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tranquility, sleepiness, and friendliness, while carbohydrate rich meals induce tension and hostility, and increase activity in the sympathetic nervous system.^{1,2} The bidirectional link between the gut and emotion is so strong that the gut might usefully be regarded as part of the limbic system! However, I remain cynical of the cumbersome and dated tryptophan hypothesis that is so frequently trundled out to explain the effects of food on human mood and behaviour, and would favour a more direct action via afferent nerves.

I have read the paper by Dr Ledochowski and colleagues that was published in *Digestive Diseases and Sciences*. Of 30 healthy female volunteers, six showed evidence of lactose malabsorption and had higher scores on Beck's Depression Inventory. Analysis of the individual data presented in this paper is less convincing as they are biased by two lactose malabsorbers who scored very highly for depression. The scores of the remaining women were within the range seen in people that absorbed lactose normally. Although the authors concluded that lactose malabsorption induced anxiety and depression, their data could be equally well explained by the effects of psychological tension on gut function.

Psychological tension can accelerate small bowel transit, which in turn can compromise absorption, particularly of foods that are more slowly absorbed. Most of the world's adult population are lactose malabsorbers, but they are not all depressed. Indeed, depression seems to be more common in people that absorb lactose and come from Northern Europe.

Finally, is lactose deficiency or fructose malabsorption truly more common in patients with IBS than in normal subjects? The accumulated data are unconvincing. What seems more likely is that the hypersensitive and hyper-reactive gut of patients with IBS responds more vigorously to an osmotic load, by generating symptoms of diarrhoea, bloating, and pain.

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- 1 Wells AS, Read NW, Uvnas Moberg K, et al. Influences of fat and carbohydrate on postprandial sleepiness, mood and hormones. *Physiol Behav* 1997;61:679–86.
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Is isolated idiopathic pancreatitis associated with CFTR mutations?

EDITOR,—In one of two recently published studies which looked at a link between mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene and idiopathic pancreatitis,^{1,2} Cohn *et al* estimated that 37% of a cohort of 27 patients with idiopathic pancreatitis had at least one abnormal CFTR gene, which is 11 times the expected frequency.¹ Furthermore, the authors concluded that additional CFTR mutations might be detected by more comprehensive DNA testing, because they had tested DNA samples for only 16 of the more than 800 mutations associated with cystic fibrosis.

Table 1 Characteristics of 10 patients with idiopathic pancreatitis

Patient no	Sex	Current age	Age at diagnosis	CFTR genotypes		
				Sequence changes	IVS8 TGn-Tn	1540 A/G (M470V)
1	M	77	75	—/—	TG11-T7/TG11-T7	G/G
2	F	52	41	3041-71A/G 4002A/G	TG11-T7/TG11-T9	A/G
3	M	44	42	4404C/T	TG10-T7/TG11-T7	A/G
4	F	70	69	875+40A/G	TG11-T5/TG11-T7	A/G
5	M	62	61	125G/C	TG11-T7/TG11-T7	G/G
6	F	52	50	1716G/A	TG11-T5/TG10-T7	A/A
7	M	41	38	125G/C	TG11-T7/TG12-T7	A/G
8	M	64	36	—/—	TG10-T7/TG10-T9	A/A
9	M	72	69	1506V 875+40A/G	TG10-T7/TG11-T7	A/G
10	F	18	NA	—/—	TG11-T7/TG12-T7	A/G

NA, not available.

In order to document further whether a proportion of adults presenting with idiopathic pancreatitis carry alleles linked to mild abnormalities of CFTR functions, we conducted a complete scan of CFTR sequences by denaturing gradient gel electrophoresis (27 exons) and other appropriate methods (four intronic regions), in a sample of 10 patients with isolated idiopathic pancreatitis (ascertained by standard criteria) in the south of France. As some CFTR alleles of specific DNA marker haplotypes have recently been shown to produce incomplete or less functional CFTR protein,³ we also thoroughly studied the TGn-Tn loci in the branch/acceptor splice site in intron 8 and the 1540A/G locus (named M470V) in exon 10. Exclusion criteria included the ingestion of more than two alcoholic drinks per day (20 g ethanol), cancer, drug or trauma related pancreatitis, and familial chronic pancreatitis. None of the patients had any clinical manifestation or family history suggestive of cystic fibrosis or CFTR associated diseases. The study was approved by our ethics committee.

