Barns Medical Practice Service Specification Outline: Menopause

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Introduction

Menopause is when menstruation ceases permanently due to loss of ovarian follicular activity. It occurs with the final menstrual period and therefore can only be diagnosed with certainty after 12 months after the last period. This can occasionally be premature, for example if there is a family history of premature ovarian failure or if the ovaries are removed surgically. In the UK, the average age at the menopause is 51 years.

Perimenopause = characterised by irregular cycles of ovulation and menstruation and ends 12 months after the last menstrual period.
Postmenopause = time after a woman has not had a menstrual period for 12 consecutive months
Early menopause = cessation of ovarian function between 40 and 45 years, in the absence of other causes of secondary amenorrhoea.
Premature ovarian insufficiency = clinical syndrome defined as the transient or permanent loss of ovarian function before the age of 40 years.

Diagnosis

Diagnosis is mainly clinical. About 75% of women in the UK will experience menopausal symptoms in their lifetime and 25% of them will find the symptoms distressing. Menopausal symptoms are usually self limiting, lasting between 2 and 5 years. Symptoms commonly include:

- Hot flushes and night sweats.
- Sleep disturbance.

- Urinary and vaginal symptoms, including vaginal discomfort and dryness. This can manifest as pain when having sex or symptoms of recurrent urinary tract infections.

If a woman is experiencing menopausal symptoms under 45 then blood tests are commonly undertaken to assess hormone levels.

Treatment of Menopausal Symptoms

There are several treatment options for women to help with menopausal symptoms and everyone should consider general lifestyle measures in the first instance as all medical therapy carries risks of side-effects.

Lifestyle Advice for Menopausal Symptoms

Encourage all women to make lifestyle modifications to reduce menopausal symptoms as many of these problems are all linked and treating one can make great differences to other symptoms:

Exercise:

- May help reduce the severity and frequency of flushes
- Promote better sleep
- Reduce risk of osteoporosis
- Reduce cardiovascular disease and reduce weight
- Improve mood by boosting natural serotonin levels

Diet:
A balanced diet is very important to maintain an adequate nutrient and mineral balance. This will not only make a woman feel more energised but also boost her mood. Cutting out processed foods, sugars and fatty foods will promote weight loss and help prevent cardiovascular disease.

Adequate intake of calcium is important to prevent loss of bone density following the menopause as oestrogen is protective against osteoporosis.

Other minerals of importance are: magnesium, copper, iron, zinc, selenium.

There is a host of information online regarding the benefits of a balanced diet and patients should be encouraged to explore this information. More information regarding important vitamins and minerals are available on websites such as *Menopause Matters* (see link below).

Sleep:
Sleep is important to help reduce stress and help the body regenerate after the day. Healthy sleep reduces stress, anxiety and low mood. Sleep disturbance is common during menopause and good sleep hygiene tips should always be followed

- Maintain a regular bedtime
- Maintain adequate hydration through the day to avoid waking up with thirst or a full bladder in the night
- Try to ensure body temperature is not too high before bed: avoid hot baths or exercise in the 2 hours before bed
- Maintain a regular bedtime even if sleep is disturbed throughout the night
- Avoid daytime napping
- No caffeine after midday
- Avoid excessive alcohol or cut out altogether
- Try sleeping in a cooler room, it is much easier to warm up than to cool down

Smoking:

- This has been found to lower oestrogen levels therefore worsen menopausal symptoms
- It is also linked to osteoporosis and heart disease as is menopause so patients should be informed of this if they are continuing to smoke after the menopause
- There are overall health benefits to stopping smoking like reducing risk of heart attacks and stroke, reducing cancer risk and reducing lung disease.

<u>Over the counter alternatives</u>

There are some complementary therapies that many women have found effective. There are many products to choose from and it is often confusing as to what they contain. It should be noted that just because a treatment is deemed 'natural' it is not always safe. If a patient is expecting the medication to work they must also expect that it may come with side-effects as with any other medication. An open and honest discussion between patient and doctor should be had if a patient would like some advice about taking these treatments. If no contraindications to these medications are found they should also be advised to stop taking it if they have been using for over 3 months as they are often expensive. Women can also be directed to a reputable therapist who has been trained in natural medicine. These can be found via the College of Practitioners of Phytotherapy.

