THOMAS BENNETT RUSSELL: We're going to talk about a couple topics. First, we're going to talk about the evaluation of microcytic anemia including talking about some treatment modalities. We'll very quickly talk about the newborn screening. And then we'll talk about some of the new guidelines for ITP. And if time allows, we'll have room to talk about neutropenia.

I really want this to be a practical experience for you guys, an interactive. So if at any time you have any questions, please do not hesitate to raise a hand and we'll get to it. So we're going to start with a case presentation. And this is a 19-month-old African-American male that presents with a low WIC hemoglobin. We've all met this patient, right?

So other clinical factors include the baby is term, the baby was exclusively breastfed for approximately seven months, and now consumes way too much milk, about eight ounce bottles of milk per day. And we instinctively get a CBC to assess them for anemia.

So let's start with the definition of anemia. The definition of anemia is a physiologic one versus a practical one, one being the hemoglobin level too low to meet the cellular oxygen demands. We all care for patients with sickle cell disease that walk around with a hemoglobin of anywhere from 5 to 10, and they somehow are able to deliver oxygen in their tissues very efficiently.

Alternatively, we more commonly or practically use a hemoglobin level greater than two standard deviations below the mean value for age and gender, and sexual maturation, ethnicity, and altitude. Case in point-- boys as they mature-- and this correlates, directly parallels, Tanner-- gain about a gram to a gram and a half per deciliter hemoglobin content over their female counterparts for the same age. Ethnically, we know that African and African-Americans often have a hemoglobin about a gram per deciliter less than Western Europeans. And as you go up an altitude, about every 5,000 feet above sea level you gain about a gram per deciliter, which tends not to be too big of an issue here in North Carolina.

This slide is really to illustrate that as a hematologist, I every single day have to look at this to look at age gender norms, because it's impossible to memorize this. In fact, it's not very helpful to memorize it. But when you guys call me on the phone for a consultation, I don't have this little thing memorized in my head, and sometimes it's not available to me. So I have a couple tricks that I want to share with you guys.

So a real smart guy out of Dallas developed these, and they're on your slides. And their two rules. One is called the 11 plus 0.1 rule. And the second one is called the 70 plus 1 rule. And these are tools you can use for children at the age of one till about 10 years of age.

And they're quick ways in your mind to kind of cheat to figure out if they're anemic and they're microcytic. So the first one and forgive the math, but I'll try to make it pretty simple. You take 11 and you add their age times 0.1-- so a one year old, 11.1; two-year-old, 11.2, et cetera, et cetera. So when I get that call and you tell me there's a three-year-old, first thing I think is, oh, three-year-old, 11.3.

OK. When it comes to if they're microcytic, you again choose 70 and you multiply or you-- sorry, add that to their age plus 1. So again-- a one-year-old, 71; a two-year-old, 72; three-year-old, 73, et cetera. And that works until you basically turn 10. And then we use the MCV of 80 to 100 which is equivalent to the adult. So case in point, if you take a three-year-old with a hemoglobin of 11.4 and an MCV of 73, that's age appropriate. If you take those exact same numbers and apply that to a six-year-old, they are not only anemic but microcytic.

OK, so back to Patient 1. Remember that's our 19-month-old African-American patient that presents with some features concerning for iron deficiency, and you guys get a CBC. So I'm going to ask you to ask three questions every sign every time you assess a patient with microcytic anemia. The first few questions I absolutely know that you guys know. The last one is the one I want to drive home to you as probably the most important question.

One-- is he or she anemic for age? Yeah, absolutely, and the next slide will kind of go through this. Two-- is the patient microcytic for age? And lastly, is the red blood cell production up or down? So here's those parameters with the age norms.

And as you guys very instinctively did, said yes, this kid's anemic. Yes, this kid has microcytosis. But in this case, the red blood cell production is down. OK, all right. That's about as good as I get at making my slides interesting. OK. And my wife had to help me.

So I'm going to try to convince you that the hematopoietic system is essentially a factory. It makes three products. It makes white cells, red cells and platelets. And we're going to concentrate our efforts on the red blood cells right now. And I want to convince you that red blood cells represent the number of cars that come out of that factory. And I want to convince you that the hemoglobin represent what's in the car or essentially what's the quality of that car.

