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There's been a lot of research in recent years into irritable bowel syndrome. We've heard a lot about the epidemiology and the impact of the disease and how it is affecting a variety of different symptoms. But we need to try and understand rather better what may be going on in terms of the underlying pathophysiology. So I'm going to ask Eamonn Quigley to give us an update into our current understanding.

Well I guess the first question that many sufferers or patients ask is, what is the cause of irritable bowel syndrome? And my answer always is, "There's probably no single cause." This is probably a group of symptoms which have multiple causes. But there has been progress, and I think probably the most significant single piece of progress to me has been the realization that some individuals can develop irritable bowel syndrome for the very first time after a gastroenteritis episode, and we call that post-infectious irritable bowel syndrome. And I think that observation, which has been made in many parts of the world, has really changed our approach to the research in irritable bowel syndrome.

As we've mentioned already, stress is another important trigger in some people, and there's been a whole body of research about the role of stress and factors associated with stress and various hormones in irritable bowel syndrome. Certain foods trigger IBS for some people, and we talk a lot about this later on. And again, just recently there's been a whole load of research about various foods and how they might trigger irritable bowel syndrome, and there are probably many more factors.

Now a very useful way of looking at irritable bowel syndrome; in fact the way that most researchers look at it, is the so-called gut-brain axis. And in this cartoon, which you can see on your screen, you can see the patient with pain, with discomfort, clearly having an emotional reaction to this in terms of the brain. And this interaction between the brain and the gut is very important in irritable bowel syndrome. And for example, we can look at this from two perspectives. First of all, if we take it that— in some people the main problem may be in the gut; there may be a reaction to food or there may be a reaction, as I mentioned, to an infection. And this has an impact on the gut where it affects gut muscle, causing spasm, or it leads to increased sensitivity, so we call it "visceral hypersensitivity." And this is a situation where the gut is hypersensitive to any stimulus, and that then leads to pain and discomfort, and of course, this then leads to an interaction with the brain, where the patient is uncomfortable; it upsets them.

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Then you can take another situation, for example, where the individual is stressed, they're anxious, they're depressed, which of course would be brain symptoms, if you like. And we know from a lot of research that this can impact on the gut and cause abnormal motility and abnormal sensitivity in the gut and lead to gut symptoms. And this interplay between the brain and the gut is critical in the development of symptoms; in some patients it may be more gut, in other patients it may be more brain, in others it may be a bit of both. I think that's a very useful way of looking at the causation of irritable bowel syndrome in many different people.

Well, Anton Emmanuel is a neurogastroenterologist with a great deal of knowledge about the myenteric plexus and the way that the functions of the gut are regulated. So I'd like to ask him how he, from that specialist point of view, sees the pathophysiology of this condition.

I think this is an important question, because patients often like to know why they've got this condition. And I think it's important for doctors because it also helps us to explain to the patient. And I think, as Eamonn's alluded to, a very important issue is this issue around the guts being sensitive, they feel things too easily. And it's important to try and understand that, because there is this constant sort of dialogue between the brain and your tummy; that's how you know when you're hungry, that's how you know when you've had enough to eat, that's how you know when you need to open your bowels. There's this messages coming up from here, up to here, and in turn there are messages coming from here, back down to here to tell you to stop eating now or to go to the toilet or whatever else. And if that kind of delicate dialogue is interfered with by infection or by emotional triggers or anything, either at this end or this end, that is when things can go wrong. And those little insights, like the infectious insight, like the relationship with stress in some individuals – not every individual, but some individuals – those are really critical things, because they help the patient understand why they suffer, but they also begin to help us understand a little bit more about how maybe we can target our treatments in a more useful way for patients.

And if I could add just another point, I think it's very important for IBS sufferers to understand that the sensitivity is in the gut. They're not wimps, they're not sensitive to everything. In fact, there's lots of research showing that, in terms of other sensitivities, they're completely normal. So this seems to be a peculiar predilection that they have to being sensitive in the gut.

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So Pali we've heard some quite esoteric suggestions as to what may be going on in the background of IBS. Do you find it helpful in the primary care setting to give an explanation that takes these new concepts into account when you're managing your patients with IBS?

