

CHAPTER 4



RESULTS

A. LABORATORY EVALUATIONS OF CEFTRIAXONE TO SHIGELLA SPECIES

1. Results of Antimicrobial Susceptibility Tests

From the disc agar diffusion method mentioned before, the results of the tests were as follows :-

1.1 Susceptibility to Ceftriaxone

Thirty isolates of *Shigellae* of various strains were tested with Ceftriaxone 30 µg discs, all of them were sensitive to the drug as shown by diameter of more than 16 mm with an average zone diameter of 30.7 mm (range from 17.6 to 40 mm.) The test included strain of *Shigella* with higher MIC of eight (8) µg/ml (which will be mentioned in details on p.85), the overall results are shown in table 21.

1.2 Susceptibility to other antimicrobial agents

Another 6 antimicrobial agents discs were tested against 74 - 77 isolates of *Shigella* of various strains, 30 isolates from title 1.1 were included, all of the results are shown in table 21.

The percentage of sensitive strains to trimethoprim / sulfamethoxazole, tetracycline, neomycin, cephalothin, chloramphenicol and ampicillin were 76.6, 5.3, 77.6, 85, 6.6 and 14.3 respectively, while the percentage of sensitive strains isolated from the studied

patients are quite similar, and this is shown in table 22.

The test organisms had 16 patterns of antibiotic resistance as shown in table 23. Most of them (39 of 74 or 53 %) showed the same pattern, i.e. they were susceptible to TMP/SMX, neomycin and cephalothin and were resistant or moderately sensitive to tetracycline, chloramphenicol and ampicillin.

The shigellae isolated from the studied patients had a similar distribution of resistance pattern as shown in table 24.

2. Results of Determination of Minimal Inhibitory Concentration (MIC)

103 isolates of shigellae of various types were obtained from various places in Thailand. They were isolated from rectal swabs or stool cultures of the patients from Chantaburi, Nakorn-Sridhamarat, Nondhaburi, Bangkok, Saraburi, and others for 57, 4, 16, 14, 8 and 4 isolates respectively.

The results of the test are shown in table 21, 22 and 23. The data showed that 97 % (100 isolates) of the organisms tested were inhibited at the MIC \leq 0.03 μ g/ml. And 100 % (103 isolates) were inhibited at 8 μ g/ml.



Table 21 The results of antimicrobial susceptibility test of shigellae to ceftriaxone and other antimicrobial agents.

number	code	Shigella group and types (phase)	zone diameter to ceftriaxone (mm)	Susceptibility to other antimicrobials					
				TMP / SMX	Tetracycline	Neomycin	Cephalothin	Chloramphenicol	Ampicillin
1	94	D (I)	33.0	S	R	S	S	R	R
2	77	D (I)	17.6	I	R	S	S	S	S
3	22	B 2a	29.1	S	R	S	S	I	R
4	4	B	29.2	R	R	S	I	I	R
5	65	C	28.0	S	I	S	I	S	S
6	2	A 2	28.8	S	R	S	S	R	S
7	62	B 4	33.7	R	R	S	I	R	R
8	60	B 6	32.1	R	R	R	R	R	R
9	91	D (I)	33.7	S	R	R	S	R	R
10	78	D (I)	33.6	S	R	S	I	R	R
11	25	B 2a	33.7	S	R	S	S	I	R
12	8	B 1b	36.7	S	R	S	S	I	R
13	67	C 2	40.0	S	R	S	S	R	S
14	80	D (I)	29.2	S	R	I	I	R	R
15	81	D (I)	30.5	S	R	S	I	R	R
16	32	B 2a	32.4	S	R	S	S	I	R
17	50	B 2b	31.6	S	R	S	S	I	R
18	79	D (I)	32.3	S	R	S	S	R	R
19	33	B 2a	29.6	R	R	R	S	R	R
20	18	B 2a	31.0	S	R	S	S	I	R
21	100	D (I,II)	33.1	S	R	I	I	R	R
22	54	B 3e	30.0	S	R	S	S	R	R
23	96	D (I,II)	31.0	S	S	S	I	S	R

