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Take-home points

- Consider screening for coeliac disease in those with persistent diarrhoea but also those with functional dyspepsia and constipation with bloating and flatulence
- Food intolerance – rather than a true allergy – is more likely in patients with functional GI disease
- Amitriptyline can be useful in IBS patients, but SSRIs less so, unless there is underlying depression
- Evidence now supports the use of probiotics in patients with IBS
- Some patients labelled as having IBS actually have very treatable pathologies on further investigation
- Slow transit constipation is related to GI neuromuscular dysfunction
- A trial of cholestyramine in patients with suggestive symptoms can be offered in primary care to avoid complex testing

Gastroenterology specialist Professor Qasim Aziz answers Dr Linden Ruckert's questions on the role of stress, whether IBS is a useful term and the use of probiotics

1 IBS is said to affect 20% of the population. Do you think it is a useful or meaningful term?

The term is useful insofar as it suggests that there is no obvious and readily recognised pathology for the symptoms. But I often find physicians lose interest in patients once they are labelled as having IBS and this is where mistakes are made because sometimes treatable causes for symptoms are missed. The differential diagnosis of IBS is very wide and many different conditions can produce symptoms identical to this condition – like coeliac disease. Or IBS can be a manifestation of hitherto undiagnosed conditions such as connective tissue and neurological disorders or diabetes. So IBS often becomes a diagnosis of convenience for doctors when an easy solution is not available.

2 Foregut problems such as functional dyspepsia are very difficult to manage. Do you have any tips?

Milder cases of functional dyspepsia can often be managed by PPIs and eradication of *Helicobacter pylori*, but management can be very frustrating in more resistant cases. Again, one has to explore underlying causes. In patients with a previous history of gastroenteritis, psychological stress or a strong history of atopy I look into the dietary history carefully as there is evidence for increased small bowel permeability in these conditions, which can potentially cause delayed hypersensitivity reactions (see question 5, opposite).

Food elimination in selected patients who are well motivated can be very rewarding. I also explore the possibility of underlying causes and investigate further for neuromuscular disorders of the gut. If delayed GI motility is identified I often use prokinetics, probiotics and sometimes antibiotics if bacterial overgrowth is suspected or confirmed on breath testing.

In really difficult cases where nothing works, a multidisciplinary approach with psychologists, dieticians and pain management experts can be helpful.

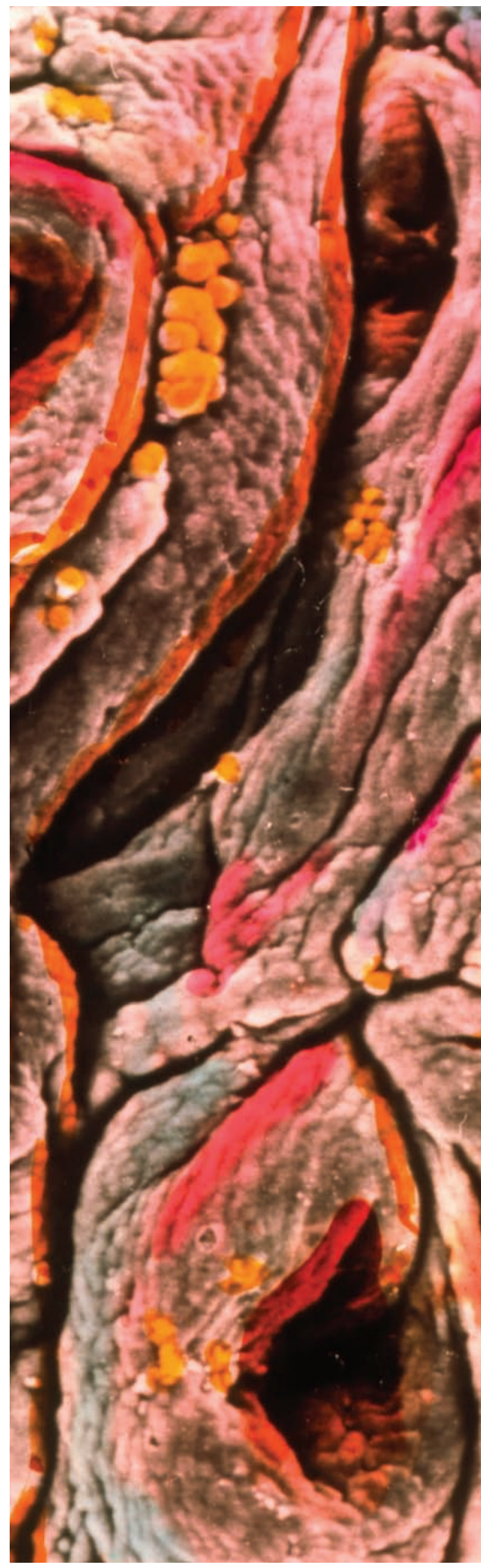
3 The new NICE guidelines recommend serological screening for coeliac disease in patients with IBS. I have read prevalence levels of one in 300 to one in 100 in the adult population. Are symptoms a reliable guide to the possibility of coeliac disease? How far should we pursue this as IgA-based screening may give a false negative?

