REPORT NO. 32
MARCH 1973

center for disease control

SHIGELLA

surveillance

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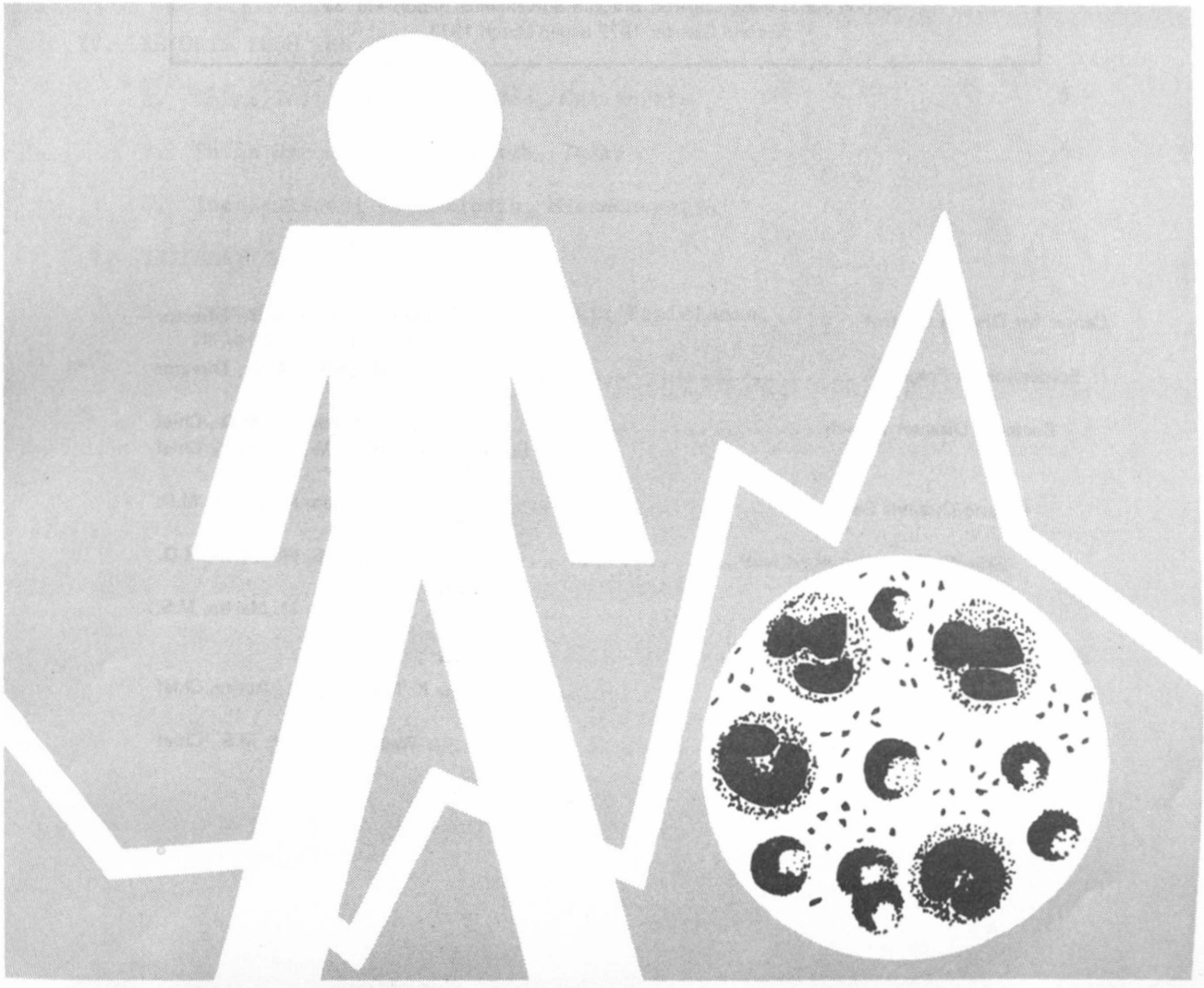
for the
Second Quarter 1972



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

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
Attn: Shigella Surveillance Activity
Epidemiology Program
Atlanta, Georgia 30333

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Center for Disease Control . . . . . David J. Sencer, M.D., Director

Epidemiology Program . . . . . Philip S. Brachman, M.D., Director

Bacterial Diseases Branch . . . . . John V. Bennett, M.D., Chief
Eugene J. Gangarosa, M.D., Deputy Chief

Enteric Diseases Section . . . . . William H. Barker, M.D.

Shigella Surveillance Activity . . . . . Jack B. Weissman, M.D.

Statistical Services . . . . . Stanley M. Martin, M.S.

Epidemiologic Services
Laboratory Section . . . . . George K. Morris, Ph.D., Acting Chief

Enteric Diseases Unit . . . . . Wallis E. DeWitt, M.S., Chief

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I. SUMMARY

For the 2nd quarter of 1972, 3,514 shigella isolations from humans were reported. This represents an increase of 716 (25.6%) over the 2,798 isolations reported for the preceding quarter, and an increase of 277 (8.6%) over the 3,237 isolations reported for the same quarter 1 year earlier (Table I).*

II. REPORTED ISOLATIONS

A. Human

1. General Incidence. For the 2nd quarter of 1972, 66.1% of reported isolations were from children under 10 years of age (Table II); this is consistent with previous quarters. The highest attack rate was in the age group 1-4 years and the 2nd highest attack rate was in the age group under 1 year.

2. Serotype Frequencies. Fifty-one of the 54 reporting centers in the Shigella Surveillance Program reported isolations of shigella; 22 different serotypes were reported (Table I). The 6 most frequently reported serotypes for the 3-month period were the following (Table 1).

Table 1

Rank	Serotype	Number Reported	Calculated Number**	Calculated Percent**	Rank Last Quarter
1	S. sonnei	2,782	2,831	80.5	1
2	S. flexneri 2a	118	205	5.8	3
3	S. flexneri 6	99	131	3.7	4
4	S. flexneri 3a	66	116	3.3	2
5	S. flexneri 4a	34	51	1.5	5
6	S. flexneri 2b	27	47	1.3	7
Subtotal		3,126	3,381	96.1	
Total (all serotypes)		3,514	3,517		

**Table III

Table III is calculated from data compiled during the 2nd quarter of 1972. This table shows the frequencies 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 frequencies of reporting of the more common shigella serotypes in the United States. S. sonnei accounted for approximately 79% of all reported isolations. Table IV shows the distribution of shigella serotypes reported from mental institutions.