Table 1 summarises the CFTR genotypes identified in the 10 patients with idiopathic pancreatitis. Of these, no patient had a cystic fibrosis mutation and seven were instead heterozygous for one or two sequence changes that have been classified as DNA sequence polymorphisms/variants (a complete list of these variations can be found on the cystic fibrosis mutation database: www.genet.sickkids.on.ca/cftr).

Although variant 1716G/A (no change at glutamine 528) may result in exon 10 skipping and has been reported in CFTR related diseases,^{4,5} the involvement of this variant in cystic fibrosis remains controversial. The frequency of the IVS8-5T allele (10%) was 2.3 times the observed frequency in the general population (4.3%). It is unlikely, however, that this allele is a variant which predisposes towards idiopathic pancreatitis because it is carried on a TG11-M470 haplotype background, which is not a deleterious combination.³ Finally, when we screened the whole coding/flanking CFTR sequences of 10 random individuals, six polymorphisms/variants (125G/C and 875+40A/G twice, R75Q, 5T) and one cystic fibrosis mutation (AF508) were observed.

In conclusion, extensive analysis of CFTR sequences in a subset of patients from the south of France does not confirm a link between CFTR alterations and isolated idiopathic pancreatitis.

We thank Ms Freiss for contributing clinical data and Ms Seguret for statistical advice. This research was supported by the Direction de la Recherche Clinique, CHU, Montpellier, France (UF7533).

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Did prostaglandin E₂ stimulate glucose absorption in rat intestine?

EDITOR,—I read with interest the recent paper by Schotka *et al* (*Gut* 1999;44:490–496) which reported that prostaglandin E₂ (PGE₂) stimulated glucose absorption via the sodium dependent glucose transporter-1 in rat intestine.

The authors suggested that PGE₂ raises sodium dependent glucose transporter (SGLT₁) and thus increases glucose absorption. However, earlier papers contradicted this theory and we are now in a state of confusion. Kimberg and coworkers^{1,2} and Klacveman and colleagues³ have suggested that prostaglandins increase membrane bound adenylate cyclase activity in the small intestinal mucosa, and thus inhibit Na⁺-K⁺-ATPase activity of gut mucosa.^{1,2} Recently, Sundaram and colleagues⁴ reported that inflamed ileum (excess prostaglandin) express low levels of SGLT₁ in rabbits, which indicates that

prostaglandin may inhibit SGLT₁ activity. Furthermore, a decrease in active absorption of glucose due to increased levels of prostaglandins and cytokines has been observed both in patients with severe intestinal inflammation⁷ and surgical patients.^{8,9}

Can the authors explain an alternative mechanism for their findings?

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Reply

EDITOR.—We see no reason for confusion over the acute increase of PGE₂-stimulated glucose absorption via SGLT₁ in rat small intestine. By using isolated perfused rat small intestine and rat villus tip enterocytes, we showed that PGE₂ acutely increased glucose and galactose absorption via SGLT₁ with cAMP, raised by the actions of PGE₂ receptor subtypes 2 and 4, which served as the second messenger.

As the maximum PGE₂ effect was reached after four minutes, the underlying mechanism can only have been stimulation of SGLT₁ activity, rather than an increase in the amount of SGLT₁ by *de novo* synthesis. Our findings are concurrent with previous data which showed that forskolin (an adenylate cyclase activator) stimulated a glucose dependent inward current of Na⁺ acutely, in the jejunum of CFTR knockout (cystic fibrosis) mice, and that cAMP increased glucose uptake into brush border membrane vesicles of rat jejunal enterocytes.³

Dr Somasundaram now claims that earlier reports contradict this theory. Kimberg, Klaeveman and colleagues showed that prostaglandins stimulated membrane bound adenylate cyclase activity in the small intestine, which is in line with our findings. Mozsik *et al* showed that 5'-AMP, cyclic 2',3'-AMP, and cyclic 3',5'-AMP inhibited Na⁺/K⁺-ATPase activity in human stomach, indicating that this effect was not specific. Furthermore, Parkinson *et al* found that Na⁺/K⁺-ATPase activity in plasma membrane preparations of rabbit jejunum decreased three hours after

cholera toxin treatment; they did not study the direct acute effect of cAMP or PGE₂. Sundaram and colleagues, using a rabbit model of chronic ileal inflammation (cells isolated 13–15 days after intragastric inoculation with *Eimeria magna* oocytes), concluded that Na⁺-glucose cotransport reduction was secondary to a decrease in the amount of SGLT₁; PGE₂ involvement in this chronic alteration was not examined.

