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Continuity in Care: Strategies for Managing Growth Hormone Deficiency Through Life's Stages

Announcer:
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Chapter 1

Dr. Maniatis:
Hello, I'm Dr. Aristides Maniatis, a pediatric endocrinologist at Rocky Mountain Pediatric Endocrinology, and I'd like to welcome you to our Patient-Clinician Connection on continuity in care of growth hormone deficiency.

In this episode, I'll take you through clinical case scenarios to help you learn how to recognize the early signs of growth hormone deficiency and navigate the complexities of growth hormone testing. We'll also examine how to optimize care during the critical transition from pediatric to adult endocrinology, ensuring patients continue to receive appropriate therapy. Lastly, we'll demystify the evolving landscape of long-acting growth hormone treatments with a focus on IGF-1 monitoring and patient-centered transition strategies. So let's dive right in.

Growth hormone deficiency is a rare but significant health issue affecting both children and adults that can be overlooked, leading to delay in diagnosis. The diagnosis of growth hormone deficiency is based on clinical, biochemical, and radiological diagnostic criteria.

The single most important clinical presentation of children with growth hormone deficiency is growth failure, and careful assessment of growth velocity is essential for diagnosis. We consider growth concerns to be clinically significant when a child presents with severe short stature, defined as a height more than 3 standard deviations below the mean, or when their height is more than 1.5 standard deviations below their midparental target height. Additionally, a height below -2 standard deviations and a growth velocity that's dropped more than 1 standard deviation over the past year, or a decrease in height SD of more than 0.5 SDs over the past year. In the absence of short stature, a growth velocity less than -2 standard deviations in 1 year or less than 1.5 standard deviations over 2 years raises concerns for growth hormone deficiency, signs of midline intracranial lesions, signs of multiple pituitary hormone deficiency, or signs of neonatal growth hormone deficiency.

Once growth concerns are flagged, we move to blood work. We start by ruling out nonendocrine conditions, such as poor nutrition, and systemic illnesses, like anemia or liver or kidney disease. We obtain a CBC, CMP, FOS, ESR, CRP, and celiac panel. In addition, for endocrine conditions we obtain screening thyroid levels. Random growth hormone levels are not useful secondary to pulsatile release of

growth hormone at night. Instead, IGF-1 levels are stable in a steady state during the day and should be measured to screen for growth hormone deficiency. However, the levels may be artifactually low with associated malnutrition or chronic systemic diseases. A karyotype should be done in girls to rule out Turner syndrome and in boys with genital abnormalities. Based on physical stigmata, specific genetic testing should be obtained for other rare genetic disorders such as Prader-Willi syndrome, Noonan syndrome, or SHOX deficiency. Birth weight and length should be obtained to assess for potential of being small for gestational age, which is defined as parameters less than -2 SD. A thorough family history for timing of puberty and constitutional growth delay should also be taken.

Also getting a left hand and wrist x-ray helps assess bone age, which is considered delayed if it is more than 1 year below chronologic age. A cranial MRI might be needed in patients with midline defects or other features that point to congenital malformation of pituitary or pituitary tumors.

The next step is confirmatory testing with formal provocative growth hormone stimulation testing.

Today, I'm going to walk you through a clinical scenario involving 6-year-old Matthew, whose mother, Mrs. Hosack, is in my office for a follow-up visit for an evaluation of growth hormone deficiency. Matthew was born preterm at 33 weeks with birth length and weight appropriate for gestational age. And on his 2nd birthday he was noted to be falling behind in height with a deceleration in his growth velocity. He was less than 1 percentile for height and low in weight, too. Nonendocrine causes were ruled out, and thyroid levels were normal as assessed by his pediatrician. His family history is unremarkable. At their last visit we ordered an IGF-1 and bone age. His IGF-1 was low and his bone age was delayed by 1 year. Today, his mother and I are discussing doing a growth hormone stimulation test.

Dr. Maniatis:
Mrs. Hosack, hello. It's great to see you today.

Mrs. Hosack:
It's great to see you too.

Dr. Maniatis:
So as we discussed, Matthew has a low IGF-1 level, delayed bone age, and continues to fall behind in height. I think this is a good time to test him further to confirm the diagnosis. I would like to do growth hormone stimulation testing.

