Providing High Value Care: Examples from Pediatric Endocrinology - Pediatric Grand Rounds-10-31-2025-Meeting Recording

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Calderon, Delia started transcription

Ranch, Daniel 0:03

Looks great. Thank you.

0:05

Thank you.

Ranch, Daniel 0:34

All right, it's 7:30, so we'll get started. Good morning, everybody, and thank you for attending University of Texas Health San Antonio Pediatric Grand Rounds. A couple of reminders as you log in, please don't forget to mute your devices. Also, the Grand Rounds attendance code will be placed in the chat box periodically, so you.

You can just scroll through there for the code. Otherwise, it is my pleasure to introduce Doctor Amit Lahudi. He's an attending physician in the Division of Pediatric Endocrinology and an Associate Professor of Pediatrics at The Ohio State University. He's also the Program Director for the Pediatric Endocrinology Fellowship Program. Doctor Lahodi completed his medical school at Maulana Azad Medical College in New Delhi, India. He did his residency in pediatrics at Children's Hospital, Michigan before completing his pediatric endocrinology fellowship at Cullen Children's Medical Center in New York. He initially joined the faculty at Le Bonheur Children's Hospital in Memphis in August 2014 and was there.

There until June 2022, when he joined the team Nationwide Children's Hospital in Columbus, Oh. His clinical interests include type one and type 2 diabetes, medical education and high value care. He has published several research articles and reviews and presented at national and international conferences.

He has served in professional studies in various roles, including nationally as co-chair of the Paediatric Endocrine Society Drugs and Therapeutic Committee from April

2022 to May 2020, April 2020 to May 2022 and in the PDSS Education Committee. He was the recipient of the 2023 Paul Kaplowitz Endowed Lectureship by the AP and PAS, recognizing his work in cost-effective care. Doctor Lahouti, you have the floor.

Lahoti, Amit 2:15

Thank you so much for that warm introduction. And once again, thank you for inviting me to talk to you all. I'll be virtually, but hopefully we'll be able to connect today on this topic that I think goes much beyond endocrinology. The topic that I'll be talking about today is providing high value care with.
examples from pediatric endocrinology.
The objectives for my talk today is to understand what is high-value care, review some common scenarios in which screening endocrinology tests are ordered in primary care settings, and then apply some principles of high-value care to determine appropriate screening tests in these common endocrine scenarios.
A little bit of background of why we are wanting to talk about this topic. I think we are all probably aware to some degree about the rising healthcare cost in the United States. The healthcare costs in the United States have increased drastically over the past several decades, which used to be about like 5% of our entire GDP is ranging somewhere between 15 to 20.
Percent of our GDP over the past 50-60 years.
United States per capita healthcare spending is about two times the average of other wealthy countries. However, we are also sorely aware that this does not translate to better health outcomes in United States compared to several of these countries which spend less than us.
Healthcare experts have estimated that about 25% of total healthcare spending goes to unnecessary, ineffective, overpriced and wasteful services.
How do we determine if an intervention is wasteful or provides or does provide actually high value?
So to understand and answer that question, let's first understand what is high value care. So high value care is defined as a care which is the best for the patient with producing optimal results for the circumstance and is delivered at the right place, right price.
Another way to look at it is value is equal to quality over cost, where quality is includes the outcomes of the patient as well as patient experience and cost includes both direct and indirect costs.

Based on this equation, it would appear that value is directly proportional to quality and value is indirectly proportional to cost.
However, there are some nuances which I think will be helpful and important to know before we apply this principle. So let's use some visual examples to explain further if you have an intervention which is high in cost.
But does produce high quality. It produces high value, so simply high cost does not equal to low value.
On the other hand, if you have an intervention which is low in cost but does produce low quality, it also produces low value. So simply less costly interventions are not high value.
On the other hand, if we have something which costs a lot but does roduce low quality, definitely causes low value.
Our focus today would be to talk about how can we change this high cost intervention into a lower cost.
At the same time, focus on providing higher quality and thus change the value to a high value care.
Now with that background and knowing these principles, I think the time is ripe for us to examine our practices and reduce wasteful, cost non-efficient healthcare practices.
Today we will discuss about opportunities for doing so in evaluation of some common endocrine conditions.
Before we move forward, I want to put in my disclaimer that I'm not an expert at this topic. However, I'm a clinician and educator who feels passionate about talking about it with my peers and my mentees.
In the hope that my real objective is that may you all pause for a few seconds before you click OK or sign for the next order for your patient, whether the next order relates to endocrinology or not.
As I said, these principles of providing high value care apply to pretty much all the fields of medicine and the if I want, there's one goal that I have at the end of this presentation, it's for you all.
To at least think before you sign your next order and kind of try to think it with the lens of does it provide high value care.
All right. As we move forward, I am. I have.
Designed this presentation in in terms of cases. We'll go through several cases to highlight a few points, and these are the different cases that we'll talk about. We'll

