

An outbreak of Shigella sonnei dysentery in Buffalo, N. Y., in 1959 led to an epidemiologic and immunologic study. The findings are reported in the following paper. Diagnostic and control measures are discussed.

EPIDEMIOLOGIC AND IMMUNOLOGIC STUDIES OF SHIGELLA SONNEI DYSENTERY

Erwin Neter, M.D., F.A.P.H.A.

MODERN sanitation has substantially reduced the incidence of salmonellosis and shigellosis, particularly of water and food-borne outbreaks in certain parts of the world. Nonetheless, these infections are not under satisfactory control even in this country. Elsewhere, these diseases still contribute greatly to morbidity and even to mortality. For example, Olarte¹ in 1960 reported that in Mexico an average of 16,000 deaths per year are due to shigellosis. An outbreak of *Shigella sonnei* dysentery in Buffalo, N. Y., during 1959 afforded the opportunity to study several facets of this infection, namely, the presence of overt and subclinical infection, the spread of the illness in households and a hospital, and the antibody response of patients as a tool for immunologic diagnosis. The results of this investigation are presented here.

Plan of Study

All patients with diarrhea admitted to the Children's Hospital or seen at its Out-Patient Department were studied bacteriologically. Included in the study were also family members of patients with enterobacterial infections. Rectal swabs were obtained for cultural exami-

nation. The material was seeded on blood agar, Endo or MacConkey, S.S., and desoxycholate citrate agar, as well as in broth and enriching fluid (selenite broth). The latter, after incubation at 37° C for 18 hours, was subcultured on the above differential and selective culture media. The pathogens isolated were identified by means of the conventional biochemical and serologic methods.

The antibody response of these subjects was determined by means of hemagglutination tests, described in detail previously.^{2,3} Whenever possible two or more blood specimens were obtained. All serum specimens from each patient and from all members of a single family were titrated simultaneously. Antibodies against *S. sonnei* were determined by the monovalent hemagglutination test. For control purposes, the titers of antibodies against five serogroups of salmonellas (B to E) and five representative serotypes of enteropathogenic *Escherichia coli* were determined in the polyvalent hemagglutination test. The antibody response was considered significant, if there was at least a fourfold rise between two specimens from an individual, or if the antibody titer against *S. sonnei* was at least fourfold higher than that of antibodies against any and all ten heterologous pathogens.

Table 1—Enterobacterial Infections, 1959

Months	Number of Cases		
	Shigella sonnei	Shigella flexneri	Salmo- nella
January	2	0	3
February	1	0	4
March	0	0	2
April	1	0	2
May	12	0	1
June	16	4	2
July	32	1	5
August	34	2	5
September	44	0	8
October	53	1	3
November	30	1	1
December	18	0	1
Total	243	9	37
Grand Total	289		

The Epidemic

During 1959 a diagnosis of shigellosis or salmonellosis was made bacteriologically in 289 individuals. As can be seen from the data shown in Table 1, 243 of these patients had infection due to *S. sonnei*, nine due to *S. flexneri*, and 37 due to salmonellas. The table shows, furthermore, that there was a striking increase in the number of *S. sonnei* isolations starting in May and with a peak in October. No parallel increase occurred in the isolation rates of the other enteric pathogens. This increase in *S. sonnei* infection was not due to the isolation of the pathogen from family members of patients, for a parallel increase was noted in the number of cases and of families. A total of 130 families with two or more members each were available for study. In 41 or approximately 31 per cent of these families *S. sonnei* infection was proved bacteriologically in two or more members. Two cases per family were observed 24 times, three cases nine times, four cases five times, five cases twice, and eight cases once.

In the majority of patients the clinical illness was mild, as evidenced by the fact that 214 subjects were seen in the Out-Patient Department. Only 29 patients needed hospitalization or acquired the infection in the institution. Even during a mild epidemic, however, *S. sonnei* infection may result occasionally in serious consequences, as illustrated by the following case. A five-year-old child with lymphatic leukemia in clinical remission developed severe vomiting, profuse watery diarrhea, and a temperature of 106° F and succumbed less than 40 hours later. On post-mortem examination, acute *S. sonnei* enterocolitis and leukemia in state of remission were found. Whether the primary disease or the treatment with prednisone and/or aminopterin was responsible for the rapidly fatal outcome cannot be answered with certainty. From an epidemiologic point of view it is significant to point out that four siblings had diarrhea prior to the onset of the infection of the patient.

