LETTERS TO THE EDITOR

Radioisotope determination of regional colonic transit in severe constipation

EDITOR,—We were interested to see the article by van der Sijp *et al* (*Gut* 1993; **34**: 402–8) on a scintigraphic method of colonic transit measurement compared with the conventional radiological method. There are, however, several points that we would like to raise. They have dismissed the method using methacrylate coated capsules as unnecessary and resulting in unpredictable release point. In an early study (30 patients, unpublished data) we examined the colonic transit without the use of pH sensitive capsules and often found overlap of the activity in the small and large bowel in the first day images particularly, if there was slow gastric emptying. Although this is not important in patients with severe chronic constipation, it is a problem when dealing with patients with normal or fast transit (such as some patients with inflammatory bowel disease). The method of methacrylate coating of the capsule, however, is important and in our preliminary studies using capsules with several coatings, there was delayed release in two of 10 patients. As we have modified the method of coating by reducing the number of coatings to two[1] only in one of 130 patients studied so far has the capsule failed to open before reaching the ascending colon. One should aim for capsule release somewhere in the small intestine, having passed intact through the stomach, as activity tends to collect in the terminal ileum before its release into the colon. In our experience there is no need to obtain release precisely in the terminal ileum.

A fundamental problem arises in the use of 'centre of mass' (COM) to describe colonic transit and to compare the two methods of studying transit. COM is useful for examining groups of patients with colonic disorders. The radiologic and scintigraphic methods seem to be no different from each other in this study as only the COM is used to compare groups for both methods. It is of limited value, however, in reporting and treating individual patients, especially when a full range of colonic motility disorders is under study. COM ignores all detailed information obtained by the scintigraphic method, which is essential for correct classification of different patterns of colonic movement. This is best achieved using parametric images.

A final point is the activity given for these investigations. We have found a four day study sufficient to identify all patterns of colonic motility disorders even in those with severe constipation. The shorter study allows us to use smaller ^{111}In activity (2 MBq) and still obtain good image quality, reducing the whole body irradiation even further than that described by van der Sijp.

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1 Notghi A, Kumar D, Panagamuwa B, Tulley NJ, Hesslewood SR, Harding LK. Measurement of colonic transit time using radionuclide imaging: analysis by condensed images. *Nucl Med Commun* 1993; **14**: 204–11.

Reply

EDITOR,—I am interested in the comments by Dr Notghi and his colleagues about our paper on colonic transit. Even though about half of our severely constipated patients have slow gastric emptying[1] we did not find overlap of the small and large intestine to be a problem (in constipated patients or healthy controls).

I believe that a pH sensitive capsule is satisfactory if the goal is only to study colonic transit. Many patients with disturbances of colonic motility, however, have a disorder that affects much of the gut.[1] The use of a coated capsule precludes the gathering of detailed information about upper gut motility. The use of a radiolabelled meal,[2] however, allows the assessment of upper and lower gut transit during the same study.

The 'centre of mass' measurement was just one of the methods we used to describe colonic transit. It provides a useful single numerical guide to the effectiveness of transit. We also described in detail, however, the quantitation of transit through each colonic region.

In some patients with delayed colonic transit we have found a four day study inadequate for assessing transit through the left colon. Any reduction in radiation dose, however, without the loss of information should be welcomed.

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1 van der Sijp, Kamm MA, Nightingale JMD, Walker E, Granowska M, Britton K, *et al.* Disturbed gastric and small bowel transit in severe idiopathic constipation. *Dig Dis Sci* (in press).
2 Mather SJ, Ellison D, Nightingale J, Kamm MA, Britton KE. The design of a two-phase radiolabelled meal for gastric emptying studies. *Nucl Med Commun* 1991; **12**: 409–16.

Polyunsaturated fatty acid pattern and fish oil treatment in inflammatory bowel disease

EDITOR,—We read with great interest the paper by M Esteve-Comas *et al* (*Gut* 1992; **33**: 1365–9). The authors claim that patients with inflammatory bowel disease have different plasma fatty acid patterns by comparison with controls, mainly characterised by an increase in n3 series and a decrease in some n6 series (20:3 n6) and that these differences are more pronounced, in an inversely proportional manner, accordingly to the severity of the disease. These data suggest an increased polyunsaturated fatty acid biosynthesis and consumption in active inflammatory bowel disease, especially of the n3 series, raising some doubts on the use of high doses of fish oil in the treatment of acute inflammatory bowel disease. These results, however, need to be carefully considered. The authors did not separate the different lipid fractions containing the plasma fatty acids (phospholipids, triacylglicerols, cholesterol and free fatty acids), by thin layer chromatography. This would have been of great benefit as the main source for the eicosanoids' synthesis is the fatty acid stored in the phospholipids and also because each fraction has different representation of every single fatty acid.[1,2] Moreover, V Schacky *et al* have shown that the variability in the plasma fatty acid pattern is enormous and that the alimentary habit and the quality of lipid intake can modify the pattern in a few hours.[3] For this reason an overnight fast is certainly insufficient to guarantee the stability of the plasma fatty acid pattern.

