HORMONE REPLACEMENT THERAPY (HRT)
RECENT CLINICAL STUDIES

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There is no doubt that estrogen deficiency in women after menopause can cause unpleasant symptoms as well as health problems. Since women’s expected life span in modern societies is increasing, more attention is now paid to the quality of life during and after menopausal transition. In fact, women may now expect to live half of their adult life after menopause! It is obvious that we should all strive to spend these mature years in good physical and mental health—by preventing degenerative diseases and associated discomfort. In women such problems tend to become aggravated both by advancing age and by estrogen deficiency.

Symptoms that appear around the time of menopause typically include hot flashes, dizziness, sweating and sleep disturbances. Estrogen treatment (combined with progestins in women who have not had their uterus removed) is very effective in eliminating these unpleasant complaints. In addition, there are other well-documented beneficial effects of estrogens on women’s health:

- Preventing bone resorption, osteoporosis, fractures, and tooth loss.
- Preventing atrophic changes of skin, vaginal wall, and urinary tract.
- Dilating blood vessels and improving blood supply to heart and brain.
- Antioxidant and anti-inflammatory effects on tissues.
- Lowering LDL (“bad cholesterol”) and increasing HDL (“good cholesterol”).
- Maintaining neuronal structures in the brain.
- Decreasing likelihood of colon cancer.
- Preventing or delaying onset of cataracts, macular degeneration and blindness.
- Decreasing muscle and bone pain.

It is a well-known fact that many women after menopause feel better taking estrogens. This has led to the common practice of “hormone replacement therapy” (HRT). This recommendation has been, however, the subject of recent controversy and has been questioned both by doctors and by women patients. There are several reasons for these doubts:

- Recent reports in medical journals and the popular press about harmful effects of HRT. Examples include “Heart and Estrogen/Progestin Replacement Study” (HERS), which failed to find beneficial effects of HRT for women after heart attacks; another study found progression of atherosclerosis in women with coronary artery disease in spite of estrogen treatment. Yet another report described a group of women who have suffered strokes and were treated with HRT—the results of the study did not show decreased incidence of recurrence. The newest publications\textsuperscript{(1,2)} from the “Women’s Health Initiative” (WHI) study demonstrated that in the group of women taking HRT, there was slightly increased frequency of blood clots, heart attacks and strokes (as well as dementia in women taking HRT after 65 years of age). However, it should be remembered that women participating in the WHI study were considerably older than typical patients who initiate HRT at the time of menopause. It is also emphasized that only one dose of one type of estrogen/progestin preparation was tested.

- On the other hand, studies confirming beneficial actions of estrogens continue to be published. For example, one study has shown that heart attacks are less likely to be fatal in women who have taken estrogens prior to their heart attack. The majority of studies also confirm the ability of HRT to prevent osteoporosis and bone fractures and reduce risk of colon cancer.\textsuperscript{(1)}
• Women after menopause do not want to continue menstrual bleeding—which is often a consequence of “cyclic” administration of estrogens and progestins. For this reason HRT is often given as a “continuous” therapy; even then “breakthrough” bleedings are not uncommon. Another option has been the possibility of using very small doses of estrogen (unlikely to cause bleeding), which nevertheless still have the ability to slow down bone resorption and prevent osteoporosis.

• Women are afraid of uterine and breast cancers which are known to be, at least partly, hormone dependent. It has been known for a long time that the risk of uterine cancer can be minimized by combining estrogen treatment with progesterone or synthetic progestins (as a cyclic or continuous method) and by lowering the dose of estrogen. It is the connection between estrogen and breast cancer that women fear the most. The majority of studies do not show significantly increased risk of breast cancer during short-term HRT. Even during long-term HRT, the increase in risk in absolute numbers can be considered small. For example, in one publication it is estimated that in a cohort of 1000 women, when all have used HRT from 50 to 55 years of age, there will be two more breast cancers by age 75 that can be attributed to HRT—79 women instead of 77 women with breast cancer.\(^{(3)}\)

• Studies among breast cancer survivors who took HRT after treatment for primary breast cancer do not show any increase in risk of recurrence or breast cancer mortality. In some studies even a decrease in breast cancer mortality was observed.\(^{(4-6)}\) However, these findings need to be viewed with caution until results from the clinical trial HABITS (Hormone Replacement Therapy After Breast Cancer-Is It Safe?) become available.

Recently a whole new field of science has appeared — postmenopausal therapy with selective estrogen receptor modulators (SERMs). These compounds have “selective” affinity to estrogen receptors in different tissues in the body. In this way they may have a beneficial effect on one tissue, e.g., bone; and be devoid of undesirable side effects, e.g., on the uterus. There is some evidence that SERMs may have an ability to protect breast tissue against cancer. SERMs already in clinical use include tamoxifene (used to prevent breast cancer recurrences) and raloxifene (approved for prevention of osteoporosis). Raloxifene has no effects on the uterus and does not induce bleeding. Unfortunately, raloxifene does not reduce hot flashes. Currently studies are underway comparing tamoxifene with raloxifene for breast-cancer prevention in high-risk women.

Many scientists believe that in the future long-term HRT will involve as yet undiscovered new SERMs — compounds with only desirable properties and devoid of side effects. Such drugs are already being developed by two leading pharmaceutical companies and are expected to be available in 2005.

Meanwhile, it is recommended that HRT for post-menopausal women be individualized (as has always been practiced by physicians), taking into account patients’ symptoms, lifestyle, risk factors, weight, cholesterol level, bone density, presence or absence of other problems, e.g., diabetes, hypertension, vascular disease, as well as psychologic and other factors. An important benefit of such an individualized approach is the opportunity to include the patient in the process of deciding whether or not to undertake long-term hormone treatment.

Our Patients—Dear Ladies, please let’s not panic. In most studies, including the most recent ones, the actual risk of suffering complications from HRT is minimal (below 1%) and its use has not resulted in the statistical increase of mortality. In spite of the media’s alarmist reporting of recent findings, there is really no reason to be unduly concerned!