It can be assumed that the cases diagnosed at this hospital represent only a minor fraction of the total of *S. sonnei* dysentery in the community. It is not surprising, therefore, that the infection was introduced into surgical and maternity units. In fact, nine cases on the surgical ward were recognized. In part, this was due to the fact that patients admitted because of illness other than dysentery were in the incubation period of this infection. For example, a patient admitted because of a severe laceration of the eye developed *S. sonnei* diarrhea within 12 hours after admission. Error in diagnosis resulted in admission of a patient with "bloody stools" and a history of previous rectal bleeding to the open surgical floor; study revealed that the patient had, in fact, *S. sonnei* dysentery. Several cross-infections occurred on the Surgical Service because of the inadvertent admission of such cases. In addition, *S. sonnei* infection was recog-

nized in two maternity cases, and in one of them the infection was transmitted during delivery to the newborn infant. The control measures initiated will be discussed briefly below. Finally, it is not surprising that infection occurred also in two nurses, an aide, and a medical house officer. These individuals had taken care of dysentery patients. It was not possible, however, to ascertain whether the infection was acquired in the institution or outside. Clearly, these subjects in turn could be possible sources of infection of patients.

Immunologic Diagnosis

It is a recognized fact that fecal or rectal cultures on patients with bacillary dysentery do not always reveal the presence of the pathogen, particularly if only one specimen is available. Furthermore, the isolation of an enteric pathogen from the feces does not furnish unequivocal evidence of disease caused by this pathogen, because it is conceivable that a patient, who is a carrier of the pathogen, has diarrhea due to other causes, microbial or noninfectious. For these reasons, the demonstration of a

specific antibody response in patients with diarrhea can supply important information. First it may yield supportive evidence for the etiologic diagnosis; second, it may make possible the recognition of infection in bacteriologically negative subjects. The latter possibility applies particularly to individuals, such as family or household members, who had a recent infection and no longer excrete the pathogen.⁴ An illustrative example of the potential of immunologic diagnosis of *S. sonnei* infection in a family is presented in Table 2. Perusal of the table reveals that only the original patient had clinical diarrhea and excreted *S. sonnei*. Study of the antibody response of these subjects clearly showed that four siblings and the mother had high antibody titers against *S. sonnei*, but not against ten heterologous pathogens. It was shown previously⁴ that elevated antibody titers are not maintained for many months. It may be concluded, therefore, that recent infection with *S. sonnei* was present in five family members of a patient with dysentery, and that the diagnosis in these subjects was made by immunologic, but not by cultural, examination.

Table 2—Family Incidence of Shigellosis

Family Members No. 19		Diarrhea	S. sonnei Culture		Hemagglutinin Titers (Reciprocal)			
Name	Age (Years)		Date	Result	Date	S. sonnei	Salmonella Polyvalent	Enteropathogenic E. coli Polyvalent
L.L.	3	+	7/27/59	+	8/12/59	640	40	40
S.L.	2	—	8/ 4/59	—	8/12/59	160	20	40
R.L.	4	—	8/ 4/59	—	8/12/59	640	20	40
P.L.	5	—	8/ 4/59	—	8/12/59	320	40	40
W.L.	8	—	8/ 4/59	—	8/12/59	640	40	40
W.L.	(father)	—	8/ 4/59	—	8/12/59	20	20	40
J.L.	(mother)	?	8/ 4/59	—	8/12/59	320	40	40

Table 3—Clinical, Bacteriologic, and Serologic Data on Patients with *Shigella sonnei* Infection and Family Members

Clinical Status	Total Number of Cases	S. sonnei Culture	Serologic Response			
			Positive	Negative	Equivocal	
Number and Percentage of Cases						
Diarrhea	127*	Positive	109 (85.8%)	81 (74.3%)	24 (22.1%)	4 (3.6%)
		Negative	18 (14.2%)	12 (66.7%)	5 (27.8%)	1 (5.5%)
No diarrhea	45†	Positive	19 (42.2%)	16 (84.3%)	2 (10.5%)	1 (5.2%)
		Negative	26 (57.8%)	17 (65.4%)	9 (34.6%)	0 (0%)
Unknown	25‡	Positive	6 (24%)	3 (50.0%)	3 (50.0%)	0 (0%)
		Negative	19 (76%)	8 (42.2%)	11 (57.8%)	0 (0%)
Total	197	197	137 (69.6%)	54 (27.4%)	6 (3.0%)	