Table 21 (continued)

number	code	Shigella group and types (phases)	zone diameter to ceftriaxone (mm)	Susceptibility to other antimicrobials					
				TMP / SMX	Tetracycline	Neomycin	Cephalothin	Chloramphenicol	Ampicillin
24	71	C 4	32.0	S	R	S	S	R	R
25	64	C	27.0	S	R	S	S	R	R
26	21	B 2a	27.0	R	R	R	R	R	R
27	72	C 4	31.0	S	R	S	I	R	R
28	6	B	28.0	S	R	S	S	R	R
29	116	B	31.2	S	R	S	S	R	R
30	17	B 2a	26.0	S	R	S	S	R	R
31	104	B		S	R	S	S	R	R
32	105	B		S	R	S	S	R	R
33	106	B		R	R	S	S	S	R
34	107	B		R	-	-	-	-	R
35	108	B		R	S	R	-	R	R
36	109	B		R	R	R	-	R	R
37	110	B		S	R	S	S	R	R
38	111	D		S	R	R	S	R	R
39	112	B		S	R	S	S	R	R
40	113	B		S	S	S	S	R	S
41	114	B		S	R	S	S	R	S
42	115	B		S	R	S	S	R	R
43	129	B		S	R	S	S	R	R
44	117	B		S	R	S	S	R	R
45	118	C		S	S	S	S	S	S
46	130	B		S	R	S	S	R	R
47	119	B		S	R	S	S	R	R
48	120	B		S	R	S	S	R	R

Table 21 (cont.)

number	code	Shigella group and types (phases)	zone diameter to ceftriaxone (mm)	Susceptibility to other antimicrobials					
				TMP / SMX	Tetracycline	Neomycin	Cephalothin	Chlorampheni- col	Ampicillin
49	121	B		S	R	S	S	R	R
50	122	B		S	R	S	S	R	S
51	123	D		S	R	S	S	R	R
52	124	B		S	R	S	S	R	R
53	125	B		S	R	S	S	R	R
54	126	B		S	R	S	S	R	R
55	127	D		S	R	S	S	R	R
56	128	B		S	R	S	S	R	R
57	150	B		R	R	S	S	R	R
58	151	B		S	R	S	S	R	R
59	131	B		S	R	S	S	R	R
60	132	B		S	R	I	S	R	I
61	133	B		R	R	S	S	R	R
62	134	B		R	R	I	S	R	R
63	135	D		R	R	R	S	R	R
64	136	B		R	R	R	S	R	R
65	137	D		R	R	R	S	R	R
66	138	B		R	R	S	S	R	R
67	139	B		S	R	S	S	R	R
68	140	B		S	R	S	S	R	R
69	141	B		S	R	R	S	R	R
70	142	B		S	R	R	S	R	S
71	143	B		R	R	R	S	R	R
72	144	B		S	R	S	S	R	R
73	145	B		S	R	S	S	R	S

Table 21 (cont.)

number	code	Shigella group and types (phases)	zone diameter to ceftriaxone (mm)	Susceptibility to other antimicrobials					
				TMP / SMX	Tetracycline	Neomycin	Cephalothin	Chlorampheni- col	Ampicillin
74	146	B		S	R	S	S	R	R
75	147	B		S	R	S	S	R	R
76	148	B		S	R	S	S	R	S
77	149	B		S	R	S	S	R	R
TOTAL NUMBER OF SUSCEPTIBLE ORGANISMS				59	4	59	63	5	11
TOTAL NUMBER OF TEST ORGANISMS				77	76	76	74	76	77
PERCENT OF SUSCEPTIBLE ORG ^m				76.6	5.3	77.6	85	6.6	14.3

N.B. S = susceptible

I = intermediate (moderately) susceptible

R = resistant.

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Table 22 The antimicrobial susceptibility test of shigellae isolated from studied patients to antimicrobial agents

number	code	Shigella group and types (phases)	zone diameter to ceftriaxone (mm)	Susceptibility to other antimicrobials					
				TMP / SMX	Tetracycline	Neomycin	Cephalothin	Chloramphenicol	Ampicillin
1	65	CC	28.0	S	I	S	I	S	S
2	64	CC	27.0	S	R	S	S	R	R
3	6	B	28.0	S	R	S	S	R	R
4	116	B	31.2	S	R	S	S	R	R
5	104	B		S	R	S	S	R	R
6	105	B		S	R	S	S	R	R
7	106	B		R	R	S	S	S	R
8	107	B		R	-	-	-	-	R
9	108	B		R	S	R	R	R	R
10	109	B		R	R	R	-	R	R
11	111	D		S	R	R	S	R	R
12	112	B		S	R	S	S	R	R
13	113	B		S	S	S	S	R	S
14	114	B		S	R	S	S	R	S
15	115	B		S	R	S	S	R	R
16	117	B		S	R	S	S	R	R
17	118	C		S	S	S	S	S	S
18	119	B		S	R	S	S	R	R
TOTAL NUMBER OF SUSCEPTIBLE ORG ^M				14	3	14	14	3	4
TOTAL NUMBER OF TEST ORGANISMS				18	17	17	15	17	18
PERCENT OF SUSCEPTIBLE ORG ^M				77.7	17.6	82.4	93.3	17.6	22.2
PERCENT OF SUSCEPTIBLE ORG ^M FROM									
77 TEST ORGANISMS (Table 21)				76.6	5.3	77.6	85	6.6	14.3

