HRT troubleshooting

Dr Sam Morgan

Menopause Fellow BNSSG Training Hub, GP & BMS Accredited Menopause Specialist

Sharon Hartmann

Specialist Nurse Contraception, Menopause and Sexual Health, Nurse Prescriber

Today we are going to go through some common presentations in primary care

- **“My HRT’s not working”**
- **“Can you help with my vulval symptoms, I’ve had breast cancer”**
- **“I’m bleeding all the time”**
- **“My mood is worse”**
- **“I’d like to start testosterone”**
- **“I’m so fed up I can’t get hold of my HRT, can I change to a tablet”**
- **“Can you take over my private script for 8 pumps of gel please”**
- **“Do I need to stop my HRT, my sister has breast cancer”**

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Case 1

Amanda, aged 47, presented to your GP colleague 3 months ago with typical perimenopause. She started Lenzetto® at 2 sprays/day and micronised progesterone (Utrogestan® or Gepretix®) 200mg in a cyclical regime, 2 weeks on 2 weeks off. She has booked with you for her 3-month review and is really fed up as she doesn’t feel any better at all.

“It’s not working”

Lifestyle

Diagnosis

Reviewing HRT - “3 Ds”

- Dose – very high doses can be needed in premature ovarian insufficiency (POI) to relieve symptoms
- Duration – symptoms can improve at different timescales
- Drug & route of administration – 20% of women don’t absorb well transdermally, oestradiol levels can sometimes help here

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Lifestyle & Diagnosis - Amanda is having a really difficult time at work, she feels unsupported and is going to speak to her line manager.

Dose, duration, drug - Amanda has memory symptoms & finds she often forgets to apply her spray. She decides to try the patch instead.

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Questions?

Case 2

Bhavna, aged 61, is booked with you for a medication review. She had a diagnosis of breast cancer 9 years ago and takes tamoxifen. At the end of the consultation, she asks you to prescribe some treatment for her recurrent thrush.

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Bhavna doesn’t have a discharge. You know recurrent thrush could be GSM.

Vulval care - Bhavna has always washed with soap, she agrees to stop & try an emollient.

Local oestrogen - Bhavna is really worried about this idea, so you agree to write to her oncologist and consider a referral to the menopause oncology clinic.

Local oestrogen and breast cancer

Fine to prescribe if on tamoxifen or no active treatment.

Do not prescribe if on aromatase inhibitor (Anastrozole® etc).

Don’t forget [vulval care](), emollient & lubricant advice (Yes range)

Consider other diagnoses e.g. Lichen sclerosis

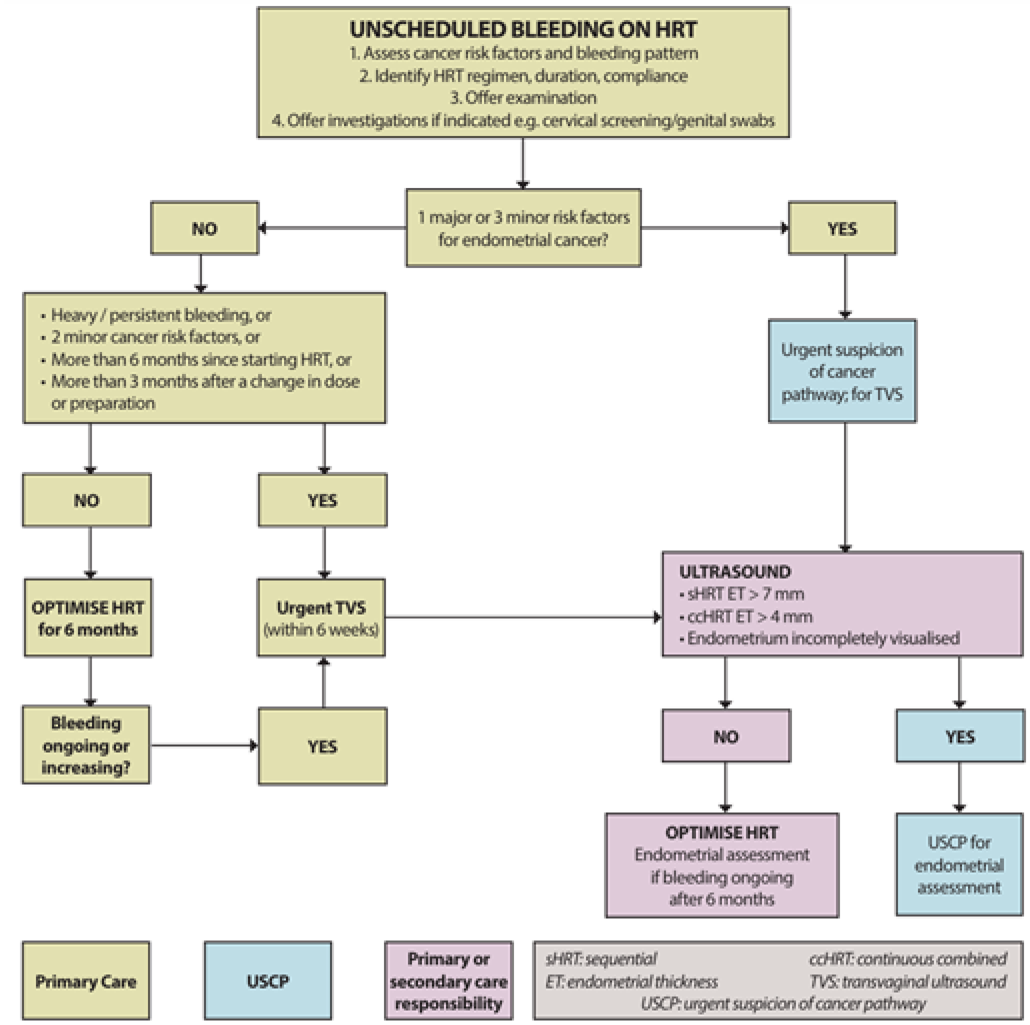
Remember the Menopause Oncology Clinic at St Michael’s

