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## Lower GI Issues

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Video <https://youtu.be/UWLVsR4PX1Y>

[00:00:00]

[00:00:07] **Dr. Qasim Aziz:**

Thank you for that kind introduction. I agree, gastroenterology just doesn't roll sometimes, properly on the tongue. So, we're going to talk today about lower gastrointestinal, problems in this talk, and suffice it to say, I think, as I usually do, just to remind you what the – what the gut actually, looks like my – some of my patients when they come to see me in the clinic are a tiny bit surprised when I show them this figure.

[00:00:38]

But, nevertheless, it actually starts from the oral cavity, and via the pharynx into the esophagus, often described as the gullet, as well. There's a valve at the lower end of the esophagus, which opens up to allow the food to get into the stomach, which is a little reservoir or a mixer, and it actually mixes all the food with acid, clears up all the bacteria, breaks the

food into small particles, and then sends that into the small bowel, where the absorption of the food takes place. All the waste then goes into the colon, and then it is evacuated. When it arrives in the rectum and you get a sense that you need to, need to go.

[00:01:23] So today we're going to focus mainly on the small/large bowel and the rectum, and how these areas are involved in patients with Ehlers-Danlos syndrome.

[00:01:35] Just to give you an idea of what the structure of the gut is, if you look at a cross section, right in the middle, that target zone, is the lumen or the inside of the bowel, where the food, all the different juices, etc., reside. The finger-like projections that you see are projections of the mucosa or the lining of the gut, which contains a number of cells, and it actually has these finger-like projections just to increase the surface area for absorption. If it was flat, then the absorption wouldn't be so good. And this is actually what happens when the small bowel gets damaged, for instance, in celiac disease, that it becomes flat.

[00:02:16] Just behind that, is the submucosa. I'm sorry, we don't have a pointer to actually, point towards it directly, but just behind this, these finger-like projections, is an area called the submucosa, and within that there is a very rich plexus of nerves called the submucous plexus. These are nerves that are sensing what is actually going on in the inside of the, of the gut, of the lumen of the gut, and what's happening at the cells and [inaudible] level and so on.

[00:02:46] And then the muscle layer starts, and first muscle layer is the circular muscle layer, which is the inner muscle layer, and then the outer muscle layer is called the longitudinal muscle layer, and between them there is, again, a very vast plexus of nerves called the myenteric plexus. So, this, the gut is rich in nerves, and as you will see it is also rich in immune cells, as well, and I'll show that to you later. But if you actually take a section and look at all these different areas [in] a little bit more detail, and to see where the connective tissue is within these layers, and it seems that the main, mainly the connective tissue is in the muscle layers of the gut.

[00:03:29] At the bottom half you see the inner circular layer and the upper half you see the outer longitudinal muscle layer, and in the longitudinal muscle layer you see these connective tissue scaffolds coming down, these dark red lines coming down, and in between the two muscle layers, the, the circle that you – big circle that you see, are the myenteric nerves. These

are the nerves of the gut. And you see that there is a lot of collagen fibers and elastin fibers around the nervous system of the gut.

[00:03:58]

So it shouldn't be surprising that if there is a problem with, with this connective tissue or the collagen, there could be dysfunction in the muscle layers of the gut, but also in the nervous system of the gut, and, indeed, we have shown that recently in animal studies that there is a problem, because the – if you have the certain connective tissue proteins like tenascin-X, if there is a problem with that, that directly affects some of the nerves in the, in the gut.

[00:04:30]

So here's a slide which accumulates all the symptoms that have been described in patients with, you know, previously in previous literature this was all JHS and, uh, EDS hypermobility, but is—now according to the new classification this would cover both HSD and hEDS as well. You can see at the top there is a lot of epigastrium and intestinal symptoms, but we will talk about that in my next presentation, so, we are going to focus on the lower GI symptoms. As you can see, most of the studies describe abdominal pain as a very common symptom range between 58–98%, but an average of about 76% of the patients with HSD and hypermobile EDS complain of abdominal pain.

[00:05:18]

About 39–40% of them have irritable bowel syndrome-like symptoms. Constipation and diarrhea appear to be almost equal, and alternating bowel habits, where patients complain of constipation alternating with diarrhea, seems to be much more common, and that's certainly true of my clinical experience as well, that in terms of alt – you know – change in bowel habits, it's the altered bowel habits that seem to be the most common problem, and I'll explain to you how and why that might occur.

[00:05:52]

There's a recent very, um, nice, um, study in large number of patients that has compared the prevalence of gastrointestinal symptoms in EDS hypermobility type. Again, the old classification, which again would include HSD and, and hEDS patients, and other forms of EDS, including classic vascular, unclassified, and so on. And if you look at the prevalence of more lower GI symptoms, which I've highlighted in red then bloating seems to be equally common in about 12, 11–12% of patients.

