Aetiology of protracted gastrointestinal complaints after travel in the (sub)tropics

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This article presents a prospective study of the aetiology of chronic diarrhoea or persisting gastrointestinal complaints after travel in the (sub)tropics. Inclusion criteria were diarrhoea or gastro-intestinal complaints that had started during travel in (sub)tropical countries or within two weeks after return, and persisted for at least two weeks.

This report is the third part of a study concerning chronic gastrointestinal problems after travelling in the subtropics (Van Gompel et al, 1994). In part three an extended prospective survey was performed in order to establish the most frequent microbiological or parasitic causes of protracted gastrointestinal symptoms after travel or stay in the (sub)tropics. The predictive value of liquid stools for presence of pathogens was also checked. Of the stools studied, a bacterial pathogen was found in 8.2%, and a parasite in 9.6%.

The most frequent pathogens found were *Campylobacter jejuni* and *Giardia lamblia*. The low amount of pathogens found in the stool contrasts with higher yields obtained in studies of acute diarrhoea. Liquid stools predict the presence of bacterial pathogens, not of parasites.

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Material and methods

We included all patients who presented at the post-travel clinic from March 1992 until May 1995 with persisting diarrhoea or other gastrointestinal complaints (anorexia, nausea, vomiting, abdominal pain or discomfort, meteorism, flatulence — symptoms which were sufficiently disturbing to necessitate consulting a specialized post-travel service).

The diarrhoea must have started during the travel in (sub)tropical countries or within two weeks after return. All patients were asked to submit a fresh stool sample for parasite detection and bacterial culture, regardless of previous antibiotic treatment.

In addition to routine cultures, more elaborate techniques were used. To isolate *Campylobacter upsaliensis*, the faecal material was filtered for 30 to 60 minutes on on a cellulose triacetate membrane filter (diameter of 0.45 micron, SM 11106050N, Sartorius Gmbh,Vander heyden.), then incubated on Mueller-Hinton agar with 5% sheep blood at 37 °C, aerophilic, over three days (anaerocult C, 1 16 275, Merck) (Goossens et al, 1990a; Goossens et al,

1990b). For *Salmonella sp.* the stool was enriched on selenite at both 37 °C and 42 °C for five days. For *Yersinia sp.* stool was enriched both on Rappaport (BPF7601, International Medical) and on phosphate buffer (pH 7.2 at 4 °C) for one week. To detect *Escherichia coli 0157: H7* the stool was incubated on Fluorocult E. coli 0157: H7 agar (Merck, 4036).

Table 1. Frequency of bacterial pathogens cultured in the stools

Campylobacter jejuni	11/330
ETEC	6/330
Shigella sp.	4/330
Salmonella sp.	3/330
Clostridium difficile	1/330

Table 2. Frequency of parasites found in the stools

Giardia lamblia	15/312
Entamoeba histolytica	9/312
Trichuris trichiura	5/312
Ancylostoma	3/312

We searched for ova and parasites by SAEX concentration-technique (Loughlin and Spitz, 1947). Since routine stains used for stool parasitology are not sensitive for the identification of *Cryptosporidium* oocysts, a fuchsine staining technique was performed (Heine, 1982). For patients suspected to have strongyloidiasis, Baermann's method was used (Jones and Abadie, 1954; Pereira-Lima and Delgado, 1961). The liquid or more firm aspect of the stools was noted in the laboratory (WHO, 1991).

Results

Three hundred and thirty stool samples of different patients were examined microbiologically and 312 parasitologically. In 27 (8.2%) samples a bacterial enteropathogen was isolated (*Table 1*) and the most frequent bacteria cultured was *Campylobacter jejuni*. In 30 (9.6%) a parasite was found in the stools (*Table 2*), *Giardia lamblia* being the pathogen most frequently found. In eight cases several micro-organisms were found in the same stool sample. In total we found a pathogen in 15.2% of the stools. In one patient, suffering from diarrhoea for five years, an overwhelming infection with exclusively vegetative forms of *Entamoeba coli* was found. After treatment with tinidazole 2g/d for seven days all his symptoms and the vegetative forms of *Entamoeba coli* disappeared.

