

# PERSPECTIVES ON ACUTE ENTERIC DISEASE EPIDEMIOLOGY AND CONTROL<sup>1, 2</sup>

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*Annual mortality from enteric disease ranges from 10 per 100,000 in highly developed countries to as much as 500 per 100,000 in developing countries. This article reviews the major epidemiologic features of acute enteric diseases and outlines a general strategy for their prevention and control in developing countries.*

## Introduction

The acute enteric diseases may be defined as a group of gastrointestinal disorders caused by ingesting one of a wide variety of infectious or toxic agents. While clinical manifestations may be specific for a few well-known enteric diseases (e.g. rice-water diarrhea is specific for severe cholera, bloody diarrhea and tenesmus for severe Shiga dysentery, and sustained fever with headache for typhoid) clinical features in the majority of enteric illnesses are quite nonspecific. Some form of diarrhea is generally present, and incubation periods are generally short, ranging from a few hours to a few days.

Basic epidemiologic attributes of the various enteric disease agents are also quite similar. The reservoir of most agents is the intestinal tract of either humans or animals. The mode of spread is either by direct person-to-person contact (via the fecal-oral route) or through ingestion of contaminated food or water.

## Morbidity and Mortality Patterns

Mortality statistics testify to the significant impact of acute enteric diseases in many parts

of the world. A recent World Health Organization report shows yearly death rates of 200 to 500 per 100,000 attributed to diarrheal disease in certain developing countries. Overall, diarrheal disease accounted for between 20 and 35 per cent of total mortality in those countries. These rates contrast strikingly with rates in the more developed countries, which reported fewer than 10 deaths from diarrhea per 100,000 people—indicating that these diseases accounted for less than 1 per cent of total mortality. In all countries, however, the well-known specific types of enteric disease—typhoid, dysentery, and cholera—accounted for less than 5 per cent of the reported diarrhea mortality (1).

Estimates of enteric disease morbidity in terms of incidence, prevalence, and relative frequency of various etiologic agents have been reported in numerous surveys from different parts of the world (2, 3). As in the case of mortality statistics, there are great differences in the rates reported for different countries, and the rates tend to vary inversely with levels of socioeconomic and industrial development.

The agents most often incriminated by laboratory-based studies of endemic enteric disease have been enteropathogenic *Escherichia coli* and shigellae; but in the past such investigations have failed to identify the etiologic agents responsible for most of the cases studied (4-8). A number of agents whose enteropathogenicity has only recently been recognized may account for some of these cases. This group of agents would include the non-cholera vibrios (9),

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toxin-producing strains of *E. coli* that may not agglutinate in standard enteropathogenic *E. coli* diagnostic antisera (10), and viruses (11). In tropical countries, infestation with one or more intestinal parasites is also common; but the high background prevalence of these parasites often makes it difficult to ascertain their etiologic significance in cases of acute enteric disease.

### *High-Risk Groups*

Certain definable subgroups of people run a particularly high risk of acquiring enteric diseases. Age is the prime consideration. In all societies, children under ten years of age (especially those between one and four) have the highest rates of morbidity and mortality from enteric disease. "Weanling diarrhea," the well-known high incidence enteric illness which occurs in children of developing countries when they are weaned from the breast, is a particularly serious component of this problem, and one which has been the subject of extensive study (12). Residents of institutions for the mentally retarded also have a disproportionately great chance of experiencing acute enteric diseases, especially shigellosis (13). And visitors to foreign countries, particularly developing tropical countries, run a relatively high risk of acquiring "traveler's diarrhea," a febrile gastroenteritis syndrome usually lasting only a few days, which may be caused by one of a variety of agents (14).

### *Epidemics*

Besides endemic patterns of morbidity and mortality, one must consider the well-known potential for enteric disease to occur in epidemic form. These epidemics range in size from the small community outbreak of staphylococcal foodborne disease following a common meal, or the propagated outbreak of shigellosis in a custodial institution, to nationwide outbreaks—such as that due to *Salmonella typhi* which occurred in Mexico in 1972-1973 (15); to region-wide outbreaks—such as that due to Shiga's bacillus, which spread through several

Central American countries in 1969-1972 (16); and ultimately to pandemics—such as that due to El Tor cholera, which spread from East Asia to the Middle East, Africa, and parts of Southern Europe over the past decade (17, 18).