[00:06:30]

Functional constipation means constipation without pain. Um, so these are classification according to the Rome Criteria of Functional Gastrointestinal Disorders, so functional constipation is constipation without pain, again. Similar prevalence, in both HEDS and non-HEDS patients.

[00:06:50]

Diarrhea, again, very low prevalence in this, but IBS is very prevalent, about 55–58%. Again, equal representation in both groups. And the reason that constipation and diarrhea is low in this study is that most of the constipation and diarrhea is going to come under irritable bowel syndrome, because irritable bowel syndrome can be constipation predominant, diarrhea predominant, or mixed bowel habits, so I suspect that all of that is actually, being classified under irritable bowel syndrome because pain is so common. So, the classification or definition of IBS is bowel symptoms associated with pain, and therefore, most of these patients are getting diagnosed with irritable bowel syndrome.

[00:07:35]

So, if you look at why people get problems in the gut, and I sort of simplify that for myself as well when I actually try and understand what the problem is, into three categories, three main categories. One is mechanical problems in the gut, the gut may be more sensitive, or there is immune dysfunction in the gut, and it's just – it's not necessary that all of these will act independently in a patient. They could actually be a combination of two or three factors that could be contributing to the symptoms in a given patient.

[00:08:08]

So let's look at mechanical problems in the gut. I often give this, you know, so I use this analogy of a hose pipe versus tap water. So when you open the, you know, kitchen tap, hopefully water gushes out, and that's because there are metal pipes that are bringing water to the kitchen tap. And there's a basic law of physics that flow in a tube, depends on how elastic the tube is. So, the more rigid the tube, the faster the flow. The more elastic the tube, the slower the flow. And that's why usually, it's, at least in the old-fashioned hose pipes, the flow would be a lot slower, although I know that there are all these new fancy hose pipes where the ... actually, water gushes out better than your kitchen tap, I suppose.

[00:08:55]

But, but because we imagine that collagen is more elastic and stretchy in the gut, and therefore the gut, which is a tubular organ, long tube, that may be more elastic and stretchy, and therefore may not move so well. However, this has not been necessarily proven by the research studies, which are few and far between, but the small number of studies that we have seen, at least in the stomach, the stomach doesn't appear to be more stretchy in patients with, with EDS, but the bowel may well be – and the bowel appears to be quite sluggish, but it seems that quite often the problem is actually in the nerves and in the muscle layers themselves. We talked about how connective tissues are in the muscle layers and in the nerves, and therefore it seems that its dysfunction is being caused

by directly affecting nerve and muscle, um, function in, um, quite a lot of patients, but much more research is really needed to clarify this.

[00:09:54]

So let's look at constipation. What you see in this X-ray is there are these white dots in different shapes that are scattered around the, the bowel, and this is called a shape study, so you ask the patients to swallow a number of different capsules. These open up like cluster bombs into many different shapes that then go around your gut, and you – we – after administering these capsules, we take an X-ray five days later. In five days you should have passed all of these shapes.

But as you can see in this patient that most of the shapes are still there. They're scattered round about, but particularly dense on the left side of the bowel, okay? And this, on the X-ray that would show up on your right side. So that's the descending bowel and the rectum, and that's where most of them – so, this tells us two things. One, that transit is slow in the gut. In five days, this patient hasn't cleared all of these markers, and secondly, the transit is slow mainly in the left or the lower part of the bowel, and this may be because there is difficulty in evacuating the stool, and that may be what's causing that blockage.

[00:11:06]

So we would call this secondary delay in transit because of difficulty in evacuation. In some patients we see these markers scattered all the way around the bowel equally, which means that there is a primary problem in, in transit. And in terms of evacuatory dysfunction, very common in the patients that we see, and this is why constipation treatment often fails, because people fail to pick up on the fact that the pelvic floor – there is a problem in the pelvic floor and in the evacuatory mechanism. No matter how much you push from the top, laxatives, stimulants, *etc.*, they're still not going to be able to evacuate because there may be an anatomical problem. And as you can see in this figure, on the left-hand side of your figure is a normal rectum, and it's got a slight S-shaped loop, because it connects with the sigmoid colon, which is S-shaped, and then the rectum smoothly enters into the anal canal.

[00:11:59]

But on the right side of the picture you see that there is a big bulge in the rectum. This is called a rectocele, or it's a pocket, that sort of presses on the vagina a little bit, and this pocket can trap the stool. So, as the stool passes over the rectum, some of it drops into this bucket and you, uh, evacuate, but the patients still feel that there is something left behind, and this causes a lot of disfaction – dissatisfaction. They try again and again,

but because it's stuck in the pocket, it may not come out, and therefore there will be a lot of dissatisfaction caused by this. This is surgically correctable, and if you don't pick up and there is a large pocket like this, this rectocele, this can cause quite a lot of discomfort.

