

Detailed Study Notes: Episode 445

Dr. Hazel Wallace - Nutrition for Women's Health

Quick Overview

- Cravings can change across the menstrual cycle, typically highest in the luteal phase. This also lines up with an increased energy expenditure (via increased resting metabolic rate) of up to 100-300 kcal.
- Pre-menopausal women should pay particular attention to getting enough of certain 'at risk' nutrients, i.e. those that are typically low in the diet and/or have specific importance in this population. They include: Iron, folic acid, iodine, and DHA.
- Functional hypothalamic amenorrhea describes the loss of the menstrual cycle for non-clinical reasons. Commonly this is seen in cases of low energy availability where calorie intake is insufficient to meet the energy requirements driven by high exercise levels.
- A number of supplements have been hypothesized to help with symptoms of PMS. However, the research is currently very limited and weak.
- Physiological changes occur at menopause that impact a number of health parameters. Estrogen levels decline at this time significantly. And estrogen can have a protective effect on heart disease risk. Similarly there may be impacts on bone health.
- In order to help mitigate the changes at menopause, there is a potential role of diet. For CVD risk, paying more attention to dietary patterns that keep LDL-C/ApoB low is important. And there may be a beneficial role for including soy foods due to their isoflavone content, as isoflavones may have some estrogen-like effects.
- Women with significant menopausal symptoms can talk to their doctor about HRT, with the greatest benefit:risk ratio generally being in those under 60 years of age.

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Introduction to this Episode

When it comes to specific questions related to diet and health for women, there is often a shortage of consensus answers from research, for a variety of reasons. In addition, there are clearly aspects of biological sex that have implications for health and also the interaction with diet. For example, the impact of the menstrual cycle, of menopause, and differences in nutrient requirements.

In this episode, Dr. Hazel Wallace discusses some of these key considerations. Some things covered include: the impact of menstrual cycle phase on cravings, at-risk nutrients in pre-menopausal women, functional hypothalamic amenorrhea, interaction of diet and PMS, the physiological changes at menopause and potential role of diet.

Connection to Previous Episodes

In this episode Dr. Wallace raising several specific topics which have been discussed in previous episodes of the podcast. Here's a short list of the most relevant episodes, if you wish to dive into the details of any of the listed topics:

1. In [episode 279](#) of the podcast the topics of **estrogen, menopause and HRT** were discussed by Drs. Avrum Bluming, MD & Carol Tavaris, PhD.
2. Hypothalamic amenorrhea was discussed in [episode 135](#) with Dr. Nicola Rinaldi, PhD.
3. In our episode on bone health ([episode 411](#)), the impact of phytoestrogens/isoflavones was discussed.
4. [Episode 430](#) was all about soy and isoflavones. Of most relevance here was how that relates to breast cancer (38:24) and then cardiovascular disease and menopause (53:51).

Menstrual Cycle Basics

- Average 28 days – but anything between 21 and 40 days is considered normal.
- Menstruation occurs on day 1 and usually ends on day 5 or 6.
- The cycle is split into two main phases:
 - the follicular phase
 - the luteal phase
 - ovulation occurs in between these phases (approx day 14)
- Four hormones play a central role:
 - Estrogen
 - Progesterone
 - Follicle-stimulating hormone (FSH)
 - Luteinising hormone (LH)

