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### Diagnostic & Management Updates for Abnormal Uterine Bleeding

Narrator:

Welcome to CME on ReachMD. This segment: *Effective Management of Abnormal Uterine Bleeding*, is provided by Omnia Education. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements, as well as the learning objectives.

Dr. Zurawin:

This activity will discuss the updated diagnostic and treatment algorithm to manage abnormal uterine bleeding, using a minimally invasive surgical approach, a better understanding of the broad umbrella of bleeding that occurs outside of normal cyclic menstruation, proper patient workup, risk management options, and selection between techniques will also be discussed. Dr. Munro, welcome to the program.

Dr. Munro:

Glad to be here. Thank you very much for inviting me.

Dr. Zurawin:

Oh, you're very welcome. We're always eager to hear your opinions about this very important topic that you're a renowned expert in. So, let's just start off in saying, Dr. Munro, what comprises abnormal uterine bleeding, or AUB, in the reproductive years, and what are the potential causes?

Dr. Munro:

Well, abnormal uterine bleeding is an abnormality in 1 or a combination of 4 variables: the frequency, regularity, duration, or/and perceived volume of bleeding. The categorization can be further broken down into acute or chronic, so that women with chronic abnormal uterine bleeding we've defined as having more than 3 of their previous cycles in the past 6 months, for example, effected in this way. Alternatively, you have acute abnormal uterine bleeding which is usually an episode of heavy menstrual bleeding that, in the opinion of the clinician, is of sufficient volume to require urgent or emergent management.

Dr. Zurawin:

So, for the purpose of this discussion, we're going to exclude acute uterine bleeding or heavy menstrual bleeding. So, how do we really start when faced with such a patient? For example, we often see patients who have perceived heavy bleeding, but in reality, clinically, it's not. So, are there any useful laboratory tests?

Dr. Munro:

Well, first of all, it's really important with our FIGO systems to recognize, in fact, that there are two systems, and the history, which I think has not very well been taught or appreciated, is the critical first step. So, a structured history really has to be performed because this is the key to the identification of some of the potential causes that aren't detectable by imaging or laboratory tests. So a history that documents the cycle length, the regularity of that cycle, which we now know is probably give or take 4 days, and we know now that the frequency should be between 24 and 38 days, not 21 and 35 as was previously perceived, the duration is normally up to 8 days, and the volume, which really is something that the patient really has to determine. When we say that maybe they really don't have heavy

bleeding, we don't think that's important. If a woman says, "I've got heavy bleeding" and you say, "You don't, because your hemoglobin is normal," that doesn't really help her, because if her quality of life is affected by what she perceives to be heavy bleeding, then we take that seriously and respect that decision, even if her hemoglobin is normal. So, while measuring the hemoglobin and the red cell indices is very important, the absence of anemia, for example, or the absence of evidence of iron deficiency, while reassuring to a certain extent, does not mean that this patient doesn't qualify for some type of intervention if she desired. Now, with respect to other tests to try to sort out ovulatory function, for example, or coagulopathy, there are a few, but history really trumps them in most instances; however, in some women the history is unclear and performing, for example, a serum progesterone level in what is anticipated to be the luteal phase can be useful, at least for that cycle, and of course if the woman has ovulatory dysfunction, if that's what we assume, there are a number of potential causes of that which include: abnormal thyroid function, hypoprolactinemia, etc. that can be tested in a laboratory. The assessment for a coagulopathy which is present far more than perceived by many, can be first detected or suggested at least, by a structured history, and if that structured history is suggestive of coagulopathy then there are a number of assessments that can be performed and we'll talk about those later.

Dr. Zurawin:

Well, one of the things that you mentioned that's, I think, of great interest to our listeners, is the perceived rate of bleeding. Because I don't think we can argue with frequency, regularity, or duration in terms of critical components of the history and a structured history. Many clinicians are stymied by patients who complain of hemorrhaging and when they get a hemoglobin or hematocrit they see that it's normal. What, at this point in the history, do you really recommend our clinicians do when they're faced with that?

