Café-au-lait Spot - Pediatric Grand Rounds-1-24-25-Meeting Recording

January 24, 2025, 1:29PM

56m 24s

Kamat, Deepak M started transcription

Kamat, Deepak M 0:24

Nina, you're ready.

I'm gonna introduce you and OK. Yeah.

CN

Champaigne, Neena 0:27

Absolutely. Thank you.

Kamat, Deepak M 0:30

Good morning and welcome to pediatric grand rounds.

The CME code is in the chat box and we keep repeating it.

It's my great pleasure to introduce this morning's grand Round speaker, doctor Nina Champagne, who is the clinical geneticist with expertise in biomedical genetics.

She's a clinical associate professor and devotion chief for genetics in Department of Pediatrics at the Medical University of South Carolina.

She specializes in the diagnosis and management of children and adults with inborn errors of metabolism.

And provides newborn screening.

Follow up in South Carolina.

Doctor, Champagne earned her Bachelor of Science degree in molecular genetics from the University of Rochester in New York.

She received her medical degree from the University of Texas Medical Branch at Galveston, where she also completed her residency training in general Pediatrics.

She completed additional residency training in clinical genetics at the University of Texas Health Sciences Center at Houston.

She's certified by the American Board of Medical Genetics.

And genomics in the clinical genetics and genomics and medical biomedical genetics, she holds memberships in the American College of Medical Genetics and Genomics Society for innovative metabolic disorders, American Medical Association,

South Carolina Medical Association, and American Academy of Pediatrics.
Doctor Champin, thank you very much for accepting our invitation and the floor is yours.

Champaigne, Neena 1:54
Thank you so much for having me.
It's great to be at least virtually back in my home state of Texas.
My previous stomping grounds, as was shared. I did all of my training in the Houston Galveston area and still visit quite frequently.
I've been out in South Carolina for almost 20 years, but I wanted to share a talk that I've given to a lot of trainees and different pediatricians and.
Really looking for subtle clues that everyone should be.
Aware of when you're thinking about a genetic diagnosis just a little bit of background.
I always enjoyed solving puzzles and mysteries, and so that's probably what drew me to genetics.
Some of you may recall Sherlock Holmes.
But one of my favorites was ALWAYS Nancy Drew.
So that's again where I get my love. Probably for a lot of this particular fields.
So just to start off with, I have no relevant.
Disclosures related to this talk and I will be covering evidence based medicine that's free of commercial bias.
With that, we'll go ahead and go through the learning objectives.
So by the end of this presentation, you should be able to recognize minor anomalies that are red flags indicating the presence of a specific occult major anomaly.
List further evaluation that should be considered for each of these common anomalies, and then also Council families about prognosis.
Of a child with a structural anomaly based on the mechanism which occurred.
So, as Sherlock Holmes says, my name is Sherlock Holmes. It is my business to know what other people do not know.
So we start with what you can know.
So Dysmorphology is actually a field that was first coined by David Smith back in the 1960s, and he used this really to study the area of human congenital malformation.
And this particular area of genetics specializes in birth defects and really combines the knowledge of several areas.

So developmental mechanisms, the Natural History of congenital abnormalities, as well as the genetic principles.
However, when we're talking about dysmorphology, you have to think about just morphology and what is normal. And so part of that is what we'll go through and kind of understanding.
When things do not go correctly.
So thinking just about.
The etiology of birth defects. We know that 2 to 3% of all newborns are born with a a birth defect and they account for 25 to 30% of pediatric admissions.
You can see here some statistics that are a little bit old, but probably are still consistent in that one in 33 babies born in the United States each year has a birth defect, which I think is is.
A pretty impressive number.
When you look a little bit at the etiology, there's several categories that we can look at. Most of them have an unknown etiology. So at this point, we think of them as sporadic and there may be other mechanisms we just haven't clearly defined a good number of them.
Are due to chromosomal abnormalities, and we'll reviewing some of those and then further, we know that different things including single gene disorders or genetic abnormality is account for another portion followed by teratogens or even just the timing of of the birth.
So a lot of different etiologies to think about when we're evaluating a birth defect.
So we talked about just, you know, thinking about the timing and the way that our organs develop over time.
So when we think about the different categories of development, it's good to break them out into three different categories.
So the implantation, the embryonic stage and followed by the fetal stage.
And so if we think about that, the time frame for implementation is fertilization till the end of the third week.
This is a time period of rapid cell proliferation.
All of those initial.
Circulatory connections are having are are being made as well as early cell differentiation.
This particular is is more of an all or none, and so this is where if things don't go in the correct order or.

