1. Introduction

Dr. Eyal Ben-Isaac: Hello and welcome to the Perspectives on Pediatrics podcast. I am your host, Dr. Eyal Ben-Isaac, recording from CHLA – Children's Hospital Los Angeles,

Tamar Minasyan: And I am your host Tamar Minasyan, PR Director at the AECP – Armenian EyeCare Project, recording from our office in Yerevan, Armenia.

Dr. Eyal Ben-Isaac: The Perspective on Pediatrics podcast is CME-accredited in Armenia, so if you're interested in receiving credits, please go to the links in the show notes or to our website at www.learnwithopen.org to take the accompanying quiz questions that go with this episode.

Tamar Minasyan: In our show, we showcase multiple medical practitioners from the US and from Armenia in the field of pediatric care. Note that that means some of the practices discussed may differ between physicians. Also note that since we have international guests and hosts, portions of this show have been translated and re-recorded by voice actors.

Dr. Eyal Ben-Isaac: If you like to read as much as you like to listen, we also have an OPEN newsletter where we share additional tips and updates on pediatric care.

Dr. Eyal Ben-Isaac: In our first episode we review how to best approach abnormal uterine bleeding. One of the most common concerns parents and patients express to pediatricians relates to the start of menstruation, any irregularity in the periods, and the amount of bleeding.

Tamar Minasyan: We review the pattern of cycles after the start of menarche, the variations of normal cycles, and if and when any work-up should be considered.

Dr. Eyal Ben-Isaac: In the first half of the episode, I talk to my good friend Dr. Tanaka, an Associate Professor of Pediatrics and a clinician-educator who has spent over 20 years delivering evidence-based care to adolescents and young adults. She is the medical director of the Teenage and Young Adult Health Center here at Children's Hospital Los Angeles.

Tamar Minasyan: And I follow up with a conversation with Dr. Nelly Aleyan, who is a pediatric gynecologist in the "Arabkir" Institute of Children and Adolescent health in Yerevan. She is one of the few gynecologists in the country specialized in adolescents and young adults' care.

We talk about abnormal uterine bleeding and contrast what is done in the American versus the Armenian context.

Dr. Eyal Ben-Isaac: To start off, here is my conversation with Dr. Tanaka.

2. Interview with Dr. Diane Tanaka

Dr. Eyal Ben-Isaac: Hello and welcome to the perspectives on pediatrics podcast. I am your host, Dr. Eyal Ben-Isaac, recording from Children's Hospital, Los Angeles. I had the pleasure of talking to Dr. Diane Tanaka. Dr. Tanaka is a good friend of mine, and is an Associate Professor of pediatrics and a clinician-educator who has spent over 20 years delivering evidence-based care to adolescents and young adults. She is also the medical director of the Teenage and Young Adult Health Center here at

Children's Hospital Los Angeles. I got to chat with Dr. Tanaka on the topic of abnormal uterine bleeding. I think one of the most common concerns parents and patients express to pediatricians relates to the start of menstruation, any irregularity in the periods, and the amount of bleeding.

Dr. Eyal Ben-Isaac: Dr. Tanaka did a wonderful job giving us the variations of normal cycles and when a clinician should consider investigating. We reviewed the pattern of the cycles after the start of menarche, the variations of normal cycles, if and when any workups should be considered, and how to manage abnormal uterine bleeding. It was a very educational and clinically applicable session. Here's my conversation with Dr. Tanaka.

Dr. Eyal Ben-Isaac: Hello everyone. Today, we are here with Dr. Diane Tanaka from Children's Hospital Los Angeles. Welcome Diane.

Dr. Diane Tanaka: Hello.

Dr. Eyal Ben-Isaac: And we're going to go over a case that we see relatively commonly. I think as pediatricians, when teenagers and mothers and parents come into a clinic and it's regarding concerns about menarche, maybe how long the periods are going, the irregularity that they might be experiencing, and the amount of bleeding.

So let's start with a case today, and we're going to go over… Maybe we'll start with a 17 year old female who comes in for regular checkup. She has been healthy throughout her life and reached menarche at age 15. On review of systems, she tells you her periods occur every 30 days, but at times they can be every 45 days

according to her monitoring. She feels some months that she has a lot of bleeding for five to seven days.

Dr. Diane Tanaka: Yes. This is a common issue that comes up I think for many practitioners that work with adolescents. And I think it gets confusing sometimes about, should I be worried? Do I need to do a workup? Or can I just do watchful waiting, right? And with time, this teens menstrual periods will regulate.

Dr. Eyal Ben-Isaac: And when do we usually say, "It's enough time?" So she started menarche at age 15, do we say, "Oh, it usually takes about one year." Can we give them up to two years before we expect it to be more regular?

Dr. Diane Tanaka: Yes. It takes on average two years to reach regular ovulatory cycles. The one thing we should keep in mind is the younger the adolescent starts their periods, so just this past week, I saw an 11 year old, when you start that young, you tend to reach regular ovulatory cycles in less than two years. It could be more like a year, maybe year and a half. Whereas the mid adolescent, like in this case where she was 15, when she started her menstrual periods, it takes more like two years.

However, keep in mind, it can take as long as five years to reach routinely ovulating every cycle. So just because somebody's hit two years and they're still skipping some periods or having some type of irregularity, I would not panic at that point, knowing that it could take three or four years, or even up to five years. However, if it's been four or five years since they started having their periods and they're still having very irregular periods, then I would start working them up.

Dr. Eyal Ben-Isaac: Very good to know. Something we could definitely tell the families when we realize that they just started menarche and give them some anticipatory guidance on when to expect normal cycles. On that note, what is considered to be a normal cycle typically? What is the range of days that they should not be worried about?