3. Geographical and Seasonal Observations. There were more reported isolations of S. sonnei than S. flexneri in all but 5 states--Montana (4:4), South Dakota (3:8), Mississippi (1:7), South Carolina (1:1), and Arizona (53:82) (Figure 1). This trend 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.

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

Figure 3 shows the number of reported isolations per million population by state for April-June utilizing 1970 census figures. Approximately 17.2 isolations per million population were reported during the 2nd quarter of 1972.

Table IV shows the general type of residence of those patients from whom shigella was isolated.

Figure 1 PERCENTAGE *S. flexneri* AND *S. sonnei* OF TOTAL SHIGELLA ISOLATIONS REPORTED FROM INDICATED REGIONS UNITED STATES, APRIL – JUNE 1972

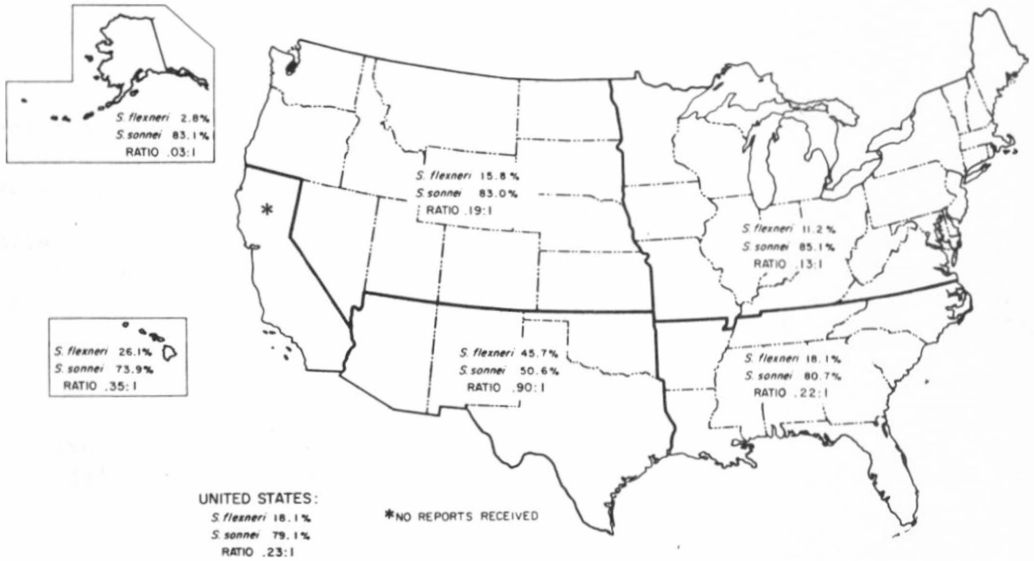
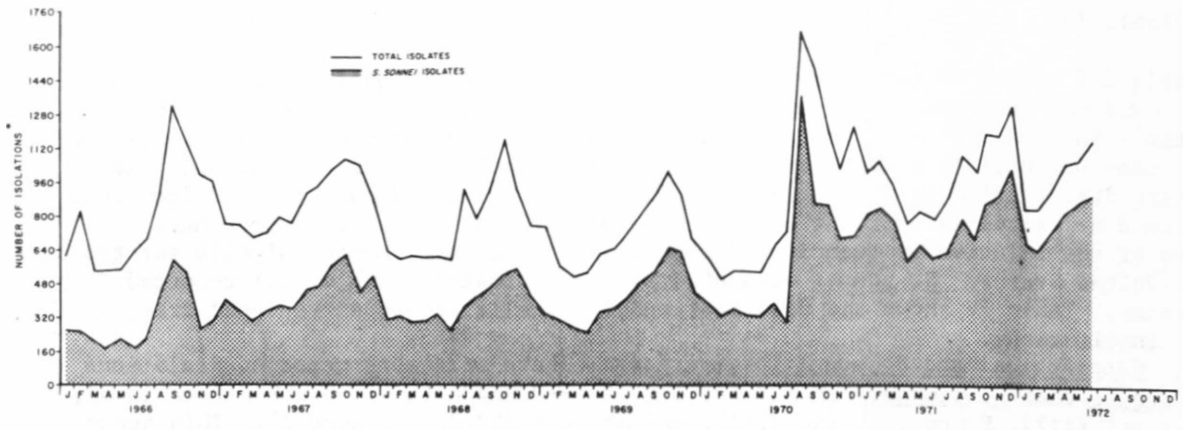
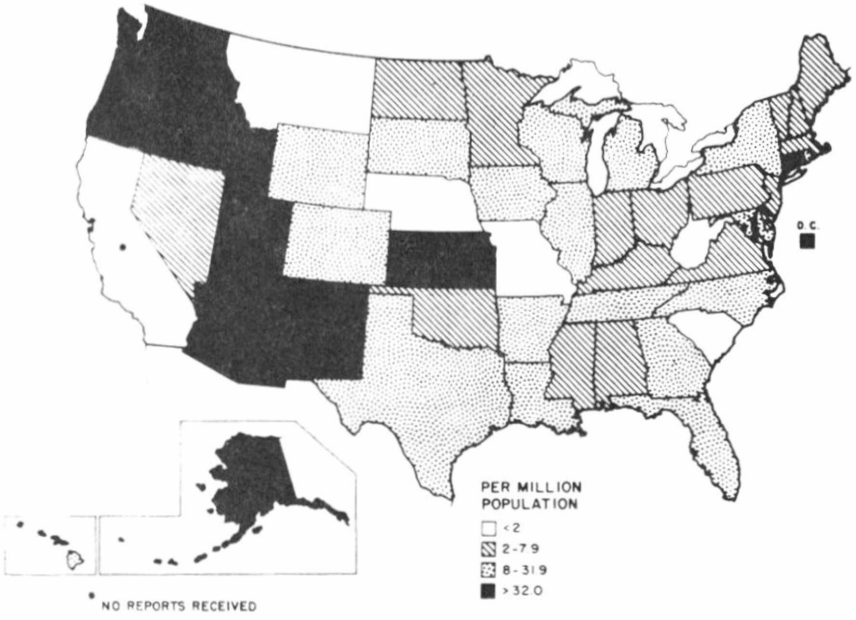


Figure 2 REPORTED ISOLATIONS OF SHIGELLA IN THE UNITED STATES



* ADJUSTED TO 4-WEEK MONTH

Figure 3 ATTACK RATES OF SHIGELLOSIS, BY STATE, APRIL – JUNE 1972



B. Nonhuman

During the 2nd quarter of 1972, 13 isolations from nonhumans were reported. Most of these were from primates:

