**Peri and Post-Menopausal Bleeding Problems Transcript**

**April 2021**

**Dr Jayne Clarke-Williams. Faculty Trainer, BMS Menopause Specialist and Trainer.**

**0.01 Chair:** Good evening, everyone. I'm really pleased to welcome you all to this webinar tonight. This is the third in our series on women's health. And today we'll be talking around bleeding issues around the menopause. From the first webinar there are lots of questions about bleeding and hopefully we will have time to finish off answering the ones that we couldn't answer on the actual day. Without further ado, I am going to introduce you to Dr Jane Clarke-Williams who is going to take us through this webinar. Thank you, Jane.

**0.36 Speaker:** Thank you so much for joining us. Today I'm talking about the problems of menopausal bleeding around the peri and post-menopausal times. It's quite a common problem in practice. People often come in and this is something that you might often hear in surgery. ‘My periods have changed. I think I must be starting the menopause’.

So funny bleeding in your 40s and 50s. Very, very common, and really what we need to do is decide, is this normal or is this something to worry about? Because, of course, bleeding is normal, but we need to be aware of when we have to think again. So in a regular cycle that changes its length or changes the amount of bleeding is very, very common. And actually, it's nearly always due to obesity and fibroids and not hormonal changes. Of course, we know that fat is metabolic and oestrogenic, and that is why if you have more fat, you have more exposure to oestrogen and therefore your you are likely to have more bleeding problems.

**2.01 Speaker:** So what causes funny bleeding? I don't know how many of you, perhaps quite a few people use this thing to remind – it is PALM and COEIN.

And so the PALM part is things that you might find - the Polyps, Adenomyosis, Leiomyoma, (that's obviously fibroids) or Malignancy. But it could be due to funny bleeding or people on Warfarin, Ovulatory dysfunction, something in the Endometrium (for example Endometriosis) can be caused by things we've done (Iatrogenic) and then obviously the N is the not otherwise classified. Of this list the most likely are fibroids and ovulatory dysfunction.

**3.02 Speaker:** So most of these causes are non-worrying and we have the NICE guidance on heavy menstrual bleeding, which I won't go into tonight, but obviously that is something we can cover. If they do have heavy bleeding, then it's sensible to give some non-hormonal treatment like Tranexamic acid and Mefenamic acid while you’re waiting for any investigations you’ve requested. Tranexamic acid has a greater action on reducing the amount of bleeding but Mefenamic acid has a bit more pain relief. The Mirena is always a good option. And remember, the other thing that is licenced for heavy menstrual bleeding is Qlaira, which is an estradiol containing contraceptive pill. It is one of the things, unfortunately, that has been in short supply. Luckily, most of the HRTs have come back, but Qlaira doesn't seem to have appeared in the chemist very frequently at the moment.

**4.08 Speaker:** So why does your bleeding change as you get older? The average age we start our bleeding now is 12.5 and we're very used to people when they first start at periods having them irregularly, because we're waiting for the whole system to mean that you ovulate every month. And the perimenopause is exactly the same in the reverse. It's very common towards the end, that the cycle shortens, or you start skipping periods and you're not going to ovulate each time. And this is because there's less follicles, your hormones and FSH are going up and down and you're getting these increasingly frequent anovulatory cycles.

**5.01 Speaker:** So as a GP, what are you going to do when this lady comes in? Bleeding is normal, but it has such a massive effect on so many women and therefore, we know that 1 in 20 of our 30-49 year olds are going to come in to see us each year for funny bleeding. And we know that at least 70% of these presentations for heavy menstrual bleeding are in that perimenopausal age range. So this is a large bit of work for us and therefore it's always helpful to know how to deal with it.

So the first question when you're taking a history, it's very important to know whether they are on any contraception. I mean, people often to come in and talk about their funny bleeding and then when you say, ‘what are you taking?’ they say ‘Oh yes, I'm on the progesterone only pill/ I’m on the combined pill and I'm taking it continuously. Very often people are on contraception. They haven't mentioned it. And it is vital because obviously that has a massive impact on their bleeding. And different contraceptives have different bleeding patterns that are expected. Always think about pregnancy. I mean, I had a lady who was in her mid-50s. She'd been infertile, never been had a successful pregnancy, her period stopped, assumed she was through the menopause and blow me down a few months later, there was the baby. So I always considered pregnancy risk. It is unlikely, but it is always there. It is worth knowing what age they started their periods. And obviously it's always important to know their sexual history, relationship history and the family history. We do need to measure them because the BMI is important.

