Epidemiologic and Microbiological Study of a *Shigella flexneri* Outbreak

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MODERN SANITATION and hygiene are sometimes reputed to have controlled shigellosis to the point where cases are rare, or at least sporadic. Examination of data reported for the United States gives reason for a cautious attitude regarding progress in shigellosis control, however, for the number of reported cases has remained at nearly the same level for the past 11 years. Although the total cases reported in the United States decreased from 32,215 in 1951 to 13,846 in 1954, the annual average has since remained in the range of 10,000 to 13,000 cases. In 1964, a total of 12,984 cases were reported (*1*). Further, it is clear that the number of cases reported annually represent only a small fraction of the total that occur. Two recent epidemics of shigellosis involving a total of more than 200 cases in Erie County, N.Y., further emphasize the magnitude of the shigellosis problem. The first of these epidemics, described in this report, occurred during the summer of 1964.

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The recognition of *Shigella flexneri* infection in a few children with ethnically similar family names attending the outpatient department of Children's Hospital in Buffalo prompted investigation of the epidemiologic aspects of the illness. Within a few days 28 definitive or probable cases of infection had been found among 35 members of seven related households.

All persons known to have been infected were Indians who lived in the core of the city of Buffalo, N.Y., or on the Cattaraugus Indian Reservation approximately 35 miles south of Buffalo. All were of low socioeconomic status. Those living in the city had running water and municipal sewerage systems in their homes; those living on the reservation had individual wells and poorly constructed cesspools, septic tanks, or privies. Their below-average personal hygiene resulted in an efficient person-to-person spread of *S. flexneri*.

The illness was generally characterized by several days of diarrhea, in many cases accompanied by mucus or blood, abdominal cramps, and fever. One child was hospitalized; the other patients infected were treated on an outpatient basis. Several persons excreted the organism but denied illness.

Methods

Epidemiologic investigation. Each household in which illness occurred was visited by a physician and public health nurse. A standard

questionnaire was used to gather sanitation information and data on each family member regarding age, sex, race, date of illness onset, signs and symptoms, duration of illness, laboratory examinations, treatment, and possible contacts. Epidemiologic investigators also asked if household members knew of other persons who had had recent gastrointestinal illness, and queried anyone so designated. Fecal and blood specimens were collected during these visits as well as at the hospital clinic. During home visits discussions were held with the family members regarding the nature and causes of their illness and about means to prevent the spread of enteric organisms. When indicated, medications, including tetracycline, were dispensed. It was emphasized that family members should not visit other families for several weeks.

Microbiological investigation. Bacteriological study was carried out on rectal swabs with the material seeded on Endo, *Salmonella-Shigella* (SS) agar, and desoxycholate citrate agar, as well as in selenite F enriching fluid. Nonlactose fermenting colonies, obtained from the primary culture media or the subcultures of the enriching fluid or both, were studied by conventional methods, including motility, biochemical activities, and antigenic analysis by means of polyvalent and group-specific *Shigella* antiserums. Multiple specimens were taken from these nonlactose fermenting colonies.

Antibody studies were carried out by means of the hemagglutination test, previously described in detail (*2–4*). The usefulness of this method has been recently confirmed by Haltalin and associates (*5*). Briefly, all serum specimens obtained from an individual patient were titrated simultaneously in the following manner. Serum in twofold serial dilutions (0.2 ml.) was mixed with equal amounts of antigenically modified human erythrocytes of blood group O. Antigen was obtained from cultures grown on brain veal agar, the organisms being suspended in phosphate buffer and heated at 100° C. for 30 minutes. The supernate obtained after centrifugation at 23,500 gravity for 20 minutes was used as antigen in a dilution of 1:10. The red blood cells were treated with *S. flexneri* antigen from the strain associated with the epidemic for 30 minutes at 37° C. and then washed to remove excess antigen. Separate systems of red blood cells that had been modified with antigens from five serogroups of *S. flexneri* other than the epidemic type, *Shigella boydii* and *Shigella sonnei;* antigens from five serogroups of salmonellae (groups B, C_1, C_2, D, E); and with antigens from five serologic groups of enteropathogenic *Escherichia coli* were used as controls.

The mixtures of serum and antigenically-modified erythrocytes were incubated in a water bath at 37° C. for 30 minutes, and the resulting hemagglutination was read grossly after centrifugation at 1,300 gravity for 2 minutes. An antibody response to the epidemic strain was considered significant if at least a fourfold rise in titer occurred between the acute and convalescent serum specimens in the absence of an associated rise of the titer of antibodies against the control antigens, or if a similar fall in titer occurred between convalescent and late blood specimens, or the *S. flexneri* antibody titer in a single serum specimen was at least fourfold higher than the titers against the three mixtures of five antigens each used for control purposes.

