

# CHLORAMPHENICOL RESISTANT STRAINS IN SALMONELLOSIS IN JAKARTA

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## INTRODUCTION

Resistance to chloramphenicol in individual strains of *Salmonella typhi* has been reported in various areas of Southeast Asia (Butler *et al.*, 1974; Linh, 1974; Brown *et al.*, 1975). In additional chloramphenicol resistant *S. typhi* caused an epidemic in Mexico in 1972 (Anderson and Smith 1972) and transmission of the bacterium was attributed to contaminated drinking water (Gonzales-Sortes *et al.*, 1973). Physicians have been aware therefore, that this drug resistant problem may occur also in Jakarta, Indonesia. However, it was not until January 17, 1978, that the first patients infected with chloramphenicol resistant *S. typhi* and *S. enteritidis* were seen in Sumber Waras hospital. The results of our observations of these patients, during the years 1978-1979 are presented herein.

## MATERIAL AND METHODS

During a 20 month period, from January 1978 through August 1979, a study was carried out on 123 cases comprising of 70 males and 53 females ranging in age from 17 days to 14 years.

All were admitted to the Pediatric Department of the Sumber Waras Hospital. This hospital is a general hospital for the Western part of Jakarta. It draws patients from the western, northern, southern and central regions of the city. The criteria for the selection of cases were the presence of fever and clinical manifestations suggestive of enteric

fever together with a positive blood, stool, urine or cerebrospinal fluid culture for *S. typhi* or *paratyphi*, or a seroconversion or a rising *S. typhi* O titre in the case of typhoid fever or a rising group A, B or C titre in the case of *S. enteritidis* infection with or without a concomitant rise in the *S. typhi* 'O' titre.

Blood from patients with suspected typhoid fever was inoculated into thioglycolate liquid medium and stool specimens were inoculated into selenite and tetrathionate broth and into *Salmonella-Shigella* and MacConkey agar. *Salmonella* organisms were identified by routine bacteriological and serological methods using poly O, and H antigens (Difco). Antibiotic susceptibility patterns were determined by a modified Kirby-Bauer single-disk method using DST (Diagnostic Sensitivity Test) agar (Oxoid). Widal serology, complete blood count and urinalysis were performed. If *S. typhi* or *S. enteritidis* could be isolated from the blood, stool, urine or spinal fluid, a second bacterial examination was performed 7 to 10 days later and continued until negative cultures were obtained. Other laboratory tests were done depending upon the clinical picture.

The patients were treated with oral chloramphenicol at a dosage rate of 50-75 mg per kg body weight/day. If after 7-10 days the patients showed no improvement clinically, treatment was changed according to the resistance test. Intravenous fluid therapy and other drugs were given when indicated. Close observations were made on (1) clinical cure, (2) the time for the temperature to

become normal, (3) resistance pattern of the isolate from a positive blood or stool culture after treatment had begun, (4) adverse drug reactions and (5) if relapse occurred, the recurrence of fever together with positive blood or stool cultures. The first four *S. typhi* strains resistant to chloramphenicol were found in our laboratory and were then sent to the Microbiology Department at NAMRU-2, Jakarta for confirmation. Thereafter all isolates from the blood, stool, urine and spinal fluid were also sent for serological typing and further antibiotic susceptibility studies to NAMRU-2.

### RESULTS

Over a 20 month period, 123 infants and children clinically suspected with salmonellosis were admitted. In 105 cases, *S. typhi* or *S. enteritidis* were isolated from the stool, urine, blood or cerebrospinal fluid. The *Salmonella* strains isolated included 66 *S. typhi*, 16 *S. sero-group A*, 3 *S. sero-group B* (Schwartzengrund) and 19 *S. sero-group C<sub>1</sub>* (Oranienburg) (Table 1).

There were 27 (26%) *Salmonella* strains resistant to chloramphenicol. In 1978, 9

(32%) *S. typhi* isolates resistant to chloramphenicol were likewise resistant to sulfa and tetracycline. Some were also resistant to ampicillin, gentamicin and cephalixin, but still sensitive to sulfamethoxazole-trimethoprim. Sixty seven percent (6/9) *S. sero-group C<sub>1</sub>* were sensitive only to sulfamethoxazole-trimethoprim and gentamicin. In 1979, no chloramphenicol resistant *S. typhi* were found. However *S. sero-group C<sub>1</sub>* resistance to chloramphenicol increased to 90% (9/10). They were resistant also to sulfamethoxazole-trimethoprim, but still sensitive to gentamicin and cephalixin. In 3 patients *S. sero-group B* could be isolated from their stool and blood. Two of the isolates were resistant to chloramphenicol, sulfamethoxazole-trimethoprim, ampicillin, tetracycline and sulfa but still sensitive to gentamicin and cephalixin.

