Understanding Bone Health in Children - Pediatric Grand Rounds-5-9-25-Meeting Recording

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Kamat, Deepak M started transcription

Kamat, Deepak M 0:25

It's 7:30. Morning in the morning and let's get started with our pediatric grand rounds again.

This will be the second presentation by our fellows, graduating fellows and today's Doctor Radhika Pillai, who will be presenting her grand rounds and Dr. Doctors Suki Reyes, who is her mentor, will be introducing her.

Doctor Reyes, go ahead and introduce Doctor Pillai, please.

Rayas, Maria S 0:50

Wonderful. Good morning.

So it is an absolute privilege to introduce Doctor Radhika Pillai.

She is a pediatric endocrinolog.

Ist she earned her medical degree for a Medical College of Georgia and Augusta and completed her residency at the Children's Hospital of San Antonio, Baylor College of Medicine.

Her research has focused on cystic fibrosis, leading projects on obesity and cardiovascular health, which he has presented at local, regional and national conferences.

Last year she was awarded 3rd place for her oral presentation at Pediatric Research Day, which makes me so lucky to be her mentor. Doctor Pillai's clinical interests include calcium growth and puberty disorders, pediatric diabetes and obesity, and the use of diabetes technology to improve.

Patient outcomes.

She's passionate about providing quality care, equitable care and strives to empower patients and their families to be actively involved in their health journey this year after caring for children with complex bone disorders, she developed a really strong interest in rickets and osteoporosis and will present to us on.

Understanding bone health in children.

Pillai, Radhika 2:00

Thank you so much, Doctor Rayas, for the kind introduction and thank you Doctor Kamat for this opportunity.

I'm really excited to be speaking today, so let's get started.

I have no financial disclosures.

So for my talk today, I'll be covering rickets and osteoporosis.

My objectives are to review risk factors and clinical presentation, describe the approach to diagnosis and discuss management strategies.

Phone health is an important and often underappreciated pediatric concern.

Bones are necessary not only for body structure and movement, but they also protect our organs.

House bone marrow.

Bone also serves as a reservoir for calcium and phosphorus, and has an endocrine organ in its involvement with renal phosphate handling glucose metabolism and the vitamin D endocrine pathways, and so incorporating bone health considerations into routine clinical practice is important.

This is a summary slide just to highlight the point that when we're evaluating for bone disorders.

There are important aspects of the assessment that will help with uncovering the diagnosis.

And it starts with getting a good history and exam.

In terms of bone health history, you want to ask about birth history.

And individuals diet and activity.

Brittle development and growth.

Are they meeting milestones?

You want to ask about their dental health.

Whether there have been any delays or early dental eruptions, any concerns about enamel or frequent cavities you want to ask about illnesses and current and previous medication use?

And fracture history asking about the mechanism of fractures, the impact and the healing process.

And you also want to get a family history understanding if there are a history of fractures in the family.

Osteoporosis, connective tissue disorders, or any underlying chronic illnesses, and on

an exam you want to assess for growth parameters, motor function, limb deformities, spine asymmetry and puberty progression.
So let's see what this looks like with a clinical case.
It's after hours and you're the on call.
Endocrinologist and you receive a call from a Community pediatrician regarding a 16 month old African American male with concerns for leg bowing. And as you can see on the growth chart, there's concerns regarding the decline in growth trajectory both for weight and for length.
I just want to make a point about measurements for any of our learners in the audience.
So it's really important to ask how the patient was measured and to assure to make sure that the measurements were done accurately. So in the case of infants to measure their length accurately on a stadiometer, you want to have them laying flat on their back on the meas.
Board.
Ensure that their head is against the headboard in the vertical plane and that their feet are against the footboard and this is usually going to be a two person job, one person to secure the head in place and the other to make sure that the feet are touch.
The footboard for ambulatory children. This means that there's a stadiometer that's attached to a wall so that the child can stand against it with their head.
Shoulders and heels.
Touching, you want to make sure there are no head, accessories or shoes on and that their head is in the horizontal axis of vision.
So if there is any concern about measurements, it's always important to ask how are the measurements done and to repeat them if there's concerns.
So back to our patient.
We learned that he was born term via an uncomplicated pregnancy, his parents noted. Boeing at 11 months with delay dental eruption at 12 months.
He is meeting his developmental milestones.
He was exclusively breastfed until 15 months and so far he's a fairly picky eater.
Only eats or in foods in limited quantities. He was not on vitamin D supplementation, and he also learned that his brother, who's now three, had a similar history of leg bowing and infancy.
They are a single income household and there are concerns for food insecurity.

