EPISODE 28 - Inborn Errors of Metabolism with Danielle Vice

Transcript

I got to work one morning , opened my email and saw a message from the geneticists that we had a new PKU baby. The newborn screening for the baby came back positive. The baby was 6 days old and was the first baby born to this couple. I had to come up with the nutrition protocol and would see the family in clinic that week. For the first few days, the baby had to be on a Phenylalanine or Phe free formula to get the Phe levels down. Once the baby's levels were down, we had to start the process of introducing Phe back to the diet either by adding breastmilk or infant formula. We had to then check the Phe levels to see the patients threshold for Phe. Everyone is a little different but in this case, the baby had a classic case of PKU and had a fairly standard threshold for Phe. Whether we're dealing with PKU or any other inborn error of metabolism, finding that sweet spot for these patients is key to managing their nutrition and maintaining safe levels.

[Music and Intro]

Well, hey there. I'm so happy for this weeks episode. You're gonna learn about inborn errors of metabolism. And who better to learn from than Danielle Vice, a metabolic dietitian. I can't wait for you to hear this interview. Danielle is seriously gonna blow your mind.

But first, I want to give a huge shout out to Kylie Mignon who just passed the RD Exam. She's amazing and she's got an incredible journey ahead of her. I'm so honored the podcast helped her get across the finish line. Congratulations Kylie. I'm so excited for you to use those hard earned RD credentials. You earned it, you deserved it and the next journey is gonna be amazing.

Ok so I won't keep you waiting any longer. Danielle is one of the smartest dietitians I know. She's a metabolic dietitian and is really good at her job. I've been wanting to cover inborn errors of metabolism for a while, and who better to speak with than Danielle.

I'm so excited for today. I have Danielle Vice, who is a dear friend of mine. We've been friends ever since I became a clinical dietitian. She actually taught me pediatrics and metabolics, which is why she's here today. She's been working in metabolics for many years. So, Danielle, why don't you tell us a little bit about yourself?

Danielle: Thank you for having me, Jana. I feel honored that you asked me to participate. Yes, I've been a dietitian for 16 years now, and it sounds crazy to hear you say I taught you pediatrics and Metabolics. I don't ever remember it or think of it that way. That was where we met, in California. I'm a dietitian in Texas right now in a metabolic clinic. But my first exposure to inborn errors of metabolism other than a brief, maybe half class on PKU in undergrad - I really didn't understand what it was until I did my dietetic internship in California where we met. And the hospital we worked at together had a metabolic clinic. And so during my internship, I always knew I wanted to do pediatrics, so I tried to get more pediatric rotations and this program that included the opportunity to work in this metabolic clinic. And it was part time. I think we had clinic like, one day a week. But even having clinic one day a week, I spent a large portion of my time and energy and focus helping these patients. And that's really just where I fell in love with it. And I worked there for about six years, I think. And I didn't start in that metabolic clinic right away. I got a job as a pediatric dietitian. And then this opportunity to be the dietitian for the metabolic clinic came early on. It was a little scary at first. Felt like maybe I was too new or too young of a dietitian to take that on. But I loved the patient population, so that's what I did for six years. Did it, like, part time. And then I came to Texas and worked in a pediatric ICU where I wasn't a metabolic dietitian. But when the metabolic patients for that outpatient clinic were admitted to the ICU, I worked with the genetics dietitian there to help with their care plans. And then I ended up in the clinic where I am now. So I finally get to do full time metabolics, which I truly love. It is definitely my passion.

Jana: Absolutely. I would agree with that. And you're so good at it, and yeah, you did. It is crazy to think about it that you are the one who taught me pediatrics and genetics that Thursday afternoon in clinic.

Danielle: That’s right. My favorite day.

Jana: It was a lot of fun. So, I know there's so many different conditions out there, and we were kind of going over which ones would be helpful. So maybe we can start with PKU since that's kind of a common condition that we see, it's kind of similar to some of the other inborn errors of metabolism.

Danielle: Yeah, that sounds great. Definitely. In the clinic that I am in now, I have more than half of our patients are patients with PKU. And yes, if we talk about PKU first and the management, the management of PKU is similar to the management of other amino acidopathies of other disorders of amino acid metabolism. But since you're more likely to get a question on the exam about PKU and more likely to meet someone with PKU in your career, I think it's a good one to start with.

Jana: Okay, perfect.

Danielle: So PKU results from a deficiency of the enzyme that normally processes Phenylalanine, which I will say Phe for short. I'll give that preface now. Widely used in our clinics, patients, families, we use Phe instead of Phenylalanine. So if I say Phe, I'm referring to phenylalanine. But there's a deficiency in that process where Phe is converted into Tyrosine, and this causes elevated blood Phe levels, which is neurotoxic. There's a lot going on, but it, in simplified terms, causes demyelination in the brain. And since the Phe can't be fully converted to Tyrosine, there's a deficiency of Tyrosine in these patients. And we need Tyrosine to make neurotransmitters like epinephrine, hormones like thyroxine and melanin for our skin pigment. And so this disruption in the formation of these neurotransmitters and normal brain function causes problems with executive functioning and mood. So difficulties with concentration, memory, reading comprehension, organizing, planning and prioritizing, impulse control, anxiety, depression, irritability - things that all of us can experience. But if a PKU patient has high levels for a long time, high Phe, low Tyrosine, they can experience these at a much higher frequency and a higher severity. So to reduce this influx of Phe into their bloodstream, that can then cross the blood brain barrier. To help prevent these symptoms so that they can function day to day, these patients have to follow a protein restricted diet. Right. Because that's the only way we can restrict how much Phe is going to get into the bloodstream. It is one of the most challenging diets I feel. I'm sure you feel the same way. Most patients if you think traditional, so, like, no pharmaceutical interventions which we can talk about what's available, but traditionally, that's about four to 10 grams of protein a day, and ten is generous. Most patients, it's three, four, five, six grams of protein a day that they can allow. And I'm sure the listeners, being experts in nutrition, can comprehend just how challenging that can be.

Jana: Yes. A slice of bread has 2 grams of protein. So that's pretty much your entire day's worth.

Danielle: Exactly. Yeah. So a general rule of thumb that we teach patients, or I teach patients, is any food that contains more than 2 grams of protein per serving, like if they're reading the label, is really kind of off limits because there's just no way you can fit it in the diet. So that means no meat, no poultry, fish or shellfish, beans or lentils, nuts, seeds or nut butters, like peanut butter, no eggs, dairy, soy, like even plant based proteins have the Phe. I sometimes hear it described as like a vegan diet, but it's really much more restrictive than that.

Jana: Right.

Danielle: Because if you think a glass of milk, 8 grams of protein, an egg, 6 grams of protein, an ounce of meat, poultry, seven grams of protein, those are just out of the question. And so the safe foods that are allowed that won't sort of spike their blood Phe are fruits, vegetables and grains. But even starchy vegetables and grains like

bread, like you said, can really add up quickly if you think like corn, peas, potatoes, sweet potatoes. Some of those can have 4 grams of protein in a portion, like a normal portion that we would eat. So we sort of teach them to avoid those restricted foods, read the label, and only choose things that have zero of 2 grams of protein per serving and really build their diet around fruits, vegetables with more focus on nonstarchy vegetables and then grains. But everything has to be either measured or weighed because it's just so easy to go over that 4 grams a day or 5 grams a day.

