140 Harley Street
London W1N 1AH

The Endocrine & Dermatology Centre

Telephone 01 935 2440
Telex 8955552 Endoc G

EDC NEWSLETTER: MARCH 1989

sHRT AND OSTEOPOROSIS: OVERDOSING ON OESTROGEN?

Almost 50 years have elapsed since Fuller Albright predicted the value of sex Hormone Replacement Therapy (sHRT) in the prevention of Osteoporosis (1). Despite this less than 8% of the 9.6 million women in the United Kingdom over 45 years at risk from postmenopausal Osteoporosis are receiving sHRT. **Why?** There are two main reasons. Firstly, the scarcity of Osteoporosis Screening Centres to detect the condition early and for follow-up. Secondly, an intuitive fear by Doctors and Patients of the possible side effects of longterm sHRT. Such fears are justified. From 1960 studies showed that endometrial (uterine) cancer was 3-4 times more common in women receiving unopposed oestrogen therapy ie without progestogen supplementation compared to those who were (2). Although longterm studies with present oestrogen/progestogen oral or topical preparations have yet to be published, early evidence indicates no increased risk of endometrial cancer but with a reduction in strokes (3), coronary artery disease (4) and relief of the Postmenopausal Syndrome (PMS). The verdict on breast cancer is less clear (5). Additionally certain patients may experience breakthrough bleeding, breast tenderness, nausea, increased blood pressure, migraine, mood changes, water retention or return of hot flushes.

To reduce unwanted side effects and future potential dangers to a minimum, we consider it **mandatory** that before receiving sHRT all patients are fully evaluated with a **GBH** Screen: **G**ynaecology (Mammography, Colposcopy and Cervical Smear or post-hysterectomy Vault Smear, Ovarian Ultrasound, Serum CA 125 where appropriate), **B**one (Bone Density Scan), **H**eart (ECG, Cholesterol, lipids) with the exclusion of anaemia, liver disease, renal disease, diabetes mellitus, thyroid dysfunction, hypertension etc. Subsequently, circulating oestrogen levels should be measured to ensure that the individual patient receives the **Minimum Effective Dose of Oestrogen (MEDO, 6)**. The dose of sHRT (a) for longterm safety, (b) to protect and stimulate the skeleton, while (c) relieving PMS should provide circulating oestrogen levels (as oestradiol 17B) at a minimum of 150pmol/L since this has been shown to prevent bone loss and PMS (7) but below 440pmol/L being the upper limit of the normal follicular phase range (first half) of the menstrual cycle (8) **MEDO Therapy, which we advocate, contrasts sharply with the overdosing on oestrogen produced in women in whom oestradiol/ testosterone implants have been used (9). These may produce blood oestradiol levels between 2 to 15 times greater than necessary (ranging from 372-2370 median 725pmol/L) and being sustained continuously (Figure).** Such levels are equivalent to those of a woman in a permanent state of ovulation. This is clearly not a physiological approach to the menopause. Also such high levels of oestrogen may be insufficiently opposed by standard progestogen dose supplements. Failure to appreciate the significance of maintaining physiological hormone levels with sHRT have inevitably rekindled fears of a rise in uterine, possibly breast cancer and

other side effects. For this reason **MEDO Therapy** is recommended to enable patients to obtain the maximum clinical benefit from sHRT with the minimum of risks during longterm treatment.

OSTEOPOROSIS AND MENOPAUSE CLINIC
The Endocrine and Dermatology Centre
140 Harley Street
London W1N 1AH

References

1. Albright F, Smith PH, Richardson AM (1941) Postmenopausal Osteoporosis: Its clinical features. Journal of the American Medical Association 116: 2465-2474.

2. Smith DC, Prentice R, Thompson DJ, Herrmann WL (1975) Association of exogenous estrogen and endometrial carcinoma. New England Journal of Medicine 293: 1164-1167.

3. Paganini-Hill A, Ross RK, Henderson BE (1988) Postmenopausal oestrogen treatment and stroke: A prospective study. British Medical Journal 297: 519-522.

4. Beaglehole R (1988) Oestrogens and cardiovascular disease: Postmenopausal oestrogens seem to reduce coronary heart disease. British Medical Journal 297: 571-572.

5. Hunt K, Vessey M (1987) Long-term effects of postmenopausal hormone therapy. British Journal of Hospital Medicine 38: 450-460.

6. Mortimer CH, Perry W (1988) Osteoporosis: Prevention, Detection, Treatment. EDC update Series. EDC Publications.

7. Selby PL, Peacock M (1986) Dose dependent response of symptoms, pituitary, and bone to transdermal oestrogen in postmenopausal women. British Medical Journal 293: 1337-1339.

8. Mortimer CH, Perry W (1988) Skeletal effects of oestrogen and testosterone in postmenopausal women. British Medical Journal 297: 687-688.

9. Savvas M, Studd JWW, Fogelman I, Dooley M, Montgomery J, Murby B (1988) Skeletal effects of oral oestrogen compared with subcutaneous oestrogen and testosterone in postmenopausal women. British Medical Journal 297: 331-333.

OSTEOPOROSIS AND sHRT: OVERDOSING ON OESTROGEN