On exam you do confirm the bilateral leg bowing.
You also notice metaphysical flaring in the long bones, as seen in this forearm frontal bossing and prominence of the costochondral junction were also referred to as Rickidic Rosary.
And so based on the history and the exam, this helps to guide further evaluation in terms of imaging. We think about getting a skeletal survey to assess for fractures and if there's concern about bone mineral density, then we think about getting dexa scans.
And in terms of laboratory testing, we have a whole host of bone health labs that we like to.
Assess.
Including parathyroid hormone levels, calcium, magnesium phosphate, alkaline phosphatase.
The two vitamin D levels, the 25 hydroxy and 125 hydroxy and then assessing renal function with electrolytes and urine studies.
So in our patient radio graphic imaging does confirm the various bonding.
There's also the prominent Costochondral junction.
And then there's broadening, copying and writing of the of the longborn metaphyses.
On laboratory testing, we see that there's market hypocalcemia hypophosphatemia elevated alkaline phosphatase and parathyroid hormone levels and that the 25 hydroxy vitamin D and 125 dihydroxy vitamin D are both low. And so this constellation of features from the history, the exam.
Our imaging and laboratory testing leads us to suspected diagnosis.
Is the vitamin D deficiency for kids now I want to take a step back and discuss calcium and phosphate homeostasis and the role of vitamin D in this process.
So vitamin D in its inactive prohormone form comes as vitamin D2 or ERGOCALCIFEROL and vitamin D3 holy calciferol.
And the easy way to remember which vitamin D is, which is there are two C's in ergocalciferol.

JF **Jane Fried** 9:39
Thank you.

PR **Pillai, Radhika** 9:41

And three C's in Colicalciferol or vitamin D3. Now we can get vitamin D2 and D3 from our diet, and we can also make vitamin D3 in our skin through exposure to UV sunlight.
This vitamin D is then hydroxylated in the liver to become 25 hydroxy vitamin D or calcidiol and this is the storage form of vitamin D.
That we most often are measuring on laboratory testing because it has a more stable half life.
It then is hydroxylated again in the kidney by 1A hydroxylase to become the active form, or 125 dihydroxy vitamin D, also referred to as Calcitriol, and this calcitriol is involved in maintaining our calcium and phosphate levels within target range by stimulating calcium and phosphate abs.
From the gut.
By by regulating.
Bone modeling and resorption and also indirectly being involved in phosphate absorption and excretion in the kidney. It also feeds back to the parathyroid gland and serves as a modulator of parathyroid hormone release, which is involved in regulating this process of calcium and phosphate homeostasis as well.
So when we look at our patients labs in this pathway due to the vitamin D, the low vitamin D intake.
And this lead to low levels of Calcidiol and Calcitriol, and because the body was not able to have the substrate of Calcitriol to absorb adequate amounts of calcium and phosphate, the parathyroid hormone.
And alkaline phosphatase, which is a marker of bone turnover, were elevated to try to counter regulate the insufficient quantities of Calcitriol.
And so, because this system was not able to re achieve homeostasis, this led to the findings of hypocalcemia and hypophosphatmia as well.
So rickets, what is it?
It is a generalized bone disorder that's associated with decreased mineralization of the bone matrix.
And again, this occurs because the body is trying to do all that it can to maintain calcium and phosphate levels in within target range.
And it comes at the expense of the mineralization process of the Bony matrix.
And so this leads to softer and weaker bones.
This is occurring at the growth plate of the long bones and actively growing children, and this same process.

When it occurs after growth is complete or after the growth plate closes, is referred to as osteomalacia.
In terms of causes of rickets, we can classify them as either due to calcium deficiency and or phosphate deficiency.
In terms of Calcipeic rickets, we have vitamin D deficiency and calcium deficiency, which are globally the most common causes of nutritional rickets. And then there are rare forms of calcipe and crickets due to abnormalities of vitamin D metabolism or action.
Which are due to deficiencies in the 25 hydroxylase enzyme 1A hydroxylase enzyme and end organ resistance due to mutations in the vitamin D receptor that lead to vitamin D resistant rickets.
So I want to take a minute to talk about nutritional rickets.
There are certain risk factors that can predispose a child to develop nutritional rickets and are important to take into account.
In preterm infants, because the in utero mineralization process that is occurring in the third trimester is interrupted as well as the increased nutritional demands, they are at a higher risk of developing rickets.
In infants who are exclusively breast fed due to the low content of vitamin D in breast milk, as well as if there is maternal.
Vitamin D deficiency? They are more likely to be at risk for rickets.
Children who have darker skin pigmentation have higher melanin content.
Which reduces their skin's ability to produce vitamin D from sunlight, and this can be particularly problematic in countries at high latitudes or in colder climates where sunlight exposure might be limited.
As well as with more frequent use of sunscreen which impairs our skin's ability to make vitamin D in terms of malabsorptive disorders, any disease processes that impair absorption, for example, celiac disease or inflammatory bowel disease, can lead to nutritional records as well.
And if there are any dietary restrictions, whether that's being on a vegetarian or vegan diet.
Or limiting dairy intake if there's, for example, lactose intolerance, and then it's also important to consider socioeconomic factors. So if there's limited access to healthcare or nutritional education or limited access to foods that are fortified, this can lead to a diet that's deficient in essential nutrients, which was.
A concern in our in our patients case.

