

PATHOLOGY OF THE FEMALE GENITAL TRACT

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Research***

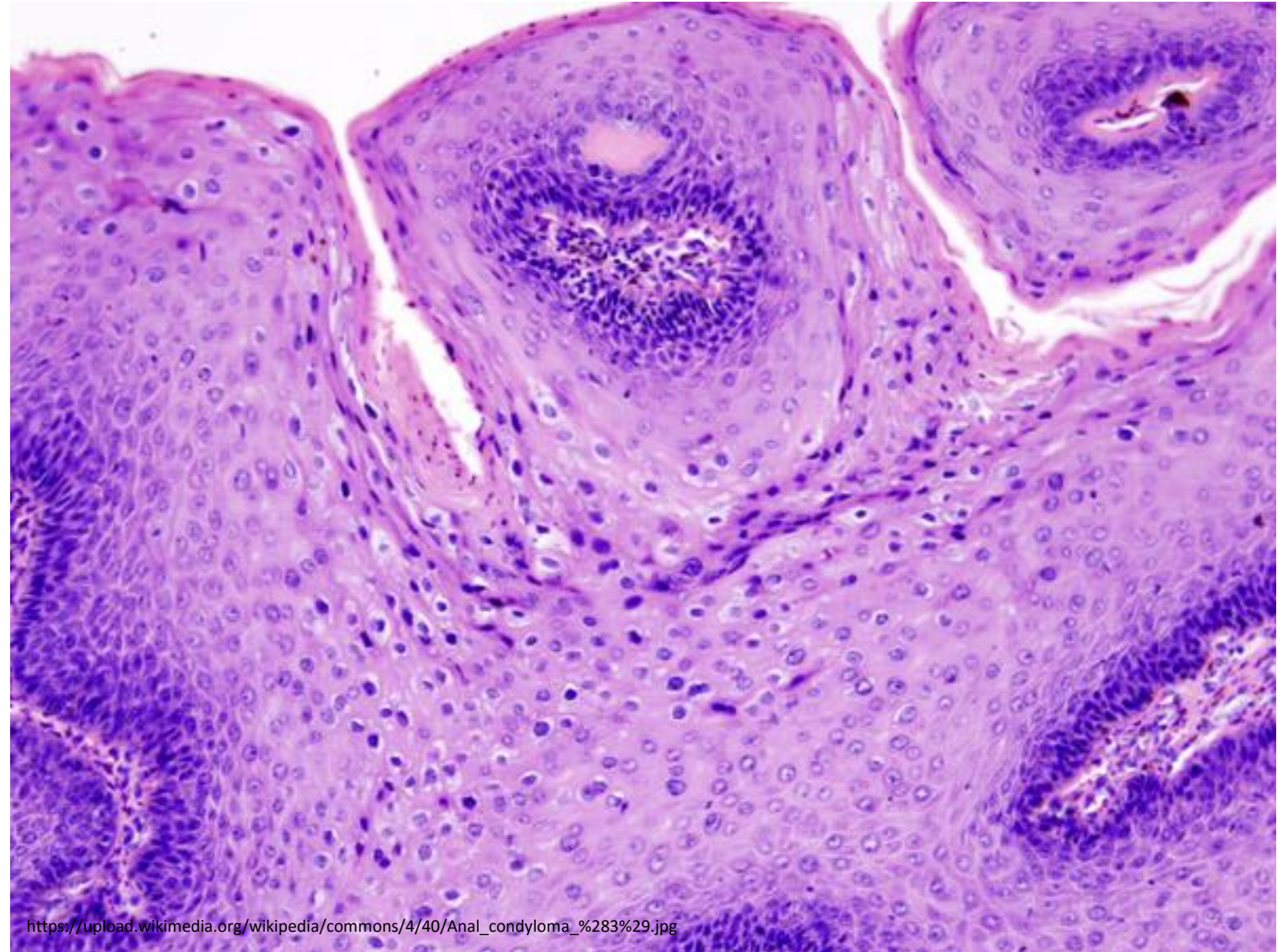
2020.



