# Migraine, menopause and MHT

**Prof Dr Anne MacGregor:** So my name is Anne MacGregor. I'm a doctor in London and I work in sexual reproductive healthcare, and today I'm going to talk about migraine, the menopause and HRT. So the subjects I'm going to be covering, I'm just going to do an overview about the epidemiology, I'm going to then talk about diagnosing headaches, and then look at the relationship between migraine and menopause, and move on to using hormone replacement therapy for women with migraine, and then end it, round it all off with some practical recommendations. One of the biggest problems that I've recognised in my work is how women, when they come to a menopause clinic, they don't often talk about their headaches. They're so focused on what they think the doctor needs to know, or the healthcare professional needs to know, about vasomotor symptoms, but they often won't mention headache. And when we have looked at the proportion of women who actually have headache coming to a menopause clinic, 57% of the women that we surveyed actually reported headache.

And when we broke down into the types of headache that they experienced, 29% of those women were experiencing migraine and 10% had daily headache. Now when you put that into the background, an average in a population, you would expect, of women to experience migraine would be around 15%. So you can see that the prevalence in this particular population of women seeking care for menopause is much higher than the expected prevalence in the background population. So we know from epidemiological data that during the productive reproductive years that women are twice as likely to experience migraine as men. And this tells us very much that there is a definitive hormonal component to women's migraine that we need to consider and to manage. So the particular times that women are most likely to experience troublesome migraine is when it starts, around the time of puberty, where the rate of prevalence markedly increases, and secondly, at the time of perimenopause where again we see another increase in the prevalence of migraine affecting women. So on that basis, we've discussed about the epidemiology of migraine. What about diagnosing migraine? How do we understand what a migraine is compared to just a headache?

So migraine headaches will typically last between part of a day and up to three days in women or men who are otherwise completely free of symptoms. So it's an otherwise healthy population. And we then need to ask them about whether or not they have specific symptoms that accompany their headache that can help distinguish the type of headache that they experience. So the first question we'd ask is, 'When you have a headache, does light bother you more than usual?' Secondly, 'Do your headaches limit your ability to work or carry out your usual daily activities?' So for example, if you would think about doing something different from what you had planned as a consequence of the headache that you're experiencing. And finally, 'With your headaches, do you ever feel nauseous or sick or even do you vomit?'

So if we have women who can answer 'yes' to at least two out of three of those questions that accompany their episodic headaches and are fine between those attacks, that has a positive predictor value for migraine of 93%. And if they say 'yes' to three out of three of those questions, then the likelihood, the positive predictor value of migraine is up to 98% in those women. So it's a really simple screener that you can use in your clinical practice to identify whether or not women have migraine. It's interesting to note that one of the most common misdiagnoses of migraine is sinus headache. So one study that was actually looking at a large group of 2,991 patients with a previous diagnosis of sinus headache, actually 80% of those women fulfilled the criteria for migraine without aura. So anybody who talks about, oh, they have these terrible sinus headaches that affect them infrequently, it's very useful to actually screen for migraine, because the sinuses just block up within the front of the face during migraine attacks, and many people then think that the headaches they are experiencing are a consequence of sinusitis rather than just a consequence of vasodilation within the sinuses as part of a typical migraine attack.

So there are three main types of migraine that you are likely to come across in clinical practice. Most commonly is migraine without aura. So that's a sick headache that we've just been diagnosing. And that accounts for about 70 to 80% of attacks that people will experience. Then about 20 to 30% of attacks are migraine with an aura, and these are the typical migraine without aura preceded by aura symptoms that I'll be explaining in a little bit more detail. So migraine aura is neurological symptoms that precede the typical migraine attack that follow the premonitory symptoms that actually herald a migraine. So premonitory symptoms are what we call 'hypothalamic' symptoms, where people can feel very hungry, craving for very sweet foods, feeling very light-sensitive, feeling very, very tired, feeling a little bit low, sometimes feeling on top of the world. And those can last for about 12 to 24 hours before the onset of the typical migraine headache.

