Pediatrician's Corner
A Conversation with a Pediatric Gastroenterologist

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Shea Fleming, MD: Hi, and welcome to the Pediatrician's Corner podcast series brought to you by PNCE.org and the Annenberg Center for Health Sciences. I'm Dr. Shea Fleming, managing partner, owner and pediatrician of Peachtree Park Pediatrics in Atlanta, Georgia. It's great to have everybody here with us today.

Our guest today is Dr. Benjamin Gold. Dr. Gold is a pediatric gastroenterologist, past president of NASPGHAN, and is a partner and owner of GI Care for Kids, LLC, Children's Center for Digestive Healthcare, LLC, in Atlanta, Georgia. Thanks for joining us today.

This is going to be great. So, what I thought we would cover today are the following areas: first, I think it would be great to dig into the topic of the microbiome, how it's influenced and shaped early in life and how this impacts our overall health. Then we can talk a little bit about allergy, food vs skin allergy, and how to approach the evaluation of suspected allergy. And then I know you get—and I have certainly sent—a lot of referrals for constipation, so we're going to make sure we get into that topic. And last, we'll touch on feeding challenges and try to help guide pediatricians in the right direction when these present themselves.

Most pediatricians understand that the establishment of the gut microbiome early in life impacts long-term GI health, but how can we help to positively shape this through our recommendations to parents, and how we guide caregivers, is not always clear. So, what factors do you, Dr. Gold, think pediatricians should be mindful of in the first 1,000 days, and what practices or behaviors are most important to support a balanced microbiome?

Benjamin Gold, MD: A wonderful, multilayered question, and I think one of the things to recognize is that if there's any area in medicine and science that is a hot topic and that actually may give us the explanation to lots of things, both pathways to health and disease, is understanding the microbiome. And I think people don't recognize—and now there's data within the past 2 to 3 years—that actually the microbiome gets established even in gestation. So, proper dietary habits, well checks during pregnancy, influences the microbiome. In fact, the founding species, if you will, of the microbiome in the infant gut happens sometime between 16 to 20 weeks' gestation. Then, how people are born, whether they're born by C-section or by vaginal delivery, that's a key event in establishing the infant's microbiome. We all try to strive to have a natural birth and some of us can't, both of my kids unfortunately, one because failure to progress and the other one came early, were born by C-section and, interestingly enough, as per your question, there are ways that moms can actually do things if, for example, they're born by C-section vs vaginal delivery.

The delivery is one of the key events, and then things that they go through in the first few months, few weeks of life, that establish that microflora. So, whether they're breast-fed or whether they're bottle-fed, and then the type of formula that they choose and whether or not they use—and I know we'll get to this at some point—probiotics or prebiotics or both in the first few days to weeks of life help establish that microbiome. So, we've gone from a world where people were playing in the dirt and living in rural spaces to almost being uber-hygienic and I think we're still reeling from the impact of the pandemic and what it did to our hygiene, if you will. Unfortunately, being hygienic, and interrupting transmission of infectious diseases, has resulted in less healthy, if you will, less diverse, less robust microflora. And so, therefore, you're getting infants and children early in life that are starting down pathways, if you will, that could potentially cause disease, particularly if they have the genetic predisposition vs health.

Shea Fleming, MD: Right, so missing out on that good bacteria that we always talk about.

Benjamin Gold, MD: Exactly, for example, if you look at people who were born and raised in rural environments, and in Georgia there's still a lot of people who live on farms and have farm animals, those microbiomes are much more diverse and rich than people who were born in urban environments. And if you look at long-term studies comparing risk for allergy development by age 10, autoimmune diseases, even in families where there's no family history, those children who were born in urban environments are more at risk for having disease than those who were born in rural environments. I'm one of those who, being a 4-legged child owner, dogs and cats are

actually going to become surrogates, if you will, of the microbiome that we're not getting in the urban environment because you come in the front door and you're getting the licks and they're sharing your food and with the kids. So, actually a child born in the house with a dog or a cat is less likely to develop dog or cat dander allergies by age 10 than a child who a dog or cat is brought in later on.

Shea Fleming, MD: That goes back to the exposure, like even when we begin talking about early exposure to allergens which we're going to get to a little bit later, a naive system is going to react much differently than one that has some intel already.

Benjamin Gold, MD: We can, for example, elective C-section rates in the United States are still way too high and there's lots of reasons behind that and we won't go into that at this point in time and for this broadcast. But one of the things to know is that between 30% to 40%, depending upon where you live and what zip code you live in, babies are being born by C-section. So, they're already starting, if you will, behind the 8-ball. There are 2 national studies going on, multicenter studies actually, looking at giving vaginal flora to infants who are born by C-section to see if that can enhance the diversity of their microbiome and prevent disease. For those who can't, then supplementing with things like probiotics or prebiotics or both and then, if they can breastfeed, even better. Then they get the chance to sort of catch up, if you will, in terms of developing a more rich and diverse microbiome.

Shea Fleming, MD: That's very interesting. Touching on the probiotic concept, what is the most current evidence that you can share with us about probiotic use in common pediatric GI conditions and how do you approach recommending those? I always find that very interesting because parents ask me a lot about should I be on a probiotic and honestly, it's a little bit of a loaded question because it depends on all of those things that you've already discussed, but other things as well. So, it's good for us to think about how do you usually go about doing that.