Mrs. Hosack:
Growth stimulation testing? What's that?

Dr. Maniatis:
The growth hormone stimulation testing checks whether your child's body can actually produce enough growth hormone when we give it a little push. We do this by giving certain medications that stimulate the pituitary gland that makes growth hormone. We give 2 different agents through an IV and then we measure the response by doing serial blood levels every 30 minutes for 4 hours. A normal response is when we see serum growth hormone concentrations of more than 10 ng/mL. If he fails, then we complete the pituitary evaluation for both structure and function with a cortisol stimulation test and MRI of the brain.

Dr. Maniatis:
The diagnosis of growth hormone deficiency is confirmed by performing growth hormone stimulation testing. The most common provocative agents include arginine, glucagon, clonidine, and L-dopa. The idea of the growth hormone stimulation testing is to challenge the pituitary and measure its capacity to secrete growth hormone. Typically, to make a diagnosis of growth hormone deficiency, 2 different agents are used. Serial growth hormone levels are then measured every 30 minutes for 4 hours with a cut off peak growth hormone of less than 10 ng/mL, indicating the diagnosis of growth hormone deficiency.

However, the Pediatric Endocrine Society recommends that one should not solely rely on growth hormone stimulation testing as the diagnostic criterion for growth hormone deficiency. A growth hormone stimulation test is not needed to establish the diagnosis in patients who meet the auxologic criteria, have a low IGF-1 level, as well as 3 or more pituitary hormone deficiencies, children with documented genetic mutations or structural hypothalamic pituitary lesions, or infants with severe hypoglycemia and a low random growth hormone level at the time of low glucose.

Finally, for children in the peripubertal range, which is greater than 11 for boys and greater than 10 for girls, sex steroid hormone priming can be considered.

Let's return to our discussion about reaching a diagnosis.

Mrs. Hosack:
Okay, that sounds more involved. Is it safe? Are there any side effects?

Dr. Maniatis:
Yes, it's generally very safe, though we monitor closely for symptoms such as low blood sugar, low blood pressure, or nausea and vomiting, which can happen during the test. Low blood sugar can present with lightheadedness, sweating, and nausea, and low blood pressure can also present with lightheadedness or drowsiness. This gives us the most reliable data to assess a patient's growth hormone secretion ability. Injection site reactions and serious allergic reactions are extremely rare.

Mrs. Hosack:
Okay, so you look at all of these tests together?

Dr. Maniatis:
Exactly. No one test gives us the full picture. We'll interpret the results in context—his growth chart, physical findings, genetic potential based on midparental target height, lab values, and imaging—to make a clear, accurate diagnosis and decide on next steps together.

Mrs. Hosack:
So if he fails the tests, you said he'll have to start growth hormone. But isn't that what bodybuilders use? That sounds risky.

Dr. Maniatis:
That's a common misconception, but I'm glad you brought it up. The growth hormone we use in pediatric endocrinology is carefully dosed to replace what the body isn't making on its own. With athletic abuse, super high doses of growth hormone are used to enhance performance. In children with true deficiency, growth hormone is a medically necessary therapy that supports not only normal growth but also metabolism and bone health. It's not about enhancement—it's about restoring what's missing safely and responsibly.

Dr. Maniatis:
So that is an easy way to assess and provide care to a patient.

Chapter 2

Dr. Maniatis:
Transitioning care from pediatric to adult endocrinology is another critical phase for patients with growth hormone deficiency. Optimizing this process ensures continuity of treatment, reassessment of growth hormone status, and long-term health outcomes.

In the next clinical scenario, we'll explore strategies to streamline the transition of care, foster collaboration, and empower patients through coordinated, age-appropriate management planning.

Now we're following the case of Sam, a 17-year-old with a history of idiopathic isolated growth hormone deficiency. Sam was diagnosed at the age of 13 years with a deceleration in growth velocity falling below the 4th percentile. A low IGF-1 and failed growth hormone stimulation testing confirmed the diagnosis. He began daily recombinant growth hormone therapy at 14 years and 3 months of age, starting from a height of 4'11". His response to therapy has been favorable, with a steady height gain of approximately 1 inch every 3 months. An aromatase inhibitor, anastrozole, was added to delay epiphyseal fusion and give more time for growth. Now 17 years old, Sam has achieved a height of 5'9", which is appropriate for his genetic potential based on midparental target height. He is now approaching a critical point in his care, the transition from pediatric to adult endocrinology services.