VULVA

BENIGN TUMORS OF THE VULVA: CONDYLOMA (ACUMINATUM)

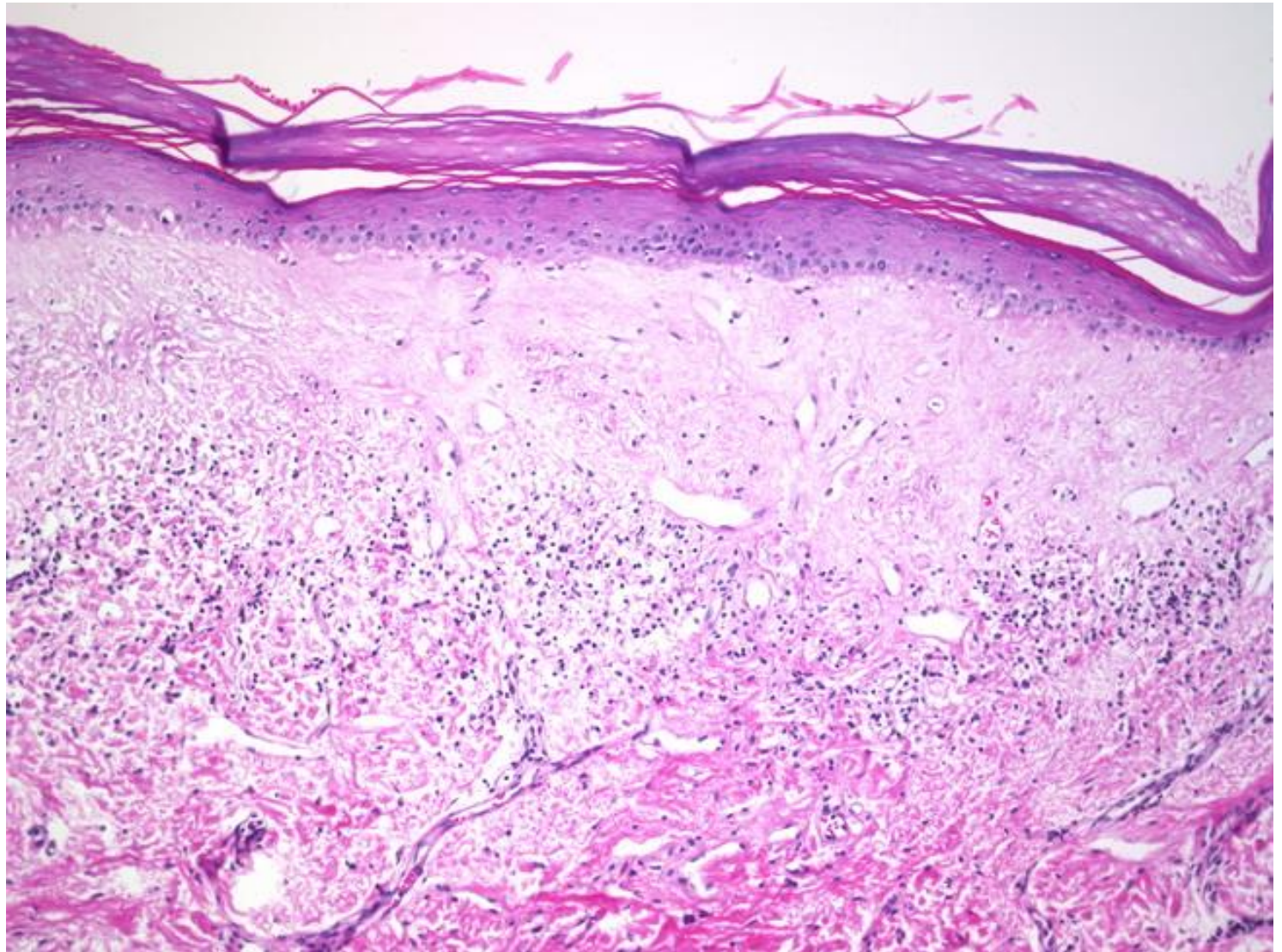
**HPV-associated:
LSIL!**



VULVA – LICHEN SCLEROSUS



