Managing Unscheduled Bleeding In Women on Hormone Replacement Therapy

University Hospitals of Leicester NHS Trust

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Contents

1. Introduction and Who Guideline applies to

This guideline is intended for use by Primary Care and Secondary care.

Background: The risk of endometrial cancer is significantly lower in women taking HRT presenting with unscheduled bleeding as compared to the cohort of women presenting with Post-Menopausal Bleeding (PMB) who are not taking HRT (Hormone Replacement Therapy). This is especially true of women who were not experiencing bleeding irregularities prior to starting HRT.
2WW referral is therefore not routinely indicated in women with unscheduled bleeding on HRT. These 2 studies were published in PRH journal confirming the low risk of malignancy in women taking HRT.

- **Endometrial cancer rate in Hormone replacement therapy users with postmenopausal bleeding: Retrospective cohort study published 08-22**
- **Outcomes of endometrial assessment in women with unscheduled bleeding on hormone replacement therapy 03-2018**

The BGCS (British Gynaecological Cancer Society) suggests stopping HRT for 6 weeks to see if bleeding settles prior to referral, however this would have detrimental effects on women and they would suffer return of their symptoms and increase follow up in primary care, “Advice and Guidance” and demands on secondary care menopause services. This approach is not supported by the British Menopause Society.

Related UHL Documents:

Post-Coital Bleeding UHL Gynaecology Guideline
Menopause UHL Gynaecology Guideline
Imaging Referral – Gynaecology UHL Imaging Guideline

2. Unscheduled bleeding on HRT

Consider other non-pathological causes of unscheduled bleeding on HRT before changing HRT or investigating further.

2.1 In primary care, consider the following when assessing *Unscheduled Bleeding on HRT in Primary care*:

- **Pregnancy** (unlikely over the age of 55y)
- **Symptoms suggesting recent ovulation** - Unscheduled bleeding can occur as a result of a women's own endogenous ovarian activity that can be intermittent in the perimenopause
- **Bleeding pattern before HRT was started**
- **Change of regime-** has the prescription or route changed?
- **Compliance** - has the woman omitted doses, taken sequential HRT incorrectly
- **Continuous combined HRT vs Sequential HRT –** monthly (or 3 monthly depending on regime) scheduled bleeding after the combined Estrogen & Progesterone part of the regime is normal on sequential HRT
    - **To reduce risk of endometrial cancer - switch to ccHRT if**
        - **over 54y OR**
        - **on sequential HRT >2y if under 50y or >1y if over 50y**
- **Suboptimal absorption –** malabsorption/ gastrointestinal upset
- **Other medication and interactions**
- **Lower genital tract pathology – e.g. vulva, vagina, cervix**
- **Infection**
- **Risk factors for endometrial cancer** (obesity, diabetes, nulliparity, history or chronic anovulation, history of polycystic ovarian syndrome, late menopause, FH of hereditary nonpolyposis colorectal, endometrial or ovarian cancer)

2.2 Do not discontinue HRT in the first instance with unscheduled bleeding on HRT

Given that the risk of malignancy is so low in women on HRT with adequate endometrial protection with progesterone, it is unnecessary to stop the HRT. This practice leads to unnecessary distress for the patient and does not resolve the underlying issue causing the bleeding.

2.3 Two Week Wait (2WW) endometrial pathway

Women with unscheduled bleeding on HRT do not usually require referral on 2WW endometrial pathway.
Unless an USS pelvis is suggestive of invasive endometrial malignancy, women with unscheduled bleeding on HRT do not require 2WW referral.

2.4 Unscheduled bleeding on HRT in the first 6 months of administration

Where women experience unscheduled bleeding on HRT in the first 6 months of taking HRT – consider a trial of increased progesterone in the HRT regime unless there was abnormal uterine bleeding before the HRT was commenced. Where this does not settle the bleeding, consider Ultra Sound Scan and refer on Suspected Endometrial Pathology (SEP) pathway.

Based on joint advice from the Royal College of Obstetricians & Gynaecologists, Royal College of General Practitioners, Royal College of Nursing, Faculty of Sexual & Reproductive Health and the British Menopause Society, do not refer to secondary care at first presentation. Bleeding within the first six months of taking HRT is extremely common and unlikely to be associated with underlying pathology.