### **Epidemiologic Determinants**

Three basic epidemiologic determinants—the agent, the host, and the environment—each contribute in some way to every case of disease; the agent through its ability to persist in the environment and to cause pathophysiologic changes in the host; the host through behavioral and biological characteristics which may serve to increase or decrease the risk of disease; and the environment by providing a means for transmitting the agent to the host.

### *Agent Factors*

Table 1 lists a selection of known enteric disease agents and their basic epidemiologic attributes. The list includes various bacteria, viruses, parasites, and chemicals. The most common reservoir of infection is the human body, although some agents reside in domestic animals or the inanimate environment. Ingestion of contaminated food and water is the most general mode of transmission, but person-to-person spread through fecal-oral contact is also very important.

Each of the various agents, when ingested in sufficient amounts, causes human illness in one of various ways. The amounts needed have been estimated for several agents by means of volunteer feeding experiments. These tests have pointed to an important relationship between the minimum infectious dose of various bacterial pathogens and their mode of transmission: Shigellae, with an infectious dose as low as  $10^2$  organisms, are particularly likely to be spread by the person-to-person route (19, 20); *Vibrio cholerae* and *Vibrio parahaemolyticus*, with infectious doses in the range of  $10^6$  to  $10^8$ , are spread mainly if not entirely by food and water (21, 22); and typhoid as well as non-typhoid salmonellae, with infectious doses in the range

TABLE 1—Epidemiologic profiles for selected agents of acute enteric disease.

Agents	Reservoir		Mode of transmission		
	Human intestine	Other	In water	In food	Person-to-person
<b>PARASITES</b>					
<i>E. histolytica</i>	+		+	+	
<i>G. lamblia</i>	+		+		
Intestinal helminths	+		+	+	+
<b>BACTERIA</b>					
<i>Clostridium perfringens</i>		Animal intestines		+	
<i>Clostridium botulinum</i>		Soil		+	
Enteropathogenic <i>E. coli</i>	+		+	+	+
<i>Salmonella typhi</i>	+		+	+	+
Non-typhoid salmonellae		Animal intestines	+	+	+
<i>Shigella</i> spp.	+		+	+	+
<i>Staphylococcus aureus</i>		Human skin, nasopharynx		+	
<i>Vibrio cholerae</i>	+		+	+	
<i>Vibrio parahaemolyticus</i>		The marine environment		+	
<b>VIRUSES</b>					
(Echo, Parvo, ?)	?	?	?	?	+
<b>CHEMICALS</b>					
Organic		Marine and plant life		+	
Inorganic (metals, pesticides, food additives, etc.)		The inanimate environment	+	+	

of  $10^4$  to  $10^5$ , are spread primarily by food and water but undergo some definite person-to-person spread as well (23, 24).

Pathogenic mechanisms, which for many agents are poorly understood, may be broadly categorized as either toxic or invasive. Well-studied models of toxic and invasive mechanisms include the watery diarrheal syndrome of cholera, which is attributed almost entirely to the effects of enterotoxin released by the growing organism on the mucosa of the small intestine (25), and the bloody mucoid diarrheal syndrome of Shiga dysentery, which results primarily from invasion of the mucosa of the large intestine and proliferation by the Shiga bacillus (*Shigella dysenteriae*, type 1) (20).

Besides pathogenic mechanisms, the other major factors that account for an agent's capacity to cause illness are its ability to survive in nature and to withstand host defenses and therapeutic interventions. These abilities are illustrated by two recent enteric disease experiences. First, the relative hardiness of the El Tor biotype of *Vibrio cholerae*, relative to the

classical biotype of *V. cholerae*, is thought to have contributed to the rapid and wide dissemination of the former organism through Asia, Africa, and Southern Europe over the past several years (17, 18). Second, the appearance and rapid spread of the Shiga bacillus in Central America and the attendant severe clinical disease which it caused in the early 1970's is attributed, in part, to the resistance of the epidemic strain to various commonly employed antibiotics (26, 27).

#### Host Factors

Host factors that contribute to enteric disease include behavior patterns promoting host exposure to pathogenic agents and biological conditions rendering the host susceptible to them.

*Behavior patterns.* Choices of food and drinking water sources, ways of handling food before eating, and habits of personal hygiene all involve host behavior which may unwittingly increase the risk of exposure to enteric disease.

