



Női genitális traktus II. A méhtest patológiája

Dr Madaras Lilla PhD
egyetemi docens

*250 years of EXCELLENCE
in medical education,
research & innovation
and healthcare*

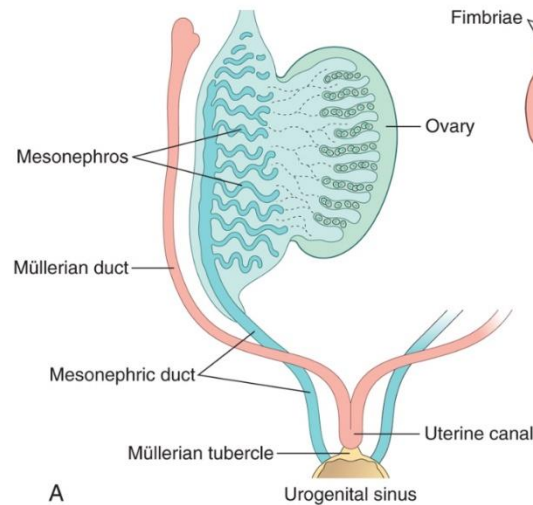
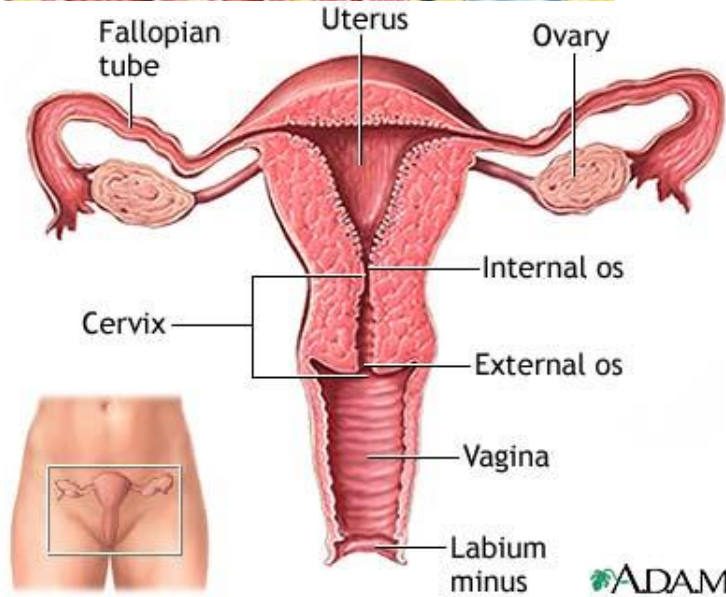
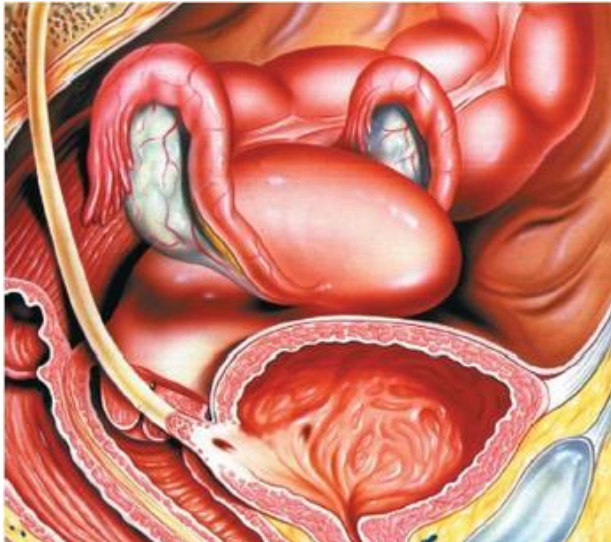
2022. április 7.



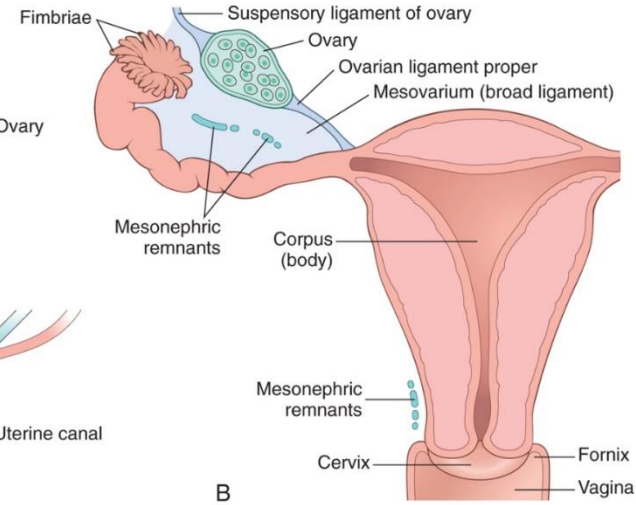
FYI

A kék csillaggal jelölt diák a legfontosabbak, ezek tartalmát a szigorlaton tudni kell. Természetesen a többi info is fontos (elsősorban jövő nőgyógyászok és patológusok számára (-:)

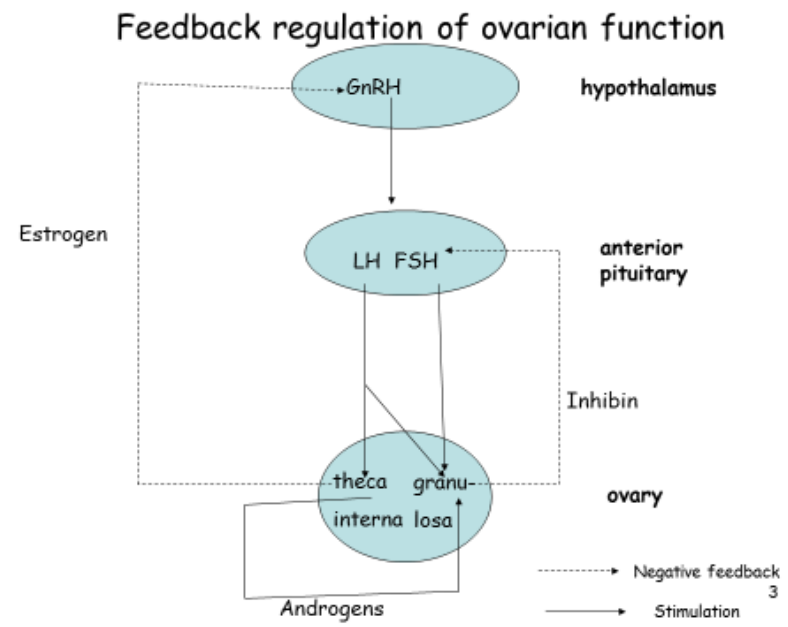
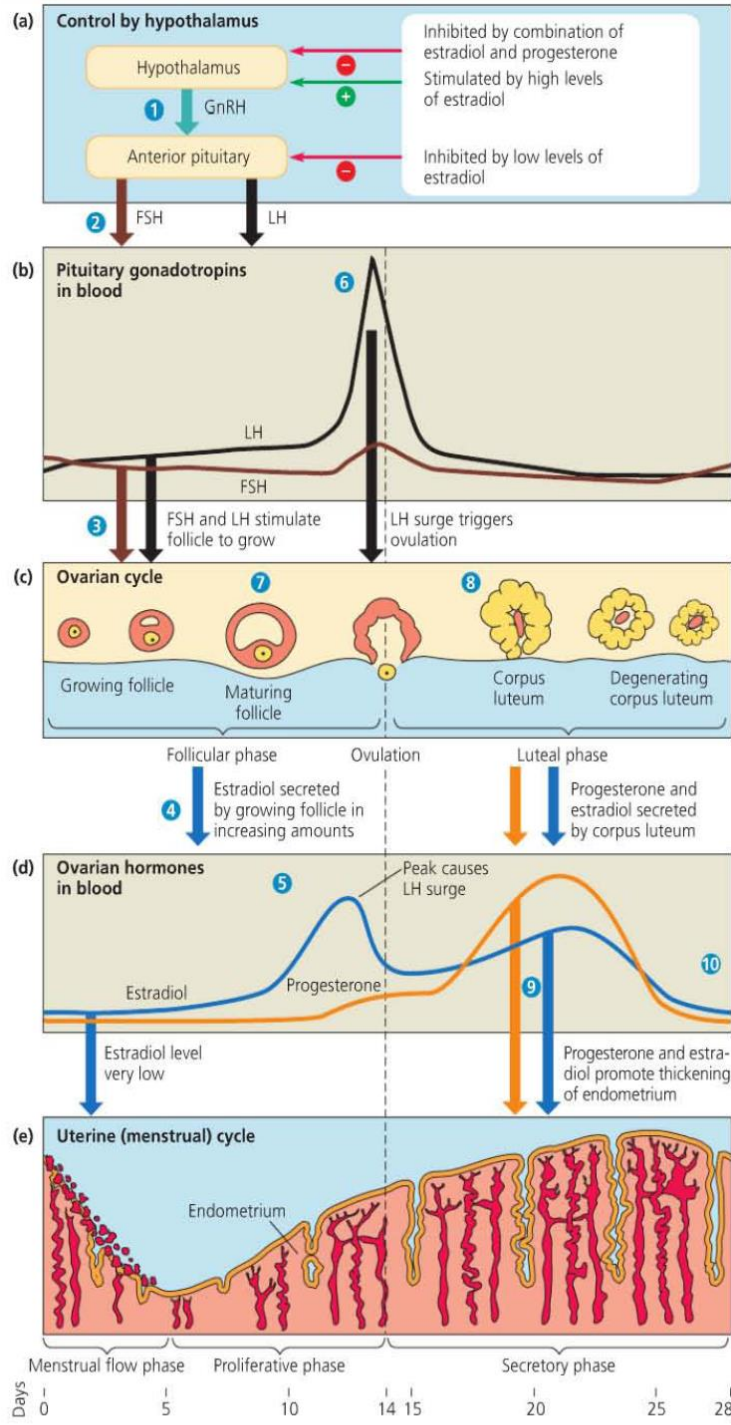
Anatomia, fejlődés



A



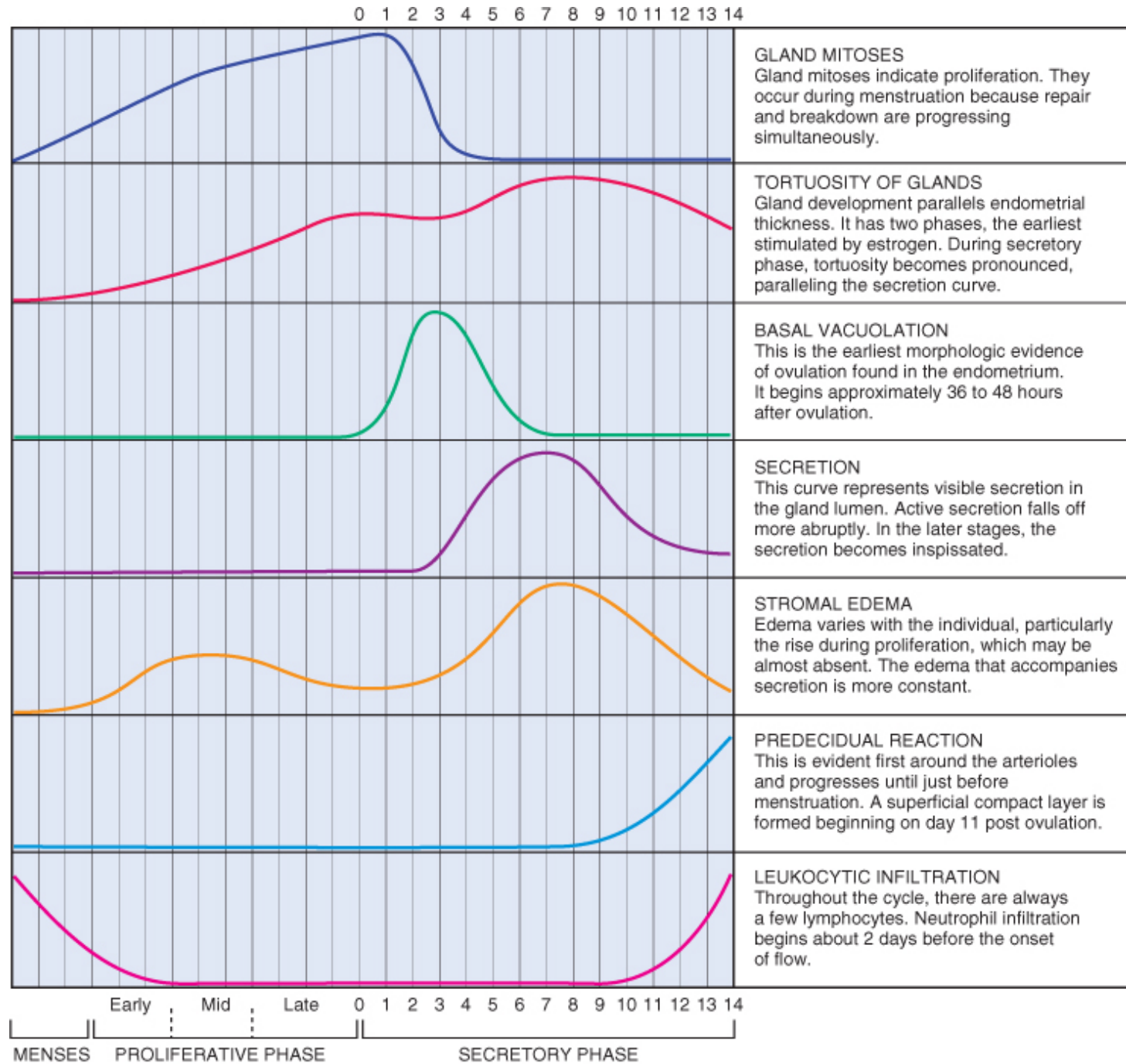
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Az ovariális és endometriális ciklus szabályozása

Az endometrium „datálása”

Az endometrium datálása



GLAND MITOSES
Gland mitoses indicate proliferation. They occur during menstruation because repair and breakdown are progressing simultaneously.

TORTUOSITY OF GLANDS
Gland development parallels endometrial thickness. It has two phases, the earliest stimulated by estrogen. During secretory phase, tortuosity becomes pronounced, paralleling the secretion curve.

BASAL VACUOLATION
This is the earliest morphologic evidence of ovulation found in the endometrium. It begins approximately 36 to 48 hours after ovulation.

