



Estrogen replacement for women with cardiovascular disease: Why don't physicians and patients follow the guidelines?

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What's the matter with cardiologists in Toronto? Recent Canadian and US guidelines advocate the use of hormone replacement therapy (HRT) to protect women with cardiovascular disease from secondary events.^{1,2} However, in this issue Dr. Michelle R. Wise and colleagues³ report that only 21% of women seen in a general cardiology clinic in a tertiary care hospital in Toronto were documented users of HRT. Even if we include the additional 6% of women who were using HRT without documentation in the clinic record, we must conclude that current HRT guidelines were being followed in less than a third of eligible women and that cardiologists were actively treating an even smaller number.

The Toronto experience is not unique; studies conducted in the US have also demonstrated that only a small minority of women with coronary artery disease use HRT.⁴⁻⁶ Physicians are not alone in being slow to adopt the new guidelines; it appears that most Canadian women remain unaware that HRT may reduce their risk of heart disease. Moreover, a recent survey conducted by the Heart and Stroke Foundation of Canada⁷ showed that few women discuss the matter with their physician. Does this indifference to current expert opinion represent a lack of knowledge by physicians and patients or a healthy skepticism about medical dogma? I would argue the latter.

The epidemiologic data supporting the use of HRT to prevent cardiovascular disease in postmenopausal women and recurrent events in women with diagnosed cardiovascular disease are consistent. Grady and colleagues⁸ analysed 32 epidemiologic studies that evaluated the relation between noncontraceptive estrogen use and coronary artery disease. Most of these studies demonstrated that the risk of coronary artery disease was lower among women who used estrogen than among women who did not. The pooled estimates for the relative risk of coronary artery disease among estrogen users versus nonusers in this and 2 other similar meta-analyses ranged from 0.55 to 0.65.^{9,10} In one subanalysis involving women with angiographically proven coronary artery disease, the protective effect of estrogen was even greater, reducing the risk of recurrent disease by 84%.¹¹ Accordingly, there is excellent epidemiologic data to

suggest that HRT may be efficacious in both primary and secondary prevention. On the other hand, epidemiologic data do not provide sufficient evidence to assure us that the potential benefits of HRT demonstrated in observational or case-control studies will actually be realized among specific patients.

The associations observed in epidemiologic studies may represent a true protective effect; on the other hand, if the women who choose to take hormones are simply healthier than those who do not, these associations may reflect only a selection bias. Only a randomized clinical trial can provide the efficacy data needed to confirm the benefits of HRT. As Wise and colleagues acknowledge, the only completed study to date — the Heart and Estrogen/progestin Replacement Study (HERS) — was disappointing in that the incidence of cardiac events was not reduced among women with established disease.¹² Although negative results of a single study should not stifle our interest in the protective effect of HRT, it must dampen our enthusiasm for prescribing HRT to prevent secondary cardiovascular events in postmenopausal women. Although we may expect the results of other trials to be reported over the next few years, HERS remains the only randomized clinical trial published to date. Unfortunately, the efficacy of HRT in primary prevention may be even more difficult to prove, given the fewer events expected among asymptomatic women.

The potential benefits of HRT in preventing cardiovascular disease remain seductive. If the expected reduction in risk is realized, the associated increase in life expectancy and decrease in cardiovascular disease could be substantial. While we await the results of future clinical trials, women need not stand by passively. Strong and consistent data from randomized clinical trials demonstrate that the treatment of other cardiovascular risk factors such as hypertension and lipid abnormalities can result in a reduction in coronary risk consistent with the earlier promise of epidemiologic studies. Our risk reduction efforts must focus first and foremost on modifiable risk factors for which clear scientific proof is available. In a thoughtful editorial written 2 years before the HERS results were known, Jacques Rossouw¹³ cautioned that the HRT data might mimic those



on antioxidants: great epidemiology but disappointing trial results. We need not be discouraged that cardiologists and their patients appear to be making thoughtful decisions based on the weight of the current scientific evidence.

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