Table 24 The drug resistance patterns of 15 strains of shigellae isolated from the studied patients.

pattern number	Susceptibility to antimicrobials						number of organisms	percentage
	TMP / SMX	Tetracycline	Neomycin	Cephalothin	Chloramphenicol	Ampicillin		
1	S	R	S	S	R(I)	R	9	60
2	S	R	S	S	R	S	1	7
4	S	R	R	S	R	R	1	7
10	R	R	S	S	S	R	1	7
12	S	I	S	I	S	S	1	7
15	S	S	S	S	R	S	1	7
16	S	S	S	S	S	S	1	7

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Table 25 .The MICs of ceftriaxone to shigellae

No.	organism	type	obtained from (province)	MIC ug / ml
1	<u>S. dysenteriae</u> (group A)	2a	C	≤ 0.00195
2			S	0.0039
3			NB	≤ 0.00195
4			NB	0.03
5			NB8	0.0078
6			NB	0.0078
7			C	0.0039
8			NB	0.03
9			B	0.125
10			C	0.03
11	<u>Shigella flexneri</u> (group B)	2a	C	≤ 0.00195
12			S	0.0078
13			C	0.0525
14			C	≤ 0.00195
15			NB	0.0078
16			B	0.0078
17			NS	0.0039
18			S	0.0039
19			B	≤ 0.00195
20			B	0.0039
21	B	0.0039		
22	C	0.0039		
23	C	≤ 0.00195		
24	C	0.0039		
25	B	0.03		
26	NB	0.03		

Table 25 (cont.)

No.	organism	type	obtained from (province)	MIC $\mu\text{g} / \text{ml}$	
27	↑ <u>Shigella flexneri</u> (group B) ↓	↑ 2a ↓ 2b ↓ 3a	NB	0.03	
28			C	0.03	
29			C	0.03	
30			C	0.03	
31			C	0.03	
32			C	0.03	
33			C	0.03	
34			C	0.0078	
35			C	0.0078	
36			C	0.0078	
37			C	0.0078	
38			C	0.0078	
39			C	0.0078	
40			C	0.0078	
41			C	0.0078	
42			C	0.0078	
43			C	0.0078	
44			C	0.03	
45			C	0.03	
46			C	0.03	
47			C	0.03	
48			C	0.03	
49			S	0.003	
50			B	0.03	
51			S	0.03	
52			C	\leq 0.00195	
				C	



Table 25 (cont.)

No.	organisms	type	obtained from (province)	MIC ug / ml
53	<i>Shigella flexneri</i> (group B)	type 3c 3a	C	0.0039
54			NS	0.0039
55			NS	0.0039
56			NB	≤ 0.00195
57			C	0.0039
58			C	0.0039
59			C	0.03
60			B	0.0039
61			NB	≤ 0.00195
62			C	0.0039
63	<i>Shigella boydii</i> (group C)	type 6	C	≤ 0.00195
64			NB	≤ 0.00195
65			NB	0.0039
66			C	≤ 0.00195
67			C	0.015
68			C	0.015
69			C	0.03
70			C	0.0039
71			Cholburi	0.0039
72			B	0.0039
73	<i>S. sonnei</i> (group D)	type 4	NB	0.03
74			C	0.03
75			C	0.0078
76			C	0.0078
77			C	8
78			Samutra-sakorn	0.015

Table 25 (cont.)