The Epidemic

Figure 1 shows the dates of onset of illness by week in the 23 persons with cases or probable cases about whom reliable information could be obtained. An irregular epidemic pattern is illustrated with the onset of the peak number of cases occurring during the week of June

Figure 1. Onset of cases by week, *Shigella flexneri* epidemic, Buffalo, 1964

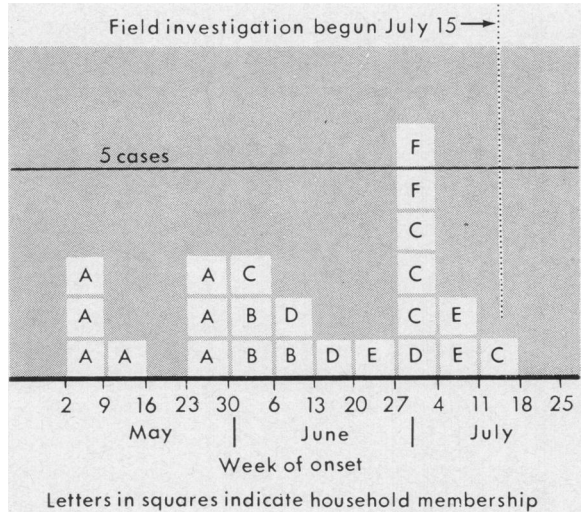
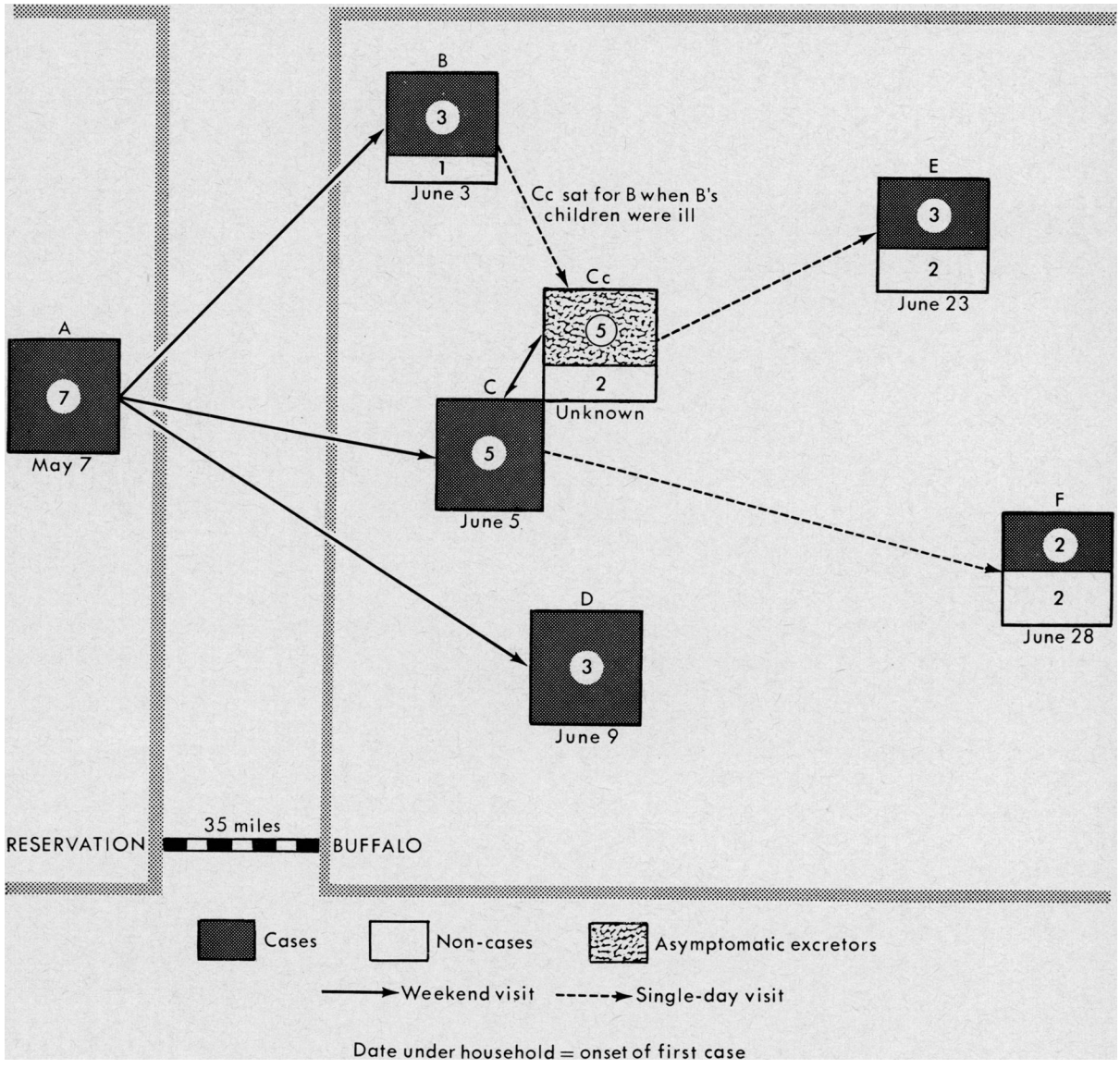


Figure 2. Chain of infection, *Shigella flexneri* epidemic, Buffalo, 1964



27–July 4. The onset of only three cases occurred after that time. The epidemiologic investigation was begun on July 15; the followup was continued into September.

