CHAPTER 12

Escherichia coli
Diarrhea

Herbert L. DuPont

1. Introduction

During the 1940s and 1950s, a series of outbreaks of diarrhea in hospital newborn nurseries were reported in which the etiological agent appeared to be *Escherichia coli* identified by serotype. These strains became known as enteropathogenic *E. coli* (EPEC). Little information has been gathered about these strains in recent years, although it is generally recognized that they are responsible for diarrhea among children under 2 years of age.

In 1969, a strain of *E. coli* was shown to be responsible for diarrhea in a group of British soldiers stationed in the Middle East. The strain was later shown to produce an exotoxin that caused fluid accumulation in a ligated rabbit loop preparation. Such enteroxigenic *E. coli* (ETEC) strains have proven to be causes of diarrhea with worldwide distribution. The strains are responsible for approximately 40% of the diarrhea among United States travelers to developing countries.

Certain nonenterotoxigenic *E. coli* strains are pathogenic by virtue of possessing the ability to penetrate intact epithelial cells. These invasive *E. coli* (IEC) strains produce bacillary dysentery clinically indistinguishable from that produced by *Shigella* strains. This form of diarrhea is not common.

In this chapter, we will review information available about EPEC, ETEC, and IEC. Since the organisms are biochemically similar (each represents an *E. coli*), they will be discussed in the same sections even though their clinical features and epidemiology are distinctly different.

2. Historical Background

In 1945, Bray(6) identified an organism with similar antigenic properties in stools obtained from 42 of 44 infants who acquired a diarrheal illness during a hospital-nursery outbreak. Several years later, Giles(30) and Taylor et al.(87) described similar outbreaks of diarrhea due to serotype-identified *E. coli*. During the 1950s, serological procedures were outlined that allowed the fingerprinting of *E. coli* strains according to their somatic (O) and flagellar (H) antigens. It was reported soon thereafter that EPEC strains had a worldwide distribution. The mechanism or mechanisms of virulence of these strains have yet to be resolved.

Taylor et al.(88) reported in 1961 that *E. coli* isolated from stools of a number of children with a diarrheal syndrome gave a positive rabbit-loop reaction (dilatation from transudation of fluid and electrolytes),...
while strains recovered from healthy infants, from well water, or from the urine of patients with urinary-tract infection produced a negative reaction. In 1970, an O148 strain of E. coli was reported to have produced diarrhea in British soldiers stationed in Aden. This strain was later shown to be enterotoxigenic. In the mid 1970s, two different enterotoxins were shown to be produced by E. coli pathogenic for swine. The toxins could be differentiated by a variation in heat susceptibility. In 1971, it was shown that for disease to be produced, ETEC bacteria had to be able to colonize the upper gut of the infected host, and later, colonization fimbriae were identified with this adherence property. ETEC strains have been shown to be the most important cause of diarrhea among United States travelers to Mexico (see Section 5.1).

IEC strains were first demonstrated as causative agents of diarrhea in Japan and Brazil. The similarity of these strains to Shigella in causing bacillary dysentery was demonstrated in volunteer studies. Except for a single but extensive outbreak of diarrhea in the United States during November and December 1971 traced to contaminated imported cheese from France, these strains have been shown to be rare causes of diarrhea in nearly all parts of the world.

3. Methodology

3.1. Sources of Mortality Data

Since E. coli diarrhea is not a reportable disease, little is known about the true incidence and mortality of illness. It is necessary to rely on outbreak data or information obtained from prevalence or short-term incidence surveys. The mortality of EPEC diarrhea has varied widely from 0 to as high as 70%. The average mortality rate is 5–6%, with an age-specific mortality rate in the neonatal period of 16%. Risk factors that relate directly to increased mortality are age, in that the neonatal period and prematurity are associated with higher death rates, and strain variation, in that there appears to be a different virulence of EPEC strains. Escherichia coli O111 is generally associated with a more striking clinical illness and higher mortality rate. There is a prevailing attitude that mortality of EPEC illness has lessened in recent years.

ETEC strains produce mild disease in healthy persons from the United States traveling to Latin America, but severe choleralike illness has been reported in patients studied in cholera-endemic areas. Mortality is unusual with ETEC, but it undoubtedly occurs in areas of the world where health standards are low and where fluid and electrolyte replacement is not established in those with dehydrating illness.

IEC is a rare cause of bacillary dysentery. There are no accurate data on mortality rates, but the reported studies suggest that deaths would be unusual. These reports describe the disease primarily in healthy Western adults. There is good reason to consider the mortality to approximate that seen in shigellosis.

3.2. Sources of Morbidity Data

Again, since E. coli diarrhea is not a reportable disease, data on morbidity must come from survey information.

3.3. Surveys

Sporadic cases and hospital-nursery outbreaks of EPEC diarrhea have been documented in nearly every country where appropriate studies have been carried out. Three types of studies have been done to determine the importance of EPEC illness: surveys of the relative frequency of recovering EPEC strains in populations with diarrhea, study of newborn-nursery outbreaks of EPEC disease, and finally surveillance of the strains during short periods in communities under study. While it is impossible to state the prevalence and incidence of diarrhea with accuracy, in approximately 10% of diarrhea episodes in infants and young children, an EPEC strain can be recovered from stools. Surveillance studies during community epidemics have verified the epidemic potential for EPEC strains.

Surveys of ETEC and IEC diarrhea have been restricted to short-term studies of diarrhea cases in several regions of the world.

3.4. Laboratory Diagnosis

3.4.1. Isolation and Identification of Organisms. The methodology for E. coli isolation is readily available in microbiology texts, and any diag-