No.	organism	type	obtained from (province)	MIC μg / ml
79	↑ <u>Shigella sonnei</u> (group D) ↓	↑	B	0.03
80			B	0.03
81			B	0.03
82			Cholburi	0.03
83			C	0.015
84			C	0.03
85			C	0.03
86			C	0.0078
87			C	≤ 0.00195
88			C	≤ 0.00195
89		I	NS	≤ 0.00195
90			S	≤ 0.00195
91			B	0.0039
92			C	0.0039
93			NB	0.0039
94			S	0.0039
95			C	≤ 0.00195
96			S	0.0039
97			C	0.015
98		II	NB	0.0039
99		I	B	0.0039
100			Samutra-sakorn	0.0039
101			NB	0.0039
102			C	0.0078
103		II	C	≤ 0.00195

C = Chantaburi , NS = Nakorn-sridhamarat
 NB = Nonthaburi , B = Bangkok , S = Saraburi

Table 26 The summarized data of the MICs of ceftriaxone to each Shigella group

organisms	group	types	No. of isolate (N)	modal MIC (µg/ml)	(n) of mode	% of mode $\frac{n}{N} \times 100$	MIC range (µg/ml)
<u>S. dysenteriae</u>	A	2, 2a	3	≤0.00195	2	67	≤0.00195 - -0.0039
<u>S. flexneri</u>	B	1b, 2a, 3a, 3b, 3c, 4a, 6	61	0.0312	20	33	≤0.00195 - -0.0625
<u>S. boydii</u>	C	2, 4	11	0.0039	4	36	≤0.00195 - 0.0312
<u>S. sonnei</u>	D	I, II I° II	28	0.0312	6	21	≤0.00195 - -8
<u>Shigella spp.</u>	A, B, C, D	various	103	0.0312, 0.0039	29 29	28 % 28 %	≤0.0195 - 8

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Table 27 The summarized number of shigellae isolates which have the same MIC of ceftriaxone

MIC (ug / ml)	No. of isolates (%)	cumulative % inhibited	No. of shigellae isolates of each group			
			A	B	C	D
≤ 0.00195	18 (17)	17	2	8	2	6
0.0039	29 (28)	45	1	16	4	8
0.0078	19 (18)	63	-	15	-	4
0.0156	5 (5)	68	-	-	2	3
0.0312	29 (28)	97	-	20	3	6
0.0625	1 (1)	98	-	1	-	-
0.125	1 (1)	99	-	1	-	-
8.0	1 (1)	100	-	-	-	1
total	103		3	61	11	28

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The MIC₅₀ and MIC₉₀

The activities of ceftriaxone against 103 strains of Shigella is shown in table 26 and figure 8 as the relationship between the cumulative percentage of the inhibited organisms and log MIC values. By interpolating the graph to meet the minimum inhibitory concentrations from 50 and 90 cumulative percentage inhibited, the MIC₅₀ and MIC₉₀ obtained were 0.00465 and 0.0262 ug/ml respectively.

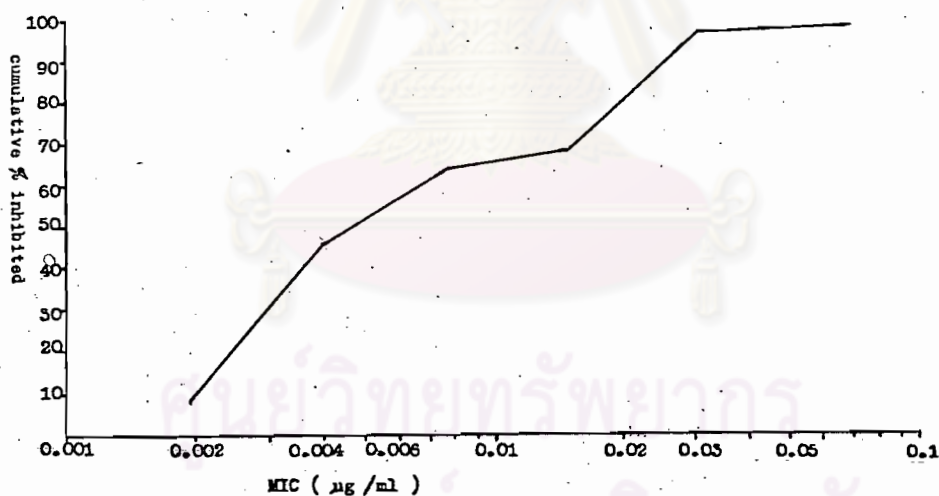


Figure 8 The activities of ceftriaxone against 103 strains of Shigella spp.

The details of the organism with higher MIC of ceftriaxone

There is 1 isolate of Shigella which was inhibited at the MIC of 8 ug/ml.

The Shigella sonnei (no. 77) which had the MIC at 8 µg/ml was obtained from the rectal swab of a girl admitted in Chantaburi Hospital in the year 1983 and it was sensitive to ampicillin, chloramphenicol but was resistant to tetracycline and was moderately sensitive to co-trimoxazole. It gave 17.6 mm zone diameter with the Ceftriaxone 30 µg disc, which was much lesser than the average. This girl had no history of Ceftriaxone treatment.