Table 2

Serotype	Number	Source	State
S. flexneri 2a	1	monkey	Hawaii
	1	monkey	Illinois
S. flexneri 4	2	monkey	Georgia
S. flexneri 4a	1	monkey	Texas
S. flexneri 4b	1	monkey	Connecticut
	1	monkey	Illinois
	1	monkey	Louisiana
S. flexneri 6	1	unspecified animal	Illinois
S. sonnei	1	monkey	Hawaii
	1	cat	Idaho
	1	dog	Idaho
	1	monkey	Maryland

III. CURRENT TOPICS

A. The Changing Status of Antimicrobial Therapy for Shigellosis

It is well established that appropriate antimicrobial therapy is effective in the treatment of shigellosis.[1] Recent studies have shown that antibiotics will significantly decrease the duration of diarrhea and excretion of shigellae in the stool, and will abbreviate the clinical course of both mild and severe disease.[2,3]

In the early 1940s the sulfa drugs were introduced as therapy for bacillary dysentery, and they rapidly became the treatment of choice. As early as the mid-1940s however, many workers began to note increasing sulfa resistance of shigella isolates. By 1949, sulfonamides had become virtually ineffective against shigella in Japan because of resistance,[4] and a study of almost 1,500 cases in Korea in 1953[5] showed almost all strains to be sulfa-resistant, reflecting a worldwide trend.

The tetracyclines enjoyed a brief period of preference, but the next major breakthrough in the antibiotic management of shigellosis came with the discovery of ampicillin, and its use became widespread in the 1960s. In 1967 Nelson and Haltalin[2] compared ampicillin with placebo in the therapy of hospitalized children in Texas with shigellosis and found significant differences both clinically and bacteriologically. The antibiograms of the shigella isolates showed 63% resistance to sulfa, 12% resistance to tetracycline, and 11% resistance to chloramphenicol, but only 3% resistance to ampicillin. Between 1961 and 1964, shigella isolations also showed about 3% of strains resistant to ampicillin. The low level of ampicillin resistance noted in Texas[2,3] was initially the same as that found in Atlanta[10] and elsewhere.

Ampicillin therapy resulted in bacteriologic clearing of the stool in 61-94% of cases within 48 hours and in virtually all within 1 week[2,6] as opposed to a 75% bacteriologic failure rate in patients treated with placebo. Relapse or late convalescencent carriage occurred only rarely in ampicillin-treated patients. However, although ampicillin was effective in the treatment of individual cases in large epidemics, it appeared of dubious value as a chemoprophylactic agent; the traditional practice of isolation of infected persons was still necessary to abort an outbreak.[7] Adequate antibiotic therapy was effective, on the other hand, in the treatment of the individual asymptomatic carrier.[8] (One should not confuse this treatment with that for salmonellosis where antibiotic therapy will actually prolong the excretion of salmonellae.[9]) In general, then, while ampicillin proved its worth in the treatment of clinical cases, its use in epidemic situations, in treatment of contacts or persons who were asymptomatic, was not encouraging.

Some shigellae are known to be multiply drug resistant, including ampicillin resistant, and in vitro R factor transfer from Escherichia coli to shigella had been demonstrated. In Japan more than 50% of all shigella isolates became resistant to ampicillin by 1969.[12]

Despite these trends abroad and despite the widespread use of ampicillin, low levels of resistance persisted in this country, and as late as 1970 it was stated that "...it would appear that R factors are not as important in promoting resistance in shigellae in some areas as they have been reported to be elsewhere."[3]

In the years 1967-1971, marked increased in ampicillin resistance were noted in shigella isolates in Washington, D.C., reaching 95% by 1971, compared with 8% in 1967 in the population which was studied. Increases in resistance to the cephalosporins, tetracyclines, streptomycin, and carbenicillin, though less pronounced, were also noted. In Tennessee, increasing ampicillin resistance was also reported[14] with about ½ of the isolates showing multiple drug resistance in 1971 compared with 6% in 1967.

In a recent communication, Haltalin has confirmed increasing ampicillin resistance in Dallas isolates in the first 10 months of 1972, 25% for S. sonnei compared with 1% in 1971, 14% for S. flexneri, up from 7% the previous year.[15] He further states that "ampicillin is less useful than formerly thought and cannot be regarded as the drug of choice for shigellosis in all areas of the country."

It is not unreasonable to assume that the rapid increase in ampicillin resistance that often occurs coincident with multiple antibiotic administration may be consequent to the acquisition of episomal material from gut bacteria. As Ross[13] pointed out, multiple antibiotic resistance may develop rapidly after antibiotic administration in previously sensitive enteric organisms which receive R factors from resistant bacteria. The use of broad spectrum drugs such as ampicillin results in major changes in the normal enteric flora and consequently exerts selective influence on sensitive organisms which can more successfully survive by conjugating with resistant strains and acquiring genetic material which confers resistance.

In choosing the appropriate antibiotic to treat shigellosis, it should be borne in mind that in the average case shigellosis is a self-limited, relatively mild illness in which bacteriologic clearing of the stool occurs in 30-70% of untreated patients within a week of onset of disease and in which long-term carriage (and shedding) of shigella is uncommon (Hardy and Halbert, 1948; Hardy, et al, 1952; Garfinkel, 1953).[6] It is unjustified, therefore, to treat mild cases of shigellosis when toxic drugs or drugs with significant potential toxicity are the only effective antimicrobials

demonstrated *in vitro*. Antimicrobial therapy should be reserved for patients whose illness is severe enough to warrant the hazards of the appropriately effective drugs.

In deciding on the proper therapeutic agent after the decision to treat has been made, one should also consider that *in vitro* sensitivities may not correlate well with *in vivo* action. Specifically, non-absorbable antibiotics, when administered orally, may be ineffective,[16] probably reflecting the pathogenesis of shigellosis in which penetration of the colonic epithelium is essential. Drugs such as oral kanamycin or neomycin, for example, would not be optimal agents regardless of *in vitro* susceptibilities.

The somewhat discouraging history of antimicrobial therapy for shigellosis again points to the preeminent roles of isolation, sanitation, and adequate hygiene in the control of this disease. The effectiveness of an appropriate drug in the treatment of the single clinical case is insufficient for the prevention or control of epidemic disease.