Benjamin Gold, MD: It's interesting that you bring that up because they come in with their downloads from Dr. Google, Nurse Wikipedia and Medical TikTok and they're telling you what probiotics they're on and there are a lot of probiotics that are out there, almost too many to mention or even describe. And some of them have some pretty, how shall I say, unscientific claims, that you can walk on water and heal all mankind, but there are really a few that truly have data, even from infancy. And there's a recent paper published by the group that's on the European side, ESPGHAN, and there's a working group here in the United States that are starting to look at the type of probiotics and different disease states they can help. So, there's lots of data, for example now, in infantile colic, even in NEC prevention, so in preterm babies who are at risk for a very serious GI condition called NEC, there's data on probiotics in that. There's data on probiotics in patients who have functional abdominal pain. There's really exciting data now looking at, in particular, risk for long-term diseases and mental health, and administration of probiotics early in childhood. When I get asked that question—and invariably they have something that they've looked up on the internet—and because it says it's organic or it's natural, then it must be better, there's really only 4 that we truly recommend. So, Culturelle and the strain is called *lactobacillus rhamnosus*, is probably the best studied and widest used. *L. reuteri* is one that's found in BioGaia and was found in the Gerber Soothe Drops and VSL#3 which is actually the only multistrain probiotic, all of those have data in a variety of different conditions. And there are a few other ones that are now getting to the point where there's good data.

The FDA, in the 90s—and the paper came out in early 2000s—actually established 2 specific genera, so the genus of a bacteria, as generally-recognized as safe for human consumption, that being *lactobacillus* and *bifidobacter*. So, if you're looking at a probiotic and you can't find the Culturelle or you can't find the BioGaia, then look at the label, and if they have *lactobacillus* species in it or they have *bifidobacter* or both, then that at least is safe and you probably won't do any harm. Whether or not you're going to get any benefit remains to be seen. Lastly, there's a recent paper, actually 2 well-done studies, that looked at kids with upper respiratory infections, given all the wonderful viruses we've had this year—and you know this as a pediatrician and we're seeing it on the GI side—there's actually data saying that probiotics shorten the course of the illness, prevent actually more severe or help prevent severe sequellae and actually help speed route to recovery. And *L. reuteri* was the one that was studied in these particular recent studies, just published in the last couple of months. Lastly, if you get antibiotics and that's one of the things that I didn't touch on when I was talking about those first 1,000 days because clearly antibiotic exposure puts you at risk for a variety of different illnesses and diseases, both short-term and long-term, but if you get antibiotics, all of the ones that I just listed, the probiotics that I just listed, they'll get wiped out by the antibiotic. *Saccharomyces boulardii*, it's a yeast,

and the trade name is Florastor, is one of those that you can take in conjunction with the antibiotic and that has been shown in some studies to actually help prevent antibiotic-associated diarrhea.

Shea Fleming, MD: Would you generally suggest to somebody like myself, I've been in practice for over 20 years, should that be something that should be in our 2-month, 4-month, 6-month, 9-month, I mean, where does this land in terms of risk/benefit, right? So, people ask us and you say, oh sure, I think that's a great idea, let's go ahead and start a probiotic and we give our suggestions, would that be something that would be standard? Where does that land?

Benjamin Gold, MD: That's a great question and I think we all sort of wrestle with it because the data still is evolving, and I think our understanding of characterizing the microbiome and what that role of probiotics really take is still not there. I think I would have that discussion. I often will wait, if the parent brings it up, asks the question, then I think that's a great time to ask about it or if, for example, you're treating a child with antibiotics for an ear infection, for otitis media, and the parent asks, "Well, is there anything I can do to prevent other things from happening?" that might be the opportunity. I think it's not yet in terms of prime time as an anticipatory guidance type of topic to use because I don't think the data is quite there yet. The other thing to recognize is all of the studies were done in 6- to 8-week increments, so nobody's really looked long-term in terms of whether or not these are good. Now, I gave this talk to general pediatricians in the state of Georgia for the Georgia Chapter of the American Academy and, after I finished the talk, this individual—and I never guess a person's age—came up to me and sort of, in this braggadocio way, said, "How old do you think I am?" and, of course, I didn't ask his age and he said, "I'm 89!" I mean, he did not look 89. And he said, "And I've been drinking kifer for 25 years," and kifer, the sort of liquid yogurts, has live cultures of probably the most strains of any of the yogurt compounds. And I was like, "Oh good," and he said, "So I recommend it to all my patients." Whether or not that's something I would do, no, I probably wouldn't, but again it gets back at the thing that things that can enhance our microflora, things that can help with its richness and diversity can actually help and have some benefit.

Shea Fleming, MD: For somebody specific who comes in and maybe has had more illnesses than the parent feels is natural for them, in a particular year or something, it might be something that we, as general pediatricians, can consider that maybe wouldn't have come up otherwise.

