Gynaecology and Menopause in a primary care setting

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Issues Covering:

- Abnormal Uterine Bleeding and menorrhagia
- PCOs and Endometriosis
- Common vaginal/vulval lesions
- Menopause and HRT

Menorrhagia

- **Definition of menorrhagia: Passing of more than 80mls of blood in each cycle**

- **Take a detailed clinical history:**
  - The nature of the bleeding (flooding, clots) and the impact on the woman's quality of life.
  - Her age — in the first year after menarche, and in the perimenopause, heavy bleeding is associated with irregular cycles which may be due to anovulatory bleeding.
  - Cervical screening history — to confirm she has attended as scheduled and results were normal.
  - Details of the woman's normal menstrual cycle (such as length of the cycle, number of days of menstruation) and any variation of this pattern.
  - Sexual history — this should include current contraceptive use, contraceptive plans, and future plans for a family, as this may impact on the choice of treatment.

Menorrhagia

- The possibility of pregnancy should be considered and excluded
- Family history — particularly ask about endometriosis and coagulation disorders that may have a hereditary component (for example von Willebrand disease).
- Medicines (for example hormonal contraceptives) — these may cause irregular bleeding.
- **Consider the possibility of an underlying systemic disease**. For example, look for signs of hypothyroidism (goitre) or PCOs (acne, hirsuitism)
- Other associated symptoms that might suggest an underlying cause for menorrhagia, for example:
  - PCB or IMB
  - Dyspareunia or pelvic pain/pressure
  - Dysmenorrhoea.
  - Vaginal discharge.

Further Investigations

- **Perform an abdominal and bimanual pelvic examination:**
  - To exclude an underlying cause, such as ascites, fibroids or gynaecological cancer.
  - If the levonorgestrel intrauterine system (LNG-IUS) is being considered.
  - **Perform a speculum examination of the vagina and cervix.**
  - Swabs should be taken if infection is suspected.

- **Arrange a blood test to check for iron deficiency anaemia, Thyroid disorders and any other appropriate investigations.**

- **Consider referral for pelvic u/s scan if suspect any fibroids or other abnormal pathology**

Fibroids

- **Uterine fibroids (leiomyomas) are benign tumours** — they are a mixture of smooth muscle cells and fibroblasts, which form hard, round tumours in the myometrium.
- **Fibroids develop in women of reproductive age** — oestrogen and progesterone control the proliferation and maintenance of uterine fibroids.
- They can be single, or multiple, and their size varies from a few millimetres to 30 cm or larger.
- Subserosal and submucosal fibroids may become pedunculated — attached to the myometrium by a pedicle containing their blood supply.

Fibroids: Risk Factors

- **Increasing age** — the risk of fibroids increases progressively from puberty until the menopause.
- **Early puberty** — the risk of fibroids is increased in women who experienced early puberty and decreased in women who experienced late puberty.
- **Obesity** — weight gain and central distribution of body fat increase the risk of fibroids.
- **Black ethnicity** — incidence is higher in black and Asian women than in white women, and multiple fibroids are more common. In addition, they tend to occur at an earlier age, are larger, and are more likely to be symptomatic.
- **Family history** — risk is higher in women who have first-degree relatives who have fibroids.

- **The risk of fibroids is reduced by pregnancy** and decreases with an increasing number of pregnancies.
- **Note:** there is no evidence that combined hormonal contraceptives (CHCs) increase the risk of developing fibroids.
  - Progestogen-only injectable contraceptives and oral contraceptives reduce the risk of fibroids.

When to Refer Menorrhagia

- **Urgently** if physical examination identifies ascites and/or a pelvic or abdominal mass (which is not obviously due to uterine fibroids).

- **Using a suspected cancer pathway referral** (for an appointment within 2 weeks) if she has a pelvic mass associated with any other features of cancer (such as unexplained bleeding, or weight loss).

