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The concurrent prevalence of chloramphenicol-sensitive and multidrug-resistant *Salmonella typhi* in Vellore, S. India

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SUMMARY

A multidrug resistant (MDR) variety of *Salmonella typhi* emerged as the cause of epidemic typhoid fever in some Asian countries including India, during the late 1980s. We faced the epidemic from April 1990 to the first quarter of 1993. However, during this period we continued to isolate chloramphenicol sensitive (CS) *S. typhi* also. The relative prevalences showed that the frequency of CS variety was unaffected by the epidemic of MDR variety. This is an unusual epidemiological pattern, which indicates that there may have been factors which favoured the epidemic of the MDR variety but not the CS one.

Salmonella typhi resistant to chloramphenicol (C), ampicillin (A) and trimethoprim-sulphamethoxazole (TMP-SMZ) became prevalent in some Asian countries during the late 1980s and early 1990s [1–4]. It is generally believed that this multidrug resistant (MDR) variety emerged in southern China [2] and then spread to the neighbouring countries. We had previously reported its presence in the Vellore region in 1990 [3] and shown that the drug resistance was plasmid-mediated [5]. A review of the relative frequencies of chloramphenicol-sensitive (CS) and MDR strains of *S. typhi* obtained in our laboratory during 1989–94 is presented here to illustrate certain unusual epidemiological features.

Blood for culture was collected from patients with suspected typhoid fever and inoculated and processed by standard recommended procedures [6]. Biochemical and serological confirmation of *S. typhi* was also carried out using standard techniques [7]. Antibiotic susceptibility testing was performed by the disk diffusion technique of Kirby and Bauer [6] using *E. coli* (25922) and *S. aureus* (ATCC 25923) as control strains.

The numbers of isolates of CS and MDR strains of *S. typhi* by month, during September 1988 through May 1995 are shown in Fig. 1. There has been no month without the isolation of *S. typhi*. The very first isolate of a MDR strain was obtained in January 1989 and the next one in March. Following intermittent isolation of one or two isolates per month till March 1989, there were 2–5 isolates per month from April 1989 to March 1990. Thereafter the numbers increased steeply, indicative of an epidemic, which lasted till the first quarter of 1993. During this entire period of 6 years the CS strains continued to be isolated. During the period of the epidemic of the MDR variety (April 1990–March 1993) there was neither an increase nor a decrease in the prevalence of the CS variety.

The unusual phenomenon we describe here is the behaviour of the CS and MDR varieties of *S. typhi* as though they were epidemiologically independent pathogens. If the mode of transmission and the risk factors for infection by both CS and MDR were identical, we would have expected the prevalences of the two varieties to be more or less parallel to each other. In other words, if there were epidemiological factors which favoured the epidemic spread of *S. typhi* in the community around us irrespective of their drug sensitivity pattern, then we would have expected both varieties to participate in the epidemic. However, only

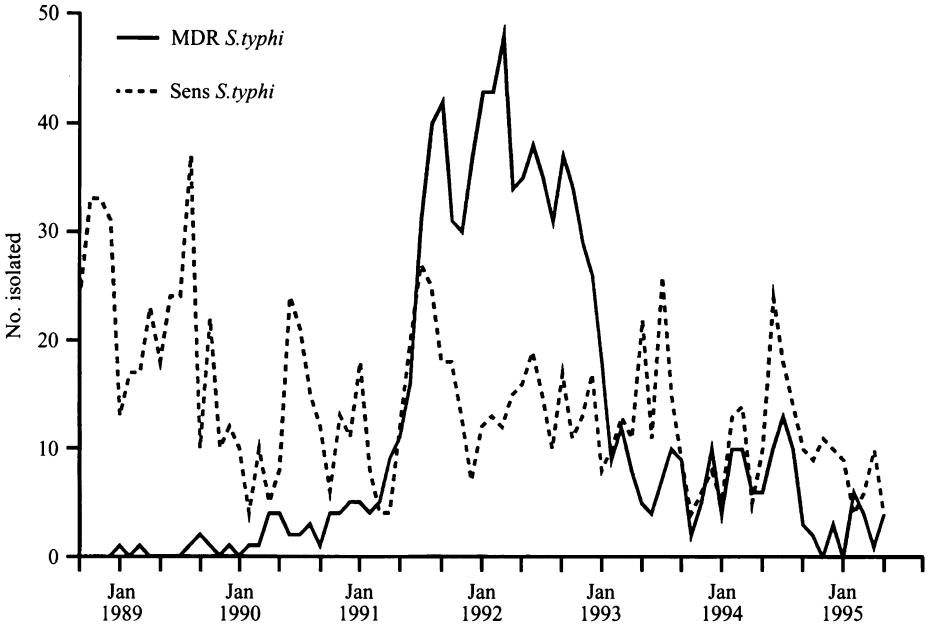

Fig. 1. Isolation pattern of *S. typhi* from blood culture. —, MDR *S. typhi*; ----, Sens *S. typhi*.

the MDR variety became epidemic, not the CS one. This implies that the factors involved in the transmission or establishment of the organism were not identical for the two varieties.

Recently, the epidemic replacement of *Vibrio cholerae* O1 by O139 [9] was attributed to the fact that the local population had previously not experienced serogroup O139 and were immunologically naive [10]. Thus, an epidemic, such as that of the MDR variety of *S. typhi*, indicates epidemiological conditions conducive for its rapid spread and/or a community with an unusual gap in immunity. Earlier we argued why epidemiological conditions conducive for the rapid spread of *S. typhi* could not have explained the epidemic since the CS variety did not participate in the epidemic. Was there a gap in immunity to the MDR variety of *S. typhi* alone, but not to the CS variety? Such an explanation requires that there should be differential immunities against the CS variety and the MDR one, rather like those to the O1 and O139 serogroups of *V. cholerae*. There is no evidence to suggest that this is the case since both organisms are identical in their microbiological characteristics; both are Vi positive, and both have the classical *S. typhi* O and H antigen specificities. Therefore we raise the question of whether other factors involved in immunity could be different between these two varieties.

Thus, we propose that properties other than MDR status may be conferred on *S. typhi* by the plasmid which specifies resistance to several antimicrobials [5]; there have been reports that show the severity of typhoid fever and or the frequency of complications to be more commonly associated with the MDR variety than the CS variety of *S. typhi* [11, 12]. Thus, increased virulence may be another property conferred by the MDR plasmid.

Currently following MDR epidemic period that lasted about 2 years, both the CS and MDR appear to be endemic and not in competition, as shown in Fig. 1.

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