Endocrine Care in Prader-Willi Syndrome

Ages 3–9

2026 FPWR Family Conference • Dr. Amy Fleischman, pediatric endocrinologist

This transcript was lightly edited for readability. Brackets mark unclear wording or an omission in the transcript.

Introduction

Karine Kabundi, FPWR board member representing FPWR-Canada since 2024

Hello everyone. All right. Welcome to the session on endocrine recommendations for ages 3–9 with Dr. Amy Fleischman. My name is Karine Kabundi and I am a mother of two and my six-year-old has syndrome and I'm from Canada. So in this session Dr. Fleischman will provide an overview of care for people with PWS across the age continuum including medical needs, medications, supplements, and behavior management. Dr. Fleischman has served as a faculty member in the division of endocrinology at Boston Children’s Hospital for 20 years where she has developed expertise in clinical care and research in obesity management in children mechanism of insulin resistance the endocrine sequelae in cancer survivors and endocrine management of children with PWS as a director of the Optimal Wellness for Life Clinic at the Boston Children’s Hospital.

She has overseen a clinic of multidisciplinary staff evaluating high-risk children with obesity. So please help me welcome Dr. Fleischman. Thank you. [applause]

Dr. Amy Fleischman

Thank you so much for the introduction. Good afternoon everybody. I'm sure it's been a long and exciting day. It certainly has been for me. I really enjoyed Dr. Roy’s talk for those who were also here on the babies. But I'm very privileged and excited to talk about that transition phase from a cute baby to these little folks who are developing their personalities and becoming into their own and joyful and challenging and all of those things as we kind of move into this phase.

[Part of the session introduction is unclear in the source.] We're a small group, so I have a couple of red slides which we'll do like some hand raising and group participation just keep. And some of them I feel like have probably some right answers and some really don't have some right answers. So feel free to with that as you wish. So some quick disclosures. We work with now Neurocrine. I'm a consultant related to the VYKAT XR studies and was involved in the clinical trials and I always put up the tag that medication use we might discuss some medications that are not approved for individuals with PWS or in this context and Dr. We've talked at the end a little bit about things like supplements.

So they're not approved. So that's disclosure. So we're going to talk today a little bit about how the brain works, hormones and growth, endocrine care, that's what I do and we think a lot about how this matters in PWS. A bit about food and appetite because that's always something that comes into question particularly in this age range. And a little bit about research and [unclear].

Hunger, the brain, and hormone systems

So let's start with a question. See how we're awake. Which one of these is true about Prader-Willi syndrome? A, if children with PWS are monitored very closely, they will not have any issues with food. B, the hunger in PWS comes from the brain, not really from the stomach. C, growth hormone treatment is what makes the appetite increase. And D, children with PWS will outgrow their hunger drive by the teen years. So, what do you guys think? A B. You got a lot of B's.

C D Okay, so it sounds like we this group thinks there's a right answer here. Okay, and I would agree. I think the point here being the hunger and PWS does come from the brain, right? Not the stomach. And we're going to talk a lot about the hypothalamus and the pituitary gland. And if you were here for Dr. Roy’s talk, she talked a lot about the hypothalamus and the pituitary gland. And some of that is [unclear]. So we're really focused on this gland. Pituitary glands are right behind your nose here between your eyes.

It's our master gland. It controls a lot of things, but you also think it's logical to talk about because it really does lead to a lot of things we have to think about in our kids. So, it's a small area. It's at the base of the brain. It doesn't always work in a typical way. One of its jobs is to kind of integrate all of the satiety signals to tell us we’re full, and sometimes that message just doesn't get right. That's why things like willpower and rewards and consequences don't fix that signal because signaling is still there.

And that same control panel impacts growth, thyroid hormone, cortisol, puberty hormones. That's why we have to think about a lot of those things in PWS located. So this is the point one small area of the brain has a lot of jobs. It's a small area but appetite growth hormones. So, I'm going to talk a lot about thyroid, adrenal puberty. Dr. Stafford tomorrow will talk even more about thyroid adrenal puberty and more puberty in the in the teen years. Temperature dysregulation.

Some of our young kids have some body temperature dysregulation, right? They run cold, they run hot, they may not feel as cold. That's again from that area of the brain that may not be appropriately signaled sleep. So, we know daytime, disrupted night sleep, early awakening. These are all really common things we hear about our kids. And again, the circadian rhythm and hormones in that portion of the brain can have an impact on how you regulate day and night and how you regulate energy, pain, and stress.

So, many patients don't have the typical pain signals. Pain may be blunted. Kids are really tough, but they don't feel that pain as much. So, we have to be a little more worried when they're complaining or not complaining. Stress responses can be strong emotionally. So all of that can have origin in this same location. So let's think a little bit about hormones and growth, right? That three to nine year old age range, we're seeing a lot of growth in development and there's lots of important systems we want to think about from an endocrinology stand.

So I'm going to talk a bit about these seven hormone systems. So we're talk about growth in body composition. Here's the idea. Low growth hormone, neurosctory dysregulation as we call it. So either there's not enough growth hormone or it's not being secreted in a typical fashion. Often leads to lower muscle, lower muscle mass, maybe more fat mass, and that results in less calories needed than you would expect typically because muscle is tends to be what brings up those calories.

We're going to talk about thyroid. Dr. Roy talked a lot about thyroid and how often we have to think about thyroid a little bit differently. So the most common cause of low thyroid in the population comes from the thyroid here being attacked by antibodies and not working. But here we're going back to the brain and often in kids with PWS the signal to the thyroid is what's low. And so it's a less common cause of thyroid hormone deficiency called central hypothyroidism.