**7.08 Speaker:** So which things do they tell us that make our ears prick up?

* As you get older, you're more likely to have problems. So age is important.
* Smoking. As we know, smoking has a bad effect on a lot of things.
* Anything that means you have been exposed to oestrogen. And this is obesity. As I said, a very common cause. Someone who has not ovulated, for example, those with polycystic ovary syndrome. And obviously in the history, we will check that they haven't been taking unopposed oestrogen tablets or tamoxifen.
* People are more likely to have problems when they have an early menarche, a late menopause. Often a trigger for an early menarche can be weight and body mass, and so these all these things are connected,
* We are more worried if the bleeding is between period times or after intercourse.
* Pelvic pressure or pain is something we definitely need to take note of.
* Diabetes and hypertension are two things that can make us have a higher index of suspicion. But of course, all these things we want, whether it's cause or effect, because if you've got metabolic fat that has the effect of giving you excess oestrogen exposure and diabetics, hypertensives often have this alongside.
* Then if people do have a condition that makes them more prone to have cancer and the one mentioned at the bottom of the slide is Lynch Syndrome, which is non-polyposis colorectal cancer, these people can have a much higher incidence of endometrial and other cancers.

**9.18 Speaker:** So this patient, what are we going to do, we really need to know where the bleeding is coming from because they can notice it on their pants or their pads, but there are lots of things that can cause that bleeding. So it is important. Have a look, can you see where the bleeding is coming from? A bimanual will help us check out the uterine size and the adnexal mass. And of course, we might think about pregnancy again.

**9.54 Speaker:** But what are we looking for? So where is this bleeding coming from? When we think about the womb there are various causes.

* We're going to atrophy where we're talking about the peri and post-menopausal years. As we've talked about in previous webinars, the lack of oestrogen has a profound effect on all the tissues down there and therefore, it is quite common to get bleeding from where the skin has got thin and dry and has micro abrasions and things.
* Polyps. You can have an intrauterine polyp.
* Fibroids are obviously important and that you'd be able to check out with your bimanual.
* Endometritis. Infection is important and definitely with me working in the genitourinary medicine department, we always think about infection and we like to do swabs.
* Endometrial hyperplasia. This causes more bleeding. Most individual hyperplasia is quite simple to treat and settle down, but obviously they can continue on to endometrial carcinoma.

**11.17 Speaker:** So what about the cervix? Again, you can have polyps. We've all seen ectropion – they are very, very common. Cervicitis. Of course chlamydia can happen at any age and gonorrhoea, we're seeing a lot more of this in GUM. So do remember that infection is quite a common cause of funny bleeding. Some ladies, you're quite surprised when you look, and you realise that you can actually see the cervix without the speculum. And some people get really horrible sores where their cervix, because of the prolapse has rubbed on things and they can bleed. Very nasty. Or obviously there can be cervical carcinoma. But you're only going to take a smear if it's due.

**12.11 Speaker:** So the vulva. Again, atrophy can bleed. They can scratch. Dermatological conditions can be excoriated. Don't forget, Herpes can occur at any age and remember in the peri and post-menopausal period it makes the skin much more likely. Herpes can be more common. Age is no reason for people not to catch it. But also, if your skin is atrophic, you might get more recurrences. And then you can have good old warts, they can bleed. And again, vulval carcinoma.

**13.03 Speaker:** And then, of course, the other site is the vagina. I have had a lady who was pouring postmenopausal bleeding. And you think, oh, no, she's going to have CA endometrium. But then you read the notes and she's had a hysterectomy. People who've had hysterectomies so they can bleed quite a lot. And very often that is with atrophy, with the atrophic vaginitis. And obviously any trauma can cause bleeding from anywhere. Now, don't forget endometriosis. I have mentioned this in the past. If you've had surgery to remove everything, even if you've had a hysterectomy and you've removed the womb and they feel that they've removed all the endometriosis deposits from the peritoneum, these ladies, if they've got widespread endometriosis, the chances of removing every last cell is very low. And if there's any oestrogen still around and certainly these ladies may have been given because they've had a hysterectomy, we've just given them some unopposed oestrogen. Don't forget endometriosis, even if you've got a couple of cells, that they can build up again and cause problems. And in fact, if the endometrium deposit is in the vagina, that makes it easy for us to identify and know what the cause is. Obviously, if you're getting abdominal pain because the endometriosis deposit has built up in the peritoneum, unfortunately, then we don't have such a clear cut diagnosis. We have to find it another way. Again, infection and carcinoma.