I agree with NICE that IBS patients should be screened for coeliac disease because this is easily treatable and a misdiagnosis can lead to considerable morbidity. I routinely perform serological tests for coeliac disease in patients with diarrhoea-predominant symptoms. But because of the varying presentation of this condition I would consider serological screening for patients with functional dyspepsia and even constipation associated with bloating and flatulence. I request small bowel biopsies for patients undergoing upper GI endoscopy and would consider referral for endoscopy and biopsy if the serological test was positive. There is a small chance of a false negative serological test for coeliac disease. But in cases with considerable suspicion – especially those who respond very well to a gluten-free diet – a small bowel biopsy should be considered after a gluten challenge if necessary.

It should be noted latent coeliac disease is increasingly being recognised in patients with abnormal serology but normal biopsy, or even normal serology and biopsy but with tissue transglutaminase antibodies present in the small bowel mucosa[1]. Patients with latent coeliac disease often respond well to a gluten-free diet.

4 Many patients develop IBS and have it attributed to stress and yet they have been stressed for ages. It doesn't answer the 'why now' question...

I agree. More often than not, once the diagnosis of IBS or another functional GI disorder (FGID) is made there is a misconception that symptoms must be



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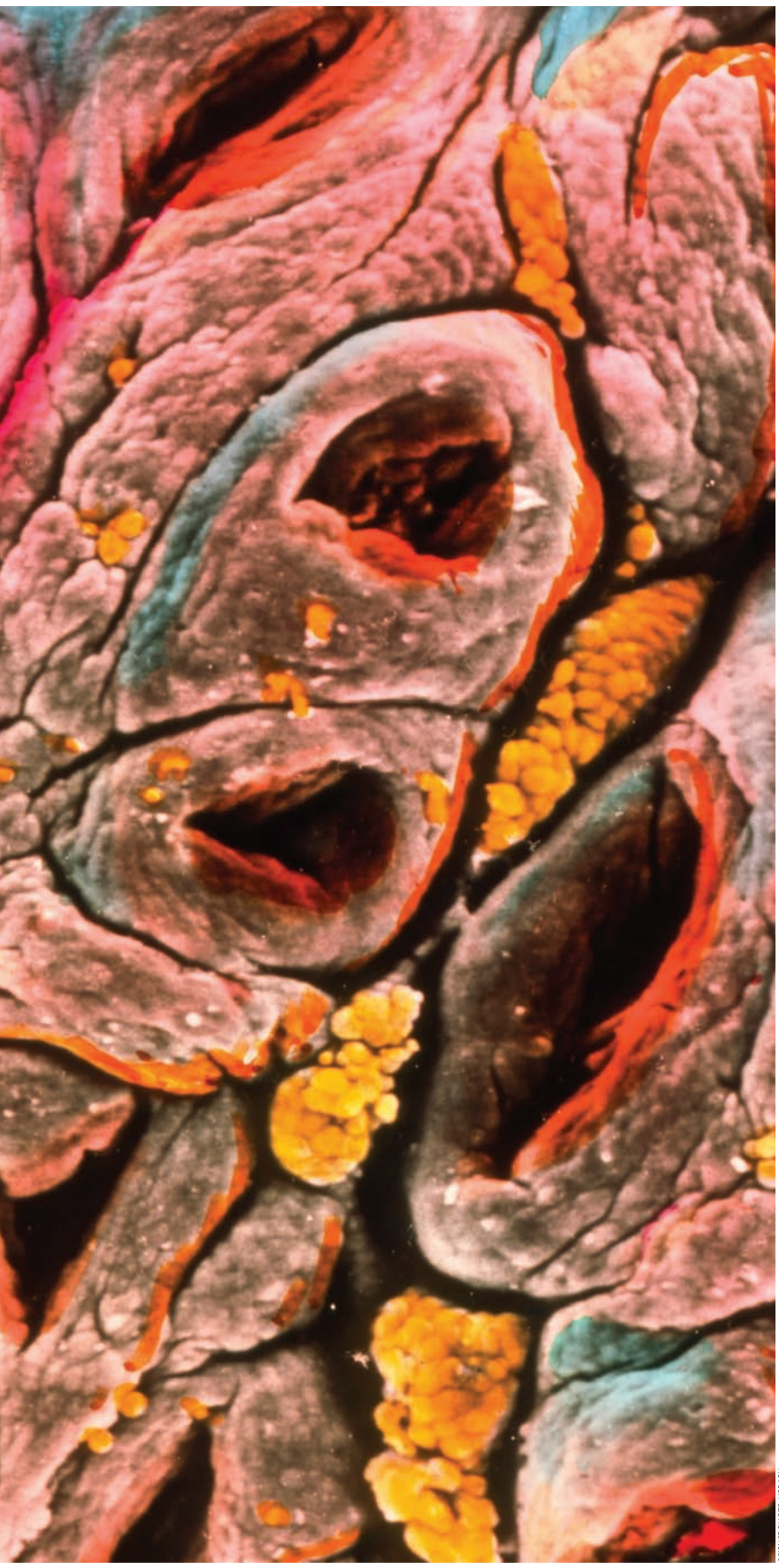

