REPORT NO. 34
Issued November 1973

center for disease control

SHIGELLA

surveillance

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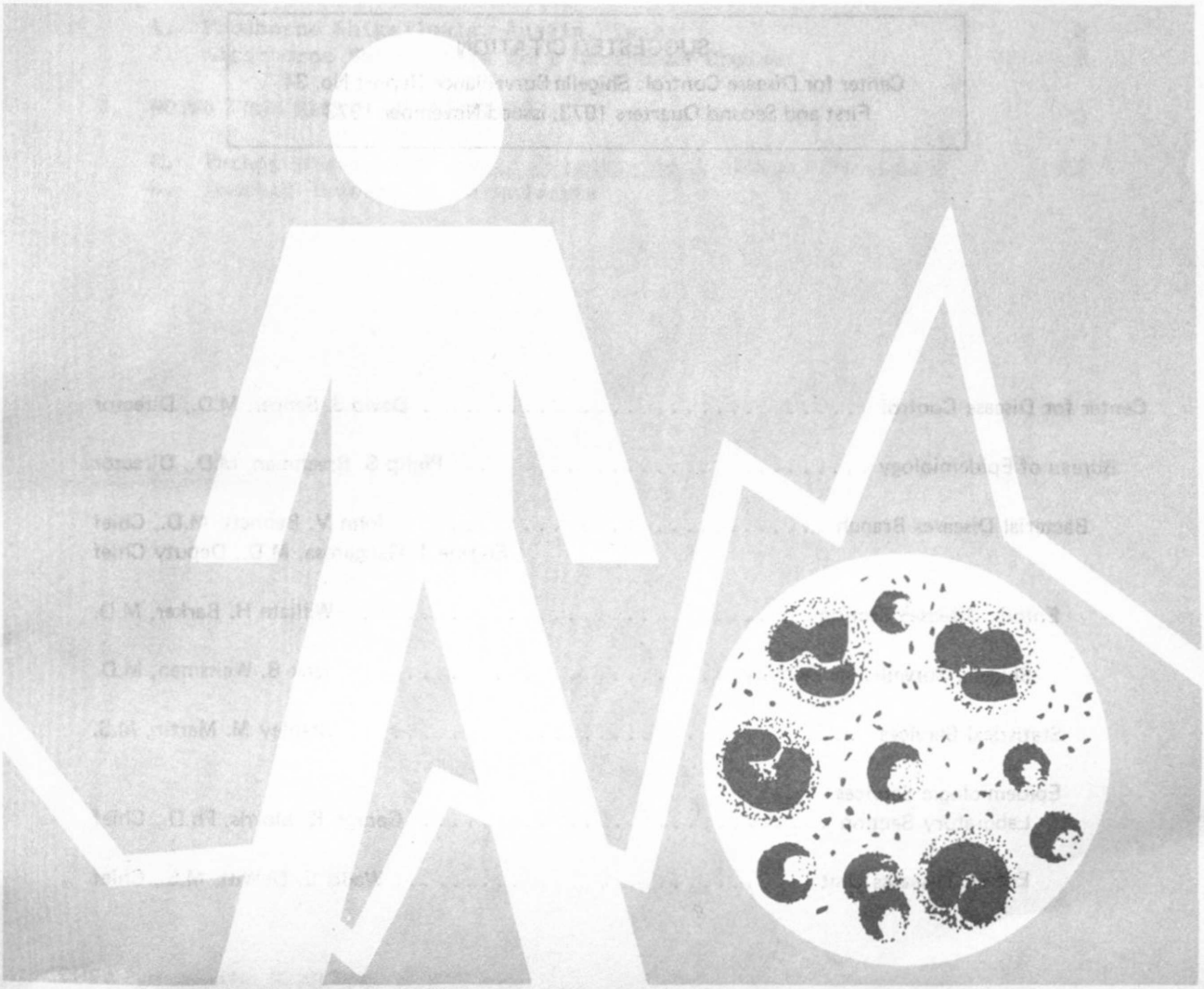
for the
First and Second Quarters 1973



U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE: PUBLIC HEALTH SERVICE

PREFACE

This report summarizes data voluntarily reported from participating state, territorial, and city health departments. Much of the information is preliminary. It is intended primarily for the use of those with responsibility for disease control activities. Anyone desiring to quote this report should contact the original investigator for confirmation and interpretation.

Contributions to the surveillance report are most welcome. Please address to:

Center for Disease Control
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SUGGESTED CITATION

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First and Second Quarters 1973; issued November 1973

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I. SUMMARY

For the period January-June 1973, 6,581 shigella isolations from humans were reported. This represents a decrease of 905 (12.1%) from the 7,486 isolations reported for the preceding 6 months and an increase of 269 (4.3%) over the 6,312 isolations reported for the corresponding months of 1972 (Tables I-A - I-B, pp 13-16).*

II. REPORTED ISOLATIONS

A. Human

1. General Incidence

For the first half of 1973, 67.4% of reported isolations were from children under 10 years of age (Table II); this is consistent with previous 6-month periods. The highest attack rate was in the 1-4 age group, and the second highest attack rate was in the less than 1 year age group.

2. Serotype Frequency

Fifty-three of the 54 centers participating in the Shigella Surveillance Program reported isolations of shigella; 23 different serotypes were reported. The 6 most frequently reported for the 6-month period were the following (Table 1).

Table 1

Rank	Serotype	Number Reported	Calculated Number**	Calculated Percent**	Rank Last Period
1	S. sonnei	5,403	5,429	82.5	1
2	S. flexneri 2a	218	419	6.4	2
3	S. flexneri 3a	112	171	2.6	3
4	S. flexneri 6	134	161	2.5	4
5	S. flexneri 2b	57	110	1.7	5
6	S. flexneri 4a	52	81	1.2	6
Subtotal		5,796	6,371	96.8	
Total (all serotypes)		6,581	6,580		

**From Table III

Table III is calculated from data compiled for the first half of 1973 and shows the frequency of reported isolations of the various serotypes; the isolations in each of the unspecified categories are distributed over their subgroups in the same proportions as the completely specified isolations of that group. The resulting distribution in the tables is called the "calculated number," and from this is derived a "calculated percent" for each serotype. These provide approximate indices of the relative frequency of reporting of the more common shigella serotypes in the United States. S. sonnei accounted for approximately 82.5% of all reported isolations. Table IV shows the distribution of shigella serotypes reported from mental institutions.

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*No laboratory reports were received from California or the Virgin Islands.

3. Geographical and Seasonal Observations

There were more reported isolations of S. sonnei than S. flexneri in all but the following 6 states: Montana (12:19), North Dakota (5:16), South Dakota (4:25), Wyoming (0:3), Mississippi (15:23), and Arizona (69:128) (Figure 1). This is consistent with what has been observed in the past in that the reported incidence of S. flexneri is, in general, decreasing while the reported incidence of S. sonnei is increasing. The seasonal distribution is depicted in Figure 2. Approximately 35.0 isolations per million population were reported for the first half of 1973. Figure 3 shows the number of reported isolations per million population by state for the period January-June utilizing 1970 census data. Table V shows the general type of residence of those patients from whom shigella was isolated and reported.