Jana: Right.

Danielle: And there are specialty companies, I guess, that make food specifically for these disorders or protein metabolism that patients sometimes have access to. They can be expensive, and they're not always covered by insurance. And the availability of them, I'd say state to state, varies widely. But there are, I think, three or four, maybe five companies that devote their efforts in making these specialty breads, rice, pasta, breakfast items. And so, for example, you mentioned bread. Most has about 2 grams of protein per slice. But the specialty bread they can get might have, you know, 0.2 grams per slice. So they can still get some calories and more variety and more volume of food without going over their phe tolerance if if they can afford it and and obtain it. Luckily, the landscape of allowed foods has increased in variety over the years. As to what's available in our grocery stores. If you think about just more people choosing to follow a dairy free or vegetarian, vegan lifestyle, these food manufacturers have responded with more options to accommodate these diets. And often they're lower in protein as well. Not always. Definitely focus on reading labels, but there are a lot more options out there for these patients to choose from the regular grocery store, even if they can't afford the specialty items online. So there's a lot of vegan cheeses, often like oil based, and there's coconut milk yogurts, and there's nondairy milks, tortillas made out of cassava flour, which are lower in protein. Think about like, zucchini noodles and cauliflower rice and jackfruit and gluten free products that can sometimes be lower in protein. Those are much more widely available in our grocery stores today than they were, I'd say, even ten years ago.

Jana: Yeah, definitely. That's really helped a lot. Some of these specialty or more plant based diets for me because I can't eat gluten anymore. I'm so thankful for all of the gluten free products that are available.

Danielle: There's a lot more options.

Jana: There are, yeah.

Danielle: Before the pandemic, I have not restarted them really since 2020. But prior, I would host grocery store tours with patients. Sometimes it was just one family. It might be one or two families. And we would just go up and down the aisles of a popular grocery store here in Texas, and I would just point out the items that are available, because sometimes it can be overwhelming as a new parent or a patient to go in these huge grocery stores and find something that you can have. So the grocery store tours were really helpful in helping them see what they or their kids can have.

Jana: Yeah. Oh, that's fun.

Danielle: Yeah, I loved it. I hope to start it up soon again.

Jana: Yeah, that would be really helpful. Just so that they can I mean, I know grocery tours are popular anyways, but especially for these families who are so overwhelmed when they're told the ginormous list of things they can't eat. Just to have somebody go with them to a grocery store and show the things that they can have probably reduce a lot of their anxiety and worry, knowing that there are some options for them.

Danielle: Yes. I've had parents just cry at the end. Like, just cry, like good tears, like happy tears. Or just to know that it didn't. It sounds less restrictive, kind of, when you go through it, because yeah, we're eliminating entire food groups from their diet.

Jana: Yeah.

Danielle: Definitely overwhelming.

Jana: Yeah. I mean, and food is just one of those things that, as parents, we worry about anyways with our kids when they're younger. Are they getting enough? Am I doing it right? So when they're told they can't have these entire food groups. It's hard. It's really hard for them. I remember too, having so many parents in clinic just cry. It's just heartbreaking.

Danielle: It is. It's a challenging diet. It is. And we teach them to read the labels because it's just important to learn because you are going to be choosing foods that are out there in the grocery stores and restaurants. But we in clinic sort of figure out how much phe, milligrams of phe they can have. That's much more accurate. And once we figure out how much phe they can have, then we can translate that into roughly like grams of protein they can have per day. So a typical phe prescription, again, for a PKU patient who is just on formula diet, no

pharmaceuticals, it's probably between 200-400 milligrams of phe per day is pretty common. And there is on average - it varies - but on average, there's roughly 50 milligrams of phe (of phenylalanine) per 1 gram of protein. So it ranges probably like 30 to 70 milligrams per gram of protein, depending on if you're comparing a fruit or a grain. But of the foods that they are allowed to have on their diet, it's an average of 50. So that's a good tool they can use. If they're going into those grocery stores and looking at a label and something says 1 gram of protein, we would teach them to estimate that to be about 50 milligrams of phe. So, like I said, it's not uncommon for it to be less than 10 grams per day, but that's the way they can track it. And then there's an excellent website called How Much Phe. I think we recommend every patient. And it's an online sort of database that tells you the milligrams of phe and thousands of foods: name brand foods, restaurant foods. Not everything you look for will be in there, but I mean, a good bulk of them. We even have patients who will only eat something if it's in that database, so they know exactly how much phe they're consuming. And you can track it on there too. They allow you to put in your phe prescription and sort of enter the foods that you eat during the day. And so it sort of tracks it for you, it adds it up, and then it even allows you to send your food log for the day or the week to your dietitian. Like, just straight from the website, it'll email it to your dietitian. So it sort of makes that relationship we have of food records and helping make recommendations based on the food records really easy, and it helps them track it day to day. And it's the most accurate way we have. Definitely.

Jana: Wow. Things have come a long way since I've been working with inborn errors of metabolism. That would have been amazing.

Danielle: Yes, it is. It basically took that binder. Do you remember the binder we had with different color like fruits and vegetables on the outside that it was just pages and pages of these lists? Basically those food lists. It's the same group that made those books. They just put it online now, but they're able to update it in real time. They can update it anytime they get a new amino acid profile from a manufacturer. They can update it right away versus waiting to print the next edition of that book.

Jana: Right. Oh, my goodness. That's amazing. That's really helpful.

Danielle: Yeah. And it tracks your calories. You can enter your formulas in. And that, I guess, leads us to the formula. I'm sure these nutrition experts listening are like, how can you survive on 4 grams of protein a day? It would lead to nutritional deficiencies, poor growth in children malnutrition. And so really, their main source of nutrition is these formulas made specifically for PKU. The insurance term for them, because you can obtain through a prescription only, is medical food. But they are truly medically necessary for them because they supplement what they can't get in their diet, so they can still get their calories and carbohydrates and essential

fatty acids and vitamins and minerals. And then because of that pathway where we're not converting phe into tyrosine, for them, tyrosine becomes a conditionally essential amino acid. The formulas fortified with tyrosine so that they get enough. So they come in the form of a liquid, ready to drink, or a powder that you can mix with water or a protein free beverage. And you typically drink them sort of three times a day, like you would kind of like a meal replacement. And often they provide up to 80, 85% of their total nutrition needs. So their 4 to 5 grams of protein is important. They do need that phe. But really the bulk of their nutrition comes from their formula. So that brings a lot of education to the families about their plates are just going to look a little bit different than maybe the rest of the families because so much of their nutrition is coming from their formula.