start with the first case, which is it is the thyroid.
Uh.
So we'll start with case number one, which is a 13 year old boy with no past medical history. The patient is referred to endocrinology for abnormal thyroid function tests. The thyroid function tests are checked for excess weight gain over the preceding one year. He denied Constipation, poor growth, changes in skin or hair.
And there's no family history of thyroid disease. When you look at the thyroid function test, the TSH is 5.89 micro international units per mil, which is above the reference range of 0.4 to 4.5. The free T4 of 1.3 nanograms per deciliter, which is within the reference range, and a total T3 of 150 nanograms per deciliter, which is. Also within the reference range.
When you do a physical examination and review the growth charts, the growth chart shows the patient has been growing steadily. The weight percent and BMI percent have indeed increased in the past year, and the body mass index is now at the 98th percentile for age.
The patient does not have any goiter. The patient has ten or two pubic hair with bilateral testes about 6ML and hence is in early puberty. So in summary, your case one is the is a case of a child who who has an isolated mild TSH elevation.
With history of recent rapid weight gain.
So what are the differential diagnosis for isolated mild TSH elevation with normal free T4?
The one possibility is that this can be a normal variant. As we all know, any reference range for any blood test that you're looking at from the lab, the way that reference range is created is by including 95% of healthy individuals who have undergone that test.
So we do recognize that any reference range actually has 5% of healthy individuals, about 2.3% which will be having a value below the reference range, and about 2.3% who will be having a value above the reference range, like in any normal curve.
Who will be still healthy but have a value for the that particular blood test slightly outside the reference range. The second possibility is TSH elevation associated with obesity and this little diagram here kind of depicts how.
Obesity may cause a TSH elevation. Obesity is a condition of leptin resistance, so the body makes extra leptin, excessive leptin from the fat cells, and these high high leptin levels stimulate TRH release from the hypothalamus, which in turn.
And leads to TSH release from the pituitary gland and hence we end up having a

condition in which obesity can cause high TSH levels without an underlying thyroid pathology. And the reason we know this is obesity related is because in good in. Well-planned studies, when these patients were made to lose weight through lifestyle intervention, the TSH did come back down to normal. So mild TSH elevations can be seen just with obesity without an underlying thyroid disease. The patient can also have early compensated or subclinical hypothyroidism indeed.
This could be the start of Hashimoto thyroiditis in this patient and we are seeing it at a very early state. Or this patient could be recovering from CQ thyroid syndrome. As you all may know, CQ thyroid syndrome is a condition in which the thyroid gland. Indeed, slows down to conserve energy for more vital function. So if and a patient is critically ill, like in an ICU, you do not want to spend a lot of energy kind of maintaining body temperature or burning, burning calories for heat.
And that is why the body intentionally lowers down your thyroid hormone levels. And the classic picture of patients with CQ thyroid syndrome is a low TSH and a low or low normal free T4. However, as you recover from CQ thyroid syndrome and the patient recovers clinically.
The TSH does indeed go from very low to slightly in the higher range to kind of how I explain myself as kind of to wake up the sleepy thyroid gland. So you can see mild elevations in TSH as somebody's recovering from a critical illness or a sickness.
Now.
This is a common referral for endocrinology as a lab finding and I I want to kind of show some data that we collected during my fellowship several years ago now in New York is we actually looked at our reference for abnormal thyroid function tests and this is a pie diagram showing the various thyroid function test abnormalities. For which end token referrals were made and you see right at the top, high TSH with or without additional abnormality comprised almost 63% of our referrals. Interestingly, follow-up TSH levels was normal in over 50% of patients after about 6 to 8 weeks of the initial testing, and only 20% of these patients who were referred for suspected hypothyroidism truly had thyroid dysfunction. So the vast majority of these patients.
Did not have anything truly wrong with them. Some high value practices for thyroid function testing that I do want to highlight based on this case is weight gain alone is unlikely to be a symptom of hypothyroidism in a child growing at a steady pace, that is if the patient has stable height percentile and normal for age growth velocity.
If you're screening for primary hypothyroidism, TSH with or without free T4 is the

preferred test and T3 level is not needed to be checked for hypothyroidism testing or treatment monitoring.
It is also to note that mild abnormalities in TSH with normal free T4 in an asymptomatic child often resolve spontaneously. So in terms of kind of putting this through the equation of value or equal to quality over cost, this is relatively a high cost intervention given the number of thyroid function.
Test these patients end up getting because of that initial abnormal test and does not bring much value to you.
In a recent article by Allen et al, they did put this explain this concept a little bit further of what is probably an appropriate process when you do find abnormal thyroid function test. I think they even before you perform tests, make sure you're doing the testing in an appropriate setting, but if you are performing the test.
Or clinical concerns and you do find a low free T4 and an elevated TSH, then refer to endocrinologist. Patient most likely has true hypothyroidism. If this patient has low free T4 but the TSH is normal or low.
The next step would be to do a free T4 by direct dialysis. Now you may wonder what is direct dialysis versus the free T4 assay that you may get it in your own lab in in hospital. Most hospitals do not do free T4 by direct dialysis. Direct dialysis is a much more time consuming, labor intensive and expensive test.
However, it does measure free T4 directly. And how does it differ from the quote UN quote direct free T4 measurements in most commercial labs? Because free T4 constitutes about less than 1% of your entire.
T4 in the blood. So most of your T4 is actually bound to proteins and less than 1% is the free T4 component. So when you are measuring that, most commercial labs actually estimate the free T4 using various assays. So it's not a direct measurement of the actual free T4 level just because it's such a small end amount.
However, that leads to some possible interferences and there are several studies that have been done that showing the same blood sample. If made to measure free T4 in multiple different labs, you get very different values. Certain labs have the test better calibrated than the others.
However, if you do end up in a situation where your lab findings do not match up with what you were expecting for the patient, especially for free T4, do consider a direct free T4 measurement in which they actually use the dialysis membrane to actually dialyze out the free T4 and then measure it. It's generally a standard.

Matos, Johanna 15:33
Yeah.

Lahoti, Amit 15:36
Out test to a specialty endocrine specialty laboratory and if the free T4 by direct dialysis comes back as low, then this patient should be referred to endocrinology because may truly have central hypothyroidism in this case because the free T4 being low and the TSH not being elevated is an inappropriate TSH.

Matos, Johanna 15:41
Right.

