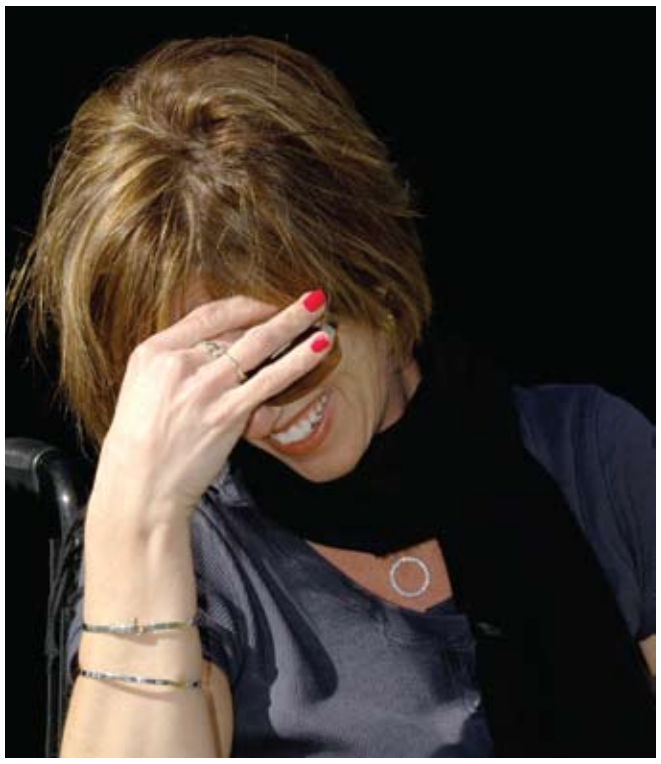
HRT: Practical prescribing options

Helen Roberts *combines her role of senior lecturer in women's health at Auckland University with that of research manager for the Family Planning Association's northern region. Dr Roberts' key research interests are contraception and menopause. She was the clinical leader for NZGG's hormone replacement guidelines*



Many women obtain symptom relief with low doses of oestrogen

Evidence

This article, the second in a two-part series, looks at prescribing hormone replacement therapy in general practice. The first article (*New Zealand Doctor*, 13 February) looked at original findings from the Women's Health Initiative (WHI) studies published five years ago alongside their recently published age subgroup data and results from the Women's International Study of Long Duration Oestrogen after Menopause (WISDOM). The article also considered the evidence on the safety of HRT, and indications for HRT in relation to recommendations published in 2004 by the New Zealand Guidelines Group (NZGG).

When to prescribe HRT

On review of the more recent evidence the key messages about HRT prepared by the NZGG[1,2] remain current (Panel 1). HRT is an appropriate treatment for women with moderate to severe menopausal symptoms[1,2] and is at present the most effective therapy for this indication.[3]

What to do before starting therapy?

Flushes can start while a woman is still having periods. Hormone levels fluctuate at this time and are not useful in making the decision for treatment. A full personal and family history will identify those women with risk factors who should not use oestrogen (Panel 2).

Risk assessment for cardiovascular disease should include measurement of BMI, blood pressure and lipid levels. Individual risk can be assessed. For example, HRT increases the risk of stroke by 40 per cent (relative risk 1.4). A woman with a 5 per cent baseline risk then has a 7 per cent (5 x 1.4) risk with HRT – a 2 per cent increase. If, however, she has a 25 per cent baseline risk of stroke, then the risk with HRT is now 35 per cent (25 x 1.4), a 10 per cent increase.[3]

The NZGG cardiovascular risk assessment coloured charts,[4] online at www.nzgg.org.nz and in the back of *New Ethicals*[5] aid in the discussion with women.

The absolute risks of therapy for women aged 50–79 years, derived from the WHI studies are outlined in Table 1.[6–8] Healthy women in early menopause are at a low absolute risk whether they take hormones or not, and are unlikely to face substantially increased risks when using hormones for a few years.[9]

Starting HRT

Many women obtain symptom relief with low doses of oestrogen. Start HRT with oral therapy at doses of 0.3mg conjugated equine oestrogen or 0.5–1.0 mg of 17-beta oestradiol or oestradiol valerate. Women with a uterus will also require separate prescribing of progestogen. Table 2 outlines the doses required for endometrial protection.[10] At present there is only one low dose combined continuous package regimen (Kliovance: 1mg of 17-beta oestradiol with 0.5mg norethisterone acetate). The dose of hormone(s) can be increased if relief of symptoms is not adequate after two months.

