Management of Endometrial Hyperplasia

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V4	February 2023	Saadia Naeem Tim Duncan Gynaecologists	Minor amendments, update to fit Trust Docs template
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Previous Titles for this Document:

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None	Not applicable

Distribution Control

Printed copies of this document should be considered out of date. The most up to date version is available from the Trust Intranet.

Consultation

The following were consulted during the development of this document:
Gynae-oncologist, Gynaecology consultant and Postmenopausal nurse specialists

Monitoring and Review of Procedural Document

The document owner is responsible for monitoring and reviewing the effectiveness of this Procedural Document. This review is continuous however as a minimum will be achieved at the point this procedural document requires a review e.g. changes in legislation, findings from incidents or document expiry.

Relationship of this document to other procedural documents

This document is a clinical guideline applicable to Norfolk and Norwich University Hospital NHS Foundation Trust. Please refer to local Trust's procedural documents for further guidance, as noted in Section 5.

Management of Endometrial Hyperplasia

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1. Introduction

Endometrial hyperplasia (EH) is usually detected following investigation for abnormal uterine bleeding[1]. This can occur in pre and postmenopausal women and management must take into account fertility wishes, medical co-morbidities and risk of cancer progression

1.1. Rationale

Classification of EH has varied over the years. The World Health Organization (WHO) 2014 classification is recommended [2]. These separates EH into two groups based upon the presence of cytological atypia:

Types of EH	Risk of progression [3]
• Hyperplasia without atypia	<5% over 20 years
• Atypical hyperplasia	30%

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1.2. Objective

The objective of the guideline is to provide clinicians with up-to-date evidence-based information regarding the management of endometrial hyperplasia.

1.3. Scope

This is a guide for the clinician to the management of women diagnosed with endometrial hyperplasia on endometrial biopsy. It includes identifying and addressing the risk factors, treatment, and follow-up required.

1.4. Glossary

The following terms and abbreviations have been used within this document:

Term	Definition
EH	Endometrial hyperplasia
WHO	World Health Organisation
PCOS	Polycystic ovary syndrome
PMB	Postmenopausal bleeding
IMB	Intermenstrual bleeding
HRT	Hormone replacement therapy
LNG-IUS	Levonorgestrel-releasing intrauterine system
BMI	Body mass index
AEH	Atypical endometrial hyperplasia
BSO	Bilateral Salpingo Oophorectomy
IUS	Intrauterine system
MRI	Magnetic resonance imaging
CXR	Chest x-ray
MDT	Multidisciplinary team
MPA	Medroxyprogestrone acetate

NET	Norethisterone

2. Responsibilities

Mrs Saadia Naeem, Consultant Gynaecologist, Document lead.

3. Policy Principles/ Service to be delivered/Processes to be followed

Endometrial hyperplasia (EH) is usually detected following investigation for abnormal uterine bleeding[1]. This can occur in pre and postmenopausal women and management must take into account fertility wishes, medical co-morbidities and risk of cancer progression.

Classification of EH has varied over the years. The World Health Organization (WHO) 2014 classification is recommended [2]. These separates EH into two groups based upon the presence of cytological atypia:

	Risk of progression [3]
Hyperplasia without atypia	<5% over 20 years
Atypical hyperplasia	30%

Associated factors which increased incidence and risk of progression of EH include [4-7]:

- Unopposed oestrogen therapy.
- Obesity (BMI>35).
- Nulliparity.
- Diabetes.
- Tamoxifen.
- PCOS (anovulation).
- Oestrogen secreting tumours (e.g. ovarian granulosa cell tumour).

Symptoms:

- PMB.
- IMB.
- Menorrhagia.
- Irregular cycle.

EH can be reliably diagnosed by Pipelle biopsy or hysteroscopic biopsy [8], however, focal abnormalities within polyps can be missed with Pipelle endometrial sampling.

Hysteroscopy should be undertaken where EH has been diagnosed within a polyp by Pipelle sampling or if there is suspicion of a polyp on ultrasound assessment. Polyps should be removed in their entirety to ensure focal lesions such as areas of carcinoma are identified.

For investigation of PMB see guideline G39.