Jana: Yeah, and the formula, I'm sure they've come a long way, but as time went on, they really did like their formula. But if anyone else tried it, it was just not very tasty at all. But they get used to it from such a young age and I know over time they've come up with a lot more products available. And that was happening as I was kind of leaving metabolics, but I remember that being such an eye opening thing for the parents. I don't know how she drinks this. It's terrible tasting, but they get so used to it from when they're babies.

Danielle: It's true. Yeah. And there are a lot. Oh, man, I wish I had a count of how many PKU formulas there are. I would say 50. I don't know. So they do have a lot of options, which is great, but yes, just that synthetic nature of, like, adding these amino acids can just make them not very palatable. And even if a child or adult finds one that they like, and they can drink three times a day, maybe after two years of that, they don't like it as much anymore. We call that flavor fatigue. And it's a real thing, I think. Just imagine drinking the same thing for three times a day every day, day in, day out, month after month, year after year. So there are definitely some who are sort of still on one that's similar to what they had at birth. And maybe now they're teenagers and that's still their preference and they like it. But some, after they get introduced to more foods, natural protein foods, it maybe changes their outlook on the taste of the formula. And so they want to try different things. So I always send patients samples of new ones just so that they kind of see what's out there and in case they find one that would be easier for them to drink, they have that opportunity. And it definitely comes up a lot. We're constantly coming up with ways to mix it to make it taste better, sampling new ones. I'm a huge proponent of combination prescriptions where they don't have to just pick one formula. If they want to pick one or two or even three, that they may be drinking three different ones during the day, they're less likely to get tired of those. And it all depends on if insurance will cover it. But we'll definitely fight for them if that's what it's going to make their day to day life easier.

Jana: Yeah, absolutely. Because I can imagine. Yeah. I'd get so bored of having the same thing all day, every day. After a while, it would just be like, I don't want this anymore.

Danielle: Yes. And I have all of the dietetic interns that rotate with me. And in our genetic clinic, some of the residents and med students that come, we offer them to try it because it may sound easy on paper. You know follow this. Lots of fruits and veggies and grains. And then drink this formula. If you just think, think of our culture and the way it's centered around food, and it's really hard to do day to day. It may sound easier on paper, but when they taste these formulas and think, like, okay, and they took a sip, and it's like, all right, now drink three of these today, they're like, well, I don't know that I could do that. And that sort of just helps make them a little more empathetic to what these patients go through to stay healthy.

Jana: Right. And it changes it when, oh, my goodness, I have to drink that much every day. It is a lot harder. And, yeah, on paper, it looks easier, but in reality, it's a lot harder.

Danielle: Yeah. So if we can find a formula they enjoy, that is just the greatest day, many of them just find one that they will tolerate, sort of. But for those who truly find one that they like and enjoy, it's definitely makes managing their diet a lot easier. And PKU patients also have to look out for, aspartame. I'm sure a lot of the listeners have seen the labels. This food contains aspartame, and it's not safe for ketonurics. That's another thing that's different from the other amino acid disorders that they have to look out for as well. And that's because the aspartame molecule itself contains phe, but it's like phenylalanine is part of it, but it's not a whole protein, so it's not always accurately reflected on the label. It may say 0 grams of protein on the label, so they have to look out for that message on the label. And we just try to teach them, you know, when that still might fit in their diet, when it might not. So, for example, a twelve ounce Diet Coke that uses aspartame as its sweetener has 100 milligrams of phe, but the label won't say 2 grams of protein. Right. But it has 100 milligrams of phe, and it's all from aspartame. So that might not be a good choice if you have 300 milligrams for the day. But then, on the other hand, a wriggly sugar free gum has ten milligrams a phe, I think, per stick. And so that, you know, they may be able to have a piece of gum that's a lot different than 100, but that's also something they can look up in that How Much Phe database for a lot of the foods. There's just something else to look out for when educating patients with PKU.

Jana: That’s a good point, because aspartame is a lot of places. So just being in there, yeah.

Danielle: Less and less with time, with other alternatives, but it's still out there for sure.

Jana: And so do you still do the camps? Or did the pandemic kind of put those on hold too? Or you want to share a little bit about those? Because they really are amazing.

Danielle: Sure. I think I've been going for about nine years to a summer camp for kids with PKU aged six to 18 here in Texas. And, yeah, we did a virtual camp in the year 2020, and then we did a smaller there are some restrictions on the camp in 2021, but this past summer it was back to normal, as we like to say. So close to like 75 campers and all the activities. So it's back in the swing of things. But, yeah, it's a week long. The parents drop the kids off, which some of these parents have never dropped their child off for an overnight camp because no other camp would accommodate their nutrition needs, their diet, or their formula. And here it's taken care of. So there is a menu that's created ahead of time, and the campers go online a couple of months before and actually select their menu that's personalized for them based on their phe prescription. So they're able to put in, I can have 400 milligrams of phe a day, and then they can choose from the foods on the menu and make it match their phe prescription. And then we all make formula together, drink formula together. And all the foods on there are really low in protein. They're mostly made from scratch. We have three chefs that help prepare the meals, and so just when they're made from scratch, sometimes they're a little tastier. So in camp, really, their plates look normal. Sometimes their plates are so full they have a hard time finishing it, which is not always the case at home for them. Another dietitian and I will lead low protein cooking classes while they're at the camp. That's one of their activities. They have all the usual fun summer activities like zip lining and horseback riding and archery and canoe and dancing and campfire stuff like that. But it's a way that they can go and enjoy all those things and feel assured that their diet needs are going to be met and they're not going to be singled out. Everyone at the camp is eating low protein foods and drinking formula, so it's very inclusive. And some of the foods we have, like, for breakfast one day, we have a potato, apple, hash. So even, like, hash browns can kind of add up in protein pretty quickly. So we do like shredded potatoes with shredded onions and apples. And so adding those onions and apples kind of makes the phe a little bit lower, but the volume is still a good size portion. We make low protein pizza with low protein cheese and veggies. We make barbecue jackfruit sandwiches. We make low protein ice cream from nondairy creamer and nondairy whipped toppings. So it's a tasty menu, but everything is safe for them to eat.

Jana: That sounds amazing. That would be such a fun camp to go to.

Danielle: I'm biased, but I think it is. It's truly one of my favorite aspects of my job is going to this camp. Truly.

Jana: Oh, my goodness. That is so fun. And to just be able to be around so many other kids, kids who are just like you, just to feel like you're not alone, that part is amazing. And cooking is always fun for kids, so I love that. That is amazing. And I'm glad that you're able to do that again. I'm sure the kids missed it when they couldn't do it.

Danielle: They absolutely did. Yeah. And it gives the parents just a week to kind of know that their children are in a place where they're being taken care of and where other times, they send them to places where they know it might be challenging to navigate their diet.

Jana: And then that creates a whole sense of worry. And it's just one of the worst things if you're worried about your kids. So there's no peace for you as a parent. So just knowing that your kids are taken care of, their needs are met, that their diet is not at all a concern, because that is one of the primary things taken care of at this camp. That would just give such a sense of relief. And to know that they're having fun.