There are recommended dietary.
Period allowances for both calcium vitamin D, as well as phosphorus by age. It's fairly easy to achieve the amount of daily phosphorus that's needed because our diet is rich in phosphorus. However, it can be challenging to achieve the amount of calcium and vitamin D that's necessary on a.
Daily basis.
And as you can see the required amount varies by age.
Reaching up to 1300 milligrams per day for 9 to 18 year olds and from 400 to 600 international units of vitamin D daily.
And so just to put this into perspective, in terms of the challenge.
For vitamin D, there are foods that are fortified, dairy products, cereals.
There are various types of fish that have vitamin D.
But to achieve that amount of 400 to 600 international units of vitamin D daily would require having at least four to five servings of high rich vitamin D food. For example, in a glass of milk that's vitamin D fortified, there's about 40% of that daily.
Recommended amount and so it can be challenging when we're counseling our patients to.
Help them achieve that.
Daily required amount.
And the same with calcium.
There are dairy products, fish, vegetables, fruits again that have calcium in them. But there is the added challenge with calcium that it's important to space out the intake over the day to optimize its absorption.
And that adds a layer of added complexity in children who have active schedules or who might be on other medications that could have impaired absorption of taken with.
It is preferred for calcium to be obtained through the diet.
There are some studies in adults that show adverse cardiovascular effects, and so we do.
We do try to reserve calcium supplementation if we're concerned that dietary intake is not sufficient.
In terms of supplementation for vitamin D, either formulation of D2 or D3 are equally effective.
And the goal of vitamin D levels is to maintain within a range above 20 to 30.
In terms of calcium supplementation, I wanted to just point out that there are many

calcium formulations and it's important to be mindful that these formulations have varying amounts of elemental calcium. One of the more common forms is calcium carbonate, which has about 40, which has 40% of.
Elemental calcium.
And so as an example, if a 1000 milligram calcium carbonate tablet has 40% elemental calcium, this amounts to 400 milligrams.
And so being mindful of that when you're calculating the doses is important.
In terms of Ricketts vitamin D management, it's recommended that oral treatment is done to restore vitamin D.
Levels and as I mentioned, either D2 or D3 are equally effective.
If the dosing ranges from 2000 to 6000 units, depending on the age and it's advised to prescribe this regimen for a minimum of three months at that time, it's important to assess for biochemical improvement.
So checking labs and some children may require longer treatment during.
During that time, it's also important to replace calcium in the diet or via supplementation.
Because.
When the body starts to see the improved vitamin D, it will try to compensate for inadequate calcium by continuing to pull from the bones and so to avoid this, this hungry bone picture that we might encounter, we supplement with some calcium as well.
As well, and once the concern for rickets has resolved, it's recommended to continue maintenance dosing at anywhere from 400 to 600 international units daily.
There are some studies that have looked at single dose treatment with equivocal findings, but for ease of use and compliance, it is an option that can be considered.
So in terms of Calcopaedic brickets, we've talked about nutritional rickets. I just wanted to take a few minutes to talk about some of the rare abnormalities that can occur from vitamin D metabolism or action that can also lead to rickets.
So 25 hydroxylase deficiency is where there's a mutation in 25 hydroxylase that inactivates it.
And as a result, there's a similar presentation as vitamin D deficiency rickets, where there's low levels of calcidyl and Calcitriol, which lead to hypocalcemia and hypophosphatemia and the counter regulatory hormones alkaline phosphatase, which is that marker for bone turn number is elevated as well as parathyroid hormone levels.

