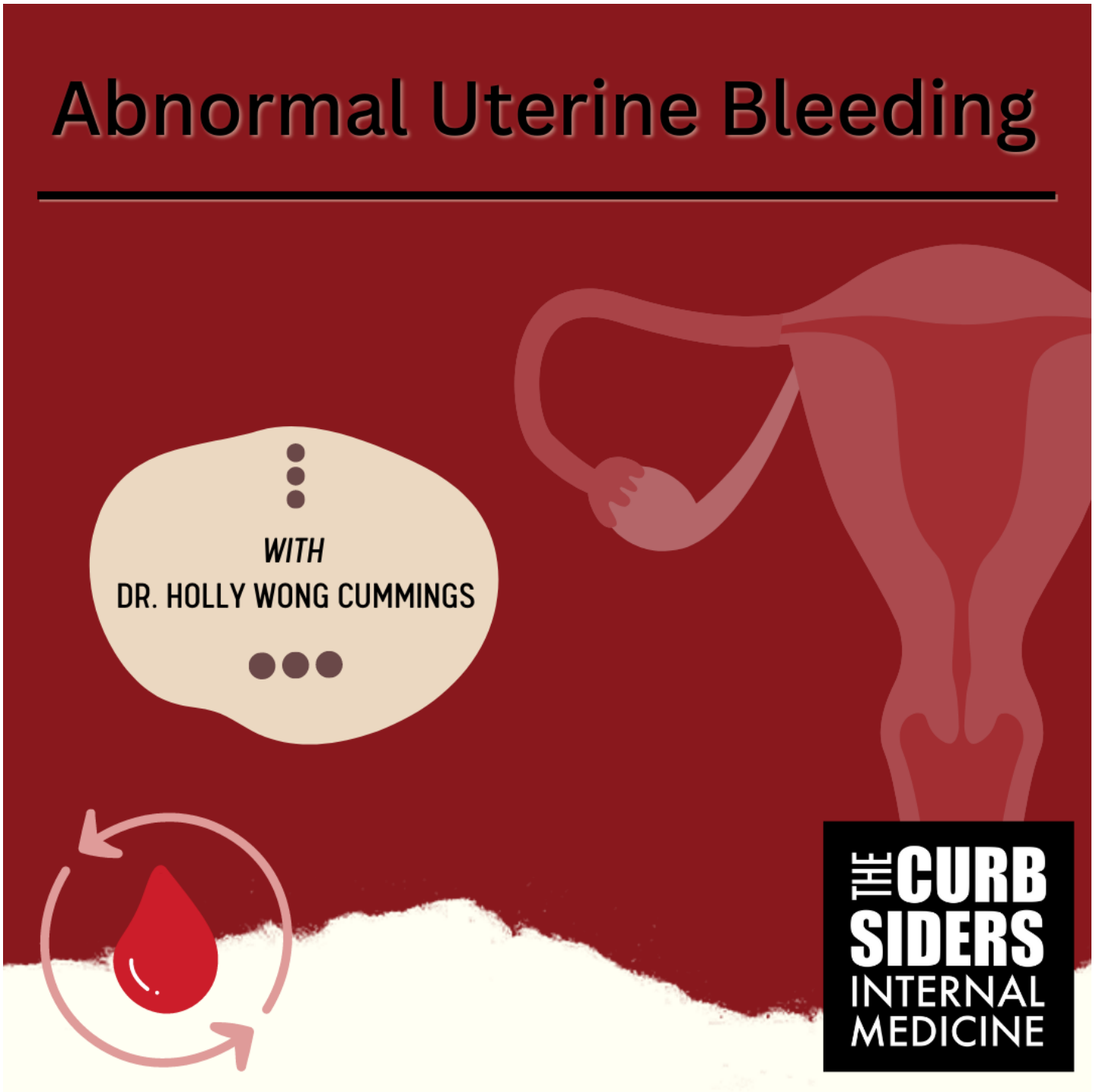
#382 Abnormal Uterine Bleeding

With Dr Holly Wong Cummings



Matt: Paul, why did the uterus get kicked out of Hollywood?

Paul: I don't know, Matt. Why don't you tell me?

Matt: It's because it was overreacting.

[laughter]

Matt: No. Nothing. You want me to explain it, Paul?

Paul: No, I think the lesson is probably better.

Matt: All right, I'll just hang my head in shame and let's start the show.

Molly: I know, Matt. I can't believe you went there. I mean, jokes about women's health are not funny.

Paul: Boo.

Matt: Double team, Paul.

Paul: Boo to all of this.

[laughter]

[Disclaimer]

[Curbsiders theme]

Matt: Welcome back to the Curbsiders, I'm Dr. Matthew Watto, here with my great friend, Dr. Paul Nelson Williams. On tonight's show, we're talking about abnormal uterine bleeding with a fantastic guest, Dr. Holly Wong Cummings. Paul, before we introduce our fantastic cohost and our guest, can you please remind the audience what is it that we do on The Curbsiders?

Paul: Sure, happy to as always, Matt, we are *the* Internal Medicine Podcast. We use expert interviews to bring your clinical pearls and practice-changing knowledge. And as you alluded to keep the audience's suspense for all 3 seconds. I will now reveal our exciting cohost.

[laughter]

Paul: The amazing producer extraordinaire, medical educator extraordinaire, everything extraordinaire, Dr. Molly Heublein. Dr. Heublein, how are you?