<u>Phyto-oestrogens</u>

These are naturally derived compounds which have properties similar to oestrogen and therefore can give some relief from menopausal symptoms. There are many dietary forms of these compounds and it has been studied that menopausal symptoms are much more tolerable in women of Asia, particularly Japan. This is thought to be related to the high dietary intake of phyto-oetrogens. These can be naturally found in:

Cereals: oats, barley, rye, brown rice, couscous and bulgar wheat.
Seeds: sunflower, sesame, pumpkin, poppy, and linseeds.
Pulses: soya beans and all soya based products.
Beans: chickpeas, kidney beans, haricot beans, broad beans, green split peas.
Vegetables: red onions, green beans, celery, sweet peppers, sage, garlic, broccoli, tomatoes and bean sprouts.

These phyto-oestrogens can also be found in capsule or tablet form and some women find they can give great support over the peri-menopausal and menopausal years. They should be used with great caution in those who have hormonal dependent diseases such as breast cancer as the oestrogen mimicking effect can stimulate the cancer cells.

Herbal Remedies

Many herbal remedies may or may not contain phyto-oestrogens but the doses per product may vary wildly and if a patient would seriously like to try this type of medication she should be advised to thoroughly research the products and, if necessary, consult a phytotherapist. Many of these medications have properties which not only help hormonal symptoms but, like any other medication, interact with prescribed medication such as hormonal contraception, anti-epileptic medication, warfarin or antidepressant medications. The following herbal products have all been used to treat menopausal symptoms.

- Agnus castus
- Black Cohosh
- Sage
- Gingko Biloba
- St Johns Wort

Other non-prescribable alternatives

Include: massage, relaxation techniques, magnet therapies, aromatherapy, accupuncture, reflexology or homeopathy.

These may enhance a woman's feeling of overall well-being and mood and must always be recognised if it helps the individual. What may work for one woman may not work for another. Whilst it is important to remain open-minded, non-judgemental and have the patient's best interests at heart, it is also important to remain scientific and objective and to protect a woman from making financial losses on non-NHS funded treatments if they don't seem to be helping her.

Peer support

Is often under-estimated and sometimes talking with others going through a similar experience can be very helpful. This could involve encouraging the patient to talk to friends of a similar age, or researching forums online.

Prescribable Non-Hormonal Treatments

Clonidine

- 50mcg twice daily. Can increase to 75mcg if required.
- Useful for vasomotor symptoms

SSRIs or SNRIs

- 2 week trial of Fluoxetine 20mg, Citalopram 20mg or Venlafaxine 37.5mg
- Can help vasomotor symptoms in those whom HRT is contraindicated although can interact with tamoxifen.
- Should not be offered as 1st line for vasomotor symptoms alone
- No clear evidence SSRIs or SNRIs ease low mood in those who do not have a formal diagnosis of depression

Vaginal moisturiser eg Replens

- Can be used alongside vaginal oestrogens.

CBT – useful for symptoms of low mood

Testosterone – useful for symptoms of low libido despite HRT

<u>Prescribable Hormonal Treatments</u>

For some women, hormone replacement therapy (HRT) may be useful, but the risks and benefits of treatment must be considered for each woman. Aim is to prescribe the lowest dose for the shortest possible duration.

Hormone replacement therapy (HRT) is effective for:

- Treating vasomotor symptoms (for example hot flushes and night sweats).
- Treating urogenital symptoms (for example vaginal dryness, pain during sex as a result of vaginal dryness, recurrent urinary tract infections, and urinary frequency and urgency).
    - Topical HRT is very effective and doesn't carry the level of risk that HRT patches or tablets do.
- Managing sleep or mood disturbances caused by hot flushes and night sweats.
- Protects against osteoporosis - due to the risks associated with long-term use, HRT is not normally used as first-line treatment for long-term prevention of osteoporosis in women over 50 years of age, except when other treatments are contraindicated, not tolerated, or ineffective.
    - Protection maintained whilst on treatment but decreases once stopped.
    - Benefit may last longer if on treatment for longer
- Protects against loss of muscle mass

In every woman considering HRT advise about:

- Modifying their lifestyle to reduce symptoms.
- The risks and benefits of hormone replacement therapy (HRT).
- The expected duration of treatment - for vasomotor symptoms, most women require 2–5 years of treatment, but some women may need longer.
    - This judgement should be made on a case-by-case basis with regular attempts to discontinue treatment.