This case represents a common but complex scenario in which both clinical decision-making and communication strategies must be aligned to support patients and families through a safe and effective transition process. He is in the office today with his mom, Megan, to talk about next steps.

Dr Maniatis:
Hi, Sam. How are you?

Sam:
Hey. I'm good, thanks.

Dr. Maniatis:
Great. Well, I wanted to take a few minutes to talk about the next phase of your care. You're now 17 and approaching final adult height, and we have been preparing for you, in the past few visits, to plan the transition from pediatric to adult endocrinology.

Sam:
What exactly does that mean? Will I not see you anymore?

Mrs. Broeckert:
He's been doing well on treatment. Will that change?

Dr. Maniatis:
That's a great question. Many children with idiopathic isolated growth hormone deficiency, like Sam, need reevaluation once they've finished growing and have a bone age of around 16. There's a possibility that his growth hormone levels have normalized, which is very common. So before we make any decisions about continuing therapy into adulthood and the possibility of needing an adult endocrinologist, we'll reassess whether he still meets the criteria for growth hormone deficiency.

Sam:
And how do you do that?

Dr. Maniatis:
We'll temporarily stop therapy and do a month's washout with nothing in your system and then repeat the growth hormone stimulation testing now based on the adult criteria. This helps us see how your body responds without the support of medication, as it has implications for bone density, muscle strength, the cardiovascular system, and body composition. Based on that testing, if you still show clear signs of deficiency, we'd recommend continuing treatment, though the goals shift from supporting growth to maintaining metabolic health, bone density, and quality of life.

Dr. Maniatis:
During the transition from pediatric to adult care, repeat growth hormone stimulation testing is recommended for most patients who are diagnosed with childhood-onset growth hormone deficiency and treated with growth hormone therapy, except for certain high-risk groups.

Patients who need repeat growth hormone stimulation testing include children and adolescents with idiopathic isolated growth hormone deficiency. The majority of patients with idiopathic isolated growth hormone deficiency require retesting at the end of growth, when near-final height is achieved and pubertal development is complete to determine if growth hormone deficiency persists into adulthood. Idiopathic refers to not having clear structural or genetic cause, and isolated refers to no other additional hormone deficiency. A substantial portion of these patients will have normal growth hormone secretion on retesting and do not require ongoing growth hormone therapy as adults.

Patients with deficiency of only 1 additional pituitary hormone—those who, in addition to growth hormone deficiency, are deficient in only one other pituitary hormone, not multiple—should also be retested. Patients with ectopic posterior pituitary—this structural abnormality is not consistently associated with permanent growth hormone deficiency, so retesting is appropriate. Patients who have received brain irradiation, these individuals are at risk for evolving pituitary dysfunction and should be retested, as not all develop permanent growth hormone deficiency.

Patients who do not need repeat growth hormone stimulation testing:

- Patients with 3 or more pituitary hormone deficiencies. Those with 3 or more pituitary deficiencies and low IGF-1 levels are considered to have permanent growth hormone deficiency and do not require repeat growth hormone stimulation testing at transition.
- Patients with confirmed genetic mutations or irreversible structural lesions affecting the hypothalamic pituitary axis. Retesting is not needed if growth hormone deficiency is due to a known genetic defect or a clear permanent structural abnormality other than an ectopic posterior pituitary.

Timing and protocol: retesting should be performed after growth hormone therapy has been discontinued for at least 1 month and when the patient has reached near-final height with a growth velocity of less than 2 cm per year and is pubertally mature.

Let's return to our conversation with Sam and his mother.

Mrs. Broeckert:
Do you think Sam will be ready to take responsibility for managing his medication?

Dr. Maniatis:
That's something we'll assess together. Transition readiness is key. It includes helping Sam understand his condition, manage his medication, and feel confident talking to his providers. Based on our discussion, I know that he has been taking the shots himself with minimal assistance.

Mrs. Broeckert:
Right.