B. RESULTS OF CLINICAL STUDIES

1. The clinical response of patients treated with Ceftriaxone
The overall clinical results are shown in table 28.

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Table 28 The clinical results of patients treated with ceftriaxone

No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	total	
No. Patient No.	36	37	39	40	41	42	43	45	46	1	2	3	5	8	11	13	14	21	22	25	27		
1. age (yrs.)	$\frac{2}{12}$	$\frac{10}{12}$	5	$\frac{3}{12}$	$\frac{8}{12}$	$\frac{8}{12}$	$\frac{2}{12}$	2	1	$\frac{4}{12}$	2	$\frac{1}{12}$	$\frac{2}{12}$	11	8	$\frac{3}{12}$	$\frac{10}{12}$	6	$\frac{5}{12}$	2	$\frac{6}{12}$	$\frac{10}{12}$	
2. sex, male		✓		✓	✓		✓	✓	✓	✓	✓			✓		✓		✓	✓			✓	13
female	✓		✓			✓						✓	✓		✓		✓			✓			8
3. causative organisms																							
<u>S.dysenteriae</u>																							0
<u>S.flexneri</u>		✓	✓		✓		✓	✓	✓			✓	✓			✓	✓	✓	✓			✓	13
<u>S.boydii</u>	✓			✓		✓																	3
<u>S.sonnei</u>										✓	✓			✓	✓						✓		5
3.1 susceptibility to																							
ampicillin	R	R	R	S	R	S	R	R	R	S	S	R	S	S	S	S	S	R	S	R	R	R	$R=\frac{11}{12}$
TMP / SMX	S	S	S	S	S	S	S	R	R	S	S	R	S	S	S	S	S	S	S	S	S	S	$R=\frac{3}{12}$
4. dose of 100mg/ml(ml)	5	8.5	6	4	3.5		5	3.3	1.5	5	1.5	1.5	12	9	7.5	2.5	6.5	3	5.5	4			
5. route of administration																							
intravenous	✓	✓	✓	✓	✓	✓	✓	✓		✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	19/21
intramuscular									✓		✓												2/21
6. fever before treatment start (X)	X	X	X	-	-	X	X	-	-	X	-	X	-	X	X	-	X	X	X	X	X	-	13/21
7. afebrile after treatment (/)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	X	✓	✓		19/21
8. first afebrile day	1	1	1	0	0	1	1	0	0	1	0	1	0	2	1	0	6	6	1	1			

Table 28 (cont.)

No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	total	
No. Patient No.	36	37	39	40	41	42	43	45	46	1	2	3	5	8	11	13	14	21	22	25	27		
9. frequency of stool ≤ 3 / day (./) first admission day	X	X	X	X	X	-	X	X	X	-	X	X	X	X	X	X	X	X	X	X	X	X	19/21
after treatment	./	./	./	X	X	-	X	./	./	-	./	X	./	./	./	./	./	X	X	./	X	12/19	
days after treat ment	4	7	5	76	75	0	75	3	2	-	5	75	1	1	1	5	4	76	76	3	76		
10. abnormal stool characteristics days required to recover	X	X	X	X	X	X	X	X	X	-	X	X	X	X	X	X	X	X	X	X	X	X	20/21
11. days to recover other symptoms	5	7	4	76	5	3	5	4	3	-	-	76	2	3	3	5	3	76	76	6	76		
vomiting																3						1	
gastric distention			1	1																			
abdominal pain													1				2						
dehydration	1	-	1	1	1	-	1	1	-	-	-	-	1	-	-	1	-	1	-	1	1	11/11	

** became febrile after 5 days of treatment

*** became febrile after 4 days of treatment

1.1 Age and sex distribution of patients

There were 21 children, who were suffered from Shigellosis and were treated with ceftriaxone, The age and sex distribution of the patients are shown in table 29. Fifty-two percent of them were under 2 years of age and the patients age range was between 1 month to 11 years old with the ratio of the male to female is 13 : 8 (62 % : 38 %)

Table 29

Age and sex distribution of patients

Age group (years)	range (years)	male	female	total
< 2	$\frac{1}{12}$ - $1 \frac{6}{12}$	9	2	11
≥ 2 - 12	2 - 11	4	6	10
total number of each group		13	8	21

1.2 Causative organisms

The most common causative organisms which were isolated from the patients' stool were S. flexneri (62 % or 13 in 21 cases) and the other included were S. sonnei (24 %, 5 in 21) and S. boydii (14 %, 3 in 21).