Benjamin Gold, MD: I think that's a great point. In fact, actually I'm thinking of my grandson who is now in daycare and the number of infections that he's had over the past year, and there's actually a really cool study that's being done now by 3 different centers who are looking at daycares and they've got 2 different groups. One is control, 1 is being given probiotics. Same type of daycare in terms of the mix and populations and they're just looking at numbers of illnesses and seeing if the probiotics actually influence outcome. So, stay tuned. So, I think there's some really neat things that are happening.

Shea Fleming, MD: The discussion of microbiome seems to sort of segue really nicely into allergy. So, let's talk a little bit for our listeners about how allergies develop and how the microbiome plays a role here. Can you help us understand how the role it plays, you know, has a place in that early allergy development?

Benjamin Gold, MD: I think that's an important question, and I alluded to that, too, when I was talking about cat and dog exposure and risk for allergies. You can, I mean, hit child allergy, food allergy on Google and the top 10 you're going to get every, I mean, all the lay press and scientific press, you're finding articles over and over again about whether it's the stress in the family, who's got a child who's got food allergy, whether it's change in quality of life for a child who's starting school, preschool and has a bunch of allergies. We get it when we fly on airplanes, when somebody says there's somebody on the plane that has a peanut allergy, we are not going to be serving nuts today.

I think there's clear data that shows, over the last 2½ to 3 decades, allergy prevalence. And for those who don't know epidemiology, prevalence is the frequency of a condition in a population at 1 time, and incidence. So, if you follow populations over time, looking at that same group, both—and it's the frequency of that condition as you follow that population over time—both are going up. And it's interesting, if you look at the map of the United States, the highest increase is in the South as it's becoming less rural, more urban and we're dropping off in terms of our exposures. We're not playing in the dirt as much and we're not being exposed to other things that enhance our microbiome. So, thinking about ways, it's not like I had 1 allergist who said maybe we should change the 5-second rule when something hits the floor to 2 or 3 minutes, or even lick the floor actually, no, I would never advocate that!

Shea Fleming, MD: Many people into orbit if we change that!

Benjamin Gold, MD: It brings up that thought process that we've almost become too hygienic in what we do. A perfect example—and I know this isn't quite getting at your question—but I have 2 kids, as you know. My son is the older of the 2. My daughter never did pacifiers. My son, we thought would graduate from high school with his pacifier. Thankfully, he got rid of it during elementary school, but if pacifier ever fell out, you'd see me doing an ESPN Top 10 highlight diving to try to catch it before it hit the floor; my wife looking at me, saying, "I've got 5 other ones in my purse and they're all sterilized, just pick that 1 up and give him 1 of the clean ones and we'll sterilize that when we get home." And then my mother who's very good at embarrassing me at the right time or wrong time who said, "Ben, you had a pacifier when you were little. When it fell on the floor, I'd pick it up, I'd lick it off and I'd shove it right back in your mouth." Oh, that explains it, okay. Anyway, but again, the concept being that we need to really rethink of how we're approaching things and what we're exposing kids to, how kids are staying inside, not playing outside and what foods that we give and how we might be able to enhance what they do.

There are 2 types of main allergies and there's a sort of third type and not to get too much into the weeds, but there's the ones that people know about. It's the ad they have on television now where it's a group of high schoolers that are at a party and somebody is having an anaphylactic reaction and it's for EpiPens. Those are IgE-mediated allergies, so those are classic IgE type allergies. Those are the ones that all the tests, the blood tests, the skin prick tests that the allergists do, the patch testing that some allergists do, are based on. And the EpiPen is based on those kids that are having IgE-, severe IgE-mediated allergy to stop that approach. IgE-mediated allergies are fast in their onset. They're sort of classic, you get hives, you get a stuffy nose, you start getting the throat closing. Those are your IgE-mediated allergies.

What's dramatically on the rise, and this is in my world and the kids that you, as pediatricians, send to us, are the non-IgE-mediated allergies. And, in fact, that's one of the faster rising and there's an inflammatory component, there's no tests and the things that you stop it, unfortunately, are more for the symptoms rather than the trigger. The other thing is that the triggers for IgE-mediated allergies, if you focus specifically on foods, are different in some ways than those that are non-IgE and there's more cross-reactivity in those that are non-IgE.

Shea Fleming, MD: That's fascinating. We're going to get into allergies, which I think is going to be interesting. I find parents have such a hard time understanding a non-IgE-mediated allergy. They really aren't aware at all that there's that subclass. They really don't know.

Benjamin Gold, MD: You may not be surprised, but there was a recent study done in both Canada and the US that more people think that their child has food sensitivities and/or allergies than they actually do. And I think this is an important area, really, where lots of education needs to go, both amongst primary healthcare providers and I think even specialists, but also to parents, in terms of understanding what's real food sensitivity and what's not and what to be worried about and what really they may just be disagreeing with the food.

Shea Fleming, MD: As we talk about the different types of allergies, what are the most common signs and symptoms? We talked a little bit about an IgE-mediated allergy as what I think is what parents fear. It's the throat closing, it's the coughing, it's the swelling, those physical signs for that type of allergy and that's why parents have such a hard time understanding that there's a different subclass of allergies. But let's talk a little bit more about those non-IgE-mediated allergies and how those look.

