Managing Pediatric Functional Constipation – Transcript

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Hello Everyone. Good evening and Welcome to this managing Pediatric Functional Constipation Symposium. You know that many of you are still enjoying your meal, which is wonderful. Please continue to do so. For those who haven't had a chance yet, there's still a buffet that's open in the back.

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I want to point your attention to what you all may see here in front of you. At each table there are some index cards. There's also ways to communicate with us. That'll be one way that you'll be able to go ahead and submit some questions as we go through this presentation, and we certainly welcome those.

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There will also be a mic right here in the middle of the room. There will also be some opportunities if you'd like to just personally go ahead and ask a question as well. We certainly welcome that.

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So I'd like each of us to introduce ourselves and, first hello, I'm Bruno Chumpitazi. I'm a division chief of pediatric GI at Duke University School of Medicine. And previous to joining Duke I was the director of the Neurogastroenterology Motility Program at Texas Children's Hospital. It's a real pleasure to be here with you all.

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Hi, everyone. Welcome. My name is Julie Khlevner. I'm a pediatric gastroenterologist over at Columbia New York, and I head our motility center there.

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Hello, I am Sharon Perry. I'm a nurse practitioner at Rainbow Babies and Children's Hospital in Cleveland, and I do constipation along with general GI.

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Wonderful. So the, the format for this evening will be to go through case presentation and slides. We will go ahead and then open up the rest of the session to a Q and A format.

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A couple of housekeeping items to go through. There's a recording that's going on. As you can see, there's a camera here to my left just to let you all know we, in terms of electronics, if please go ahead and turn our turn off or silence your devices, and please refrain from checking your email during the meeting.

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From a Q and A standpoint, as we mentioned, there will be an opportunity at the end of the meeting, and then please complete a post-meeting survey. We'd like to hear your feedback on this presentation. Some ways that we can continue to do things that seem to work well and improve on in other areas.

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In terms of the objectives for today, after participating in this activity learners should be able to first implement strategies to improve the recognition and accurate diagnosis of functional constipation, which we'll term FC in pediatrics. The second will be to evaluate the most recent clinical data associated with current and emerging treatments for pediatric FC. And then finally, to review patient-centric decision-making management strategies and counseling pearls in pediatric FC.

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Here is our disclaimer slide. So I know that many of the room are here see functional constipation and constipation on a frequent basis. And this, all of you are, are quite good at taking care of patients with this issue. What's interesting is that constipation certainly can seem straightforward to us as physicians and as clinicians, but sometimes for our patients and those that we're seeing, it actually can be a little bit confusing.

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Another might have relatively frequent bowel movements, but have difficulty passing stool. If you suspect constipation in newborn one tip off is firm stools less than once a day. As you can see, there are different themes that are coming out here in terms of issues with stool form, frequency, difficulty passing, and it some to our patients, it can actually be difficult to grasp, well, what is constipation and what, and what do you mean by that?

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Many of you are very familiar with the Rome IV constipation diagnostic criteria. Rome V group is currently meeting now, and we are reviewing this. What you're seeing here, the two sides, one on the left here for infants and toddlers less than four years of age. And here on the right, the criteria for older children, there's a significant amount of overlap, but you're going to hear these themes about forms and frequency in other aspects.

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But just to go through it, for infants and toddlers, less than four, they need to have for one month of at least two of the following, two or fewer bowel movements per week, a history of excessive stool retention, a history of painful or hard bowel movements, a history of large diameter stools or presence of a large fecal mass in the rectum.

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If that in toddler or older child is toilet trained, then you get to these criteria here in which you have at least one episode per week of fecal incontinence and a history of large diameter stools that may obstruct the toilet.

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For the older children, you're seeing a lot of overlap here, two or more falling once per week over one month. Again, you're talking about frequency here, two or fewer bowel movements per week. History of excessive stool retention, history of painful or hard bowel movements, presence of a large fecal mass in the rectum, at least one episode per week of fecal incontinence and history of large diameter stools that may obstruct the toilet.

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So you can see the different, different aspects here in terms of what we need to be thinking about. And I want to point, at least from a stool form scale, there are different ways to measure this. I think many of us are familiar with this. I know in our, in our practice, we actually have these on the walls, and sometimes kids giggle a little bit, right when you ask them about stool form, but sometimes it's the easiest way for them to actually point to something objective and actually describe to you without using words what their stools are looking like.

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As you're seeing here, the Bristol stool form scale goes from a type one all the way to type seven with a type one being these hard balls here, hard lumps, and you slowly but surely get to just softer and softer consistency until you actually get to a diarrhea type. Type seven looks like a milkshake or a watery stool. So that's one way. And to take a look at constipation when you're speaking with your patients.

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And we'll be discussing some of these facets too. And we talk about some of the clinical trials. Here on the left, just going through some of the diagnostic criteria, again, just, it's just a myriad of these different factors, including in infrequent defecation, incontinence, withholding behavior, painful defecation, heart or large diameter stools.

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And so it's not always, a one fits all type of picture. Well, how prevalent is constipation if you take a look at the data, it can comprise about 25% of our pediatric GI practices can be an issue that's seen in about 3% of general pediatrician practices. And this is the reason, what you're seeing here is the geographic distribution of constipation in children presented in median prevalence rates, and it's color coded here.

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So those darker bars here correspond to prevalence rates of anywhere from 30 to 40% here in the United States. We're here anywhere from about 10 to 20%. If you take a look at the different surveys, this, this is literally affecting millions and millions of children worldwide.

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Well, what's the impact despite this high prevalence? Well, when you take a look at the data here in the United States, there's increased healthcare visits, so increased number of outpatient visits, and ED visits. I think many of us are very familiar with frequent calls to our offices, frequent touching base with us about how to best take care of, of these children. And so we are very familiar with the fact that this can increase the number of contacts with our, our patients and families.

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And then this also increased medical costs about $3.9 billion per year, which is an astronomical sum. And when you compare children who are constipated versus those who are not constipated, we're looking at about $3,430 per year in medical expenses for those who are constipated versus slightly under $1,100 per year for those who are not. It also leads to lower school functioning, health related quality of life scores are lower, and those who with constipation compared to those who are healthy.

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And then there's also the potential, unfortunately, for these children to continue to have symptoms over a several year period even into adulthood. So now that we've seen the impact, what is the pathophysiology?

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And this is something that I think we're all very familiar with in terms of the model, and that's one related to voluntary stool withholding. What you're seeing here is the cycle in which there's a painful defecation leading to voluntary withholding that leads to prolonged fecal stasis reabsorption of the fluids in the rectum, and that leads to larger and harder stools, which then leads to more pain. And you get this vicious cycle that that is continuing.

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What you're seeing here is, is that fecal impact starts getting larger. There's actually data that shows that the rectum increases in, in compliance. And so the child, as many of us see clinically can have a larger and

larger fecal impaction before they actually are able to recognize that sensation of needing to use the restroom.

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That can lead to issues of ongoing fecal impaction as well as problems such as fecal incontinence. What are factors that we're seeing in, in clinical practice that seem to augment this problem? I think many of us are seeing children with ADHD or attention deficit hyperactivity disorder that increases the risk for constipation.

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There can be pervasive developmental delay or autism spectrum disorders, some studies showing that up to a prevalence up to three times as high in this group of children. In terms of having fecal functional constipation, there's a lot of interest in looking at the gut microbiome in terms of how does the micro gut microbiome potentially relate to functional constipation in children.

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While there's not a lot of great data actually showing that the composition or what the makeup is of the microbiome in terms of causing constipation. There's growing and growing evidence looking at some of the activity and affecting motility. So what I mean by that is, for example, for bile acids, our bacteria actually convert primary bile acids to secondary bile acids.

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And certain secondary bile acids have actually been shown to decrease colonic motility. And so if you have a gut microbiome that's actually producing those secondary bile acids, that may be an issue.

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In addition, one of the biomarkers that seems to correlate with really slow transit is having increase in methane production, and methane is not something that's produced by the microbiome in all of us. It's actually only present in certain individuals. And so we're seeing that increased methane is something that can be associated with constipation in children.

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If you actually do a clean out in that same child and the amount of methane goes down, there also seems to be a correlation with improved colonic transit. We're also seeing psychosocial factors that are playing a role, including toilet training, timing and, and the processes as well as unfortunately factors such as abuse that can increase the risk for functional constipation.

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There is a subset of children, and this is something that's still being evaluated and looked, looked at that actually have colonic dysmotility or what is known as slow transit constipation, and we'll go into the ways to evaluate for that.