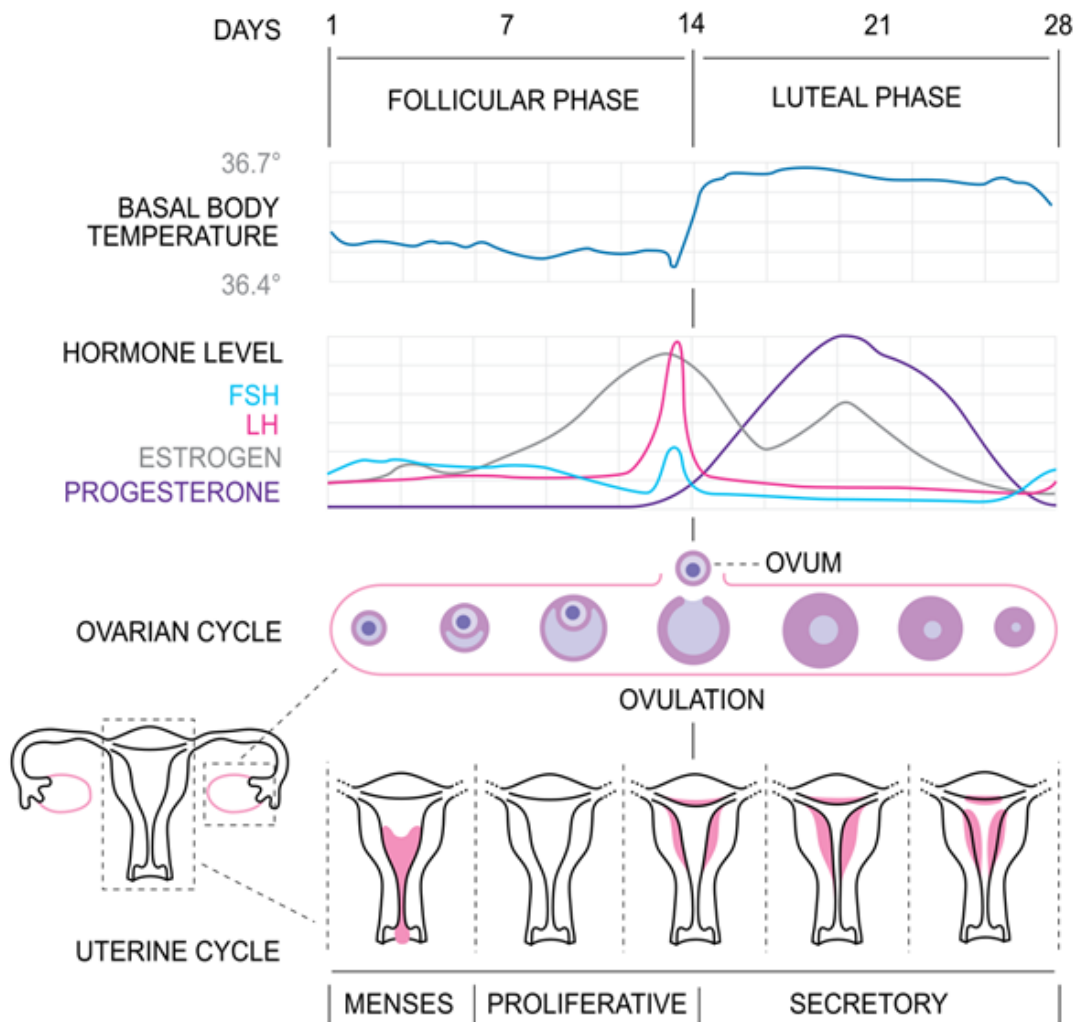


Image created by [Isometrik](#), Wikipedia

Pre-Menopause: Key Nutrients

Pre-menopausal women should pay particular attention to getting enough of certain 'at risk' nutrients, i.e. those that are typically low in the diet and/or have specific importance in this population. They include:

1. Iron
2. Iodine
3. Folic acid
4. DHA

In Europe, [61–97% of women](#) have a dietary iron intake below 15 mg/day, with differences between countries in both total intake and percentage of iron coming from heme iron. In women aged between 18 and 25 years old, 77% had iodine intakes [below the recommended intake](#), while 96% of women across reproductive ages (defined as 18-42 in this study) had intakes of folate and iron below levels recommended specifically for pregnancy.

The [most common nutrient insufficiencies](#) (i.e., below the lower reference nutrient intake) in women of reproductive age between 18-42 include:

- Iodine
- Iron
- Potassium
- Selenium

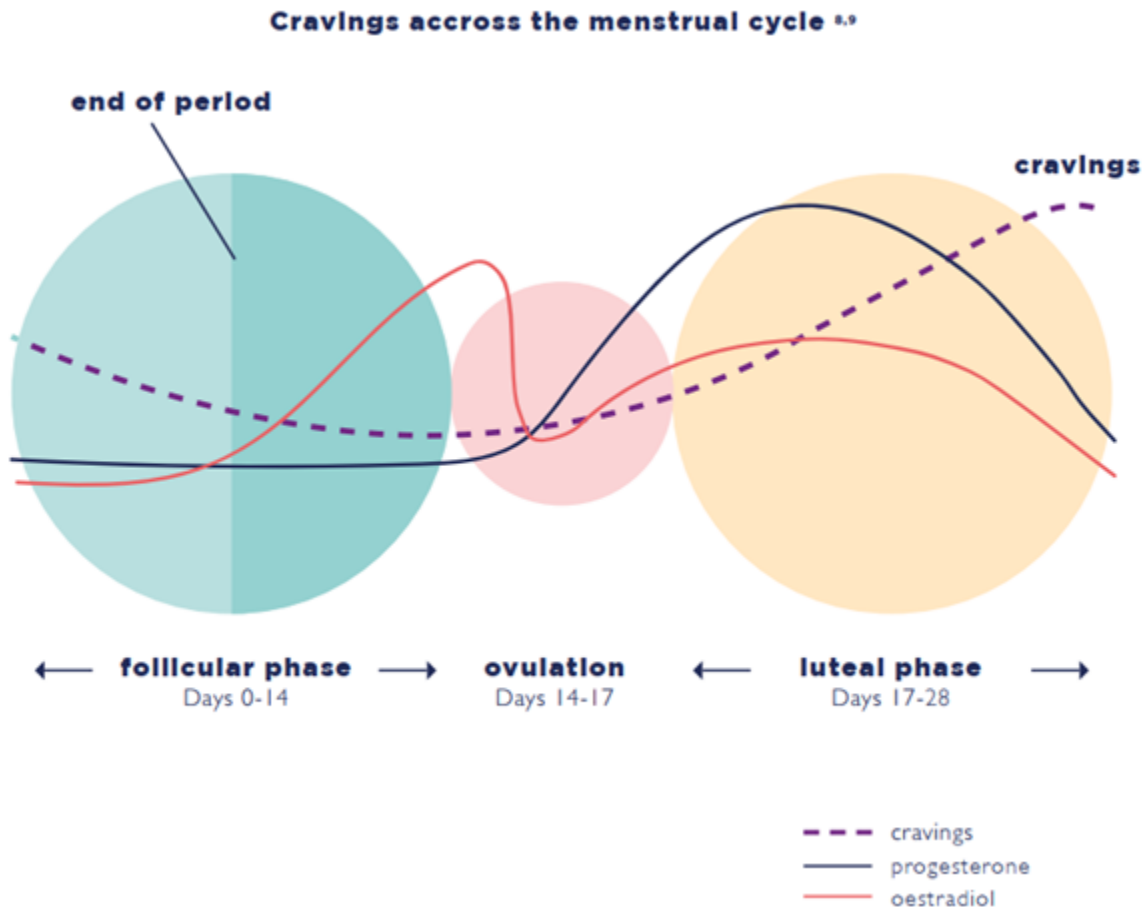
For pregnancy nutrition specifically (where folate and DHA are crucial), see previous episodes with Drs. Julie Abayomi (441), Kevin Klatt (443), and Leanne Redman (402).

Diet & the Menstrual Cycle

- Over the course of a menstrual cycle, calorie and nutrient requirements change due to fluctuations in the sex hormones; progesterone and oestrogen.
- These hormones influence body temperature, metabolism, hunger and food cravings.
- As iron is carried in red blood cells, monthly menstruation puts pre-menopausal women at an increased risk of iron deficiency and iron deficiency anaemia.
- Low energy availability (via eating too few calories relative to energy demands) can lead to irregularities with, or even complete loss of, periods.

Cravings, RMR & Hormonal Fluctuations

- In the luteal phase, progesterone is high and estrogen remains relatively high (at the start of the luteal phase). [See chart on page 4].
- At this time there is an increase in resting metabolic rate (RMR), which could mean an increased energy expenditure of up to 100-300 kcal per day (based on estimates from work by [Benton et al., 2020](#)).
- This could potentially explain the often reported increased in cravings. As Dr. Wallace framed it: *“And the thing is the human body is really intuitive and very clever at adjusting for changes. And so that's why we think that's why we see this natural increase in food craving and food intake. And when it comes to cravings, it's particularly for carbohydrate and fat.”*



Source: [The Female Factor: Making women's health count – and what it means for you by Dr Hazel Wallace is published on 7th July 2022 \(Yellow Kite, £20\)](#)

PMS (Premenstrual Syndrome)

PMS (premenstrual syndrome) is the name for the symptoms women can experience in the weeks before their period. Dr. Wallace mentioned how there have been up to 150 different symptoms reported by women during this time.