Lahoti, Amit 15:56
response. So you are then concerned about a pituitary or hypothalamic disorder. However, if the free T4 comes back normal, no need to further work up. The other possibility could be that the free T4 is normal, but the TSH is elevated below 10, so it is a mild elevation in TSH instead of referring these patients immediately.
To endocrinology, it may be reasonable to repeat the thyroid function test in about two to three months because in several cases the TSH is normalizes or starts to normalize on its own and you avoid unnecessary consultation and expensive cost to the family as well as.
Interpretations in the family. Several of these families come up very worried because they are concerned that the child truly has a thyroid disorder. On the other hand, when you repeat these blood tests and the TSH is stable or is trending up, then you may indeed have a problem and then go ahead and refer them to endocrinology for further evaluation.
And last scenario is you have a free T4 which is normal, but the TSH is over 10. This looks like compensated hypothyroidism. And then yes, these patients should be referred to endocrinology for further evaluation.
So follow up of our case, the history revealed that for the past one year the child has had a change in diet with increased fast food as mother had to pick up an extra job. He is also not enrolled in basketball team over this past year and the repeat thyroid function test about 8 weeks later showed a similar TSH of about 5 micro international units per mil and the free T4.

Was in the normal range. The diagnosis for this patient was obesity associated TSH elevation. Now I will say some people may consider checking thyroid autoimmune antibodies in some of these patients, especially if there is a family history present for autoimmune thyroid disease.
So you can check anti TPO antibodies and antithyroglobulin antibodies if you want to distinguish obesity associated TSH elevation and autoimmune thyroid diseases.
All right, we're done with thyroid. This next case is a case of insulin resistance.
So this is a 16 year old boy who's referred for elevated insulin levels. Another frequent referral to endocrinology. 3 year old history, sorry, three-year history of progressive weight gain and growth spurt. The rate of weight gain has exceeded, however, the rate of height gain and the BMI has increased from.
85% to greater than 99%. The child has poor diet and sedentary lifestyle, no polyuria or polydipsia. The labs at the primary care physician's office showed fasting glucose of 97, hemoglobin A1C of 5.6%, both of which are normal. However, the patient's insulin level fasting insulin level was 55 micro international units.
A mill, which is elevated based on the reference range.
So in somebody you have a 16 year old boy with severe obesity and with a history of recent weight gain who presents with who has a kinthosis and has high insulin level.
So what does he have? Insulin resistance, insulin resistance, insulin resistance.
Now it's important to understand something about insulin resistance that acanthosis nigricans is a clinical sign of insulin resistance. With increasing insulin resistance, body typically responds by releasing more insulin in the blood to maintain normal glucose levels.
This is a well-renowned kind of well-established chart to kind of show how this works and I'm going to walk you through this for people who are not familiar with it. On the X axis you have insulin sensitivity. So the more to the left you are, the less insulin sensitive or more insulin resistant you are.
And on the Y axis you have insulin release. So if you are on this white chart, which is in the white line, sorry in the green curve, depending on how insulin sensitive you are, you do you do make insulin appropriately. So if you are more insulin sensitive, you'd need less insulin if you are less insulin.
Sensitive, you do make more insulin. So as long as you stay in this curve you may have and as you move from right to the left, that is when as the weight increases for a patient, they often move towards left and up on this curve because they are having lesser insulin sensitivity or greater insulin resistance.

And they compensate by making more insulin. And as long as patients are along this line, they do not develop diabetes. Essentially, if your body can compensate for the insulin resistance by making more insulin, you are still able to maintain your glycemia. The problem happens when the pancreas.
Is unable to keep up with how much insulin it needs and the insulin production goes down. So then you transition from having normal glyphemic control to impaired glucose tolerance and then eventually to type 2 diabetes. So the insulin levels are not clinically used to determine management plan and.
Insulin resistance. So what is clinically used in these scenarios? Lab testing should be directed towards screening for type 2 diabetes and not to proving insulin resistance, because the physical presence of akanthosis is enough to prove that this patient has evidence of insulin resistance.
So question comes what you we should screen for type 2 diabetes in appropriate scenarios and what are the appropriate scenarios for screening for type 2 diabetes in asymptomatic children and adolescents. It is based on their individual risks. So the screening should be considered in youth greater than 10 years or which are pubertal who have overweight which is greater than 85th.
Percentile of their of the BMI or obesity greater than 95th percentile for BMI and who have one or more additional risk factors including either a maternal history of diabetes or gestational diabetes mellitus during the child's gestation, family history of type 2 diabetes and 1st or second degree relative high risk race, ethnicity or ancestry.
And signs of insulin resistance or conditions associated with insulin resistance and acanthosis nigric cancer is right up there. So if you're worried about somebody having type 2 diabetes, then screen accordingly with a fasting glucose and I'll come to that in a minute.
The Hba-1C or fasting plasma glucose or insulin level is not a useful test to diagnose prediabetes or diabetes and should not be done in clinical settings and we should avoid routinely measuring thyroid function tests or insulin levels in children with obesity. So again in if I put this again in the equation.
Measuring insulin level is relatively higher cost, does not bring enough value and hence does not provide high value care for these patients in whom you're concerned about prediabetes or type 2 diabetes.
All right, I'll move on to our third case, which is this patient has a vitamin D level which would not rise.

