Estrogen Therapy During Menopause
Practical Treatment Recommendations

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Summary

The potential benefits of estrogen replacement therapy (ERT) for postmenopausal women are now generally recognised, and no scientist involved in this field of research will deny the gratifying results of hormone therapy. However, in the risk-benefit equation the adverse effects of ERT must be carefully considered.

Most of the harmful adverse effects of ERT have been related firstly to the absence of progestational balance, and secondly to the fact that most of the estrogens previously available for clinical use were artificial and administered orally, resulting in intensive hepatic metabolism, leading to metabolic disturbances. The need for the addition of progestogen leads also to consideration of the adverse effects of these substances.

During the past decade therapeutic improvements have been achieved. Knowledge...
about the different types of steroids now available, the right choice of dosage and duration of therapy according to the needs of the patient, and the new alternative delivery systems improves day by day.

Various steroids are now available for clinical use. Among the estrogens, orally administered drugs, natural derivatives of estradiol, and nonoral drugs delivered by injection, implant, vaginal ring or cream, ointment or transdermal system are at the prescriber's disposal. Among the progestogens available to the prescriber and recommended to be added to ERT, the molecules derived from testosterone [norethisterone (norethindrone), norgestrel] are less prescribed than the molecules derived from progesterone (dideoxosterone) or from 17-hydroxyprogesterone (medroxyprogesterone acetate). In menopausal therapy the latter derivatives from progesterone or 17-hydroxyprogesterone are preferable, but low doses of any type of progestogen could be both protective of the target organs and devoid of harmful effects. Careful consideration of contraindications of treatment and regular follow-up are prerequisites for safe therapy.

Recent epidemiological data now demonstrate clearly that the use of ERT under these conditions affords protection against osteoporosis and cardiovascular disease. Clear benefits to women's health may therefore be obtained from the adequate choice and surveillance of therapy.

In 1987 the world population reached 5 billion, and by the beginning of the next century it will reach 6 billion. Parallel with this dramatic increase, life expectancy will also rapidly increase in both the developed and the developing countries. By the year 2025, 23% of the population will be aged 60 and over in the developed countries and 12% in the developing countries (Diczfalusy 1984). Among the huge problems related to these changes, menopause will become a major area of concern. Among the major health disorders related to menopause, osteoporosis, bone fracture risk and ischaemic heart disease will become overwhelming in both the developed and the developing countries.

1. Rationale for Estrogen Replacement Therapy (ERT)

As a result of the increase in life expectancy, about one-third of a woman's life is now after the menopause. While menopause is a so-called physiological event, oestrogen deprivation leads to non-physiological clinical symptoms and moreover to increased risk of severe diseases such as bone fractures and cardiovascular disease. Therefore, the rationale for ERT, and its benefits, appear obvious.

2. Osteoporosis

Among the many symptoms and disorders that occur during the menopause, osteoporosis and bone fractures represent the heaviest burdens for ageing women and for society. Since Albright et al. (1941) published their findings, it has been recognised that oestrogen deficiency at menopause could lead to osteoporotic fractures. More recently, the preventive effect of ERT on these fractures has been demonstrated in long term double-blind studies (Hutchinson et al. 1979; Nachtigall et al. 1979). The role of oestrogen deprivation on accelerated bone loss and the benefits of ERT in the prevention of fractures are now widely recognised. In a recent analysis ERT was shown to decrease hip and wrist fractures, with a fracture rate 3 times lower in treated than in untreated postmenopausal women (Weiss et al. 1980). Not all women are at risk of osteoporosis, but while Albright et al. (1941) stated that 1 out of 4 women will develop osteoporosis after the menopause, more recently Jensen et al. (1982) showed that 43% of a female population was at risk of bone fracture.

The search for accurate and cheap markers of bone loss would be of great benefit in identifying women at risk in large screening programmes and in making the decision to use ERT. Nevertheless,