[00:12:43]

And there is another condition that we see which is in lay language described as a prolapse, internal prolapse of the rectum into the sigmoid, into the anal canal. So, the rectum, if it's more elastic, and stretchy, and floppy, instead of squeezing the stool out, it just flops onto itself and this is what you see in these three pictures. In the first picture, on the left, you actually see the rectum is starting to collapse into the anal canal, and this becomes bigger and bigger, and eventually in some people, it actually prolapses all the way out.

[00:13:17]

So these are anatomical problems that can be fixed with surgery, and without fixing them sometimes management of constipation can be difficult. And we have therapists who work with patients to strengthen the pelvic floor and improve evacuating function and pelvic floor function, which can sometimes help to reduce the straining, which often causes this internal prolapse.

[00:13:41]

Now, constipation. I've said that a lot of our patients have alternating bowel habits. They have constipation, then diarrhea, constipation, diarrhea, and this pattern keeps occurring. So why does that happen? So, this happens because secondary to the severe constipation you get stagnation in the bowel. There's a tubular structure, which is blocked at one end and there is a lot of stagnation, and you've got food, fluid, stool, all mixed in together. Ideal median, medium for developing a swamp-like situation in the bowel. So, you've got a lot of horrible stuff just sitting there fermenting and not going anywhere. So it's become a bit like a pond rather than a flowing river that it should be.

[00:14:23]

And in this swamp are a lot of bacteria. Normally there are millions of bacteria. There are more bacteria in our gut than the number of cells in, in our body, and the alternative theory of evolution is that man was created for the bacteria really, because they have a great time in our bodies when we're alive, and then they consume us when we're dead, so, you know, it's a win-win situation for them. So, so there's lots of these bacteria. They're usually healthy, they're helpful to us. It's, you know, in their interest that we survive as long as possible. But, you know, when you've got a stagnant gut you start to get quite unhealthy bacteria growing in there that will

cause fermentation of food, which will produce a lot of gas, flatulence, and bloating and pain and cramping and this diarrhea. You start to get what we call, you know, diarrhea caused by bacterial overgrowth. And this is exactly what it looks like in that swamp. It's got undigested material, because you may start mal-absorbing food, particularly fat. It's oily, it floats on the water, it's difficult to flush, it's smelly. So, you know, that's a tell-tale sign of diarrhea occurring secondary to the stagnation that's going on inside in the bacterial overgrowth.

[00:15:39]

You also get overflow diarrhea. So, the idea here is that the bowel is so packed up with stool that the only way it can get out is by breaking down and coming down as liquid stool. So just like, you know, on the left of the picture you actually see this beautiful waterfall, but above that there is a glacier. Okay? So, this solid block of ice and water is melting and coming down as, as a waterfall. So, the same thing is happening in a very, very severely constipated patient. There is so much stool backed up in the bowel that the only way that it can really get out is bits break on the edges and come down as liquid stool. And actually, that is like a waterfall when it happens. It is urgent. You have to rush, um, and sometimes accidents can happen. It's just watery liquid stool. So, people feel, "Oh, I've got terrible diarrhea." They take more Imodium. Stop this. And, you know, it just – the bowel just keeps getting fuller and fuller and fuller, and the problem just keeps on getting, getting worse. And then the bacterial overgrowth starts as well, and then you get the malabsorption diarrhea sometimes, and sometimes the overflow diarrhea. It just becomes incredibly confusion as to what is actually going on.

[00:16:50]

And then you take the laxatives, more of this overflow occurs, because when you take the laxative it breaks on the edges first and the overflow diarrhea starts. And they say, "Oh, gosh, this is a terrible laxative. It's giving me terrible diarrhea and cramping, so I have to stop this laxative." And you just [*inaudible*] vicious cycle.

[00:17:08]

Now the gut knows. As we've said, there are lots of nerves in the gut. This is, again, another picturing showing the number of nerves, and it just gives you an idea of the extent of the nerves. Just underneath the mucosa is the submucosal plexus, and then the myenteric plexus behind that, between the muscle layers. And there are more nerves in the gut than the spinal – there are nerves in the spinal cord. So, people forget that, how nervy this, this organ actually, actually is, and therefore dysfunction in these nerves can cause dysfunction in the, in the entire gut.

[00:17:47]

But there are also pathways that go from the gut up to the brain, and there are a number of different pathways that go via the spinal cord and they travel up to different parts of the brain and the pain centers in the brain, um, such as the MCC and ACC that you see is the cingulate cortex, part of the limbic cortex. You might have, might have heard of the saying, "This person has gone limbic." Limbic means they've gotten very emotional. So, these are the emotional centers of the brain. And then on the outer side you see a little arrow, green arrow going up, that says primary somatosensory cortex. That is, that is where the sensation is perceived and the intensity of the pain is perceived.