Dr. Diane Tanaka: Right. So we count menstrual cycles from first day of the menses to the first day of the next menses. So I can't tell you how many times I asked one of my patients, when was your last period? And they give me a date. So let's say November First. And then I've learned to ask, is that the day it started? Because most of the time, I'd say 90% of the time they give you an answer, that's the last day of the period. So we count cycles first day of the menses to first day of the menses and anywhere between 21 to 45 days is within a normal range.

Dr. Diane Tanaka: So many times, families will come to you saying that, "My daughter is having her periods sometimes every 24 days, sometimes every 32 days, sometimes 38 days, she has irregular periods." And so once we understand that, then we, as providers can think in our minds, "Well, she's within 21 to 45 days. We're good." Right? And you can just reassure the family and let them know that our bodies run on their own timeline. And so we are not as regular as a clock. We will have some variability and as long as it's within 21 to 45 days, we're all right.

Dr. Eyal Ben-Isaac: Great point. Just another great thing to let the families know so they don't worry. Oftentimes we get a complaint that they are bleeding too much, and we don't really know how to quantify that amount of bleeding. Do you have any

tips or tricks on how you can figure out how much bleeding that is and is it too much or not?

Dr. Diane Tanaka: Yeah. So this is a very common question that comes up. Just so that the listeners are aware, the American college of OBGYN recently changed the terminology that we use to describe how much girls are bleeding. And so heavy menstrual bleeding like Eyal said at the top of this podcast, is the new terminology that we use. And really it's defined as what the patient considers heavier than what their typical would be. So, in the past, we were trying to figure out, the definition is more than 80 CCs over the entire period. I don't know how anybody's going to practically measure that, right?

Dr. Diane Tanaka: The other tips I use to figure out if somebody is bleeding heavier is one, I'll ask them, is this period heavier than your typical periods? If the girl answers, yes, then I go by number of pads or tampons used per day. So I will ask her for instance, "How many pads on your typical periods or normal periods do you use per day?" She says, "I use four." That's pretty average. And then I'll ask her, "With your heavy period, how many pads were you using per day?" She says 8 or 10. Okay. She served as her own internal control. I know she's just doubled the number of pads she's using and I've got a pretty good idea this is definitely heavier than usual.

Dr. Diane Tanaka: Other things that providers can ask are, "How often do you need to change your pads or tampons because they're pretty soaked?" And if they're saying every one hour, every two hours, that's very frequent. So again, I'll take that as she's bleeding heavy, heavier than usual. Another question you can ask

is, “Do you ever have overflow bleeding?” So what that is, she’s been sitting at our desk, sitting down in a chair. She goes to stand up and then suddenly she feels this “gush,” kind of this rush of blood. And she can feel that it’s like flowing over her pad or past her tampon and her underwear is getting wet. That’s heavy bleeding.

Dr. Diane Tanaka: And then the final thing that you could think of to ask is, “Do you pass blood clots?” So now many girls may pass small blood clots. We’re talking, what do I mean by small, like the size of a dime. So maybe less than a centimeter, let’s say, because I know this, this is an international audience. The ones that are larger that we consider larger or things that are like two centimeters, three centimeters, maybe the size of a quarter. Anything larger like that, or significantly large blood clots again, that tells me she’s bleeding heavier.

Dr. Eyal Ben-Isaac: So we’ll continue that story because that’s what mom is concerned about. She says she’s concerned about the amount of bleeding her daughter’s experiencing. And mom asks if we should do any blood tests today or any ultrasound to find out why she’s bleeding so much. How do you pursue and when do you decide to do a workup when you’re concerned or not?

Dr. Diane Tanaka: Yes. When I determined that she is bleeding heavier or heavily, so she’s telling me… Let’s say we get the history, Eyal, she’s changing our pad every hour. She sometimes soils her underwear because the bleeding has just extended beyond the margins of her menstrual pad or through her tampon. And she’s passing fairly large blood clots or large blood clots, then I’m going to want to work her up. And so some tests you could think of running are: thyroid dysfunction is probably the most common etiology of irregular or changes in menstrual periods.

It's either you're bleeding too much or you're not bleeding enough, you're skipping periods. And thyroid disorders are fairly common. And luckily, even just running a thyroid stimulating hormone test is fairly inexpensive. So I would at a minimum do that.

Dr. Diane Tanaka: I would also want to check a CBC, not to determine the etiology, the bleeding, but just to get a sense of what's the sequelae of this heavy bleeding, is she already anemic, right? Because that's going to help us decide, is this a young woman who needs to be hospitalized because her anemia is so severe we are concerned? Or she may require transfusion with packed red blood cells. So that's another reason why I would obtain that. The other advantage of CBC gives you is you can look at your platelet count. So she's thrombocytopenic. You may then be picking up an etiology for her heavy bleeding, right?

Dr. Diane Tanaka: Other labs, your coagulation studies. So a PT and PTT is typically useful in these situations. In addition, I would ask key historical questions such as, "Do you notice that you have more frequent bruising or a bruise that's larger than you would expect for the amount of trauma in that area?" So it's typical for all of us to hit our knee against something, or you knock your shin against the edge of the table. Typically we get bruises that are small to size, or nothing that's significant, but if she says, Oh yeah, let me show you doctor. This bruise I got, I accidentally kicked the table and she has a bruise at six, seven centimeters large. You're like, that's pretty big for that level of trauma.