Somasundaram *et al*, who used a rat model of extraintestinal inflammation (six hours after formalin injection into hind leg pad), showed that glucose absorption was impaired in the jejunum, and that this impairment could be prevented by the anti-inflammatory drug, oxyphenbutazone; again PGE₂ involvement was not investigated. Ohri and colleagues reported that monosaccharides were malabsorbed in coronary artery bypass patients, because of significant hypoperfusion of the intestine; they did not study the involvement of PGE₂. Finally, Wicks *et al* concluded that enteral feeding was as effective as total parenteral nutrition in orthotopic liver transplantation; they also did not examine the involvement of PGE₂.

In summary, Dr Somasundaram has not presented any evidence that PGE₂ lowers SGLT₁ activity and acutely or chronically decreases glucose absorption. There is no discrepancy between our findings and any previous study. As PGE₂, or any similar hormone or mediator, may have different short term acute and long term chronic actions, and because an appropriate distinction has yet to be made between the state of health and the state of disease, we see no reason for any confusion and no need to provide an alternative mechanism for our findings. We are sure that Dr Somasundaram would be happy to agree.

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NOTES

11th Annual International Colorectal Disease Symposium

The 11th Annual International Colorectal Disease Symposium will be held at the Marriott Harbor Beach Resort, Fort Lauderdale, Florida, USA, on 17–19 February 2000. Further information from: Cleveland Clinic Florida, Department of Continuing Education, 2950 West Cypress Creek Road, Fort Lauderdale, Florida 33309, USA. Tel: +1 954 978 5056; fax: +1 954 978 5539; email: jagelms@ccf.org

5th World Congress on Trauma, Shock, Inflammation, and Sepsis

The 5th World Congress on Trauma, Shock, Inflammation, and Sepsis will be held in Munich, Germany, from 29 February to 4 March 2000. Further information from: Prof Eugen Faist, Department of Surgery, Ludwig Maximilians University Munich, Klinikum Grosshadern, Marchioninstrasse 15, 81377 Munich, Germany. Tel: +49 89 7095 5461/2461; fax: +49 89 7095 2460; email: faist@gch.med.uni-muenchen.de

Second Annual Gastrointestinal Cancer Update: A Multidisciplinary Approach

The Second Annual Gastrointestinal Cancer Update conference will be held at the Yarrow Hotel and Conference Centre, Park City, Utah, USA, on 15–19 March 2000. Further information from: Rosalie Lammle. Tel: +1 801 581 8664; fax: +1 801 581 3647; email: rosalie.lammle@hsc.utah.edu

European Courses on Laparoscopic Surgery

The European Courses on Laparoscopic Surgery will be held at the University Hospital Saint Pierre, Brussels, Belgium, on 4–7 April 2000 and 21–24 November 2000. Further information from: Conference Services S.A., Drève des Tumuli, 18, B-1170 Brussels, Belgium. Tel: +32 2 375 1648; fax: +32 2 375 3299; email: conference.services@skynet.be

Third Scandinavian Course on Inflammatory Bowel Diseases

The Third Scandinavian Course on Inflammatory Bowel Diseases will be held at the Wilanderselen, Örebro Medical Centre, Örebro, Sweden, on 12–14 April 2000. Further information from: Kurskansliet, Region-sjukhuset, S-701 85 Örebro, Sweden. Tel: +46 19 15 37 05; fax: +46 19 15 37 95.

XVIIIth European Workshop on Gastroenterology and Endotherapy

The XVIIIth European Workshop on Gastroenterology and Endotherapy will be held in Brussels, Belgium, on 26–28 April 2000. Further information from: Administrative Secretariat, Ms Nancy Beauprez, Gastroenterology Department, Erasme Hospital, Route de Lennik 808, B-1070 Brussels, Belgium. Tel: +32 2 555 4900; fax: +32 2 555 4901; email: beauprez@ulb.ac.be

Digestive Disease Week

The Digestive Disease Week will be held at the San Diego Convention Centre, San Diego, California, USA, on 21–24 May 2000. Further information from: DDW Administration, 7910 Woodmont Avenue, 7th Floor, Bethesda, Maryland 20814, USA. Tel: +1 301 272 0022; fax: +1 301 654 3978; website: www.ddw.org

International Hepato-Pancreato-Biliary Association 4th World Congress

The International Hepato-Pancreato-Biliary Association 4th World Congress will be held in Brisbane, Australia, from 28 May to 1 June 2000. Further information from: Intermedia Convention and Event Management, PO Box 1280 (Intermedia House, 11/97 Castlemaine Street), Milton, Queensland 4064, Australia. Tel: +61 (0)7 3369 0477; fax: +61 (0)7 3369 1512; email: hpb2000@im.com.au