There's a problem that this will end up in a miscarriage, so these usually have very early.
Issues.
Followed by the embryonic stage. This is from the 4th week to the end of the 7th week, and this is particularly important in terms of looking at birth defects, because this is where we see.
See again that early primary tissue differentiation.
We have closure of the neural tube and then you have definitive organ formation and you can see here in this the the heart in particular and and other solid organs are being made. So you can have significant defects that occur at this point.
Lastly, the fetal stage.
So that's eight week to birth. And so this is more where organs start to differentiate and grow in size and then you just have overall enlargement.
Of the skeleton, muscle and brain. And so this is more where you get definition of those major organs. And so you can think about just in terms of timing how.
An abnormality or a change in any one of those timings can have a difference in terms of outcomes.
So looking at the pathogenic mechanisms, it could be normal or abnormal and cause an anomaly, and we typically categorize the different mechanisms.
And these four different categories and we'll be reviewing them.
So deformation disruption, malformation and dysplasia. Of course, in some conditions there is a little bit of overlap between these mechanisms.
So looking at the first mechanism, this is deformation.
So this really refers to a normal developmental process or tissue, and there's some mechanical force.
It's either extrinsic or intrinsic that has changed the way that that tissue looks so extrinsic. Examples are an abnormal uterus.
Where there could be compression also multiple gestation where there's not enough.
Room for the fetus or fetuses.
To move low amniotic fluid is another extrinsic. And then you can have some neuromuscular abnormalities that again affect the placement of that normal tissue.
So looking at just the types of deformations, this accounts for two to 2% of newborns who have things like club feet, arthrogryposis or even plagiocephaly.
And this because there's normal tissue tends to have a very good prognosis.
So they may resolve spontaneously, or they may just need something of treatment

like physical therapy, casting or braces or external fixations or helmets.
So again, usually a very good prognosis.
So here is an example that you may have seen along in your practice of club feet.
So again, this is a deformation where typically there was not enough room in the womb.
We also see Arthra griposis and so that's again some contractures that.
Can be again due to placement, but can also have a genetic cause on occasion, but typically can improve with time. And then lastly, an example is plagiocephaly so we know that again infants that are placed differently within the uterus can have a different shape to their head and.
With some time or helmets, that's will resolve.
So our next category looking at.
Pathogenic mechanisms.
Is disruption. So this again is normal tissue that has developed, but there is a destructive force that acts upon that specific tissue and examples of this include amniotic bands, ischemia or a teratogen. And in this situation, you'll see that there are several dish different tissue types that are.
Well demarcated on a specific anatomic region.
So you have specifically an area that was affected.
By this destructive force.
And so when we look at examples of this, here's an example and many you may have seen different versions of this of an amniotic band sequence.
And again, it can affect various parts of the body. You can see here that in this baby it amputated the entire an entirety of his left hand.
So again, multiple tissues affected, but otherwise was forming normal up until that point.
Looking at another condition that we may be familiar with Poland anomaly. This is usually thought to be a destructive force related to the vascular system.
So there's usually.
Poor vascular supply to one area of the upper arm and that affects the development of the pectus muscle as well as the arm involved, and can include even differences in the fingers and anatomy based on that.
That lack of blood flow during a critical time of development.
So again, the tissues were normal originally, but because of that vascular.
Interruption. There's a disruption in terms of the?

Development of that area.
And then lastly, looking at another cause for disruption, here we go. Is thal thalidomide.
And so this is one that some of us may be familiar with.
We don't use it anymore.
But this was a drug that was given back in the 1950s and 60s for as an anti medic during pregnancies and again it was destructive and affected the supply to all of the extremities.
And so you had a babies born with these types of disruptive anomalies.
Moving on, so the first two deformation and disruption were normal tissue.
The next category, dysplasia, is actually abnormal tissue.
So this is where we start getting into more likely to be genetic and cause. So you have abnormal organization and function of specific tissues and will go through these examples.
These are things that may or may not.
Improve over time and they may even worsen with time.
So good examples of this category of dysplasia is hemangiomas, renal dysplasia, even skeletal dysplasia.
So.
Hemangiomas are a pretty mild example of this, and so many of us have seen either a single or multiple.
But this is an abnormal growth of vessels that grow and then regress, usually by childhood.
And this is again a dysplasia.
That's discrete.
Versus a renal dysplasia?
So we sometimes see autosomal recessive polycystic kidney disease or adult onset polycystic kidney disease.
And again, this is abnormal renal tissue.
That typically is due to a renal.
And the last category in this is skeletal dysplasia.
So we see quite a variety of different skeletal dysplasias and you can see here a family that was featured on one of the television networks that included individuals that had both achondroplasia and the father who had camped Amelia.
Dysplasia and so again, these are all different and abnormal development of the

