Guidelines for Management of Menopause

2010

Sultanate of Oman
Ministry of Health
Directorate General of Health Affair
Department of Family & Community Health
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</tr>
<tr>
<td>--------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>BID</td>
<td>Twice a Day</td>
</tr>
<tr>
<td>BMD</td>
<td>Bone Mineral Density</td>
</tr>
<tr>
<td>BP</td>
<td>Blood Pressure</td>
</tr>
<tr>
<td>CBC</td>
<td>Complete Blood count</td>
</tr>
<tr>
<td>D.M</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>FBC</td>
<td>Fasting Blood Sugar</td>
</tr>
<tr>
<td>HRT</td>
<td>Hormone Replacement Therapy</td>
</tr>
<tr>
<td>HTN</td>
<td>Hypertension</td>
</tr>
<tr>
<td>LFT</td>
<td>Liver Function Test</td>
</tr>
<tr>
<td>LMP</td>
<td>Last Menstrual Period</td>
</tr>
<tr>
<td>mcg</td>
<td>Microgram</td>
</tr>
<tr>
<td>OD</td>
<td>Once per Day</td>
</tr>
<tr>
<td>RFT</td>
<td>Renal Function Test</td>
</tr>
<tr>
<td>TID</td>
<td>Three Times a Day</td>
</tr>
<tr>
<td>TVS</td>
<td>Trans-vaginal Scan</td>
</tr>
</tbody>
</table>
Preface

In Oman the population pyramid in 2008 shows that 14.16% of females are in the ages of 40 years and above. This percentage is expected to increase, taking into account the current life expectancy, which is 75 years. It is well known that females in this age group usually enter a life cycle change due to peri-menopause and menopause, which usually affect their quality of life. Hence, the special health needs of this category of women have to be attended to.

To meet women’s peri-menopausal and menopausal health needs and to improve their overall health, the program of menopausal health care has been included in the 7th five-year plan.

The objectives of this program are:
1. Screening of medical problems and malignancies common to menopausal age
2. Managing existing health conditions and symptoms related to estrogen reduction

Hence, in-order to build and strengthen the capacity of providers in giving standardized comprehensive health care to peri-menopausal, menopausal and postmenopausal women, the Dept. of Family and Community Health of Ministry of health - Oman developed practical clinical guidelines at different service level.

The guidelines are divided into six sections, these are:
1. Section One : Policy Guidelines
2. Section Two : Tasks of Menopausal Health Care
3. Section Three: Understanding Menopause
4. Section Four: Management of common peri-menopause and menopausal symptoms & conditions
5. Section Five : Hormone Replacement Therapy
6. Section Six : Abnormal vaginal bleeding in post-menopausal women

These Guidelines are not meant to replace textbooks. Hence, when-ever detailed information is required, textbooks and other latest references should be used for gaining in-depth knowledge and understanding of the subject.
Section One
Policy Guidelines
Section One: Policy Guidelines

Menopause is a major event in the women’s life cycle where remarkable physiologic changes take place at both physical and psychological levels with occurrence of symptoms and conditions that affect the quality of life. In order to address these changes, the Ministry of Health is extending its services with the following goals:

- To improve woman’s physical and psychological health
- To reduce mortality and morbidity of peri-menopausal and menopausal women

Hence, services for evaluation and management of common peri-menopausal and menopausal medical conditions will be provided as an essential and integral component of maternal and child health services through the Ministry of Health network of health centres and hospitals of all levels in all regions.

The Services will target

1. Women of age 40 years and above who present with symptoms related to menopausal change.

2. Women with premature menopause (refer to annex –1 page 41).

These Services will include

1. Clinical services: clinical evaluation, investigation and management. The provision of these services will vary from the primary to referral health care level

2. Counseling: will be done at all levels by the providers trained in counseling skills.

3. Health education: through sessions and provision of educational material
Section One: Policy Guidelines

Who will provide these services

All health personnel who are trained on peri-menopausal and menopausal health change, its related symptoms and conditions and their management.

Services at different levels:

- **At Primary Health Care Level**
  
The staff at this health care level care will conduct initial evaluation, screening and preventive measures as well as first line management and referral of cases to secondary health care level whenever needed.

