

## HORMONE REPLACEMENT THERAPY: WHERE DO WE GO FROM HERE?

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### INTRODUCTION

In July 2002, the National Institutes of Health closed a portion of the Women's Health Initiative that was studying the relationship between hormone replacement therapy (HRT) and its possible risks and benefits. The study had involved 16,608 healthy women, ages 50 to 70, who took either estrogen and progestin or a placebo.

Women's Health Initiative (WHI) stopped the study when it identified small but significantly increased risks of breast cancer, coronary artery disease, stroke, and vascular events. The benefits included lower risk of fractures and colon cancer. There was no difference in the death rates between the group on combined HRT (cHRT) and the group taking placebo.

"The ground rules have changed in how to prescribe hormone replacement therapy," Dr. Mary Jackson said. The purpose of her presentation at the Primary Care Conference was to review the findings and to help health professionals determine how to advise their patients who ask, "What do I do now?"

### WHAT ARE THE RISKS?

#### Coronary Artery Disease

Women's Health Initiative (WHI) showed a small but significant increased risk for events such as non-fatal heart attacks. The risk for heart disease was 29% higher for the group taking combined HRT than for the group taking a placebo. For example, the number of heart disease events for women in the combined therapy group averaged 37 per 10,000 during a year, while the number for women on placebos averaged 30 per 10,000. "This risk appeared in the first year of cHRT use," Dr. Jackson said.

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#### Invasive Breast Cancer

The risk of invasive breast cancer was 26% higher in the group on cHRT. The average per year was 38 cases per 10,000 women on cHRT vs 30 cases per 10,000 women on placebo. This increase was apparent after 4 years of cHRT use and appeared to be cumulative over time. "The risk in the cHRT group increased at a higher rate than the risk that would occur normally with advancing age," Dr. Jackson said.

#### Stroke

There was a 41% increased risk for the group on cHRT. The average per year was 29 cases of stroke per 10,000 women on cHRT vs 21 cases per 10,000 women on placebo. "The risk appeared in the second year of combined therapy use and continued into the fifth year of the study," Dr. Jackson said.

#### Vascular Events

"Not surprisingly, the group on cHRT had 2-fold greater rates of blood clots than the group on placebo," Dr. Jackson said. The average per year was 34 cases of blood clots per 10,000 women on cHRT vs 16 cases per 10,000 for women on placebo.

### WHAT ARE THE BENEFITS?

#### Colon Cancer

"The risk of colon cancer was reduced by 37% in the combined therapy group," Dr. Jackson said. The average per year was 10 cases of colorectal cancer per 10,000 women on cHRT vs 16 cases per 10,000 women on placebo. "This amounted to 6 fewer cases per year," Dr. Jackson pointed out. "The benefit appeared after 3 years of use and became more significant over time," she said.

#### Bone Fractures

The average per year was 10 cases of hip fracture per 10,000 women on cHRT vs 15 cases per 10,000 women on placebo (5 fewer cases per year). In the cHRT group, there was a 34% reduction in hip fractures and a 24% reduction in total fractures. "The WHI study was the first to show a decreased risk of osteoporotic fractures with HRT use," Dr. Jackson said.

## WHAT DO WE TELL OUR PATIENTS?

Dr. Jackson offered these guidelines for advising patients about hormone replacement therapy:

- Women taking "estrogen only" need not change.
- We can keep giving long-term HRT to women younger than age 50.
- Women over age 50 who take cHRT solely to prevent chronic disease should consider stopping the therapy.
- Other regimens, such as lower doses or other combinations, may not be better.
- Women who stop cHRT should be assessed for osteoporosis risk.

"Many patients have vasomotor symptoms, such as hot flashes and night sweats, and we need to evaluate these women

on a case-by-case basis," Dr. Jackson said. "Find out if the patient has other risk factors for heart disease or breast cancer. Determine how disabling the vasomotor symptoms are to the patient and ask if she is willing to try alternative therapies not approved by the FDA."

Herbal therapies include soy products, black cohosh, dong quai, and Vitamin E. "Many of these have shown some decrease in vasomotor symptoms," Dr. Jackson said. Pharmacologic therapies include Megestrol acetate (Megace), Clonidine (Catapres), Fluoxetine (Prozac) and Venlafaxine (Effexor).

For patients with urogenital atrophy, Dr. Jackson said there are topical estrogens and herbal therapy, including chasteberry for vaginal dryness. For loss of libido, there is ginseng as an herbal therapy.

"There is no standardization for herbal therapies, and I am not confident that there will be more studies of such therapies in the future," Dr. Jackson concluded.