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Osteoporosis and ERT—The jury is still out

As most readers of JAMWA will know, the Public Health Service formed a Task Force on Women’s Health Issues in 1983. Each agency of the Public Health Service now has a Women’s Health Coordinating Committee. The committee at the Centers for Disease Control has decided to focus on publicizing selected women’s health issues as well as providing a forum for discussion and debate. Although the Task Force issued a two-volume report, many of the issues covered in the report have not had the publicity we think they deserve. We hope that airing the issues will be a catalyst to action for researchers and public health authorities as well as physicians dedicated to patient care. That is why we have initiated this new column in JAMWA.

Our first topic, osteoporosis, has received much media attention, perhaps too much, especially in women’s magazines. But there are still some questions—about the wisdom of estrogen replacement therapy, for example—that deserve closer consideration and further research. This report is based on an NIH-sponsored workshop, “Research Directions in Osteoporosis,” held February 9–11, 1987, and a critical review of the data by Barrett-Connor.

—CDC Women’s Health Coordinating Committee

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Bone loss in women accelerates immediately after menopause, often leading to osteoporosis and an increased risk of bone fractures. In 1985, 247,000 hip fractures occurred in people over 45 years of age. Among those who live to be 90, one-third of women and one-sixth of men will experience hip fractures. Six months after fracture, 25% of victims will not be able to carry out their usual activities, and 50% will need assistance to do so. Hip fractures are not only a serious cause of morbidity but they also increase the risk of mortality in older people. Because the proportion of the population over 65 will increase steadily, from 11% in 1981 to 22% in 2050, the estimated number of hip fractures will triple by the year 2050.

Established risk factors for osteoporosis include being thin, white, and female. Alcohol consumption, cigarette smoking, and low dietary calcium may also increase risk. Estrogen use retards postmenopausal bone loss and reduces the risk of osteoporosis. The risk of hip fracture is considerably reduced in women who use postmenopausal estrogens. For maximum effect, estrogen should be started as soon as possible after menopause. The suggested dose is 0.625 mg, but the optimal duration of use is unknown. Experts suggest a minimum of five to ten years.

Should all women be advised to take postmenopausal estrogens? It has been estimated that at present approximately 40 million women in the United States are functionally postmenopausal, but only about 4 to 5 million of them are taking estrogen. Other factors besides the beneficial effect on osteoporosis must be taken into consideration before deciding on the use of postmenopausal estrogen.

In a recent review, Barrett-Connor stated that postmenopausal estrogen replacement was associated with an established increased risk of endometrial cancer and a possibly increased risk of breast cancer and an established decreased risk of both osteoporosis and cardiovascular disease. She emphasized that almost all risk data available were based on estrogen therapy with conjugated equine estrogen (Premarin®) given in doses ranging from 0.625 mg to 1.25 mg without a progestin. It cannot be assumed that other estrogen preparations have the same risks and benefits. Nor can it be assumed that estrogens given with progestins will have the same effects.

Multiple case control studies have found an association between endometrial cancer and estrogen replacement therapy with the risk generally increasing with dose and duration of use. The American College of Obstetrics and Gynecology has recommended that estrogen replacement therapy include a progestin to reduce endometrial cancer. Although biologically plausible, not enough data exist to definitely state that the addition of a progestin will mitigate the increased risk of endometrial cancer associated with estrogen replacement. And even more worrisome are the possible adverse effects of added progestins on breast cancer and cardiovascular disease.

Exogenous estrogen use has not been associated with breast cancer in most studies; however, long-term follow-up is necessary to exclude risk. The addition of progestin to estrogen replacement has not been studied sufficiently to determine its effect on breast cancer, although one study suggests that estrogen-progestin therapy was protective against breast cancer compared to estrogen alone or no estrogen. For women over age 65 in the United States, the death rate from myocardial infarction increases dramatically each year, and it greatly exceeds rates for both breast and endometrial cancer. If postmenopausal estrogen therapy had a benefi-

*Trade names are used for identification purposes and do not constitute endorsement by the Centers for Disease Control or the U. S. Public Health Service.
cial effect on cardiovascular risk, a stronger case might be made for its use in the prevention of ischemic heart disease than in the prevention of osteoporosis. However, the data on estrogen use and risk of heart disease are conflicting. In two studies published together in 1985, one showed an increased risk and the other showed a decreased risk of coronary artery disease associated with exogenous estrogen use. The weight of the evidence at present, however, suggests that postmenopausal estrogen use decreases the risk of cardiovascular disease. Barrett-Connor points out that a progestin supplement may reverse the potential cardiovascular benefit of estrogen use by blocking the estrogen-induced increase in high density lipoprotein cholesterol.

One side effect of estrogen replacement therapy is vaginal bleeding. This may lead to an increase in diagnostic dilation and curettage procedures and to an increased rate of hysterectomy. If progestins are added, menstrual periods will likely ensue. Many women may refuse estrogen-progestin replacement therapy because they do not want to continue menstruating after menopause. In fact, very little information is available on how women decide whether or not to take estrogen replacement at the time of menopause. Another side effect of estrogen replacement therapy is an increase in gall bladder disease.

One interesting new area is the use of transdermal estradiol. Preliminary evidence suggests that estrogen taken by nonoral routes may be effective against osteoporosis and have fewer side effects than oral estrogens. However, transdermal patch estradiol has not yet been studied in well-controlled trials.

As this summary suggests, many questions exist concerning the use of postmenopausal estrogens. The decision to prescribe estrogen must be made after considering the risks and benefits to the individual patient. Women receiving estrogen should be examined frequently for complications, especially vaginal bleeding. Frequent breast examinations and annual mammography are also advised.

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References