[Vaginal Estrogen Therapy Use and Survival in Females With Breast Cancer PMID: 37917089]()

Questions?

Case 3

Cherry, aged 46, comes in for an HRT review. She is happy with her symptom control, but worried that she has been getting some vaginal bleeding. Could this be serious, she asks? Do I need to stop my HRT?



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From new BMS guideline

[Management of unscheduled bleeding on HRT]

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HRT troubleshooting

1 major / 3 minor = 2ww referral

2 minor = urgent USS

MAJOR risk factors for endometrial cancer

- BMI ≥ 40
- Genetic predisposition (Lynch / Cowden syndrome)
- Estrogen-only HRT for > 6 months in women with a uterus
- Tricycling HRT (quarterly progestogen) for > 12 months
- Prolonged sHRT regimen: use for more than 5 years when started in women aged ≥ 45
- 12 months or more of using norethisterone or medroxyprogesterone acetate for < 10 days / month or, micronised progesterone for < 12 days / month, as part of a sequential regimen

MINOR risk factors for endometrial cancer

- BMI 30-39
- Unopposed estrogen > 3 months but < 6 months
- Tricycling HRT (quarterly progestogen) for > 6 but < 12 months
- > 6 months but < 12 months of using norethisterone or medroxyprogesteorne acetate for < 10 days / month or, micronised progesterone for < 12 days / month, as part of a sequential regimen
- Where the progestogen dose is not in proportion to the estrogen dose for > 12 months (including expired 52 mg LNG-IUD)
- Anovulatory cycles, such as in Polycystic ovarian syndrome
- Diabetes

HRT troubleshooting - “I’m bleeding all the time”

Optimise HRT regime - consider

- increase progestogen dose and / or number of days administered
- change method of progestogen delivery e.g. IUS
- change type of progestogen e.g. synthetic
- add in local oestrogen if GSM
- reduce oestrogen dose.

Oral progestogens are associated with less bleeding, but many of those with risk factors for endometrial cancer will also have risk factors for VTE with oral HRT.

Case 3

Cherry, aged 46, comes in for an HRT review. She is happy with her symptom control, but worried that she has been getting some vaginal bleeding. Could this be serious, she asks? Do I need to stop my HRT?

Diagnosis - Cherry had her IUS removed and smear taken with the ANP 8 weeks ago, and the exam was normal then. She started Utrogestan® at this point.

Cherry uses Oestrogel 2 pumps daily and Utrogestan® 100mg every night. She is really good at remembering to take it and doesn't have any risk factors for endometrial cancer. She has started within the last 3/12 so you agree to monitor, ask her to track her symptoms and come back if the bleeding is heavy or ongoing.

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Questions?

Case 4

Farhana feels her mood has been worse since she started HRT, and wonders actually whether she is depressed not perimenopausal.

HRT troubleshooting - “My mood is worse”

Transient side-effects - “4 bs” bloating, breasts, bleeding, blues

With any side-effect it can be helpful to think about whether it relates to the oestrogen or progestogen - easier to tell if on a sequential regime.

Progestogen side-effects - low mood, acne

Oestrogen side-effects - breast tenderness, nausea

“My mood is worse” - progesterone sensitivity

PMS, PMDD, postnatal depression, mood effects with hormonal contraception.

If using a synthetic progestogen could switch to micronised progesterone, or IUS.

If mood has dipped on oral micronised progesterone could consider off licence vaginal use of micronised progesterone.