1. Recommend a trial of increased progesterone in the regime (see boxes A&B below) for at least a month before considering further investigation
2. If bleeding not settling, arrange a pelvic USS whilst remaining on HRT.
3. If the ET (endometrial thickness) is ≥8mm or there is other suspected endometrial pathology (polyp / cystic / irregular / vascular appearance) seen on the scan - refer on SEP pathway.
4. If the ET is <8mm[1] and there is no other pathology seen on the scan, and the bleeding settles with the increased dose of progestogen – do not refer. Continue the progesterone at the higher dose long-term.
5. If bleeding problems don't improve within 3 months despite the ET <8mm and no other pathology seen on the scan – refer on SEP

2.5 De novo unscheduled bleeding taking HRT for more than 6 months

Where women experience de novo unscheduled bleeding taking HRT for more than 6 months, arrange an USS pelvis and consider referral on Suspected Endometrial Pathology pathway where the endometrium is 8mm or more, is vascular or cystic or irregular in appearance. Where the endometrium is <8mm and regular consider a trial of increased progesterone in the HRT regime prior referral. Women who continue to experience unscheduled bleeding on HRT despite increased progesterone in the HRT regime should be referred on the Suspected Endometrial Pathology pathway

When unscheduled bleeding occurs after the patient has been established on HRT for more than 6 months, the risk of benign pathology is slightly higher, although the risk of malignancy remains very low unless she has been taking unopposed oestrogen inadvertently.

1. Arrange TV USS Pelvis
2. If ET ≥8mm or there is other suspected endometrial pathology (polyp / cystic / irregular / vascular appearance) seen on the scan - refer on SEP pathway
3. If ET <8mm, recommend a trial of increased progesterone in the regime (see boxes A&B below) before considering referral
4. If the bleeding settles with the increased dose of progestogen – do not refer. Continue the progesterone at the higher dose long-term.
5. If bleeding problems don't improve within 3 months despite the ET <8mm and no other pathology seen on the scan – refer on SEP

3. Education and Training

None

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Women with unscheduled bleeding on HRT are offered supplementary progesterone before being referred to Secondary care unless otherwise contraindicated				
Patients are referred on SEP when they experience unscheduled bleeding on HRT that has not responded to supplementary progesterone				

5. Supporting References

1. Unscheduled bleeding on HRT -do we always need to investigate for endometrial pathology? October2017· Volume 6· Issue 10 Page 4174 International Journal of Reproduction, Contraception, Obstetrics and Gynecology LouYYet al. Int J Reprod Contracept Obstet Gynecol. 2017Oct;6(10):4174-4178www.ijrcog.org DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20174391

2. Unscheduled bleeding with hormone replacement therapy Fulva Gajjar Dave MBBS MD MRCOG, Tolu Adedipe MBBS MRCOG, Stewart Disu MRCOG, Raphael Laiyemo MRCOG First published: 16 January 2019 https://doi.org/10.1111/tog.12553 https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/tog.12553

6. Key Words

Bleeding, HRT, Unscheduled bleeding

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details			
Guideline Lead (Name and Title) Miss Olivia Barney - Consultant			**Executive Lead** Chief medical officer
Details of Changes made during review:			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
October 2023	**1**	Mr Marwan Habiba – Consultant HoS Miss Subashini Sivalingam – Consultant Gynaecology Governance Committee	**New guideline**

Appendix 1: How to increase the progesterone in HRT

How to increase the progesterone in HRT

A. Continuous combined HRT regimens

Increase the dose of progestogen:
For women on a regime that already includes micronized progesterone (***Utrogestan***) 100 mg daily; increase to 200 mg daily on continuous basis.

For women on continuous combined HRT patch or tablets or oestrogen plus Mirena Add one of: Micronized progesterone (***Utrogestan***) 100mg
Medroxyprogesterone acetate ***Provera 5mg OD***
Norethisterone 3 tablets of ***Noriday*** to their HRT regimen.