Now this is a 10 year old boy who's referred for low vitamin D level and abnormal PTH. This patient's average height and weight has average height and weight with stable growth and weight gain. He has a healthy, balanced diet with vegetables, fruits and lean meats.
He's, however, lactose intolerant and does not drink any dairy and does not like seafood concerned for possible vitamin D deficiency. The pediatrician appropriately does lab testing for vitamin D and it shows.
25 hydroxyvitamin D3 of three nanograms per ML. There were also tests that were done for 125 dihydroxyvitamin D, however, which was 70 picograms per ML, which was in the normal range, a calcium level which was 9.4 milligram per deciliter. Again the normal range. A PTH was actually also.
Check, which was low at 10 picograms per mil, where reference range being 15 to 65. The comprehensive metabolic panel was normal including the alkaline phosphatase and there were no clinical signs of rickets. He was then treated with a once weekly dose of ergo calciferol 50,000 units once weekly and.
For 12 weeks and this boy was happy getting that vitamin. Upon follow up in three months, his vitamin D level was rechecked and was as follows. 25 hydroxyvitamin D3 still at 5 nanograms per ML. Calcium was normal and the PTH was similarly at 12 micrograms per ML.
So in summary, you have a 10 year old boy with vitamin D deficiency due to poor intake. However, his levels do not improve with vitamin D replacement. He also has a low PTH. So what is the etiology of his persistent low vitamin D and PTH levels?
To understand this better, I will take us all for a quick brief review of vitamin D metabolism.
This actually came in one of my peds board exams, so I I generally never forget this that the question asks what is the precursor for vitamin D in our skin. So the answer is 70 hydrocholesterol. So 70 hydrocholesterol when.
Exposed to UVB rays gets converted to cholecalciferol or vitamin D3 in our skin. You can also get cholecalciferol, vitamin D3 in diet and through animal products, or you can get ergocalciferol. Sorry for the typo, it's ERGO ergocalciferol or vitamin D2 through plants.
Sources and any vitamin D3 or D2 you get in our body gets 25 hydroxylated at the liver to make 25 hydroxy vitamin D There's no negative regular control regulation at this step, and the conversion directly depends on substrate availability.
This vitamin 25 hydroxyvitamin D is bound to vitamin D binding protein and is the

storage form of vitamin D, which is how it stays in our body.
For further use of this vitamin D, it has to be one alpha hydroxylated at the level of kidneys to make 125 dihydroxy vitamin D or also called as known as calcitriol as the active form of vitamin D This is also bound to the vitamin D binding protein, but this is the.
Vitamin D metabolite, which eventually binds to the vitamin D receptors to produce vitamin D related actions. The conversion of 25 hydroxyvitamin D to 1A125 dihydroxyvitamin D is tightly regulated by several factors.
Including PTH, which stimulates or activates this conversion and calcium phosphorus, FGF 23 and 125 dihydroxyvitamin D itself inhibits this conversion from 25 hydroxyvitamin D to 125 dihydroxyvitamin D as kind of a feedback loop to maintain and regulate.
The levels of activated hormone.
So you see there are two different forms of vitamin D you can get depending on the source of vitamin D, and as a result you get both 25 hydroxy vitamin D3 and 25 hydroxy vitamin D2 which could be present in our blood. Now assays for vitamin D should be capable of measuring both D2 and D3.
Derivatives. Most commercial labs either have chemiluminescent protein binding assays or radioiminoassays, which use the monoclonal antibodies. This continues to remain as an area for more work and improvement because the assays have struggled with variable results and lack of reproducibility whenever you measure by.
Vitamin D So two labs measuring the vitamin D level for a same person at the same time may get slightly different results. So understanding the limitations of the lab, whatever lab test you are getting done is also equally important to ordering the knowing the right lab.
So this answers one of our questions, which is I think this patient was getting Argocalciferol, which was D2 and we were measuring 25 hydroxyvitamin D3. So I'll take that back for a minute just to make sure we catch captured that this patient had received Argocalciferol and the lab had measured D3 initially.
Initially as well As for follow-up and D3 would not rise in this patient, but if the lab had actually reported total D vitamin D, we would have gotten a much better response as long as the patient took the medication.
All right. The another question that came up was this patient's PTH measurement.
And for those of you who are not seeing this normogram, it's a very interesting normogram that I want you to guys to again walk through. On the X axis you have

total serum calcium here and on the Y axis you have PTH levels.
And this green line kind of shows how a healthy PTH level may change based on the calcium levels. So what is an appropriate response if your calcium level is as long as as your calcium levels drop, you should have a spike in your PTH if your calcium levels are high.
Should have a suppression in your PTH level. However, you see this steep of normalcy. That means when your calcium level is a normal range, you can have a very variable PTH response and sometimes honestly slightly even below this square.
So a PTH level cannot be interpreted or is honestly not needed when your calcium level is normal and should not be performed in the first go.
So So what are the high value practices for screening calcium and vitamin D disorders? 25 hydroxyvitamin D total is the best measure of vitamin D status and should be used whenever needed to screen as well As for monitoring these patients who are on treatment. Serum calcium, phosphorus, magnesium, alkaline phosphatase levels will additionally help.
Assess the biochemical profile of a patient with vitamin D deficiency and PTH level is not routinely needed or useful if electrolytes are abnormal. Hence do not routinely measure 125 dihydroxyvitamin D unless the patient has hypercalcemia or decreased kidney function also. So if you have to measure one test.
For assessing somebody's vitamin D status, it should be total 25 hydroxy vitamin D.
Alright, we'll transition to our next case, which is case #4 and it's early puberty, so everybody please brace yourself.
This is a 7 year old girl who's referred for concern of precocious puberty. The patient has had pubic hair growth since about six years old and the parents are coming in because of concern for precocious puberty because mom is concerned the patient may have a period anytime soon.
The patient, however, has not had any growth acceleration. Mother had menarche at age of 10 years and as I said, she's concerned that the child will also start soon. The labs that were sent with the referral included an FSH of 1 million international units per mil, which was within the Tanner 1 reference range and LH of 0.02 million international units.
Per ML, which was also in Tanner stage one, had an estradiol of less than 5 picograms per ML. On physical examination, the girl had a normal BO body mass index, had Tanner 1 breasts and Tanner 2 cubic hair. In summary, you have a 7 year old girl for concern of precocious puberty. However, exam is consistent with