So from the headlines, 2004, doesn't matter. Ford Brazil halts truck production due to steel shortages, OK? So if you have a Ford plant and you have to make big Ford trucks that weigh 6,000 pounds on average, and you run out of steel, your factory essentially closes down. But luckily, the human body is much more adaptable to that.

So in the context of our micronutrients iron being deplete or becoming deplete because iron deficiency in no way is a static thing-- it's always a continuum. Our bodies have adapted to start making smaller cells. So given the fact that you lack some iron, instead of making those big Ford trucks, you can now make little Ford Focuses, which is essentially that microcytic red cell, right?

Who's familiar with Mentzer Index, raise your hand? Or have used it? Who has to Google about every other week? I do, I always forget it to be honest with you, because I don't use it very often. But it's actually a really good way to kind of prove this point.

So the Mentzer Index is defined by the MCV divided by the red blood cells. And if it's greater than 13, it favors iron deficiency. If it's less than 13, it favors thalassemia. And case in point, our patient, if you do the numbers, his Mentzer Index is 20.3, which would put him certainly in the place where you think he has iron deficiency based on his history. That all makes a lot of sense.

So I want to introduce you to the concept that we call proportional versus a disproportional microcytic anemia. So in iron deficiency anemia, go back to that plant, or that factory rather. As that micronutrient becomes deplete or deficient, there is a microcitosis that is proportional to the decrease in red cell production. Right? And that is a proportional thing that happens over time.

In thalassemia, and this is really the first time we've talked about thalassemia, there is a very different pathophysiology that's occurring. You always, always have a microcytic product. And we'll talk a little bit about that. But the body still has the responsibility of delivering oxygen to the tissues. And so now you have a bunch of cars that aren't great, and the way you deal with that on a production line basis is you can increase your production of cars. OK? And henceforth, as the denominator gets bigger, it drives that ratio down, which allows that Mentzer Index to be helpful.

So very quick, a slide on the pathophysiology of thalassemia. You have a decreased production of globulins. That imbalance leads to excess globulin precipitation that leads to damage to the red cell membrane, which leads to the microcytic of a very different pathophysiology. But what ultimately happens is that the patients become anemic because basically the cars on the road don't last that normal 90-100 days.

You get expansion of the marrow space, because I told you-- it's a factory. It's responsible for making three products. And if you have to make double or sometimes triple your red blood cell content to keep up with oxygen delivery, you have to expand the size of your factory. And then ultimately, you get little Yugos. They don't last very long, and they're not very good cells.

But what I want to convince you of is that there are plenty of red blood cells in the body. The quality of those red blood cells are just bad. And so that's the difference. So to drive that point home, we're going to talk about patient number two. You can only do this in slides, right, in presentations.

Another 19-month-old African-American comes in with a low WIC hemoglobin, right? He's also term, also breastfed for seven months. Consumes a little bit less milk than our first patient. And we get a CBC, and we're going to ask the same exact. questions.

One-- is the kid anemic? Absolutely. Is the kid microcytic? Absolutely. Is the patient's red blood cell production up or down? Yeah, absolutely.

So that's why that third question is so important. Because you're talking about production of red blood cells and how the body deals with either you have a bad-- or sorry, a lack of micronutrient in this case, iron. Or you actually just have a bad production line, which is the red blood cell production.

Again, we use that Mentzer Index. And lo and behold, that Dr. Mentzer was pretty smart and figured this out. And that this favors thalassemia.

This slide is just to kind of show a number of geographic distributions of different hemoglobinopathies, including thalassemia which is represented in yellow. The reason I show the slide is it just reminds all of us that people from France, Spain, Italy, Greece, et cetera, et cetera-- people that look like Western Europeans can actually have thalassemia. Very briefly we're going to talk about the newborn screen and then we're going to go right back into talking about iron deficiency anemia.

And these are things you can use in the future. These are very self-explanatory slides. But things that I don't feel like I arrived to understanding until I got to fellowship was all detectable hemoglobins are reported. Now there are hemoglobin species that basically they're so unstable that they basically fall out and they're not represented. Which is why this is a great screening tool, but it's certainly not the definitive test if you have to assess for hemoglobinopathies.

They're also reported in decreasing funding. Case in point, the first hemoglobin you see on the left is the highest quantity, although they don't tell you the percentage, and moving forward. So the case in point, if you get a newborn screening that shows FAS, that means the fetal hemoglobin at that moment is the highest proportion of hemoglobin, followed by hemoglobin 1A followed by S.

