Antibiotic–Resistant Typhoid Fever

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OBJECTIVE: To determine the prevalence and degree of antibiotic resistance among *Salmonella typhi* isolates from typhoid fever patients at Children's Hospital and to correlate the *in vitro* pattern of resistance with the phage types of *S. typhi* and the clinical response to therapy.

BACKGROUND: Antibiotic–resistant strains of *S. typhi* have been isolated from patients with typhoid fever at Children's Hospital. These *S. typhi* strains have resistance patterns and transferable R factor similar to strains isolated from Mexico, India and Vietnam. Chloramphenicol has been ineffective therapy in patients infected with Chloramphenicol–resistant *S. typhi*.

DESCRIPTION: Isolates of *S. typhi* from patients with clinical typhoid fever at Children's Hospital were obtained and disc sensitivities performed by the Kirby–Bauer method, and minimal inhibitory concentrations (MIC) by the plate dilution technique. *S. typhi* isolates from other parts of Thailand, and from Cambodia and South Vietnam were similarly studied.

The presence of R factor in antibiotic resistant strains was determined by the transfer of antibiotic resistance to a sensitive strain of *Escherichia coli*.

Phage typing of the *S. typhi* strains was performed through Dr. E.S. Anderson at the Enteric Reference Laboratory, London, England.

PROGRESS: Forty–four *S. typhi* isolates from Children's Hospital obtained between 28 March 1974 to 11 March 1975 were studied; seventeen (39%) were resistant to Chloramphenicol.

The Kirby–Bauer Disc method showed the resistance Pattern I, Chloramphenicol, Streptomycin, Sulfadiazine, and Tetracycline (C S Su T) in eight strains and the resistance Pattern II (Ampicillin C S Su T) in nine strains.

The disc sensitivities are presented in Table 1 and the minimal inhibitory concentrations to Chloramphenicol, Ampicillin and Trimethoprim/Sulfamethoxazole (TMP/SMZ) are illustrated in Figure 1. In Figure 1 the MIC for TMP/SMZ refers to the μgm/ml of TMP in a 1:20 ratio of TMP:SMZ.

Each Chloramphenicol–resistant strain of *S. typhi* possessed R factor capable of transferring Chloramphenicol resistance to a sensitive *E. coli*. The strains that were also resistant to Ampicillin transferred both Chloramphenicol and Ampicillin resistance to sensitive *E. coli*.

Vi phage type results are available on *S. typhi* strains obtained from Children's Hospital since November 1973. Their distribution by Chloramphenicol sensitivity is illustrated in Table 2. Most of the *S. typhi* strains resistant to Chloramphenicol but sensitive to Ampicillin have been phage type 53. All of the Ampicillin and Chloramphenicol resistant strains of *S. typhi* have been phage type D 1 (variant).

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Table 1. Antibiotic Disc Sensitivity of *Salmonella typhi* strains (44)

Antibiotic	Sensitivity (percent)
TMP/SMZ	100%
Kanamycin	100%
Gentamicin	100%
Cephalothin	100%
Ampicillin	80%
Chloramphenicol	61%
Tetracycline	61%
Sulfadiazine	30%
Streptomycin	0%

The 10 patients with phage type D 1 (variant) came from scattered locales in Bangkok and nine were hospitalized during the months of May, June and July 1974. Initial therapy with Chloramphenicol or Ampicillin was ineffective in these patients; however, therapy with Trimethoprim/Sulfamethoxazole resulted in satisfactory clinical improvement.

Twenty five strains of *S. typhi* from Vietnam and ten strains of *S. typhi* from Siriraj Hospital, Bangkok, Thailand were confirmed to be resistant to Chloramphenicol by disc sensitivity and MIC. All of the strains exhibited resistance Pattern I, C S Su T. No Ampicillin resistance was detected.

One *S. typhi* strain from Cambodia, and two from Songkla, Thailand were sensitive to Chloramphenicol. One of seven strains of *S. typhi* from the Bumrasnaradura Infectious Disease Hospital exhibited resistance Pattern I, while the remainder were sensitive to Chloramphenicol. All of the 21 *S. typhi* strains from Chiangmai were sensitive to Chloramphenicol and Ampicillin.

DISCUSSION: The emergence of Chloramphenicol–resistant *S. typhi* strains with demonstrable *in vitro* and *in vivo* resistance which was first noted in 1973 has continued and a number of strains have been resistant to Ampicillin as well. All strains have been sensitive to TMP/SMZ and satisfactory clinical responses have been observed with this drug. The potential emergence of resistance of *S. typhi* to TMP/TMZ, remains; however, since resistance to TMP/SMZ is seen in other enteropathogens. Approximately 10% of Shigella isolates at SEATO Laboratory during the past year have demonstrated *in vitro* resistance (disc method) to TMP/SMZ. Continued surveillance of antibiotic resistance patterns of *S. typhi* will continue.