After menopause
Before puberty



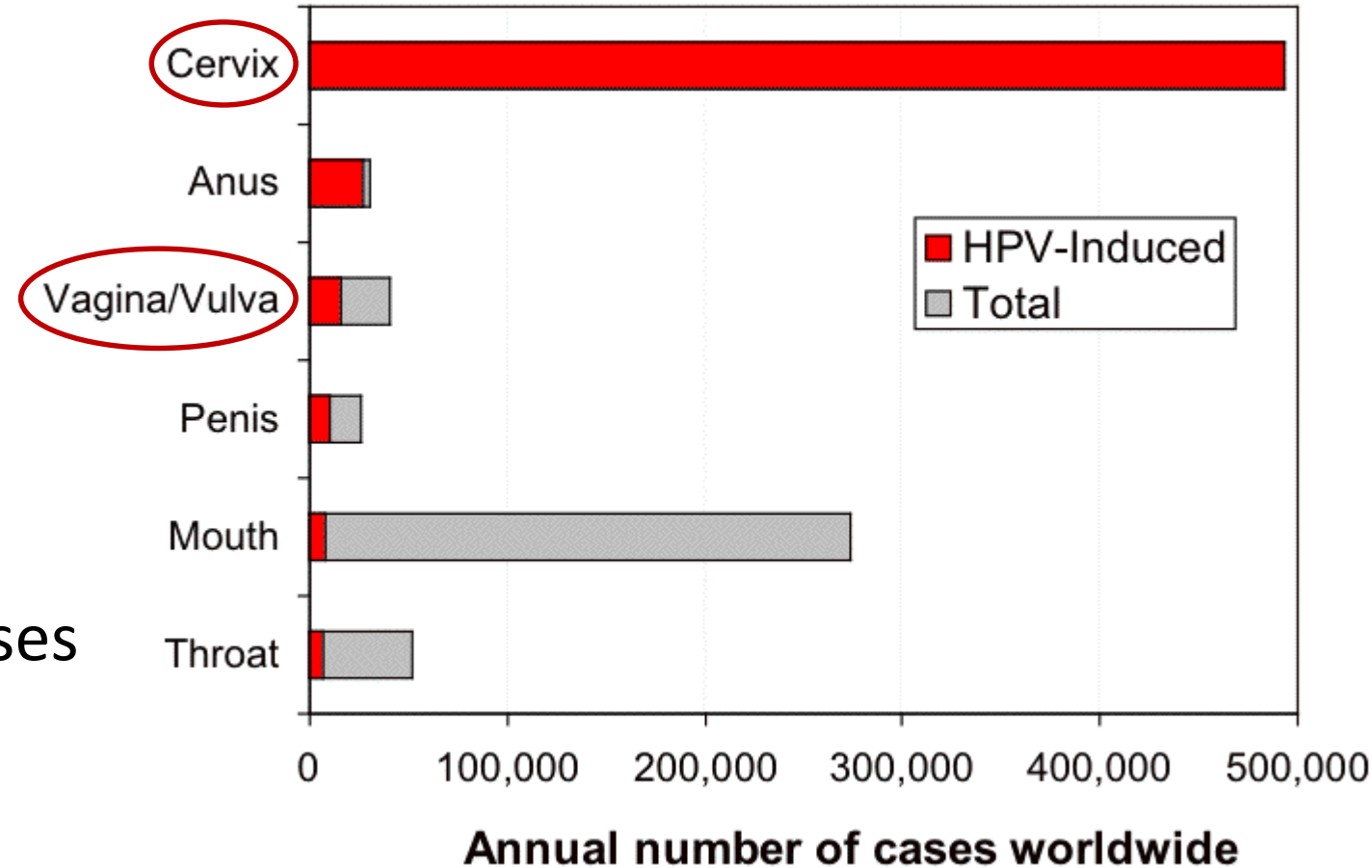
http://www.webpathology.com/slides-13/slides/Vulva_LichenSclerosusEtAtrophicus1.jpg