- **At Secondary & Tertiary Health Care Level**
  
  Gynecologist in menopause clinic will further evaluate and manage referred women, and might collaborate with other specialties in the facility if needed.
Section Two
Tasks of Menopausal Health Care
In order to achieve above-mentioned goals the following tasks must be carried out:

- **At primary health care level**

  The staff at primary health care level will perform the following tasks:

  - History taken and physical examination including:
    - Evaluation of individual risk factors for conditions such as breast cancer, endometrial cancer, cardiovascular conditions and osteoporosis etc.
    - Perform investigation according to clinical findings
  - Counsel on possible risk and necessary lifestyle modification
  - Train on breast self examination (refer to screening for breast cancer - Operational guidelines)
  - Refer to secondary care level for further management if needed

### Evaluation of peri-menopausal & menopausal women

- **Menstruation, contraception and symptoms**
  - Date of LMP (could she be pregnant)
  - Contraception
  - Frequency, heaviness & duration of period
  - Hot flushes & night sweats
  - Vaginal dryness
  - Dyspareunia, urinary symptoms

- **Personal, family & medical**
  - Breast, ovarian or endometrial cancer in close family members
  - Risk factors for osteoporosis
  - Risk factors for heart disease & strokes
  - Deep vein thrombosis or pulmonary embolism
  - Liver disorders

* Refer to annex- 3 for BMI page 42
**(refer to screening for breast cancer- Operational guidelines)
Section Two: Tasks of Menopausal Health Care

- At Secondary Health Care Level

Gynecologist at secondary health care level should perform the following:

- Further evaluate the referred women
- Management including Hormone Replacement Therapy (HRT), calcium and vitamin D according to clinical evaluation and individualized women’s needs. These drugs should not be started without baseline workup.
- Consult other specialties like surgeon, etc.
- Refer women to tertiary health care if needed

- At Tertiary Health Care Level

- Referred women will be clinically re-evaluated, investigation previously done will be reviewed and further special tests required will be carried out like Bone Mineral Density (BMD) etc.

All along woman should be kept informed about the finding of clinical evaluation, investigation and management planned.
Section Three
Understanding Menopause
Section Three: Understanding Menopause

Definition

The word menopause means the cessation of menses due to failure of ovarian follicular development, and is commonly used instead of climacteric, a wider term for events leading up to and following the menopause (refer to annex-1 page 41). The median age at which the menopause occurs is 51 years, with a range of 41-55.

Diagnosis of menopause

Menopause is usually diagnosed by the presence of amenorrhea for a period of 6-12 months together with occurrence of hot flashes. Confirmation of menopause can be done if in doubt by hormonal assay of serum levels of LH, FSH and estradiol.

<table>
<thead>
<tr>
<th></th>
<th>FSH (U/liter)</th>
<th>LH (U/liter)</th>
<th>Oestradiol (p mol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-menopause</td>
<td>2-20</td>
<td>5-25</td>
<td>100-600</td>
</tr>
<tr>
<td>Post-menopause</td>
<td>40-70</td>
<td>50-70</td>
<td>60</td>
</tr>
</tbody>
</table>

The change in hormone levels, particularly the decline in estrogen levels that occurs during the climacteric phase, causes acute symptoms such as vasomotor symptoms and chronic conditions like osteoporosis.

ACUTE (short term squeal) → CHRONIC (long term squeal)
and/or early onset and or later onset
Table 1: common symptoms & conditions of menopause

<table>
<thead>
<tr>
<th>Vasomotor symptoms</th>
<th><strong>Psychological symptoms</strong></th>
<th>Uro-genital tract symptoms</th>
<th>Skeletal</th>
<th>Cardio-vascular disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>• *Hot flushes</td>
<td>• Emotional liability.</td>
<td>• Vaginal atrophy (dryness, burning)</td>
<td>• ***Osteoporosis</td>
<td>• Ischemic heart disease</td>
</tr>
<tr>
<td>• Sweats</td>
<td>• Anxiety</td>
<td>• Dyspareunia</td>
<td>• Vertebal crush fracture</td>
<td>• Cerebro-vasuclar disease</td>
</tr>
<tr>
<td>often associated with palpitation</td>
<td>• Depressed mood</td>
<td>• Prolapse</td>
<td>• Femoral neck fracture</td>
<td></td>
</tr>
<tr>
<td>• Panic attacks</td>
<td>• Poor memory concentration</td>
<td>• Urgency</td>
<td>• backache</td>
<td></td>
</tr>
<tr>
<td>• Insomnia</td>
<td>• Irritability</td>
<td>• Frequency</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Decrease libido</td>
<td>• Dysuria</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Urinary incontinence</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Voiding difficulties</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Hot flushes and night sweats are the most common symptoms of menopause, although they may begin before the cessation of menses. The prevalence of flushes is highest in the first year after the final menstrual period. Hot flushes have been reported in up to 75% of women undergoing natural menopause and in almost all women undergoing surgical menopause.

- Women with hot flushes have twice the rate of insomnia as women without hot flushes. It is important to note that there are many additional causes of insomnia; so attributing insomnia to menopause simply because of a woman’s menopausal transition status is not advised.