Become elevated.
In 1A, hydroxylase deficiency, the loss of function mutation is in 1A hydroxylase, the enzyme in the kidney, and this leads to.
Markedly low levels of Calcitriol the 25 hydroxy vitamin D, or calcidyl levels may be normal.
And again, we see the hypocalcemia and hypophosphatemia at much significant levels.
And markedly elevated alkaline phosphatase and PTH.
And this is because that active vitamin D is not able to reach its target organs and so these counter regulatory pathways are ramped up.
And in vitamin D resistant rickets, this is an an organ resistance due to vitamin to vitamin D due to receptor mutation and so the body feels that there's not adequate 125 hydroxy vitamin D and so this leads to hypocalcemia and hypophosphatemia when in reality.
The Calcitriol level are actually markedly elevated.
But not able to interact with the target organs.
And again, alkaline phosphatase M PTH respond by ramping up.
And calcidyl levels again can be normal.
Another unique feature of vitamin D resistant rickets is that there are there can be varying degrees of alopecia with the Vonage deformities characteristic of rickets.
In addition to calc rickets, there are also phospholipenic rickets.
In developed countries, dietary phosphate deficiency or impaired by availability is fairly rare.
However, it is important to be aware of, particularly in preterm infants, who can be at risk for phosphate deficiency due to their increased nutritional needs, especially when they are breast fed and also if there are antacids being used which can bind to phosphate and lead to hypophosphatemia.
In terms of renal defects, if there's Vanconi syndrome, which is a generalized reabsorptive defect in proximal convoluted tubule which leads to loss of amino acids, glucose, phosphate in the urine leads to proteinuria, and hypophosphatemia and metabolic acidosis.
There's also hereditary hypophosphatemic rickets with hypercalceuria.
Which is due to a defect in the sodium phosphate transporter, and this leads to an early onset hypophosphatemia due to renal wasting along with the rickets and the unique findings are there are elevated 125 vitamin D levels and increased urinary

calcium excretion.
The other category of phosphenic rickets are those that involve FG23, whether that's in increase in in thyroglast growth factor 23 secretion or an impairment in its degradation. What is fibroblast growth factor 23, it's made by the bone and the way it interacts in this.
Vitamin D calcium phase is pathway.
Is that?
It it feeds back to the kidney when it there are adequate levels of calcium and phosphorus.
To to slow down 1A hydroxylase and the production of 125 dihydroxy vitamin D.
It also interacts in the kidney.
At the level of phosphate absorption and excretion.
And there are various forms of FGF mediated hypophosphatemic rickets.
There's X linked hypophosphatemia, autosomal recessive hypophosphotmic rickets which are both due to increased FGF 23 secretion.
There's also autosomal dominant hypophosphatemix due to impaired degradation of FGF 23.
And then more rare entities.
Such as tumor induced osteomalacia where there are tumors that produce excess FGF, 23 and fibrous dysplasia such as Mccune Albright, which is associated with increased FGF secretion via the activation of the protein kinase 8 pathway.
I want to talk about XLH or X link dominant hypophosphatemic rickets for just a moment.
It's one of the most common causes of inherited hypophosphatemic.
Rickets occurring in one per every 20,000 live births. This isn't due to a mutation in the gene called fax, which is located on the X chromosome, and it's normally expressed in osteoblasts, and its role is in inactivating phosphatonins like FGF 23 that promote phosphate excretion and.
So when there is a loss of function mutation in fax, this leads to.
And increased secretion in activity of FGF 23 and as a result in the kidney there's impaired phosphatase absorption and increased phosphate excretion in the urine.
As I mentioned, FGF 23 also has a role in down regulating calcium trial production and so.
Via these two paths, due to decreased absorption of phosphate at the kidney.
Level and decreased phosphate absorption from the gut due to low levels of calcine

trial.
Overall, there's low serum phosphate and this impairs bone mineralization.
Conventionally, treatment has included supplementation with phosphate, calcitriol and vitamin D.
To counteract this, L increased FGF activity in 2018, the FDA approved gross and AB, which is a fully human monoclonal IDG 1 antibody that neutralizes FGF 23 for children one year and older.
And the way it works is that it blocks the FDF 23 signaling.
And this leads to improvement in phosphate absorption in the kidneys and improves production of calci trial. And because these two paths are restored, there's improved phosphate absorption and improved bone mineralization.
And this has been really exciting in terms of prognosis for XLH.
I now want to switch gears a bit and talk about osteoporosis in childhood, and I want to take a minute to 1st review bone anatomy.
So bone is divided into 3 anatomic regions. We have the diaphysis or the shaft of the bone. The METAPHYSIS, which includes the Epithio or growth plate and then the epiphysis which is the rounded articular surface and the bone.
And it's at this epithysial growth.
Plate, where there's cartilage which is the site of bone formation and allows for long bone growth in childhood.
At a macroscopic level, we have two types of bone, trabecular bone or or spongy bone and cortical bone, which is the majority of our skeleton. It's found in the shaft of our long bones and it's more dense and offers mechanical support.
Are trabecular bone is at found at the end of the long bones are vertebrae and flat bones and it's metabolically active in hematocoesis.
There are two main players in terms of.
Our gross profit level.
And those are our osteoblasts and our osteoclast and these two cells are involved in bone formation and resorption.
So our osteoglasts help with forming bone and our osteoclasts are involved in releasing bone mineral for our bodily.
Use and we need this.
We need both of our both of these processes to occur in balance to achieve normal bone mass and bone mineral density, and this process of remodeling and and modeling is going on throughout our lifetime and it allows our bone to grow and