Molly: I'm doing great. It's great to be back with you guys and happy to be back with the regular Curbsiders team here. We had a great conversation today with our guest, Dr. Holly Wong Cummings. We talk about how to diagnose abnormal uterine bleeding, go through the PALM-COEIN framework for thinking about what's causing the abnormal bleeding, and then review practical steps to treat that so that our patients don't need to suffer. Really the majority of this is things that primary care providers can do. Most of the treatments are not surgical and so we should feel more confident helping our patients manage this. Holly Wong Cummings, MD,

MPH is an assistant professor of clinical obstetrics and gynecology at the Perelman School of Medicine at the University of Pennsylvania. Dr. Cummings is the full-scope OBGYN with clinical interests in breastfeeding medicine and transgender gynecologic care including frivolous surgical practice. Her academic interests lie in medical education and legislative advocacy. Outside of work, she finds peace in her garden.

Matt: We got to start the garden, Paul.

Paul: [crosstalk]

[laughter]

Matt: We keep saying it. [laughs] All right, before we get right into the interview, a reminder that this and most episodes will be available for CME credit through VCU Health at *curbsiders.vcuhealth.org.* Holly, it's been so great to meet you and now for the audience to meet you, thanks for joining us on the show.

Holly: Thank you for having me. I'm excited to be here.

Matt: We're going to jump right into it. Molly, do you want to bring us to a case from Kashlak?

Molly: So, we have Melissa, she's a 46-year-old woman, she's a nonsmoker, her BMI is 30, she has a history of PCOS and she's coming in today complaining of heavy menstrual bleeding. She says in the past four months or so, her periods have just been uncontrollably heavy. She'll bleed for about 10 days and three or four of those days will be really very heavy. In the past two cycles, she's had kind of shorter cycles, only every 21 days. She feels like she's bleeding all the time. When she comes in today, she says the bleedings went heavy for about five days this cycle and she just wants it to stop. For the past few days, she's bleeding through a tampon in less than 2 hours and seeing more clots. Let's just start by taking a step back and review what happens during a normal menstrual cycle.

Holly: Yeah. For many of us, this might not be something we've thought about since medical school, and you may have put it out of your brain the same way I've put many other things out of my brain. When we think about the menstrual cycle, the job of the female reproductive system and so that's anybody with ovaries and a uterus is to try to get us pregnant. Mother Nature wants us to procreate and pass on our genes. The menstrual cycle is this really intricate pattern and interplay of a whole bunch of different hormones that are coming from the hypothalamus, the pituitary, and then the ovaries and they are sending messages to the uterus. What those hormones are doing are telling your ovary to ovulate or release an egg and then simultaneously telling the lining of the uterus, the endometrium to build up and then shed. The shedding happens if the person who ovulates does not get pregnant, if that egg is not fertilized by sperm.

Classically, we time the menstrual cycle by the first day of bleeding. So, we'll call that cycle day one. Cycle day one through maybe five to seven would be the period itself, the menstrual period, or the time of the days of bleeding and then the bleeding stops, the egg is released, so ovulation happens generally around day 12 to 14. That's when you would expect fertilization to occur if it's going to and then if fertilization doesn't occur, then usually around day 27, 28 the shedding of that endometrial lining happens. That would be day one of your next cycle. That's the normal menstrual cycle in a nutshell.

Matt: Paul, you remember all that right?

Paul: Yeah, absolutely. I was actually going to graph out for you guys all the different phases of the hormones if that was going to be helpful for you. [Matt laughs]

Holly: I'm sure you remember the chart where there's like the FSH or the progesterone and the LH.

Paul: Things are spiking, yeah, it's-- [crosstalk]

Holly: Yep, absolutely.

Paul: This is where I reveal that I'm a dumb guy. I do find the nomenclature around abnormal bleeding kind of bewildering like menorrhagia, metrorrhagia, menometrorrhagia, dysfunctional uterine bleeding, and abnormal uterine bleeding. Can you talk us through the accepted nomenclature for what we're describing in this case and so how to talk about it, so we don't sound as confused as I am sometimes?

Holly: There used to be a lot of those terms that people would use, the ones that you mentioned. Maybe around 2011 or so, the International Federation of Gynecology and Obstetrics, which is abbreviated FIGO, the FIGO organization decided to all come together and agree on a standard nomenclature that's all based on abnormal uterine bleeding or AUB. We no longer use DUB or dysfunctional uterine bleeding. I never use metrorrhagia or menometrorrhagia. I will sometimes still say menorrhagia, which specifically just means heavy periods. Although even there, the accepted terminology is really just heavy menstrual bleeding. So, you have heavy menstrual bleeding and then AUB.

Within the overarching category of AUB or abnormal uterine bleeding, it's broken up into two categories and it's often referred to as the PALM-COEIN nomenclature. What I draw this out for my students I literally draw the PALM-COEIN across the top and down the left I write PALM. Those are the four structural causes of abnormal uterine bleeding. P is for polyps, A is for adenomyosis, L is for leiomyoma which is fibroids, and then M is malignancy or premalignancy or hyperplasia.

Down the right side of your table, you'll have COEIN, although it's not spelled correctly, it's C-O-E-I-N and these are nonstructural causes. So, C is coagulopathy. You've got things like von Willebrand's disease, O is ovulatory dysfunction, so things like PCOS, I is iatrogenic, which would be any number of medications that we give to people that cause bleeding. Patients who are on therapeutic anticoagulation, people who are on hormonal types of contraceptives that are then interfering with the menstrual cycle and things like that and then e is endometrial. Endometrial causes of abnormal bleeding would be things like low-lying endometrial infections or even frankly cervical infections if you're not sure where the bleeding is coming from. So, like a low-lying endometritis, chronic endometritis would be an example of an E, and then N, not otherwise specified, so all those other things that you can't figure out.

Matt: Really crammed in the acronym there, Paul.

[laughter]

Holly: Oh yeah, all of it, PALM-COEIN.

