



# If not hormones – then what?



**BACKGROUND** The Women's Health Initiative study has made women reconsider their use of hormone therapy and made medical practitioners review the risks and benefits to each patient. The significance of lifestyle, nonprescription, and prescription therapies for menopause management are of increasing relevance.

**OBJECTIVE** This article reports on the evidence from randomised controlled clinical trials and population based cohorts on nonhormonal management of menopause symptoms and on the role of diet and exercise in osteoporosis prevention. Personal tips are included.

**DISCUSSION** Menopausal consultations should include a discussion of diet and exercise, and education of available over-the-counter therapies. For those women in whom oestrogen is contraindicated, prescriptions of serotonin noradrenergic reuptake inhibitors or clonidine may be indicated.

**Table 1. Osteoporosis treatment and prevention tips**

- Exercise slows the rate of bone loss in older women by about 1.5% per year
- It's never too late to start increasing weight bearing exercise and dietary calcium

## Lifestyle strategies

Addressing lifestyle factors such as the benefit of weight management, moderation in alcohol use, smoking cessation, stress management, exercise and diet for cardiovascular disease prevention and wellbeing, should be included in an annual health check or biennial Pap test and general health check. The importance and overwhelming evidence supporting the role of these strategies is assumed and will not be discussed further in this article.

## Exercise

*Advise your patients it is never too late to start* Australia's national physical activity guidelines recommend that adults accumulate at least 30 minutes of moderate intensity exercise such as walking, most days of the week.<sup>1</sup> A Swedish study reported that regular exercise reduced the intensity of hot flashes. The Melbourne Midlife cross sectional study found no association with exercise and hot flashes.<sup>2</sup>

Regular exercise decreases anxiety and depression. Strenuous exercise releases endorphins and also increases monoamine neurotransmitters that impact on stress and depressive reactions. A daytime walk provides light exposure – light therapy is effective for winter depression and might also be helpful for non-seasonal depression.<sup>3</sup>

Exercise is a major contributor to osteoporosis prevention and treatment (*Table 1*). Exercise must stress the skeleton to be effective in preventing bone loss. Walking, aerobics and tennis are more effective than swimming and cycling where the body's weight is supported.<sup>1</sup> Moderate to high intensity weight bearing aerobic exercise, high intensity progressive resistance training and impact loading such as jumping, increase bone density in pre- and post-menopausal women with positive effects seen at both the femoral neck and lumbar spine. Exercise appears to slow the rate of



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bone loss in older women by about 1.5% per year compared with sedentary controls.<sup>4</sup> Most exercise studies have shown significant slowing in bone loss with exercise programs of 1 hour three times per week. More energetic exercise appears to produce greater effects, but the ultimate exercise prescription still awaits randomised control trial evidence.

Resistance training can include resistance bands, free weights, and exercise machines. These increase back muscle strength and generate muscle tension on bones. Exercise programs should also include balance training to assist with postural sway and strength training to increase muscle strength, muscle mass and mobility.<sup>2</sup> These programs are associated with reduction in falls in the elderly. Supervision is recommended particularly in those with low bone mass. Whether weight and balance training exercises translate to fracture risk reduction is not known.<sup>4</sup>

### Dietary recommendations

A balanced diet with adequate fibre, low in saturated fat and with daily variety is recommended. Calcium and vitamin D have a major role in osteoporosis prevention.

#### Calcium

*Most women need to increase calcium intake*

A Cochrane review<sup>5</sup> reports that calcium supplementation alone has a small, positive effect on bone density with data showing a reduction in vertebral fracture. Most Australian women have calcium intake below the recommended daily dietary intake of 800 mg (premenopausal) and 1000 mg (postmenopausal). Dairy products are the main dietary sources of calcium and 1000 mg can be achieved with 3–4 servings per day. Nondairy sources include tinned fish with bones, fortified breakfast cereals and soy products. Calcium supplements are well absorbed. Supplements and milk powder are equally effective at slowing bone loss at the hip.<sup>1,4</sup>

#### Vitamin D

*Have a little sunlight every day*

Low serum vitamin D is increasingly widespread. Vitamin D is produced in the skin as a result of sunlight exposure and decreases with age, frailty, skin pigmentation, sun-block creams and extensive body covering when outdoors. Nutritional supplementation with calcium combined with vitamin D or ostelin 1000 IU per capsule is recommended for osteoporosis prevention.<sup>4</sup> To date there are no national guidelines, however, encouraging patients to have 15 minutes of sunlight every day may be advisable.