As per the NHS, the most common symptoms of PMS include:

- mood swings
- feeling upset, anxious or irritable
- tiredness or trouble sleeping
- bloating or tummy pain
- breast tenderness
- headaches
- spotty skin
- greasy hair
- changes in appetite and sex drive

Diet/Nutrients & PMS

- Dr. Wallace discussed how, anecdotally lots of women have been told that sugar and/or carbohydrates can increase your risk of having PMS symptoms.
- However, evidence suggests there is no clear link between total, or type of, carbohydrate intake and the risk of PMS ([Houghton et al., 2018](#))
- Dr. Wallace mentioned that there is some observational evidence that women with higher intakes of non-heme iron tend to have lower symptoms of PMS. Whether this is causal is unknown.
- One pragmatic recommendation Dr. Wallace gave is to potentially look at reducing caffeine intake (and/or alter timing) during this phase.
 - During the luteal phase, body temperature is increased by up to 1°C (1.8°F) higher, which can negatively impact sleep. Insomnia like symptoms are common.
 - In addition, symptoms like anxiety and bloating are common at this time.
 - As caffeine can impact sleep, anxiety and gut symptoms, Dr. Wallace suggests it may be prudent to lower intake during this phase.
- Vitamin B6 is often recommended but the evidence is actually quite weak.
- Some suggestive evidence for various extracts (e.g. The [vitex agnus-castus fruit](#), also known as chasteberry) in supplement form. But again, evidence isn't that strong.
- Potential benefit of soy isoflavones, due to estrogenic effects ([Kim et al., 2006](#))

Functional Hypothalamic Amenorrhea (FHA)

Key terms:

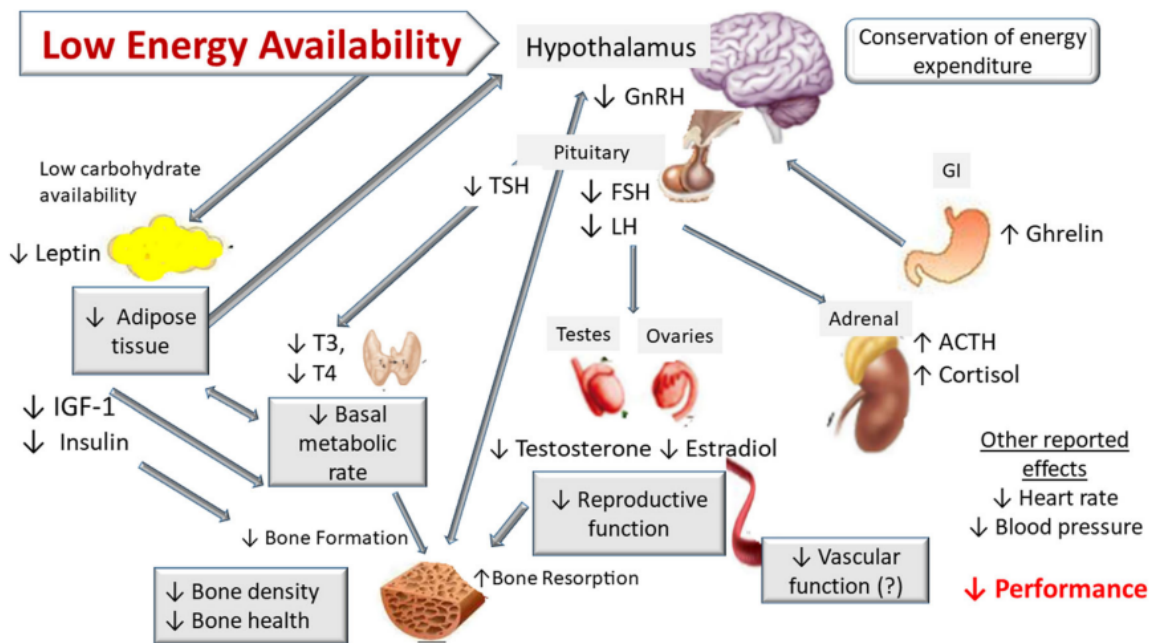
- **Amenorrhea:** “the absence of menstruation, often defined as missing one or more menstrual periods”
- **Energy availability (EA):** “the amount of dietary energy remaining to support remaining metabolic systems in the body after the energy cost for a particular system has been removed: In the case of athletes, energy availability is the amount of energy remaining to support all other body functions after the energy expended in exercise and sporting activities is removed from energy intake. (EA=Energy intake—Energy expended in exercise relative to fat-free mass)”
- **Low energy availability (LEA):** “occurs when an individual’s dietary energy intake is 3 insufficient to support the energy expenditure required for health, function and daily living, once the cost of exercise and sporting activities is taken into account”
- **Relative Energy Deficiency (RED):** “relative energy deficiency connotes that low energy availability can occur even in the scenario where energy intake and total energy expenditure are balanced (i.e. there is no overall energy deficit)”