Dr. Diane Tanaka: Also bruising that occurs on the anterior chest or maybe the upper back, those aren't areas you're typically hitting anything. And you want to

also make sure they're not being abused, but if they're getting these smallish or small bruises in those areas, that's abnormal, right? Also asking about oozing gums or bleeding gums, having frequent nosebleeds or nosebleeds that are prolonged, like they don't stop with pressure. So if you get any of that type of history, you also want to definitely check your coagulability studies to determine if that's abnormal and lending itself to her having heavier periods.

Dr. Diane Tanaka: And then the key question is people oftentimes ask me, "Well, should I be running Von Willebrand tests?" Right? "Should I be obtaining those?" And that's a really key question. And the times at which I think about running Von Willebrands studies and I don't get it on all girls that are bleeding heavily, the key things I'm really looking for are typically these girls may have heavy periods from their very first menses. So there are menarche tends to either have heavy flow and/or it's prolonged. So what do I mean by prolonged? The period lasted longer than eight days.

Dr. Diane Tanaka: So you get a history and she says, "Oh yeah, my first period was 10 days long. And every period since then has been anywhere from 10 days to two weeks." Right? That's a long amount of time. And I've met girls who, when I've asked if they've ever sought medical attention for it, they say, "Oh no, because mom told me, this is the way we are in our family. All the girls have heavy periods." And again, as we know, that's also a red flag to start thinking about Von Willebrands is probably an issue in this family.

Dr. Eyal Ben-Isaac: That is a great point because oftentimes, we don't delve into the family history and the teenagers might think this is normal for their family. So

maybe recapping, we're talking about ordering a CBC, looking both for anemia at the platelet count, looking at thyroid function and possibly coagulation studies and Von Willebrand factor, especially if it's heavy bleeding right from the start-up menarche. And also if it's prolonged bleeding.

Dr. Diane Tanaka: Yes.

Dr. Eyal Ben-Isaac: Wonderful. Is there any utility of ever getting a pelvic ultrasound?

Dr. Diane Tanaka: Yeah, that's a great question. And oftentimes I know providers obtain one and I understand why, because you're like, "There's something different happening in that pelvic area. And maybe there's something structurally occurring in the uterus that's contributing to this." And for the most part, the majority of girls that have heavy menstrual bleeding don't tend to have structural issues. So what do I mean by structural issues?

Dr. Diane Tanaka: The most common would be, could she have fibroids in the uterus? We know that fibroids are associated with heavy menstrual bleeding. Fortunately, they're not very common in adolescent girls. Adult women, absolutely, you should be thinking about that. So given that, and even with polycystic ovarian syndrome, which more typically you have infrequent periods, meaning the history is that the patient is skipping periods. Maybe they only get their periods every two to three months, or even as long as four or five months. The issue becomes there is no standard about how many cysts in an ovary is consistent with polycystic ovarian syndrome in an adolescent girl because by virtue of their age, being adolescents,

being on the younger reproductive age range, it's pretty typical for adolescent girls to have multiple cysts in their ovaries.

Dr. Diane Tanaka: So you obtain the ultrasound, the radiologist reads it and says, "Oh, there's multiple follicular cysts in the ovaries." Then the primary looks at it and they tell the patient and this ramps up people's anxiety really quickly because they're like, "Oh my God, that sounds really bad. Do I need surgery? What do we do about this?" Some parents know something about polycystic ovarian syndrome. There may be somebody else in the family, maybe her sister, so the patient's aunt has this. And then the mom's like, "Oh my God, she's never going to be to have a baby." And it creates all sorts of feelings that are negative in the family. And the reality is that's not sufficient for us as pediatricians, adolescent medicine doctors to say, "Yep, Jenny's got polycystic ovarian syndrome."

Dr. Diane Tanaka: Because we need to have a history of changes in the menstrual cycle. Typically, she's having less frequent menses and some biological, or depending on what criteria you're using to diagnose this because there's different criteria, but typically you need to see some biochemical changes too. Like she has an elevated testosterone level. That's probably one of the more common ones.

Dr. Diane Tanaka: So in short, because I know that was a long answer. I typically do not obtain ultrasounds on the routine when I meet a young girl who is having heavy menstrual periods. I consider it if with my intervention in my treatment, it's just not working. Then I would consider, "You know what, maybe there's something more going on than I'm just not aware of. Let's at least get a pelvic ultrasound to make sure I'm not missing one of those zebras that are out there."

Dr. Eyal Ben-Isaac: Good to know because parents frequently asked for imaging studies. So it's a good take to reassure them when it really is indicated. So going along those lines, mom is wondering if there's any treatment options for her daughter, should she be taking iron or any other medications? So how do you decide when treatment is indicated? And if so, what would you try?

Dr. Diane Tanaka: Great questions. I consider treatment options if number one, the amount of bleeding is really interfering with the teens quality of life. So if I'm getting a history and I will ask, "Are you missing school because of these periods?" And if she's, mom and the daughter are nodding their heads and saying, "Oh yeah, every month she misses three or four days of school when her period's the heaviest." That's not sustainable. That's a lot of school to miss every month. So in that situation, I will intervene by offering medications. If also, let's say the parents are, "I'm not so sure. Do we really have to use medication?" I will then say, "Let's see what the lab results show us."

Dr. Diane Tanaka: If her CBC returns, and typically you can get that result fairly quickly or you might even in your office, want to just do a finger stick check of their hemoglobin. And if that's low and what do I mean by low? Oh, it comes back at nine. It's coming back at eight. Okay. I'm not going to mess around. And she's still bleeding. I'm going to go ahead and say, you know what? We really need to start treatment.