    - Symptoms may recur for a short time after stopping HRT. Topical (vaginal) oestrogen may be required long term.
    - Regular attempts (at least annually) to stop treatment are usually made.

Risks of HRT

- Venous thrombo-embolism
    - Reduced risk with transdermal use of HRT compared to oral preparations.
    - Low-dose transdermal use carries no increased risk compared to baseline.
- Coronary heart disease and stroke
    - Multifactorial and varied from woman to woman
    - Studies have shown no increased CHD risk when started below the age of 60
    - Oestrogen only is mildly protective against CHD
    - Small increased risk of stroke in <60 and in those using oral HRT
    - HRT does not increase the risk of dying from CHD.
- Breast cancer
    - Risk varies from person to person
    - Oestrogen only HRT is associated with little to no increased risk of breast cancer
    - Combined HRT associated with increased risk that is dependent on the length of time on HRT. Risk reduces once HRT is stopped
    - No difference based on preparations used.
- Ovarian cancer may be increased by HRT use.
    - Risk declines the longer ago HRT was stopped.

Adverse effects of HRT

- Oestrogen-related adverse effects
    - Fluid retention, bloating, breast tenderness, nausea, headaches, leg cramps, and dyspepsia.
    - Can try adding vaginal oestrogen if urogenital symptoms not controlled.
    - Oestrogen type can be changed ie. From estrodiol to conjugated oestrogens.
- Progestogen-related adverse effects
    - Fluid retention, breast tenderness, headaches or migraine, mood swings, depression, acne, lower abdominal pain, and headache.
    - Tend to be more cyclical
    - Can try changing the androgen type. Ie. From norethisterone and norgestrol to medroxyprogesterone and dydygesterone
        - Medroxypoxyprogesterone, dydrogesterone and drospirenone may be better tolerated than norethisterone or levonorgestrel as they are less androgenic.
    - Once postmenopausal, change to continuous
- Weight gain is very common around the time of the menopause and HRT does not significantly contribute to further weight gain.
    - Some evidence that the tendency towards central abdominal obesity is ameliorated by oestrogen therapy.

- Studies generally indicate a reduction in overall fat mass, improved insulin sensitivity, and a lower rate of development of T2DM with HRT.

Vaginal Bleeding

Monthly Cyclical

Monthly cyclical regimens should produce regular predictable bleeding starting towards or soon after the end of the progestogen phase.

It is mandatory to investigate unexplained bleeding before changing treatment, to exclude pelvic pathology.

- Visualize the cervix, check smears are up to date, and refer for transvaginal ultrasound to exclude pelvic abnormalities.
- Check for compliance with treatment, drug interactions (for example with anticonvulsants), or gastrointestinal upset (which can interfere with absorption).

Altering the progestogen part of the regimen may improve bleeding problems:

- For heavy or prolonged bleeding = increase the duration or dose of the progestogen, or change the type of progestogen.
- For bleeding early in the progestogen phase = increase dose or change the type of progestogen.
- For irregular bleeding = change the treatment regimen or increase the dose of progestogen.
- Idiopathic menorrhagia may be helped by using the levonorgestrel-releasing intrauterine system (Mirena®) combined with an oestrogen delivered orally or transdermally.

The absence of bleeding whilst taking a cyclical regimen reflects an atrophic endometrium and occurs in 5% of women.

- Exclude pregnancy in perimenopausal women or women with ovarian failure.
- Check compliance if the progestogen component is taken separately.

Continuous Combined or during long cycle regimens

Irregular breakthrough bleeding or spotting is common in the first 4–6 months of continuous combined HRT. Bleeding beyond 6 months or after a spell of amenorrhoea requires further investigation or referral.