For example, one classic case described by John Snow involved a lady who contracted cholera because she had the unusual habit of drinking water brought many blocks across London each day from the contaminated Broad Street Pump (28).

Several contemporary examples of the relationship between host behavior and exposure to enteric disease agents can also be cited. For instance, several studies of enteric disease incidence among infants suggest that the mother's choice to breast-feed affords protection against such illness (3, 29). Whether this is the result of some transferred immunity, or (more likely) reduced ingestion of contaminated foodstuffs, or both, is subject to speculation. In addition, various observations suggest that an individual increases his risk of acquiring traveller's diarrhea by choosing to eat fresh vegetables or fruit, or by drinking water from unreliable sources (30). Also, holding food at temperatures conducive to bacterial growth prior to eating has been documented as the commonest factor contributing to the occurrence of food-borne diseases in the United States (31); this is probably a factor, to varying degrees, in all societies. Finally, with regard to personal hygiene, studies from several parts of the world suggest that hand-washing reduces the incidence of enteric diseases, particularly shigellosis (32, 33).

*Biological conditions.* Among the biological factors that determine host susceptibility, both specific and nonspecific protective mechanisms should be considered.

Field trials of orally administered attenuated shigella vaccines and parenterally administered killed cholera vaccines have demonstrated moderate but generally short-lived protective effects (34, 35). Typhoid vaccines have provided moderate levels of protection that have been sustained for several years (23). The possible protective role of secretory antibody, whether passively acquired by an infant from the mother's colostrum or actively secreted by the gastrointestinal mucosa, is a debated but unresolved subject.

There is considerable experimental evidence that gastric acid provides a major nonspecific barrier against a wide variety of enteric pathogens; therefore, situations which compromise an individual's capacity to produce gastric acid might be expected to increase his susceptibility to enteric disease (36).

Existence of a correlation between nutritional status and the occurrence of acute enteric disease has frequently been reported.<sup>4</sup> When exposed to an enteric pathogen, a malnourished host is likely to experience a longer, more severe, and more dangerous illness than his well-nourished counterpart. Furthermore, an episode of diarrhea will often aggravate borderline malnutrition, leading to kwashiorkor (3).

#### *Environmental Factors*

Food, water, and human waste are the principal environmental ingredients involved in spreading human enteric disease.

Inadequate facilities for hand-washing and for disposal of fecal waste have both been linked to increased risk of enteric disease (32, 37). Deficiencies in such facilities can contribute both to person-to-person spread of enteric disease agents and to their spread through contaminated food and water. If removal of fecal wastes is inadequate, flies may serve as intermediaries by transferring pathogens from sewage to food or water (38).

The role of contaminated drinking water in enteric disease transmission, first documented on sound epidemiologic grounds by Snow's investigations of cholera in mid-nineteenth century London (28), has been well-established for a variety of parasitic, bacterial, viral, and chemical agents (39). In most instances the introduction of these agents into water supplies is attributable to contamination with human fecal waste. Studies from both North and South

<sup>4</sup>See M. Béhar, The role of feeding and nutrition in the pathogeny and prevention of diarrheic processes, *Bulletin of the Pan American Health Organization*, Volume IX, No. 1, 1975, pp. 1-9.

America indicate an inverse relationship between the quality of drinking water and the morbidity and mortality rates for typhoid fever and general diarrheal disease (3, 40).

Food, like water, can serve as the vehicle for transmitting a wide variety of disease agents. This role of food has been documented by epidemiologic investigations of food-borne disease outbreaks in many parts of the world. Less direct evidence comes from observing the incidence of "weaning diarrhea," which occurs shortly after breast-fed babies are put on a diet of cow's milk and food. Primary causes of food contamination include improper processing or packaging, practice of poor personal hygiene by food handlers, lack of adequate cooking, and failure to keep cooked or fresh food properly preserved before eating. These errors can either introduce pathogenic agents into food or allow microbial agents to proliferate until they reach potentially harmful levels.

### Prevention and Control

Preventive health programs can employ any of three types of measures: first, those directed at reducing the agent's presence or its ability to cause disease; second, those directed at increasing the host's resistance to disease agents; and third, those directed at countering environmental factors which contribute to disease transmission. Successful use of each type of measure can be cited, such as 1) prophylactic use of antibiotics to eliminate infectious agents from persons exposed to tuberculosis and syphilis; 2) administration of specific vaccines to immunize the host against smallpox, measles, polio, etc.; and 3) application of insecticides to remove malaria and yellow fever vectors from the environment.