Dr. Diane Tanaka: If you were to get a finger stick and her hemoglobin is 11, and let's say the patient's telling you, "Oh yeah, my bleeding's already stopping. Or I'm not on my period right now. That was the last period. And it's only happened one

time." I don't jump to start medication for that. I will say, "Let's just wait and see what happens." And can you keep track of how your periods are doing and I'll see you back in three months or six months and see what's going on. We can check in through a [online] video visit. If you have the capability to do that, you could have them come into the office. Or if you have a really busy practice, you could even just have your nurse or you yourself give that mother a call and a couple of months, two or three months, and just check in, see how her daughter's doing. If she's continuing to have heavy periods. Then you're going to definitely want to bring her back into the office and then start a treatment.

Dr. Eyal Ben-Isaac: If we do start treatment, what are the options that we usually have for us? And what would you discuss with the families about why we're doing it and for how long?

Dr. Diane Tanaka: Yeah. So when we talk about treatment, we're really always talking about a hormonal treatment. So this creates feelings also, it creates some anxiety in quite a few of our mothers that we talk to. And typically, I'm seeing mothers because usually when it comes to this type of complaint, the girl to come in with their mom, the mom wants to be, their dads are kind of like, "Yeah, no. You women have this. I'll stay at home and watch the younger kids. Right?"

Dr. Diane Tanaka: And typically, what we're using is birth control pills, so that already, alarm bells. I can see it on parents' faces on the mom's face. The minute we say, whether it's me or one of our trainees says, "We can use birth control pills. We have a treatment. We can use birth control pills to control this bleeding." And I see in the mom's eyes, like they get bigger and there's alarm bells ringing behind them.

And I know exactly what they're thinking. And I've had many conversations with mothers around this, which is, "My daughter's not having sex, number one. And number two, oh no, you don't. You are not going to give my daughter birth control pills, and then she's going to go out and have sex. Because she's going to think it's okay because now she's protected."

Dr. Diane Tanaka: So what's really important is, and our hematology colleagues do this very well also, is to introduce and say, "Good news. We have medicines that we can use to treat this heavy menstrual bleeding, and it will slow down or stop and lighten the periods that your daughter or Debra, that you're having." So talking to the patient or talking to the mom, then we say, "It's a hormonal medication. It's commonly known as birth control pills.

However, we are not using it for birth control. These pills can be used as medication also. Most people know them as birth control pills, but the beautiful thing about them is they can be used for many things aside from just birth control. And this is one of the most important ways in which birth control pills can be used, other than protecting one from an unplanned pregnancy, is treating heavy menstrual bleeding so that your daughter doesn't have to miss three to four days of school every month, right? And her grades are suffering."

Dr. Diane Tanaka: So when you frame it like that and lead with it's a medication, it's a treatment. Oftentimes, you see that anxiety go down. There's context for the parent and the patient to understand why you're introducing this idea. And then you just start your treatment with a birth control pill.

So you may be wondering, “Okay, that sounds great. How do I do that? Now I have to actually prescribe it. What do I do?” And it’s fairly straight forward. So if she has stopped bleeding, when you come to see her, you get your hemoglobin result back, whether that’s a finger stick or you see the CBC the next day or the next couple of days, and her hemoglobin, like I said is 11.

Okay. Not a big worry, but it’s enough that she’s missing school. I would just have her start with one pill a day and she could start at any time just reminding her to try and take it about the same time every day. It’s not as critical as when you’re using it for birth control to make sure you’re taking it at the exact same time every day.

Dr. Diane Tanaka: The reason we say that for birth control is we don’t want the levels to drop enough that you can actually end up with an unplanned pregnancy. We’re trying to control bleeding. So it’s not as critical.

However, we don’t want her missing days because then she could have breakthrough bleeding on those days she misses it. If you see your CBC or she’s come to you. And this happens to us in our clinic quite a bit, she’s sitting there in front of you and she’s like, “I’m on my period still. It’s been three weeks. It’s not slowing down. I’m still bleeding the same amount.” Then I would start with a higher dose of the birth control pills, not higher, so much in terms of the content of each pill, but prescribing more than one pill per day.

Dr. Diane Tanaka: Typically, some people will start at two pills a day until the bleeding stops. And then you can go down to one pill a day. The advantage of starting at only two pills a day is there tends to be less side effects from the pills

because remember, there is estrogen in each pill. So when you start taking more than one a day, nausea can become a problem. However, she's bleeding heavily and her hemoglobin comes back more at nine or 10, I'm probably not going to want to start at just two pills a day. Then I would start at more like four pills a day. Now don't give them all to the girl all at once, because then she definitely will get nauseous, she may vomit the dose and then they're like, "We're done. That medicine's nasty. I don't ever want to take it again."

Dr. Diane Tanaka: So what we do is we either have the patient take it one pill four times a day, although I've taken four times a day medications before, and it's hard to get that fourth dose in. Or what's probably easier and still more tolerable in terms of side effects, is two pills twice a day. And emphasize that the girls should take it after meals because taking that much estrogen on an empty stomach is definitely going to make her nauseous.

And I let the family and the patient know that. So she could take two pills after lunch, two pills at bedtime. She could do two pills after dinner and two pills at bedtime. And especially right now, when people are doing all remote learning, they tend to be going to bed later, so you could have a good four hours, five hours between dinner and bedtime.

Dr. Diane Tanaka: It doesn't matter how much you space it out because you could give her all four at once, but I don't recommend it because of the side effects like I just said. So she would just take it after each meal, whatever meal she chooses until the bleeding stops. And then she can go down to three pills a day.

I mean one pill after dinner, two pills at bedtime, and then step it down again after three days to two pills a day. So those two pills at bedtime or two pills after dinner, whatever you want to use. And I've been saying lunch, dinner or bedtime, because most adolescent girls I work with skip breakfast. So breakfast may not be a great time.