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There's also this subset of children that have defecation dyssynergia, in which from an involuntary standpoint, they have very poor coordination in the sense that rather than having good increase in abdominal pressure and a decrease in their anal sphincter relaxation as they, as you may have here in which the sphincters are relaxing and opening and stool is able to pass through very easily. Instead with dyssynergic defecation, typically one is seeing a lack of good coordination here, so that even though perhaps there's good abdominal pressure that should be propelling the stool outwards. The anal sphincters are not relaxing appropriately leading to increased accumulation.

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And finally, with diet poor, fiber intake is associated with functional constipation. We'll talk about how that may be related to some of the treatment that we recommend for these children. Now, let go into a case study that we'll be following through the presentation.

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We have a seven year old boy with functional constipation who presented with infrequent painful bowel movements since the age of three. Per the mother the patient has intermittent abdominal distension that resolves after having a large bowel movement. There's a denial of emesis. The child's a picky eater, particularly when constipated and the child mostly drinks apple juice throughout the day.

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From a toilet training history standpoint, he was successfully toilet trained for urination, but will only defecate in pull-ups in a standing position hiding from the family. There will be stool in the underwear in most days, almost constantly. On physical examination, he's well developed well-nourished boy, and when you feel the abdomen, you can quickly palpate that there's a large amount of stool in the abdomen.

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Let's touch base on some of the aspects related to diagnosis. So I think we're very familiar with seeing these children and also the concept of when we're examining somebody doing a comprehensive physical examination and history taking to try to identify red flags. This is a table here of red flags based on the Rome criteria that they asked you to consider when you're making this evaluation in the patient that you're seeing.

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Here first is the passage of meconium. If it takes greater than 48 hours in the term newborn, given the increased risk for Hirschsprung's disease, if that's present, whether if the constipation is actually starting in the first month of life. If you take a look at prevalence data in infants with constipation, it's a very low prevalence of constipation in those children who are less than two months.

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So if you're actually seeing an infant that you truly believe has constipation and they're that young, that is a red flag and deserves further evaluation. If there's a family history of Hirschsprung disease if there's ribbon stools or blood in the stools in the absence of anal fissures, failure to thrive, bilious vomiting, severe abdominal distension and abnormal thyroid gland, abnormal positioning of the anus.

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And we'll be talking a little bit about that here in just a little bit. And absent anal or cremasteric reflex, decreased lower extremity strength tone or reflex that may signify a neurologic issue, a sacral dimple, tough to have hair on the spine again, or gluteal cleft deviation, kind of pointing to potential issues related to the spinal cord or even anal scars that unfortunately may relate to abuse.

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If any of these are present, there should certainly be more of an evaluation in, in my clinical practice. We certainly would then proceed with these laboratory evaluations, including the TSH/T4, celiac serologies, electrolytes and directed evaluation based on the alarm or red flags. Now, one of the things I wanted to focus on a little bit that perhaps we don't do enough of is actually a rectal examination when we're evaluating these children.

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I think there is different perspectives in terms of whether or not, you should have this proctored. I think for the most part, most of us recommend having someone else in the room to assist you. They're usually the patient's in the left lateral position and as comfortable as possible with tthe head completely flat with the

table being completely flat.

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I do recommend washing hands, donning a pair of disposable gloves speaking to the patient in developmentally appropriate language in terms of what you're going to do prior to doing it and gently separating the buttocks and inspecting the, the cleft and the anal verge.

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You're going to be looking for fissures, rashes, hemorrhoids, warts, et cetera. And, going to be trying to identify if there is a lesion where it is on the clock, as many of us know, the posterior part when you're when we're reading a note, this is the six o'clock position anterior s 12 o'clock, and the findings that we'll be looking for here, leaked stool congenital defects such as imperforate anus, particularly in the infants interior location of the anus, which we'll be going into sacral dimples, hairy patches, fissures fistula, or external hemorrhoids.

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Another aspect of the rectal examination that we can certainly do further, again to dig a look for neurologic issues includes the anal cutaneous reflex. This is a reflexive contraction of the external anal sphincter. What you should see is a symmetric contraction to due to a light stroking of the perineal or perianal skin. And there's a lot of things that you can use to actually elicit this reflex, including using a pin, a Q-tip.

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Perhaps most of us actually in our clinical practice have tongue depressors. And if you actually break this tongue depressor, and you can have these what appear to be jagged edges, you can actually use that as well. I think a lot of children get very anxious when they see this, and what you can actually do is just quickly just touch their skin on their hand or their arm and show that it's actually not particularly painful at all, and they become more comfortable usually and allow you to do this part of the evaluation.

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The nice part of the sensation is you can ask the patient, so you're actually trying to see what is the actual recognition of the sensation that's occurring, and you're really assessing the segments of the lower spine cord from S2 to S5.

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I mentioned the anal position, and this is something that intermittently we'll get questions about from general pediatricians in our practice. Concern about an anal, anterior placement. And one of the things to take a look at is something called the a, the API, Anal Position index.

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And what it is a measure from in females from the posterior fourchette in terms of the ratio of posterior fourchette to the central part of the anus, divided by the length here from the posterior fourchette down to the coccyx.

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And in boys it goes from the posterior part of the scrotum and you have a similar ratio. What you can see here is that females have a lower ratio of approximately 0.4, or as boys have a ratio of approximately 0.5. One of the things that I was taught as a fellow is that the anal opening should be at approximately right in the middle but actually for females, and this is something that I think many of us get questions about in clinical practice, it's actually just slight again, 0.4, so it's actually slightly closer to the posterior fourchette.

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If you'd like to, you can certainly measure this in your clinical practice if there's still a concern. What about other aspects of the rectal examination while there's the voluntary squeeze. And again, you're going to be asking that patient to see if they're able to follow commands.

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There can be what, what appeared to be very mature children that you'll ask them to go ahead and squeeze, and they'll even strain, they'll turn red, but they're unable to actually increase the pressure in their rectum, which really seems to show a discoordination in terms of how to control their external anal sphincter. And you can also assess for anal sphincter tone.

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Other aspects include the digital rectal examination. In the child with fecal incontinence, you're going to be looking for the amount of fecal material in the rectum to see if it's retentive or constipation related, in terms of an impaction. If you do not feel a lot of fecal material, and this doesn't happen very much one of the things on that, your differential should actually be that rare child that may have non retentive fecal incontinence in which the fecal incontinence that may be occurring is not due to a fecal impaction at all, but actually due to rapid transit.

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I think in my clinical practice, I've only caught a very small handful of children like this. You're also be feeling for masses. And then from a Hirschsprung standpoint, as on finger withdrawal, if you withdraw and there's a large gush, the differential will include Hirschsprung's, and that's because you're relieving pressure when you do this.

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What about other diagnostic modalities outside of the physical examination? Well, abdominal radio radiography has really been getting a bad rap as of late. And, in fairness, the data actually suggests that we should be trying to avoid this in our clinical evaluations. The sensitivity of an abdominal radiograph and identifying constipation is not great and ranges anywhere from 60 to 80%. In terms of specificity, which is to say that the child that you're seeing, if you get an X-ray, they actually do not have constipation.

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The ability of an abdominal radiograph to actually tell you that that patient does not have constipation can be as low as 43% all the way to 99%. There's very poor inter-rater reliability, which means that if you, for example, were to compare your read to the radiologist read and you were to do this in a blinded fashion, there would be very poor reliability data.

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There is moderate inter-rater reliability. What this means is that if you are the only one that's doing the rating and you're, you have your own system and you're just consistent in that system, you yourself could actually do a moderate job in terms of being able to, to be reliable in your reads as to whether or not someone's constipated or not. But it's not fantastic.

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This is a wonderful quote by Dr. DiLorenzo, which I think is one perfect in this scenario. The colon is supposed to hold stool, big deal. So it's really not a fantastic way to diagnose constipation. I think the only time to really consider using abdominal radiography is in the area of Sitz marker evaluation. And if you really cannot get a good abdominal examination or a rectal examination, the Sitz marker evaluation uses radio opaque markers. There's one company that typically has about 24 of these markers that come in one capsule.

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One of the ways to do this is to give the child the capsule and to get a picture on day zero. That's the day of ingestion. Then to get a film two days after. If all the markers are gone within a two day period, that patient may actually have non retentive fecal incontinence or the bowel regimen that you have the patient on, if you do this on a bowel regimen, is perhaps too aggressive.

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What you're seeing here is the ideal in which you do not have a lot of markers. If you have more than 20% of the markers still there on day plus five. So just to go through an example, if you were to the child were to ingest the, the Sitz marker capsule on a Wednesday, if you were to go ahead and get a film on Monday and you saw more than 20% of the markers, that's too many. There can be different patterns that you can see with the Sitz markers evaluation.

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This pattern here can either be slow transit constipation in which the markers are going through too slowly. Unfortunately, the other differential for this is still dyssynergic defecation, at least in the adult studies. What you're seeing here is something that we commonly see when doing Sitz marker studies is that all the markers they're not evacuated, but they're all here down in the rectal sigmoid area.