Reversible risk factors such as obesity and the use of hormone replacement therapy (HRT) should be identified and addressed if possible [9,10]. Where relevant, weight loss is advised, although the evidence of enhanced regression rates are lacking. Women on HRT should have the indication and preparation reviewed as this may be an opportunity to influence the likelihood of spontaneous regression

3.1. Management of EH without atypia

3.1.1. Conservative Management

EH without atypia progresses to endometrial cancer in less than 5% of cases over 20 years. The majority will regress spontaneously during the follow-up [1-2].

Observation alone, with follow-up endometrial biopsies (6 monthly) to ensure disease regression, can be considered especially when identifiable risk factors can be reversed.

Women should be informed that the treatment with progestogens has a higher disease regression rate compared with observation alone [11].

Progestogen treatment is indicated in women who fail to regress following observation alone for 12 months.

Conservative management in symptomatic women with abnormal bleeding is rarely advised.

3.1.2. Medical Management

Both continuous oral and local intrauterine [Levonorgestrel-releasing intrauterine system (LNG-IUS)] progestogen is effective in achieving regression.

The LNG-IUS should be the first-line medical treatment because compared to oral progestogens it has a higher disease regression rate and more favourable bleeding profile and fewer adverse effects [12].

Continuous progestogens (medroxyprogesterone 10-20 mg/day or norethisterone 10-15 mg/day) should be used for women who decline the LNG-IUS.

Cyclical progestogens should not be used because they are less effective.

Treatment with oral progestogens or the LNG-IUS should be for a minimum of 6 months in order to induce histological regression [13].

If adverse effects are tolerable and fertility is not desired, women should be encouraged to retain the LNG-IUS for up to 5 years as this reduces the risk of relapse.

After commencement of treatment an outpatient endometrial biopsy is recommended at 6-months. Once reversal has been achieved at least two consecutive negative biopsies, taken 6 monthly, should be obtained prior to discharge [14-15].

Due to the high relapse rates in women with a BMI>35 longer term follow-up should be considered with 6 monthly biopsies for 2 years. Following this the decision for ongoing follow up will be at the discretion of the responsible consultant [14-15].

Women should be asked to seek a further referral if abnormal bleeding recurs after completion of treatment because this may indicate disease relapse.

3.1.3. Surgical Management

Hysterectomy should not be considered as a first line treatment for hyperplasia without atypia.

Indications for hysterectomy:

- Progression to atypical hyperplasia.
- No histological regression after 12 months of treatment.
- Relapse.
- Persistence of bleeding in spite of reversal.
- Women who decline endometrial surveillance and/ or medical treatment.

Whenever possible a laparoscopic hysterectomy or vaginal hysterectomy should be offered.

Post-menopausal women requiring hysterectomy should be offered a bilateral salpingo-oopherectomy.

Due to the potential risk of residual hyperplasia both subtotal hysterectomy and endometrial ablation are contraindicated.

For premenopausal women the decision to remove the ovaries should be individualised; however, bilateral salpingectomy should be considered as this may reduce the risk of a future ovarian malignancy. The evidence regarding the effectiveness of prophylactic salpingectomy and the potential effects on ovarian function are yet to be established [17].

3.1.4. HRT and endometrial hyperplasia:

All women taking HRT should be encouraged to report any unscheduled vaginal bleeding promptly. Women with endometrial hyperplasia taking a sequential HRT preparation who wish to continue HRT should be advised to change to continuous progestogen intake using the LNG-IUS or a continuous combined HRT preparation. Subsequent management should be as described in the preceding sections of the guideline

Women with endometrial hyperplasia taking a continuous combined preparation who wish to continue HRT should have their need to continue HRT reviewed. Discuss the limitations of the available evidence regarding the optimal progestogen regimen in this context [7]. Consider using the LNG-IUS as a source of progestogen replacement. Subsequent management should be as described in the preceding sections of the guideline

3.2. Management of atypical EH

Atypical endometrial hyperplasia (AEH) carries a much greater risk of progression to endometrial cancer (up to 50%). Rates of concurrent endometrial cancer may be as high as 40% in patients diagnosed with AEH [3]. Management of patients should be discussed through the Gynaecological Oncology Multidisciplinary Team Meeting.

A pre-treatment pelvic MRI to rule out invasive endometrial cancer or coexisting ovarian cancer is recommended.