Hot flushes → Disturbing normal sleep → insomnia, irritability and difficulty in concentration.
Note:

** These psychological problems are also likely to be associated with past problems and current life stresses such as lack of social support and previous history of depression including postpartum depression.

*** Osteoporosis is defined as a reduction in bone mineral density by $\geq -2.5$ S.D of the mean. It increases risk skeletal fragility and fractures.
Section Four
Management of Common Symptoms & Conditions
Vasomotor symptoms:

- Evaluate risk factors
  - Modifiable risk factors that increase the risk of hot flashes: cigarette smoking, spicy food, caffeine, alcohol, smoking, change in temperature, and body mass index > 30 kg/m².
  - Non-modifiable risk factors: menopause (natural and surgical)

- Exclude other causes of hot flashes as clinically indicated.
  These can be:
  - Hyperthyroidism
  - Pancreatic mast cell disease
  - Systemic mast cell disease
  - Panic disorder
  - Carcinoid syndrome
  - Pheochromocytoma

- Counseling (refer to annex-3 page 43)

- Pharmacological treatment: Alleviation of vasomotor symptoms after failure of general lifestyle modification measures.
  - Hormonal Replacement Therapy (refer to section Five page 27). Short-term treatment should be continued for a minimum of 6 months up to longer period (4-5 years) if required.
Section Four: Management of Common Symptoms & Conditions

- HRT alternatives (Fluoxetine 20mg orally daily) if in case of contraindications to HRT or if woman dose not wish to use hormone therapy.

Urogenital tract symptoms:

- Treat urinary tract infection if present
  - Simple versus complicated or according to urine culture
  - Amoxicillin 500 mg TID for 5-7 days

- Counseling (refer to annex-3 page 43)

- Hormonal treatment:
  - Hormone replacement therapy: preferably topical vaginal preparation
    (Premarin vaginal cream, if HRT is being prescribed solely for uro-genital symptoms (refer to section Five page 27)

- Conservative management
  - Pelvic floor exercise
  - Pessary (if prolapse present & woman has risk for surgery

- Surgical management of
  - Uterine prolapse
  - Urinary incontinence
Psychological symptoms

- **Evaluate underlying contributing factors:** past problems and current life stress such as lack of social support, economic status, emotional issues, and previous history of depression including postpartum depression.

- **Counseling** (refer to annex-3 page 43)

- **Pharmacological treatment:**
  - Hormone replacement therapy appears to improve mood and sleep quality. Its use should be preceded with informed choice (refer to section Five page 27)

- **Referred to psychiatrists if needed**
Section Four: Management of Common Symptoms & Conditions

- **Osteoporosis:**

  It is defined as a reduction in bone mineral density by equal or more than - 2.5 S.D of the mean.

- **Evaluate risk factors for osteoporosis:**

  The most important risk factors for osteoporosis in clinical practice are shown in table 2

### Table 2: Risk factors for osteoporosis

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic</td>
<td>Family history of adult fracture (particularly in a first degree relative with hip fracture)</td>
</tr>
<tr>
<td>Constitutional</td>
<td>Low body weight / low BMI</td>
</tr>
<tr>
<td></td>
<td>Early menopause &lt; 45</td>
</tr>
<tr>
<td></td>
<td>Personal history of fall / fracture</td>
</tr>
<tr>
<td>Environmental</td>
<td>Low calcium intake/ vitamin D Deficiency, high protein diet</td>
</tr>
<tr>
<td></td>
<td>Cigarette smoking/ high caffeine intake</td>
</tr>
<tr>
<td></td>
<td>Alcohol abuse</td>
</tr>
<tr>
<td></td>
<td>Sedentary lifestyle/immobilization/ Poor sun exposure</td>
</tr>
<tr>
<td>Drugs</td>
<td>Use of Corticosteroids, &gt; 7.5 mg prednisolone or equivalent daily</td>
</tr>
<tr>
<td></td>
<td>prolonged heparin therapy</td>
</tr>
<tr>
<td>Diseases</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td></td>
<td>Hyperparathyroidism</td>
</tr>
<tr>
<td></td>
<td>Hypogonadism</td>
</tr>
<tr>
<td></td>
<td>Cushing’s disease</td>
</tr>
<tr>
<td></td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td></td>
<td>Malabsorption syndromes</td>
</tr>
<tr>
<td></td>
<td>Diabetes Mellitus type I</td>
</tr>
</tbody>
</table>
**Section Four: Management of Common Symptoms & Conditions**