premature.
Adrenarchy and the gonadotropins and estradiol are in pre-pubertal range. Now that I have spoken these two different terms, precocious puberty and premature adrenarchy, I do want to spend a couple minutes talking and differentiating between the two that will help us come to our high-value take-home messages for this from this patient.
So what is precocious puberty? Precocious puberty is defined as the early activation of the hypothalamic pituitary gonadal axis, which in physical exam manifests as presence of breast development in a girl and testicle enlargement in a boy with or without other signs of puberty.
Now, for it to be considered precocious, changes have to happen at less than 8 year old in a girl or less than nine years old in a boy. It is also to be noted that growth spurt is typically present in girls with the start of true precocious puberty, though it may not be apparent in boys early on because.
Growth spurt in boys is typically a late pubertal event. Now we contrast this with premature adrenarche, which is defined as the activation of the adrenal glands, resulting in the early onset of secondary sexual characteristics, specifically pubic hair, axillary hair, acne, body odor, but is not associated.
With growth spurt or breast or testicular enlargement. If you do see in addition to the body hair, if you also see gonadarchy or testicular enlargement or breast enlargement, then this patient does not have premature adrenarchy but rather true central precocious puberty.
And again, for it to be considered premature, changes have to happen at less than 80 year old in a girl and less than nine years old in a boy. I'll dive further in premature adrenarche a little bit in terms of what causes premature adrenarche in the next slide.
So in terms of etiology, premature adrenarche which this patient had.
What are the different possible causes? So it could be due to an exogenous androgen or anabolic steroid exposure. This is 1 history which is very important to take, and honestly, if taken a good history, most of times you are able to rule in or rule out this possibility.
Though important to ask questions like does the parent or a grandparent in the family uses any hormone creams or gels that the child could have been exposed to, even if the child may not be directly applying the creams or gels on themselves.
Just by sometimes use laying on the same bed that the parent who had used topical creams of testosterone. If the child lays on the same bed, he may be exposed to it.

Honestly, sometimes laundering the clothes together for both the parent and the child may expose the child to the topical.
Testosterone which eventually gets systematically absorbed in the patient to produce changes. So taking a good detailed history about possible exogenous exposure is important. The other possibility is non classical CAH or other rare disorders of adrenal steroid metabolism you all are probably familiar with.
The classical CAH, which we screen for in the newborn screen and these patients have to be immediately put on treatment with cortisol and flutrocortisone to prevent adrenal crisis. However, if the deficiency of these adrenal enzymes is not absolute, these patients may go on to have.
Fair amount of cortisol and mineralocorticoid production, but do produce excess androgens, which can present itself as premature adrenarchy in older age group. The third possibility is a virilizing tumor either of the adrenals or of the gonads, which can also produce.
Virilizing changes, including excess body hair. However, typically these patients would also have other signs of virilization, including in a girl it can lead to clitoromegaly. In a boy it can lead to penile enlargement and excess body hair or acne.
And typically also would lead to growth spurt. So typically the virilizing tumors have more features than a patient with idiopathic premature adrenarchy. And that's why I put in these devil's horns in there because these patients.

35:19
OK.

Lahoti, Amit 35:28
The physical changes are generally remarkable and the 4th possibility is the idiopathic premature anarchy, which basically says that we have ruled out other causes of premature anarchy and that is the current standard of care that for you to diagnose with somebody with idiopathic premature anarchy.
When you have ruled out the other possible causes of virilization.
Now there are some key similarities and differences between premature adrenarchy and precocious puberty, and I tried to summarize both these conditions in this in this slide. And this is a good take home slide for the trainee especially is when you see premature adrenarchy and precocious puberty, it is in part.

Suspicion for precocious or early puberty. It's important to differentiate at the very minimum is this patient having premature adrenarch or precocious puberty and that will be based on first your clinical changes. So if there are only adrenal changes present including pubic hair, axillary hair, musty body odor.
With no gonadal development, then you most likely have premature adrenarchy if it occurs less than eight years in a girl or less than nine years in a boy. And on the other hand, if you have changes due to gonadal development, that is breast or testicular enlargement and other pubertal signs, then you probably have picochous puberty.

Lynch, Jane L 36:38
So.

LA **Lahoti, Amit** 36:45
Both these conditions are more common in girls than in boys, and more commonly idiopathic in girls and higher chances of organic pathology in boys. Typically, premature eternality is not associated with any growth acceleration, and growth acceleration is usually present in patients with precocious puberty.
The lab evaluation for these conditions is not identical and depending on our differential diagnosis. So for our premature adrenarchy we had a differential diagnosis for non classical CAH. That is why we are going to screen with 17 hydroxyprogesterone. We had differential for virilizing tumors. That is why we will check for testosterone and DHGS sulfate.
And on the other hand, in precocious puberty, when you are concerned about true activation of the hypothalamic pituitary gonadal axis, you do screen with LHFSH, estradiol or testosterone.
Now the bone age advancement is often absent, but can be seen in patients with high BMI when it is premature adrenarchy. However, if your patient has precocious puberty, bone age advancement is often present.
So bone age is generally not very helpful as a screening test in premature adrenarchy. Unless you are eventually, unless you are concerned about based on your screening test that this patient has non-classical CAH or a virilizing tumor, then a bone age will probably be helpful to figure out how long this has been happening and what kind of prognosis does this patient have.
Have in terms of height outcome.
So when we think about organic pathology versus idiopathic premature adrenarchy,