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This is something that's very concerning for dyssynergic defecation and not a significant motility issue. Now, there can certainly be refractory cases, where you will be considering doing other diagnostic evaluations, including the barium enema, anorectal manometry, rectal suction biopsy and colonic manometry.

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I'll go into this, but I think one of the things to really be thinking about is when should you refer a patient to a motility program? I think different motility programs have different parameters and thresholds, but these are just some general considerations. You know, if you have a patient with intractable constipation, how, how might you define that? As someone that has refractory constipation, despite an aggressive bowel regimen that's involving stimulants and osmotics, and perhaps even enemas that even on this aggressive bowel regimen you do a Sitz marker evaluation and you're confirming that there is very poor transit suggesting that there may be a significant motility issue.

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Other aspects that I think you should have a low threshold for referral to motility program includes identification of megacolon or a history of sigmoid volvulus, a history of anorectal or spinal malformation, and issues with fecal incontinence, for example, or a history of Hirschsprung’s disease in previous history of colorectal surgery, I think we're very familiar with the idea of a barium enema, taking a look for a transition zone for Hirschsprung’s disease, which you're seeing here is a very, a narrowed part of the colon as you hit this transition zone in which things become more dilated.

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This is the part that does not have the ganglion cells in Hirschsprung’s disease. You're also looking for perhaps excessive bowel dilation, particularly in the sigmoid area and or a redundant sigmoid. Many of us are able to do anorectal manometry without going to a center that specializes in this, and that's fantastic.

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One of the key parts of this is the insertion of the catheter with a balloon on the end, an inflation of this balloon within the rectum to try to elicit what's known as the recto-anal inhibitory reflex, which occur in here, is that the, there's a relaxation of the internal anal sphincter pressure. If that is not present on the

differential, there would be Hirschsprung's disease or internal anal sphincter achalasia.

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During the anorectal manometry, you can ask the patient to push as they would at home. That can be, if there's abnormalities in that area, there can be dyssynergic defecation, and that is by far the most abnormal, the most common abnormality that you'll see in anorectal manometry evaluations, particularly once you get past the age of infants.

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You'll be able to assess anal tone and squeeze sensation, and then there are catheters that are available that can actually give you a 3D view, and particularly in those patients that have had previous anorectal surgery, you can actually get a full 3D view of the sphincter anatomy.

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Well, what are the comparisons of some of these evaluations I mentioned in terms of identifying Hirschsprung's? This is a really nice study that was published several years ago that took a look at contrast enema, the sensitivity being around 70% for identifying Hirschsprung's disease with a specificity of 83%. ARM is anorectal manometry. The sensitivity goes up to 91% and specificity of 94%. RSB is the rectal suction biopsy in which you have a sensitivity of 93% for identifying Hirschsprung's disease specificity of 98%.

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And with both the anorectal manometry and rectal suction biopsy, if you compare that to the contrast enema, this, the sensitivity is statistically higher in the other two modalities. If you compare anorectal manometry versus rectal suction biopsy, there's no difference in the actual sensitivity statistically, at least based on their review. And if you go to, if you refer a patient or in your own center, you have a lot of experience with evaluation of infants using Hirschsprung's disease. I think you can feel quite confident that anorectal manometry will be able to help you and potentially avoid or rectal suction biopsy. If you do not have anorectal manometry available, then the rectal suction biopsy would be the way to proceed with the evaluation.

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Now, just to touch base with that very briefly, this is a schematic here in which you're seeing the rectum, the anal canal. You're seeing the dentate line here, the squamous mucosa and the kind of cutaneous skin on the outside. You have the internal anal sphincter, which provides the majority of the anal sphincter pressure and the external anal sphincter, and you would insert the rectal suction biopsy device.

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There's several, there's two particular devices that are common. One of the things that you want to be careful about as you're inserting this is that you're not inserting it in an area that's too low. And sometimes you'll be able to tell that if the pathologist in the pathology report comes back and says that they're identifying cutaneous tissue. You also typically want to go beyond a centimeter, sometimes two, three or four centimeters above the dentate line.

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And that's because again, there can actually be an anal transition zone that's normal physiology in which you actually do not have ganglion cells there. So if you're biopsying too low you may end up getting concerns for Hirschsprung's disease when they're actually not present. Ultimately, if you do a rectal suction biopsy and you're not seeing ganglion cells, that patient should be referred to a pediatric surgeon for full thickness biopsies.

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Now, we did talk a briefly about a referral to motility programs. just wanted to very briefly introduce, well, what are some of the things that they can be done from a diagnostic standpoint? Well, this is, here is

an X-ray of a catheter that had been placed. What you're seeing here is it's entering into the rectum, rectal sigmoid area. The sigmoid is really quite redundant in this patient. Before you finally get into the portions here, going to transverse colon, the ascending colon, all the way to the cecum, there are things that one can measure here, including the gastrocolic reflux in which you're giving a patient a meal during this, this is prior to the meal. You're seeing a lot of bluish color here.

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And then once the meal is actually given as indicated in this arrow, you're seeing this increase in kind of greenish colors from the top sensor here in the cecum all the way down to the sensors down towards the rectum. Significant find that this patient has an intact gastrocolic reflux. That's a sign of colonic health. Another common sign of colonic health that can be identified during colonic manometry is the high amplitude propagating contractions. Again, you have the same radiograph here identifying the positioning of the catheter within the patient. And here now you're seeing these lines that are kind of extend from the top and extend downwards to the bottom right, signifying contractions that are going from the proximal colon and nicely propagating down to the more distal portion.

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Signifying again that there can be intact colonic health absence of an HAPC can signify colonic inertia in a patient that may actually need a surgical intervention. At this point, I'll go ahead and transition to Dr. Khlevner.

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Thank you Dr. Chumpitazi, for that nice overview. Feel free to take more food, you guys. Alright, so I'll initially talk about the management, which is non-pharmacological, and then move into some pharmacological options.

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So in terms of non-pharmacological interventions, we think about some behavioral and physical interventions that we can implement. And one of the things that we can help our children with is appropriate sitting behaviors when they're sitting on a toilet, if they're getting to be toilet trained or are already toilet trained. So you want to make sure, you recommend for them to sit in a toilet five minutes after, after meals for about five minutes. And when they do sit, they should really try to relax as much as possible and really try to get their knees as high as possible during a sitting position.

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And that can be aided with a step stool or any sort of device that can really lift your legs up as they're sitting on a toilet. Parents should be encouraged to provide some positive reinforcement if possible. This is not to give patients hundreds of dollars for going on the toilet for successful defecation, but something small, a sticker or a clap or something positive that allow children to really be interested in continuing that positive behavior. And then there's also options for pelvic floor physiotherapy, which may help constipation symptoms as well.

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And remember, if there is a behavioral component that's associated with patients, particularly in the setting of behavioral challenges or oppositional behavior, sometimes involving a behavioral specialist, like a psychologist or a therapist, may be helpful to really implement some of the things that we just talked about for better outcomes. So in terms of diet, the ESPGHAN/NASPGHAN guidelines from 2014. I really recommend that children should be getting adequate fiber and water. They shouldn't be getting more than what is age appropriate.

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So higher fiber and higher water content does not improve constipation, but really having appropriate amounts of fiber and water in the diet is really what's recommended. So for example, a really easy way to think about it is if you have a child at their age, plus five to 10 grams of fiber per day. So if you have a

three year old, it should be about eight to 13 grams per day of fiber. Hydration also tends to matter on the age, but anywhere from 32 to 64 ounces of liquid intake outside of non-dairy liquids. I know Dr. Chumpitazi mentioned a little bit about the microbiota changes that we sometimes can see in patients with constipation, but unfortunately at this point there are no probiotics that are effective in the treatment of functional constipation.

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Stay tuned. Perhaps this will change. And in terms of this biofeedback pelvic floor physiotherapy, it really helps the child to sort of understand what muscles are to be used at the time of defecation. There's a lot of studies reporting its benefit. Some studies report that there is no benefit. It really is very much dependent on who's performing this and what expertise that performer has. And the ESPGHAN/NASPGHAN Guidelines currently does not recommend behavioral therapy for biofeedback. This may change. We're actually as part of the neurogastro motility committee, we're trying to revamp the guidelines a little bit to really summarize what has been done since 2014.

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So this may change, but this is really the most updated guidelines that we have right now. So moving on to pharmacologic interventions. When we think about treatment for our patients, it really is a three step process. We want to disimpact our children, we want to maintain them, and then we want to wean whatever we started.