Dr. Maniatis:
We can use a few tools, like transition checklists, to guide this process and make sure he's supported emotionally and practically. We can also discuss potentially switching to a long-acting growth hormone at a different visit.

Sam:
Will I continue to see you?

Dr. Maniatis:
Well, we will test you here, and we'll guide you through every step. But once we confirm the path forward and if you need to continue with therapy, we'll coordinate with an adult endocrinologist to ensure a smooth handoff. Our nurse can provide you with a transition guide to help you understand the process, know what to expect, and consider important questions along the way.

Dr. Maniatis:
So as you saw above, transitioning care isn't just about switching providers—it's about empowering young adults like Sam to take ownership of their health. With the right tools, a supportive team, and a stepwise approach, we can ensure that this next chapter builds on the progress we've already made.

Most patients with idiopathic isolated childhood-onset growth hormone deficiency should undergo repeat growth hormone stimulation testing after reaching near-final height and discontinuing therapy for at least 1 month. Retesting is not necessary for those with 3 or more pituitary hormone deficiencies or confirmed genetic or permanent structural causes.

Clinicians should assess transition readiness by evaluating the patient's ability to manage their condition and communicate with providers. Tools such as checklists and educational handouts can help ensure a smooth and supported shift from pediatric to adult endocrine care.

Chapter 3

Dr. Maniatis:
Now let's go back to Mrs. Hosack and her son. In the first vignette you saw me counsel Mrs. Hosack about the diagnostic pathways.

Matthew went on to fail 2 growth hormone stimulation tests and was started on daily growth hormone. He has been on daily injections for the past 3 years but now he's beginning to get fussy before his injections and has developed a phobia of injection time. Adherence is getting to be a challenge, and he and his mother are interested in switching to long-acting growth hormone. In today's visit, we'll be talking all about how to get him started on that switch and how to monitor from there on. So let's dive in.

Dr. Maniatis:
Hello, Mrs. Hosack, good to see you again. So what brings you in today?

Mrs. Hosack:
Hello, Dr. Maniatis. Matthew has been on daily growth hormone injections for some time now, and until recently, he was doing fine with it, but now it's becoming a struggle every single night. He gets anxious as soon as he sees the pen. He's calling it “injection time,” and it's like we're gearing up for battle. Last night, he cried and told me he didn't want to grow anymore if it means another shot.

Dr. Maniatis:
I'm really sorry to hear that. Injection fatigue can be tough, especially in kids who've been on long-term treatment. It's more common than people think, and you're not alone in this.

Mrs. Hosack:
I understand he needs this to grow and stay healthy—believe me, I do—but I can't keep forcing him like this. It's becoming traumatic for both of us. Is there anything else we can consider, maybe something that doesn't need to be given every single day?

Dr. Maniatis:
Yes, absolutely. It sounds like Matthew might be a good candidate for a long-acting growth hormone option. These formulations are designed to be given once weekly instead of daily, which can really ease the emotional burden and improve adherence. If he's otherwise doing well on therapy, this could be a very reasonable next step.

Mrs. Hosack:
Yes, that would be such a relief—for him and for us. I just want him to keep progressing without the fear and stress every day.

Dr. Maniatis:
Several long-acting growth hormone products are now approved globally, each using distinct mechanisms of action to extend half-life and alter pharmacokinetics.

Three are approved in the US. While all 3 agents are designed to reduce injection frequency and improve adherence, they differ significantly in structure, mechanism, and formulation.

Lonapegsomatropin uses transient PEGylation. It's a prodrug with a polyethylene glycol carrier, a linker, and somatropin. Once in the body, the linker dissociates, releasing unmodified somatropin.

Somapacitan uses a noncovalent albumin-binding strategy. The somatropin molecule has a single amino acid substitution with a hydrophilic spacer that then binds the serum albumin.

Somatrogon is a fusion protein. The somatropin molecule has 3 carboxy terminal peptides from human chorionic gonadotropin, or hCG, attached to it.

When initiating long-acting growth hormone, we start with weight-based dosing. This is consistent with how we approach daily growth hormone but with a few important nuances.

Now a key caveat here—consider a lower initial dose in certain populations. Specifically, this applies to children with obesity or those at increased risk of hyperglycemia, intracranial hypertension, severe growth hormone deficiency, or those with known genetic or chromosomal abnormalities. These individuals may have heightened sensitivity or altered pharmacodynamics, and starting conservatively can help minimize adverse events.

