Top tips: menopause

Dr Alice Scott and **Dr Louise Newson** offer ten top tips on diagnosing and managing the menopause and premature ovarian insufficiency

Read this article to learn more about:

- when laboratory testing is and is not needed to diagnose menopause
- the advantages of using body-identical and transdermal hormone replacement therapy (HRT) over alternatives
- how the benefits and risks differ between different types of HRT.

0.5 CPD CREDITS

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1 Diagnose menopause based on clinical presentation

For most women, menopause is a clinical diagnosis and it is rarely necessary to arrange any specific tests. Menopause is the cessation of menstruation due to ovarian failure, and is diagnosed retrospectively after 1 year of amenorrhoea.[1] The mean age for the natural menopause in the UK is 51 years.

It is important to note that there are many menopausal symptoms. There is a widespread presence of oestrogen receptors throughout the body, so when the hormonal balance of oestrogen changes multiple systems in the body are affected. Symptoms often commence during the perimenopause and can continue post menopause, persisting for a median 7 years.[1]

Around 75% of women will experience vasomotor symptoms of night sweats and hot flushes, which are often associated with palpitations and anxiety. Other systemic symptoms include aching joints, fatigue, difficulty concentrating, poor sleep, mood changes, low libido, headaches, dry skin, hair changes, and genitourinary symptoms.

Serum follicle-stimulating hormone (FSH) should be measured only in women with menopausal symptoms who are aged 45 years and under.

Owing to daily fluctuations in hormones in the transitional period,[1] a normal FSH in the perimenopause should not be a reason to deny treatment for symptoms.

2 Recognise premature ovarian insufficiency

Premature ovarian insufficiency (POI), defined as menopause before age 40 years, is more common than many doctors realise; it is estimated to affect 1% of women.[1,2] The identifying features of POI are:

- no or infrequent periods for more than 3 months
- raised FSH
- low oestradiol levels.

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Elevated FSH levels on two blood samples taken 4–6 weeks apart are diagnostic of POI.[1] Further investigations may be considered to determine underlying causes; however, in 90% of cases of spontaneous POI no cause will be identified.[3]

Premature ovarian insufficiency is associated with an unpredictable pattern of intermittent ovarian function; 5–10% of women with POI find that they are spontaneously able to conceive.[4]

A diagnosis of POI can be difficult for patients to accept due to both the physical symptoms and the psychological adjustment often required. Prolonged absence of oestrogen increases the risk of cardiovascular disease, osteoporosis, and dementia.[2]

Therefore, provided they do not have any contraindications, women with POI should be treated with hormone replacement therapy (HRT) until the average age of menopause to reduce the risk of developing other chronic conditions.

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Adequate replacement can be provided by way of combined hormonal contraceptive (CHC) for those under the age of 50 years, which may be more acceptable to younger women. However, there is less evidence that CHC affords protection to bones and the heart compared with HRT.[5,6]

During a consultation, the opportunity should be taken to emphasise modification of lifestyle factors (e.g. diet and physical activity) to reduce cardiovascular and osteoporotic risk.

3 Know the benefits of hormone replacement therapy

The treatment of choice for many menopausal symptoms is HRT.[1] Hormone replacement therapy containing oestrogen can help alleviate vasomotor symptoms, low mood, and altered sexual function. Vaginal oestrogen can relieve symptoms of urogenital atrophy.

If HRT is started below the age of 60 years and/or within 10 years of the menopause, it has been shown to have a beneficial effect on cardiovascular health, reduce the chances of type 2 diabetes, and to increase bone density.[7]

Unopposed oestrogen in a woman with a uterus can lead to endometrial hyperplasia, therefore, a progestogen licensed for endometrial protection should be given simultaneously.[8] Sequential preparations are usually given if the last menstrual period (LMP) was less than 1 year ago, otherwise a continuous combined preparation is usually indicated.

Taking a continuous combined regimen provides better endometrial protection.[9,10] Most women can be given a continuous preparation after they have taken a cyclical preparation for 1 year.

4 Be aware that different types of HRT do not have equal risks

The risks of HRT differ depending on the route of administration (oral or transdermal) and on whether the preparation contains a body-identical or synthetic hormone.