Benjamin Gold, MD: The non-IgE allergies, to get at your question, vs the IgE-mediated allergies, we're seeing more in kids with eczema, so skin allergy, atopic dermatitis is probably the appropriate term, and then GI allergy, the Es, if you will, so the eosinophilic diseases. And some of those we couldn't spell 10 years ago. So EOE, until the early 2000s, eosinophilic esophagitis—which I won't say 5 times fast—was something that we really rarely saw. And the only way to make the diagnosis, and still the only way to make the diagnosis, is to have an endoscopy and biopsy. But the number 1 cause of meat impactions in the United States, in 11- to 17-year-olds, is eosinophilic esophagitis, at least by the *Annals of Emergency Medicine* published just within the past couple of years. So, it's clearly a condition on the rise and when you think about the non-IgE equivalent to the anaphylaxis that you're describing that parents really are scared about, is a condition called FPIES, F-P-I-E-S. Which again, we couldn't spell 10 years ago. And that means Food Protein-Induced Enterocolitis Syndrome. In those kids, the reaction can be anywhere from an hour or 2 to 12 to 24 hours later, and they present with profuse vomiting and/or diarrhea or, unfortunate for the parents, both ends coming out at the same time and violently. In fact, there's been a couple of studies that have looked at the number of kids

that got admitted to the hospital with septic shock and they presented with vomiting and diarrhea, and it was because of FPIES and translocation of bacteria in the gut to become septic and then getting them really sick. So, for those kids, it's stopping the vomiting. So a protocol that we give parents, knowing what the food triggers are and remembering that this isn't an allergy, that you can do the testing and find it. So, it's really doing a good basic history and knowing, okay, when I gave the bananas, within 6 hours, they were just puking their guts out. And then eliminating that and coming up with a good careful approach to how you give safe foods and start introducing the not-so-safe foods.

Shea Fleming, MD: With FPIES, I just have a quick question. The earliest I've ever seen a child with that was really within the first couple of weeks of life, actually one of our colleagues, someone I went to residency with, her son had a reaction like that. Is that unusual to see FPIES hit that early or when should we be watching for that?

Benjamin Gold, MD: That's a good question. Actually, the original description of FPIES, the best sort of larger series that was published, just described it in infants and it's like you described within the first few weeks of life to the first few months of life. Oftentimes, a peak you see around 4 months of age when they're starting to introduce different types of solid foods, although I've actually seen them when it's something that mom eats and she's breastfeeding and they get it through the breast milk. Unfortunately, or fortunately, depending upon what part of the healthcare provider universe you live in, there's now a childhood form. There's an adolescent form and then, within the past year, there's now an adult form of FPIES. So, this is something that potentially could be seen at almost any age.

Now, your question might then be do they ever outgrow it and that's one of the neat things I think that we still don't understand—if that could be a neat thing about allergies—is that many children do outgrow it and the key is finding them a good, balanced diet of safe foods, going through a process of reintroduction of the more offending foods, and monitoring their growth and their development.

Shea Fleming, MD: When they're going through that process, some approaches include small little exposures, some include completely avoiding, is that individual to what's going on with the child or is there some debate back and forth about what the right way to do that is, or I guess it would just depend on what allergy, what pathway of allergy they have, right?

Benjamin Gold, MD: Correct. We typically, even with those kids, will have them IgE tested to see if there's some things that we can identify. I'm also a believer that they probably should get environmental testing at some point in time So I feel a multidisciplinary approach is better for those children, involving the allergist and involving our dieticians because they're the ones that really can help work with the parent on counseling them on balanced foods, alternative choices, for example if they've got a bunch of foods that they're not . . and I think it depends upon the severity and type of allergy that they have and what they react to. I'm still a believer in there's lots of data that shows that early introduction, smaller amounts, can help either prevent or induce tolerance, which is something we all should have, both in the immunology/allergy world and otherwise. No I'm not going to be political. But it's also the fact that you can induce that over time with giving small amounts and allergists know how to do this. There's a lot of exciting work looking at what's called OIT, oral immunization and inducing tolerance, oral induction of tolerance, which is kind of like the allergy shots, you know, where they give small amounts over a frequent time and then they eventually start increasing the amounts and then delay the duration until you don't react to those proteins.

Shea Fleming, MD: When you're looking at the diagnostic approach to allergies, which tests do you think are the most useful and which ones aren't? And sort of piggybacking on that, celiac is something that comes up a lot, I think, in general peds, that it's the kind of great masquerader. It can present itself very unusually, at least in my experience with some of my patients. So, I tend to throw a celiac panel on a lot of times when I have things that don't make a lot of sense to me for a patient. But expound on that or explain to me why that wouldn't be a good idea and tell me what else that you think we should focus on when we're looking at testing.

Benjamin Gold, MD: I am more aligned with what you do, say, in terms of your approach. Celiac is also on the rise. What I think is interesting, is that how it presents is very, very different, depending upon where you live, where you grew up, and what you're exposed to. So, back to some of the points that I made earlier, there's actually some really cool studies that are going on at MGH in Boston, University of Maryland, and in Denver, that are actually showing that in at-risk families—that means 1 or more relatives has to have biopsy-proven celiac disease—early introduction of gluten can actually help in preventing or delaying development of celiac disease. If you look at celiac disease prevalence here in the US compared to Europe, where in

Europe the guidelines say if you've got a relative who's been biopsied, has celiac disease, all you've got to do is get the serology. Here in the US, it's still you get the serology if you're positive, then you have to go to the gastroenterologist and get the biopsies done. And, in part it's because, although the frequency isn't different, how it presents is different.