Dr. Diane Tanaka: And then how long do you keep them on the pill? That's the other big question. So I have them remain on one pill each day for anywhere between three to six months. And I gauge that by two things. One, how low was their hemoglobin when I started? And two, is how reluctant does the family seem to be? Or how uncomfortable are they about her not having any more periods while you're treating her?

Because keep in mind, they are not going to be taking the placebo pills. The girl will only be taking the active pills. So she will not be having a period for as long as you have or taking the active pills. So some families will tolerate three months, but beyond that, they start getting really nervous because they think, "How safe is this? Is this natural?"

Dr. Diane Tanaka: Just so that we all know as providers it's perfectly safe. She could not have a withdrawal bleed for a year and still be fine. We tend not to go that long. So some families, I'll say, they really have a lot of questions or I can really sense a lot of hesitation in the mother's questions or around her acceptance of the treatment, I will say, "Let's try this for three months. And then after three months we can stop the pills and see what happens. If she continues to have a heavy periods again, then we can just restart it again. It's not a big deal. Right?"

Dr. Diane Tanaka: And if you're just that calm about it, they tend to like calm down too and say, "Yes, I like that idea." If you feel like they really need to be on for six months to really just stop the bleeding so that their anemia can resolve. And yes, to your earlier question, Eyal, you do want these patients on supplemental iron because they all are iron deficient and anemic due to their heavy bleeding, then I will go out for six months. They take their iron, they're taking their one pill a day. Once they step down to that dose of active pill for those six months, and then you can try taking her off and see what happens.

Dr. Eyal Ben-Isaac: So are there times where you would consider admitting the patient because maybe you're a little concerned and also when might you seek out additional help, for example, maybe seeking out help from or consultation from a hematologist?

Dr. Diane Tanaka: Yes. And this does come up at times. So when I think about admitting a patient that is experiencing heavy menstrual bleeding is for one of two reasons or both, which is she's severely anemic. So what do I mean by that? I see her hemoglobin result and it's under seven. I think we would all agree that's quite low. And oftentimes, those adolescents require a blood transfusion or at least it would be a consideration.

So you see the CBC results or you've done a finger stick hemoglobin and the result comes back five or at six. Then I would definitely want to admit her. I'm wanting to make sure, especially if she's still bleeding, I want to make sure that she doesn't to decrease her hemoglobin level because that's problematic as we all know.

Dr. Diane Tanaka: The other reason that would lead me to want to admit an adolescent who comes to me with heavy menstrual bleeding would be if she has orthostatic changes in her blood pressure. And oftentimes I'm clued into that because the mom or the patient has told me that she feels lightheaded. She has actually passed out once or almost passed out when getting out of bed or was in class and stood up and saw black. So if that happens, then I would definitely want to check orthostatic changes in her vital signs. If she is orthostatic that tells me she's significantly volume depleted, and I would want to admit her for further management and close observation.

Dr. Eyal Ben-Isaac: Wonderful. And would you maybe consider getting consultation with a hematologist either as an outpatient or an inpatient based on things aren't getting better or you have abnormalities in your labs, how would you consider when you should maybe reach out for additional support?

Dr. Diane Tanaka: Yes, absolutely. So there'd be a couple of times that I would definitely immediately think, "I need help from my hematology colleagues." One would be if in obtaining the history of the heavy periods from the patient or the mother or both, they tell me that even her very first period was heavy and or prolonged. So she was bleeding and passing large blood clots. She was needing to change her menstrual pads every hour, and she was passing large blood clots.

I would immediately start to suspect that this adolescent actually has a bleeding disorder or could have one. And so I would definitely obtain a Von Willebrand titer at that point and also really think about having my hematology colleagues also evaluate this patient because even if the Von Willebrand result back normal, she

could have another cause of a platelet dysfunction, some of the more rare etiology, so I would definitely want their expertise.

Dr. Diane Tanaka: The other time at which I would have hematology evaluate is if after, let's say this is a patient who requires admission because she has a hemoglobin of five when she presents to you, she's been presyncope or actually experienced syncope because of her anemia and then once she's admitted in the hospital and let's say, you're having trouble controlling the bleeding, she's requiring more blood transfusion than you would think would be typical.

And typically, if we do need to transfuse packed red blood cells for these patients, it's usually only one unit at most, two units. But if you're getting beyond that, I'm definitely calling in hematology because that's really outside of the norm for just typical heavy menstrual bleeding.

Dr. Eyal Ben-Isaac: Thank you again. This was incredibly informative and very educational. Are there specific takeaway points that you would love our audience to keep in mind?

Dr. Diane Tanaka: Yeah. So one, obtain a careful history because the history will tell you most of what you need to know. So I've already highlighted key elements of the history.

Second takeaway would be you don't need to obtain a pelvic ultrasound as part of the initial workup. Think about it if you're running into more challenges with managing this than you expected, or the patient's having even more pain than you would expect, then I would get a pelvic ultrasound.

And the third thing would be keep in mind if this bleeding is really heavy or she's having other signs of bleeding abnormalities, such as prolonged nose bleeds or frequent bruising, then definitely calling hematology. Don't be shy about reaching out to your colleagues and asking for help.

Dr. Eyal Ben-Isaac: Thank you so much, Diane. Thank you for always educating me and thank you for educating our audience today. It was really great.

Dr. Diane Tanaka: Well thank you very much. I very much enjoyed being here and thank you all for listening.

3. Interview with Dr. Nelli Aleyan

Tamar Minasyan: Hello, Dr. Aleyan!

Nelli Aleyan: Hello!

