MALIGNANCY IN THE ENDOMETRIAL POLYPS

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- Endometrial polyps are one of the most common etiologies of abnormal uterine bleeding (AUB) in both premenopausal and postmenopausal women.

- *Obstet Gynecol 2010;116(5)*

- **Endometrial polyps are common pathologic findings in gynecologic pathology and their prevalence range is between 16% to 34% depending on characteristics of the population studied and detecting methods.**

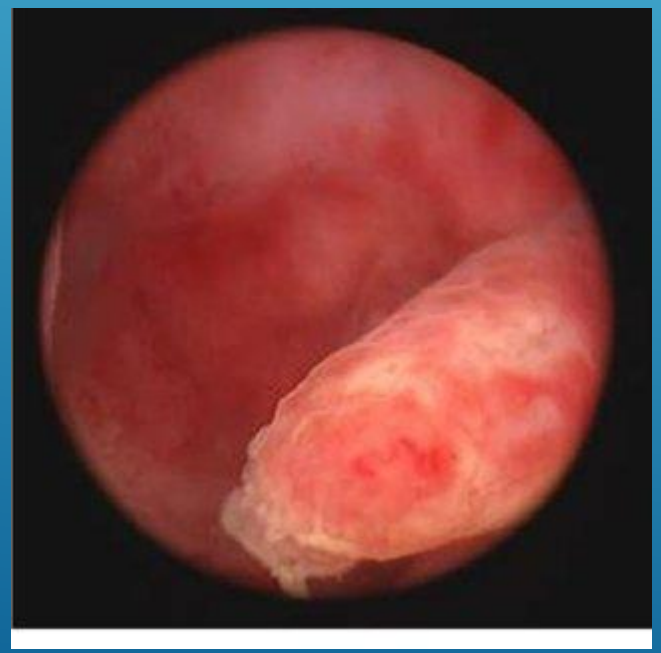
- ***Int J Gynecol Pathol. 2009;28(6):522–8.***

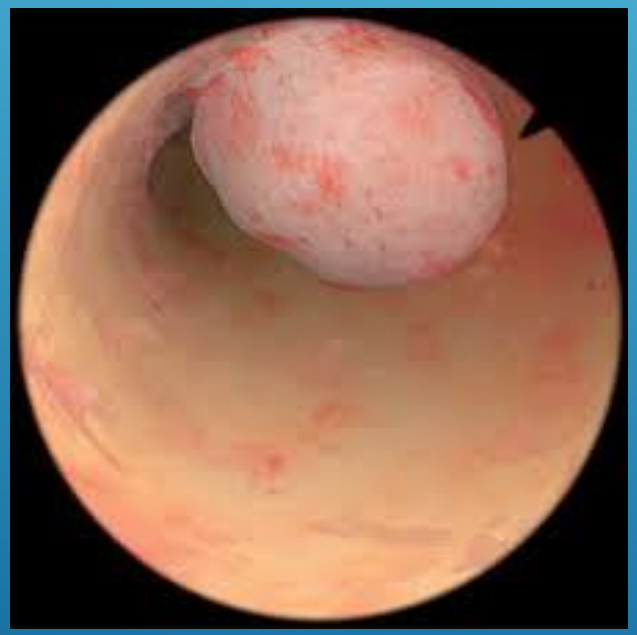
- The exact prevalence of endometrial polyps is not known, however, Dreisler et al. reported 82% of the women who had histopathology verified polyps were asymptomatic. Nevertheless, endometrial polyps have been implicated **in about 50% of cases of abnormal uterine bleeding and 35% of infertility.**

- Hysteroscopy is widely used because of its ability to detect endometrial polyps with a specificity of 93% and sensitivity of 90%.

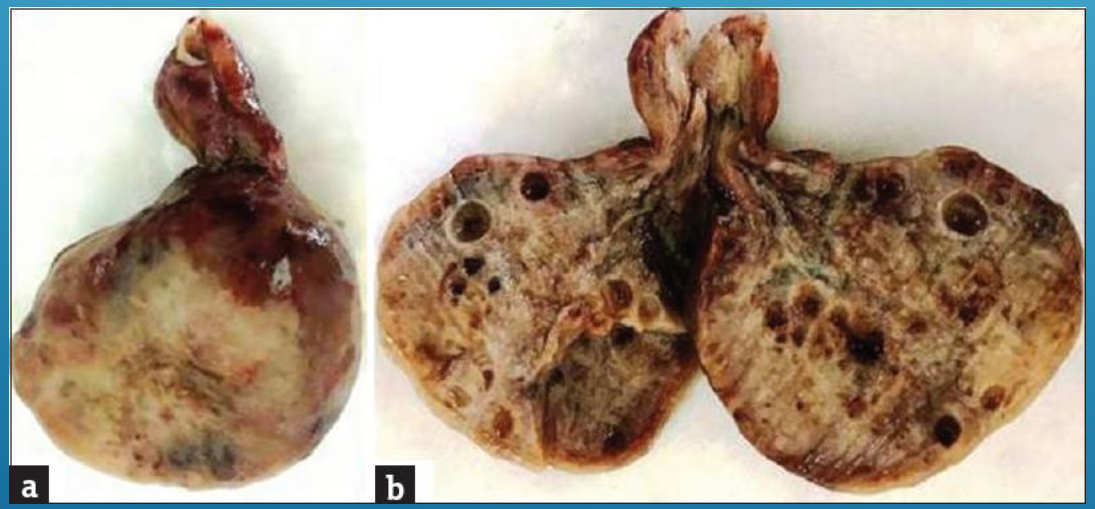
- *Arch Gynecol Obstet 2015;291(6):1347e54.*
- *Minim Invasive Gynecol 2011;18(5):569e81.*

- Endometrial polyps are benign, localized overgrowth of endometrial glands and stroma that are covered by epithelium and project above the adjacent surface epithelium.