### Phytoestrogens

*A high isoflavone intake is one component of a healthy lifestyle, without being able to assign a particular health benefit to one dietary component*

Phytoestrogens are included in a routine dietary discussion as they are metabolised from plant foods high in fibre. These include soybeans, legumes, vegetables and cereals. The plant derived compounds, daidzein and genistein, act as oestrogen receptor modulators predominantly binding to the oestrogen receptor  $\beta$ . There are three main classes: isoflavones, lignans, and coumestans; with isoflavones the most widely studied. Isoflavones are found in whole foods such as soybeans, soy grits, isoflavone supplements, and fortified foods such as breads and breakfast cereals.<sup>1</sup> The Melbourne Midlife cross sectional study reported that Australian women have a wide range of intake of isoflavone rich foods. For those women with a higher isoflavone intake, it is one component of a healthier lifestyle that includes greater intake of fruit and vegetables, greater exercise, lower mean body mass index, lower negative mood score, and higher bone mineral density of the femoral neck without being able to assign a particular health benefit to one dietary component.<sup>6</sup>

### Nonprescription treatments

#### Core body temperature

*Lowering core body temperature may help prevent hot flushes*

Evidence suggests that core body temperature has a role in initiating hot flushes. At menopause, increased sensitivity to heat with a narrow 'thermoneutral' zone often occurs. One study reported that women with hot flushes had a significantly narrowed thermoneutral zone compared with asymptomatic women.<sup>7</sup> It is rational to assume that practices that lower core body temperature may be beneficial. Observational studies have reported that lowering air temperature reduces hot flushes. Perhaps hot foods or drinks should be avoided.

#### Relaxation techniques

*Slow breathing can reduce hot flushes*

Paced respiration including slow, controlled diaphragmatic breathing has some efficacy in reducing hot flushes when performed when the flush begins (*Table 2*). Randomised prospective trials have reported that paced respiration lowers flush frequency by more than 50% compared with controls. Paced respiration was superior to muscle relaxation in reducing hot flushes.<sup>7</sup>

**Table 2. Paced respiration**

- Stand or sit erect
- Inhale steadily through the nostrils
- Fill the lower part of the lungs, lower the diaphragm
- Fill the middle part of the lungs, push out the ribs
- Fill the higher portion of the lungs, the inhalation is continuous
- Retain the breath a few seconds
- Exhale slowly
- Breathe at a rate of 6–8 cycles per minute

## Complementary and alternative therapies

Australians spend \$2.3 billion a year on complementary and alternative therapies (CAM). In a cross sectional survey of the Australian Longitudinal Study on Women's Health it was reported that women at mid-age (45–50 years) were more likely than younger women to use CAM, more likely to live in nonurban areas, and appear to use CAM in conjunction with general practitioner, specialist and hospital services – selecting therapies according to their perceived health needs.<sup>8</sup>

Many women use nonprescriptive medications for hot flushes including isoflavones, black cohosh, progesterone topical cream and dong quai. Attending a qualified practitioner is recommended as issues of the whole person can be addressed and side effects minimised from self medication. There is a paucity of data regarding efficacy and long term safety of CAM.<sup>7</sup>

### Soy derived isoflavones

*Add two tablespoons of soy grits to breakfast cereal to increase isoflavone intake*

The position statement of the North American Menopause Society states that: in general, vasomotor symptoms are only slightly reduced in women who consume soy derived products in randomised controlled clinical trials.<sup>7</sup> The majority of studies report no benefit above placebo with up to 40–45% improvement in both the treatment group and controls.

Comparing studies is difficult because of the natural resolution of flushes over time, the variation in products, and study design and duration. Some studies included dietary intervention with soy flour, soy fortified foods drinks and breads, and other dietary

supplements. The isoflavone amount varied from 40–80 mg per day. Advising patients to add 2 tablespoons of soy grits to breakfast cereal can achieve comparable increases. Two common sources for isoflavone supplements are soy and red clover. Whole foods may be preferable to supplements due to the risk of unintentional overdose with supplements.

### Red clover derived isoflavones

Red clover contains a rich supply of daidzein and genistein. Randomised controlled trials have found no benefit above placebo for treatment of hot flushes with rimostril (57 mg/day isoflavones) or promensil (40 mg/day isoflavone) one tablet daily for 3 months.<sup>7</sup> However, isoflavone supplementation 80 mg per day has decreased hot flushes by 44% compared with placebo after 12 weeks.<sup>9</sup> Minimal side effects have been reported from red clover isoflavones, although long term safety has not been confirmed.

### Black cohosh (*Cimifuga racemosa*)

Preparations from black cohosh, commercially named 'remifemin', have been studied for some years and results have been inconsistent. One randomised trial with black cohosh equivalent to 40 mg per day showed no benefit above placebo,<sup>10</sup> and the second trial showed a response equivalent to hormone therapy for treatment of hot flushes.<sup>11</sup> An earlier formulation improved menopausal symptom score and vaginal epithelium above placebo.<sup>7</sup>

The German government's 'commission E' (regulating herb efficacy and safety) has 6 months of safety data for remifemin. Reports that postulated black cohosh to have oestrogenic effects have now been refuted. Further clarification is required until it can be presumed safe in women with breast cancer. Serious adverse effects or drug interactions have not been reported.

