Diarrheal Diseases

Microorganisms in Childhood Diarrhea[1]

The last decade has been an exciting one for clinicians and scientists interested in acute childhood diarrhea. In addition to well-known microbial causes of human diarrhea *(Vibrio cholerae, Salmonellae, Shigellae,* and certain strains of *Escherichia coli),* rotavirus, *Campylobacter,* and *Yersinia* are now recognized and our knowledge of the mechanisms involved in *E. coli* diarrhea has grown.

Epidemiological studies have highlighted the worldwide importance of rotavirus and *E. coli* diarrhea and this review will concentrate on these organisms.

Rotavirus

Rotavirus causes perhaps 50 per cent of childhood diarrhea increasing to 80 per cent in temperate climates during the winter. It was first identified in children in 1973, but had previously been found in other young mammals.

In young patients, watery diarrhea preceded by vomiting should suggest rotavirus infection. Dehydration occurs particularly rapidly because of vomiting and, although recovery is usually uneventful with proper rehydration treatment, deaths do sometimes occur. Though a proven cause of diarrhea, rotavirus has been found in the stools of healthy, newborn infants.

Loss of electrolytes and water. Rotavirus is thought to cause diarrhea by destruction of the cells lining the small intestine. The cells replacing those shed into the intestinal lumen are less able to absorb sugars. Unabsorbed sugar draws fluid from the rest of the body into the intestine by osmosis. At the same time, the process of sodium and water transfer, which depends on sugar absorption in the upper intestine, becomes less efficient. The overall effect is a huge loss of electrolytes and water from within the small intestine which the large intestine is then unable to reabsorb. The result is diarrhea and further dehydration.

Escherichia coli

Only certain strains of *E. coli* cause diarrhea in humans and these strains are classified in three groups:

- Enterotoxigenic *E. coli* (ETEC). These *E. coli* produce enterotoxins which stimulate the small intestine to secrete electrolytes and water. Two enterotoxins of *E. coli* are recognized: a high molecular weight protein readily destroyed by heating—heat-labile toxin (LT) and a low molecular weight heat-stable toxin (ST).
- Enteroinvasive *E. coli* (EIEC). EIEC invade the mucosa of the ileum and the colon, unlike ETEC, which remain on the mucosal surface.
- Enteropathogenic *E. coli* (EPEC). EPEC do not produce either LT or ST, nor do they invade the intestine; yet they certainly cause diarrhea. They have been implicated by epidemiological means in outbreaks of diarrhea in infants.

Serologic classification. E. coli can also be classified serologically on the basis of a bacterial cell wall antigen (O antigen). At present, 164 distinct O serogroups are recognized. ETEC, EIEC, and EPEC strains tend to have distinctive O serogroups (Table 1). However, *E. coli* possessing these O serogroups are not always pathogenic and *E. coli* which have not been serotyped may also cause diarrhea.

Nevertheless, the serotype of *E. coli* is a useful epidemiological tool since other means of identifying potentially pathogenic *E. coli* are difficult, expensive, and not widely available.

Infections. Infections with ETEC cause copious, watery diarrhea and are an important cause of warm season diarrhea in young children in developing countries.

EIEC produces fever, abdominal cramps, urgent and painful defecation (tenesmus) and watery diarrhea, followed by scanty discharges of blood and mucus (dysentery). Microscopic examination of methylene-blue stained fecal mucus shows pus and red cells.

EPEC can produce sudden cholera-like diarrhea in adults, whereas in infants the disease often tends to be more prolonged, with high mortality. It is possible that these organisms produce uncharacterized enterotoxins.

Another factor which may determine the ability of *E. coli* to cause diarrhea is whether they can produce hair-like structures called *fimbriae* or *pili.*[2] These *fimbriae* an-

Table 1. O Serogroups in which ETEC, EIEC, and EPEC strains commonly occur.

Escherichia coli strain	Serogroups
ETEC	O6, O8, O15, O20, O25, O78, O115, O148, O159
EIEC	O28, O112, O115, O124, O136, O143, O144, O147, O152
EPEC	O55, O86, O111, O127, O128, O142

[1]Rohde, J. E., and R. S. Northrup. Taking science where the diarrhoea is. Acute diarrhoea in childhood. *Ciba Found Symp* 42:339-366, 1975.

[2]Stickiness and sickness. *Diarrhoea Dialogue* Issue 2, 1980, page 3.

chor *E. coli* to the lining of the small intestine, overcoming the attempts of the intestine to expel them and allowing colonization.

Vibrio cholerae

The vibrio associated with cholera was probably confined to the area around Calcutta until 1813 when a series of pandemics occurred. Improved sanitation in industrialized countries now keeps cholera at bay, but it is still endemic in parts of Asia. Diarrhea caused by cholera looks like rice water and a liter or more of fluid can be lost every hour for several days. An enterotoxin almost identical to LT is the cause of this sympton.

Campylobacter

Campylobacter have been reported mainly from Europe, South Africa, and North America where as high as 15 per cent of infant diarrhea may be due to this organism. Abdominal pain, fever, diarrhea and, occasionally, dysentery are the usual features. Pet dogs, poultry, and milk are likely sources of infection.