Oestrogen alone is prescribed for women who have had a hysterectomy; women with a uterus need the addition of progestogen.

A sequential regimen (continuous oestrogen and 14 days' progestogen) is used for perimenopausal women or those having less than one year since the last period. If periods are still present, commence oestrogen on day one with the progestogen for the last 14 days of the cycle. A hormone withdrawal bleed should occur at or near the end of the progestogen tablets. For those women who bleed earlier, the dose of progestogen can be increased.

A combined continuous regimen (oestrogen and progestogen every day) is used for women having one year since the last menstrual period. On this regimen women have no bleed, though some irregular spotting is not uncommon in the first six months of use. This usually disappears with time or with increasing the dose of progestogen.

If irregular bleeding persists during treatment, compliance should be checked and cervical malignancy or infection ruled out before investigation for endometrial abnormalities.

Treating genitourinary symptoms

Oestrogen improves genitourinary symptoms of dry vagina and dyspareunia (level of evidence A) and recurrent urinary tract infections (level of evidence B).[3] These symptoms are usually present long term – vaginal oestrogen should be used by these women. Current low dose vaginal preparations have minimal absorption. Recent position statements support long term use as long as distressing symptoms remain, without the need for progestogen for women with a uterus.[11]

Ending treatment

Good evidence is lacking on the best way to discontinue treatment. Most women stop HRT within two years of use, often without needing to visit a healthcare provider. Initial advice could be to end treatment within a few years of starting therapy to see if symptoms have resolved. Women with severe return of flushes could then be advised to restart therapy but to decrease the dose slowly over the next few months. The addition of other non-hormonal treatments for flushes has been suggested to help women who have severe symptoms on withdrawal, particularly those with a high risk of adverse events while using therapy.[3] Women with long term debilitating symptoms will need to balance symptom relief with ongoing risks from HRT. D

Useful resources

Women's Health Initiative study: www.nhlbi.nih.gov/whi

This website contains a video, information kit, and details of publications from the WHI study

New Zealand Guidelines Group resources

- Hormone replacement therapy. Summary document 2004 www.nzgg.org.nz/guidelines/0078/HRT_summary_web.pdf
- Pamphlet for women re combined oestrogen and progestogen www.nzgg.org.nz/guidelines/0078/FINAL_Web_HRT_Summary.pdf?%20

Hormone replacement therapy: use

Panel 1

- HRT remains an appropriate treatment for women with moderate to severe menopausal symptoms.
- HRT should not be used for the prevention of chronic disease.
- Treatment should be at the lowest dose for the shortest time necessary to control symptoms.
- Women should be advised of the increased risk of stroke, deep vein thrombosis and gallbladder disease with both combined and oestrogen-only therapy.
- Combined therapy is associated with increases in the risk of breast cancer and dementia (in women aged over 65).
- Low dose vaginal oestrogen is an effective treatment for vaginal dryness, dyspareunia and to prevent recurrent urinary tract infections and can be used as long as symptoms remain.

Contraindications to oestrogen use

Panel 2

- previous breast cancer
- previous heart attack
- previous stroke
- previous VTE
- high risk CVD

Absolute risks of therapy

Table 1

Absolute risk increase over placebo per 10,000 women per year (for women aged 50–79 years)[6-8]

Outcome	Oestrogen + progestogen	Oestrogen only
Stroke	+8	+12
Pulmonary embolus	+8	+7
Breast cancer	+8	–
Dementia (>65 years)	+23	–

For references go to **www.nzdoctor.co.nz** under 'References'

This column is coordinated by the New Zealand Guidelines Group. NZGG is an independent, not-for-profit organisation set up to promote effective delivery of health and disability services, based on evidence. NZGG works with a broad-based collaborative network of clinical leaders, opinion leaders and consumers, designing tools to promote an evidence-based culture within the New Zealand health and disability sector. **www.nzgg.org.nz**

Individual prescribing of low dose HRT[10]

Table 2

Continuous oestrogen	Sequential progestogen for 14 days if <1 year postmenopausal	Continuous progestogen if >1 year postmenopausal
0.3mg conjugated equine oestrogen or 0.5–1mg 17-beta oestradiol or 0.5 –1mg oestradiol valerate	5mg medroxyprogesterone acetate or 0.7mg norethisterone (2 Noriday) or 0.06mg levonorgestrel (2 Microlut)	2.5mg medroxyprogesterone acetate or 0.35mg norethisterone (1 Noriday) or 0.03mg levonorgestrel (1 Microlut)