And that can be missed depending on what is tested. So it's an important thing to remember again back centrally this is what's going on. We have to think about where how the brain is playing a role in we talk a little bit about the adrenal gland and the cortisol production. I think Dr. Talked a bit about this. Is the signal weak? Some data shows it can be more commonly weak in some folks. Some data shows it's really not much of a problem. We'll try to talk a little bit about what that means for your kids.

Early pubic hair and underarm hair, super common, often really concerning for folks. Most of the time it's pretty benign and not something we have to worry about. But what do we need to think about to figure out that it's not something we have to worry about and how do we evaluate in the context? Puberty and sex hormones. Most of that I'm going to leave for Dr. Stafford to talk about tomorrow because by age nine, we're really not expecting puberty to fully kick in.

But most kids will begin having some levels of sex hormone, but it might be low. Often puberty starts but may stall. So thinking about how do we evaluate that and why is that important? And we'll talk a little bit about why is that important for example for bone and for growth. So why do we have to start thinking about this in that early kind of pre-teen phase? Bone density may be low. So we do have to think about how do we optimize bone density? What are the hormones that can contribute?

What are the activities that can contribute? What are the nutrients that can contribute? Curvature of the spine is common. Episode was talking about in the baby section looking at the hips but then looking at the spine making sure that any concern gets evaluated and getting an orthopedist on your team to be following that over time to decide whether any additional intervention is needed. And then blood sugar and metabolism. So diabetes risk not typically in this age range but certainly can be true in adolescence and adults and we know there's some medications now particularly VYKAT XR which we'll talk briefly about that can alter blood sugar so it's something on forefront

Growth hormone and monitoring

so let's start with growth hormone that's often what we're starting with often the first thing I get asked when I meet a new family is when can we get on growth hormone and that's in the baby phase for most people which is wonderful so by the time Most kids get to three these days. They're already getting some growth hormone. So why is that important? Growth hormone adds height. Children reach a more typical adult height consistent with those in their family.

This is a growth chart of one of my patients down there. You can see maybe you can see it's a little small. But you can see that mom and dad are pretty average in height and this child has been on growth hormone since infancy and has grown pretty average in height. And this is a standard growth group. So we really often see it's normalized with with use of early age. That's not to say like if you're all short people your child's not going to be you know 7 feet tall they're going to be aligned with their genetic

potential kind of where they should should be most typically versus historically when individuals with Prader-Willi syndrome were characterized as being quite short.

So growth hormone does generalize that importantly builds muscle and lowers fat mass. And so we know that we said inherently there's this mis mismatch with higher fat mass, lower lean mass for any given absolute weight. And so increasing that lean mass, strength, endurance, all of that is really important. And then that helps support activity levels, right? And we know the other thing we can do besides adding growth hormone is adding physical activity to whatever capacity is possible.

But using those muscles is always incredibly important in addition to growth hormone in order to build muscle, building muscle and improving metabolism. Some studies do also suggest some benefits for learning. And so you know lots of studies on all this other associated benefits. So what to know before before and during Dr. I talked a little bit about sleep study and sleep assessments and oxygenation assessments at the start and then again ongoing with growth hormone during this age range.

She mentioned you know that's when we sometimes can start seeing hypertrophy of the tonsils or adnoids that needs if there's new concerns about sleep snoring more obstructive sleep apnea that needs to be evaluated by a sleep specialist so that we can make sure that the child's safe. It typically is caused during severe illness. And that's mostly related to some older studies now that showed when people were put on growth hormone during severe illness, they tended to do worse.

I'm not sure that there's good data in like if your child is on replacement growth hormone that is good or bad to stop it, but often it's stopped if somebody's critically ill. And what we typically will monitor IGF-1. So that's the downstream marker that the liver makes. That is the best measure of growth hormone. Growth hormone itself goes up and down and is not easily measured. So we tend to measure IGF-1 and try to make sure that stays either in the upper end of the normal range or sometimes slightly above that normal range but not skyhigh and not super low.

And as Dr. Roy mentioned, we also monitor thyroid. We'll talk more about monitoring thyroid anyway, but we think about when we put something in growth hormone that it kind of may like wreck the thyroid system. So, we also want to check that we're not having more problems with thyroid as time goes on. We often will check a bone age. That's an X-ray of the left hand. Why we do that? I think of a bone age as a clock. Girls grow till their bone age is about 15.

Boys grow till their bone age is about 17. So, it's nice to kind of know where your child is marching along toward that done phase. There's a theoretical possibility that too much growth hormone could push that bone age farther along. That differences in hormones could push that farther along. And so child's growing great, but their bone age is way advanced. That's not going to get us to the height that we were expecting. So typically on the doses that we're using in the conditions that we're talking about, we're not seeing major advancement or delay, but it's reassuring to kind of see that bone age is marching along pretty close to your child's age.

Did you say left hand? Left hand. What just because that's what we do. So there's there's literally a book of left hands that are average, you know, that show like this is what 10-year-old looks like. This is and so, you know, you can't switch because it's very much arbitrary, but it's what you and then scoliosis. So

growth doesn't cause scoliosis. It can with any rapid growth, you can see scoliosis progressing more rapidly. So you need to be on board with whoever is following the scoliosis.

Hey, we're on growth hormone. We got to maybe take some extra x-rays. Maybe we're getting seen a little more frequently. So, it's more of a monitoring status. And sometimes, you know, I have had a couple patients where scoliosis was progressing so rapidly that we wanted to come down and maybe even stall up a little bit just to kind of balance those risks. So, growth and body composition. So, just a little aside, I'm like why does the same meal do something different, right?

Like two children. You may have two children. You may have more than two children. Maybe they're eating the exact same thing. Why do I have to think about my child who has PWS differently? Well, we said there's less muscle to like burn up those calories, right? So muscle burns the fuel, more less lean mass means really your body needs fewer calories. And that what we call resting energy expenditure. Like what we're burning just sitting around here, it's less if you have less muscle.