They are not aura, whereas aura is very definitive in the type of symptoms that people experience, and they will last anything up to an hour before the onset of the typical migraine headache and resolve before the onset of that headache. Now the important thing to recognise is these aura symptoms can occur without subsequent headache. So the headache may be very, very mild and people only notice a headache if they actually just stick their head between the knees and shake their head. They'll be aware of a sort of pressure or a headache that they're not otherwise noticing unless they provoke it. But that can even occur without any accompanying headache at all. That can make it hard to make a diagnosis because you're often asking about symptoms that precede a headache, but in fact it's not so difficult because most women will have experienced typical migraine without aura at some stage in their past. So you'll get a past history of migraine at some point, and you can still ask about visual symptoms that they might experience.

99% of auras are visual. So even if the woman experiences sensory or speech aura symptoms, that will also be preceding and resolving before the headache, we can make the diagnosis of aura mostly on these visual symptoms. And different from ischemic events is that the aura develops slowly, so it's moving across the field division, it will last for less than an hour, typically 20 to 30 minutes. with complete reversibility. So these symptoms resolve spontaneously, of their own accord, without intervention. And then they will be followed by the headache if that indeed is going to occur. Sensory aura, it rarely occurs in absence of visual aura, and people will often describe it, they'll describe it as a weakness but actually it's sensory. So there is no motor loss in typical sensory migraine aura, and it's a bit like that feeling when your arm has gone to sleep, that you feel that you can't move it around but actually you're waving it around at the same time, but it's that tingling feeling. And for sensory aura, it'll often start in the fingers, travel up one arm, often up into the side of the face and into the mouth. So the leg is very rarely affected with the aura of migraine and it's unilateral, affecting one side.

What you need to recognise is that you don't need eyes to see an aura, because the aura is coming from the visual cortex at the back of the brain, and one of the diagnostic features of aura is that it's still present when the person closes their eyes, they can still see an aura. So we can put all these factors together to come up with a simple way, simple questions that you can ask in clinic to help diagnose whether or not the woman is experiencing typical migraine aura. And the questions you need to ask is, 'Do you ever have visual disturbances that have started before a headache, they last for less than an hour, they resolve before the onset of the headache, and they persist with the eyes closed?' And if you want to ask about whether or not they can draw the aura, often they will just wave in the air their finger, and draw zigzaggy lines, and that is diagnostic of migraine aura, it can't be anything else.

So you now know how to diagnose migraine headache. You now know how to diagnose migraine aura. So what happens to migraine around the time of the menopause? Well one factor that we are aware of is that migraine is actually a risk factor for onset of menopause symptoms, and we typically in clinic will see the majority of women that present for management of migraine will often be in their mid-forties seeking help for migraine. And very quickly they will start to progress to more typical migraine symptoms, vasomotor symptoms, for example, irregular periods. The other factor that we're aware of is that migraine predicts more frequent vasomotor symptoms. So we can see in this study from the States that women presenting with vasomotor symptoms are actually far more likely to have be experiencing migraine as well.

More frequent vasomotor symptoms have their own associated factors as well, particularly severe depression, anxiety, and sleep disturbances, which are all factors that we need to manage. So there's a whole package of symptoms. It's not just migraine that we're needing to manage, it's the vasomotor symptoms and all these other accompanying comorbidities as well. Now the type of menopause that women experience will also have an effect on migraine. So we know that women who are experiencing a natural menopause, that their migraine is more likely to improve with time since their last menstrual period. So about 67% of women with migraine will improve with time following a natural menopause. So this is actually mirroring the same decline in ovarian function. So while we have, during the perimenopause, we have the increase in ovarian activity, we have spiking high oestrogen levels, we have a lot more vasomotor symptoms, we have a lot more migraine around that time as well.