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So from a disimpaction standpoint, the recommendation is really to try oral disimpaction first, and that usually is accomplished with PEG. And it can be done in one to 1.5 grams per kilo per day for three to six days. Or you can use rectal disimpaction. So for some families, rectal route is sometimes more effective or more convenient. And these are some of the agents that have been utilized as an enema preparation for disimpaction. So you can see that there is bisacodyl, sodium docusate, sodium phosphate, sodium chloride, et cetera, and mineral oil.

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Again, these are all enema preparations right here. And some of the recommended dosages are for you here as well. Again, the oral route is the preferred, unless PEG is not available or a patient cannot tolerate or it's a family's preference to use the rectal route instead.

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And then when we think about maintenance, these are the medications that we use on daily basis. It really helps to prevent the re-accumulation of stool whenever possible. And treatment can take one to two weeks before you see some good effect. And we should really continue this treatment for at least two or more months. Symptoms can resolve in a month or so, but what my rule of sort of maintenance is a patient has to do really well for at least two months for me to think about weaning this medication and preparing the weaning stage. Some of the pharmacological options that are available for maintenance includes laxatives that are osmotics like PEG, lactulose or magnesium oxide stool softeners or prescription agents that we'll talk about.

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And then weaning. The good news is probably 50% of children with functional constipation can discontinue medications in six to 12 months after initiation maintenance. So when patients and their parents come to us, they really want to know when is the weaning going to take place. They don't care about anything else but the wean. So it's nice to have some data and some education that we can provide to our patients. And weaning can certainly be considered if a patient is having at least three bowel movements per week and maintenance should be gradually reduced to prevent relapse.

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If the child is being toilet trained, the recommendation is to really keep the laxative on-board through

toilet training and then try to wean after, because toilet training is a huge trigger for relapse. So we try to keep the maintenance on board till toilet training is complete. So in terms of our osmotic laxatives, the options that we have again is PEG, lactulose and magnesium hydroxide. High dose PEG for three to six days is what we use for oral disimpaction, and I've mentioned that already, and the ESPGHAN/NASPGHAN 2014 guidelines again recommend that to be a first line treatment options for patients with functional constipation.

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If that is not available, then you will disimpact with an enema protocol. And then for maintenance, you use about 0.4 mg per kilo per day for patients on PEG. Lactulose is recommended as a first line maintenance therapy when PEG is not available. And magnesium hydroxide can be used as an additional agent or a second line agent, but it should not be used in patients with severe renal impairments. There've been studies looking at patients and whether magnesium actually goes up in the serum. And what we've seen from the studies is that magnesium can actually go up, but it's still within the norm.

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So it doesn't go into huge issues unless there's renal impairment in the child, and it shouldn't be used in children less than two years of age. So stimulant laxatives are also an option. It can be an additional or a second line agent. So if you have a patient who's failed PEG or cannot take PEG for whatever reason or you need to step up your regimen, then a stimulant laxative is a good option. It's administered orally and it can take anywhere between six to 12 to sometimes 18 hours to show it’s effect. It can also be given rectally as rescue or as part of that disimpaction plan we talked about.

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It is not advised for children less than two and not orally advised for children less than three. And senna, which is another type of laxative also is recommended as an additional agent to the primary PEG or first line treatment or a second line treatment just like bisacodyl. And it is not recommended in children less than two years of age, although I'm sure some of us have used it in way smaller patients than two.

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So in terms of what the guidelines are showing and recommending to us, it's that we use PEG as a first light treatment per maintenance. And again, it's 0.4 grams per kilo per day and it can be adjusted based on the response. So if a patient is not really getting the effect from it, you can increase it to 0.7 grams per kilo as needed. Lactulose is given one to two grams per kilo one to two times a day in sort of smaller children or infants. It's usually one ml per month, one to two times a day. And that's usually recommended if PEG is not available or not tolerated.

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Magnesium oxide, again, it's dosed by age. You want to really be careful about using it in small kids and in those that are renally impaired and it can be considered as an additional agent to your primary or first line agent or a second line agent. There are multiple data and meta analyses on PEG that I'll quickly review with you and to show you that really the current recommendation from the data that we have is PEG is the first line treatment for functional constipation.

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So this is sort of a summary of all the studies that are available that were either made analysis of systemic reviews, on PEG in patients with functional constipation. I'm not going to go through all of them, but everyone probably has heard about some of them. PEG versus lactulose, there's six studies on that. And this sort of looks at the corresponding risks of mean difference in stools per week. So you could see that PEG was more beneficial and more effective at 0.7. There's PEG versus placebo. So PEG allowed 2.61 increase in the stool as compared to placebo.

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PEG versus liquid paraffin. And really what it shows is PEG is probably most superior to most of these agents. It also looked at comparing high versus low dose of PEG, so 0.7 grams versus 0.4. And there could be potentially a benefit to using a higher dose, but again, depends on the child. Make sure that the child is not having too much of loose stools or worsening accidents if sort of encopresis or fecal incontinence is an issue. The quality of evidence unfortunately is quite low. We of course in pediatrics need more robust data and more robust trials, but this is what we have.

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So in terms of the stimulant and lubricant laxatives, we talked a little bit about the bisacodyl and senna. There's mineral oil in terms of the lubricants. And the guidelines currently recommend stimulant laxatives, and mineral oil be used as additional or second line agents as mentioned. And while there's clinical experience that suggests that Senna may be effective, there are really no large randomized controlled trials that have been performed on this.

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Data suggests that bisacodyl can be helpful to improve symptoms and that studies support efficacy of some use of mineral oil, but overall the quality of studies are poor. So when we think about these sort of osmotics versus stimulants, we always sort of think about what is the mechanism of action, what is going to be more beneficial to our patients. So unlike osmotic stimulants promote colonic motility to induce bowel movements and lubricants basically just soften and lubricate stools.

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If there's anyone who's still using docusate as a way to sort of maintain your patients, there really isn't any benefit. And that's been sort of reported in the last few years that docusate really is ineffective in treating patients with functional constipation. So it's not better than a placebo. This is that sort of study where I quickly mentioned that bisacodyl can be helpful in patients with refractory to standard therapy for constipation.

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This was a study, it was a retrospective chart review looking at the use of bisacodyl. And what you saw at the end was that patients went from two bowel movements per week to four bowel movements per week on the use of bisacodyl at about five mg per kg. So again, some of us are using it not only as an agent but as a additional agent. So it's not unlikely to have PEG plus bisacodyl or if someone has failed PEG, we go to bisacodyl. We use bisacodyl with other agents that are available. And the factors that were associated with responders versus non-responders was that the duration of therapy was very important.

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It was really important to keep these patients on for 14 months as opposed to 11 months of that were non-responders. And 57% of patients actually had response to therapy, which is a pretty good number. I mean, this wasn't a comparison trial, this was a retrospective trial of the use of the bisacodyl. But again, it's a viable agent for us to use for functional constipation.

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So moving along at the case study that Dr. Chumpitazi presented. This is a patient who's seen a prior pediatric gastroenterologist and was started on daily PEG without much of a success. There are multiple barriers to this child's getting pegged. One was that the patient refused to drink it. I'm sure a lot of us deal with that, not everybody likes the taste, not everybody wants to drink it. And when the child did take it at the appropriate dose, it actually caused more frequent fecal incontinence episodes, which obviously is not helpful when patients are dealing with fecal incontinence as a part of their symptomatology of constipation.

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So as you think about this case, it's going to come back again to you. So as a group we can discuss sort of what are the options for this patient who's now not able to take our first line recommended therapy based on the 2014 guidelines. So we do have thankfully some novel therapeutics, one prokinetic called Prucalopride, and then some, secretagogues, lubiprostone and linaclotide, and I'll show you some of the data.

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So in terms of the Prucalopride, how it works is that it is a 5HT4 agonist, and what it does is it sort of binds to the 5HT4 receptor in the myenteric plexus where neuromodulator is released and acetylcholine is used to stimulate the contraction of the smooth muscle within the colon. And hence it's a prokinetic. It is not FDA approved in pediatrics whatsoever. This drug was recently approved in adult chronic idiopathic constipation, but no approval in pediatrics.

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And initially we saw some promising results from a small open label trial that was done. But then unfortunately a multicenter, randomized phase three double blinds placebo control trial of the use of prucalopride in functional constipation, this was a European study. It enrolled about 215 patients 6 months to 17 years of age. They were either randomized to a placebo or prucalopride at the dose of 0.04 milligrams per kg per day. And it was adjusted to the maximum dose of two milligrams per day versus placebo. And the primary endpoint was actually not met. There was no statistically significant difference between placebo and prucalopride for this patient population. And some of the treatment emergent adverse events included headaches, pyrexia, vomiting and abdominal pain. And then constipation was actually an adverse event in in one patient who was on prucalopride. So again, no great data about this medication use at this time for functional constipation and we don't even have it approved.