**14.50 Speaker:** And don't forget, this lady can be saying she's having bleeding, it could be from her urethra again, that can be from lack of oestrogen, but it can be some from your bladder tumour or anything that causes inflammation in the urinary system. And inflammatory bowel disease and haemorrhoids and obviously tumours. So in other words, we need to examine the patient to know where the bleeding is from.

**15.18 Speaker:** And other causes of funny bleeding. As I said, contraception, HRT, anticoagulants, and other carcinomas like the fallopian tube.

**15.36 Speaker:** So when are we going to refer this lady to Gynaecology? Now post-menopausal bleeding. This is people who bleed after a year of no periods at all. If they're over 45 and you're concerned they tick all those high risk boxes and certainly if they're under forty five and things just haven't settled down with the simple treatments that you've tried in practice. So the inter-menstrual bleed the post-coital bleed - again, you're going to refer if you haven't located the source and been able to treat it.

**16.15 Speaker:** So what about those ladies who are not taking HRT and they are post-menopausal? As we know, if you have bleeding and this can be repeated bleeding or a single heavy bleed, please know that you can refer these along the two-week wait. However, when you're looking at how many of these people actually have endometrial carcinoma with these ladies who aren't on HRT, it varies between 1% and 24%. When you look at ladies who are on HRT, the conversion rate for referral along the two weeks wait pathway to actually serious pathology is only 2% for sequential and 1% for continuous combined.

**17.19 Speaker:** So when's ultrasound useful? Well, it is useful because we want to know what those ovaries are up to. We are checking the anatomy. But don't forget that thickness, that endometrial thickness, it's no use at all, really, with people who are having regular periods because it varies so much. And it's not predictive; it doesn't have any predictive value. When people are on sequential HRT, again, the lining is building up, shedding, building up. And again, it's of little value. So that's not really what we're looking at. If you do feel you want to do one and want to look at the endometrial thickness, you need to do it immediately after the withdrawal bleed. But in the premenopausal and those on sequential, if you're doing an ultrasound it's because you want to check the other bits in the pelvis, not the endometrial thickness. And so what we're looking for is post-menopausally. This is where the individual fitness can be useful, and when you're not taking HRT, we don't really want it thicker than 4mm. And if you're on HRT, we start being more concerned over 5mm. But as we said, the conversion rate to cancer in this group can often be very low. Obviously, it's important that those people are referred, and we do find it. But if the endometrial thickness is greater than 8mm, all groups show a much higher rate of carcinoma.

**18.55 Speaker:** Ultrasound reports - we get them through, we don't have the pictures and sometimes you look at it and think, well, what does this mean?

Post endometrial ablation. When they've done that, it's tricky for everyone to assess. Ultrasound and hysteroscopy because of the scar tissue and everything. Unfortunately, in these ladies it is very tricky sometimes to try and just decide what's going on. That's why I'm always much happier when people have done the individual ablation, it's always NICE if they put it in the Merina at that point, because at least then we can be happy about the endometrium.

So another thing that they say, endometrial fluid and you are thinking, what does that mean? And so there were lots of reasons for endometrial fluid. And they do say that if your endometrial thickness is 3mm or less, I wouldn't worry about the endometrial fluids. If it's more, then I would carry on and refer on. Sometimes we've done an ultrasound for something else, and we get a note of an increased endometrial thickness in a lady who's got no symptoms. So certainly you would refer for biopsy and the advice is - if it's over 6.75mm, certainly refer. But it's rare that there's any pathology in asymptomatic ladies if the thickness is less than 11 millimetres. But obviously we don't want to miss that one person, do we?