These organisms had percentage of resistance to ampicillin and co-trimoxazole of 92 % (12 in 13) and 25 % (3 in 12) respectively. Their patterns of drug resistance are shown in table 22 (page 75) and table 24 (page 77).

1.3 Fever response

Sixty-two per cent of the patients (13 in 21) had a body temperature above 38° C at the time of admission, before treatment started and 85 % of them (11 in 13) became afebrile within 48 hours after treatment (range 1-2 days, with an average of 1.08 days). The other two cases did not respond and were still febrile after more than 5 days, Two cases which had no fever before treatment became febrile after ceftriaxone treatment, this is 11 % of the whole patients receiving ceftriaxone or 25 % of the afebrile patients (2 in 8). These are shown in table 30.

1.4 The change in frequency and characteristics of stools

The change in frequency and characteristics of the patients' stools are shown in table 31

Table 30

Fever Response

	No/total	percentage
Having fever before treatment started	13/21	62
Afebrile within 48 hours	11/13	85
no./ % of recurrent fever	2/21	9.5
mean afebrile day (range)	1.08 (1-2 days)	
Those with normal temperature on admission who developed fever after treatment	2/8	25

Table 31

Frequency and characteristics of stools

	No./total	percentage
<u>Frequency of stool \leq 3/day</u>		
before or on the day treatment started	2/21	62
within 5 days	11/19	58
average (range)	3.1 \pm 1.56 (1 - 5)	
failure	8/19	42
<u>Characteristic of Stool</u>		
patients with abnormal stool characteristics before treatment	19/20*	95
well-formed stool within 5 days	12/19	63
average (range)	3.75 \pm 1.01 (2 - 5 days)	
failure	7/19	37

* one patient had no record of the stool characteristic.

The percentage of patients who had bowel movement \leq 3 times/day within 5 days were 58 % (11 in 19 cases), with 42 % failure (8 in 19). Sixty-three per cent (12 in 19) of the patients with abnormal stool characteristic had well-formed stool within 5 days after treatment, with the average of 3.75 days with a range between 2 to 5 days. There

are 37 % (7 in 19) failure rate in this point .

1.5 Response of other symptoms

Other systemic or gastrointestinal tract symptoms such as dehydration, vomiting, abdominal pain and distension disappeared within 48 hours after treatment as shown in table 32

Table 32

Other symptoms and their disappearance after treatment

Symptoms	days to recover		no. of patient
	average	range	
- dehydration	1	1	11
- vomiting	2	1 - 3	2
- abdominal pain	1.5	1 - 2	2
- abdominal distension	1	1	2

2. The bacteriological response in patients

The overall bacteriological results of patients' stool culture are shown in table 33

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Table 33 Results of patients' stools' culture

No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	total	
No., Patients'	36	37	39	40	41	42	43	45	1	2	3	5	8	11	13	14	21	22	25	27		
1. age (yrs.)	2 $\frac{10}{12}$	5	3 $\frac{6}{12}$	8 $\frac{8}{12}$	8 $\frac{8}{12}$	2 $\frac{6}{12}$	2	1	2	1 $\frac{1}{12}$	2 $\frac{2}{12}$	11	8	3 $\frac{10}{12}$	2 $\frac{2}{12}$	6	5 $\frac{5}{12}$	2	1 $\frac{6}{12}$	10 $\frac{10}{12}$		
2. causative organisms																						
group A																						
group B		/	/		/		/	/			/	/			/	/	/	/		/	13	
group C	/			/		/															3	
group D									/	/			/	/						/	5	
3. susceptibility to																						
ampicillin	R	R	R	S	R	S	R	R			R	S				S	R	R	R	R	R = 11/12	
TMP / SMX	S	S	S	S	S	S	S	R			R	S				S	S	S	S	S	R = 3/12	
cephalothr																						
in	S	S	S	I	S	S	S					S				S	S	S	S	S		
4. results of stool cultures, on admission																						
day, 1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	20/20
2	+	+	+	-	+	-	+	+	+	-		+	+	+	-	-	+	+	+	+	+	14/19
3	+		+	-	+	-	+	+	+		-	-	+	-	+	+	+	+	+	-	+	11/17
4		+	+		-		+		+		-	-	-	-	-	-	+	+	+	+	+	8/15
5		+	+		-		+				-		+	+	+	+	+	+	+	+	+	11/13
5	+								+								+	+				4/4

* S. typhi was isolated.