So you just don't burn as much in your day-to-day living. So generally we think about kids with PWS having a lower calorie requirement for that reason. And there may just be an inherent turnown of that like thermostat in the sense of like burning again just sitting around. Growth hormone helps you know it increases lean mass and it's thought to increase metabolism as well. So it's an important part of thinking about why growth hormone works and is helpful.

So when we think about kind of like what to ask for, what are you thinking about dietary recommendations and growth expectations for your child with PWS, right? So just making sure whoever's looking at those growth parameters and thinking about those dietary recommendations know there are some differences.

Thyroid function

So thyroid thyroid is super important. It gets monitored on many newborn screens, but to note, even though we're not doing the baby talk, it can get missed if it's a TSH only assay. And that is because thyroid stimulating hormone, like we said, comes from the pituitary. Thyroid hormone comes from here. What we really want to know is there enough thyroid hormone? Because that TSH signal may be altered. And roughly one in five kids with PWS will have low thyroid signal coming from the brain.

It often shows up in the first two years, but it can show up later. And the symptoms kind of hide in plain sight. So what are symptoms? Like low tone, sleepiness, constipation. Kids have these things, especially kids with PWS, right? So we're not going to know from the symptoms. So we're going to have to just look. So there needs to be a regularly screened because this is, you know, this is something we need to know about. We need to treat impacts metabolism, brain development, day-to-day energy.

So much. And just point being pret. So, we need to look at both otherwise we could miss it. A normal TSH does not rule this out. Should be checked about every 6 months. Sometimes every year when kids get older because it's also a very easy thing to treat. It's a small pill. You can chew it, you can crush it, you can swallow it. And once treated, kids need to be checked regularly to make sure they're on the right.

Adrenal function and cortisol

And what about cortisol? This one's a little bit more controversial because I think as I said here, there's studies that really disagree. Like some studies show nobody has this problem, like zero. And some studies show up to like 50% of kids have this problem. And I think if you ask 10 endocrinologists, even 10 endocrinologists who specialize in DWS, you'll get potentially 10 different answers, although we maybe kind of try to get more of a consensus as Dr. I was just discussing.

So what is this whole story? So cortisol is a hormone the body needs particularly during injury, illness, fever, surgery. It has to get ramped up. I think our thought is most of the time we think kids with PWS can ramp up that hormone. But there's a theor a thought that perhaps some kids can't ramp it all the way up for like significant procedures. The tests are pretty imperfect. And we also worry a little bit because sometimes kids with PWS won't have a fever, won't complain as much about pain.

So like we might kind of missing a lot. Okay. So I think this is a discussion to have with your providers. Often we'll get a morning cortisol. Just make sure that is adequate, looks good, looks normal. If you have a kid who's had a normal cortisol andor had a bunch of procedures and did awesome probably they don't have this problem. But there's a discussion about you know if they could and maybe they do, we talk about something called stress-dose steroids.

So that may be a term you've heard. That basically just means you get highdose steroids just when your kid is sick, just when your kid is going for surgery. And having, you know, if we're if we're going all in that we need to have like a backup and plan if if your kid gets sick and you can't do that. So it's a discussion to have. If you've decided that there is a high risk that your kid maybe is in this category, then you do need a plan. Then how do we get those stress steroids?

How do we do it? And then who do we call if we have a question about whether to use it? So discuss with your endocrinologist whether your kids in that category

Early adrenarche and puberty

Premature adrenarche. I get so many questions about this because it's really really common. I think Dr. Stafford actually did a study quite a bit of time ago now and showed how very common it is. So many of our patients with PWS in this 3 to nine year old age range get pubic or underarm hair or oily skin or acne or body odor. So studies show about one in four to maybe even one in three kids with PWS have this and it's often noticed in that like 4 5 6 7 8 range.

So what's happening? This is not the pubertal switch. This is a different switch. So this is from the adrenal glands which are these little triangular glands that sit over your kidneys and make that cortisol like we were just talking about. But they also make androgens, these male hormones that girls and guys have because it's what gives you the lovely body hair and acne in everybody. And so this is a this is a switch that turns on. The adrenals start making these androgens.

It is not not always at the same time as puberty turns on which comes from the brain. LH and FSH turn on. This is can happen at the same time does in some kids but can as is often true in PWS happen earlier and separate. So the central signal the puberty signal the LH and the MSH that's what gives you the estrogen and the testosterone that's what gives you the enlarged tests the breast development

ultimately periods two different things. So most of the time in PWS when we see this body here that is what's going on.

Two different things and it's most commonly benign and not related to timing of puberty and not something to worry about but still worth bringing up because we need to make sure that's true. How do we make sure that's true? So back to that bone age. So if there's a lot of hormones going on, if estrogen is on board, if there's a lot of testosterone, that bone age is likely to get pushed ahead, get advanced. That's that's really what advances potentiation.

We'll often measure other adrenal androgens like DHEAS, 17 hydroxy progesterone to rule out that something else is going on with the adrenal to make X-ray androgens. And sometimes if we're not sure if it's central puberty, we'll measure those puberty hormones. And once we've done all that and we've said it's not puberty, bone age isn't super far advanced. This is just benign premature adarchy. That's what it is, you know. And most of the time that's what's going to be true and it's not going to have a huge impact on growth or development.

It's just kind of going to be there and then we watch it over time. So important to bring up but most of the time not super important to worry about.

So one more question make sure everybody's wait so your six-year-old suddenly has body odor and pubic hair. Most likely explanation puberty started early and needs to be stopped. The adrenal glands have woken up early, which is common in PWS, usually harmless. Growth hormone is causing it and should be stopped. Something has gone wrong with the diet. Okay, what do we got? A B C D. You're such an agreeable group. Okay, so I think I would agree. B. So usually the adrenal glands have woken up early which is really common in PWS and it's usually harmless.