[laughter]

Holly: So, when I write my notes, for instance, like all right the patient has AUB-L if they have fibroids. It's really helpful when you're talking to people and when you're working this out in your head to organize it in those ways. And people can have multiple causes too.

Matt: I wanted to ask if there's anything else about the history because basically, you're giving us a differential diagnosis there with those categories. What do you listen for in the history that makes you start to key in on one or the other as far as your differential?

Holly: In terms of differential, I think a lot about the timing. For instance, this patient, I know we're saying the past two cycles were only 21 days apart. First of all, I want to make sure that the patient is measuring that from the first day of bleeding till the first day of the next bleed. Sometimes you'll have patients measuring from the last day of one bleeding episode until the first day of the next bleeding episode. So that's artificially short count. I want to make sure that patient's counting correctly from day one to day one, what were the periods like before that? I don't necessarily need, like the last 10 months of dates of somebody's periods, but nowadays many people are tracking them on apps and their phone calendars and so they often can tell me all the days in the last year they've been bleeding.

I also think about whether the patient, presumably this patient based on the case hasn't skipped any cycles, but have there been any months where they don't get a bleed? Also importantly, has there been any intermenstrual bleeding? Any spotting between periods, any other unexpected bleeding, and things like that.

In terms of other history, because as we know from medical school, the answer is always you want to know more history, I want to know how she's preventing pregnancy, [laughs] how is she preventing pregnancy and what are her plans for pregnancy. In my day, it's not fair to assume that somebody at age 46 is not planning any more pregnancies, so I always ask.

Molly: Excellent. What do you think of the role of the physical exam here? Many of those things you can't really evaluate on physical exams. What would you recommend that we check out for someone like this?

Holly: Yeah, so I'm aware that the ACIP does not recommend routine bimanual exams. I would argue that in this case, this is not somebody coming for a well checkup who potentially is getting a pelvic exam for no good reason. I think there is value to the pelvic exam here. I think on abdominal exam sometimes you'll find patients with really massive fibroids that are palpably on an abdominal exam, so that's always notable. On a pelvic exam, I think it's helpful to do a speculum exam and look at the cervix because sometimes you'll see gross abnormalities on the cervix and the bimanual exam in this case, I think can be really helpful for determining the size of the uterus.

Molly: I would say it is helpful when I do these exams and find a polyp. Not so much for someone who's bleeding this heavily, but having interventional spotting to just say this is most likely the situation here. We see a polyp let's deal with it and hopefully manage your symptoms.

Holly: Yes, absolutely. It feels really good to be able to do something there.

Matt: It seems like someone with my skill level, probably the patient is going to be getting some other workup, imaging or lab. For a patient like this that we've presented here, what might be your next steps if you didn't clinch the diagnosis with just the physical exam?

Holly: I know you're being self-deprecating there, but I would encourage you to do pelvic exams. I really appreciate my primary care and internal medicine colleagues who are doing this kind of care for our shared patients. It's really helpful. I think it's a skill that you have and that you can definitely use, and maybe you need more practice, but I would definitely encourage you to do it. So actually, I don't mind sharing that my primary care doctor does my Pap tests, so I think it's definitely something that your patients can get from you and there's a value and an added bonus. That said, I now forget exactly what you asked me. Matt, I'm sorry.

Matt: Our patient, Melissa, she's 46, right? This is the patient we had presented to you. The question was, if we had done the physical exam, did a bimanual exam, a speculum exam, did an abdominal exam, if we didn't clinch the diagnosis from that, what another workup might you be doing for her?

Holly: I think the role of a blood count, it's not unreasonable to check some blood work. In my experience, if somebody's only had four months of really heavy periods, they're probably not anemic, but it's always worth checking if there's no real reason not to check labs. A hemoglobin would be useful, a TSH would be useful because thyroid dysfunction can result in abnormal bleeding. A pelvic ultrasound is always useful. I send my patients to radiology as well for that, so that's definitely helpful to have.

Paul: Is there a step-wise approach? I mean, obviously, look at the patient in front of you, but they're used to wait for the labs to come back before you do ultrasound. I feel like that's always. I shouldn't say always, but in practice, if you see a patient like this, you might order a battery of labs, expect them to come back normal, give them an ultrasound in the hand. I guess the question is, like, does every patient want an ultrasound? It just seems from the outside, potentially kind of been based on comfort for the patient. You almost want to avoid it if you can, even though I don't think that's necessarily the right thing to do. But, I mean, I guess how are you making the determination who gets ultrasonography, who does not? Where is that in terms of helping you triage things?

Holly: Yeah. I think this might depend on what your plan is with the patient for how much you're going to manage this bleeding versus are you going to refer to GYN. I think if you're going to refer to GYN, it is helpful to have an ultrasound. Not mandatory, but certainly helpful. I think if this patient then gets to me, I would probably order an ultrasound if nothing else, very clear, has come up from the physical exam. In terms of invasiveness, it generally does involve both a transabdominal and transvaginal scan. The transvaginal probes are pretty small and I always mention to patients that they have the right to decline the vaginal portion if they prefer. In my experience, the sonographers are really good about showing the patient the probe, lots of positioning and mitigation techniques for managing the discomfort. I don't know what this patient's pregnancy history is, but honestly, most patients who have given birth are comfortable, willing to tolerate the transvaginal ultrasound in the name of potentially getting useful information out of it.

If we have an ultrasound that shows nothing clear, I think it is still helpful to know. There's a benefit to the negative test here. I think if you or I were seeing the patient and we're making an empiric plan for management, maybe this is the medications, it's reasonable to do that without getting an ultrasound first, with the consideration that maybe if things aren't better or things have changed in three to six months, then an ultrasound is something to remember we haven't done yet.

Molly: I was going to ask do you try to counsel your patients to get the ultrasound done on a particular day of their cycle or it doesn't really matter.