The patients with chloramphenicol-resistant *Salmonella* infections remained febrile for 7 or more days after chloramphenicol treatment was started. They became afebrile within 5 days when they received antibiotics according to the sensitivity tests, except in one case. Those patients who had chloramphenicol sensitive organisms, became afebrile

Table 1

The number of isolates and the strains resistant to chloramphenicol.

<i>Salmonella</i>	1978 (12 months)			1979 (8 months)		
	Total	CMS.	CMR.	Total	CMS.	CMR.
<i>S. typhi</i>	28	19	9	38	38	0
<i>S. serogroup A</i>	10	10	0	6	6	0
<i>S. serogroup B</i>	0	0	0	3	1	2
<i>S. serogroup C</i>	9	3	6	10	1	9
<i>S. serogroup H</i>	1	0	1	0	0	0
Negative	12	12	0	6	6	0
Total	60	44	16	63	52	11

CM = Chloramphenicol, S = Sensitive, R = Resistant.

within 1 to 8 days after onset, except in 3 cases (10 days).

A series of questionnaires were completed by the parents of 4 children who had chloramphenicol resistant typhoid fever. They had never travelled outside Jakarta. These four cases lived in different parts of the city and had no connection with one another. Samples of food, well water and drinking water from jars were collected for bacteriological analysis and kept under refrigeration until processing in the laboratory. The results were negative.

In 105 patients, the diagnosis of salmonellosis was confirmed by isolation of the organism in blood, stool, urine or cerebrospinal fluid. Only 22 (21%) of the 105 patients seroconverted. The diagnosis in 18 cases (15%) was based on clinical findings and highly suggestive seroconversion. The death rate was 7% (9/123) following complications or associated diseases. Intestinal perforation occurred in 3 cases, bronchopneumonia and heart failure in 2 cases, bronchopneumonia and encephalopathia in 1 case, otitis media in 1 case and *S. enteritidis* sero-group C<sub>1</sub> meningitis and disseminated intravascular coagulation (DIC) in one case. Four of the fatal cases belonged to the chloramphenicol resistant group.

#### DISCUSSION

In our previous studies (Komalarini and Sanborn, 1975, Komalarini *et al.*, 1976), chloramphenicol resistant *S. typhi* was never isolated, nor was *S. sero-group C<sub>1</sub>* isolated from the blood or urine in *S. enteritidis* infections. There were only 5 cases of *Salmonella* meningitis out of 85 patients admitted with acute bacterial meningitis during a 5 year period (1971-1976) in the department of Pediatrics (Erawan *et al.*, 1976). The CSF revealed the presence of *S. typhi* in 3 cases,

*S. sero-group B* in 1 case and *S. sero-group C<sub>1</sub>* in 1 case. In our present study 32% (9/28) of the *S. typhi* isolated in the year 1978 were resistant to chloramphenicol *in vivo* as well as *in vitro*. Of particular interest is the fact that in the next year (1979), no *S. typhi* resistant to chloramphenicol was found. Chloramphenicol resistant *S. sero-group C<sub>1</sub>* (Oranienburg) increased from 67% (6/9) in 1978 to 90% (9/10) in 1979. According to Smith (1975) most *Salmonellae* can cause human gastroenteritis and only some are invasive. The fact, that in the last 2 years *S. sero-group C<sub>1</sub>*, could be isolated so often from the blood and urine suggests that this bacterium in Indonesia has become more important as a cause of gastroenteritis and also has a higher degree of resistance to antibiotics than formerly. We could have fairly well predicted this present situation based on prior studies showing a yearly increase in *S. enteritidis* caused gastroenteritis (Komalarini *et al.*, 1977; Sanborn and Komalarini, 1976).

#### SUMMARY

During an observation period of 20 months (from January 1978 to September 1979) 123 children with clinically suspected salmonellosis were admitted to the Department of Pediatrics, 70 males and 53 females varying in age from 17 days to 14 years. *S. typhi* or *S. enteritidis* was isolated from the stool, urine, blood or cerebrospinal fluid in 85% (105/123) of the cases. The results of the microbiologic examination showed that 28 out of the 105 cases (27%) were resistant to chloramphenicol of which the *S. sero-group C<sub>1</sub>* was predominant. It appeared that 28 cases conformed to the clinical data. In all these cases chloramphenicol was replaced by other antibiotics according to the sensitivity test. The mortality rate was 7% (9/123). Four of the fatal cases were from the chloramphenicol resistant group.

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