International Menopause Society

Promoting education and research on midlife women's health

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The evidence base for Hormone Replacement Therapy (HRT): what can we believe?

The 'facts' that most women and clinicians consider in making the decision to use, or not use, HRT are frequently wrong or incorrectly applied says Professor Robert D Langer in a paper entitled The evidence base for HRT: what can we believe?, which will be published in the forthcoming April edition of the journal of the International Menopause Society, Climacteric. It raises serious questions about the 'facts' that have led women and their doctors to believe hormone therapy (often called HRT) is unsafe.

The incendiary reports surrounding the early termination of the Women's Health Initiative (WHI) clinical trial of a specific form of HRT (conjugated equine estrogens with medroxyprogesterone acetate), in 2002, were highly misleading. They indicated that the study was stopped because HRT caused breast cancer and heart attacks, when in reality the study was stopped for more subtle reasons and there was no statistically significant harm for either breast cancer or heart attacks. Nonetheless, that stunning report quickly resulted in women across the world abandoning HRT.

Professor Langer, one of the principal investigators in the WHI, describes in his paper the process that led to the distorted reporting of the WHI findings that triggered the sensationalised cascade of fear, and the flight from appropriate use of HRT. He reports that, in an unprecedented departure from accepted practice, the incendiary initial results paper was written by a small group of individuals and kept secret from the vast majority of scientists in whose names it was submitted until after it was accepted by the journal. The unfortunate result was that the paper misrepresented the findings, and made inflammatory claims that were not supported by the data when viewed according to the pre-established study protocol -- which was largely abandoned in this and subsequent reports.

Professor Langer also points out that the WHI was conducted to test if the benefits that had been seen in women starting HRT near menopause would be found in women starting this treatment a decade or so after going through menopause, and that the study purposely did not include enough recently menopausal women to assess outcomes in that age group. Nonetheless, the initial results were generalized

from the older women to younger women, twisting the logic of the study in a scientifically inappropriate manner. The aftermath has been that women with significant menopausal symptoms such as hot flushes, night sweats, sleep disturbance, joint pain, anxiety and lowered mood (approximately 1 in 3 women), have been mostly untreated for 15 years. Not only have women been denied symptom relief but they have also been denied the other benefits of HRT- including unarguably protection against bone loss and reduced risk of fracture.

Professor Langer points out that the second half of the WHI HRT trials, the study testing conjugated equine estrogen alone in women with prior hysterectomy, found trends in breast cancer and heart attacks that were the opposite of the results in the first paper. The results suggested a reduced rate of breast cancer with that form of HRT, and reduced rates of heart attacks in women who were less than 60 years old when they began HRT. Those results, reported 2 years after the initial paper, were lost in the by then well-established climate of fear. He notes that -- as those contrasting results demonstrate -- there are important differences in HRT regimens and that the available HRT regimens have expanded tremendously, built upon the lessons of the WHI and other recent clinical trials.

In a cautionary note, Professor Langer cites recent data that show an increase in major diseases that HRT could prevent, including hip fractures and heart attacks, in the wake of the WHI.

Professor Rodney Baber, Editor in Chief of the journal and lead author of the IMS recommendations on HRT concludes in the April edition editorial “This new study raises serious questions about due process surrounding the data evaluation, writing, author approval and publication of the original WHI paper. It seems not all principal investigators were consulted during the data evaluation and writing phases. There may have been protocol violations and the paper was prepared and published prior to review by all authors. Other WHI investigators may hold different views, but this study points to the need for reappraisal and potential change in our overall understanding of the relationship between HRT use and risk”

Professor Mary Ann Lumsden, IMS President comments “All clinicians constantly reappraise treatment modalities and look at the balance of risk, but now is time for us to recognise that hormone therapy prescribed to healthy postmenopausal women within 10 years of their last menstrual period, is an effective intervention, and for most women benefits outweigh risks. It can help avoid the many symptoms women suffer during this transitional period of their lives. We welcome the release of this paper, which reinforces the advice provided in our evidence based IMS Recommendations on HRT”