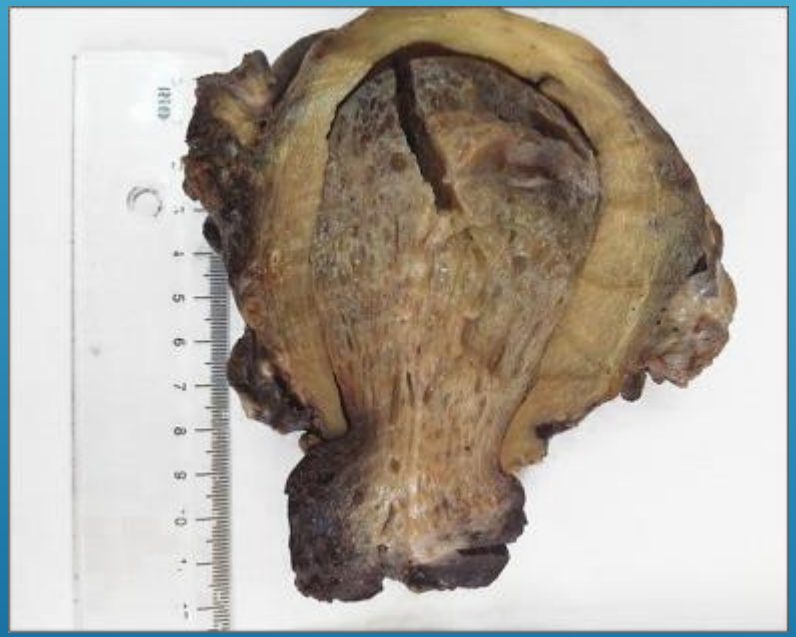


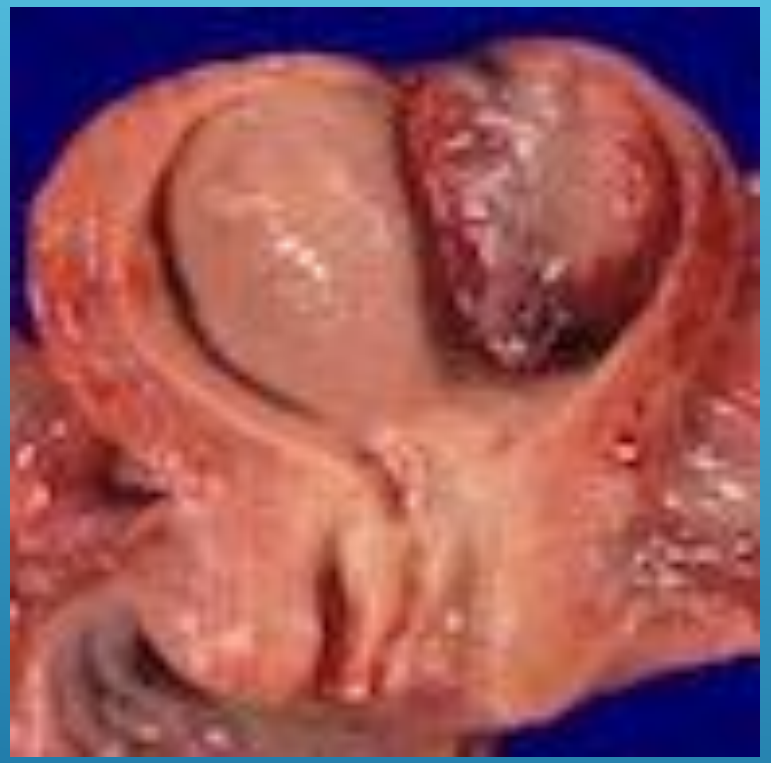


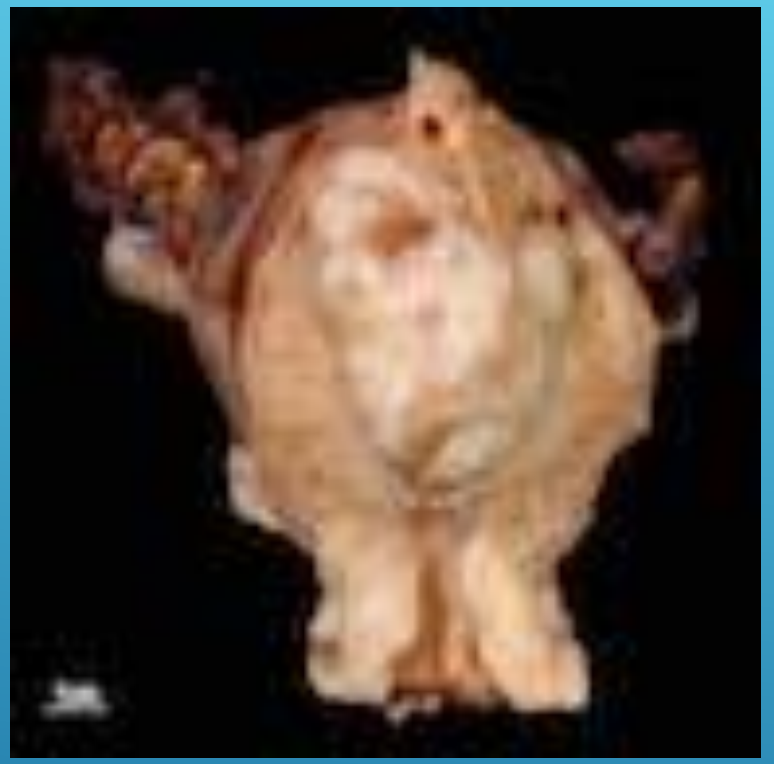
- Polyps are common in women over 40 years of age and extremely rare before menarche.
- In addition to common clinical findings(intermenstrual bleeding, menometrorrhagia and postmenopausal bleeding), a polyp should be considered if abnormal bleeding persists after curettage because polyps that contain a delicate, pliable stalk may elude the curettage.



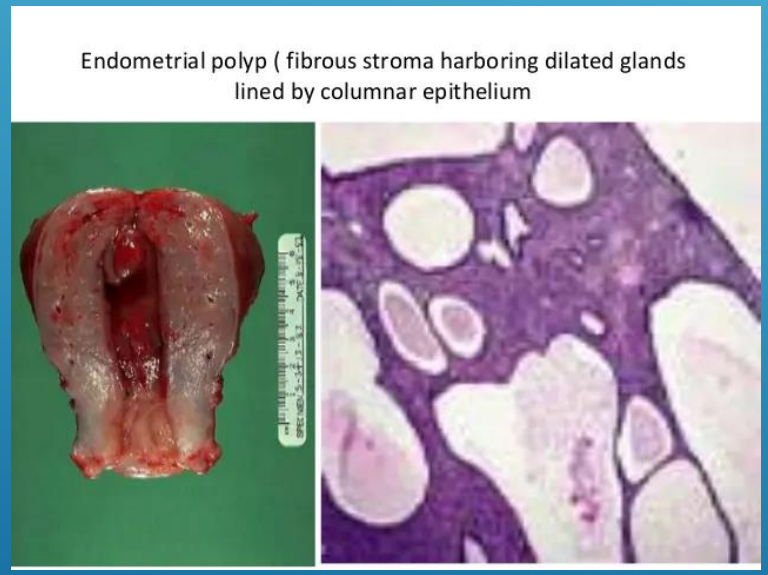
- A polyp may entirely fill and distends the endometrial cavity.