Shea Fleming, MD: The frequency between the US and Europe isn't different?

Benjamin Gold, MD: It isn't different.

Shea Fleming, MD: That's, not what's sort of touted often. It's often that it occurs a lot more here than it occurs there.

Benjamin Gold, MD: Part of the problem is that it's not comparing apples to apples. So, when you look at populations, here the presentation is much more atypical, they present later, they present not with the . . . for example when I was at Sick Kids in Toronto, the Queen's face is still on the dollar up there, so it's a commonwealth country, so you're getting the influence of Europe and the UK, if you will, we were seeing classic celiac, 18 months to 2½ years, typically blonde hair, blue eyes, big belly, little butt, evil as all get-out, and you diagnose celiac, take gluten out of the diet and in 6 to 8 weeks, you'd have like a completely different child running around your room. Whereas here, there was an adult gastroenterologist who recently retired who had a very boutique practice just looking at adults with celiac. She probably had 1 of the largest adult-diagnosed celiac populations, bar none, in the US, and of her adults, at least a quarter probably had symptoms before their 18th birthday, they just didn't connect the dots. But, if you look at it on the other side, 75% of her population developed the disease as an adult. And so, because it's an autoimmune, because it's an inflammatory disease and because something, exposure or exposures, flipped the switch on, you get some of these developing later on in life. And I think that's also part of the, at least to me, the fascinating thing about some of the diseases that we're starting to see and how we can think about what's going on in early childhood, back to the very beginning of our discussion, and what you can do to make a healthy microbiome, healthy microflora and potentially change the pathway of these conditions.

Shea Fleming, MD: That's fascinating. So, I derailed us a little bit. So, when we talk about those diagnostic approach and the tests, celiac sounds like 1 that you also agree with, but what else do you think we should be looking for?

Benjamin Gold, MD: With celiac, if you can get the panel, unfortunately the panel doesn't always include the endomysium antibody, so I would recommend, if you're really thinking about it, it's the TTG, tissue transglutaminase, IgA and IgG, and then endomysium antibody that are really the 2 sensitive and specific for celiac. There's a bunch of really exciting work looking at other markers, but that's what I would include in terms of thinking about celiac. For example, again, 1 other point on celiac, there's been a study going on at least 3 decades or more, called the TEDDY study, where there's juvenile-onset diabetes that the endocrinologists will screen the siblings, because it's the same genetic pathway, for celiac. So, we get a lot of referrals in GI who have been screened, completely asymptomatic, growing, doing fine, who their brother or sister had diabetes and the endocrinologist did the celiac screen and they're positive and then we end up doing the evaluation and testing. IgE-mediated antibodies, or IgE-mediated allergy is the 1 that all the tests are based on. So, either, and again, this is very, very depending upon who you talk to, but the ImmunoCAP or the Quest, the lab that look you can do a food allergy panel, those are all based on IgE. There's some more in research and if you're getting into the weeds, there are IgG and IgG subclasses that people do, but the bottom line is those check the box on the Quest or the Labcorp test and you can get a panel, and at least get the screen. And then what I tell parents is that if I've got high positives, then the next step is to refer them to the allergist who will then do the skin prick testing that's also based on IgE-mediated allergy and confirm those or not confirm the specific allergy.

Shea Fleming, MD: If you're doing a food panel test, are you looking specifically at the seafoods, you're looking at nuts, you're looking at eggs and that panel takes . . .

Benjamin Gold, MD: That panel takes all of sort of what are the 9 major food antigens that the FDA, last year, labeled as the most likely to cause IgE-mediated allergy. And so it's a pretty comprehensive panel that you're going to get, and then if you got high positives, moderate-to-high positives, then that's 1 that I typically recommend going to the allergist and get confirmatory testing and, at minimum, think about those foods. I also send them to our dietician and then they're probably going to get an EpiPen.

Shea Fleming, MD: And sesame is now on that we said, right?

Benjamin Gold, MD: Yes, sesame is actually a new addition to the group, unfortunately for lots of different reasons, but

yeah it has been included. One other point on that is that if you have an IgE-mediated allergy to milk, to dairy proteins, which is not lactose intolerance, that's a whole other topic, you can still drink soy. If you have a non-IgE-mediated allergy to dairy, then soy can cross-react in 40% to 60%. So, you have a very different approach, at least as the pediatrician or the pediatric gastroenterologist or allergist, in terms of guiding the diet of those children.

Shea Fleming, MD: When should a general pediatrician or when do you, once we send somebody to you, when do you suspect something other than an allergy? So, you touched a little bit on EOE, there's behavioral things, there's all sorts of subclasses that we can look at when we're looking at something other than an allergy, where are your red flags for things like that? Where do the key elements in your grabbing of their history and sort of their clinical presentation that you decide what you're going to do for a work-up?

