5. PATIENT COMPLIANCE

This card will focus on the various strategies which should be employed to minimise the side effects of HRT and thus maximise the benefit: risk ratio. It will also provide data regarding the risks of HRT and help put these into context. This information should help to maximise continuation with therapy and improve initial rates of uptake.

SIDE EFFECTS OF HRT

BLEEDING PROBLEMS

Sequential therapy

If heavy bleeding occurs: increase duration (from 14/28 to 21/28) and dose (eg norethisterone 5mg to 10mg) of progestogen; switch to continuous combined HRT (ccHRT); change to a more androgenic progestogen (eg norethisterone); and/or reduce the dose of oestrogen *(eg* from 2 to 1 mg). If bleeding persists >6 months refer to gynaecologist.

Continuous combined HRT

Start with a low dose preparation unless specific problems exist such as established osteoporosis or psychological problems. If possible, aim for a single pilVpatch regimen to maximise adherence to therapy. If breakthrough bleeding (BTB) occurs:

- Allow a minimum of 3 months before a change in strategy and reassure the patient.
- After3monthseithercontinuefor3monthswiththesamepreparationorswitchto:ccHRTwithmore androgenic progestogen; ccH RT with less oestrogen; tibolone; or sequential H RT.
- If BTB continues for more than 6 months or if it starts de novo when bleed free for 1 year, the patient should be referred to a gynaecologist.

PROGESTOGENIC SIDE EFFECTS (MAINLY PMS AND ANDROGENIC SIDE EFFECTS)

If `PMS - like' progestogenic side effects occur (progestogen intolerance)':

- Decrease duration of progestogen to 10 or even 7 days: the incidence of endometrial hyperplasia increases and timing of bleed may be unhelpful to detect hyperplasia.
- Decrease the dosage of progestogen with the same proviso as above.
- Use a product with less androgenic progestogen.
- Gynaecologists may use a natural progesterone as progestogenic opposition, eg cyclogest orcrinone or use the local route -eg levonorgestrel-releasing intrauterine system.

WEIGHTGAIN

There is no evidence from research of increase in weight with HRT[2]. Weight increases as age increases due to slowing down of basal metabolic rate.

OESTROGENIC SIDE EFFECTS (MAINLY BREAST TENDERNESS AND NAUSEA)

- Encourage perseverance as symptoms usually settle within 3 months.
- Use a non-oral route to allow monitoring of oestradiol levels.
- Use lower dose of oestrogen (esp. >60 years), ie1 mg rather than 2 mg orally or 25µg transdermally.

ASSOCIATED RISKS

BREAST CANCER

The best data are from the ICRF and WHI studies. There is a35 percent (ICRF) and a26 percent (WHI) increase in incidence after5 years of usage of HRT, but no increase in mortality''.

If the woman has been previously diagnosed with breast cancer the practitioner should liaise with breast surgeons and oncologists. The benefits versus risks should be evaluated according to: symptoms, risks of osteoporosis, etc. versus oestrogen receptor (ER) status of tumour, node involvement, duration since diagnosis and treatment.

There arefew data concerning HRT in women with afamily history of breast cancer. The benefits versus the number of relatives affected should be evaluated. Inherited tumours are usually ER negative and probably not related to increased risk with HRT

Benign breast disease is not a contraindication, but therapy may exacerbate symptoms.

HYPERTENSION AND CARDIOVASCULAR DISEASE

Hypertension is not a contraindication for HRT Since the results of HERS' and WH [14], HRT is not currently indicated forthe secondary or primary prevention of cardiovascular disease. However data are required from studies in younger populations with other H RTformulations. Women with pre-existing coronary heart disease, already on or wishing to start HRT, should seek specialist advice.

VENOUSTHROMBOEMBOLISM (VTE)

There is an increase in risk of two to fourtimes baselinewith HRT(typical increase from 15 to 30 per 10,000 per annum)'. If there is previous orfamily history of VTE the patient should be screened for thrombophilia prior to commencing HRT. If the screen is positive the risk: benefits should be carefully evaluated and an alternative product considered. HRT should be stopped 4-6 weeks priorto and for4 weeks after major surgery. No change in therapy is needed for minor surgery.

ENDOMETRIAL CANCER

Risks should be minimised by switching to ccHRT as soon as possible'. A previous history necessitates a risk: benefit evaluation based on symptoms, risk of osteoporosis versus differentiation, stage and prognosis of lesion.

OVARIAN CANCER

Recent prospective observational (unrandomised) studies suggest a small increase in the risk of ovarian cancer in long-term HRT users'. However, further data are required to clarify the issue.

KEY REFERENCES

1. Panay N, Studd J. Progestogen intolerance and compliance with hormone replacement therapy in menopausal women. *Human Reproduction Update 1997;* 3(2):159-171.
2. NormanRJ,FlightIHK,ReesMCROestrogenandprogestogenhormonereplacementtherapyforperi-menopausal and post-menopausal women: weight and body fat distribution (Cochrane Review). In: *The Cochrane Library,* Issue 1, *2002.* Oxford: Update Software.
3. Collaborative group on hormonal factors in breast cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of *52,705* women with breast cancer and 108,411 women without breast cancer. *Lancet 1997;* **350** *(9084):1047-1059.*
4. WritingGroupfortheWomen'sHealthInitiativeInvestigators.Risksandbenefitsofestrogenplusprogestinin healthy postmenopausal women: principal results from the Women's Health Initiative. *JAMA 2002;* ***288*** *(3):321-333.*
5. HulleyS,GradyD,BushTetal.Randomisedtrialofestrogenplusprogestinforsecondarypreventionofcoronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research *Group. JAMA 1998;* 280(7):605-613.
6. JickH,DerbyLE,MyersMW,VasilakisC,NewtonKM.Riskofhospitaladmissionforidiopathicvenous thromboembolism among users of postmenopausal oestrogens. *Lancet 1996;* ***348 (9033):981-983.***
7. Beresford SA, Weiss NS, Voigt LF, McKnight B. Risk of endometrial cancer in relation to use of oestrogen combined with cyclic progestagen therapy in postmenopausal women. *Lancet 1997;* ***348(9050):*** *458-461.*
8. RodriguezC,PatelAV,CalleEE,JacobEJ,ThunMJ.Estrogenreplacementtherapyandovariancancermortalityina large prospective study of US women. *JAMA 2001;* 285(11):1460-1465.

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