Phases of female reproductive cycle

- Regular cycles
  - ‘premenopause’
- Change in cycle frequency
  - ‘early perimenopause’
- Cycles up to 3-12 months apart
  - ‘late perimenopause’
- Final menstrual period
  - ‘menopause’ (average age 51 years)
- No menstrual cycles >12 months
  - ‘postmenopause’

Based on symptom report only. Hormonal screening unreliable due to unpredictable fluctuations. FSH levels may be helpful in young women.

Commonly reported menopausal symptoms include:

- Hot flushes
- Night sweats
- Muscle/joint pains
- Anxiety
- Irritability
- Sleep disturbance
- Lessened concentration
- Vaginal dryness
- Painful intercourse
- Fatigue
- Crawling sensations on skin
- Overall diminished wellbeing
- Low libido

Routine screening

Menopausal women are at increased risk of:
- heart disease, osteoporosis, central adiposity, mood disorders.

- Exclude – thyroid, diabetes, iron deficiency, drug side effects
- Bleeding changes – recent changes in bleeding pattern including heavy bleeding
  - Investigate for iron deficiency and gynaecological pathology
- Check last cervical screening test and mammogram
- Metabolic syndrome – monitor BP, cholesterol, blood glucose, abdominal girth and weight
  - discuss with patient the need to increase activity and monitor caloric intake
- Bone density – see bone health section
- Smoking – discuss with patient the need to cease smoking

Key messages

- Hot flushes – dress in layers, natural fibres, reduce weight, reduce alcohol, increase activity, reduce caffeine, healthy diet
- Dry vagina – local treatments: vaginal oestrogen cream, pessaries and tablets. Encourage patients to select vaginal lubricants and moisturisers most similar (in pH and osmolality) to natural vaginal secretions, as this may make them less likely to cause irritation
  - There are many vaginal lubricants (for use during intercourse) for urogenital symptoms and vaginal dryness. Those listed in pink meet the suggested pH and osmolality composition: Astroglide®, KY® Jelly, pjur® and Yes®. It is also possible to use natural oils eg olive, sweet almond oil
  - Vaginal moisturisers (for regular, twice weekly use): Replens®, Yes®
- Emotional health – ask initial screening questions (back page)
- Stress management – discuss with patient the need to actively manage stress and mood eg activity, mindfulness, social connectedness
- Diet – phytoestrogen diet may assist in symptom reduction

Use of natural supplementation

There is some evidence of effectiveness for the following supplements:
- Black cohosh (Remifemin® and Femular®) – decrease hot flushes. Monitor for signs of liver toxicity.
## HRT/MHT* candidates

- Women experiencing menopausal symptoms (peri or postmenopause)
- Women with early or premature menopause (bone sparing and reduces CVD risk)
- Women with osteoporosis <60 years
- Women within 5-10 years of last period for vasomotor symptoms

**In general use:** lowest effective HRT/MHT dose for the short-term relief of menopausal symptoms, except for early/premature menopause – higher dose and long-term therapy. Effectiveness monitored by self-reported symptom control.

## Contraindications for HRT/MHT

(consider referral to menopause specialist)

- Breast cancer (hormonally sensitive)
- Thrombophilia/past venous thrombo-embolic event (VTE)
- Undiagnosed vaginal bleeding
- Active liver disease
- Uncontrolled hypertension
- CVD risk or disease

## Alternatives to HRT/MHT

### Pharmaceutical

<table>
<thead>
<tr>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escitalopram</td>
</tr>
<tr>
<td>10-20mgs daily</td>
</tr>
<tr>
<td>Venlafaxine</td>
</tr>
<tr>
<td>37.5-75mgs daily</td>
</tr>
<tr>
<td>Desvenlafaxine</td>
</tr>
<tr>
<td>50-100mgs daily</td>
</tr>
<tr>
<td>Paroxetine**</td>
</tr>
<tr>
<td>7.5-10mgs daily</td>
</tr>
<tr>
<td>Gabapentin</td>
</tr>
<tr>
<td>300-900mgs daily</td>
</tr>
<tr>
<td>Clonidine</td>
</tr>
<tr>
<td>50-150mcg daily</td>
</tr>
</tbody>
</table>

** (not to be used with Tamoxifen)

## Women with a uterus: important to note that HRT/MHT is not a contraceptive

### Early (<45 years)/premature (<40 years) menopause

Continue HRT/MHT until 50 years unless contraindicated. Higher doses usually required.