B. Cyclical HRT regimens

Increase the dose or duration of progesterone:

- For women on a regime that already includes micronized progesterone (***Utrogestan***) 200 mg for 12 days of the month – increase this to 300 mg for 12 days a month

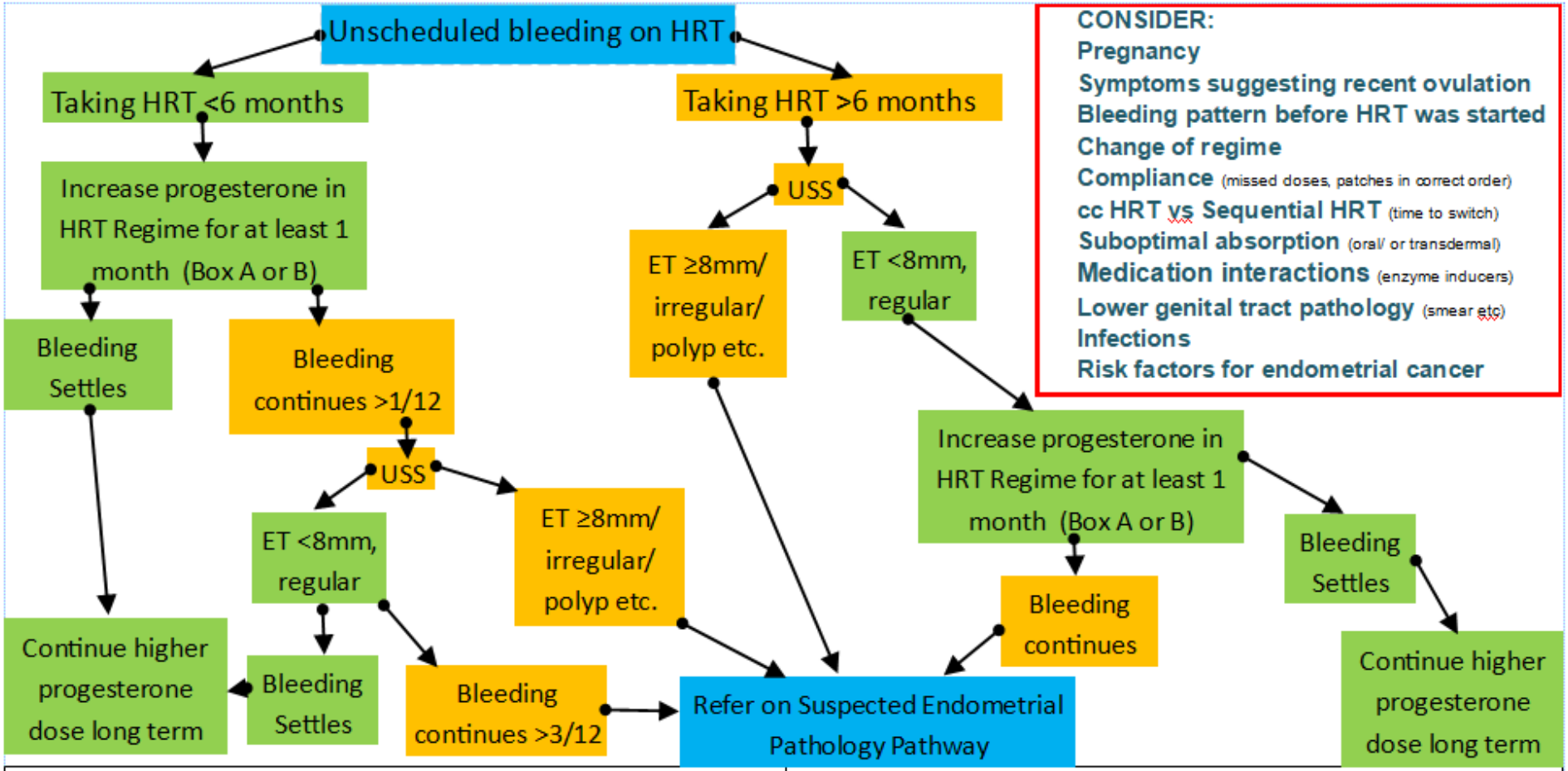
or
Change the progesterone to ***Provera 10mg OD*** for 12 days of the months or 3 tablets of ***Noriday*** a day for 12 days.
or

- Increase duration of progestogen to 21 days out of a 28-day HRT cycle

or

- switch to continuous regime if she has been on Sequential HRT for more than a year over the age of 50y. This will also minimise the risk of endometrial hyperplasia. The timing of switching from sequential to continuous combined HRT should be considered in relation to the woman's age and the frequency of her menstrual cycles (prior to commencing HRT). Women under the age of 50 who had shorter durations of amenorrhoea before starting HRT are likely to need to continue on sequential intake for a longer duration before switching to continuous combined HRT intake.

Appendix 2: unscheduled bleeding on HRT pathway



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