DELTA Centre
Derby Endoscopic & Laparoscopic Training & Academic Centre

Derby Teaching Hospitals NHS
NHS Foundation Trust

Classification and Management of Endometrial Hyperplasia

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Taking pride in caring

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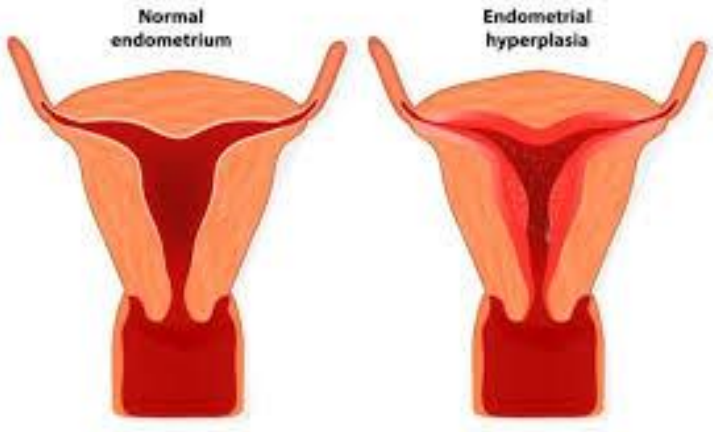
What is endometrial hyperplasia?

'An irregular proliferation of the endometrial glands with an increase in the gland to stroma ratio compared with proliferative endometrium'

Most common presentation is abnormal uterine bleeding eg. HMB, IMB, PMB, irregular bleeding or unscheduled bleeding on HRT.



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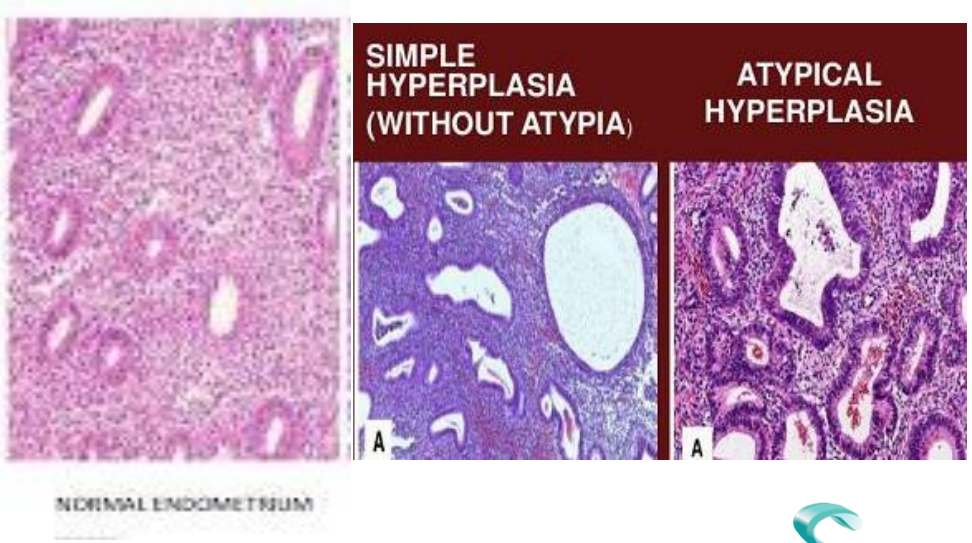


RCOG GTG no. 67, February 2016

Risk factors

1. Increased BMI ≥ 35
2. Anovulation associated with perimenopause or PCOS
3. Oestrogen secreting tumours eg. Granulosa cell tumour
4. Drug induced endometrial stimulation

Diagnosis and surveillance

2014 WHO classification – endometrial hyperplasia with or without atypia

- Histological examination of endometrial tissue
- Consider diagnostic hysteroscopy for endometrial sample
- TV USS may be useful in diagnosing hyperplasia in pre/post-menopausal women
- Direct visualisation and biopsy of cavity with hysteroscopy should be undertaken where hyperplasia has been diagnosed within a polyp or discrete focal lesion.