Notes:

- Amenorrhoea can be primary or secondary:
 - Primary amenorrhoea = if you went through puberty, but you just never got a period.
 - Secondary amenorrhoea = previously had a period and then you lost it. There's lots of reasons why that may be (e.g. thyroid problems or PCOS).
- Low energy availability (LEA) is estimated to be the cause of 30% of *secondary* amenorrhoea cases.
 - Caution before you just assume that it's down to exercise your nutrition. Speak to your doctor.
- A sub-type of amenorrhoea, that is due to LEA, is termed '**functional hypothalamic amenorrhoea**':
 - 'functional' because there is no physical problem
 - 'hypothalamic' meaning that it's coming from hypothalamus
 - 'Amenorrhoea' meaning loss of the menstrual cycle
- Functional hypothalamic amenorrhea is a common form of secondary amenorrhea resulting in estrogen deficiency in young premenopausal women. The cause of this disorder is related to psychological stress, excessive exercise, disordered eating or a

combination of these factors resulting in suppression of the hypothalamic–pituitary–ovarian axis

- FHA occurs at a time when female athletes are in their peak reproductive years, which may result in infertility.
- For some athletes this may be emotionally distressing, however, it has been widely observed that many female athletes see the absence of menses to be positive.
- Many, generally feel well and avoid the regular symptoms of menses disturbing their training cycles. However, the long term fertility repercussion (i.e., infertility or increased risk miscarriage) should be communicated to female athletes by the athletes health team during health risk assessment.



From: [Dipla et al., Hormones volume 20, pages 35–47 \(2021\)](#)

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Menopause

- The perimenopausal period represents an important life stage with regard to chronic disease risk and associated nutritional factors.
- A number of changes occur that impact health:
 - declines in estrogen
 - rise in blood pressure
 - change in body fat distribution
 - lipid profile changes
- Such changes can in turn influence risk of:
 - Cardiovascular disease
 - Osteoporosis or fragility fracture
 - Breast cancer

Perimenopausal Period

Important lifestage transition to consider with regard to chronic disease risk and associated nutritional factors.

Cardiovascular Disease Risk

Breast Cancer Risk

Osteoporosis Risk

SIGMA NUTRITION .com
with Danny Louie

The infographic features a black background with yellow and white text. It includes three icons: a red heart with a white ECG line, a pink breast cancer awareness ribbon, and a yellow bone with a black jagged fracture line. The Sigma Nutrition logo is in the bottom right corner.

Menopause & CVD

- In Europe before the age of 65, there are 490,000 deaths from CVD each year in men compared to 193,000 in women.
- However, in later life [women's CVD risk increases](#). Some of this may be attributable to changes in estrogen and other mechanisms.
- The decline in estrogen is associated with notable shifts in cardiovascular disease (CVD) risk post-menopause.
- Whether due to changes in oestrogen or via other mechanisms, there seems to be an [alteration in blood lipid profiles](#) between pre- and post-menopause.
- The magnitude of risk reduction for major coronary and cardiovascular events per unit reduction in LDL-C from statin therapy [is similar in women as with men](#).
- Practically, in order to mitigate some negative changes, following the typically dietary advice aimed at keeping lipids low is recommended. Specifically:
 - Increase dietary fiber intake (with extra benefit from inclusion of viscous fiber, such as beta-glucans in oats)
 - Reduce saturated fat intake to less than 10% of calories
 - Increase unsaturated fat (in particular polyunsaturated fats and omega-3 fatty acids) in place of the saturated fat
 - For additional benefit, based on the Portfolio diet (see [episode 439](#)), consume:
 - ~2g/d phytosterols
 - ~30-60g/d nuts
 - ~25g/d soy protein