We recently quoted the plasma phospholipid fatty acid profiles in a group of Crohn's disease patients in comparison with a group of healthy controls and we did not find any significant differences. On the contrary we studied, in the same groups, the phospholipid fatty acid profiles in red blood cell membranes and we found remarkable differences: a significant decrease in all polyunsaturated fatty acids and a significant increase in the main saturated fatty acids (palmitic and stearic acids).[4] Actually, the fatty acid profile in red blood cell phospholipid membranes is much more stable; six to eight weeks of a very high dose of n3 fatty acid supplementation (fish oil) is needed to modify its composition and occurs during cell formation.[5] Regarding the use of fish oil in active inflammatory bowel disease, it should be noted that the incorporation of n3 fatty acid in the neutrophil membranes occurs by the replacing of arachidonic acid, the main source for LTB4 production and one of the most powerful inflammatory mediators.[6,7] Our findings would suggest that the authors' results could have different interpretations.

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2 Farkkila MA, Tilvis RS, Miettinen TA. Plasma fatty acid composition in patients with ileal dysfunction. *Scand J Gastroenterol* 1987; **22**: 411–9.
3 Von Schacky C, Weber PC. Metabolism and effects on platelet function of the purified eicosapentaenoic and docosahexaenoic acids in humans. *J Clin Invest* 1985; **76**: 2446–50.
4 Belluzzi A, Brignola C, Campieri M, Pironi L, Gionchetti P, Rizzello F, *et al.* Zinc sulphate supplementation modifies long chain fatty acid metabolism in patients with Crohn's disease. *Gut* 1991; **32**: A1241–2.
5 Von Schacky C, Fischer S, Weber PC. Long term effects of dietary marine w-3 fatty acids upon plasma and cellular lipids, platelet function and eicosanoids formation in humans. *J Clin Invest* 1985; **76**: 1626–31.
6 Belluzzi A, Hawthorne AB, Hawkey CJ. Increased neutrophil membrane w-3 fatty acids may be of clinical benefit in ulcerative colitis. *Gut* 1989; **30**: A1501.
7 Hawthorne AB, Daneshmend TK, Hawkey CJ, Belluzzi A, Everitt SJ, Holmes GKT, *et al.* Treatment of ulcerative colitis with fish oil supplementation: a prospective 12 month randomised controlled trial. *Gut* 1992; **33**: 922–8.

Reply

EDITOR,—We read the interesting comments by Belluzzi *et al* regarding our paper on polyunsaturated fatty acids in inflammatory bowel disease. We are afraid that they have misinterpreted our results when stating that the differences in polyunsaturated fatty acids profile – that is, an increase in n3 polyunsaturated fatty acids and a decrease of some n6 polyunsaturated fatty acids 'are more pronounced

in an inversely proportional manner according to the severity of the disease'. In fact, the decrease in polyunsaturated fatty acids as the disease activity increases occurred for both series, although it was more noticeable for n6 polyunsaturated fatty acids. As a consequence our hypothesis was that in inflammatory bowel disease an increased polyunsaturated fatty acid biosynthesis coexists with an increased polyunsaturated fatty acid consumption, the second being associated with the disease activity. The increased polyunsaturated fatty acid biosynthesis would be more noticeable in the n3 series as these fatty acids have the highest affinity for desaturases. Hyperconsumption, although occurring in both polyunsaturated fatty acids series, is more evident in n6 products probably because of an increased arachidonate derived eicosanoid production. This hypothesis seems to be further supported by data from recent studies in patients with non-active inflammatory bowel disease.

Of course, it will be interesting to confirm these findings in different plasma lipid fractions, as well as in colonic mucosa. We are analysing these data, which hopefully will be reported soon. Nevertheless, as far as plasma long chain polyunsaturated fatty acids (mainly n3) are concerned, their concentration in total lipids mainly reflects that found in phospholipids, as most of them are bound to this fraction.[2,3]

The dietary habits of the patients in our study were similar to that of healthy controls (standard Western diet). This type of diet contains negligible amounts of n3 polyunsaturated fatty acids (less than 1% of the total fat).[4] In addition, most of the patients included were in hospital because of moderate to severe attacks of inflammatory bowel disease. Most of them were anorectic and tended to decrease their food intake rather than change to different types of food. No patient had been on artificial nutritional support before plasma sampling was performed.

Although a 14 hour overnight fast might theoretically be a source of error, it is generally assumed that this condition provides an easily reproducible state of metabolic equilibrium. In fact, approximately 15 hours after the last meal there is a progressive decrease in carbohydrate oxidation and a rise in fat oxidation. Increased lipolysis in adipose tissue and fatty acid mobilisation are seen whereas, in the liver, fatty acid synthesis is progressively replaced by fatty acid oxidation and ketone body production.[5] Therefore, longer fasting would lead to misleading results.

We look forward to seeing the findings reported by Belluzzi *et al*[6] published in full as it is difficult to draw real conclusions from an abstract. Data on the location and extent of the disease, bowel resections, nutritional state, and other factors liable to lead to fat malabsorption would be of utmost interest as in the patients described there is a decrease in essential precursors – that is, linoleic acid, which may account for the deficiency seen in long chain polyunsaturated fatty acids. In fact, similar data were also reported by Färkkilä *et al*[7] in plasma lipids from a series including many Crohn's disease patients with bowel resection. So, the findings by Belluzzi *et al*, by contrast with our results, closely resemble the pattern of essential fatty acid deficiency.