Essential to explain the progesterone is to protect against endometrial cancer and must be continued.

Risk assess, offer support and safety-net.

HRT prescribing - body-identicals - who are they really advantageous for?

Medical indications for micronised progesterone

- higher breast cancer risk
- higher VTE risk
- PMDD/severe PMS/progestogenic SEs with contraception
- higher c-v disease risk

Not suitable for those with a soy or peanut allergy

Femoston® is the most breast-friendly and lipid-friendly of the oral preparations

Case 4

Farhana feels her mood has been worse since she started HRT, and wonders actually whether she is depressed not perimenopausal.

Farhana has always had quite severe PMS, and experienced postnatal depression after the birth of her first child. She tried the combined pill in her early 20s and stopped it as her mood dipped.

She is currently using a sequential patch, and her tracker shows her mood dips when she is using the progestogen. She is not keen on an IUS, but likes the idea of micronised progesterone alongside an oestrogen only patch.

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Questions?

Case 5

Davina, aged 55, would like to start testosterone, as her friends have all told her it is great for libido.

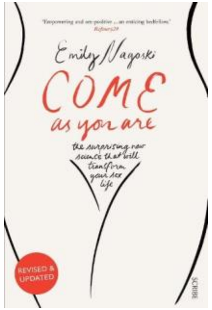
Testosterone

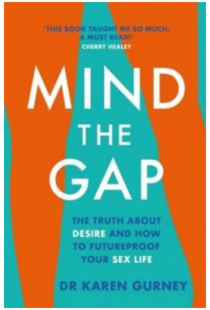
NICE & BMS “Consider testosterone for menopausal women with low sexual desire if HRT alone not effective & biopsychosocial approach excludes other causes.”

Remember the impact of SSRIs on libido.

Optimise oestrogen (switch to transdermal oestrogen if on oral).

Ask about GSM and offer local oestrogen. Lubricant advice.





Testosterone

Some women particularly benefit - surgical menopause and POI

Side effects can include acne, local hair growth and weight gain

Applied topically to lower abdo/thigh, 3-6 month trial, review with repeat bloods.

BMS “Randomised clinical trials to date have not demonstrated beneficial effects of testosterone therapy for cognition, mood, energy and musculoskeletal health.”

Case 5

Davina, aged 55, would like to start testosterone, as her friends have all told her it is great for libido.

Davina is on oral HRT, so you change to transdermal oestrogen.

She has GSM, so you advise about vulval care, lubricants and start local oestrogen.

It can be helpful to explain your practice's position on testosterone Rx/local formulary decision making at this point to help expectations around next steps.

Questions?

Case 6

Ellie, aged 62, is really frustrated that again the pharmacy can’t get hold of her HRT. She uses Oestrogel® and Utrogestan®. She asks about changing to a tablet instead as this is the third time there have been stock difficulties.

HRT prescribing - shortages

Changing oestrogen products, BMS guide to equivalence:

Estradiol – equivalent doses*

	Ultra low	Low	Medium	High
Oral	0.5mg	1mg	2mg	3-4mg
Patch	Half 25	25	50	75-100
Gel-pump	½ pump	1 pump	2 pumps	3-4 pumps
Gel-sachet	½ x 0.5mg sachet - 0.25mg	0.5mg	1-1.5mg	2-3mg
Spray	1 spray	2 sprays	3 sprays	—

* The table has been drawn up as a practical guide based on a combination of pharmacokinetics, clinical trials and clinical experience. The dose equivalents are subject to significant individual variations in absorption and metabolism.

BMS supply updates publicised to members

HRT prescribing - shortages

Utrogestan® / Gepretix® standard dose alternatives

- IUS
- Medroxyprogesterone acetate (Provera®)
  - 10mg for 14 days if sequential (licensed)
  - 2.5mg-5mg daily continuous combined (unlicensed)
- Norethisterone
  - 5mg for 14 days if sequential (unlicensed)
  - 5mg daily continuous combined (unlicensed)

Not covered by HRT-PPC..

HRT prescribing - matching higher oestrogen doses with higher progestogen doses

- Higher oestrogen dose - 4 mg oral, 4 pumps gel, 100mcg patch, 6 sprays
- Utrogestan® - 300mg for sequential or 200mg for continuous combined

Management of unscheduled bleeding on HRT - new BMS guidance April 24 (47 pages..useful summary pages 4-6)

Progestogens and endometrial protection - BMS guidance

HRT prescribing - medical indications for trans-dermal oestrogen

- age over 60
- migraine
- BMI >30
- higher VTE risk
- higher cardiovascular disease risk
- liver / gallbladder disease
- hypothyroid on thyroxine
- G-I conditions that can affect absorption.