Figure 1 PERCENTAGE *S. flexneri* AND *S. sonnei* OF TOTAL SHIGELLA ISOLATIONS REPORTED FROM INDICATED REGIONS UNITED STATES, JANUARY-JUNE 1973

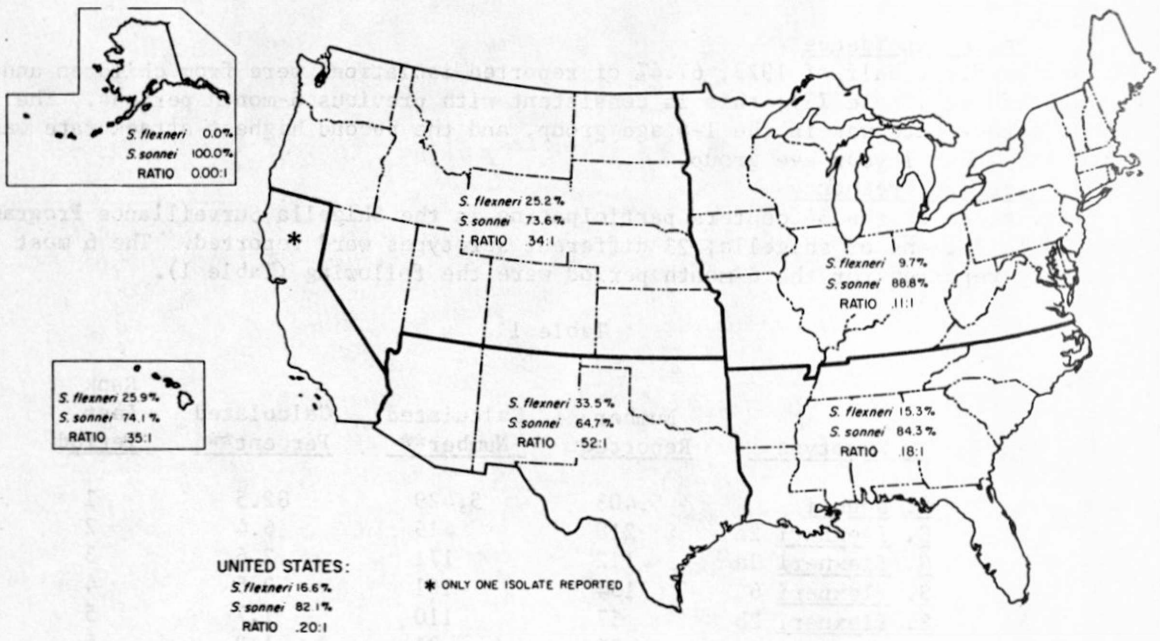


Fig. 2 REPORTED ISOLATIONS OF SHIGELLA IN THE UNITED STATES

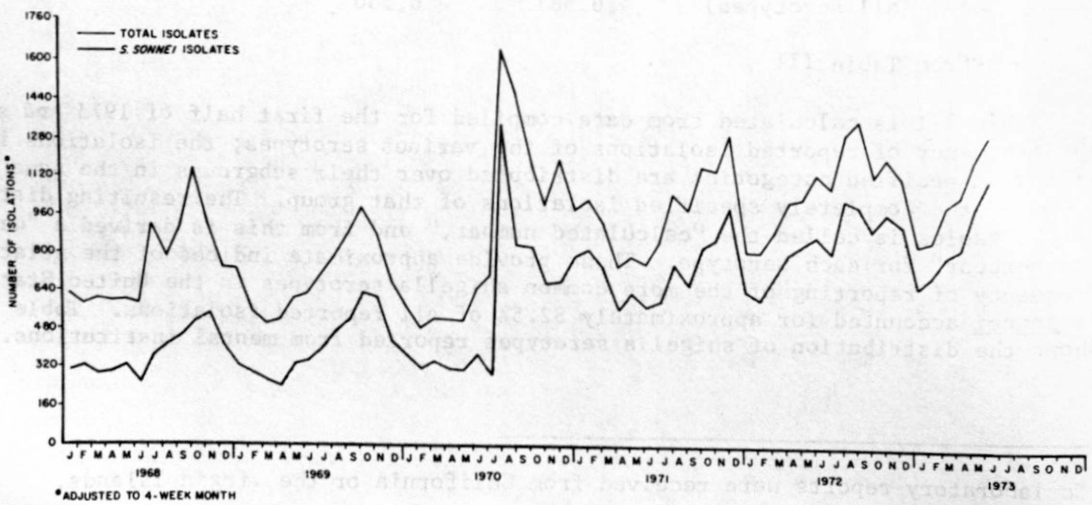
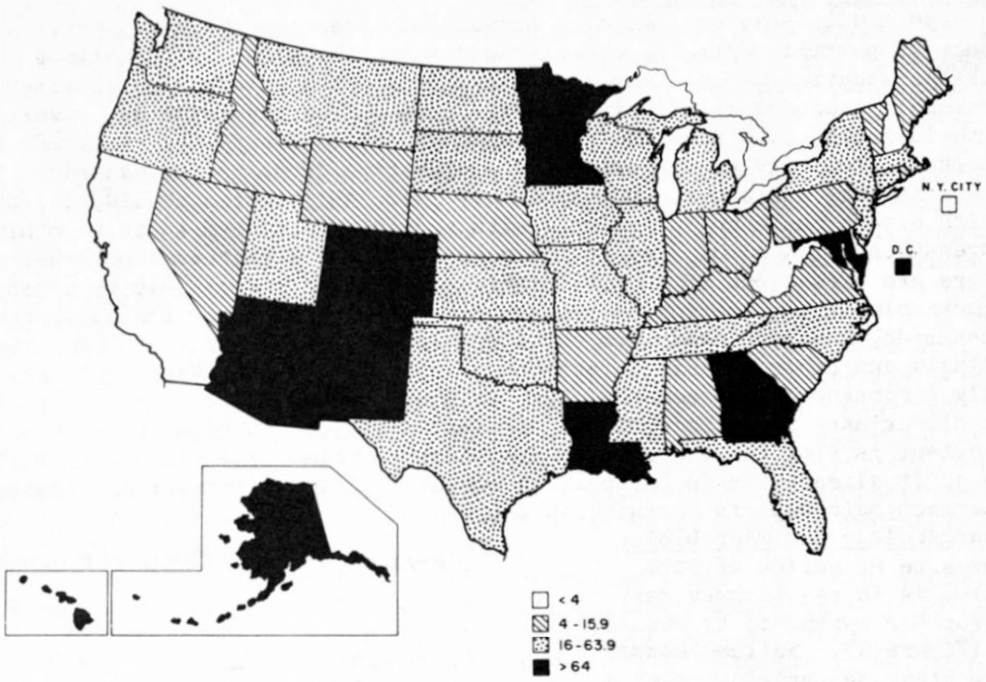


Fig. 3 ATTACK RATES OF SHIGELLOSIS, BY STATE, JANUARY-JUNE 1973



B. Nonhuman

For the period January-June 1973, 40 isolations from nonhuman sources were reported, 36 of them from primates.

Table 2

Serotype	Number	Source	State
S. boydii 12	1	unknown	Connecticut
S. dysenteriae 2	1	monkey	Illinois
S. flexneri (unspec)	1	monkey	Iowa
S. flexneri 2 (unspec)	1	monkey	Maryland
	2	rhesus monkey	Maryland
	2	stumptailed monkey	Maryland
	1	monkey	Ohio
S. flexneri 2a	1	monkey	Connecticut
	5	monkey	Illinois
	1	monkey	Louisiana
	2	monkey	Ohio
S. flexneri 3 (unspec)	1	unknown	Hawaii
	2	monkey	Hawaii
	1	chimpanzee	Maryland
	1	rhesus monkey	Maryland
S. flexneri 4 (unspec)	1	rhesus monkey	Maryland
	1	primate	Ohio
S. flexneri 4a	3	monkey	Illinois
	1	baboon	Texas
S. flexneri 4b	1	monkey	Illinois
S. sonnei	1	monkey	Hawaii
	6	monkey	Illinois
	1	cat	Michigan
	1	canine	Washington
S. species	1	monkey	Connecticut