Just like with daily growth hormone, dose titration for long-acting growth hormone is ultimately at the provider's discretion. We base adjustments on a range of clinical indicators, including IGF-1 levels—if these rise above the target range, that's our first signal to reassess the dose; annualized height velocity—are we seeing the expected growth; pubertal staging—as the child progresses through puberty, growth velocity changes; bone age, which gives us a sense of maturation versus chronologic age; and estrogen supplementation in girls, which can impact growth and growth hormone responsiveness. If you're seeing elevated IGF-1 levels, the general recommendation is to reduce the dose by about 15% to 20%.

This brings us to an important pharmacologic principle. Because each long-acting growth hormone molecule has its own unique pharmacokinetic and pharmacodynamic profile and its own molecular weight, the per-milligram dosing calculations are not interchangeable. That means you can't compare milligram doses between different long-acting growth hormone formulations or between long-acting growth hormone and daily growth hormone on a 1:1 basis. Direct milligram-to-milligram comparisons are simply not appropriate.

It's important to understand the pharmacokinetics and pharmacodynamics of long-acting growth hormone therapies when monitoring IGF-1 levels. IGF-1 levels fluctuate over the dosing interval and the timing of lab sampling is critical for accurate interpretation.

For daily growth hormone, IGF-1 levels remain relatively stable across the week with minor day-to-day fluctuations. For long-acting growth hormone, IGF-1 rises to a peak 2 days after the injection then gradually declines to a trough before the next dose. Point B represents the average IGF-1 level, which is the target for long-term monitoring. The consensus recommendations suggest drawing blood near the average IGF-1 timepoint: lonapegsomatropin, day 4.5; somapacitan, day 4; somatrogon, day 4.

Let's return to our appointment with Matthew's mother.

Dr. Maniatis:
Let's walk through what that transition might look like. You would have to give it every week. The great thing about it is that, since it is weekly, you won't have to worry about giving him shots every day.

Mrs. Hosack:
Is it as good as the daily injections?

Dr. Maniatis:
Yes. Studies have shown that long-acting growth hormone works just as well as daily growth hormone. The main difference is how it moves through your system. With daily growth hormone, your IGF-1 levels stay pretty steady. With long-acting, the levels rise after the shot, peak a couple days in, then drop before your next dose. That's totally expected. It's how the medication is designed.

As far as safety is concerned, to date, the safety profile of long-acting growth hormone is comparable to that of the daily growth hormones.

Dr. Maniatis:
In early clinical experience with long-acting growth hormone, it has been observed that patients already accustomed to traditional daily growth hormone therapy may exhibit greater hesitation to transition to long-acting growth hormone compared to treatment-naïve individuals who may be more open to newer therapeutic options. This reluctance often stems from familiarity with daily growth hormone regimens and uncertainty around the pharmacokinetics, dosing adjustments, and monitoring protocols associated with long-acting growth hormone.
Across all pivotal phase 3 trials, the 3 currently approved long-acting growth hormone therapies—lonapegsomatropin, somapacitan, and somatrogon—have demonstrated noninferiority to daily growth hormone in promoting annualized height velocity over a 52-week period. This evolving landscape underscores the importance of patient education and shared decision-making when introducing long-acting growth hormone as a therapeutic alternative.

When initiating a new long-acting growth hormone, the key principle is to avoid overlapping dosing. For patients switching from daily growth hormone, the previous dose should be discontinued the night before, ensuring at least 8 hours between the last daily injection and the first long-acting growth hormone dose. For those transitioning from another long-acting growth hormone formulation, it's important to discontinue the prior long-acting growth hormone at least 7 days in advance to prevent cumulative exposure.

When selecting a long-acting growth hormone, it's important to consider device features and dosing format. Regardless of which long-acting growth hormone is used, more than one injection may be needed regularly based on weight threshold.

Lonapegsomatropin uses an autoinjector with fixed weight-based cartridges. It has a 60.5-kg threshold for requiring 2 injections and the full dose is delivered per cartridge. Somapacitan and somatrogon are pen based. Their thresholds for 2 injections are 50 kg and 45 kg, respectively. They offer more flexible dose graduations but will more frequently require 2 injections based on partial remaining dosage in the pen to avoid waste.