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So moving on to a secretagogue, lubiprostone, this is a chloride channel agonist. So what it does is it binds to the chloride channel, it sort of forces chloride to stay in the lumen and then the water and sodium follow allowing for the effect of softer stools and propelling the stools down. Again, not approved in pediatric functional constipation. And we do have a phase three randomized control trial in pediatric functional constipation. And unfortunately that also did not meet its primary endpoint. So this is the trial that I'm sure you guys are quite familiar with. This also enrolled patients 6 months to 17 years of age and they were randomized two to one to receive lubiprostone at 12 micrograms. And if patients did not do better on 12 micrograms, they were escalated to 24 micrograms twice daily. And that was based on the body weight versus placebo.

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And as you can see, there's really no statistically significant difference in the overall spontaneous bowel movements between the placebo and lubiprostone. So again, something that we were hoping to get some better results in, and unfortunately we did not meet the primary endpoint. And nausea seems to be the most adverse event that patients report. And some of the things that patients can do to bypass that is to take this medication with a meal as opposed to an empty stomach. And that sometimes helps navigate the nausea a little bit. But again, we don't have it approved, nor is it exceptionally helpful based on this randomized control trial.

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Linaclotide, as some of you may have been hearing, has recently been approved for pediatric functional constipation for 6 to 17 years of age. There is a black box warning on the use of this agent in patients less than two years of age. And that's because the mice, the young pups, died from dehydration. And so that remains still a contraindication for the use of this medication.

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So linaclotide works by activating the guanylate cyclase C receptor and that allows for some of the fluid to the bicarb and chloride through the CFTR channel to secrete where water and sodium again follow into the lumen. The receptor is actually located in small bowel and colon and it seems that it's a more effective in the colon and hence that's why it can be quite effective for patients with functional constipation. Again, it is approved in children six to 17 years of age. And I'll go through sort of the study that allowed for the approval of this medication.

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So this was a phase three trial of linaclotide in pediatric functional constipation that enrolled about 328 patients across 64 sites and seven countries. And the protocol was, the study design was, there was a screening period, 14 to 20 days, followed by pre-intervention period, another 14 to 21 days and then followed by randomization. And for 12 weeks a patient was randomized either to placebo, linaclotide, then it was a one week post-intervention period. And again, it was one to one randomization and it was 72 micrograms dose versus the placebo. And that's the approved dose by the way, the 72 micrograms. What I want to sort of bring your attention to is that sometimes we hear, well, a lot of these studies are done in academic centers, these patients are very sort of complex.

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What do I do as a general gastroenterologist or general pediatrician? So the number of centers that were actually involved, there was private practice, there was academic centers, non-academic centers. So this is quite representative what all of us are seeing sort of in our practices. The patients that were involved, placebo versus the treatment didn't really have a difference in terms of their spontaneous bowel movements per week at baseline. So if you look placebo is 1.278 and Linaclotide was 1.157, so no statistical significance. And stool consistency at baseline was also very similar between the two groups. The study had sort of a primary and a secondary endpoint. And so for the primary endpoint that was the 12 week measurement of spontaneous bowel movement frequency.

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And there was a comparison between the placebo and linaclotide and there was a statistically significant difference and an increase in the spontaneous bowel movements across 12 weeks. But what's also interesting is that improvement in that spontaneous bowel movement frequency were observed as early as week one and maintain through the 12 week period. So sometimes families are asking, well, how long am I going to see the effect then? Is it a day, is it six months? Is it years? When should I start to see the effect? And so it's nice that we have some data to point that the effect was actually seen within the first week.

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And then the secondary endpoint was a change in stool consistency. And as you can see, there was a statistically significant change in stool consistency between the two groups, the placebo versus linaclotide, although the clinical difference is, is a bit unclear at this point. The adverse events were actually not very different from adult studies. All sort of adverse events. There was 35 in the placebo and 28 linaclotide and diarrhea has been previously reported by our adult colleagues seems to be more prevalent with the use of linaclotide. You can see covid 19 rates unclear what that means. And then in terms of the serious adverse events, that led a patient to discontinue, the medication was again one in the linaclotide group, one nausea and one dehydration. The dehydration was serious, but the patient actually did well after hydration in the hospital.

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Again, dehydration is in the setting of just severe diarrhea from the medication. So what do we do when

these things fail us? Well, we move on to other interventions including transanal irrigations and that could be utilized in patients who sort of failed your oral laxative regimen. And you basically irrigate the rectum in the colon of normal saline, 10 to 20 milliliters per kilogram to clear stool output. And some retrospective studies have demonstrated improved response in terms of patient symptoms. When you think about the antegrade continence enema or ACE, it really is sort of an intervention that is done for refractory symptoms and those that have sort of failed your routine aggressive outpatient regimen. It can be used in patients with functional constipation, but we really try to do that as almost like a last resort when everything else fails.

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And then botulinum toxin injection can sometimes be utilized in patients with punctual constipation, particularly in the setting of dyssynergia or high anal resting tone for example. What it does is it relaxes the anal sphincter and facilitates improved passage of stool, but we always want to keep our patients on top of what things to expect. And sometimes urinary and fecal incontinence can be a short-term effect that obviously gets better after the botulinum toxin weans off. So, when we think about sort of functional constipation and how we tackle this, this is sort of the Rome diagnostic proposed flowchart. So child, passing heart painful stools with some withholding behaviors. You do a good medical history, you provide dietary intervention, so age appropriate fiber, age appropriate water intake, you provide psychosocial changes you get a good psychosocial history and you may do a rectal exam, which is really helpful.

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I know Dr. Chumpitazi talked about it. I think the point about rectal exams is you really want to make sure to have a proctor near you no matter where you are. I think it's, it's a good practice and if there really aren't any alarm features, then you diagnose a patient with functional constipation using the Rome IV criteria and then you sort of embark on your disimpaction/maintenance/weaning protocol. And if the treatment is ineffective, then you're sort of thinking about, okay, well is there anything else I'm missing? And you go back to trying to figure out if there's an abnormality. You may want to get some blood work done, particularly in a setting of alarm signs.

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It could be an organic etiology, it could be celiac disease, inflammatory bowel disease, it could be some sort of a malformation, et cetera. So you want to always make sure you reevaluate your decision making, particularly if a patient is not responding to routine regimen. So this is a proposed treatment approach for otherwise previously healthy children more than one years of age. This is just mostly expert opinion. This is not pulled based on any data, but I think this helps to conceptualize how we care for these patients.

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So you have a patient functional constipation, you maintain them on some sort of an osmotic plus/minus stimulant laxative. You provide the proper behavioral modifications, toilet training, toilet sitting, etc. And if a patient doesn't do well, then you're thinking about doing some other lab workup. For example, a thyroid or celiac antibody. You want to escalate your maintenance regimen if a patient is still not doing well. And the above workup is nonrevealing. And you may want to consider doing an anorectal manometry to really understand the defecation dynamics, if the anorectal manometry shows a concern. So absence of that rectal anal inhibitory reflux, you want to make sure that you follow up with the rectal biopsy.

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It could be full thickness based on the patient's age. It could be rectal suction. And you refer to surgery if RAIR is not present on anorectal manometry. If dyssnergia is present based on your anorectal manometry evaluation or even a rectal exam evaluation, that can give you some signs of dyssnergia as well. You really want to understand whether physiotherapy plus minus feedback is a good option for your patient. And then you want to consider botulinum toxin potentially if your maintenance medications are not

working. And if there is no dyssynergia, then you may want to consider a sitz marks test that we talked about earlier in the lecture. And if the patient continues to have difficulty, you really want to utilize your motility specialist to see what else they can do to help understand what's happening.

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You may want to order a lumbar sacral MRI if there are risks for it, or if you're concerned, you don't need to refer to a motility specialist to do that. You don't need to refer to a motility specialist to get a barium enema that can be done anywhere. But things like colonic manometry you will only probably find in a motility expertise center. And then consider transanal irrigation, cecostomy and botulinum toxin as we discussed. All right, now I'll invite Sharon Perry to continue this presentation.

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All right, thank you. So now we're going to talk about the collaborative and integrative management strategies. So this really is a multidisciplinary team approach. It, it takes a village. It really does take a village. It takes more than just the medical provider to manage constipation. It takes the medical provider, whether that's a physician or a nurse practitioner. It takes nursing because they're the ones that are fielding the phone calls from parents, they're the ones that are doing the prior authorizations for medications. It takes your social worker because parents are missing work, children are missing school for this.

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If you have a dietician, they're the ones that are managing the dietary concerns because kids are not getting enough fiber, kids are picky eaters, things like that. So you really need to work with your entire team if you have a child that has any surgical concerns, because you found some abnormal testing, things like that. If you have children that are coming from a small center to a larger academic center. So you really do need to work multidisciplinary for this.