III. CURRENT TOPICS

A. Co-trimoxazole and Shigellosis

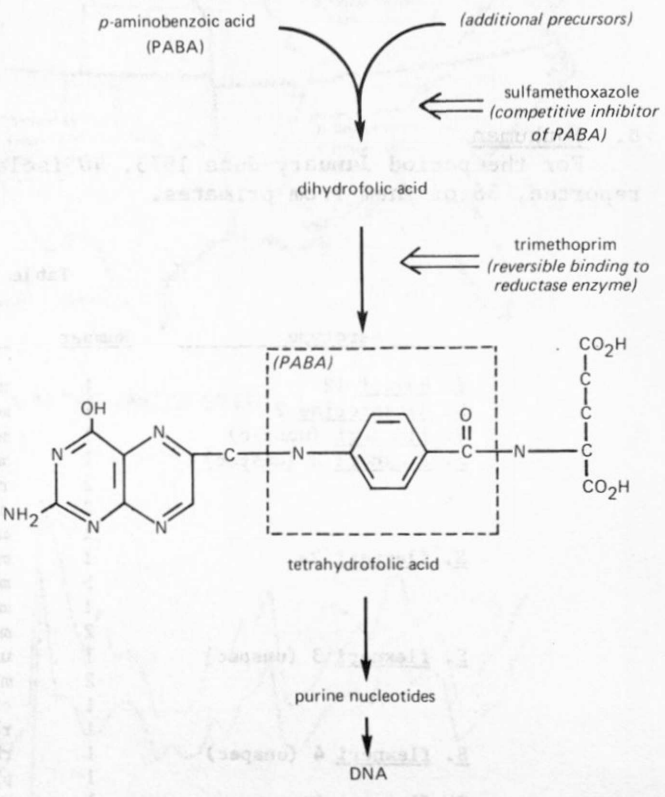
As reported in previous shigella surveillance reports and elsewhere,[1] the rising frequency of multiple antibiotic resistance among shigellae has sometimes created serious therapeutic problems for clinicians faced with an organism resistant to the most commonly used and relatively nontoxic drugs. The physician may wisely choose to withhold antibiotics from the individual whose illness is self-limited, because the potential toxicity of the appropriate effective drugs is too hazardous to risk their use in patients who are not seriously ill. Antibiotics should, in fact, be used with discretion even in patients with sensitive organism so as to minimize selective pressures which might lead to the acquisition of R factors from other gut flora.

There are situations of course in which antibiotic therapy may be essential. Co-trimoxazole, a combination of trimethoprim, an antibiotic, with sulfamethoxazole, a sulfonamide, has been used with considerable success in Europe in the treatment of shigellosis and other enteric infections in the past several years. It has been recently licensed in this country, but its use is currently limited to the treatment of chronic urinary tract infections. However, this combination may some day become an important part of the therapeutic armamentarium against shigellosis in the United States as it already has in Europe. This report will summarize the salient clinical and pharmacologic aspects of this new drug.

Pharmacology and Microbiology

The site of action of both molecules is in the pathway responsible for the synthesis of nucleic acids (Figure 4). Sulfamethoxazole acts to block bacterial synthesis of dihydrofolic acid by competing with paraaminobenzoic acid (PABA). Trimethoprim binds to and reversibly inhibits dihydrofolate reductase, the enzyme catalyzing the reduction of dihydrofolate to tetrahydrofolate. In combination, these drugs exert a "double-pronged" effect at 2 consecutive steps in the nucleic acid synthetic pathway: sulfamethoxazole, as other sulfonamides, resembles PABA and competes with it for incorporation into dihydrofolic acid; trimethoprim prevents the catalysis of dihydrofolates to tetrahydrofolic acid.[2] Their efficacy as antimicrobials lies in the inability for mammalian cells to utilize endogenous folate, and the many thousand-fold greater affinity of trimethoprim for the bacterial reductase than for the corresponding mammalian enzyme.

Figure 4 Folic acid synthetic pathway



The efficacy of this drug combination is thought to rest in the strong synergism observed in vitro against susceptible bacteria.[3,4,5] Synergism has sometimes occurred when the organisms are sulfa-resistant although this has not been a uniform observation. In addition, the development of resistance has thus far not been a significant problem when this

combination is prescribed, and there is evidence to suggest that the development of resistance to trimethoprim is retarded when used in combination with a sulfonamide. With use of this drug combination the dosage that would be required if each drug were used singly can be reduced, thereby reducing the likelihood of dose-related side effects or toxicity.[6] Lastly, although both sulfamethoxazole and trimethoprim are bacteriostatic drugs, there is some evidence to show that when used together they may be bacteriocidal.[6] Antagonism between the 2 drugs or with other concurrently prescribed antimicrobials has not been observed.

In vitro studies have demonstrated that most sensitive organisms are inhibited by trimethoprim concentrations of 0.25 - 2 mg/ml. The minimum inhibitory concentration (MIC) for E. coli, salmonella, and shigella is usually under 0.25 mg/ml. MICs for sulfonamides are harder to demonstrate because of widespread resistance, but for sensitive organisms they are generally in the range of 5-50 mg/ml. The degree of synergistic potentiation depends upon the ratio of sulfamethoxazole to trimethoprim used and tends to be maximal when the ratio of drug concentrations is similar to their MICs making the optimal sulfa:trimethoprim ratio about 20:1. Currently marketed preparations contain 400 mg of sulfamethoxazole and 80 mg of trimethoprim; this ratio of 5:1 has empirically been shown to produce a 20:1 drug ratio in serum.[6] Synergism has been demonstrated by several authors and is usually 2-fold to 8-fold (including potentiation of action against E. coli, salmonella and shigella), but potentiation by factors up to 64-fold has been observed against some organisms, notably gonococci and Proteus mirabilis.

The drugs are rapidly absorbed from the gastrointestinal tract, reaching peak blood levels 1-4 hours following oral administration. Excretion is primarily by the kidneys; consequently dosage must be adjusted in patients with impaired renal function. The half-life in serum is 10 hours for sulfamethaxazole and 16 hours for trimethoprim. The principle manifestations of co-trimoxazole toxicity are blood dyscrasias, primarily leukopenia and thrombocytopenia.

Use in Enteric Infections

The approved use of co-trimoxazole in the treatment of urinary tract infections has been adequately documented and will not be dealt with in this discussion. Several reports in the literature have evaluated the use of these drugs in treating salmonella infections.[7,8,9,10] Reports have differed as to the efficacy of treatment. Eighty-nine of 92 patients from South Africa with proven typhoid responded to therapy, with minimal side effects and no relapses or persistent carriers, leading the authors to state "we are satisfied....that trimethoprim-sulfamethoxazole is an effective treatment for typhoid fever."[8] On the other hand, 103 children with typhoid fever treated with trimethoprim-sulfamethoxazole in Britain were felt to have had an "unsatisfactory response to treatment" when compared with 40 patients treated with chloramphenicol, leading the authors to state that "at present chloramphenicol is still the drug of choice for typhoid fever."[9] They acknowledged, however, that other studies demonstrated as good or better results with co-trimoxazole as with chloramphenicol. The Medical Letter has indicated that for typhoid strains resistant to chloramphenicol and ampicillin, co-trimoxazole may offer the best therapy available;[11] such strains have recently been isolated from a small number of patients with typhoid fever in Mexico.

Shigella Infections

Several studies have explored the effectiveness of co-trimoxazole against shigellae. In vitro sensitivity testing of 209 S. sonnei strains by Jarvis[12] showed all strains sensitive to trimethoprim at a concentration of 0.32 μ/ml or greater. Only 26% were sensitive to sulfamethoxazole at a concentration of 6.4 μ/ml, however, and 74% remained resistant at a concentration of 100 μ/ml.[12] The authors also demonstrated synergism by showing a reduction in the MIC for trimethoprim in the presence of sulfamethoxazole (Table 3). However, potentiation of trimethoprim was well marked only with sulfa-sensitive strains; there was little or no potentiation against sulfa-resistant organisms.

