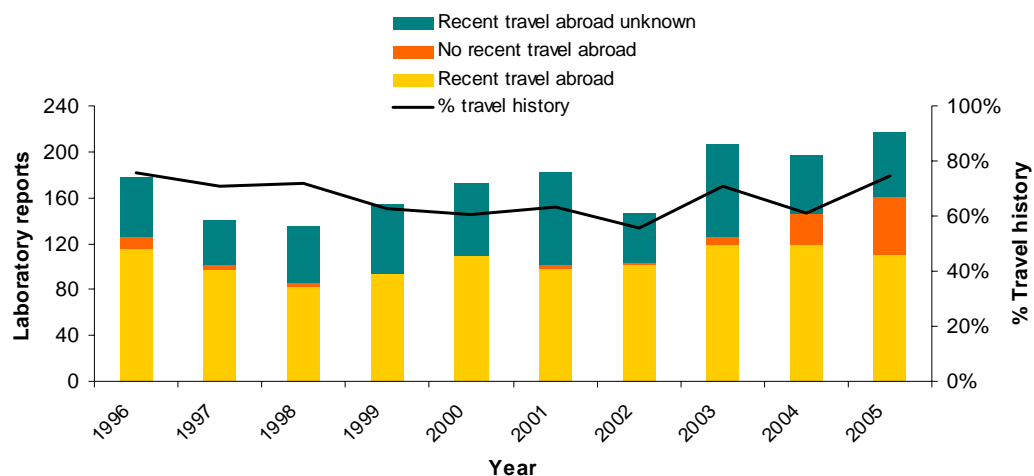
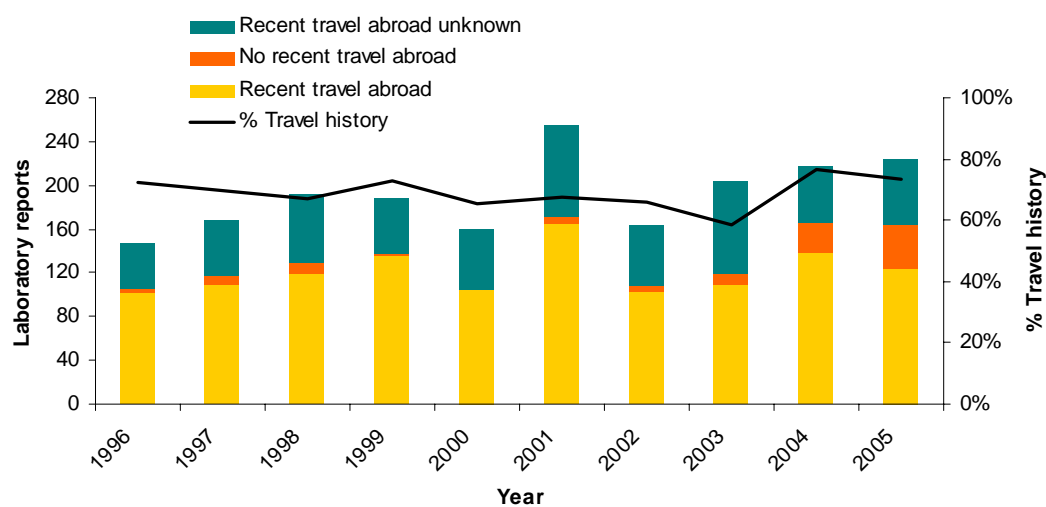
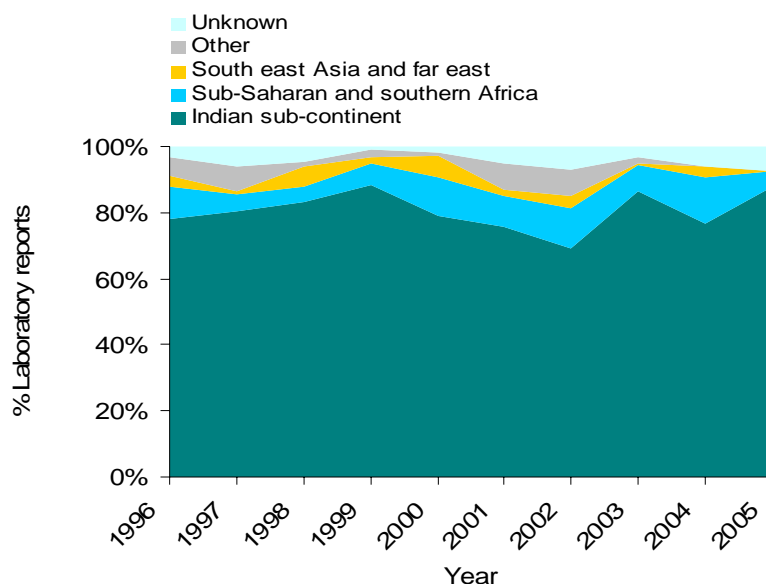


Figure 2: Laboratory reports of *Salmonella* Paratyphi by travel history, England, Wales, and Northern Ireland: 1996 to 2005. [5]



The Indian sub-continent (ISC) is the most commonly reported region of acquisition of typhoid since 1996 [Figure 3], with India and Pakistan being the most common in 2005 (39 and 38 reports respectively). In recent years, cases have also been associated with travel to sub-Saharan and southern Africa, in particular Nigeria (four reports in 2005 and 12 in 2004) [5].

Figure 3: Laboratory reports of *Salmonella* Typhi by country of travel, England, Wales, and Northern Ireland: 1996 -2005. [5]



Salmonella Paratyphi A is the most commonly reported paratyphoid infection in England, Wales, and Northern Ireland, with nearly all cases associated with travel to the ISC. In 2005, there were 61 reports of *S. Paratyphi* A that were associated with travel to India, and 31 to Pakistan. In recent years, *S. Paratyphi* B has mainly been associated with travel to South America (three in 2004 and six in 2005)[5]. Currently, imported cases of paratyphoid exceed the number of cases of typhoid.

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 for travellers to the Indian sub-continent (India, Pakistan and Bangladesh) [6]. For British travellers to the Indian sub-continent the risk has been estimated at 30 cases per 100,000 visits compared with 1 case per 100,000 visits to other low income countries [7]. 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 [8].

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 [9]. The carrier state is more common in women and those with biliary tract abnormality [8,9]. 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 [9].

Treatment

From its introduction in 1948, chloramphenicol was the drug of choice to treat typhoid [10], 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 [11]. 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 [12]. In 1997, a large outbreak of multi-drug resistant typhoid was reported in Dushanbe, Tajikistan involving 8,901 cases and 95 deaths [13]. Drug-resistant strains have also 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) [14].

Typhoid can be successfully treated with appropriate antibiotics. Treatment is usually with fluoroquinolones, cephalosporins [15], or azithromycin in cases that are resistant to fluoroquinolones [16]



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 [17].

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 [17]

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 [17].

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	Istituto Sieroterapico Berna s.r.l Distributed by MASTA	3 capsules 1 st on day 1, 2 nd day 3, 3 rd day 5	1 year	Adults and children from 6 years of age
Viatim (combined hepatitis A and typhoid vaccine)	Sanofi Pasteur MSD	Single dose of combined vaccine	<p>Component</p> <p>Typhoid Revaccination with single dose purified polysaccharide typhoid vaccine every 3 years</p> <p>Hepatitis A 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>Component</p> <p>Typhoid Revaccination with single dose purified polysaccharide typhoid vaccine every 3 years</p> <p>Hepatitis A 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 [18,19,20].

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