skeletal tissue and again it's genetic.
And then our last category is malformation.
And so this entails just an abnormal developmental process. When we talked about again the timing in and development between implantation.
The embryo and the fetus.
Something in that early phase has been impacted and caused the either arrest, delay or misdirection of early development of that tissue or organ.
And so again, these may be some, you know internal cause, but generally they're going to be either a gene defect, a teratogen or a stochastic which is just a fancy word to say that we can't predict the events that preceded it for that process.
So when we look at this, this is a category that fits into that 2 to 3% of newborns who are born with a major significant malformation.
These are typically going to have serious medical and cosmetic consequences.
And often need medical and or surgical intervention. So I've listed some examples here and we can look at those and so examples that fall into this category include cleft lip and palate.
And again, you can have various types all the way from an incomplete pallet to a complete cleft pallet to bilateral cleft, lip and pallet. And so certainly we've seen various varieties of this. While we do know that there are multi factorial causes for cleft lip and or pal.
There are definitely single gene disorders that we have now identified as being causative of this particular finding.
The next condition that we're looking at is a neural tube defect, and again this is something that occurs early during the pregnancy, usually by the 4th week where the neural tube fails to close and again is considered to be a major malformation.
And then the last example that I share with you is an amphalocele.
And so this again is a pretty significant malformation that often requires surgical correction. And this particular finding is associated with a variety conditions that we will review. But the ones that come to mind are Beckwith, Wiedemann syndrome as well as some other chromosomal defects. So this is somet.
Where again, genetics should be at the forefrfr of your mind.
This would be a clue that further evaluation is required.
So those were major malformations, but a lot of us have minor malformations and in fact these effects 15 to 40% of healthy people, they're really not significant in that.
They don't require any medical or surgical intervention and they can be normal

variants, but they can also be.
Very important, subtle clues that give you information about an underlying genetic diagnosis.
So the one I think that we think about the most when we're evaluating is what we call a single transverse Palmer crease.
And I'll show an example of that and then we have some other common minor anomalies that we can look at.
So here's a single transverse Palmer crease.
Again, 3% of the population has this unilaterally, and if it's bilateral, it's more.
An indication of hypotonia.
And so that's because there's decreased movement.
In utero, but by itself again is just a minor anomaly or malformation. Another common minor malformation is 2/3 toesindactyly.
So you can see here where this fusion happens between the second and third toes, and here it is from an anterior view.
Again, this is quite common, but also can be associated with different genetic conditions if it's.
Seen in combination with other malformations.
Here we have a double whirl hair whirl, so normally most of us just have one that runs in a clockwise fashion.
And sometimes you can see two again.
This is a normal variant, but can be indicative of an underlying CNS problem.
So something to look at.
And then last, sorry for our next anomaly.
We all see a lot of hair preauricular pits as well as tags.
And these again can be a minor anomaly that can again be indicative of a of a bigger anomaly or condition.
And then lastly, Cafe Olay macules or spots again, we see these regularly within our practice and a single Cafe Ale macule by itself or a couple really are not concerning and common among the population.
But when we see multiple greater than six in combination with other findings, then again we start to get concerned about a a particular genetic condition like neurofibromatosis type 1.
So.
Here's just a summary of all the minor malformations that we have categorized, and

this is something again that you can find in an article here.
That's referenced and so we talked about a lot of these different findings, but they can involve the head and neck, the eyes again the eyes, it could be the slant of the palpebral fissures. The ears could be the shape or position mouth as well, could be related to.
The shape or position?
The.
Extremities may have abnormalities. Again, that don't require any surgical intervention.
We talked about, you know, theal, but a minor malformation correlate would be the umbilical hernia. And then lastly these skin findings.
So again, these are quite prevalent, but in combination can be suggestive of an underlying genetic etiology.
And what we found in actuality.
While the good majority have.
Only none to one major anomaly.
The more minor anomalies that you have.
So when you get to 3, the likelihood that there's another major malformation goes up, but it goes up significantly when you have 4 minor anomalies.
So again, the more minor anomalies are likely to be associated with at least one or more major malformations.
So that's something that again is a key take away.
From this talk.
So we talked about mechanisms and now I want to switch and talk about patterns.
So we now can look a little bit differently about the patterns of anomalies.
And so we talked about different areas and so they can involve just a single system. It can be an association, meaning there's multiple anomalies that we know are associated with each other, but we don't know the underlying genetic diagnosis.
It can be a sequence, meaning that it's triggered by one initial event, or it can be a a complex basically where it involves a particular area.
And then lastly, we have the term and and group that we are probably the most familiar with, which is syndromes.
So again, you know, these anomalies are typically sporadic and maybe multifactorial.
We then have the category of syndromes which encompasses about 25%.
And then the last group is 15%.