- **Perform Bone Mineral Density (BMD) if woman:**
  1. Has primary amenorrhea or secondary amenorrhea including that resulting from oophorectomy + hysterectomy at age less than 45 years
  2. Older than 50 years and suspected to be osteoporotic on x-ray or clinically through height loss or low impact fracture such as Colles’ radial fracture or fracture of any peripheral bone excluding the digits 3.
  3. Has a medical condition that predisposes to osteoporosis such as metabolic bone disease, thyroid disease, liver disease, mal-absorption syndromes
  4. Has used or is using systemic corticosteroid with a daily dose > 7.5 mg prednisolone or equivalent for a projected duration of 3-6 months or longer.
  5. Has a history of fracture, particularly hip fracture in a first degree relative

- **Counseling** (refer to annex-3 page 35)
  
- **Prevention:**
  - life style modification (smoking cessation, moderate exercise)
  - Calcium supplementation 500 – 800 mg / day
  - vitamin D 800 IU / day

- **Pharmacological treatment:**
  - calcium supplement: 1000-1500 mg/ day
  - vitamin D (Alfacalcidol) 0.25 mcg OD
Section Four: Management of Common Symptoms & Conditions

- Bisphosphonates: alendronic acid 10 mg daily or 70 mg once a week for the treatment of osteoporosis and 5 mg daily or 35 mg once a week for prevention of osteoporosis. Woman should be counseled to swallow the tablets with full glass of water at least 30 minutes before breakfast (and any other medication) and not to lie down after swallowing the tablets for at least 30 minutes.

- Calcitonin: Calcitrol 0.25mcg BID

- With or without Hormone replacement therapy: usual recommended dose at least 0.625mg conjugated equine estrogen (Premarin) orally daily or equivalent (see section Five page 31)
Algorithm 1: Screening and Management of osteoporosis

Previous fragility fracture or x-ray evidence of fracture

Low estrogen due to premature menopause, prolonged amenorrhea, etc

Family history of osteoporosis or fracture in a first degree relative

Medical disorders
- Hypothyroidism
- Malabsorption
- Liver disease
- Metabolic bone disease

Glucocorticoid therapy > 7.5mg oral prednisolone / day

Investigate with BMD

Management
Guided by BMD results/age/patient preference

Consider investigations for secondary causes

Investigate with BMD

Normal
Life style advice
Exercise & high calcium diet
Observe for change

Mild osteopenia
Treatment
- calcium & vitamin D
- Life style advice (Exercise & high calcium diet)

Severe osteopenia or osteoporosis
Treatment
- Dietary and exercise advice
- calcium & vitamin D biphosphonates
- (+/-) HRT

Refer to endocrinologist for
- Severe osteoporosis
- Treatment failure
- Suspected secondary osteoporosis

Follow up
Cardiovascular disease:

- Control risk factors for cardiovascular disease such as BP, diabetes, hyperlipidemia, lifestyle stressor…etc.

- Counsel on lifestyle modification

- Refer to physician if indicated

- HRT should not be used for treatment of primary cardiac lesion

HRT should not be used for primary or secondary prevention of cardiovascular diseases
### Table 2: Management of Common Peri-menopausal & Menopausal Symptoms and Conditions according to health care facilities levels

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Primary Health Care Level</th>
<th>Secondary Health Care Level</th>
<th>Tertiary Health Care Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasomotor symptoms</td>
<td>▪ Counseling</td>
<td>▪ HRT</td>
<td>▪ HRT</td>
</tr>
<tr>
<td></td>
<td>▪ Health education</td>
<td>▪ Alternative therapy to HRT</td>
<td>▪ Alternative therapy to HRT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Health education</td>
<td>▪ Health education</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Counseling</td>
<td>▪ Counseling</td>
</tr>
<tr>
<td>Urogenital atrophy</td>
<td>▪ Rx of urinary tract infection if present</td>
<td>▪ HRT (local)</td>
<td>▪ HRT (local)</td>
</tr>
<tr>
<td></td>
<td>▪ Counseling</td>
<td>▪ Management of uterine prolapse and urinary incontinence if resources available</td>
<td>▪ Management of uterine prolapse and urinary incontinence</td>
</tr>
<tr>
<td></td>
<td>▪ Health education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>▪ Evaluation of risk factors</td>
<td>▪ Calcium supplement/ Vitamin D</td>
<td>▪ Bone Mineral Density (BMD)</td>
</tr>
<tr>
<td></td>
<td>▪ Health education</td>
<td>▪ Bisphosphonates</td>
<td>▪ Calcium supplement</td>
</tr>
<tr>
<td></td>
<td>▪ Counseling</td>
<td>▪ HRT</td>
<td>▪ Bisphosphonates</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Health education</td>
<td>▪ Vitamin D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Counseling</td>
<td>▪ Calcitonin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>▪ HRT</td>
</tr>
<tr>
<td>Psychological symptoms</td>
<td>▪ Evaluation of underlying contributing factors</td>
<td>▪ HRT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Health education</td>
<td>▪ Referral to psychiatrist if needed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Counseling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular symptoms</td>
<td>▪ Evaluation of risk factors</td>
<td>▪ Management in collaboration with cardiologist/physician</td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Control of HTN, D.M, weight management</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Algorithm 2: Summary of Management of the Menopause / use of hormone replacement therapy