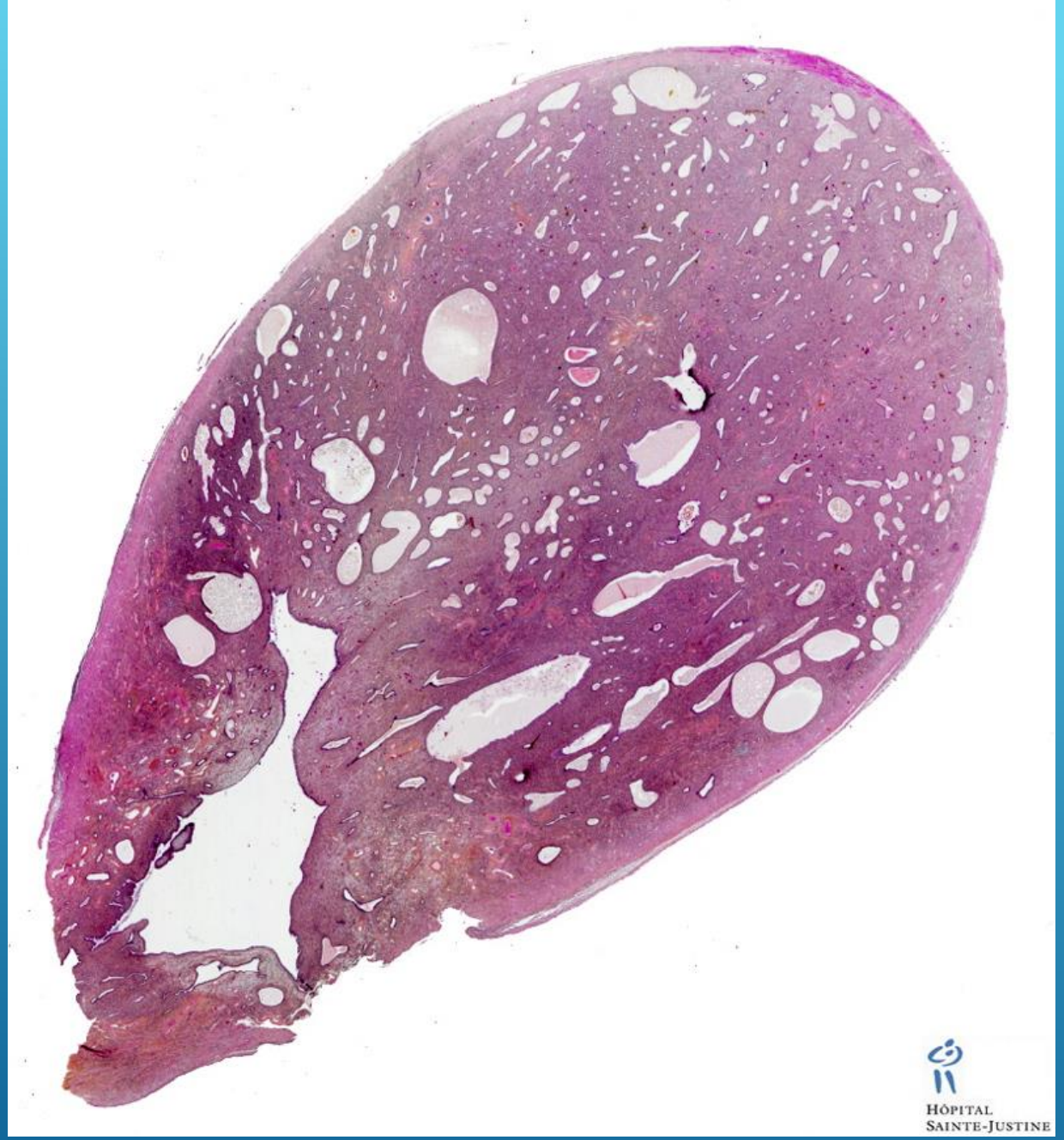






- The majority of polyps are located in the fundus, often in the corneal area, and in this area there are obvious technical difficulties for removal by curettage.

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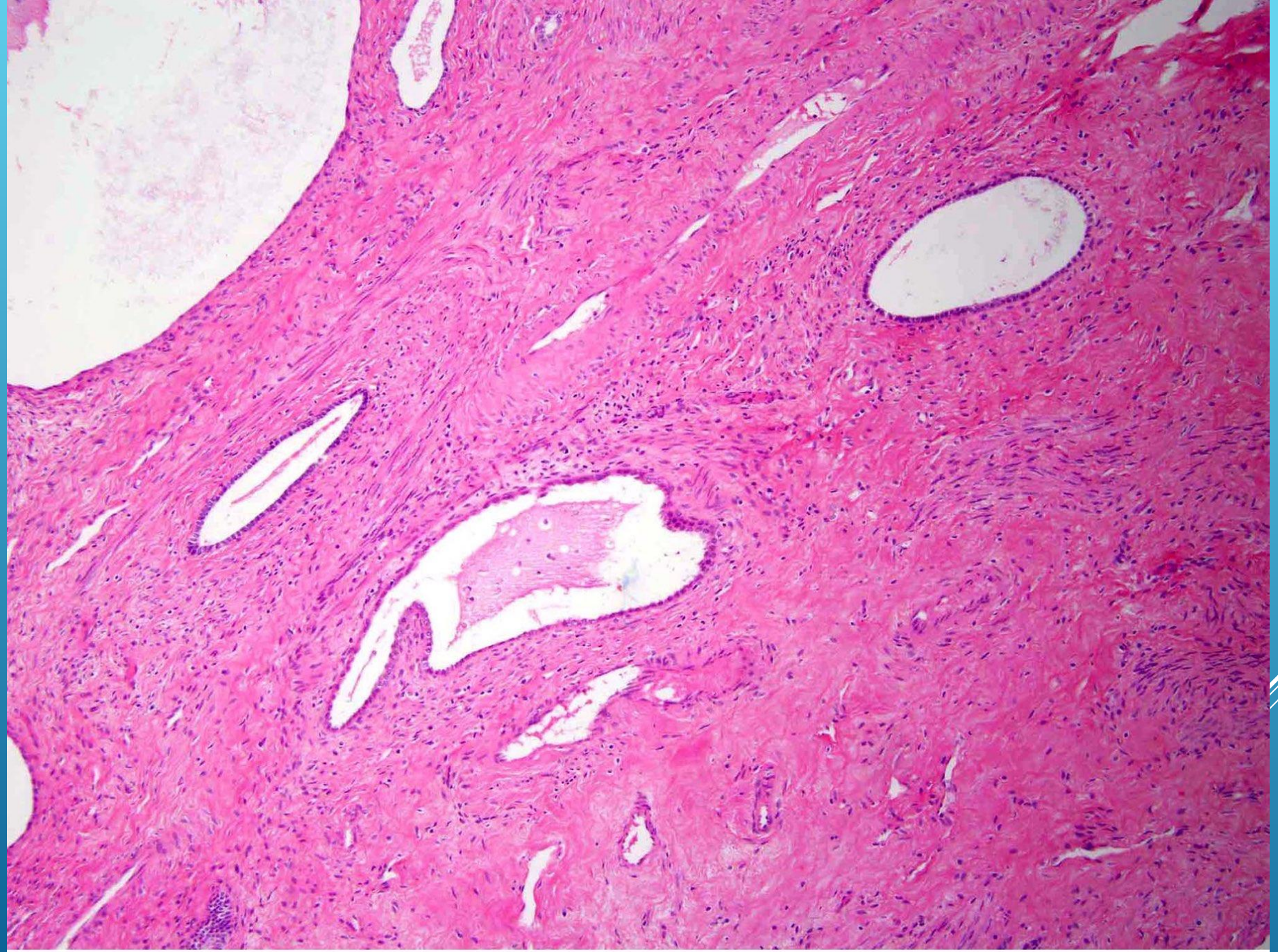
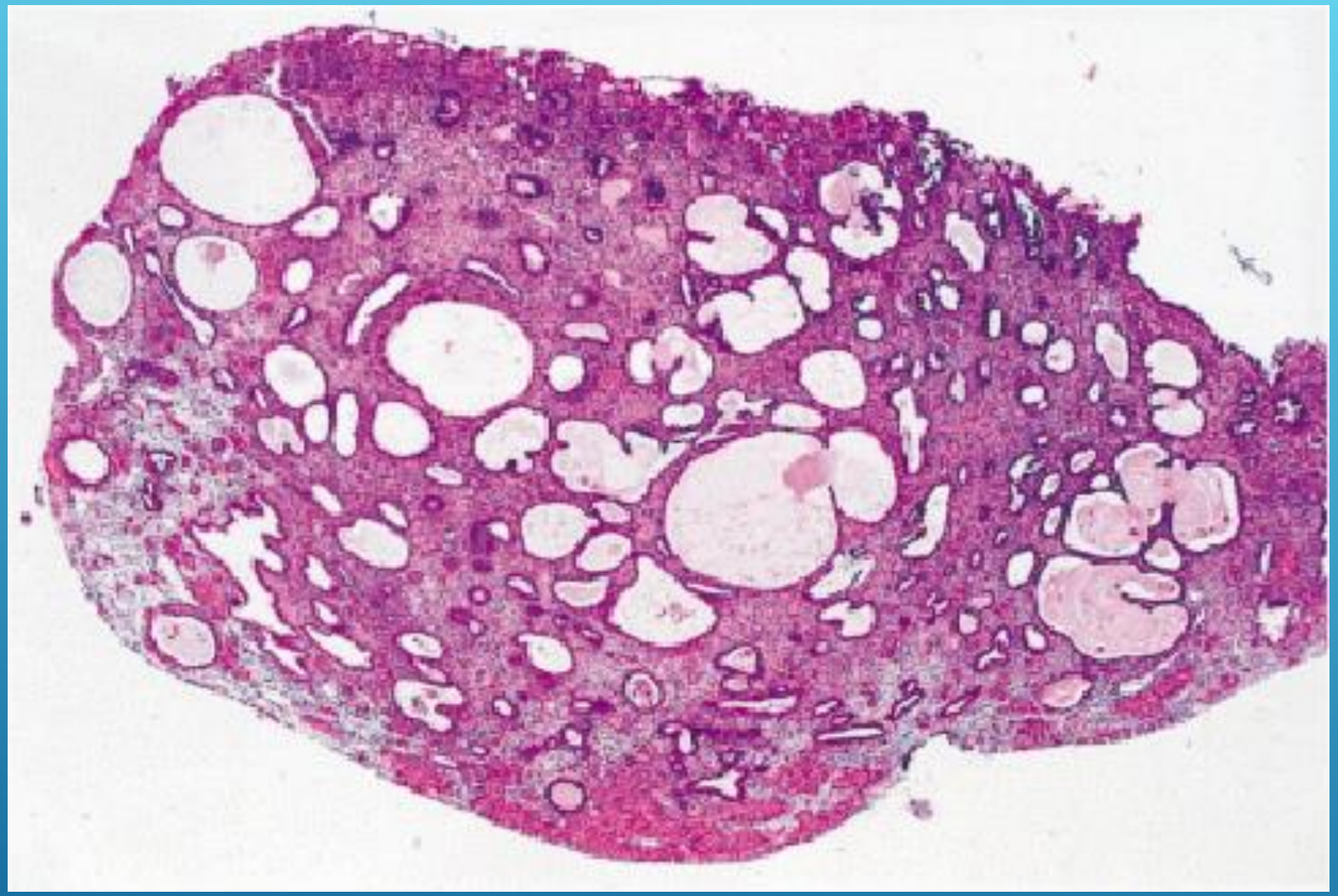


