

REPORT OF EXPERT COMMITTEE

Convened by the Therapeutic Goods Administration
to assess the findings of a report on the safety of the

US Women's Health Initiative

(combined Hormone Replacement Therapy) trial.

Presented to the Hon Trish Worth, Parliamentary Secretary to the
Commonwealth Minister for Health and Ageing, by the Chair of the
Expert Committee, Professor Martin Tattersall

July 11, 2002

Overview

- The US Women's Health Initiative has released important information about the long-term safety of oestrogen plus progestin combination hormone replacement therapy. In a trial enrolling more than 16,000 women, they report an increase in the incidence of heart attacks, stroke, clotting events and breast cancer. These were balanced to some extent by protective effects, against bowel cancer and osteoporotic (*major*) fracture. There is no difference over the 5 year follow-up in overall mortality in those receiving combination hormone therapy versus placebo.
- This trial was designed to investigate the efficacy and safety of long-term hormone replacement therapy in preventing diseases, such as coronary heart disease and hip fracture, in post menopausal women. It was not designed to study the effects of hormone replacement therapy being used in women to treat symptoms experienced at the time of menopause. The women enrolled in this study had a mean age of 63, with two-thirds being over 60. On average the women were overweight, and one-third were obese. Fifty percent were previous or current cigarette smokers when they entered the study. One-third had received treatment for high blood pressure and over ten percent had raised cholesterol levels requiring medication. The presence of these factors may have increased the harmful effects caused by hormone therapy.
- The absolute increase risk in disease risk for an individual woman shown in this study is small. In 10,000 women in the age group studied, and with their characteristics, taking the combination hormone replacement therapy for a year, there would be 7 more cases of coronary heart disease (37 vs 30), 8 more cases of invasive breast cancer (38 vs 30), 8 more cases of stroke (29 vs 21) and 8 more cases of blood clots on the lungs (15 vs 7), but 6 fewer bowel cancers (10 vs 16) and 5 fewer hip fractures (10 vs 15) than in those not using therapy.
- The increase in harm was smaller in the first two to three years from starting treatment than with three or more years of use.

Conclusions

- The Committee agrees with the conclusions of the authors that combination hormone replacement therapy in any form should not be used for long-term disease prevention in post menopausal women because the benefits are not sufficient to justify the risks of such use. The Committee believes that this conclusion is not necessarily restricted to the particular products used in the trial, but could potentially apply to all oestrogen/progestin combination hormone products.
- The relevance of these findings to the use of hormone replacement therapies in the short term treatment of symptoms in women at the time of the menopause is less certain. Women can be assured that short-term use of combination hormone replacement therapies and other products to manage symptoms of menopause remains an appropriate treatment option, but women should discuss their particular medical circumstances with their doctor, as individual factors may affect the risks and benefits of treatment for them. This is even more so for younger women with premature menopause, in whom the benefits of hormone replacement would be expected to be greater, and the risks are probably smaller.
- The continued use of combined hormone replacement therapy for women with established

osteoporosis is also an acceptable option for many but women should discuss the benefits and risks with their treating doctor.

- In another arm of this study, which has not been discontinued, the use of oestrogen alone for the prevention of disease in post menopausal women who have had a hysterectomy continues under investigation. It is unsafe for women who have a uterus (womb) to use oestrogen without progestin, as use of oestrogen alone increases the risk of uterine cancer.

Recommendations for Future Action

- The Committee supports the TGA in its actions to ensure updating of product and consumer information for all products used in combination hormone replacement therapy.
- The Committee recommends a full review of the use of combination hormone replacement therapy in long-term treatment and prevention of osteoporosis.
- The Committee recommends that the TGA review all ongoing Australian trials using combination hormone therapy for chronic diseases.