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CLINICAL MANIFESTATIONS AND MANAGEMENT

Intestinal Manifestations of Invasive Diarrheas and Their Diagnosis

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Data from studies of 916 children with diarrhea, including 122 from whom shigellae were isolated, and data on patients affected in an epidemic due to Shigella dysenteriae type 1 were analyzed to determine whether a diagnostic clinical profile of shigellosis could be identified. Blood and/or mucus in stool, increased frequency of stool, abdominal pain, rectal tenesmus, and fever were noted more frequently in patients with shigellosis. The diagnostic confirmation of shigellosis depends on the isolation of the organism, but in the clinical situation early initiation of appropriate antibiotic therapy can be based on clinical judgment that utilizes local perceptions regarding dysentery.

Invasive diarrhea may be broadly defined as the response of the human gastrointestinal tract to enteric pathogens—such as bacteria (Shigella, Salmonella, Campylobacter, and enteroinvasive Escherichia coli), viruses (rotavirus), and parasites (e.g., Entamoeba histolytica and Trichuris trichuria)—that have the capacity to invade and damage the mucosa of the small and/or large intestine. Among this variety of pathogens, only those that specifically invade and damage the mucosa of the large intestine and rectum give rise to bloody, urgent, frequent stools and rectal tenesmus, the clinical features of dysentery. Data from several recent reports on patients with dysentery who reside in tropical developing areas suggest that, except for some diseases that have specific geographic distribution (e.g., amebiasis and schistosomiasis), the Shigella organisms are probably the most frequently isolated pathogens. In addition, the term shigellosis often is used interchangeably with the terms dysentry and invasive diarrhea. Since early initiation of therapy with appropriate antibiotics is essential for reduction of morbidity and mortality due to Shigella infection, the identification of a diagnostic group of intestinal manifestations would help the clinician treat patients in an efficient, effective manner.

In this paper, data from two studies are presented and data from other relevant literature are reviewed to determine if a diagnostic clinical profile of shigellosis can be identified. The first study was a selected analysis of symptoms and findings for a group of children who were part of a detailed investigation of etiologic agents associated with acute diarrhea in patients at a tertiary care hospital in southern India. Nine hundred sixteen children with diarrhea were enrolled in this 2-year study. During the course of the study, all 916 children were <3 years old, had had diarrhea (or dysentery) for <72 hours, and presented at the hospital with no history of therapy. A detailed microbiologic examination (with the use of the recommended methods of the World Health Organization [1]) of stool specimens from these children was carried out to identify enteric pathogens. The rate of isolation of pathogens for this group of patients was compared with that of a control group of 587 children who were matched for age, sex, and socioeconomic status. The participants of the control group were selected from either children attending well-baby clinics or children without infectious diseases or intestinal symptoms who were attending a pediatric clinic. The details of this study will be published elsewhere.

The second study was of patients affected in an epidemic in a village where Shigella dysenteriae type 1 (the Shiga bacillus) was the sole enteric pathogen that was detected. Although a report on this epidemic (which was due to fecal contamination of an ostensibly protected water supply) has been published elsewhere [2], the clinical data from studies of these patients who belonged to all age groups are reanalyzed herein.

Comparative Analysis of Control Subjects and Children with Diarrhea

In this study, one or more enteric pathogens were isolated from 74.2% of the 916 patients and from 48.6% of the 587 control subjects. Shigella was the sole pathogen isolated from specimens of stool from 75 patients, and for another 77 Shigella was isolated in association with one or more other enteric pathogens (bacteria, viruses, or parasites). Shigella was the sole pathogen isolated from the stool specimens from seven control individuals (1.2%), and for another four Shigella was isolated in association with other pathogens.
Diarrhea was the first presenting symptom of almost all patients, but in 17.8% of children for whom *Shigella* was the sole pathogen identified, fever was the first presenting symptom. A significantly higher proportion of patients from whom *Shigella* was isolated (either alone or in combination with other enteric pathogens) had blood and mucus in their stool, complained of abdominal pain and fever at the time of presentation, and were more likely to have a history of >10 stools per day (table 1). One-third of the patients from whom *Shigella* was the sole pathogen isolated had no blood in their stools. For 68% of patients from whom *Shigella* was the only pathogen isolated, >15 leukocytes per high-power field were found on methylene blue–stained fresh fecal smears; in contrast, less than one-third of other patients’ fecal samples had >15 leukocytes. *Shigella* was not isolated from children who were exclusively breast-fed.

### Intestinal Manifestations of Diarrhea Due to *S. dysenteriae* Type 1

During the 1970s several epidemics of acute diarrhea occurred in southern Indian villages where multidrug-resistant *S. dysenteriae* type 1 was the sole intestinal pathogen isolated from patients [3]. During a 6-week period that began the last week of October 1972, in a village with a population of 2,050 there were 546 people who were affected in an epidemic of diarrhea and dysentery; cases of this disease occurred in 278 of the 497 households [2]. The epidemiologic characteristics of this epidemic suggested that the disease was from a common source and was transmitted secondarily from person to person. During the first 2 weeks of the epidemic, *S. dysenteriae* type 1 was isolated from 43 of 59 specimens of stool that were examined.