Yes, indeed. I think that from the general practitioner's viewpoint, all the items that you've discussed in the last few minutes can be very nicely brought together to say a patient is a person and their pain and discomfort is part of what they feel as a person, and that you cannot separate the gastrointestinal system from other parts of the person, which is the thinking mind, the so-called brain-body axis, or whatever other phrase we might use. And certainly one very good and clear explanation for irritable bowel syndrome is that the lining of the gut has become over-sensitive and that this is sending messages to the brain which cause a perception of great discomfort and in return, of course, then the individual gets a reaction to that.

So this oversensitivity or hypersensitivity of the gut I'm not sure that we necessarily understand clearly how this happens and how it can be dealt with, but that is to me the most obvious explanation for the symptoms that a person sees.

Is it one you find the patients understand readily?

Yes, because I think patients understand that if their bowel system is oversensitive to either what's happening inside or to pressure inside the gastrointestinal tract then these perceptions and these signals are abnormally transmitted and received, hence the discomfort and the pain.

Well thank you for that. Of course, one of the concerns about persistence in terms that have not necessarily been fully explained, is whether something else is going on. And of course the individual symptoms might be caused by a variety of different disorders. And since we have no specific test for IBS, that tends to amplify some of these concerns. But of course there is good news, because if you are young, you have typical IBS symptoms of abdominal pain which is fluctuating with altered bowel habit, as is being discussed, and you have no warning signs, or red flags as we call them, such as weight loss, blood loss in the stool, vomiting, then the diagnosis is very likely to be accurate and it's very unlikely to change over time, as we have heard.

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But patients and sufferers from IBS will question whether they need investigation and to what extent that investigation might go. Typically if as we've said, the patients are young, the symptoms are typical, very few tests may need to be done. These days typically your doctor might test for celiac disease since there is a slight increase in celiac disease amongst IBS sufferers. Usually a test will be done to check for anemia and some evidence of inflammation. Stool might be tested for infections or for blood in the stool. And depending upon age and various other factors there may be a need to image the bowel, either with x-rays or with endoscopy. So this is the usual path of approach to the patient with IBS symptoms.

Let's now ask our experts how they view this need for investigation first in the primary care setting, Pali.

I think that it's normal human nature to think the worst, and I think both the sufferer, the patient, and the doctor will want to make sure that there isn't anything drastic going on. Let's be honest about it, some patients will fear, and indeed their doctors might fear that the patient has some form of cancer or some other more dangerous disease. Indeed more commonly now in many European countries with a greater awareness of ovarian cancer, many women might fear that they have ovarian cancer problems.

Having said that, I would like to reiterate what you've mentioned, which is that a positive diagnosis of irritable bowel syndrome is possible made on the basis of symptoms, the length of history, also with the use of simple blood tests to exclude anything like celiac disease or anemia, a stool test to rule out infection, perhaps other blood tests to rule out inflammation. Once those things are out of the way the chances of the diagnosis not being IBS are very, very low. And we know that irritable bowel syndrome is not a condition that turns into something more dangerous or worrying over a period of time. So in the vast majority of patients we can be quite confident of the diagnosis based on the history and the examination.

At the specialist level, Anton, you're going to look at this somewhat differently perhaps. How do you view the need for investigation in patients who come to you with IBS?

I think the right thing to do is to come again to the patient's symptoms. And I think when the symptoms are bloating and pain, I think there's a very particular set of things, which I think Pali alluded to, the gynecological features. Because the diseases in the

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gynecological systems can very, very easily and very commonly mimic gut symptoms. And we have really no way of examining for that. And so an ultrasound examination, maybe some blood tests, those things would be important in a female patient to be sure that there's nothing going on within that system. And it can be horrible diseases of the sort Pali mentioned, or it can be quite benign things which can mimic this condition.

And as far as the gut goes, again, I think Pali has raised a very important point about this need for – or possible need for colonoscopy, this examination of the bowel, or x-ray examination of the bowel. And this is quite tricky, because I think, you know, patients often get a bit nervous about this, but on the other side feel the need to have it done to be absolutely sure, because unfortunately bad things that happen in the bowel are very prevalent and we all know somebody or have somebody in the distant family whose had something like this, and it's quite a tricky area, I think.