Danielle: It's great. Yeah. And it's been going on over 25 years, this particular one. So, I mean, I didn't start it, and many of the menu items were already created before me, but, yeah, it's been going strong for a little over two decades.

Jana: That's awesome. Yeah, very fun. So a little earlier you mentioned pharmaceuticals and I was wondering if maybe you can share a little bit about what those are with the listeners.

Danielle: Sure. There are two sort of pharmaceutical options. There is a ton of research right now with clinical trials for different treatment options for PKU, which is is fantastic. But on the market now, there is an oral medication that I think was FDA approved in 2007. So it's been around a long time. Many patients are on it. It is an oral form of the cofactor for the enzyme that they are deficient and for that PAH enzyme. So it's sort of a synthetic form of the cofactor. So the thought process is that if you give them more of the cofactor, it will improve whatever residual enzyme activity they have. It comes in a tablet or powder form. It cn be started pretty early in childhood, even like less than one year of age. And theoretically, it should work for most patients. It's not quite clear why, but it doesn't affect each patient the same. Truly, you have to just sort of trial it on every patient to see how adding that cofactor helps them process more phe into tyrosine, if at all. But if it does, if it allows them to process more phe into tyrosine, then they can eat more natural protein and they require less formula. So sometimes adding that medication may give them a couple of extra grams of protein per day, which is still a big deal especially if you can only have four. And in some more rare cases, it can't allow them to have an extra 30, 40, 50 grams of protein a day. So it's definitely worth trialing patients. And then yeah, as the dietitian, you sort of, like, help if they are able to eat more protein, you sort of help give them ideas of how we can add more protein, how much less formula they may need. And it's taken once a day, so relatively easy to incorporate in their day.

Jana: Yeah.

Danielle: And then a newer medication, as of I think it was FDA approved in 2018. It’s not an oral medication. It's a subcutaneous injection. It's an enzyme substitution. So where the other one was sort of giving them a synthetic form of the cofactor, this one is synthetic enzyme substitution. And so it, over time, can allow for a larger liberalization of the diet to incorporate high protein foods that can replace formula as well. But because it's injections, it does come with a lot of side effects, and it takes months, maybe even years, to get them to a dose where they can reach efficacy in their body to where the enzyme is processing their phe. So they start maybe with a once weekly injection and slowly work up to one, maybe even two or three injections per day. So it doesn't sort of act in the body as quickly as the oral form, but the benefit may be much larger.

Jana: Okay.

Danielle: And once you sort of reach efficacy, for most patients, that means a regular diet. They slowly incorporate all those food groups back in. They may go from eating 7 grams of protein a day to 70.

Jana: Wow.

Danielle: Quite fascinating. But it's a long road to get there, so we definitely make sure patients understand that. But it's so rewarding to see and be a part of. But as a dietitian, many of these patients have never eaten some of those food groups. So you're there to sort of help see what they're interested in. Maybe they're not interested in meat, but they're interested in beans and lentils and eggs and helping them come up with recipes or ways to incorporate them. Cooking classes on just how do you cook eggs, how do you grill chicken. So it has changed, I guess, sort of what a PKU dietician teaches patients.

Jana: Yeah.

Danielle: Where we go from teaching them low protein foods to high protein foods, but it's really rewarding to be a part of. It’s just a long journey for some patients. They may experience a lot of side effects before reaching that goal, but for a lot of them, it's still worth it.

Jana: Yeah. That's amazing. Science, again, like I always say, is amazing. And just that this is an option for some of these patients is really remarkable.

Danielle: It is. And so right now in the US. It's approved for 18 years and up, and they're doing trials for adolescents. But I think in our clinic, we have about 20 to 25 patients who are on injections. It's it's a new part of teaching PKU patients.

Jana: Yeah. You spend so much time going over low protein, and then all of a sudden it switches when they're able to. To how do you incorporate these foods?

Danielle: And we used to do exclusively, like, low protein cooking classes, something else we did before the pandemic that we hope to bring back again soon. But now we're talking about having low protein cooking classes for those who are still on a low protein diet, but also high protein cooking classes for those who have transitioned and have just never cooked with these foods.

Wow. Amazing what's happening. And it's just going to get hopefully better for these patients with time and with discoveries.

Danielle: It’s amazing to be a part of.

Jana: Yeah, I can imagine. And rewarding for the patients and for their families, because just to see that they can eventually potentially go back to eating, quote unquote, a normal diet must feel so great to so many of them.

Danielle: Yes. To have options. Right.

Jana: I mean, that's really what we want is for them to have options. And for so many years, it could feel like they don't have a lot of options. So even though they do, the fact that you're saying there are that many formulas, even when I was doing inborn errors of metabolism years ago, there were formulas, but there weren't that many formulas available. And so just to hear what has happened over the years and the discovery of new ones and the development of these products for patients s really great and really incredible.

Danielle: It is. Yeah. There are a lot of people out there trying to make their quality of life as good as it can be.

Jana: Yeah. So we talked about PKU, but there's another condition that is not as commonly seen, but I definitely saw several kids with it: Homocysteinuria. So maybe we can talk a little bit about that one since it is kind of similar with regards to the low protein diet. It just involves a different amino acid.

Danielle: Yeah. Homocysteineuria is caused by an enzyme deficiency that impairs the normal metabolism of the amino acid methionine. So the result is a build up of methionine, but also homocysteine, as well as a deficiency of cysteine. And so, normally, methionine in our bodies is converted to homocysteine, and then it can be converted to cysteine. The two separate enzymes. And sort of in that process is where we find this enzyme deficiency that results in homocysteinuria. And those enzymes use vitamin B6 as a cofactor. So we sort of have this block here where the homocysteine can't be converted to cysteine as efficiently as normal. But that's not the only fate of homocysteine in our body. There's also a re-methylation cycle. I like to think of it as like recycling, so where the homocysteine can be converted back to methionine for protein synthesis. So instead of like a pathway that falls like a straight line, I kind of picture this in more of like a circle, like it can go back to methionine. And that re-methylation process occurs through two more enzymes. One of which incorporates the folate cycle and requires B12 as a cofactor. So it uses Folate and B12. And then the other enzyme uses a methyl group from Betane in our bodies. And that helps sort of turn the homocysteine back to methionine. And so we can support the pathway by reducing the amount of methionine the body has to process by following a low protein diet very similar to PKU. And then we can supplement sort of the residual enzyme activity they have by giving them vitamin B6, vitamin B12, Folate, and there's a synthetic form of betane too, so they can take Betane, which makes more available for the homocysteine to go back into methionine since it can't go down this other pathway to be converted to cysteine. And it's not necessarily the methionine that causes the negative symptoms in homocysteinuria. We restrict the methionine to reduce the total homocysteine levels, but it's the homocysteine levels that are what can cause the problem. So those who aren't treated can suffer damage to several organ systems. So they can have eye problems, osteoporosis, scoliosis, intellectual disability, seizures, blood clots, stroke, pulmonary embolism, psychiatric disease. So there's a lot of things they can experience to multiple different organs, and a lot of it is attributed to that elevated homocysteine level and a deficiency of cysteine. Because we need cysteine, it's important for a synthesis of proteins, including collagen and antioxidants. And so we measure the homocysteine level, sort of our guide to manage treatment. But the only way to control that level is by following a low protein diet so that you control the amount of methionine that's available to be converted to homocysteine. It's a complicated pathway.