Figure 2 illustrates diagrammatically the apparent chain of transmission from one family to another. The 28 persons with cases, probable cases, and asymptomatic excretions were found among 35 members of seven households. The first person with a case of illness was a 3-year-old boy in household A, located on the Indian reservation, whose illness began on May 7. Within 2 days his 5-year-old brother and 8-year-old sister had also experienced diarrheal episodes; by May 25 two younger siblings as well as the mother and father had developed similar symptoms. *S. flexneri* was cultured from fecal specimens collected from four of these seven persons 9 to 21 days after the onset of their illnesses.

Weekend visits to household A by members of households B, C, and D continued throughout this period, despite the spread of illness among the permanent residents of household A. While the person with the index case still excreted the organism, as evidenced by positive

isolations from stool cultures, the first case of illness appeared in household B. Members of household B were still excreting the organism when the first members of households C and D became ill.

Members of household C not only visited those of household F about three times a week, but also shared the first floor of an apartment with household Cc and may have spread the infection to that household as well. Members of household Cc, in turn, were frequent visitors of household E, and one teenager also was a babysitter in household B while members of the family were ill. This person was found to be an asymptomatic excretor of shigellae.

All but one of the households involved were generally unkempt and dirty with abundant houseflies. Household A, no exception, posed even more of a sanitation hazard because its drinking water was primarily from a shallow drilled well located about 30 feet from a poorly constructed septic tank. Water from this well harbored coliform organisms in large numbers. However, fluorescein dye studies failed to reveal evidence of cross-contamination between the septic tank and well. Household A is discussed because it was the weekend gathering place, and apparently the source of infection, for members of households B, C, and D (fig. 2).

The table shows the number of infected persons and subjects at risk in the seven households. Infection rates in all households were high, ranging from 50 to 100 percent. It is noteworthy that of 14 exposed persons under 4 years of age, 13 developed clinical infections and 1, a subclinical infection, thus comprising more than half of the known cases. The 100 percent infection rate for these children was strikingly higher than the 58 percent rate for persons over 20 years old. The overall infection rate of 80 percent includes five subjects who were recognized as asymptomatic excretors or who had only immunological evidence of infection. If these cases are not included, the attack rate, defined as the percent of those in exposed households who experienced clinical symptoms, becomes 66 percent.

Clinical illness was thus present in 23 persons. Six of these persons with characteristic diarrheal illness occurring during the epidemic period were included as probably infected, although laboratory examinations failed to supply definitive evidence of *S. flexneri* infection. Subclinical infection, based on the finding of a specific antibody response, was found in two additional subjects. Three asymptomatic excretors were detected at the time of the outbreak.

Infection rates, *Shigella flexneri* epidemic, Buffalo, 1964

Patient classification	Persons exposed	Persons infected	Percent infected
Household:			
A	7	7	100
B	4	3	75
C	5	5	100
Cc	7	[1] 5	71
D	3	3	100
E	5	3	60
F	4	2	50
Age (years):			
0–4	14	14	100
5–19	9	7	78
20–49	12	7	58
Sex:			
Male	13	12	92
Female	22	16	73
Total	35	28	80

[1] 3 asymptomatic excretors and 2 inapparent cases.

Bacteriological examination revealed the presence of *S. flexneri* in 18 of the 29 (62 percent) subjects tested during the epidemic. Unfortunately, serotyping on the isolated strains was not carried out. Absorption experiments with serums from patients, however, revealed that a single serotype was involved in the outbreak. Nine of these 18 patients with positive stool cultures exhibited a specific immunological response to the pathogen. Four additional subjects, whose fecal cultures were negative for *S. flexneri*, also developed antibodies against the etiological agent, strongly suggesting that they, too, had been infected. Two of these four had diarrheal symptoms. Paired serums were available from 22 subjects. Had second blood specimens been available from all 35 subjects, a higher rate of positive serologic results might have been obtained.