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3. Haltalin KC, Kusmiesz HT, Hinton LV, et al: Treatment of acute diarrhea in outpatients. Double-blind study comparing ampicillin and placebo. Am J Dis Child 124:554-561, 1972
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14. Harbin RL, Ratner HB, Schaffner W: Increasing resistance of shigellae to antibiotics. J Tennessee Med Assoc 65:999, 1972
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16. Haltalin KC, Nelson JD, Hinton LV, et al: Comparison of orally absorbable and non-absorbable antibiotics in shigellosis. J Pediat 72:708, 1968

IV. REPORTS FROM THE STATES

A. *Shigellosis, San Francisco, California.*

Reported by Selma K. Dritz, M.D., Associate Director, Bureau of Disease Control; Francis J. Curry, M.D., Director of Public Health; and John Garcia, Ph.D., Acting Chief, Microbiology Laboratory, San Francisco Department of Public Health.

For the 1st quarter of 1972, 78 cases of shigellosis due to *S. sonnei* were reported to the San Francisco Department of Public Health, representing a sharp increase over the 10 cases reported for the 1st quarter of 1971, and the 116 cases reported in all of 1971; 47 cases were reported in 1970. Although reportable under California law, shigellosis reporting is considered to be incomplete but consistent over recent years.

All areas of the city reported cases, without discernable patterns. The incidence of disease was somewhat higher in the lower income areas, but the difference between these areas and the rest of the city was not statistically significant. The greatest number of cases were reported at the end of January. There was no evidence for a common source, and no evidence of imported disease in recently returned travelers. Two of the cases investigated occurred in food handlers, but there was no evidence that any secondary cases resulted from exposure to these individuals. Cases clustered within households frequently. Inadequate sanitation did not appear to be a common factor in the cases, although crowding was.

In 9 of the households investigated, the index cases occurred in children under 12 years of age, 3 of whom attended the same school. There were 35 secondary cases in the homes of these 9 youngsters, 12 of which were culture-confirmed. In all, they accounted for 56.4% of the total cases reported for the quarter; children under 12 accounted for 60.2% of the 78 cases reported.

Editorial Comment: This report, based upon San Francisco Department of Public Health surveillance data, is illustrative of a continuing trend in the Pacific coastal states of Washington, Oregon, and California, where shigella isolates have increased markedly in the past year. In Washington and Oregon, shigella isolates have increased in each corresponding quarter of 1972, compared with 1971 (Table 3). In the 1st half of 1972, the number of isolates increased in Washington State by a factor of 2.5 over the 1st half of 1971, and by a factor of 8.3 in Oregon.

Table 3

Shigella Isolations

	1st Qtr 1972	2nd Qtr 1972	1st Qtr 1971	2nd Qtr 1971
Washington	56	186	55	42
Oregon	155	87	5	24

As in California, there was nothing to suggest a common source, likewise there was little available data to implicate any of the common factors (apart from overcrowding), such as poor sanitation, contaminated water supplies, institutional environment and the like, often associated with shigellosis. Preliminary data from Washington State shows a pattern of 6-7 year cyclic peaking in the incidence of shigellosis, however, the reason is not well understood.

In the investigation of focal increases in S. sonnei, the predominant serotype in the U.S. currently, colicin typing and other differentiating methods may prove helpful in defining the problem.[1]

Reference:

1. Reller LB: Colicin typing as an epidemiological tool. Appl Microbiol 21:21-26, 1971

B. Shiga dysentery, Fort Worth, Texas

Reported by Kenneth C. Haltalin, M.D., Associate Professor of Pediatrics, Department of Pediatrics, University of Texas, Southwestern Medical School at Dallas; M.S. Dickerson, M.D., Chief, Communicable Disease Services Section, Texas State Department of Health; and Louis A. Lobes, M.D., EIS Officer located in St. Louis, Missouri.

On May 21, 1972, in Fort Worth, Texas, a 14-month-old Latin American boy developed fever and diarrhea. Two days later, on the morning of May 23, he was seen in the emergency room of a local hospital because his diarrhea had worsened, and fever persisted. He had passed 12 watery stools containing blood and mucus in the preceding 24 hours and had vomited twice. Although acutely ill with a temperature of 102° F, the patient did not appear toxic. He was admitted to the hospital in mid-afternoon

with a diagnosis of probable shigellosis. A rectal swab was obtained, and he was placed on clear liquids by mouth. Ampicillin (250 mg IM q6h) was prescribed. Five hours after admission, before the patient had received the prescribed ampicillin, he was transferred to another hospital in Grand Prairie, a nearby town, at the insistance of his parents.

At the 2nd hospital, he was treated for gastroenteritis with clysis, and received an injection of bicillin and chloramphenicol palmitate. No specimens were obtained. On May 28, the patient experienced a generalized seizure which was treated with valium intravenously. That same day his mother had onset of bloody diarrhea, chills, and fever. A stool specimen was obtained for culture.

The patient was transferred to Children's Medical Center of Dallas in the early morning of May 29. On admission there he was pale, cool, comatose, and showed evidence of decerebrate posturing. His abdomen was distended, bowel sounds were absent, and he was passing grossly bloody urine. Admission laboratory values included a hemoglobin of 11.4 gm %, white blood count 64,800 cells/mm^3, BUN 10 mg %, sodium 112 mEq/liter, calcium 6.1 mEq/l, potassium 5.7 mEq/l; urinalysis showed 50-75 red blood cells per high power field. Serologic and rectal swab specimens were obtained for culture, and parenteral therapy with ampicillin and gentamicin was begun. On May 30, the hemoglobin dropped to 7.3 gms%, the platelets to 9,000, and the BUN began to rise.

The child's sensorium was still very clouded, and a diagnosis of metabolic encephalopathy secondary to hyponatremia was considered. Abdominal distention persisted with the frequent passage of small bloody stools. On May 31, he was seen by a surgical consultant because of the severity of the abdominal distention and diarrhea. A barium enema was performed June 1. Findings were consistent with ulcerative colitis and toxic megacolon. On June 1, the patient was evaluated by the Infectious Disease Service who felt the child's illness was compatible with severe shigellosos possibly due to Shiga's bacillus. The child's subsequent course was complicated by a severe hemolytic-uremic syndrome requiring transfusions of 9 units of packed red blood cells. He received the last transfusion June 8, the day on which his BUN peaked at 181 mg%.

By June 25 his hemoglobin had stabilized and his renal status had improved, but serious neurologic sequellae persisted. Over the next 3 days his renal status remained stable while his neurologic status greatly improved. The patient was discharged on June 29.

Rectal swabs obtained in the 1st hospital from the child, and from the mother when the child was in the 2nd hospital both grew S. dysenteriae 1 which was resistant to chloramphenicol, sulfadiazine, streptomycin, and tetracycline, but sensitive to ampicillin. Stool and blood specimens obtained from the patient on admission to the hospital in Dallas did not grow shigella. A stool specimen obtained from his mother on June 1 was also negative, as were specimens from both persons after 5 days of ampicillin therapy.