UTERINE CERVIX

TUMORS INDUCED BY HUMAN PAPILLOMAVIRUS

RISK FACTORS

- Early sexual activity
- High number of sexual partners
- HPV-infected partner
- Immunosuppression
- Smoking
- Other sexually transmitted diseases



HPV-RELATED LESIONS IN THE FEMALE GENITAL TRACT

low risk types

HPV-6, 11

condyloma (acuminatum)
(= LSIL!)

high risk types

HPV-16, 18, 31, 45

Cervical Intraepithelial Neoplasia
(CIN)

Vaginal Intraepithelial Neoplasia
(VaIN)

Vulvar Intraepithelial Neoplasia
(VIN)

Squamous cell carcinoma – vulva, vagina

Invasive carcinomas of the cervix

**Squamous
Intraepithelial
Lesion (SIL)**

CIN-1

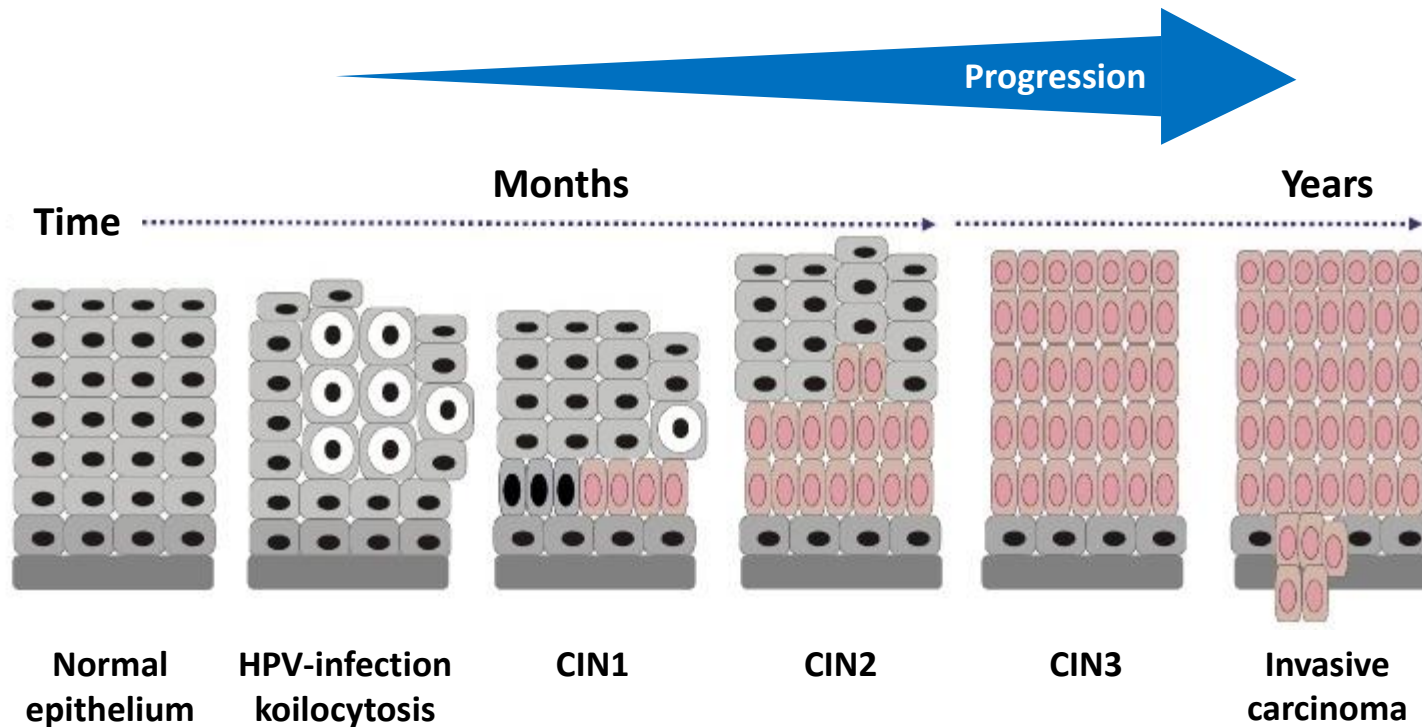
**Low-grade SIL
(LSIL)**

CIN-2

CIN-3

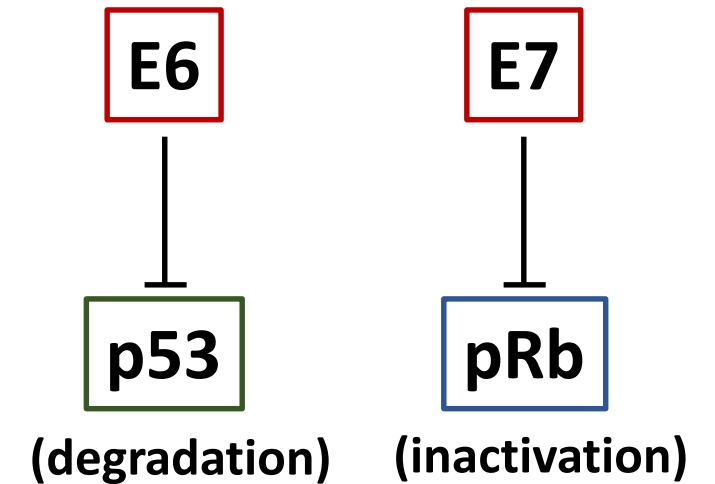
**High-grade SIL
(HSIL)**

CERVICAL HPV INFECTION



Productive infection
Low-grade squamous
intraepithelial lesion
(ASCUS/LSIL)

Genomic integration
High-grade squamous
intraepithelial lesion (HSIL)



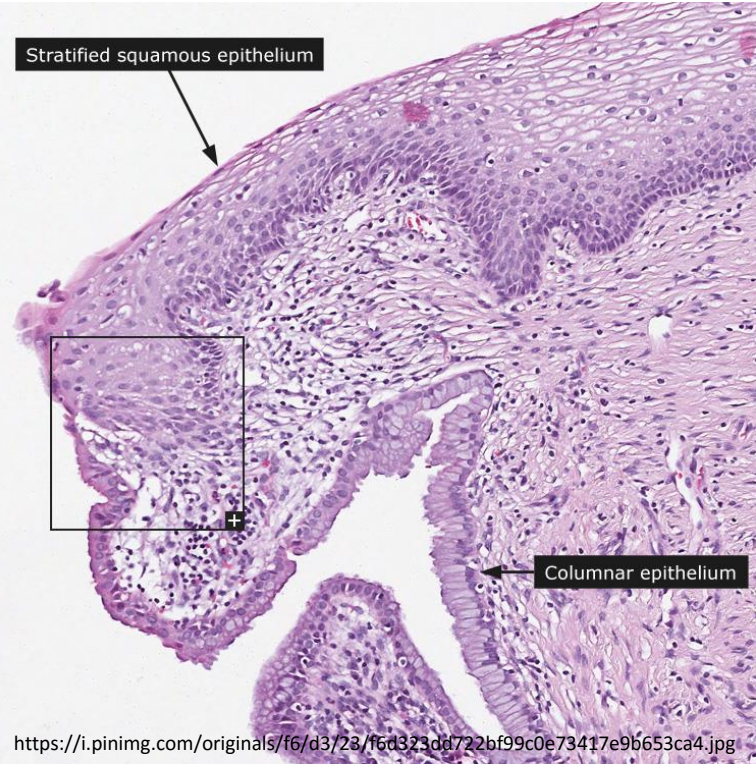
Invasive carcinoma

- Squamous cell carcinoma (75-90%)
- Adenocarcinoma (5-20%)
- Neuroendocrine carcinoma (<5%)

