Most cases of typhoid or enteric fever are caused by *Salmonella enterica* subsp. *enterica* serovar Typhi (S. Typhi), although S. Paratyphi A and B and occasionally other serotypes such as S. Virchov, S. Dublin and S. Newport are implicated. S. Typhi is solely a human pathogen and there is no animal reservoir. Although typhoid is a rare imported infection in developed countries the antimicrobial agents most readily available for therapy are ampicillin, chloramphenicol and co-trimoxazole. Unfortunately, strains of S. Typhi resistant to all three agents have emerged [5]. Multi-drug resistant strains were first reported in Pakistan in 1987 [18] and have increased in prevalence to almost 90% of S. Typhi isolates [19, 20].

All of 25 multiresistant isolates obtained from Rawalpindi in 1990–91 carried a single self-transferable c. 98 MDa plasmid encoding resistance to chloramphenicol, ampicillin, streptomycin, tetracycline, sulphonamides, gentamicin and cephalazolin was encoded on a self-transferable 98 MDa plasmid [17]. Multi-drug resistant strains were first reported in Pakistan in 1987 [18] and have increased in prevalence to almost 90% of S. Typhi isolates [19, 20].

Multi-drug resistant S. Typhi were first described in India in 1990 [21] and several different phage types carrying incH1 plasmids of 110–120 MDa have been described [22]. Multi resistant strains have also been isolated in Malaysia [23], Bangladesh [24] and Vietnam [25], and the epidemic zone in Asia now appears to stretch from Pakistan in the west to China in the east. In addition, there is a 'pseudo-epidemic' zone in the Middle East. Between 30% and 40% of the population of Persian Gulf states are expatriate workers, mainly from the Indian sub-continent and the East. These workers travel repeatedly from their home countries to work and 70–80% of multiresistant S. Typhi strains in Bahrain [26], Kuwait [27], Qatar [28] and Oman [29] are imported. In this region 5–30% of S. Typhi isolates are multi-drug resistant.

Surprisingly, multi-drug resistance does not seem to have had a major impact in Africa, or South and Central America. In Africa, cases have been described in Egypt [30] and a cluster of six cases of multi-resistant S. Typhi infection was reported from northern Natal [31]. Elsewhere in Africa and America, S. Typhi remains sensitive to one or more of the first line agents, although large outbreaks of infection due to...
The emergence of multi-drug resistance has great pathognomonic features to distinguish such infections from other antimicrobial agents continue to occur [10, 14]. In the UK, multiresistant strains now represent >18% of S. Typhi isolates [32], mostly acquired in the Indian sub-continent or the Middle East. Three such strains have been isolated in Spain but their origin is unclear [33].

The emergence of multi-drug resistance has great implications for therapy [32]. For example, children infected with such strains are more ill at presentation, have a longer duration of illness and a significantly higher mortality rate [34]. However, there are no pathognomonic features to distinguish such infections from infection with fully sensitive S. Typhi at presentation. The therapeutic options for treatment include fluoroquinolones such as ciprofloxacin or ofloxacin, and expanded-spectrum cephalosporins such as ceftriaxone [35]. Azithromycin appears to be of little value as there was a lack of clinical response by the fourth or fifth day, in three or four patients treated [36]. In comparative and open studies, fluoroquinolones appear superior to cephalosporins [35], producing defervescence within 3–4 days [20, 25]. This speed of clinical response makes them a current treatment of choice even for less resistant S. Typhi. A 3-day regimen of oral ofloxacin was safe and highly effective in treating uncomplicated multi-drug resistant typhoid [25], but the effect of such short courses on carriage of S. Typhi needs further exploration. In children, the risks of mortality and morbidity from infection with multiresistant strains greatly outweigh the risk of potential side-effects of fluoroquinolone therapy [37]. For now, empirical therapy of suspected typhoid should be a fluoroquinolone or expanded-spectrum cephalosporin. Unfortunately, ciprofloxacin-resistant strains have already begun to emerge [38, 39], and this will further limit the therapeutic options.

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