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Parents and caregiver counseling.. You have to have time and you have to have patience to work with these patients. because parents have a lot of questions. Why is my kid constipated? Why is this not getting better? I'm trained as a nurse, so I'm trained to listen to families. So I am very fortunate that I have time to sit and listen to families. And I can spend a lot of time listening and I can just sit and be, it's okay, it's okay. We will get through this. We will get through this together.

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So educating families that this did not happen overnight is not going to get better overnight. It is going to take some time. So recognizing behaviors of constipation. So it was your child doing well and then did something happen and now we are withholding? Again, acknowledging that relapse is common. So I tell families a lot, it just takes one time for missing a medication dose or one time to have a hard poop that things are going to reset themselves.

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Again, providing that positive reinforcement. So like Dr. Khlevner said, praising your child when they sit on the potty, sitting and having a poop on the potty. And again, it does not have to be a monetary value. I tell that to families a lot of times I have a lot of low-income families. So saying you get to have an extra 10 minutes of TV time or you get to have an extra 10 minutes of screen time, or you get to pick the movie that night. It does not have to be anything. Monetary toilet training. When they're not resistant to sitting on the toilet, parents want their children toilet trained, they want to get out of that diaper phase.

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If they are pooping in a diaper and they don't want to sit on that toilet, it is useless. So I tell them when they are ready to get out of the diapers, then we will work on the toilet training. And then importance of scheduling follow-up appointments. Once they're toilet trained or once the constipation is better, they have

to continue coming to appointments. They can't just drop off the radar because then they're going to show back up in clinic six months or a year later with the same problems over again.

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And then strategies preventing childhood constipation. So minimizing psychological stress. Are kids embarrassed about pooping at school? Yes, they're embarrassed about pooping at school. Nobody wants to poop at school, providing bathroom letters, letting them poop in the nurse's office for more privacy. Telling them to take the poop spray. Correct toilet training. You know, sitting up straight, putting your feet flat on the floor if you can't touch the floor, getting a step stool. Building a safe society for children. So again, pooping at school is embarrassing. A lot of kids don't want to poop at school. So we talk about that. Kids that don't want to poop in public, poop in public who cares. Everybody does it.

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I talked about when I poop in public, it's not a big deal. But taking that stigma away, Healthy dietary habits. Nobody wants to eat vegetables. Vegetables are not going to kill you. I've never seen a kid die from eating a vegetable. But making it so it's not that big of a deal. You know, talking about how to incorporate fiber into your diet, that's not so gross. You know, avoiding those sugary drinks from Starbucks, avoiding the sugary drinks from Dunkin Donuts, those kinds of things like that. Not going to McDonald's every day.

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Physical activity we talk about. The more sedentary you are, the more sedentary your gut is. You have to get up and move around. Don't be a couch potato, don't play your video games all day. You have to get up and play. And then parental attention. Parents have to be a part of this too. So I really encourage parents to like, you know, work with your kids, get up and do things as a family and things will eventually get better. And then resources. So I give families stool calendars so they can keep track with little kids. Little kids like stickers, little kids like stars, little kids like smiley faces. So this is just an example of how you can keep track of stools.

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So how many times did they sit on the toilet? How many times did they have a poop out? What was the poop like? Did they take any medicine that day? Did they have any belly pain that day? Did they have any soiling that day? And it doesn't have to be this extensive, it can just be did they poop? Yes or no? Did they sit yes or no?

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But this is a nice way for families to keep track because then they're not just jotting it down in a notebook or they're not trying to keep track of it on their phone. And this gives them something tangible that they can go back and look and see if things have gotten better. NASPGHAN and ESPGHAN have several resources available. GIkids.org has the constipation, constipation care package, which is a great resource for both providers and for families. And then, so this brings us back to our case study, our seven year old boy with functional constipation.

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We've kind of gone through the whole gamut. We've now found a treatment that seemed to be working. Our constipation has improved And we fixed him. And so now I think we're ready for questions. So again, if you have an opportunity, there's a mic right there in the middle of the room or we again encourage index cards. If you have an index card, go ahead and hold it up and, we're happy to have someone grab that and, and we'll try to answer questions as best as we can.

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Don't be shy please. And just to go back to that case, so we wanted to sort of get your opinion because the first line treatment did not work for that patient. What would you do next? This patient is refusing the

PEG. What are your choices at this point? Knowing what we just sort of presented? Love to hear your opinion as well. This is really informal.

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Just come on up and answer them if you want and ask if you want. Oh, we have. Alright. So the first question is, given the fact that anal achalasia and HD have similar ARM findings, do you recommend only ARM for HD corrective surgery, AKA not using rectal suction biopsy? So the difference on from internal anal sphincter acylation to Hirschsprung's it really comes down to a biopsy. So your ARM findings are going to be very similar between those two patient groups. You're going to have lack of rectal anal inhibitor reflux. What we know about rectal suction biopsy is there are no ganglions for Hirschsprung's disease, but you actually will see some ganglions for internal anal phi acylation. They're dysfunctional ganglia, they don't secrete nitric oxide and hence your ARM is abnormal.

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So that's really the only way that you can differentiate those two types of patients to accurately start treating those two types of patients. Unlike the Hirschsprung's disease for internal anal sphincter achalasia, Botox may be a really good initial treatment step for that patient. They may eventually need my, you know, myectomy, but botulism toxin is, is still a really good way to start addressing those patient symptoms. I don't know if that addressed it, but Yeah, hopefully that addressed it.

01:13:21.965 --> 01:13:32.555
I agree. Oh, we have a few other questions. Oh, go ahead please. Yeah. All right. So are we still concerned for melanosis coli on long-term stimulant use?

01:13:34.715 --> 01:14:14.965
So melanosis coli for stimulant use, is that a, is that a concern? There used to be a concern for that if in the, in the past, but as we've gotten to learn more about the effects of melanosis colli, it's actually not been shown to have any detrimental effects on patients either from a physiologic standpoint in terms of the colon working or even, you know, in the past there have been concerns about perhaps increased risk for cancer and things of that nature. That's actually not been shown to be an issue. What can be difficult is when we're doing the colonoscopy in these patients, sometimes it can be quite dark in there and can be difficult to complete the evaluation. But other than that, there are no adverse physiologic effects that we know of.

01:14:15.985 --> 01:14:34.885
It was actually a nice study that came out of the colorectal group who are using really high dose stimulant laxatives in their patients. I mean, those patients tend to be more unlike anal rectal malformation, Hirschsprung's disease. But even long term there hasn't been any concerns for dependency or ill effect or anything on the use of those stimulants.

01:14:34.985 --> 01:15:27.465
So that's something very different than what our patients tends to know about these types of agents. Right. And then experiences with linaclotide and insurance approval? So I think you have to get very creative despite the six to 17 year old age approval, insurance till doesn't want to cover it. They still say it's not approved in pediatrics. So I still generally I will start with the 72 micrograms and then dose it based on response. But I will get very creative in my appeal letters. Yeah, I think the right thing to do Is make sure that you code the indications correctly.

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So you want to code as functional constipation in children. And the other thing that is helpful is when I write letters of appeal, I will quote every single study abstract, anything I can get my hands on and include that and then my last sentence is, if this is not approved, my next step is a surgical intervention. Please let me know what you feel about that. I have to say in New York as difficult it is to get some of these agents

approved, I think we're pretty lucky to get, I would say more than 80% of the times I can get this agent approved.

01:16:02.775 --> 01:16:36.545
Only thing I'd add really quickly, and I agree with everything that's been said, is that it can sometimes depend on the panel that the insurance company is working with from a, from the drug standpoint. So some companies seem to be more comfortable with certain secretagogues such as linaclotide versus lubiprostone. Others will give you a hard time all the way around. It does help to, to send the clinicals as they call it in terms of the documentation and to show that there have been other first line therapies that have failed. And I think that can help.

01:16:39.255 --> 01:17:20.765
What doses of botulinum would you use? So I use six units per kilogram per full injection and max at a hundred. So if it's a small infant who weighs five kilograms, then it's sort of 30 units divided into four quadrants. But if it's an older child and they're over, let's say, you know, 30 kilograms or whatnot, 20 kilograms, then you really max at a hundred. We use the same dosing as well. And, and I think there's been some discussion about whether or not one can use higher dosing. That's just what the literature has actually really shown and that's where most people call us at six units per kilograms.