**Options:**

1. Continuous oestrogen
   - (high dose oestrogen due to age)
   - + cyclical or continuous progestogen
2. Combined contraceptive
3. Tibolone

### Menopausal transition

Dosage: lowest effective dose monitored by self-reported symptom control

**Options:**

1. Low dose combined contraceptive
   - (if low CVD risk & <50 years)
2. Continuous oestrogen
   - + cyclical progestogen 10-14 days each month
   - + contraception (including barrier, sterilisation)
3. Continuous oestrogen
   - + levonorgestrel IUD for progestogen and contraception

### Postmenopause

Dosage: lowest effective dose monitored by self-reported symptom control

**Options:**

1. Continuous oestrogen
   - + continuous progestogen
   - (if menopause >1-2 years ago)
2. Continuous oestrogen
   - + cyclical progestogen
   - (if menopause <1 year ago)
   - or levonorgestrel IUD
3. Tibolone (if menopause is >1-2 years ago)
4. Tissue-selective oestrogen complex (TSEC)

**Review:** initially 2-6 months then assess benefits/side effects, address concerns, titrate regimen to suit the individual woman – assess need, new development/options, CVD and breast cancer risk. Then annual review.
**Special considerations**

**After hysterectomy**
Continuous oestrogen or tibolone.

**Androgen deficiency**
Not OCP or oral oestrogen; use transdermal oestrogen to lower SHBG; consider testosterone if low calculated free testosterone, or tibolone.

**Breast cancer**
Refer to HRT/MHT contraindications. Vaginal oestriol for vaginal and urinary symptoms.

**Cardiovascular disease (hypertension, diabetes, hypercholesterolemia)**
Use transdermal if menopausal symptoms bothersome.

**Compounded hormones**
Advise against compounded bioidentical hormone therapy as not TGA approved.

**Endometrial cancer**
Tibolone or HRT/MHT (refer to menopause expert/ liaise with oncologist/gynaecologist), usually only stage 1.

**Endometriosis**
OCP, levonorgestrel IUD + oestrogen, tibolone, continuous combined HRT/MHT; with post-surgical menopause need to consider added progestogen/tibolone.

**Fibroids**
No special regimen; theoretically may increase in size – less likely with tibolone or transdermal oestrogen and progestogen.

**Hirsutism**
Oral oestrogen to increase SHBG: cyproterone, dydrogesterone, drospirenone or oral progesterone as progestogen. Can also use spironolactone.

**Liver disease, gallstones**
Transdermal.

**Mastalgia**
Lower dose, transdermal oestrogen, tibolone, testosterone, evening primrose oil caps.

**Migraine**
Transdermal oestrogen and progestogen, lower dose, avoid oral progestogens; continuous therapy, not cyclic.

**Obesity/morbid obesity**
Transdermal.

**Ovarian cancer**
No special regimen. Liaise with oncologist/ gynaecologist, as some cancers are hormonally sensitive.

**Progestogen side effect**
Change progestogen, tibolone.

**PV bleeding**
Investigate to determine cause and exclude pathology prior to treatment – transvaginal ultrasound +/- hysteroscopy.

If atrophic endometrium (<4mms on US), reduce progestin/increase oestrogen. Otherwise, increase progestin dose/ length/type; levonorgestrel IUD.