[00:18:26]

So there is this sort of communication going on between the gut and the brain, and sometimes these nerves can get sensitized. So, what happens under normal circumstances is that normal sensation in the gut is transmitted to the brain, and you may get a little sensation. Normally we don't feel any sensation, but if there's a big bolus or something is not going down properly, you may feel it and sense it, but after injury, inflammation, etc., these nerves may get sensitized and you get a much larger signal going up to the brain, which causes much greater activation of the brain areas that process pain, and that will produce quite severe pain. And this is a system where the nerves have become sensitized.

[00:19:05]

But there's an alternative situation where the pathway from the gut to the brain is absolutely normal, but in those limbic areas of the brain the processing is somehow enhanced – enhanced, and that occurs because of stress, anxiety, depression, and therefore normal signals are amplified, and, and that can also cause, cause pain. So, the same sensation which is not painful when you're not stressed, during stress may become painful.

[00:19:31]

So this is a good way of describing it that you could have actually in the, in the gut. You can have sensitization of nerves, describing it – described as peripheral sensitization, which can lead to sensitization occurring at the level of the spinal cord, which is described as central sensitization. And yesterday Professor Dan Claw described very nicely, and I went up quickly and got this figure, from Google Images of the guitar and the amplifier. So, the guitar is at the, the strings are at the level of the gut, you know, so, you know, they can be playing, but if your amplifier is actually set at very high, so the same signal coming from the guitar will get amplified and go up at a very high level to the brain, and sometimes the problem is in the amplifier rather than in the strings, and that is what is called a central

sensitization. And, of course, as we have said, psychological stress, *etc.*, modifies all of that and can, can amplify the signals in any case.

[00:20:25]

I can't talk about pain and not talk about this condition called anterior abdominal wall pain. About 30% of my patients with EDS have this, and this is because the muscle in the middle called the rectus muscle extends for about 5–6 cm on either side of the midline have a lot of nerves that are branches of spinal nerves that come underneath the muscle and go through the muscle like that. So, you've got this white cord coming through the muscle, and then goes, uh, underneath the muscle, goes through the muscle in this fibrous canal and comes out. And you can get a nerve entrapment of this, um, nerve, of these nerves as they go through this muscle. And this can produce severe excruciating pain. And these patients have a frozen abdomen. They can't move. If they lie in a certain way it's more painful. They bend down to pick something, it's more painful. This is not coming from your bowel. This is coming from these trapped nerves on the, on the abdominal wall. And this can be treated and I'll show you some information about that.

[00:21:28]

So let's talk about immune dysfunction quickly. As I've said, the gut has an extensive immune system. There are lots of bacteria, fungi, *etc.*, in the lumen, and these are all protect – the, the, the cells protect against this because they are very tightly bound together, and there's a very rich immune system underneath it which is helping to regulate everything, and then included in that immune system are the mast cells as well.

[00:21:23]

And the gut microbiota is an extensive organ really within the gut itself, and they communicate with all the types of cells, with the immune cells, epithelial cells, nerves, muscles, *etc., etc.*, and they also communicate with the brain through the autonomic nervous system, which is the nervous system of the organs of the body and the hypothalamic pituitary axis, which are the part of the brain which responds to stress and releases steroid glucocorticoid hormones, *etc.* So, it's communicating through the brain. It's communicating vastly in the gut. So, any problem that occurs in the gut microbiota gets transmitted up to the prob – to the brain, which can lead to functional and neuroplastic changes that can occur in the brain. And sometimes with [*inaudible*] at either end, either at the brain level because of stress, life, adverse events, changes in environment or at the gut level through diet, pathogens, inflammation, you can actually get problems throughout this gut-brain axis modulated by the gut microbiota.

[00:22:42]

And you've all heard of leaky gut syndrome, where the epithelial or the cells that line the gut become leaky and articles of food and bacteria, *etc.*, get through and then the immune system reacts to that. And the immune system can become over-reactive, and this can lead to food allergy and intolerance of normal immuno – even autoimmunity, leading on to other autoimmune diseases, can be a factor in, in leaky gut syndrome. And I think in a lot of our patients with mast cell activation disorder, *etc.*, this is the problem here because the mast cells react to these antigens coming through the lining, which is leaky lining, and then you get release of histamine, *etc.*

[00:23:25]

And mast cell activation disorder, I am not going to dwell on that very much, because it was described very nicely by Dr. Maitland yesterday, but suffice it to say when histamine and mast cells are active, you can get a lot of tummy symptoms of diarrhea. This is another cause of diarrhea which is related to eating. Flush. People feel flushed. They can get itchy. Palpitations, severe diarrhea. That can occur within an hour of a meal with abdominal cramps and a lot of flatulence, *etc.*, as well.

