DOSES, DURATION, AND STARTING AGE FOR HRT TREATMENT: THE AMERICAN VIEWPOINT

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The United States must be recognized as both a melting pot and a mosaic. It would therefore be presumptuous to give an "American viewpoint" on anything. Nonetheless, it is possible to review the concept of postmenopausal hormone replacement therapy (HRT) with regard to dose, duration of therapy, and starting age, from several perspectives.

The Consumer Perspective

Discussions about menopause among women is now common behavior in the United States, and the broad availability of information, good and bad, has led to widespread interest. In general, the American culture is youth-oriented, and a major consideration in women's thinking regarding menopause management relates to issues of prevention of aging.

Scientific information published in weekly journals, such as The New England Journal of Medicine, are received by the media before the medical community. Presentation of this information, sometimes with appropriate review and sometimes with misinterpretation of data, is rapidly disseminated. The public is therefore often confused and the health provider not given the opportunity of adequate study of the scientific papers before bringing the information into line in therapeutic considerations. This can sometimes lead to miscommunication between the patient and doctor.

The North American Menopause Society (NAMS) has conducted Gallup Surveys in 1994 and 1997 on a broad range of questions, including women's perceptions of the menopause, use of hormone replacement, and reasons for discontinuation [1,2].

In the 1994 NAMS/Gallup Survey, almost 90% of women were aware of estrogen therapy and 20% were aware of androgens. The women aged 45-65 reported a current use of 34%, past use of 8%, with 58% having never taken any form of hormone replacement. Of the 34% current users, 59% were on estrogen, 37% on estrogen and progestin, and 2% on estrogen and androgen.

The main reasons for discontinuation were side effects reported by 34%, fear of cancer by 18%, and the rest believing that they did not need the medication or that the problem had been resolved.

In the 1997 Gallup Survey [2], a greater proportion of women reported that their physicians had spent considerable time with them discussing issues of hormone replacement
and in about 40% of instances had also discussed alternate therapies.

The overall lesson learned from this information is that women are far more aware of the issues concerning menopause and the potential treatments including hormone replacement, but that they maintain a serious concern regarding potential long-term side effects. Among these is certainly the fear of breast cancer, and despite the increasing information on this and on the risks of cardiovascular disease, concern for the problem persists.

**Compliance**

It is generally accepted that no more than 25% of women prescribed ERT or HRT will still be on therapy after 24 months. Moreover, the side effects induced by progestins result in many postmenopausal women never filling their prescription for this component, and either discontinuing therapy or remaining on estrogen only. Thus, continuance remains a major problem, and has lead to considerable rethinking amongst providers with regard to the dose and starting age for HRT therapy.

**Dose and Starting Age for HRT**

Traditionally, hormone replacement therapy was started after menopause or with the onset of specific symptoms such as hot flashes. The majority of HRT users are therefore in the age range 45-55. Poor continuance has led to far fewer users beyond the age of 55. The 45-55 year age range is also the time of maximal increase in the incidence of breast cancer. This probably accounts for part of the suspicion women have for long-term use of this therapy.

There appears to be a general consensus that the slight increase in the incidence of breast cancer in HRT users develops after 5-10 years of continuous use. The major increase in incidence of ischemic heart disease develops after the age of 70, as does the incidence of hip fractures. It must be recognized that current users of HRT show essential protection against coronary heart disease whereas previous users tend to lose this protective effect. Moreover, in relation to osteoporosis, women discontinuing therapy after 10 years of continuous use at age 60, would be at similar risk by age 70 for fracture as never-users.

The above factors have led to a trend to either recommend hormone therapy from menopause onwards without discontinuation, or a more serious consideration of starting HRT at an older age. The previous misconception that HRT was of minimal benefit if started beyond age 65 has now been replaced by a developing belief that it would be satisfactory and valuable to start therapy for the first time beyond age 65.

Clinical experience has suggested that side effects are higher on standard doses in older patients. There is therefore an increasing research focus on using lower doses of estrogen in older women. Good data with safety and efficacy results are still lacking, and this has become an area for increased research.