

# Escherichia coli Strains As Etiological Agents Of Diarrheal Disease

FRED J. PAYNE, M.D.

A GREAT DEAL of evidence has been compiled during the past 15 years indicating that certain strains of *Escherichia coli* are intimately associated with diarrhea of the newborn. These *E. coli* strains are associated not only with cases of diarrhea occurring in hospital nurseries in the newborn but with sporadic cases occurring outside the hospital. In spite of the evidence, there is considerable doubt in the minds of many highly competent individuals that this association is one of cause and effect.

This paper reviews the currently available evidence concerning these organisms in an attempt to shed further light on this rather complex situation.

The idea that at least some strains of *E. coli* might be a causative agent of epidemic diarrhea of the newborn is not a new one. Adam described a biochemical type of *E. coli* which he felt was responsible for such an outbreak in Germany in the 1920's (1). He labeled his strain "dyspepsi-coli." However, biochemical variations do not permit a satisfactory classification of the genus *Escherichia*, and the work was not followed up.

Bray (2), working in Great Britain in the early forties, noted that the seminal odor which characterized the stools of infants with summer diarrhea originated from the *E. coli* found in them. Serologic studies showed the coli from

these cases were of one antigenic type. This strain, which was called *E. coli* var. *neopolitatum*, was recovered from 100 percent of the sick infants and only 4 percent of the healthy infants in their series.

This work was followed by that of Giles and co-workers (3) who were able to incriminate a strain of *E. coli* by similar methods as the etiological agent of an outbreak. The strain was called *E. coli* alpha type. The same authors subsequently described another serologically distinct strain found in a second outbreak, which they named *E. coli* beta type. Taylor and co-workers (4) in London later described a strain called *E. coli* D-433 as the probable cause of an outbreak in a nursery there.

By this time Kauffmann (5) had completed work on a serologic typing schema for *E. coli*. He described the *E. coli* beta type of Giles and associates as belonging to O group 55 of his schema, with an envelope antigen B5. The type strain for this O group had been recovered earlier from the pus of a middle ear infection. He further demonstrated that the *E. coli* var. *neopolitatum* of Bray, the alpha type of Giles and associates, and the D-433 of Taylor, all belonged to a new O group, which he designated 111, and that these strains had the same envelope antigen, B4. Since that time *E. coli* O55B5 and O111B4 have been found in widely scattered outbreaks of diarrhea of the newborn throughout the world. A number of other serotypes of *E. coli* have subsequently been found to be involved with this disease in single or multiple outbreaks. A recent review of this problem, with extensive bibliography, has been presented by Neter (6).

In most of the epidemics in which these organisms have been incriminated, the pattern has been similar. The particular coli type has been found to be present in almost pure culture in the stools of sick infants and has been found infrequently in the stools of healthy infants in the same environment.

I have had the opportunity to investigate five such outbreaks during the past 6 years. Two were associated with *E. coli* O55B5, two with *E. coli* O111B4, and one with *E. coli* O127B8.

Rarely were members of the nursery staff found to be infected with the epidemic strain in these outbreaks. The source of four of the

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*Dr. Payne is assistant chief of the Phoenix, Ariz., field station of the Communicable Disease Center, Public Health Service. The article was presented as a paper at the 17th annual conference of the U.S.-Mexico Border Public Health Association in Brownsville, Tex., and Matamoros, Tamaulipas, Mexico, on March 31, 1959.*

outbreaks could not be clearly determined. But in one instance an infant acutely ill with diarrhea was admitted to an open pediatric ward and ignited an outbreak.

As an increasing number of outbreaks associated with these organisms were reported, the problem of their epidemiology outside the hospital became more pressing. A study done by the Public Health Service in New Orleans in an effort to find O groups 55 and 111 in healthy infants and children disclosed one O111 in 576 children. Similar studies carried on in Denmark on an even larger scale showed a similarly low yield (7).

### More Etiological Agents

Subsequent studies have contradicted these earlier findings. Gamble and Rowson (8) reported that they had found enteropathogenic *E. coli* in 20 percent of their routine stool examinations in infants under 1 year of age. Their reason for designating some of the serotypes in their investigations as enteropathogens is not clear; however, they include types which are not generally accepted as enteropathogenic. This serves to illustrate a fundamental problem in working with these organisms. We must be exceedingly careful in our designation of a type as enteropathogenic. Only for three serotypes, O111B4, O55B5, and O127B8, do we have what amounts to conclusive evidence that their association with diarrhea is one of cause and effect. They have been found repeatedly throughout the world associated with epidemic diarrhea of the newborn, and they have been shown experimentally to be capable of producing a gastroenteritis in human adults when ingested in large numbers.

In addition to these three types, evidence is mounting that certain other types alluded to earlier in this paper may be etiological agents as well. These are O26B6, O86B7, O112B11, O119B14, O124B17, O125B15, O126B16, and O128B12. In all, about a dozen types fall under scrutiny as possible or probable enteropathogens on the basis of previous involvement in nursery outbreaks. Until we are sure not only of their pathogenicity but also of their epidemiological characteristics, we must be careful about interpreting data which lump them all

together. For the present, the data for each type must be analyzed separately and evaluated on its own merits.