- For further investigations, if clinically indicated eg if scan shows possible endometriois or multiple fibroids that may require surgical intervention

Treatment – Non Hormonal

- Tranexamic acid 500mg tablets, one or two three times a day, for up to 4 days (max 8 a day)
- Treatment should be stopped if not effective after 3 cycles
- NSAIDs - Only mefenamic acid is specifically licensed for menorrhagia. However, there are concerns that it is more likely to cause seizures in overdose, and it has a low therapeutic window which increases the risk of accidental overdose.
- The following doses are recommended:
  - Mefenamic acid — 500 mg three times daily.
  - Naproxen — 500 mg as the first dose, then 250 mg every 6–8 hours.
  - Ibuprofen — 400 mg three or four times daily

Treatment- Hormonal

- Consider initially stopping heavy menstrual bleeding by prescribing:
  - Oral Norethisterone 5 mg three times daily for 10 days — bleeding usually stops within 48 hours. Inform the woman that a withdrawal bleed will occur a few days after stopping treatment.
  - If bleeding is exceptionally heavy ('flooding'), 10 mg three times daily for 1 week, may provide more effective results. This should then be tapered to 5 mg three times daily for one week, once bleeding has stopped, depending on clinical judgement.
- Prescribe oral norethisterone longer term (5 mg three times daily) from days 5–26 of the menstrual cycle (the follicular and luteal phases) — this dose is off-label
- Note latest studies suggest Norethisterone carries similar clotting risks to CHC

Treatment - Hormonal

- Medical treatment is recommended first-line for women with menorrhagia who:
  - Have no symptoms that suggest an underlying pathology.
  - Are awaiting the results of investigations.
- Depending on the acceptability to the woman, consider treatments in the following order:
  - Levonorgestrel intrauterine system (LNG-IUS) provided long-term (at least 12 months) use is anticipated
  - Combined oral contraceptives (COCs). When menorrhagia coexists with dysmenorrhoea, NSAIDs should be prescribed in preference to tranexamic acid.
  - Consider POP or Depo for those not suitable for above options

Treatment - Surgical

- For patients who do not respond to medical treatments, have other complicating factors, or when other methods are not suitable consider referral to gynaes for surgical options.
- Endometrial Ablation
- Fibroidectomy
- Hysterectomy

Intermenstrual Bleeding: Causes

- Endometrial polyps.
- Cervical lesions such as polyps or ectropian
- Unscheduled bleeding due to a contraceptive method
- Endometrial hyperplasia or carcinoma or, rarely, uterine sarcoma
- Endometritis or PID – AUB in women with symptomatic chronic endometritis may present as intermenstrual bleeding or spotting, postcoital bleeding, or heavy menstrual bleeding (HMB).
- In women with AUB, the presence of pelvic pain, cervicitis, or vaginal leukorrhea should alert the clinician to the possibility of endometritis.
- Endometritis is most likely to occur in women with a recent history of childbirth or an intrauterine procedure (eg, pregnancy termination, IUD insertion).
- Endometrial abnormalities related to previous endometrial trauma (eg, a caesarean scar defect)
- Among women with regular menses, intermenstrual spotting occurs in less than 3 percent of cycles and may represent physiologic intermenstrual bleeding associated with ovulation

Other investigations

- Transvaginal ultrasound is the investigation of choice to look for structural abnormality.
- Ultrasound should ideally be done immediately postmenstrually, as the endometrium at its thinnest and polyps and cystic areas tend to be more obvious.
- Evidence of endometrial thickening should prompt referral for biopsy.
- Women with PMB (bleeding after more than 12 months of amenorrhoea if 50yrs and after 24 months <50yrs) require an **urgent** 2ww referral to gynaes for endometrial biopsy to exclude endometrial Ca, unless bleeding is likely to be HRT related

Post Coital Bleeding

- Within General Practice approximately 6% of patients will present with post coital bleeding.
- ·PCB occurs in 0.7-39% of women with cervical cancer.
- The incidence of finding a woman in the community presenting with PCB who has cervical cancer is 1 in 44,00- of 20-24 year olds and 1 in 2,400 of 45- 54 year olds.