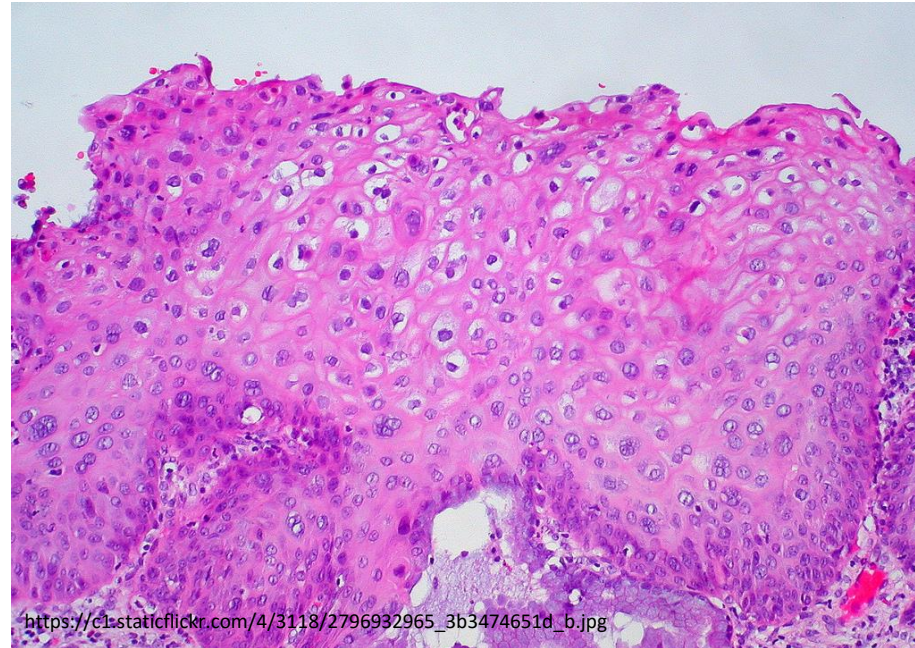
ASCUS: atypical squamous cells of unknown significance

Burd EM, Clin Microbiol Rev 2003; 16:1-7.
Solomon D, et al. JAMA 2002; 287:2114-2119.

