

New Scientific Statement on Menopausal Hormone Therapy (MHT) by the Endocrine Society – July 2010

A new Endocrine Society scientific statement published in the July 2010 issue of the *Journal of Clinical Endocrinology & Metabolism* evaluates benefits and risks for postmenopausal hormone replacement therapy (HRT), now known as menopausal hormone therapy (MHT).

Although MHT was in widespread use in the 1990s in hopes of lowering cardiovascular disease risk as well as to treat menopausal symptoms, the Women's Health Initiative (WHI) Study showed that MHT was actually associated with an increased risk for heart disease, stroke, and breast cancer. However, recent evidence suggests that these risks may be affected by time after onset of menopause when MHT was started, a factor not considered in the WHI assessment of MHT safety and efficacy.

"Before the WHI, MHT was believed to prevent heart disease, fractures, memory loss and dementia in addition to relieving uncomfortable menopausal symptoms," said task force chair Richard J. Santen, MD, professor of medicine at the University of Virginia in Charlottesville, in a news release. "Following the WHI reports of increased health risks associated with MHT, MHT use declined by 80%. New data however show that these health risks may not apply to all women using MHT, and that MHT may in fact be very beneficial to some women."

Controversy regarding WHI's applicability to women just entering menopause stems from the fact that the average age of participants was 63 years, and only 3.5% of the women were aged 50 to 54 years, which is the age range when women typically decide whether to start MHT. Furthermore, WHI did not address menopausal symptom relief. Therefore, this scientific statement considered new data from later studies evaluating the effects of MHT in women aged 50 to 55 years.

Compared with women who begin MHT after age 60 years, those who begin MHT a short time after onset of menopause at ages 50 to 59 years appear to benefit. According to recent evidence, women within a short time after onset of menopause using MHT for 5 years had a 30% to 40% reduction in mortality risk and no increased cardiovascular disease risk. In addition, they had a 90% decrease in hot flashes, overactive bladder, or other menopausal symptoms.

"Some women in this group still developed breast cancer but only with the combination of estrogen plus a progestogen, not with estrogen alone," Dr. Santen said. "This may be due to the stimulation and uncovering of very small, undiagnosed breast cancers, rather than causing these cancers de novo."

Conclusions Reached

Below is a list of some of the conclusions (with level of evidence A) reached by the task force after evaluation of the new data along with WHI:

- "Standard-dose" estrogen used with or without a progestogen is associated with marked reduction in frequency and severity of hot flashes. For many women, lower doses of estrogen are also effective.
- For symptoms of vaginal atrophy, very low doses of vaginal estradiol are effective.
- Symptoms of overactive bladder may be reduced by estrogen given vaginally or systemically.
- Vaginal estrogen is associated with lower rates of recurrent urinary tract infections.

- For women in postmenopause, estrogen given with or without a progestogen is as effective as bisphosphonate therapy for preventing postmenopausal bone loss and increasing bone mass.
- Use of estrogen alone and estrogen plus a progestogen is associated with a lower incidence of hip and vertebral fractures.
- Treatment with the selective estrogen receptor modulator raloxifene is associated with increased bone mineral density and lower rates of vertebral, but not hip, fractures.
- Use of MHT containing estrogen plus a progestogen is linked to a lower risk for colon cancer.
- Raloxifene is associated with a lower risk for breast cancer.
- Mammographic density is increased in women taking estrogen alone or with a progestogen.
- Sexual function is improved by physiologic amounts of transdermal testosterone, but not by dehydroepiandrosterone.
- Risk for venothrombotic episodes is approximately doubled in women using MHT, and this risk is multiplicative with baseline risk factors such as age, increased body mass index, thrombophilias, surgery, and immobilization.
- Use of raloxifene is associated with an increased incidence of venothrombotic episodes.
- Raloxifene is not associated with any increase in stroke risk.
- In older women with preexisting vascular disease, hormone use does not reduce stroke incidence.
- Although continuous estrogen plus a progestogen does not cause endometrial cancer, estrogen alone without a progestogen is associated with an increased incidence in endometrial cancer.
- Risk for gallbladder disease is increased in women using estrogen alone or with a progestogen.
- MHT started after age 60 years does not improve memory.

"It is important to remember that most women considering MHT are between the ages of 50 and 55 and in this group MHT may have many benefits," Dr. Santen concluded. "Physicians and their patients need to re-think the use of MHT based on data pertinent to the 50-55 year old and therapy should be individualized based on symptoms and underlying risks of breast cancer and heart disease."

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