Dr. Munro:

Accept the patient's definition. Let me give you an example. If you're an individual and you leave the house every day not knowing whether you're going to have a bleed or not, your life's affected. It doesn't really matter if it's heavy or not heavy, but it can affect what you wear, where you sit, when you're going to have sex. It can be any of those things. So, the notion that hemoglobin drives this decision is a fallacious one. The National Institute of Clinical Excellence in the United Kingdom has really determined that heavy menstrual bleeding is that which is of sufficient abnormality or quantity so as to affect quality of life. And so, I am one, for example, who really is behind the notion that we have to move from suggesting that women don't have a problem if they don't have an anemia, to accepting and respecting the definition of the woman.

Dr. Zurawin:

So, over and above laboratory tests, is there a role for uterine imaging in determining the cause of chronic abnormal uterine bleeding?

Dr. Munro:

Absolutely, and this is very critical, particularly in determining the presence or absence of structural abnormalities that may, or in some cases may not, cause the bleeding that is witnessed or experienced by the patient. So, probably the most important one, particularly for gynecologists because they have ready access in general to this, is transvaginal ultrasound. So, transvaginal ultrasound is very important. It can help with the diagnosis of endometrial polyps, adenomyosis, and leiomyomas, and can even be suggestive or helpful in determining women with ovulatory disorders. So not only simple transvaginal ultrasound is important, but also the use of contrast and that contrast is generally saline but also can be with gel and this is an assessment that, I think, has been under-taught throughout the United States, but one that is very easy to do as long as you know how to do it. The catheter that can be used is as simple as an insemination catheter and the infusion device is as simple as a 10 mL syringe full of saline. And by placing this fluid in the endometrial cavity, one can identify endometrial polyps, one can identify the relationship of leiomyomas to the endometrium, and these 2 features are very important and can really be helpful in a relatively rapid identification of possible contributors to the bleeding. Of course there are other imaging assessments as well; MRI has a use that's very important, particularly in women who have combination of adenomyosis and leiomyomas, or where the uterus is very large and it's very difficult transvaginally to identify or evaluate the uterus. It's also of value in women who can't be examined with transvaginal ultrasound because of, for example, virginal status, or those who are postmenopausal and have a very sensitive vagina that limits the evaluation. So, there are a number of places where transvaginal ultrasound can have a role. Now, I consider that imaging also can include hysteroscopy, although most people don't use it in that context, but if we think of the full package, if you will, of imaging, diagnostic hysteroscopy, preferably in an office environment, is also very useful. It doesn't though evaluate for adenomyosis and has some limitations in determining the relationship of the leiomyoma to the endometrium. On the other hand, hysteroscopy can provide a see-and-treat approach where one can hysteroscope the patient and at the same time, or in the same setting at least, removal an endometrial polyp or sample the endometrium in a directed fashion.

Dr. Zurawin:

You were one of the key authors of the PALM-COEIN system of classification of abnormal uterine bleeding. And with a mind towards utilizing that system to see and treat patients within 1 or 2 visits if possible, can you go over some of the key points of the PALM-COEIN algorithm for us?

Dr. Munro:

Well, first of all, I wouldn't call PALM-COEIN an algorithm, but it is the second of the 2 FIGO systems. The first is the one I mentioned, obtaining that structured history and without that structured history, one can't really do a PALM-COEIN categorization. So this PALM-COEIN system, if you will, breaks down the various possible contributors in a given individual in a way that allows one to perhaps design therapy after determining causes. And in many women, more than 1 positive finding can be present at the same time, and some of those findings may or may not contribute to the bleeding. For example, a type 5 leiomyoma that doesn't impact, by definition, the endometrium probably has nothing to do with abnormal bleeding; many polyps don't have anything to do with the bleeding, and adenomyosis often has nothing to do with the abnormal uterine bleeding, but they all can. So PALM-COEIN allows you to collect all of these potential causes and then try to address the patient in a way that meets her needs and desires, with respect to fertility and degree of intervention. So, for the structural entities: the polyps, ABP; adenomyosis, ABA; and leiomyomas, ABL; all require some type of imaging and, as we've said, ultrasound is the beginning. While polyps, for example, can be suggested with simple transvaginal ultrasound, addition of contrast to that ultrasound can be very helpful and really as sensitive as hysteroscopy in making a diagnosis. Adenomyosis typically doesn't require the contrast, but there are a number of features including heterogeneity, the presence of striae, lakes, little micro-cystic areas, thickening of the myometrium, particularly posteriorly but sometimes globally; all of those are independently suggestive of adenomyosis and the more of them that are present the more likely the diagnosis is there. And indeed, in reasonable hands, transvaginal ultrasound is equivalent to MRI for this diagnosis when compared to histopathological examination at the time of hysterectomy. And then, finally, leiomyomas often can be identified by transvaginal ultrasound, but it is our understanding that when leiomyomas contribute to the genesis of abnormal uterine bleeding, which by the way is generally heavy menstrual bleeding, so it's cyclical if the woman's ovulatory, when that leiomyoma is contributing to the bleeding, in order to do so, it should be in contact with the endometrium, because in those circumstances the diffusion of substances like TGF beta 3 from the leiomyoma can influence the factors in the endometrium that are responsible for hemostasis. So it's very important, before you ascribe the cause of the bleeding to a specific leiomyoma, that you demonstrate that it be adjacent to the endometrium. So, that is something that can be very effectively determined by transvaginal ultrasound with contrast, or contrast hysterosonography, and for most Americans that's SIS, saline infusion sonography, but MRI can be effective there as well. So, those are basically, in a nutshell, the ways of distinguishing among those 3 structural entities. The fourth one which is hyperplasia, and for this system we're really talking about what we used to call atypical hyperplasia which is now evolving to endometrial intraepithelial neoplasia. That, of course, requires histopathological diagnosis with biopsy and those individuals are categorized further according to the FIGO and WHO systems that are appropriate.

Dr. Zurawin:

Okay, well then, is it really necessary to perform all of the investigations in all patients? Are there some kinds of acceptable shortcuts that will get us to where we need to be?

Dr. Munro:

First of all, we want to be careful. We haven't really talked very much about iatrogenic and the non, or not yet, or not otherwise classified groups, but that them, what you might get, for example in your history, you might find that if a woman had a Cesarean section she might be at higher risk for having bleeding from what we call an isthmocele. Women with acute bleeding after having interventions could have an AUB malformation. So, we have to think about those, but in general, if we can find a group of women who are very low risk, at least at first glance and at first impression, not all of these investigations are going to be necessary.

Dr. Zurawin:

So, Dr. Munro, we've talked about different aspects of the PALM-COEIN system and some of them seem to lend themselves to therapies like endometrial ablation, and others seem to lend themselves towards resection and other kinds of operative treatments. Can you talk a little bit about how you would relate to the PALM-COEIN system and to these different surgical options?

Dr. Munro:

Sure, Rob. Well, of course, medical therapy for many circumstances is what's going to be most appropriate, but for polyps, for example, we have no predicate example of medical therapy. We don't think medical therapy works. So, polyps are an example of an entity that requires a surgical approach and we now know that hysteroscopically-directed polypectomy is the most appropriate with respect to therapeutic efficacy. We know that a lot of individuals put a hysteroscope in, take it out, put a polyp forceps in, pull out the polyp, and then go back in and look to see if they got the job done. We know that the failure rate with that approach is probably 15 times that of hysteroscopically-directed polypectomy with some type of device, be it scissors, be a resectoscope, be it a tissue-removal system. So polypectomy is one that's very amenable to that approach. And for women who certainly desire fertility, and have submucous myomas, myomectomy is the approach of choice. And so for them, that should be done by the least invasive approach possible and generally that approach is hysteroscopically-directed myomectomy. Now, the discrimination between those women who are appropriate for hysteroscopic myomectomy and an approach from above, be it laparoscopic or laparotomic, that requires a critical evaluation with