Yersinia

Yersinia enterocolitica has been identified as a cause of gastroenteritis in children in Canada, Europe, Japan, and South Africa. It produces pain severe enough to suggest a surgical emergency. *Yersinia* are invasive and also produce ST. Special bacteriologic techniques are needed to grow *Yersinia* and *Campylobacter* from stools. During incubation, high temperatures favor *Campylobacter* and low temperatures encourage *Yersinia.*

Shigellae and Salmonellae

Shigellae are an important cause of diarrhea in infants aged six months to two years. Since shigellosis is spread by person-to-person contact, incidence is higher where environmental health and personal hygiene are poor.[3] As few as 10 swallowed bacteria are enough to cause the disease.

Salmonellae are foodborne and contamination of animal carcasses in slaughterhouses is the usual source. Symptoms resemble those produced by *Campylobacter.*

Salmonellae and *Shigellae* are invasive and probably release toxins from inside the intestinal cells. These cause secretion of fluid in the upper intestine and cell damage in the lower intestine.

Protozoal infections

Giardia lamblia and *Entamoeba histolytica* are single cell microorganisms (protozoa) which have been reported in most countries. *G. lamblia* grows in the small intestine and is thought to be a cause of both acute and chronic diarrhea, by unknown mechanisms. *E. histolytica* prefers tropical zones and causes ulceration of the large intestine.

Other causes

Diarrhea may be due to infections outside the intestine, such as pneumonia, and this possibility must be considered in any child with diarrhea.

Conclusions

At present, the main treatment for acute diarrhea is replacement of water and electrolyte losses. Even in rotavirus infections, when sugar absorption is impaired, the intestine has sufficient reserves to allow successful treatment of diarrhea by oral rehydration with sugar and salt solutions.

In the future, it may be possible to offer specific preventive measures or treatment for specific causes of diarrhea. Simple, low-cost methods for detecting the causative organisms will then be of great importance. Rotavirus can already be detected in stools by a test relying on antibodies against the virus (enzyme-linked immunosorbent assay—ELISA) which can be carried out without expensive equipment such as electron microscopes.

The use of simpler tests in the field will mean that specific therapy will be given only when necessary (Table 2) and that antibiotics will not be administered when contraindicated (e.g. rotavirus) or where such drugs may actually prolong the illness (e.g. *Salmonellae*). Accomplishing these goals will depend on the ability of health workers to recognize the causative organism in the early stages of the disease.

Oral Rehydration in Costa Rica

Since a trial oral rehydration therapy (ORT) project was begun in Costa Rica at the beginning of 1978, ORT has proved an effective life-saver in both bacterial and rotaviral infant diarrhea, including neonates.[4,5] Routine implementation of OR in the National Children's Hospital has resulted in more than an 80 per cent reduction in mortality. The technique is easily understood both by

[3]Kahn, M. U. Soap, water, and shigellosis. *Diarrhoea Dialogue,* Issue 2, 1980, page 3.

[4]Nalin, D. R., *et al.* Oral rehydration and maintenance of children with rotavirus and bacterial diarrhoeas. *Bull WHO* 57:453-459, 1979.

[5]Pizarro, D., *et al.* Evaluation of oral therapy for infant diarrhoea in an emergency room setting; the acute episode as an opportunity for instructing mothers in home treatment. *Bull WHO* 57:983-986, 1979.

Table 2. Clinician's guide to the etiology of diarrheal diseases.[a]

Complaint	Associated clinical features: Common	Associated clinical features: Others	Incubation period	Epidemiological features	Organisms	First line treatment
Acute watery diarrhea (The stool takes the shape of the container)	Vomiting Fever	Severe dehydration in some	24-72 hours	Infants and young children Common worldwide in all socioeconomic groups Peak in colder seasons in temperate climates	Rotavirus	Rehydration therapy
	Nausea Vomiting Abdominal pain	Fever Malaise Severe dehydration	6-72 hours	Infants and young children in developing countries Travelers diarrhea in adults	Enterotoxigenic *Escherichia coli* (ETEC)	Rehydration therapy
	Nausea Vomiting Fever Chills Abdominal pain	Malaise	8-36 hours	Children Common worldwide Foodborne outbreaks (animal products) Warmer seasons	Non-typhoid *Salmonellae*	Rehydration therapy
	Abdominal pain Fever Malaise	Chills Blood and pus in the stools	3-5 days	Worldwide distribution In developed countries may be foodborne (animal products) or transmitted by handling of animals	*Campylobacter*	Rehydration therapy Erythromycin in severe cases
	Vomiting Abdominal pain	Severe dehydration Circulatory collapse, "shock"	1-3 days	Children in endemic areas Adults in newly affected areas Not found in Latin America	*Vibrio cholerae*	Rehydration therapy Tetracycline
	Nausea Vomiting	Fever	6-72 hours	Nursery outbreaks in developed countries Uncertain in developing countries	Enteropathogenic *Escherichia coli* (EPEC)	Rehydration therapy
Dysentery (The stool is soft and watery with blood and/or pus)	Fever Abdominal pain	Malaise Vomiting Urgency to defecate Painful spasm on defecation	36-72 hours	Children Poor hygiene Malnutrition Institutions Warmer seasons	*Shigellae*	Rehydration therapy Ampicillin or Trimethoprim-Sulfamethoxazole
Prolonged diarrhea (or dysentery)	Abdominal discomfort		2-6 weeks	All age groups Worldwide distribution	*Entamoeba histolytica*[b]	Metronidazole
(For at least 7 days, stools have been more frequent or of softer consistency, with or without blood or pus)	Abdominal distension Flatulence	Anorexia Nausea Malabsorption Frothy stools	1-3 weeks	Young children Some travelers Poor hygiene Worldwide distribution	*Giardia lamblia*[b]	Metronidazole