Low power image of endometrial polyp with cystically dilated glands lined



- It in not necessary to report simple hyperplastic change inside the endometrial polyps, howerever complex hyperplasia and Endometriod Intraepithelial Neoplasia-EIN should be reported because theses change may be seen in the non-polypoid endometrium in a significant proportion of the cases.

AETIOLOGY AND PATHOGENESIS

- The pathogenesis and natural history of endometrial polyps are not very clear and exact cause of endometrial polyps is unknown, however, there are several theories proposed relating to the aetiology and pathogenesis of these lesions.

- 1. They are believed to be related to oestrogen stimulation, this may be as a result of an increased concentration of oestrogen receptors (ERs), predominantly ER-alpha in polyp glandular cells compared with normal endometrium, and a decreased expression of progesterone receptors (PRs) A and B in polyps compared with normal endometrium.

- 2. The role of B-cell lymphoma-2 (Bcl-2) marker, which is an inhibitor of apoptosis, and Ki67 protein, which is a cellular marker for proliferation and cell mitotic activity, has been reported.

- Miranda et al. reported that the expression of Ki-67 were significantly higher in the polyp samples from tamoxifen-treated women compared with those samples from women using no hormone.

- Cytogenetic studies have suggested that chromosomal abnormalities may have a role in the development of endometrial polyps. Endometrial polyps arise as a result of chromosomal rearrangements (translocation) in the stromal cells.

- **Endometrial polyp formation may be the result of localized chronic inflammation in the endometrium.** Mast cells and are known to initiate and control inflammation through their secretion of cytokines and growth factors.[32] Cyclooxygenase-2 (COX-2), a key enzyme involved in the production of prostaglandin in mast cells, was also found to be significantly higher in polyps compared with normal endometrium.[33] Inflammation results in the formation of new blood vessels and growth of tissue.

RISK FACTORS

- The risk factors for endometrial polyp formation include **increased endogenous oestrogen and exogenous oestrogen** administration. **Tamoxifen** (a uterine oestrogen agonist used to treat breast cancer in pre- and postmenopausal women) **have an increased likelihood of developing endometrial polyp.**

- Polyps are the most common endometrial lesion associated with tamoxifen therapy, being present in as many as **30% of these patients.**

- **Tamoxifen induced polyps** tend to be **larger and multiple**. In addition these polyps **may recur after resection**.

- Similarly, **postmenopausal women on hormone replacement therapy (HRT)** have been found to have a higher incidence of endometrial polyps.

MALIGNANCY IN THE ENDOMETRIAL POLYPS

- Overall the prevalence of malignant and premalignant lesions found in the endometrial polyps ranges from 0.8% to 4.8%.

- *Am J Obstet Gynecol. 2003;188(4):927–31*

- In a 12-year experience including 1242 cases, histological diagnosis identified **95.2% of the polyps as benign**, and the remaining 4.8% as either **premalignant (1.3%)** or **malignant (3.5%**) lesions confined to the polyp. Univariate analysis identified ***older age, menopausal status, presence of abnormal uterine bleeding, and hypertension as significant factors*** associated with premalignancy or malignancy of Eps.

- **Obstetrical & Gynecological Survey: February 2010 - Volume 65 - Issue 2 - p 96-97**

- At multivariate analysis, polyp's diameter was the only variable significantly associated to an abnormal histology (cancer, polypoid cancer, and atypical hyperplasia) in asymptomatic women.

- Am J Obstet Gynecol. 2009;200(3):235.

- Although the majority of endometrial polyps are benign, they can be associated with premalignant or malignant entities including endometrial hyperplasia and carcinoma. Polyps are detected in pre and postmenopausal women and can be asymptomatic or present with symptoms such as abnormal uterine bleeding. **Postmenopausal status, Tamoxifen induced polyps and abnormal bleeding are significant predictors of malignancy** associated with polyps and thus indications for excision.

- The most common subtypes of endometrial malignancy which have been reported in endometrial polyps are “Endometriod carcinoma”, “Clear cell carcinoma” and “serous carcinoma”.