Also means that FAS is absolutely not the same as FSA. These are the slides you just can use in the future to kind of drive these points home. Normal, what we consider normal would be FA, because we know that the fetal hemoglobin is the predominate species of hemoglobin at birth.

If you have a Barts, this is where things get really confusing. We know Barts is associated with thalassemia. It's basically where you get a of tetramer of gamma. That's that inappropriate ratio, because you lack the alpha globulin.

But what's very interesting is the proportionality. How much Barts they see is actually what distinguishes the different types of thalassemia. The only other way to really prove that point is actually to do the genomic testing and very few people do that.

Additionally, when you look at-- I think this is a nice slide to look for sickle cell disease, which we're not going to spend much time. But the way I always remember it-- if A is higher than S, that's trait. If S is higher than A or A is not there, only thing you get is FS, then that's the disease. And one little trick for the kid that came out of the NICU-- if they got transfused, that A will be the predominate species, because they're getting adult blood. So that could be a bit confusing.

So back to our patients before we talk about therapy. As you can see every single one-- many of the parameters, rather-- other than red blood cells are exactly the same. The hemoglobin content's the exact same. The MCV is the exact same.

The only thing different in these two patients that I created is that red blood cell production in these are up or down. So when I look at a CBC, I always look at that, those three questions. Are they anemic? Are they microcytic? Is the red blood cell production up or down?

Back to Patient 1. So this is our patient that, based on the history and that CBC and our Mentzer Index, we think has iron deficiency anemia. So what are we going to do about that?

So what I want to convince you guys of is when you're counseling patients on iron deficiency, I want you to convince them that this is a therapy. And I want you to use that word, because that word has meaning. It convinces them that this is important to my child. This is not supplementation.

I think sometimes what happens with iron deficiency is, it's considered a micronutrient, a vitamin, and it's not really given the credit that it probably deserves. I give my patients their iron either once or twice a day. If you look historically, hematologists often said you can give it anywhere from three to four times a day. I can tell you as a parent, if I have to hold my kid down once a day or twice a day or four times a day, I'm going to choose the once a day opportunity.

And I have a different population. I have adolescent, predominantly female patients that I will prescribe four 325 milligram tablets of iron or ferrous sulfate to be given once a day. And I always get a call from a pharmacy, because it really scares them that I would give that much at one time. But it definitely helps with the compliance, if they can tolerate it.

We always want to identify their potential sources of blood loss. So I always document if there's urine or GI losses. And then we want to counsel them on contributing factors, medication history, diet, specifically milk intake, et cetera, et cetera. So why should we care?

Well, there's a clear association of iron deficiency with poor cognitive development, motor development and behavioral problems. And those are thought to only be partially reversible. And in fact, we don't actually think this is an issue of anemia. This is an issue of iron deficiency.

We just heard a great lecture from someone that was talking about autism, where the newest data says about one in 88 kids, right? This is a disease that affects, if you look lower on the slide, about 15% of the population, our young population. Only about a third of that population will actually have iron deficiency anemia. So those are diseases that we somehow need to separate.

Worldwide, we know this affects a lot of women and children. And in fact the WHO put it on the top 10 risk factors for contributing to a death. Now that's obviously not an issue in the first world, but that's a real big issue in the third world.

And why as a hematologist am I talking about iron? Well, it's because about 2/3 of iron is in a hematopoietic system. But where it really, really, really matters is all those enzymes that our body needs for normal function. And specifically, the neurologic system that needs iron to have normal function.

All right, we're back to Patient 1. We identified a patient that we are concerned has iron deficiency. We counseled them on their milk intake. We arrived at a place where we introduced that therapeutic iron. And now we're going to see him back in two weeks.

And I can tell you this is probably more conservative than you guys are used to. Because most of the time when we prescribe iron, we say we'll see you in three months. But I can tell you there are so many issues with compliance and tolerance and side effects, et cetera.

And if you're really trying to convince a family this is a therapy and they need it, then seeing them back in two weeks whether that's a physician, nurse practitioner, PA visit, or just a nurse visit to get a CBC and a retic count, and to make sure that compliance in iron therapy is going well. What I want to see in about two weeks-- in fact it happens as early as seven to 10 days. But I think to be practical about a two week follow up-- is I want to see an increase in their hemoglobin content by no less than a gram per deciliter and want to demonstrate they have a reticulocytosis.