The patient, his parents, and his grandparents had not left the United States in recent years. On May 8, however, friends who had recently returned from San Luis, Mexico, visited the patient and his family; these friends stayed for several days. While they were visiting, their 16-month-old child experienced fever, irritability, anorexia, and diarrhea of several days duration; her illness was treated symptomatically. Shortly thereafter, the patient's 4-year-old sister had onset of anorexia, fever, and diarrhea with mucus, alternating with constipation. Her illness persisted for 8-10 days and ended spontaneously without specific therapy.

Serum specimens were obtained from the patient's family, the grandparents, and the visiting family on June 26. Titers of S. dysenteriae 1 antibodies were elevated ($\geq$1:40) in the serum specimens from the patient's mother and sister, and the mother of the visiting family. Stool specimens from the 2 families were negative.

Editorial Comment: Beginning in 1968 an epidemic of dysentery caused by S. dysenteriae 1 was noted in many Central American countries. Since 1970, increasing numbers of cases of shigellosis due to Shiga's bacillus have occurred

in the United States, with 42 cases in 1971 compared with 28 in 1970. The 4 states bordering Mexico accounted for 46% of cases in 1970 and 91% of cases in 1971. Perhaps more significant than proximity to Mexico is the fact that in 1970, 82% of cases had a history of recent travel outside the United States whereas in 1971 only 48% gave such a history. These changes in the epidemiology of Shiga's bacillus suggest that transmission of this disease is occurring in the United States.

This case is illustrative of this point. The patient seems clearly to have been infected within the United States by exposure to a member of the visiting family who had just returned from Mexico. It is probable that his mother and sister acquired their illnesses from the same source. This is supported by the incubation period (usually 5-7 days) and the serologic evidence.

It is important to emphasize that this disease, although still rare in the United States, is occurring with increasing frequency. Its severity compared with other forms of shigellosis, as well as its infrequency, often lead to delays and confusion in diagnosis. Most commonly confused with Shiga dysentery are ulcerative colitis, amebiasis, and "non-specific gastroenteritis."

Although ampicillin resistance has been an increasing problem in the treatment of other forms of shigellosis, S. dysenteriae 1 strains have to date been universally sensitive to ampicillin; however, multiple resistance to other antibiotics is frequently encountered in S. dysenteriae 1. This resistance has been shown to be due to an R factor.

C. Institutional Shigellosis, Massachusetts.

Reported by Nicholas J. Fiumara, M.D., Director, and George E. Waterman, M.D., Assistant Director, Division of Communicable Diseases, Massachusetts Department of Public Health; and David Freeman, M.D., EIS Officer located at the Massachusetts Department of Public Health.

In mid-April 1972, an outbreak of shigellosis was reported from a school for the mentally retarded in Massachusetts. Within 3 months, 97 of 1,437 residents at the school had clinical illness with symptoms of fever, sometimes up to 105° F, and watery, occasionally bloody diarrhea. Stool specimens from 36 of the affected individuals were positive for S. flexneri 2a.

Epidemiological investigations disclosed that the illness was confined primarily to 5 of 20 resident buildings, with 91% of cases limited to those facilities. In total, 9 resident buildings were involved. Although the epidemic continued for 24 weeks (Figure 4), the 5 most heavily infected houses were affected sequentially, in each building about 90% of total cases occurring within a different 3-4 week interval (Table 4).

Figure 4

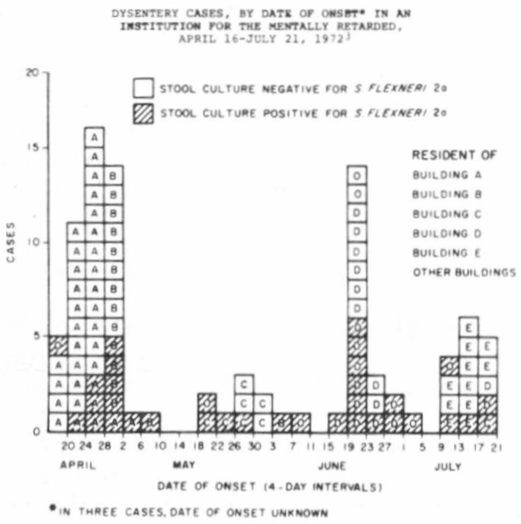

Table 4

Diarrheal Illness at a Custodial Institution, Massachusetts
April 1972

	Bldg A	Bldg B	Bldg C	Bldg D	Bldg E
Total Cases	33	15	8	20	11
Peak of outbreak (weeks)	1-3	4-6	9-12	16-19	22-24
Number of cases during peak weeks	31	14	7	18	11
Percent of cases during peak weeks	94%	93%	88%	90%	100%

Clinical attack rates ranged from 2 to 36%, with an overall attack rate of 6.8% for the entire institution. For culture proven cases, the age specific attack rate was 2.9%, below age 35, and 1.2% for the older residents. Analysis by degree of mental retardation showed that the epidemic involved exclusively those individuals classified as moderately to severely retarded.

Of the 9 buildings in which cases occurred, 4 were residences housing ambulatory but severely retarded patients. There were fewer cases in non-ambulatory residents.

Editorial Comment: Shigellosis is frequently endemic or epidemic in mental institutions and presents a continuing problem in caring for the mentally retarded. In 1967, 9% of 11,405 shigella isolates reported to the CDC came from mental institutions.[1] A survey of mental institutions representing 75% of this country's total institutionalized population disclosed that over 2/3 considered shigellosis a serious problem at those facilities.[2]

As is illustrated by this report, outbreaks are often confined primarily to those buildings which house the most severely retarded who present the greatest difficulties in maintaining adequate hygiene. Spread is usually by person-to-person transmission. In this epidemic, however, separate explosive outbreaks in 5 buildings over a 4-month period suggested the possibility of common source outbreaks in each building, although person-to-person spread within houses may have played a role. The mode of spread between buildings was not demonstrated, but patients from different buildings have varying degrees of contact with one another and personnel may visit several buildings during the day.