Holly: Ideally, you want to get it done in the follicular phase, so that's the first half of the menstrual cycle after the heaviest bleeding has stopped, but before ovulation has occurred because that's the time in the cycle when the endometrial lining is thinnest. If it's going to be a scheduling issue for the patient, then I'd rather have any ultrasound than make a big deal about timing.

Paul: I was going to ask, could you talk just a little bit about sonohysterography, which I may be mispronouncing? I feel like we read some practice bulletins in advance of this and they're letting talk about how great it was examining internal topography and that kind of stuff. It's not something that was on my radar at all, embarrassingly. So, is that something that is uncommonly in practice, should we be thinking about that at all, or is that best deferred to the experts?

Holly: Even in my world, it's not something that I do personally and the radiology department at my institution doesn't perform them routinely. You definitely need to know what your institution offers and who's able to perform it. I do have a couple of subspecialty colleagues who can do them, but because they're not readily available to me, I don't routinely do them either. But the idea is that you're injecting some sort of generally saline into the uterus. You place a catheter through the cervix into the uterine cavity and inject saline off it in through that and then simultaneously, you're doing a transabdominal ultrasound so that you can see the fluid pass through the uterine cavity and then out the fallopian tubes, and it can give you an idea of the internal contours of the endometrial cavity.

Molly: How does that differ from a hysterosalpingogram?

Holly: So, a hysterosalpingogram is logistically slightly similar. This is generally done in radiology because it's done under fluoroscopy. A catheter is placed into the patient's cervix, and they're placed under the x-ray machine, and then some sort of a fluoro dye is injected into the uterine cavity and a series of x-ray films are snapped. They'll inject the dye into the uterus and then have the patient turn to one side and then the other. You're actually looking to see if the dye spills out of the tubes. The hysterosalpingogram is technically only designed to check for tubal patency, but often in the process you can get a sense of the endometrial cavity as well.

Molly: So, bottom line, we don't need to feel bad that we have not [crosstalk]

[laughter]

Holly: You do not need to feel bad that you are not ordering those, yeah. I think a regular pelvic ultrasound is perfect and honestly, if I have a pelvic ultrasound that shows something abnormal, my next step would be direct visualization meaning, like, in the operating room. I usually, in my routine cases, would not follow up an ultrasound with a hysterosalpingogram or a sonohysterogram.

Matt: I guess the last part of work up you gave us the differential diagnosis includes malignancy. Endometrial biopsy is something that's considered. Does the age of the patient ever make-- I know postmenopausal, it seems like typically those patients are getting an ultrasound and a biopsy, but does the age matter, are most patients with abnormal uterine bleeding getting biopsies at some point if it goes on?

Holly: Yeah, that's a great question and it's one that when I was in training, I struggled a lot to wrap my head around, and my current residents are trying to wrap their heads around it. So, when do we biopsy, when do we not? Strictly speaking, you'll hear people say that anybody in their 40s with any abnormal uterine bleeding of any sort should have endometrial sampling. Many of us either currently train or have trained in Philadelphia, which is not a great place from a medicolegal liability standpoint. [Matt laughs] So, certainly there's an attitude of you should biopsy it if you can to make sure you're not missing anything. I think from an objective perspective, I really do think about the patient in front of me and what their goals are and I think this is a place where shared decision-making is really important. Personally, I never surprise somebody with, "We should do an endometrial biopsy today no matter what before you're leaving if they weren't planning on that" because I do think that's a little bit cruel because it is uncomfortable and people deserve to have taken some ibuprofen in advance and prepped themselves mentally for it.

So, I'm perfectly fine with starting a workup or even initiating an empiric plan maybe with a plan to come back for a biopsy if needed in the future. Other times, I have patients who I know from the time they've made the appointment and the phone triage that the biopsy is recommended. I'm recommending the biopsy and this has been told to the patient and they're on board with it. There is a plan in place for that. I also think the way I practice, if what we're worried about with an endometrial biopsy is endometrial hyperplasia or neoplasia and one of the treatments potentially is hormonal medication like progesterone. If the ultimate plan that the patient's walking out of the room with that day involves a progestin, then in my mind we're covering our bases. I do think it's safe to continue on for a few months and see how the symptoms resolve before jumping straight to a biopsy.

Matt: You said if they're going on a progestin is that because it won't be building progesterone or progestin is not going to be building up the lining and potentially growing anything that might be there, so you feel comfortable delaying the biopsy as opposed to someone who is going home on an estrogen?

Holly: Probably nobody would be going home on an estrogen alone, but if we think back to how does endometrial hyperplasia occur in the presence of unopposed estrogen on the endometrial lining and one of the treatments for hyperplasia can be with counseling progesterone treatment. So, for instance, you'll hear about people who have endometrial hyperplasia or sometimes even early endometrial cancers who are treated with progesterone therapy or progestin intrauterine devices, IUDs, because the progesterone is protective for the endometrial lining. If your treatment is going to involve the progestin already, right. You're covering your bases even if there is a secret hyperplasia that you haven't identified yet by not doing a biopsy.

Matt: Got it. Okay. I'm dangerously close, Molly, to pulling us into talking about treatment, but I don't think we're ready there yet. Did you want to ask more about imaging? I know that was part of it.

Molly: Well, I think also just thinking about this patient who's 46. She has to BMI of 30. She has a history of PCOS. Do those historical features kind of push you more towards biopsy that she's somebody at a little higher risk or you're still comfortable just kind of watching and if you can manage the bleeding medically not being as concerned?

