

Delhi Belly, Hong Kong Dog, Casablanca Crud, Montezuma's Revenge, Turista

BY WHATEVER SYNONYM, travelers' diarrhea remains a taxing problem for the physician trying to give practical advice in advance of travel. Despite the renaissance of information emerging from recent studies of bacterial diarrheas,¹ little has come forth to advance our knowledge of the cause, treatment or prevention of travelers' diarrhea. These points are well reviewed by Dr. Barrett-Connor in this issue of CALIFORNIA MEDICINE.

Etiology. The relatively few bacteriologic and virologic studies conducted on travelers' diarrhea have shown that most cases are not due to viruses or to the commonly accepted enteropathogenic agents, including salmonellae, shigellae, the enteropathogenic serotypes of *Escherichia coli*, *Entamoeba histolytica*, and *Giardia lamblia*. Nevertheless, epidemiologic evidence strongly implicates an infectious process.

A most attractive hypothesis to explain travelers' diarrhea holds that the "normal" bacterial population of a person's intestinal tract changes during travel as a result of exposure to the "normal" intestinal bacterial population in a new environment.² In this process of change, so the hypothesis goes, for many persons diarrhea is an intermediate stage. The pathogenesis of such diarrhea may include the invasion by foreign coliforms of upper levels of the intestinal tract,^{2,3} areas that are normally sterile or nearly so. A recent important finding was the isolation of "nonpathogenic," toxin-producing *E. coli* from sites in the jejunum, duodenum, and stomach of indigenes (not travelers) in India, who were experiencing acute episodes of diarrhea.³

Future studies of travelers' diarrhea should include serotyping of *E. coli* strains before departure, and during and after episodes of diarrhea. In addition, studies should attempt to isolate coli-

forms as well as anaerobes temporarily colonizing the upper intestinal tract. Basic to the latter work, however, is further clarification of the normal anaerobic intestinal flora.

Efforts to determine factors that predispose to diarrhea should be continued. Immunity may play a role. Reduction of intestinal motility by opiates has been reported in animal studies to enhance the pathogenicity of certain bacteria in the upper small intestine. Speculative but intriguing is whether the changing diet of travelers might yet be shown to contribute to the invasiveness of ordinarily nonpathogenic enterobacteria. In support of this notion, a recent report by Bullen et al⁴ suggests that the iron-binding proteins of mother's milk play an important part in the resistance of breast-fed infants to *E. coli* infection as well as related physiologic conditions in the small intestine.

Therapy. Dr. Barrett-Connor's suggestion that allowing diarrhea to continue may serve a useful purpose by eliminating the infective organism or enterotoxin is provocative but needs further study. Meanwhile, patients should be provided symptomatic relief by such agents as compound of opium (paregoric) or diphenoxylate hydrochloride (Lomotil®). The comparative effectiveness of the two drugs is not established. Additional therapy includes rest, fluids, and an appropriate diet for diarrhea. If, however, diarrhea and prostration persist for longer than the usual one to three days, or if blood or mucus appears in the stools, or if temperature elevation is more than low grade for about a day, the patient should be advised to see a physician for diagnosis. Such symptoms often indicate salmonellosis, shigellosis or amebiasis.

Chemoprophylaxis. No drug can be recommended at present for the prophylaxis of either

travelers' diarrhea or for enteric bacterial or protozoal pathogens. The efficacy and safety of the drugs promoted for these purposes are in dispute or need additional confirmation. Promising perhaps in selected cases is the use of oral nonabsorbed sulfonamides or antibiotics (with full recognition, however, of their potential for adverse side effects). Travelers to areas with poor sanitation and hygiene still do best to eat only what is cooked or peeled, and to drink only boiled or bottled water.

Of immediate concern is the drug iodochlorohydroxyquin (Entero-Vioform®), often prescribed in advance of travel or available abroad without prescription. Studies of its effectiveness for travelers' diarrhea are not convincing. The recent fascinating-tragic report from Japan^{5,6} of an association between the use of Entero-Vioform and the onset of a severe neurologic disease—subacute myelo-optic neuropathy (SMON)—in thousands of persons, has led the Food and Drug Administration in this country to recommend that the drug not be used for travelers' diarrhea. Although a causal relationship between the drug and the syndrome has not been established, the association is strong. A suggestive case of SMON was recently described⁷ in a returning citizen following use of Entero-Vioform abroad. Since Entero-Vioform is a hydroxyquinoline, we should be alert to the possible occurrence of the SMON syndrome following therapeutic use of the chemically related drug diiodohydroxyquin (Diodoquin®), a major drug for the treatment of amebiasis. For this disease, it seems prudent to withdraw Entero-Vioform pending further studies, but to continue to use the equally effective Diodoquin.

ROBERT GOLDSMITH, MD

Associate Professor of Tropical Medicine
Department of International Health and
Division of Ambulatory and Community
Medicine
University of California, San Francisco

REFERENCES

1. Grady GF, Keusch GT: Pathogenesis of bacterial diarrheas (first of two parts). *N Engl J Med* 285:831-841, Oct 7, 1971
2. Eichenwald HF, McCracken GH Jr: Acute diarrheal disease. *Med Clin N Amer* 54:443-453, Mar 1970
3. Gorbach SL, Banwell JG, Chatterjee BD, et al: Acute undifferentiated human diarrhea in the tropics—I. Alterations in intestinal microflora. *J Clin Invest* 50:881-889, Apr 1971
4. Bullen JJ, Rogers HJ, Leigh L: Iron-binding proteins in milk and resistance to *Escherichia coli* infection in infants. *Br Med J* 1:69-75, Jan 8, 1972
5. Kono R: Subacute myelo-optico-neuropathy, a new neurological disease prevailing in Japan. *Japan J Med Sci Biol* 24:195-216, Aug, 1971
6. Schultz MG: Entero-Vioform for preventing travelers' diarrhea. *JAMA* 220:273-274, Apr 10, 1972
7. Kean BH: Subacute myelo-optic neuropathy. *JAMA* 220:243-244, Apr 10, 1972

Controversial Ethical Issues in Medicine

THE ARTICLE, "Euthanasia—An Overview for Our Times," which is to be found elsewhere in this issue, marks the second in a new series, "Controversial Ethical Issues," in CALIFORNIA MEDICINE. As far as is known the Committee for Continuing Study of Evolving Trends in Society Affecting Life is the first of its kind to be established in any medical association. It has a difficult but an enormously important assignment. It is the primary instrument of organized medicine in California to explore the many new and complex ethical issues affecting life which are already confronting physicians, their patients and the families of patients and society as a whole. These issues are not likely to go quietly away. They are certainly not to be swept under the rug. Nor will they be easily resolved.

We live in a time of changing values, or at least in a time when traditional values are being questioned and reassessed. This, coupled with scientific progress in medicine and human biology which is likely to be nothing short of fantastic within the foreseeable future, and the certainty that the cost of applying this mushrooming knowledge and technology in practice will be equally fantastic, foreshadows the need for many new kinds of value decisions affecting human life and well-being. These decisions will generally be made by patients, their families, or in some way by society, but physicians and even the medical profession as a whole cannot but be involved in them.

It is appropriate that these emerging ethical issues be more openly discussed and it is appropriate that the medical profession be an important part of these discussions. It is not too soon to begin to get our thoughts in order, both as physicians and as a profession particularly concerned with human life and the quality of life.

—MSMW