Oestradiol is body-identical oestrogen and should be considered the oestrogen of choice as synthetic conjugated equine oestrogens contain a mixture of different hormones, including equine specific steroids which have unknown properties in humans.[6,11]

Studies show that transdermal oestradiol (as a patch or gel) does not have the increased risks of venous thromboembolism,[12,13] ischaemic stroke[12,13] and gallbladder problems that are associated with oral oestradiol.[10]

Oestrogen-only HRT does not increase the risk of invasive breast cancer, but when oestrogen is combined with a synthetic progestogen (e.g. noresthisterone, norgestrel, levonorgestrel, medroxyprogesterone acetate, or drospirenone) there is a small increased risk of breast cancer.[14,15] In contrast, studies have looked at the combination of oestradiol and body-identical micronised progesterone (oral or vaginal micronised progesterone) and found no increased risk of breast cancer for the first 5 years of taking it.[16]

There is also evidence that, compared with synthetic progestogens, micronised progesterone has a safer cardiovascular profile, a neutral effect on blood pressure, and a favourable effect on lipids.[17]

The optimal HRT regimen associated with the lowest risks appears to be transdermal oestrogen and micronised progesterone, if a progestogen component is required.

There will be some women who may prefer oral HRT or a combined patch (these are currently only available with a synthetic progestogen component); when prescribing these types of HRT it is important to discuss with the patient the slightly increased risks of these methods compared to body-identical hormones.

For women who require ongoing contraception, who are experiencing heavy menstrual bleeding in the perimenopause, or who may find compliance an issue with the two separate components, the Mirena intrauterine system (IUS) could be used instead of the micronised progesterone.

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The synthetic steroidal compound tibolone has oestrogenic, progestogenic, and androgenic activity[1] and is licensed for menopausal symptoms in postmenopausal women.[18] It can be considered to have the same risk profile as oral HRT; however, the Medicines and Healthcare products Regulatory Agency has warned that using tibolone substantially increases risk of stroke in women older than 60 years.[19]

5 Investigate persistent HRT side-effects

Most women do not experience side-effects when taking a combination of transdermal oestrogen

and micronised progesterone, and most side-effects settle within 3–6 months. Therefore, if women are already on oral HRT or preparations containing synthetic progestogens and develop side-effects, it makes sense to switch them to body-identical HRT.

Bleeding within the first 6 months of continuous HRT is not uncommon; however, bleeding beyond 6 months in women who are experiencing menopause should be investigated,[14] to exclude pathology including possible endometrial cancer as per the NICE guideline on *Suspected cancer: recognition and referral*.[20]

Once pelvic pathology is excluded, either a Mirena IUS can be used to control the bleeding (and then as the progestogen component of the HRT) or, if bleeding occurred following the switch to continuous combined HRT, treatment can be switched back to a sequential regimen for a further 6–12 months. If bleeding is heavy or erratic on a sequential regimen, then the dose of progestogen could be doubled or the duration increased to 21 days.[14]

Low libido is a complex symptom due to interplay between biological factors such as dyspareunia from vulvovaginal atrophy, sweats leading to poor sleep, fatigue and mood changes, and non-biological factors such as happiness in the relationship.

If the woman is adequately oestrogenised, systemically and locally (vaginal oestrogen can be given in conjunction with systemic HRT if needed), and there are no relationship issues NICE recommends that testosterone treatment can be considered.[1]

It should be noted that at the time of publication (July 2018), testosterone was not licensed for altered sexual function in the menopause; the prescriber should follow relevant professional guidance, taking full responsibility for all clinical decisions.

Informed consent should be obtained and documented. See the General Medical Council's guidance on *Good practice in prescribing and managing medicines and devices* for further information.[21]

6 Balance benefits against risks in long-term HRT use

Most women require 2–5 years of HRT for vasomotor symptoms but some women require it for longer.[1] There is no arbitrary age cut-off for HRT and it can be continued as long as it is felt that the benefits of symptom control outweigh the risks.

