

View this article online at: patient.info/doctor/endometrial-hyperplasia-pro

Endometrial Hyperplasia

Definition

Endometrial hyperplasia is an abnormal proliferation of the endometrium (ie greater than the normal proliferation that occurs during the menstrual cycle). It is a risk factor for the development of endometrial carcinoma.

Pathogenesis^[1]

The 2014 World Health Organization (WHO) classification divides endometrial hyperplasia into two types on the basis of presence or absence of cytological change:

- Hyperplasia without atypia
- Atypical hyperplasia

Atypical hyperplasia is considered a pre-malignant condition. Management is therefore dependent upon the presence of cellular atypia. Histological examination of endometrial tissue is mandatory for diagnostic classification.

For hyperplasia without atypia, the risk of progression to carcinoma is less than 5% over 20 years. The risk in atypical hyperplasia is 28% over the same time period^[2]. Statistics vary, which may be due to the poor diagnostic reproducibility^[3].

Risk factors

Endometrial hyperplasia is caused by oestrogen, which when unopposed by progesterone, stimulates endometrial cell growth by binding to oestrogen receptors in the nuclei of endometrial cells. Most established risk factors are therefore those which cause raised oestrogen levels.

- Obesity (androgens are converted to oestrogen within adipose tissue).
- Exogenous oestrogen use (without cyclical progesterone)^[4].
- Oestrogen-secreting ovarian tumour. (Up to 40% of those with granulosa cell tumours have endometrial hyperplasia.)
- Tamoxifen use; it has an anti-oestrogen effect on the breast but a pro-oestrogen effect on the uterus and bones.
- Polycystic ovarian syndrome (due to anovulation).
- Nulliparity.
- Hereditary non-polyposis colorectal carcinoma.
- Diabetes.

NB: use of combined oral contraceptive decreases risk^[5].

Presentation

Endometrial hyperplasia usually presents clinically as abnormal vaginal bleeding - intermenstrual bleeding, irregular bleeding, menorrhagia or postmenopausal bleeding. There may be vaginal discharge.

Investigations^[1]

Endometrial biopsy

A definitive diagnosis of endometrial hyperplasia, and which type, is made by histology.

Historically, endometrial samples have been obtained by dilatation and curettage under general anaesthesia (GA). Nowadays it is more usual to obtain a sample by outpatient endometrial sampling, most commonly a pipelle biopsy. Occasionally this has to be performed under GA. All methods of sampling the endometrium will miss some hyperplasia and some cancers.

Hysteroscopy

Hysteroscopy and biopsy (curettage) should be considered as a more accurate method of diagnosis, and is the preferred diagnostic technique to detect polyps and other benign lesions. Where endometrial hyperplasia has been found within a polyp or other focal lesion, biopsy with direct visualisation by hysteroscopy is essential. Hysteroscopy may be performed as an outpatient procedure, although some women will require GA.

Transvaginal ultrasound

Ultrasound may be useful in both pre-menopausal and postmenopausal women in assessing abnormal vaginal bleeding, although if clinical suspicion is high, histological examination should take place regardless of the results.

- In postmenopausal women, the endometrial thickness may be used as a guide to help establish which women should have a biopsy and/or hysteroscopy. A cut off of 3-4 mm for endometrial thickness is usually advised; where the endometrium measures more than this, further investigation is required^[6].
- In pre-menopausal women, the thickness is less helpful due to cyclical change and the overlap between normal proliferative endometrium and hyperplasia. Ultrasound may be used to identify structural abnormalities such as polyps, and endometrial thickness below 7 mm is unlikely to represent hyperplasia.

Suspected cancer guidelines from the National Institute for Health and Care Excellence (NICE) advise referral under the two-week wait system for women over the age of 55 years with postmenopausal bleeding^[7].

Management^[1]

Management of hyperplasia without atypia

- **Reassurance:** explain to women that the risk of progression to cancer is less than 5% over 20 years and that most of this type of hyperplasia will return to normal either with or without treatment.
- **Address any risk factors:** help with obesity where this is an issue, and review hormonal medication which may be contributing.
- **Watchful waiting:** may be an option in asymptomatic women. Follow-up biopsies are required; women should be advised that regression is more likely with active treatment.
- **Progestogen treatment:** this is the usual management. The levonorgestrel intrauterine system (IUS) is the first-line option, as it is more effective in inducing regression and is associated with fewer adverse effects^[8]. The second-line option is continuous oral progestogen treatment, in the form of medroxyprogesterone (10-20 mg per day) or norethisterone (10-15 mg per day). Treatment with either is used for at least six months, although ideally the IUS should be left in situ for the full five years.
- **Follow-up:** endometrial biopsies are required six-monthly until two consecutive biopsies have been negative. Annual biopsy thereafter should be considered in women at higher risk (eg, BMI ≥ 35), and women should be educated to report any further bleeding as relapse may have occurred.
- **Hysterectomy:** this is not normally indicated but may be used where:
 - Regression has not occurred despite a year of progestogen treatment.
 - There is change to atypical hyperplasia.
 - There is relapse after treatment.
 - The woman wishes to have surgery rather than long-term medical treatment and regular biopsy.

Women on hormone replacement therapy (HRT) with endometrial hyperplasia should be advised to use the IUS as the progestogen, rather than a sequential HRT.