Contraindications to HRT

Absolute

- Current, past, or suspected breast cancer.
- Known or suspected oestrogen-sensitive cancer.
- Undiagnosed vaginal bleeding.
- Untreated endometrial hyperplasia.
- Previous idiopathic or current venous thromboembolism (deep vein thrombosis or pulmonary embolism) unless the woman is already on anticoagulant therapy.
- Active or recent arterial thromboembolic disease (for example angina or myocardial infarction).

- Untreated hypertension.
- Active liver disease with abnormal liver function tests.
- Pregnancy
- Thrombophilic disorder

Caution
- Porphyria cutanea tarda
- Diabetes mellitus (increased risk of heart disease)
- Factors predisposing to VTE
- History of endometrial hyperplasia
- Migraine and migraine-like headache.
- Increased risk of breast cancer

HRT may need to be stopped *immediately* if any of the following occur:
- Sudden severe chest pain (even if not radiating to left arm).
- Sudden breathlessness (or cough with blood-stained sputum).
- Unexplained swelling or severe pain in the calf of one leg.
- Severe stomach pain.
- Serious neurological effects, including unusual severe, prolonged headache, especially:
    - If it is the first time, or getting progressively worse, or
    - There is sudden partial or complete loss of vision, or
    - Sudden disturbance of hearing or other perceptual disorders, or
    - Dysphasia, or
    - Bad fainting attack or collapse, or
    - First unexplained epileptic seizure, or
    - Weakness, motor disturbances, or very marked numbness suddenly affecting one side or one part of body.
- Hepatitis, jaundice, or liver enlargement.
- Blood pressure above systolic 160 mmHg or diastolic 95 mmHg.
- Prolonged immobility after surgery or leg injury.

Prescribing HRT

<u>Options</u>

Systemic HRT
- With a uterus = **combined oestrogen–progestogen** preparations, unless they have Mirena coil in which case they can have oestrogen only
- Without a uterus = **oestrogen-only** preparations

Vaginal oestrogen
- Low-dose natural oestrogens, such as estriol (cream or pessary) or estradiol (tablet or ring) preparations, are suitable for vaginal use.

- Endometrial effects should not be incurred therefore a progestogen is not needed with such low-dose preparations.
- Synthetic or conjugated oestrogens should be avoided as they are well absorbed from the vagina and may potentially result in endometrial stimulation.

Tibolone is an alternative no-bleed regimen for post menopausal women.

- It is a synthetic steroidal compound with oestrogenic, progestogenic, and androgenic activity.
- It may be used as an alternative to combined HRT for **postmenopausal** women who wish to have amenorrhoea.

Advise the woman that she may still get pregnant if contraception is not used:

- A suitable method of contraception should be used for 1 year after the last menstrual period if the woman is more than 50 years of age, or for 2 years after the last menstrual period if the woman is less than 50 years of age

<u>Regimen</u>

- Women who do not have a uterus - oestrogen-only hormone replacement therapy (usually taken continuously).
- Women *with* an intact uterus - combined oestrogen and progestogen therapy
    - If LMP <12 months: cyclical HRT
        - Monthly cyclical regimens — oestrogen is taken daily and progestogen is given at the end of the cycle for 10–14 days.
        - Three-monthly cyclical regimens — oestrogen is taken every day and progestogen is given for 14 days every 13 weeks (this is better if the woman is intolerant to progestogenic side-effects)
    - If LMP >12 months: continuous combined
        - Continuous combined regimens — oestrogen and progestogen are taken every day.
        - Continuous combined HRT may produce irregular bleeding or spotting for the first 4–6 months of treatment.
            - Bleeding should be investigated if it persists beyond 6 months, becomes heavier rather than less, or occurs after periods have been absent for over a year whilst on HRT

Vaginal oestrogen regimens depend on the preparation used

- One vaginal tablet daily for 2 weeks, then reduced to 1 vaginal tablet twice weekly
- One applicator daily for 3-4 weeks then reduced to 1 applicator twice weekly
- One pessary daily for 3 weeks then reduced to 1 pessary twice weekly
- One vaginal ring inserted into the upper third of the vagina and worn continuously, to be replaced at 3 months. Max durations is 2 years.