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IBS patients should be screened for coeliac disease (gut wall pictured left with missing villi)

related to stress. Although I don't disagree that stress can exacerbate and perpetuate GI problems, there can still be an underlying pathology.

These patients have often been ill for a long time and suffer considerable morbidity. They may have lost their jobs and/or partners and have an uncertain future. It is understandable that they will be stressed, anxious and depressed.

It is increasingly recognised that IBS symptoms should be considered within the framework of biological, psychological and social factors[2]. I work closely with colleagues in psychiatry and psychology to manage these patients, but often find underlying biological causes for symptoms which are worsened by the psychological co-morbidity. Once the biological factor is treated it is very rewarding to see a remarkable improvement in psychological health. Nevertheless, there are some patients with considerable psychological issues who need to be dealt with very sensitively by colleagues experienced in managing such patients.

5 Patients are very keen on the idea of testing for food 'allergies' or intolerance. How useful is this in practical terms? I note the NICE guidance recommends avoidance of unabsorbable fibre.

I agree that a large number of FGID patients describe food-related symptoms. I don't regard this as a food allergy but rather as intolerance. It is rare for a food allergy to develop in adults because these allergies are usually evident from childhood. There is evidence for increased gut permeability in patients with IBS and it is therefore conceivable that delayed hypersensitivity reactions develop to food antigens getting past the mucosal barrier. Indeed evidence of increased IgG-mediated food hypersensitivity has been reported[3].

A delayed hypersensitivity reaction could take up to 72 hours to manifest. Hence it is not surprising that there is a poor correlation between dietary intake and symptoms in IBS patients. Of course, consuming too much junk food will also have more direct effect – for instance, from the direct effect of fat on gut function – and needs to be explored in patients.

When I suspect food intolerance I don't organise allergy tests unless I suspect an immediate IgE-mediated hypersensitivity to food. In that case I will consider a RAST test to common food allergens.

Instead I tend to try dietary therapy, in the form of eliminating the two most common foods that cause intolerance in my experience – wheat and dairy products. I might consider a proper elimination diet for patients who are well motivated and at the severe end of the spectrum.

6 How do you use amitriptyline or SSRIs in IBS and how do you 'sell' them? Especially as there's the problem of constipation with them too.

I tend to use amitriptyline in IBS patients to manage their pain and visceral hypersensitivity – that is excessive sensitivity to experimental gut stimulation. It's a useful strategy, particularly in patients with diarrhoea-predominant symptoms as the drug has anticholinergic effects. But I have often used it in patients with constipation as well, where pain is a major feature. I often compensate for the use of amitriptyline by using additional doses of laxatives and more often than not constipation does not get worse in these patients.

Other drugs that I sometimes use in patients with pain as a predominant symptom are pregabalin or duloxetine.

I don't use SSRIs very much unless there is an underlying depressive disorder.

I 'sell' these drugs by explaining the importance of brain-gut communication for normal gut function and why pain is caused by abnormal communication. I explain to them that the nerves in the gut are too sensitive and they are sending exaggerated signals to the brain and that low-dose amitriptyline reduces the intensity of these signals and hence reduces pain. I also explain that the doses used to treat depression are much higher and most accept this explanation.

