

Shigella Infection in Breast-Fed Guatemalan Indian Neonates

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SEVERAL cases of neonatal shigellosis have been reported recently in industrialized areas.¹⁻³ Practically all the *Shigella* infections reported were accompanied by serious clinical manifestations, mainly diarrhea, with several deaths. In the present paper, the authors want to advance observations on *Shigella* infections in neonates from a semiprimitive Mayan village of Guatemala, because the behavior of infections in these infants departs from that described by the American authors.

The cases herein reported were observed during a longitudinal study in which a cohort of children is followed in their natural environment from the time of birth, in order to observe their general health condition, their growth, their diet, and the colonization of the intestine by parasites, yeasts, bacteria, and viruses. Only the infection by *Shigella*, observed in infants under 1 month of age, will be described and discussed in the present paper.

Methods

Study Area.—Since February 1964, children born in the Guatemalan village of Santa María Cauqué (approximately 1,300 inhabitants; altitude, 6,100 feet), have been recruited for study. Sanitary conditions in the village are extremely inadequate; running water, as well as adequate disposal of excreta and garbage, are nonexistent in the homes. Knowledge and practices of personal hygiene are also poor; deliveries are in the homes under unhygienic conditions. Prolonged

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breast-feeding is universally practiced in the village (mean of complete weaning, 28 months); practically no supplementary foods are offered before the sixth month of life.

Field Procedure.—A clinic and laboratory have been established in this village. Children born in the community are studied at birth and then followed periodically with anthropometric measurements, physical examinations, and studies of dietary intake. The characteristics and duration of disease are determined by regular visits to the homes. Feces are examined every day during the first week when feasible, and at least once weekly thereafter.⁴ Each sample is investigated for parasites, yeasts, Enterobacteriaceae, and viruses.⁵

Laboratory Investigation of Shigella.—Fecal specimens were collected at the homes in half-pint cartons, transported to the field laboratory, and processed within one hour of evacuation. The SS and MacConkey agar plates and selenite broth were inoculated. At least ten colonies, suspicious for *Shigella*, were transferred to triple sugar iron agar tubes, when available. Suspicious cultures were screened in Christensen's urea, Simmons' citrate, and motility agar, and the presumptive *Shigella* cultures were tested in group- and type-specific antisera. Positive cultures were confirmed by biochemical tests.⁶

Results

During a four-year period, February 1964 to February 1968, a total of 210 children were born in the village. One hundred and nine (52%) were studied during their neonatal period or for a longer period. Of these, four children (3.6%) were found infected with *Shigella* within the first 28 days of life, and will be described in detail.

Report of Cases

CASE 1 (3-022-02-07).—This girl was born prematurely (after a pregnancy of 35 weeks) on Oct 1, 1965, with a weight of 1,635 gm (3 lb 9 ounces), and her delivery was uneventful. Her mother developed a psychosis in the third month of pregnancy, which worsened toward the end. During delivery, and over the following two months, the mother was extremely depressed and indifferent to her maternal responsibilities. She also suffered from diarrhea with blood and mucus during the second and third week after delivery. Because of her mental state, she frequently defecated in bed, where her baby often stayed. No dysentery or diarrhea was observed in other members of the family during the study period. The girl could not be nursed by the

mother during her first month of life. During this time she was nursed by an aunt (a common practice in the village in these cases). After the first month she was nursed by her mother. In addition, and because her weight was not progressing satisfactorily, she was given a whole reconstituted powdered acidified milk (Pelargón) prepared in the clinic, beginning on the tenth day of age. The bottle was not handled or kept under proper sanitary conditions in the home. The weight at 16 weeks of age was 2,190 gm (4 lb 9 ounces).

The weekly examination of the feces of this baby gave a culture positive for *S flexneri* 1 in the third week. The same serotype was isolated again from the fifth to the ninth week. The cultures taken in the 10th to 13th week were negative for *Shigella*, but in the 14th week the same serotype was isolated again. No *Shigella* was isolated during the remainder of the first year of life. The baby did not have diarrhea during the period of *Shigella* excretion; the only illness observed during this period was purulent conjunctivitis in the 10th and 11th week, with a relapse in the 14th week. The eye discharge was not cultured for *Shigella*. For this infection she received procaine penicillin G (four doses of 400 units daily, intramuscularly) and chloramphenicol ophthalmic ointment, but no treatment was instituted for the *Shigella* infection.