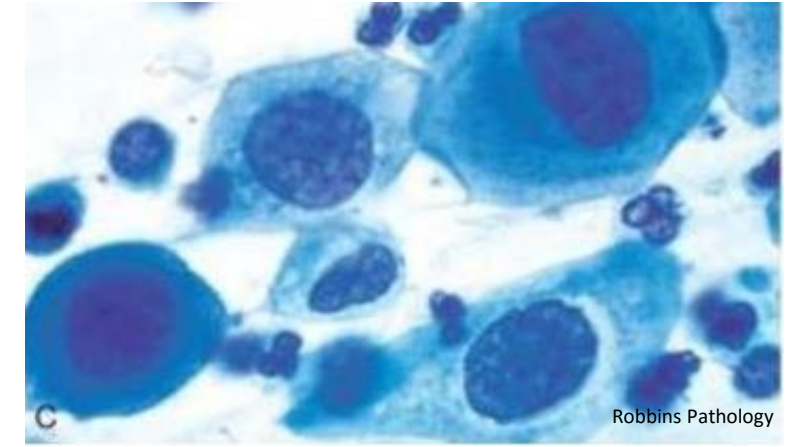
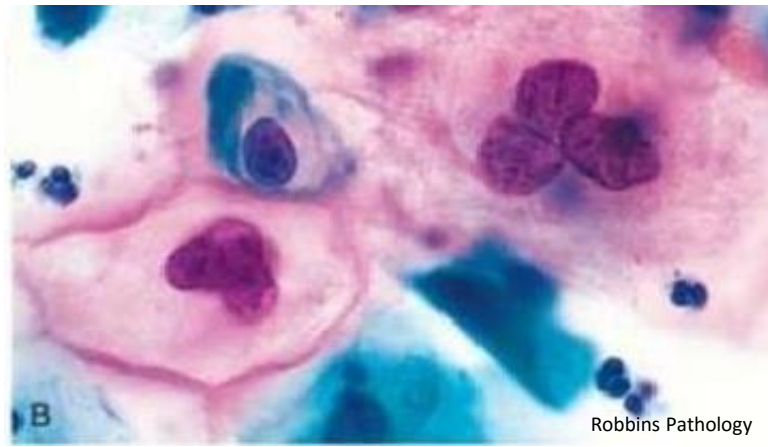
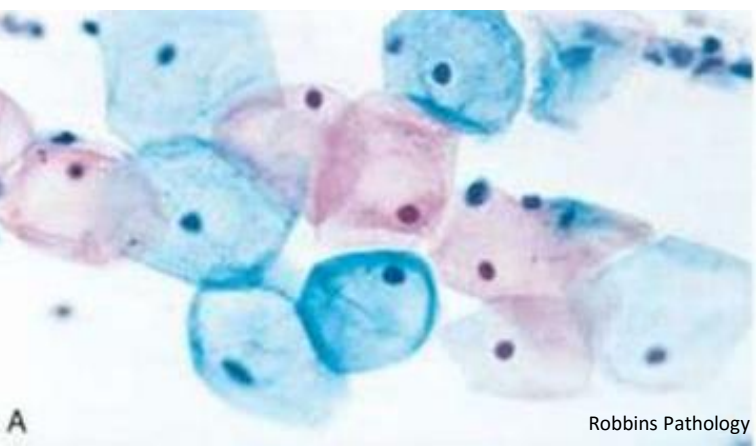
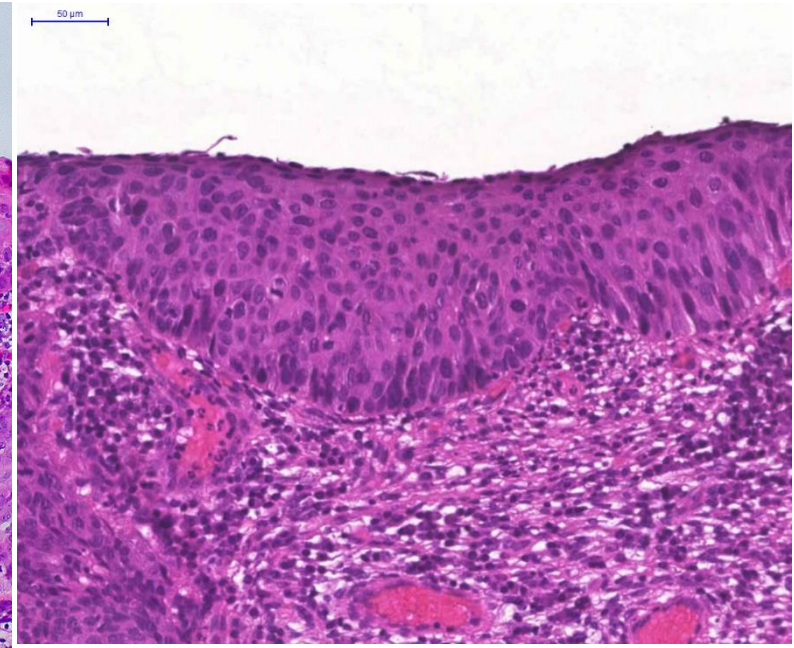
Normal cervix



Low-grade SIL (LSIL)
CIN-1; koilocytosis!