change.
If there's an imbalance in this process where there is an inadequate bone formation and increased bone resorption, then this can lead to impaired bone strength and bone fragility and risk for osteoporosis.
There are many intrinsic and extrinsic factors that influence our bone health. Our peak bone mass is achieved in adulthood and it is heavily influenced by genetics 60 to 80%. However, that remaining 20 to 40% of our peak bone mass is impacted by nutrition and diet which?
We talked about extensively physical activity.
Hormones and pubertal progression. Steroids and chronic disease.
And it's important for us to be mindful of these modifiable factors because these are things that we can address with our patients on a regular basis in clinic in terms of physical activity, bone adapts to mechanical load. And so when muscle pulls on bone, this strengthens our B.
Which is why wheat bearing exercise is important.
In terms of our hormonal milieu and pubertal progression.
And our growth factors and sex hormones play a major role in our peak bone mass accrual, which is why 50% is accrued in adolescents. Estrogen plays a role in osteoblast survival and osteoclast apoptosis, which promotes bone mass formation.
And our androgens like testosterone stimulate bone formation.
On the outer surface of bone as well.
And then of course, our growth hormone and and growth hormone factors are anabolic agents that are important in skeletal growth.
In individuals who are on steroid therapy, this can impaired bone health by by impairing osteoblast function and increasing osteoclast activity.
It can also suppress growth factors and sex hormones, which can impair linear growth in bone mass.
And in chronic disease, there are many ways that bone health can be affected through the inflammatory processes that can promote osteoclast activity.
Malabsorption, which can lead to nutritional deficiencies and immobility, which can reduce mechanical loading and of course, chronic disease can also impact endocrine function in terms of.
Growth hormones.
Sex hormones and the thyroid axis.
Bone does have this intrinsic ability to model and remodel, and this is what allows us

to repair our bone throughout life.
In terms of normal bone growth or accretion, 39% of our total bone mineral is acquired during the four years that surround our peak in bone accretion. And in girls, this is occurring between the ages of 10 to 14.
Team and then voice is typically occurs between the ages of 12 to 14.
By.
Four years following that peak, 95% of bone mass has been achieved and this is one of the reasons why it's so important for us to consider pediatric bone health in our patients to ensure that we're doing everything we can to prevent low bone mineral density in.
Our at risk patients.
There is, as you can see, a delay between peak growth velocity and peak bone mass accrual. Both invoice and curl and it it's due to this that there's an increased fracture risk in this window between 11 1/2 and 12 1/2 in girls and thir.
And a half in 14, 1/2 in boys. And it's thought that this increased fracture rate in childhood is due to this lack.
Between the peak growth velocity and peak bone mass accrual.
And so just to emphasize cortical density and structural strength does continue to increase into the third decade.
So even after this four year window, there is continued bone mass accrual into the third decade. And so optimizing accrual during that growth period is essential to prevent current and future fractures.
So childhood fractures are common. As I mentioned, we see tons of kids with fractures and it can be very challenging to know as a pediatrician which ones to worry about, about 50% of children have at least one fracture prior to adulthood, and the most frequent side is.
The forearm, which accounts for 50% of all fractures.
So how do we know when to be concerned?
And again, it goes back to that history.
And asking important questions.
So you want to ask about fracture characteristics, the location of the fractures? Were they in the long bones?
Were the what was the OR in the vertebrae?
What was the mechanism of injury?
Was it falling from?

A Cliff? Or was it simply from climbing a flight of stairs?
You want to ask about any unusual features.
Whether or not.
The healing process was impaired.
And you also want to assess for clinical findings suggestive of an underlying bone fragility disorder.
So looking for looking.
For discoloration of the sclera, skeletal deformities, dental appearance, dental appearance, any limb abnormalities.
Joint or skin laxity?
And chest wall deformities and asking about family history, whether there were any early fractures, frequent fractures or known diagnosis of bone disorders in close relatives.
So what is osteoporosis?
How do we define it?
It's characterized by low bone mineral density and impaired microarchitecture.
Which leads to decreased bone strength and fragility fractures.
And it's been increasingly recognized, particularly in children with genetic disorders, causing bone fragility, and then those with chronic illness. And the way that we measure bone mineral density is through a dexa scan, which looks like this.
So dexa or dual energy X-ray observed optometry is the preferred method. As I mentioned for assessing areal bone mineral density.
It's reproducible, inexpensive and low radiation exposure.
However, it is important that the technicians are trained to work with children and that comparison of images over time are conducted on the same machine, ideally with the same technician and with pediatric software that has normative data for comparison.
The preferred sites for dexa measurements on the lumbar spine.
And total body less head and in children who may not be able to be assessed at these sites.
There, the distal forearm, proximal hip and lateral distal femur can be used, and this is usually in the case where they might have hardware or reduce weight bearing or are non ambulatory.
The DEXA scan generates bone mineral density Ross scores.
That are then converted to age and sex matched Z scores and there are additional

