



Menopause – Combined Hormone (Replacement Therapy)

Women generally undergo menopause between the ages of 45 and 55 years. Around the time of menopause, women may experience symptoms such as hot flushes, sweats, anxiety, dry vagina, loss of libido, irritability, headaches, poor memory, poor concentration, dizzy spells, and muscle/joint pains. Oestrogen therapy is effective in relieving these symptoms but if taken by itself increases the risk of cancer of the endometrium (lining of the uterus). Women who have not had a hysterectomy are usually advised to take a progestin as well, because it protects against this cancer. Daily hormone therapy/hormone replacement therapy (HT/HRT) containing oestrogen plus progestin, a synthetic form of the natural hormone, is referred to as combined hormonal therapy. This therapy can be used either continuously (when oestrogen and progestin are used throughout the whole month) or cyclical (when oestrogen is used for 14 days followed by 14 days of oestrogen plus progestin).

Types of oestrogens

- Oestrogens are available as tablets, patches, gels, nasal spray or as an implant under the skin.
- Tablets are often used and are acceptable to most women. The tablets include conjugated equine oestrogen, oestradiol, oestrone and oestriol.
- Women who have problems with absorption from the gut e.g. diarrhoea or taking medications for oesophageal reflux may respond better to non-tablet forms.
- A benefit of using a patch, gel, nasal spray or implant is the avoidance of effects on the liver and this may be beneficial for women with liver problems or nausea with tablet therapy.
- Women with high triglyceride levels may be better using a patch which does not increase triglycerides as well as possibly not increasing the risk of deep venous thrombosis (DVT). (See Menopausal Treatments and the Risk of Blood Clots).
- Vaginal oestrogen in creams or pessaries is available for women suffering vaginal dryness or painful intercourse.

Types of progestogens

- Progestogen is a term encompassing both progesterone, the naturally occurring hormone, and synthetic versions called progestins.
- Progestogen tablets for HT/HRT are medroxyprogesterone acetate, norethisterone, dydrogesterone and cyproterone acetate.
- An alternative method would be the use of an intrauterine device containing the progestin, levonorgestrel.
- Troches have not been evaluated. Progesterone creams are ineffective in reducing endometrial thickening and there is no evidence they protect the endometrium.

How the hormones are taken

- Continuous combined HT/HRT comes in many forms including combined tablets and combined patches. Oestrogen can be taken as a gel, nasal spray or implant combined with a progestin tablet.
- The doses depend on how a woman's symptoms respond and her well-being.
- Progestogens can be taken cyclically, so the woman has a predictable monthly bleeding pattern, or continuously, which suppresses the withdrawal bleeds.
- Women going through menopause are usually given cyclical therapy because the lining of the uterus is thicker and irregular bleeding more common.
- Older women are better suited to continuous combined therapy.
- For women who cannot tolerate progestin tablets, an alternative is to try the levonorgestrel intrauterine system.
- A small number of women are unable to tolerate any progestins, and if they want to take oestrogen to control menopausal symptoms they should discuss their options with their doctor.



The benefits of HT/HRT

- By reducing menopausal symptoms HT/HRT improves concentration and quality of life.
- Combined HT/HRT reduces the risk for postmenopausal bone fracture, including hip fracture. Oestrogen increases bone density.
- HT/HRT reduces the risk of bowel cancer.
- HT/HRT may improve mild depressive symptoms, however moderate to severe depression should be treated with antidepressant and other therapies.

Side-effects of HT/HRT

- Common side-effects due to the oestrogen component, which are usually temporary, include breast enlargement and nausea. Side-effects usually related to the progestin component include fluid retention and headache.
- Irregular bleeding or heavy withdrawal bleeding may result from an imbalance in doses of the oestrogen and progestogens and needs to be investigated by a doctor.
- Some women associate HT/HRT with weight gain. Studies show that HT/HRT does not cause weight gain. Women going through the menopause have a tendency to gain weight due to their body metabolic changes and more sedentary lifestyle. A potential benefit of HT/HRT is that if women feel better they may be more motivated to exercise.
- Side-effects may be reduced or eliminated if the dose is tailored individually.

The risks of HT/HRT

- All drug therapies have potential side-effects. Every medication needs to be used for a reason.
- It is recommended that HT/HRT taken to relieve symptoms should be short-term and HT/HRT should not be used for long-term preventative therapy.
- These guidelines follow the shut-down of part of the Women's Health Initiative (WHI) trial in the United States which looked at whether one form of combined HT/HRT - conjugated equine oestrogen 0.625 mg daily plus medroxyprogesterone acetate 2.5 mg daily - could prevent chronic disease.
- The WHI trial found that breast cancer risk increased for women on combined HT/HRT after five years of use. This result cannot necessarily be applied to other combination therapies, to use of oestrogen alone (see Menopause - Oestrogen Only Therapy), to SERMs (see The Role of SERMs Post Menopause) or to younger women (See Early Menopause Spontaneous and Unexpected Ovarian Failure).
- The WHI trial also found a small increase in stroke.
- The women in the WHI trial were older (on average 63 years when they started) and had more health risk factors such as high blood pressure than women in Australia and New Zealand likely to be taking HT/HRT to relieve symptoms.
- The use of HT/HRT is associated with increased risk of blood clots, particularly as women age (see Menopausal Treatments and the Risk of Blood Clots).
- In older women, the use of HT/HRT is associated with increased risk of gallbladder inflammation (cholecystitis).

Managing the risk

- Women considering HT/HRT use are recommended to have a pre-treatment breast check and mammogram. Regular examinations and mammograms are prudent.
- A decision to use HT/HRT should be reviewed annually by the woman in consultation with her doctor. Personal benefits versus risk should be discussed with a doctor.
- HT/HRT should not be used for cardiovascular protection.
- If menopausal symptoms are present short-term use of HT/HRT is recommended. Use of the lowest dose which relieves symptoms should be considered.
- Women who do not have symptoms but require treatment to reduce their risk of osteoporosis should consult a physician to discuss all treatment alternatives.
- If a woman using HT/HRT develops symptoms suggesting DVT she should seek medical attention promptly. (See Menopausal Treatments and the Risk of Blood Clots).

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