Jana: It is a complicated pathway. And visual, it's a little bit easier to break down when you can actually see it. But it's a reminder of all of the biochemistry and chemistry classes that we took to get to where we are as dietitians, because it just might come up, especially if you work in metabolics.

Danielle: It would be amazing if I know some of the listeners may be driving a car, working out, but if you're able to pull up the pathway as we talk about each one, it definitely helps you sort of visualize it and have it sink in a little bit easier.

Jana: Yeah, definitely.

Danielle: But the management of homocysteinuria is very similar to PKU in that they follow a low protein diet and they have a formula as well. But instead of it being a phe free formula that's supplemented with Tyrosine, theirs is methionine free and it's fortified with cysteine. So it sort of follows the same guideline for the PKU formula. And I don't know your experience. Most of my homocysteinuria patients have also needed 10 grams or less of protein a day. So pretty restrictive.

Jana: Very low.

Danielle: They also need a lot of formula. But in addition to all the formula they're taking, they take Folate, B6, B12, the Betane, the cysteine. So I feel like their medication or supplement list tends to be a little longer than patients with PKU.

Jana: Yeah, and then, like you said, they have their formula, too. Are there as many formulas available for these patients? Because there weren't when I was working in metabolics.

Danielle: Good question. No, there still aren't. If I had to guess. I don't know, ten or 15 maybe. So less than half? Yeah. So, yeah, there's just less available. So sometimes with these patients, if they're struggling, we may try the same formula over and over every few years because their taste buds may have changed, or maybe they didn't like what was available two years ago, but that could change over time. But because it's a rare condition, there are less formula options for them.

Jan: And just like with PKU, the low protein foods are available for these patients too, right? They can get the low protein foods.

Danielle: Yes. So they would go to the same websites and these companies give breakdowns of the phe and the foods. They also give breakdowns of the methionine in the foods. They don't have that website like I told you. How much phe? They don't have something similar for methionine. It's actually just a lot harder to get exact milligrams of methionine to get that information for food. So many of them, it is just more logistically realistic, honestly, to count grams of protein. But some of them can still use that website. How Much Phe because it will also give the gram of protein and the milligrams of phe. So some of them use it to get that exact unrounded protein amount. But otherwise we also teach them to read the food labels. And there are some websites that

have the milligrams of methionine. They're just not quite as user friendly, maybe, as the one for PKU. But there's an excellent, like, patient advocacy organization, and so maybe they're working on making that easier for these patients.

Jana: That would be amazing. But that's good that they have a little bit of crossover. And so the resources that we have for our patients with or people with PKU, they can use it for people with homocysteinuria.

Danielle: Yeah. And so there are some low protein cooking classes that are for patients with PKU. Or they may be disease specific, I guess, but then oftentimes and then I know in our clinic, we try to just have low protein diet education, whether it be grocery store tours or cooking classes that are for all the patients who follow low protein diets, not just one condition, because there's so much overlap.

Jana: Yeah. Absolutely.

Danielle: They can all use the same recipes and buy the same things in the grocery store.

Jana: Yeah, that's great. That's a great resource. Yeah. So, let’s talk a little bit about maple syrup urine disease.

Danielle: MSUD

Jana: I feel like we learned about that a lot in school. I remember hearing that one in school a lot. PKU. Yes. And then maple syrup urine disease.

Danielle: I agree. I feel like those are the two I learned in undergrad. Yes. Maple syrup urine disease. We say MSUD, just for short, involves the branch chain amino acids. So, isoleucine, leucine, and valine. So there's a deficiency in the enzyme complex that breaks these branch chains down. They do have that characteristic sweet smelling maple syrup odor in the urine. Also in the ear wax, which I didn't learn until a couple of years into being a metabolic dietitian. Personally, I have not had a patient or a baby who has that smell. You know me, I don't have a good sense of smell, but I think that some of our physicians haven't either. And it could be in part to newborn screening. And so it may be that we're diagnosing the babies earlier, before maybe their levels get so high that we pick up on that odor. But it's definitely a true thing that happens. Like, I've seen babies in the ICU who end up being diagnosed with MSUD, and we did not have that smell on them. So it's not like they have to have that smell for you to consider MSUD. So and while all the branch chain amino acids are involved, it's really leucine and its keto acid that are the toxic substances in this case that can cause damage to the brain, sort of

once it crosses that blood brain barrier, it can disrupt the normal homeostasis and signaling in the brain. It's another interesting pathway to really dive deep in. It's really complicated and again, not fully understood, but we do know it's the leucine that we need to keep at a safe level. So shortly after birth, these infants will decompensate and in a couple of days and maybe they go home from the hospital, feeding fine, healthy, but they suddenly present with poor feeding that may lead to either weight loss or they're not gaining weight. They become very lethargic. May start vomiting, become very irritable. They can have sort of a fluctuating muscle tone where they're kind of floppy hypotonic and then more rigid hypertonic. And without emergency treatment, cerebral edema and seizures and death can occur. So it's why it's one of the conditions on newborn screenings. Hopefully you can get a diagnosis within a couple of days, but even still, some of the really severe cases may present to the hospital before that newborn screening is even resulted at day five. So it is one of those conditions that you can't just depend on picking up a newborn screening. You may see it in an ICU setting before you get that diagnosis. So it's definitely something that the intensivists have to consider if they have a baby come in with this presentation.

Jana: Yeah, I was going to say because the newborn screening does take roughly around a week to come back. So if a baby starts to show signs that something's not right, they would go to the hospital or they would at least be assessed before even the results are back from the newborn screening.

Danielle: Exactly. Yeah. And once we know if it's MSUD, let's say it's an infant in that condition, for example, the emergency treatment would aim to reduce that blood leucine level as quickly as possible to hopefully prevent swelling in the brain. And you do that by immediately, like stopping all intact proteins. So if they're on a traditional infant formula or breast milk, sort of stopping that and initiating again a medical food of formula. So similar to the one with PKU and homocysteinuria, but in this case for MUSD, they're free of the branch chain amino acids. So it's Leucine free, isoleucine and Valine free. And you want to initiate that with giving them maybe 20% to 50% more calories than baseline to sort of promote this anabolic phase so that the Leucine goes into protein synthesis and gets out of the bloodstream and less into the brain. And they may also need dialysis sort of concurrently with this just to reduce those leucine levels. And once they're stable, then you can continue that leucine free formula, but you're able to slowly add back whatever their intact protein source was, whether it was breast milk or infant formula. And so, similar to how we figured out the exact milligrams of phe a patient needed or methionine a patient needed, we also have to work as a team to figure out how much leucine can a patient with MSUD tolerate before they experience these side effects. So there's a range that we want to keep their blood level in. So in the beginning, it's kind of a trial and error process as you're making changes to formula. At the same time, you're frequently getting labs. But once you find that sweet spot, again, they're on that combination of the two formulas. And then as they get older and they're on solid food, table food, their diet

