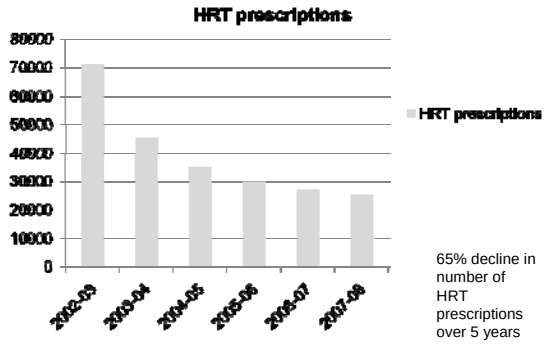
Contemporary Management of the Menopausal Woman

Dr Ailsa Gebbie
ESHRE October 2008

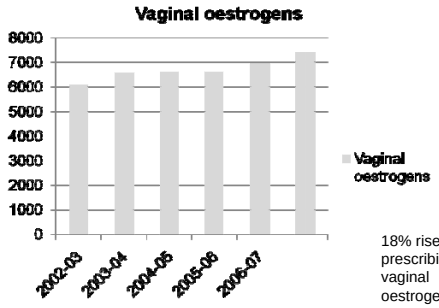
Prescribing of HRT in NHS Lothian, Scotland, UK



65% decline in number of HRT prescriptions over 5 years

Data from Prescribing Information System Scotland

Prescribing of local vaginal oestrogens in NHS Lothian, Scotland, UK



18% rise in prescribing of vaginal oestrogen preparations over 5 years

Data from Prescribing Information System Scotland

Case Study
Mrs JG aged 56 years
teacher

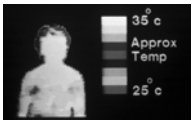
- HRT for 6 years (Prempak C 1.25 mg)
- Prescribed for severe flushes and sweats, poor sleep, chronic fatigue, low mood
- Heavy regular withdrawal bleeds
- Smokes 10 cigarettes per day, BMI 24, unfit
- FH of stroke (father aged 60), breast cancer (maternal aunt aged 54), osteoporosis (mother aged 80)
- GP insists she stops HRT as 'too dangerous'
- Terrible return of vasomotor symptoms
- Referral for specialist advice

Issues to discuss with this lady

- Starting, stopping and restarting HRT
- [Benefits and risks of HRT]
- [Osteoporosis]
- Choice of preparation
- Alternatives
- Sources of information
- Local and national guidance in the UK for healthcare professionals

Starting, stopping and restarting HRT

Vasomotor symptoms



- Cochrane Systematic review – 'HRT is highly effective and sustained treatment for vasomotor symptoms'
- All routes, combinations and dosages effective
- *Average* duration of HRT use 2-5 years in UK
- No fixed duration of use

- '*Individual assessment and annual review*' – some women have more 'risk factors'

Choosing HRT

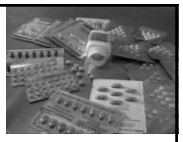
WISDOM study focus groups:

'*Qualitative content analysis of discussion transcripts'*

- Overwhelming reason for HRT was perceived improvement in quality of life
- Decisions made on basis of own health experience and that of family/friends
- High degree of trust in GP
- Often decide on HRT without reference to absolute increase or decrease in risk or benefit
- Decision making viewed as personal choice

[Welton 2004 Climacteric]

Stopping HRT



- GPs lack confidence with 'stopping HRT' more than 'starting HRT'
- Male doctors (44%) less confident than female (59%)
- GPs in deprived areas (56%) less likely to restart HRT than in middle-class areas (72%)
- Areas of particular confusion – premature menopause and risk of osteoporosis

[Cogliano Br J Gen Pract. 2004]

- Wean down with reduced doses over 6 months
- 'Tapering HRT' did not reduce recurrence

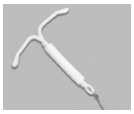
[Haskell 2004 JWH]

Choosing the optimum preparation

Transdermal preparations

- Risk of VTE - ESTHER Study data differential association between oral and transdermal HRT
  - case control study 155 cases
  - odds ratio: oral HRT 3.5 (95% CI 1.8-6.8)
    transdermal HRT 0.9 (95% CI 0.5-1.6)
    [Scarabin 2003 Lancet]
- Choice of progestogen also significant [Canonico 2007]
- Recent meta-analysis/SR confirms oral>transdermal [Canonico 2008]
- Arterial disease?
- Transdermal contraception patch no safer

Intra-uterine system



- Licensed in Europe for endometrial protection in HRT regimens
- Often unacceptable to women
- Technically more difficult to fit
- Does very low serum progestogen confer any long term breast advantage?