In the case of enteric diseases, caused as they are by such a wide variety of known and unknown agents, agent-specific preventive programs are likely to have only limited effect. Instead, one must think primarily in terms of measures aimed at host and environmental factors common to many enteric disease agents.

### Primary Prevention

Specifically, preventive programs should focus on improving nutrition, improving personal hygiene and food handling habits, and providing safe water supplies and sewage disposal systems. Long before antibiotics or vaccines were available, these measures accounted for a major drop in the incidence of enteric disease among the world's industrialized countries. The continuing strength of such barriers against enteric disease has been confirmed by recent experiences in which epidemic strains of *Vibrio cholerae* from Asia, *Shigella dysenteriae* 1 from Central America, and *Salmonella typhi* from Mexico were accidentally introduced into the United States or countries of Western Europe; for in each case the existence of these barriers prevented the agent from establishing endemic foci of infection (41-43).

Where there is an unusually high risk of exposure to a specific enteric pathogen, vaccination may be an important primary preventive measure. For example, a shigella vaccine could be very useful for protecting residents of custodial institutions where shigellosis is a serious endemic problem.

### Clinical Treatment

While primary prevention of enteric disease is the ultimate object, reducing current mortality by effectively treating cases and by recognizing and controlling epidemics is a more immediate practical goal.

The vast majority of enteric disease deaths result from diarrheal fluid loss with attendant dehydration, serum electrolyte imbalance, and acidosis. A simple regimen of oral glucose-electrolyte fluid replacement has been shown highly effective in ameliorating these life-threatening complications (44, 45). Because of its simplicity, relatively low cost, and wide applicability, this form of treatment should have the highest priority in an enteric disease control program.

Specific antibiotic, chemotherapeutic, or an-

toxic treatments may play a major role in reducing morbidity and mortality from certain enteric diseases involving invasion and systemic spread of the agent. Examples of such treatments include use of antibiotics against typhoid fever, shigellosis, and amebiasis; employment of chemotherapeutic agents to treat intestinal helminthic infections; and use of type-specific antitoxin to treat botulism.

### *Epidemic Control*

The coming of an epidemic, superimposed upon the usual background incidence of disease, always signals some significant shift in the existing balance between host, agent, and environment. A prompt and thorough investigation of the cases that arise should shed light on the responsible factor or factors and should serve as a guide in selecting control measures to prevent further spread. Several recent examples from Western Hemisphere countries illustrate this principal of epidemic investigation and control.

In April 1971 widespread increases in the incidence of typhoid fever cases were noted in Trinidad. The cases occurred primarily in school-age children, and careful epidemiologic analysis of the children's eating habits implicated the products of an ice cream company. As a result, a number of hazardous practices in the processing plant were uncovered and corrected (46).

In June 1973 an explosive outbreak of shigellosis involving over 500 passengers occurred on board a Caribbean cruise ship. An investigation implicated the ship's potable water system (47). This investigation resulted not only in correction of the water system on that specific craft, but also in an extensive survey to assess the risk of diarrheal illness on cruise vessels (48).

Local investigations of Central America's Shiga dysentery epidemic of the early 1970's and Mexico's typhoid epidemic of 1972-1973 implicated both contaminated water and person-to-person spread (15, 16). In these instances, the widespread lack of proper hygienic practices and the prevalence of unsafe water systems made it impossible to take dramatic corrective measures, and both epidemics persisted for one or more years. However, the investigations did provide important informa-

tion about resistance of the epidemic strains of Shiga bacillus and *S. typhi* to commonly employed antibiotics, thus contributing to a decrease in mortality by improving the choice of antibiotics.

### **Administrative Considerations**

Effective administration of a program for acute enteric disease prevention and control requires both allocation of appropriate resources to deal with the problem and ongoing evaluation of the program's results. The problem in developing countries, as already noted, requires a public health program directed at improving treatment methods, nutritional status, personal hygiene, food handling practices, and water and sewerage facilities. To implement such a program, one must consider the relative worth of contributions made by physicians, nurses, sanitarians, health aides, and other personnel, and of hospitals, laboratories, community health centers, and other facilities.

