MHT (HRT) – a step by step guide to prescribing

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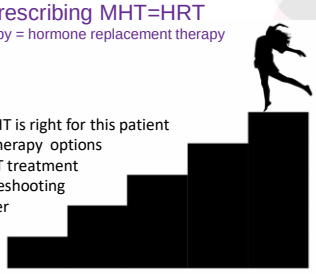
A step by step to prescribing MHT=HRT

Menopausal hormone therapy = hormone replacement therapy

Steps

Step 1 – Assess if MHT is right for this patient
Step 2 –Hormonal therapy options
Step 3 –Starting MHT treatment
Step 4 –R/V &Troubleshooting
Step 5 –When to refer



Step 1 – Is MHT is right for this patient ?

The first menopause consultation

- What are her presenting symptoms and concerns ?
- What is her personal and family history?
- Where on the menopausal transition does this woman sit?

This is an opportunity for a midlife woman's health assessment

- Focus on top 3 concerns
- May not want treatment just information
- Shared decision making
- Set up review

Goal of MHT

- **Relieve menopausal symptoms**
- Most effective treatment for VMS
- QOL, joint pain, mood changes and sleep disturbances may improve
- Effective for vulvovaginal atrophy/GSM -if VVA only symptom, use vaginal E and does not require P
- Benefits outweigh risks when started <60 yrs or within 10 yrs of the menopause

Contraindications

- Unexplained vaginal bleeding
- Estrogen dependent cancer
- High risk of VTE/DVT or thrombophilia
- Severe active liver disease
- Untreated hypertension/CHD
- Personal wish not to use hormones

Assessing other benefits

MHT (inc tibolone and CE/BZE)

- Effective in reducing bone loss > reduces vertebral, hip fracture
- Initiated in early menopause has no effect on cognition, may prevent Alzheimer's in later life
- May improve mood in perimenopausal/early menopausal women
- Reduction in colorectal cancer

E only therapy

- Decrease risk of AMI, all-cause mortality in women <60yrs or within 10 yrs of the menopause

E + P

- May decrease AMI risk dependent on the progestin used

Assessing risks

VTE

- Oral combined MHT different effect compared to oestrogen alone. MPA and norpregnane derivatives may be associated with a higher risk than progesterone
- Transdermal MHT has little or no effect on coagulation factors
- Highest risk within first year of starting treatment and dose related. Increased risk persists throughout the time of taking MHT
- In clinical practice previous provoked VTE in "low risk" patient – transdermal estrogen and reduced oestrogen dose is preferred

Breast cancer risk is complex

1 in 8 lifetime risk for Australian women (12%)

- No increased risk on E therapy alone up to 20 years of use
- Combined therapy (E&P) absolute risk of 0.5% over 7 years of treatment
- 9 extra breast cancers per 10,000 women per year compared with 34 per 10,000 women per year in placebo group

Consider risk factors:

early menarche, late menopause, late 1st birth,
obesity, alcohol, lack of exercise,
personal hx LCIS, atypical hyperplasia, chest irradiation
mammographically dense breast tissue
strong fhx or BC gene mutation (eg BRCA1, BRCA2)

Risks

- **Cerebrovascular disease** - no impact in women <60 years, May cause small increase in women >60 years
- **Cardiovascular disease** – may reduce risks if started within 10 years of the menopause, may increase risks if started after 60 years of age
- Oral MHT – given to women> 65yrs may increase risk of dementia

Migraines and MHT

- **Study reviews WHI data to demonstrate lack of association between migraines, cardiovascular disease and hormone therapy; opens door to increased use of hormones to treat migraines.**

11 October 2017:
North American Menopause Society (NAMS) Annual Meeting

- Modification of HRT regimen, dose and delivery may be appropriate in women with hormonally sensitive migraine.
- Transdermal oestrogen delivery is less likely to trigger migraine than oral oestrogen delivery
- Monitor and cease therapy if migraines worsening

Primary Ovarian Insufficiency - endocrinological disorder

- High FSH and low E with irregular menses in women ***less than 40 years***
- May be spontaneous or rarely due to genetic, autoimmune, and environmental or toxic causes.
- 4 months of amenorrhoea with a FSH and E levels in the menopausal range on two occasions at least 6 weeks apart
- Untreated POI increases the risk of osteoporosis, heart disease, cognitive impairment, and premature death
- MHT until ave age of menopause (50-51 yrs)
- Contraception may still be required