comparisons that can be made by race and ethnicity of the. However, this is a limitation because the only reported race and ethnicity options are white, black and Hispanic, and those clearly don't represent the.
Of any person's identity.
Bone Age is something that can be used in children who might have delayed or advanced puberty to adjust for the age adjusted Z scores.
So for example, if there's a child who's chronologically 15 years of age but may have delayed puberty and their Bone Age is close to that.
Of a 12 year old, you would want to use their Bony age.
For the age adjusted C scores.
Similarly, the DEXIS can because it's a 2D image of a 3D object, has potential for calculation error in individuals who are taller or shorter.
For their age and so in individuals who are short, their bone mineral density may be falsely low because they have smaller bones and taller individuals may have falsely elevated bone mineral.
Density due to having larger bones and so adjusting for height is also important and and the Children's Hospital of Pennsylvania has an excellent calculator that can help with this. If the software doesn't have it already built in.
This is just an example of a dexa scan report. On the left you can see the total body less head where.
It is showing the parts of the body.
The full body.
Minus the skull is being assessed and the reason for that is because.
The skull is not considered a major osteoporotic site, so it's excluded from the scan and then age match percentiles and Z scores are generated and the same for the lumbar spine.
You can see that the area that is being scanned as well as the age matched percentiles and Z scores.
In terms of diagnostic criteria for osteoporosis, it's defined as having either one or more vertebral fractures or the presence of a clinically significant fracture. History and bone mineral densities. Disease growth less than -2.
What is a clinically significant fracture history having either having two or more long?
Low trauma fractures by age 10 or three or more.
Low trauma long fractures.
By age 19, it's important to note, however, that having a bone marrow density Z

score that's above -2 does not preclude the possibility of skeletal fragility or increased fracture risk.
And this is important to remember in patients who have bone fragility due to an underlying disorder. For example, patients who might have leukemia or chronic kidney disease, or neuromuscular disorders.
And of course osteogenesis imperfecta, where there are bone marrow densities, these gorme be normal, but we know that they are at an increased risk of sustaining fractures.
So what is low trauma fracture? There are various definitions which create a bit of a challenge in terms of diagnosis.
One is fractures occurring outside of motor vehicle accidents or falling from 10 feet or less.
Now, 10 feet is quite quite a high height and so this can create a bit of a of a Gray zone in terms of moderate and mild trauma with respect to falls in high risk chronic illness, setting a more conservative definition has been used of falling from a.
Standing height or less at no more than walking speed.
And again, as I mentioned these.
There are limitations to diagnosing osteoporosis. In addition to the challenge of defining low energy trauma, the diagnostic criteria can also lead to under diagnosis.
The question arises of do we wait for two or or three fractures? If that first long bone fracture was significant?
Also, with the bone marrow densities, these scores, they can vary depending on the reference database that was used to generate the Z scores.
And so this can create challenge in terms of assessing the bone mineral density as well. If that individual for example was not able to obtain the the scan in the same machine.
So we've talked about osteoporosis.
We've defined it.
We've reviewed the role of DEXA scans.
How do we approach this clinically if we have a patient coming into our practice with fractures and so this is a summary slide.
We've talked about rickets, but that first step is to is to perform an evaluation for biochemical assessment so that you can roll out rickets.
And it involves getting good history and exams.
And laboratory testing.

And I want to make a note here that it's also important during this process to consider non Occidental trauma on the differential.
Because these conditions are critical to ensure that appropriate intervention.
Is provided. They're not related with an underlying bone issue.
And so the treatment is going to be very different from osteoporosis.
So if you see a child who's not ovulatory, or if there are delays in care or unexplained bruising with with.
Fractures in various stages of healing or an unclear mechanism of history of injury.
It's very important to involve our child abuse specialist to undergo the proper evaluation.
And so that leads to imaging consideration. So getting the skeletal survey to assess for fractures in terms of bone fragility, this can also help identify skeletal deformities or, for example, like were wormian bones, which are those extra skull bones that can be seen in osteogenesis imperfecta.
You also want to think about getting lateral spine radiographs.
To look for vertebral fractures. And then we've talked about getting dexa scans when we're concerned about bone mineral density.
The next step is to determine whether there's a primary or a secondary cause of osteoporosis.
So again, this is where we look for features of of osteogenesis imperfecta such as blue glace, glera, skin laxity, long bone deformities.
Chest wall deformities and if there's a family history that's suggestive as well.
The majority of childhood osteoporosis, however, is going to fall under secondary osteoporosis and each one of these could really be a lecture in and of itself.
But some things to highlight. Many of our patients will fall under overlapping categories, for example, those with chronic disease who are also on long term steroid therapy.
In the endocrine category, as we've discussed, the role of.
Growth hormone in terms of osteoblast activity are sex hormones in terms of osteoblast activity as well.
And the parathyroid gland in both modulating osteoblasts and osteoclast activity.
Any impairments in these processes can affect Bron fragility as well as thyroid dysfunction, type one diabetes and Cushing's syndrome, which all lead to increased osteoclastic.
Activity and bone resorption.