Twenty out of 21 cases of patients from title no. 1 were studied, with an exclusion of one patient on whom stool culture was not performed after treatment (patient no. 46).

On the first hospital day all patients had positive stool cultures for Shigella.

On the second day of hospitalization (2 days after Ceftriaxone administration), 74 % of the patients (14 out of 19) gave positive stool cultures. The percentage of positive cultures for Shigella gradually decreased each day but the organism disappeared from the stool only temporarily. At the end of the fifth day of treatment, 11 out of 13 cases (85 %) had persistent organisms. These datae were shown in table 34

Table 34

Bacteriologic response

Day (s) after treatment	positive shigella /no. in stool culture tested	percentage
1	20/20	100
2	14/19	74
3	11/17	65
4	8/15	53
5	11/13	85

3. The sera levels of Ceftriaxone

The overall data on serum Ceftriaxone concentrations were shown in table 35 and their relationship with time were shown in figure 7.



There were 24 children of the age not more than 12 years in the study, all of them were admitted with diarrhea causes. Seven of them were the patients from the group of clinical study in title no 1 p.85 Twenty of them did not receive any other antimicrobial therapy while the sera were being drawn, but 4 of them were treated with furazolidone suspension orally at the time the sera were drawn with a dosage of between 8.3 - 16.7 mg each time for 2 to 4 times daily (2.7 to 10 mg/Kg/day). The dose distribution of furazolidone in 4 cases was shown in table 37 while the summarized data of all patients were shown in table 36.

Furazolidone was tested for antibacterial properties against S. lutea, the test organism in assay of serum Ceftriaxone. Usually the drug was absorbed very slightly through the intestinal wall.⁵⁷ The absorbed con.ⁿ of it was unknown, so, the researcher tried to find its effects to S. lutea to see whether it could inhibit it in the highest concentration, it possible to appear in the sera or not. The result was that it could not, as shown in table 38.

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Table 35 The sera ceftriaxone concentrations in children.

No.	patient No.	sex	age (yrs)	wt. (kg)	dose (mg)	mg/kg	sera concentration (µg/ml)					
							1	2	5	8	24	48
1	11	F	3,10/12	15	750	50	179.5	-	-	69.3	-	-
2	8	M	8	18	900	50	228	-	-	-	-	-
3	7	F	6/12	6	300	50	205.5	-	105	-	9.4	-
4	6	M	11/12	8.5	450	53	160.	-	132	-	14	-
5	10	M	5/12	8	400	50	-	159	-	-	-	-
6	89	M	-	-	-	50	175.5	-	-	-	5.91	-
7	3a	M	4/12	6	300	50	-	-	-	-	9.5	1.76
8	3	F	2/12	3.3	150	45.5	-	154.5	-	-	10.3	1.68
9	46	M	4/12	3.4	150	44.1	-	156	-	-	10.4	1.7
10	4	F	2/12	3.4	170	50	-	-	-	103.5	15.3	-
11	5	F	11	24	1200	50	240	-	-	97.5	10.7	-
12	12	M	10	-	-	50	243	-	-	93.5	6.8	-
13	90	M	-	-	-	50	199.5	-	-	-	5.8	-
14	91	M	-	-	-	50	217.6	-	-	117	6.2	-
15	92	F	-	-	-	50	211.5	-	-	114	11.3	-
16	93*	M	5/12	6	300	50	273	-	-	114	2.9	-
17	94*	M	9/12	9.8	500	51	199.5	-	-	62.5	1.5	-
18	95*	M	1 5/12	10	500	50	243	-	-	72	2.1	-
19	96*	F	6/12	6.6	350	53	259.5	-	-	109.5	-	-
20	97	M	6/12	7.6	400	52.6	307.5	-	-	81	-	-
21	98	M	-	-	-	50	243	-	-	-	-	-
22	27	M	10/12	9.5	450	47.4	-	-	-	-	5.9	-
23	99	F	-	-	-	50	175.5	-	-	-	-	-
24	13	M	2/12	5	250	50	-	-	-	94.5	-	-
number (n)						24	17	3	2	12	16	3
average(\bar{X})						49.9	221.3	156.5	118.5	94	8.0	1.7
							+ 39	+2.3	+ 19	+ 19	+ 4	+ 0.04
range							160-	154-	105-	69-	1.5-	1.6-
							307	159	132	117	15	1.7

* Received furazolidone (see tables 37 and 38).

