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Perimenopause and menopause as oestrogen deficiency while ignoring progesterone

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In their recent Primer article (Menopause. *Nat. Rev. Dis. Primers* **1**, 15004 (2015))[1], Susan Davis and colleagues describe the life phases that every woman (surviving long enough) will experience. However, they do not include in their description the evidence that the 'cause' of menopause (oestrogen loss), related to the key hormonal and other changes of perimenopause and menopause, disappears when ageing and socioeconomic, lifestyle, genetic, racial and cultural factors are taken into account[2].

The pleomorphic experience changes that women describe, especially in perimenopause, often do become symptomatic, causing women to seek medical attention. However, the pervasive medicalization of perimenopause and menopause is related to a lack of accurate, woman-centred information; the concept (alive and well in this Primer) that menopause means 'oestrogen loss' and 'oestrogen deficiency' (REF. 1) is the height of misinformation given that this is a normal life phase. The authors do admit that perimenopause is associated with higher than normal oestrogen levels[1].

In a physiological context, changes in oestrogen levels during menopause must be considered in conjunction with the concomitant decreases in progesterone levels, which are more pronounced than any decreases in oestrogen levels. Why? With the menstrual cycle as the gold standard, oestradiol levels are measured in picomoles, whereas progesterone levels are in the nanomolar range; in percentage terms, from cycle day 1, oestradiol levels rise 225% to its mid-cycle peak, but ovulatory progesterone levels rise 1,400% to its luteal-phase plateau (admittedly, for only 10–16 days of the average ovulatory cycle)[3]. In this Primer, discussion of progesterone, the second main gonadal steroid in women, is virtually non-existent; it is even missing from a diagram of menstrual cycle hormones[1].

In addition, there is a persistent, non-scientific conflation of perimenopause and menopause, their symptoms (ambiguously called 'menopausal symptoms') and their therapies. If discussing perimenopausal symptoms, menometrorrhagia[4,5], mastalgia[6], headaches and nausea[7] should take centre stage. These two life phases do share hot flushes and night sweats (that is, vasomotor symptoms), and vaginal dryness; although vaginal dryness occurs in perimenopause for unknown reasons. However, hormonally, perimenopause and menopause are as different as chalk and cheese. Compared with premenopausal women, oestrogen levels are erratically higher in perimenopause[8] and stably lower in menopause; progesterone levels silently decline and become lower in the perimenopausal years before the last flow[9]. In contrast to conventional wisdom[10], perimenopause begins with changes in experiences within regular cycles at a time when oestrogen levels are already higher and progesterone levels already lower than in premenopause[11].

Vasomotor symptoms, which are a key adverse experience of both perimenopause and menopause, are discussed in a way that creates confusion, includes no primary physiological references and alludes to the old hypothesis that low oestrogen levels cause these symptoms[12]. Why, then, do perimenopausal women experience vasomotor symptoms when they 'have rather high levels of oestrogens' (REF. 1)? The authors state that: "Hypothalamic insensitivity to oestrogens also explains why menopausal symptoms — such as hot flushes and night sweats — commonly occur at this stage [perimenopause]… as well as why exogenous oestrogens are effective in reducing the symptoms" (REF. 1). Randomized controlled trials have shown that menopausal vasomotor symptoms are effectively treated by oestrogen or oestrogen–progestin[13], medroxyprogesterone[14], or oral micronized progesterone alone[15]. However, I challenge the authors to provide data from randomized controlled trials in perimenopausal women showing that oestrogen therapy decreases vasomotor symptoms more than placebo.

The Primer puts forward a version of these normal and universal life phases in women as 'oestrogen deficiency', but this is a decades' old, non-physiological perspective.

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Competing interests
The author declares no competing interests.