Benjamin Gold, MD: When I think of other things, first of all, and anybody can do this in the primary care space, is a really good family history. Drill down on both mom and dad and their relatives. If there's 1 or more individuals who have an autoimmune history in that household, then you really need to start thinking about risk for autoimmune type of diseases, inflammatory bowel disease being 1 of those, or others. And then, depending upon the symptom complexes that they're coming in, if it's just belly pain, or periodic vomiting or sort of mucousy stools, you may not necessarily realize that the classic cow's milk protein allergy in an infant is bloody, mucousy stools. And that still is by and large the single most likely cause of why that child is having bloody stools. But it's other things that are going on that might trigger my thought process, both family history, looking at their growth and development, other organ systems being involved that you might want to think that there may be something else that's going on and you need to think about sort of broadening the net, if you will.

Shea Fleming, MD: Where do you think that would be a good line to draw between, as a general pediatrician, if you're going to refer to either a pediatric allergist, pediatric GI? Skin involvement, is it some sort of symptom complex or do you, maybe if we rank them, you're always going to say peds GI first, don't know, but if you had to pick between the 2, is there a reason that you would pick one vs the other?

Benjamin Gold, MD: It's pretty comprehensive and I think the bottom line is I think we try to partner with you guys because it's a team and I think the more comprehensive. I mean you and I were trained sort of in the same era and by people who you would be embarrassed if you didn't rule ABCXYZ out before you sent them to the specialist. Because a lot of times I'm undoing and redoing when I'm getting the referral and actually having to provide basic anticipatory guidance before I kind of get into the meat of why that child, infant or teenager is there to see me. So, the more that you can do in terms of screens, like the celiac, like a food allergy panel, like stool studies where you look at markers of malabsorption or markers of inflammation, a test called fecal calprotectin, for example, or fecal white cells, those are things that tell me, a, this is your thought process and, b, those are tests I'm not going to have to repeat.

Shea Fleming, MD: Right, tee it up for you so that you can go in 1 direction or another.

Benjamin Gold, MD: Right, I find that much more healthy and helpful and the other thing that it does is it also allows me to partner with you because, in the end of the day, they're still going to be coming back to you for immunizations, for well-child checks, because we do get them better. And for good anticipatory guidance in terms of growth and development. So, the more I can streamline my approach, doesn't necessarily mean the next day I'm going to do a scope, but the more I can streamline my approach because of what you've done is a help to me.

Shea Fleming, MD: The next thing we're going to look at is the challenges of constipation in infants and children. So, we deal with a lot of constipation in general peds. A lot of it we can handle on our own; some of it gets a little bit more complicated and we end up needing to move it along and transfer that care to you or get your feedback about what we're supposed to do with it. What is your approach to differentiating functional constipation from other causes, and what red flags, for a general pediatrician, should prompt us to be thinking about a little bit more urgent investigation?

Benjamin Gold, MD: Yes, fecal urgency is 1 of those things that we worry about and I think it literally is 40% of the patients that we see. And if you think about it, again getting back to the microbiome, the reason why constipation is such a huge problem is not that we're not eating enough diet, kids just don't hydrate well enough. And when we think about constipation as a whole, there's really a couple of key developmental age groups if you start to see an increase. First that you'll see it is when kids start introducing solids or

infants start introducing solids and then there are some things that you should be thinking about, both as a parent, but also as the primary pediatrician. And the types of questions that you're going to ask in terms of what happened when you start introducing solid foods, how frequent are the bowel movements, how difficult are they to pass. Normal infants can have a poop after every time they eat to 1 or 2 a week. The key is they're not getting bloated, they're not having pain when they have their poop, they're not getting gassy, they don't fall off of feeds because they're full. So, there are certain things that you should be thinking about in your history in the infant that, even if they go infrequently, it could still be normal for that child.

Shea Fleming, MD: My tag line for parents is always constipation is not the frequency of your stool; it's the consistency of your stool. And is that pretty much accurate, right?

Benjamin Gold, MD: Right, and how difficult a time is it that you're getting it out. So, the 6-year-old that's spending 45 minutes in the bathroom, and they do not have their iPad or something that they're playing on, because they're trying to poop, and you're hearing grunting and groaning noises, I think I'd worry a little bit about the constipation.

Shea Fleming, MD: When you talk about some of the more medical issues that kids can have, like a Hirschsprung's or something like that, is there anything that tops your list in terms of red flags? Something where you say, gosh, you know, if you all see this, this is something, you know, blood in the stool with a newborn, hopefully the people that are seeing those kids know enough to rule out milk protein allergy and all that other kind of thing, but when you're looking at like a true medical diagnosis that would be of concern, is there something that really jumps out for you?

Benjamin Gold, MD: If a parent gives me the history that they didn't pass meconium in the first 24 hours and they were sent home and they didn't have their first poop for 2 or 3 or 4 days, and actually we had to stick a rectal thermometer in to stimulate them to go or a glycerin suppository, so things that say, okay, this is out of the range of normal. And then I have parents who come in and say, well you know, the only time that they poop actually is when I put in the windy or I have to stimulate them to get them to go. That's telling me that the normal reflexes that would be occurring in that infant are not happening.

Then the other times that you'll start to see an increase is potty training. One of the things—and you and I have talked about this a lot, and I wish I could broadcast to all the daycares—is that by age 3, they expect children to be completely potty-trained and, I'm sorry, but developmentally, at least 25% to 30% of children are just not ready.