Table 36 The summarized data of patients treated with ceftriaxone in the determination of sera levels

route of administration	IV	
	range	mean
exact dose (mg / kg)	44.1-53	49.9
age (years)	2/12-11	
weight (kg)	3.3-24	
sex	male	female
	(%)	(%)
	16(67)	8(33)

Table 37 The oral dose distribution of furazolidone in 4 patients

patient no.	sex	age (yrs.)	body wt. (kg)	Furazolidone taken			
				dose (mg)	mg/kg	times/day	mg/kg/day
93	M	5/12	6	8.3	1.38	2	2.77
94	M	9/12	9.8	8.3	0.85	4	3.39
95	M	1 5/12	10	8.3	0.83	4	3.32
96	F	6/12	6.6	16.7	2.53	4	10.1

Table 38 Test of furazolidone's activity against Sarcina lutea

furazolidone conc ⁿ (ug/ml)	average inhibition zone diameter (mm)
66.7	0.88
33.3	0.84
16.7	0.91
8.3	0.92
4.1	1.1
2.08	0.84

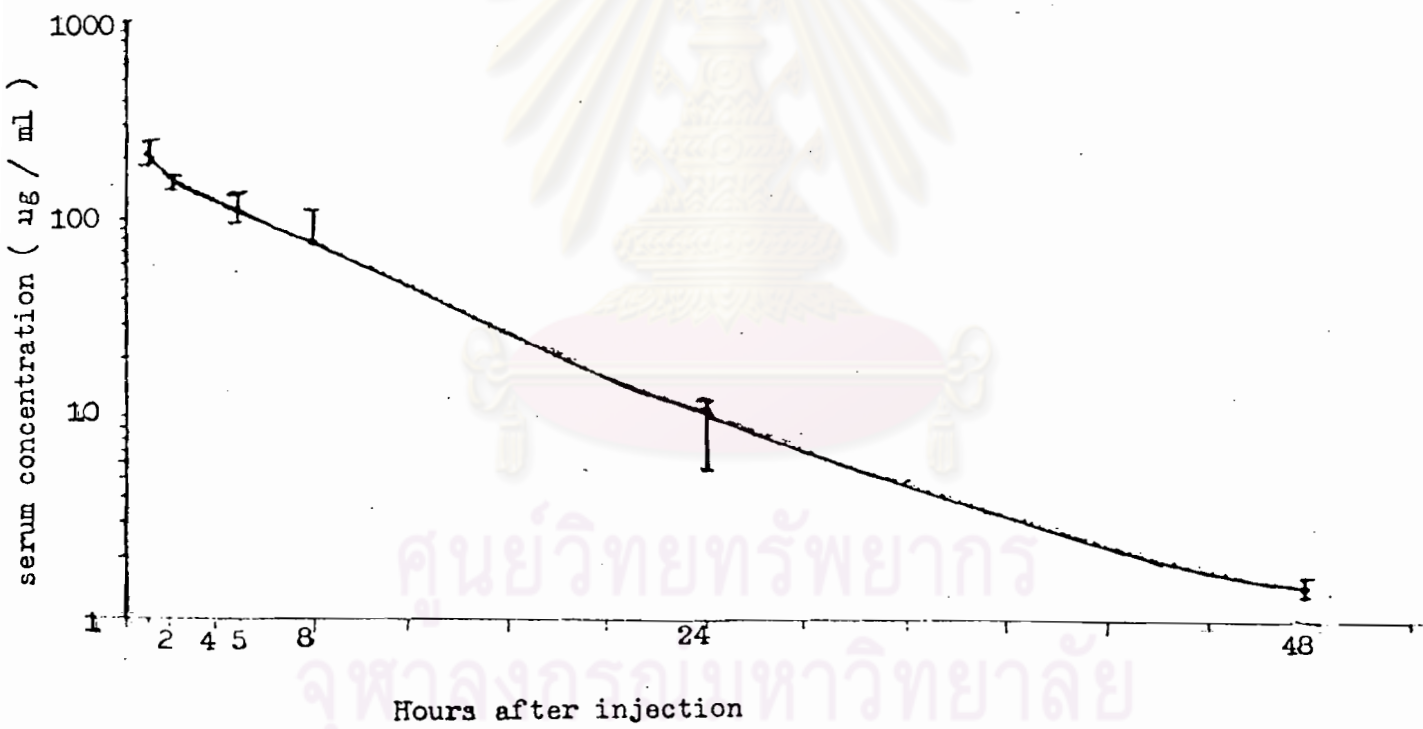


Figure 7 Sera ceftriaxone concentrations after a 50 mg/kg IV dose in 24 children.