is similar to what we've discussed with PKU and homocysteinuria. So the protein restricted diet, a lot of fruits, vegetables, grains, all measured. And they can also, like, read food labels. Again, the milligrams of leucine is a little bit less readily available than for Phe. But we can also, a gram of protein contains approximately, on average, 60 milligrams of leucine. So they can kind of estimate the same way as we discussed with PKU. So if they're limiting their protein in their diet to obtain a certain blood leucine level, so they're restricting the diet to get to a certain amount of leucine. The valine and isoleucine content of protein in our food is half that of leucine. So, as you can imagine, if they restrict their leucine to where it's a safe place, they would probably become deficient in valine and isoleucine because there's half the amount in that protein. So it seems very counterintuitive to a lot of students who are learning about it, but they end up getting a supplement of valine and isoleucine daily. And it's just because of what we just said. If they restrict their leucine to where they need to be, they just can't get enough valine and isoleucine. So they keep it out of the formula so that the clinicians can kind of control how much they get. But they do need that valine and isoleucine supplement to maintain their levels in a normal range, because what we don't want is for them to restrict their leucine and then they over restrict their valine and isoleucine, which can then trigger catabolism. And if the body goes into catabolism and starts breaking down our muscle and protein, that would trigger a spike in blood Leucine again and you'd sort of be on this cycle. So you want to give them enough valine and isoleucine that their bodies don't become catabolic looking for those branched chain amino acids.

Jana: Yeah, and that's a really good point. I remember working in the clinic, and anytime any of these people would get sick. So if their intake stopped or slowed down because they weren't feeling well, we always would tell them right away to come to the hospital and make sure that we would give them an IV and dextrose or really monitor their intake so that they wouldn't go into catabolism. Because when they start breaking down their protein, it then feeds into the pathway and increases their levels, which is harmful.

Danielle: Yes. Can be deadly.

Jana: Absolutely, yeah.

Danielle: Catabolism comes up all the time in metabolics. It is just a state that can trigger a lot of problems for these patients. So any metabolic dietitian, you truly got to understand the anabolism and catabolism processes. And for all of them, we try to avoid catabolism, whether it's a carbohydrate disorder or fat disorder or protein disorder. In most cases, that catabolism could cause increased levels of whatever their toxic analyte is that they can't process.

Jana: Yeah. Very big, important conversation I remember having regularly with the patients and with the geneticists who were overseeing the cases. And a really important point to bring up to the families that you come immediately for help if anything starts to show signs of not eating or anything like that at home, go and get the help you need.

Danielle: Yes. Very low threshold for going to the emergency room, especially think about pediatrics. It's just when we're exposed to a lot of viruses, we just get sick a lot as babies and toddlers and children, and so they spend a lot of time in the hospital. Whereas maybe a patient without MSUD could stay home, get a little TLC, just rest, try to hydrate as well as possible. It can be deadly for them. So they have to go into the hospital where they can be given hydration and a source of glucose and calories in the form of these special formulas, where we're not giving them too much leucine, but we're giving them all the other amino acids that they need so that their body doesn't break down their own protein sources and contribute leucine to the bloodstream. I always tell patients, like, you have PKU or MSUD, but when your body becomes catabolic, it's not like we can tell it, no, release all the other amino acids, but keep the leucine, keep the phe. It doesn't work that way. It releases all of it. You'd think that your body would be, like, communicating with itself, but it doesn't. It releases all the amino acids. And so if you are trying to control any one of those, catabolism makes it very hard to do so. We just try to avoid catabolism or prevent it from becoming very severe or prolonged.

Jana: Yeah. Really scary.

Danielle: It is, yes. So they have sick day diets where if they're even starting to show signs of illness, that they start and contact the clinic immediately. And then definitely, like I said, a low threshold. If they're vomiting, fever, it's pretty much go to the ER and will help take care of you there. Which, as a metabolic dietitian, can be a good balance of both outpatient and inpatient nutrition therapy.

Jana: Yeah. Do you still see the patients when they are admitted?

Danielle: Yes. We still work with the inpatient team. Yes, I'd say it's less often at this clinic than my previous clinic. We have less cases who decompensate regularly, but yes, absolutely.

Jana: Okay. I really liked that balance of the outpatient and inpatient and following them, or at least being aware of what's going on all across the board. So, that was one of my favorite parts, really? Was having like, that oversight.

Danielle: Yes, you really developed…it's what I love about the field is the relationship you develop with the patients and their families because you're with them through the healthy wellness checks and checkups. You talk to them on a fairly regular basis because you can imagine the questions they have about diet or formula. You're also there with them during these really stressful times when they're sick or their baby sick. And so you're part of their team through so much of their life.

Jana: Yeah. And that's a good way of putting it. It is such a relationship you establish with the families.

Danielle: But again, if we think back to what we've talked about, the diet for MSUD once they're on table foods is very similar to what we've discussed with PKU and homocysteinuria. And they also have access to those specialty low protein food companies. They also list the leucine content in their foods. And there are probably about as many formulas as homocysteinuria as there are for MSUD. So not quite as many options as with PKU, but there are multiple companies who each have a handful of formulas that they could try to find the one that works best for them.

Jana: That's amazing. And yeah, they would. Just like we previously talked about with the patients with PKU, it's the same thing. They can get fatigue of the formula that they're taking.

Danielle: Absolutely.

Jana: Yeah. So let's talk a little about urea cycle disorders.

Danielle: Yeah. So following on this pathway of disorders of protein metabolism. The medical nutrition therapy for urea cycles is similar, but it's slightly different because with the urea cycle, all amino acids are contributing to the nitrogen pool, which they then get formed into ammonia and then go down the cycle where it's excreted as urea. It's definitely helpful to pull up the pathway if you're in a place where you can do that. It's definitely like a circle sort of pathway. So there are six enzymes and two transporters in the cycle, and so a urea cycle defect can occur at any one of those eight places. And if our protein intake exceeds our need for protein synthesis or again, for having catabolism with protein degradation - normally the waste nitrogen is converted to ammonia, which then enters the cycle and is excreted as urea. But if the ammonia cannot be processed correctly through this pathway, the ammonia levels in the blood will build up, which are very neurotoxic. Same thing can cause cerebral edema, death in a very short amount of time. I think they usually have a couple of days to kind of get the ammonia level down. So initially if there's an ammonia level that's building up, you can get poor feeding and vomiting, lethargic, maybe fussiness in a baby or like confusion in an older child or adolescent. But eventually it

