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

Press Statement

ISSUED ON BEHALF OF THE INTERNATIONAL MENOPAUSE SOCIETY BY
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Postmenopausal hormone therapy and coronary disease – the truth of the matter

With each new publication of coronary artery disease (CAD) data from the Women's Health Initiative (WHI) study, the inevitable reaction is "Why on earth did the WHI investigators claim in 2002–2004 that postmenopausal hormone therapy has deleterious effects on the risk for CAD, when, from the beginning, they were aware of the importance of the age factor in this clinical scenario?". Women in the age group of 50–59 years who participated in the estrogen-alone arm of the WHI study were asked immediately after the early cessation of the trial to become part of an ancillary study – the WHI-CACS – which looked at the magnitude of coronary calcifications measured by ultra-fast coronary CT. Coronary calcium deposits develop as part of the atherosclerosis process and correlate well with findings of coronary angiography. The results of WHI-CACS, now published in the *New England Journal of Medicine* [1] are very encouraging, since women who were randomized to the estrogen arm of the WHI had significantly smaller calcification scores than their counterparts in the placebo arm. The effect was recorded for all degrees of severity, with estrogen users having a 20–30% reduction in the likelihood of being categorized as having a mild to moderate increase in calcification scores (less than 100), and a more than 50% reduction in the likelihood of being categorized as advanced cases with calcification scores above 100. This study re-affirms what was actually known for many years, based on animal data and observational studies in women. Estrogen has a wide range of well-documented beneficial metabolic and vascular effects: it reduces the pace of accumulation of atherosclerosis, and decreases the risk of coronary events, provided that treatment is started *early* in the menopause. In addition, the CT in the WHI-CACS was performed at a mean age of 64.8 years, 7.4 years after randomization to the WHI trial, which suggests a new "safety margin" for age and duration of estrogen therapy, as women can be reassured that estrogen therapy is cardioprotective at least until age 65.

One of the main arguments that were raised at the time of publication of the preliminary data of the WHI 5 years ago, in attempt to explain the disconcordance between the results of previous large-scale, long-term, observational studies and the WHI cardiac data, was that randomized, placebo-controlled trials are always better and suffer less bias. With randomized trials being Level I evidence and observational trials considered Level II evidence, devaluation of good observational data became

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state-of-the-art. The recent post-hoc analyses from WHI show that, by the end of the day, the observational studies did give valuable information, which was comparable to that obtained by the randomized trials. Even for the issue of coronary calcifications and hormone therapy, a literature search shows that "lower grade" encouraging clinical data were there for at least 10 years. Clearly, a real long-term, randomized, double-blind, placebo-controlled study on hormone therapy cannot be performed. The IMS therefore suggests that available long-term data from the Nurses' Health Study and other major observational studies should be considered while making decisions on hormone therapy in clinical practice. Since most, if not all, women do not start hormone therapy at an old age, safety concerns on its possible adverse cardiac effects are actually invalid for the vast majority of hormone users. In fact, treatment seems to be associated with reduction of risk for coronary artery disease if initiated early.

Reference

1. Manson JE, *et al*. *N Engl J Med* 2007;356:2591

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