So looking just at the single system defects again, that comprises the majority of the defects, this accounts for about 60% and usually the specific cause is difficult to identify.
Again, there's probably a combination of genetic and environmental factors that lead to these particular findings.
So these conditions include things like.
Clap, clip clubfoot, pyloric stenosis, congenital hip dislocation and congenital heart disease.
So these are again are common major malformations that we see in the newborn period.
The association.
That many of you are probably most familiar with is voctural, which stands for vertebral **** cardiac, TE fistula, renal and limb defects.
And this really just denotes that we have an association.
Or a group of malformations that we know occur together more often than expected by chance.
So it seems non random, but we don't know that there is a common etiology and so this again is an association that we still have not figured out the inciting 'cause.
I will say that there are a lot of what I call phena copies.
So conditions that have some of the features of factorial that we now have genetic.
Single gene causes for but we still have a lot.
That we have not been able to identify.
Our next pattern to look at is a sequence.
So this is again where a group of anomalies arises from an initial malformation, and we have several examples of this that we see.
So the conditions that we look at are Potter sequence, holoprosencephaly sequence and Robin sequence.
So here's Potter sequence, so this usually.
Will come from a renal defect.
That causes a lack of urine.
Subsequently, there's not enough amniotic fluid for the baby and what you see is that there's pulmonary hyperplasia.
They get fetal compression.
They end up being in a breach position and they have abnormal positioning of their hands and feet due to that fetal compression and so again the instigating factor was

that renal defect that caused the lack of urine.
And again, that may be caused by a number of of renal abnormalities.
Another sequence that we see quite regularly is called holoprosencephaly sequence.
So this is failure of the mid face or the forebrain to develop.
Again, what we see and you can see here demonstrated by this infant who is significantly affected is that they have a midline cleft lip and palate.
They have hypotelorism, meaning that.
Their eyes are are closely spaced and then on, if we were to do a brain MRI, they would have holoprosencephaly.
So again, those midline defects, this is something that has again a very variable expression.
And in this child's mother, it's hard to appreciate. Maybe on the level of the picture, but her she has the same genetic condition and her only feature is a single central incisor.
So that's the only malformation.
That she had as a clue for this particular condition, and this is due to a gene defect.
And the last sequence to discuss is Robin sequence, also referred to Pierre Robin sequence.
And so you can see here there's a number of inciting features that can result in this Pierre Robin sequence.
So it could be just a neurogenic hypotonia where the tongue is displaced.
It could be extrinsic from oligohydramnios or not having enough amniotic fluid.
Or there could be a genetic condition again.
Affecting the collagen that ultimately leads to mandibular hypoplasia.
So the mandible does not form, it pushes the tongue back and then we end up with AU shaped cleft as well as the micro nathia.
And so again that comes from this inciting feature that leads to that antibular hypoplasia.
So both non genetic and genetic causes.
The other area that has created some just discussion amongst our group is.
The complex, also known as a developmental field defect.
So again, this is where a noxious influence acts on a particular geographic area of the developing embryo. I mentioned the path, the pathogenic mechanism of disruption.
So this falls into that category and again most of them are going to be vascular anomalies. I mentioned earlier, Poland anomaly where you have an interruption of

the blood supply.
To one extremity, typically the the left upper arm.
But you can see similar patterns of vascular causes of again a field defect with sacral agenesis or even hemifacial microsomia.
So again, there's a particular area that has been affected and normal tissue from developing appropriately.
And lastly, syndrome syndrome is a word that we use quite regularly. It's not.
I try not to use it as much when I'm talking to patients because I think it can have.
Somewhat of a negative connotation, and really this word comes from the Greek running together and it's a group of recognizable anomalies that come from a single genetic etiology. And so prior to having a lot of sophisticated genetic technologies and molecular sequencing, the conditions that we observed were descri.
As syndrome. So these group of anomalies that were appreciated.
And now are known.
Going to have a variety of of genetic causes, so some of them are chromosomal disorders that are due to number or structure. Some are due to gene defects and then others can be caused by teratogens including infectious etiologies.
So let's just talk a little bit about what that looks like before we switch over to looking at some different syndromes.
Hopefully you can assess again the detective.
Can be either the pediatrician or you know the.
Geneticists. But we have to put it all together in terms of gathering all of the information. So the history knowing about the pregnancy, the birth, the health and development, as well as growth and family history, and then ultimately the exam and looking at the different anatomic regions, the.
Organ systems, measurements, photographs, again, all together to help us find all of those.
Unique clues that would be a red flag and hopefully.
Convince you that there may be something underlying that's genetic and requires further evaluation.
So when you're thinking about these findings, you wanna again think about the timing, the mechanism, the pattern. And we have a variety of resources that we can look at for that, that I'll share at the end. And then ultimately we want to do some confirmatory testing and that.
Can include anywhere from laboratory testing, imaging and then.