We evaluated the association between the consistency (liquid or normal) of the stools and the presence of pathogens (*Table 3*). There is a significant association ($P< 0.05$) between liquid stools and all pathogens. This association is even more significant with bacterial enteropathogens but no association was found with

Table 3. Association between liquid stool and the presence of pathogens in the stool:

	positive likelihood ratio	negative likelihood ratio	odds ratio	*P*
any pathogen	1.4	0.7	1.78 (1.29<OR<2.46)	0.044
bacterial	1.6	0.5	3.15 (1.81<OR<5.49)	0.011
parasite	1.2	0.8	1.55 (1.05<OR<2.27)	0.265
Campylobacter jejuni	1.7	0.5	3.67 (1.62<OR<8.53)	0.046
Giardia lamblia	1.6	0.9	2.66(1.38<OR<5.14)	0.063

parasites. Normal stool consistency does not exclude the presence of pathogens: if only patients with liquid stools were examined, we would have missed 7/27 (26%) of stools positive for bacterial enteropathogens and 18/30 (60%) of stools with parasites.

Discussion

Gastrointestinal symptoms frequently occur during or after travel or stay in the (sub)tropics and protracted diarrhoea is often encountered (Sharp et al,1995; Ericsson et al,1995). In the first part of this study, diarrhoea lasting for more than two weeks was seen in 19.6% of patients complaining of diarrhoea (Van Gompel et al, 1994). Diarrhoea lasting for more than one month is seen in 2% (Kelsall and Guerrant, 1992; Ericsson et al, 1995).

In this study we could only detect a causal agent in 15.2%. This low yield is consistent with the data obtained in the earlier part of the study (Van Gompel et al, 1994). A possible explanation for this phenomenon is that there are several non-infectious causes for chronic diarrhoea or persistent gastrointestinal complaints. They may be due to disruption of the normal architecture and functioning of the small bowel, possibly as a consequence of infection, such as in tropical sprue and lactase deficiency.

Irritable bowel syndrome can be a late complication of salmonella or other bacterial infections (McKendrick and Read, 1994). Other causes are bacterial overgrowth, inflammatory bowel disease, and hormonal dysfunction (Kelsall and Guerrant, 1992; Donowitz et al, 1995). The low level of detected enteropathogens might be due to insufficient sensitivity of the detection methods used in the study or to the non-exclusion of patients with previous antibiotic and/or parasitic therapy (Van Gompel et al, 1994). A new ELISA technique to detect *Giardia lamblia* in stools with a sensitivity of 92% and a specificity of 98% is important in this perspective (Wanke et al,1987; Donowitz et al, 1995).

In studies on acute diarrhoea, enteropathogens are more often found. (Mattila et al, 1992; Gascon et al, 1993; Haberberger et al,1994; Ericsson et al,1995).

The spectrum of enteropathogens isolated differs in acute diarrhoea and chronic diarrhoea. In acute diarrhoea *ETEC, EAEC , Shigella sp.* and *Campylobacter jejuni* are mainly found depending on the season and geographical region (Mattila et al, 1992; Haberger et al, 1994; Sharp et al, 1995; Ericsson et al, 1995).

Our data give the highest prevalence for *Giardia lamblia* (4.8%), *Campylobacter jejuni* (3.3%) and *Entamoeba histolytica* (2.9%). Steffen found *Giardia lamblia* in 10/73 (13.7%) and *Entamoeba histolytica* in 13.7% of patients with chronic diarrhoea (Steffen et al, 1987). Van Gompel et al (1994) found *Giardia lamblia* in 6.3%, which was also their most frequent diagnosis in patients with chronic gastrointestinal complaints. Liquid stool and the presence of bacterial pathogens, particularly *Campylobacter jejuni*, are positively related. Such an association does not exist between parasites and liquid stool. These findings, however, do not allow us to forgo a culture of formed stool in patinets with chronic gastro-intestinal complaints. Had we adopted such a strategy, we would have missed 25.9% of bacterial pathogens in this study.

Conclusion

In more than 80% of patients with protracted diarrhoea or other gastro-intestinal complaints after travel in the (sub)tropics, no parasitic or microbiological cause can be obtained by means of extended laboratory testing. The most common pathogens associated with chronic complaints are *Giardia lamblia* and *Campylobacter jejuni*. There is a significant association between liquid stools and bacterial pathogens, but not with parasites. Because of the low predictive value of liquid stools for the presence of pathogens, examination of formed stools should always be performed when patients have complaints, especially when looking for treatable bacterial causes.

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