Table 3

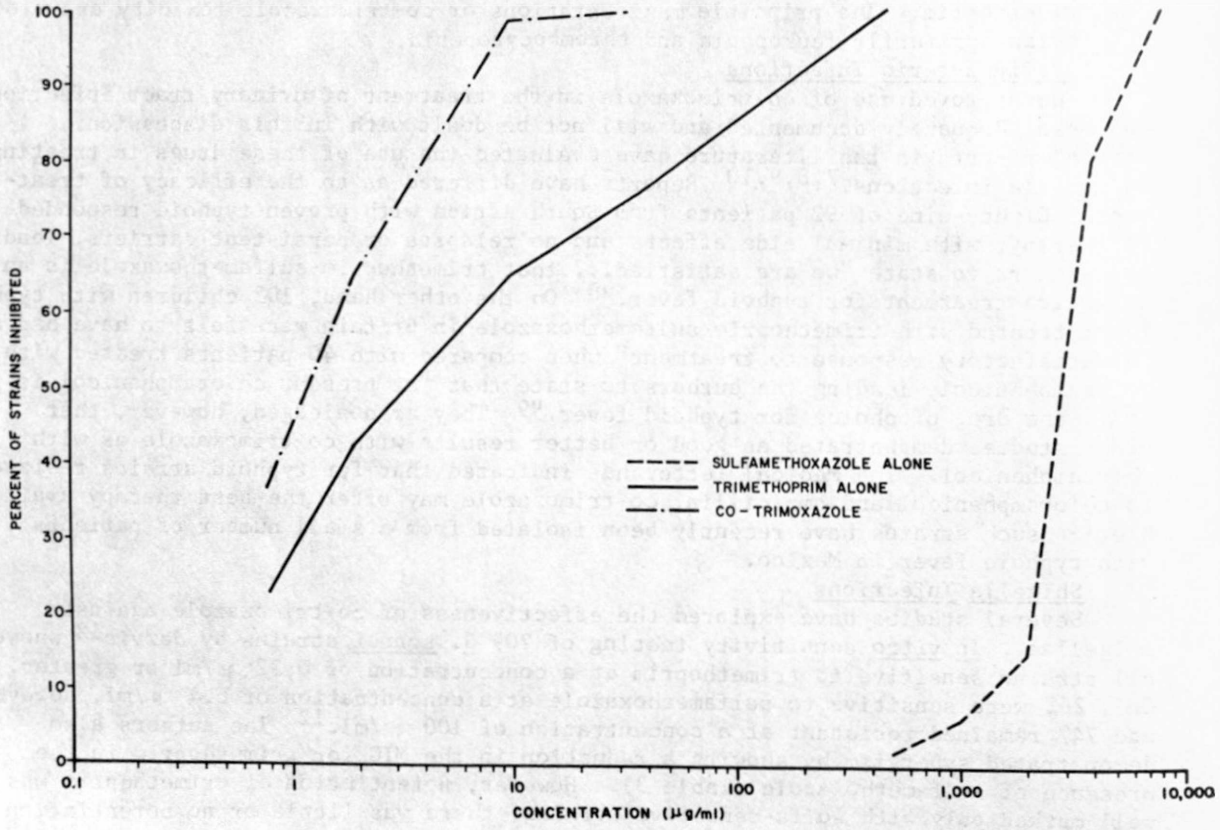
Potentiation of Trimethoprim by Sulfamethoxazole Against Sulfonamide-Sensitive and Resistant Strains of S. sonnei

Potentiation of trimethoprim †	Number of strains showing the stated amount of potentiation among: Sulfonamide-sensitive strains	Sulfonamide-resistant strains
x½	0	4
x1	0	110
x2	0	40
x4	22	1
x8	32	0
Total	54	155

† Factor by which the MIC of trimethoprim was reduced by the presence of sulfamethoxazole.

Clinical studies have indicated that co-trimoxazole is of substantial therapeutic value in the treatment of shigellosis. In a Bangkok study, comparison of co-trimoxazole with furazolidone demonstrated that those treated with co-trimoxazole recovered more quickly and the drug eliminated shigellae from their feces more rapidly than those treated with furazolidone.[13] Moreover, although all 104 shigella isolates tested were resistant to 500 mg/ml or more of sulfamethoxazole, and 30% of strains were resistant to trimethoprim (at a concentration of 12.5 mg/ml), all strains were sensitive to co-trimoxazole, and the MIC of co-trimoxazole was significantly lower than for either drug alone (Figure 5).

Fig. 5 **MINIMUM INHIBITORY CONCENTRATIONS OF SULFAMETHOXAZOLE, TRIMETHOPRIM, AND CO-TRIMOXAZOLE FOR 104 STRAINS OF SHIGELLAE***



*data from Lexomboon[13]

Significant abbreviation of shigella carriage was also seen in 31 Swedish patients treated with co-trimoxazole when compared with untreated controls.[3] No patient with an organism sensitive to both sulfa and trimethoprim had a positive culture beyond the third day of treatment. Three patients with sulfa-resistant organisms, however, remained positive for 5 days and 1 child remained positive 23 days after therapy, although she was subsequently cured with a second course of co-trimoxazole. In an institutional outbreak of S. sonnei, co-trimoxazole again was effective in achieving bacteriologic clearance of shigella from the stool, but there was no difference between co-trimoxazole-treated patients and controls who received no antibiotics in terms of duration of symptoms or other clinical parameters.

Discussion

The routine use of antibiotics in the treatment of shigellosis has been previously called into question not only because the illness is generally self-limited and the spontaneous cure rate high, but also because the repeated emergence of antibiotic resistant strains following widespread use of 1 or another antimicrobial has made it important, from an epidemiologic standpoint, to avoid "environmental contamination" by the indiscriminant use of these agents.[1] Resistance to co-trimoxazole has already been demonstrated in E. coli, and such resistance has been shown to be transferrable.[11] In Britain, trimethoprim resistance was demonstrated in 18 of 725 coliforms isolated from patients over a 4-month period in 1971;[14] five came from patients who had previously been treated with co-trimoxazole. Shigella resistance to sulfonamides has been widespread for many years. It would seem, therefore, that the increasing development of R factor-mediated resistance to co-trimoxazole--at least to trimethoprim--is a distinct and ominous possibility. If co-trimoxazole should be licensed in this country for use against shigella, consequently, it is unlikely that there will be reason to change current recommendations of avoiding specific therapy when the patient's shigella is resistant to innocuous antimicrobials, unless the severity of the patient's illness warrants the hazards of the use of appropriate drugs.[1] However, when faced with a patient whose clinical status warrants specific therapy (in his physician's judgement) and who is excreting a multiply-resistant organism, co-trimoxazole may be a valuable therapeutic alternative to potentially more hazardous drugs.

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IV. REPORTS FROM THE STATES

A. Foodborne Shigellosis, Austin, Texas

Reported by J. Yoas, R.N., Supervising Nurse, E. Gentry, M.D., Director, Communicable Diseases, and J. Sessums, M.D. Director, Austin-Travis County Health Department; and M.S. Dickerson, M.D., State Epidemiologist, Texas State Department of Health.

On February 13, 1973, an elementary school in Austin, Texas, noted a sharp rise in absenteeism. Within 2 days, 116 of 232 pupils and 6 of 30 staff members were absent with fever and gastroenteritis (Figure 6). A day care center located in the school building experienced a similar rise in absenteeism, with 15 of 25 preschoolers absent because of gastrointestinal illness. Stool specimens from 36 of 38 symptomatic individuals who were cultured were positive for S. sonnei.

Epidemiologic investigation disclosed that only those individuals who had eaten lunch at school on February 12 had become ill. In addition, food histories obtained from 30 adults showed that only those who had eaten tuna fish salad became ill (Table 4).

Fig. 6 PERCENT OF STUDENTS ABSENT, AUSTIN, TEXAS ELEMENTARY SCHOOL, FEBRUARY 1973

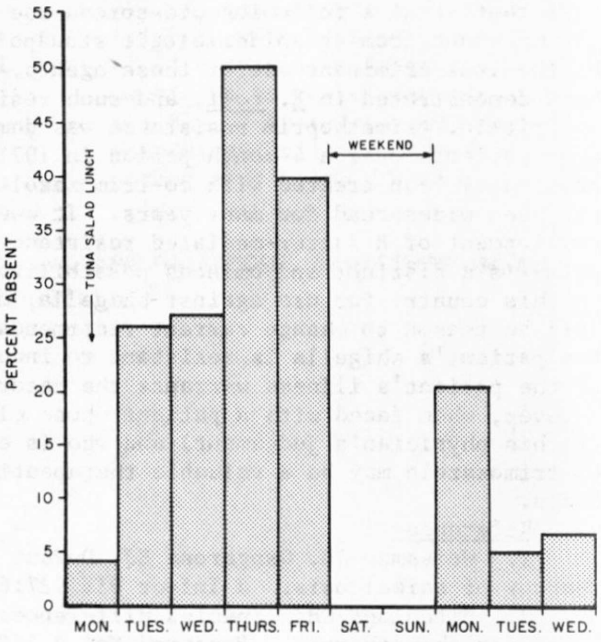

Table 4

Diarrheal Illness in 30 Adults, by History of Eating Tuna Salad, Austin, Texas, Elementary School, February 12, 1973

	Ill	Not ill
Ate tuna salad	6	9
Did not eat tuna salad	0	15

p = .008

Stool specimens were obtained from all 4 kitchen workers who were involved in food preparation. The specimen from the worker who had prepared the incriminated tuna salad was positive for S. sonnei. She denied having had a recent diarrheal illness but said she had had an "upset stomach" the week before. However, both her children, ages 7 and 13, had been ill the week before with fever and diarrhea. Both children had positive stool cultures for S. sonnei.