imaging, but certainly the use of a resectoscope, or a tissue-removal system, or one of the methods that we have described which is the use of a bipolar needle and a tissue-removal system, that can be done very effectively; in fact it can be done even in an office system. Those women are not going to be appropriate for medical therapy because, for example, their abnormal uterine bleeding and their infertility, if that's the case, are actually related. Medical therapy isn't going to help with the infertility aspect. Now, on the other side, if you have AUB-E, AUB-O, or even cases of AUB-C, all of those are treatable with endometrial ablation, and indeed for women who do not wish to ever become pregnant in the future, endometrial ablation can be useful for some types of submucous myomas. So, AUB-LSM.

The other place that endometrial ablation can be of some value is in women with submucous myomas who do not wish to become pregnant ever in the future. Now, this is not part of the original randomized trials, but there are a number of studies showing that in some women with submucous myomas, endometrial ablation can be effective. So, the individual surgeon who is suggesting this should be careful that whatever technique they use is appropriately and effectively performed with the submucous myoma that they're dealing with, and generally this means that the submucous myomas are type 2's and it generally means that they're less than 3-or-so cm in diameter. With respect to adenomyosis, it's a difficult circumstance. We have evidence that women with adenomyosis can do well with endometrial ablation, but we're not sure which techniques are most appropriate and we do know that a relatively high proportion of women who fail endometrial ablation do have adenomyosis. So, I think information on the appropriateness of endometrial ablation in women who have adenomyosis is not well determined or worked out at this time.

Dr. Zurawin:

So, you've talked about tissue extraction and operative hysteroscopy and you do so many hysteroscopies, and both diagnostic and operative, have you seen a change in the approach to operative hysteroscopy for polyps and fibroids with the advent of the new technologies using morcellation as opposed to the 25 years that we had beforehand where we only had resectoscopes and rollerballs and so on.

Dr. Munro:

Well, anything that I say about this has to do with local perceptions and what I perceive is going on throughout the country, and it is my impression that more people are utilizing these techniques because they never felt comfortable with radiofrequency resectoscopes and with the aid of industry who are helping them, and the relative simplicity of these devices, it's been my impression that there is a bit of a uptick, if you will, in the utilization of these devices, at least for removal of polyps. Leiomyomas is another story and I must say that I do have concerns because it's my impression as well that more women are having their leiomyomas partially treated, because as we know, these morcellating or tissue-removal devices do have some limitations when used on their own; they aren't particularly useful at getting at type 2 myomas. So we see more referrals from women who have persisting disease than I was experiencing in the past. We did, as I mentioned before, publish a technique, one that was originally published by Betoki from Italy, but we actually do it all in 1 setting where we use a radiofrequency needle electrode to actually incise into the pseudocapsule and typically these type 1 or type 2 myomas, if they're appropriately selected, they tend to extrude into the cavity and one can then dissect along the pseudocapsule and have a much greater chance of getting them out in a single setting than was the case if you just used the tissue-removal device on its own. So, I think there's great promise for these devices. I think they perhaps are more consistently effective with polyps, but in the right hands, with the right combination of techniques, they can be very effective for leiomyomas as well.

Dr. Zurawin:

That's great, Dr. Munro, because at the end of the day, we're all working towards providing our patients with the optimal care and the most efficient and accurate diagnosis that we can for their problems, as well as the safest and most cost-effective treatments, so I think that the work that you've done has been critical in achieving those goals and I really thank you for talking with us today regarding abnormal uterine bleeding, the different diagnostic and treatment algorithms, and the associated challenges associated with this common clinical problem. Thanks so much.

Dr. Munro:

It was my pleasure, Rob.

Narrator:

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