Holly: Yeah, those are definitely additional risk factors for hyperplasia. I'm curious about what exactly her history of PCOS is personally. Is she somebody who has gone long amounts of time,

multiple months in a row without a period in the past, that is the time frame over which the endometrial hyperplasia can build up or develop? A higher BMI is a risk factor for endometrial hyperplasia as well because it's the excess adipose tissue in our bodies. I don't know what the examples are of this in the internal medicine world, but I know I was always trained that fat cells are inert and inactive, but we now know they're hormonally active, and so they are converting peripherally to estrogen as well. Anybody with a higher BMI, in essence, has excess unopposed estrogen in their system. So, those are definitely risk factors. Again, I'm not saying I would never biopsy her. I would bring it up if this patient were willing to do the biopsy today and I have had patients who say, absolutely, I wasn't planning for it, but I'm here, let's do it. It's totally reasonable. If they say, "Well, let's get the ultrasound first, let me come back in a month, let me try this medication." I think that's reasonable as well.

Molly: I like that because I don't know if they're actually true guidelines, but I feel like I've definitely read anyone over 40 or over 45 should be biopsied and that's like all of my patients, but-

Holly: Right?

Molly: -most of them don't want to have that happen.

Holly: Exactly. I think that's our general recommendation as well, so I'm not saying don't biopsy. I guess what I'm narrowing in on is the timeline in which we're doing that with the patient. You'll have some patients who, after counseling, don't want anything done in the office, and they would prefer to do a D&C, a dilation and curettage in the operating room and that's something I would offer too. I know that's not what you're offering, but it's all worth a discussion. I think the number of people who make it through their 40s with no biopsy is potentially on the lower side. It's a very common occurrence. I think it's a little bit of existential question of if it's overkill or not. We do find abnormalities and so, I think those patients are happy that we found them.

Matt: Let's do a little bit of a recap. Paul asked you the question about nomenclature and we're using the term abnormal uterine bleeding now, we don't have to remember the metrorrhagia, those things.

Paul: Or, how to spell them more importantly.

Matt: Yeah, how to spell them.

Holly: Yeah.

[laughter]

Matt: And we split them into two columns. There's the structural, that's the PALM part of the mnemonic, and the nonstructural that's the COEIN part to the structural polyps, adenomyosis, fibroids are leiomyomas, and malignancy or hyperplasia. And then on the nonstructural side, we have coagulopathy, I believe it was ovulatory dysfunction, endometrial causes, iatrogenic causes, and then not otherwise specified. The work up, we're going to do a pelvic exam, speculum exam, look at the cervix and attempt a bimanual exam as well. The low ab workup is pretty basic, make sure they're not pregnant you said, a CBC, check of their thyroid, and a pelvic ultrasound, which we talked about extensively, and then whether or not they get an endometrial biopsy was where we're just at in the discussion. So, Molly, where are we going to go to next with this case?

[music]

Molly: Yeah, so were excellent internists and ordered a pelvic ultrasound, which showed a 2-centimeter subserosal fibroid, adenomyosis, and a 16-millimeter endometrial stripe. Let's break it down a little bit. Which fibroids are actually related to heavy bleeding and when should a PCP consider referring patients for specific fibroid treatment with Gynecology versus just initiating hormonal treatment that might be pretty much the same whether they have a fibroid or not?

Holly: Yeah, that's a great question. So, fibroids are really common. Up to 65% to 75% of people with a uterus have fibroids and they range from really small 1 cm, sub-centimeter ones, because our radiologists are so good and the ultrasound machines are so sensitive, we can pick them up to people with multiple massive fibroids who are walking around looking like they have a full-term pregnancy. In my world, a 2-cm fibroid is small. I would say anything under about 4 to 5 cm is considered small, but regardless of size or location, they all contribute to heavier periods. So, somebody with a fibroid, any fibroids, any size, is going to have heavier periods in general than somebody without fibroids.

The fibroids, if you recall, can be in three different locations in the uterus, so they can be like, really hanging off the outside of the uterus. I refer to them with patients as like Mickey Mouse ears and those would be the pedunculated ones, they can be subserosal as in this patient, so that's in the uterine muscle layer, and often if you're looking directly at a uterus or you're directly looking at the ultrasound, you can see that there's a bulge there, but it's certainly within the muscle layer of the uterus, and then you could have submucosal fibroids, which are ones that are pushing into the endometrial cavity. In general, the submucosal ones will cause more heavy bleeding than the subserosal or the pedunculated ones, but they can really all contribute to heavy bleeding.

In terms of when do fibroids need to be referred to GYN, I think, would be if either you suspect or the patient desires surgical management would really be the only true reason to refer. There are primary care doctors who do IUD insertions and so if that's you, you can go ahead and manage this with an IUD. If you would be referring to GYN for an IUD, you can refer for that. But yeah, if you're going to manage with an oral medication of some sort, then I don't think you have to refer to GYN at all.

Molly: I feel like we're seeing adenomyosis more and more on ultrasounds as kind of the technology is improving. How do you talk to patients about that? What's your spiel for explaining it?

Holly: I'm a visual learner and I'm a visual teacher, so I always draw a picture to the patient. Usually like at our office, the face sheet gets put on the door and at the end, it gets thrown out if we don't do anything else with it. On the back of it I draw the patient's uterus and a little schematic, and I'll draw on the diagram of where their fibroids are so they really get that visual. What I explain about adenomyosis is that the lining cells of the uterus, those endometrial cells, that's what usually builds up and then sheds each month and adenomyosis is a condition where those endometrial cells get into the muscle layer of the uterus. We don't really know how or why it happens, but it does and because our ultrasound technology has gotten so good, we're able to see that more often these days than say 20, 30 years ago.

So, adenomyosis is the condition in which those endometrial cells get into the uterine lining or into the uterine muscle layer. When the lining cells bleed and shed, the bleeding is also happening in the uterine muscle and so that's a very painful process. Adenomyosis is a condition characterized by heavy periods and also painful periods.