Growth hormone does not cause this. It is worth watching to make sure that the bone age is not getting advanced and there's nothing else going on there and puberty isn't turning on early which can happen. Not super common in PWS but can happen. So need to check. So what about your reading behaviors? Like I said, I'm going to leave most of that to the teen talk because that's when we think these things are happening. But just kind of talking about what happens when it comes a little bit early because by early usually we're just talking about premature hierarchy.

So puberty is normal in girls starting at age 8 and boys starting at around age nine. So that can happen. You can start going into puberty. But about eight and 10 kids with PWS will actually have low central pubal hormone levels, LH and FSH. That doesn't mean they don't go into puberty. They may go into puberty and it may kind of stall or get prolonged over time. And so in boys, as we talked about in the baby talk, unended testes are very common. So that's often treated in the first year of life if needed.

They may also stay small, the testes may stay small if the signal is not as robust. And so testicular positioning and surgical procedures are sometimes necessary early on. Girls may start developing breast development and get some estrogen but very often it will stall. Periods may come. They may come on time. They may come a little bit late or they may not come at all. So like what do we have to care about in the 3 to 9year-old range? Mostly just you know if there are concerns about premature accur early puberty it should be worked out just like any child.

We don't expect that puberty is going to rapidly be progressing in this age range. So mostly we want to be tracking growth. We want somebody taking a good exam, looking at testes, looking at breast development, making sure so that if puberty does stall out, you have some time to think about that with your provider when we need to supplement the estrogen and testosterone and why do we need to think about that? And I'll put in a plug for it's not just about the point of going through puberty, but those are the hormones that make our bones as strong as they can be.

There's a lot of other benefits to having those hormones. So, thinking about if the body's not producing them, when we need to add them in, that kind of brings me on time.

Bone health, blood sugar, and endocrine visits

So, again, lower growth hormone and lower sex hormones can contribute to lower bone density. So, we have to think about that. We have to make sure we're maximizing our bone builders. Less muscle, less pull on the bone. Less weight bearing exercise, less pull on the bone. So, maximizing activity, weightbearing activity, maximizing that smooth muscle mass again with growth hormone, but also with nutritious eating and physical activity. I'm probably going to say that multiple times because I'm a really big fan of physical activity being the absolute best medicine for all of my patients.

So, my patients hear that a lot. And we know that sometimes that's really complicated and can have its challenges, but in any way that works for you and your family and your child, physical activity will help in a lot of these things. Vitamin D and calcium intake are important to maximize and make sure that is true. And when we're working with nutrition, we're often so hyperfocused on calories and intake. We want to make sure they're also thinking about vitamin D and calcium and making sure there's enough of that in the diet so that the bones are getting as absolutely strong as possible because we also worry a little bit with this like less pain, high pain tolerance, you know, is there a small fracture?

Is there an injury? We really want to make the bones as strong as possible to try to prevent that from scoliosis. This is an age when it this scoliosis can progress. Can really appear at any age. So, needs to be looked for. Just looking at at the spine, having a orthopedic surgeon on your on your team if possible to be keeping a close eye if anything needs to intervene with. And just to make a point again, scoliosis is the growth hormone itself doesn't cause the scoliosis, but any rapid growth phase can make things change quickly.

So treatment, you know, can just be watching or some kids will need bracing and some may need surgery. So, what do you ask for when you're a senior provider? Thinking about vitamin D assessment, thinking about the time, focusing on daily weight bearing. I said that and walking, climbing, dancing, whatever is being in a standard upper body exercise, all of it is good. And considering a supplement with calcium and vitamin D if that's not something that can be worked into the diet in a successful way.

So, what about blood sugar? I think that question comes up a lot and I think in the setting of IAT and it's coming up even more. So type two diabetes is rare in this age group in any individual. Risk does climb in the teen years and it does climb with weight. Also with family history other risk factors obesity can occur in individuals with PWS. We know not all individuals have this problem but it can occur. So monitoring with metabolic screening hemoglobin A1C which is a diabetes screening lab and other metabolic

markers such as like lipids looking at liver function that's something I introduce depending on the child's growth pattern but certainly by this age grouping and certainly by the time a child reaches puberty.

So growth hormone theoretically can increase blood glucose and we know that's true because somebody who is profoundly growth hormone deficient will have low blood sugar. It's actually just a hormone that we need to keep our blood sugar normal. Kids with PWS don't usually have profound growth. They don't make none. So they don't usually end up with issues with low blood sugar. And on balance we think that because it makes lean and metabolism better there isn't a huge uptick in blood sugar certainly not at this age I think as we think about adult parameters and metabolic risks and things like that there may be other thoughts there but generally certainly in this age group we don't really see growth hormone worsening blood sugar typically but now we're adding vicat which blocks insulin secretion directly in some individuals who are choosing to take that.

And so, you know, I think we're going to have to learn what those those two medications do together and whether there's any difference there. But generally, growth hormone metabolically positive. I don't think about it as as being metabolically negative. So, what do we check? Height, weight, blood pressure, A1C, lipids, liver. And then more often if a child is gaining weight quickly or if they're on VYKAT XR, we have to keep a closer eye on blood sugars.

So, kind of a summary, what gets checked. So, what do we typically do in our endocrine visits? So every visit we're getting a height, we're getting awake, we're getting BMI, blood pressure, a quick look at the spine, a longer look if we're worried. Cubital staging, what's going on there? Dietary planning, discussion about physical activity about every 6 months looking at an IGF-1 level if they're on growth hormone and looking at thyroid again in addition to the TSH.