Women on tamoxifen are at higher risk of endometrial hyperplasia. The IUS reduces the risk of hyperplasia; however, the balance of risks and benefits has not yet been established so this is not routinely recommended^[9].

Management of atypical hyperplasia

Total hysterectomy is advisable for all women, due to the risk of malignant progression, with bilateral salpingo-oophorectomy in addition for postmenopausal women. A laparoscopic approach is preferable. For women who wish to preserve fertility, progestogen options may be used as above, with regular monitoring by three-monthly endometrial biopsy, and advice to have a hysterectomy as soon as potential fertility is no longer required. A 2013 Cochrane review concluded there is not yet the evidence of safety and efficacy for the routine use of IUS to be convincing in women with atypical hyperplasia^[10].

Women who wish to conceive should be advised to wait until regression on medical treatment has occurred (at least one negative biopsy). Referral to a fertility specialist is advisable, and assisted conception may be considered.

Complications

Recurrence after treatment may occur. Endometrial hyperplasia may develop into endometrial carcinoma. Women who don't have atypical changes have a very small risk of developing a cancer. As many as 30-40% of women diagnosed with atypical hyperplasia are found to have a concurrent carcinoma^[11]. The rest with atypical changes are at significant risk as above. Risk increases after menopause.

Further reading & references

- **Clement NS, Oliver TR, Shiwani H, et al**; Metformin for endometrial hyperplasia: a Cochrane protocol. *BMJ Open*. 2016 Aug 16;6(8):e013385. doi: 10.1136/bmjopen-2016-013385.
- 1. **Management of Endometrial Hyperplasia**; RCOG/BSGE Joint Guideline (2016)
- 2. **Lacey JV Jr, Sherman ME, Rush BB, et al**; Absolute risk of endometrial carcinoma during 20-year follow-up among women with endometrial hyperplasia. *J Clin Oncol*. 2010 Feb 10;28(5):788-92. doi: 10.1200/JCO.2009.24.1315. Epub 2010 Jan 11.
- 3. **Lacey JV Jr, Chia VM**; Endometrial hyperplasia and the risk of progression to carcinoma. *Maturitas*. 2009 May 20;63(1):39-44. doi: 10.1016/j.maturitas.2009.02.005. Epub 2009 Mar 13.
- 4. **Furness S, Roberts H, Marjoribanks J, et al**; Hormone therapy in postmenopausal women and risk of endometrial hyperplasia. *Cochrane Database Syst Rev*. 2012 Aug 15;(8):CD000402. doi: 10.1002/14651858.CD000402.pub4.
- 5. **Schindler AE**; Non-contraceptive benefits of oral hormonal contraceptives. *Int J Endocrinol Metab*. 2013 Winter;11(1):41-7. doi: 10.5812/ijem.4158. Epub 2012 Dec 21.
- 6. **Timmermans A, Opmeer BC, Khan KS, et al**; Endometrial thickness measurement for detecting endometrial cancer in women with postmenopausal bleeding: a systematic review and meta-analysis. *Obstet Gynecol*. 2010 Jul;116(1):160-7.
- 7. **Suspected cancer: recognition and referral**; NICE Clinical Guideline (2015)
- 8. **Abu Hashim H, Ghayaty E, El Rakhawy M**; Levonorgestrel-releasing intrauterine system vs oral progestins for non-atypical endometrial hyperplasia: a systematic review and metaanalysis of randomized trials. *Am J Obstet Gynecol*. 2015 Oct;213(4):469-78. doi: 10.1016/j.ajog.2015.03.037. Epub 2015 Mar 19.
- 9. **Dominick S, Hickey M, Chin J, et al**; Levonorgestrel intrauterine system for endometrial protection in women with breast cancer on adjuvant tamoxifen. *Cochrane Database Syst Rev*. 2015 Dec 9;(12):CD007245. doi: 10.1002/14651858.CD007245.pub3.
- 10. **Luo L, Luo B, Zheng Y, et al**; Levonorgestrel-releasing intrauterine system for atypical endometrial hyperplasia. *Cochrane Database Syst Rev*. 2013 Jun 5;6:CD009458. doi: 10.1002/14651858.CD009458.pub2.
- 11. **Saso S, Chatterjee J, Georgiou E, et al**; Endometrial cancer. *BMJ*. 2011 Jul 6;343:d3954. doi: 10.1136/bmj.d3954.

Disclaimer: This article is for information only and should not be used for the diagnosis or treatment of medical conditions. Patient Platform Limited has used all reasonable care in compiling the information but makes no warranty as to its accuracy. Consult a doctor or other healthcare professional for diagnosis and treatment of medical conditions. For details see our [conditions](#).

| | | |
|-----------------------------------|-------------------------------------|--------------------------------------|
| Original Author: Dr Colin Tidy | Current Version: Dr Mary Harding | Peer Reviewer: Miss Shalini Patni |
| Document ID: 2096 (v23) | Last Checked: 22/03/2017 | Next Review: 21/03/2022 |

View this article online at: patient.info/doctor/endometrial-hyperplasia-pro

Discuss Endometrial Hyperplasia and find more trusted resources at [Patient](https://patient.info).

© Patient Platform Limited - All rights reserved.