The food handler and her children were kept at home until 3 consecutive negative stool cultures had been obtained. Elementary school students were permitted to return to class when they were clinically recovered.

Editorial Comment

In 1973, over 300 outbreaks of foodborne disease occurred in the United States;[1] shigellosis accounted for 2.2% of these outbreaks, but 6.7% of cases were attributed to shigella. Although staphylococcus, *Clostridium perfringens*, salmonella, and *C. botulinum* rank above shigella as causative organisms, foodborne shigellosis may account for significant morbidity. In 1971, outbreaks due to shigella averaged 100 cases of clinical illness each. Because of adverse growth conditions, competition from other bacteria, improper culture techniques, and frequent unavailability of the implicated foods, shigella is not often recovered from the food vehicle.[2] In 1970 shigella was recovered from food in only 1 of 7 reported outbreaks.[3]

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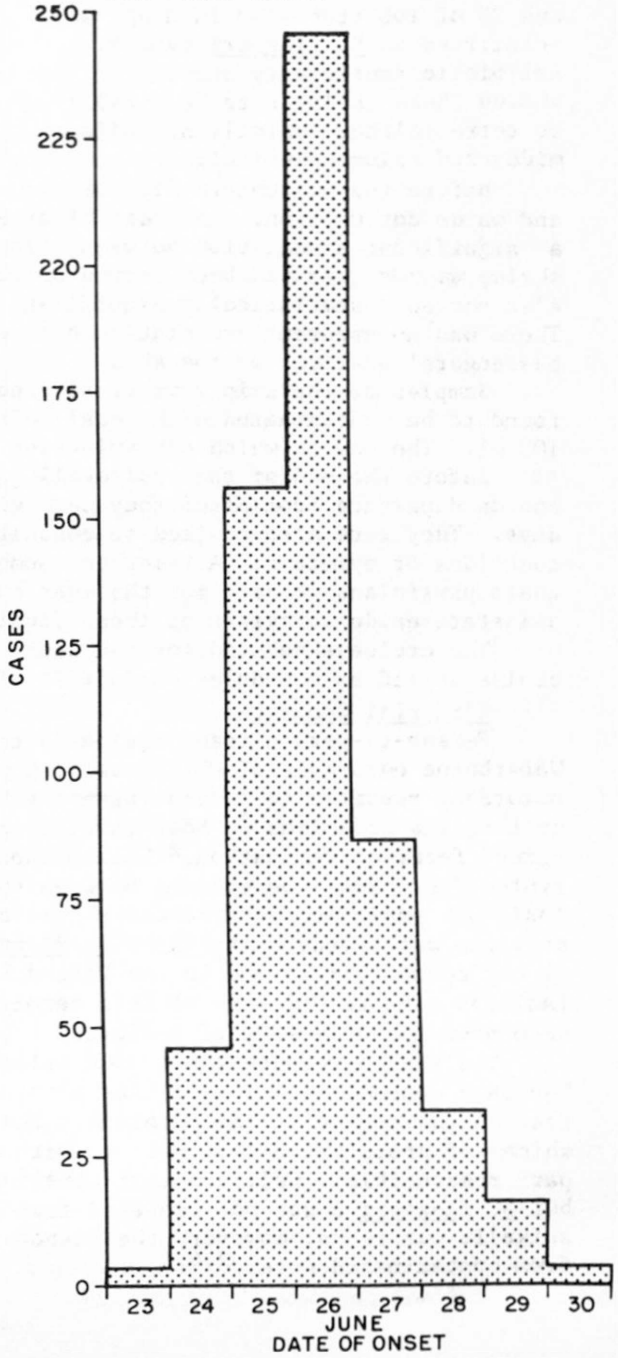
B. Waterborne Shigellosis on a Caribbean Cruise

Reported by Mrs. Marla Dolores Gonzalez de Vazquez, Supervisor, Department of Sanitary Bacteriology, Institute of Laboratories, Puerto Rico Department of Health; Ferdinand A. Nicholson, Director, Bureau of Public Health Laboratories, Virgin Islands Department of Health; Milton S. Saslaw, M.D., Director, Joel L. Nitzkin, M.D., Chief, Office of Consumer Protection, Boone Carey, Jr., Engineer, and Harry S. Workman, Sanitarian, Dade County Department of Public Health.

Between June 23 and 30, an outbreak of acute gastroenteritis occurred on a Caribbean cruise ship. Approximately 90% of the 650 passengers and 35% of 299 crew were affected. The ship was on a 1-week tour with stops at Haiti, Puerto Rico, St. Thomas, and Nassau. Because of the outbreak, the ship by-passed Nassau on June 29 and arrived at Miami at 4:30 AM on June 30.

In the outbreak which began on Saturday, June 23, a total of 586 cases occurred in the passengers (Figure 7). Explosive watery diarrhea was the dominant symptom, accompanied by abdominal cramps

Fig. 7 CASES OF SHIGELLOSIS ABOARD CARIBBEAN CRUISE SHIP, JUNE 23–30, 1973



and chills, headache, and nausea (Table 5). Documented fever of 100°-102°F was not unusual, and in 1 case it was 104°F. Vomiting was relatively infrequent. Symptoms generally lasted 3-5 days. In Miami, 3 of the passengers were hospitalized for short periods; the others were released to proceed home or to other destinations.

Table 5

Distribution of Symptoms of Passengers and Crew

Symptom	Passengers	Crew
Diarrhea	98%	84%
Mucus	19%	12%
Blood	6%	8%
Tenesmus	31%	25%
Cramps	85%	37%
Headache	66%	39%
Nausea	59%	22%
Vomiting	27%	17%
Muscle aches	55%	26%
Chills	54%	25%
Fever	47%	24%

Isolates from 3 of 16 stool cultures obtained from ill passengers and crew processed in public health laboratories in San Juan, Puerto Rico, 6 of 13 processed in St. Thomas, Virgin Islands, and 23 of 108 processed in Miami were identified as S. flexneri type 6. Antibiotic sensitivity studies showed these isolates to be sensitive to tetracycline, ampicillin, sulfonamide, and chloramphenicol.

Before the passengers disembarked, they and the crew were questioned as to food and water consumption. Analysis of attack rates by food and water exposure disclosed a significant association between illness and passengers' water consumption. Two shrimp dishes that had been served on ice on Saturday, June 23, and Monday, June 25, also showed a statistically significant association with the occurrence of illness. There was no apparent association between the risk of illness and the location of passengers' quarters on the ship.

Samples of the ship's water studied in Puerto Rico and the Virgin Islands were found to be contaminated with fecal coliforms ranging from 13 to 49 organisms per 100 ml. The way in which contamination occurred was not determined.

Before the end of the cruise, all passengers were started on oral tetracycline, and on departure from Miami they were given a supply of tetracycline to take for 6 days. They were also advised to consult their family physician if they had further questions or symptoms. A telephone number of CDC was provided for passengers or their physicians to call for the most current information and advice. CDC informed all state epidemiologists of these findings by telegraph.

The cruise scheduled for the week of June 30-July 7 was cancelled. The next cruise sailed as scheduled on July 7. There was no further illness aboard ship.