[00:23:56]

So, as you can see, there are three causes of diarrhea here that we've already seen in our patients, and it's a matter of trying to actually figure out which one of these is the most likely.

[00:24:05]

In terms of management, it's important to reassure patients to say, "Well, we, we think we know that there is a cause." It's not just irritable bowel syndrome, and, you know, nothing can be done about it. There are problems. There are issues. We understand what those issues are. And, and one tries to go through these problems and try and understand what the basis is for the symptoms and try and manage them. An MDT approach with dieticians, pain management, other colleagues who understand POTS and joint problems and urinary involvement, *etc.*, is very helpful, and psychologists, because a lot of stress is caused by undiagnosed symptoms over years and years, which, which needs management in its own right.

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We need to do some basic investigations, blood, X-rays, scans, *etc.*, to rule-out and make sure we're not missing anything. And conditions that can overlap, sometimes with hypermobile EDS are inflammatory bowel disease, like colitis or Crohn's disease, celiac disease, autoimmune connective tissue disorders, and there is some suggestion that there is a higher incidence of these conditions in people, patients with EDS. And we do some

physiol – physiological tests of hydrogen and methane tests to see if there is bacterial overgrowth in the gut or a colonic transit study as I explained, and we have anorectal physiology studies that can pickup whether you've got a rectocele or intussusception or a collapse, internal collapse, etc. So, all of these problems can be, can be diagnosed through tests.

[00:25:30]

Food intolerance, again common in irritable bowel syndrome, common in our patients that we see and I've talked about how increase in fermentation in the gut, particularly of carbohydrates, can be a problem, and this is where FODMAPs, which are foods that are high in fermentable carbohydrates, can be problematic in these patients where there is a lot of blockage, there is a lot of fermentation, and then the bacteria, in the gut. You might have heard of low histamine diet. The research studies in patients with gastrointestinal symptoms are few and far between, but certainly, in those patients with mast cell activation problems, looking at the histamine in the diet and seeing whether there are histamine-related triggers, can be helpful. And sometimes antihistamine and mast cell stabilizers, as Dr. Maitland described yesterday, can be helpful in those patients where there are features of of mast cell activation disorder.

[00:26:22]

I'm going to go a couple of minutes over time, I'm afraid.

[00:26:24]

So there's a recent study showing that low FODMAP diet in both patients with irritable syndrome, but in those with EDS and IBS, the response seems to be better in that group compared to IBS alone. And all the symptoms improve, pain, bloating, constipation, diarrhea, etc., all symptoms improved on the low FODMAP diet. This is certainly something to consider. This is the first study of, you know, dietary study in irritable bowel syndrome patients.

[00:26:53]

This was discussed yesterday about avoiding opiates, but particularly relevant to the, to the gut, because you get opioid-induced constipation and you get narcotic bowel syndrome in long-term use of opioids, where actually, the pain gets amplified. The short-term opioids are excellent for certain conditions, but long-term opioids can play havoc with your nervous system, with your immune system, particularly your gut, so this has to be thought through very, very carefully. And then on top of opioids, because you're getting opioids, then you get overflow diarrhea, you've got bacterial overgrowth, etc., people start taking, uh, drugs to stop the diarrhea, which makes the bowel even more and more constipated, and this becomes a nightmare to, to manage.

[00:27:35]

And for sensitive nerves, again, Dr. Claw discussed this yesterday, just pain modulators like a gabapentin, pregabalin, amitriptyline, serotonin, noradrenergic inhibitors like duloxetine, *etc.*, they can be helpful in gut pain as well, where there is some suggestion that there may be sensitized nerves. But, of course, psychological factors like, you know, approaches like CBT, hypnotherapy, slow deep breathing, SSRIs, they're all helpful as well, and quite often you need a combination of these therapies to really manage, um, manage the pain in our patients.

[00:28:10]

And for patients who have this, these, trigger points on the tummy wall and they have these trapped nerves, you can do trigger-point injections with local anesthetic and steroids, and that can produce quite a lot of relief, but physiotherapy, really working with a good physiotherapist who can actually, understand why people are taking so much pressure, usually because of poor core strength or use abdominal muscles a lot, and, and rectifying that can be helpful for this as well.

[00:28:35]

For constipation, try and keep the stools soft and dietary fiber particularly soluble fiber, but, of course, this can cause more bloating and discomfort in some of our patients. So, stool softeners such as Movicol I find, which is a PEGylated solution, there may be a different name here in the US, uh, is often helpful to just soften the stools. I often add Senokot or Dulcolax as stimulant laxatives as, as step two in our patients, and sometimes we need to use a pro-kinetic, which is a drug like Resolor, which I don't think is available in the US, Prucalopride is the other name, which helps, helps to stimulate the nerves to produce stronger contractions, in-in-in the gut.