Cervical ectropions and Polyps

- Ectropion Often induced by hormones such as COC or pregnancy
- These may resolve spontaneously if the COC pill is stopped, or following pregnancy.
- They can be treated conservatively or cauterised with silver nitrate.
- Other treatment options include thermal cautery and diathermy, cryosurgery, laser or microwave therapy

- **Cervical and endometrial polyps**
- Cervical polyps should be avulsed and sent for histology.
- A systematic review and meta-analysis found that the incidence of cancer within an endometrial polyp in women of reproductive age was only 1.7%, compared with 5.4% in postmenopausal women[12].

PCB: Investigations and Examination

- **ALWAYS** exclude the possibility of the patient being pregnant. If this is positive then the patient requires urgent referral to early pregnancy clinic for an ultrasound +/- serial serum β-HCG. This will help to exclude an ectopic pregnancy.
- **Screening for STIs –** This can be performed by a self-obtained low vaginal swab. This swab will allow for you the patient to be tested for Chlamydia and Gonorrhoea.
- **Cervical Smear –** A speculum examination will allow for you to have a look at the vaginal wall for any evidence of vaginitis, an abnormal cervix, an ectropion or any obvious mass. A smear is not routinely performed unless the patient is due for a smear. A negative smear, with persistent post coital bleeding should be referred.
- **Bimanual examination** – Feeling for a palpable mass consistent with a polyp or carcinoma, or cervical excitation/tenderness, which would indicate pelvic inflammatory disease.
- **Bloods** – may not be routinely performed but you can perform FBCs (looking for infection and anaemia), Clotting, Thyroid function and FSH/LH levels (if you suspect the onset of menopause).

Post coital Bleeding: Key Points for Referral

- >35 years with persistent PCB for more than 4 weeks require URGENT referral to be seen within 2 weeks
- Any features suggestive of cervical cancer must be referred urgently
- A patient with persistent intermenstrual bleeding with a negative pelvic exam should be referred urgently
- Unexplained vulval lump
- Vulval bleeding due to ulceration

- **POST MENOPAUSAL BLEEDING IS ENDOMETRIAL CANCER UNTIL PROVEN OTHERWISE!**

Differentials

Cervical Polyps

- Cervical Polyps: treatment is removal, which can be done in the GP surgery or gynaecology clinic simply by twisting the polyp. Note risk of bleeding and need to arrange a pelvic scan to exclude endometrial lesions
- This can only be done if the patient has a small cervical polyp. Larger more persistent polyps should be removed by the Gynaecologist.

Cervical Ectropion/Erosion

- These are commonly seen in teenagers and patients taking the OCP. Treatment can be with cryocautery

- **Cervicitis**
- Treatment should be tailored towards the results of the swab taken.
- Chlamydia or GC consult local GUM clinic for latest treatment regimens
- Bacterial vaginosis (Metronidazole 400mg BD for 7 days)

Endometriosis

- Long term condition where tissue similar to the endometrium grows in other places eg fallopian tubes, ovaries, bowel

- Aetiology is unknown: ? Retrograde of menstruation, spread of endometrial tissue via the blood or lymphatic system; immune system reacts with endometrial tissue; genetics

- Symptoms include:
- pelvic pain often related to menstruation
- Dysmenorrhoea
- deep dyspareunia
- cyclical dysuria
- May result in infertility

Endometriosis Diagnosis

- A detailed history including menstrual history
- Physical examination- pelvic examination to check for pelvic tenderness and cervical excitation as well as any obvious pathology
- Laparoscopy often only way to confirm diagnosis –visual mapping of the lesions and histological confirmation

Endometriosis - Treatment Options

- Drug treatments induce atrophy of ectopic endometrium, either by altering the effect of oestrogen on endometriosis tissue or by reducing circulating oestrogen levels, which may reduce menstrual bleeding or induce amenorrhoea.
- **If the woman does not wish to conceive, consider prescribing a 3-6 month trial of hormonal contraception (off-label use).**
- Monophasic combined oral contraceptive (COC) preparations containing 30–35 micrograms of ethinylestradiol and norethisterone, norgestimate, or levonorgestrel are usually first choice.
- Advise the woman to start a 3–month trial of a conventional regimen, then switch to tricycling or continuous use if this does not control symptoms.
- POP (desogestrel 75 micrograms), depot (Depo-Provera® or SAYANA PRESS®), subdermal implant (Nexplanon®) may all help
- Mirena IUS may also be considered, after a full discussion of the advantages and disadvantages.