Case 6

Ellie, aged 62, is really frustrated that again the pharmacy can't get hold of her HRT. She uses Oestrogel® and Utrogestan®. She asks about changing to a tablet instead as this is the third time there have been stock difficulties.

Ellie has been using 4 pumps of Oestrogel® and 100mg Utrogestan® every day. Her BMI is 34 so you advise to continue transdermal oestrogen & Utrogestan®. She previously tried Sandrena® and didn't get on with the sachets.

She opts to try a patch. You check the latest on supply updates and start Evorel® 100mcg with 200mg Utrogestan® daily.

Questions?

Case 7

Hannah, aged 42, asks whether you can continue her private script for Oestrogel 8 pumps daily on the NHS

HRT prescribing - higher than licensed doses

- Higher doses often needed in POI, also sometimes after surgical menopause
- How is the product being used e.g. are patches peeling off
- Have bloods been done re absorption?
- What is she using for endometrial protection?
  - Women's Health Forum safety alert BMS, FSRH, RCGP, RCOG & RCN
- Concerns re tachyphylaxis
  - Tachyphylaxis with HRT BMS

Case 7

Hannah, aged 42, asks whether you can take over her private script for Oestrogel 8 pumps daily on the NHS

Hannah’s history is of surgical menopause at age 38. She had very little response to HRT at standard levels, tried oral and transdermal products and gradually increased her dose to this level, which gives good symptom control. She has an in date IUS for endometrial protection. Recent oestradiol level on 8 pumps 450.

Surgical menopause: a toolkit for healthcare professionals BMS

Questions?

Case 8

George, aged 58, asks whether she should stop her HRT as her younger sister has just been diagnosed with breast cancer.

HRT prescribing - FH breast cancer

- Take a family history
  - Classification, care and managing breast cancer in people with a family history of breast cancer NICE
- What other risk factors does she have? weight, smoking, alcohol, exercise
  - Understanding the risks of breast cancer WHC infographic
- If keen to continue is she on a lower risk preparation?
  - HRT and breast cancer risk BMS Tool for clinicians
- Is she aware of non-hormonal alternatives?
  - Prescribable alternatives to HRT BMS

Symptom management for those who can’t or don’t want to use HRT

SSRIs

Clonidine® (licensed) for vasomotor symptoms if bp not low!

Gabapentin® & pregabalin® for vasomotor symptoms, ? sleep and mood too

Oxybutynin® for vasomotor symptoms

Fezolinetant coming soon

Case 8

George, aged 58, asks whether she should stop her HRT as her younger sister has just been diagnosed with breast cancer.

George has no other relatives with breast cancer. She drinks 20 units alcohol per week and did not realise this was a risk factor, so decides to stop. She takes HRT to help with a number of different symptoms, not just vasomotor symptoms, so on balance decides she is happy to continue with her current regime.

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Questions?

HRT prescribing - top tips!

You can cut patches in half - best on the diagonal

Estradot® has the least skin reactions of the patches, and is the smallest

You can split gel / spray dose to bd - useful if on higher doses

Lenzetto® is great for swimmers (15 mins vs 6 hours for gel)

Lenzetto® has 56 doses in each device, doesn't feel empty..

"Window of opportunity" 10 years for heart, 5 years for brain

Local oestrogen leaflet still very misleading, daily Rx for 4 weeks if severe symptoms

HRT prescribing - new products

Bijuve® - oral continuous combined (micronised progesterone)

Gina® - OTC (> age 50 and LMP >1 year ago) local oestrogen

Intrarosa® (prasterone) - DHEA vaginal pessary

Qlaira® - COC with estradiol, amber on formulary for POI if contraception and HRT needed

Ideas for QI projects - HRT

Changing from sequential to continuous combined HRT if still on at 5 years or 54

Offering a switch from oral to transdermal oestrogen at age 60

Expired IUS being used for endometrial protection

Matching oestrogen and progestogen dose

Including progestogen on oestrogen only prescription e.g. 2 pumps daily with Mirena (change due October 25)

Useful resources

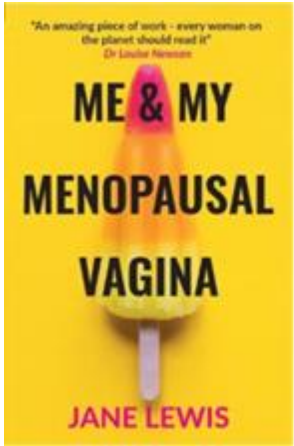
BMS resources & PPMC toolkit

Women’s Health Concern

PCWHF & Rock my menopause

Menopause Easy Read HRT guide - Learning Disability Wales

Perimenopause and HRT leaflets - University of Bristol, available in English, Arabic, Punjabi, Somali and Urdu



Questions?

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Any further questions?

Next webinar - 21st May POI