Potential Public Health Significance of Non-\textit{Escherichia coli} Coliforms in Food

ROBERT M. TWEDT* and BRENDA K. BOUTIN

Division of Microbiology, Food and Drug Administration
1090 Tusculum Ave., Cincinnati, Ohio 45228

(Received for publication June 19, 1978)

\textbf{ABSTRACT}

Several coliform species other than \textit{Escherichia coli} are often associated with and possibly responsible for acute and chronic diarrheal disease. Recent evidence suggests that non-\textit{Escherichia coli} coliforms may be capable of colonizing the human intestine and producing enterotoxin(s) in high yield. Whether these organisms are newly capable of causing disease because of infestation with extrachromosomal factors mediating pathogenicity or simply because of inherent pathogenic capabilities that have gone unrecognized, they pose a potential health hazard. Food, medical, and public health microbiologists should be aware that the non-\textit{E. coli} coliforms contaminating foods may be potential enteropathogens. This possibility may make determination of their pathogenic capabilities even more important than identification of their taxonomic characteristics.

Colonization of the small intestine by enterotoxigenic \textit{Escherichia coli} with attendant toxin production is well recognized as being responsible for acute and chronic diarrheal diseases that have affected humans of all ages in Africa (18), Asia (17), Japan (21), Brazil (4), Mexico (14, 19), and the United States (20). Adherence of \textit{E. coli} to epithelial surfaces, which promotes colonization of the gut, is mediated by specific, heat-labile surface antigens. These antigens exhibit a fine filamentous or pilus-like structure and include the K-88 antigen of swine-specific enterotoxigenic \textit{E. coli} (6, 25), the bovine- and sheep-specific K-99 antigen (16, 26), and the human-specific colonization factor antigen (1, 2). Each of the host-specific adherence factors of \textit{E. coli} is plasmid-mediated (2, 15, 26). Production of enterotoxins by some strains of \textit{E. coli} is also mediated by transmissible plasmids (5, 23, 24) that are transferred between strains of the species in a manner analogous to the spread of R-factors determining antibiotic resistance (13).

Investigators studying R-factor-mediated antibiotic resistance related the widespread appearance of resistant bacterial strains among the healthy human population to a reservoir of R-factors (30). They warned that indiscriminate use of antibiotics may result in multi-resistant strains that can transfer such resistances in the human gut (27). The transfer of plasmids coding for toxin production (5) or for mucosal adhesion (31) among intestinal bacteria could create reservoirs of enteropathogenicity.

Recently, Wachsmuth et al. (28) demonstrated the plasmid mediation and transmissibility of heat-stable enterotoxin production and multiple antibiotic resistance in \textit{E. coli} 078:K80:H12 epidemiologically incriminated in a hospital outbreak of infantile diarrhea. They showed that the conjugal transfer of the responsible plasmids into \textit{E. coli} K-12 was signaled by concurrent transfer of resistances and enterotoxin production.

\textbf{OTHER COLIFORMS}

Non-\textit{E. coli} coliforms also appear to be capable of colonizing the human gut and producing potent enterotoxins in high yield. During the last few years, strains of \textit{Klebsiella}, \textit{Enterobacter}, and \textit{Citrobacter} (some shown to be enterotoxigenic) have been isolated from stools or the intestinal tract of children and adults in several epidemiological studies of acute and chronic diarrheal diseases (3, 4, 9-12, 29, 30). Reasons for induction of bacterial activities, unexpected in genera considered to have minor pathogenic significance, are as yet unclear. It is possible that a family of enterotoxins may exist among the various \textit{Enterobacteriaceae}. Recent findings suggest that plasmids encoding for enterotoxin production may spread between related species. In fact, the intergeneric transfer of plasmids among the \textit{Enterobacteriaceae} was one reason cited by Sanderson (22) for the difficulties he encountered when studying the genetic relatedness of the family.

\textbf{THE TOXINS}

In a recent study, Klipstein et al. (8) compared the enterotoxigenicity of 12 strains of coliforms (\textit{Enterobacter cloacae}, \textit{Klebsiella pneumoniae}, and \textit{E. coli}) isolated from the gastrointestinal tract of persons ill with diarrhea with that of 13 strains of coliforms from urine cultures. They studied the effect of purified heat-labile or...
heat-stable toxins from these isolates in the rat jejunal perfusion model. All 12 gastrointestinal strains, but only six of the 13 urine strains (one \textit{E. cloacae}, two \textit{K. pneumoniae}, and three \textit{E. coli}), elaborated one or both forms of enterotoxin. In addition to the difference between the two groups of cultures in the proportion of enterotoxin producers, there was also a million-fold quantitative difference in the potency of the toxins produced. Toxins produced by the gastrointestinal strains had minimal effective concentrations as low as 0.1 to 10 ng/ml. In contrast, urine cultures produced toxins of weak potency.

In a companion study, Klipstein and Engert (7) compared the relationship of cholera toxin and the heat-labile and heat-stable toxins of enterotoxigenic \textit{E. coli} to the toxins produced by intestinal isolates of \textit{K. pneumoniae} and \textit{E. cloacae}. They compared the capacity of equine anti-cholera toxin and rabbit antiserum prepared against the heat-labile toxin from each of the coliforms to neutralize homologous and heterologous toxins by the rat jejunal perfusion technique. Their results indicated that the close immunological relationship of cholera toxin and \textit{E. coli} heat-labile toxin extends to the heat-labile toxins of \textit{Klebsiella} and \textit{E. cloacae} and, to a lesser extent, to the heat-stable toxins of \textit{E. coli} and \textit{Klebsiella}.

The immunological similarity between enterotoxins of \textit{E. coli} and other coliforms, demonstrated by Klipstein and Engert (7), supports the hypothesis that these toxins are mediated by plasmid(s) transmissible between species and genera resident in the human intestine.

In an epidemiological investigation of a recent nursery outbreak of diarrheal disease, Guerrant et al. (3) identified nine different serotypes of three different species of enterotoxigenic organisms—\textit{E. coli}, \textit{Klebsiella}, and \textit{Citrobacter}. To support their contention that the outbreak could have been related to the intergeneric spread of toxigenicity by a plasmid, the authors offered three main observations: (a) multiplicity of strains in the epidemic, (b) inability to demonstrate a single, common serotype, and (c) disappearance of toxigenicity despite persistence of identical strains in convalescence. Present evidence strongly supports the thesis that acute and chronic diarrheal disease in humans can result from colonization of the small intestine by enteropathogenic \textit{E. coli} whose ability to adhere to mucosal epithelium and to produce potent enterotoxins is mediated by transmissible plasmids.

Food, medical, and public health microbiologists should be aware that non-\textit{E. coli} coliforms may also develop pathogenicity as a result of acquiring a plasmid(s) while maintained in the environment or in the human host. Strains that are routinely dismissed on taxonomic grounds during microbiological examinations of suspect food may actually pose a potential public health hazard. Recognition of these organisms should therefore rely on tests for enteropathogenic capabilities. Tests for enterotoxigenicity and adherence of \textit{E. coli} should be investigated to determine their applicability for testing other coliforms that contaminate food.

REFERENCES