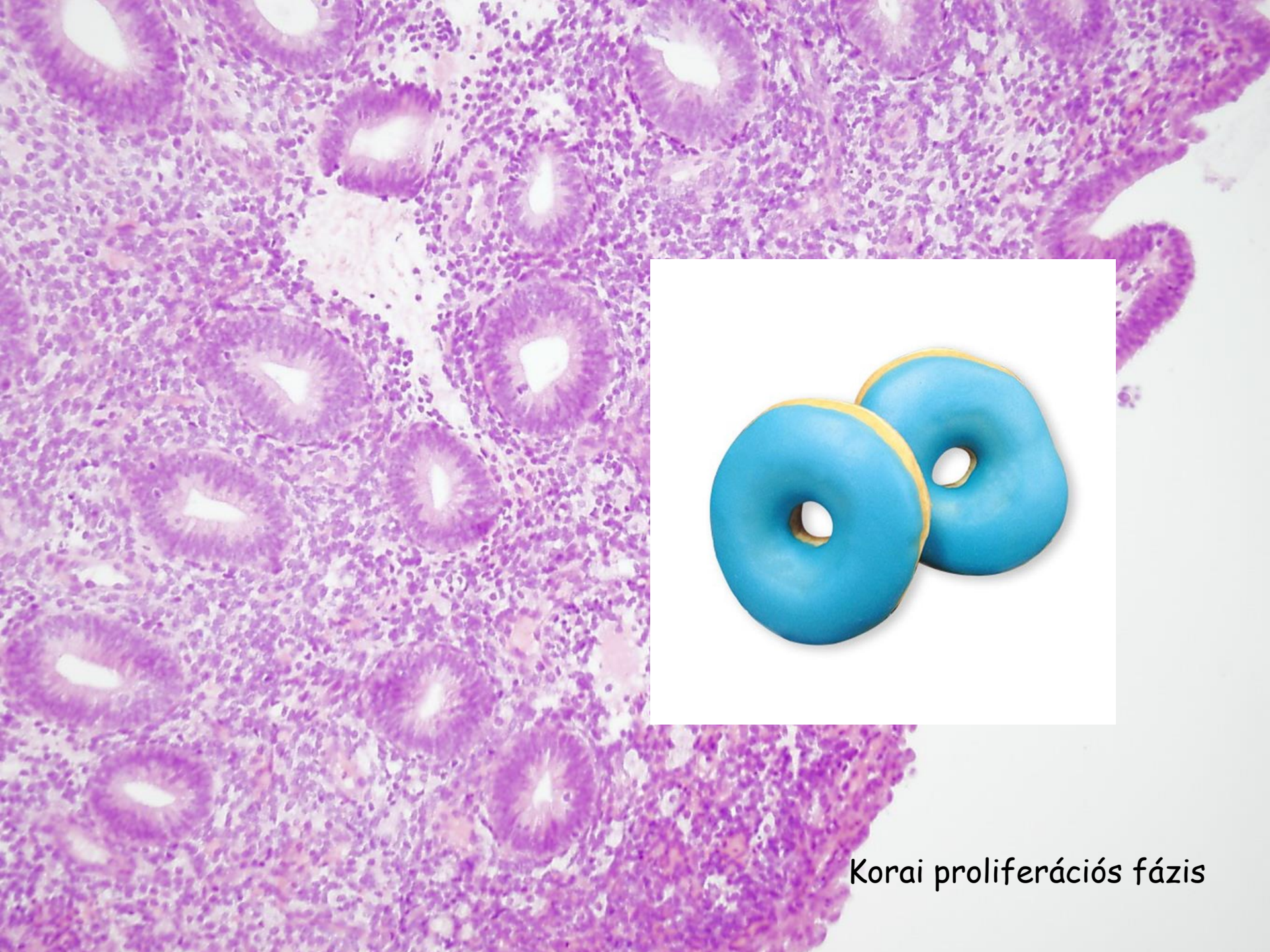
SECRETION
This curve represents visible secretion in the gland lumen. Active secretion falls off more abruptly. In the later stages, the secretion becomes inspissated.

STROMAL EDEMA
Edema varies with the individual, particularly the rise during proliferation, which may be almost absent. The edema that accompanies secretion is more constant.

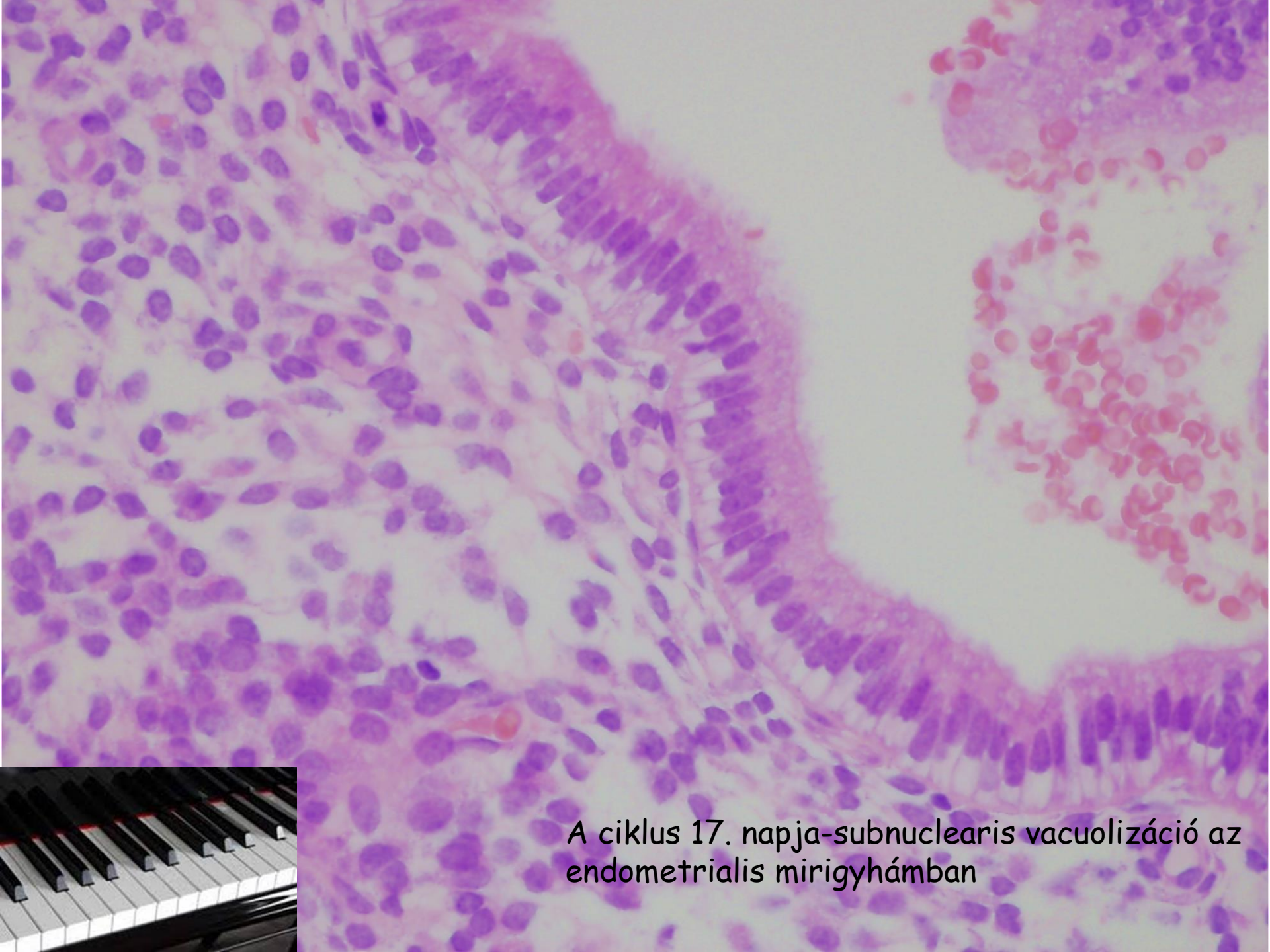
PREDECIDUAL REACTION
This is evident first around the arterioles and progresses until just before menstruation. A superficial compact layer is formed beginning on day 11 post ovulation.

LEUKOCYtic INFILTRATION
Throughout the cycle, there are always a few lymphocytes. Neutrophil infiltration begins about 2 days before the onset of flow.

Early Mid Late 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
 MENSES PROLIFERATIVE PHASE SECRETORY PHASE