3.2.1. Surgical Management of Atypical Hyperplasia

Women with atypical hyperplasia should undergo a total hysterectomy because of the risk of progression or underlying cancer. A laparoscopic approach is preferable.

Due to the significant risk of concurrent endometrial cancer, postmenopausal women should also undergo a bilateral salpingo-oopherectomy. In premenopausal women the decision should be individualised, however, it is likely that removal of the ovaries through a second operation would be required if endometrial cancer was identified in the hysterectomy specimen.

Due to the potential risk of residual hyperplasia and / or cancer both subtotal hysterectomy and endometrial ablation are contraindicated.

3.2.2. Non-Surgical Management of Atypical Hyperplasia

Prior to considering medical management, where feasible, the patient should undergo hysteroscopy to reduce the risk of missing an occult carcinoma.

Medical management can be considered in the following situations:

- Fertility preservation.
- Medically unfit for surgery.
- Extreme obesity.
- Patient unwilling to undergo surgery.

Women should be counselled about the significant risk of underlying or subsequent progression to endometrial cancer which may be at an advanced stage. There is also an associated risk of concurrent ovarian cancer (up to 4%). These factors all have potential prognostic implications (30-50%) [8,18]. The need for close monitoring and follow-up needs to be emphasised. The effectiveness of conservative treatment is yet to be established.

First-line treatment with the LNG-IUS is recommended, with oral progestogens as a second-best alternative[19].

Once fertility is no longer required, hysterectomy should be offered in view of the high risk of disease relapse.

Follow up [20]

- 6 monthly until two consecutive negative biopsies.

- Evidence for duration of follow up, once regression has occurred, is limited.
- Recurrence risk is highest in the first 2 years, follow up with two annual biopsies is recommended. Following this the decision for ongoing follow up will be at the discretion of the responsible consultant.
- Once discharged patients and General Practitioners should be made aware of the symptoms of potential recurrence.
- Hysterectomy reconsidered at 12 months if regression has not occurred and also in patients who develop recurrent disease.

4. Training & Competencies

Not applicable

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6. Audit of the process

Compliance with the process will be monitored through the following:

Key elements	Process for Monitoring	By Whom (Individual / group /committee)	Responsible Governance Committee /dept	Frequency of monitoring
100% of women with endometrial hyperplasia without atypia should have at least two negative endometrial biopsies prior to discharge	Audit	Gynaecology team	Gynaecology Governance	3 yearly
100% of postmenopausal women with atypical hyperplasia should undergo a total hysterectomy and bilateral salpingo-oophorectomy if not medically contraindicated	Audit	Gynaecology team	Gynaecology Governance	3 yearly

The audit results are to be discussed at relevant governance meetings (Gynaecology clinical Governance meeting) to review the results and recommendations for further action. Then sent to (Gynaecology Guideline committee) who will ensure that the actions and recommendations are suitable and sufficient.

7. Appendices

7.1. Appendix 1 – Management of Endometrial Hyperplasia Without Atypia

7.2. Appendix 2 – Management of Atypical Endometrial Hyperplasia

8. Equality Impact Assessment (EIA)

Type of function or policy	New/Existing (remove which does not apply)

Division	Women and Children's Division	**Department**	Gynaecology
Name of person completing form	Mrs S. Naeem	**Date**	08/03/2023

Equality Area	**Potential Negative Impact**	**Impact Positive Impact**	**Which groups are affected**	**Full Impact Assessment Required YES/NO**
Race				No
Pregnancy & Maternity				No
Disability				No
Religion and beliefs				No
Sex				No
Gender reassignment				No
Sexual Orientation				No
Age				No
Marriage & Civil Partnership				No
EDS2 – How does this change impact the Equality and Diversity Strategic plan (contact HR or see EDS2 plan)?				

- **A full assessment will only be required if: The impact is potentially discriminatory under the general equality duty**
- **Any groups of patients/staff/visitors or communities could be potentially disadvantaged by the policy or function/service**
- **The policy or function/service is assessed to be of high significance**

IF IN DOUBT A FULL IMPACT ASSESSMENT FORM IS REQUIRED

The review of the existing policy re-affirms the rights of all groups and clarifies the individual, managerial and organisational responsibilities in line with statutory and best practice guidance.