And as that ovarian function declines, then subsequently so does the migraine. Now the fact that you need to put across to women here is, they think that when they have their last menstrual period, that's it, migraine is going to get better. But we know that as their vasomotor symptoms take time to improve following their last menstrual period, so will it take time for their migraine to improve. Just following that same timeline as well. The factor that aggravates migraine is surgical menopause. So we know that even when the ovaries are left in place and women just have their womb removed, that that still increases the likelihood of migraine worsening. If they have ovaries removed and the womb removed as well, then that is markedly accompanied by an increase in migraine that needs to be managed, again in the same way that menopause symptoms will worsen following a surgical menopause,

likewise, migraine symptoms worsen as well. And management becomes management of the menopause symptoms, which can often also manage the migraine too. Which segues us nicely into the link between migraine and HRT. Here we know that the root of delivery can markedly affect women's response with respect to migraine. So we know that oral oestrogens can actually increase the frequency of migraine attacks, because it's increasing the fluctuations in oestrogen levels, and consequently increase the number of days with headache. So we want to avoid oral oestrogens, very much in favour of transdermal oestrogen, which because it provides much more stable levels in the oestrogen levels, we know that it doesn't have any adverse effects in itself on women's migraine, and in some cases may actually benefit migraine too. What about the regimen of HRT? Does that make a difference to migraine? So the standard regimens that are usually given are cyclical combined, where a woman is taking oestrogen across the entire 28-day cycle, and then she will just use cyclical progestogen to provoke a bleed and provide endometrial stability during that time.

Postmenopause, women can have continuous combined, where they have oestrogen continuously and progestogen continuously as well. Now we know that for migraine we need to try to push women to a continuous combined regimen as quickly as we possibly can, because anything that interrupts or causes hormone fluctuations can actually adversely affect migraine. So because we know that progestogens oppose oestrogen, that you'll create a change in a woman's response to the oestrogen by adding back the progestogen cycle. So by providing the progestogens continuously will minimise the adverse effects of the fluctuation on migraine in itself. So in the perimenopause, how can we provide a continuous combined regimen? Well, the obvious answer is the Mirena intrauterine system, which has the added advantage of providing contraception and managing bleeding in the perimenopause as well. So that would be the preferred option for managing migraine in the perimenopause for women with migraine.

Then postmenopause, women don't need contraception, and we can benefit from micronised progesterone, which has several advantages. We know that it's breast neutral. It doesn't confer the increased risk of potential breast cancer on women that the synthetic progestogen do. It also has the advantage of being sedative, which can benefit sleep, and because sleep disturbance is a trigger for migraine, it a benefit on that trigger as well. And it's anxiolytic as well, so it can reduce the anxiety symptoms that women can experience through menopause. Now what about testosterone? Because that's become a question that many women ask about, because they hear a lot in the press that testosterone can be good for menopause as well. We only have three studies, the first harking back to 1955, on testosterone and migraine. And so from those three studies, is there any data that we can glean about the effects of testosterone on migraine?

Well, there would appear to be some benefit, but the honest answer is we really don't know. We wouldn't advocate additional testosterone specifically for management of migraine, but for those women who might need add-back testosterone for other reasons, for hormone replacement therapy, there may be some benefit, and certainly there does not seem to be any adverse effect from add-back testosterone and migraine. What about aura? We know that there is a concern about aura in the younger population, and risk of ischemic stroke. So we know that migraine aura marks out people who experience aura as being at a higher risk of ischemic stroke, although the aura itself is not triggering an ischemic stroke, it's just marking out an individual who potentially is at risk. We know that, with respect to risk of ischemic stroke and aura, that age matters. So it is typically the younger population who are at risk rather than the older population.

So we know that in women who have migraine without aura, there is no statistically significant increased risk of ischemic stroke in either the younger or the older population. Now if we actually look at migraine with aura, the increased risk is very much in the younger population, the population under age 45 who might be using contraception. So by the time women are approaching age at menopause, that risk becomes less significant. It's a 1.25 increased risk of ischemic stroke in that population. And that is because the other factors become more prevalent that are associated with increased risk of stroke in the older population. So things like hypertension, diabetes, obesity. So that migraine aura on its own is less of an issue, which is great news if we have any concerns about this population using, perhaps, specific types of oestrogen therapy.

The other factor about migraine and ischemic stroke is that the additional risk factors matter. So with respect to the risk of ischemic stroke and the type or route of delivery of oestrogen, if we look at oral versus transdermal oestrogen, then you can see that oral oestrogen itself carries an increased risk of ischemic stroke. So we want to try to avoid adding additional risk factors in anybody who might already have baseline risks. So if we then shift to looking at the transdermal oestrogen, we see a very different pattern. So as you can see from this slide, transdermal oestrogens confer no increased risk of ischemic stroke, so they can then safely be used by anybody who might otherwise be at risk, whether it's venous thrombosis or people who are at high risk of cardiovascular disease, can use transdermal oestrogen.