can lead to coma or death. So we try to limit total protein to the patient's tolerance, so that we limit how much ammonia is being being formed, since it may not be able to be properly processed in this pathway. Also, again, we want to prevent catabolism. So it's total protein we're looking at, not one or a few offending amino acids. So what I may not have mentioned with PKU and homocysteinuria and MSUD, is that if a patient reaches their protein goal from food, they've eaten all the protein they're sort of allowed for the day, and they consume their normal formula prescription, we tell them, if you want more formula, you can always have more formula. Because, again, it doesn't have Phe, it doesn't have methionine or leucine. So that could be a way that they can still get satiated. However, with urea cycle disorders, their formula, their medical food, is supplemented with only essential amino acids. And so if they have more formula than you prescribe, that is still going to contribute to that nitrogen load and that ammonia formation. And so we kind of figure out their total protein goal, like, how much protein can you tolerate before having a high ammonia level that's going to send you to the ER and possibly cause irreversible, reversible harm. And of that total protein, how much of it can come from intact protein from food, and how much of it needs to come from this essential amino acid protein source. Because they often need less formula. I'm sure that was your case. They need less formula than PKU or homocysteinuria because they can tolerate more protein in general than the other disorders we've discussed. But let's say even if you can have 20 grams of protein, you still have to make some good choices to get all your nutrients in a small amount of protein. So they still need some formula, but maybe it's not as much. But really, once they've hit that threshold from food and formula, they really can't go over it. They'd have to choose, you know, foods that are only carbohydrates or only fats. Otherwise they're placing themselves at risk for hyperammonemia. And you can use protein free modular formulas out there that are either just carb, just fat, or a combination of carbon and fat. And there are some that are also fortified with vitamins and minerals as well. So it's sort of like a protein free but otherwise complete formula that they can have in their diet as well. But their, you know, food choices are similar and they can also have access to those specialty low protein foods, but the amount of protein that they can tolerate is a little bit higher in general.

Jana: Yeah. So just for the listeners to put like a kind of a frame of reference. So you had mentioned, say, around 20 grams of protein. Well, a typical renal diet is around 60 grams of protein, and that already is low in protein for those patients and can be a struggle. Granted, they typically, a lot of times, have lived a life of eating a normal, quote unquote diet where they didn't have to monitor their protein, and now all of a sudden, they have to restrict it. Where these people from the very beginning have to restrict their protein. But it's still a low protein diet to be on a renal diet, getting 60 grams or less. So to only have around 20, it just kind of puts it as a frame of reference for the listeners, like, wow, that's still low. That's still low in protein.

Danielle: It is. It's tough. And even restricting to the DRI. How many of us exceed the DRI for protein? So even if you had a patient that's, like, you can only tolerate exactly the DRI 0.8 grams per kg protein, that still requires a lot of education and planning and calculating as the day goes on and what you're eating. But if it's life threatening to go over that amount, it just becomes very important to figure out a way to follow it.

Jana: Yeah. And in this Western culture that we have, we are protein consumers.

Danielle: Yeah, man. I said there's a lot of low protein foods available, more so than when I started as a dietitian. They're also adding protein to so many foods that they didn't before. We see it on both sides. Also have to be careful that you don't get a protein fortified juice or coffee or what.

Jana: Yes.

Danielle: Accidentally.

Jana: Yes, everywhere.

Danielle: So they may have a little bit more flexibility in the amount of protein. Maybe they can have more of those starches and grains than a patient with PKU, but the risk that they experience if they exceed that amount is very immediate and acute, and like we said, can be can be deadly.

Jana: Do you see long term complications from following such a low protein diet? Like, do you see issues with muscle tone or ability to participate in activities in people with urea cycle defects?

Danielle: That’s a good question. I think so. To be honest, I don't have a lot that are older. Yes. Lower muscle tone, for sure, I feel like can be something we see. The activities, it would, I guess, depend on what activity they wanted to do, how easy it is for us to keep them anabolic. Like, if you think of a lot of sports and things, it's so easy to become catabolic. So it would just you have to come up with a good plan as a team for what they're going to have before the activity and during the activity and after the activity and to make sure that they're getting enough calories to prevent catabolism. Yeah, it would definitely be like a team approach and probably very specific to the individual because so if you think of the urea cycle as that like sort of as a circle, if you have a defect that's further up towards the top of the cycle, then those patients are at risk for higher ammonia levels and are much more sensitive to their levels getting higher versus a patient who maybe has a defect in the last enzyme in the process. Like their ammonia is sort of like maybe been able to go through part of the cycle. So if

that makes sense. So a patient with an enzyme deficiency of the last enzyme in the cycle is going to have less risk for these acute hyperammonemic crises versus someone with a defect in the first enzyme of the cycle. That may be play a big part as well in how much protein they can tolerate, what activities you would be okay with, and their risk for these encephalopathic crises.

Jana: Yeah, that makes a lot of sense. And seeing the pathway definitely will help.

Danielle: It helps tremendously. Yeah. And these patients also have access to, we call them nitrogen scavenging medications. So it's these prescription medications they can take that basically kind of go in the body and find all this excess waste nitrogen and get rid of them through alternative pathways. And so that may allow a patient to tolerate more protein from food than they would otherwise. I mean, I think all the patients are on the nitrogen scavenging medication. One or two. And they're also used during an acute crisis as well to get the ammonia level down as quickly as possible.

Jana: Okay. Well, that definitely is helpful. At least helping it liberalize a little bit. Give them a little bit more options to eat.

Danielle: A little bit of breathing room. Yeah.

Jana: So let's segue a little bit away from protein and talk about Galactosemia.

Danielle: Yeah, I'm sure. I guess I thought we will learn about this in undergraduate now that we're going through this. I think I learned about PKU, MSUD. Galactosemia is one I think maybe more people are aware of. So the disaccharide lactose in our diet is broken down to the monosaccharides glucose and galactose in our body. And then the glucose can be used right away. And then the galactose is converted to glucose through a series of steps that occurs in the liver. And galactosemia is the result of an enzyme deficiency in that part of the process. And so the goal for nutrition therapy is to restrict the intake of lactose in the diet. So basically now, and I can get into how it's changed, but no dairy. And then they're supplemented usually with calcium and vitamin D. Infants who are suspected to have galactosemia, maybe because they have an abnormal newborn screen or their presentation is suspicious for Galactosemia, they are switched to a soy formula immediately because the risk of morbidity and mortality in the neonate is high. It kind of gives you some buying time to figure out what is going on. And usually there's no harm in placing a baby on soy formula because they can develop sepsis, liver dysfunction with jaundice, coagulopathy, coma, hypotonia, poor feeding, vomiting. These are all very serious symptoms they can have. So they can switch to soy maybe while we're waiting for the newborn screen results to

come back. But that's what we're trying to prevent is further complications from those symptoms. And then if it's determined that the baby truly has Galactosemia, then they stay on a soy formula. And then as they get older and are transitioning to table foods, we help educate the families again, label reading, recipe substitutions and like, finding nondairy alternatives so that we can continue to restrict the amount of lactose that's consumed. So it used to be when I was with you at the hospital in California, we gave them, I think it was like eight pages long of this whole list of fruits and vegetables and legumes and all these things that they had to avoid because they had galactose. And with technology, science, as you say, we've been better able to - scientists - have been better able to differentiate between bound galactose in food and free galactose in food. So there are a lot of foods, a lot of fruits and vegetables and legumes that have galactose in the body, but it's bound galactose, so it's never actually broken down and released in our system. And so it's actually safe for a patient with galactosemia to eat versus dairy has a lot of free galactose, so it will be released into their bloodstream. And so the education has changed to be, in my mind, like, less restrictive. So it's felt really nice to be able to tell these patients that really they have to restrict dairy. Milk, cheese, yogurt, and also organ meats and fermented foods contain some free galactose as well. So depending on their diet, if that's something that they commonly have in their family or in their tradition, educating them on those. But the main focus these days is to avoid dairy, which is much easier to do than the whole list that we used to give patients. It was almost every bean was restricted, tomatoes and it was much harder for them to follow. And so we were compromising their nutrition too, because it's what we knew at the time. But now their nutrition can be improved because they can have a bigger variety of food in their diet so they get access to more nutrients. And like we said earlier when we're talking about protein, just the access to non dairy alternatives is better now than it was then. So they can usually find an alternative to milk, non lactose containing cheeses and yogurt. So it's easier to find a substitution for that patient or for that child to make their diet a little bit easier.

