Enteric Fever: Emerging Trends

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Enteric fever is still regarded as a major public health problem globally. Worldwide there were an estimated 22 million cases of enteric fever, with 2,00,000 deaths in 2002. The incidence is highest (>100 cases per 1,00,000 population per year) in South Central and South East Asia. It is estimated that there is one case of paratyphoid fever for every four cases of typhoid fever, but the incidence of infection associated with *S paratyphi A* appears to be increasing, especially in India. In this issue Gupta et al [1], from Bangalore report that 20% of their 81 cases of culture positive Enteric fever were due to *S paratyphi*. Another study of 119 culture positive cases from Mumbai shows that 39% of their cases were of *S paratyphi* infection [2].

Traditionally, it has been believed that enteric fever has a lower incidence and a benign course in preschool children. However, recent population based studies in South Asia show that the incidence is highest in children less than five years of age with higher rates of complications and hospitalization [3].

Enteric fever is a potentially lethal disease but its course can be altered favourably if appropriate antibiotics are exhibited early in the illness. However, given the non specific nature of presentation there are no discerning clinical clues which aid the physician. One can only resort to a high index of suspicion. In the tropics, the presentation is indistinguishable from malaria, viral hepatitis, bacterial enteritis, dengue, rickettsial fever, leptospirosis and amoebic liver abscess. Given the name Enteric Fever, one would expect an illness dominated by gastro intestinal manifestations. However, abdominal pain (30-40%), vomiting (18%), diarrhea (22-28%) and constipation (13-16%) do not constitute the hall mark features of the disease [4]. Constipation was not encountered at all in the Mumbai series of 119 cases [2]. The oft quoted relative bradycardia is an inconsistent finding [2,3]. However, two thirds of the 81 cases reported in this issue by Gupta et al [1], had relative

bradycardia. The classic mode of presentation with a slow and “step ladder” rise in fever is seldom seen and “Rose Red” spots are elusive in Asians. The incidence of splenomegaly is variably quoted. The Kathmandu group found splenomegaly in 5-6% of their 669 cases while the Mumbai study encountered splenomegaly alone or as part of hepatosplenomegaly in 20% of the cases [2,4]. Gupta et al [1], however report a much higher occurrence of splenomegaly to the tune of almost 60%. It can well be concluded that there is nothing typical about the presentation of enteric fever and the threshold for considering the diagnosis has to be low. To make matters worse, a “hepatic” presentation may be encountered in 4.8 to 8.6% of the cases [5].

How far does the laboratory come to the rescue? Leucopenia or a normal leucocyte count is the norm in enteric fever but leucocytosis is common in children and in those with complications. However, the presence of leucocytosis casts a doubt on the diagnosis of typhoid fever. Leucocytosis was seen only in 4 out of 119 culture positive cases of the Mumbai study [2]. The same study found absolute eosinopenia (AEC=0) in 77% of the cases and the authors propose this to be a useful marker of enteric fever. The Widal test lacks sensitivity and specificity and at best is a rough screening tool. The “Gold Standard” for diagnosis is culture positivity. The Mumbai study [2], found cultures positive in 52.6% of their cases in whom “Enteric Fever” was the diagnosis at discharge. It was heartening to observe that a substantial (46.2%) number of cases which were culture positive had received prior antibiotics. Therefore, antecedent antibiotic therapy should not dissuade a physician from sending cultures. Bone marrow cultures are said to retain a high sensitivity (90%) despite antibiotic therapy but the obvious constraints are that the test is invasive and more applicable to the hospital setting. Culture of intestinal secretions (best obtained by a non invasive duodenal string test) can be positive despite a

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negative bone marrow culture [6]. It would be interesting to extrapolate this to endoscopically obtained duodenal secretions at least in the centers where endoscopy is available and see if a relatively non invasive method for culture becomes available. Newer serological diagnostic techniques such as Typhidot, Typhidot M and Tubex detect the IgM response and are stated to have good sensitivity and specificity but have not proved to be robust enough in the community setting [3].

A high incidence of nalidixic acid resistant *Salmonella typhi* (NARST) isolates is reported in the study by Gupta et al [1] and the study by Jog et al [2], viz 86% and 79% respectively. In therapeutic terms, this portends fluoroquinolone resistance. Fortunately, resistance to third generation cephalosporins is not an issue at present, though a substantial relapse rate with ceftriaxone is an area of concern. Oral azithromycin is an exciting prospect that gives cure rates which are better than quinolones and comparable to ceftriaxone, with the added advantage of lower relapse rates [7].

Salmonella infection has challenged physicians since the times of Aristotle and still continues to do so today. Diagnosis can be elusive since the disease can be protean in its manifestations. The third world physician would do well to consider enteric fever in all the short

term febrile illnesses that he encounters. Multidrug resistance is an area of concern but thankfully the pharmacological armamentarium has kept pace. Above all, it is the early exhibition of an appropriate antibiotic which will salvage many a patient.

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