When to Refer

- **Referral to confirm the diagnosis of endometriosis**
- Both guidelines recommend visual inspection of the pelvis by laparoscopy with histological examination of specimens collected during laparoscopy to confirm the presence of endometriosis.
- Establishing a diagnosis of endometriosis on the basis of symptoms alone can be difficult as symptoms are variable and may mimic other conditions
- Expert opinion of CKS external reviewers stated that there are no investigations in primary care that are helpful in confirming a diagnosis of endometriosis. A normal ultrasound scan of the pelvis does not exclude endometriosis but can be reassuring, particularly as it can exclude an ovarian endometrioma that can be associated with endometriosis.
- There is no evidence that hormonal treatments improve the chance of pregnancy in women with endometriosis-associated subfertility
- The recommendation that laparoscopy is the gold standard diagnostic test for endometriosis is based on the Royal College of Obstetrician and Gynaecologists guideline *The investigation and management of endometriosis*[RCOG, 2006] and the European Society of Human Reproduction and Embryology (ESHRE) guideline *Management of women with endometriosis*[Dunselman et al, 2014].

Polycystic Ovarian Syndrome (PCOS)

- Chronic anovulation/ oligomenorrhoea
- clinical or biochemical hyperandrogenis
- polycystic ovaries on ultrasound
- Predisposes to Cardiovascular disease, Type 2 diabetes, obesity, thrombosis
- Genetic link

Causes PCOD

- Poorly understood
- characteristic polycystic ovary emerges when a state of anovulation persists for a length of time.
- Patients with PCOhave persistently elevated levels of androgens and oestrogens, which set up a vicious cycle.
- Obesity can aggravate PCOD - fatty tissues are hormonally active and they produce estrogen which disrupts ovulation .
- Overactive adrenal glands can also produce excess androgens, and these may also contribute to PCOD.
- These women also have insulin resistance (high levels of insulin in their blood, because their cells do not respond normally to insulin) of androgens and estrogens in PCOD

Treatments - polycystic ovary syndrome:

- Measure fasting glucose annually or If the fasting glucose level is 5.6 mmol/L or greater, perform an oral glucose tolerance test.
- Alternatively offer a glucose tolerance test every 2 years.
- weight loss – often cycles will come back to being regular if BMI is reduced and into a normal range
- Treat infertility if pregnancy is desired
- hormonal- oestradiol

Treatments – Polycystic Ovary Syndrome

- **Oligomenorrhoea or amenorrhoea -** If the woman has prolonged amenorrhea (less than one period every three months), abnormal vaginal bleeding, or excess weight:
  - Prescribe a cyclical progestogen (such as medroxyprogesterone 10 mg daily for 14 days) to induce a withdrawal bleed, *then*
  - Refer for a transvaginal ultrasound to assess endometrial thickness

- Medroxyprogesterone is indicated for endometrial protection from oestrogenic hormone replacement therapy as a 14-day course within each 28-day oestrogen hormone replacement therapy cycle

- A cyclical progestogen, such as medroxyprogesterone 10 mg daily for 14 days every 1–3 months.

Infertility in PCOs

- The National Institute for Health and Care Excellence recommend:
  - Clomifene citrate *or*
  - Metformin *or*
  - Clomifene in combination with metformin.
- Some experts recommend avoiding the use of metformin alone.