* Includes 3 adults
 † Includes 7 adults
 ‡ Includes 24 adults

Comparative data on the diagnosis of *S. sonnei* infection by cultural and immunologic methods are summarized in Table 3, and the findings are related to the presence or absence of clinical illness. The table shows that among 127 patients with diarrhea a significant antibody response was found in 93 cases (73 per cent), and cultural examination was positive in 109 subjects (86 per cent). In contrast, among 45 subjects without diarrhea, a diagnosis of *S. sonnei* infection by means of the antibody test was obtained in 33 cases (73 per cent), whereas cultures were positive in only 19 cases (42 per cent). Further, a significant antibody response was obtained in 37 (60 per cent) of 63 subjects whose cultures were negative for *S. sonnei*. It should be emphasized that two blood specimens were not available from each subject. Had this been the case, it is possible that the immunologic diagnosis could have been made on additional individuals. This assumption appears to be justified, for only 53 per cent of single serum specimens from 62 subjects and 77 per cent of two or

more serum specimens from 135 individuals were positive.

It was of interest to determine whether the young infant responds with antibody formation to infection with *S. sonnei*. To this end, the relationship between antibody response and age of subjects was analyzed. It was found that 9 (69 per cent) out of 13 infants less than one year of age formed these antibodies. Twelve of the infants were older than four months, and antibodies appeared in one infant between the age of 7 and 12 days. By comparison, 63 per cent of children between one and two years of age, 71 per cent of those between two and six years, and 80 per cent of those between 6 and 16 years produced *S. sonnei* antibodies. It may be concluded, therefore, that even the young infant can form detectable antibodies after infection with *S. sonnei*.

Determination of the antibody response of patients and family members also yields information useful for the analysis of the sequence of infection. The data on such a family are presented in Table 4. It is evident that two sub-

jects without diarrhea were infected prior to two patients whose diarrhea commenced on July 29, 1959, for the former on this day already had a high antibody titer, whereas the latter two children did not, but did so later. The source of infection of the two children with clinical illness may well have been one of the siblings who did not have clinical illness and yet excreted *S. sonnei*.

If, as assumed, the infection is predominantly due to contact, then, it can be expected that the incidence of *S. sonnei* infection in mothers be more common than in fathers of the dysentery patients. Analysis of our data revealed that this assumption is correct. Based on cultural examination of 99 parents, 28 per cent of mothers and only 14 per cent of fathers harbored *S. sonnei*. Similarly, significant titers of *S. sonnei* antibodies were found in 30 per cent of mothers and in only 12 per cent of fathers.

In the studies just reported the hemagglutination test was used. It was

deemed of interest to compare the sensitivity of this method with that of the conventional agglutination test. A titer of 1:50 or higher was considered to be significant in the latter method. The results of the study on 74 subjects done in parallel are shown in Table 5. Perusal of this table reveals that an immunologic diagnosis of *S. sonnei* infection was made by means of the agglutination test in 43 per cent and by the hemagglutination method in 75 per cent. The table reveals, furthermore, that the hemagglutination test proved to be more sensitive in both groups of subjects, with and without clinical illness. It must be emphasized that as yet the immunologic procedures, and particularly the hemagglutination test, are adjuncts to, and not substitutes for, bacteriologic diagnosis of bacillary dysentery.

Discussion

The present study on patients of the Children's Hospital, Buffalo, N. Y., has revealed that during the summer and

Table 4—Family Incidence of Shigellosis

Patients No. 21	Age (Years)	Diarrhea	S. sonnei Culture		Hemagglutinin Titers (Reciprocal)			Entero- pathogenic E. coli Poly- valent
			Date	Result	Date	S. sonnei	Salmo- nella	
T.P.	2	—	7/29/59	+	7/29/59	320	80	40
			8/ 6/59	—	8/ 7/59	160	40	20
H.P.	5	—	7/29/59	+	7/29/59	640	40	40
			8/ 6/59	+	8/ 7/59	160	40	40
E.P.	1	+	7/29/59	+	7/29/59	40	20	10
			8/ 6/59	—	8/ 7/59	160	10	10
G.P.	4	+	7/29/59	—	7/29/59	20	80	40
			8/ 6/59	+	8/ 9/59	160	40	40
C.P. (mother)		?	7/29/59	—	7/29/59	20	40	40
			8/ 7/59	+	8/ 7/59	40	40	40

Table 5—Serologic Diagnosis of Shigellosis by Hemagglutination and Agglutination Tests