**20.37 Speaker:** So unscheduled bleeding on HRT. Remember the risk of pathologies low in this group, but we don't want to miss it when that it is there. So check about the combined HRT and remember, you want combined HRT if there's any endometrial tissue. So these are ladies who have got a womb, who have had a subtotal and left a cervical stump, which we're going to check whether there's any endometrial by giving them a progesterone challenge. And if they get a bleed, you're going to put them on a combined regime. Ladies who’ve had endometriosis, if you're going to give them endometrial protection, because they are if they truly have had widespread endometriosis, they will still have deposits. And of course, these are really tricky. The bleeding gives you a hint, but those who have just peritoneal deposits, these are ladies to watch out for, if they've been given unopposed. So on sequential HRT, if they have been on it more than five years because of the gaps, it doesn't give us adequate endometrial protection. And therefore, these people are more likely to get endometrial hyperplasia. So that's why we tend to swap about the continuous combined. Don't leave them on the sequential for more than five years. And if they're on the continuous combined HRT, remember, there is a significantly lower risk of endometrial cancer. It decreases your risk by 80%. Funny bleeding is common, but endometrial carcinoma is a lot less common in these ladies.

**22.28 Speaker:** So what do you expect when you take the HRT? The sequential HRT - up to 90% are going to bleed and remember that endometrial thickness is varying. But they say up to 38% of ladies have some unscheduled bleeding in the first year of use. So this is bleeding at other times from when they'd expect with that withdrawal bleed. So that's quite a high number of ladies. And this isn't to panic about. This is common.

On continuous combined remember that it can take up to a year to truly get rid of any bleeding. It's extremely common to get spotting in the first six months. And as since we know that continuous combined HRT does not increase your risk of endometrial cancer.

So, yes, that doesn't mean that people don't get it, but the HRT does not increase your risk because you've given the progesterone. As long as you give it enough progesterone.

And so you don't stop your HRT pending investigation because for these ladies it's not the HRT, but it's other risk factors that may have caused the endometrial pathology. So 41% of women on continuous combined will have unscheduled bleeding in that first year of use and we don't really talk about this. We often say, oh, you know, you on stuff, you won't bleed at all. And this obviously creates worry for us.

So up to 50% of ladies, stop the HRT because of unscheduled bleeding in their first year. So when we stop people on the progesterone only pill, I hope that all of you say to them: ‘your bleeding will do its own thing, you might not bleed for months and you might bleed for a couple of weeks and then not bleed for months, but your bleeding will do whatever. Continuous combined HRT is exactly the same for the ladies with their bleeding patterns on progesterone only pill. We should always counsel those and so we're going to counsel the people on HRT. So the bleeding rate at one year is about 10% of people on HRT.

**24.52 Speaker:** When are we going to worry? The HRT doesn't stop those people who were going to get endometrial carcinoma necessarily. So if you've been on HRT for over six months or you've had absolutely no periods, then, you know, we just need to check it out. That's really what we're saying. Don't ignore it. We know that the risk is low of endometrial carcinoma, but don't ignore it. It could happen even if it's only in 1% of people.

Now, NICE say report funny bleeding at the three month review. If you remember it from the NICE guidance, we review our patients when we start them, we review them at three months and then we review them annually after that. So the three months review is that time when we see them. So you want them to tell us at the three months review if you are you getting any bleeding. That's not because that's when we worry. It's because we need to keep an eye on those ladies and reassure them that it's normal and common. Check that there isn't any extra thing going on, that there's no infection or anything else to concern. And probably to those, we might say: ‘I'll give you a phone review at six months or can you ring up and book a phone review if you continue to bleed?’

But what if the periods were a certain style and then they become heavy or painful? You know, if the timing's changed/something else has gone on? Of course, if we find that on the bimanual that the uterus is enlarged in size or whatever. And obviously if we have an abnormal ultrasound. There are lots of things we can do to help settle the bleeding. But if the things we've tried don't work, then it is definitely worth asking for further advice. And remember those risk factors obesity, diabetes, hypertension, polycystic ovary syndrome, early menarche, late menopause. These are the people who would have had excess personal oestrogen over their lives and therefore they are at higher risk.