Step 2 – MHT options

MHT is the most effective treatment for VMS

- Oestrogen alone (E) - in hysterectomised women
- Oestrogen plus Progestogen (E&P)
  - For endometrial protection
  - Cyclical regimen in peri - & early post menopause
  - Continuous in women more than 1 year post menopause

MHT options

- Low dose OC pill in women <50 years old and without significant cardiovascular risk factors, non smokers, no VTE
- Tibolone
- TSEC (tissue-selective oestrogen complex) i.e. oestrogen + SERM (selective oestrogen receptor modulator)

Different routes MHT

- Transdermal - patch, gel
- Oral
- Vaginal
- Intrauterine (Mirena – levonorgestrel)

Different progestins

- Oestradiol and dydrogesterone - Femoston
  - low dose cyclical (1mg oestradiol/10mg dyhydrogesterone)
  - medium dose cyclical (2mg oestradiol/10mg dyhydrogesterone)
  - low dose continuous (1mg oestradiol/ 0.5mg dyhydrogesterone- Femoston-conti)
- Lower incidence of progestogenic side effects/risks including mood symptoms
- Lower risk of VTE
- Greater breast neutrality (do NOT tell patients these are “breast safe”)

Micronised progesterone -Prometrium

Body-identical hormone therapy (Nick Panay 2014)

Available in Australia since 2016
Soft gel capsule 100mg
Considered the preferred progestin by many experts (see uptodate:MHT)

Oral dosage: cyclical 200 mg per day for 14 days
continuous 100mg per day
consider 200mg if on E 75-100 mcg for endometrial protection
Sedative so use at night.

Vaginal dosage: 100mg alt nights (John Eden 2017). May lessen side effects

Davis SR, Micronised progesterone. MedicineToday 2017; 18(1): 53-55

Tissue Selective Oestrogen Complex (TSEC) =Selective Estrogen Receptor Modulator + Estrogen

Differing agonist or antagonist effects at the oestrogen receptor in different tissues > "selective". The outcome is distinct from administering either component alone.

Available 2017 - CEE 0.45mg with Bazedoxifene 20mg (Duavive)

- Improves hot flushes, sleep
- Improves BMD
- Neutral effect on the endometrium
- Improves VVA symptoms
- Less bleeding than with CEE/MPA
- Less mastalgia then CEE/MPA

- For use in postmenopausal women with a uterus

Baber R, what's new in menopausal hormone therapy. Medicine Today April 2018
Pickar J, et al TSEC:a review Menopause, 2018;25 (9)

Non-hormonal treatments

- SSRI/SNRI (paroxetine, escitalopram, venlafaxine, desvenlafaxine)
- Gabapentin
- Pregabalin
- Clonidine
- Oxybutynin ER
- Stellate ganglion blockade
- Hypnosis
- Cognitive Behaviour Therapy (CBT)
- Weight loss for obese women

Natural Therapies

Complementary and alternative medicines
-mixed data or little if any benefit in clinical trials

- Black Cohosh – Remifemin®, Femular®
- Soy and plant phytoestrogen products
- Vitamin E
- Flaxseed
- Evening primrose oil, dong quai, ginseng, wild yam
- St John's wort
- Yoga/acupuncture
- Exercise

Bioidentical therapy

- Combinations of hormones in a troche (lozenge) – e.g. oestrogen, progesterone, testosterone, DHEA
- Manufactured in compounding pharmacies
- Not approved for use in Australia by TGA
- Minimal data on efficacy and safety
- Some concerns regarding endometrial carcinoma
- Expensive, marketing is misleading

Global Consensus Statement on Menopausal Hormone Therapy Climacteric 2016;19:313-315

Step 4 – starting MHT treatment

Address **her** concerns:

- **Localised urogenital symptoms**
  vaginal lubricants, moisturizers
  vaginal E therapy--- does not require progestogen
  possibly MHT
- **Moderate to severe menopausal symptoms**
  hormonal Tx = E (no uterus), E+P, E + BZA, Tibolone
  non hormonal options
- **Sexual dysfunction**
  consider tibolone/testosterone therapy
- **Concerns, no distressing symptoms**
  advice on lifestyle management
  evidenced based information

A practical approach

First line management

Uterus intact

A. Combined transdermal (E+P) patch
B. Transdermal E patch or gel plus oral P or LNG-IUD
C. Oral E plus oral P or LNG-IUD
D. Tibolone
E. TSEC (E +SERM)

Post hysterectomy

A. Transdermal E patch or gel
B. Oral E
C. Tibolone

Jane and Davis; A practitioner's Toolkit for the Menopause

Dosing

AMS gui

the prod d the

composi

E.g.

