

Hormone Replacement Therapy: Definition and Adverse Effects

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Many of the symptoms and signs of menopause can be attributed to the cessation of the production of estrogen by the ovaries in the menopausal stage. The most common complications that women face during menopause include vaginal dryness, soreness, dyspareunia, urinary frequency, and urgency. Mood changes are also common during menopause and in postmenopausal women. Vasomotor instability can cause hot flashes, sweating, and palpitations in menopausal women.



Overview

Menopause refers to the period of a woman's life during which there is a cessation of cyclic menstruation, thereby signaling the end of one's reproductive ability. It begins with a perimenopausal period that precedes and warns about the arrival of the menopausal period, which is characterized by amenorrhea for > 12 months. The timing of menopause varies widely, but it generally occurs in the 4th or 5th decade of life, with the mean age of occurrence at 51 years.

Symptomatically, menopause is characterized by irregular menses, increased sweating,

hot flashes, heat intolerance, headaches, irritability, loss of libido, vaginal and mammary atrophy, and mood swings. Many of these symptoms can be attributed to the loss of the normal cyclic production of estrogen and progesterone by the ovaries. Thus, hormone replacement therapy (HRT) has emerged as a solution to prevent these unpleasant symptoms. **HRT is available in topical or systemic formulations.**

Another important effect of menopause on women's health is **impaired bone metabolism and progressive loss of bone density**. Some studies have estimated the prevalence of osteoporosis in postmenopausal women to be around 1 in 3 women. Another important effect of menopause on women is the increased risk of coronary artery disease.

Definition

Hormone replacement is the administration of synthetic estrogen and progesterone to replace depleting levels of hormones in menopausal women.

Forms and Application of HRT

- HRT is available in the following forms:
 - Estrogen-containing methods
 - Combined estrogen and progesterone methods
 - Selective estrogen receptor modulators
 - Gonadomimetics

Hormones can be prescribed via:

- Local methods (hormone-based creams, pessaries, and rings)
- Systemic therapy (oral formulations, transdermal patches or gel, and implants)

Hormones can also be grouped by schedules of administration, including those taken daily or via cyclic schedules, such as for progesterone-containing methods.

Indications

The 3 main indications for the prescription of HRT in menopausal women are:

1. To relieve vasomotor symptoms of hot flashes, swelling, and palpitations
2. To improve urogenital symptoms of dyspareunia, urinary frequency, and urinary urgency
3. To prevent osteoporosis

It is important to understand that **HRT has been statistically proven to only prevent the initial development of osteoporosis; thus, therapy is only effective if started during the first 5 years after menopause**. HRT is therefore indicated for women with low bone mineral density or a history of osteoporotic fractures.

Contraindications

There are no absolute contraindications to HRT. **Relative contraindications** include:

- Previous history of breast cancer or endometrial cancer
- Porphyria
- Severe active liver disease

- Hypertriglyceridemia
- Undiagnosed vaginal bleeding
- Endometriosis
- Fibroids
- Thromboembolic disease

HRT also has some important side effects that women should be aware of. **Nausea, bloating, fluid retention, and mood swings** are common. Weight gain after starting HRT has always been a debatable subject and is controversial, to say the least.

Because of these risks, **baseline laboratory and imaging studies should be performed** before commencing HRT. These investigations can include fasting lipid profile, blood sugar levels, ultrasonography to assess endometrial thickness and the ovaries, electrocardiography, Papanicolaou test, and mammogram.

Forms

HRT can contain estrogen alone or have a combination of an estrogen and a progestin. **The most commonly used estrogens are equine estrogen, micronized 17-beta-estradiol, and ethinyl estradiol.** The most commonly used progestins are medroxyprogesterone acetate and norethindrone acetate. The usual dose used in combined therapy is 0.625 mg of equine estrogen, combined with 2.5 mg of medroxyprogesterone acetate.

Women who have had a hysterectomy should receive estrogen alone. **The rationale behind adding progestin to the regimen is to oppose the effects of the estrogen** on the endometrium, as this can be associated with an increased risk of carcinogenesis. Women who have undergone a hysterectomy do not need the opposing effects of progestin.

Postmenopausal women who have an impaired lipid profile or an increased risk of osteoporosis may benefit from **selective estrogen receptor modulators.** These drugs can mimic the effects of estrogen or antagonize the effects of estrogen. They are known to prevent osteoporosis and have fewer adverse effects compared with conventional hormone replacement therapy.

Systemic Hormone Replacement

Systemic HRT has been proven to improve the symptoms of menopause related to vasomotor disturbance. These symptoms include hot flashes, sweating, and palpitations. Systemic HRT is also effective in **managing the urogenital symptoms of menopause, such as vaginal dryness, superficial dyspareunia, and urinary frequency or urgency.** Topical estrogen creams can be used to relieve vaginal dryness and superficial dyspareunia. Urogenital symptoms usually improve after prolonged and continuous HRT and are known to recur after stopping the treatment.

Systemic HRT is also very effective in preventing osteoporosis, although the strongest protective effect of HRT in this regard has been shown to occur within the first 5 years after the onset of menopause.

Premature ovarian failure is also associated with an increased risk of osteoporosis, and HRT has been proven to significantly lower this risk. These effects appear to be lost after women stop taking HRT.

Guidelines

The United Kingdom's National Institute for Health and Clinical Excellence and the International Menopause Society issued guidelines to aid general practitioners and gynecologists when prescribing HRT in menopausal women:

1. HRT is the mainstay treatment for vasomotor symptoms of menopause. The best option is combined equine estrogens with medroxyprogesterone acetate, or equine estrogens with bazedoxifene (see table below).
2. The risk of breast cancer is very low when estrogen is used alone but slightly higher when combined therapy is used. It should also be explained to women taking HRT that the risk of cardiovascular disease is not significantly affected.
3. Women with several relative contraindications to HRT should be started on selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors in addition to gabapentin to control mood and vasomotor symptoms.
4. The optimum time to start HRT is before 60 years of age or within the first 10 years after menopause.

Oral Estrogen	Oral Estrogen-Progestin Combinations	Oral Estrogen-Testosterone Combinations
<ul style="list-style-type: none">• Estrace (estradiol)• Menest (esterified estrogen)• Premarin (conjugated equine estrogen)• Cenestin (conjugated synthetic estrogen)	<ul style="list-style-type: none">• Prempro (conjugated equine estrogen + medroxyprogesterone)• Prefest (estradiol + norgestimate)	<ul style="list-style-type: none">• Esterified estrogen + methyltestosterone

References

[Menopausal Hormone Replacement Therapy](#) via medscape.com

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Notes