

Chloramphenicol—Resistant *Salmonella typhi*

Principal Investigators: Richard M. Lampe, MAJ, MC
Chiraphun Duangmanee, M.D.
Pethai Mansuwan, M.D.¹

Associate Investigators: Michael W. Benenson, MAJ, MC
Douglas R. Stutz, MAJ, MSC

OBJECTIVE: To determine prevalence and degree of chloramphenicol resistance among *Salmonella typhi* isolates from typhoid fever patients at Children's Hospital; and to correlate the *in vitro* pattern of resistance with epidemiological data and clinical response.

BACKGROUND: Chloramphenicol—resistant *S. typhi* has recently been reported from Mexico (1), India (2) and Vietnam (3). R factor transfer of resistance has been demonstrated in these strains, and is believed to be the manner in which chloramphenicol resistance develops. Typhoid fever is endemic in Thailand. Approximately 100 cases are seen annually at Children's Hospital. Enteropathogens isolated in Thailand are resistant to multiple antibacterial drugs, and this resistance is transferable (4). The occurrence of chloramphenicol—resistant *S. typhi* at Children's Hospital has been suspected for several years but has only recently been documented.

Five of fifty *S. typhi* isolates from hemocultures at Children's Hospital were resistant to chloramphenicol (30 µgm Kirby—Bauer discs) during the period Jan—Jun 1973.

DESCRIPTION: Children with suspected typhoid fever had hemocultures, rectal cultures, and Widal tests performed on the day of admission, day 5, and day 10. Bone marrow cultures were obtained when deemed necessary by the ward physician. *S. typhi* isolates had disc sensitivities performed by the Kirby—Bauer method. Plate dilution minimum inhibitory concentration (MIC) was determined for chloramphenicol, ampicillin, tetracycline and trimethoprim—sulfamethoxazole.

PROGRESS: *S. typhi* has been isolated from 41 patients since the beginning of the project 1 Nov. 73. Thirteen of these (32%) have been resistant to chloramphenicol. In each resistant case the same pattern of resistance has been found; resistance to chloramphenicol, tetracycline, streptomycin and sulfadiazine. MIC data for the resistant *S. typhi* isolates are reported in Table 1.

Two of the isolates were resistant to ampicillin. All chloramphenicol—resistant isolates were sensitive to trimethoprim—sulfamethoxazole.

Of thirteen resistant cases eight were from Wang Noi, Ayutthaya, 2 from Nonthaburi, 2 from Bangkok and 1 from Lopburi (see Figure 1). The sensitive cases were from scattered locales, predominantly in the Bangkok area. The home of a family living in Wang Noi, with chloramphenicol—resistant *S. typhi* isolates from two of their children was visited, and rectal swabs were obtained from the parents and three additional siblings. Canal (klong) water, drinking water and duck feces were also cultured. No *Salmonella typhi* was found. Conversations with personnel at District Hospital and the District Health Center revealed no recognized problem with typhoid fever, unresponsive to therapy.

One patient with chloramphenicol—resistant *S. typhi* lived in an orphanage, Baan Rajvithi, in Bangkok. Eighteen contacts, children living in the same cottage as the patient, had rectal swabs taken as did the six food handlers for the orphanage. None were positive for *S. typhi*.

¹ Chief of Pediatrics, Children's Hospital, Bangkok, Thailand

Table 1. MIC Values for Chloramphenicol-Resistant *S. typhi*

| Antibiotic | No. of <i>S. typhi</i> isolates | MIC ($\mu\text{g/ml}$) |
|------------------------|---------------------------------|--------------------------|
| Chloramphenicol | 13 | 256-512 |
| Tetracycline | 13 | 256-512 |
| Ampicillin | 11 | 0.5-1.0 |
| Ampicillin | 2 | 256-512 |
| Trimethoprim (TMP) | 13 | 0.4-1.6 |
| Sulfamethoxazole (SMZ) | 13 | 16384 |
| TMP-SMZ | 13 | 0.1/1.9-0.8/15.2 |

Four chloramphenicol resistant isolates of *S. typhi* from 1973 and one resistant isolate from 1965 have been phage typed at the CDC, Atlanta, Georgia. The 1965 isolate was phage type E-1; the four 1973 isolates were untypeable.

Transfer of chloramphenicol resistance to a sensitive strain of *E. coli* has been demonstrated in the 3 resistant isolates of *S. typhi* on which this has been attempted.

Patients from whom chloramphenicol-resistant isolates have been obtained have demonstrated clinical resistance when treated with chloramphenicol. Therapy with ampicillin or trimethoprim-sulfamethoxazole has proved satisfactory in the resistant cases.