The next step is to evaluate for spontaneous recovery, so deciding whether or not. Aggressive medical intervention is needed, or if the patient has the potential to recover without more aggressive medical therapy, and so individuals who might have less potential would be those who are on prolonged steroid therapy of more than three months, chronic impaired mobility.
Or an underlying disease that's poorly controlled or due to a genetic condition.
Older age because there's less growth potential and having higher severity vertebral fractures.
Are risk for less potential for spontaneous recovery. Conversely, being on short term steroid therapy having short term immobilization and well controlled underlying disease?
Bone for more potential.
As well as well as younger age and lower severity vertebral fractures.
Now I want to make a point about spontaneous recovery.
It's not this magical.
Recovery that just happens.
There are still supportive measures that need to be put into place to assure that the patient recovers from the fracture, so this includes prescribing calcium supplementation.
Vitamin supplementation and as able recommending physical therapy to help in the healing process.
And so in terms of drug therapy and osteoporosis, bisphosphonates are the mainstay of therapy.
And and the way that bisphosphonates work is that they impair osteoclast activity. They deposit at the bone matrix and then are ingested by the osteoclast, which leads to impaired activity and apoptosis. And there are two forms of IV bisphosphonates.
A.
Pomedronate and zoledronic acid and it's been shown that the IV formulations are superior to oral in terms of bioavailability.
Important considerations in terms of preparing for infusion include making sure that you calcmia.
Normal ranges of phosphate and vitamin D are achieved prior to the infusion.
During and after the infusion.
There is risk, particularly with the first infusion of having flu like symptoms and of precipitating hypocalcemia and hypophosphatemia. So it's important to monitor

calcium and phosphorus levels very closely after the infusion.
Additionally, in patients who might be on chronic steroid therapy, the infusion can precipitate an adrenal crisis type picture.
And so it's important to have these patients on stress dosing.
Not only prior to the infusion, but to continue for the 2448 hours after the infusion as well.
Just to quickly highlight there, the 24 formulations, I won't go into all the details, but the dosing varies by age as well as the frequency it becomes.
It's more frequent in the younger age because there's more bone turnover.
And the same forz electronic acid. This is all electronic. Acid is more frequently used.
Used in clinical care because of the ease of less frequent dosing intervals and the shorter infusion time compared to premedronate and the dose varies by age as well as the intervals.
There are some rare side effects that have been reported.
Iriditis anecdotally, so it's important to have children who might have any eye issues, undergo ophthalmologic evaluation, atypical femoral fractures.
Have been reported with the studies being more in the adult population and so it might not be drug related in the pediatric population and is not necessarily an indication for treatment cessation.
It's been shown to be a risk in adults with prolonged bisphosphonate therapy of greater than than five years and then osteonecrosis of the jaw.
There, there aren't any published reports occurring in children.
Childhood. However, it is important to emphasize routine dental care and.
To intervene, if necessary, and then in childbearing individuals, it's important to counsel on a on the importance of avoiding pregnancy for at least 12 months after therapy.
And this is because bisphosphonates have a really long half life of 10 years or more.
And so the risk for fetal development.
Is not clearly understood and so it's important to Council.
In terms of dose adjustments and duration, the duration of therapy in children is not well defined, but it's tailored to the individual patient's response and their clinical condition. So generally treatment is continued until they're significant. Bone mineral density improvement or until the patient reaches skeletal maturity.
So you start at osteoporosis stabilization doses and then you try treatment.
To achieve normal bone mineral densities, these fours and if there are no new