- Maturitas. 2007;57(4):415–21
- Am J Obstet Gynecol. 2009;200(3):235.
- Hum Pathol. 2005;36(12):1316–21.

- Various frequencies of the association of hyperplasia without atypia, atypical hyperplasia and carcinoma with endometrial polyps have been reported in the literature, ranging from 11.4–25.7%, 1.1–12% and 0.8% to 3.5% respectively.

- Ann Diagn Pathol. 2016 Aug;23:29-31

- In a systematic review and meta-analysis performed on total of 51 studies in which reporting data on 35,345 women were included , the prevalence of malignant polyps was 2.73% (95% CI 2.57-2.91) with very high heterogeneity among studies and symptomatic vaginal bleeding and postmenopausal status in women with endometrial polyps increased the risk of malignancy.

- Eur J Obstet Gynecol Reprod Biol. 2019 Jun;237:48-56

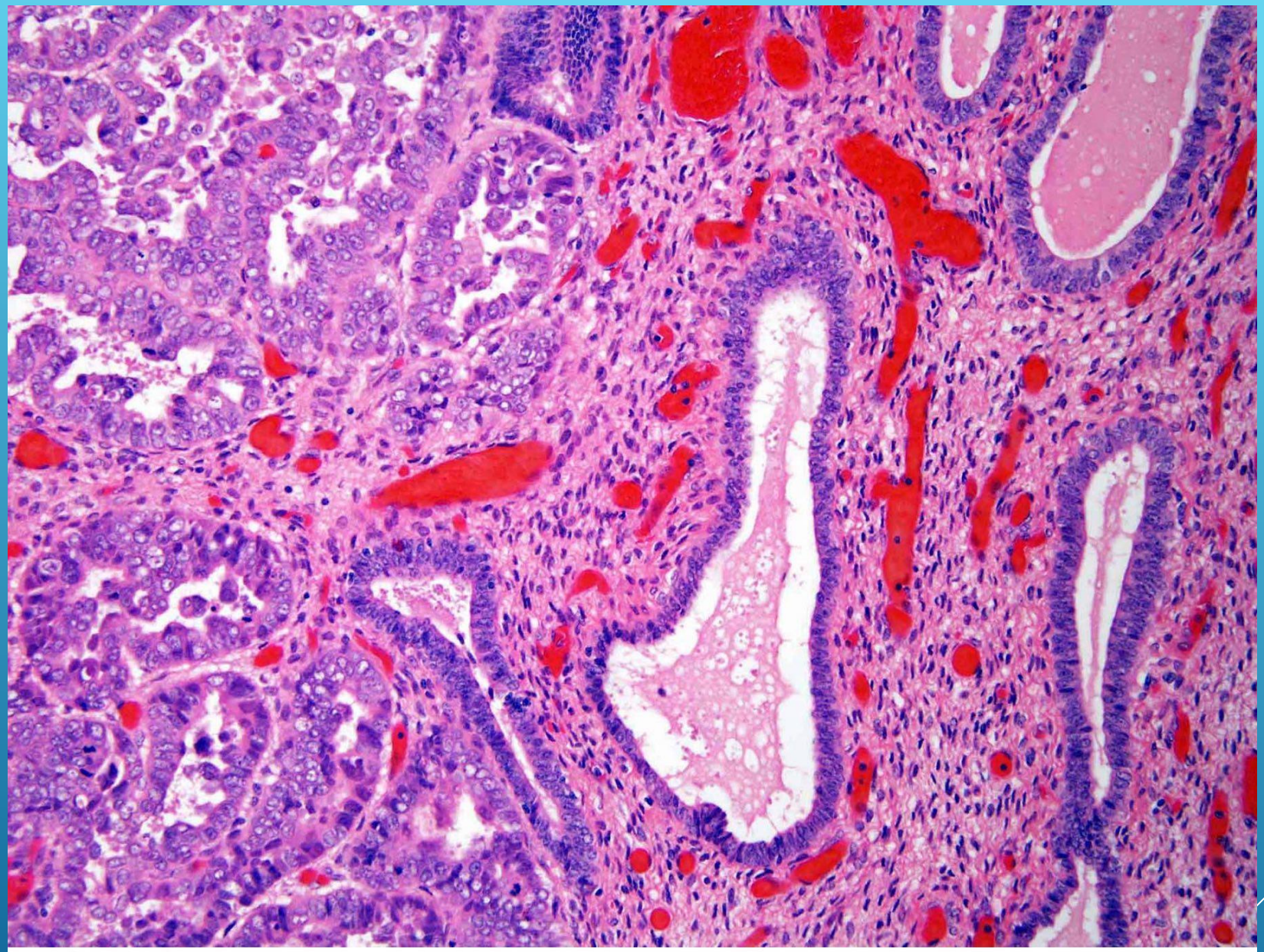
- In another study the prevalence of premalignant and malignant lesions was 3.4% **Abnormal uterine bleeding**, **menopausal status**, age >60 years. diabetes mellitus , systemic arterial hypertension , obesity and **tamoxifen use** were associated with endometrial polyp malignancy.

- J Minim Invasive Gynecol. Jul-Aug 2018;25(5):777-785

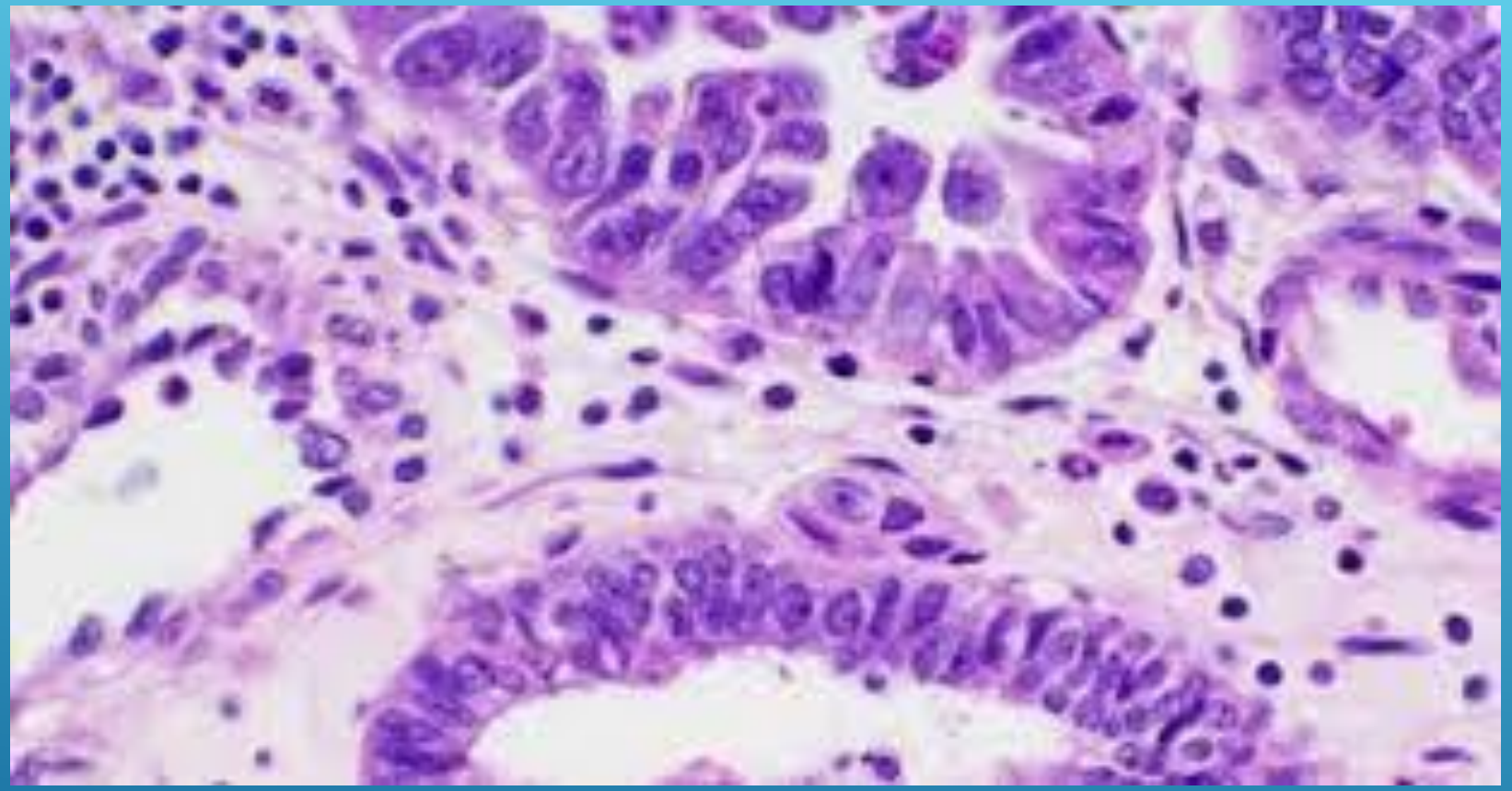
- **Metastatic breast lobular carcinoma involving tamoxifen-associated endometrial polyps: report of two cases and review of tamoxifen-associated polypoid uterine lesions.**