**27.18 Speaker:** So these people who are bleeding on their HRT.

Those on sequential preparations. They must have at least 12 days a month because we know that if they don't, the endometrial cancer risk is increased three times. I just think it's easier to say to people, you know, two weeks on, two weeks off. I don't know how people remember otherwise, although you can say take it for the first to the 12th, but each month varies in length, doesn't it, between 28 days and 31 days. So I think it's much easier to say two weeks on, two weeks off rolling programme, if they've got separate progesterone and oestrogen. And remember to swap to continuous combined preparation before five years of use.

**28.09 Speaker:** So the progesterone does matter, doesn't it? This is just a little table of the doses that you need to give to try and give adequate endometrial protection. So really, a rule of thumb is whatever you give every single day for continuous combined, if you're giving it half the time, you give twice the dose. The thing about ones like the Dydrogesterone and the Norethisterone - the 1mg tablets are no longer available, unfortunately, so you can't get that one separately. So, Norethisterone you give whatever's in that tablet preparation. But the ones that are available, the Medroxyprogesterone and the Micronised Progesterone - basically it's whatever dose every day. So half the time you give twice the dose.

**29.11 Speaker:** There are swings and roundabouts as everything's a balancing act. So the bioequivalent progesterones, the micronised progesterone and the dydrogesterone, they are really good because there's a beneficial effect on your lipid profile. They've got lower risk of breast cancer, clotting. But the downside, the dydrogesterone is only available in those Femoston combination tablets. They are not absorbed transdermally. They're more expensive. In fact, the micronised progesterone is an amber drug, which traditionally has been under expert advice. And they give less good control to bleeding.

So the progestogens. That's Medroxyprogesterone/Norethisterone. Unfortunately they have an adverse effect on your lipid profile. They have a higher risk of breast cancer in the combination than the bioequivalent Progesterones. Norethisterone - we all need to remember that 1mg of Norethisterone is converted in the body to six micrograms of ethinyl estradiol and therefore it has extra clotting risk. But they are cheaper. Norethisterone is absorbed transdermally and in fact it works very well in the patches and they give a much better control of bleeding.

**30.40 Speaker:** So this lady with her troublesome bleeding on her HRT. There are several things you can do. You can increase the dose of progesterone. For example, they are on the hundred milligrams every single night of their micronised progesterone. Step it up to two hundred. Increase the number of progesterone days for the sequential regimes. So for the number of progesterone days for sequential, you're going to say, especially if they are only on 12, you can say 14. You might go up to three weeks or whatever. More progesterone days for the sequential regimes can help. And then change the progesterone. As I said, it is swings and roundabouts. You are on the micronised progesterone, you know, that's the lowest risk. Do you step it up? They need transdermal because of the clotting risk, for example, then you might go to the Medroxyprogesterone, which has better cycle control. But you know that it then has an adverse effect on the lipid profile. Anyway, so it's a balancing act. And that is why do consider the Mirena IUS. For anyone who's perimenopausal, once you've fitted that IUS, you know you don't have to worry the same. The lady doesn't have to worry because her bleeding hopefully will all settle down.

**32.10 Speaker:** So why do I recommend considering the Mirena IUS? I don’t have shares in Mirena. It's a shame. I have been fitting coils since before they were brought into the market and it was fantastic when they arrived because actually, they have fulfilled the promise that they told us before we got them. They result in a systemic concentration. So if you do a blood test on someone with the Merina, it's a lot less than half the circulating progesterone that that caused by the progesterone pill. And therefore, you're doing a very good job on a very low dose. And remember that, the Kyleena is not is not licenced for the progesterone part of HRT at the moment. So if you had your IUS in situ for five years, this gives you a 50% reduction in endometrial cancer. If it's been in for ten years (so obviously, that be you two or if it's fitted at forty five, you could leave it in) 75% reduction in endometrium cancer. So the IUS is very, very good at protecting the endometrium. And if this lady, as long as the IUS is still in date or sufficiently youthful for the progesterone part of HRT (the licences for 4 years, the faculty supports five years). If you add oestrogen into the IUS, there's no change in bleeding pattern. It has no adverse effects on lipids or insulin resistance and for control of bleeding with HRT, it was shown that the IUS was best in 93% of cases. So it really, really is worth it. A lot of people say: ‘Oh, what about the coil?’ The lady says: ‘Well, I don't think so’. ‘Oh well, never mind’. But actually I think we just need to explain. Yes, it goes through a very undignified and uncomfortable route. But on the other hand, it gives so many benefits. Nothing suits everyone all the time. And I would never suggest that it was the right thing for everyone. However, I think if you explain to the lady, then you'll be surprised at how many people say: ‘Yes, that's a good idea’.