Shea Fleming, MD: It's very stressful for those families, absolutely.

Benjamin Gold, MD: So, it throws the family into this tizzy. They want to get them into the daycare, and they did all the preamble and Joey's or Sarah's not potty trained yet. And you can see, if you think about most normal child development, when they're ready to potty train, 24 hours and they're done and they're potty trained. So, the key is to destress them and to recognize that they may not necessarily be ready, and this is a time that they need to kind of take a back off. And we often will write letters to the school to say that so-and-so is not quite ready, they're working on it, we're setting up a VAL program. And then the other time that you'll see a peak is the beginning of school. And it's interesting because if you look at the frequency of constipation, there's not a huge difference between boys and girls. It's who has the problems and, unfortunately, and I'm a Y chromosome that's about to say this, we are the weaker link and, in part, it's because when we start school, we avoid, at all costs, going to the bathroom to sit down and have a bowel movement. And that oftentimes runs into issues.

Shea Fleming, MD: How would you let families know about what the timeline of treatment would be for somebody that's got some chronic functional constipation because you do have families that feel as if they have a deadline or they just need a target sometimes, right? So, what's a reasonable expectation for somebody to think about with something like that?

Benjamin Gold, MD: I somewhat individualize it based on the family, the degree of stress, how much stress they're putting on the child, the age of the child, how long that child has had that problem, what things they may have tried, or the pediatrician might have tried. But I think, in the end of the day, the 3 main components that we use in terms of treatment are hydration, hydration, hydration. They've got to be drinking enough, even if I have to write a letter to the school to say they need to carry their Swiftie or their whatever water bottle with them. Second, that they need to be on a stool softener. I like the phrase you've taught me that you use in terms of what's the right consistency.

Shea Fleming, MD: I tell parents that you can hold clay or Play-Doh, but you can't hold humus. So, when you've got kids that their stool is too hard, they're able to hold and they're able to pass through the bodily methods that they need to go. So, but it's hard for parents to accept that sometimes.

Benjamin Gold, MD: It is, it truly is. And then there's the reports of Miralax and behavior changes and so I have to go through, and I do view this through the mounds of data that show—in fact, a longitudinal study in thousands of children that Children's Hospital of Philadelphia did—that shows the safety of these medications, short- and long-term. So, the key is hydration, a stool softener and really behavioral training, teaching that child, setting up a schedule, it's about control really. When you're young, the only things you control are what goes in and what goes out. And so, teaching them to set a schedule where they sit regularly and being consistent with that schedule and, if they get the sense, oh I gotta go, they don't wait.

Shea Fleming, MD: Right, and that gastrocolic reflex, as I remember, is usually a certain period after you eat, right?

Benjamin Gold, MD: Best time. Anywhere you go in the world, the most common time people have a poop, first thing in the morning.

Shea Fleming, MD: That digestive tract turns right on. Alright, so we're going to wrap up a little bit with talking a little bit about feeding challenges, picky eating, ARFID which is the Avoidant/Restrictive Food Intake Disorders, those kinds of kids. A lot of kids struggle with feeding challenges and obviously the origin of these can be huge, right? So, when do you look at something like that and you say, what's the importance between the parent and the caregiver and the child when it comes to feeding and how can we help parents manage a child's developing a good relationship with food and being adventuresome and that sort of thing? How do you manage that?

Benjamin Gold, MD: Shea, that's an actually amazing question and this is, we could spend a whole hour talking about these sort of things. And again, I try to group it into the age of the child and where the problem is occurring. I mean, you can't imagine, or you probably can, how many infants where they're not latching right, they're fussing and screaming, they may be doing okay on their growth curve, but everybody's stressed. And what the first part is is explaining to them, mealtimes are supposed to be fun, they're supposed to be pleasurable, it's a bonding experience. I mean, it's why if you look at where the microbiome clusters are, guess where? It's in the kitchen. It's because that's where people conglomerate and so, it's destressing that process and making them understand that that baby has that uncanny and intangible connection between the parents, and particularly with mom, and if mom's stressed, that baby can feel that and that baby's going to be resonating, like okay, why is mommy so upset, why is mommy so uptight and not relaxed. And then, they get irritable and then you run into the feeding problems. So, part of it is trying to destress and then tease out what might be something that's organic. So, a condition that might be contributing to the child not being able to eat well, suck well, swallow well if it's an infant or, if it's an older child, being more of a picky eater. My son was meat and potatoes. If we went to a Japanese or Chinese restaurant, we'd be stopping at Burger King or McDonald's on the way, even when he was a teenager. Then he went to Stanford and he came back with this very sophisticated palate, go figure. But it's understanding that sometimes just being a picky eater doesn't mean that they have an eating problem. As long as they're gaining weight, as long as it's the 3 staple foods, but they get a basic balanced diet and so those are sort of things to think about. So, separating out what might be organic vs what is behavioral and then kind of focusing on both of those areas.