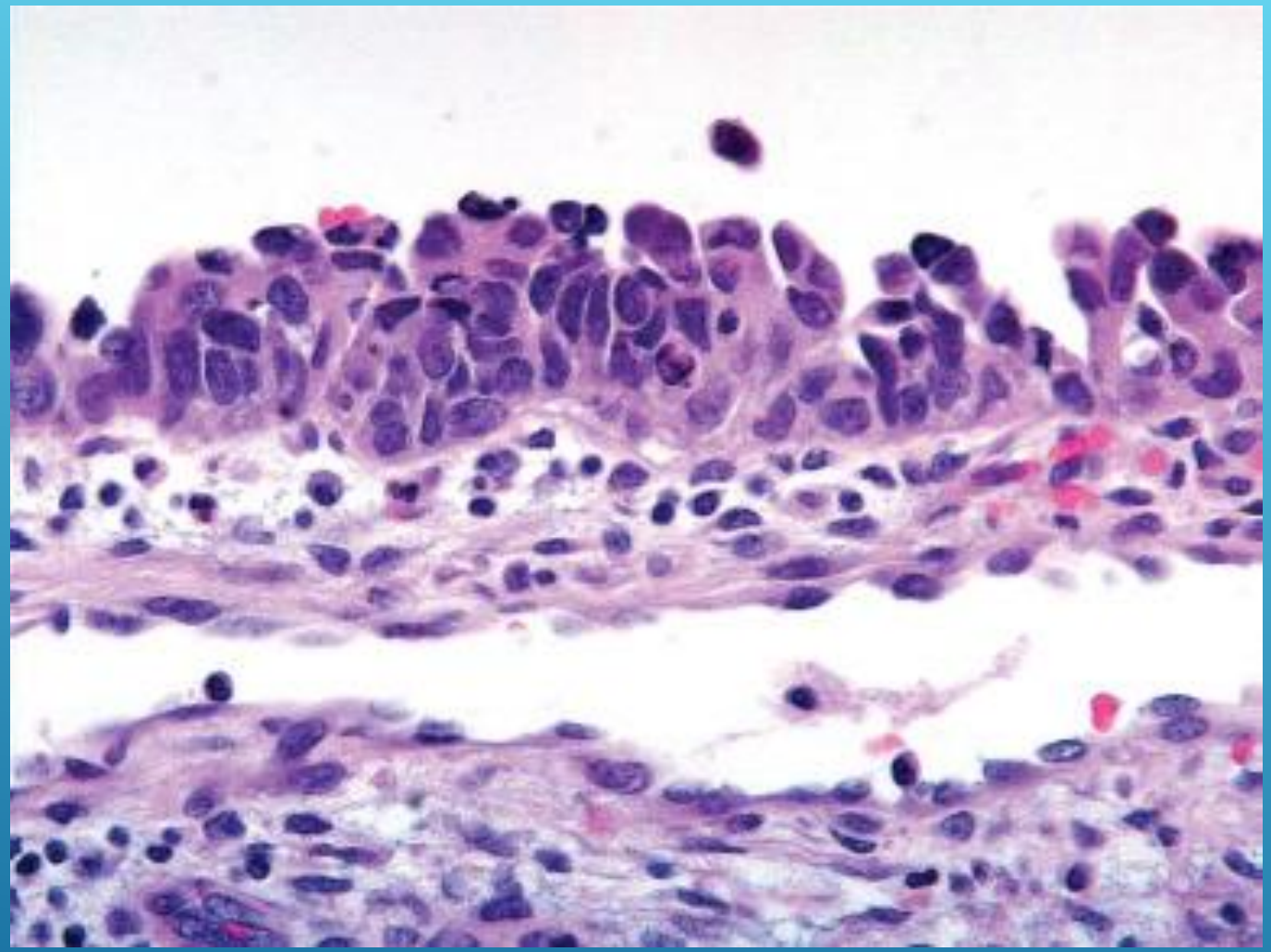
- **Mod Pathol. 2003 Apr;16(4):395-8**

- The most important issue in this context is that these metastatic lesions **(metastatic lobular breast carcinoma)** can be **missed easily in the endometrial polyps.**