And then once a year again more if it's rising or white hat in bone A1C lipid panel vitamin D levels and then when indicated so sleep studies certainly in the early phases of growth hormone and then as concerns arise bone ages typically annually when on growth hormone because we're looking at premature adenarchy. Adrenal testing plus or minus once it's done and it's reassuring we don't necessarily have to do it all the time. A DEXA scan. So, usually that's more an adolescent thing, but that is a bone density evaluation.

So, if there's any concerns, certainly if I have patients who are starting to report fractures or get an X-ray, their bones look really washed out, we might move to get a DEXA scan earlier to try to see like how how worried are we about the bone strength and how much do we have to think about maximizing those bones. And then spotting if we'll worry about scoliosis.

Hunger, food security, and family routines

So, a quick foray into food and appetite because that's also a passion of mine. And hard to do a talk in PWS without talking about food and appetite because a lot of times that's what we think about. So, why is hunger different in PWS, right? So, we talked about a lot of this comes from our satiety signals in our brain. They just don't arrive in the same way as might in other individuals. They don't register that the body is full. So, signals continue to go on and eating is continually stimulated.

Lower lean mass means there's lower calorie needs than would be typical with a certain weight. And hunger doesn't really take a break, right? So, if the satiety signals don't turn things down, it's just kind of

constant, right? It's there. And it can be uncomfortable. It can be distracting. So the goal is not to teach self-control around food. The goal is ultimately to build a world in which we could have a whole world to not have to practice that self-control, right?

To be able to respond to the question of where's the food, where is it? Now, this slide I'm putting up here, and I know it's a little bit controversial. Some people love this, some people absolutely hate this paradigm. I have found it helpful in many of my patients, so I throw it out there. You're allowed to hate it. Because I think I hate saying things like no doubt, no hope. It's sounds horrible. But I think the no doubt, no hope, no disappointment actually gives you hope.

And why I say that is I find that when when we talk to patients about no doubt food is coming. You're getting food. We know exactly when you're it's coming. You we promise you will get breakfast, you will get lunch, you will get your snacks. There will be a meal that is never questioned. And that does not depend on your behavior. You don't have to be good to get your lunch. It's happening. The idea of no hope is like there's no extra. Don't negotiate. Don't cry.

It's like that's it. You're getting what you're getting. There's no extra. And then no disappointment is what was promised appears. Mhm. If the plans change, we talk it through. And we know that's hard. We know like no disappointment like we all have a disappointment in life. You know, best late plans don't always. So we know that this is an impossible plan for every day, but maybe it's a possible plan for most days. And in doing so, I have seen families have great success with it.

Because I do think it lowers anxiety and a lot of my patients will articulate. So my patients who are older and can really tell me will say that they are much less anxious when they know the plans aren't going to change, right? And they're much less anxious when they're at school and they know that somebody's watching exactly what they're getting for lunch and there's no possible opportunity for them to get anything else. It makes them feel better. And I spent every time we talk about this, especially with my patients as they start to be in that 3 to 9, you know, 7 8 9 age range where we may be looking for hyperfasia, but that they're old enough to articulate this to me.

I will say, is there any part of your life where you're not feeling this security, where you're not feeling safe around food? And it's amazing what comes out. You know, I had a patient the other day who said, "Yeah, you know, I used to have somebody sit next to me at lunch and you know, that person's been out on leave." And it's been really hard not to get like a second lunch because I know nobody's looking and mom had no idea, right? And so, you know, that child was telling me like, I felt much better when there was somebody sitting next to me making sure I didn't go back and get a second lunch.

And now it's really stressful. And he hadn't mentioned it, but when mom said, "Would you feel better if we got somebody sitting back next right?" So I think anxiety is less when these constraints are in place in a way that the child can feel supported and safe. So, this is going to look different in everybody's house, but just as an example, some of the literature discusses actually like posting a meal plan, putting pictures or writing up the plan so like it can be seen like here's today's meal plan.

We're having breakfast at this time and eating this and having a snack at this time and having lunch at this time. Because we know not every day is the same, right? Every time I see a patient in clinic, their family, you know, the kid even themselves will articulate this day was just a mess because I wasn't

eating at the right time because I had to drive here and see you. Of course you did. And that's really disruptive to your day. I completely appreciate that.

But even though there's all kinds of signs about like not eating in the room, if my patient is there and if we're running into 12:00 and 12:00 was their lunch time, I'm like, "You go ahead because let's try to make this plan work. Let's try to keep the plan." so you know, this includes walking, this includes eating at consistent times and really has to try to be an everywhere plant, which again, you know, can't be, but in theory needs to be on the school bus and at the school and trying to get your whole village around you.

Supporting this. So, this one I don't necessarily think there's a great answer. I'll throw it out there right now because I think there's a couple ways you could look at this, but it may happen to you. I think it happens in lots of homes. Grandma wants to bring a treat. I'm coming over. So what do you tell her? Fine. It's one time. It'll make her happy. Let's just do it. B, no treats ever. C. Yes to treats, but only ones that are planned, announced ahead of time, and part of meal plan.

Or D, let the kid decide. I'm throw my guess there. Let let the kid decide whether they want to eat that treat.

so what do you guys think? A B C. Okay. D. So I mean, when I wrote it, I was thinking C. But you know, I think there's also the idea that like sweets are really, really hard, right? So depending on what that treat is. We, you know, we try to avoid like the really sugary stuff, the stuff that's going to cause sugar cravings. Dr. White pointed out like trying to delay that to like the older years, not not trying to give the super sweet foods for that like super sweet taste to littles.

But I think the reality is when we get to school age kids like treats will be part of the world and we're not going to say don't look over there, right? But planned announced part of the plan part of the meal plan. You know, I have lots of patients, especially in their older teenage years where they're in their high school programs and like every Friday they walk to X, right? X, whatever it is, and their whole week is spanned around like what are they going to get on that Friday walk to and it's really important to them and it's really special and they look forward to that and that can work really well.