Tamar Minasyan: Thank you for accepting our invitation! Our colleagues at Los Angeles Children's Hospital talked about uterine bleeding at the onset of menstruation, any menstrual irregularities and the amount of blood loss. In general, how does the presented situation differ from the Armenian reality and what are the main reasons for the differences?

Nelli Aleyan: Of course, by and large, we mostly adhere to the same protocols, as our American colleagues, but considering the geographical location of our country and some cultural factors, there are differences.

Tamar Minasyan: What are the main differences between the American context that has been presented, and the context in Armenia?

Nelli Aleyan: The main differences are that the standards are slightly different, such as, for example, the number of sanitary pads used or the patient's subjective feeling, whether her blood loss is greater than usual.

We do not pay much attention to the subjective factor, because it is purely subjective. Very often it can simply confuse us, as children are usually afraid of blood, so even when there is a little more blood, they present it as bleeding. However, after collecting detailed information about other factors that are specific for bleeding from the parent, we understand that it is simply her subjective opinion that she has heavy bleeding.

Tamar Minasyan: What are the most common problems in this field in Armenia and are they specific to Armenians only or do they represent a consistent pattern?

Nelli Aleyan: The most common menstrual problems in adolescents are mild disorders after the onset of the menarche and, of course, bleeding, as a functional disorder. We basically observe problems caused by the same etiological factors and manifesting in a similar way in the region and other countries. We meet children with problems like this very often.

Tamar Minasyan: What is the normal menstrual period? What are the evaluation criteria?

Nelli Aleyan: The criteria for assessing the normality of the menstrual period are the onset of menstruation at the age of 10 to 15 years, the duration of the period up to 7 days and the number of hygienic pads used – up to 7 tampons or pads. There is one more criteria, which is definitely a little subjective, – blood passing to underwear or clothes.

Tamar Minasyan: Got it! So how do you usually identify any issues? What are the signals that the adolescent has a problem and there is a need to follow up or intervene?

Nelli Aleyan: Very often the parents decide to turn to a doctor at the stage of the bleeding. If they do not decide on their own, they may turn to a doctor based on someone's advice to check, if their situation involves any disorders. I believe educational programs for parents should be implemented. Parents with adolescents should know the criteria of what is considered a normal menstrual period, so that they know when to talk to a physician.

Tamar Minasyan: People usually turn to a doctor when it's too late. What is the situation with gynecologists?

Nelli Aleyan: This statement is applicable to gynecology, too, yet given that the situation relates to children and reproductive organs, people are more cautious.

Tamar Minasyan: Is the situation any different in Yerevan as compared to other, more rural regions in Armenia?

Nelli Aleyan: Compared to rural regions, the situation is better in Yerevan. The challenge with the rural regions is that they turn to a doctor at a later stage, maybe because they deem it to be normal or because the mother may have had similar bleeding at that age and the problem disappeared without medical intervention, so they do not see it as a problem and turn to a doctor later. It should also be mentioned that there is a strong demand for pediatric gynecologists in our rural regions, as there is a lack of specialists there. The children are observed either by pediatricians or district therapists, who, of course, are not specialized. They can help the child as much as their professional knowledge allows. If they encounter problems, where they are simply not authorized to take action or intervene, they refer the child to specialists in Yerevan.

Tamar Minasyan: Do you encounter complicated cases more often?

Nelli Aleyan: I encounter both complicated and uncomplicated cases. Certainly there have been more complicated cases during the Covid period. I believe it is related to the total lockdown during the Covid period and the stressful situation. Not going to school and doing remote classes from home have added to the children's stress, and stress may cause period disorders, which in turn mostly causes dysfunctional uterine bleeding. I have had both complicated and uncomplicated cases before the Covid pandemic as well, it depends on the mentality of the family or the mother.

Tamar Minasyan: By the way, is there an established link to Covid or any related causalities?

Nelli Aleyan: No link or causality has been established yet, since Covid 19 is considered a relatively new infection and there will definitely be more research ahead. There may be some kind of link between dysfunctional uterine bleeding and Covid in children.

It is worth mentioning the fact that children with Covid have the mild form of the disease and are very often asymptomatic, which makes it difficult to identify Covid in children, so it is possible that there will be no statistically significant evidence. But this is a subjective estimation, purely based on the cases that I have encountered. And in case of children that also take anticoagulants this will affect the amount of blood loss from dysfunctional uterine bleeding, too.

Tamar Minasyan: What are the actions to be taken in this case?

Nelli Aleyan: If we have deviations from the norm, it should be a red signal for the parent to see a doctor. These are the quantity of used sanitary pads exceeding 7 per day and the abundant blood secretion for more than 7 days.

An adequate child usually mentions that during the given cycle, on a given day she has more blood loss than usual. If a lot of blood passes to the mattress or underwear, then the girl should be taken to the nearest medical facility. If there is no opportunity for an examination, diagnosis or medical assistance, they should turn to a specialized hospital.

Tama Minasyan: Very good! When does an adolescent usually visit a gynecologist for the first time? And what diagnostic steps are taken if there is no specific problem?

Nelli Aleyan: There is a Government program in our country that is aimed at early detection of infertility and gynecological problems in children and adolescents, at increasing the chances of treatment, and thus reducing the level of infertility.

If there are no complaints, the adolescents visit a gynecologist at the age of 15. A pelvic ultrasound examination is performed to identify the availability of any pathology. If no pathology is revealed, future visits to a gynecologist will be based on need.

If the adolescent has complaints, she will be examined by a specialist. If there are complaints before the age of 15, she should be seen by a doctor by all means.