Certainly, our results may be interpreted in different ways. On the one hand, as n3 polyunsaturated fatty acids are increased, it would not be necessary to supply them in increased dietary amounts. Conversely, a plasma long chain n3 polyunsaturated fatty acid increase might be seen as an unsuccessful attempt to prevent an excessive production of arachidonate derived eicosanoids. In such cases the slight clinical response seen when fish oil is given, despite modifying eicosanoid production, could suggest that the amount of n3 polyunsaturated fatty acids given should be increased. All these data, however, provide an attractive insight into the pathogenesis of inflammatory bowel disease, in which the true role of fatty acid treatment also has to be investigated further.

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1 Esteve-Comas M, Núñez MC, Fernández-Bañares F, Abad-Lacruz A, Gil A, Cabré E, *et al.* Abnormal plasma polyunsaturated fatty acid pattern in non-active inflammatory bowel disease. *Gut* (in press).
2 Cabré E, Periago JL, Mingorance MD, Fernández-Bañares F, Abad A, Esteve M, *et al.* Factors related to the plasma fatty acid profile in healthy subjects, with special reference to antioxidant micronutrient status: A multivariate analysis. *Am J Clin Nutr* 1992; **55**: 831–7.
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Open access gastroscopy

EDITOR,—Dr Bramble and colleagues describe a most efficient and well run open access endoscopy service (*Gut* 1993; **34**: 422–7). Even they, however, only achieve a mean waiting time of 17 days for open access endoscopy. Most of us would fair far worse and therein lies one important problem of open access endoscopy. Do we deprive out symptomatic patients of effective ulcer healing treatment for 17 days so as to obtain a 'pure' endoscopic diagnosis but subject patients to 17 days of unnecessary symptoms and risk of complications, or do we treat patients in the knowledge that if an ulcer is present it may well have healed by the time the patient has an endoscopy, especially – as is increasingly so – the general practitioner has prescribed a proton pump inhibitor.

A short outpatient visit in a general clinic or a specialist dyspepsia clinic would seem a better solution. General practitioners can be encouraged to treat patients as they see fit and the patients seen on treatment. If still symptomatic and, if it is appropriate, they can have an endoscopy immediately. If asymptomatic they can be asked to complete their treatment and arrangements made for the patient to book themselves in for endoscopy by telephone if and when their symptoms next occur before starting treatment. Additional investigations can be arranged and the patient counselled as to the likely result of the endoscopy; normal endoscopy still being the single commonest finding. In our experience with this system[1] 35% of patients will be spared endoscopy.

We found 68% of patients that had an endoscopy preferred this system to open access endoscopy despite the need for two hospital visits and if those spared endoscopy are taken into account 81% preferred the clinic appointment first.

Pressure from general practitioners to set up open access endoscopy is considerable. We feel a clinic appointment first, however, is a more logical solution and the one favoured by the patient. The endoscopies saved may also make it more cost effective.

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1 Saunders BP, Trewby PN. Is an out patient visit of value in patients suitable for open access endoscopy? *Gut* 1992; **33** (suppl 1): S50.

Reply

EDITOR,—We are grateful for the opportunity to respond to the comments of Drs Trewby and Saunders. There is a basic misunderstanding in their letter. Our provision of an efficient open access gastroscopy service does not in any way deprive patients of effective treatment. We have not made any attempt to discourage general practitioners from treating patients with dyspepsia on clinical grounds. Our guidelines point out that it is appropriate to refer patients for investigation if it is felt that a diagnosis is important before treatment is given or if this has happened and there has been a failure to respond after a reasonable time. The general practitioners in our district have a range of options for patients with dyspepsia and almost one in three of dyspepsia referrals are still by standard letter to a targeted consultant. The type of service described by Drs Trewby and Saunders is still available in Middlesbrough alongside the open access system. (In the case of open access endoscopy, the general practitioner has a further choice of asking for 'report only' or giving the endoscopist discretion about treatment and further management. 'Report only' is specified on about 50% of open access endoscopy referral forms.) We are currently setting up a pilot scheme with a number of GP practices, which will allow them to gain direct access to our open access endoscopy computer scheduling system. This will mean that the general practitioner can give our system the details and obtain the booking and instruction sheet while the patient is still present. It is quite likely that this will bring the time from request to 'investigation' down to about 12 days.

There is no basis to an assumption that screening patients through a specialist hospital clinic will have much effect on the results of endoscopy. The proportion of different abnormalities found on our open access endoscopy lists is very similar to those lists generated from patients seen in clinic and to those published figures in other series. We are developing the software to permit us to send regular feedback to our general practitioners about their use of the open access endoscopy service. This will be similar to the information they receive regularly about their prescribing practice. It will be possible for them to see how they compare with their peers in terms of number of referrals, age, sex, and findings. General practitioners already deal with most cases of dyspepsia that they see.