Like they know on Friday they go and they pick out their long and that's what they eat and that can work for families. I have a family where their child from a very young age knows that her ice cream is in the sample cup and that's just what she gets and she's very happy with it and she likes her sample cup ice cream and when the family goes out for ice cream once a week I think in the summertime that's what she gets and she's pleased with it but that's not going to work for everyone.

That might be terrible for some families. So, you know, again planning seeing what's right for your family and your child. So the idea here was just like that not that there can't be no treats, but that doesn't seem like a feasible option, but that there there it's not a surprise, right? It's not a like here are the treats. Go for it cuz that's stressful. I think that's stressful.

Current treatments and emerging research

So, just to take a couple minutes here at the end because what's going on in research and I will say I wrote this before the last two days. I kind of wish I could have updated it because I learned so much in the last couple days at the FPWR research symposium. There is so much happening is so exciting in this space. So many companies trying to develop drugs and think about this. So many researchers looking at genetics and genetic modification. So many people looking at different hormone modulators and ways to impact the hypothalamic signaling.

Really new novel mouse models and cellular models. So I think we have to really keep looking at this space, right? Those of us who work in the space are super excited and I'm glad that you guys are coming to these meetings and learning about it because obviously this is a total team sport, right? We can't do studies without you guys. And so thinking about, you know, what of these areas of research are most important to you is most important to us. And also thinking and learning and all of us together as we go.

So what's approved? What's been new? What's what's what do we got? So we have prothone. It is approved in prairie syndrome. I was just having a conversation with a patient outside who and we were, you know, discussing how sometimes even though that's true, it can still be get hard to get approved or used with insurance companies and now they're not approving it. But just to say out loud, it is approved by the FDA in individuals with greater Willie syndrome and considered standard of care.

So hopefully that is something we can argue for through most insurance providers and get it covered because it's super expensive. So we don't really expect that anyone's going to be able to pay for this out of pocket. But sometimes it's a battle and really it's super expensive. So insurance companies are going to make it a battle. But hopefully as a team you guys can get that get that covered if it's right for your child. The general standard of care is to start early certain certainly now the focus is within the first year of life with the idea that it should improve height muscle body fat strength and stamina sleep study and sleep assessment making sure there's safety there getting blood work getting the bone age x-ray as they get older I don't usually start that till like five or six there just aren't that many bones to look at but once you get older and certainly if you're thinking about the puberty hormones And then VYKAT XR.

VYKAT XR was approved in March of 2025. That is also FDA approved for specifically hyperasia in PWS but down to age four. So it definitely comes in that way in this age group for some people. The studies showed that it did reduce hypervasion in some participants. And now we're seeing that although at first it was said could take up to six months now in clinical use some some folks are noting that it can take even up to 12 months to see an effect. So we're learning a lot now that it's out in the world.

You guys may be learning a lot. You may have personal experiences or experience of friends and colleagues. So more to come on this and you know not only were there studies to approve the drug there are now many studies you guys may be part of them to study what it looks like in real life to do some of the surveys that are sponsoring to write about your experiences because hopefully you know every conference we can come back and we'll know more about this drug and other drugs out there.

So we only know what we know so far. Blood sugar has to be closely monitored. So diazoxide is a medication as endocrinologists we have used for many years to raise blood sugar. Blood sugar is low in

babies. So we know this is a different compound that it raises blood sugar. That's what it does. And so we need to make sure that it raises it into a you know as it's raised it's it's still in a safe range. So it has to be carefully monitored. The other two things we're certainly looking for are any fluid retention and swelling as well as extra body growth.

So many people don't find that really find that but it does happen in many. So what else is out there? This is just a taste of what out there. There's so much out there right now. But lots of studies in appetite signaling again targeting the hypothalamus some of the brain chemistry oxytocin. Somebody asked about that earlier on. So some of those pituitary related hormones are being studied both in infants and in older children. And then some of these gene directed work, right?

Can we edit the gene can we turn things on that are turned off? Certainly animal models are looking really exciting in that and these are moving really fast. So stay updated. So looking ahead I think ages 3 to 9 is really a build the system time. So building the system around like your food security, making sure growth hormone's going okay, monitoring the schedule, making sure you have a plan. Because when kind of that hyperphasia comes in, I think Dr. Roy said it well.

It's not usually a switch. It's not usually like yesterday it wasn't there and tomorrow it is, but sometimes you can see that kind of creeping in during these years. So getting out ahead of it with the plan, with the support, with making sure the school's on board, all of that can make that transition so much easier. I think as we get to the 9 to 12 and plus now we're watching the switches. So like when did entrarchy happen? When did puberty happen? What's going on with all of that and as kids are becoming more independent out in the world?

We have to come up with more creative plans like what about those treats? What about those trips with friends? What about doing different things? How are we going to integrate that? At the same time, we have to think about how all of these other things are changing with their growth and development and then of course adulthood which is own has many of its own challenges with transition and care providing etc. So couple things I think to take home you can take home [unclear] but the hunger from the brain it's not anyone's fault.

It's there you just have to work with it. Thyroid. Make sure we ask for a free T4, not just a TSH. If we find low thyroid, it's easy to fix and it's really important for mental and physical health. Discuss the six day sick day plan for emergencies. Decide whether that's something your child and you need to be concerned about. If so, make a plan. Early pubertic care is common in PWS. It's usually harmless, but it should still be evaluated. And growth hormone and food security are both working to improve growth, strength, and metabolism kind of together.

So, that's a view from the Charles River of looking out into Boston. So, come visit. But thank you guys for that. I'm going to hand this off before we get to questions for a little plug for how you can be part of the research team. Thank you.