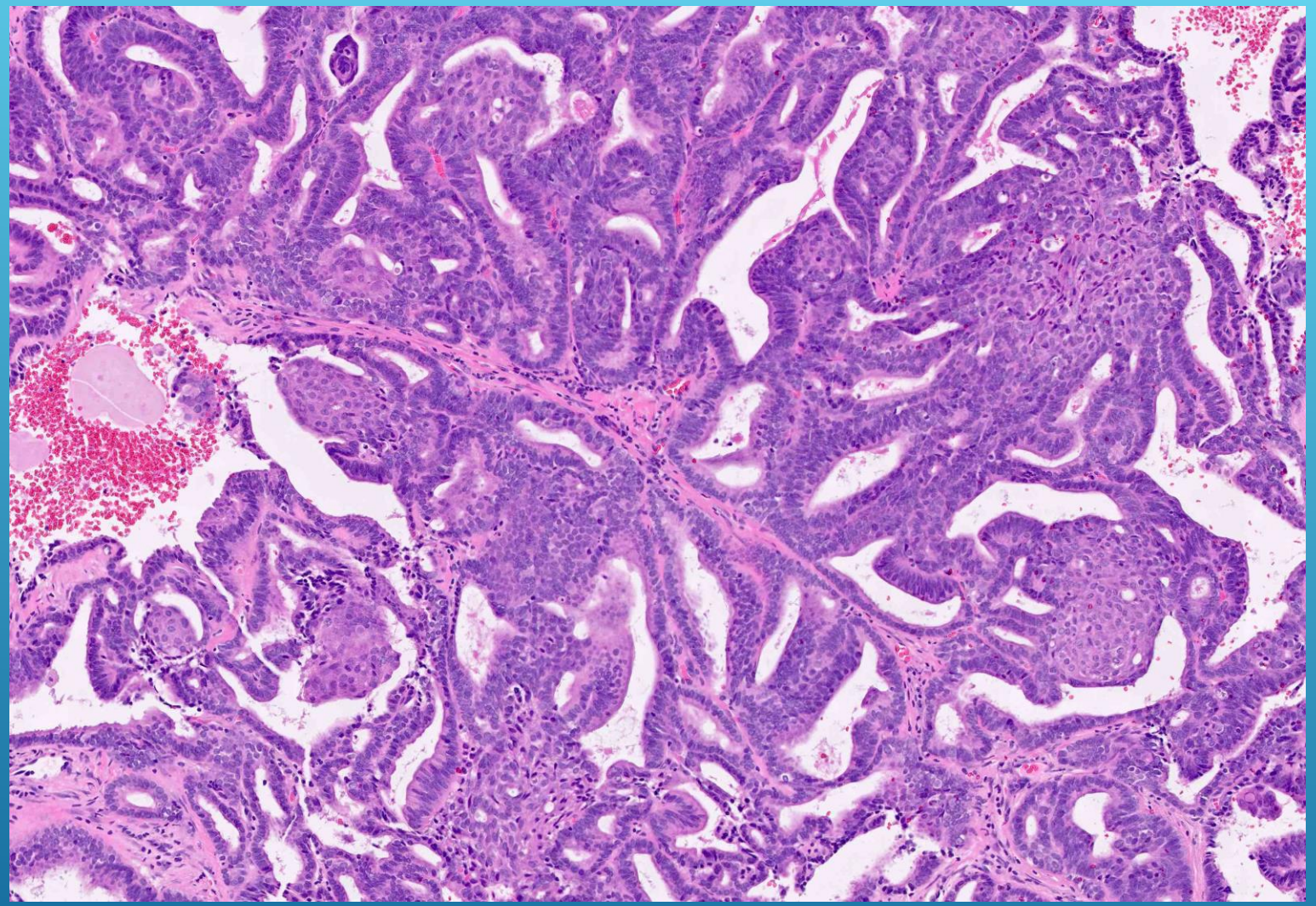
High grade serous carcinoma arising in an endometrial polyp in a postmenopausal female, H&E, 200x

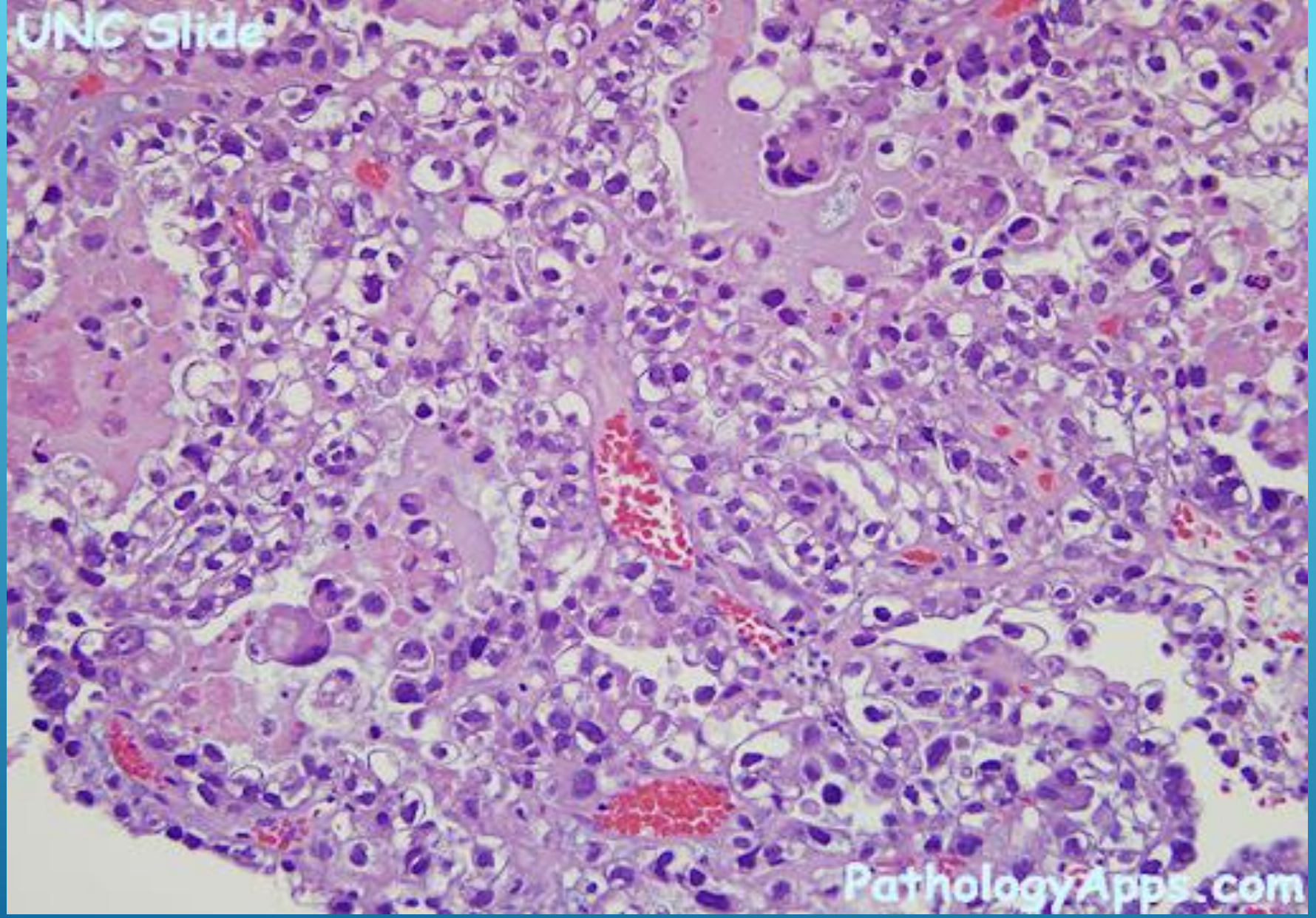




EIN (ENDOMETRIOD INTRAEPITHELIAL NEOPLASIA)

EIC (ENDOMETRIAL INTRAEPITHELIAL CARCINOMA)