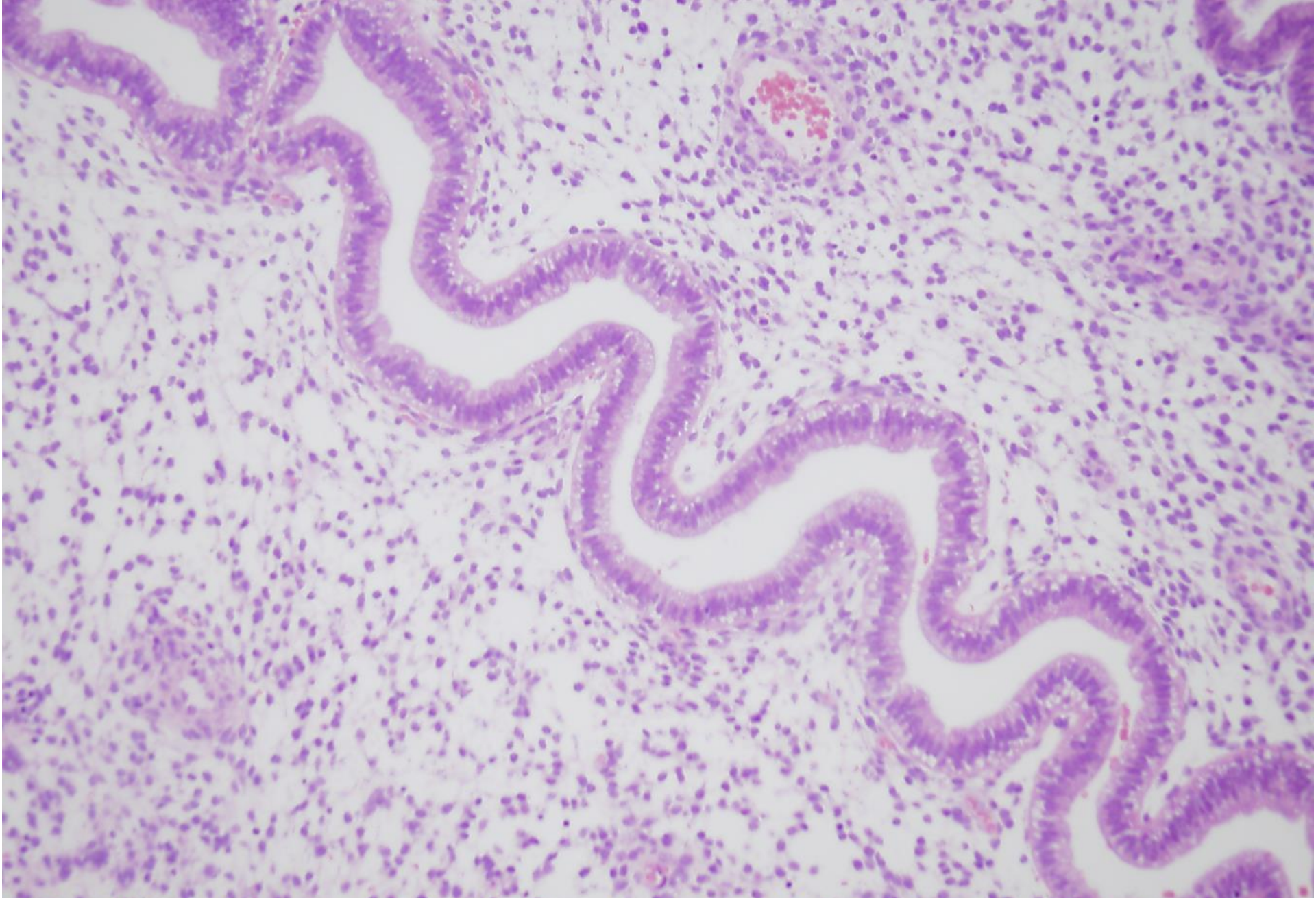


Korai proliferációs fázis

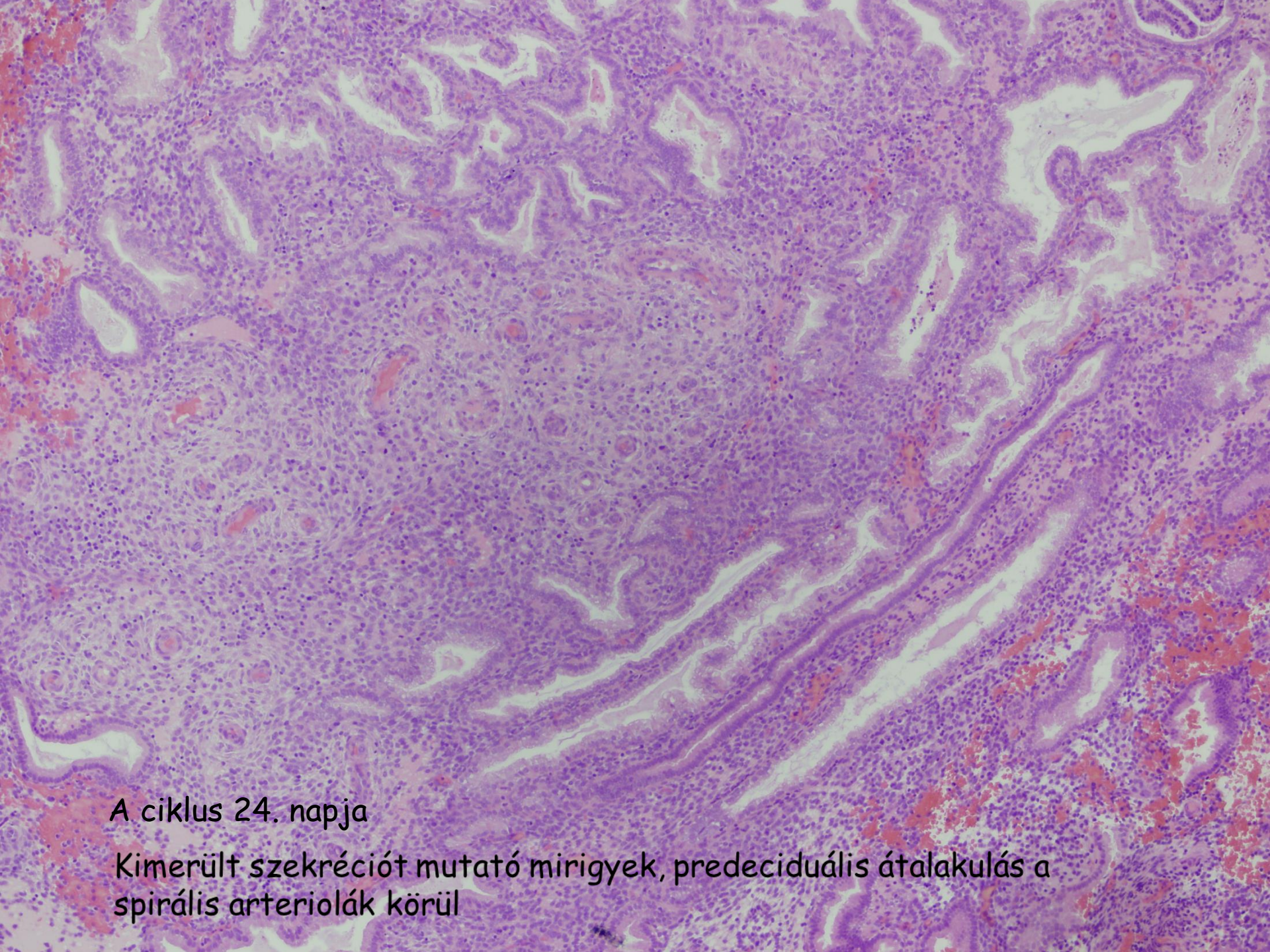


A ciklus 17. napja-subnuclearis vacuolizáció az endometrialis mirigyhámban



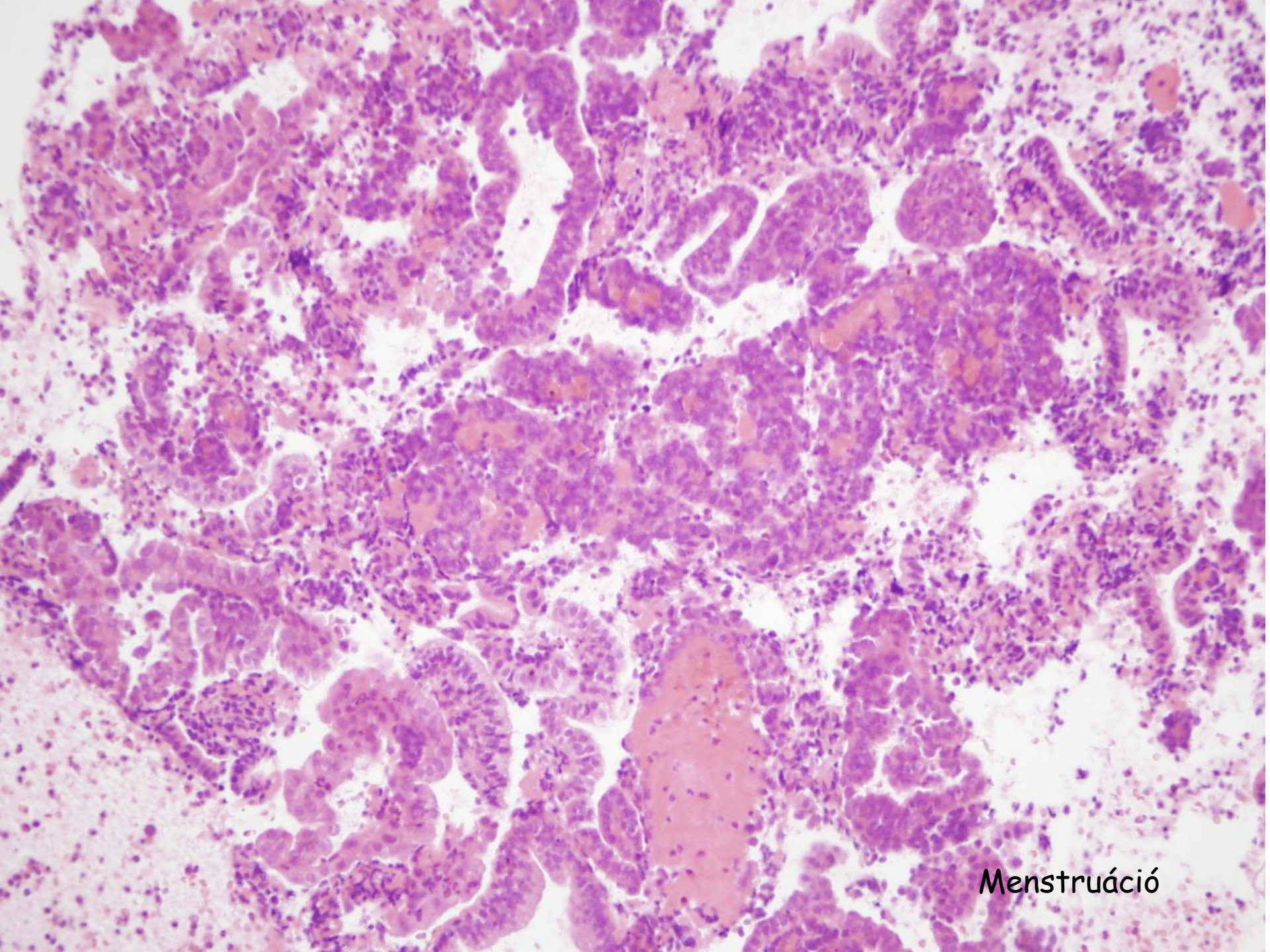


A ciklus 18. napja: kanyargós mirigyek, szub-és szupranukleáris vakuolizáció

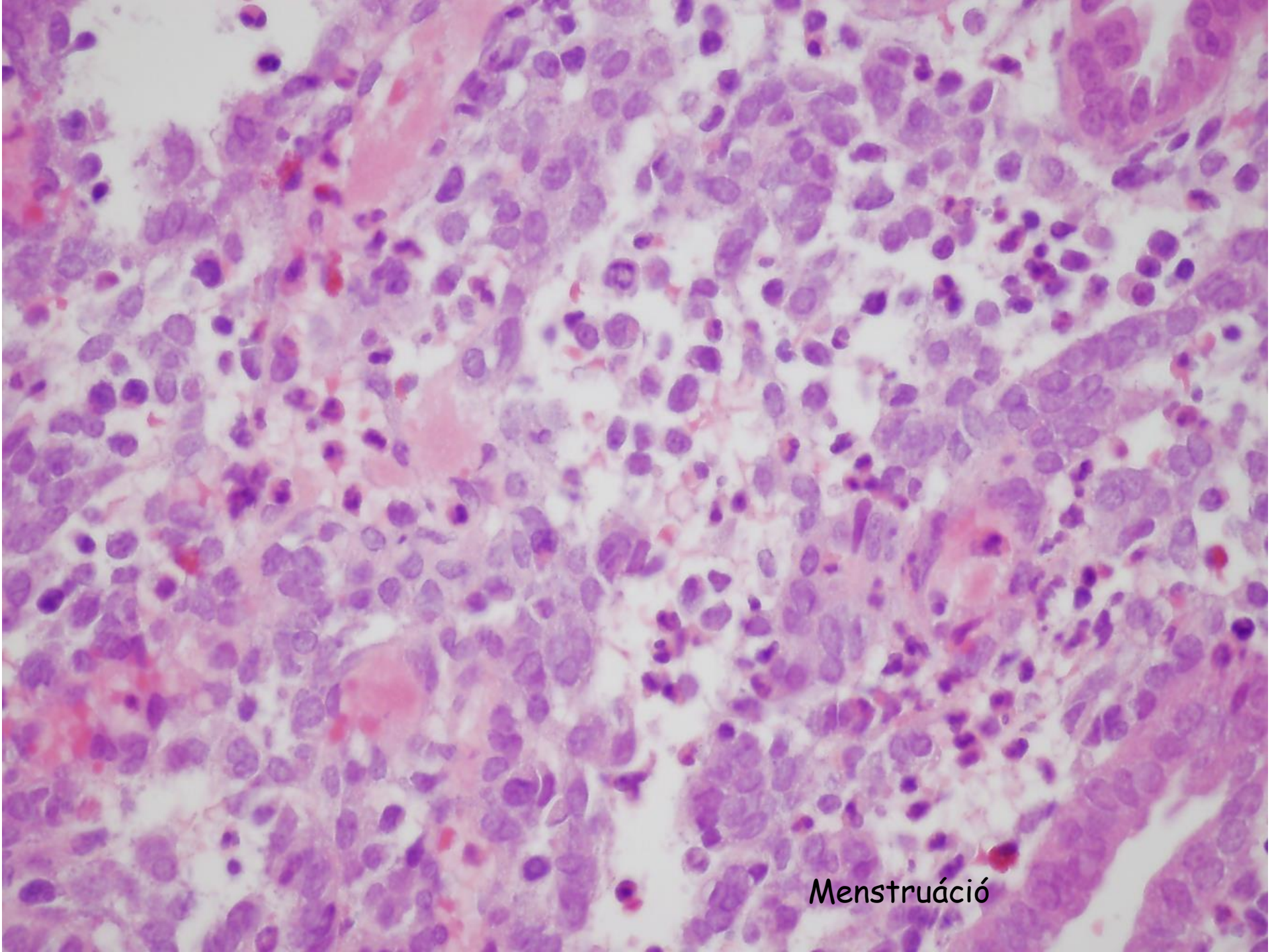


A ciklus 24. napja

Kimerült szekréciót mutató mirigyek, predeciduális átalakulás a spirális arteriolák körül



Menstruáció



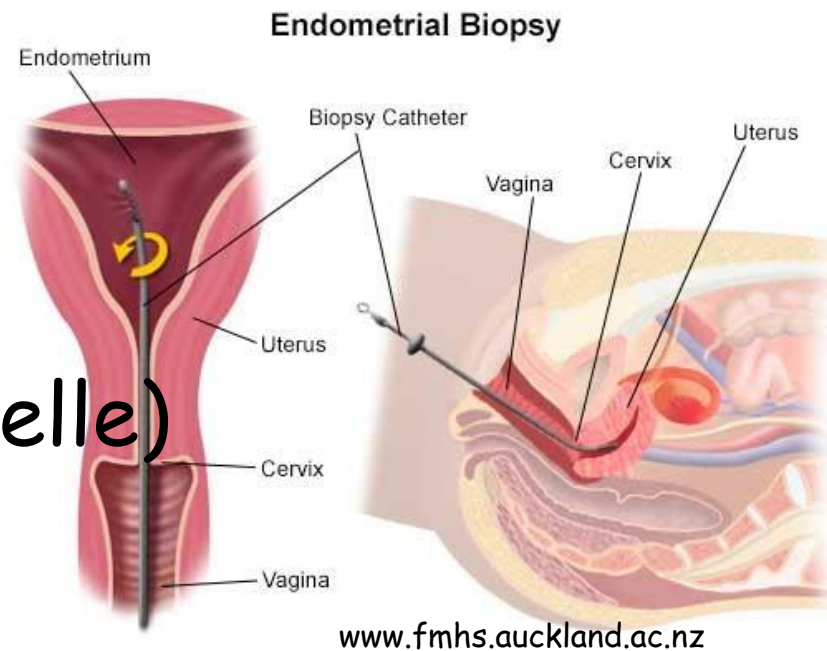
Menstruáció

Az endometrium vizsgálata

- Mintavétel
- Hysterectomia (lehet TAH és BSO, laparoscopos hysterectomia, Chrobak műtét, Wertheim műtét...)

Mintavételi technikák

1. Curettage
2. Fractionalt curettage
3. Hysteroscopia+
polyp/endometrium ablatio
4. Endometrium biopsia (Pipelle)



Endometrium-mintavétel- mikor?

- AUB (abnormal uterine bleeding)-
rendellenes méhvérzés
- Conceptuum kiürítése
- Infertilitás esetén az endometrium
datálása
- Hormon hatás megítélése pl. HRT,
Tamoxifen kezeléskor

Az endometrium patológiája

- Gyulladás
- Vérzészavarokhoz kapcsolódó klinikai fogalmak
- AUB
- Endometrium hyperplasia
- Adenomyosis és endometriosis
- Az endometrium daganatai



Gyulló

- **Acut endometritis**
 - abortus után, postpartum
 - group A hemolytic streptococcus
- **Chronicus endometritis**
 - gestatio szövet retenciója utáni
 - PID
 - IUD (actinomyces!)
 - tuberculosis (salpingitis tuberculosa)
 - chlamydia - plasma sejtek!
- **Pyometra**
- **Asherman syndroma (intrauterin amenorrhoea)**



Semmelweis Ignác Fülöp
(1818-1865)

Semmelweis

Klinikai fogalmak

- ~~Dysfunctionalis méhvérzés~~
- ~~Oligomenorrhoea, polymenorrhoea~~
- ~~hypomenorrhoea ↔ menorrhagia~~
- ~~Metrorrhagia, metropathia haemorrhagica~~
- ~~Dysmenorrhoea stb.~~



- Rendellenes méhvérzés (abnormal uterine bleeding) AUB

AUB tények

- Premenop AUB- nőgyógyászati vizitek 1/3-a emiatt
- Peri- és postmenop AUB- nőgyógyászati vizitek 70%-a
- FIGO Menstrual Disorders Working Group-2011
- American College of Obstetricians and Gynecologists (ACOG)-2013



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SPECIAL COMMUNICATION

FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age

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AUB definíciók

- AUB: az uterus corpusából származó, a normálistól szabályosságában, mennyiségében és gyakoriságában eltérő vérzés
 - Heavy menstrual bleeding (HMB)
 - Intermenstrual bleeding (IMB)
- Acut AUB: azonnali intervenciót igénylő erős vérzés illetve minden AUB, ami 6 hónapnál kevesebb ideje áll fenn
- Chronicus AUB: 6 hónapon túl fennáll

AUB in reproductive ages

PALM/COEIN

P olyp	}	S ubmucosal
A denomyosis		
L eiomyoma		O ther
M alignancy & hyperplasia		

C oagulopathy
O vulatory dysfunction
E ndometrial
I atrogenic
N ot yet classified



PALM

- Polyp-AUB-P
- Adenomyosis AUB-A
- Leiomyoma AUB-L
- Malignitás és hyperplasia AUB-M
- Szövettanilag és képalkotók által igazolható laesiók

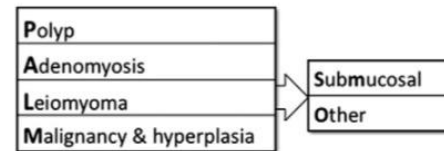


A rendellenes méhvérzések (AUB) okai

Prepubertas	Pubertas praecox (hypothalamicus, hypophysealis vagy ovarialis ok)
Serdülők	Anovulációs cyclus
Reproductiv kor	Terhességi komplikációk (abortusz, trophobl.betegségek, ectopiás terhesség) Organicus laesiok (leiomyoma, polyp, adenomyosis, endom. hyperplasia, cc) Anovulációs cyclus
Perimenopausa	Anovulációs cyclus Organicus laesiok (cc, hppl, polyp)
Postmenopausa	Organicus laesiok (carcinoma, hyperplasia, polyp) Endometrium atrophia

Dysfunctionális méhvérzés (AUB COEIN)

- **Elégtelen proliferációs fázis**
 - Eltérés a várt és a ténylegesen megfigyelt endometriális szöveti kép között a proliferációs fázisban
- **Elégtelen lutealis fázis**
 - alacsony progesteron szint
 - infertilitás
 - amenorrhoea vagy rendellenes vérzés
 - endometrium vizsgálata 2 nappal a várt menstruáció előtt!
- **Szabálytalan méhnyálkahártya leöködés**
 - a ciklus nem hosszabb, de a menstruáció 7 napnál tovább tart
 - az endometrium a menstruáció 5. napján egyszerre mutat menstruációs, késői szekréciós és korai proliferációs részleteket



Coagulopathy
Ovulatory dysfunction
Endometrial
Iatrogenic
Not yet classified



(Dysfunctionalis méhvérzés)



- **Anovulációs cyclus**

- leggyakoribb serdülőkorban és premenopausában, általában enyhe hormonális zavar okozza
- Ritkább okai:
 - **endocrin** okok: pm, mvese vagy hypophysis betegségek
 - **ovarialis** okok: PCO, granulosa sejtes tumor
 - **szisztemás** metabolicus okok: obesitás, malnutritio (anorexia nervosa!),
- nincs ovulatio → prolongált kiegyensúlyozatlan oestrogen stimulatio → persistáló proliferációs endometrium → endometrium hyperplasia → rendellenes méhvérzés