- GPs should prescribe clomifene citrate only as part of a formal shared-care agreement between primary and secondary care.
  - Women with PCOS should be offered clomifene citrate for a maximum of 6 months.
  - Women should be informed of the risk of multiple pregnancies associated with clomifene citrate.
  - Women undergoing treatment with clomifene citrate should be offered ultrasonographic monitoring during at least the first cycle of treatment, to ensure that they receive a dose that minimizes the risk of multiple pregnancy.

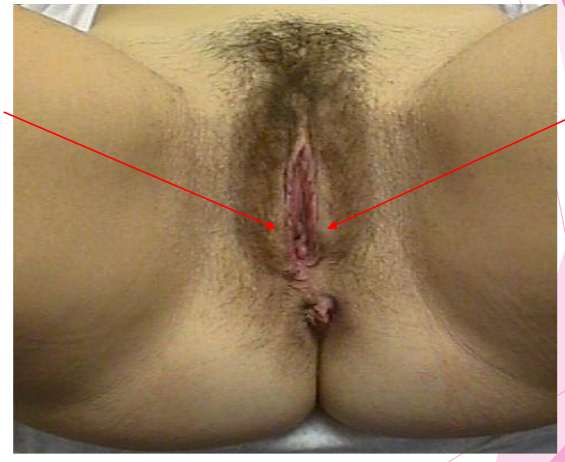
- No significant difference in number of live singleton births between metformin, metformin with clomifene and clomifene alone.

Gynaecological Lesions

- Abnormal lesions in the vagina, vulva and labia areas can be quite common and often easily treatable
- Need to be able to recognise common benign lesions to know when something is more unusual and may need a referral
- A good history of the lesion or condition is key to differentiating likely benign or sinister problems

Bartholin'sglands

- Two in number.
- Lie posteriolaterallyto the vaginal orifice, one on either side
- Normally not seen nor felt.
- If enlarged, can be a cyst or painful abscess



Bartholin's Gland Abscess (Bartholinitis)

- Signs and symptoms:

- Usually present with acute onset of pain and swelling, may have had previous episodes of similar lesions
- Perineal pain, fever, labial oedema, chills, malaise, and purulent discharge
- Systemic infection if not treated promptly
- Medical diagnosis based on history and examination
- Visual inspection; culture and sensitivity if weeping and open
- Treated with oral broad spectrum antibiotics such s co-amoxiclav but need review to ensure not developing an abscess as some require I&D

Pruritis Vulva

- **Take a history** to find an underlying cause for the vulval itch. Ask about:**Location, duration and onset of symptoms.**
  - Extragenital itch may indicate a more generalized problem such as eczema/dermatitis
  - Lichen sclerosus is normally confined to the vulva, typically does not affect the vagina and very rarely involves the oral mucosa
  - lichen planus may affect the vagina, skin, hair, nails, as well as genital and oral mucous membranes.
  - Acute onset is associated with allergic contact dermatitis, or vulvovaginal candidiasis (which is the most common cause of acute vulval itch).
  - Nocturnal vulval itching may indicate threadworm infestation (particularly if combined with perianal itch).

Medical history

- A personal or family history of skin disorders or atopic conditions such as hayfever, asthma, or eczema — a positive family history is observed in about 10% of patients with vulval lichen sclerosus, and up to 75% of people with lichen simplex chronicus have a personal or family history of atopy.
- Diabetes mellitus — the risk of candidal infection is increased.
- Systemic illness, such as renal or hepatic impairment, or anaemia can cause generalized pruritus.
- Faecal or urinary incontinence — these can damage the vulval skin either directly, or indirectly, by the use of sanitary products, or over washing.
- Menopause — symptoms may be caused by atrophic vaginitis.
- Breastfeeding can result in lowered oestrogen levels and consequent vulval symptoms.
- Consider Sexual History of appropriate to exclude any STI
- Stress or psychological issues can lead to itching