Of the patients affected in this epidemic, 89.4% complained of bloody, mucoid, small, frequent stools as well as crampy abdominal pain and rectal tenesmus. However, 10.6% of patients from all age groups only had watery or semifomed stools in which no blood or mucus was present. One-quarter of the patients had a history of fever at or before the onset of diarrhea. The mean duration of diarrhea or dysentery ranged from 14.2 days for children <5 years old to 10.8 days for adults.

### Diagnosis of Invasive Diarrhea

The intestinal manifestations of diarrhea that are associated with invasive enteric pathogens that affect the large bowel are the presence of blood and mucus in the stool and systemic symptoms such as fever. Such symptoms imply invasion of the organism beyond the epithelial layer that is associated with an inflammatory response in the lamina propria mucosae. The results reported here for patients from all age groups from southern India supplement those from earlier reports [4–7] that document the significantly higher frequency of bloody stools, fever, and abdominal pain of patients with shigellosis. For about two-thirds of patients, these clinical features can suggest a diagnosis and therefore are of poor sensitivity.

One of the confounding issues in the clinical diagnosis of shigellosis involves the fact that for all age groups of patients, ~10%–35% of individuals from whom *Shigella* can be isolated may not have visible blood and mucus in their stool. For a small proportion of the patients, a careful review of their history may reveal an initial instance of watery diarrhea as well as the subsequent development of small, bloody, mucoid stools; this may suggest that the initial event is a secretory response (presumably in the small intestine) and that the colon and rectum are subsequently invaded, a process leading to dysentery. Although highly suggestive, the presence of leukocytes and red blood cells on stool smears did not unequivocally distinguish shigellosis from other diarrheal diseases [6]. In southern India, a vascular lesion (localized Shwartzman reaction) was found in the rectal mucosa of patients with acute diarrhea that was unrelated to the type of enteric pathogen that was isolated from the patients [8]. It is possible that the presence of this lesion also contributes to the number of fecal leukocytes.

Physicians’ diagnoses of a group of symptoms can range from clinical impressions to confirmed diagnoses that are supported by the identification of pathogenic microbes and/or histopathologic evidence. A variety of terms, such as invasive diarrhea, dysentery, shigellosis, and invasive enteritis, that are often utilized without precise definition are used to describe the response of the human rectal and colonic mucosa to invasion by enteric pathogens. A variety of microbial pathogens—including rotavirus (which invades, multiplies in, and leads to the desquamation of enterocytes in the duodenum and upper jejunum), the parasite *Strongyloides stercoralis* (which causes widespread enteritis of the upper small intestine), and *Salmonella typhi* (which invades and proliferates in the Peyer’s patches, especially in the ileum, and produces a systemic infection of the reticuloendothelial cells)—can invade the intestinal mucosa. Although all of these pathogens

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence (%) of symptoms in children from whom indicated pathogen was isolated</th>
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<tbody>
<tr>
<td></td>
<td>Shigellae alone (n = 75)</td>
</tr>
<tr>
<td>Blood in stools</td>
<td>63.5</td>
</tr>
<tr>
<td>Mucus in stools</td>
<td>70.2</td>
</tr>
<tr>
<td>11-20 stools per day</td>
<td>38.7</td>
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<tr>
<td>&gt;20 stools per day</td>
<td>16.0</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>66.2</td>
</tr>
<tr>
<td>Respiratory illness</td>
<td>95.4</td>
</tr>
<tr>
<td>Fever</td>
<td>56.2</td>
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</tbody>
</table>

Table 1. Prevalence of selected symptoms in relation to isolation of pathogens from children with diarrhea.
give rise to invasive enteritis, none of them would be considered the cause of invasive diarrhea. Before the diagnosis of shigellosis can be confirmed, the Shigella organisms must be isolated from stool or rectal swab specimens. However, for up to one-third of patients from whom Shigella was isolated, there may not be any blood in their stool. The significance of mucus in the stool is difficult to assess. At this symposium, data on the increased mortality among children with mucoid diarrhea rather than watery diarrhea were presented, but their relation to shigellosis is difficult to evaluate.

In most tropical developing countries, there are specific local names for the dysenteric illnesses caused by invasive organisms. In southern India (Tamil Nadu) they are referred to as rakthabedi or sheethabedi. The people of these areas recognize that these two types of diarrhea are different from other types of diarrhea. In addition to a full understanding of the vernacular and regional names for the disease, the clinician can arrive at the diagnosis of the illness based on the frequency of stools and the presence of blood and/or mucus in the stool, abdominal pain, rectal tenesmus, fever, and other constitutional symptoms as well as mild tenderness over the left colon on palpation of the abdomen. The presence of an increased number of fecal leukocytes or a bacillary exudate can contribute to the confirmation of the diagnosis, and a fecal smear can also exclude amebiasis as a cause of dysentery. It has been suggested [9] that children with bloody diarrhea that was discovered by community health workers should be treated with appropriate antibiotics. However, for the initiation of proper therapy, it is important for the physician to understand the comparative prevalence of E. histolytica versus other pathogens that can cause this disease among inhabitants of the particular region as well as of the pattern of antibiotic sensitivity of the most prevalent pathogens. Until a single applicable diagnostic test is available, the physician's diagnosis of invasive diarrhea due to Shigella that leads to appropriate therapeutic intervention must be based primarily on clinical judgment.

References