But you're going to, in that setting, age 50-ish positive blood in the stool, you're going to do it anyway. Family history perhaps, particularly of young onset of malignancy.

Absolutely. And I think that's exactly the point. So it's – or as you say, exactly to do with the symptoms and the context of the patient. So where there is a high likelihood of disease, of course it's our job in hospitals to persuade the patient, who may be a bit unwilling, to have these tests done.

Equally importantly, there are situations where we can be really very confident. We got a very positive message from the GP saying, "This is a patient I've known for decades." We take a history where they sort of tick the boxes of the criteria which fulfill what we consider IBS, where there's no alarm features, the things you mentioned as red flags. And when that's the situation, we need to be able to be strong enough to give the patient confidence as well in our clinical acumen and that the diagnosis is secure. And as Pali and Eamonn said earlier on, this is a diagnosis which we can be confident of making and be confident that if we do it positively we can be fairly sure that patients won't go on to get something horrible.

Yes. And I think reassuring the fact that colon cancer rates in IBS sufferers are certainly no higher, and possibly a little lower than in the general population.

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And there is a risk in continuing to investigate the patient.

Absolutely. I agree.

Because that may convey to the patient your uncertainty, and it also conveys to the patient that IBS really isn't that important, and we're trying to find the important things. And that's not the way you should be approaching it. I completely agree that there are a number of situations which both Pali and Anton have identified where investigation is appropriate. And I would add one other one, and that's the patient who has continuous diarrhea, because there we do begin to think of celiac disease, which has been mentioned, and we think of inflammatory bowel disease and some other gut inflammations.

But if you take the 25-year-old female with constipation, with bloating, with these intermittent symptoms, there really is very little need for much in the way of investigation, and continuing to investigate that patient is going to expose them to a lot of discomfort, a lot of distress, as Anton has mentioned, and is really going to be fruitless.

Eamonn, let me for a moment though take the opposite viewpoint. Let's assume that I am a patient with the kind of symptoms that you've mentioned. I know that as my doctor you would try to reassure me as much as you can that I have irritable bowel syndrome and nothing more dangerous. But if I still have a doubt in my mind and I'm not completely convinced, and if a great deal of my anxiety is about the fact that I might have a hidden dangerous disease, then how do you think you as my doctor should handle my situation?

Well the way I would handle it is as follows. I think first of all I would say that, you've got irritable bowel syndrome. This is a real entity, it's a very important entity, and in your case it's a disabling entity. And that we know from a lot of experience that severe irritable bowel syndrome can be as disabling as heart failure, as high blood pressure, as a lot of other "serious" diseases. That's the first point I would make.

The second point I would make is that the likelihood of as you've already mentioned, in a 25-year-old female with these symptoms and not having this and not having that, having cancer is zero. And so I think that is the way I would approach it. And I think you have to keep that dialogue with the patient. And as you've mentioned and you've all mentioned, if you've, in your first contact with the

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patient, gone into the history in detail, made it clear to the patient that you understand not just their symptoms, but how they're affecting them, then it should not be a problem.

Surely, is this not one reason why some sufferers go from one doctor to another, because in spite of the explanation, they're not as reassured as we would prefer them to be?

But I think I've been here, because I think we have a major responsibility as physicians to always draw a bottom line. And a lot of physicians these days I think are a little reluctant, because they worry themselves about being wrong. And if you convey that to the patient as Eamonn already said, I think that is as much of a problem in perpetuation of the anxiety, if not the symptoms, that it is important to say, "You're a 25-year-old, you're a female, you've got the classical symptoms. You do not need a colonoscopy."

And it's interesting that in recent years I've noticed a change. I've noticed patients saying, "I think it might be irritable bowel syndrome, Doctor. Is it irritable bowel syndrome?" Ten years ago the approach was that the last thing that was left after everything else was negative was irritable bowel syndrome. Now patients are saying, "Is it irritable bowel syndrome?" and if you say yes they say, "Fine. Now let's talk how we're going to deal with it."

This is a very good point for me to move to the next topic.

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