**34.27 Speaker:** This is a bit of a busy slide, I do apologise. This is the flow diagram that they give for people presenting with abnormal bleeding and we're going to send the slides out later. So you can just see that basically this flow diagram says what we've already said.

And basically this is if that's unscheduled bleeding on HRT, you can follow this down. But if you've got an intact uterus, check that they are taking continuous combined with no breaks. Some of the leaflets in with continuous combine - so if you look at the gel - the micronised progesterone and the EstroGel, they do sometimes say take a couple of days break and you think ‘Oh, I'm not quite sure about that’. But if the lady is very good at reading the leaflet, they may follow those instructions and not the ones you give her. So just check that there are no breaks otherwise you will get bleeding.

And obviously you're going to examine the urine to check the blood isn't there and you're going to check where is this bleeding coming from. If everything's normal and if you're still a bit worried, an ultrasound, but not for those ladies who are perimenopausal. And if this is normal, we're very happy. Allow it to settle. But as I said, you could increase the dose, change the progesterone dose or consider fitting a Merina IUS. The first three to six months, obviously, we should remember, to counsel these ladies and let them know that they do take the time to settle down. Don’t worry. We do report it. Do let me know, but don't worry. And again, if it's a nuisance, really consider the IUS.

So if they've had a hysterectomy and they're bleeding, you're going to think, where is this bleeding coming from? So check for infection. Think about that endometriosis lady and you're going to add that progesterone. Look for any sign of tumours. But obviously, the atrophic vaginitis is going to be the commonest cause of any bleeding in a lady who has had a hysterectomy. So remember that 25% of people, even if they are on HRT, NICE guidance is to add the vaginal oestrogens as well and continue them when they stop the systemic HRT, continue those oestrogens, the vaginal oestrogens, because the symptoms of the urogenital atrophy will always come back if you stop those vaginal oestrogens. And really there's no end to us needing vaginal oestrogens. If in doubt refer.

**37.32 Speaker:** So in summary, bleeding is very, very common, and so it's not something to worry about, but it's something to try and sort out. Those that we all are a bit worried about and need to look further and those that we’re not worried about, but we reassure. So remember, they rarely have a sinister cause and we're very good at treating it in primary care. We just need to be clear what's the cause and what are we treating. Always identify the site of the bleeding. You can't treat it if you don't know where it comes from and you're not going to know where the bleeding comes from unless you look. So obviously we could order a urine specimen, but we need to actually have a little look. And that involves a speculum and look at the cervix. If these ladies are very uncomfortable because they are postmenopausal, then don't forget, you won't run into problems with the vaginal oestrogens to allow a more comfortable look. But obviously, you don't want to delay. If you have a high index of suspicion, you're going to refer them before. Continuous combined, HRT decreases the risk of endometrial carcinoma and funny bleeding is very common. So we need to counsel them when we're prescribing, but we need them to tell us whether you're getting any bleeding. Don't worry but tell us and we can then follow that up. Progesterone does matter, which progesterone you give them, which dose, how long it each month. Beware those ladies with risk factors have a much lower threshold to refer. And don't forget, never forget the vaginal oestrogens. But the intrauterine system is a really good choice.

So thank you for listening and I think there might be a few questions.

**39.42 Chair:** Yes, there are. Thank you very much, Jane. And so there's a couple of easy ones. Is Qlaira expensive?

**37.50 Speaker:** Qlaira is expensive, but as I said, the problem at the moment is that it is one of the medications that's been unavailable. However, because it's got a license for heavy menstrual bleeding, it is quite a useful thing to think about. It is a combined contraceptive, so you've got your UKMEC guidelines, but it's estradiol not ethinylestradiol. So for the perimenopausal lady who needs contraception and has heavy menstrual bleeding, it's quite a good option. But it is going to cost more than Micogynon, but then we're talking about that group of ladies where probably you wouldn't be giving them Micogynon and if they had heavy menstrual bleeding, you'd probably also be giving them an Tranexamic acid etc whatever, medroxyprogesterone for their holidays. So in the long run, it might work out cheaper if it suits and if it's available.

