



# INTERNATIONAL MENOPAUSE SOCIETY

THE SOCIETY FOR THE STUDY OF ALL ASPECTS OF THE CLIMACTERIC IN MEN AND WOMEN

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## Press Statement

ISSUED ON BEHALF OF THE INTERNATIONAL MENOPAUSE SOCIETY BY  
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*July 24, 2007*

### **Breast cancer and hormone therapy: a looking-glass mirror?**

The medical community has been debating for many years whether, and to what extent, postmenopausal hormone therapy (HT) use is associated with a higher risk of breast cancer, says Professor Amos Pines, President of the International Menopause Society. Although it is agreed that long-term HT slightly increases that risk, the definition of long-term use is still unclear, particularly in view of data showing that it may vary significantly by type of HT (estrogen-alone vs. estrogen-progestin, brand of progestin, dosage). A new study from the Kaiser Permanente health plan<sup>1</sup> raises the question whether trends in breast cancer incidence and use of HT over the past 25 years may be directly linked.

The Women's Health Initiative (WHI) trial was a landmark in menopause medicine since it provided information based on the best available study methodology<sup>2</sup>. By adopting its results as the ultimate source of information, many organizations, medical societies and health authorities actually declared that data derived from observations in the postmenopausal population are less valuable. Nevertheless, during the past few months, several studies have used databases on the incidence of breast cancer, on the one hand, and sales of HT on the other hand, in order to suggest a direct link between trends of hormone use and the number of newly diagnosed breast cancer patients. While such information, by itself, is very important and interesting, conclusions must be drawn with great caution. It is tempting to simplify the observed year-by-year figures on HT use and breast cancer incidence and establish a 'mirror glass' equation: the more postmenopausal hormone use, the more breast cancer, and vice versa. But human biology is far too complicated and the pathophysiology of breast cancer is far too complex to adopt such a mechanistic approach, as the authors of those studies and related Editorials rightly say.

The mere fact that the incidence of lung cancer is higher among people carrying a lighter in their pocket does not mean that lighters cause lung cancer. Thus, having two parallel time trends, for breast cancer incidence and for hormone use, still makes it necessary to investigate further in order to better understand if and how those trends could be linked. For example, a third important player has now been added, namely the rate of mammography screening, which has proved to have similar fluctuations as HT use and breast cancer incidence<sup>1</sup>. According to the Kaiser Permanente registry<sup>1</sup>, the rate of women aged 45–59 undergoing screening mammography in 2002–2004 (post-WHI period) decreased from 48% to 44%. Thus, awareness of the need for periodic breast examinations may ease, and the likelihood

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of women coming to be examined may decrease in a population that uses HT less frequently, which could lead to under-diagnosis of breast cancer.

On the other hand, the 28% increase in breast cancer incidence between the early 1980s and the early 1990s observed in the Kaiser Permanente cohort probably reflects the outcome of implementation of the mammography screening program during that period. The largest group among HT users in most of the countries (excluding the USA) has always been women younger than 60 years. The Kaiser Permanente data show that, for women aged 45–59, the 70% drop in HT use (defined as dispensation of at least one hormonal prescription) in the year 2006 (post-WHI period) as compared to the year 2000 (pre-WHI period) was associated with a *non-significant* decrease of 4.9% in breast cancer incidence, which translates into a reduction of less than one case of breast cancer per 10,000 women per year.

Furthermore, a welcome but unexplained fact is that, in younger women (age groups < 45 years and 45–59 years), the incidence of invasive breast cancer started to decrease *before* the year 2000 (see Figure 1 in Glass *et al.*<sup>1</sup>). The same has been shown for the incidence of localized cancers (Figure 2<sup>1</sup>) and the age-adjusted annual incidence rate of both estrogen receptor-positive and -negative breast cancers (Figure 3<sup>1</sup>). Therefore, the decrease of breast cancer incidence analyzed from different angles by Glass and colleagues cannot be attributed simply to the drop in HT use, which started after the publication of the WHI study. There must be another, non-hormonal and still unknown factor explaining, at least in part, these changes in incidence since 1998.

Professor Pines concludes that the new epidemiological data coming from the Kaiser Permanente study do have scientific merits, but may be confusing when interpreted for the lay public. Health-care providers should stay with the first-grade information coming from the WHI study when discussing this issue with their patients: breast-wise, in women younger than 60, HT (particularly estrogen-alone) is safe. Long-term use may be associated with a small increased risk, in the order of one extra case per 1000 women per year. Discontinuation of HT brings this risk back to the values for age-matched non-users after 3–5 years. Weighing the overall benefits and risks of HT in the younger postmenopausal population clearly favors the use of HT for symptomatic women.

## References

1. Glass AG, Lacey JV Jr, Carreon D, Hoover RN. Breast cancer incidence, 1980–2006: combined roles of menopausal hormone therapy, screening mammography, and estrogen receptor status. *J Natl Cancer Inst* 2007;99:1152–61
2. Rossouw JE, Anderson GL, Prentice RL, *et al.* Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321–33

## THE INTERNATIONAL MENOPAUSE SOCIETY

The aims of the Society (IMS) are to promote knowledge, study and research on all aspects of aging in men and women; to organize, prepare, hold and participate in international meetings and congresses on menopause and climacteric; and to encourage the interchange of research plans and experience between individual members. The Society is a non-profit association, within the meaning of the Swiss Civil Code. It was created in 1978 during the first World Congress on the Menopause. In addition to organizing congresses, symposia, and workshops, the IMS owns its own journal: *Climacteric*. See website: [www.imsociety.org](http://www.imsociety.org)