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V. INTERNATIONAL NOTES

A. Transferable Multiple Antibiotic Resistance, Melbourne, Australia.[1]

The authors examined 48 antibiotic-resistant shigella species which had been isolated from patients at a mental institution in Melbourne, Australia, between 1952 and 1968. (These cultures had been lyophilized and stored at the time they were obtained.) By conjugating these organisms with sensitive E. coli and subsequently testing the E. coli for resistance to a variety of antibiotics, they were able to show that 42 of the 48 shigella strains examined donated their entire resistance patterns to their E. coli recipients at a rate too great to be explained by

spontaneous mutation. Antibiotic resistance was transferable from the E. coli, now acting as donors, to other E. coli recipients, again transferring the entire antibiotic resistance pattern (Table 5). There were 5 strains resistant to sulfonamides and 1 resistant to streptomycin in which resistance was not transferable. The authors felt the ability to transfer the entire pattern of antibiotic resistance represented evidence of the presence of R factors in the shigellae (Table 6).

Table 5

Transfer of Resistance Determinants by Shigella
In Melbourne Institutions, 1952-1968

Year of Isolation	Number of Strains Examined	Drug Resistance Pattern	Number of Strains With Pattern	Number Transferring Resistance
1952	2	Su	2	2
1955-56	7	Su	4	4
1958-59	14	S,T,C,Su	1	1
		S,C,Su	8	8
		*Su	2	1
1963	5	S,T,C,Su	1	1
		T,Su	1	1
		**S	1	-
1967-68	47	S,T,C,Su	17	17
		S,C,Su	3	3
		S,Su	3	3
		T	1	1
		*Su	4	-
TOTAL	75		48	42

S = streptomycin, T = tetracycline, C = chloramphenicol
Su = sulfathiazole
*Strain resistant to sulfathiazole not transferring resistance determinants
**Strain resistant to streptomycin not transferring resistance determinants

Adapted from Davey and Pittard[1]

Table 6

Patterns of Resistance Transfer

Number of Drugs Resistant	Number of Strains	Number Transferring Resistance	Percent Transferring Resistance
1	14	8	57%
2	4	4	100%
3	11	11	100%
4	19	19	100%
1-4	48	42	87.5%
>1	34	34	100%

Data from Davey and Pittard[1]

Historically, antibiotic therapy at the institution investigated had been confined to culture-proven cases and included chloramphenicol, nitrofurantoin, ampicillin, and other drugs. Streptomycin and tetracylcine, while not employed in treatment of shigellosis, were frequently used in the therapy of other illnesses. The authors felt that the R factors identified in the isolates which were studied did not originate within the institutional setting because some appeared chronologically before the widespread use of the antibiotics to which resistance was conferred. The R factors identified, they felt, were probably part of an individual's microflora at the time of admission.

Editorial Comment: The occurrence of multiple antibiotic-resistant shigella has become a problem of significant concern to clinicians who may be faced with a limited range of perhaps toxic drugs to which the organism in question is sensitive. The problem has been discussed in detail elsewhere in this issue (see "Current Topics" p 3). Multiple drug resistance has been shown to be carried and transferred by an episome.[2] In a single epidemic, a given shigella strain may be completely sensitive in some patients and multiply resistant in others; in fact, the same person may excrete both sensitive and multiply resistant bacteria at the same time.

The microbiology of R factors has been investigated in detail.[3,4] Still unexplained is the origin of these bits of extrachromosomal genetic material. It seems clear that R factors did not arise as a consequence of antibiotic administration, although their widespread use has contributed to the exponentially increasing isolation of these factors. The evidence for their preexistence is supported by the Australian paper discussed here, in which the appearance of R factors antedated the use of antibiotics to which resistance was conferred. Watanabe has proposed that the definitive evidence to support this concept would be to identify R factors within an "antibiotic virgin" population which had never been exposed either directly (through drug administration) or indirectly (through food or contact) to antimicrobial agents. Three such populations have been identified.[4] A group of Kalahai bushmen in Rhodesia who had had no contact with humans for 10 years, had drug resistant gram negative bacteria in 57 of 582 stool specimens examined, but none with R factors. On the other hand, in an isolated community on the Solomon Islands, an R factor was isolated from 1 of 21 stool specimens and 1 of 19 soil specimens examined, each conferring resistance to streptomycin and tetracycline. One hundred twenty eight stool specimens from villagers in North Borneo disclosed 6 bacterial species with R factors (Table 7).

Table 7

R Factors from Villagers in North Borneo[4]

Number of Strains	R Factor
2	Su-S-C-T
3	Su-S-T-A
1	Su-S-C-T-A

Su=Sulfa, S-Streptomycin,
C=Chloramphenicol, T=Tetracycline,
A=Ampicillin

If R factors conferring resistance to antimicrobials antedate the antimicrobials themselves, it is not unreasonable to expect that such factors would not be "discovered" until the discovery of the antibiotics to which resistance was conferred. However, most antibiotics are produced by soil organisms, and naturally occurring antibiotics are ubiquitous in nature; hence, it is possible that the presence of an R factor in an organism may have protected it from trace antibiotics in the environment, a function of an R factor which would have insured its evolutionary survival. Resistance to the sulfa drugs, however, would not be explained by such a hypothesis. (Sulfonamides do not occur spontaneously in nature.)

Another possibility, admittedly speculative, is that the enzymes produced by R factor carrying bacteria (e.g. penicillinase) may have properties other than catalyzing antibiotic inactivation; hence, they would be of use to their hosts for an additional, as yet unexplained, purpose.

Whatever its value to the host, either currently or in the course of evolution, the origin of a "first" R factor and whether or not all R factors are descendants from a single episomal parent are questions that still remain unanswered.

References:
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TABLE I
SHIGELLA SEROTYPES ISOLATED FROM HUMANS
SECOND QUARTER, 1972

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	
A. *S. dysenteriae*																																						
1																										0												0	0
2				1							1															2										1		1	3
4																										0												0	0
9																										0												0	0
Total	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	1	0	1	3
B. *S. flexneri*																																						
Unspecified	2		3		3	2				1	21		9		1	10	2	12		1			4			71	13							7	8		1	29	100
1 Unspecified									1																1	2									1	4	5	7
1A				1						1	1															3												0	3
1B																										0		1										1	1
2 Unspecified									5		1														2	8			1						4	8		13	21
2A	2			15						10	1	1							2							31		2	5	1		2						10	41
2B				1																						1		6	3									9	10
3 Unspecified									1				2		1										1	5			2							4		6	11
3A	1			34																						35												0	35
3B																										0												0	0
3C											1	2														3												0	3
4 Unspecified																										0										1		1	1
4A				1						1	1								1							4			2							5		7	11
4B												1														1			1							8		9	10
5				2																						2		1										1	3
6	1			5					3		1															10			4	3		1			1	6		15	25
Variant Y																										0		2										2	2
Total	6	0	3	59	3	2	0	0	10	13	27	4	11	0	2	10	2	12	3	1	0	0	4	0	4	176	13	12	18	4	0	0	3	7	8	19	23	1	108	284
C. *S. boydii*																																						
Unspecified																										0				1					1			2	2
2			1																							1										4		4	5
4																										0												0	0
7																										0												0	0
9																										0										1		1	1
14																										0												0	0
Total	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		1	0	0	0	0	1	0	0	0	1	1	4	0	7	8
D. *S. sonnei*	156	1	86	152	29	76	10	15	107	19	125	7	112	6	16	18	36	145	42	26	11	1	60		81	1,337	48	51	152	4		3		80	3	64	158	4	567	1,904
Unknown			49															7								56												0	56
TOTAL	162	1	139	212	32	78	10	15	117	32	153	11	123	6	18	28	38	164	45	27	11	1	64	0	85	1,572	61	63	170	8	1	3	3	87	12	84	186	5	683	2,255