CASE 2 (3-105-11-08).—This girl was born on Jan 3, 1966, with a weight of 2,620 gm (5 lb 12 ounces) and her delivery was uneventful. Her mother did not suffer from any illnesses during pregnancy or the month after delivery, but her 2-year-old sister developed diarrhea, which began one day before this girl's birth and lasted one month.

The child was breast-fed by the mother. Except for sugar water, given in small amounts during the first three days of life, the only food received during the first four months of life was mother's milk. Her weight progressed satisfactorily. The weekly stool cultures in the newborn showed *S flexneri* 3 in the fourth and fifth weeks of life. The same serotype was again isolated in the 14th, 17th, 21st, and 22nd weeks of life. No *Shigella* was isolated during the remainder of the year.

No gastrointestinal symptoms were found in association with the initial *Shigella* infection. However, four consecutive days of diarrhea with mucus were observed during the 13th week, preceding the isolation of *Shigella* in the 14th week. Only symptomatic treatment (a kaolin mixture with pectin [Kaopectate] per os) was given. In addition, this girl suffered from bronchitis starting in the seventh week, which lasted for 36 days and was treated with aspirin, expectorant, and procaine penicillin G (four doses of 400 units

daily, intramuscularly). She also had an upper respiratory disease during the 16th week, which lasted eight days and was treated with aspirin.

CASE 3 (3-029-03-05).—This girl was born March 6, 1966, with a weight of 2,200 gm (4 lb 13 ounces) from an uneventful delivery. A few days before delivery, the mother developed an abscess in the left elbow and cellulitis in the arm and forearm, lasting until two weeks after delivery. The mother suffered from acute pain and did not nurse the child during this period, complaining that the movements of the child accentuated the pain. She refused surgery but consented to receive an antibiotic, procaine penicillin G (seven doses of 400 units daily, intramuscularly). Finally, she allowed the physician to drain the abscess 14 days post partum. No disease was observed in other members of the family.

Due to the condition of the mother, she did not nurse the child during the first month of life. Three ladies from the village served as foster-mothers but nursed the child very irregularly. During the evening the child was given water with sugar with the aid of a spoon. At 8 days of life, a vegetable mixture (INCAPARINA⁷) was initiated but in insufficient quantity. These foods were administered under unsanitary conditions. The mother began nursing the child at 1 month, discontinuing the other foods. The weight of the child could not be collected adequately; only the birth weight and the weight at 16 weeks of age—4,535 gm (10 lb)—were recorded during the study period.

The child developed diarrhea at 10 days of age with more than ten bowel movements per day. Blood and mucus were present the 11th day and dehydration and fever became established on the 12th day. Electrolyte solutions were then administered (per os and intravenously) with resulting decrease in the number of bowel movements and normalization of consistency of feces. Increased number of evacuations, however, persisted until the 21st day of life. *Shigella flexneri* 2 was isolated in the 12th, 18th, 20th, and 22nd days of life. No additional cultures were made after 1 month of age.

Bronchopneumonia appeared in the 17th day, and lasted for three days. It was treated with procaine penicillin G (three doses of 400 units daily, intramuscularly) and kanamycin sulfate (Kantrex) (three doses of 10 mg/kg body weight daily).

CASE 4 (3-042-04-14).—This boy was born Dec 8, 1967, with a weight of 2,970 gm (6 lb 8 ounces) after an uneventful delivery. No diseases were observed in the mother during pregnancy nor in any of the relatives during the neonatal period.

This child was breast fed by a foster-mother during the first three days of life, and thereafter

by the mother. This is the common practice in the village. He did not receive any other foods in the neonatal period. The weight gain was adequate.

A fecal culture of this child was positive for *S sonnei* on the 28th day of life, followed by negative cultures in the following 12 weeks. Quantitative studies of the culturable fecal microflora were conducted in this particular child. The counts at the time *Shigella* was isolated showed a predominance of bifidobacteria (10^{11} to 10^{12} /gm of wet feces) with aerobes in the order of 10^7 to 10^9 /gm. This is the usual flora of breast-fed children in this area (unpublished observations). *Shigella* were estimated at 10^3 to 10^4 bacilli/gm of wet feces.