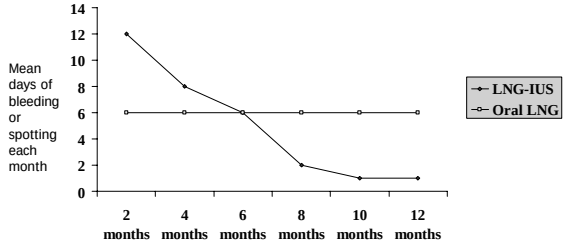
Intra-uterine release of LNG for HRT

- 40 perimenopausal women
- 2 mg oral oestradiol
- LNG-IUS *or* oral levonorgestrel for 10 days each cycle
- LNG-IUS - more bleeding days initially, well tolerated, no progestogenic symptoms, endometrial atrophy
- Same relief of menopausal symptoms

(Andersson et al, Obstet Gynecol 1992)

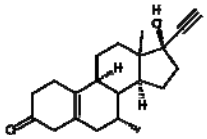
Intra-uterine LNG versus oral LNG in combination with oestradiol

(Andersson et al 1992)



"The perimenopausal woman who has a Mirena for contraception will surf on through into the menopause"

Tibolone



- First line treatment for menopausal symptoms
- Second line treatment for osteoporosis prevention in the UK
- Favourable effect on libido

UK advice for healthcare professionals to consider before prescribing

Tibolone: "Every woman's overall risk of stroke, breast cancer, and, in those with an intact uterus, endometrial cancer should be assessed carefully, taking into consideration any baseline risk factors, the increased risk due to tibolone use, and her therapeutic preferences

(MHRA 2007)

Tibolone

LIFT Trial discontinued in 2006 as had reached its objectives and shown increased stroke risk

>4500 osteoporotic women aged 60-85 (Cummings NEJM 2008)

- Decreased risk of spinal fracture RH 0.55 [95% CI, 0.41-0.74]
- Breast cancer – RH 0.32 [95% CI, 0.13 to 0.80]
  (Million Women Study 2003 RR 1·5 [95% CI 1·3–1·7])
- Increased risk of stroke RH 2.19 [95% CI, 1.14 to 4.23]
- Endometrial cancer
  (Million Women Study RR 1.79 [95% CI, 1.43-2.25]

'Do not use in older women and those with risk factors for stroke'

Alternatives to conventional HRT

Alternatives to HRT
SSRI / SNRI

- Generally short trials
- Most data for venlafaxine 37.5mg bd
  60% reduction v 27% placebo over 4 weeks
  [Loprinzi 2000 Lancet]
- Desvenlafaxine 64% reduction at 12 weeks
  [Obstet Gynecol 2008]
- 9 months of fluoxetine/citalopram no better than placebo [Suvanto 2005 Menopause]
- Side effects (nausea) a problem

Alternatives to HRT
Progestogens

- megestrol (20mg bd)
- norethisterone (5mg bd)
- medroxyprogesterone (20-50 mg)

- Megestrol 74% reduction in VMSx - placebo 20%
  in 8 week crossover study (Loprinzi 1994 NEJM)
- NE conversion to ethinyl estradiol (Chu 2007 JCEM)
  5mg NE equivalent to 30 µg EE
- VTE risk RR 5.3 (CI 1.5-18.7) (Vasilikis Lancet 2000)
- Breast effects unknown

Alternatives to HRT
Lifestyle and natural therapies

- Exercise – aerobic, sustained and regular such as swimming and running
  -50% reduction in women who sustained exercise
  [Lindh-Astrand 2004 Maturitas]
- Avoidance alcohol (caffeine) [Greendale 2005 AJM]
- Weight reduction / healthy eating programmes
- Herbal/Food supplements:
  black cohosh,
  phyto-oestrogens etc.
  very mixed results