we do just learn. We didn't just learn that the girls are more often diagnosed with premature adrenarchy or develop and hence are more often referred than boys. So most of the referrals for premature adrenarchy are indeed girls.
And premature drenarchy is idiopathic in vast majority of girls. Nonetheless, the current screening protocols for premature drenarchy do not stratify our evaluation based on the risk of organic pathology. So it made me wonder, are we truly providing high value care by using the same screening protocols for everybody under the?
Son who developed premature anarchy irrespective of their risk.
So it made me actually look at our referrals back when I was in Memphis and we conducted A retrospective study looking at our patients who were referred for premature adenarche. We had a total of 273 children who were referred with premature adenarche. 266 of these subjects had idiopathic premature adenarche. One subject that was.
Was diagnosed with non-classical CAH, two with late onset CAH and four subjects exogenous androgen exposure. While all the patients underwent lab evaluation, which was pretty similar, non-classical CAH or late diagnosis of CAH was seen in less than 1% of subjects. None of these patients were black and none had virilizing.
To.
So the need for evaluation is it's same for all for premature and it's an important question to ask because this laboratory evaluation comes at a high cost.
You talk about prices for each of these tests and I actually inquired the pricing at several institutions as well as several commercial labs, including the possibility of self-paying and the roughly the cost of if you add up all these costs, it comes out to be around 417 to $1100 per patient for one.
Set of these lab testing and you add on these costs with a cost for endocrine consultation, phlebotomy charges, wage lost when multiplied with the number of patients equaled evaluated, the cost quickly adds up.
So.
Is should the end of premature adrenality evaluation be the same for all patients? It can potentially be stratified in girls, especially at greater than six years of age based on individual characteristics of patients. There are some things that we do know that there are certain patients who are at a higher risk for developing.
High risk of having an underlying pathology and in all kind of if we look back at the differential diagnosis for premature adrenarchy, we talked about exogenous

exposure, we talked about virilizing tumor, we talked about non classical CAH and the idiopathic premature adrenarchy, the ones which are the hardest to distinguish based.
On just physical examination alone are the non-classical CAH patients and the incidence of non-classical CAH is not identical throughout the entire population. So I think there is need for us to kind of revisit our evaluation for premature adrenarchy by.
Kind of understanding what is my patient truly at risk for. I do not have right answer for this. However, it's not a bad thing finding out that you don't have all the answers, you just need to start asking the right questions. So this is an area that needs more studies to understand how we can best stratify our approach so that we don't miss out pathology.
But can reduce the number of unnecessary evaluations that we're performing for premature adrenarchy.
So some take home points for high value practices for evaluating premature adrenarchy is #1 to know that adrenarchy and gonadarchy are two parallel but separate processes and growth spurt and menarchy in a girl is tied to gonadarchy and not to adrenarchy. So in this patient honestly speaking as regards her concern of early menarchy.
She could have been reassured that their child is not going through gonadarchy and so while we need to possibly think about what we need to do about adrenarchy evaluation, but don't be worried, this patient is not at risk of having an early period based on what we are seeing right now and hence you should avoid ordering LH and FSH and either estradiol or testosterone.
for children with pubic hair and or body odor, but no other signs of puberty.
The testosterone may be needed as a part of your evaluation for premature adrenarchy. However, generally estradiol is not needed in a girl who has with premature adrenarchy alone.
All right, but towards the end, and this last case is a child who has not grown in the past year and he truly wants it now. All right, I have split this this case scenario into two cases, 5A and 5B. So we'll start with the case 5A first. This is a 13 year old boy who's referred for.
Concern for short stature. He's shorter than several of his teammates on his football team, and the parents want to know if he's a candidate for growth hormone therapy. The pediatrician, being listening to the concerns from the parents, did a screening

evaluation which included a complete blood count, a comprehensive metabolic panel, thyroid function tests.
And ESR, a celiac screen, IGF one and IGF BP3 as surrogate markers for growth hormone and they were all normal. He had a bone age study done which was 12.5 years at his chronological age of 13 years and hence was average.
On exam he was healthy appearing, asymptomatic and proportional. On a GU exam he was in early puberty with a testes of about 6 to 8 ML. So in summary, this is a 13 year old early pubertal boy who's shorter than average height but still growing steadily and is within the range for his family.
His mid parental height is at about 50th percentile. He has been growing more so around the 25th percentile. So what does this patient have is the height, which is those shorter than average is within normal range for his family. Now contrast this with the second case, which is a 13 year old girl who's referred for evaluation of poor. Growth and lack of pubertal changes. There are no significant medical issues except for frequent otitis media as an infant, and she's developmentally normal, good school performance except for geometry in which she struggles. So you do the similar test testing that the first patient got, including a complete blood count, a comprehensive metabolic path.
Thyroid function tests, ESR, celiac disease screen IGF1 and IGFBP 3, which are screening for various causes of growth failure or short stature in a patient. And as you notice on this growth chart, this patient's height had been at the lower end of the growth chart for entire life, significantly below the mid.
Parental height, which is still at the 50th percentile. This child was growing just at the 5th percentile and not until recently is when this patient actually started drifting further off from the growth chart and now is below the growth chart.
On the bone age evaluation, the child's bones are younger at 11 years old, and on exam she's well appearing with a normal GU exam of 10 or one breasts, but she does have 10 or two pubic hair. So in summary, this patient has a 13 year old prepubertal girl.
Because she does not have true breast development and puberty is truly when gonadarky happens with long standing height being plotted below the expected for family, but now also has growth failure. So further evaluation of this patient actually showed that this patient has a Kerotype of 45X or Turner syndrome.
So before we move further, I do want us to kind of understand and learn what is short stature, how do we define it to make sure we are kind of seeing our patients

with the correct lens.
So short stature is defined as if length or height Z score is less than -2 standard deviation, which corresponds to a height that is less than 2.3 percentile on our growth charts. That is called short stature and this patient should be evaluated.
If height is, however, above the 2.3 percentile or greater than the -2 SD, so still within the growth chart, generally no further specific evaluation is needed unless there are additional reasons for concerns, such as progressively decreasing height percentile.
So if a patient was initially growing at less 75.
5th percentile and now growing at 25th percentile. Although the height is greater than the -2 standard deviation, this patient should be evaluated because this patient is now having growth failure if the patient has dysmorphic features to be concerned of an underlying syndrome.
Has evidence of underlying systemic disease, so symptoms of IBD or symptoms of celiac disease, or if they are growing well below their genetic potential. So if a patient is growing consistently at the 10th percentile but the mid-parental height is at the 90th percentile.
Even though the growth may be steady, that is a reason for concern and they should be evaluated. That is, if the parents are very tall and the child is staying very short, it's it's worthy of further evaluation.
However, how well do we apply these principles when we are studying or when we are evaluating our patients or seeing them in our clinic? And are there some health disparities in how we apply these principles as I tried to highlight with the cases that I just presented?
The boy, although.
Was within range for his family, did undergo the same evaluation at around 13 years of age, while the girl who was significantly much shorter than her parents was watched for much longer before indeed an evaluation was done and the.
Literature on evaluation of our short stature is has abundant literature by some stalwarts in this field like Doctor Ada Greenberg who have looked at how we are, what are the health disparities in our evaluation and what they found is that males are referred for short.
Evaluation more often than girls, even with the same degree of shortness. So essentially if they have the same height standard deviation, boys are referred for evaluation much more often than girls and the data from US Kings database, which is the US data of world's largest post marketing surveillance database of pediatric