**40.56 Chair:** You mentioned about a progesterone challenge. Can you just explain that, please?

**41.03 Speaker:** So if you're wondering whether it is endometrium that's capable of bleeding, then you'd give them, for example, this lady who's had the subtotal hysterectomy, you don't know whether there's any endometrium left in that stump. You can give them, for example, 10 mgs of medroxyprogesterone twice a day for five to seven days and stop it and see if they have a withdrawal bleed. If they have no withdrawal bleed, you might do it another time and just see if there's any sign of bleeding. And that's a progesterone challenge.

Also, whilst we're talking about progesterone challenges, if a lady who has polycystic ovary syndrome and is on no medication at all (not got the implant in, not got the IUS in) if she has no bleeding for over six months, she's going to be a lady you're going to give a progesterone challenge to because that is a lady who may get endometrial hyperplasia.

So that's the progesterone challenge to see if they're bleeding. However, if they don't bleed and you start them on the oestrogen only and then they start to bleed, then I would swap them to a continuous combined. Does that make sense?

**40.56 Chair:** So can you go through when people should be made on combined cyclical HRT, both patches and tablets? So when should they be bleeding?

**43.00 Speaker:** So with the sequential, you're going to give it to those ladies who have bleeding but need HRT and want regular bleeds rather than run the risk with the continuous combined of bleeding all over the place. Or people you've tried to continuous combined with but are bleeding all over the place and would prefer a regular bleed. So the two types tablet in their box or their patches. Once they're established on it after two or three cycles, they'll know when they're bleeding happens. And it'll be a couple of days after the change in tablet colour or patch. So it's much like the combined pill. Most people find that they either start on day two or whatever, so they establish their own pattern. And they do say that if the withdrawal bleed gets lighter and later than those ladies, they will be absolutely fine if you swap onto a continuous combined.

**44.21 Chair:** Thank you. The transdermal Norethisterone - does it have the same risk as oral?

**43.27 Speaker:** It doesn't seem to have the same clotting risks because it's transdermal and misses the liver, so it shouldn't be extra clotting. However, Evorel Conti – brilliant patch. Loads of people use it. Ideal if they won't have an IUS and they've got migraine. It's the only slow release progesterone available until they bring back FemSeven, which may come back in about September/October this year. But that's another progestogen. And so, yes, so it doesn't give as good a cycle control transdermally, but it gives enough endometrial protection. The clotting risk you don't have to worry about with the transdermal patches. It's just obviously it's not a beneficial progesterone in the same way as the micronised progesterone.

**45.30 Chair:** Thank you. By endometrial fluid, do you mean oedema of the lining and is it due to the individual thickness? Where'd you get the fluid from?

**45. 45 Speaker:** Well, the ultrasound report will often say endometrial fluid. That's what they tend to say in the report. And obviously endometrial fluid can be blood or whatever. So ultrasound reports sometimes just mention endometrial fluid. And that's why it's just one of those reports that we get and we think, well, what do they mean? Do we worry about that or not? And as I said, it's really only if only if there were other reasons to worry.

**46.18 Chair:** Thank you, Jane. If there's a lady over 60 who has been on continuous HRT and she's been seen in the post-menopausal clinic a few years ago for unscheduled bleeding, all the results/investigations are normal. The HRT was changed as a consequence to different preparation at that point. But then she represents several years later with unscheduled bleeding. What would you do? Would you re-refer or do an ultrasound?

**46.42 Speaker:** I think it's difficult because obviously, as I said, the different progesterones have different actions. And if she's been changed to a different progesterone, some people… I mean, the trouble is with oestrogen bleeding is normal. That's what happens. We build up the lining of our wombs and we bleed. And that's why it's so important to give endometrial protection. I mean, the likelihood of there being a problem is very low. On the other hand, if she's a large lady who had polycystic ovary syndrome, diabetes, hypertension, then I might be more worried. This is a lady who actually when she was seen in clinic, they should have fitted an IUS because then you wouldn't have the concern because any hyperplasia or anything would be sorted out by that. I would probably refer that. But the chances of that being a problem is very, very low. Yes, an ultrasound. I would do an ultrasound to check the thickness.