That allows us to predict the clinical course and then provide families with long term outcomes as well as resources.
And so that's essentially what we do in our clinic on a, on a regular basis is get all that information, get a detailed history and physical and exam and then start to put it all together so that we know what the next steps are for confirmation.
So when you have a limited eliminated the impossible. Whatever remains, however probable, must be the truth.
And so now I just like to usually this portion of the of the presentation is a little bit more interactive.
So hopefully when we when I share the pictures that you'll take the time to take a good look at the photo that I'm showing you and then we'll go through the different features that again give us the diagnosis.
So here's our first condition that we're going to.
To review.
And if you take this picture, hopefully most of you are noticing a number of of of features, minor anomalies, that again suggest a major anomaly.
So for this child you can see that he has upslanted palpebral fissures.
So the opening of the eye is slanted upwards. If we were to look at his profile.
The face face is a bit flat.
Looking at his hand here, he has a single transverse Palmer crease.
His hands also look a little bit broad and if we were to look closely, he would have a little bit of clinodactyly or curved to his fifth finger. If we were to look at his eyes, he may have a brushfield spots and it's a little bit hard here.
But he does have some minor epicanthal folds.
And so hopefully when you looked at this picture.
Initially, the overall Gestalt would have suggested Down syndrome, and so again, many of us are familiar with these particular features.
But it's important again to look at what each of those individual features include.
So those craniofacial abnormalities the hands.
And then if we were to look at the feet, there would be a gap between the 1st and 2nd toes.
Why is this important?
What information or long term health?
Concerns can come from this well Down syndrome. As we all know, has intellectual disability. 50% of these individuals have congenital heart defects.

Over time, they can have a number of health complications, including ear infections, hearing loss, vision problems, thyroid disease, GI disease and in some.
Leukemia. So again, making this diagnosis helps us in terms of health maintenance. And evaluation to ensure that we provide appropriate and adequate care. So we'll move to another picture.
Here's a cute little girl.
And if you look at her, you may see some features that appear particularly striking.
So we can notice here that she has blonde hair.
Her eyes here they look a little bit puffy, and so she has kind of this supraorbital.
Fullness.
Looking here, her philtrum is a little bit flat.
And if we look a little bit closely, her mouth is a bit fuller with this full lower lip.
And so this particular.
Facial feature is common in in Williams syndrome, so this is another condition that we see regularly. And so we saw those, but the prominent lips with a large mouth is a very key feature that would suggest this condition.
So again, why is this important?
What health consequences can individuals with Williams syndrome experience?
These are board questions for the pediatric resident. So we always see or can see supervalvular aortic stenosis.
So when that cardiac feature is identified, we should always think of William syndrome.
In addition, they can have other anomalies of the kidneys.
Joint limitations and they usually have an intellectual disability.
That can be deceiving because they're very chatty and friendly and very musically inclined.
And I included here a documentary that was shared in 2013 about a woman who had Williams syndrome and shares some of her experience. If you're interested in looking at that further.
So again, another genetic condition that may present in your clinic that warrants further evaluation and management.
Here's another little girl. Very cute.
And again, you can look at a variety of different features that may stand out to you.
I imagine that probably the most notable thing here is her macro glacia or her large tongue.