Jan: Yeah. And I remember when I first was training with you, even finding coconut yogurt, you'd have to go to like one store.

Danielle: Yeah.

Jana: And now it's all over the place. And in some parts of the country, it might not be as accessible as other parts.

Danielle: Very true. Good point.

Jana: That is something that we have to keep in mind. But it is more available than it was, and so that definitely helps a lot.

Danielle: Yes, you bring up a good point. Yeah, I have some patients, definitely like in Texas, that live in more rural areas where these foods aren't as readily available as they are for us, in some of the metropolitan areas. And they often take they call it like a grocery store field trip where they may go sort of like out of town, like once a month, to kind of stock up on some items. So it is still not easy for them, but easier than it was before.

Jana: Yeah.

Danielle: There are even some aged cheeses. So the process of aging cheeses over time naturally reduces the galactose level. And so there are even a handful of aged cheeses. It's the ones you find in the specialty cheese section. They're often really expensive but that are safe to have. And so it feels really nice to be able to tell a new family that they can have some cheeses and to give them a less restrictive list of foods. But it can be challenging for a patient who is older and has been following the sort of the previous diet recommendations all their life. It can be psychologically hard for them to try this cheese and feel confident that they won't become really sick. So if that's the case, we don't want you to do anything you don't feel comfortable with. I just want you to know that our science and our technology has changed, and now we know more than we did. And so if you want to try cooking with these or having these as a source of calcium, vitamin D, protein, it's now available to you. But many of them still need supplements, and we check their bone density scans to assess their osteopenia or osteoporosis. And unlike other metabolic disorders where we can say, if you follow these treatment guidelines, you can live a healthy, long life, galactosemia is a tough one where even with early detection and compliance, long term complications like developmental delays or speech delay and premature ovarian insufficiency can still occur, even with the most compliant patient. And that's due to our we think, again, it's one of those not fully understood pathways, but we think it's due to our endogenous galactose production. So our body endogenously makes galactose as well. And so sometimes we have to do what we can control and restrict the amount of exogenous galactose that we contribute, what we can't really change at this point in time, how much endogenous galactose we produce. And so for some patients, that may still contribute to complications.

Jana: Well, hopefully with our amazing scientists, they'll discover something that will help with that down the road.

Danielle: Yes, there are clinical trials for new treatments for galactosemia as well. Very exciting.

Jana: Yeah, that would be helpful. Well, Danielle, thank you so much. We covered a lot, and I'm sure the listeners are, well, for one, impressed by you as I am, because you are just so smart, so brilliant, and I'm so happy and honored to be your friend and to have known you all these years. But thank you so much for coming on and for sharing all of your knowledge and giving us a good lesson on inborn errors of metabolism.

Danielle: Thank you for having me. I feel honored to have you say that. You're also brilliant and I respect you a lot, so I appreciate you having me on. And I will say, if any of the listeners are interested in metabolics, it's a fantastic field to be a part of. And if you are, I would recommend Metabolic University. It happens in Colorado, I think, twice a year. It's sort of like a good crash course for new dietitians in metabolics. And then our professional organization is GMDI Genetic Metabolic Dietitians International is also just an excellent resource for new and long term metabolic dietitians. So those are sort of my go to things to help me stay up to date for caring for these metabolic patients.

Jana: That's really helpful. I'll also put links to both of those in the show notes so the listeners can go and learn more.

Danielle: Because we don't have a specialty certification. We have the CSP, the CNSC, the CSR. We don't quite have one of those. So this is kind of a way to get some of that specialty training.

Jana: Yeah, that's awesome.

Danielle: But thank you, Jana. I really appreciate you having me.

Jana: Thanks, Danielle.

Danielle: Good luck on the exam to all the listeners.

Jana: Yes, they're going to do amazing.

Danielle: That's right.

Isn't Danielle amazing? She is such a fabulous mentor. And really, I am so grateful for the years I've got to work with her and for her friendship. I hope this episode resonated with you, and, if anything, that it shows how truly amazing our role as dietitians is. I look back when I was a metabolic dietitian. We had clinic every Thursday, and

that's when I got to see all my genetic patients, because they'd come to clinic. Of course, not every single week, but that's when I got to see them. And I only really saw the patients who had nutrition needs, primarily the patients with inborn errors of metabolism, like the ones we talked about in this episode. But every once in a while, someone would need some advice and guidance about nutrition. And I was always happy to see those people, too. Honestly, Thursdays were so fun. For one, metabolics was a great experience and learning opportunity. I'd been the cross cover for genetics long before it became my permanent clinic. So I had established a relationship not only with the team, but actually with the patients, because I would see them when I was cross covering. But once it became my clinic and the patients were fully my responsibility, I really got to form some amazing connections with the patients in the clinic. And I got to tell you, there were so many happy moments and also some really sad moments too. When we get a new positive newborn screening, parents would be really scared. Totally understandable. And it's also really confusing for families because food is a way so many people and cultures show love. So to have a child who can't eat traditional foods or really any of the foods kids commonly eat, is so hard for families to process. I can't tell you how many times I've had families cry to me, and then I end up in tears too, because I'm only human. And it's really hard. The pain and the fear they have is so real and completely understandable. And from there, that vulnerability that we share with each other really helps create beautiful working relationships. Being able to see these kids grow and do so well on their diet even though it's such a hard diet to follow, it's really such a good feeling. It's definitely an area of nutrition that really helped shape me not only as a dietitian, but also into who I am today. Every family left an imprint on my heart and oh my goodness, I've said this before, but seriously, geneticists are so stinking and smart. My learning and growth while working in the clinic was exponential and something I'll forever be grateful for. No matter where you end up, don't ever doubt the impact you have on others. You're here for a reason, and the world is waiting for you. Whether you're still studying for the exam - I See You - or you're an Rd, listening in for some amazing metabolic information on this episode. I'm so thankful you're here. Keep doing you. Keep going, keep learning, and stay on top of your steady gain. There is no limit to achieving the success you so deeply desire. Until next time.

[Music and Outro]