Regardless of product, it is important to rotate sites to avoid lipoatrophy and always document day and time of the dosing.

When it comes to missed doses of long-acting growth hormone, each product has a specific makeup window. For lonapegsomatropin, the missed dose should be given within 2 days of the scheduled shot. For somapacitan and somatrogon, you have a 3-day window. If the dose is missed outside of that window, skip it and resume dosing on the next scheduled day. Most importantly, emphasize to patients and caregivers that consistent dosing is critical. Missing doses can reduce efficacy and pose potential safety risk, such as hypoglycemia.

As far as safety is concerned, to date, the safety profile of the long-acting growth hormone formulations is comparable to that of daily growth hormone. These formulations have several potential advantages over daily growth hormone, including the potential for improved adherence, reduced treatment burden, and positive impact on quality of life.

Now let's see if Matthew's mother has any more questions.

Mrs. Hosack:
Is the dose the same as what Matthew takes now?

Dr. Maniatis:
Not quite. The milligram dosing is different because it is a different molecule designed for once-weekly use. But don't let the higher number throw you off. We'll calculate a starting dose based on Matthew's current weight and adjust it based on his labs and how he responds.

Mrs. Hosack:
Okay, so will the monitoring be the same?

Dr. Maniatis:
We'll still check his IGF-1 levels, but we'll time the blood draw differently. Depending on the medication, we might ask you to come in on day 4 or 4.5 after the injection. That's when we get the most accurate reading. We'll use that to fine-tune the dose if needed.

Mrs. Hosack:
What about side effects? Do you think he'll have any side effects? We've been really lucky. He's done great on daily injections, but now that he's developing a fear of injections, I have to chase him down every night. I'm tired of all the crying, and it's painful to watch him go through this every day.

Dr. Maniatis:
So far, it's been very well tolerated. Nothing new or unexpected has shown up compared to daily growth hormone. The side effects profile of the long-acting growth hormone products is the same as that of daily growth hormone.

Mrs. Hosack:
Do a lot of people switch?

Dr. Maniatis:
Many do, especially parents whose children are taking multiple medications or those who are expressing difficulty with daily growth hormone adherence and are looking for something less burdensome. It's not for everyone, but it can be a good fit if you're consistent

with follow-up.

Dr. Maniatis:
When considering long-acting growth hormone therapy, think about children who may struggle with daily injections. These include teenagers and others with a history of poor adherence; children on multiple medications; or those with neurodiverse conditions, like autism or ADHD, who may find injections especially distressing; children or caregivers with injection-related fear or anxiety, where treatment could impact the parent-child dynamic; children with more than 1 home where coordinating treatment across locations can be challenging; those with busy schedules like travel for sports, music, or frequent sleepovers, where daily dosing becomes a burden; and families facing socioeconomic challenges for whom growth hormone therapy adds stress.

It's important to note that long-acting growth hormone is approved for pediatric growth hormone deficiency from as early as 1 to 3 years of age, depending on the country and product.

Currently, 3 globally approved long-acting growth hormone formulations—lonapegsomatropin, somapacitan, and somatrogon—have shown noninferiority to daily growth hormone in efficacy with comparable safety profiles.

While long-acting growth hormone holds promise beyond growth hormone deficiency, more data are needed. Until then, our best outcomes will continue to come from early intervention, thoughtful transitions, and collaborative informed choices with our patients and their families.

As we reflect on the cases we've discussed today, several themes come into focus. First, the importance of early diagnosis in growth hormone deficiency—timely recognition sets the foundation for better long-term outcomes.

Second, the need for structured, individualized transitions to adult care, especially as patients complete growth and move into new therapeutic goals focused on metabolic health and quality of life.

We've also seen how shared decision-making plays a central role, whether it's preparing a teenager to manage their care independently or supporting a family exploring alternatives to daily injections. For some, this includes transitioning to long-acting growth hormone therapy, which offers the potential for improved adherence, decreased treatment burden, and positive impact on quality of life.

Thank you for joining me for our Patient-Clinician Connection vignettes on growth hormone deficiency. I hope this program will be helpful for your practice.

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