This child did not present diarrhea during the study period. The illnesses observed were conjunctivitis and impetigo in the first week, lasting four weeks; oral thrush beginning in the second week of life, lasting ten days; otitis media associated with conjunctivitis at 2 weeks, lasting seven days; and upper respiratory disease, without fever, in the fourth week, lasting eight days.

Thrush was treated with gentian violet; otitis media was treated with procaine penicillin G (four doses of 400 units daily, intramuscularly) and the upper respiratory infection with aspirin.

Comment

Infection of the intestinal tract of the newborn with myriads of microorganisms is accomplished within a few hours after birth.⁸ In the village infants studied, who are raised under inadequate sanitary conditions and fed almost exclusively from the breast, an indigenous microbiota, constituted predominantly by bifidobacteria (10^{11} to 10^{12} /gm of wet feces) is soon installed. ~~Cribs~~^{9,10} *Cribs* forms, enterococci, and others are less numerous (10^6 to 10^{10} /gm). Pathogenic species of parasites, bacteria and viruses, highly prevalent in older children and adults from the village, also reach the gastrointestinal tract during the first days of life.^{9,10} It seems, however, that the early acquisition of these pathogenic microorganisms generally is asymptomatic and does not result in persistent infection. The incidence of diarrheal disease, high in children during the second half of their first year and during their second year of life, is lower in the first three months of life.⁴

Preceding cross-sectional studies in this community showed a prevalence of *Shigella* of 7% in children under 10 years,^{11,12} with epidemics of shigellosis occurring regularly.¹³ Despite this and the constant contamination of the child, only four cases of *Shigella* infection were found among 109 infants studied during the first month of life, through weekly (or more frequent) fecal cultures. In other similar developing areas *Shigella* infection is also rare in the first months of life,^{11,14} suggesting that breast-feeding is a responsible factor. It is significant to note that cases 1, 2, and 3, receiving other foods in addition to mother's milk during their first month of life, appeared with *Shigella* infections. The agent was isolated more than once in all three. Case 4, exclusively breast-fed, showed *Shigella* in only one instance. Furthermore, case 3, where the finding of neonatal *Shigella* infection was associated with severe diarrhea, was an unsatisfactorily breast-fed child, who was receiving foods other than milk under unhygienic circumstances and in insufficient quantity. The infection in cases 1 and 4 was completely asymptomatic. In case 2 the infection observed in the fourth and fifth weeks was not associated with symptoms, although the child suffered from mild diarrhea on the 13th week preceding the reisolation of *Shigella* the following week. Longitudinal studies now in progress show that *Shigella* infection increases with age, particularly during the weaning period. Also, infections tend to be more frequently associated with diarrhea as the child grows older.⁴

With the exception of the premature baby (case 1), the birth weight of the patients here described did not depart significantly from the birth weight of the children of the village, ie, $2,675 \pm 311$ kg (5 lb 14 ounces \pm 11 ounces),¹⁰ and were similar to those described elsewhere in neonatal shigellosis.¹⁻³ The environmental conditions and dietary practices prevailing in the village under study probably have in these cases greater importance

than the low birth weight (and nutrition endowment) as determinants of *Shigella* and other infections.

The cases of shigellosis reported by Haltalin¹ were in infants who apparently were receiving artificial feeding. In these cases the disease was serious and the administration of antibiotics was considered opportune. In contrast, the infections reported here were frequently asymptomatic and were spontaneously eliminated without the administration of antibiotics or sulfonamides. Two of the cases were consistently negative for over one year after the infection was demonstrated, and one was negative for several weeks up to the present time. In the other (case 3) an antibiotic (orally administered kanamycin) was given for another reason; this case could not be followed up.

Differences in the intestinal microflora of breast-fed and artificially fed infants, or other factors such as antibodies or antibacterial substances in breast milk, may be responsible for the different behaviour of *Shigella* infection in the present cases. These two factors could be of particular importance in areas where the environmental conditions, and childbirth and rearing practices, favor early exposure of the host to infection by pathogenic microorganisms.