The association of certain phage types with antibiotic resistant strains of *S. typhi* suggests that certain phage types are more likely to be associated with R factor. The phage type associated with antibiotic–resistant strains of *S. typhi* are different than phage types noted in Mexico and in Vietnam and determination of the phage type may prove useful in determining the source of infection in the future.

Table 2. Distribution of Vi Phage Phage Types by Sensitivity (53 *S. typhi* strains)

Phage type	Chloramphenicol sensitive	Chloramphenicol resistant
A	5	
D2	5	
M1	4	1*
53	4	13*
E10	3	
Degraded Vi (7)	2	
E1	1	
E2	1	
E3	1	
D6	1	
Degraded Vi (8)	1	
Vi negative		1*
D 1 variant		10**
Total	28	25

* Pattern I: C S Su T
** Pattern II: A C S Su T

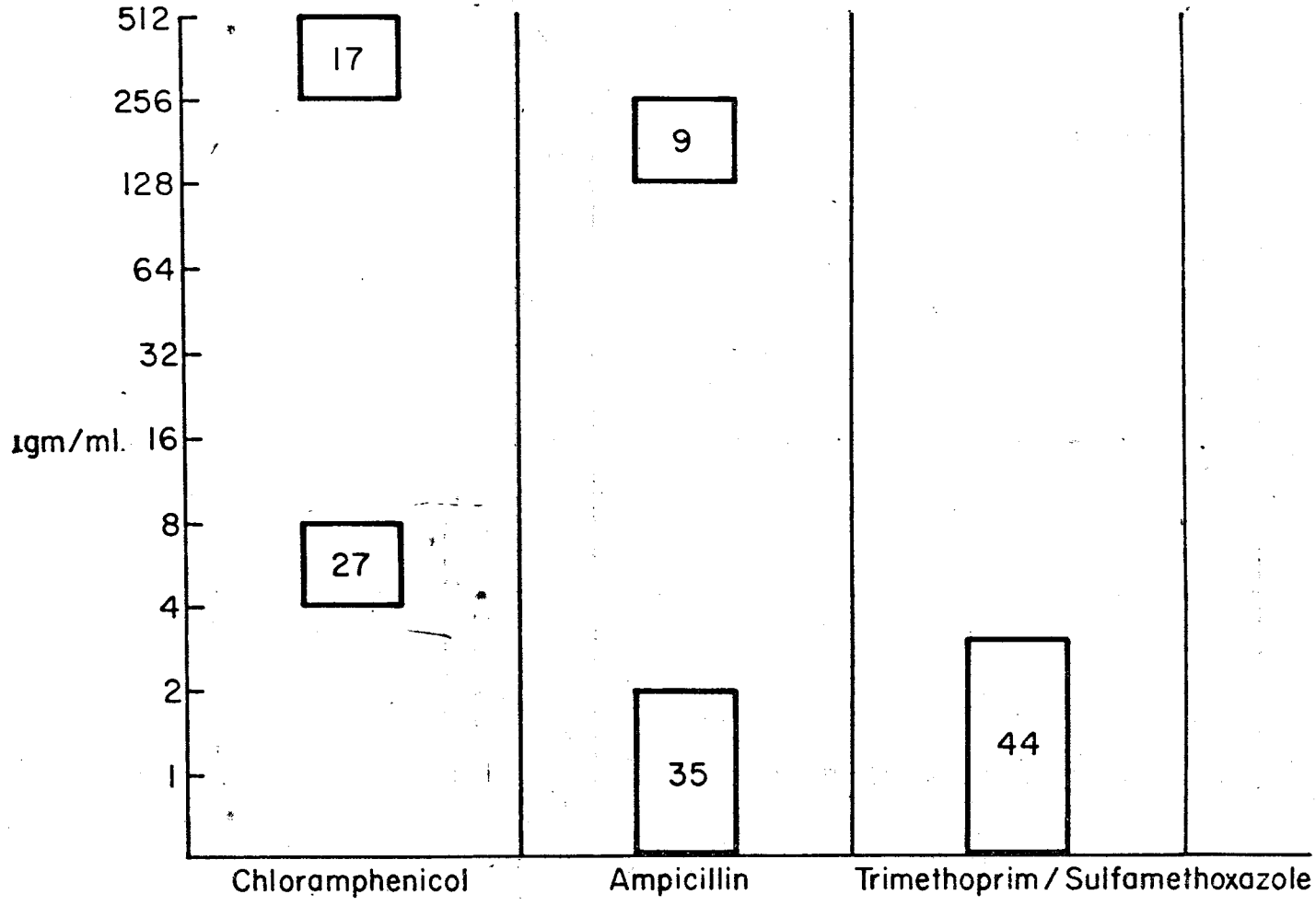

Figure 1. Range of Minimal Inhibitory Concentrations (for 44 S. typhi Strains)