- Generally poor absorption
- Should not be used for endometrial protection
- Claimed to have *'no side effects'*
- But has *'no effects'* either

Sources of information

Sources of information

- Healthcare professionals
- Friends and relatives
- Magazines, books, booklets
- Newspapers

guardian.co.uk **"The truth about HRT"**

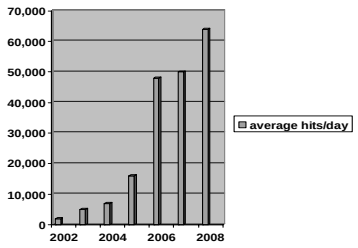
The Guardian newspaper 2007

- "RCOG in schism ....(about HRT)
- "A vocal minority of doctors, mainly gynaecologists, who specialise in treating the menopause.. refuse to believe it (the evidence of harm with HRT"
- "Many of them (gynaecologists) receive funding from the drug companies in the shape of lecture fees and consultancies"
- "...how tightly knit and influential the group of pro-HRT doctors is"
- "The message that seems to have filtered through is doubt not about HRT but about the studies warning of the risks of HRT"

- Electronic – 'e-health'
  - -Google 'menopause'
  - -14,000,000 sites in <1 second
  - -limited 'kite marking': HON Foundation

(Health on the Net)

www.menopausematters.co.uk

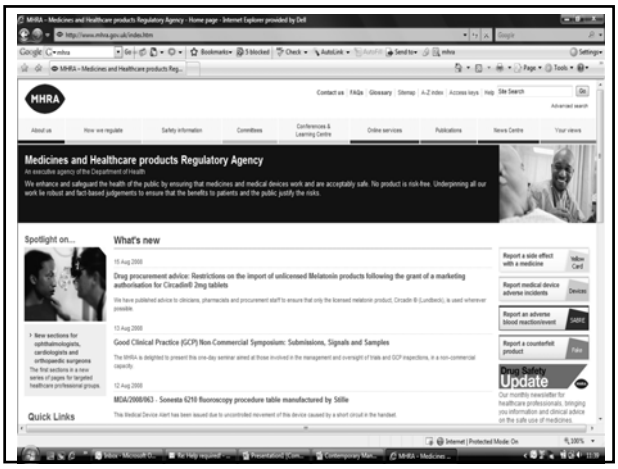


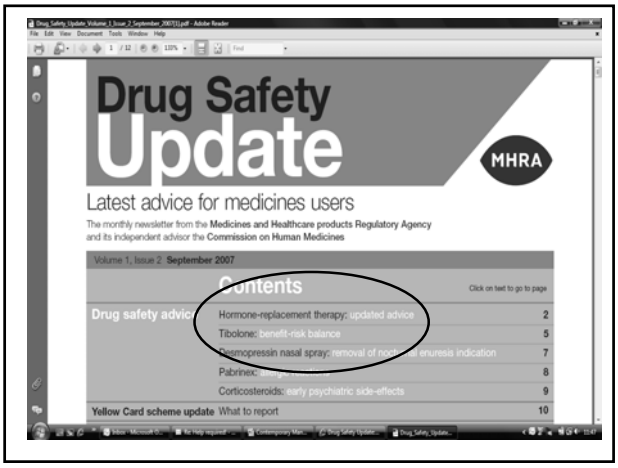
- Up to date information
- Support groups
- Online consultations
- 'Ask the experts'
- Email alerts
- Online surveys

Local and national guidance

Local and national guidance

- Local specialist clinics
- Local formularies for HRT prescribing
- Specialist societies: BMS Meeting the challenge of menopause
- The Regulators - UK MHRA
  "***For all women, the lowest effective dose (of HRT) should be used for the shortest time."***





Case Study
Mrs JG aged 56 years
teacher

Management in 2008

- Consultation at specialist menopause clinic
- Written information, website support
- Make informed choice whether to take HRT or not
- Consider 'no period', transdermal E_2, tibolone, IUS
- If not keen on HRT, try SNRI/SSRI or progestogen
- Encourage to stop smoking, take more exercise, keep normal weight
- Osteoporosis a separate issue
- Once retires, try to phase out E_2 slowly by reducing dose
- Vaginal oestrogens if sexually active when stops HRT