tissues and it contributes to the tumorigenic process through the promotion of cell survival, stimulation of angiogenesis, and enhancement of invasion and metastasis.[8 10] The current investigation highlights the critical role of the microenvironment in transcriptional regulation, whereby an extrinsic fine-tuning mechanism is instigated to favour those events that particularly promote tumour progression.

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References

1 **Morin PJ**, Sparks AB, Korinek V, *et al*. Activation of β-catenin-Tcf signaling in colon cancer by mutations in β-catenin or APC. *Science* 1997;**275**:1787–90.
2 **Reya T**, Clevers H. Wnt signalling in stem cells and cancer. *Nature* 2005;**434**:843–50.
3 **Batlle E**, Henderson J, Beghtel H, *et al*. β-catenin and TCF mediate cell positioning in the intestinal epithelium by controlling the expression of EphB/ephrinB. *Cell* 2002;**111**:251–63.
4 **Holmberg J**, Genander M, Halford M, *et al*. EphB receptors coordinate migration and proliferation in the intestinal stem cell niche. *Cell* 2006;**125**:151–63.
5 **Clevers H**, Batlle E. EphB/EphrinB receptors and Wnt signaling in colorectal cancer. *Cancer Res* 2006;**66**:2–5.
6 **Batlle E**, Bacani J, Begthel H, *et al*. EphB receptor activity suppresses colorectal cancer progression. *Nature* 2005;**435**:1126–30.
7 **Harris AL**. Hypoxia: a key regulatory factor in tumour growth. *Nat Rev Cancer* 2002;**2**:38–47.
8 **Semenza GL**. Hypoxia, clonal selection, and the role of HIF-1 in tumor progression. *Crit Rev Biochem Mol Biol* 2000;**35**:71–103.
9 **Kaidi A**, Williams AC, Paraskeva C. Interaction between beta-catenin and HIF-1 promotes cellular adaptation to hypoxia. *Nat Cell Biol* 2007;**9**:210–7.
10 **Lal A**, Peters H, St. Croix B, *et al*. Transcriptional response to hypoxia in human tumors. *J Natl Cancer Ins* 2001;**93**:1337–43.

Inflammatory bowel disease: reviewing an old study under a new perspective

We would like to comment on the paper by Professor S Shivananda and colleagues (*Gut* 1996;**39**:690–7), which examined whether there was a difference in the incidence of inflammatory bowel disease (IBD) between northern and southern Europe.

Shivananda *et al*. conducted an epidemiological study across Europe from 1991 to 1993, and concluded that IBD, which includes ulcerative colitis (UC) and Crohn's disease (CD), is possibly not more frequent in the north than in the south.