[00:29:15]

The medicine called Linzess, which I think is available here, which, uh, the, it's a – linaclotide is the other name for it – which helps to release fluid in the small bowel and softens the stool, but it can produce – like a diuretic of the gut, but it can be problematic in patients with POTS, and I'm very cautious because it can lead to dropping the blood pressure because of fluid loss. So, one has to be careful. But otherwise it's, it's good for treatment of constipation and for evacuatory dysfunction, suppositories, enemas, sometimes rectal irrigation, biofeedback is often very helpful to help strengthen the pelvic floor muscles, and in a bowel that is blocked, if an X-ray shows you've got a backed-up bowel that's just completely blocked, you have to clear it out with bowel prep that you take for colonoscopies, *etc.* Without that, things will not really settle down, and, and will result in overflow. And sometimes really in, in severe constipation, we have to consider surgery when nothing else is working, but that is rare.

- [00:30:12] Probiotics. There's a whole range of probiotics that are commercially available, and I've mentioned these where there is some evidence that they can help with gastrointestinal symptoms. Which one for which patient we don't quite know, so there's a little bit of blind therapy, and one of – some respond better to others, to one type or the other, so there's a bit of trial and error within all of this. But patients with bacterial overgrowth in the gut, low FODMAP diet helps to reduce some of the bloating, pain, and discomfort, but antibiotics, such as rifaximin, *etc.*, are sometimes also helpful, in these patients.
- [00:30:34] For mast cell activation disorder, as I said, diet, avoid the histamine triggers, antihistamines, this has been discussed all day yesterday, so I'm not going to go into any great detail. Both Type 1 and Type 2 antihistamines, leukotriene inhibitors, which are inflammatory mediators, and montelukast is very good, so it's usually an add-on diet, antihistamine, leukotriene, with mast cell stabilizers like Ketotifen and sodium cromoglycate (Nalcrom) are often things that we will use in our patients.
- [00:31:10] Enteral and parenteral nutrition sometimes becomes necessary in those who have intestinal failure; however, there's a very high failure rate of these types of therapies. Infections are common, pain is common, so one has to think it through carefully what the benefit might be of either using feeding direction into the gut or intravenously. And one has to be also aware, in a very small tip of the iceberg, really small proportion of patients, psychological issues like eating disorders, *etc.*, can present in this way, and there usually is a high failure rate of these types of nutritional therapies in those patients.
- [00:31:48] Just to finally say it's, we know that JHS or EDS is a multiple, you know, multisystem disorder and really one needs multidisciplinary team management, you, and we need commissioned services for this, which really doesn't exist at the moment. And finally, just to thank all the people who have contributed and all the funders, and particularly the Ehlers-Danlos Society, EDS UK, Bowel & Cancer Research, who have given us the funds to do the research. Thank you very much.
- [00:32:22] **Sandra Aiken Chack:**
- Is this on yet? It's so fun how that does that. Thank you, Professor Aziz. Some questions here, and I am probably going to mispronounce some of these words, so in – apologies in advance. I'll just show it to you if I can't figure it out at all.

[*Laughter*]

Um, can you see a rectocele, is that what it's, what it's called?

[00:32:41] **Dr. Qasim Aziz:**

Can you see a rectocele?

[00:32:43] **Sandra Aiken Chack:**

Yeah. In a colonoscopy.

[00:32:45] **Dr. Qasim Aziz:**

No. It's not so easy to actually see a rectocele in a colonoscopy. You can feel it during a rectal examination, but because it's just a sagging, it's not really a firm pocket, it's just a sagging of the mucosa, it can be quite difficult to pick up on a, on a colonoscopy. But a good physician can pick it up during a rectal examination, but the best way to pick it up is a proctogram. It's a barium X-ray where you put a bit of barium in the back passage, and then ask the patients to evacuate that on a commode which has got an X-ray machine attached to it, and that will very nicely pick up a rectocele, as well as an internal prolapse and an intussusception.

[00:33:24] **Sandra Aiken Chack:**

Thank you. How do, how do we resolve overflow diarrhea?

[00:33:30] **Dr. Qasim Aziz:**

You have to clear the bowel out. You really have to clear the bowel out. It can be painful, it can be difficult, because there's an – in the initial phases you, you take – I tend to use a bowel clearing medicine called Picolax, which just you dissolve the powder in a glass of water, and I just say take, take one sachet a day for five – anywhere between three to seven days until you start to see clear fluid coming out. So, you – some patients actually say to me, "I never had any stool come out. It was all liquid, and therefore it didn't clear me out." You take an X-ray and it's absolutely clean, the bowel. So, what happens is all you do is you get overflow. It just starts breaking on the edges, comes down as liquid stool. You keep rushing to the toilet passing liquid, liquid, liquid, and you keep expecting something solid is going to come, but it doesn't. It's just like a block of ice melting, okay? So, it actually just melts away. And, and there's no other way. You just have to persevere and get that out.