Summary

During a four-year period, 109 breast-fed children out of 210 born in an Indian village, were followed by serial fecal cultures and other examinations during the first month of life or longer. Four of the children studied (3.6%) were infected with *Shigella* in the neonatal period. The infection was transient and asymptomatic in one child who was exclusively breast-fed. It was asymptomatic but persistent in two children receiving food supplements. In the other child who had deficient nursing and inadequate food supplementation, *Shigella* infection was associated with severe diarrhea. All patients recovered spontaneously without antimicrobial treat-

ment. One child was premature. The birth weight was low in the other three, but within values common in the village. It is suggested that the intestinal microflora that develops in breast-fed children favors resistance to *Shigella* infection or elimination of the agent when it is acquired. Other factors (inhibitors in the milk) should also be considered.

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Generic and Trade Names of Drugs

Chloramphenicol—*Chloromycetin*.

Kaolin mixture with pectin—*Kao-Pek*, *Kaopectate*, *Keotin*, *Paocin*, *Pektamalt*.

Aspirin—*Aspirdrops*, *Crystar*, *Measurin*, *Pentaprin*, *Taasa*.

Kanamycin sulfate—*Kantrex*.

References

1. Haltalin, K.C.: Neonatal Shigellosis: Report of 16 Cases and Review of the Literature, *Amer J Dis Child* 114:603-611 (Dec) 1967.
2. Salzman, T.C.; Scher, C.D.; and Moss, R.: *Shigellae* With Transferable Drug Resistance: Outbreak in a Nursery for Premature Infants, *J Pediat* 71:21-26 (July) 1967.
3. Whitfield, C.; and Humphries, J.M.: Meningitis and Septicemia Due to *Shigellae* in a Newborn Infant, *J Pediat* 70:805-806 (May) 1967.
4. Mata, L.J.; Urrutia, J.J.; and Gordon, J.E.: Diarrhoeal Disease in a Cohort of Guatemalan Village Children Observed From Birth to Age Two Years, *Trop Geogr Med* 19:247-257 (Dec) 1967.
5. Mata, L.J.; Beteta, C.E.; and García, B.: Estudio Longitudinal de Las Colonizaciones Intestinales en el Niño, *Salud Pública* 7:735-742 (Sept-Oct) 1965.
6. Edwards, P.R., and Ewing, W.H.: *Identification of Enterobacteriaceae*, Minneapolis: Burgess Publishing Co., 1962.
7. Bressani, R.; and Béhar, M.: The Use of Plant Protein Foods in Preventing Malnutrition, in *Proceedings of the Sixth International Congress of Nutrition*, Edinburgh: Aug 9-15, 1963, pp 181-206.
8. Rosebury, T.: *Microorganism Indigenous to Man*, New York: McGraw-Hill Book Co., Inc., 1962.
9. Kotcher, E., et al: Acquisition of Intestinal Parasites in Newborn Human Infants, *Fed Proc* 24: 442 (March-April) 1965.
10. Mata, L.J.; Urrutia, J.J.; and García, B.: Effect of Infection and Diet on Growth: Experience in a Guatemalan Village, in *Ciba Foundation Study Group No. 31, Nutrition and Infection*, Boston: Little, Brown & Co., 1967, pp 112-126.
11. Beck, M.D.; Muñoz, J.A.; and Scrimshaw, N.S.: Studies on Diarrheal Diseases in Central America: I. Preliminary Findings on Cultural Surveys of Normal Population Groups in Guatemala, *Amer J Trop Med Hyg* 6:62-71 (Jan) 1957.
12. Mata, L.J., et al: Prevalence of *Shigella*, *Salmonella* and Enteropathogenic *Escherichia coli* in Six Mayan Villages, *Amer J Public Health* 55: 1396-1402 (Sept) 1965.
13. Gordon, J.E., et al: Studies of Diarrheal Disease in Central America: VI. An Epidemic of Diarrhea in a Guatemalan Highland Village, With a Component Due to *Shigella dysenteriae*, Type 1, *Amer J Trop Med Hyg* 14:404-411 (May) 1965.
14. Floyd, T.M.; Higgins, A.R.; and Kader, M.A.: Studies of Shigellosis: V. The Relationship of Age to the Incidence of *Shigella* Infections in Egyptian Children, With Special Reference to Shigellosis in the Newborn and in Infants in the First Six Months of Life, *Amer J Trop Med Hyg* 5:119-130 (Jan) 1956.