01:17:22.075 --> 01:18:16.885
Okay. Does the diagnostic approach differ for patients behavioral or developmental disorders? I think so. I have a lot of families that are very hesitant to use medications in, in their patients with, you know, their children with developmental delays or patients with any kind of behavioral issues. It, but at the same time they want this to get better. So I think it just is very dependent on the families. I will, I'll talk about the, the safety of a medication. I'll talk about, you know, we can still work through this, you just have to be willing to work with me, but I will work with you as well. We do a lot of play therapy with that.

01:18:17.555 --> 01:19:12.805
Yeah. You know, this can be a really challenging population. Some really great work has been done for children with autism by different investigators like Kara Margolis and Kenneth Williams at Nationwide. And there's just so many considerations in terms of, well, what will the patient actually take? What will they allow you to even give sometimes in terms of medications, for example, and you know, Dr. Williams really pointed out that before you even think about doing that initial clean out, come up with that maintenance plan, somehow work with the families in terms of already identifying what it is from a maintenance standpoint you're going to be going to, rather than making that assumption. There can be some children with significant pervasive developmental disorders that for whatever reason will not take the mar PEG or they will not take the milk magnesia, but they may actually take some of the secretagogues better.

01:19:12.875 --> 01:20:00.365
Just a consideration that I've, I've seen sometimes whether it's the volume or the taste or some are other aspect, it's something to consider. Some of the other aspects in treatments that we've talked about, like bio biofeedback or physiotherapy for dyssynergic defecation, those can sometimes be very difficult to implement in certain children with developmental disorders or autism. So sometimes some of the treatments you'd like to go to can actually be limited. But having said that, there are some wonderful behavioral therapists, as many of us are familiar with, some of the behavioral therapies that, for example, children with autism are going through. And sometimes you can actually communicate with those therapists to try to integrate some of the, the toilet sitting, some of the other aspects that we were talking about into the therapy that they're already receiving and sometimes make some progress that way.

01:20:01.325 --> 01:20:22.805
I think you have to sometimes get creative with the medications as well and anticipate that they're not

going to take that medicine next week. So hiding senna in a candy bar, hiding PEG in applesauce, things like that. So you know that they will take it in the food that they eat. So you just kind of have to get creative.

01:20:28.915 --> 01:21:09.335
I can read the question. What is the site for Botox injection and what are the side effects you could teach the family? So in terms of the Botox injection, it really is proximal to the dentate line. So my technique is to use a nasal speculum. So I open up the anal canal and I actually visualize the dentate line and I go right proximal to that and inject my needle until I feel a muscle. And that's where sort of I inject each of the four quadrants. There are better techniques including an ultrasound guided injection, so it's a lot more precise I would say, but obviously that takes longer and need to have your ultrasound machine ready with you.

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But there's some really nice literature to support its use, for a more precise injection. And in terms of side effects obviously an allergic reaction and anaphylaxis from the Botox itself, but again, with the dosage that we use, that shouldn't be such an issue in terms of the systemic effects. But some fecal and urinary incontinence that I talked about earlier can be short-lived, but it's something that can be quite devastating for let's say a teenager who's never had that before and all of a sudden you do this and they can have accidents.

01:21:40.595 --> 01:22:10.015
So I'm always really careful about teaching them that this is a potential side effect. And are they're okay to proceed? Oh, thanks. I was going to just try to go back to the figure, but I couldn't. But what Dr. Khlevner is saying in terms of just going just proximal to the dentate line is because that's right where you have that transition from the external anal sphincter to the internal anal sphincter. And as we had talked about before, the internal anal sphincter is the one that's giving the most pressure in the anal in the anal sphincter complex. And so that's where you want to aim for.

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If you take a look at some of the literature, diarrhea, fecal incontinence usually only lasts for a couple of days if that occurs. There can be some cases where that can last for a couple of weeks, unfortunately. And some centers, what they'll do is they'll actually get a baseline pressure of the anal sphincter before giving the Botox. Others don't do that. But if the pressure is below, for example, 40 millimeters of mercury, then there's some centers actually won't give the Botox at all in those cases.

01:22:43.425 --> 01:23:27.525
How do you, how do you treat a child who is not responding to treatment and how long do you try a therapy before trying another treatment option? That's a good question. Zero evidence. So I guess it matters on, on the actual maintenance regimen that you're using. So anything that you utilize the recommendations is you try it at least sort of for a month, quote unquote, until you sort of understand whether things are moving in the right direction. That's sort of a very loaded answer because if someone is having significant symptoms, you're not going to keep them on a month worth of the same regimen if it's not working.

01:23:28.265 --> 01:23:50.245
So you try to escalate that one or two, whatever laxative you are using within that month period and seeing if you are aggressively maximizing that particular agent and it's still not working, then it's time for you to move on. And moving on can mean that you are adding another agent to the first agent that you started or completely switching agents.

01:23:50.785 --> 01:24:44.605
And the question is sort of to go back to our case, our patient did not find it effective to use the PEG, right? So you've tried it, the patient's refusing to take it, or when they take it at the dose it seems to be

causing more of the incontinence. What do you do with that patient? Are you going to add something to that patient as a second line, like a stimulant or move away completely from the PEG and go on to a second line like a stimulant? I think a lot of us can be quite cavalier sometimes and add on agents that have very different mechanism of action just to target all possibilities like trying a prokinetic with a asthmatic or stimulants with the prokinetic or a secret talk with the prokinetic. We do a lot of different things and try to maximize medical management before trying sort of exhausting and saying this patient needs something more aggressive than that.

01:24:45.225 --> 01:25:13.285
But it sometimes can be really difficult because we don't really have a great flow chart in terms of what the things we should be using if A fails go to B, if B fails, go to C, and how do we incorporate now the use of linaclotide now that this is the first FDA approved agent for functional constipation. Is it first line, is it second line? Is it an additive? So it's very confusing right now and I think we need to understand better how do we put that into use for our patients.

01:25:15.155 --> 01:26:19.405
Yeah, I completely agree. One thing that sometimes I try and try to be proactive with families is that after that initial disimpaction, rather than waiting to see if that maintenance regimen that you all have agreed with when you're discussing with the family, whether it's working or not, I try to get an objective measure. And unfortunately this is without evidence, but we'd sometimes recommend doing just an at home what I call an at home transit study. And that's where you ask the family to eat something that you'll actually end up seeing in the stool in a couple of days. So that'd be actually corn or a particular dye or food coloring or something of that nature. Perhaps at the week after they're done with the disimpaction, they're now in the maintenance phase. You can go ahead and have them go ahead and do this transit study and just like you saw the sits markers, you know, if you were to do this very formally, ideally, you know, especially if they're on a bowel regimen, I usually recommend that they should be seeing all the complete clearance of this dye or the corn or whatever is that they ate within probably about 72 to 96 hours at most.

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I let them know that if you start seeing that corn coming out, for example, and it comes out very quickly, but it still keeps coming out several days later, that's not a good sign that you may actually have an impaction still. And then if you see it come out too quickly, so with say within 24 hours all of the dye, all of the corn has come out and it's gone, you actually may be on a regimen that's too aggressive and in that way because the symptoms can be very difficult right sometimes for families to tell you whether or not it's successful or not.

01:26:54.785 --> 01:27:52.685
Particularly if they're soiling themselves or some other aspects. So that can be an objective way if you want to be very formal about it. You can do a maintenance regimen and do a sits marker study on the regimen and show that you're actually getting good transit. I'm sure you guys have heard of patients that don't poop for two months, right? My child has not pooped for two months and you go bang your head against the wall and you cannot prove otherwise. So I think what Dr. Chumpitazi says is really valuable because you can actually prove that particularly with sits marks look on day five, there aren't any in your colon, so you are pooping, someone is pooping and it must be you because it's your colon. So sometimes to objectify these very difficult sort of patient scenarios where they swear to you they don't poop for months and then your regimen is like, you're like un laxative number seven and no one's pooping still, what do you do with that?

01:27:52.905 --> 01:28:23.645
So I think getting some information in, Can we circle back quickly to the Botox side effects? What percentage patients who had Botox? I think what's reported is less than 1%. Is that true Bruno? I it's, it's quite rare actually. I do tons of Botox. I have to say I do a lot of it in toddlers who already have incontinence potentially. So it's really hard to know the true exact prevalence.

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But in, in sort of the older children who are completely, totally trained without accidents, I've never had it as a side effect. I believe it's low as well. I'm sorry, I don't know off the top of my head, it's probably less than 10% in my, in my clinical experience. I think I've been lucky and have not actually had issues with fecal incontinence or diarrhea for several years now, knock on wood that continues, but it seems to be relatively low.

01:28:54.505 --> 01:29:15.765
Do you repeat it? The question was do you repeat it? And so in, in terms of it's well known that for example, if a patient had Hirschsprung's disease and you know, you've given they've already had the corrective surgery and you're still trying to address, for example, that's sphincter that's too tight or achalasia. There are children that have had up to seven, you know, different Botox injections.