Paul: When the reports, God bless, like you say [unintelligible [00:32:39] are great and oftentimes if there's something to do with abnormal endometrial thickness, like OBGYN consultation recommended or sampling recommended, which bless them, but when you see those reports and look at the numbers what things stand out or what are you looking for in terms of comments on the endometrium itself?

Holly: It is important to distinguish here that we're talking about a premenopausal patient as opposed to a postmenopausal patient. In a postmenopausal patient, somebody who has gone more than a year without any periods, generally in their late 40s to early 50s, any finding of endometrial thickness in a postmenopausal patient warrants evaluation and so that would be 5 mm thickness or more. In a premenopausal patient, it's totally normal for the lining to be a different measurement throughout the menstrual cycle. If you ultrasounded someone every day for an entire menstrual cycle, you'll see that lining build up and then shed.

There is not really a number to say this is too thick and therefore it warrants biopsy. I'm concerned about hyperplasia. The day that the ultrasound is done, the thickness of the stripe could be predictive of how much bleeding, how much blood products are still in there that the patient has to bleed. If I were seeing the patient on this day, I might say, "Yeah, you've still got heavy bleeding to go versus if on the day of the ultrasound, her endometrial stripe was 2 mm. I'm not surprised if she's saying she's not bleeding. I wouldn't be explaining it too much to the patient at all. I wouldn't be making too much of a note of it.

Molly: Well, I think that is a good wrap-up for kind of ultrasound findings unless there's anything else that you look for an ultrasound or things that you see that are helpful in terms of nailing down the diagnosis.

Holly: The other thing that often we can see on ultrasound are endometrial polyps and so that would be a good reason to refer to GYN. When we see polyps, we do recommend removing them because they can have a very small risk of hyperplasia just within the polyp themselves and so that would be a reason for surgical removal. Those are the big things I'm looking for in an ultrasound, those structural causes.

Matt: Molly, is it time to get into treatment?

Molly: I think so, yeah. So, Melissa is exhausted by the amount of bleeding that she's had and really just wants it to stop immediately. What kind of options do we have for acute treatment of heavy bleeding?

Holly: In terms of acute treatment, there are a variety of medications available, hormonal and nonhormonal. So, the hormonal ones are all various combinations of estrogens and progestins, and generally, your choices are progestin-only medications. These would be things like medroxyprogesterone or norethindrone, combined hormonal contraceptives, any number of oral the contraceptive pills that are available to us, so we can totally go through selection. So, tranexamic acid, I explained to patients, is a nonhormonal medication that helps their bodies stop active bleeding. It's like when you get a cut and your body has to make a scab like we get a papercut, and that same thing is happening inside the uterus and the tranexamic acid helps with

that clotting cascade to help the clot form or that scab form on the lining of the uterus. Those are all the acute treatment options. I will further go into the more long-term treatment options, which can include those same ones and then additionally I'll add things like intrauterine devices, the arm implant, the contraceptive implant, and then surgical options.

Matt: For the acute treatments, can you speak a little bit to the doses because I don't prescribe oral contraception that often or a lot of my patients are on it and I'm just refilling it for them already. We're talking about someone with acute bleeding, they come in the office like this patient and they're asking us to stop the bleeding. Not like, "Oh, I have heavy bleeding every month, can you help me with that?" The estrogen I was reading, it's like 30 to 35 mcg daily and then for the progestins, it's like 5 to 10 mg daily. Can you just speak to what might be a typical prescription and how long they continue it in that acute setting?

Holly: Again, we're never going to prescribe estrogen alone because then you're at risk of endometrial hyperplasia, and so you're essentially choosing between a progestin alone or a combined pill. If it's going to be a combined pill, honestly, I think you can choose any birth control pill on the market and you'll be fine. Most pills on the market are somewhere between 20 mcg of estrogen and 35 mcg of estrogen, and any of those would be fine. It is possible to do a high-dose birth control pill taper. What we'll do is actually have the patient start with two pills a day or even one every 8 hours for like 24 to 48 hours. The bleeding will significantly lighten and then you can taper down. If you started at three a day, you'll taper down to two a day for a while and then taper down to one a day and finish out the whole pack.

The downside of that is that those doses of estrogen will really make people nauseous, so you just want to make sure they have an antiemetic available, like prescribe it with the antiemetic. I would really reserve that for somebody who's really acutely bleeding much more heavily than this or somebody who's soaking through multiple pads an hour. I think this patient was a tampon in 2 hours, so a tampon in 2 hours, I'm not worried about acute hemorrhage or blood loss.

For this patient, I think I would probably just start her on a regular pack of birth control pills, take one a day and the bleeding is going to stop pretty quickly. If you're concerned about using estrogen because this patient is over 40, her BMI is a little higher, and you're worried about that VTE risk, then you can get the same effect from a progestin-only. That would be the norethindrone acetate or the medroxyprogesterone and same thing I would probably start with a taper with those like three a day, down to two a day, down to one a day.

Matt: That's great. Thank you.

Holly: Mm-hmm.

Matt: Very helpful. Hopefully, this won't come up often-

[laughter]

Matt: -where I have to use this knowledge, but I'm sure we have a lot of listeners. I think some people are going to be seeing this situation more than I am, where my patients tend to be on the older side and so not as many young women. Molly any other follow-up questions about this?

Molly: Yeah, if someone is bleeding that heavily but they're hemodynamically stable, or you got hemoglobin and it's lowish, but they're okay, when do you think about sending someone to the emergency room for IV estrogen or just doubling up or tripling up on the oral work as well as IV?