Treatment

- Dermatological: Lichen Simplex – betamethasone 1-2 weeks, Anxiolytic such as hydroxyzine at night. Emollient as soap substitute.
- Seborrheic Dermatitis: Ketoconazole shampoo.
- Contact Dermatitis : For mild itching, consider prescribing a mild potency topical corticosteroid ointment, such as hydrocortisone 1% for 7–10 days.
- Stronger potency corticosteroids (such as betamethasone or clobetasol) may be considered if, symptoms are severe, if the skin is lichenified, or to break the itch-scratch-cycle.
- Refer if not improving and also remember to review recurrent lesions as nature may change over time

Vaginitis

Infective vaginitis

- Management is against the organism. The common causes of infective vaginitis include:

- - Candida Albicans (thrush) – Topical clotrimazole 500mg pessary plus vulval cream or 150mg oral Fluconazole once only dose.
- - Bacterial Vaginosis – Metronidazole 2g orally once only dose
- - Trichomoniasis Vaginalis –Metronidazole 2g orally once only dose

Vaginitis

Atrophic vaginitis

- This is often due to low levels of oestrogen resulting in thinning of the vaginal wall and decreased lubrication. There are multiple management options for this including:

- - Encouraging the patient to use a water-soluble lubricant during intercourse
- - Vaginal moisturising cream
- - Avoidance of scented soaps, lotions and perfuse
- - Topical oestrogen for the vaginal wall

- Be aware that this can cause psychosexual problems in the patients' relationship.

Menopause

- Cessation of the menstrual cycle due to ovarian failure
- Median age: 52years.
- Determined in Utero.
- 1.5 million oocytes at birth.
  - 1/3rd lost by menarche.
- Peri-menopause – increased anovulatory cycles

Menopause: Definition

- **Menopause** is a biological stage in a woman's life when menstruation ceases permanently due to the loss of ovarian follicular activity. It occurs with the final menstrual period and is usually diagnosed clinically after 12 months of amenorrhoea.
- **Perimenopause,** also called the 'menopausal transition' or 'climacteric', is the period *before* the menopause when the endocrinological, biological, and clinical features of approaching menopause commence. It is characterized by irregular cycles of ovulation and menstruation and ends 12 months after the last menstrual period.
  - **Postmenopause** is the time after a woman has not had a period for 12 consecutive months.
- **Premature menopause,** also called 'premature ovarian insufficiency' or 'premature ovarian failure', is usually defined as menopause occurring before the age of 40 years

Menopause - Clinical Features

- Clinical Features: (affects 2/3rd woman)
  - Menstrual irregularity
  - Vasomotor
  - Musculoskeletal
  - Psychological
  - Urogenital
  - Cardiovascular
  - Osteoporosis
  - Breast disease

Menopause – Clinical Features

- Vasomotor.
  - Hot flushes, night sweats, disturbed sleep patterns, insomnia, irritability, short term memory loss and concentration.
- Sexual dysfunction.
  - Multifactorial.
  - Sexual desire disorders.
  - Sexual arousal disorders.
  - Orgasmic disorders.
  - Sexual pain disorders like Dyspareunia, Vaginismus, genital pain.
- Psychological symptoms.
  - Depressed mood, anxiety, irritability, mood swings, lethargy and lack of energy.
- Urinary symptoms.

Diagnosis Menopause

- Diagnosis should be based on clinical symptoms if >45
  - Perimenopause – vasomotor Sx & irregular periods
  - Menopause – no period for 12m & not taking contraception (Sx if no uterus)
- Consider FSH if…
  - >45 years with atypical symptoms
  - 40-45 years with Sx and change in periods
  - <45 years and suspecting premature menopause
- Laboratory results
  - Consistently raised FSH >30IU/l. Repeat on 2 occasions at least 6 weeks apart
  - Raised LH
  - Low serum oestradiol.

