Leading article

Antibiotics and travellers' diarrhoea

It has been estimated that approaching one thousand million passengers will travel annually on commercial airlines by the end of the present decade. As diarrhoea is the commonest ailment affecting travellers it is an opportune time to consider the benefits and disadvantages of chemoprophylaxis in the prevention of this troublesome, embarrassing and often incapacitating disease.

Salmonellae, shigellae, *Vibrio cholerae* and *Entamoeba histolytica* have long been recognized as causes of diarrhoea in travellers, especially those visiting tropical and sub-tropical countries. More recently, rotaviruses, campylobacter species and also *Giardia lamblia* have been shown to be common aetiological agents, particularly the latter organism which is a relatively frequent cause of diarrhoea in travellers to Eastern Europe, especially visitors to Leningrad.

The most important microbiological causes of travellers' diarrhoea, however, are undoubtedly enterotoxigenic strains of *Escherichia coli*. These organisms were first definitely linked with travellers' diarrhoea by Rowe and his colleagues (1970) who isolated them from the stools of more than half of a group of British soldiers who had developed diarrhoea shortly after arriving in Aden. Gorbach *et al.* (1975) studying American students travelling during college vacations confirmed this observation and found that 72% of students (26 out of 36) who developed diarrhoea while in Mexico excreted enterotoxin-producing *E. coli* strains in their stools. The *E. coli* toxin is heat-labile and has a similar action on the intestine to that of the cholera toxin which stimulates the adenyl cyclase system in the wall of the gut thus inducing isotonic fluid and electrolyte secretion into the bowel. The ability of *E. coli* to produce enterotoxin is conferred by a transmissible plasmid, unlike toxin production in *V. cholerae* which is chromosomally mediated. Travellers most susceptible to the effects of enterotoxigenic *E. coli* strains are those from 'developed' countries with temperate climates travelling to less advanced communities, especially in tropical and sub-tropical areas of the world. It is probable that the indigenous populations of these countries, and also long-stay visitors, develop resistance to the local *E. coli* strains.

Many antimicrobial agents have been recommended for the chemoprophylaxis of travellers' diarrhoea and several have apparently been successful as judged by the results of controlled clinical trials. These include the sulphonamides, neomycin, doxycycline, furazolidine and clioquinol (enterovioform) (DuPont & Pickering, 1980). It is probable that the beneficial effect of these agents in the prevention of travellers' diarrhoea is principally related to the inhibition of toxin-producing *E. coli* strains.

Unfortunately, as happens with most, if not all, chemoprophylactic regimes there are a number of important problems associated with the use of antimicrobial agents for the prevention of travellers' diarrhoea. The most obvious disadvantage is the possibility of adverse reactions to the chosen drug. These may be relatively trivial, for example rash with the sulphonamides or ampicillin, but can be serious and potentially fatal as with the Stevens-Johnson syndrome, also associated with sulphonamides. Enterovioform has been claimed to be a cause of subacute myelo-optic neuropathy if taken continuously in high doses for prolonged periods and is no longer licenced in the United States. Neomycin can damage small bowel villae and lead to intestinal malabsorption and doxycycline may produce several unwanted effects including staining of teeth in children and cutaneous photosensitivity.

Chemoprophylaxis for travellers' diarrhoea may also be associated with unwanted microbiological consequences. In the individual patient this may result in 'superinfection' with micro-organisms such as salmonella species resistant to the agent being used for prophylaxis. An additional and extremely important microbiological hazard is the selection out and dissemination of antibiotic-resistant bacteria, including those with
multiple resistance patterns. Plasmids conferring the capacity to produce enterotoxin may be transmitted by bacterial conjugation.

Should chemoprophylaxis be used in an attempt to prevent travellers developing diarrhoea when they visit 'high-risk' countries? DuPont & Pickering (1980) recommend prophylaxis in certain circumstances which include previous severe attacks of travellers' diarrhoea and/or for key personnel making brief visits to 'high-risk' countries for important reasons such as diplomatic missions or business meetings. International sportsmen are also commonly given prophylactic agents in the hope of preventing diarrhoea which, for them, can be incapacitating and embarrassing. Further groups to be considered are those with alimentary disease such as ulcerative colitis or prior gastric surgery, and also the immunosuppressed.

It is essential that each case should be considered individually and chemoprophylaxis only prescribed after careful thought. Mass and indiscriminate use of antimicrobial agents for the prevention of diarrhoea must be discouraged for the reasons given above plus the additional disadvantage of unnecessary cost. Indeed, there are many who maintain that there is little substantiated evidence based on large-scale clinical trials for the efficacy of chemoprophylaxis for travellers' diarrhoea (Nye, 1979). I am inclined to support this view.

Which drug should be used if chemoprophylaxis is considered necessary? Doxycycline was shown to be effective in American Peace Corps volunteers arriving in East Africa (Sack et al., 1978). The antibiotic was given initially in a dose of 200 mg daily for the first week and then reduced to 100 mg daily for a further 14 days. Microbial species causing diarrhoea, however, differ in different countries and their antibiotic sensitivity patterns vary. There is, therefore, no way of predicting which drug will be effective in a particular part of the world.

An alternative approach which avoids the use of antimicrobial agents and is therefore attractive is the use of bismuth subsalicylate which may act by neutralizing E. coli enterotoxin and has been shown to be effective in the prevention of travellers' diarrhoea (DuPont et al., 1980). The disadvantage of this preparation is that it has to be carried as a suspension.

Of greater importance than chemoprophylaxis in the prevention of travellers' diarrhoea is scrupulous care in the selection of food and drink when visiting 'high-risk' countries. Wayside vendors should be avoided and meals only taken in hotels and recommended restaurants. Even these precautions, however, will not prevent the acquisition of the ubiquitous toxigenic E. coli. If a traveller does develop significant diarrhoea he should avoid food and maintain hydration with non-alcoholic fluids. A bowel sedative such as 30 mg of codeine phosphate may be helpful. However, anti-peristaltic agents, by slowing intestinal transit, may delay the elimination of bacteria and inflammatory debris and prolong the illness. They should therefore be used with caution. Travellers to remote areas without available medical advice might be supplied with co-trimoxazole and metronidazole and given instructions to commence a course of the former for diarrhoea of more than 24-h duration associated with significant systemic upset and fever. Metronidazole could be taken for 'low-grade' diarrhoea persisting for more than three days especially if associated with abdominal distention and colic; it should be continued for seven days.

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References