Holly: Yeah, I think the role of emergency evaluation is for vital sign instability. If you think somebody actually needs a blood transfusion or they are actively hemorrhaging that much--probably if they're hemorrhaging that much, you're in blood transfusion territory anyway. That's where we start thinking about IV estrogen. Generally, I don't think it's a rule, but in my experience, we're considering IV estrogen in people who've already failed some sort of oral management.

Molly: That's helpful, thanks. And I run into this a lot, patients who are maybe already on birth control pills, but they're still having breakthrough bleeding that's heavy or something like that, and thinking about tranexamic acid, which has FDA labeling suggesting increased risk of thrombosis, and then the pharmacy doesn't like to give that with the oral contraceptives if it's an estrogen-containing contraception, how do you think about that and is that something that you co-prescribe or you really stay away from co-prescribing those?

Holly: I have co-prescribed them, I agree, I think the labeling and then the actual evidence are in conflict. I think it's an area where hopefully we will have more data in the near future. I wonder if some of it has to do with the fact that originally a lot of the tranexamic acid use was in the orthopedic surgery population, which tends to be a different population than what I'm seeing for acute heavy menstrual bleeding. The reality is if somebody's bleeding that heavily, I think the benefits of stopping their bleeding outweigh the risks of potential VTE. I'm not going to say that's like a black-and-white statement, but again this is where shared decision-making and good patient counseling come into play, but I certainly have co-prescribed them.

Molly: If someone has clear indications why they shouldn't be on estrogen, high VTE risk, or active smoking, and someone on the older side or migraine with aura, potentially. How do you choose between using progesterone only versus tranexamic acid?

Holly: That's a good question. I think if they have a contraindication to estrogen, I am equally willing to offer either a progestin-only medication or tranexamic acid. Often, I'm talking to my patients about the logistics of how they're taken. The progestin-only medications are daily and it's probably going to be daily for the short to medium to long term, whereas the tranexamic acid is three times a day, but only for the first five days of your period. People will feel different ways about those options. With tranexamic acid, I'm unlikely to be able to predict no more bleeding, but it will make each of those days of bleeding significantly lighter. Whereas with many patients, I can get them to amenorrhea or no periods with progestin medications if they give me enough time and patients to work with it.

Matt: We talked about various causes of abnormal uterine bleeding. When we're talking about tranexamic acid for somebody that has abnormal uterine bleeding from ovulatory dysfunction. In those cases, do you still consider NSAIDs and tranexamic acid? Because I know for heavy menstrual bleeding, they're having their menses and it's heavy. I know tranexamic acid, I've prescribed it, and I've prescribed NSAIDs in those cases. Do they also work for other structural causes of abnormal uterine bleeding that aren't related to menses? I'm just trying to differentiate for myself and the audience, like the nomenclature thing as Paul and I were saying, the therapies we're just talking about, I think OCPs address many causes of abnormal uterine bleeding. The tranexamic acid for people who are bleeding, does that work just if it's their menses that we're trying to slow down or lighten, like, decrease bleeding or does it also work for other causes?

Holly: I think in any situation where you would think about OCPs, you can also think about tranexamic acid. You would not think about OCPs if somebody had a polyp and so then I wouldn't think about tranexamic acid there either. For any other cause of heavy menstrual bleeding regardless of whether it's from fibroids or adenomyosis or PCOS, yeah, they would all work, all be good options.

Matt: Thank you, Paul, how are we doing here? [crosstalk]

Paul: Fantastic. This is so extraordinarily helpful. No, this is great.

[laughter]

Matt: Molly, any other treatments you wanted to ask about?

Molly: No, I think that's great for the acute. Just kind of moving on to more chronic treatment. We started Melissa on whatever your favorite recommendation is after some shared decision-making and she's really happy the bleeding stopped over the next couple of days. She really doesn't want to go through this again next month. How do we think about continuing treatment for future prevention?

Holly: This is where that anticipatory guidance is really important. Say we stopped her acute bleeding with one of the progestin medications like norethindrone. If and when she stops it, she will get a withdrawal bleed and what I mean by that is we've been giving her progesterone and then she stops taking it that's the exact mimic of what happens in a normal menstrual cycle to trigger a menstrual period. Sometimes I get patients who say, "Oh, life was good. I stopped my bleeding, and then I stopped the norethindrone and my period came right back." I always sigh because that means somebody didn't counsel them appropriately. You have to counsel people that whenever you stop that progesterone-containing medications, you will get a period and that's normal.

It hopefully will not be as heavy as the acute event that brought her into you originally, but it could be. Sometimes people go, they seesaw, they'll be on norethindrone taper and then they taper off and then the bleeding comes back, and they go back on and they go through the cycle until they get annoyed with it.

Other people stay on the progestin maybe once a day indefinitely and that's perfectly safe, but what I often find is that eventually some of the other side effects become annoying to them. So, for instance, medroxyprogesterone in particular, I find makes people really moody and tends to make them bloated, norethindrone a little bit less, but it can also do that. Eventually, patients get fed up with those side effects.

I do have some patients who have stayed on tranexamic acid long term and that's great. Every month they take the tranexamic acid for five days. It controls their periods if they are heavy, but a lot of times I then have patients who want to transition to something else. Either we're talking about intrauterine devices or the arm implant or surgical interventions.

Matt: I don't think we mentioned it, but just regular combination oral contraceptive pills, those are also on the table as well. Just anyone that we want to prescribe on the market should do the trick.

Holly: Yes, yes.

Matt: On a prior episode. We talked with actually a hematologist about coagulopathy and heavy menstrual bleeding, and she was a big fan of the LARCs, as she was calling them, the long-acting reversible contraceptives just because it's so convenient and you don't have to worry about taking it at the same time every day like you do with some of the other hormonal pills. What else is available? You mentioned surgical options. How do you counsel patients about that if they're just not having luck despite long-acting contraception or the oral contraception?