Assessment of Menopause

- Assess symptoms and their severity
- Assess risk of cardiovascular disease (Qrisk)
- Assess risk of osteoporosis
- Discuss her expectations
- Consider investigation if any sudden change in menstrual pattern (IMB, post coital)

Premature Menopause

- Menopause <40 years (1%).
- Risk of osteoporosis and IHD
- Diagnosis – FSH >30 with raised LH and low oestrogen on two occasions 4-6 weeks apart
- Management
  - Should have hormonal treatment with HRT or combined hormonal contraceptive until age of natural menopause & 5-10 yrs after
  - HRT can benefit BP/ CVS risks, but both HRT and combined contraceptive offer bone protection.
  - HRT **not** a contraceptive

Menopause treatments - HRT

- Indications
  - Relief of vasomotor or other menopausal symptoms
  - Prevention of osteoporosis
  - Premature ovarian failure
- Contraindications
  - Pregnancy, undiagnosed abnormal PV bleeding
  - Active thromboembolic disorder or MI
  - Breast disease or endometrial cancer
  - Active liver disease

Menopause Treatments - HRT

- Various preparation available:
  - Different strengths.
  - Combinations or Oestrogen Only
  - Route of administration.
- “Sequential” Vs “continuous”
- Routes: oral, transdermal, subcutaneous, Vaginal.
- Can start HRT before amenorrhea begins.

HRT Medication

- **Prescribe the lowest effective dose of hormone replacement therapy (HRT) for the shortest time possible.**
- **Oestrogen dose for symptom control**
  - Older women may be less tolerant of oestrogen and need to start (and are usually maintained) on a lower dose (for example 1 mg of oral estradiol or 25–50 micrograms of transdermal estradiol).
  - Younger women may require higher doses (for example 2–4 mg of oral estradiol or 100 micrograms of transdermal estradiol) to remain symptom-free.
  - Tailor the dose to the symptoms, as the ingested or applied dose may not be well absorbed.
- **Progestogens for endometrial protection**
  - Different progestogens used in combined oral HRT provide adequate endometrial protection. For example, oral norethisterone provides:
    - In a cyclical preparation, 1 mg for the last 12–14 days of a 28-day cycle.
    - In a continuous preparation, 0.5–1 mg.

HRT Medication

- Latest studies suggest some reduced risks when using transdermal oestrogen with added progesterone cover
- Progesterone can be given as oral micronised progesterone (utrogestan) or via a Mirena IUS device
- Transdermal oestrogen can be given as a patch twice weekly or a daily dose of oestrogen gel

HRT - Counselling Points

- Irregular bleeding is common in first 3-6 months
  - (Bleeding > 6mnths/ after amenorrhoea requires Ix)
- Importance of adherence with treatment
- Remind peri-menopausal women that HRT is not a contraceptive
- No evidence that HRT causes weight gain

HRT Follow up

- 1st visit after start of treatment in 3 months.
- Then after evaluation every 6-12 months
- BP monitoring every 6/12.
- Contraception:
  - Continue contraception for 2 years after last period if women <50years.
  - One year contraception after last period if >50 years.
  - Mirena IUS only contraception that can be used as progesterone arm of HRT

Expect side effects

- Estrogen related: fluid retention, bloating, breast tenderness. Nausea, headache, leg cramps, dyspepsia
- Progesterone related: migraines, headache, fluid retention, depression, acne, mood swings.
- Common to both: weight gain, poor cycle control and BTB

Bleeding

- **Unscheduled vaginal bleeding** is a common adverse effect of hormone replacement therapy (HRT) within the first 3 months of treatment.
- **Monthly cyclical regimens should produce regular predictable bleeding starting towards or soon after the end of the progestogen phase.** Unpredictable or unacceptable bleeding may be due to non-adherence to therapy, drug interactions, gastrointestinal upset (which can interfere with absorption), or gynaecological cancer.

  If serious gynaecological pathology has been excluded, altering the progestogen part of the regimen may improve bleeding problems

  Consider use of Mirena IUS with oestrogen only prep if bleeding is problematic

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

- **Continuous combined HRT** commonly produces irregular breakthrough bleeding or spotting in the first 4–6 months of treatment.

Studies on HRT

- Women`s health initiative and Million women study .
- WHI:
  - Risk of breast cancer in estrogen alone group was 23% lower than placebo group.
  - In combined HRT group increase in risk emerged after 3 years of randomisation.
- Million women study:
  - Increased risk of breast cancer in all HRT regimen.
  - Greatest risk with combined group.
  - The pattern of progesterone administration did not change the risk.