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If you took a look at some of the literature, so folks are repeating this. Ideally what I like to tell families is that we're going to get proceeded with the Botox injection, but our goal is to try to come up with behavioral, other regimens and we don't have to keep doing this. Unfortunately sometimes we can't get to that point, but imagine you're having a child that's undergoing general anesthesia each time that you're doing this so that they can stay still and that it's not too uncomfortable of a procedure. I think that's a big deal. So really ideally you're just constantly trying to identify another regimen that will work even if you need to do repeated injections.

01:29:53.345 --> 01:30:44.755
Alright. How do you work with parents who are hesitant to have their child start treatment? So again, that can be challenging. You know, I tell them, you know, if we're not going to start treatment, I can't fix this. I'm very blunt, you know, if you're coming to see me, there's a reason. So if you're coming to see me, we're going to do medications. If you don't want to do medications, I don't know what you want me to do. Yeah, I think sort of partnering with the family and really sort of do as much as education as you can to talk about some of the manifestations you're trying to help the child with and trying to sort of give them the sequelae of what happens when it's an in not managed properly.

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A lot of the times you can really convince the families to be on board with something, even if it's something small. Start something small and then they have trust in you and then you build that trust and you escalate your therapy and once they see their child do better, they'll do anything and they'll continue to do anything as long as they see improvement. So setting sort of realistic goals, it's not going to be perfect. We may need to work on what works for your child, for your family. There isn't one regimen that works for all, particularly in the settings of the type of a patient, the type of, you know, how busy the household is and there's no time for, you know, morning administration of a medication that only needs to be done in the morning. So it just depends on who you are working with, but I think really partnering up with the family and trying to get them to trust you that you're helping them and even small things can be really helpful.

01:31:38.425 --> 01:32:00.165
Just as a quick survey in the group, how many folks here have taken care of a patient where they refuse to do any of the medications that you're recommending, but they're very amenable to actually taking a natural product that if you actually take a look at the ingredients it contains magnesium or senna? Let's go ahead and so we are probably three quarters of the room or half the room.

01:32:00.865 --> 01:32:37.165
And that's a very common scenario that I think we're all dealing within clinical practice. I am willing and I, but some, some folks are not to actually try to work with the families using that product that they're using and try to as closely as possible. For example, if they're using, if that active ingredient or is magnesium hydroxide, try to make it akin to the dosing that I would typically use for a typical magnesium

hydroxide product. Same thing with the Senna. Again, if you're, if they have Senna and that natural product that they're usually no work with, kind of keep the dosing in mind that you, that you typically use.

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Um, but it's a great point that really working with the families is very, is very important. I do work with families, let me, let me go back. I do work with them and I use a lot of the natural products, but when I'm even talking about the natural products and they don't want to do that, then I'm like, I don't, I don't know what you want me to do.

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Yeah. So I can't see with my glasses. Sorry guys. How does your treatment approach change based on the patient's age? So I think that it depends on how young they are when we start treatment, how I change it as we get older. If I'm at the school age and we need to get more aggressive then I'll add medications. If I'm at a toddler that's super picky, that's I think the hardest age to deal with because you're constantly changing things because one day they'll take something the next day they won't. I think that's the hardest age to deal with just because they're so picky. But I think it's very dependent on the age and the child themselves.

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I try to do as much as I can with as little as possible. Do you want me to try, I just to add a little bit to that maybe and I, I agree with you as well is, as you get a little bit older, you may be able to get a little bit more buy-in, especially in terms of the toilet sitting in terms of the dietary aspects that, that you may not be able to do as well in a, in a toddler. So for example, once you hit a certain developmental age, some physiotherapists say five is kind of the lowest age, maybe six, seven on up your, you have a better chance of somebody actually participating in physiotherapy in which they're working with a physical therapist.

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Some programs are once a week or once every other week to really learn how to push correctly, how to relax their bottom correctly. As you get older you can actually get a little bit more buy-in, in terms of being able to, to address this. The other, the other part I like about working with kids that are a little bit older is that you can gauge actually, well how invested are they? And ask them if you're having fecal soiling for example, how much is of this is a problem for you, do you actually care? And one of the things I feel like that's almost a sigh, you know, if they don't care that the fecal incontinence is happening.

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I think we've all seen this in clinical practice, you're very unlikely to be successful despite all your medications and all the therapies. If it's not a problem in their own mind, it's very difficult to, to get a successful outcome. But if they start caring for whatever reason, it really seems to, seems to help. Yeah, I don't think I have much more to add except for those patients that have incontinence and you start a laxative, I often hear, I'm not doing this anymore because I got worse. I'm having a lot more accidents. They're happening now more in school. The family gets super upset with you. So I think this is a really good opportunity to put in a plug for disimpaction because if you are using a laxative and someone who's full of stool, you're worsening their incontinence at baseline. So it's this vicious cycle.

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So I think the most effective way, if possible, no matter what the age is clean them out and then start something for the most sort of successful outcomes. But you have to sort of know the mechanism of action of all these medications and how long, so a child is in school and they're taking a laxative in the morning and they're supposed to be stooling two hours later. That may not work for that family and that child because they're in school, they're already having withholding issues.

01:36:20.825 --> 01:36:29.215

So you want to time things so that they're at home for potentially a more successful bowel movement. But again, that's like more of a social issue. Right.

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All right. Do you ever recommend a one day clean out with PEG and Senna on a clear liquid diet? Yeah, we sometimes do colonoscopy preps as a clean out, so use of a stimulant with a really good PEG dose in one day for sure. A lot of the times it's really hard to do for smaller children, but that's totally acceptable.

01:40:43.235 --> 01:41:30.195
Yeah. Or physical at all sometimes. And particularly for a patient who's quite impacted, it can be very helpful. I do them all the time, so. Alright. Practical tips for giving PEG, do you, I'm sorry, I can't read. What about frozen popsicles? What about juice? How much? I'm sorry. I'm sorry. I can't read this whole thing. I'm sorry. Yeah, I can't, I have really bad eyes. Sorry. So practical tips for giving PEG. Do you use other stim? What other do you use other than water? What about frozen popsicles? What about juice and how much to, I assume to mix it in?

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So the way PEG works is you need some sort of fluid without the fluid it's not going to be effective. And so the recommendation is a capsule per eight ounces or so, something like that. But you can be as creative as possible. Juice, Gatorade popsicles, it's de liquid, it's just a frozen form of it. I don't know if there are any studies about using the vehicles of how you mix the PEG. But we've been very creative.

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I think Sharon has mentioned using applesauce. I've done that applesauce have a lot of hydrating capacities and so sometimes mixing with that just you need a pretty good amount of applesauce, but that sometimes can be a vehicle for you to deliver your PEG. Thanks. I do wish there were more studies in the different vehicles that you can put it in. Generally, for some reason I think we feel that, you know, water is better and that's where the studies have been done. If it ends up being an aspect of volume where giving the PEG for that patient, they just can't take that volume for whatever reason they're, they're too sensitive or some other aspect. If you can get away from the PEG in those cases and maybe use milk magnesia just due the fact that the volume is significantly less.

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And so just something to keep in mind. The only liquid I've never recommended mixing it in is any kind of carbonated beverage because it gets super, super fizzy and it overflows and it makes a mess. But that's just the nurse in me, but you can, I just don't recommend it.

01:43:06.525 --> 01:43:52.925
So how much is too much when it comes to stimulant laxatives? I think that if you're doing an initial disimpaction or clean out, I think that you kind of give what you think you need to make them poop, right? There are guidelines, but I make them poop so I just kind of give what they I think they need. Yeah. Just to piggyback on that, I, I think I was a little hesitant initially, but working with our surgical colleagues in the colorectal programs, they all use whopping doses of, of Senna and not have any concerns with it other than the fact that if you run into side effects, so you're getting a lot of cramping, obviously that is not going to work in terms of a strategy.

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But as Sharon's mentioning, the higher the dosing if you're not having these side effects but you're still having some good bowel movements, I don't have a limit in terms of the dosing I try to use. Yeah, I agree. I mean I push those doses quite high. The only caveat is those that are diapered, it can cause a significant perianal rash and denuded skin and skin burns in some. So just be careful, particularly in the patients who are not toilet trained because that can be a huge issue.

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And, if you don't talk to the families about it, they can be really upset by it. And then the last question is, what is your idea about the longest time for giving PEG treatment? But I think we discussed that so

01:44:38.275 --> 01:44:56.325
Well, thank you very much. Thanks everybody for attending. We'll still be here if you have additional questions, but really appreciate your interaction. Have a great evening. Thanks everyone. Thank you. Thank you. That was great. Thank you so much for reading all these. You're welcome. I couldn't see them myself. The handwriting is like, so.