7 What is the role of probiotics?

I am using probiotics increasingly frequently. The role of bacterial flora in normal gut function is in no doubt and evidence suggests that abnormal flora can lead to abnormal gut immune responses in patients with IBD and IBS. Probiotics have been shown to normalise the ratio of plasma pro-inflammatory versus anti-inflammatory cytokines in patients with IBS[4]. I tend to use VSL3, now available OTC in most pharmacies. I recommend a starting dose of one sachet a day,

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going up to two if necessary in patients with previous gastroenteritis, frequent antibiotic use and abnormal gut motility where bacterial overgrowth is likely.

8 I have had a number of patients with 'low-grade inflammatory changes' on rectal biopsy attributed to the bowel prep and diarrhoea. Do you think some patients might have a 'low-grade' chronic inflammatory process?

Yes. Numerous studies in patients with a history of gastroenteritis who have gone on to develop IBS have shown persistence of low-grade chronic inflammatory processes in mucosal biopsies. It has been suggested that IBS patients may have abnormal anti-inflammatory cytokine production, predisposing them to low-grade inflammation.

It is now known that stress can activate the immune system by causing degranulation of mast cells within the gut wall, leading to release of inflammatory mediators. Indeed, there is evidence that patients who are stressed by significant life events are more likely to develop post infective IBS, compared with those subjects not exposed to such stressors.

It is important to remember that brain-gut communication can occur not only via the nerves but also via the immune system. So it is not surprising that peripheral and central factors combine to produce symptoms. Low-grade inflammation may well lead to fatigue and generalised aches and pains, which are then diagnosed as fibromyalgia or even ME.

9 Some people seem to have lifelong constipation. How do you explain 'slow-transit' problems? Is there an identifiable abnormality and how should we manage it?

There is increasing evidence that slow-transit constipation is related to neuromuscular dysfunction of the gastrointestinal tract. Increasingly abnormalities are being identified in the enteric nervous system in these patients. Why this dysfunction occurs from childhood in some patients is not clear, although developmental defects of the enteric nervous system in this condition have been reported.

These patients can be investigated in a number of ways. Their condition can be differentiated from other causes of constipation such as obstructed defecation caused by pelvic floor dyssynergia, using transit studies with either radio-isotopes or simple radiological markers. Whole-colon manometry and anorectal physiology studies are also helpful. The mainstay of treatment is lifestyle advice and adequate laxatives. However, in cases where standard laxative therapy fails, more novel forms of treatment, such as sacral nerve stimulation and antigrade continence enema (ACE) procedures to irrigate the colon, can be tried. Surgery should normally be avoided in these patients but in very intractable cases there may be a role for it.

10 Who might need cholestyramine? Is there an easy way to identify such patients in primary care?

Cholestyramine is used in patients with bile salt malabsorption, which can occur in terminal ileal disease such as Crohn's disease or in patients who have had surgical resection of the terminal ileum. However, a number of cases of bile salt malabsorption are idiopathic. One needs to consider this diagnosis when patients complain of diarrhoea that is suggestive of steatorrhoea where all other causes have been excluded. We can do a SeCHAT test to diagnose bile salt malabsorption. However, if this test is difficult to organise in primary care then an empirical treatment with cholestyramine in a patient with suggestive history may be considered.

Professor Qasim Aziz is professor of neurogastroenterology at Barts and the London School of Medicine

Competing interests Professor Aziz is currently trialling a new IBS drug for Novartis

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Extra online at pulsetoday.co.uk/clinical

Go online to read Professor Aziz's views on bowel disturbance and damage in childbirth. You can also post your own question in the comment box and Professor Aziz will answer the first two.

WHAT I WILL DO NOW

Dr Linden Ruckert considers Professor Aziz's answers to her questions

- The question of food intolerance comes up time and again so it is interesting to know about delayed hypersensitivity and small bowel permeability
- It might be worth supporting a supervised exclusion diet but resisting 'allergy testing'
- I will continue screening for coeliac disease in IBS and the notion of latent coeliac disease is helpful
- The explanation of the use of amitriptyline in IBS is a useful form of words to try with patients
- It is interesting to note that SSRIs are less useful
- The idea of a low-grade inflammatory process in the whole GI tract is an interesting one that might be acceptable to patients as part of a biosocial model

Dr Linden Ruckert is a GP in north London

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