- **Osteoporosis**
  - **-ve risk factors**
    - Observe for change
  - **+ ve risk factors**
    - BMD

- **Cardiovascular disease**
  - **+ ve risk factors**
    - Observe for change

- **Urogeential atrophy**
  - **- ve risk factors**

- **Vasomotor symptoms**
  - **Yes**

**Baseline workup**
- Physical exam.: Weight, BP, Breast exam., Pelvic exam. including speculum exam.
- Blood investigation: CBC, lipid profile, RFT, LFT, uric acid, FBS & 17 B estradiol
- Cervical smear, Trans-vaginal scan, Mammogram, BMD if indicated

**Menopausal women Candidate for hormone replacement therapy (HRT)**

- **No**
  - Evaluate for symptoms of menopause or risk factors for complication resulting from estrogen.

- **Yes**
  - Offer HRT

- **Women declines HRT**

- **Baseline workup**

- **Woman begins HRT**
  - Continue primary preventative care

**Treatment options**
- Advice to continue sexual activity
- Local estrogen
- Lubrication
- Surgery if indicated

**Treatment options**
- Avoiding trigger factors, alternation in lifestyle
- Alternative therapy

**Prevention**
- Smoking cessation
- Blood pressure control
- Lower cholesterol levels
- Diabetes control
- Exercise
- Weight reduction
- Good nutrition

**Osteoporosis**
- Treatment: Calcium, Calcitonin, Vitamin D, Bisphosphonates
Section Five
Hormone Replacement Therapy
Guiling Principles:

1. Hormone replacement therapy (HRT) is effective for symptomatic relief of menopausal symptoms and its use is justified when symptoms adversely affect quality of life. The lowest effective dose for a particular woman should be used for the shortest period necessary and treatment reappraised at least annually.

2. Alternatives to HRT should be discussed with women before starting HRT.

3. HRT can be used in younger women who have experienced a premature menopause (younger than 40 years), unless contraindicated, for treating menopausal symptoms and preventing osteoporosis until the age of normal menopause, when the therapy should be reviewed.

4. Prior to commencing HRT, contraindication to HRT should be excluded through personal history and family history.

5. All women eligible for HRT should be counseled about its benefits and risks. Its use should be with informed choice and management should be individualized.

6. When estrogen is being prescribed solely for the treatment of symptoms of urogenital atrophy, topical vaginal preparations should be considered.

7. HRT can be used up to five years for relief of menopause symptoms in women in their early 50s. In some women, symptoms may persist considerably longer than this. If a decision is made to stop HRT, it should be phased out slowly in symptomatic women.

8. Local estrogen replacement may be required for the long term to reverse the symptoms of uro-genital atrophy. It is more effective than systemic therapy. Low dose vaginal estrogen can also be used in the management of postmenopausal women with recurrent urinary tract infection once underlying pathology has been excluded.
**Table 3: Contraindication to HRT**

<table>
<thead>
<tr>
<th>Absolute contraindication</th>
<th>Relative contraindication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known or suspected breast cancer</td>
<td>Undiagnosed genital bleeding</td>
</tr>
<tr>
<td>Known or suspected endometrial cancer</td>
<td>Previous venous thromboembolic disorder</td>
</tr>
<tr>
<td>Untreated endometrial hyperplasia</td>
<td>Chronic hepatic dysfunction</td>
</tr>
<tr>
<td>Active liver disease</td>
<td>Proven coronary heart disease or recent MI</td>
</tr>
<tr>
<td>Current venous thromboembolic disorder</td>
<td>Pancreatic disease</td>
</tr>
<tr>
<td>Active thrombophlebitis</td>
<td>Migraines aggravated by estrogen</td>
</tr>
<tr>
<td>Active or recent arterial thromo-embolic disease (Angina, MI).</td>
<td>Family history of breast cancer/thromboembolism</td>
</tr>
<tr>
<td><em>Uncontrolled hypertension</em></td>
<td>Familial hyperlipidemia</td>
</tr>
</tbody>
</table>

*Note:* hypertension should be controlled before commencing HRT. Local preparation should be used.