fractures, if there is evidence of improved bone mineral density, improved functional mobility, then there is the option of reducing to maintenance therapy, which reduces includes reducing the frequency or the dose of infusions while continu.
To ensure that their abdominal density improvements.
And fracture prevention in individuals who might have transient conditions.
That are that have led to osteoporosis, for example, patients who have leukemia, who are on on cyclic glucocorticoids but may not be in remission and have improved lung, mineral density and no new fractures. Consideration of discontinuing therapy is an option usually after 6 to 12 months and in.
Those who have.
Permanent or persistent factors?
Risk factors like patients with OI or or chronic illness.
Is then you can you wanna consider lowering to maintenance dosing if they're stable and continuing until final height is achieved. It's been shown that with fracture holidays where there's intermittent bisphosphonate infusions, this can lead to.
Recurrence of fractures because of the juxtaposition of.
This fosini treated bone with new bone that's bisphosphonate naive and weaker, and this creates a site for fractures to occur.
And so in conclusion, bone Health is an essential consideration in pediatric care.
Optimizing bone mass accrual in the pediatric years is crucial in optimizing adult bone health.
And this is something that we all play a role in a thorough history. An exam can often lead to the diagnosis of rickets and osteoporosis, with the goal of early identification and initiation of therapy.
To optimize functional outcomes.
And with that, I thank you all for listening and I'm happy to take any questions.

Kamat, Deepak M 57:23
Thank you Doctor Pillai for that excellent presentation on bone health in children.
Let's see.
Doctor Williams, you have a question?

Williams, Janet F (Dr.) 57:32
I have a statement but first I want to say thank you for that outstanding presentation.
It really warms the cockles of my heart because everybody, my colleagues and house

staff who have worked with me know that I'm constantly.
Speaking about the 1300 milligrams of calcium that adolescents need and are not getting, I think that.
Your.
Under what I've seen a historic trend.
Of dairy being.
And even other quality foods. Although nobody's eating six cups of broccoli a day.
Or or eating 4/6 cups of cheese a day.
And living to tell about it anyway, that you're under this historic trend of dairy being replaced?
By sodas and and juice beverages that don't contribute at all. As a matter of fact, they can be a detriment to calcium deposition.
And.
The other thing that I see more recently is somehow Derek Milk will say, but it's dairy type substance.
Liquid is getting a bad rap and and someone is teaching our house staff to limit milk.
To 1 cup a day and I think that's really wrong.
It is true that you can drink too much of A milk type substance, even formula.
But there's nothing wrong with getting that extra 2 cups, let's say, or possibly even 3.
At times, there's 200 milligrams, as you said, of calcium in there. And it's really, really hard to get the 1300 milligrams. So what I recommend.
Religiously.
Is that all girls at adolescents? If they can hopefully swallow a pill by age 10, which is where adolescent starts for me.
Take a woman's vitamin because a woman's vitamin has a 5 to 600, usually pretty religiously 600, which is the limit you can absorb at one time of calcium daily.
And now it don't like guys.
So the boys and also girls who don't want to do that, can take Tums, which are generally.
Doable, but you have to educate them about turning the bottle around and how much they're going to get right, because that's only going to be 400 or possibly 600, usually not.

PR **Pillai, Radhika** 1:00:09
No.

Williams, Janet F (Dr.) 1:00:13

Maybe less so anyway.
I just want to say that.
You know on your bandwagon and I think it's critically important to educate the the adolescent and the family about.
Calcium intake and to do it.
In a way that they can.
It's compatible with them and also affordable.
They don't need a fancy women's vitamin or fancy Tom's.
They can buy the generic brand at Heb, Walmart, whatever, and it's it's really affordable.
So just wanna say thank you so much.

Pillai, Radhika 1:00:51

Thank you.
Those are all excellent points, I agree.
I think it's so challenging.
To achieve that dietary amount of calcium and vitamin D, and so I I really like your approach. I think that's great.

Kamat, Deepak M 1:01:07

Thank you.
Thank you, Doctor Lynch.
Go ahead and ask your question.

Lynch, Jane L 1:01:11

Oh, I just want to say that was absolutely fantastic. And as you know, those of you on the wards know we've been struggling with a tough case of a bone disease.
And so this I learned some good things.
I'm. I'm just going to do a shout out for an article that came out in January through the AAP that somehow got buried as an E article, which is a shame because it was so good and.
I put it in the chat.
It's on evaluating factors.

And young children, and we do often get endocrine consults, and you need to have a really good.
History and work up for that because when those cases end up in court, the child abuse team is super appreciative. If you've shown that there wasn't an underlying reason for those fractures and this just walks you through it. If you want to pull that up and put that.
In your resources.

Kamat, Deepak M 1:02:09
Thank you.
Any other questions? Comments for Doctor Pillai?
I don't see any.
So thank you all for attending this morning's Pillai for that excellent presentation on bone health insurance.
Again, we'll see you next week and then next week there will be another graduating fellow who will be presenting during grand rounds.
So have a wonderful week and we'll see you next Friday at 7:30 in the morning.

Pillai, Radhika 1:02:48
Thank you so much.

Kamat, Deepak M stopped transcription