TABLE I (CONTINUED)
SHIGELLA SEROTYPES ISOLATED FROM HUMANS
SECOND QUARTER, 1972

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		
																										A. *S. dysenteriae*
									0	1			2	3	3					0	3	0.1	1	0.0	1
2		2							4	1			1	2	6					0	9	0.3	4	0.1	2
									0	1			1	2	2					0	2	0.1			4
									0	1				1	1					0	1	0.0			9
2	0	2	0	0	0	0	0	0	4	4	0	0	4	8	12	0	0	0	0	0	15	0.4	10	0.4	Total
																										B. *S. flexneri*
		3			7	1	1		12		26	1	3	30	42	2		1		3	145	4.1	127	4.5	Unspecified
									0		6			6	6					0	13	0.4	10	0.4	1 Unspecified
									0	2			10	12	12					0	15	0.4	17	0.6	1A
	2			3					5	4			4	8	13					0	14	0.4	3	0.1	1B
3		4	13			4			24				1	1	25					0	46	1.3	45	1.6	2 Unspecified
	8			4				3	15	30		1	26	57	72			5		5	118	3.4	88	3.1	2A
								2	2	4			11	15	17					0	27	0.8	16	0.6	2B
1		5	1						7		6			6	13					0	24	0.7	24	0.9	3 Unspecified
				2				8	10	14			7	21	31					0	66	1.9	105	3.8	3A
									0	3				3	3					0	3	0.1	3	0.1	3B
									0				3	3	3					0	6	0.2	4	0.1	3C
			1						1		4			4	5					0	6	0.2	6	0.2	4 Unspecified
				3				1	4	14			5	19	23					0	34	1.0	40	1.4	4A
	2								2				1	1	3					0	13	0.4	2	0.1	4B
									0		2		1	3	3					0	6	0.2	3	0.1	5
		37	4						41	11	3		19	33	74					0	99	2.8	72	2.6	6
									0					0	0					0	2	0.1			Variant Y
4	12	49	19	12	7	5	1	14	123	82	47	2	91	222	345	2	0	6	0	8	637	18.1	565	20.2	Total
																										C. *S. boydii*
									0					0	0					0	2	0.1	2	0.1	Unspecified
		1							1				6	6	7					0	12	0.3	4	0.1	2
									0	1				1	1					0	1	0.0	1	0.0	4
									0				1	1	1					0	1	0.0			7
									0					0	0					0	1	0.0			9
									0	2				2	2					0	2	0.1			14
0	0	1	0	0	0	0	0	0	1	3	0	0	7	10	11	0	0	0	0	0	19	0.5	10	0.4	Total
16	23	165	123	67	1	81	1	70	547	53	70	13	110	246	793	67		17		84	2,781	79.1	2,181	77.9	D. *S. sonnei*
					3				3						3	3				3	62	1.8	32	1.1	Unknown
22	35	217	142	79	11	86	2	84	678	142	117	15	212	486	1,164	72	0	23	0	95	3,514		2,798		TOTAL

Table II

Age and Sex Distribution of Individuals Infected With Shigella in the United States, 2nd Quarter, 1972

Age (Years)	Male	Female	Unknown	Total	Percent	Cumulative Percent	Number of Reported Isolations/ Million Population*
<1	63	56		119	5.1	5.1	34.1
1-4	449	401	3	853	36.7	41.8	62.4
5-9	264	301	1	566	24.3	66.1	28.4
10-19	171	141		312	13.4	79.5	7.8
20-29	75	175		250	10.7	90.2	8.4
30-39	46	77		123	5.3	95.5	5.5
40-49	21	25		46	2.0	97.5	1.9
50-59	7	17		24	1.0	98.5	1.1
60-69	6	10		16	.7	99.2	1.0
70-79	4	9		13	.6	99.8	1.4
80 +		5		5	.2	100.0	1.3
Subtotal	1106	1217	4	2327			
Child (unspec)	15	7	2	24			
Adult (unspec)	3	12		15			
Unknown	563	572	13	1148			
TOTAL	1687	1808	19	3514			
Percent	48.3	51.7					

*Based on 1970 Census of Population, General Population Characteristics, United States Summary, Table 52, issued January 1972

Table III

Relative Frequencies of Shigella Serotypes
Reported, 2nd Quarter, 1972

	Serotype	Number Reported	Calculated Number *	Calculated Percent*	Rank
A.	S. dysenteriae				
	unspecified				
	1	3	3	.09	15
	2	9	9	.26	12
	4	2	2	.06	16
	9	1	1	.03	17
B.	S. flexneri				
	unspecified	145			
	1 unspecified	13			
	1a	15	29	.82	7
	1b	14	27	.77	8
	2 unspecified	46			
	2a	118	205	5.83	2
	2b	27	47	1.34	6
	3 unspecified	24			
	3a	66	116	3.30	4
	3b	3	5	.14	14
	3c	6	11	.31	11
	4 unspecified	6			
	4a	34	51	1.45	5
	4b	13	19	.54	9
	5	6	8	.23	13
	6	99	131	3.72	3
	Variant Y	2	3	.09	15
C.	S. boydii				
	unspecified	2			
	2	12	14	.40	10
	4	1	1	.03	17
	7	1	1	.03	17
	9	1	1	.03	17
	14	2	2	.06	16
D.	S. sonnei	2781	2831	80.49	1
	unknown	62			
	TOTAL	3514	3517		