Tamar Minasyan: What is the indicator of seeing a gynecologist in Armenia? Are there any factors like shame or fear that hinder?

Nelli Aleyan: There are factors that hinder, but happily, I must mention that during the last 5 years the number of applicants has increased. Parents have become more literate, they better distinguish a pathology from the norm and realize that there is no shame or harm for the child to consult a pediatric gynecologist. On the contrary, we help the child to get rid of the problem or identify the deviations from the norm, meanwhile the mother may not realize or know this due to a lack of professional knowledge.

Tamar Minasyan: In your practice do you use any criteria for determining a deviation from the norm that is not widely accepted as a deviation?

Nelli Aleyan: For sure, there are such. I believe all my colleagues will agree with me that almost 90% of adolescents experience pain during the menstrual period and to the question, if they have a painful period, the mother or the girl usually replies "Who does not?".

This is a misconception and in fact the menstrual period should not be painful at all. If there is pain, there is a problem. Naturally, the pain is milder in the beginning, then it gets stronger from cycle to cycle and of course it affects the child's social life, the learning process and her well-being, actually it affects everything.

And perhaps in the last three years or so, I noticed that girls with painful, extremely painful periods turn to me. This means that they had painful menstrual periods before this terrible pain, but they did not turn to a doctor, as they considered the pain to be a norm.

Tamar Minasyan: And they perhaps try to relieve the pain with painkillers, don't they?

Nelli Aleyan: They do take painkillers, yet all the children that come to me with this terrible pain always mention that they take the medicine when it is no longer possible to endure the pain. This is another misconception that you should only take painkillers when you can no longer stand the pain. No, painkillers should be taken at the very beginning of the pain for the pain to go away completely, while when one takes them at the peak pain, the pain just subsides, it does not go away completely. The pain becomes a source of stress, which is another factor that can lead to further menstrual cycle disorders.

Tamar Minasyan: What causes pain?

Nelli Aleyan: The pain is caused by many different factors, such as anatomical changes or inflammatory problems, yet at least in my practice with children inflammatory problems are not very common. The most common cause is the excess production of prostaglandins in the myometrium, which leads to a uterine contraction increase in intensity and pain.

Of course, taking antiprostaglandin drugs completely removes the pain syndrome, and since we mainly work locally, the cyclic intake of pills and suppositories helps to ensure painless menstrual periods for many years to come.

Tamar Minasyan: What should professionals do to prevent a delay in diagnosing the problems, since time is of the essence?

Nelli Aleyan: Of course, time really matters here. Just like with other diseases, the timing is important for gynecological diseases as well, because neglected problems make it impossible for a doctor to control the process.

The same goes for bleeding or the pain, because the pain has a negative effect on the child, causing fainting, nausea or vomiting. So based on the symptoms the child has, she may be tested for completely different problems, such as, for instance, gastrointestinal diseases, meanwhile in reality the whole symptom complex comes from the menstrual period pain.

Of course, there are children who are ashamed or cannot explain what is happening to them, in which case the parent comes to the rescue. We should not

ask the patient, if there is a problem at the given moment, because if the parent does not know, she will give a negative answer. When we start asking individual questions about the symptoms, we always find some problems.

Tamar Minasyan: Aside from the 3-4 mentioned symptoms are there any questions that you have formulated during your practice and they really help you to figure out the case and evaluate the situation correctly?

Nelli Aleyan: Definitely! I find that the hereditary factor matters in dysfunctional uterine bleeding or painful menstrual periods. Generally, females inherit some of the problems related to this function from maternal lineage.

With regard to the painful period, we often hear from the mother that her period had also been painful. You will often hear the same about bleeding, too – mother had bleeding at that age, now the child is having the same problem. Or we hear that the mother had not only bleeding, but also some disorders in menstrual periods that are being repeated in her daughter.

By the way, I would not call it a heredity, yet we very often see a predisposition through maternal lineage when it comes to polycystic ovary syndrome.

Tamar Minasyan: So in that case, if the mother was not treated and considered her condition normal, the daughter is not treated either, isn't she?

Nelli Aleyan: Yes, because it was taken as a norm, as they did not know that it's a disorder.

Tamar Minasyan: Unless no specific problem is voiced, what are the questions to ask for assessing the situation? And is there a problem that the doctor identifies before the patient or the parent does?

Nelli Aleyan: There are definitely questions for that. First of all, we check if the patient has complaints. If there are problems that disturb the adolescent, she will always tell about them. If not, the parent will voice them. Otherwise, we start asking questions about menarche, such as about the age when the menarche started, how many days it lasts and when it finishes.

Let's say it lasts 7 days. The doctor will ask on how many days of the period the bleeding is heavy, as it is within the norm if the period starts with heavy bleeding and decreases in intensity by its end.

If the period is painful, we will ask if the patient takes medicine. If the answer is negative, then the period is not very painful and can be considered as non-pathological.

When should medicine be taken and what drugs to take? – Very often the parents use No-Spa as a first line drug, because they consider it to have a mild effect and not rich in chemical components. Yet, it is a vasodilator medication, it relieves the pain, but it is not guaranteed that the pain will go away. If the pain went away completely, very good, if the pain decreased in intensity, what would be the next step – stand the pain or take another drug?

Or if the bleeding is heavy, at what time of the day it is so, how intense it is, because night bleedings occur due to the vasodilator effect, because the body is built that way.

It is necessary to find out all the details through consecutive questions and answers. In other cases, if, for example, the menstrual period is normal, but the adolescent notices itching or redness on the external genitalia, the only reason they turn to a gynecologist is very often the painful urination.

Or when the urinary system is being examined, and we do not find a problem, but the mucous membrane of the external genitalia is hyperemic, which is often the case, and as a result the children feel pain there.