[00:34:23] **Offscreen Speaker:**

What's that called again? The medication.

[00:34:27] **Dr. Qasim Aziz:**

The medication? Picolax. Picolax. It's sodium picosulfate that's available in liquid, but we have these Picolax, um, sachets with some powder that we tend to, but there are lots of other – the reason I use that is that you don't have to drink two liters of fluid with it, as you do with some of the other ones.

[00:34:36] **Sandra Aiken Chack:**

Can males get pelvic floor dysfunction, and, if so, how do you treat it?

[00:34:50] **Dr. Qasim Aziz:**

Exactly the same way. Yes. Males with EDS, or other connective tissue disorders, yes, they do get pelvic floor dysfunction. They get rectoceles and internal rectal prolapses as well, and you treat it exactly the same, whereas you do – you really have to start with basic, you know, sort of biofeedback type of therapy to strengthen the pelvic floor muscles, improve evacuation, but if that's not working, it's a significant rectocele or an internal prolapse, and sometimes surgical management is, is required to correct that.

[00:35:26] **Sandra Aiken Chack:**

Can gastroparesis look like roughly monthly cycles of barely no mobility for most of the time with abdominal pain, bloating, nausea, and then a day or two of emptying, diarrhea, vomiting.

[00:35:22] **Dr. Qasim Aziz:**

Hm. I'm not sure. I think gastroparesis, usually true gastroparesis will produce long-term daily symptoms that you will have, you know, fullness, bloating, early satiety. You eat a small amount and then you feel very full. And then nausea and vomiting are more severe. Now, you can have variation and you can have some good days and bad days, but most of the time you have these symptoms. Then you have a condition called cyclical vomiting, where you have normal periods of no symptoms and severe vomiting that will last for a few hours, a few days, and that will – in all of this, bowel symptoms can carry on. You can have constipation, you can have diarrhea, alongside all of this.

[00:36:32]

Now, it's usually the other way around. It's actually – if your bowel is very constipated, then your stomach will slow down. It's the motorway effect.

One car slows down, and all the cars behind have to slow down. So, if the rectum, if the bowel is not evacuating, it, it sends signals to the stomach, you know, slow down, slow down, there's too much traffic here, so just – so that, that can happen. But usually not the other way around.

[00:36:57] **Sandra Aiken Chack:**

Okay. Do you recommend virtual colonoscopy for classical EDS, and, if so, how frequent?

[00:37:05] **Dr. Qasim Aziz:**

Virtual colonoscopy is a colonoscopy done by a CT scan, and it's a very good way of looking at the, at the bowel. There are advantages and disadvantages. Disadvantage. You don't actually have to have a camera tube going all the way around, but you still have to clear your bowel out, so you can't get away from not having that bowel prep. And, and it's, we'll miss very, very small polyps sometimes, but they're usually not significant in any case with a good screening test. And the only disadvantage is you can't take biopsies. So even if the bowel looks normal, sometimes it has microscopic inflammation, increase in mast cells, eosinophils, so quite often when we ask for a colonoscopy, we ask our endoscopist to actually take lots of biopsies that we can exam. So, in a virtual colonoscopy you can't do that. But if having a colonoscopy is a problem for whatever reason, virtual colonoscopy is, is pretty good. The, the other disadvantage for young patients, it is a CT scan, so it gives you a lot of radiation.

[00:38:06] **Sandra Aiken Chack:**

Okay. A follow-up question to that. Is, are there, if you're dealing with a, with a GI who is not particularly well versed in EDS, are there any precautions an EDS patient should ask for prior to colonoscopy/endoscopy?

[00:38:22] **Dr. Qasim Aziz:**

For hypomobile, EDS and HS, they know. We don't seem to find any issues; in fact, there is a recent study that we were involved with done by our collaborators in Maastricht in the Netherlands, where they've actually even, looked at with, EDS, hypermobile EDS patients experienced more pain during colonoscopy which shows all the colonoscopies are more difficult, which is often a perception it's a very long, tortuous colon, etc., and they blinded the colonoscopists, and then they interviewed the patients, too, as well, so those who had hypermobile EDS and those who didn't, and they found no differences. There was not an increase in pain.

The amount of time it took to do the colonoscopy, the difficulty that the endoscopist felt during, nothing was different.

[00:39:08]

So, it seems that there's no issue with HSD and hypermobile EDS but we don't know about classical and vascular and so on, and of course I think there, that is where I think if precautions have to be taken. They should be taken, and so you do need to inform your, your gastroenterologist about that, because in classical and particularly in vascular EDS, there, there can be risks.