Menopause & Breast Cancer Risk

- Breast cancers that have estrogen receptors are called ER-positive (or ER+) cancers. While those without receptors are ER-negative.
- [Soy isoflavones intake](#) was inversely related to death from breast cancer among women with ER-negative breast cancer (i.e. higher intake = lower risk) but not in those with ER-positive breast cancer.
- Overall, the evidence suggests that dietary patterns inclusive of high amounts polyphenols, isothiocyanates, carotenoids, fiber, and low-fat dairy, are broadly associated with reductions in breast cancer risk, while specific reductions in total and saturated fat may be considered in cases of ER-positive and PR-positive receptor types.
- More details on this issue are discussed in episode 430 at 38:24.

Soy & Breast Cancer

- Based on mechanistic reasoning related to estrogen's effects it has been hypothesised that soy isoflavones could increase breast cancer risk, increase risk of reoccurrence, or be a problem for those with breast cancer.
- Original data on animals in the 1990s indicated the potential for increased risk.
However, this has *not* been replicated in humans.
- In fact, meta-analyses have suggested breast cancer risk reduction with soy intake; see Nachvak et al., 2019 and Qui & Jiang, 2019.

Isoflavones vs. Estrogen

While the isoflavones found in soy are often brought up due to their potential “estrogen-like” effects, it is important to clarify that they are not the same and don't have the exact same effects. Thinking isoflavones do exactly what estrogens do is a mistake.

To understand this, consider the mechanism of action:

1. There are two estrogen receptors in the human body: alpha and beta receptors
2. The hormone estrogen binds with equal affinity to both alpha and beta. (Affinity describes how ‘strongly’ a hormone binds with a receptor, i.e. how well it “fits” the receptor, and how likely it is to bind)
3. Isoflavones do indeed have estrogen-mimicking actions, but they don't act in the exact same way.
4. Rather isoflavones preferentially bind to the beta receptors, with much less of an affinity for the alpha receptors
5. Therefore they classified as SERMs (Selective Estrogen Receptor Modulators)
6. The difference in receptor binding between isoflavones and estrogen is important because the alpha and beta receptors are present in differing amounts in different tissues, and have different effects in the body when one of the compounds binds to them.
7. So isoflavones can have some estrogen-like effects in the body, but it is weaker of an effect, and it also doesn't mimic all the effects of estrogen.
8. Importantly, isoflavones don't really affect estrogen levels. So they have some estrogen-like effects, without changing estrogen concentrations. Maybe why differences in relation to risk predicted by mechanisms.
9. Finally, as they are a phytonutrient, isoflavones can have effects that are completely separate to an estrogen-mimicking effect.

Hormone Replacement Therapy & Menopause

- Dr. Wallace mentioned that there's a lot of fear around HRT and a lot of that stems from old poorly done research.
 - This is a theme that was discussed in detail in [episode 279 of the podcast](#). In that, one big example discussed was the significant issues with the Women's Health Initiative (2002) that suggested women taking HRT had an increased risk of breast cancer.
- Dr. Wallace stated that, *in general*, for most women under the age of 60 who have symptoms relating to the menopause (e.g. hot flashes, insomnia, etc.), the benefits of HRT generally outweigh the risks.
- For women under the age of 50 who go through the menopause the risks of HRT do not apply as you are “simply replacing the hormones you would normally have at this age.”
- There is potentially a decreased risk in cardiovascular disease, if HRT is started within 10 years of starting the menopause, or if you're under the age of 60.
 - Data suggesting harm was based on women over the age of 70, who were starting HRT for the first time.
- For women over the age of 60, the risk:reward balance may start to tip in the other direction.
- HRT is the most effective solution for the relief of menopausal symptoms and also carries some other benefits. However, Dr. Wallace emphasized that, like all treatment, it's not completely risk-free and it is not suitable for everyone.
- Some of that risk, for certain people/groups, is a small increased risk of breast cancer with combined HRT (estrogen + progesterone). However, there is no risk with estrogen-only HRT.