HRT Risks (over 5 years)

- Breast cancer
  - Background risk is 15/1000. 2-6/1000 extra cases
- Ovarian cancer
  - Background risk is 2/1000. <1 extra case over 5 yrs
- Endometrial cancer
  - Combined HRT protects endometrium
  - B/G risk is 2/1000. 4 extra cases over 5 yrs (oestrogen only)
- Venous thromboembolism
  - Background risk is 5/1000. 2 extra cases over 5 yrs
- Cardiovascular disease
  - No increased risks in those with no pre-existing CVS disease

HRT Risks (in perspective)

- Breast cancer
  - <>2-3 units alcohol per day increases risk by 1.5x
  - Post menopausal obesity increases risk by 1.6x
  - First pregnancy >30 years increases risk by 1.9x
  - 5 years of HRT increases risk by 1.35x

Stopping HRT

- **Explain that:**
  - **For vasomotor symptoms,** most women require 2–5 years of HRT, 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 due to oestrogen withdrawal
  - **Topical (vaginal) oestrogen** may be required long term. Regular attempts (at least annually) to stop treatment are usually made. Symptoms may recur once treatment has stopped.
  - **Women with premature menopause** usually take HRT up to the average age of the natural menopause (51 years), after which the need for HRT should be reassessed. Some women will still be symptomatic.

Stopping HRT

- **Offer women who wish to stop HRT a choice of gradually reducing or immediately stopping treatment.** Explain that:
  - Gradually reducing or immediately stopping HRT makes no difference to their symptoms in the longer term.
  - Gradually reducing HRT may limit recurrence of symptoms in the short term.
  - Symptoms of urogenital atrophy often come back when treatment with vaginal oestrogen is stopped. Consider using vaginal HRT longer term to control these symptoms

Menopause – Other treatment options

- Lifestyle Modifications – Diet, exercise, stop smoking
- Alternative Therapies – Isoflavines (red clover) and Black Cohosh, acupuncture, reflexology

- Hot flushes
  - Progestogens, clonidine, SSRI, Gabapentin, propranolol.
- Vaginal atrophy
  - Lubricants, moisturizers (Replens, sylk)
- Osteoporosis:
  - Bisphosphonates, Alendronate, SERMs like raloxifene, Strontium, para thyroid hormone, calcitonin.
- Mood changes
  - SSRI's / Venlafaxine NICE do not use SSRIs/SNRIs as first line for women in menopause

Management of Co Morbidities

- **For menopausal women with, or at high risk of, breast cancer:**
  - Provide information on non-hormonal and non-pharmacological treatments
  - Offer referral to a healthcare professional with expertise in menopause.
- **For women at increased risk of venous thromboembolism (VTE):**
  - Consider prescribing transdermal hormone replacement therapy (HRT) rather than oral HRT as less risk
  - Refer menopausal women at high risk of VTE (for example those with a strong family history of VTE or a hereditary thrombophilia) to a haematologist for assessment before considering HRT.
- **For women with cardiovascular risk factors (for example hypertension):**
  - HRT can be considered; however, cardiovascular risk factors should be managed and BP should be well controlled
- **For woman with type 2 diabetes:**
  - Consider HRT after taking comorbidities into account and seeking specialist advice if needed.
  - Advise that HRT is not associated with an adverse effect on blood glucose control.
- **For women with hypothyroidism:**
  - Monitor their thyroid function regularly to ensure that thyroid hormone levels remain in the acceptable range.

Useful websites

www.thebms.org.uk

www.menopausematters.co.uk

www.mapofmedicine.com

- Information on support groups, such as:Menopause Matters (www.menopausematters.co.uk) — provides information on the menopause, menopausal symptoms, and treatment options.
- The Daisy Network (www.daisynetwork.org.uk) — a nationwide support group for women who have suffered a premature menopause.