So back to our factory. If you prescribe iron, it goes into their body. It is absorbed into the gut. It arrives at the hematopoietic system. And you make new cars. Then you know that you have arrived at a real diagnosis.

So when does it not work? Well, there are common things that happen. And this happens all the time. As a hematologist, I would say that probably 90-95% of the time when someone's struggling with iron deficiency, it's really these top ones.

It's either not given according to the instructions, the dosing is incorrect, very common that a lot of our colleagues are dosing it based on the elemental versus just a total dose of iron. And a lot of times, patients just don't take it. And I'm convinced a lot of that is that we do a poor job of convincing them of how important this is and that this is a therapy. Occasionally, there's issues of ongoing blood loss, an absolutely incorrect diagnosis, and then very, very rare cases there's actually malabsorption.

All right. So our patient comes back at their two week visit. And we check his CBC, we get a retic, and lo and behold-- in the ideal world, on my slide, magically, everything goes perfect, right? The hemoglobin content goes up by greater than a gram per deciliter, and they have a confirmed reticulocytosis. And in fact, this is the first time we've actually confirmed the diagnosis.

Everything I've done before that is that I put them in a box based on lots of information and expertise. And I made an intervention. And now I want to test that theory. And this is the first time we can say, yes, that kid actually has iron deficiency anemia.

Then I like to check a CBC in about four to six weeks to make sure that they have normalization of their hemoglobin. I like to separate iron deficiency anemia from iron deficiency. I think those are two different things on the same spectrum. But if you have a really good family, they're very compliant, they're doing well, this is the easy one to skip. You don't need to do that.

And then I like to see them or have them come back and get a CBC and a ferritin at three months, and then every about three months thereafter to basically talk about ending therapy. And I typically, the way I remember it is ferritin at 50. I try to get that ferritin close to 50. 40 or 50 is absolutely reasonable.

So by the numbers-- same exact thing, I'm just showing it in a different format. Day 1-- I meet the patient. I'm concerned they have iron deficiency. I get a CBC. I start my therapy.

Two weeks later, I get a CBC and a retic to confirm the diagnosis and to assess tolerance and compliance. I can tell you right now, I do not prescribe iron without MiraLAX. I don't do it. Because they all get constipated, and it's a big issue with compliance. And it doesn't happen on day one or two, but it definitely happens month two, three, four when I'm really trying to get rid of their iron deficiency.

In a month I like to check that CBC to document their anemia, the anemia part is over. And then about every three and then six months I determine if there are iron repleted so that I can stop their therapy. So that's really talking about a total body iron.

Notice I have not once ordered an iron panel. And I would discourage anybody from ordering an iron panel. I very, very, very rarely order an iron panel. And in fact, the population I most commonly do is kids that have iron or anemia of chronic disease. And for the grand majority of those patients, they actually have a [INAUDIBLE].

They're also quite expensive. And they're hard to interpret. And I can tell you, I can interpret it in many different ways to fit the clinical scenario that I want. So I find them not to be very helpful to be honest with you.

Well, let's break it down. Let's talk about what's in a typical iron panel. Ferritin-- ferritin is a great, great test. And in fact, it is by far the best test to assess total body iron.

In fact, if you have a ferritin less than 10, you have a 99% specificity for having iron deficiency. It's a pretty good test. We all know that it's an acute phase reactant. And there's really great pathophysiology why that happens.

When our body perceives an infection or inflammation, the body tries to hide the iron from all that microbiota that wants that iron. In the world of the microbiota, iron is really money. It's the economy of the microbiota. It's how electrons are moved from one place to another.

Serum iron-- almost a completely worthless test. If you eat a steak and I check your serum iron, it's going to be up unless you don't absorb. So it might tell me that you're compliant, and in fact, sometimes we have patients where we worry about compliance, or more importantly worry about absorption. We actually do a test where we will bring them in, get a serum iron, give them a dose of iron and then two hours later, recheck their serum iron to see if it actually gets into the duodenum and into the bloodstream.

Transferrin's not a bad test, by any means, but I would argue you probably don't need it for most patients. Basically the way I like to think about this is when there is less iron in the body, your body makes more buses to go and find all that iron that is missing. And then another one that's reasonable is the transferrin saturation. But again, like I said, if you just rely on a ferritin, more times than not, you will be well-served.

