

AD-781 427

TREATMENT OF CHRONIC URINARY
SALMONELLA CARRIERS WITH TRIMETHOPRIM-
SULPHAMETHOXAZOLE

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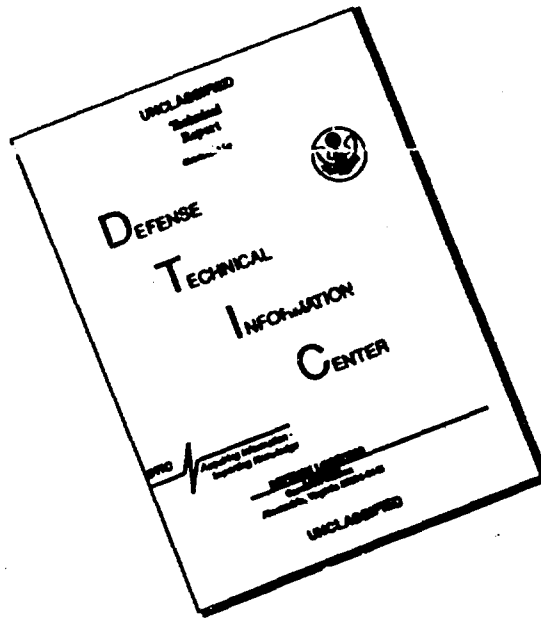
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AD-781 427

DOCUMENT CONTROL DATA - R & D		
(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)		
1. ORIGINATING ACTIVITY (Corporate author) U.S. Naval Medical Research Unit No. 3 FPO New York 09527		2a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED
		2b. GROUP
3. REPORT TITLE TREATMENT OF CHRONIC URINARY SALMONELLA CARRIERS WITH TRIMETHOPRIM-SULPHAMETHOXAZOLE		
4. DESCRIPTIVE NOTES (Type of report and inclusive dates) Technical/Scientific report		
5. AUTHOR(s) (First name, middle initial, last name) S. Bassily, Z. Farid, J.S. Lehman, Jr., N. Ayad, and J. Sippel		
6. REPORT DATE 1972	7a. TOTAL NO. OF PAGES 3	7b. NO. OF REFS 15
8a. CONTRACT OR GRANT NO.	9a. ORIGINATOR'S REPORT NUMBER (S) NAMRU-3-TR.50-73	
b. PROJECT NO.		
c. MR005.20.0308A	9b. OTHER REPORT NO (S) (Any other numbers that may be assigned this report) Acc.889	
d.		
10. DISTRIBUTION STATEMENT Distribution of this report is unlimited		
11. SUPPLEMENTARY NOTES Published in J. Trop. Med. Hyg. 75:227-229, 1972		12. SPONSORING MILITARY ACTIVITY Bureau of Medicine and Surgery Department of the Navy Washington, D.C. 20306 X 20372
13. ABSTRACT Nine chronic urinary salmonella carriers were treated with combined trimethoprim-sulphamethoxazole and niridazole and another 10 carriers (used as controls) were treated with niridazole. 8 of 9 who received combined therapy were completely cured whereas only 3 of the 10 receiving antischistosomal therapy alone were cured. Of the 7 patients who relapsed after antischistosomal therapy 5 were successfully re-treated with trimethoprim-sulphamethoxazole.		

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S/N 0101 807 8801

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14	KEY WORDS	LINK A		LINK B		LINK C	
		ROLE	WT	ROLE	WT	ROLE	WT
	Urinary Salmonella carriers Combined therapy Antischistosomal therapy alone Retreatment Eradication of salmonella Trimethoprim-sulphamethoxazole Niridazole Urinary tract Egypt						

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TREATMENT OF CHRONIC URINARY SALMONELLA CARRIERS WITH TRIMETHOPRIM-SULPHAMETHOXAZOLE

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Introduction

Treatment of chronic urinary salmonella carriers is notoriously difficult (Douglas, 1950; Miller & Floyd, 1954; Christie, 1964; Whitby, 1964) and in Egypt the problem is further complicated by the close relationship of these salmonella carriers with damaged urinary tracts caused by *Schistosoma haematobium* infection (Neva, 1949; Miller & Floyd, 1954; Halawani & Badran, 1958; Hathout *et al.*, 1966). Besides passing salmonella organisms in the urine, the Egyptian carrier frequently manifests a state of chronic salmonella bacteraemia (Farid *et al.*, 1970a). Recently Bassily *et al.* (1970) succeeded in curing 9 of 14 carriers by using combined ampicillin-antischistosomal therapy. All 5 patients who relapsed following treatment were shown to have irreparably damaged urinary tracts not responsive to antischistosomal therapy.

The purpose of the present study was to determine the efficacy of trimethoprim-sulphamethoxazole (Bactrim, Septrin) in lieu of chloramphenicol or ampicillin as the antibiotic to be administered in conjunction with antischistosomal therapy in the management of chronic urinary salmonella carriers. Trimethoprim-sulphamethoxazole is easy to administer, has minimal side effects, and has been found to be quite effective against acute salmonella and brucella infections (Farid *et al.*, 1970b; Hassan *et al.*, 1971). 19 chronic urinary salmonella excretors with recurrent bacteraemia were studied—all had been excreting the organism in the blood and urine for over a year. 9 received combined trimethoprim-sulphamethoxazole and niridazole (Ambilhar) and 10 were used as controls and treated with niridazole only.