Endometrium hyperplasia

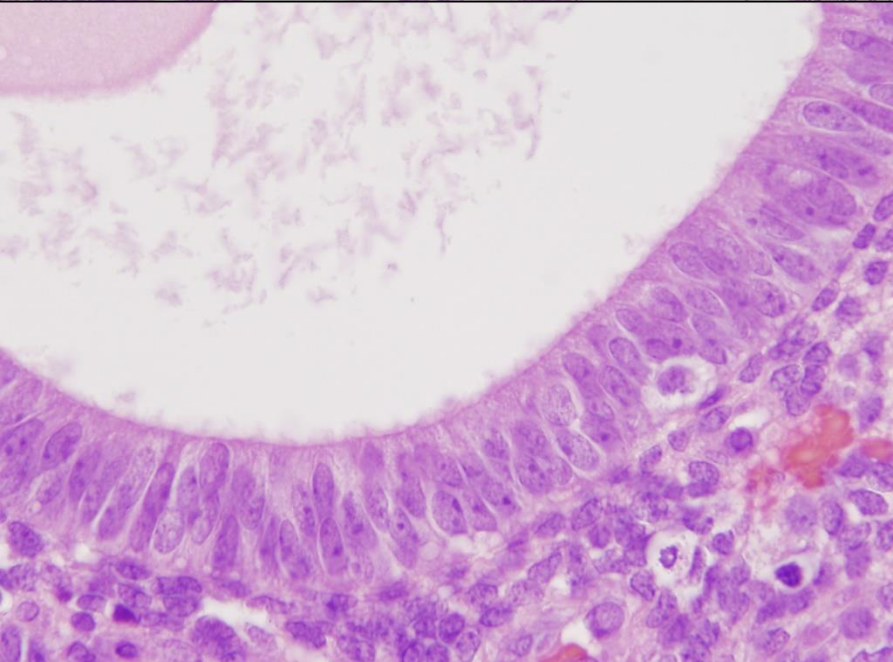
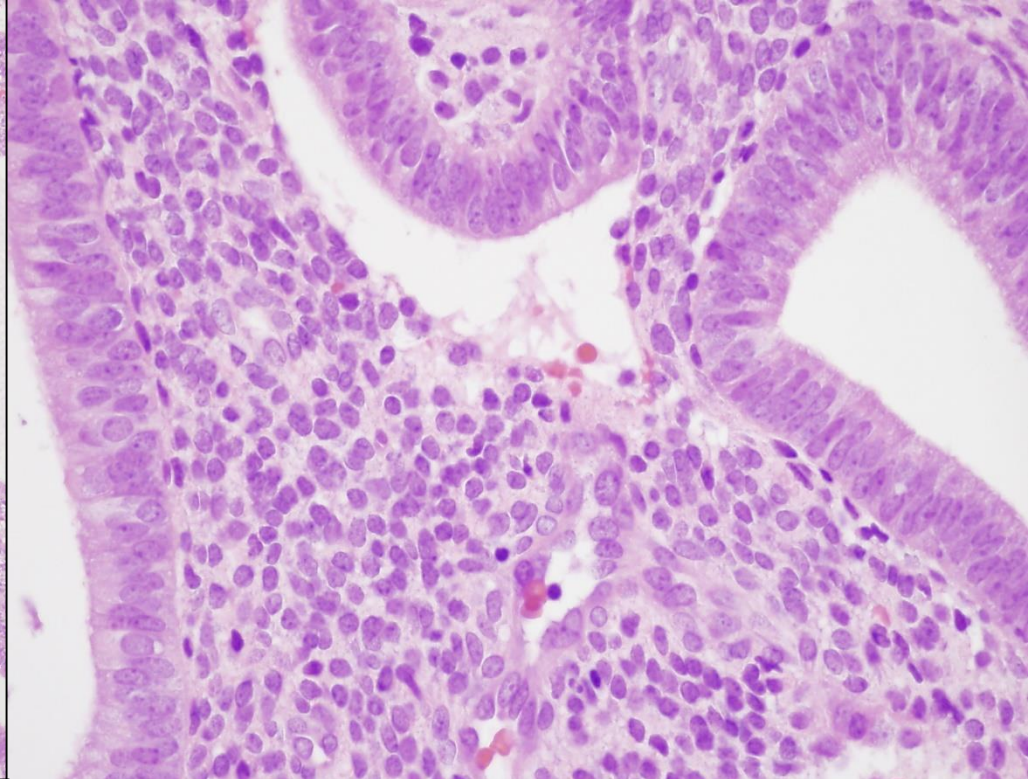
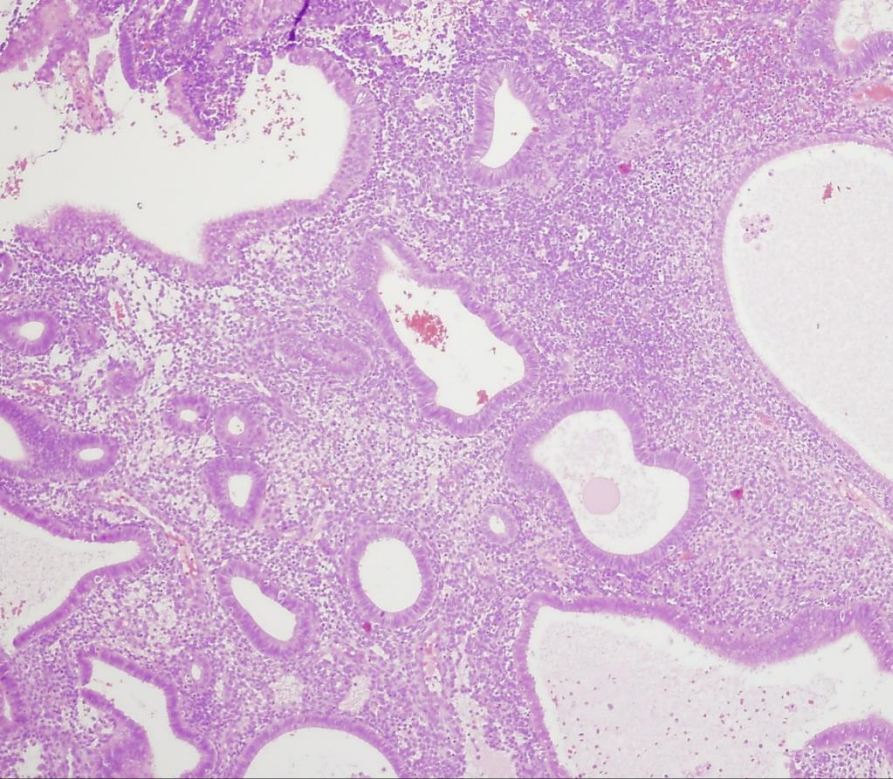
- Prolongált, kiegyensúlyozatlan oestrogen stimulatio eredménye (anovulatio vagy fokozott oestrogen productio- PCO, Stein-Leventhal sy, corticalis stromalis hppl, oestrogen pótló hormonkezelés, funkcionáló granulosa sejtes tumor)
- (Simplex) hyperplasia atypia nélkül vagy atypiával
- (Complex) hyperplasia atypia nélkül vagy atypiával



Simplex hyperplasia



- **Atypia nélkül (Glandular cysticus hppl)**
 - diffúz
 - mirigyek és stroma mennyisége megnőtt
 - mirigy-stroma arány- 1:1
 - különböző alakú és nagyságú mirigyek
 - cysticusan tágult mirigyek
 - mirigyhám: proliferatios
 - 2% carcinoma
- **Atypiával**
 - előbbi jellegzetességek + cytologiai atypia
 - Ritka
 - 8%-ukból carcinoma lesz



Simplex hyperplasia

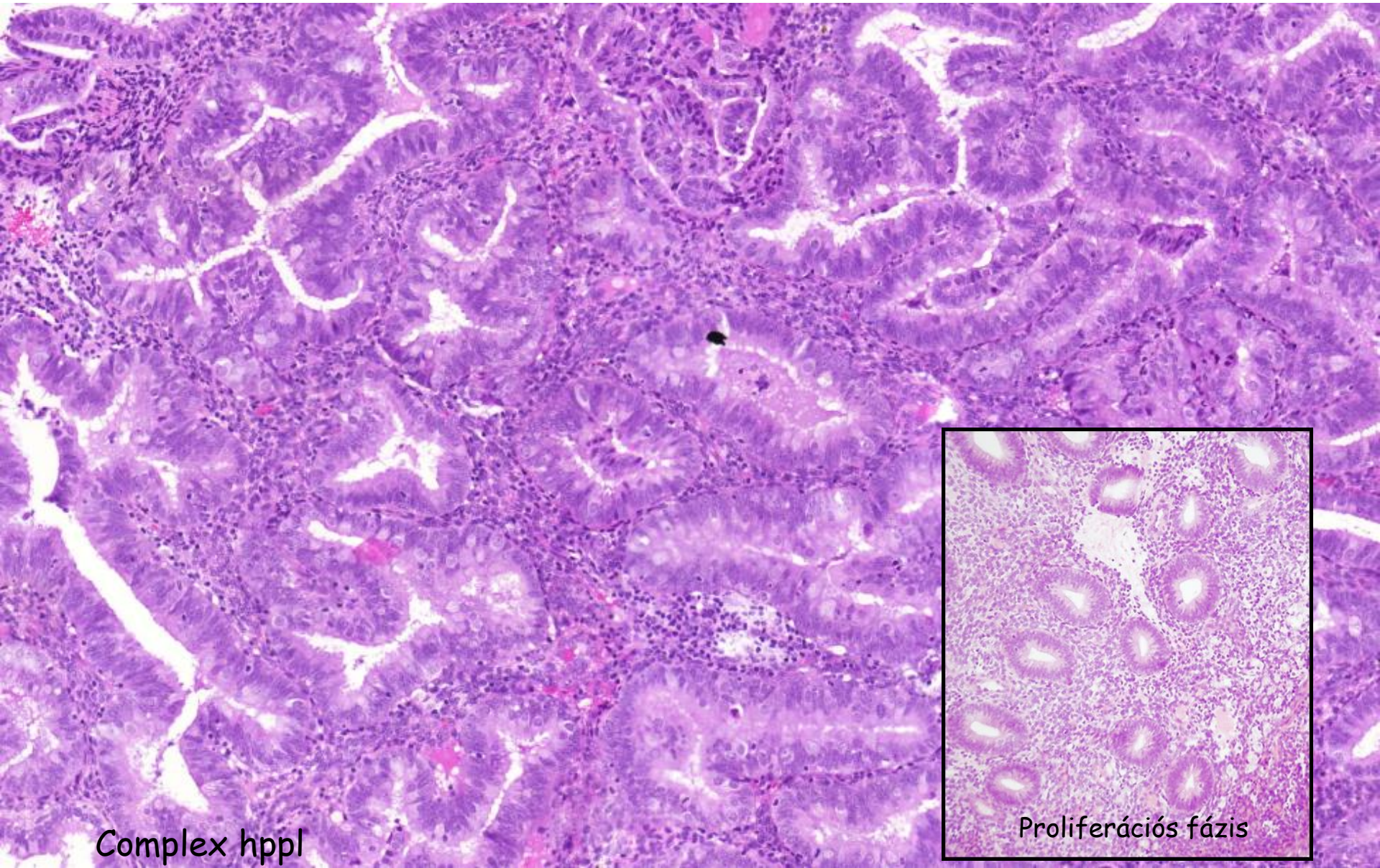


Hpp1 simplex endometrii

Complex hyperplasia

- Atypia nélkül
 - focalis
 - szabálytalan mirigyek
 - mirigy-stroma arány megnövekedett (back-to-back mirigyek)
 - 3%-ukból cc lesz
- Atypiával
 - cytologiai atypia
 - elkülönítése az adenocarcinomától nehéz
 - 25-30% carcinoma lesz



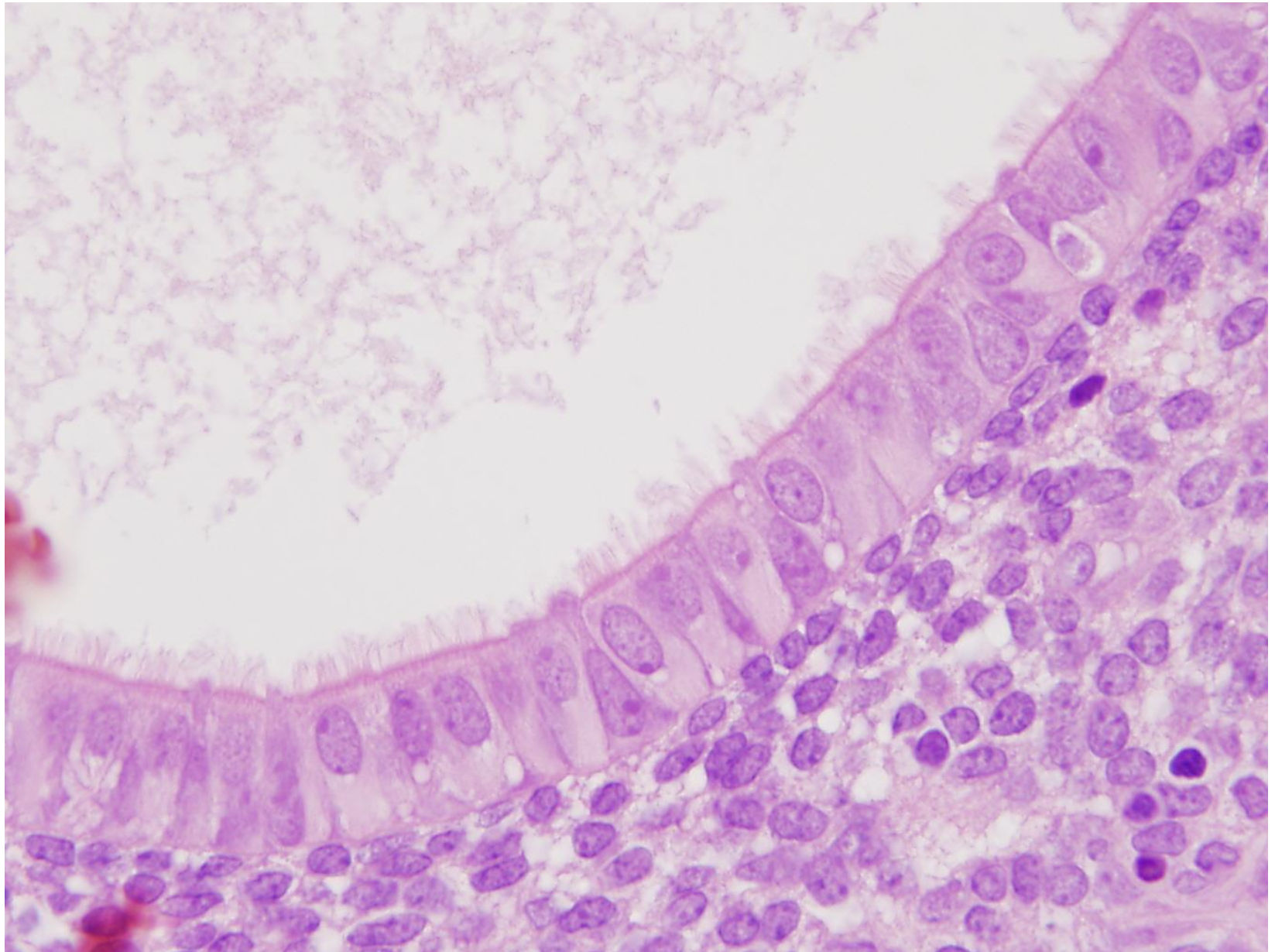


Complex hppl

Proliferációs fázis

Metaplasia

- különböző típusok: laphám, tubalis, mucinosus, etc.
- gyakran társul hyperplasiához



Tubalis metaplasia

Adenomyosis és endometriosis

- **Adenomyosis:** endometriális mirigyek és stroma mélyen a myometriumban (endometriumtól legalább 2-3 mm-re)
- **Endometriosis:** endometrialis szigetek a méhen kívül
 - Functionalis endometrium
 - Müllercső maradványaiból? implantatio? lymphaticus vagy hematogen terjedés?
 - Legyakoribb lokalizáció: ovariumok, a méh ligamentumai, peritoneum
 - pelvic pain, dysmenorrhea, infertilitás
 - DIE: deep infiltrating endometriosis