**47.43 Chair:** Thank you. Now a question about Evorel sequi. If they're having irregular heavy bleeding, which is intercepting by six months and an ultrasound scan has been normal, what do you do? Would add a progesterone? Would you just leave it and see if it improves?

**48.00 Speaker:** I would encourage them to have an intrauterine system. It's just such a good method of controlling anyone who has troubles, really troublesome bleeding an intrauterine system sorts it out. And you don't have to worry about endometrial hyperplasia because it is the treatment for endometrial hypoplasia rather than any cause. So I think perimenopausal ladies, if I'm really troubled by the bleeding, then I would tend to go to the intrauterine system. But if she's on Evorel sequi patches, then the option is an oral progesterone. So you could give her medroxyprogesterone orally because that's better at controlling the bleeding. As I say, transdermal Norethisterone is good for clotting and they are brilliant patches, but not so good for controlling bleeding. Encourage the intrauterine system. Swap her to medroxyprogesterone and perhaps try continuous combined, actually, because sometimes that just helps them all settle down. But as I say, intrauterine for the funny bleeding in that case.

**49.22 Chair:** Jane, you talked about not stopping HRT if you’ve got continuous combined while you're investigating unscheduled bleeding. What about someone is on sequential HRT after the first six months? Do you stop it while you investigate?

**49.38 Speaker:** I probably wouldn't stop it, because if they're going to go and have investigations, I mean, the gynaecologist might want to stop it. Gynaecologists aren't trained in menopause so often it depends on that level of experience with HRT and things. However, you can leave it on, and they might well stop it. But as I say, there is no reason to. But I would definitely check what progesterone they're on and make sure they're taking it and taking enough days. But yes, once you refer them, you don't know how long the referral is going to take and you don't want them to have awful menopausal symptoms in the meantime. However, if that's a lady who's really troubled and the bleeding is really getting her down, she could try stopping it to see if the bleeding settles. Because I think if you have horrible bleeding, it's just terrible for your life in general, isn’t it?

**50.47 Chair:** Thank you. For the delegates, the feedback form link is in the chat bar if people want to click on that to give us some feedback.

There is another question about the optimum time to switch from sequential to continuous combined.

**50.59 Speaker:** Certainly you don't want to leave it five years or whatever, but if the bleeding is getting lighter it's worth a try. So after a couple of years, when I did my 2 year review, you’d say, you can always try the continuous combined. So I'd certainly discuss it. But you need to say to the lady, look, it may well be that you're bleeding, then it all settles and goes away completely, but you may well get a few months of bleeding that comes whenever. So certainly, I'll discuss this with each review. But certainly the two year, three year review. I think with people who have a very early menopause and it's essential that these ladies stay on unless they've got a very good reason not to e.g. the premature ovarian insufficiency, if you're thirty five or whatever, to try and stop them getting osteoporosis, cardiac disease and all the other problems that they will get if they don't take their HRT. Some of these ladies do like a regular bleed because it makes them feel more like their peer group. But I discuss it. So certainly after two years I'd offer them the option. But explain that might be funny bleeding.

**52.23 Chair:** Thank you. And do you preferentially use transdermal HRT other than the Merina IUS? What is your preference?

**52.34 Speaker:** Well, it absolutely depends on the lady. I think that for a lot of us, a tablet every day is so easy -so if it's a young, fit person with no other risk factors. If you've got raised BMI it needs to be transdermal. If you have migraines, it needs to be slow release and transdermal. Any clotting risk. So this is something that I'd say - to minimise your risk, it needs to be transdermal. But if they've got no particular risk factors, they're fine, then a tablet can be so easy. And the Femoston range, I don't like being an advert, but unfortunately that's the only way you can get the dydrogesterone. They're very simple to take. But remember that it's the dose is important as well. And so like with the Femoston range, they have the one milligram their Conti is only a one milligram, which is equivalent to a twenty five microgram patch or one plunge of the gel. And so therefore for the younger fitter one, you might well need two milligrams of the Estradiol tablets. So it's entirely up to the lady. But if they have any reason why they might have increased clotting or migraines or your cardiovascular risk, then I would always advise the transdermal was better.

**54.08 Chair:** Thank you, Jane. We don't have any further questions, so I'd like to thank you for a really, really useful and clear talk. Lots of comments saying that it was a very good talk, very comprehensive in answer to the questions. So thank you very much.