[a]This table is greatly simplified. For example, some agents produce a variety of clinical features. Only agents of major worldwide importance have been included. In certain areas, at certain times, the picture may be quite different. Also, there are a number of other conditions associated with diarrhea such as infections outside the intestine (e.g. measles and malaria), malnutrition, food intolerance, etc.

[b]Can be identified on examination of the stools with a light microscope. Blood and pus from *Shigellae* and *Campylobacter* can also be identified.

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health personnel and mothers visiting the emergency unit at the hospital.[6] In addition, health centers in both urban and rural areas have also been able to introduce oral rehydration therapy.

Field Project

A field project to monitor oral rehydration therapy

[6]Pizarro, D., *et al.* Oral rehydration of neonates with dehydrating diarrhoeas. *Lancet* 2:1209-1210, 1979.

given by mothers to their children in rural areas was started by the Institute for Research in Health ("Instituto de Investigaciones en Salud," INISA) in 1980. Mothers soon learned the technique and treated children successfully. At the same time, comprehensive teaching material for health personnel was prepared by the state welfare system, while the Ministry of Health established a national program of diarrheal disease control with technical cooperation from PAHO.

Sharing Experiences

During the past three years, the Costa Rican experience has been shared with several Latin American countries. Health personnel from Bolivia, El Salvador, Guatemala, Honduras, Panama, Paraguay, and Venezuela visited Costa Rica for a first-hand view of the OR program. Visiting physicians spent a week in the emergency unit of the National Children's Hospital, INISA's rural program in Puriscal, the rural hospital in Grecia, and the Department of Maternal and Child Health of the Health Ministry.

Decrease in Mortality Rates

Since 1978, about 15,000 dehydrated children (including 160 neonates) have been rehydrated in the emergency unit of the National Children's Hospital. Mothers have been taught about the causes, transmission, and management of diarrhea as well as techniques to rehydrate and prevent dehydration among infants.

All these effort have had a considerable impact on both hospital mortality rates and overall diarrheal disease mortality in Costa Rica.[7]

(*Source: Diarrhoea Dialogue,* Issue 7, 1981.)

Editorial Comment

This article focuses on two aspects of diarrheal diseases which constitute a major cause of morbidity and mortality in children in Latin America and the Caribbean.[8]

The PAHO Diarrheal Disease Prevention and Control Program carries out the WHO expanded diarrheal disease program's commitment to reduce infant mortality and malnutrition related to diarrhea. It assumes a collaborative role with national diarrheal disease control programs, and emphasizes interdisciplinary strategies which are integrated into the existing primary health care infrastructure. These strategies include treatment through oral rehydration, maternal and child nutrition, adoption of measures aimed at improving water supplies, sewerage, and food hygiene facilities, intensification of health education efforts, and establishment of surveillance systems to detect and control epidemics and evaluate the program's impact. A final component of the PAHO program is support for research in all aspects of diarrheal diseases.

These diseases are critically important and developments in epidemiology, clinical aspects, research findings, and efforts aimed at their control should be emphasized. The PAHO *Epidemiological Bulletin* provides a forum whereby developments in the aforementioned areas are highlighted for all diseases; contributions in the specific area of diarrheal diseases are welcome.

[7] Mata, L. J. Diarrhoeal diseases. How Costa Rica won. *World Health Forum* 2:141-142, 1981.

[8] See PAHO *Epidemiological Bulletin* 1: 2, 1980.

Reports of Meetings and Seminars

Meeting on Emergencies caused by Communicable Disease Epidemics

A group of specialists from several countries met from 9-13 November 1981 at WHO Headquarters in Geneva to discuss emergency situations caused by communicable disease epidemics. Participants included staff from the six WHO regions (America, Europe, Africa, Eastern Mediterranean, Southeastern Pacific, and Western Pacific).

The main objectives of the meeting were: to find more dynamic means of cooperation among countries and between these and WHO during emergencies caused by common disease epidemics, and to establish guidelines for surveillance, prevention, and control of certain communicable diseases.

As a framework for discussions, the characteristic elements of epidemics which threaten or cause emergency situations were defined to include the following (although