**Base line workup prior to commencing HRT**

- Physical examination:
  - Weight
  - BP
  - Breast examination
    - Pelvic examination including speculum examination
- Pap smear
- Trans-vaginal scan
- Blood investigation: CBC, lipid profile, RFT, LFT, FBS and 17 ß estradiol
- Mammogram
- BMD if indicated (see page 21)
Section Five: Hormone Replacement Therapy

The regimens of treatment

- For non- hysterectomized women:

  Estrogen daily + Progesterone  for the last 10-14 days of a cycle (every 4 weeks or month) (sequentially) → monthly bleeds

  OR

  Estrogen daily for 3 months + Progesterone in 2\textsuperscript{nd} half of 3\textsuperscript{rd} month → bleeds every 3\textsuperscript{rd} month

  OR

  Estrogen + Progesterone (continuously) → generally no bleeding

  Note: The shift to the continuous combined regimen should take place after the bleed at the end of a cycle of sequential therapy.

  Progesterone is added to estrogens to reduced the increased risk of endometrial hyperplasia and carcinoma

- For Hysterectomized women

  Estrogen alone and there is no need for progesterone. Combined HRT may confer a greater risk of breast cancer than estrogen alone.
# Table 4: Doses of HRT

<table>
<thead>
<tr>
<th>1. Estrogen</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Conjugated equine estrogen (Premarin oral tablets)</td>
<td>0.3-0.625 mg</td>
</tr>
<tr>
<td>2. Estradiol gel</td>
<td>50 µ transdermal</td>
</tr>
<tr>
<td>3. Estrogen vaginal cream (Premarin cream)</td>
<td>for 7 days for treatment of vaginitis otherwise as per requirement</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Progestrogen</th>
<th>Dose</th>
<th>Regimens</th>
<th>Timing of dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sequential</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Medroxyprogesterone acetate (Provera)</td>
<td>5-10 mg</td>
<td>for the last 12-14 days of a 28 days cycle</td>
<td></td>
</tr>
<tr>
<td>2. Dydrogesterone oral (Duphaston)</td>
<td>20 mg</td>
<td>for the last 14 days of 3 months</td>
<td></td>
</tr>
<tr>
<td>2. Dydrogesterone oral (Duphaston)</td>
<td>10-20 mg</td>
<td>for Last 12-14 days of 28 days cycle (dose can be doubled if women has bleeding)</td>
<td></td>
</tr>
<tr>
<td><strong>Continuous</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Medroxyprogesterone acetate (Provera)</td>
<td>2.5 mg</td>
<td>Daily</td>
<td></td>
</tr>
<tr>
<td>2. Dydrogesterone oral (Duphaston)</td>
<td>5 mg</td>
<td>Daily</td>
<td></td>
</tr>
</tbody>
</table>
Starting HRT

- HRT is offered according to the need

- Symptomatic women should be offered HRT. It should be started after counseling regarding the risks and benefits and after baseline investigation.

- For Perimenopausal women continuous combined regimens should not be used because of the high risk of irregular bleeding. Sequential regime is preferred which produce regular withdrawal bleeding.

Follow up

- **Every six months for:**
  - Monitoring compliance
  - Relief of symptoms to adjust the doses
  - Blood pressure measurement
  - Breast examination.

- **Annually for:**
  - Blood investigation: CBC, lipid profile, RFT, LFT, FBS
  - Trans-vaginal scan for endometrial thickness
  - Pap smear
  - Mammography (after age 50)

- **Three yearly for:**
  - Bone mineral Density (BMD) if normal (depends also on medical condition)
Duration of treatment

- For vasomotor symptoms → continue for 2-4 years and may continue for up to 5 years then stop to evaluate whatever or not they have recurred
- For prevention or treatment of osteoporosis → continued for life (a minimum of 10 years) as bone mineral density (BMD) falls when treatment is stopped

Management of side effects

- Some women may experience side effects of HRT. Side effects can be related to estrogen or progesterone or combination of both (refer to annex-4 page 45).
- It is essential to discuss side effects when prescribing HRT and explain that they usually resolve.

Management startegies

- Side- effects are often transient and resolve without any change in treatment with increasing duration of use. Women should be encouraged to persist with therapy for about 12 weeks to await resolution.
- Give oral dose with food
- Start with low dose, gradually increase to therapeutic dose over few weeks
- In women with one year postmenopause, recommend continuos regimen
- With persistant side effects the options include:
  - Reduce dose: when doing this, the endpoints of treatment such as symptoms control and the prevention of osteoprosis must be born in mind in reducing oestrogen dose. Progesterone dose should not be reduced below the recommended levels for endometrial protection
  - Change type of estrogens or progesterone
  - Change route of delivery- such as from oral to gel
  - Reduce frequency for progesterone: using long cycle HRT that administers progesterone for 14 days every three months
Section Six
Abnormal Vaginal Bleeding
Section Six: Abnormal vaginal bleeding

Postmenopausal bleeding and abnormal peri-menopausal bleeding such as a sudden change in menstrual pattern, inter-menstrual bleeding or post-coital bleeding requires evaluation.