Editorial Comment

Person-to-person transmission is the predominant mode of spread of shigellosis. Waterborne outbreaks of shigellosis, however, are not uncommon. Of 358 waterborne outbreaks reported to federal agencies between 1946 and 1970, 33 (9%) were caused by shigella organisms.[1] Most involved private water supplies and were caused by direct fecal contamination,[2] back-siphonage from a nonpotable into a potable water system,[3] or cross-connections between such systems.[4] A review of waterborne shigellosis was published in a recent shigella surveillance report.[5] Although at least 1 previous waterborne outbreak of S. flexneri 6 has been documented,[2] this organism is not commonly reported in the United States. In 1972, only 3.2% of shigella isolates sent to CDC were of this serotype; in the first half of 1973, S. flexneri 6 accounted for only 2.0% of isolates.

The explosive onset, the high attack rate, and the water and ice-containing beverage consumption histories of passengers implicated the ship's water, including ice, as the source of the outbreak. The possibility exists that 1 or 2 shrimp items, which had prolonged direct contact with the ship's water, could have also been in part responsible. Coliform contamination was found in all water samples tested, but S. flexneri 6 was not isolated from any of the samples. In previous waterborne shigella outbreaks, however, the responsible organisms have usually not been isolated from contaminated water.[2,4,5]

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V. NOTES FROM RECENT PUBLICATIONS

A. Pathogenesis of Shigella dysenteriae 1 (Shiga) Dysentery

Levine MM, DuPont HL, Formal SB, Hornick RB, Takeuchi A, Gangarosa EJ, Snyder MJ, Libonati JP. J Infect Dis 127(3):261-270, 1973

The Shiga bacillus is unique among the shigellae in its elaboration of an enterotoxin; this factor, which was recognized by Shiga himself, has been felt to be responsible for the enhanced virulence of this organism over other shigella species. The authors of this important paper examined this hypothesis by investigating the pathogenetic properties of 2 fully virulent (invasive and toxigenic) and 2 modified (noninvasive, toxigenic and invasive, nontoxigenic) strains of S. dysenteriae 1.

Invasiveness was assayed by several methods that reflect epithelial penetration: the Serény test (guinea-pig-eye model), rabbit loop, and oral infection of guinea pigs. Toxigenicity was determined by the rabbit loop model and the HeLa cell assay, using both sterile broth culture supernatants and bacterial cell extracts. Adult male volunteers from the Maryland House of Corrections participated in clinical studies.

Virulent strains produced disease in volunteers in doses as low as 10 organisms. Free toxin could not be demonstrated during illness, although large numbers of Shiga organisms were excreted in the stools. On the other hand, large numbers of a non-invasive toxigenic strain (10^6 - 10^{11} organisms) were well tolerated by 85 of 86 men. An invasive nontoxigenic strain caused shigellosis in both monkeys and volunteers.

The authors have demonstrated that epithelial penetration is the sina qua non of Shiga dysentery, as it is with other forms of shigellosis; conversely, the toxin in and of itself is insufficient to cause clinical illness.

Except for the production of a positive rabbit ileal loop, the Shiga toxin has little in common with other known enterotoxins, differing in a variety of biochemical characteristics. However, nontoxigenic organisms such as S. flexneri or S. sonnei also produce positive rabbit loops, calling into question the relevance of the rabbit ileal loop test as a definitive bioassay for toxin. As pointed out by the authors, the known cytotoxicity of Shiga enterotoxin may play a pathogenetic role after epithelial cell death. The high incidence of overt dysentery seen during the Shiga pandemic in Central America has led the authors to favor a cytotoxic role for the toxin in its contribution to clinical symptomatology.

B. Lomotil* Therapy of Shigellosis

DuPont HL, Hornick RB. Presented at the National Meeting of the American Federation for Clinical Research, Atlantic City, New Jersey, April 29, 1973. JAMA 226:in press, 1973.

Since a prerequisite for shigella infection is penetration of intestinal epithelium, intestinal motility may act as an important resistance mechanism in protecting the host against bacterial invasion. The authors of this study compared Lomotil*

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*Names of manufacturers and trade names are provided for identification only, and inclusion does not imply endorsement by the Public Health Service or the U.S. Department of Health, Education, and Welfare.

(diphenoxylate with atropine) with placebo to determine if drugs which retard intestinal motility, so often prescribed for patients with diarrhea, had an adverse effect on the course of shigellosis.

Volunteers from the Maryland House of Correction participated in the study. Challenge was achieved by the oral administration of 10^4 viable shigellae. All men who passed 2 or more unformed stools were given either Lomotil* or placebo on a blind, random basis. In addition, oxalinic acid or a second placebo was begun in those patients with fever of 101°F or greater, 5 or more diarrheal stools, or dysentery; thus there were 4 separate treatment groups.

Results

Twenty-five men developed clinical illness. Characteristics of their illnesses are summarized in Table 6, which shows efficacy of Lomotil* in terms of the duration of diarrhea, although (as expected) the frequency of diarrheal stools decreased. If anything, Lomotil* may have exacerbated symptomatology, since the duration of fever was prolonged in patients receiving Lomotil* unless it was accompanied by an antibiotic. Two men receiving Lomotil* had an exaggerated and prolonged febrile response; after 36 hours placebo preparations were discontinued and ampicillin begun. Despite this therapy (against an ampicillin-sensitive organism) the men remained toxic for 5 and 6 days, respectively, until Lomotil* was discontinued; clinical improvement followed rapidly.

Table 6

Influence of Lomotil* and Oxalinic Acid on Patients With Shigellosis

Treatment group	Number of volunteers in group	Mean number of diarrheal stools	Mean days of diarrhea	Mean duration of fever (hours) †	Bacteriologic response**
Lomotil* + Oxalinic acid	6	14.2	5.5	16	1
Placebo + Oxalinic acid	6	7.8	2.3	18	4
Lomotil* + Placebo	7	17.0	4.0	48	0
Placebo + Placebo	6	44.7	5.8	21	0

† Of those with fever
** Negative stool culture within 5 days of treatment

Discussion

The authors make the point that intestinal motility patterns represent an important homeostatic mechanism whereby the intestine can prevent multiplication of or penetration by potentially pathogenic bacteria by the physiological cleansing mechanism. In the case of enteric infection by invasive bacteria, in particular, the time of contact between the pathogen and the intestinal mucosa may be important. In this study there was a slight reduction in stool frequency in men given Lomotil* compared with a placebo-treated group, yet diarrhea was not appreciably decreased by antimicrobial therapy. The favorable effect of the antibiotic was nullified by concomitant administration of Lomotil.* They conclude that drugs which retard gut motility may be harmful in patients infected with invasive pathogens and that when fever and/or dysentery occur in the presence of acute diarrhea, thus making an invasive pathogen the likely etiology, drugs which reduce intestinal motility such as the belladonna or opium alkaloids should not be employed.

