

# All women with multiple sclerosis should start hormone replacement therapy at menopause unless contraindicated: Commentary

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Thirty percent of patients seen in multiple sclerosis (MS) clinics will be peri- or post-menopausal. There is a significant overlap between MS symptoms and those caused or exacerbated by menopause. The most prominent of these overlap symptoms are fatigue and poor sleep, mood and cognitive disturbance, along with urinary and sexual dysfunction. Hot flashes, experienced by around 75% of women during menopause, may exacerbate MS symptoms. Identifying whether symptoms originate from MS or menopause is challenging.

Hormone replacement therapy (HRT) aims to replace the oestrogen which ceases to be produced by the ovaries following menopause. Unless a woman has had a hysterectomy, she will need to take progesterone, orally, transdermally or via an intrauterine device (IUD), to reduce the risk of endometrial cancer. Access to HRT varies significantly between and within healthcare systems. Women with MS can find it particularly difficult to access appropriate advice around HRT.

Regimes vary and are evolving. Oestrogen can be given orally, transdermally or topically. Oral oestrogen is converted to estrone in the liver. Oestrogens delivered via patches, gels or creams does not undergo hepatic metabolism following primary absorption, meaning they confer differing effects both in terms of risks and potentially benefits.

The proven benefits of HRT, not specific to MS, are in controlling menopausal symptoms and maintenance of bone mineral density with reduced risk of osteoporotic fractures.<sup>1</sup> Other potential benefits include a reduced risk of coronary heart disease when started early,<sup>2</sup> along with a reduced risk of colorectal cancer and type 2 diabetes mellitus.<sup>3,4</sup> The British Menopause Society does not set an arbitrary limit on the duration of treatment, supporting the use of HRT for as long as the benefits outweigh the risks.

There is, as Dr Magyari reminds us, a dearth of evidence demonstrating that HRT provides additional benefits to women with MS. She outlines the challenges faced when disentangling the effects of menopause on MS disease trajectory from those of aging in general. A Danish registry study did not suggest a benefit of HRT in terms of either relapse or progression.<sup>5</sup> It is worth noting that the number of women taking HRT was comparatively small and that the cohort pre-dates the widespread use of high-efficacy DMT.

Menopause coincides with a stage of MS where relapses become less common and progression more prominent. The role that sex hormones play in this change is unclear. Professor Voskuhl reminds us that aging consists of many processes, some of which are unpreventable but some, such as the loss of sex hormones, may be modifiable. Studies using estriol in combination with glatiramer acetate or interferon beta demonstrated an effect on relapse rate and new lesions seen in magnetic resonance imaging (MRI), respectively.<sup>6,7</sup> She highlights the importance of studying appropriate outcomes to identify the effect of HRT in both healthy women going through the menopause and those with MS. It is also important to consider the most appropriate type of oestrogen to maximise potential neuroprotective effect.

More research needs to be done to determine the effects of HRT on women with MS going through menopause, particularly where there may be synergistic or cumulative effects. Until such data are available, women with MS should be advised that HRT may have benefits in line with the general population such as the prevention of fragility fractures along with possible beneficial effects on symptom management. Having MS is far from being a contraindication to HRT. Healthcare professionals caring for people with MS need to be aware of the overlap in symptoms and the potential benefit that HRT may have on symptom control and quality of life.

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