

Hormone Replacement Therapy for Menopause

Hormone replacement therapy (HRT), also known as menopausal hormone therapy (MHT), refers to the use of estrogen or combined estrogen-progestin supplementation to treat symptoms associated with the loss of ovarian hormones during menopause.

Indications

Indications for hormonal therapy in menopause include (Harper-Harrison, Carlson & Shanahan, 2024):

- Treatment of moderate to severe vasomotor symptoms of menopause (e.g., hot flashes) in addition to other symptoms such as sleep disturbances, mood changes or depression, and joint aches and pains.
- Treatment of genitourinary syndrome of menopause (e.g., vaginal and vulvar atrophy)

Contraindications

Contraindications to HRT include existing or a history of the following conditions (Lippincott Solutions, 2021; Martin & Barbieri, 2023):

- Breast cancer, ovarian, uterine, or endometrial cancer
- Coronary heart disease (CHD)
- Deep venous thrombosis (DVT) or pulmonary embolism
- Blood clotting disorder (e.g., Factor V Leiden mutation)
- Arterial thrombotic diseases (e.g., transient ischemic attack or stroke)
- Active liver disease or dysfunction
- Migraine with aura
- Smoking
- Current pregnancy

Types of HRT

Estrogen (Harper-Harrison, Carlson & Shanahan, 2024)

- **Unopposed estrogen therapy (ET)**, estrogen-only therapy
 - Used in patients who have had a hysterectomy.
 - Medications contain ethinyl estradiol, conjugated equine estrogen (CEE), synthetic conjugated estrogens, or micronized 17-beta estradiol, identical to the estradiol produced by the ovaries.
 - 17-beta estradiol is preferred over CEE due to its associated increased risk of coronary heart disease and breast cancer.
- **Combined estrogen-progestin therapy (EPT)**
 - Used for patients with an intact uterus who need progestin to counteract potential estrogen-associated effects such as endometrial hyperplasia and uterine cancer. Estrogen alone can cause the endometrial lining to build up abnormally. Progesterone provides a protective effect by preventing the proliferation of endometrial cells.
 - Natural micronized progesterone is preferred over MPA, a synthetic progestin.

Administration (Martin & Barbieri, 2023)

Treatment selection is based on patient preference, drug availability, and cost.

- Medications are typically taken on a continuous or cyclical schedule.
- Dosing begins low and then titrated to relieve symptoms.
- Vasomotor symptoms such as hot flashes require systemic estrogen.
- Genitourinary syndrome of menopause should be treated with low-dose vaginal estrogen, not systemic.
- Females with primary ovary insufficiency may require higher daily dosing.
- If hot flashes continue after four weeks of therapy, the estrogen dose may be increased.
- Once symptoms subside and the patient tolerates MHT, the medication regimen continues for three to five years before a taper is attempted.
 - For females with severe symptoms who start MHT in their late 40s, a taper is not attempted for at least five years.
- MHT is typically discontinued by the age of 60 when the risks outweigh the benefits. However, The Menopause Society and the American College of Obstetrics and Gynecology recommend that MHT be individualized and not stopped based only on patient age.

Routes of administration include:

- Oral
 - Oral estrogens should generally be avoided in patients with hypertriglyceridemia, active gall bladder disease, or thrombophilia (e.g., factor V Leiden).
- Transdermal patch
- Topical gels, lotions, sprays
- Vaginal ring, tablet, cream

Common Adverse Effects of MHT (Harper-Harrison, Carlson & Shanahan, 2024; Martin & Barbieri, 2023)

Patients may experience adverse effects of HRT, but the effects may be mitigated by lowering the dose of estrogen or progestin. These effects include the following:

- Breast soreness
- Mood changes
- Fluid retention, bloating
- Vaginal bleeding
- Headache

PEARLS (Martin & Barbieri, 2023)

- HRT is considered safe for healthy, symptomatic patients within ten years of menopause or younger than 60 years. HRT initiation after the age of 60 is associated with an increased risk of vascular events
- HRT is no longer recommended to prevent chronic diseases such as coronary heart disease (CHD) or osteoporosis, to improve cognitive function, or to prevent dementia.
- Selective serotonin reuptake inhibitors (SSRIs) combined with HRT may alleviate significant mood changes.

References

Harper-Harrison, G., Carlson, K., & Shanahan, M. M. (2024). Hormone Replacement Therapy. In *StatPearls*. StatPearls Publishing.
<https://www.ncbi.nlm.nih.gov/books/NBK493191/>

Hormone Replacement Therapy in Menopause. (2021). In *Lippincott Solutions*. Accessed September 2024 via the Web at
<https://advisor.lww.com/lna/document.do?bid=19&did=1418644&searchTerm=hormone%20therapy&hits=hormones,hormone,therapy,therapies>

Martin, K. A. & Barbieri, R. L. (2023, November 20). Treatment of menopausal symptoms with hormone therapy [Online]. In *UpToDate*.
<https://www.uptodate.com/contents/treatment-of-menopausal-symptoms-with-hormone-therapy>