Holly: Yeah, so the surgical options will vary depending on oftentimes the size of the uterus is one consideration, so imaging would be important there and then the patient's goals. Generally, with any surgical option, patients are done with childbearing. That's an important question I always ask. But the surgical options include sometimes an endometrial ablation and that's a procedure where through different mechanisms, depending on which device you use, you essentially burn away or ablate the lining of the uterus so that the endometrial lining can't build up again each month.

Sometimes we will consider myomectomy, which is surgical removal of just the fibroids, although generally, it's not a great cure for heavy menstrual periods alone unless the patient is desiring future childbearing. I can talk about why if you're interested. Uterine artery embolization or sometimes called uterine fibroid embolization is a great procedure done by the interventional radiologists. With that procedure, a catheter is placed into one of the patients either groin or sometimes arm vessels, and then under fluoroscopy is snaked up to the uterine arteries and then they inject a material that blocks off those uterine arteries and so because the uterine arteries are blocked off, the blood flow to the uterus is diminished and the blood flow to the fibroids are diminished. The fibroids will shrink and periods get lighter.

So, I don't perform that, but you can refer to IR. I refer to IR. It's a great option for patients. And then finally there's a hysterectomy. Hysterectomy, I can guarantee somebody will have no more periods, but it certainly is major surgery and deserves full counseling. But as a surgeon, I enjoy performing it, so it's always on the table.

[laughter]

Matt: Let's do a quick recap, and then we'll see what other questions we have. We just talked about basically the treatment. There're acute treatments, which is where we may put someone on two or three pills a day of either a combined oral contraceptive pill or a progestin-only pill, and that may help slow down the bleeding, and they would taper down on those. Or we could also prescribe tranexamic acid as part of that. We talked about in long-term treatments, again, it would be potentially an estrogen-containing oral contraceptive or a progestin-only pill. You mentioned sometimes patients with the progestin-only ones don't tolerate them as well because of moodiness or bloating.

We said tranexamic acid monthly is also an option there as well. For patients who are not doing well with those therapies, something like a long-acting reversible contraceptive either an IUD or an implant could be an option. We talked about endometrial ablation, uterine artery embolization and then hysterectomy is always on the table, pun intended. I don't know if that's, yeah sorry Paul.

Paul: [crosstalk] not too bad.

[laughter]

Matt: Okay.

Holly: I always take pictures of the uterus for the patients after I remove them. They always want to see it. So, yes, we put it on the table and I take a picture.

[laughter]

Matt: I would too. I don't blame anybody for that. Molly, what other questions do you have before we get to our take-home points?

Molly: Absolutely. Well, Holly, is anything that you see in referrals that you wish that internists or primary care was doing a little bit differently or mistakes that you see made frequently that you recommend we try to work on?

Holly: One thing I want to make sure that nobody misses is getting a Pap test up to date. I think in the setting of abnormal bleeding, it's reasonable to do a diagnostic Pap test. If you guys are doing the pelvic exam already and you have the supplies to do a Pap, it's great to go ahead and do that. Even if somebody has had a Pap two to three years ago. In the setting of abnormal bleeding, it would be appropriate to do a diagnostic one.

Certainly, there have been cases of patients who think they're having heavy periods and they actually are bleeding from cervical cancer, so that's always good to get up to date. I think another question is how quickly do people need to be referred to-- or how quickly does somebody need to get in with GYN? I think this is also going to depend on your location and everybody's availability for appointments, but it's totally reasonable to make friends with your local friendly area gynecologist.

I have colleagues who will text me and say, this is the situation-- or send me a message in the EMR and say, this is the situation. Do you think she needs to come in soon or is next available next month, okay? Those are totally reasonable conversations to have because if somebody, for instance, has-- you've gotten things under control with the norethindrone, but the patient knows she wants a hysterectomy, we've got time to get her in for that appointment. If you've already tried some oral meds and it's failing, then we probably need to get her in sooner. Great to have those conversations with you guys.

Matt: Well, I think it's time to get take-home points so we can let you get back to your family this evening. Thank you so much for all your time and teaching. If you had like two or three take-home points that you really wanted the audience to remember.

Holly: Everybody can do pelvic exams. Please don't forget that part of your physical exam. Everybody can prescribe oral hormonal medicines and tranexamic acid, and everybody can order an ultrasound. If you do those things for your patients, they will all be well taken care of.

Paul: This has been another episode of the Curbsiders, bringing you a little knowledge food for your brain hole.

Molly: Yummy.

[laughter]

Paul: I'm glad I waited this time. Get your show notes at *thecurbsiders.com*. And sign up for our mailing list to get our weekly show notes in your inbox. Plus, twice each month you'll get our Curbsiders Digest recapping the latest practice-changing articles, guidelines and news in internal medicine.

Matt: Yeah, they should check us out on YouTube as well, Paul, because we're doing video now,

Paul: Sure, if you want.

Matt: We're committed to high-value practice changing knowledge and to do that we need your feedback so please subscribe rate and review the show on Apple Podcasts or on Spotify or on YouTube. And you can also send an email to *askcurbsiders@gmail.com.* And a reminder that this and most episodes are available for free CME through VCU Health at *curbsiders.vcuhealth.org*. I wanted to give a special thanks to our writer and producer for this episode, Dr. Molly Heublein, and to our whole team. The Curbsiders is produced and edited by the team at Pod Paste. Elizabeth Proto and Jen Watto run our social media, Stuart Brigham composed our theme music. And with all that, until next time, I've been Dr. Matthew Frank Watto.

Molly: And I've been Dr. Molly Heublein. Good night.

Paul: And as always, I remain Dr. Paul Nelson Williams. Thank you and goodbye.

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