Endometrial hyperplasia without atypia

- 5% risk of cancer over 20 years
- The majority of cases resolve spontaneously
- Important to address reversible causes
- Treatment with progestagens has higher regression rate than observation alone
- Treat with progestagens if failure to regress with observation alone or if symptomatic for AUB

Management – 1st line

- Continuous oral or local intrauterine progestagens
- LNG-IUS is 1st line treatment, if declined continuous progestagens (medroxyprogesterone 10-20mg/daily or norethisterone 10-15mg/daily
- Avoid cyclical progestagens

Evidence

Meta-analysis of LNG-IUS versus oral progestagens

- Higher regression rates:
  - 3 months – OR 2.3 (95% CI 1.39-3.82)
  - 6 months – OR 3.16
  - 12 months - OR 5.73
  - 24 months - OR 7.46

- Less likely to need a hysterectomy
- No difference in rates of irregular vaginal bleeding

Abu Hashim et al. LNG-IUS vs oral progestins for non-atypical endometrial hyperplasia. AJOG 2015

- Minimum treatment duration = 6 months
- Endometrial surveillance minimum 6 month intervals with at least 2 negative biopsies prior to discharge
- Woman must seek further referral if AUB after treatment
- High risk of relapse if BMI ≥35 or treated with oral progestagens, recommend 6/12 biopsy for 2 years. If 2 negative biopsies, consider long-term follow up with annual biopsies

Management – 2nd line

- Indications for hysterectomy:
  - If disease progresses to atypia
  - If no regression after 12 months of treatment
  - If relapse after completing treatment
  - If persistent bleeding
  - If treatment declined/non-compliant

- If post-menopausal consider BSO
- Preferably laparoscopic approach
- Endometrial ablation is not recommended

Endometrial hyperplasia with atypia - management

- A total hysterectomy is recommended +/- BSO
- Laparoscopic approach is preferable
- No benefit from lymphadenectomy
- Endometrial ablation is not recommended

Evidence: case control study of 794 women with atypical hyperplasia had a risk of developing cancer of 8% in 4 years, 12.4% in 9 years and 27.5% after 19 years. 43% association with concomitant cancer.

Trimble et al. Concurrent endometrial carcinoma in women with a biopsy diagnosis of atypical endometrial hyperplasia. Cancer 2006.

Management – fertility sparing

- Need pre-treatment investigations to rule out invasive cancer or co-existing ovarian cancer (4%) eg. Histology, imaging (TVS, MRI), tumour markers
- Review investigations at MDT and plan on-going surveillance
- 1st line treatment = LNG IUS
- 2nd line = oral progestagens
- Consider hysterectomy once fertility no longer desired
- Routine endometrial surveillance (biopsy) every 3/12 until 2 consecutive negative samples
  - If asymptomatic, long-term follow up with biopsies every 6 -12 months until hysterectomy

Endometrial hyperplasia & fertility

- Need evidence of disease regression with at least 1 negative biopsy before attempting to conceive
- Referral to fertility specialist to discuss options, assessment and treatments
- Consider assisted reproduction
- Prior to treatment, regression of hyperplasia is advised

Endometrial hyperplasia & HRT

- Systemic estrogen only HRT is not recommended in women with a uterus
- Encourage women to report any unscheduled bleeding
- Women with hyperplasia taking sequential HRT should be advised to change to continuous progesterone using LNG IUS combined HRT