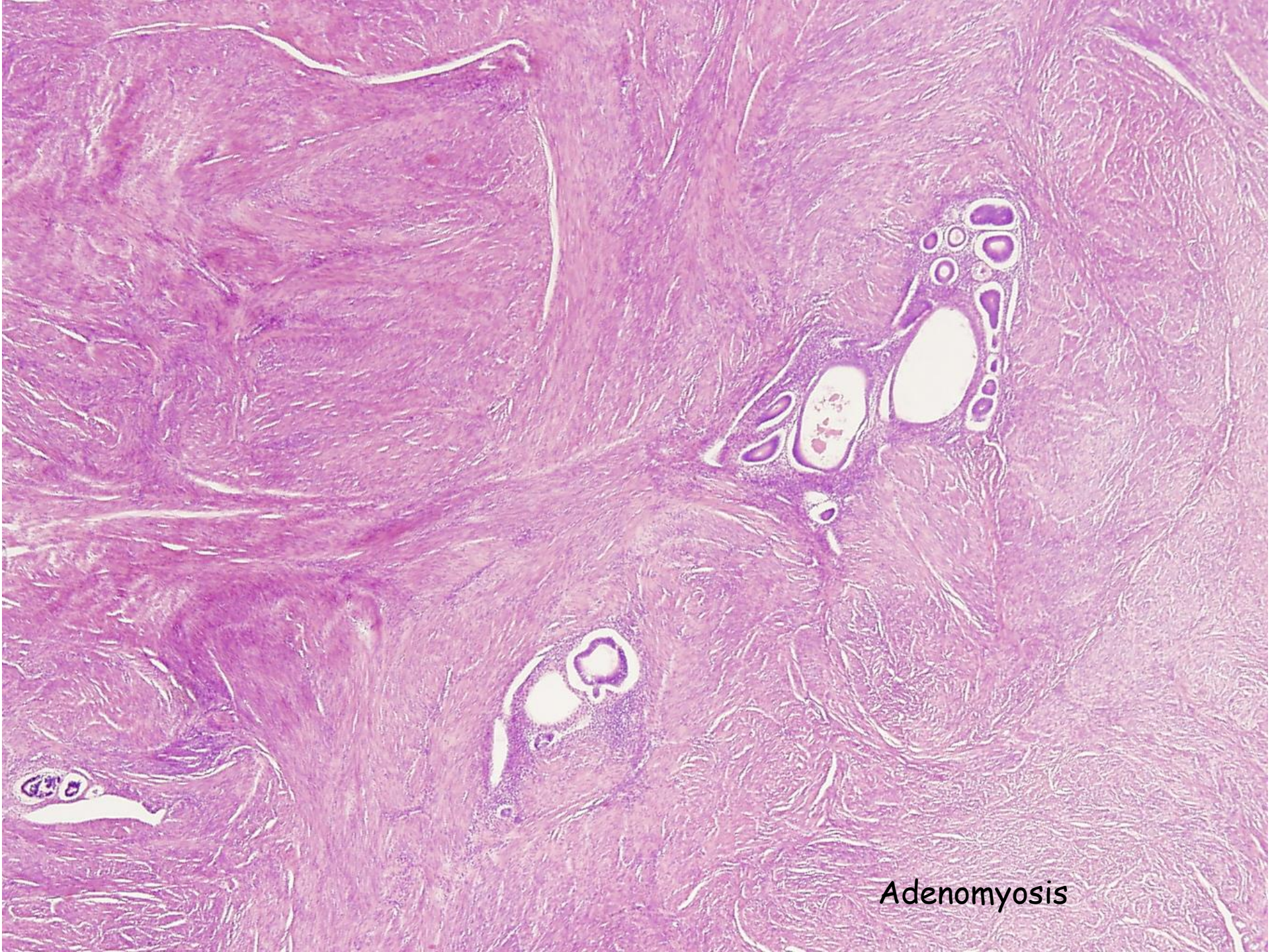


Adenomyosis és endometrialis polypus



Adenomyosis

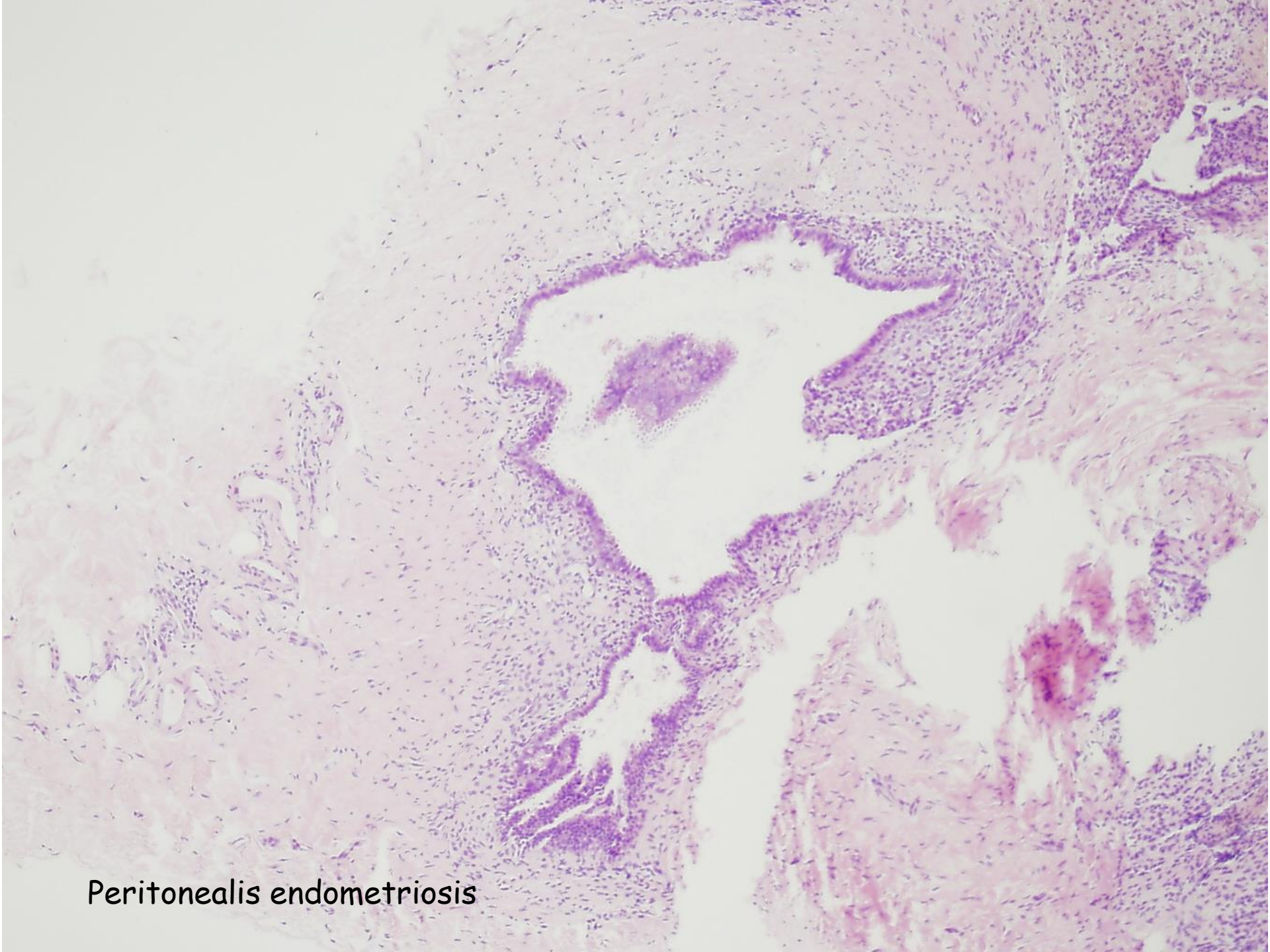
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Adenomyosis



Endometriosis - ovarium- csokoládécysta



Peritonealis endometriosis

Endometrialis polypus

- nem valódi daganat
- Tamoxifen terápia szövődménye lehet
- tünetmentes vagy rendellenes méhvérvérzést okoz
- MA: a méhürbe emelkedik
- MI: cysticusan tágult mirigyek, fibrosus stroma és **vaskos falú erek**
- adenocarcinoma kialakulhat állományában



A méhtest daganatai

Kiindulás helye		Benignus	Malignus
Endometrium	Endometrialis mirigyek	-	Endometrioid carcinoma Serosus cc Clear cell cc
	Endometrialis stroma	Stromalis nodulus	Stroma sarcoma
	Endometrialis mirigyek és stroma	Adenofibroma Adenomyoma	Carcinosarcoma Adenosarcoma
Myometrium		Leiomyoma	Leiomyosarcoma

WHO classification of tumours of the uterine corpus

Endometrial epithelial tumours and precursors

	Endometrial hyperplasia without atypia
8380/2	Atypical hyperplasia of the endometrium
8380/3	Endometrioid adenocarcinoma NOS
	<i>POLE</i> -ultramutated endometrioid carcinoma
	Mismatch repair-deficient endometrioid carcinoma
	p53-mutant endometrioid carcinoma
	No specific molecular profile (NSMP) endometrioid carcinoma
8441/3	Serous carcinoma NOS
8310/3	Clear cell adenocarcinoma NOS
8020/3	Carcinoma, undifferentiated, NOS
8323/3	Mixed cell adenocarcinoma
9110/3	Mesonephric adenocarcinoma
8070/3	Squamous cell carcinoma NOS
8144/3	Mucinous carcinoma, intestinal type
9111/3*	Mesonephric-like adenocarcinoma
8980/3	Carcinosarcoma NOS

Tumour-like lesions

Endometrial polyp
Endometrial metaplasia
Arias-Stella reaction

Mesenchymal tumours specific to the uterus

8890/0	Leiomyoma NOS
8890/0	Lipoleiomyoma
8890/0	Leiomyoma, apoplectic
8890/0	Leiomyoma, hydropic
8890/0	Dissecting leiomyoma
8892/0	Cellular leiomyoma
8896/0	Myxoid leiomyoma
8891/0	Epithelioid leiomyoma
8893/0	Symphastic leiomyoma
8890/1	Leiomyomatosis NOS
8890/1	Intravencous leiomyomatosis

8897/1	Smooth muscle tumour of uncertain malignant potential
8891/1*	Epithelioid smooth muscle tumour of uncertain malignant potential
8896/1*	Myxoid smooth muscle tumour of uncertain malignant potential
	Spindle smooth muscle tumour of uncertain malignant potential
8898/1	Metastasizing leiomyoma
8890/3	Leiomyosarcoma NOS
	Spindle leiomyosarcoma
8891/3	Epithelioid leiomyosarcoma
8896/3	Myxoid leiomyosarcoma
8930/0	Endometrial stromal nodule
8931/3	Endometrial stromal sarcoma, low grade
8930/3	Endometrial stromal sarcoma, high grade
8805/3	Undifferentiated sarcoma
8590/1	Uterine tumour resembling ovarian sex cord tumour
8714/0	Perivascular epithelioid tumour, benign
8714/3	Perivascular epithelioid tumour, malignant
8825/1	Inflammatory myofibroblastic tumour
	Epithelioid myofibroblastic sarcoma

Mixed epithelial and mesenchymal tumours

8932/0	Adenomyoma NOS
8932/0	Atypical polypoid adenomyoma
8933/3	Adenosarcoma

Miscellaneous tumours

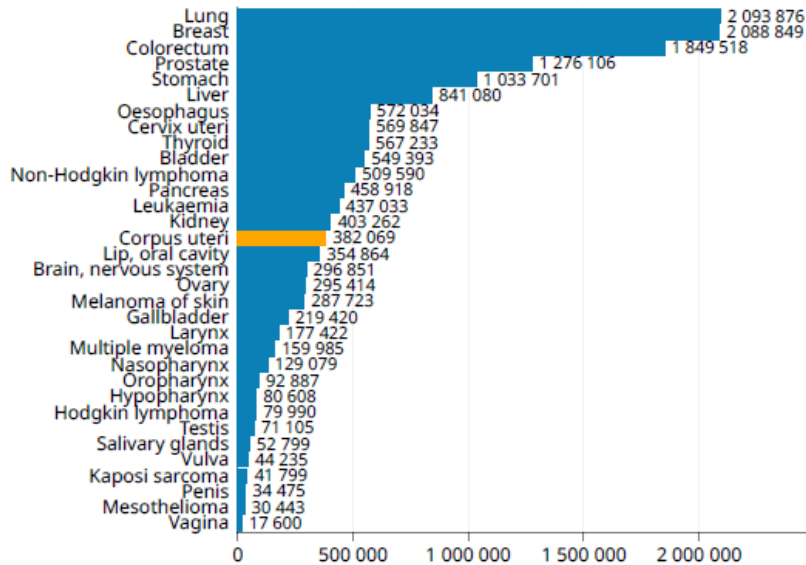
9473/3	Primitive neuroectodermal tumour NOS
9064/3	Germ cell tumour NOS
9071/3	Yolk sac tumour NOS
9080/0	Mature teratoma NOS
9080/3	Immature teratoma NOS