[00:39:36] **Sandra Aiken Chack:**

Thank you. I'm interested in knowing if there is a higher prevalence of Crohn's disease in those with EDS, and if you're treating both, you know, what is the –

[00:39:50] **Dr. Qasim Aziz:**

Yeah?

[00:39:50] **Sandra Aiken Chack:**

The roadmap there?

[00:39:52] **Dr. Qasim Aziz:**

So, there is one study which seems to suggest that there is higher prevalence of EDS in Crohn's, and at least in our experience, even if they don't have full-blown EDS, a lot of patients that I've seen with Crohn's will get referred to me because the Crohn's been treated, but the symptoms don't go away and they think, oh, this patient has IBS in IBD, so when the symptoms – inflammation has healed, symptoms carry on, it's always classified as IBS, and in that subgroup, I find a lot of patients with generalized hypermobility, they don't have all the classical features of either HSD or HEDS, but generalized, joint hypermobility is very common in these patients. I don't know exactly how it links in, but I suppose it links in through changes in gut permeability. You've got a gut which is more leaky. You've got more antigens, got more autoimmune disease, and in some people with a, with a certain genetic profile, they're going to get Crohn's. Others will get ulcerative colitis and so on. But it's all unproven. This is just my, my hypothesis.

[00:40:52] **Sandra Aiken Chack:**

Okay. Are there diagnostic tools for hypersensitivity of GI nerves?

[00:40:57] **Dr. Qasim Aziz:**

Yes. So, you can diagnose, particularly in the upper gut and in the lower gut. In the esophagus we can look at sensitivity to acid. There's a test called the Bernstein test, where you infuse acid and see how people – sensitive people are. You can do balloon distention, mechanical stimulation in the esophagus, electrical stimulation in the esophagus, and the same in the rectum. For the rest of the gut, it's more difficult. So, so there are sensitivity tests that can be done in the upper and lower gut.

[00:41:24] **Sandra Aiken Chack:**

Okay. This is a per – I, I try to stay away from the personal questions, but I think it, it speaks to the, a larger group. Loading up on multiple kinds of digestive enzymes have helped me more than probiotics alone, but I have to take huge amounts and varieties for this benefit. Any danger in this?

[00:41:46] **Dr. Qasim Aziz:**

No, I don't think there's any danger in taking lots of digestive enzymes. Some patients with pancreatic insufficiency, for instance, have to have very high doses, but I would just strongly recommend that you actually have some tests done to make sure that you don't have pancreatic insufficiency. There's a simple stool test called fecal elastase that we do all the time in patients with pancreatic exocrine, which means pancreatic digestive enzyme deficiency, so there's a test that you can have done, and there are other tests, but it would be worth, worth looking at, at that.

[00:42:19] **Sandra Aiken Chack:**

Okay. Any correlation between EDS or HSD and gastrointestinal migraines?

[00:42:26] **Dr. Qasim Aziz:**

Gastrointestinal?

[00:42:27] **Sandra Aiken Chack:**

Migraines. And I don't know if that's a thing or not. I'm just asking the question on the sheet.

[00:42:32] **Dr. Qasim Aziz:**

Can I see it?

[00:42:32] **Sandra Aiken Chack:**

Yep.

[00:42:32] **Dr. Qasim Aziz:**

Where is it?

[00:42:33] **Sandra Aiken Chack:**

Right here.

[00:42:33] **Dr. Qasim Aziz:**

Migraines, migraines.

[00:42:34] **Sandra Aiken Chack:**

Migraines. Oh, it's m-me.

[00:42:37] **Dr. Qasim Aziz:**

Uh, okay.

[00:42:37] **Sandra Aiken Chack:**

I'm sorry.

[00:42:37] **Dr. Qasim Aziz:**

Migraines, or migraines.

[00:42:37] **Sandra Aiken Chack:**

Migraines.

[00:42:37] **Dr. Qasim Aziz:**

Sorry. I didn't get that. Yes, there is. And this is the subgroup of patients where I suspect mast cell if they have EDS, if they have migraines, if they have a lot of allergies, asthma, [*inaudible*] atypical predisposition, asthma, eczema, hay fever, urticaria, and then they have gastrointestinal symptoms as well. This combination, then they get cyclical – one, some of them get cyclical one thing, some of them get cyclical abdominal pain, so this is a subgroup that I recognize now quite well, and these are the ones that do respond to low histamine diets and antihistamines and so on.

[00:43:21] **Sandra Aiken Chack:**

Okay. I'm sorry, we're out of time. Thank you so very much, Professor.

[00:43:24] **Dr. Qasim Aziz:**

**All right. Thank you.**

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