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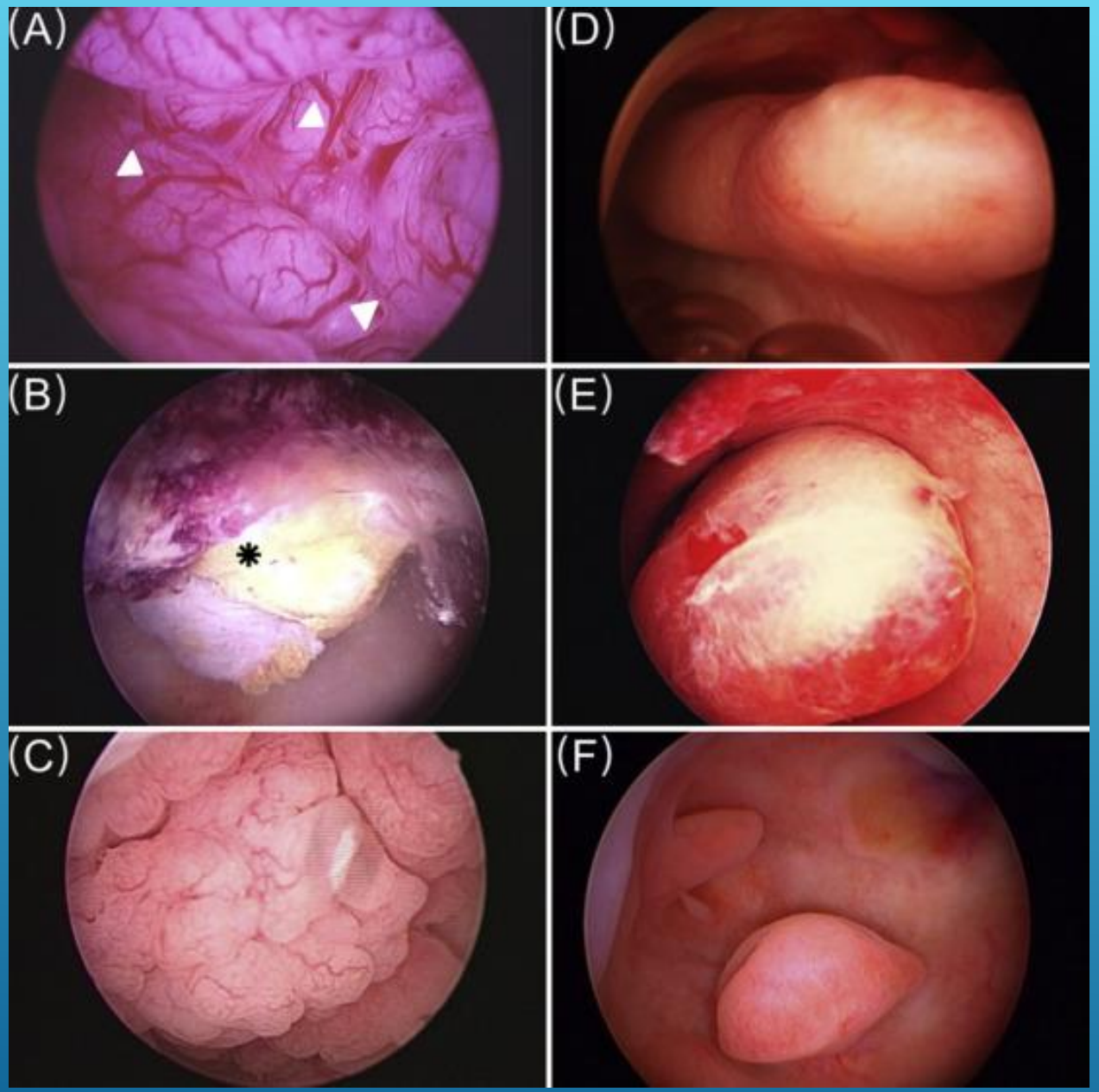
- **Prediction of Premalignant and Malignant Endometrial Polyps by Clinical and Hysteroscopic Features**
- Five hundred fifty-six women were included in the study. Their mean age was 55.4 ± 12.4 years, and 322 (57.9%) were menopausal. Endometrial carcinoma was found in 26 (4.7%) cases, whereas endometrial hyperplasia was found in 5 (0.9%) cases. **Endometrial carcinoma or hyperplasia** was significantly associated with **patients' age**, **menopausal status**, **increased polyp vascularity on hysteroscopy**, **and the presence of 3 or more polyps on hysteroscopy** (p <.01 for all comparisons)..

- J Mininm invasive Gynecol.Nov-Dec 2019;26(7):1311-1315.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- When an endometrial polyp(S) showing involvement by serous carcinoma, some studies suggest that serous carcinoma involving endometrial polyps may represent one aspect of a multicentric disease. In such multicentricity, the entire female genital tract and the abdominal peritoneal surfaces would be at high risk for concurrent or subsequent involvement by serous carcinoma even in the absence of myometrial or lymphovascular invasion.

- Mod Pathol. 1990 Mar;3(2):120-8

- **Endometrial hyperplasia and carcinoma in endometrial polyps: clinicopathologic and follow-up findings**
- **Approximately two thirds of the patients with atypical hyperplasia and 90% of patients with adenocarcinoma in endometrial polyps show endometrial pathology on subsequent hysterectomy. The above findings reinforce the need for hysterectomy especially in postmenopausal women with atypical complex hyperplasia or carcinoma in endometrial polyps even if these changes appear confined to the polyp in initial sampling.**

- Int J Gynecol Pathol. 2008 Jan;27(1):45-8.

TAMOXIFEN AND ENDOMETRIAL PATHOLOGY

- In 1993, Cohen and colleagues described the endometrial changes in postmenopausal women treated with tamoxifen for breast cancer. These included endometrial hyperplasia, polyps, and cancer. A year later, Van Leeuwen and co-workers reported that women who had used tamoxifen for more than two years had a 2.3 times greater risk of endometrial cancer than those who had never used tamoxifen. **The risk increased with the duration of use and the cumulative dose**.

- For asymptomatic women, the risk of developing endometrial cancer is 1.7 per 1,000 women years, and this is increased two- to threefold by tamoxifen therapy. Despite this fact, the benefit of tamoxifen in the treatment of breast cancer is irrefutable.

- Factors associated with endometrial pathology during tamoxifen therapy in women with breast cancer: a retrospective analysis of 821 biopsies
- Parity, endometrial thickness, and the presence of abnormal vaginal bleeding, but not age, body mass index, and menopausal status, may be associated with endometrial pathology during tamoxifen use in women with breast cancer. This finding might provide useful information for gynecological surveillance and counseling during tamoxifen treatment.

- Tamoxifen is a synthetic non-steroid anti-estrogen that has been used effectively for several years in the adjuvant treatment of breast cancer. Although its therapeutic effect is due to its anti-estrogenic properties, the drug also shows modest type B estrogen-receptor agonist activity during the menopausal period in which estrogens are at a low level. Owing to the fall in estrogen levels in menopause, tamoxifen provokes an up-regulation of both estrogen and progesterone receptors at an endometrial tissue is a direct consequence of this.

- **Adenosarcoma** as a subset of Malignant Mixed Mullerian Tumors (MMMT), is in differential diagnosis of endometrial polyps particularly **the larger one**. Presence of periglandular cuffing, atypical stromal cells and increased mitotic activity in the stromal component are factors in favor of uterine adenosarcoma.

- Microscopically lower uterine segment endometrial polyps may show mixed pattern of endometrial and endocervical polps.

- It is not necessary to report simple endometrial hyperplasia in the endometrial polyps histology if exists.


Thank You!