Route of delivery

- Oral tablets remain the most common preparation for convenience purposes
- Transdermal preparations are becoming increasingly appropriate as they carry less VTE risk. Additionally they may be generally preferred if
    - Symptom control is poor with oral treatment.
    - Oral treatment causes adverse effects (such as nausea).
    - The woman is taking a hepatic enzyme–inducing drug (for example an anticonvulsant drug).
    - The woman has a bowel disorder which may affect absorption of oral treatment.
    - The woman has a history of migraine (when steadier hormone levels may be beneficial).
    - The woman has lactose sensitivity (most HRT tablets contain lactose).
- Low-dose vaginal oestrogen (tablet, cream, pessary, or vaginal ring) may be used for urogenital symptoms alone.
- The levonorgestrel-releasing intrauterine system (IUS) (Mirena®) is an alternative route of delivery of progestogen to protect the endometrium. Since levonorgestrel is delivered locally to the uterus, a much lower daily dose is used, which also results in low systemic levels of levonorgestrel.

Offer the levonorgestrel-releasing IUS when:

- The woman is below the age of 55
- The woman is experiencing persistent progestogenic adverse effects from systemic HRT, despite changes in type and route of progestogen.
- Contraception is required along with HRT in the perimenopause.
- Withdrawal bleeds on sequential HRT are heavy, after investigation if indicated.
    - The licence for use of the levonorgestrel-releasing **IUS for the progestogen part of HRT is currently 4 years, as opposed to 5 years when used solely for contraception.**

Follow Up

Review the woman 3 months after starting hormone replacement therapy (HRT) and once she is settled on treatment, follow up annually.

At the initial 3-month review:

- Assess the effectiveness of treatment and if necessary, adjust treatment to achieve better symptom control. Enquire about any adverse effects and manage appropriately. Enquire about bleeding patterns.
- Check body weight and blood pressure.
    - Stop HRT *immediately* if blood pressure is above systolic 160 mmHg or diastolic 95 mmHg.

Once each year**,** repeat the above checks and also:

- Consider switching from cyclical HRT to continuous combined HRT, if appropriate.

- Interrupt treatment with intravaginal oestrogen and consider stopping systemic HRT, to re-assess the need for continued use.
- Discuss the advantages and disadvantages of continuing HRT, especially the increased risk of breast cancer with long-term HRT.
- Perform a breast or pelvic examination if indicated by personal, clinical or family history.
- Encourage participation in the national breast (as appropriate for their age) and cervical screening programme.

Making Changes to HRT

Switching from cyclical to continuous combined HRT

- Continuous combined preparations are generally preferred because they do not induce bleeding and may have a reduced risk of endometrial cancer compared with cyclical HRT
- Consider switching from cyclical HRT to continuous when the woman is considered to be postmenopausal. I.e
    - They are more than 54 years of age (it is estimated that 80% of women will be postmenopausal by this age).
    - They have had previous amenorrhoea or increased levels of follicle-stimulating hormone (FSH). E.g Women who experienced 6 months of amenorrhoea or had increased FSH levels in their mid-40s are likely to be postmenopausal after taking several years of cyclical HRT

Consider a trial withdrawal (if a woman is symptom-free) after 1–2 years.

- Advise the woman that symptoms may recur for a short time once HRT is stopped.
- Counsel the woman about the possible risks of HRT if she wishes to continue treatment, particularly if treatment is being used for longer than 5 years.

Topical (vaginal) oestrogen may be required long term as symptoms can recur once treatment has stopped.

- Stop treatment at least annually to re-assess the need for continued treatment.
- Detection of a risk factor which contraindicates treatment.

Concerns re. Treatment Failure

- Check that the hormone replacement therapy (HRT) has been used as recommended for at least 3 months to ensure full effect.
- If applicable, check that patches are adherent.
- Review the woman's expectations. HRT can help reduce symptoms due to oestrogen deficiency, but it is not an answer to all problems.
- Consider an alternative diagnosis.

Treatment options include:

- Switching from oral to a non-oral route of administration (for example if absorption is poor owing to a bowel disorder, or if a drug interaction is present).

- Switching delivery system, if patch adhesion is poor.
- Altering the dosage or type of hormone.

Stopping HRT

Some women do not notice any symptoms even with abrupt cessation of hormone replacement therapy (HRT), while others may experience a recurrence of hot flushes and sweats.