Taking part in the Global PWS Registry

Thank you, Dr. Fleischman. Was very informative and I appreciate you being so thorough on your information being provided. I told Dr. Roy, I feel like even though my son is 20 at this point, every time I listen to somebody talk, I take away a nugget. So, thank you. I'm going to put up a slide here really quick about the registry. So, I'm Lisa Mattis. I work for the Foundation for Prader-Willi Research and I'm an administrator for the Global PWS Registry and I also have a son who is 20 with PWS.

One of the ways that parents can very actively participate in research from the comfort of your home is being in the registry. So, if you have not yet put together a registry account or you have and it's been a while since you visited, please go in update your information. We've launched our registry onto an updated platform. Everything you have previously filled out still lives there. If you're not sure if you have an account, you think maybe I filled one out, but I can't remember, come find me.

I'll be glad to tell you if you have an active account. But just to give you a quick snapshot of things that you are contributing when you complete those surveys. There are active studies occurring in the registry at all times. Dr. Roy has an active survey in there with some colleagues. Looking at new experiences. So that is targeting our families who have a child age five or younger. We need your feedback. We want to educate physicians that work in the NICU and pediatricians and all of those that are encountering families at that very vulnerable stage to understand what the experience is now so we can help influence and make it a better experience for those that maybe didn't have the most positive experience.

Other things that are in there. There's a project in there that's looking at predicting challenging behaviors in PWS and it's a longitudinal survey that you go in and fill out every 6 months. And so we really want to see how things change as your child ages. So there are really critical pieces in there. And from those surveys, these researchers and clinicians, they publish that information. And why that's so important is because it allows people across the United States that care for our children, our clinicians, our researchers, our therapists to access information in free and open ways.

But it also gives you access to the information so you can go in educating your physician who may not know the answers to your questions and present them with information so they can learn too. So, please fill out your surveys. There's some handouts on the table. It has a QR code. I also put it up here. And, you know, it takes a couple of minutes. You can go in at your leisure. Don't get overwhelmed. There are a lot of surveys in there, but they don't have to all be done in the same time.

So, pick and choose what you have time for, visit it again at another day, and if you have questions, you can email me, info@pwsregistry.org or and I'll be happy to help. And I can give you guys my phone number, too, if you need it, which is [phone number omitted]. And you can call or text that number anytime. So, thank you. I'm going to let Dr. Fleischman answer any questions you may have. I know we're at time, but I want to make sure people have an opportunity to have those questions answered and I'm happy to stick around after people have questions.

I just want to put in another plug. I mean, I think we've all been saying in our research group like if you meet one individual with PWS, you meet one individual with PWS, right? Everyone's really really different. So, the only way we can really learn is to get input from everybody, right? Like the only way we

can answer any of these questions. So much of what we end up saying is like we don't know, we don't have data, right? So that way we can answer questions.

But if anybody has any, happy to answer them. Hi regarding the Do you know what the percentage of the kids with

Audience questions and answers

[The audience question is partially unclear in the source.] So it's a good question. So I talked about two different things, right? I talk about premature adrenarche where they have the body there but not actually the central puberty turning. So that in some studies is like 25 to 30%. But early puberty itself is not increased risk from the rest of the population. So not always quite rare in fact happens. So we look for it and make sure we roll it out but not very common in our study is actually closer to 65.

Wow. Okay. In in the Boston children's really really common.

So that's but the central puberty turn on not very common

question go back like two slides I want to think if I want slides sure

I'll let you ask so do

you ever Oh it's a great question I always ask my patients that right like I'm for you. So, you know, then you get into the whole like how much do we want to go chemical free, which I think in kids this age, we probably do. So, one of the more natural ones. But then my patient would come tell me they don't work that well. But some of the some of the brand aluminum free you looking for kind of the more natural versions I think in this probably makes the most sense to go.

But I don't have like a particular go-to Dr. I just say deodorant rather than antipersperent. Yeah. Because it's the antipersperants that have that have you know all mostly more chemicals in them. But Arman Hammer and Tom have less

like there's a bunch of those now that are like the more natural non-chemical ones. I was going to say one of the my son went through this when he was that age and this is going to sound unusual but I used to rub his armpits with vinegar to kill the bacteria and then we put him in the shower and use soap and water and that really seemed to like address the issue that had maybe gotten quite potent and then continue to use those deodorants that don't Yeah, I think all of that is good idea.

I also get asked about like cheating when you're playing girls. I think that's just a first emotions, right? Like I don't think there's anything particularly good or bad about that. It just depends on what makes you and your child most comfortable.

Do you have any opinions on is it okay? Do you have any laugh opinions on protein based sweeteners? Proteinbased sweeteners. So they're coming along to prevent and also towards the insulin shock, you know, like diabetic shock of like sweet things for PWS. Yeah, I don't know that there's that much data specifically in PWS. I will say some I've done some work in general weed management and some studies on been involved in some studies on for example sugar sweetened beverages artificial sugar sweetened beverages and then like non-sweetened beverages right and there is some data that

suggests that even if you go with the artificial sweetened like the zero calorie you can have alterations in your hormones that resemble the sugary ones.

It's also usually the artificial sweetener, and I don't know about some of the novel ones, but they're often like hyper sweet, right? Like they're extra sweet. And so there's a thought that they may actually hyper stimulate some of the receptors that cause some of the addiction to sweetness, right? And so that may actually be worse than some of the artificial sweeteners than even sweet. So, don't know that there's been much done in PWS. It' be interesting to think about how that response is different, but I do tend to try to dissuade a lot of artificial sweeteners even though there's no calories there because I think there are some form of reactions to artificial sweeteners.

Now, if that's what's being craved, a little bit of artificial sweetener versus a lot of sugar may still be the optimal way to do that. But there's likely still to be that triggering of some of that addictive tendency toward children that everyone ends up having.