- Oestr
  - -lo
  - -cy
- Oestr
- Proge
- Vagin

AUSTRALASIAN MENOPAUSE SOCIETY
NEW DIRECTIONS IN WOMEN'S HEALTH

INFORMATION SHEET

AMS Guide to Equivalent MHT/HRT Doses
Australia Only

This Information Sheet has been developed as a guideline only to approximately equivalent doses of the different MHT/HRT products available in Australia in March 2017. HRT is now referred to as Menopausal Hormone Therapy (MHT). The intention of this sheet is to help physicians change their patients to higher or lower approximate doses of MHT if needing to tailor therapy, or remain within the same approximate dose if needing to change brands of MHT. Private/non PBS script products are marked with an *.

Oestrogen and progestogen combination MHT

Use cyclical oestrogen and progestogen combinations at peri-menopause or if less than 12 months amenorrhoea

Product	Presentation	Composition
Low Dose		
Femoston	tablet	1mg oestradiol/10mg dydrogesterone
Medium dose		
Trisequens*	tablet	1 and 2mg oestradiol/1mg norethisterone
Femoston	tablet	2mg oestradiol/10mg dydrogesterone
Estalis sequi 50/140	transdermal patch	50mcg 17 B oestradiol/140mcg norethisterone acetate (twice weekly application)
Estalis sequi 50/250 (same oestrogen, more progestogen than Estalis sequi 50/140)	transdermal patch	50mcg 17 B oestradiol/250mcg norethisterone acetate (twice weekly application)

Continuous oestrogen and progestogen combinations

Should be used if 12 months since LMP or after 12 months cyclical MHT

Product	Presentation	Composition
Low dose		
Angeliq(1/2*)	tablet	1mg oestradiol/2mg drospirenone
Femoston-conti	tablet	1mg oestradiol/5mg dydrogesterone
Kliovance*	tablet	1mg oestradiol/0.5mg norethisterone
Other Low dose hormonal options		
Livial*, Xyvion*	tablet	2.5mg tibolone
Duavive* (oestrogen/SERM combination)	tablet	0.45mg conjugated equine oestrogens / 20mg bazedoxifene
Medium dose		
Kliogest*	tablet	2mg oestradiol/1mg norethisterone
Premia 2.5 continuous*	tablet	0.625mg conjugated equine oestrogens/ 2.5mg medroxyprogesterone acetate
Premia 5 continuous* (same oestrogen, more progestogen than Premia 2.5 continuous)	tablet	0.625mg conjugated equine oestrogens/ 5mg medroxyprogesterone acetate
Estalis continuous 50/140	transdermal patch	50mcg 17 B oestradiol/140mcg norethisterone acetate (twice weekly application)
Estalis continuous 50/250 (same oestrogen, more progestogen than Estalis continuous 50/140)	transdermal patch	50mcg 17 B oestradiol/250mcg norethisterone acetate (twice weekly application)

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Cyclical

Regular periods

-start MHT on D1 of period , will get monthly withdrawal bleed at this time each month

-if using ocp as MHT and symptoms in pill free week add E patch in this time

Irregular periods or < 12/12 from LMP

-start MHT possible irregular bleeding for a few months.

-can use ocp up to 50 years (oestadiol often better than CEE containing pills)

Continuous Dosing

No period for 12 months

Changing cyclical to continuous therapy

Cyclical/sequential MHT

↓ 12 months

Trial of continuous

↓ BTB → Further 12 months cyclical MHT

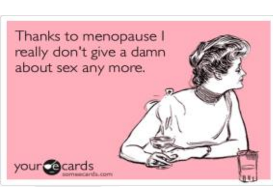
↓ Continuous MHT

Will hormone therapy make me put on weight ?

MHT does not cause weight gain

- Weight creep related to aging not menopause
- Redistribution of body fat from gynoid to android shape at menopause
- MHT may help prevent some of central adiposity and associated metabolic changes
- Losing weight may help lessen VMS in overweight women

Will hormone therapy help my libido?