High priority should be given to early and practical ways of reducing the poor prognosis for common diarrheal diseases of young children. Such a reduction may be most effectively achieved by providing nutritional services and simple glucose-electrolyte fluid therapy by community health centers. This task, one of direct service combined with health education, will be most appropriately carried out by trained community health workers and nurses. The same community health facilities and personnel should also serve to educate families about personal hygiene and food handling practices, with a view to primary prevention of disease.

To effect a permanent reduction in acute enteric diseases, one must shift the focus of treatment from the host to the environment. A long-range strategy of investment in the construction and maintenance of safe water and sewerage facilities is called for. The engineering expertise and resources for this undertaking should originate at the regional or national level of the Ministry of Health. The task of maintaining such facilities should be allocated to com-

munity health workers who have received basic training in environmental sanitation.

Finally, consideration must be given to combatting the relatively less-reported but potentially life-threatening enteric pathogens (*Salmonella typhi*, *Vibrio cholerae*, *Shigella dysenteriae* 1, and *Clostridium botulinum*) as they occur in either sporadic or epidemic form. Effective management of such outbreaks requires specific diagnosis and therapy. This component of the enteric disease program will generally require the services of physicians, microbiological laboratories, and hospitals.

### Epidemiologic Surveillance

Surveillance—the ongoing collection, analysis, and dissemination of data on the occurrence of disease—should be viewed as a public health activity serving three basic purposes. First, it provides the basis for administrative guidance and evaluation of ongoing disease control programs. Second, it assists in obtaining new knowledge about disease agents and their transmission. And third, it facilitates recognition of epidemics and provides guidance for their investigation. With any surveillance system, one must determine the geographic area to be covered, the diagnostic criteria for reporting cases of disease, and the persons and institutions responsible for collection, analysis, and use of the data being obtained.

Surveillance should play a major role in guiding and evaluating control efforts in areas of high enteric disease endemicity. Cases and deaths should be diagnosed on the basis of simple clinical criteria for diarrhea. There should be little if any need for laboratory diagnosis at this level of surveillance, and the surveillance unit might appropriately be limited to the area served by a community health center. The case-finding and reporting could then be the task of community health workers. Ongoing analysis and preparation of reports could be performed at the community or regional level. Either an ongoing count of all cases or a simple periodic prevalence survey could be employed. The effectiveness of exist-

ing control measures and the need for modifications could then be assessed on the basis of disease trends over time.

The role of surveillance in recognizing and investigating enteric disease epidemics has been illustrated by the recent experiences already cited. Recognition of an epidemic requires several things, the first being a reliable reporting system that points up unusual disease increases or disease types. In addition, people with epidemiologic field training are needed at the health ministry level to analyze the pattern of an epidemic. Also, as a guide to both case diagnosis and determination of the disease source, laboratory facilities for diagnostic microbiology and other activities would generally be required.

### Conclusions

Morbidity and mortality from acute enteric diseases generally vary inversely with levels of socioeconomic and industrial development. In some countries, diarrheal disease is the leading reported cause of death; those at greatest risk are infants and young children, who account for most of the diarrhea fatalities. In these age groups, malnutrition markedly decreases the enteric disease patients' chances for survival.

Despite the many different agents of acute enteric disease, the major clinical manifestations (diarrhea, dehydration) and epidemiologic determinants (malnutrition, inadequate personal hygiene, contaminated food and water) are quite similar. Programs for prevention and control should focus on these common factors rather than on traditional agent-specific measures such as antibiotics or vaccines. Several recent cost-benefit studies support this argument (49, 50).

Such a program should place its main emphasis on community paramedical manpower and facilities rather than on physicians, diagnostic laboratories, and large hospitals. Also, a surveillance system should be developed to direct and evaluate the program, as well as to detect epidemics and guide control efforts.

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## SUMMARY

This paper reviews the major epidemiologic features of the acute enteric diseases and outlines a plan for their prevention and control in developing countries. Annual mortality from enteric diseases ranges from 10 per 100,000 in highly developed countries to as much as 500 per 100,000 in developing countries.

Most agents of enteric disease are spread by one of two routes: direct person-to-person contact or ingestion of contaminated vehicles (food or water). An effective control program

should therefore focus on common epidemiologic factors, rather than on agent-specific remedies such as vaccines or antibiotics. The major operational components of such a program should include oral fluid replacement therapy, improvements in environmental sanitation, health education to promote personal hygiene and proper food handling, and epidemiologic surveillance to monitor public health needs and evaluate the impact of health measures.

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