In studies carried out in Phoenix, Ariz., from October 1957 through February 1959, enteropathogenic *E. coli* have been associated with 25 percent of some 474 cases of acute diarrhea in children under 2 years of age admitted to three hospitals in the area. *Shigella* infections accounted for an additional 25 percent. Among 98 infants under 2 months of age in this series, however, these *E. coli* types were found in 40 percent, whereas shigellae were found in only 8 percent. It is obvious that in the age groups where the highest mortality occurs, enteropathogenic *E. coli* constitute a very important cause of diarrhea. Almost half (46 percent) of the *E. coli* infections in this age group were with O groups 111 and 55.

In an attempt to piece together the epidemiology of the enteropathogenic *E. coli* as it exists outside the hospital, we have carried out studies on the families of infants who are admitted to the hospital infected with one of these organisms. We found that the infection rate among 244 contacts of all ages for all types of *E. coli* was 12.4 percent. Only rarely was a type encountered other than the one found in the index case. The rate varied little by age group. It was 14 percent in the age group 0 to 4 years and 13 percent in the age group 20 to 49 years. The secondary infection rate varied somewhat by type; however, the rate was 17 percent for O55 compared with 10 percent for O111 and 7 percent for O126. The numbers of other types were too small for individual analysis, but collectively their secondary infection rate among family contacts was 11 percent.

These rates are somewhat higher than those obtained for salmonellae in the same study. The secondary infection rate among family contacts of patients with salmonellosis was 8 percent. One must be cautious in interpreting this difference, however, because the ability of the laboratory to recover salmonellae and enteropathogenic *E. coli* from carriers is probably quite different. With better tools, the rate for *E. coli* could be expected to be considerably higher. No evidence has been uncovered as a result of these investigations which would

allow us to draw hypotheses as to the epidemiology of these organisms. All of the families were poor since our cases were principally charity cases. Pets or livestock were found infrequently on the premises. The diets of these people are marginal, but overt malnutrition is uncommon.

### Conclusion

There appears to be a cause and effect relationship between at least three serotypes of *E. coli* and diarrhea of the newborn. In addition, there appears to be a relationship between eight or nine other serotypes and this disease. Perhaps still others will be found in the future.

The natural history of these types outside hospital walls remains obscure, but they constitute a leading cause of cases of severe diarrhea among infants under 2 months of age whose onsets are at home as well as those occurring in hospital outbreaks. There is no assurance that environmental control measures now in vogue for diarrheal diseases will be effective in the control of these agents.

### REFERENCES

- (1) Adam, A.: Dyspepsie-Koli. Zur frage der bakteriellen aetiologie der sogenannten alimentaren intoxication. Jahrb. Kinderheilk 116: 8-40 (1927).
- (2) Bray, J.: Isolation of antigenically homogenous strains of *Bact. coli neopolitanum* from summer diarrhea of infants. J. Path. & Bact. 57: 239-247, April 1945.
- (3) Giles, C., Sangster, G., and Smith, J.: Epidemic gastroenteritis of infants in Aberdeen during 1947. Arch. Dis. Childhood 24: 45-53, March 1949.
- (4) Taylor, J., Powell, B. W., and Wright, J.: Infantile diarrhea and vomiting. A clinical and bacteriological investigation. Brit. M. J. 2: 117-141 (1949).
- (5) Kauffmann, F.: The serology of the coli group. J. Immunol. 57: 71-100, September 1947.
- (6) Neter, E.: Enteritis due to enteropathogenic *Escherichia coli*. J. Pediat. 55: 223-239 (1959).
- (7) Dupont, A.: On the occurrence of *Escherichia coli* O:55:B:6 and *E. coli* O:111:B:6 in fecal samples from infants with diarrheal disease and in control material. Acta. paediat. 83: 95 (1951).
- (8) Gamble, D. R., and Rowson, K. E.: Incidence of pathogenic *Escherichia coli* in routine fecal specimens. Lancet 273: 619-621, 628, September 1957.

## New Radiation Health Publication

The first issue of a new monthly technical publication giving levels of radioactivity in the environment appeared in April 1960.

Entitled *Radiation Health Data*, the publication is prepared by the Public Health Service as an outgrowth of a directive by the President in August 1959 that the Department of Health, Education, and Welfare "intensify its radiological health efforts and have primary responsibility within the executive branch for the collation, analysis, and interpretation of data on environmental radiation levels."

Data on radiation levels in the air, water, and milk comprise the bulk of this issue of the periodical, which presents facts compiled from a number of sources by the Public Health Service's Division of Radiological Health, with the assistance of a board of editorial advisers representing the Departments of Health, Education, and Welfare, Defense, Agriculture, and Commerce, and the Atomic Energy Commission.

Among the contents of this issue are data on strontium 90 in milk collected during November 1959 at 12 locations in the United States by the Public Health Service; milk collected during the same month at 3 locations by the Atomic Energy Commission; and monthly milk collections for the year ending August 1959 at 6 locations in Minnesota as reported by the State health department.

Most of the radiation measurements carried by the new publication will be in the form of raw data which will be susceptible to meaningful analysis or interpretation when these data accumulate and more knowledge of the biological effects of radiation begin to come out of research by Federal, State, and local agencies, and by industry and universities.

The price of the publication is 50 cents an issue or \$3 per 6-month subscription. It is available from the Office of Technical Services, U.S. Department of Commerce, Washington 25, D.C.