Shea Fleming, MD: That's great advice. It's a very stressful period for people nowadays. They just get so much information and they're so worried about doing it the right way and there really isn't just 1 right way to do it and I think that's what people stress themselves about a little bit. So, we're getting close to the wrap-up. So, I think what we should probably think a little bit about is the biggest thing, I think for me, would be what is the best way for general pediatricians and medical subspecialists to improve communication and sort of sharing of knowledge? You know, podcasts, obviously these things are great getting people connected in that way. I think social media is obviously great, but how do you like to be connected to your community of pediatricians around and what do you find effective?

Benjamin Gold, MD: I love things like this, continuing medical education where we can talk about topics, we can share examples, shared vignettes. The day of people with their busy schedules being able to go out for a dinner presentation is becoming a thing of the past although I love doing those sort of things. There's a lot of sort of the younger, next up-and-coming generation who are interested in med-ed that are doing and using and

exploiting social media, but giving proper information and sound bites and in vignettes that allow people to take home that information. Being open, I frequently am talking to my primary care colleagues who have sent me a child either if there's issues that I'm concerned about or saying, you know what, I don't really need to see this patient anymore, but if ABCXYZ starts to happen again, let me know and then we'll get them right back in. So, having a dialogue and then using platforms, such as the American Academy of Pediatrics which has a chapter in every single state and that's an opportunity, there's a meeting at least twice a year, to have people get together and interact with colleagues.

Shea Fleming, MD: I think the other thing that's gone a little bit away is visiting each other in offices. You know, there's hospitalists now, so we aren't in the hospital quite as often as general community pediatricians, so we miss that camaraderie. But in days of old, some of the subspecialists would circulate around and here's my number and give me a ring if you have any questions, but if there's anyone out there that's listening and is willing to share their personal information with those community pediatricians or vice versa, it can cut through a lot of red tape so that you can get the right test ordered or the right people referred instead of that wall of inability to communicate.

Benjamin Gold, MD: Right, there shouldn't be and the newer generation, which still being involved actively in medical education nationally, now with residents during their training, pediatric residents being pulled out of the hospital, so not knowing what they don't know and not being able to recognize really sick kids, that's where it's even more important to have that dialogue and that 2-way street, feeling open and willing to talk to the subspecialists and vice versa. The subspecialists talking to the pediatrician about the patient that they sent so that they're working as a team. And in the end, the parents appreciate that.

Questions and Answers

Shea Fleming, MD: I think that's true. We have just a couple of questions. I'm going to start real quick. We've touched on some of the testing and some of the things . . .

Can you share any insight on emerging biomarkers that might help us identify children at risk for autoimmune GI disorders earlier in the disease process? So, we talked a little bit about the diabetics and how there's a little bit of crossover, that Ven diagram with the celiac, is there anything else that's on the forefront that maybe some of us in the community haven't heard about in terms of research and things like that?

Benjamin Gold, MD: I'm beginning to start seeing more pediatricians recognizing that in addition to the SED rate, the CRP and now procalcitonin that are used in blood to look at inflammatory markers and the presence or absence and the sort of semiquantitative way of how much inflammation is there. There's also a marker that you can look at in the stool called a calprotectin which is quantitative and actually has been at least calibrated based on certain disease states and can give you an idea, at least in children about 1½, 2 years of age and up, whether or not there's active inflammation, and, in particular, inflammation in the large bowel and the very end of the small bowel.

Shea Fleming, MD: When would you recommend doing that because that is 1 that I know my partners and I order in our office, but for those out in podcast land that are listening, where would be a good indicator of where you would recommend they do that if they're going to run a panel of labs?

Benjamin Gold, MD: I would say if you've got a child that you're thinking about something based on their symptoms and their signs and your physical exam in terms of what you're evaluating, that there may be some inflammatory process and, in particular, something involving the bowel and more lower bowel, so frequency of bowel movements, presence or absence of blood, falling on their growth curve, those would be things that I would think, okay, getting a calprotectin is actually going to be extremely helpful for us to kind of decide how we're going to direct our work-up when that child comes to see us in the office.

Shea Fleming, MD: There's always the question that we get that revolves around mucousy stools. So, how much is that a marker for concern for kids when you look at small children and infants?

Benjamin Gold, MD: One of the first things that I try to explain to parents is that the colon itself has 5 different mucin-producing genes and makes different types of mucins that can come out in the stool. If you make somebody completely NPO and they happen to have a bowel movement, it's going to be predominantly mucous because those cells don't start working. So, the quantity, whether or not there's presence or absence of blood, that being one that I would worry about a little bit more. If I've got a regular bowel movement that happens to have, looks

like somebody has some snot that's gone on top of it, I'm probably not going to worry too much about that.

Shea Fleming, MD: If they're growing well and they aren't fussy, you know, there's all of the sort of general symptoms are okay.

Benjamin Gold, MD: Exactly. So, other things are sort of checking the box to say that, okay, I'm not too worried. If you've got a child who's starting to fall on the growth curve, who's sort of falling off on what they're doing in terms of their intake, has sort of chronic symptoms, maybe even if they've gotten some labs and they're iron deficient, I'm going to start thinking that that mucous may actually be something that's a forebearer of an inflammatory process.

Shea Fleming, MD: On behalf of the Annenberg Center for Health Sciences, myself and Dr. Gold, thank you so much for taking time to learn with us today. We are so grateful for your attention. Have a great day! This ends our podcast.

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