- Vaginal bleeding demanding evaluation in women using HRT are:
  1. With sequential HRT, abnormal bleeding is denoted by a change in the pattern of withdrawal bleeds or breakthrough bleeding
  2. In women who take continuous combined or long cycle regimens, breakthrough that persists for more than 4-6 months or does not lessen
  3. Women on continues regimen who bleed after amenorrhea

General management:
- Perform a rapid evaluation of the general condition of the woman, including vital signs (pulse, blood pressure) and proper history taken (if possible)
- Check the severity of the bleeding
- If woman has *heavy bleeding start an IV infusion and infuse IV fluid
- Check Hb level

Diagnosis
- It is essential to exclude carcinoma of the endometrium or cervix and pre-malignant endometrial hyperplasia
- For those who are on HRT determine:
  1. When does the bleeding occur with respect to the estrogen and progesterone phases of HRT
  2. Duration and type of flow (mild, heavy).
  3. Whether or not there was a period of amenorrhea before the HRT was commenced,
  4. Whether or not there is a problem suggesting poor compliance

* Heavy bleeding: takes less than five minutes for a clean pad or cloth to be soaked
Algorithm 3: Evaluation of vaginal bleeding in postmenopausal woman

**Section Six: Abnormal vaginal bleeding**

**Post-menopausal woman with abnormal vaginal bleeding**

### At Primary Health Care Level

- **History**
  - History of episodes
  - Check compliance if on HRT
  - Risk factors for endometrial cancer
    - Nulliparity
    - Late menopause
    - Diabetes
    - Obesity
    - Chronic anovulation
  - Family history of endometrial cancer

- **Examination**
  - General exam: vital signs, pallor, skin turgor, lymph node, weight.
  - Abdominal examination
  - Pelvic examination

- **Investigation**
  - CBC

### Refer to Secondary Health Care Level

- **Routine referral if**
  - Woman is stable with normal examination
  - Refer for Ultrasonography scan & Pap smear (if indicated)

- **Urgent referral if**
  - Abnormal findings

- **Transfer after stabilization if**
  - In shock
  - Heavy bleeding

- **Ultrasound**
  - Scan preferably TVS for ovarian pathology & endometrium pathology

- **Endometrial thickness ≤ 4 mm**
  - Follow up for further episodes

- **Endometrial thickness > 4 mm**
  - Further assessment:
    - Endometrial biopsy
Annexures
Menopause: is defined as the permanent cessation of the menstruation resulting from the loss of ovarian follicular activity. Natural menopause is recognized after 12 months of amenorrhea that is not associated with any other pathologic / physiologic cause. Although the term is used to describe all the various symptoms that occur at this stage, the actual meaning of the word is just what it says ‘stoppage of menstruation’ with transitional phase lasting for 1-5 years. The time at which menopause occurs depends on race and family history. It does not depend on the age when menses first started or on the number of pregnancies a woman has had.

Technically, natural menopause is the transition between peri-menopause and post-menopause, the entire process culminating with the ceasing of the menses. This natural menopause process itself is usually identified retrospectively, when it has been a year since a last menses.

Climacteric: is the phase encompassing the transition from the reproductive state to non-reproductive state. The menopause itself is thus a specific event during the climacteric- just as the menarche is a specific event that occurs during puberty.

Perimenopause: the time immediately prior to the menopause and the first year during which menstrual cycle and endocrine changes are occurring, and ends 12 months after the last menstrual period.

Premenopause: the time up to the beginning of the perimenopause, but is also used to define the time up to the last menstrual period.

Postmenopause: begins at the time of the last period.

Premature menopause: menopause below the age of 40 years. It could be due to premature ovarian failure, surgical menopause and medical menopause.

Osteoporosis: is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture.
## Annex 2: Body Mass Index (BMI)

### Index and Analysis

<table>
<thead>
<tr>
<th>Body Mass Index</th>
<th>Weight (Analysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 18.50</td>
<td>Underweight</td>
</tr>
<tr>
<td>18.50-24.99</td>
<td>Normal</td>
</tr>
<tr>
<td>≥ 25.00</td>
<td>Overweight</td>
</tr>
<tr>
<td>≥ 30.00</td>
<td>Obese</td>
</tr>
</tbody>
</table>

Body Mass Index = weight in kg / (height in meters)^2
### Goals of counseling:
- Listen to woman problem and build trust with her
- Train woman on how to cope with signs and symptoms of menopause
- Explain to her the concept of healthy life style (healthy nutrition, exercise, emotion wellbeing,
- Make her understand the need for seeking medical help if symptoms persist.