Corpus uteri

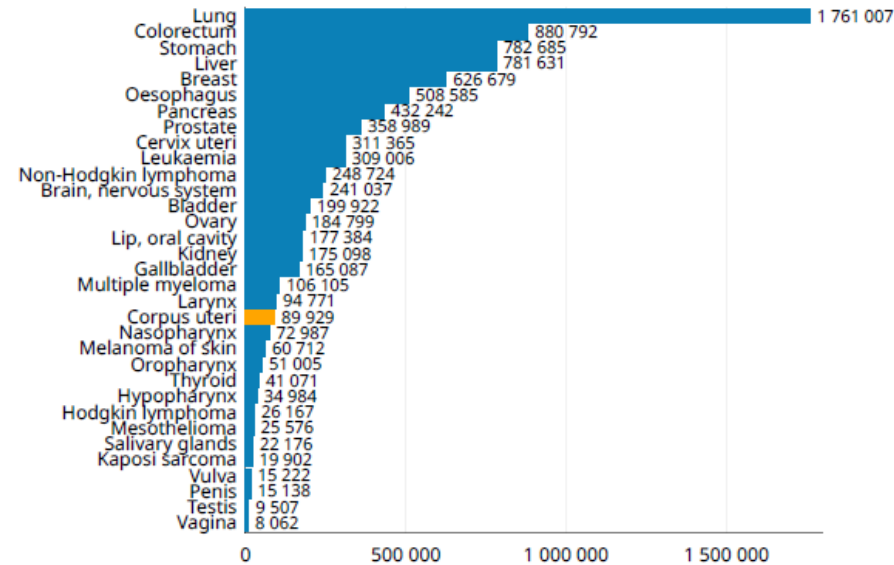
Source: Globocan 2018

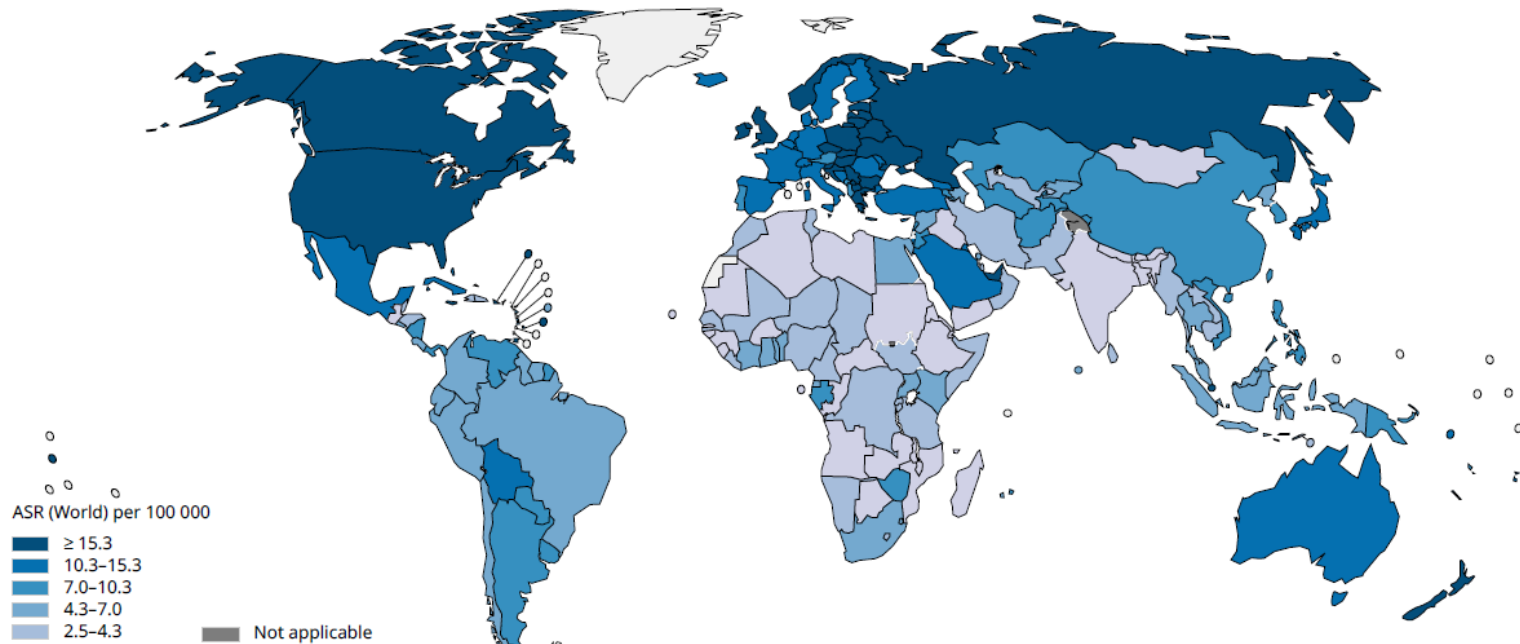


Number of new cases in 2018, both sexes, all ages

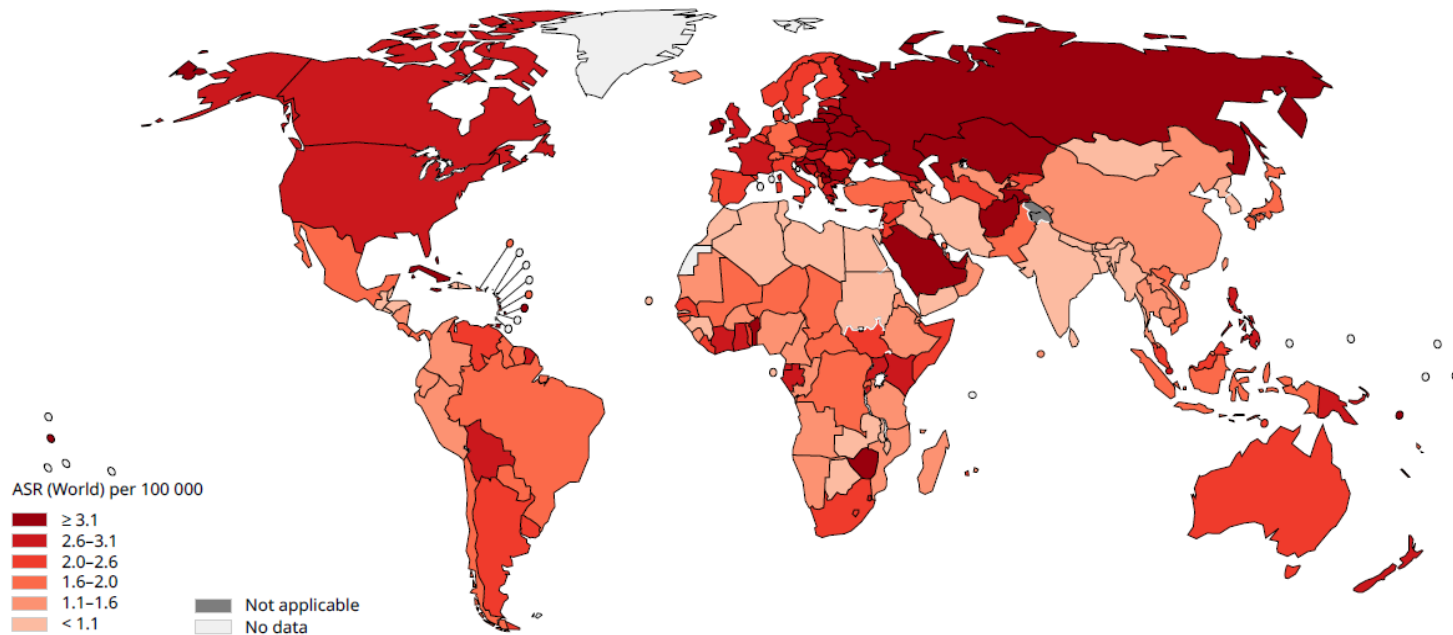


Number of deaths in 2018, both sexes, all ages





Age standardized (World) mortality rates, corpus uteri, all ages



Endometrialis carcinoma

- a nőket érintő malignus tumorok 7%-a
- peri- és postmenopausa (55-65 év)
- Lynch szindrómához asszociált lehet

- Tünete: postmenopausalis vérzés



Endometrialis carcinoma

- Korábban 2 fő típus (patomechanizmus szerint-Bokhman-féle osztályozás, I-es és II-es típus)
 - Endometrioid carcinoma (korábban I-es típus)
 - endometrium hyperplasia talaján
 - Obesitas, diabetes, hypertensio, infertilitás, Stein- Leventhal sy, oestrogen hormonpótlás, Tamoxifennel kezelt emlőrákos betegek
 - kedvezőbb prognosis
 - általában jól differenciált



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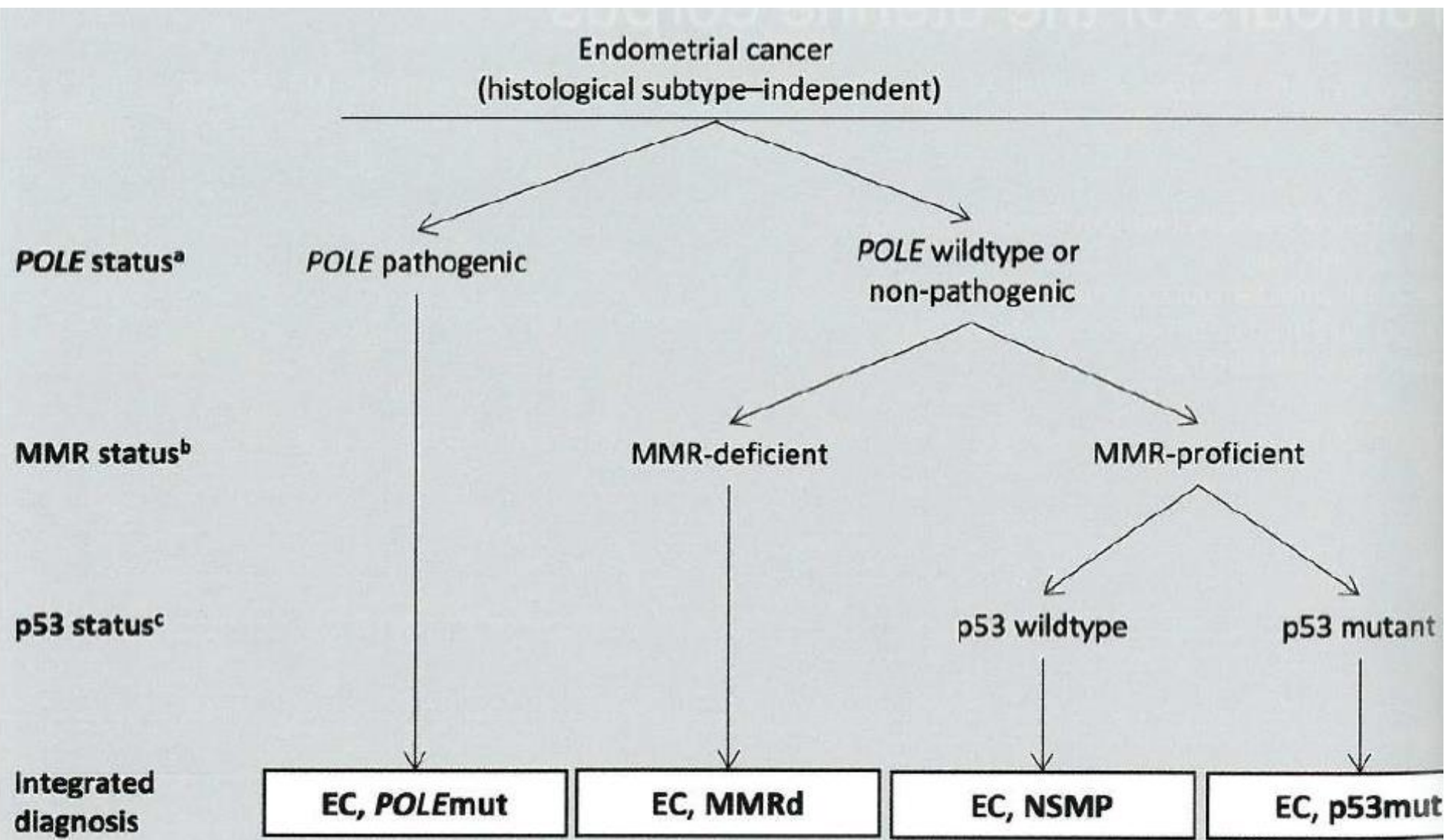
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WHO, 5. kiadás, 2020



Az endometrialis endometrioid carcinoma molekuláris klasszifikációja

WHO 5.kiadás, 2020 (ProMisE (Proactive Molecular Risk Classifier for Endometrial Cancer))

POLEmut: hotspot mutációk a DNS polimeráz epsilon (*POLE*) exonukleáz doménjén

MMR: mismatch repair

Endometrialis carcinoma

- **Endometrioid carcinoma (folyt)**
 - *Grading*
 - *Grade 1: ha < 5% solid komponens*
 - *Grade 2: ha < 50% solid komponens*
 - *Grade 3: ha > 50% solid komponens*

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Mesenchymal tumours specific to the uterus

8890/0	Leiomyoma NOS
8890/0	Lipoleiomyoma
8890/0	Leiomyoma, apoplectic
8890/0	Leiomyoma, hydropic
8890/0	Dissecting leiomyoma
8892/0	Cellular leiomyoma
8896/0	Myxoid leiomyoma
8891/0	Epithelioid leiomyoma
8893/0	Symphastic leiomyoma
8890/1	Leiomyomatosis NOS
8890/1	Intravencous leiomyomatosis

8897/1	Smooth muscle tumour of uncertain malignant potential
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8896/1*	Myxoid smooth muscle tumour of uncertain malignant potential
	Spindle smooth muscle tumour of uncertain malignant potential
8898/1	Metastasizing leiomyoma
8890/3	Leiomyosarcoma NOS
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8931/3	Endometrial stromal sarcoma, low grade
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8825/1	Inflammatory myofibroblastic tumour
	Epithelioid myofibroblastic sarcoma

Mixed epithelial and mesenchymal tumours

8932/0	Adenomyoma NOS
8932/0	Atypical polypoid adenomyoma
8933/3	Adenosarcoma

Miscellaneous tumours

9473/3	Primitive neuroectodermal tumour NOS
9064/3	Germ cell tumour NOS
9071/3	Yolk sac tumour NOS
9080/0	Mature teratoma NOS
9080/3	Immature teratoma NOS

Endometrialis carcinoma

- **Serosus carcinoma (II-es típusú korábban)**
 - nem endometrium hyperplasiahoz társul
 - atrófia talaján jön létre
 - agresszív
 - high grade cytologiai atypia, necrosis
 - TP53 mutációja kimutatható
 - Prekurzor(?!): Serosus Intraepithelialis Carcinoma (SEIC)



Endometrialis carcinoma

• Terjedés és metastasis

- Localis terjedés: myometrium és cervix
- extrauterin terjedés: pelvicus és paraaorticus nyirokcsomók, ovarium
- Serosus carcinoma: peritoneum, transtubalis terjedés

TNM Categories	FIGO Stages	
TX		Primary tumour cannot be assessed
To		No evidence of primary tumour
T1	I ^a	Tumour confined to the corpus uteri ^a
	T1a	IA ^a Tumour limited to endometrium or invading less than half of myometrium
	T1b	IB Tumour invades one half or more of myometrium
T2	II	Tumour invades cervical stroma, but does not extend beyond the uterus
T3	III	Local and/or regional spread as specified here:
	T3a	IIIA Tumour invades the serosa of the corpus uteri or adnexae (direct extension or metastasis)
	T3b	IIIB Vaginal or parametrial involvement (direct extension or metastasis)
N1,N2	IIIC	Metastasis to pelvic or para.aortic lymph nodes ^b
	N1	IIIC1 Metastasis to pelvic lymph nodes
	N2	IIIC2 Metastasis to para.aortic lymph nodes with or without metastasis to pelvic lymph nodes
T4 ^c	IV	Tumour invades bladder/bowel mucosa