There are other tests or tools out there. I do not use these. The one that is of most interest is what's call hepcidin, and unfortunately, hepcidin is not commercially available. There's the disease called iron refractory iron deficiency anemia, where essentially this population of people make this liver protein called hepcidin. It's actually a great name, which essentially blockades the absorption of iron in the gut.

So in the context of inflammation or anemia of chronic disease, what happens is is the liver produces this protein blockades iron absorption. Which again, from an evolutionary standpoint, is a protective mechanism to essentially disgard any iron that might go to the microbiota that are trying to attack you.

All right, in summary, microcytic anemia-- look at those red blood cells. That's where it's at. Iron deficiency anemia-- think of it as a therapy. Assessing of a therapeutic response-- I like to look in about 10 to 14 days. And I want to demonstrate a gram per deciliter increase in the hemoglobin content and a reticulocytosis.

About a month later, I like to make sure that that anemia is gone. And about three months to six months thereafter, I like to make sure that that iron deficiency is gone. And I remember ferritin to 50. Questions before I move to another topic? We will move on. We good? OK.

Maybe we'll skip the neutropenia because-- well, maybe not. Wow. I said interactive. And you guys meant it. OK. We'll talk fast. All right, moving on. All right.

Next patient, Patient 3 is a five-year-old female who presents with acute petechial rash. Pertinent history is a normal growth and development. Her past medical history is unremarkable.

She's absolutely no associated constitutional symptoms and her exam is otherwise unremarkable except for the petechial rash. Specifically, she has no mucosal symptoms. And as you can see down there on the bottom, her platelets are 6.

So things have changed in the ITP world. And it's hard for even hematologists to sometimes agree on this topic. But I can tell you at Brenner we have a united front, and we really, really, really believe these to be true. So we've changed the name. We no longer call it ITP, which is an acronym for immune thrombocytopenia purpura. We've gotten rid of the word purpura, because guess what? Very few kids with ITP develop purpura.

We usually think of ITP patients to have a platelet count less than 20,000. So the patient that has a platelet count of 80,000, you probably don't need to worry about them too much. When you look at a smear, we often see large platelets. It helps us identify that this is in fact ITP, but in the office that is really not something you need to worry about because there are other factors that can help you arrive at the diagnosis.

Skin and mucosa symptoms-- in the context of an otherwise normal exam, sorry-- you should otherwise have a normal exam in the context of these symptoms, if it is in fact ITP. And when it comes to the things that we really worry about that were driven home to us a lot of times in our training is, well, if you have a platelet count of six, what happens if you develop an intracranial hemorrhage? That would be horrible.

And I agree. The interesting thing is-- that was probably too obvious, right? Dr. Obvious. The truth is that regardless of whether we intervene, the risk of developing a serious bleeding event-- and most commonly the one we worry about is that intracranial hemorrhage-- is about one in 10,000. It doesn't matter what we do.

Now in a court of law, does that matter? Absolutely not. The judge couldn't care less. And of course, if I intervene and I do something aggressive, I'll be praised. And if I do nothing, somehow then I might be the bad guy.

So things that are concerning-- systemic symptoms-- that's a concern, particularly chronic fevers, bone pain, et cetera. Other cytopenias, particularly hepatosplenomegaly and adenopathy, those are concerning features. And then I might disagree with this last one-- failure to respond to standard therapy. There is just a number of patients that for reasons we don't completely understand, don't have a great response.

So what's the natural history of the disease? Well, there's a reduction and cessation of new skin findings in about three to seven days. So really if your patient presents, within about a week or two their symptoms should start resolving.

And their platelet count, if you check, and we'll talk about checking, usually takes a couple weeks to really start going up. And it often correlates with their clinical skin findings. And when you look at the normalization of platelets, the point is is it takes a long time. In fact about 50% at three months, and about 80% will have complete resolution by a year.

So in the old ITP world, we said that the diagnosis was when it was less than 150. Acute was defined as from time of diagnosis to six months, and chronic was any time thereafter. And we base severity on what your platelet count was.

And so what really drove therapy historically was what your platelet count was. If it was five, that was really scary. If it was 20, that was less scary. And disease resolution is when you arrive back to 150, which is normal.

In the new world, the diagnosis is really when it's less than 100,000. So we're trying to get rid of some of those patients that walk around with a platelet count of 120. And they're fine. It's probably just their normal physiology.

We've gotten rid of the word acute, which I can't do. It's hard for me to do. And we call it newly diagnosed, and that represents that first three months.