growth hormone.
Has more white boys, which are overrepresented, and black girls are particularly underrepresented among patients treated with growth hormone for idiopathic short stretch or ISS.
So this is this is the chart on the right side. It shows the observed versus expected frequency of subjects treated for idiopathic short stature for both black girls and boys and white girls and boys. So as you can see, the white boys are much significantly higher represented.
About 200% higher than what you would have expected, versus girls are much significantly underrepresented in this cohort.
Children of white race are overrepresented compared to expected rates for US Census data, and Hispanic black children are underrepresented for all indications of growth hormone therapy also in this. So if you look beyond even idiopathic short stature compared to the other causes of.
Receiving growth hormone including congenital growth hormone deficiency and small for gestational age patients continue to be over represented. So we currently need a lot of work to be done in terms of how we are providing equitable care to all our patients and not having biases of who deserves evaluation and who.
Does not deserve evaluation in our patients.
Some high value practices for evaluating short stature that I want to highlight is that short stature in a girl, even in the absence of other abnormal clinical signs or physical exam features, should be suspicious for Turner syndrome, and screening with a carer type should be strongly considered in a girl who is growing much below expected for their family or is below the growth chart.
And avoid ordering screening tests looking for chronic illness or an endocrine cause including CBC, CMP, IGF1, thyroid studies and celiac antibodies in healthy children who are growing at or above the 3rd percentile for height with a normal growth rate and with appropriate weight gain. And I will add to that appropriate for their family.
So our first patient honestly needed a lot of reassurance rather than an evaluation to prove that he was healthy. And again, going through this same paradigm of value is equal to quality versus cost. When I look at our first patient, a karyotype is relatively a low cost intervention.
For which produces a very high quality, very high value to early diagnosis and management of Turner syndrome, while doing all these additional tests are expensive for somebody who does not have the right indication and hence does not

provide high value.
So some take home messages and practical tips for the for everybody listening in. More testing does not always equate to better care. I would encourage everybody to incorporate discussions on providing high value care in your clinical care decisions and case discussions.
And consider using costs of individual tests as a visual reminder to practice thoughtfulness when ordering tests. So certain clinics have kind of actually reached out to their lab and asked for what are the what are the costs for some of the common tests that I order in my clinic. If you can let me know the cost, I'll print them out in a sheet and just.
Put it there in your workroom. Just looking at the cost may help you re rethink. Do I really need this test or not? Here are some references for additional reading and thank you so much for inviting me and patiently listening in and being engaged with on today's discussion. This is a QR code for my contact information.
I encourage everybody, if this is an area that kind of moves you or you're passionate about, reach out to me, connect and we can, I'll be happy to collaborate. Thank you so much.

Ranch, Daniel 52:24
Doctor Lahuri, thank you for that wonderful presentation and very practical as well. If you have a question, please feel free to raise your hand or enter in the chat. And I see Doctor Lynch has a question. Go ahead and unmute yourself, Chief.

Lynch, Jane L 52:37
All right. Am I on the? I don't know if my. Oh, here, my camera's working. So happy Halloween, everyone. I'm just back from Paris and I have this for sale. It's a little broken, but you can buy it.

LA

Lahoti, Amit 52:47
Happy.

Lynch, Jane L 52:53
That was a fabulous talk and it came from a really cool initiative through Pediatric Endocrine Society. So one of the only caveat I have for all this fabulous information is that when you do send a bone age, realize that we disagree.

With a huge percent of the readings of bone ages and we really disagree when they're done at outside institutions. So sometimes that triggers A referral and we repeat the bone age and the parents are charged for a repeat X-ray and and in fact we read it as very differently.
So just what a wonderful talk about being thoughtful in how you order and work up kids and how Mother Nature does raise the TSHA bit when you're trying to lose weight as a child who's.
Gaining rapidly on fast food and to realize some of these nuances, but thank you so much. This was really great.

Lahoti, Amit 53:53
Thank you so much, Doctor Lynch. It was good to see you.


Lynch, Jane L 53:56
Yeah, you too.

Lahoti, Amit 53:57
And I'll be changing in my costume of Waldo soon.


Ranch, Daniel 54:07
Are there questions from the audience?
There's one question in the chat from Doctor Janet Williams and she asks, is it also worth considering the psychological cost and pain and fear of blood draws when deciding whether blood draws are needed?

Lahoti, Amit 54:30
Yeah, it's an excellent point. Obviously, as we all may remember our own childhoods and we see our patients every day. Naming up that the child's going to have a blood draw is the child is. It's not a welcome sentence or statement for any patient. So I think we should be thoughtful kind of definitely.
Thinking about the cost, but also the psychological cost that I'm told that it takes and not only the pain of blood draw, but honestly speaking, several of these parents come worried into the clinics about the fear of unknown. They've been kind of they feel abnormal lab value and now they're worried that their child has something really sinister or dangerous.