Endometrioid carcinoma

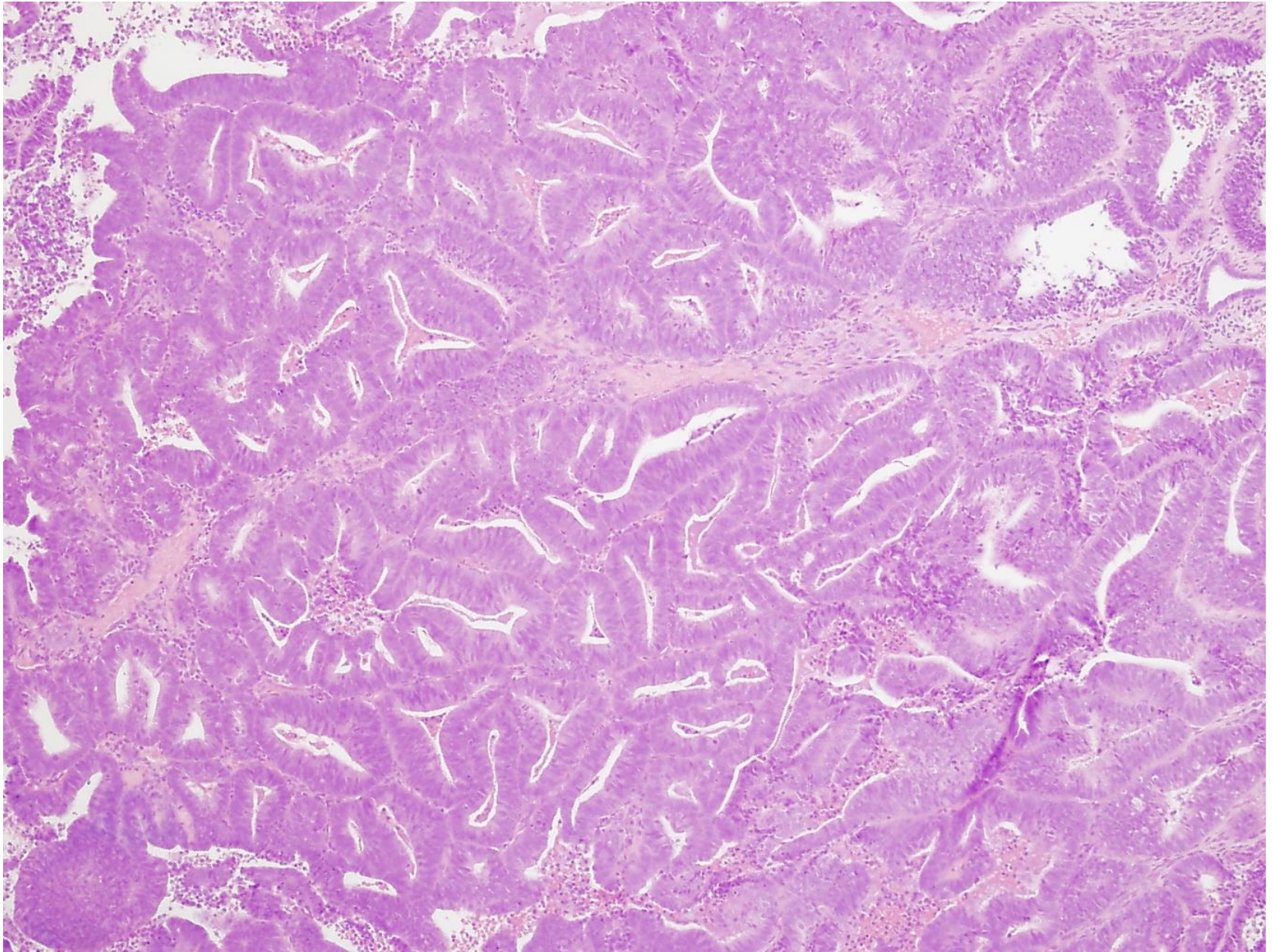


Endometrioid carcinoma

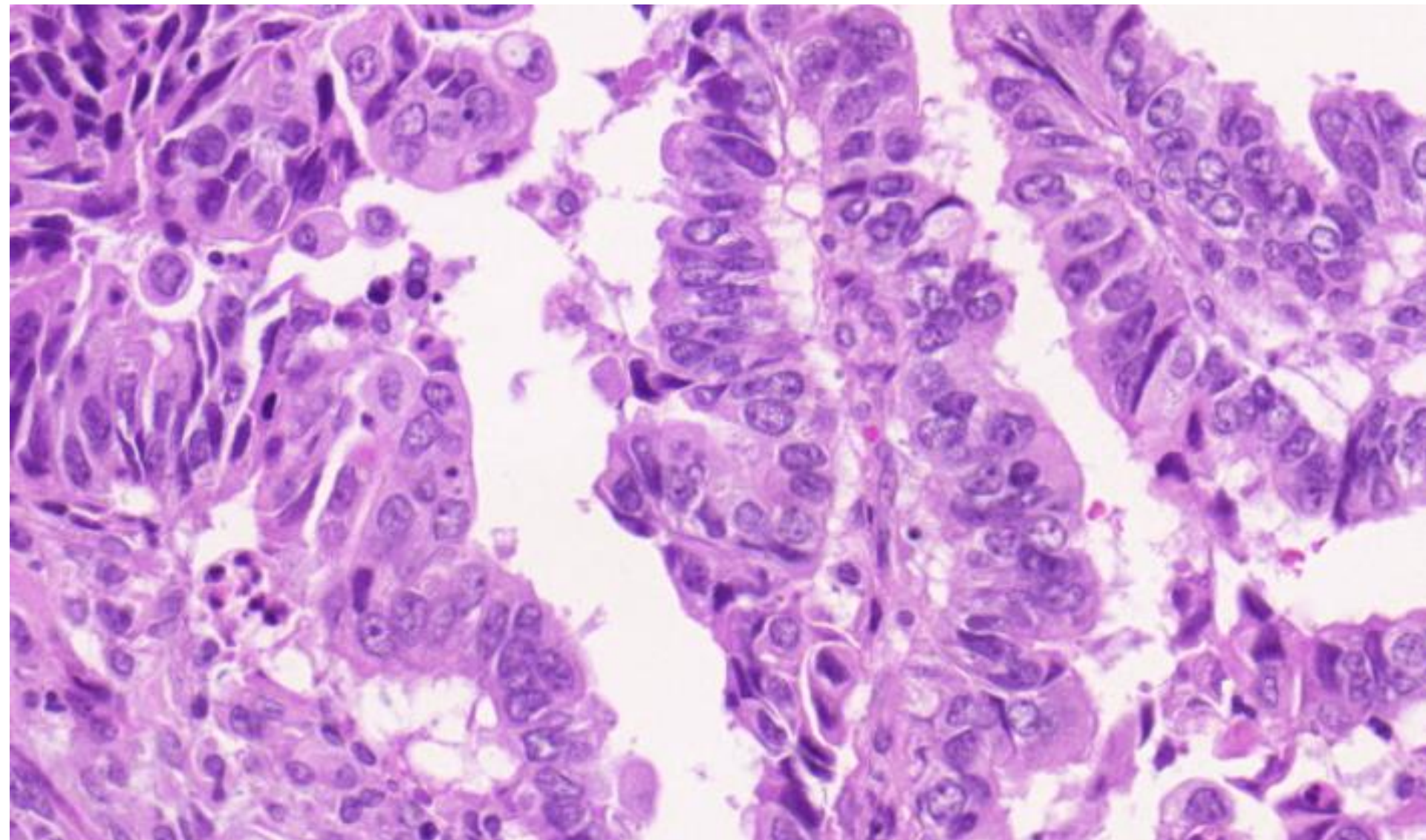
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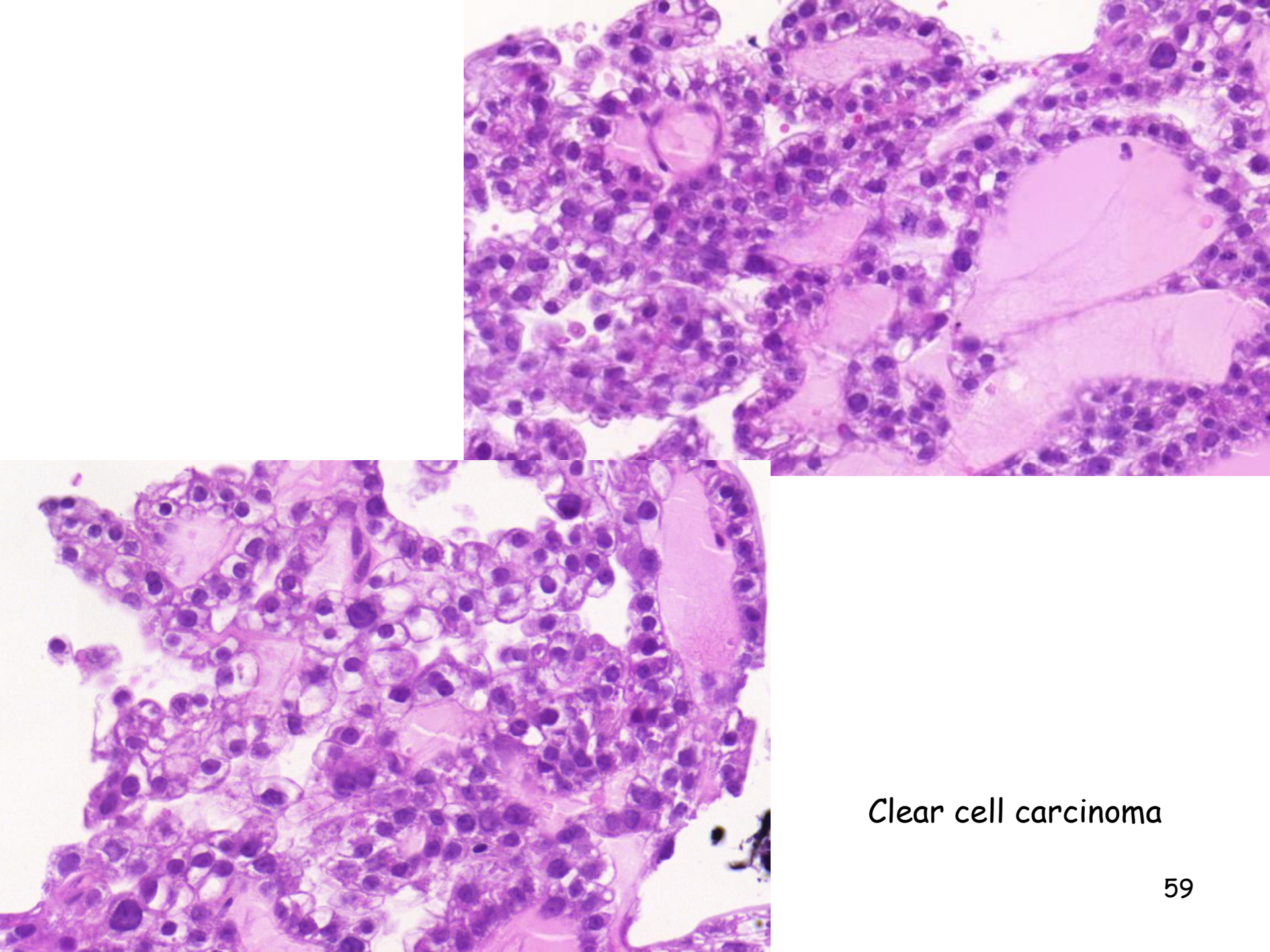
Endometrioid cc



Endometrioid carcinoma (Grade1)



Papillaris struktúrák, high grade cytomorfológia- Serosus carcinoma



Clear cell carcinoma



A méhtest daganatai

Kiindulás helye		Benignus	Malignus
Endometrium	Endometrialis mirigyek	-	Endometrioid carcinoma Serous cc Clear cell cc
	Endometrialis stroma	Stromalis nodulus	Stroma sarcoma
	Endometrialis mirigyek és stroma	Adenofibroma Adenomyoma	Carcinosarcoma Adenosarcoma
Myometrium		Leiomyoma	Leiomyosarcoma

WHO classification of tumours of the uterine corpus

Endometrial epithelial tumours and precursors

	Endometrial hyperplasia without atypia
8380/2	Atypical hyperplasia of the endometrium
8380/3	Endometrioid adenocarcinoma NOS
	<i>POLE</i> -ultramutated endometrioid carcinoma
	Mismatch repair-deficient endometrioid carcinoma
	p53-mutant endometrioid carcinoma
	No specific molecular profile (NSMP) endometrioid carcinoma
8441/3	Serous carcinoma NOS
8310/3	Clear cell adenocarcinoma NOS
8020/3	Carcinoma, undifferentiated, NOS
8323/3	Mixed cell adenocarcinoma
9110/3	Mesonephric adenocarcinoma
8070/3	Squamous cell carcinoma NOS
8144/3	Mucinous carcinoma, intestinal type
9111/3*	Mesonephric-like adenocarcinoma
8980/3	Carcinosarcoma NOS

Tumour-like lesions

Endometrial polyp
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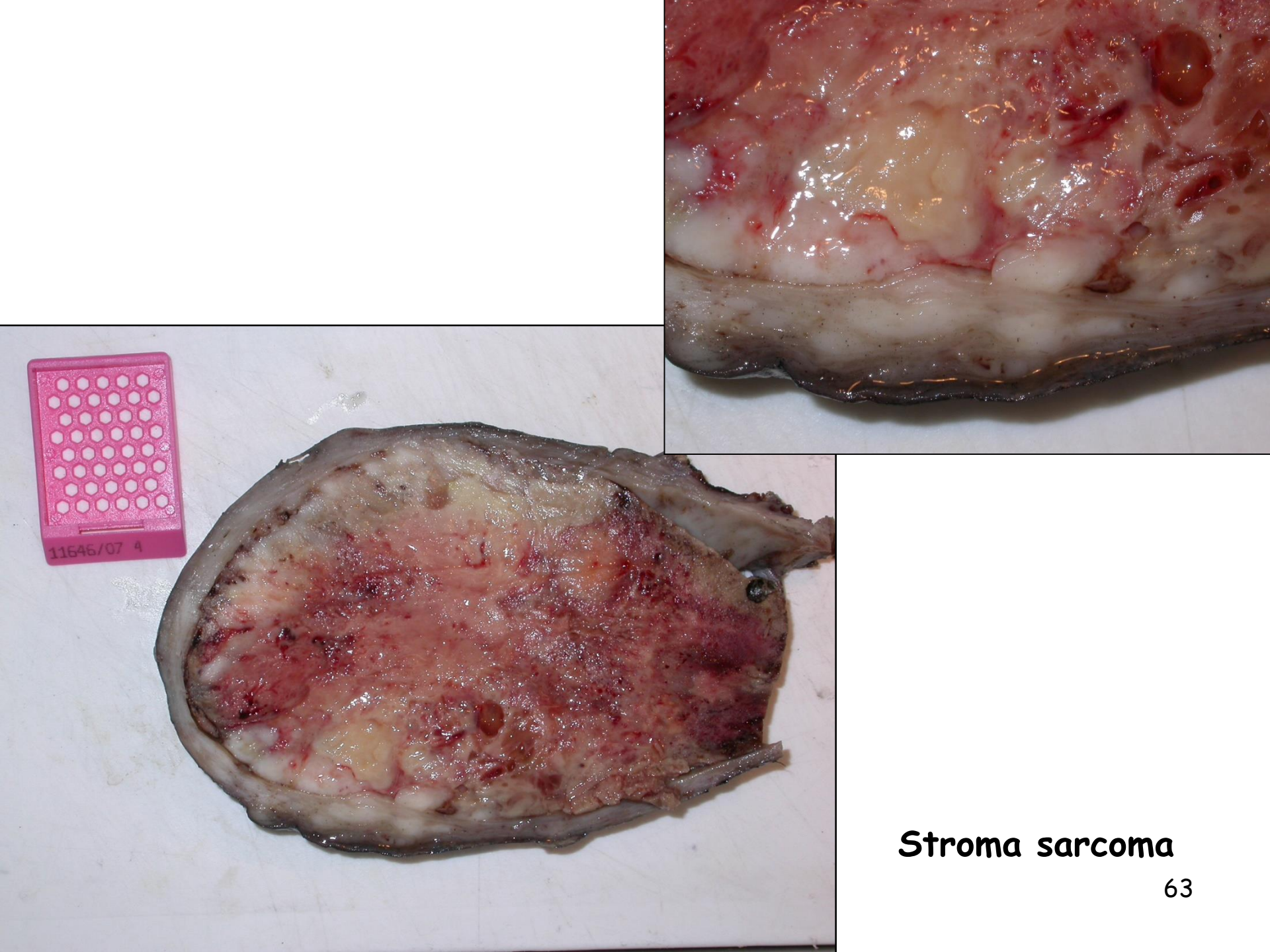
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WHO, 5. kiadás, 2020

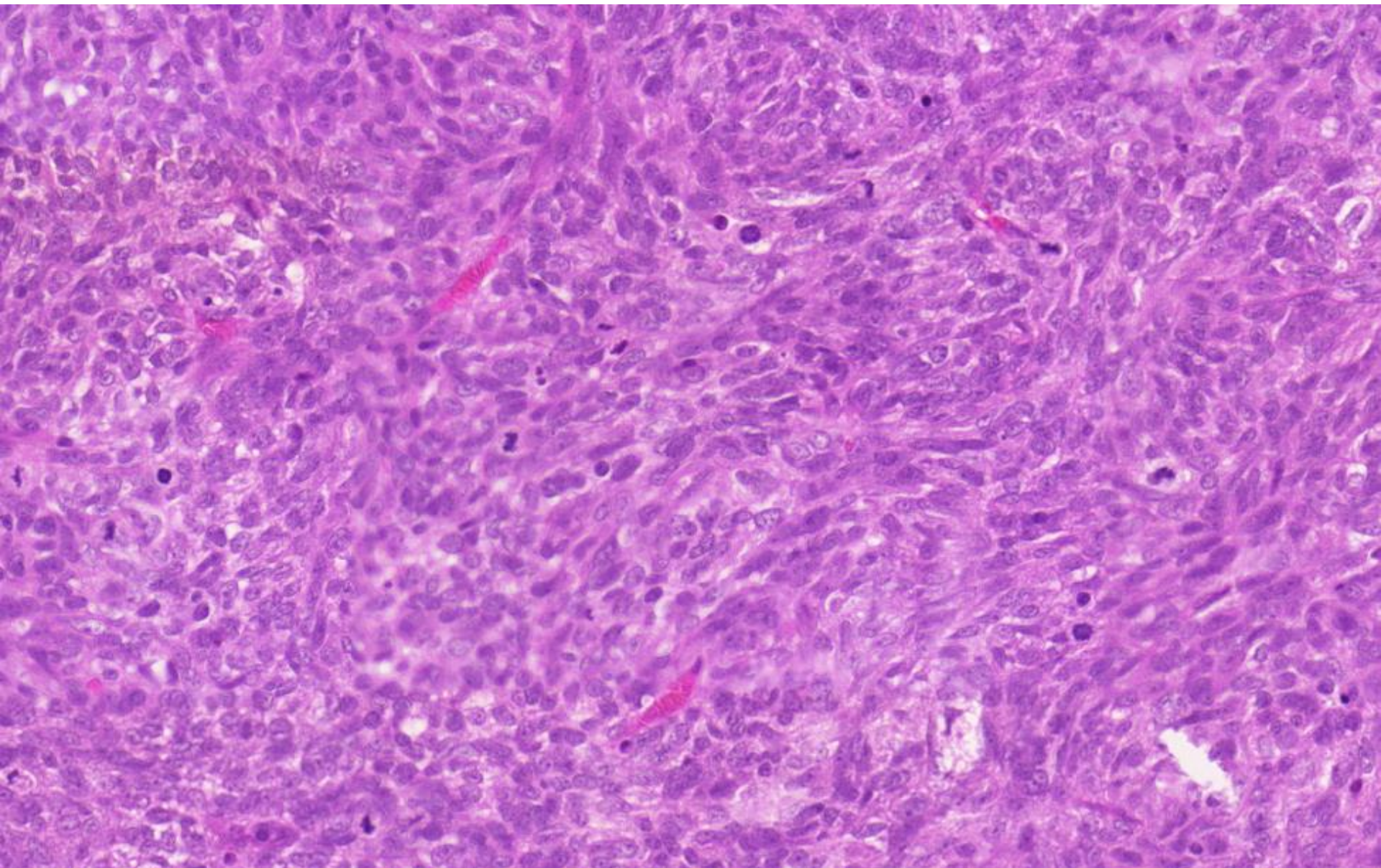
Endometrialis stromalis tumorok

- középkorú nők (átlag 45 év)
- a daganatsejtek az endometrialis stroma sejtjeire emlékeztetnek
- **Endometrialis stromalis nodulus**
- **Endometrialis stroma sarcoma**
 - alacsony és magas malignitású