* Ibid

Standard Tables I - VII

TABLE I-A

SHIGELLA SEROTYPES ISOLATED FROM HUMANS
FIRST QUARTER, 1973

SEROTYPE	NORTHEAST																													NORTHWEST													
	CONN	DEL	DC	ILL	IND	IOWA	KY	ME	MD	MASS	MICH	MINN	MO	NH	NJ	NY-A	NY-BI	NY-C	OHIO	PA	RI	VT	VA	W VA	WISC	NORTHEAST TOTAL	COLO	IDAHO	KANS	MONT	NEB	NEV	ND	ORE	SD	UTAH	WASH	WYO	NORTHWEST TOTAL	NORTH TOTAL
S. dysenteriae																																										
Unspec																	1									1	1			1										2	3
1																										0														0	0
2																										0														0	0
3																										0														0	0
6				1																						1														0	1
Total	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2	1	0	1	0	0	0	0	0	0	0	0	0	2	4
S. flexneri																																									
Unspec			2		3					2	1		6	1		4	2	16		3		2	2			44	15		1		2		1	1	12				32	76
1 Unspec									3																1	4											8		8	12
1A				3						1		1														5													0	5
1B				1																						1													0	1
2 Unspec									10		2		1												7	20										5	8		13	33
2A	5			14						10	3	2														34				6			3					9	43
2B				13																						13													0	13
3 Unspec	1								1		2		1		1											6										2		2	8
3A				17							1															18													0	18
3B				1								1														2													0	2
3C											1															1				1									1	2
4 Unspec											1														1	2													0	2
4A				3						3		1														7			1	3					1			5	12
4B											2															2									1			1	3
5																										0											1		1	1
6	1			3					2	2	2															10									2	2		4	14
Total	7	0	2	55	3	0	0	0	16	18	15	5	8	1	1	4	2	16	0	3	0	2	2	0	9	169	15	0	2	10	2	0	4	1	12	9	21	0	76	245
S. boydii																																								
Unspec											1															1													0	1
1																						1				1													0	1
2													1													1													0	1
4											1														1	2									1				1	3
10				1																						1													0	1
14																										0													0	0
Total	0	0	0	1	0	0	0	0	0	0	2	0	1	0	0	0	0	0	0	0	0	1	0	1	6	0	0	0	0	0	0	0	0	0	1	0	0	1	7
S. sonnei	39	0	24	221	25	77	28	3	148	78	85	76	57	0	69	18	11	80	49	31	3	2	7	1	109	1,241	45	3	39	0	5	3	1	41	1	26	27	0	191	1,432
Unknown			16			1					3					5										25								1					1	26
TOTAL	46	0	42	278	28	78	28	3	164	96	105	81	66	1	70	27	14	96	49	34	3	4	10	1	119	1,443	61	3	42	10	7	3	5	43	13	36	48	0	271	1,714

TABLE I-A (Continued)

SHIGELLA SEROTYPES ISOLATED FROM HUMANS

FIRST QUARTER, 1973

SOUTHEAST										SOUTHWEST						OTHER							PREVIOUS QUARTER		
ALA	ARK	FLA	GA	LA	MISS	NC	SC	TENN	SOUTHEAST TOTAL	ARIZ	NM	OKLA	TEX	SOUTHWEST TOTAL	SOUTH TOTAL	ALASKA	CALIF	HAWAII	VIRGIN ISLANDS	OTHER TOTAL	TOTAL	PERCENT OF TOTAL	TOTAL	PERCENT OF TOTAL	SEROTYPE
									0					0	0					0	3	0.1	2	0.1	*S. dysenteria* Unspec
									0				1	1	1					0	1	0.0	2	0.1	1
						1			1					0	1					0	1	0.0	2	0.1	2
						1			1				1	1	2					0	2	0.1	8	0.2	3
									0					0	0					0	1	0.0			6
0	0	0	0	0	0	2	0	0	2	0	0	0	2	2	4	0	0	0	0	0	8	0.3	18	0.5	Total
	2				16			1	19					0	19			1		1	96	3.4	108	3.0	*S. flexneri* Unspec
		1	3						4		2			2	6					0	18	0.6	19	0.5	1 Unspec
									0	3			9	12	12					0	17	0.6	10	0.3	1A
				1					1	5			3	8	9					0	10	0.4	16	0.4	1B
		30	5						35		7			7	42					0	75	2.7	96	2.7	2 Unspec
				4				2	6	11		3	32	46	52			5		5	100	3.5	111	3.1	2A
				1					1	3			12	15	16					0	29	1.0	22	0.6	2B
		2	1			4			7	3	4	1		8	15					0	23	0.8	21	0.6	3 Unspec
				1				5	6	10			11	21	27					0	45	1.6	63	1.8	3A
									0				1	1	1					0	3	0.1	5	0.1	3B
									0	1				1	1					0	3	0.1	4	0.1	3C
		2							2		3			3	5					0	7	0.2	8	0.2	4 Unspec
		1							1	5			7	12	13					0	25	0.9	15	0.4	4A
									0				4	4	4					0	7	0.2	3	0.1	4B
									0	2				2	2					0	3	0.1	11	0.3	5
		5	1			1		3	10	8	12		10	30	40					0	54	1.9	94	2.6	6
0	2	41	10	7	16	5	0	11	92	51	28	4	89	172	264	0	0	6	0	6	515	18.2	607	17.0	Total
									0					0	0					0	1	0.0	5	0.1	*S. boydii* Unspec
									0					0	0					0	1	0.0	1	0.0	1
									0				1	1	1					0	2	0.1	1	0.0	2
									0					0	0					0	3	0.1	10	0.3	4
									0				1	1	1					0	2	0.1	1	0.0	10
									0	1				1	1					0	1	0.0	1	0.0	14
0	0	0	0	0	0	0	0	0	0	1	0	0	2	3	3	0	0	0	0	0	10	0.4	22	0.6	Total
17	5	71	102	105	9	75	15	56	455	38	70	11	227	346	801	11	1	24	0	36	2,269	80.2	2,910	81.6	*S. sonnei*
									0	0										0	26	0.9	10	0.3	Unknown
17	7	112	112	112	25	82	15	67	549	90	98	15	320	523	1,072	11	1	30	0	42	2,828		3,567		TOTAL

TABLE I-B

SHIGELLA SEROTYPES ISOLATED FROM HUMANS
SECOND QUARTER, 1973

SEROTYPE	NORTHEAST																														NORTHWEST														NORTH TOTAL
	CONN	DEL	DC	ILL	IND	IOWA	KY	ME	MD	MASS	MICH	MINN	MO	NH	NJ	NY-A	NY-BI	NY-C	OHIO	PA	RI	VT	VA	W VA	WISC	NORTHEAST TOTAL	COLO	IDAHO	KANS	MONT	NEB	NEV	ND	ORE	SD	UTAH	WASH	WYO	NORTHWEST TOTAL	
S. dysenteriae																																											
Unspec																										0								1						1	1
1																										0														0	0
2				2																					1	3													0	3
3				3																						3													0	3
Total	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	6	0	0	0	0	0	0	0	1	0	0	0	0	1	7
S. flexneri																																										
Unspec			3		2	1				1	7		6			4	5	3		4			1			37	9		1		1			2	13			3	29	66
1 Unspec																									1	1										1	3		4	5
1A				4								1														5													0	5
1B				2								3														5													0	5
2 Unspec									2				1						1							4										7	6		13	17
2A	6			11						8	12	6							1							44			6	5			12					23	67
2B				8																						8													0	8
3 Unspec													1						1						1	3			1										1	4
3A	5			21						1																27													0	27
3B				1																						1													0	1
3C										1	1	1														3													0	3
4 Unspec											1								2							3										2			2	5
4A				3				1			1	1														6				3					1				4	10
4B																										0									4				4	4
5																										0													0	0
6				4					1	3																8				1						2			3	11
Total	11	0	3	54	2	1	0	1	3	14	22	12	8	0	0	4	5	3	5	4	0	0	1	0	2	155	9	0	8	9	1	0	12	2	13	13	13	3	83	238
S. boydii																																										
Unspec											1															1	2												2	3
2												1														1										1			1	2
4																									1	1													0	1
5				1																						1													0	1
7																										0													0	0
10																										0													0	0
14																										0													0	0
Total	0	0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	4	2	0	0	0	0	0	0	0	0	1	0	0	3	7
S. sonnei	66	2	14	298	31	55	13	8	181	30	152	241	87	2	63	60	16	78	38	139	11	2	28	1	97	1,713	85	5	42	12	0	2	4	40	3	18	63	0	274	1,987
Unknown			4								1	1														6													0	6
TOTAL	77	2	21	358	33	56	13	9	184	44	176	255	95	2	63	64	21	81	43	143	11	2	29	1	101	1,884	96	5	50	21	1	2	16	43	16	32	76	3	361	2,245

TABLE I-B (Continued)

