The genetics of hot flashes, hidden messages with a big impact.

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Research finds that hot flashes and hormone levels in postmenopausal women can be influenced by genetics. In several studies researchers sought to identify genes that not only affect a woman's chances of having hot flashes, but also affect their severity.[1,2]

Hot flashes are a predominate symptom of menopause and the major reason woman seek medical care. One of the most concerning aspect of hot flashes is the resulting poor sleep quality due to being awakened during the night by this symptom. As many as 40 million women experience hot flashes each year. Research has found that several factors can influence a woman's risk for developing hot flashes including hormone imbalances, glucose transportation into the brain, smoking, ethnicity and age of onset.[1,2]

When most practitioners think of menopause, they think low estrogen. Experienced providers knowledgeable about hormone balancing therapeutics know there is more to the story. Studies have shown that low endogenous total (bound and free) estradiol, estrone and progesterone levels are associated with hot flashes.[4-5] Interestingly, additional studies suggest changes in total androgen levels may not be associated with hot flashes.[6,7]

Gene's involved in the metabolism of estrogen, specifically a gene called CYP1B1 has been shown in studies to be linked to risk of experiencing hot flashes.[1,2] Specifically, one study found that women carrying the CYP1B1 allele (rs1800440) GG genotype had 3-fold greater odds of experiencing hot flashes for 1 year compared to the AA genotype.[8] This version of the CYP1B1 gene encodes for an enzyme that is responsible for the first step in the metabolism of estradiol to the catechol estrogen called 4-OH E1. The risk allele produces a fast version of this enzyme which most likely causing an increased rate of estradiol break down subsequently lowering estradiol levels in the body.[9] These low levels of estradiol can then lead to the kind of hormone imbalances in the body that are associated with hot flashes.[1,2]

A progesterone producing gene called 3HSD has also been linked to an increased risk of developing hot flashes.[1] The gene 3HSD encodes for an enzyme that catalyzes the biosynthesis of the steroid progesterone from pregnenolone, 17-hydroxyprogesterone from 17-hydroxypregnenolone, and androstenedione from dehydroepiandrosterone (DHEA). These processes are primarily carried out in the adrenal gland however the enzyme is also present in the ovaries or testes. It is 3HSD involvement in producing sex hormones that make this gene product influential in balancing progesterone and testosterone levels. Low levels of progesterone have been found in patients who develop hot flashes.[1]

Natural treatment options for hot flashes are in demand with patients. Balancing hormones is always the first goal of any treatment plan and knowing a patient's

genotype for alleles related to hormone synthesis and metabolization can help practitioners target those treatment solutions. If a patient carries a risk allele for a fast CYP1B1 enzyme, then a practitioner should consider adding Trans-resveratol which has been shown in vitro to lower this enzyme's activity rate.[9] If a patient has the risk allele of 3HSD the practitioner should focus on monitoring and supplementing bio-identical progesterone. Kajarin's 4Balance progesterone formula can help address all levels hormone imbalances that can lead to hot flashes and 4BalancePlus provides 1 mg of biest in addition to 32 mg of progesterone for women whos estradiol levels are truly low.

A third genetic connection was made when a study demonstrated that Caucasian women who carried the HIF1a 1744 genotype have an increased risk of experiencing hot flashes postmenopausal.[10] Though the mechanism of action is still being elucidated, it is known that HIF1a plays a key role in the regulation of genes controlling glucose metabolism associated with hot flashes. The connection lies in the fact that estrogen is needed to maintain cerebral glucose transport and concentrations. Lowered estrogen levels during menopause are believed to cause impaired cerebral glucose transport and central hypoglycemia. When blood sugar levels are low, hot flashes have been shown to occur more frequently. It has been speculated that hot flashes are the brain's attempt to maintain glucose levels. Women with the HIF1a risk allele are thought to have impaired glucose transport into the brain.[10] It is important to focus treatment on balancing blood sugar levels in patients with this risk allele as well as balancing estrogen levels with 4Balance cream.

The way women experience these can vary immensely. Environmental and hormonal levels have been shown in previous studies to be associated with risk for having hot flashes. In addition, researchers are finding links to genes that can also increase risk. Knowing a patient's genotype can benefit the practitioner by allowing them to create targeted treatment plans that follow a holistic approach.

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