Stroma sarcoma



Endometrialis stroma sarcoma

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WHO, 5. kiadás, 2020

Adenosarcoma

- a kevert, epithelialis és mesenchymalis tumorok alacsony malignitású formája
- MA: polypoid massa, amely kitölti a méh üregét
- MI: szabálytalan alakú mirigyek (cytologiai atypia nélkül!) és malignus stroma (az emlő phylloid tumorára emlékeztet)

Carcinosarcoma

(régebben Malignus kevert Müllercső daganat- MMMT)



- postmenopausa
- rendellenes méhvérzés, megnagyobbodott méh
- MA: nagy, puha, polypoid massa
- MI: carcinoma és sarcoma- szerű területek keveréke
 - carcinoma: high grade, differenciálatlan, necrosis, bevérzés
 - sarcoma: homológ vagy heterológ elemek (harántcsíkt izom, porc, csont, zsír)
 - Carcinoma, mely epithelialis-mesenchymalis transformatio-t (EMT) mutat



Carcinosarcoma-uterus

5560

Myometrium

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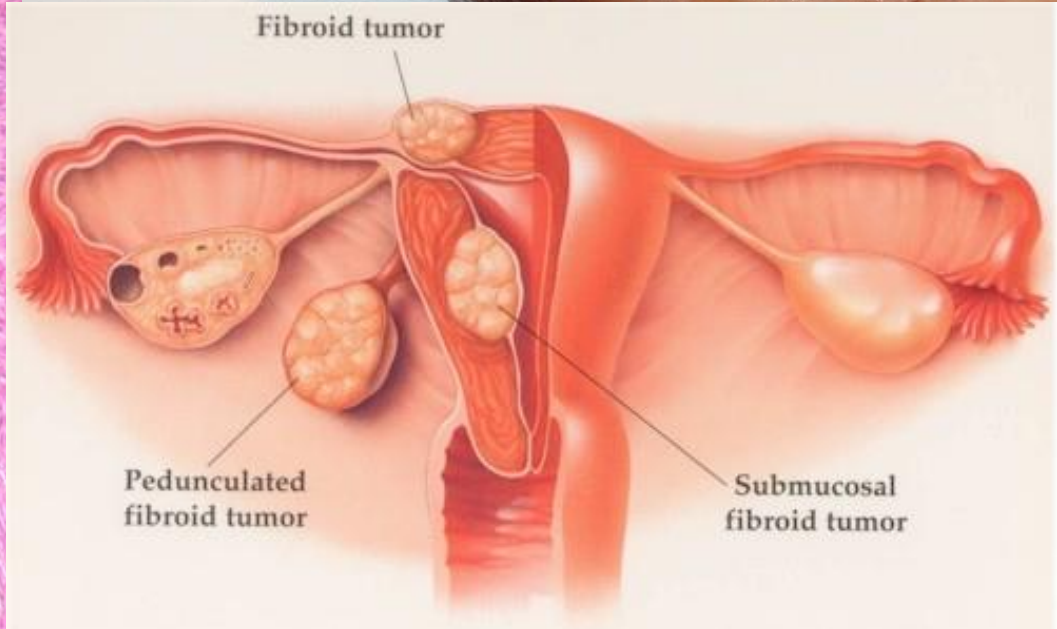
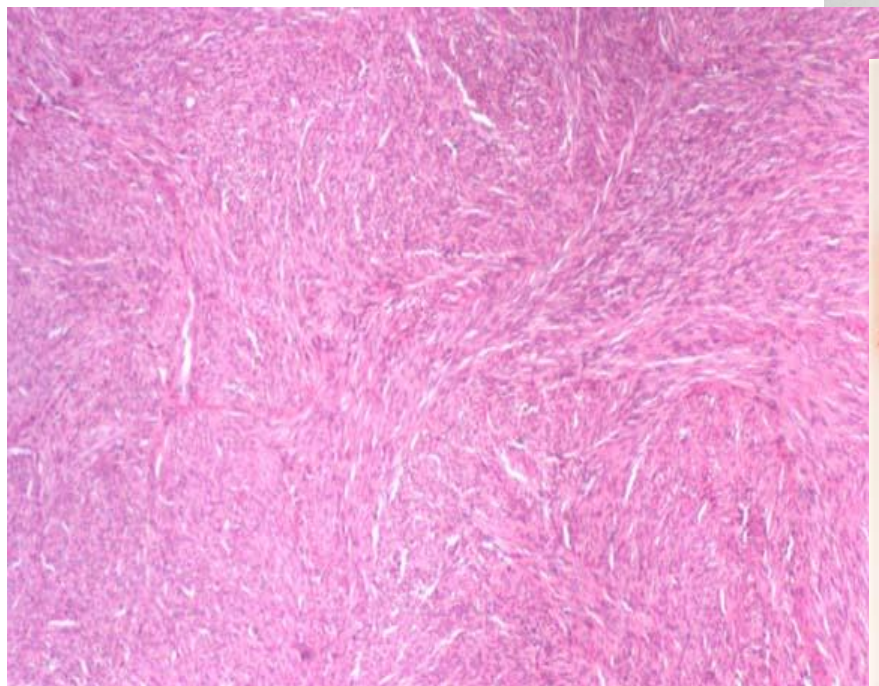
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Myometrium tumorok

- **Leiomyoma**

- az 50 év feletti nők 40%-t érinti
- **elhelyezkedés:** submucosus, intramuralis, subserosus
- **tünetek:** vérzészavar, fájdalom, spontán abortusz, infertilitás, gyakori vizelési inger
- MA: jól körülhatárolt, kerek, szürkés-fehér örvényes szerkezetű göb
- MA: monomorf orsósejtek örvényes rajtzolata, egy-egy mitosis

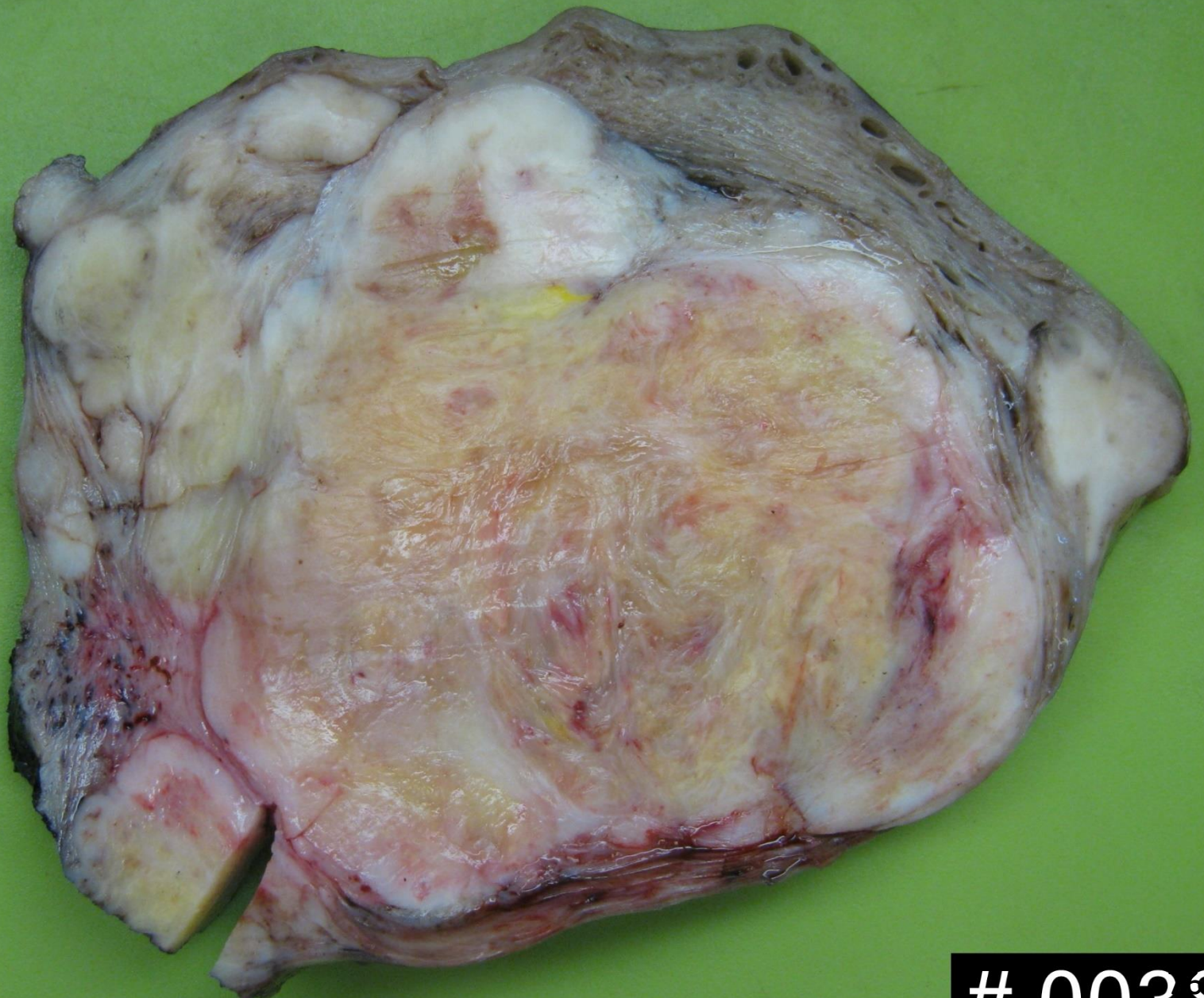




Myometrium tumorok

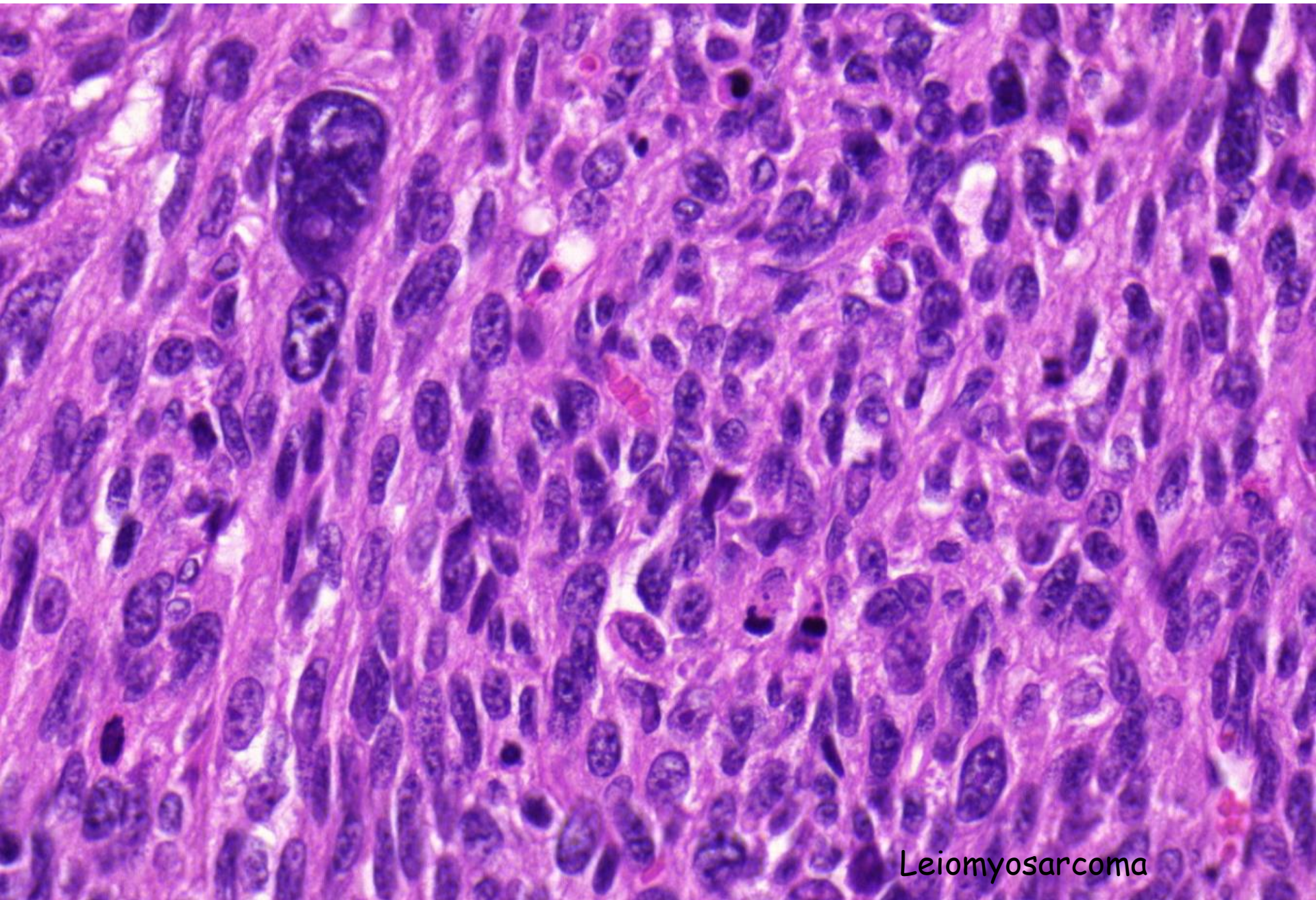
- **Leiomyosarcoma**

- idősebb nők (átlag 55 év)
- **MA**: halhússzerű, necrosist, vérzést mutat
- **MI**: hypercellularis, nuclearis atypia, pleomorphismus, emelkedett mitoticus aktivitás, atypusos mitosis, necrosis
- **Metastasis**: kismedence, tüdő, csont, agy, de a nyirokcsomó metastasis nem jellemző!



Leiomyosarcoma-uterus

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Leiomyosarcoma