Potential risks	Potential benefits	Inconclusive
<ul style="list-style-type: none"> • Small increased risk of breast cancer with combined HRT (little to no increased risk with oestrogen-only HRT).⁸¹ • Increased risk of endometrial cancer with oestrogen-only HRT – in women with a womb.⁸² (This is why oestrogen is always given with progesterone in women who still have a womb to protect the endometrial lining.) • Combined or oestrogen-only HRT taken orally slightly increases your risk of stroke.⁸³ This also depends on dose and route, so there is no increased risk with transdermal oestrogen, for example. • Increased risk of blood clots (venous thromboembolisms) in the legs or lungs with oral HRT, but not patches or gels.⁸⁴ 	<ul style="list-style-type: none"> • Reduction in menopausal symptoms including hot flushes, sleep disturbances, joint aches and pains, mood changes and vaginal and urinary symptoms.⁸⁵ This has a knock-on benefit of improving overall quality of life and relationships. • Protection against osteoporosis and risk of fracture.⁸⁶ • Many offer cosmetic benefits on skin ageing.⁸⁷ • May improve muscle mass and strength.⁸⁸ • Decrease in cardiovascular risk if started within 10 years of the menopause or under the age of 60.⁸⁹ 	<ul style="list-style-type: none"> • Possible increase in ovarian cancer, but results conflicting.⁹⁰ • Research into dementia risk and HRT is mixed and inconclusive, and so HRT is not currently recommended for the prevention of dementia.⁹¹ • Possible risk reduction in colorectal cancer.⁹²

Source: [The Female Factor: Making women's health count – and what it means for you by Dr Hazel Wallace is published on 7th July 2022 \(Yellow Kite, £20\)](#)

Hot Flashes/Flushes & Diet

- Most women will experience hot flashes when going through the menopause.
- They're often described as a sudden feeling of heat that seems to come from nowhere and spreads throughout the body.
- Individuals may also experience sweating, palpitations and flushing of the face.
- Caffeine and alcohol can make the severity of hot flashes worse in some women.
- Avoiding spicy foods is a common recommendation for women experiencing hot flashes, but [evidence to support this](#) is limited.
- Phytoestrogens could be beneficial – See episode 430 on soy

Menopausal Symptoms & Supplements

- Specific supplements are often proposed to alleviate menopausal symptoms, although the evidence is often not as robust as common indications may suggest.
- A small number of intervention studies have suggested a benefit to supplementation of dehydroepiandrosterone (DHEA):
 - [Reductions in hot flashes](#)
 - [Increased oestrogenic hormones](#)
 - [Decreased overall symptoms](#)
- A phytoestrogen supplement, Pueraria Mirifica, has been shown in [preliminary studies](#) to reduce menopausal symptoms at doses of 25-50mg/d. However, these effects need to be confirmed in larger, controlled trials.
- Black cohosh has received substantial attention as a supplement for menopausal symptoms, with [a meta-analysis of 9 studies](#) indicating a benefit in 6/9, and overall significant reduction in symptoms. However, as of yet these effects have not been consistent in larger controlled trials.

Conclusions & Practical Application

1. Cravings can change across the menstrual cycle, typically highest in the luteal phase. This also lines up with an increased energy expenditure (via increased resting metabolic rate) of up to 100-300 kcal.
2. Risk of iron deficiency increases after onset of menstrual cycle.
3. Functional hypothalamic amenorrhea occurs in cases of low energy availability where calorie intake is insufficient to meet the energy requirements driven by high exercise levels.
4. In women, estrogen appears to confer protection against visceral adipose tissue accumulation, and preferentially shift fat deposition toward subcutaneous adipose tissue accumulation.
5. Physiological changes occur at menopause that impact a number of health parameters. Estrogen levels decline at this time significantly.
6. In order to help mitigate the changes at menopause, there is a potential role of diet.
7. For CVD risk, paying more attention to dietary patterns that keep LDL-C/ApoB low is important. And there may be a beneficial role for including soy foods due to their isoflavone content, as isoflavones may have some estrogen-like effects.
8. Women with significant menopausal symptoms can talk to their doctor about HRT, with the greatest benefit:risk ratio generally being in those under 60 years of age.
9. A number of supplements have been hypothesized to help with symptoms of both PMS and menopause. However, in both cases, the research is currently very limited, preliminary and weak.