Editorial

ENTERIC FEVER THE CHANGING SCENE

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Improvements in environmental sanitation, like sewage disposal and safe water supply remain a distant dream for developing countries like India. Large population and rapid urbanization with sprawling slums have imposed a tremendous strain on limited financial resources and infrastructure capabilities in these countries. The slogan of the World Health Day for 1996 'Healthy cities for better life', therefore, is most appropriate. Enteric fever, the infection by human-adapted *Salmonella*, continues to remain a major public health problem. A large number of epidemics have been reported from India in recent years [1-5]. The disturbing aspects of these epidemics are the alarming rise in incidence of multidrug-resistant *Salmonella typhi* (MDRST), changing clinical profile, and higher morbidity. Another cause for concern is the behaviour of salmonella infection in HIV positive patients. The incidence of enteric fever in patients with AIDS is reported to be 60 times higher than that in the general population [6].

Chloramphenicol, the antimicrobial gold standard for enteric fever, was introduced for widespread clinical use in 1948. The warning that *Salmonella typhi* could become resistant to it was available as early as in 1950 [7] from England and in 1959 from India [8]. Since then resistance has also been observed to drugs like ampicillin, trimethoprim-sulphamethoxazole, furazolidine, gentamicin and cephalixin, giving rise to MDRST. Chloramphenicol acts by binding reversibly to the 50 S ribosomal subunit thus inhibiting protein synthesis by the bacteria. Resistant bacteria can render

this mechanism ineffective. Resistance on part of bacteria is due to a transferable 'R' plasmid, mutations of genes on the bacterial chromosomes and transposomes carrying resistant genes [9-11]. Large-scale use of antibiotics for diarrhoeal illnesses in humans and in farm-feed for poultry are assumed to be the causes for recent spread of MDRST [12]. The above scenario has necessitated a search for factors affecting the host-parasite relationship in case of *Salmonella typhi* infection. Krishna Menon, in an article in this issue of the journal, has demonstrated increased resistance to complement killing and higher multiplication within macrophages by MDRST. This does explain increase in virulence of MDRST and further studies are required to elucidate it.

The clinical profile of patients with MDRST infection differs from the traditional description of enteric fever. Children less than 5 years of age are being affected in greater number [2,13]. Pattern of fever ranges from low grade continuous to high grade intermittent with chills and rigors, causing confusion with malaria and other tropical infections. Approximately one third to one half of patients have hyperpyrexia. In addition duration of pyrexia may last seven to eight weeks [1]. Defervescence of fever after initiation of appropriate chemotherapy is also prolonged [2,4]. Hepatomegaly alone, rather than hepato-splenomegaly, is present in significant number of patients [14]. There is a higher incidence of complications like disseminated intravascular coagulation, myocarditis, hepatitis, circulatory collapse and nervous sys-

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tem involvement in patients with MDRST infection [1,15,16].

Patients with enteric fever due to MDRST are responsive to quinolones like ciprofloxacin and ofloxacin. Third generation cephalosporins like cefotaxime and ceftriaxone are also effective, but a few treatment failures have occurred. This has raised the cost of therapy [17]. Attempts to reduce the duration of therapy results in higher incidence of relapse or carrier rates, both of which are undesirable [18-20]. The safety of both groups of drugs in pregnancy, and that of quinolones in children, has been questioned. Recent reports suggest that the danger of arthropathy in children with quinolones is perhaps overemphasized. More than 130 cases of inadvertent use of ciprofloxacin in pregnant women have shown no maternal or foetal adverse effects [21]. Long term studies are required before these drugs can be recommended routinely for enteric fever in children and in pregnancy. However, there appears to be no choice in proven MDRST infection but to use them. Reports of increasing resistance to ciprofloxacin by *Salmonella typhi* have already started appearing. The drug is widely used and 'misused' and it is to be seen whether it suffers the same fate as chloramphenicol did.

Altered clinical profile with the emergence of MDRST needs to be closely monitored. While microbiologists are actively working on elucidating its causation, clinicians must recognize these cases at the earliest. There is a requirement of bringing down the cost of existing drugs and also to develop new cheaper substitutes.

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