SHIGELLA SEROTYPES ISOLATED FROM HUMANS
SECOND QUARTER, 1973

SOUTHEAST										SOUTHWEST					SOUTH TOTAL	OTHER					TOTAL	PERCENT OF TOTAL	PREVIOUS QUARTER		SEROTYPE
ALA	ARK	FLA	GA	LA	MISS	NC	SC	TENN	SOUTHEAST TOTAL	ARIZ	NM	OKLA	TEX	SOUTHWEST TOTAL		ALASKA	CALIF	HAWAII	VIRGIN ISLANDS	OTHER TOTAL			TOTAL	PERCENT OF TOTAL	
									0					0	0					0	1	0.0	3	0.1	*S. dysenteriae*
									0	1	1			2	2					0	2	0.1	1	0.0	Unspec
						1			1					0	1					0	4	0.1	1	0.0	1
									0					0	0					0	3	0.1	2	0.1	2
																									3
0	0	0	0	0	0	1	0	0	1	1	1	0	0	2	3	0	0	0	0	0	10	0.3	8	0.3	Total
																									S. flexneri
	5	1			7				13	1		1	1	3	16			5		5	87	2.3	96	3.4	Unspec
		5	1						6		2			2	8					0	13	0.3	18	0.6	1 Unspec
								1	1	3			8	11	12					0	17	0.5	17	0.6	1A
									0	6			5	11	11					0	16	0.4	10	0.4	1B
2		34	15			7			58		12			12	70					0	87	2.3	75	2.7	2 Unspec
				3				7	10	15		1	25	41	51					0	118	3.1	100	3.5	2A
				1					1	3			16	19	20					0	28	0.7	29	1.0	2B
		2				1			3	1	3			4	7					0	11	0.3	23	0.8	3 Unspec
		1						7	8	23			9	32	40					0	67	1.8	45	1.6	3A
									0	1			3	4	4					0	5	0.1	3	0.1	3B
				1					1				1	1	2					0	5	0.1	3	0.1	3C
		3							3		3			3	6					0	11	0.3	7	0.2	4 Unspec
		2		1					3	8			6	14	17					0	27	0.7	25	0.9	4A
									0					0	0					0	4	0.1	7	0.2	4B
				1					1		1	1		2	3					0	3	0.1	3	0.1	5
		9				1		4	14	16	17		18	51	65			4		4	80	2.1	54	0.9	6
2	5	57	16	7	7	9	0	19	122	77	38	3	92	210	332	0	0	9	0	9	579	15.4	515	18.2	Total
																									S. boydii
									0					0	0					0	3	0.1	1	0.0	Unspec
									0	1	1		7	9	9					0	11	0.3	2	0.1	2
									0	1				1	1					0	2	0.1	3	0.1	4
			1						1					0	1					0	2	0.1	0		5
		2							2					0	2					0	2	0.1	0	-	7
									0				3	3	3					0	3	0.1	2	0.1	10
									0				1	1	1					0	1	0.0	1	0.0	14
0	0	2	1	0	0	0	0	0	3	2	1	0	11	14	17	0	0	0	0	0	24	0.6	10	0.4	Total
17	19	166	255	122	6	82	11	45	723	31	65	44	252	392	1,115	13		19		32	3,134	83.5	2,269	80.2	*S. sonnei*
									0					0	0					0	6	0.2	26	0.9	Unknown
19	24	225	272	129	13	92	11	64	849	111	105	47	355	618	1,467	13	0	28	0	41	3,753		2,828		TOTAL

Table II

Age and Sex Distribution of Individuals Infected With Shigella in the United States, 1st Half, 1973

Age (Years)	Male	Female	Unknown	Total	Percent	Cumulative Percent	Number of Reported Isolations/ Million Population*
< 1	107	123	3	233	4.8	4.8	69.7
1-4	994	920	4	1,918	39.8	44.7	138.0
5-9	558	540		1,098	22.8	67.4	58.7
10-19	294	331	2	627	13.0	80.5	15.4
20-29	152	318		470	9.8	90.2	14.3
30-39	111	146	1	258	5.4	95.6	11.1
40-49	40	53		93	1.9	97.5	3.9
50-59	18	35		53	1.1	98.6	2.4
60-69	12	22		34	0.7	99.3	2.1
70-79	12	13		25	0.5	99.8	2.6
80 or Over	3	5		8	0.1	100.0	1.9
Subtotal	2,301	2,506	10	4,817			
Child (unspec)	12	18	1	31			
Adult (unspec)	8	24		32			
Unknown	846	821	34	1,701			
TOTAL	3,167	3,369	45	6,581			
Percent	48.5	51.5					

*Based on 1970 Census of Population, General Population Characteristics, United States Summary, Issued January 1972.

Table III

Relative Frequencies of Shigella Serotypes Reported, 1st Half, 1973

Serotype	Number Reported	Calculated Number*	Calculated Percent*	Rank
A. *S. dysenteriae*				
Unspecified	4			
1	3	4	.06	15
2	5	6	.09	13
3	5	6	.09	13
6	1	2	.03	15
B. *S. flexneri*				
Unspecified	183			
1 unspecified	31			
1a	34	63	.96	7
1b	26	47	.71	8
2 unspecified	162			
2a	218	419	6.37	2
2b	57	110	1.67	5
3 unspecified	34			
3a	112	171	2.60	3
3b	8	12	.18	11
3c	8	12	.18	11
4 unspecified	18			
4a	52	81	1.23	6
4b	11	17	.26	9
5	6	8	.12	12
6	134	161	2.45	4
C. *S. boydii*				
Unspecified	4			
1	1	1	.02	17
2	13	15	.23	10
4	5	5	.08	14
5	2	2	.03	16
7	2	2	.03	16
10	5	5	.08	14
14	2	2	.03	16
D. *S. sonnei*	5,403	5,429	82.51	1
Unknown	32			
TOTAL	6,581	6,580		

*Calculated number is derived by distributing the unspecified isolations in each group to their subgroup in the same proportion as the distribution of the specified isolations of that group.

Table IV

Shigella Serotypes from Mental Institutions
Number of Isolations by State, 1st Half, 1973

State	dysenteriae (unspecified)	dysenteriae 2	flexneri (unspecified)	flexneri 1a	flexneri 1b	flexneri 2 (unspecified)	flexneri 2a	flexneri 2b	flexneri 3a	flexneri 3b	flexneri 4 (unspecified)	flexneri 4a	flexneri 6	boydii 10	sonnei	Total
Florida	0	0	0	0	0	0	0	0	0	0	1	0	8	0	2	11
Georgia	0	0	0	0	0	13	0	0	0	0	0	0	0	0	3	16
Illinois	0	2	0	1	0	0	4	4	14	1	0	1	2	1	67	97
Kansas	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2
Louisiana	0	0	0	0	0	0	0	0	0	0	0	0	0	0	21	21
Maryland	0	0	0	0	0	0	0	0	0	0	0	0	0	0	41	41
Massachusetts	0	0	1	0	0	0	5	0	0	0	0	0	0	0	1	7
Michigan	0	0	0	0	0	1	0	0	1	0	0	0	0	0	17	19
Minnesota	2	0	0	0	0	0	1	0	0	0	0	1	0	0	5	9
Mississippi	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
North Carolina	0	0	0	0	0	5	0	0	0	0	0	0	0	0	2	7
South Dakota	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
Tennessee	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	4
Texas	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1
Utah	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	3
Wisconsin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	26	26
TOTAL	2	2	3	1	1	22	10	4	15	1	1	2	10	1	191	266

Table V

Sources of Reported Isolations of Shigella
By Residence at Time of Onset
1st Half, 1973

Source	Jan	Feb	Mar	Apr	May	Jun	Total	Percent of Subtotal	Percent of Total
Mental institutions	81	36	39	53	44	12	265	8.0	
Indian reservations	17	8	4	14	8	8	59	2.0	
Other residencies	433	358	455	437	714	624	3021	90.0	
Subtotal	531	402	498	504	766	644	3345	100.0	51.2
Residencies unknown	519	445	432	481	688	620	3185		47.8
TOTAL	1050	847	930	985	1454	1264	6530		100.0

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The State Epidemiologists are the key to all disease surveillance activities. They are responsible for collecting, interpreting, and transmitting data and epidemiologic information from their individual States. Their contributions to this report are gratefully acknowledged. In addition, valuable contributions are made by State Laboratory Directors; we are indebted to them for their valuable support.

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