Gradually reducing HRT may limit recurrence of symptoms in the short term but either reducing or immediately stopping, makes no difference to recurrence to symptoms in the long term.

Some experts suggest that HRT should be gradually reduced rather than stopped abruptly. Suggested strategies are:

- **For oestrogen-only tablets:** reduce from a 2 mg to a 1 mg tablet for 1–2 months, then use 1 mg on alternate days for a further 1–2 months.
- **For oestrogen-only patches:** reduce the dose gradually to 25 micrograms daily (for example step the dose down a patch strength each month). Half a matrix-type patch (12.5 micrograms daily) can be used for a further 1–2 months.
- **For cyclical combined HRT tablets:** reduce to a cyclical HRT pack containing 1 mg estradiol for 1–2 months. Cut the tablet in half for the next 1–2 months; this will ensure that the woman still receives oestrogen combined with a progestogen.
- **For cyclical combined HRT patches:** reduce the dose as for oestrogen-only patches, but ensure that the woman still uses the oestrogen-only patches for 2 weeks of the cycle followed by the combined patches for a further 2 weeks, to ensure endometrial protection.
- **For continuous combined HRT tablets or patches:** reduce the dose gradually every 1–2 months to the lowest strength tablet or patch. Then, take half a tablet or patch daily for a further 1–2 months.

If symptoms are severe after HRT is stopped, or persist for several months after stopping, the woman may wish to restart HRT after reassessment and counselling. Often a lower dose of HRT can be used (for example estradiol 1 mg) if HRT is restarted.

Referral to Secondary Services

- Multiple treatment failure, for example three or more regimens have been tried
- Those who are taking cyclical HRT if there is a change in pattern of withdrawal bleeds or breakthrough bleeding
- Those taking continuous combined hormone replacement therapy (HRT) if:
    - Breakthrough bleeding persists for more than 4–6 months after starting therapy
    - A bleed occurs after amenorrhoea.
- If, when taking tibolone, they bleed beyond 6 months of starting treatment or after stopping treatment
- Menopausal symptoms and contraindications to HRT
- Uncertainty about the most suitable treatment options

Premature Menopause

Diagnosis is based on

- menopausaul symptoms, including no or infrequent periods
- elevated FSH levels on 2 bloods samples taken 4-6 weeks apart
- Do not diagnose POI on the basis of a single blood test. Do not use AMH routinely in the diagnostic process.

Premature menopause is menopause which occurs in women younger than 40 years of age.

- Refer to a gynaecologist.
- Offer lifestyle advice.
- Emphasise the importance of starting hormone treatment until at least the age of natural menopause.
- Offer systemic oestrogen replacement therapy
    - **HRT:** the HRT regimen used will depend on whether or not the woman has undergone a hysterectomy, still has some ovarian activity, and still has periods.
        - For women who are still having periods = combined, systemic, cyclical HRT.
        - For women with infrequent periods or women who cannot tolerate progestogens = systemic 3-monthly regimen may be preferred.
        - For women who have had a hysterectomy = unopposed oestrogen replacement therapy.
    - **COC:** the decision to prescribe the COC will depend on the woman's age and the presence of associated risk factors (for example smoking).
- Advise the woman that she may still become pregnant if contraception is not used.
- Testosterone implants and patches (licensed) may be considered for treating decreased libido (especially in oophorectomized women); however, seek specialist advice before prescribing these.

Resources for Staff and or Patients

Practice specific information as per service specification

Patient information leaflet - http://www.patient.co.uk/health/menopause-and-hrt-leaflet
Patient information leaflet - http://www.patient.co.uk/health/menopause-alternatives-to-hrt
Patient information leaflet - http://www.nhs.uk/Conditions/Menopause/Pages/Treatment.aspx
GP notebook- http://www.gpnotebook.co.uk/simplepage.cfm?ID=1288699910
Menopause matters - https://www.menopausematters.co.uk
British Herbal Medicine Association - http://bhma.info
General menopausal advice for patients -https://www.avogel.co.uk/health/menopause

Staff involved and training required

- Trained clinicians, guided by appropriate protocols and committed to regular update sessions via continual professional development and appraisal systems.

Advertising of service to patients

- Practice Website: Barns Medical Practice