Other things that may be noticeable are here, and it's a little bit faint, but she has a capillary Hemangioma that's midline to her forehead, or glabella, and then looking a little bit closer at her. If we look at her ears, she has some creases, and if we were. To.
Back of the ear, there can also be pits.
So ear pits and other major anomalies that we may see is that they're overgrown. So macrosomia and that can be generalized overgrowth with visceral Begley, and then they can also have umbilical hernias.
So these are the major features that we see with Beckwith Wiedemann.
But again, this is a condition that can be associated with other malformations that we need to be aware of.
And they include fallacial. So anytime I see a baby within a fallacial, I immediately start thinking about this particular condition.
They may also have renal abnormalities hemihyperplasia with overgrowth of one particular extremity or side of the body, and they also are increased risk for tumors.
So this is about most importance to make this diagnosis, because individuals with backwith widomain undergo or require serial screening from birth until age 7 in the first four years for hepatoblastoma and then up until seven years for Wilms tumor.
So again, a very important diagnosis that we do not want to miss.
Moving on to our our next picture, here's another cute little girl and I'll give you just a moment to take a look at her before we go through her features.
I think maybe some of you will appreciate that she has curly hair.
So again this is.
I wouldn't say it's a minor anomaly, but it is something again to note, when we look at her eyes.
The openings here actually don't slant downwards, so we talked about Down syndrome, which was an upward slant.
This has a downward slant.
And if we draw a line from the most outer the outer part of the campus of the eye to her occiput, this ear is not touching that line, which it should.
And so her ears are also low set. And then looking at her nasal tip. It's a bit broad.
So she has kind of a short, broad nasal tip.
And then if we were to look a little bit closer at her neck, she has a broad neck.
As well, and so these are all features that would be suggestive of a condition called Noonan syndrome.

So again, the facial features are very typical with the wide spaced eyes, broad face down, slanty, palpebral fissures, low set ears, curly hair. We were to look at the back of her neck.
She would probably have a low posterior hairline.
And again, that short, broad neck, this is another one.
Again, that is very important to identify because there are a number of health issues that.
Actionable, of course. Over the course of this child's lifetime, these include short stature that can respond to growth hormone. They often have cardiac defects, and so again, here's that.
Board, clue or Pearl?
This condition is often associated with pulmonary valve stenosis. So when we see this, I always start to think about this particular group of conditions.
They can also have or develop cardiomyopathy.
They are at risk for a bleeding disorder and again they also have an increased risk for leukemia, so they require serial monitoring of acbc as well as a heightened awareness for that particular health risk.
Moving on, here's another little cute girl, and I'll give you just a second to kind of look at her and think about what the features are that you see. I think one of the things and again, I usually tell our students and residents to think about this.
This exam, similar to a radiologist reading an X-ray. You take it from 1 area to the next just like we do our exam.
So looking at her hair, you can see that she has a very full head of hair and that.
Her forehead is a little bit narrow with a low anterior hairline.
Her eyebrows are thin and arched with a little bit of cinniferous, so connection that's in the midline between the eyebrows.
She has these lovely, very long eyelashes that I hope you can appreciate.
She has an upturned nose and then this very flat philtrum with a thin upper lip and a downturned mouth.
So again, these are all features that make her distinctive and would give us a suggestion that she has an underlying genetic condition such as Cornelia de Lange syndrome.
And so again, she has the typical facial features, but this condition is again important to identify because they can have poor growth, moderate intellectual disability, upper limb anomalies, as well as diaphragmatic hernia.

So those are all again major concerns that could be associated with these various minor findings.
Moving on to our next condition, so I did hear someone enduring my introduction.
I am a biochemical geneticist.
Which means that I typically see a lot of inborn errors of metabolism.
So I definitely wanted to include this in my dysmorphology talk because we often don't think about metabolic disorders and dysmorphology.
But if you look at this child, he definitely has some distinctive features.
And again, if we start from, you know, the beginning, he has a full head of hair.
He has heavy, thick eyebrows.
He also has this.
Periorbital fullness.
And I hope you can appreciate here that he also has some thickness and fullness of his nose.
He is not, does not have the typical creases that we see here of the cheeks and then his.
His filter groove is is somewhat deep and pronounced, and if we were to look in his mouth he would have.
Wide spaced teeth.
And here it's hard to appreciate.
But he does have kind of fleshy, full earlobes as well.
And if we were to do an exam, he would have an enlarged liver and or spleen, as well as an umbilical hernia.
And so again, this is something that should raise concern for a condition called Hurler syndrome.
So Hurler syndrome is a mucopolysaccharidosis and they can have these very specific cranial facial features, including the hair sutism the full cheeks.
The short nose and again the wide spaced teeth.
But this is very important to identify because they can go on to have other health issues, including corneal clouding cardiomyopathy changes in their bone structure such as dysostosis Multiplex, as well as short stature.
Some states are now doing newborn screening for this condition, and so my hope is that if it is on your newborn screen.
So for MPs one that this is a child that would be identified before they.
Or symptomatic treatment for this condition involves enzyme replacement therapy