- Treat vulvovaginal atrophy – vaginal E/ MHT or both
- Consider Tibolone
- Review medications (antidepressants)
- Consider relationship and sexual counselling
- Androgen therapy

Contraception

Contraception should be offered to all women:

- under 50 until 2 years post LMP
- over 50 for 1 year post LMP

- MHT is not contraceptive (excl LNG-IUD)

- Women should be informed about the availability of the Emergency Contraceptive Pill without a prescription at pharmacies and its effectiveness up to 96 hours after unprotected intercourse

Step 4 - Trouble shooting

Bleeding on continuous combined MHT

< 6 months since starting MHT:

- Reassure and try to increase progestogen dose
  (eg change from 50/140 Estalis continuous to 50/250)

> 6/12 since starting MHT

- TVU to exclude uterine pathology
- Change from continuous to cyclical therapy

Any post coital, heavy or irregular bleeding on cyclical therapy needs investigation

Troubleshooting

Mastalgia

- Decrease oestrogen dose
- Change progestogen type or dose (dydrogesterone or micronized progesterone)
- Change to Tibolone or Duavive
- Decrease alcohol/caffeine intake
- Evening primrose oil may be helpful (1000mg tds)

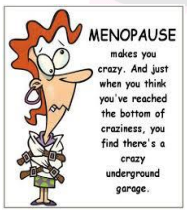
Androgenic side effects

- Change progestogen to micronised progesterone or drosperinone (Angeliq)

Trouble shooting

Mood disturbance

- Change oestrogen: oestradiol has better
- effects on mood
- Change delivery of progestogen eg patch or IUD
- Change progestogen: micronized progesterone
- has least effect on mood
- Consider TSEC
- Consider adding SSRI/SNRI



Fluid retention

- Change progestogen or decrease dose/ duration

Trouble shooting

Symptoms recur when taking inactive pills with COCP

- Take COCP active pills continuously and skip inactive pills
- Use oestrogen patch in the week of inactive pills
- Change to Zoely or Qlaira (fewer inactive pills)
- Change to Mirena + continuous oestrogen (oral/ patch or gel)

Step 5- When to refer:

- Women with ongoing distressing symptoms of menopause and
  - unable to take MHT
  - have a high risk of CVD
  - have a high risk of breast cancer (eg BRCA positive)
  - have persistent symptoms despite MHT
- Women with abnormal vaginal bleeding
- Women with ongoing bone loss whilst taking MHT
- Women with POI

North American Menopause Society Guidelines 2017

The concept of "lowest dose for the shortest period of time" may be inadequate or even harmful for some women.

POSITION STATEMENT
The 2017 hormone therapy statement of the North American Menopause Society

Take home messages

Step 1 –address a woman's concerns and assess for contraindications

Step 2 –transdermal oestrogen may reduce VTE risk compared with oral therapy, a progestogen is required in all women with an intact uterus

Step 3 –in women <60 years or within 10 years of their LMP and with no C/I, MHT is safe and effective for VMS and has additional benefits on bone and cardiovascular health

Step 4 –minimum effective dose should be used, individualized and reviewed at least annually

Step 5 –there is no specific time to cease MHT

Menopause tools

Menopause Management GP Tool

https://jeanhailes.org.au/health-professionals/tools

https://www.menopause.org.au/images/stories/documents/management-menopause-toolkit.pdf

menopause.org.au Australasian Menopause Society

jeanhailes.org.au Jean Hailes for Women's Health

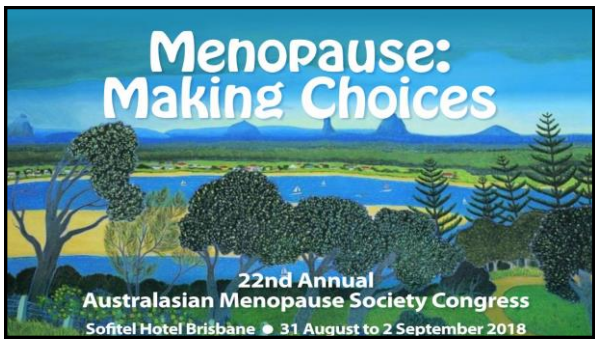
monash.edu/medicine/shpm/depts-centres-units/womenshealth Women's Health Research Program - Monash Uni

menopause.org The North American Menopause Society

imsociety.org International Menopause Society

Consensus on the use of MHT

- Treatment of Symptoms of Menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2015; 100:3975-4011
- Menopause Clinical Guideline. National Institute for Health and Care Excellence. (NICE Guideline) JAMA Intern Med 2016;176:1205-6
- 2016 IMS Recommendations on women's midlife health and Menopausal Hormone Therapy Climacteric 2016;19:109-50
- NAMS 2017 Position Statement on MHT Menopause 2017 June
- Global Consensus Statement on Menopausal Hormone Therapy Climacteric 2016;19:313-315



Thank you

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