<table>
<thead>
<tr>
<th>Complaint (symptoms)</th>
<th>Counsel on</th>
</tr>
</thead>
</table>
| **Vasomotor symptoms** | ▪ Avoiding the trigger factors if possible such as hot drinks, caffeine, spicy food, alcohol, stress, hot weather.  
▪ Use of fans, air conditioning, and light cotton clothing and layered cloths.  
▪ Dietary intake of phytoestrogen supplementation (Soya product).  
▪ Doing regular exercise.  
▪ Increase intake of fluid (water & juices) during the attack of hot flush  
▪ Taking shower or washing face during the attack of hot flush |
| **Urogenital atrophy** | ▪ Encourage regular sex activity which may help the vagina in maintaining its elasticity  
▪ Using vaginal lubricants/Moisturizers |
| **Psychological symptoms** | ▪ Possible causes of insomnia and trigger factors (e.g. drinking tea and coffee, especially in the afternoon and evening  
▪ Regular exercise such as walking  
▪ Provide women with skills and resources to modify her lifestyle and her environment to be less stressful and to practice positive thinking.  
▪ Encourage woman to share her compliant with other women with similar experience. |
| **Osteoporosis** | ▪ Risk factors for osteoporosis  
▪ Obtaining an adequate intake of dietary calcium (at least 1,200-1,500 mg/day)  
▪ Obtaining an adequate intake of vitamin D (400-800 IU / day> most women will get their recommended allowance through diet and exposure to sunlight; other can use supplements  
▪ Doing regular weight-bearing and muscle strengthening exercise. These exercises improve bone health strengthening muscles, and improve balance, which will help in preventing fall.  
▪ Fall prevention precautions e.g. taping down rugs, using night-lights etc. |
Annex 4: Side Effects & Risks of HRT

Side effects

Side effects cause by estrogen:

- Bloating
- Fluid retention
- Breast tenderness or enlargement
- Nausea
- Headache
- Leg cramps
- Dyspepsia
- Weight gain

Side effects cause by progesterone:

- Fluid retention
- Breast tenderness
- Headaches or migraine
- Mood swings
- Depression
- Acne
- Lower abdominal pain
- Backache
- Weight gain
Annex 4: Side Effects & Risks of HRT

Risks of HRT

1. Endometrial cancer
   - Unopposed estrogen replacement therapy increase risk of endometrial cancer. The relative risk is 2.3. It increase with prolonged duration of use.

2. Breast cancer:
   - Overall HRT seems to confer a similar degree of risk to that associated with late natural menopause. For every year that menopause is delayed, the risk of breast cancer increases by 2.8 %. With HRT, the risk has been estimated to increase by 2.3 % per year (an extra 2 women developing breast cancer per 1000 after 5 years of use).
   - The risk of developing breast cancer with HRT is dependent on duration of treatment, but that this effect is not sustained once HRT is stopped, when the risk after five years is no greater than that in women who have never been exposed to HRT.
   - Risk is greater with combined estrogen-progesterone replacement and less with unopposed estrogen
   - The increased risk of breast cancer with combined therapy has to be balanced against the reduction in risk of endometrial cancer provided by this therapy compared to estrogen-alone treatment.

3. Thromboembolism disease
   - Estrogen therapy has been associated with increased risk of venous thromboembolic disease with 1-2 years after initiation of therapy
   - The incidence of venous thromboembolism and pulmonary embolism was 3.5 per 1000 person year.
   - The highest risk occurs in the first year of use.
4. Gallbladder disease

- HRT increase gallbladder disease
<table>
<thead>
<tr>
<th>ICD -10</th>
<th>Diagnosis</th>
</tr>
</thead>
</table>
| N81     | Female genital prolapse  
             Excludes:  
                            genital prolapse complicating pregnancy, labour or delivery (O34.5)  
                            prolapse and hernia of ovary and fallopian tube (N83.4)  
                            prolapse of vaginal vault after hysterectomy (N99.3) |
| N95.1   | Menopausal and female climacteric states  
             Symptoms such as flushing, sleeplessness, headache, lack of concentration, associated with menopause  
             Excludes: those associated with artificial menopause (N95.3) |
| M81.0   | Postmenopausal osteoporosis |
| N95.2   | Postmenopausal atrophic vaginitis  
             Senile (atrophic) vaginitis  
             Excludes: that associated with artificial menopause (N95.3) |
| N92.4   | Excessive bleeding in the premenopausal period  
             Menorrhagia or metrorrhagia:  
                            climacteric  
                            menopausal  
                            preclimacteric  
                            premenopausal |
| N95.0   | Postmenopausal bleeding  
             Excludes: that associated with artificial menopause (N95.3) |
References
References


Who expect consultation, 2004, appropriate body mass index for Asian populations and its implications for policy and intervention strategies, lancet vol. 363 (9,403), pp.157-163