So where does that leave us with respect to practical recommendations? It means that, in contrast to the synthetic oestrogens used for contraception, which are contraindicated in women who have migraine with aura, neither migraine with or without aura contraindicate the use of transdermal oestrogen for hormone replacement therapy. So women who experience new onset migraine with aura, once they start using HRT, again there's no reason to withhold ongoing therapy. Obviously diagnostically we need to exclude a TIA, because that would need specific management in its own right, and we would have to say again, not necessarily stopping the type of HRT if they're already on transdermal HRTs, because by stopping it, can actually increase their risk of ischemic stroke. We need to reassure them once we've made that diagnosis correct. If they are on oral oestrogen, then we want to change them to transdermal. And, as is good practice, we always want to use a lowest effective dose of oestrogen that controls the vasomotor symptoms. Higher doses are not going to benefit the woman. And if the aura doesn't resolve, or actually increases in frequency, we might want to consider some non-hormonal options, and indeed there will be women who have migraine and who have vasomotor symptoms for whom oestrogens are contraindicated anyway.

So what options do we have for those? Well, none of them is going to be as effective as oestrogen, because we're treating the mechanism by using oestrogen therapy. But there are benefits can be obtained by using selective serotonin reuptake inhibitors, such as escitalopram, in doses between 10 and 20 milligrams daily. Then there are the SNRIs, the selective noradrenaline reuptake inhibitors, such as venlafaxine, and we can start with a lower than a depressive dose for vasomotor symptom control, and migraine control, starting with 37.5 milligrams but moving up if necessary. Now the major side effect of that is sedation and weight gain, which makes it difficult for some women to tolerate, but other women get on with it remarkably well. Then there's an old favourite, and because it's old doesn't necessarily mean to say it's not effective. It can be useful for some women. It's the alpha agonist that is used for hypertension as well. And it's actually licensed for use for migraine prevention and for vasomotor symptoms, and that is clonidine, starting with 50 micrograms twice daily.

The one thing to watch with that is, particularly, women with migraine have a high risk of depression as comorbidity and unfortunately clonidine can have a negative effect on depression. So you do need to watch out for women who then start to experience depressive symptoms. It may be the clonidine that's actually the aggravating factor, not just pure depression in its own right, Now, you also have to remember that there are lots of lifestyle strategies that can benefit vasomotor symptoms, menopause management and migraine also, and they can be done on their own or in conjunction with medication and hormone therapy. Exercise can have significant benefits. Weight loss and cognitive behavioural therapy have all been shown to be effective strategies on reducing vasomotor symptoms and also managing migraine. And if you haven't learned enough from this talk alone, then may I refer you to a publication in Post Reproductive Health of 2018 of exactly the same topic, where I've covered migraine, menopause and hormone replacement therapy. Thank you very much for listening to this.

End of transcript

Information about the podcast

This podcast series has been made possible by the NSW Government's Menopause Awareness Campaign. For help talking about menopause, download the [Perimenopause and Menopause Symptom Checklist](https://www.jeanhailes.org.au/resources/perimenopause-and-menopause-symptom-checklist) and take it with you to your next medical appointment. For more information visit: <https://www.nsw.gov.au/women-nsw/toolkits-and-resources/perimenopause-and-menopause-toolkit>

Hosted by Dr Sarah White, CEO at Jean Hailes

Produced by May Jasper

Sound engineering by Derek Myers

Information about Jean Hailes for Women’s Health

Jean Hailes for Women's Health is a national not-for-profit organisation dedicated to improving the health of all women, girls and gender-diverse people. For free, evidence-based and easy-to-understand health information, visit [www.jeanhailes.org.au](http://www.jeanhailes.org.au).

© 2023 Jean Hailes Foundation. All rights reserved. This publication may not be reproduced in whole or in part by any means without written permission of the copyright owner. Contact: [licensing@jeanhailes.org.au](mailto:licensing@jeanhailes.org.au)