**Testosterone therapy**
Testosterone 1% cream (for women) is TGA approved for clinically diagnosed hypoactive sexual desire disorder (HSDD) or low sexual desire with distress, when all other causes are excluded. Free testosterone is measured to exclude a high level.

**Urogenital symptoms alone**
Vaginal oestradiol/oestriol – regular use 2-3 times weekly.

**Varicose veins**
Transdermal or tibolone preferred routes of administration.

**VTE/thrombophilia**
Assess baseline risk; high risk if VTE recurrent, spontaneous, with pregnancy/OCP, family history, smokers; screen for inherited thrombophilia. If normal and low risk, use transdermal or tibolone. If high risk or inherited thrombophilia, avoid HRT/MHT unless anticoagulated; seek specialist haematological advice re use of transdermal HRT/MHT.

**Weight increase**
Not related to HRT/MHT.
## Bone health

### Indications for bone density assessment:
- Family history of osteoporosis
- Overactive thyroid or parathyroid
- Malabsorption eg coeliac disease, inflammatory bowel disease
- Some chronic diseases eg rheumatoid arthritis, chronic liver or kidney disease
- Corticosteroid use or exposure
- Some medicines for breast cancer and epilepsy and some antidepressants

### Osteoporosis
- T-score below -2.5
- Rx aim: prevent further bone loss and fracture
  - Plain X-ray thoracic lumbar spine to exclude compression fracture
- Exclude other causes:
  - Calcium, phosphate, vit D, PTH, TFT, LFT, ESR, serum/urine protein electrophoresis, coeliac antibodies
  - Use FRAX risk calculator
- Regular weight bearing exercise, optimise calcium intake + vit D levels:
  - HRT/MHT <60 years
  - Tibolone <60 years
  - Bisphosphonates
  - Raloxifene
  - Denosumab
  - Monitor bone density, DXA 2 yearly and bone markers
- If T-score between -2.0 to -2.5 and they are high fracture risk
  - Refer to specialist for consideration:
    - HRT/MHT <60 years
    - Tibolone <60 years
    - Bisphosphonates
    - Raloxifene
    - Denosumab
    - Monitor bone density, DXA 2 yearly and bone markers

### Osteopenia
- T-score between -1.0 to -2.5
- Rx aim: prevent further bone loss
  - Plain X-ray thoracic-lumbar spine to exclude compression fracture
- Regular weight bearing exercise, optimise calcium intake + vit D levels
  - Use FRAX risk calculator
- Monitor bone density DXA 2-5 yearly.

### Normal
- T-score above -1.0
- Rx aim: prevent further bone loss and fracture
  - Regular weight bearing exercise, optimise calcium intake + vit D levels
- Monitor bone density at 70 years or earlier if requested

**Note:**
- Normal: T-score above -1.0
- Osteopenia: T-score between -1.0 to -2.5
- Osteoporosis: T-score below -2.5

**Exclude other causes:**
- Calcium, phosphate, vit D, PTH, TFT, LFT, ESR, serum/urine protein electrophoresis, coeliac antibodies
- Use FRAX risk calculator
Assessment of emotional wellbeing in menopausal women

Women experiencing premature or early menopause are at increased risk of depression and anxiety. Routine screening is recommended for this patient group.

**Disclaimer:** these are general recommendations which must be modified according to the clinical presentation and desires of the individual woman after she has been fully assessed and informed of all available options.

**Initial screening questions**

1. During the past month have you often been bothered by feeling down, depressed or hopeless?
2. During the past month have you often been bothered by having little interest or pleasure in doing things?
3. During the past month have you been bothered by feeling excessively worried or concerned?

**Screening tools for depression and anxiety**

- Kessler Psychological Distress Scale 10 (K-10)
- Depression Anxiety Stress Scale (DASS-21)
- Patient Health Questionnaire (PHQ9)
- Generalised Anxiety Disorder Assessment (GAD7)

*Change in terminology: Hormone replacement therapy (HRT) is now frequently referred to as menopausal hormone therapy (MHT).*

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