If HRT is started before age 60 years or within 10 years of menopause, and HRT is provided by risk-neutral, body-identical hormones in the form of transdermal oestrogen (alone or in combination with micronised progesterone), treatment can be continued long term.[10]

> … bleeding beyond 6 months in women who are experiencing menopause should be investigated

Many women continue to take HRT indefinitely as they feel the benefits for their future health (often bone health) outweigh any potential risks. The prescribed dose of oestrogen is often lower in older women, but even low doses can lead to a reduced risk of osteoporosis.[22]

Topical vaginal oestrogen can be continued indefinitely with no need for endometrial monitoring but women should be advised to report any unscheduled vaginal bleeding.[1]

7 Consider non-pharmacological treatment options

Lifestyle modifications to improve vasomotor symptoms include: taking regular exercise, maintaining or achieving a normal body mass index, wearing loose-fitting clothing, and avoiding triggers for hot flushes such as smoking, alcohol, caffeine, and spicy foods. Sleep disturbance may be helped by sleep hygiene measures and mood disturbance can be improved with relaxation and exercise.[23]

8 Non-hormonal treatments may be effective for some women

For women in whom HRT is contraindicated, a 2-week trial with an antidepressant (off-licence) may help vasomotor symptoms; consider venlafaxine 37.5 mg twice a day, citalopram 20 mg daily, or fluoxetine 20 mg daily.[24]

Vaginal dryness may be helped with a vaginal lubricant or moisturiser. There is some evidence that isoflavones and black cohosh may help vasomotor symptoms but their safety is uncertain.[1] Clonidine at a dose of 50–75 mcg twice a day is licensed for menopausal flushing but the limited evidence for its efficacy is conflicting.[25]

9 Don't forget to offer contraception

Contraception is required until 1 year after the LMP in women aged 50 years and over, and 2 years after the LMP in those under 50. Hormone replacement

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Table 1: Recommendations regarding stopping contraception[26]

Contraceptive method	Age 40–50 years	Age >50 years
Non-hormonal	Stop contraception after 2 years of amenorrhoea	Stop contraception after 1 year of amenorrhoea.
Combined hormonal contraception	Can be continued	Stop at age 50 and switch to a non-hormonal method or IMP/POP/LNG-IUS, then follow appropriate advice.
Progestogen-only injectable	Can be continued	Women ≥50 should be counselled regarding switching to alternative methods, then follow appropriate advice.
Progestogen-only implant (IMP) Progestogen-only pill (POP) Levonorgestrel intrauterine system (LNG-IUS)	Can be continued to age 50 and beyond	Stop at age 55 when natural loss of fertility can be assumed for most women. ■ if a woman over 50 with amenorrhoea wishes to stop before age 55, FSH level can be checked ■ if FSH level is >30 IU/l the IMP/POP/LNG-IUS can be discontinued after 1 more year ■ if FSH level is in premenopausal range then method should be continued and FSH level checked again 1 year later.
		A Mirena® LNG-IUS inserted ≥45 can remain *in situ* until age 55 if used for contraception or heavy menstrual bleeding.

FSH=follicle-stimulating hormone; IU=international unit

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therapy does not confer contraception thus additional measures should be provided if necessary.[26]

Continuous combined HRT can be assumed to be contraceptive as a constant daily dose of progestogen is administered; there is no scientific evidence for this,[26] but when a woman is stable and not menstruating while on HRT it can be assumed that her HRT is having a contraceptive effect.

Contraception can be given any of the following ways:[26]

- Mirena IUS which could then act as the endometrial protective element of the HRT too (no other forms of progestogen-only contraception [POC] can be used to provide endometrial protection)
- any of the progestogen-only methods (implant, progestogen-only pill, or depo injection) alongside the HRT
- CHC can be prescribed to eligible women until age 50 years and may also treat menopausal symptoms.

If women are amenorrhoeic on POC it is not possible to use their bleeding pattern to establish whether they are postmenopausal. The Faculty of Sexual and Reproductive Healthcare guideline on Contraception for women aged over 40 years[26] provides recommendations on when to stop taking contraception based on age, contraception type, and FSH levels where relevant (see Table 1).

Note that FSH levels in women taking CHC are suppressed and are therefore not reflective of menopausal status.

10 Consider referring to a menopause specialist

Referral to a menopause specialist should be considered in the following circumstances:

- suspected or confirmed POI[1]
- difficulty in controlling menopausal symptoms or management of side-effects[1]
- women with contraindications to HRT who have not responded to the non-pharmacological and non-hormonal treatments as listed above[1]
- women who would like HRT but have a contraindication for it[1]
- any other issues which the referring clinician feels are outside of their area of expertise.

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