DISCUSSION: Chloramphenicol-resistant *S. typhi* isolates have been obtained from 32% of typhoid fever patients at Children's Hospital. The pattern and degree of resistance resembles closely those isolates from outbreaks in Mexico, India and Vietnam. Transfer of resistance has been demonstrated. The phage types of the resistant strains in Thailand are untypeable. Chloramphenicol is unsatisfactory in treating patients with chloramphenicol-resistant typhoid but ampicillin or trimethoprim-sulfamethoxazole are satisfactory alternatives.

The geographical distribution of resistant cases in Wang Noi is interesting. No explanation is available at present. Since Children's Hospital is the only pediatric hospital in Bangkok, pediatric patients with typhoid are often referred there if out-patient treatment has been unsatisfactory. The close proximity of Wang Noi to a major highway leading to Bangkok may facilitate the patient's transport to Bangkok.

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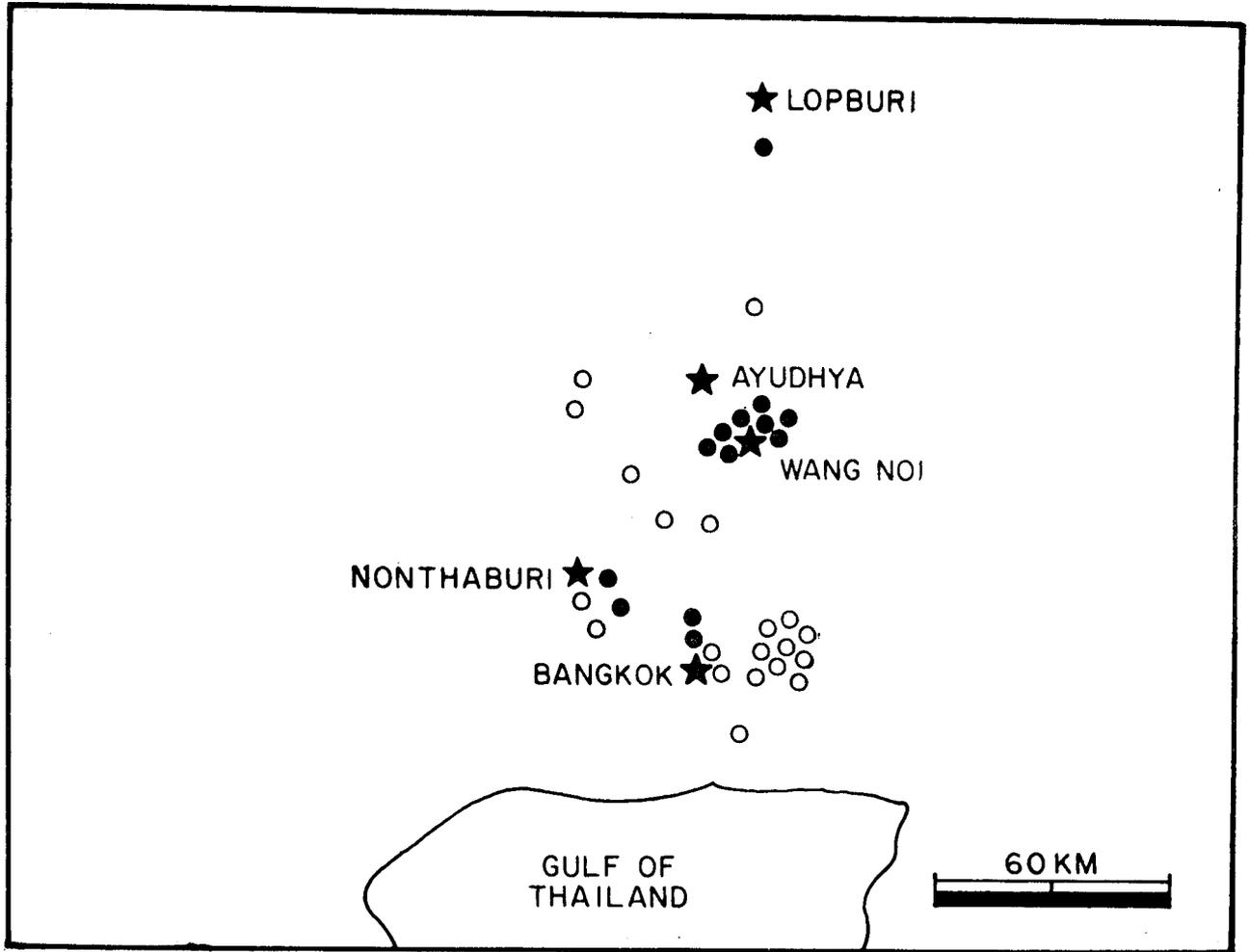


FIGURE 1: DISTRIBUTION OF TYPHOID CASES
RESISTANT (●) AND SENSITIVE (○)