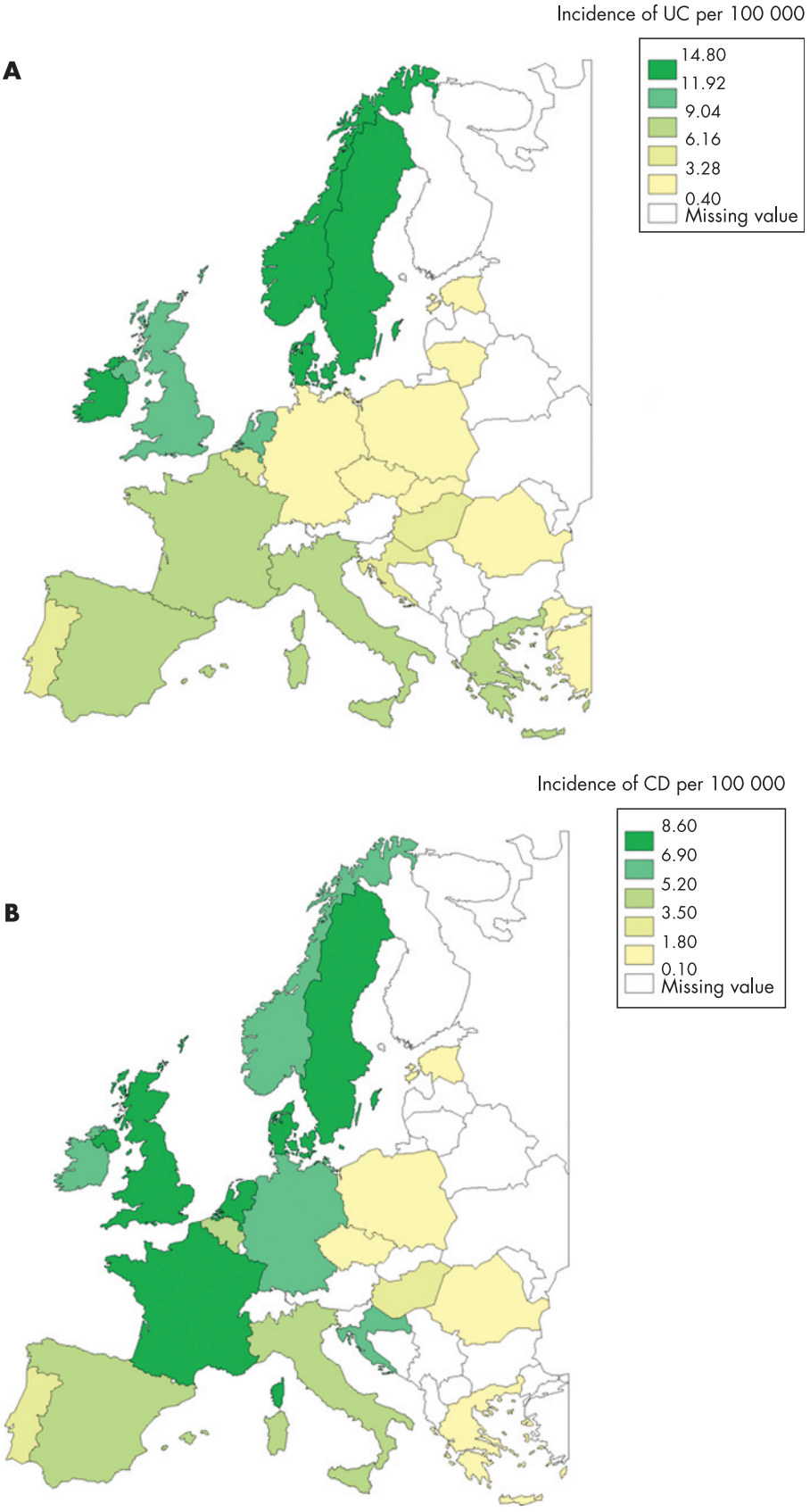

Figure 1 Incidence of IBD across Europe. (A) Incidence of ulcerative colitis (UC). (B) Incidence of Crohn's disease (CD). The maps were designed with Philcarto 4.50 for Windows (http://perso.club-internet.fr/philgeo).

Although their results are solid and groundbreaking, they did not manage to provide an explanation of the geographic distribution of the disease. A possible reason is that they did not include countries from Eastern Europe in their study.

Recent data from this area give us the opportunity to examine this issue again, providing a possible explanation. In fig 1, we present the incidence of UC (fig 1A) and CD (fig 1B) across Europe, according to data mentioned in reviews by Lakatos and Lakatos,[1] and Loftus.[2] We note some characteristics that are the basis for the new explanation:

- Although Estonia is located in northern Europe, the incidence of IBD shows pronounced differences compared with the high incidence in Scandinavian countries.[1]
- Estonia, Hungary, Romania, Croatia, the Czech Republic, Slovakia and Poland have incidence rates of UC that range from 0.5 to 5.9 per 100 000 population[1] while countries of Western Europe have an overall incidence for UC of (at least) 10.4 (*Gut* 1996;**39**:690–7). For CD, the incidence rates of the previously mentioned countries of Eastern Europe range from 0.1 to 5.7,[1] whereas countries of Western Europe have an overall incidence no less than 5.6 (*Gut* 1996;**39**:690–7).
- The countries of Eastern Europe are mainly less developed than the countries of Western Europe.[3]

Thus, is there a developed–developing gradient? The authors believe that it might be so. The development gradient is consistent with the aetiological cause of ''westernisation'' in the expression of IBD, since more developed countries are generally more westernised. Westernised lifestyle means increased consumption of refined sugar, fatty acids, fast food, cereals and bread and reduced consumption of fruit, vegetables and fibre. Furthermore, indoor and sedentary occupations as well as improved sanitation are common characteristics of westernised cultures. For all of these aspects of westernisation, there have been noted associations with IBD.[4 5]

Therefore, we can see that IBD can be better distributed according to the development of countries, instead of the north–south gradient. The underlying cause for such a distribution could be westernisation, which coincidentally explains the increase of the incidence observed in some countries (eg, according to this hypothesis, we could say that the incidence of IBD has increased in Hungary over the last few years because it has become more westernised since its level of development has risen[3]). This possible association of a wealth factor, such as the development level, with the incidence of IBD, has been noted by Ekbom, who mentions a possible influence of wealth on the incidence of IBD: ''The disappearance of the north–south gradient in Europe might be an illustration of what will happen when society gains affluence. It is therefore of extreme interest to follow the temporal trends for IBD in Eastern Europe.''[6] Similar comments have been made by other reviewers.[4 5] Finally, this theory is furthermore consistent with observations about other diseases such as type I diabetes and multiple sclerosis.[7] Specifically, Patterson *et al*.[8] note for type I diabetes that ''the strikingly higher incidence in Finland compared to ethnically-similar sub-populations in Estonia as well as the apparent decrease in type I diabetes in Germany could reflect wealth-related risk factors.''

All these observations together allow us to suppose such a distribution of IBD, an issue that would be an interesting subject of research.