Until they have had a chance to kind of talk to you and understand those lab tests. So I think the first thing that I say is definitely counsel your families about the blood test. If you have obtained a blood test and if you think this patient needs further evaluation and you're referring them, please counsel the families.
About what that blood test may mean or not mean, and do not leave it up to until they see the specialist for it. Because I think in that space of emptiness where they do not know what it means, a lot of Google searches happen and the patients are truly worried about something when it may truly not be it.
So yeah, I think in addition to the cost, do worry about the psychological impact of doing the blood test as well as the abnormalities of blood tests when the parents and the child deal with it.

Ranch, Daniel 56:00

Waiting to see in the last few minutes, there are other questions out there along the same lines and I'm sure you've experienced this. You know, typically we'll get referrals from our general pediatrics colleagues in the community and they'll be marked as urgent and the parents see that it's urgent. And in this day and age of technology, they're calling or.
Messaging my clinic, you know, frantically trying to get an appointment as soon as they can because it's an urgent referral when it may not have been truly urgent. So can you think of any mechanisms or ways we can help out our general pediatrics colleagues to so that we can make this?
Referral process smoother and hopefully decrease stress on the families who all of a sudden have to wait three months to see a specialist because quote UN quote something is wrong.

Lahoti, Amit 56:42

Sure. I think I enjoy one of the systems that we have out here at Nationwide Children's. We call it Physician to Physician Direct Connect service. So if I am a general pediatrician and I end up doing, let's say I was worried about abnormal like hypothyroidism in a patient.
And I do perform laboratory tests which are not as clear cut hypothyroidism as I would was probably suspecting, but are borderline and I'm considering this patient may need some more counseling to kind of understand this better. I think the key thing is communication and education, so if.

If you are not 100% sure how to interpret those lab results, reach out to your friendly colleagues in endocrinology and ask them, OK, I'm going to refer this patient to you, but is there something that you want me to tell the patient in the meantime? That may help at our institution. That definitely helps allay a lot of anxiety.
Amongst the patients, but the ones which have heard from their pediatrician a little bit more about what those lab tests mean. And honestly, sometimes the urgency of the referral is not urgency of the patient's disorder, but urgency of actual.
Explanation or counselling. So the counselling becomes more urgent than the actual evaluation of the patient and hence I think some counselling and education can go a long way in kind of appropriately triaging the patients as well as allying anxiety.

Ranch, Daniel 58:11
Thank you. And I guess a similar question from the chat. You know, how do you address parents who still want to see a specialist even when it's not clinically indicated?

LA

Lahoti, Amit 58:18
Yeah, that's a tough one. You finally got me, Syed. So I think we all, we all in our practices, I think will come across patients who are advocating for themselves, sometimes inappropriately so for seeking subspecialist evaluation when we in our hearts.
Minds do not feel that's needed and I think, I don't think we can undo all of it or we can probably prevent all those refers given the healthcare as it exists right now. Honestly, several of our patients self refer, they may not even need you to refer them and I do see that some of them in my practice myself.
However, the goal of this talk was to kind of help you and empower you to kind of #1 ask if that initial testing or evaluation is needed and #2 feel empowered to kind of educate your patients about that.
What is going to be probably an appropriate evaluation and not needed evaluation. If however you do feel for a patient relationship and for the parent Peace of Mind, if sometimes an evaluation has to be sent, I think it has to be sent. You cannot completely outdo those, but if you are able to spend some time understanding their concerns.
And answering them and sometimes buying time. Sometimes I think the thing that you need to tell them, I hear you, I hear your concern. At this time, I'm not as

concerned. If it's OK with you, why don't we see this in like another three months or four months and let me see you back and then we can evaluate. And if the patients seem, I'm unable to that, that may be a good.
Good approach to go to, but sometimes you do have to refer them for further counseling and sometimes the patients do want to hear from a specialist, which honestly we sometimes say the same thing as you would have said.

Ranch, Daniel 59:59
Great. Thank you for that. And we do have a question from Doctor Pearlman. Go ahead and unmute.

Perlman, Jeremy S 1:00:06
I just just a comment. So I I kind of found that pasting the the case data into or even you could probably put a whole progress note in. I think it's HIPAA complied into open evidence actually can can often provide pretty good guidance as a you know first run in terms of avoiding unnecessary stuff and.
Concepts.

LA

Lahoti, Amit 1:00:28
Yeah. Thank you so much for putting the plug about AI. Yeah, open evidence is coming up as one of the great resources that we can all begin to experiment and learn a little bit from. I think always take it with a piece of kind of caution right now. It is still relatively news and if you read something in there that always.
For.
Primary source verification. It's great to summarize the literature, but sometimes you may wanna go to the primary literature and just confirm that that indeed is what the literature is saying. Because AI is known to hallucinate and I have myself tried to prepare a grand rounds looking at and trying to find some recent references.
On a on on that particular topic and I was given it was not open evidence, it was ChatGPT at that time. So open evidence is a little bit better in that regards. But ChatGPT literally generated references for me to use only for me to find out they were nowhere to exist on PubMed.
So I think open evidence is definitely an improvised version and hopefully in coming months and years we'll see much better AI which can overcome this issue of AI hallucination. But yes, that can provide you a good summary which you can then

confirm with primary source verification and then provide something to tell your patients which is.
Is going to be evidence based.

Ranch, Daniel 1:01:47
All right. Well, it is just past 8:30, so I think we'll end it there. Doctor Lahore, thank you very much again for educating our our team and pediatricians in the community. For those who attended, please don't forget to fill out the post grand round survey. I'm sure the data is very helpful for Doctor Lahore and also supports our program. Otherwise, have a great rest of your day.

LA **Lahoti, Amit** 1:02:06
Yes.
Thank you so much for the opportunity again and look forward to hearing from you any feedback that you have about this talk. Have a great day guys and happy Halloween.

Ranch, Daniel 1:02:09
It.
Thank you. Bye-bye.

Calderon, Delia stopped transcription