Materials and Methods

Patients

All 19 patients were male. Their ages ranged from 5 to 40 years. All gave a history of attacks of fever recurring periodically for over 12 months and 13 of the 19 had received one or

more courses of chloramphenicol. All had a moderate to severe iron deficiency anaemia. 5 were excreting *Salmonella typhi* and 14 *Salm. paratyphi A* in the urine, and all patients' blood cultures were periodically positive for these organisms. 13 had active infection with *S. haematobium*, and intravenous pyelography showed that all 19 patients had damaged urinary tracts caused by this infection.

Blood specimens were cultured in Castaneda-type 2-phase bottles (Castaneda, 1947). Urine and stool specimens were cultured before and after adding selenite broth (Difco) on selective media. Blood and urine specimens were cultured at every fever spike and routinely twice weekly before, during, and throughout the 12-month follow-up period. Stool cultures were examined before treatment and once weekly during and after treatment. Intravenous pyelography was done on admission and 8 weeks after completing the antischistosomal therapy.

Treatment

9 patients were treated with oral niridazole 25 mg./kg. body-weight daily for 6 days and at the same time given oral trimethoprim-sulphamethoxazole at a dosage of 10 mg. trimethoprim and 50 mg. sulphamethoxazole per kg. daily divided into 2 portions and given every 12 hours. Treatment with trimethoprim-sulphamethoxazole was continued for 4 weeks. 10 other patients were given oral niridazole (25 mg./kg. daily for 6 days).

Results

The results are summarised in the Table. A rapid clinical response was noted in all 9 patients treated with trimethoprim-sulphamethoxazole and niridazole. All the patients became afebrile and asymptomatic within 3 to 6 days after starting treatment and 8 of the 9 patients were completely cured of the salmonella infection. One patient relapsed and began passing *Salm. paratyphi A* in the urine 4 months after completing the treatment course;

TABLE.

Treatment of chronic urinary salmonella carriers with trimethoprim-sulphamethoxazole.				
Number of patients treated	Drug given	Organisms cultured from blood and urine	Number of patients cured	Number of patients relapsed
Group I 9	trimethoprim-sulphamethoxazole + niridazole	2 <i>Salm. typhi</i> 7 <i>Salm. paratyphi A</i>	8	1 (in urine)
Group II 10	niridazole	3 <i>Salm. typhi</i> 7 <i>Salm. paratyphi A</i>	3	7* (2 in blood and urine 5 in urine only)

* These patients grew the organisms from the blood or urine within the first 2 weeks after ending therapy.

a 3-month post-treatment intravenous pyelography demonstrated persistence of bladder nodular filling defects and calcification and severe ureteral stricture with hydronephrosis.

In the control group treated with niridazole alone, 3 of 10 patients were cured of the salmonella infection. However, their clinical response to treatment was much slower than that noted in the combined therapy group. Of the 7 patients who relapsed 5 were successfully re-treated with trimethoprim-sulphamethoxazole 3 months later. The remaining 2 patients refused further therapy.

Discussion

In Egypt, the majority of urinary salmonella carriers have either an active *S. haematobium* infection or have urinary tracts damaged by this parasite. Moreover these patients continually shed the salmonella organisms into the blood, leading to a state of chronic salmonella bacteraemia. They seek medical advice only after a prolonged febrile illness; and when first seen appear toxæmic, debilitated, and severely anaemic (Farid *et al.*, 1979a).

Treatment can be summarised in 2 parts. First, the eradication of the salmonella from the blood stream is easily accomplished by one of the broad-spectrum antibiotics—chloramphenicol, ampicillin or trimethoprim-sulphamethoxazole. Second, prevention of relapse by concurrent antischistosomal therapy in an attempt to relieve the obstructive uropathy caused by active or inactive *S. haematobium* infection with the elimination of the original focus of salmonella infection.

In previous reports (Lucas *et al.*, 1966; Farid *et al.*, 1967) the effectiveness of antischistosomal therapy, particularly in the young, in reversing the urinary obstructive lesions has

been demonstrated. There will however remain a group of patients with grossly damaged urinary tracts who will not respond to antischistosomal therapy and who will relapse once antibiotic therapy is stopped. It is in this group of patients that prolonged suppressive therapy with trimethoprim-sulphamethoxazole—as described recently by Cattell *et al.* (1971) for the treatment of persistent or recurrent bacteriuria—may turn out to be most beneficial. The aim of therapy for these patients would be to suppress the bacteriuria and prevent the recurrent attacks of bacteraemia.

Summary

9 chronic urinary salmonella carriers were treated with combined trimethoprim-sulphamethoxazole and niridazole and another 10 carriers (used as controls) were treated with niridazole. 8 of the 9 who received combined therapy were completely cured whereas only 3 of the 10 receiving antischistosomal therapy alone were cured. Of the 7 patients who relapsed after antischistosomal therapy 5 were successfully re-treated with trimethoprim-sulphamethoxazole.

Acknowledgements

The authors are indebted to Captain H. A. Sparks for reviewing and correcting the manuscript.

This research forms part of Research Project MR004.20.0308A of the Bureau of Medicine and Surgery, Navy Department, Washington, D.C., U.S.A.

The opinions and assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Naval Department, the Naval Service at large, or the Egyptian Ministry of Public Health.

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