*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, 2nd Quarter, 1972

State	dysenteriae 2	flexneri (unspecified)	flexneri 2 (unspecified)	flexneri 2a	flexneri 2b	flexneri 3 (unspecified)	flexneri 3a	flexneri 5	flexneri 6	sonnei	Total
Alabama	2	0	0	0	0	0	0	0	0	3	5
Florida	2	0	0	0	0	0	0	0	37	3	42
Georgia	0	0	10	0	0	0	0	0	0	0	10
Illinois	0	0	0	6	1	0	19	2	0	13	41
Iowa	0	0	0	0	0	0	0	0	0	11	11
Kansas	0	0	0	0	0	0	0	0	0	68	68
Massachusetts	0	0	0	9	0	0	0	0	0	0	9
Michigan	0	13	0	0	0	0	0	0	0	0	13
Missouri	0	3	0	0	0	0	0	0	0	0	3
New Jersey	0	0	0	0	0	1	0	0	0	2	3
New York	0	2	0	0	0	0	0	0	0	0	2
Pennsylvania	0	0	0	0	0	0	0	0	0	1	1
Virginia	0	1	0	0	0	0	0	0	0	0	1
Wisconsin	0	0	0	0	0	0	0	0	0	36	36
Total	4	19	10	15	1	1	19	2	37	137	245

TABLE V

Sources of Reported Isolations of Shigella
By Residence at Time of Onset
2nd Quarter, 1972

Source	Apr	May	Jun	Total	Percent of Subtotal	Percent of Total
Mental institutions	76	74	95	245	14	
Indian reservations	13	6	11	30	2	
Other residencies	474	512	465	1478	84	
Subtotal	563	592	571	1753		50
Residencies unknown	483	733	520	1761		50
Total	1046	1325	1091	3514		

STATE EPIDEMIOLOGISTS AND STATE LABORATORY DIRECTORS

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.

STATE	*STATE EPIDEMIOLOGIST*	*STATE LABORATORY DIRECTOR*
	Frederick S. Wolf, M.D.	Thomas S. Hosty, Ph.D.
Alaska	Donald K. Freedman, M.D.	Frank P. Pauls, Dr.P.H.
Arizona	Philip M. Hotchkiss, D.V.M.	H. Gilbert Crecelius, Ph.D.
Arkansas	G. Doty Murphy, III, M.D.	Robert T. Howell, Dr.P.H.
California	James Chin, M.D.	Edwin H. Lannette, M.D.
Colorado	Thomas M. Vernon, Jr., M.D.	C. D. McGuire, Ph.D.
Connecticut	James C. Hart, M.D.	William W. Ullmann, Ph.D.
Delaware	Maynard H. Mires, M.D.	Mahadeo P. Verma, Ph.D.
District of Columbia	William E. Long, M.D.	Alton Shields, Dr.P.H.
Florida	Ralph B. Hogan, M.D.	Nathan J. Schneider, Ph.D.
Georgia	John E. McCroan, Ph.D.	Earl E. Long, M.S.
Hawaii	Ned Wiebenga, M.D.	George Chen
Idaho	John A. Mather, M.D.	Owen L. Carpenter
Illinois	Byron J. Francis, M.D.	Richard Morrissey, M.P.H.
Indiana	Charles L. Barrett, M.D.	Josephine Van Fleet, M.D.
Iowa	Arnold M. Reeve, M.D.	W. J. Hausler, Jr., Ph.D.
Kansas	Don E. Wilcox, M.D.	Nicholas D. Duffett, Ph.D.
Kentucky	Calixto Hernandez, M.D.	B. F. Brown, M.D.
Louisiana	Charles T. Caraway, D.V.M.	George H. Hauser, M.D.
Maine	Timothy R. Townsend, M.D. (Acting)	Charles Okey, Ph.D.
Maryland	John D. Stafford, M.D.	Robert L. Cavenaugh, M.D.
Massachusetts	Nicholas J. Fiumara, M.D.	Morton A. Madoff, M.D.
Michigan	Norman S. Hayner, M.D.	Kenneth R. Wilcox, Jr., M.D.
Minnesota	D. S. Fleming, M.D.	Henry Bauer, Ph.D.
Mississippi	Durward L. Blakey, M.D.	R. H. Andrews, M.S.
Missouri	H. Denny Donnell, Jr., M.D.	Elmer Spurrier, Dr.P.H.
Montana	Steven Kairys, M.D.	David B. Lackman, Ph.D.
Nebraska	Russell W. Currier, D.V.M.	Henry McConnell, Dr.P.H.
Nevada	William M. Edwards, M.D.	Paul Fugazzotto, Ph.D.
New Hampshire	Vladas Kaupas, M.D.	Robert A. Miliner, Dr.P.H.
New Jersey	Ronald Altman, M.D.	Martin Goldfield, M.D.
New Mexico	Nancy C. McCaig, M.D.	Daniel E. Johnson, Ph.D.
New York City	Pascal J. Imperato, M.D.	Paul S. May, Ph.D.
New York State	Alan R. Hinman, M.D.	Donald J. Dean, D.V.M.
North Carolina	Martin P. Hines, D.V.M.	Lynn G. Maddry, Ph.D.
North Dakota	Kenneth Mosser	C. Patton Steele, B.S.
Ohio	John H. Ackerman, M.D.	Charles C. Croft, Sc.D.
Oklahoma	Stanley Ferguson, Ph.D.	William R. Schmieding, M.D.
Oregon	John A. Googins, M.D.	Gatlin R. Brandon, M.P.H.
Pennsylvania	W. D. Schrack, Jr., M.D.	James E. Prier, Ph.D.
Puerto Rico	Luis Mainardi, M.D.	Eduardo Angel, M.D.
Rhode Island	James R. Allen, M.D. (Acting)	Malcolm C. Hinchliffe, M.S.
South Carolina	William B. Gamble, M.D.	Arthur F. DiSalvo, M.D.
South Dakota	Robert S. Westaby, M.D.	B. E. Diamond, M.S.
Tennessee	Robert H. Hutcheson, Jr., M.D.	J. Howard Barrick, Dr.P.H.
Texas	M. S. Dickerson, M.D.	J. V. Irons, Sc.D.
Utah	Taira Fukushima, M.D.	Russell S. Fraser, M.S.
Vermont	Geoffrey Smith, M.D.	Dymitry Pomar, D.V.M.
Virginia	Karl A. Western, M.D.	Frank W. Lambert, Ph.D.
Washington	John Beare, M.D. (Acting)	Jack Allard, Ph.D.
West Virginia	N. H. Dyer, M.D.	J. Roy Monroe, Ph.D.
Wisconsin	H. Grant Skinner, M.D.	S. L. Inhorn, M.D.
Wyoming	Herman S. Parish, M.D.	Donald T. Lee, Dr.P.H.