Thanks for the presentation. I'm father to an over here. Oh, sorry. I'm a father to an 8-year-old with PWS and considering VYKAT XR and would just be curious to hear more of your clinical experience with the drive in you know some of my shoes what I should be thinking about consider that decision. Yeah, I think it's an excellent question and we spent a lot of time in our groups the last couple days sharing experiences and looking at what the data shows.

So many of us myself included who were involved in the clinical trials and so we have some patients and individuals that we're still in touch with who've been on for now many years with the caveat being that most of our patients who stayed on in the clinical trials were doing really great on it right that's why they stayed on in the clinical trials and have been on it for many many years we're learning a lot more now that's in general population so I think for some people it has had a significant reduction in hyperasia that's been demonstrated my clinical experience is for some people it has also had some significant reduction in some of the OCD or anxiety type behaviors and certainly some of my patients who stayed on clinical trial that's why they did it.

I my experience has been that as I mentioned like pretty much universally there's some rise in blood sugar. It only makes sense your insulin's not being excreted. So but in a child if if you're starting with a totally normal hemoglobin A1C there's no worry about that then I think that risk is pretty low. It just needs to be monitored and tracked. The fluid as well. There's a lot of discussions and there's was a statement by about some of the negative consequences that have come out.

But you know thinking about knowing that the top three things we're worried about blood sugar, fluid retention and than body hair again body hair for girls tends to be more of an issue than for boys. And that could be a no-go for some for some girls. The fluid has to be the retention has to be monitored for and I discuss with your provider whether there's any increased risk in wanting to take a closer look at whether there's risk there. But we've had some patients who are very successful with it.

So I think you know keep asking those questions because we're going to learn more as we go forward. But for some people it's been very helpful and I would sorry I'm gonna add to that and say for anyone in this room whose child is taking as Dr. Replacement noted for us to learn more about how this is

impacting all of the members of our community who are using it, not just those who are in the clinical trial. There is a VYKAT experience survey in the registry.

So, you can go in and fill that out when you first start taking it and then if you've been on it for a while and your experience is changing, you can go in and update that information. And the more we learn about how people are utilizing the medication and the impact that it's having, the more informed our community will be. Yeah. I mean, I think exactly to that point, you know, you've probably seen some of the reports the FDA came out with and the statements.

So, we're going to hear negative. We're not really going to hear positive, right? And so we also we need everything. And so, you know, certainly if you're if there's negative responses, but if there's positive responses, if your kids's doing great on it, we can see that in the survey, that's going to allow us to next year to be like, hey, we have, you know, 300 kids in this survey and this many are doing great on it. So, we just don't know yet. And so, another plug for doing the surveys.

Hi, so it's been seven years since we attended this conference. But I know when you were there last there's a lot of conversation on benefits of carnitine and I don't know if that's something you have an opinion on. This is the right session to ask but curious about that. Yeah, I mean I will say it was asked at the baby session and Dr. Roy, I think you gave a good answer is that for kind of all supplements, we don't have great data on supplements like what's actually low, there's kind of variable data on there's not been a consistent signal in like in individuals with PWS X is low.

And there haven't been great studies on, you know, this makes this better. So, I don't think we know. She also mentioned, and I agree, I've had some individual patients who've been on different supplements and had some benefit from them. So, I think the plug is it has to be individualized. Talk to your provider and tell your provider. Like I always like encourage people like if you're going to if you're going to do a supplement, tell them tell them what what I liked her point is she said it really should be for something.

You know, like she was saying, sometimes patients will come in and say, "My kid's been much more sleepy. To not get through the school day. I want to try a supplement. That might be a reasonable time to try a supplement and like see if that gets better. But like let's try to try to target some something we can measure and see if it's helping. Also then look at the time point of starting it and see if it's hurting, right? Like what the negative stuff and letting your provider know so that you can kind of think together.

Any you know non-FDA supplement is a supplement. So just always like putting that out there just making sure getting it from reputable source. You know, we know it's not regulated. We kind of trusted what's in it is what's in it. I have some patients that get supplements that I don't think are regulated. Makes me a little worried. But, you know, again, let me know. I don't want to be so negative ever that people won't share it with me because I want to know what you're on.

I want to know what your kids getting so we can think together if we see positive or negative. And again, if you are using them, you can put them in our surveys because I think part of it is, you know, how things like NAC came about where people were noting that maybe had some resistance. Some people commented that was helpful. A lot of it is anecdotal, not the stuff is not well studied. So, we both need to study it. We also should probably report it.

And, you know, we can come back and say 100 people said they used a supplement and it really helped our kids energy. That's going to take us in another direction. So, it's been seven years. I don't think we've come that far on the second. Sorry about that. Yes. I have another question. So I think we have been talking about high risk people with already

and so people

such a good question and I think it's actually another controversial how it's discussed. Because historically if you look at old data you'll see things saying 30% of adults with Prader-Willi syndrome won't have diabetes but very aligned with weight gain and we know that a lot of our individuals who are becoming adults are not overweight don't have obesity and may not be at higher risk for getting diabetes than anyone else. And so I think and you know folks who've been on growth hormone, who on lean mass, like we need to kind of sus out this whole next generation to see what their risks are because I think a lot of that data in adults is from the prior generation.

So that said, we worry about metabolic health a lot of our patients. And so monitoring with [unclear]. The symptoms for true high blood sugar are extra peeing, extra drinking because that's you have to kind of pee it out. So if that tends to not be what I see in my patient with PWS, often they're like not big water drinkers, but if that switches and your child is now peeing and drinking a lot, I would bring that up and I would get that checked out. If they happen to be on VYKAT XR, they should be getting their blood sugars checked quite frequently and their A1C monitored anyway because we know you can see that without those symptoms.

But I think it's an important question to ask whether the risk is there without the weight.