### Chinese herb mixture

In a randomised, placebo controlled study of one mixture of Chinese herbs it was found that the herb mixture provided less benefit than placebo in treating hot flushes in those women who had previously used alternative therapies.<sup>7</sup>

### Vitamin E

In a cross over study of 120 breast cancer survivors with hot flushes, vitamin E 400 IU twice per day was superior to placebo in those women who had received

placebo first. However, the effect was minimal with the equivalent to a reduction of one extra flush per day. No adverse effects were noted with vitamin E use up to 1200 IU per day.<sup>7</sup>

### Progesterone cream

Commercial progesterone creams vary widely in doses and formulations. Products labelled as 'wild yam' contain oestrogen and progesterone precursors and are inert with no efficacy for treating hot flushes. A 1 year double blind placebo controlled study found that topical progesterone reduced hot flushes in 83% of women compared with 19% in the placebo group.<sup>12</sup> Other studies have failed to show any significant symptom relief. There was no protective effect on bone mineral density. Progesterone cream does not protect the endometrium from oestrogenic proliferation. There have been no reported adverse effects.<sup>7</sup>

### Other therapies

Dong quai, evening primrose oil, and panax ginseng in double blind placebo controlled studies have no benefit above placebo for hot flushes. Dong quai and ginseng are contraindicated with anticoagulants. Case reports have associated ginseng with uterine bleeding and mastalgia.<sup>7</sup>

In a control study of acupuncture for hot flushes, both groups improved with no difference between the groups. Magnetic therapy had no benefit for treatment of hot flushes in women after breast cancer.<sup>7</sup>

### St John's wort

St John's wort (*Hypericum perforatum*) has been used in folk medicine to treat depression. A Cochrane review's conclusions were that extracts of hypericum are more effective than placebo for short term treatment of mild to moderately severe depressive disorders. Side effects were reported by 26.3% of patients taking hypericum versus 44.7% for standard antidepressants.<sup>10</sup>

### Therapies for vaginal dryness

*If you don't use it, you lose it*

Regular sexual activity should be encouraged to maintain sexual health. Vaginal moisturisers such as 'Replens' used regularly are as effective as vaginal oestrogens for symptoms of dryness. 'Sylk' lubricant and vegetable oil (which is messy) have also been recommended.<sup>11</sup> Isoflavones have been shown to improve vaginal cytology in postmenopausal women,

but as yet have not been prescribed as a treatment for vaginal dryness.

### Nonhormonal prescription medications

#### Clonidine

Clonidine is an antihypertensive prescribed for hot flushes when oestrogen is contraindicated. Results have been inconsistent. In breast cancer survivors using tamoxifen, clonidine (0.1 mg/day) significantly improved hot flushes above placebo.<sup>15</sup> However, it is associated with side effects such as dry mouth, hypotension, insomnia, and pruritus in the patch form.<sup>7</sup>

#### SSRIs and SNRIs

Selective serotonin uptake inhibitors (SSRIs) and serotonin/noradrenalin reuptake inhibitors (SNRIs) are used for treatment of hot flushes when oestrogen is contraindicated. Venlafaxine, an SNRI, reduced hot flushes by 60% (75/150 mg); 37% (37.5 mg) compared with 27% reduction in placebo.<sup>16</sup> Effects were seen after 1–2 weeks. Side effects were dose dependent and included dry mouth, nausea and anorexia. Controlled release paroxetine, an SSRI, at doses of 12.5 mg or 25.0 mg, reduced hot flushes by 62% and 65% respectively after 6 weeks.<sup>17</sup> (It should be noted that only a 20 mg preparation of paroxetine is available in Australia). Fluoxetine 20 mg per day significantly reduced hot flushes over 4 weeks and was well tolerated.<sup>7</sup>

### Conclusion

For women with mild menopausal symptoms, lifestyle changes alone or in combination with nonprescription treatments such as simple cooling measures, paced respiration, dietary or supplemental isoflavones, black cohosh, or progesterone cream may be recommended. Although clinical data is lacking regarding efficacy for some of these treatments, they are not unreasonable as part of a progressive treatment plan as there are few short term adverse effects. In women where oestrogen is contraindicated and symptoms persist, prescription therapy with SSRIs and SNRIs or clonidine could be considered.

### Acknowledgment

The author would like to thank Dr Helena Teede, Dr Sue Reddish, Dr Amanda Deeks, Dr Elizabeth Farrell, Ms Julie Middleton, Ms Janet Michelmores, Dr A Newman, Mr Peter Atkinson and Ms Rita Erlich for their assistance and review of this manuscript.

### Summary of important points

- For women with mild menopausal symptoms, suggest lifestyle changes.
- Include simple cooling measures and paced respiration.
- Dietary or supplemental isoflavones, black cohosh, or progesterone cream may be recommended.
- Clinical data is lacking for CAM, but it could be considered as part of a progressive treatment plan as there are few short term adverse effects.
- In women where oestrogen is contraindicated, SNRIs are recommended.
- Clonidine can be used when oestrogen is contraindicated, but this can have significant side effects.
- Further information is available at The Jean Hailes Foundation website: [www.jeanhailes.org.au](http://www.jeanhailes.org.au).

Conflict of interest: none declared.

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