Clinical Status	Total Number of Cases	Hemagglutination Test			Agglutination Test	
		Positive	Negative	Equivocal	Positive	Negative
Number and Percentage of Cases						
Diarrhea	45	40 (88.8%)	2 (4.4%)	3 (6.7%)	23 (51.1%)	22 (48.9%)
No diarrhea	16	11 (68.7%)	5 (31.3%)	0 (0%)	8 (50%)	8 (50%)
Unknown	13	5 (38%)	8 (62%)	0 (0%)	1 (7.7%)	12 (92.3%)
Total	74	56 (75.7%)	15 (20.3%)	3 (4%)	32 (43.3%)	42 (56.7%)

fall of 1959 a marked increase in *S. sonnei* infections occurred in Buffalo, N. Y. Although in the majority of individuals the infection was mild or even subclinical, the occurrence of such an epidemic is not without epidemiologic and public health significance. It is interesting to note that a similar increase in the number of *S. sonnei* infections occurred also in the Province of Ontario. Dr. Bynoe,⁵ chief, Bacteriological Laboratories, Department of National Health and Welfare, Ottawa, Canada, informed the author on December 24, 1959, of the following monthly isolation rates of *S. sonnei* in the Ontario Public Health Laboratories in 1959: 17 in May, 17 in June, 14 in July, 50 in August, 56 in September, and 128 in October. In view of the geographic proximity of this province and Western New York, it is conceivable that we were dealing with a single outbreak involving two areas of the USA and Canada. It is of interest also that a water-borne outbreak of *S. sonnei* dysentery occurred in Ravena, N. Y., during the first week of January, 1960.⁶ Approximately 1,400 cases occurred in a population of 3,200. Increased incidence of dysentery in a community also makes possible the introduction of this infection into institutions, including hospitals. As reported here, *S. sonnei* was introduced into Maternity and Surgical Services. For

these reasons, it may be desirable to briefly summarize the control measures introduced at this hospital during the community epidemic. (1) All children with evidence or history of recent (two weeks) diarrhea were admitted to the isolation floor. (2) The same procedure was followed, if there was a history of present or recent (two weeks) diarrhea in the family or household. (3) The house-officers were instructed to obtain this information on all patients. (4) Cultural examination was carried out on all these patients, as well as on all subjects on the floors or in rooms where *S. sonnei* infection was established. (5) Patients admitted for diseases other than diarrhea on "contaminated" floors were isolated, if routine cultures revealed the presence of this pathogen or if the patient developed diarrhea. (6) In view of the susceptibility of the vast majority of strains of *S. sonnei* isolated during the epidemic, sulfonamides were recommended for therapy and, in exposed individuals on the floor, for prophylaxis. (7) New patients were not admitted to a "contaminated" floor; after discharge or transfer of remaining patients the floor was disinfected. (8) Pregnant women with evidence or history of recent diarrhea were isolated, until cultural examination ruled out *S. sonnei* infection. (9) Infants born to mothers with evidence or history of recent diar-

reha were isolated until proved to be free of *S. sonnei*. (10) The entire medical and nursing staffs were alerted to the existence of the epidemic and the above measures.

Summary

An epidemiologic and immunologic study of *Shigella sonnei* dysentery outbreak in 1959 revealed the following findings:

1. In all, 243 cases of *S. sonnei* infection were proved bacteriologically. The illness was mild, and only one fatality occurred.
2. Multiple household infections occurred in 41 or 31 per cent of the 130 families studied.
3. The infection was inadvertently introduced into Surgical and Maternity Services. The infection was transmitted during delivery from one mother to her newborn infant.
4. Determination of the antibody response of patients and family members by means of the hemagglutination test made possible the diagnosis of subclinical infection in 73 per cent of subjects without diarrhea. A significant antibody response was demonstrated in approximately 60 per cent of 63 subjects whose cultures were negative.
5. The hemagglutination test proved to be more sensitive than the conventional agglutination test for the determination of the antibody response. The former yielded positive results in 75 per cent and the latter in 43 per cent of 74 subjects.
6. Study of the antibody response of members of families made it possible to determine the sequence of infection.
7. It is concluded that the determination of the antibody response of patients with *S.*

sonnei infection is a valuable adjunct to, but not a substitute for, bacteriologic diagnosis.

8. The control measures successfully used for the prevention of cross-infection in a hospital during a community epidemic are discussed.

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Dr. Neter is associate professor of bacteriology and pediatrics, University of Buffalo Medical School, and director of bacteriology, Children's Hospital, Buffalo, N. Y.

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