Discussion

The infection rate of 80 percent among household contacts was relatively high. The actual rate was probably even higher than that observed, however, because specimens for bacte-

riological examination were not collected from some household contacts at the time of illness in the household (specimens were collected early from 29 persons and late from 4 others; no specimens were available from 2 persons) and because paired blood specimens were not available for all contacts. It appeared, because of the mildness of several cases, the presence of asymptomatic infections, and the fact that many patients did not seek medical aid, a large proportion of the infections would have gone unrecognized had this study not been done. Even if all persons who sought medical aid for shigellosis were reported to health departments (and only a fraction are reported although reporting is required by public health law in nearly all States), the true incidence of symptomatic *Shigella* infection would far exceed the reported incidence.

It is clear because of the high infection rates and the temporal sequences of infection that the *S. flexneri* were able to move with ease from person to person through the households, particularly among the young children. The proportionately large number of young children, poor hygiene and sanitation, crowded living conditions, and frequent visiting apparently combined to produce conditions quite suitable for transmission. That some or all of these factors are most important determinants of *Shigella* infection rates is further demonstrated by comparing this outbreak with a subsequent epidemic in Erie County in which an estimated 175 university students were infected by *S. flexneri* via a common source vehicle (*6*). Fewer than ten secondary cases were known in this epidemic. The hundreds of exposed persons differed from those exposed in the Indian epidemic primarily in that they were college-age, educated whites with good hygiene and sanitation who shared living quarters but ate in a central dining hall. After the epidemic was recognized, these students were given instructions on elementary precautions to prevent the spread of infection. Although an intensive bacteriological search for infected persons was not undertaken as in the Indian epidemic, surveillance was maintained and any sick persons were asked to report to the infirmary. The difference in secondary attack rates of the Indians and the students was therefore quite striking.

The immunological studies revealed a number of interesting findings. The diagnosis of infection was established in four subjects whose fecal cultures yielded negative results. In nine other cases the demonstration of a specific antibody response was in accord with the bacteriological findings. To illustrate, the antibody titer in a 17-month-old boy rose from less than 1:10 to 1:160 within a 5-day period without a change in antibody titer against other enteric pathogens. Most other cases demonstrated more leisurely antibody rises and falls, however.

In addition, immunological studies suggested the existence of *Salmonella* C_2 infection in one subject and of *S. boydii* infection in another. In line with a previous report (*7*) it must be emphasized that these serologic studies should be employed as a supplement to, and not as a substitute for, conventional bacteriological examinations with examination of multiple specimens wherever possible.

The epidemic came to a rather abrupt end during the week when the house-to-house epidemiologic investigation commenced, suggesting that the measures taken may have prevented additional infections. These measures included restriction of interhousehold visiting, administration of tetracycline to selected patients, and instruction regarding ordinary infection control precautions. However, lack of sufficient susceptibles no doubt also contributed substantially to the sudden end of the epidemic. Followup of households at risk for 2 months after the epidemic peak assured us that the end of the epidemic was not merely an apparent one caused by the cessation of casefinding activities.

Summary

The epidemiologic investigation of *Shigella flexneri* infection among children with ethnically similar names led to the finding of 28 cases, probable cases, and asymptomatic infections in seven related Indian households in Buffalo, N.Y., and on the Cattaraugus Indian Reservation during the summer of 1964. The overall infection rate was 80 percent with all of 14 preschool contacts infected; the infection rate among persons 20 years old or older was 58 percent. The probable chain of transmission from household to household and person to person was demonstrated. Immunological studies sup-

ported the bacteriological findings in 9 of 18 patients, made possible the diagnosis of 4 culturally negative persons, and suggested unrelated enteric infections in 2 persons.

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Viruses in Space Flights

A long-range study aimed at reducing the danger of virus diseases among astronauts during extended space flights has been launched by the Public Health Service.

Virus diseases present a particularly serious threat to the completion of long-term space flights, because such diseases resist the curative effects of antibiotics and because they are frequently followed by bacterial infections.

Scientists assume that every person, including a healthy astronaut, carries various kinds of viruses to which he is temporarily immune. However, a number of factors can disrupt this balance and cause clinical virus disease. One of these factors is the danger of transmitting a particular virus from an astronaut who is resistant, or immune, to a fellow astronaut who may be receptive to such a virus.

Because of these factors, the research team is attempting to find the best methods of "housecleaning" during space flights in an effort to keep the inevitable spread of these viruses to a minimum. Among the housecleaning problems receiving particular scrutiny are waste disposal, water recovery, dust control, air purification by filtration, and personal hygiene.

The researchers also are looking into the possible dangers of physiological changes in an astronaut during an extended flight that may cause him to lose immunity to his own viruses. This added hazard may be brought on by certain changes in nutrition, hormonal metabolism, emotional stress, and inactivation—the destruction of the activity of a serum by heat or other means.

Another aspect of the study is concerned with the laboratory testing of compounds that will destroy the infectivity of viruses without interfering with the life-support systems of a manned space vehicle.