They are persistent, which allots to a year. Remember that before we used to say chronic started at 12 months. So really chronic now is a year out. If you remember that, that's helpful. And then chronic ITP is as I said, it's after 12 months. And severity is based on the clinical relevant bleeding. Is the patient having symptoms of bleeding that are concerning that will drive therapy?

OK. So this patient in the ideal world, she had new onset ITP. Her history is very reassuring. That platelet count scares everybody. Everybody gets anxious and wants to intervene, but she only has skin involvement. She has no other associated symptoms.

Exam is good. Reliable, helpful family-- this is a kid I would reassess in seven to 10 days. And I may or may not get a CBC. I don't get a CBC if a history is reassuring, because I don't want to know what the number is. I want to rely on those clinical symptoms to drive therapeutic decisionmaking. I don't want to rely on that number.

Now are there things that would change my mind to either getting the CBC or intervening? Absolutely. I have a four-year-old patient who recently came in with severe autism, and he head bangs. I don't care if his platelet count is 20. I'm going to treat that kid, because that's a scary situation. Or the two-year-old that thinks he's Superman. That's a patient we might treat. Because that risk-benefit of therapy might be meaningful to that patient.

If you stop for questions, you will not have time to talk anymore.

We're not stopping folks.

Just trying to keep it moving

I'm going to get a groan either way, so let's move on. All right. Patient 4-- four year old Caucasian female presents with a mild neutropenia. Her history is her growth and development are great. She's unremarkable infectious history, other than she has a very mild respiratory infection. This is the classic kid goes to the ER with a viral URI. Someone gets a CBC, and then now we have to deal with the fact that she has a mild neutropenia.

OK. So a neutropenia represents a decrease in absolute neutrophil count below the accepted age and ethnic norms, realizing there are differences depending on the age and gender and ethnicity. Particularly in African-American patients, it's not uncommon. They have what we call either an ethnic or racial benign neutropenia, where they can live in that 900-1,100 range. And that is absolutely normal physiology and is not associated with infections.

This is a slide I think is probably really important from a practical standpoint. If you don't have neutropenia, your risk of infection should be normal, right? If you have 1,000 to 1,500, it's actually none. The risk of an infection is actually quite low. It's really the general population.

So if you have a kid with that mild range, 11, 1,200-- don't worry about it. So long as they're well. And that's really what matters, that clinical component.

In the context of moderate, that 500 to 1,000-- very low risk. It's really when we get into that severe range and really, really get into that very severe range, when it's less than 250, that infections are more of an issue. And those are kids we absolutely want to be part of their care.

And the secret behind neutropenia and what drives this is that-- remember I told you about that production line, right? We make three products-- white blood cells, red blood cells and platelets. Well, there is one cell that's unique and actually has a storage compartment or a reservoir in the marrow space. And that's neutrophils. And this we all understand. We're fine today. Tomorrow we get an infection. We go and get a CBC, and lo and behold, we have a white count or a leukocytosis. And if you look at the differential, the grand majority of that leukocytosis, what contributes to that elevated white count are neutrophils.

When you don't have that reservoir, that's when you get in trouble. So when you talk about the children with the congenital forms of neutropenia, they lack that reservoir, so on a day to day basis they can deal with the fact that they have low neutrophils. But when they get attacked, they don't have that arsenal to protect them and respond. So the most common cause of neutropenia is absolutely viruses, absolutely viruses. So in the context of a well appearing patient with an unremarkable history, just be patient.

So the way I like to think about that, there is not good recommendations that are available. I've looked and looked and looked. But what I like to think about this is in the context of severe neutropenia, if it lasts more than two to four weeks, that's a concerning feature and certainly in the context of infection, and in the moderate range if it lasts for more than a couple months.

Also, if there is more than one cell line down. If you have neutropenia and thrombocytopenia, that's a concerning feature. If you have atypical cells, that's absolutely a concerning feature. And I very much, when I talk to you guys on the phone, I really want a good abdominal exam, because features of hepatosplenomegaly are very concerning in the context of neutropenia.

So in our patient, she is well. I'm not too worried about her. She doesn't have any ongoing issues. I would say get a CBC in three months.

What happens often with neutropenia is sometimes we get CBCs once or twice a week. And that contributes a lot of pain and discomfort for our children and probably is not helpful for them. So the point is to be patient.

Question?