or, if detected within the 1st 18 months of life, they would qualify for a bone marrow transplant.
So again, a very important disorder to to have and identify early because of those available medical interventions.
Moving over now to a different condition.
Will let you look at this one for just a second and appreciate.
Hopefully that this individual, even though he's sitting, is very tall.
His arms are quite long as well as his legs, and if we take a closer look at him, you can hopefully appreciate that he has a very long face that's narrow.
His cheekbones are somewhat flat, so that's called Mailer flattening. If we were to look at his palette, it would be narrow.
And then he may or may not have a pectus.
Excavatum or Karen Adam.
So a chest deformity and then and he also has lengthening of his fingers. And if we were to look at his feet, they would be long and narrow as well.
And so this particular feature.
Would suggest a condition called Marfan syndrome.
And so again, they have a very typical craniofacial appearance with that long, narrow face, as well as down slanting palpebral fissures.
Which is a high arch palette that then leads to dental crowding.
And they again can have other physical features.
Many of you are are very good at raising concern for this particular condition, particularly when we have a individual who's tall for their family or above the 97th percentile for height, and this is a condition that again can have some pretty significant medical consequences.
Aside from lens dislocations, which can occur at any point during their life, they can have catastrophic aortic root dilatation that can lead to a rupture as well as mitral valve prolapse.
So these individuals require regular monitoring by cardiology and echocardiograms.
And again, if they see that dilatation early, there are treatments that can be.
Used to slow that process.
Or even correct it before it causes an issue.
Moving on to my last condition that I'm going to share before I just give you some pearls, here's another picture of a gentleman who actually was on a television series in the UK who catalogued his journey with his girlfriend and making the decision of

whether or not he.
Wanted to own children? This individual had some significant health issues at birth, and we can appreciate some of the physical.
Physical features similar to Marfan syndrome, he has down slanted palpebil, frischer's and a male are flattening here, so it's very flat here and that causes actually the lower lids to have a little bit of a droop and can have a cleft. If we were to look closer.
At his ears, he would have either unilateral or bilateral ear malformations.
All the way from.
A malformation to an absent ear.
In the mouth of complications that can occur with this condition, similar to the PR Robin sequence is that they get micronephia or hypoplasia that causes ultimately displacement of the tongue and can lead to cleft palate.
So a lot of very serious health issues, all the way for minor to major and a lot of these individuals often require facial reconstruction and some even require a trach in order to maintain their airway until.
Their jaw is able to grow. So again, here are the typical features that we see with this particular condition.
They can be very striking or very mild.
This is one that we can see.
It's an autosomal dominant condition that can run in families, and I've seen individuals that have very mild features, so it's very variable in its expression and sometimes even incomplete penetrance where a person may not have any of the features that would be.
Suggestive of this condition.
So again, something that's important to identify not only for the individual that's affected with this, because they are at risk for, as I mentioned, the hearing loss, the cleft palate and the airway problems.
But this is important to identify for recurrence risks, because if there is a seemingly unaffected parents, they may have, they would have a 50% risk for passing this on to their.
Any other future children?
So hopefully you've had an ability to appreciate some of the features and can now take some time when you're in clinic and when you see somebody who is distinctive. Try to go through systematically and look at what those features are and how they may be related to a specific condition, and even appreciate the mechanism or the

pattern. We have a lot of online resources that we use and I encourage.
Providers to use that is are freely available. So the first one that was originally published in book form back in the 1960s is the Mendelian inheritance of Man, which is now online, and it's called Omim. So this is a free resource from the government and it cat.
All of the genes, as well as genetic conditions that have been reported to date.
You can see here that I was able to put in earcrease and it gave me.
The top four entries that have ear creases, and we discussed #2, which is Beckwith Wiedemann syndrome number one is one of the genes that causes Beckwith Wiedemann syndrome.
So again, if you have a very unique finding, you can put this into the search engine and it will give you the top diagnosis to consider with that particular feature.
And it's very helpful and provides a lot of information in terms of all of the symptoms, the mechanisms.
As well as links to different resources and literature.
So again, online and free, the next one is a little bit more complicated and it's one that we like to play with a little bit, but it's called the phenomizer. So this is also free and it's called the. It's based on basically what we call HPO terms or.
Human phenotype ontology and so you can take all of these different features so you can see here I pulled up.
The different toasted actales and you can add them.
And create a list of all of the major and minor features, and then do a search to see which conditions match those features best.
And so this is one way that we can use to try to narrow down the potential diagnosis or etiology for a variety of minor and major malformations.
So again, it's a little bit more complicated to use, but can be of interest if you have again.
A patient that presents with some findings that are unique.
So I know that when I first started training in genetics, there was a lot of conversation.
You know, if it's genetic, what can you do about it?
Can't change our genes.
I really want to just take.
The clinical utility of genetic and genomic services.
This has continued to evolve as our knowledge has expanded and we've again began