There are children with vaginal discharge or inflammatory problems. I often see prepubertal adolescents with insignificant discharge, which we consider normal if the examination does not reveal any problems.

We explain to them that it is normal, all girls have insignificant discharge, and they should not worry about it. They are often upset that their menstrual period is not happening yet, but they have some discharge. Of course, they accept the fact that they have grown up with difficulty.

Tamar Minasyan: What are the disorders of the menstrual cycle?

Nelli Aleyan: An irregular cycle or the absence of a daily cycle is the case, when a child with a regular cycle has an absence of a period for 3 months and longer,

meanwhile for a child with an irregular cycle it will be an absence of a period for 6 months and longer.

Heavy menstrual bleeding or blood secretion may be considered an irregularity, and vice versa – short length of the period and the small amount of secreted blood secreted are also irregularities. All the mentioned cases are considered to be irregularities and a doctor should be seen in all the cases. If for some external reasons the amount of the secreted blood is small or the length of the period is short for one month, we consider it normal. Yet, if the clinical manifestations repeat regularly, it is a sufficient reason for concern.

Tamar Minasyan: What are the criteria for determining what the small amount is and what is not?

Nelli Aleyan: They usually tell us their subjective assessment that the amount of the bleeding was less than usual. For example, if she used 3-4 sanitary pads per day as a standard, this month she used 1 or maximum 2 sanitary pads per day. Or that there were fewer traces of blood on the pad than usual. Of course, during the examination we check it to understand whether it is an objective estimation and there is a problem, or the child's feeling is subjective. Very often children approach me and when I ask about the number of the sanitary pads used by them, they may mention 15. When I ask, if the pad was fully soaked in blood when they changed it, they give a negative answer and mention that they changed the pad because of a discomfort feeling. This is a completely subjective feeling, the number 15 does not scare me, because the child just wants to changes the pad.

Tamar Minasyan: Does the doctor have advice for this situation?

Nelli Aleyan: No, the doctor has nothing to do here, because the blood loss is normal, the child changes the pad because of discomfort.

Tamar Minasyan: We realize that every problem has its cure, yet what is the treatment of irregularities in general?

Nelli Aleyan: The treatment of irregularities definitely depends on etiological factors. We see children with different problems. In case of bleeding, after performing the necessary tests, we prescribe oral contraceptives, if they do not have coagulation problems. I personally prescribe anticoagulants and antiprostaglandins, which also helps to stop the bleeding. In my practice, I reach nearly 99% effect when using these three drugs together.

I do not favor and do not accept oral contraceptives as monotherapy. A positive outcome can be reached for sure, but I obtain much better results with the three drugs combined.

If we have a case of amenorrhea, then it depends on the etiological factors. For example, oligomenorrhea is often caused by thyroid problems. Of course, in this case I do not treat the patient, the endocrinologists control the level of the TSH hormone in the blood, which leads to the normalization of the cycle, as the initial cause was the thyroid disorder.

In the case of hyperprolactinemia we prescribe drugs that reduce the level of prolactin in the blood and we constantly monitor the level of the hormone to

understand how to change the dose of the drug. We gradually increase or decrease the dose of the medicine in order to avoid the occurrence of adaptation and we achieve great results.

Tamar Minasyan: Do people avoid taking drugs?

Nelli Aleyan: They may do, if they got the wrong treatment before. When it comes to taking oral contraceptives, they avoid it due to concerns of possible insomnia, weight gain or unwanted hair, but I explain to everyone that they should use the drug only in the right dose and according to the right scheme to avoid problems.

Of course, all oral contraceptives have their contraindications and side effects, and we inform the patients about them to make sure that they are aware about possible consequences of the drug.

Tamar Minasyn: Given the lack of specialists in the regions, what interesting case could you share that will be interesting to know for your colleagues?

Nelli Aleyan: There are many cases. I would like to tell about one of them. A 14-year-old child visited the pediatrician at the local polyclinic, when her first bleeding happened. The doctor advised her to use some medicine to stop the bleeding, but it did not stop and the parent decided to wait a little, and give the medicine some time to work. Of course, they are not specialists, they can't make right assumptions, so they decided to wait for some 30 days.

By the time I saw the girl, she was already pale and the amount of hemoglobin in her blood was very low. She had to use long-term control mediations, since her

breathing during the examination was shallow and rapid, i.e. she had respiratory failure and the amount of hemoglobin reached nearly 80%. This was the hemoglobin indicator at that point, because our body always tries to compensate the high level, just like during labour.

What made her mother take her daughter to a doctor? Because that morning she found the mattress completely in blood. It frightened the mother. From the first day 3 drugs were prescribed and this ensured a positive progress. Afterwards I was monitoring her and there have been no cases of bleeding so far. Hemoglobin is within the normal range, all other functions have been restored, meaning the child has a regular cycle every month.

Tamar Minasyan: Thank you very much for the interesting and educational conversation! In conclusion, what advice would you give to your colleagues regarding menstrual disorders or bleeding?

Nelli Aleyan: I would advise my colleagues to evaluate the situation correctly and if they are unable to give the right solution, refer the child to the right specialist, so that we avoid endangering the child's health. Children are our generation, they are our future.

Tamar Minasyan: Thank you so much, Dr. Aleyan! I hope our conversation will be helpful for the related specialists.

Nelli Aleyan: I hope so, too. Thank you for the invitation. I believe we will provide our regional colleagues with the necessary educational materials and assist them in

treating patients with discussed problems, so that there is no need to send them to Yerevan for treatment.

Tamar Minasyan: Thank you very much!