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References

1 **Lakatos L**, Lakatos PL. Is the incidence and prevalence of inflammatory bowel diseases increasing in Eastern Europe? *Postgrad Med J* 2006;**82**:332–7.
2 **Loftus Jr EV**. Clinical epidemiology of inflammatory bowel disease: incidence, prevalence, and environmental influences. *Gastroenterology* 2004;**126**:1504–17.
3 **The World Bank**. Country Classification 2007. http://www.worldbank.org/data/countryclass/classgroups.htm#High_income (accessed 16 June 2007).
4 **Hanauer SB**. Inflammatory bowel disease: epidemiology, pathogenesis, and therapeutic opportunities. *Inflamm Bowel Dis* 2006;**12**(Suppl 1):S3–S9.
5 **Krishnan A**, Korzenik JR. Inflammatory bowel disease and environmental influences. *Gastroenterol Clin North Am* 2002;**31**:21–39.
6 **Ekbom A**. The changing faces of Crohn's disease and ulcerative colitis. In: Targan SR, Shanahan F, Karp LC, eds. *Inflammatory bowel disease: from bench to bedside*. New York: Springer, 2005:5–20.
7 **Bach JF**. The effect of infections on susceptibility to autoimmune and allergic diseases. *N Engl J Med* 2002;**347**:911–20.
8 **Patterson CC**, Dahlquist G, Soltész G, *et al*. Is childhood-onset Type I diabetes a wealth-related disease? An ecological analysis of European incidence rates. *Diabetologia* 2001;**44**(Suppl 3): B9–B16.

Colonic colonisation with *Giardia lamblia* in a patient receiving fibrates

We read with interest the article by Troeger *et al* exploring the epithelial barrier dysfunction related to duodenal *Giardia lamblia* infection (*Gut* 2007;**56**:328–35). Not only does this protozoan interact with the intestinal epithelium but also its life cycle depends on its host's bile metabolism.

We report here on a patient for whom treatment with fibrate was likely to facilitate *Giardia lamblia* colonic colonisation. A 72-year-old woman reported a 1-year history of diarrhoea. She had a past history of type 2 diabetes, hypertension and hypercholesterolaemia. She was treated with metformin, glimepiride, enalapril, furosemide and fenofibrate. She had had a 30 kg loss of weight in the past year (from 90 to 60 kg, 157 cm) but no haematochezia, vomiting or abdominal pain.

A physical examination was normal. Repeated glycaemic controls and haemoglobin A1c were deemed satisfactory. Further laboratory tests showed iron-deficiency anaemia and hypoalbuminaemia with normal electrolytes. Human immunodeficiency virus testing was negative. Upper digestive endoscopy and biopsies showed an atrophic gastritis with *Helicobacter pylori* and a massive duodenal *G lamblia* infection with no underlying mucosal lesion. Ileocolonoscopy was normal, but colonic biopsies showed numerous trophozoites on the surface of colonic epithelium (fig 1). These micro-organisms were pear-shaped and binucleate (some being leaf-shaped on profile, some lying on the colonic epithelial surface), similar to those found on duodenal biopsy specimens and morphologically consistent with *G lamblia*. Colonic mucosa was normal.

The patient received a 7-day course of *H pylori* and *G lamblia* eradication treatment with metronidazole (1500 mg/day), clarithromycin and pantoprazole. Oral iron supplementation was started. Complete remission of diarrhoea was achieved within 2 weeks. Six months after eradication treatment was completed, the patient had gained 12 kg, and haemoglobin, plasmatic iron and albumin rates were normal.

G lamblia is a worldwide, highly prevalent, flagellated enteric protozoan. Orally transmitted as a cyst, it may turn into a trophozoite and adhere to the bowel wall. *G lamblia* intestinal infection is not usually associated with mucosal lesion (mild villous shortening and mild non-specific inflammation of the lamina propria have been reported in <5% of patients with duodenal infection).[1] The study of Troeger *et al* provides a better understanding of its pathogenic pathways, suggesting that *G lamblia* duodenal colonisation may be responsible for acute and chronic malabsorptive and secretory diarrhoea. Encystation of *G lamblia* trophozoites occurs in the small bowel. Cysts are then excreted with stools. It is therefore not common to see trophozoites in the colon[1] or in stools.[2]

In a series of 567 patients diagnosed with *G lamblia*, the site of colonisation was the small bowel in most cases (97%), but rarely the colon (two patients (0.4%), but the number of patients with colonic biopsies is not given in this study).[1] In another series of 124 patients diagnosed with *G lamblia* positive stools, 120 had only cyst (97%), four had trophozoites and cysts (3%) and none had trophozoites only.[2] Our patient had chronic malabsorption, which resolved after metronidazole treatment, and we

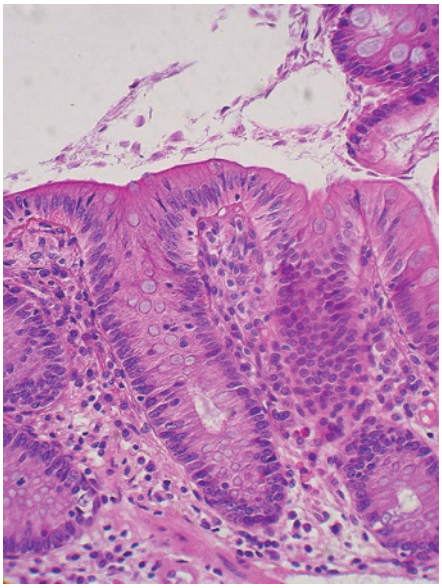

Figure 1 *Giardia lamblia* trophozoites on the surface of colonic epithelium.