to understand a lot of the pathophysiology, the genetic mechanisms, and I'll say that from the patient perspective, you know the diagnosis allows them to have a prognosis and treatment.
I always tell them that we now have a road map that we can follow for their medical management as well as.
Prevent any unnecessary testing or procedures or interventions.
Once we have a diagnosis, we can provide them anticipatory guidance and health maintenance.
That's specific for their condition and again ultimately in the future it may lead to some specific therapy or management from the family. Some of these conditions again allow us to test for at risk family members.
It allows them to then make a decision that's informed about their family planning and.
Recurrence risks for reproduction.
It also brings resolution to what we often call a diagnostic odyssey, which can often be costly and wasteful.
And then ultimately, it does bring a lot of closure to families when they are able to connect with different disease support groups and get involved and share their stories and provide again a resource for them that they can connect with regarding their child or family member.
And then ultimately, just our society as a whole.
We can understand that you know the identification and ongoing identification of these genetic conditions will ultimately lead to better research and clinical trials and ultimately hopefully reduce the economic impact on our healthcare system. And I will say that I've been in genetics now for almost 20 years and.
I have seen the revolution and impact that genetics has.
Made and continues to make.
We're now giving enzyme replacement therapies.
Is medically using gene therapies and I think there's just a lot more to come that really highlights the importance of getting these individuals diagnosed and into care.
So as my last slide, I just would like to share hopefully as you go back into your practice again, you'll start.
To look intentionally for these minor minor malformations during your physical exam.
And have a better ability to describe these distinctive facial features.

On your exam as well as the physical findings that you should be looking for when you see these facial features and then ultimately refer them over to genetics when you identify these multiple minor and major malformations for additional testing.
And with that, I will just share my references.
So there's a lot of different resources online and in the literature that you can use.
And I'll thank you for your time and open it up for any questions.

Kamat, Deepak M 52:50

Thank you, Doctor Pham Ping for that wonderful, wonderful presentation.
Let's see if anybody has any questions. I'm looking at chat box and you can also ask question directly to Doctor Campbell.
Doctor Lynch, go ahead and ask your question please.

Lynch, Jane L 53:07

Hey, that was great and so important.
I just wanted to do a shout out for it.
Is someone you probably know, Rick Giannotti.
We had him speak at a conference. We had the privilege of that last year and I'll put a link in the chat box because he just published a book on positive exposures where he's photographed kids from around the world.
In positive positive settings, which is.
In contrast to The Smiths Books, Pictures that we all grew up with, and I think it's just, I'll put the link in the chat because it was just such an amazing.
Eye opening experience to hear his talk about as a photographer, how important it is to see beauty in different ways.

CN

Champaigne, Neena 53:57

Absolutely so.
The picture that I used and you'll see that the pictures that I used. Yeah, I mean I again want to appreciate the differences and not stigmatize, but the picture from the individual with Marfan syndrome was taken from his collection. And you're exactly right. He has made. He was.

Lynch, Jane L 54:01

I recognized it.

Champaigne, Neena 54:18
A fashion photographer who then changed over to.
Again, starting with albinism, appreciating the beauty and differences.
So it it is a a great resource.

Kamat, Deepak M 54:32
Any other comments, questions or doctor Shapir?

Lynch, Jane L 54:39
There's some in the chat room.
There's one about would you consider Jeanette consult for unexplained fractures in a younger toddler with non accidental trauma injury ruled out?
I'm just reading it.

Kamat, Deepak M 54:50
Oh, OK.
Yeah, sure.

Champaigne, Neena 54:52
Yeah. So I I see that question and I would say absolutely, certainly there could be physical features and we usually do.
Again, the conditions that come to mind are osteogenesis, imperfecta and so there are resources that we could explore and just make sure that we can identify whether or not that is one of the causes for unexplained fracture.
Of course, there's other bone disorders that probably fall within the endocrinology, but there's certainly.
Idea of things to take into consideration.

Kamat, Deepak M 55:29
Other questions? Comments.
I don't see any.
Is it doctor shamin? Thank you.
Thank you very very much for that interesting talk and.
Spin your one hour with us.

Really appreciate it.
Thank you all for attending this morning's grand round.
I'm going to conclude we have a faculty meeting in 5 minutes, so thank you all.
See you at faculty meeting and thank you, Doctor Champin again.

Champaigne, Neena 56:07
Thank you.
Thank you for having me. I appreciate it.
Thank you.

Kamat, Deepak M 56:11
Thank you.

Lynch, Jane L 56:11
Thank you.

Kamat, Deepak M 56:11
Bye bye.

Williams, Janet F (Dr.) 56:12
Thank you.
Wonderful talk.

Champaigne, Neena 56:14
Thank you.

Kamat, Deepak M stopped transcription