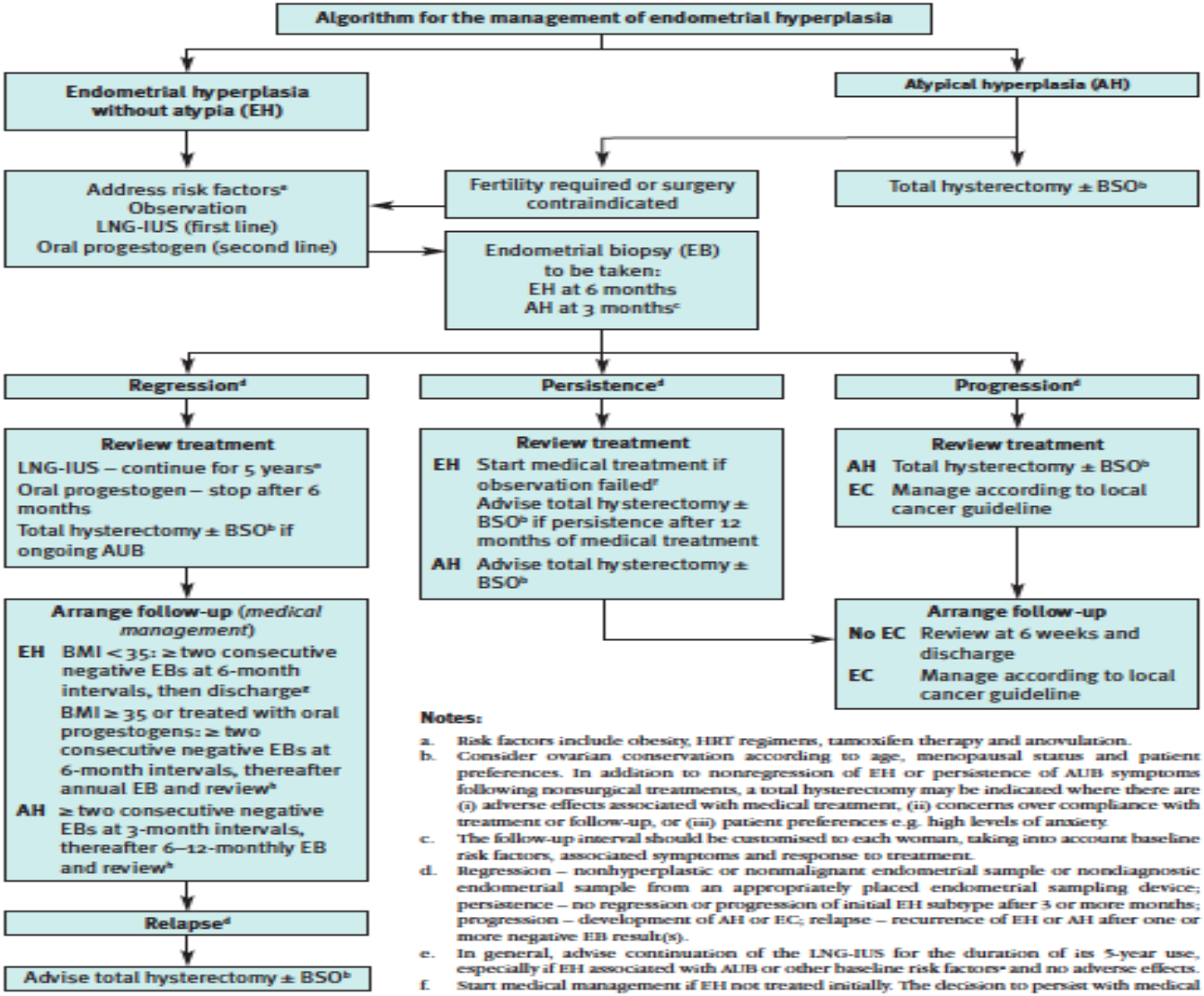
Endometrial hyperplasia & adjuvant treatment for breast cancer

- Inform women taking tamoxifen of increased risk of endometrial hyperplasia and cancer
- Aromatase inhibitors eg. Anastrazole, letrozole are not known to increase the risk of hyperplasia or cancer
- LNG-IUS prevents polyp formation and decreases incidence of hyperplasia in women on tamoxifen
- LNG-IUS effect on breast cancer recurrence is uncertain – not to be recommended
- If develop hyperplasia while on tamoxifen for breast cancer, reassess need for tamoxifen, manage according to histology in conjunction with oncologists

Endometrial hyperplasia & endometrial polyps

- Complete removal of a polyp is recommended with an endometrial biopsy to sample background endometrium

- Subsequent management is according to histological classification



Notes:

a. Risk factors include obesity, HRT regimens, tamoxifen therapy and anovulation.
b. Consider ovarian conservation according to age, menopausal status and patient preferences. In addition to nonregression of EH or persistence of AUB symptoms following nonsurgical treatments, a total hysterectomy may be indicated where there are (i) adverse effects associated with medical treatment, (ii) concerns over compliance with treatment or follow-up, or (iii) patient preferences e.g. high levels of anxiety.
c. The follow-up interval should be customised to each woman, taking into account baseline risk factors, associated symptoms and response to treatment.
d. Regression – nonhyperplastic or nonmalignant endometrial sample or nondiagnostic endometrial sample from an appropriately placed endometrial sampling device; persistence – no regression or progression of initial EH subtype after 3 or more months; progression – development of AH or EC; relapse – recurrence of EH or AH after one or more negative EB result(s).
e. In general, advise continuation of the LNG-IUS for the duration of its 5-year use, especially if EH associated with AUB or other baseline risk factors[a] and no adverse effects.
f. Start medical management if EH not treated initially. The decision to persist with medical management should be taken after careful consideration and thorough discussion with

Any questions?