High-grade SIL (HSIL)
CIN-2, CIN-3; (in situ cc.)



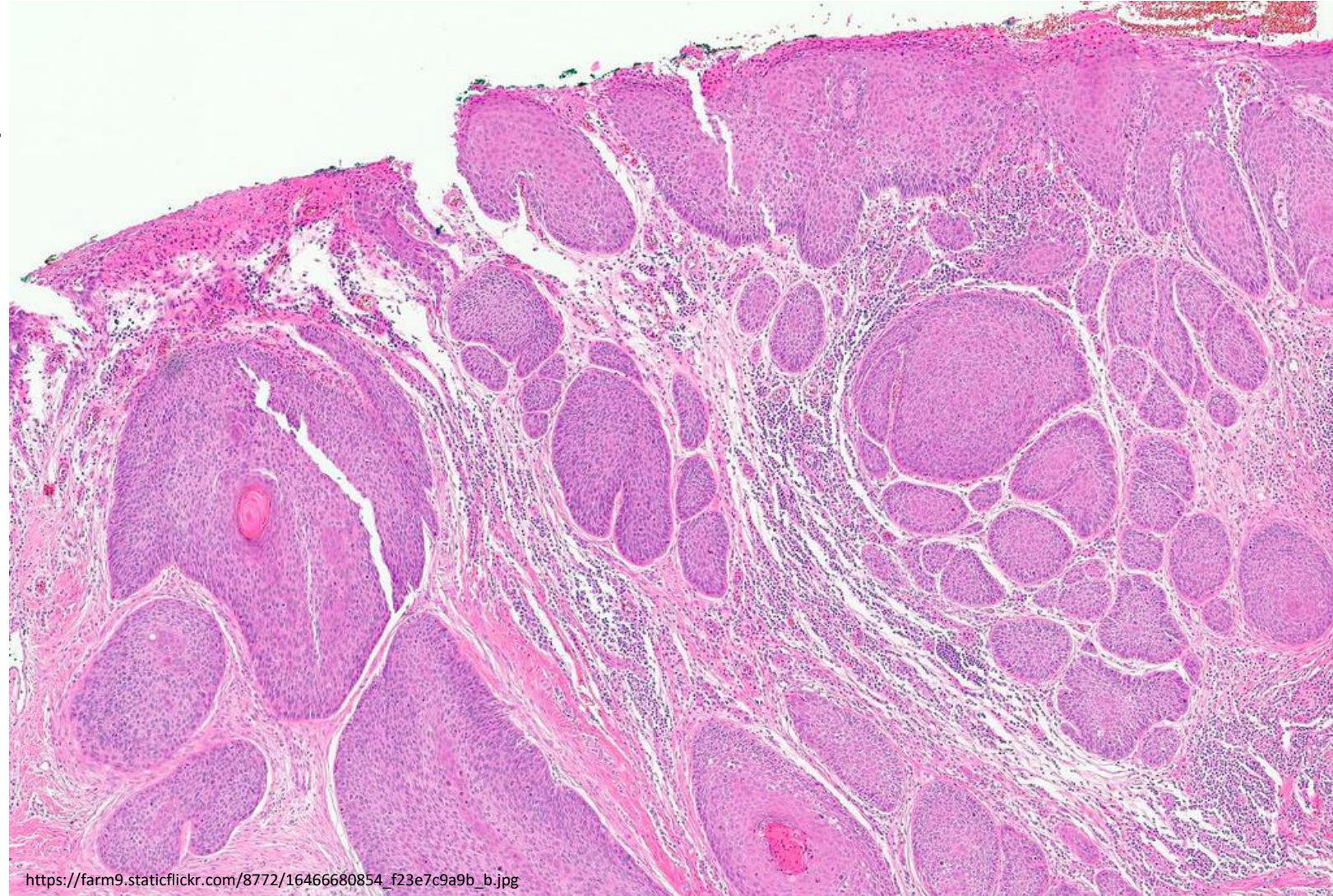
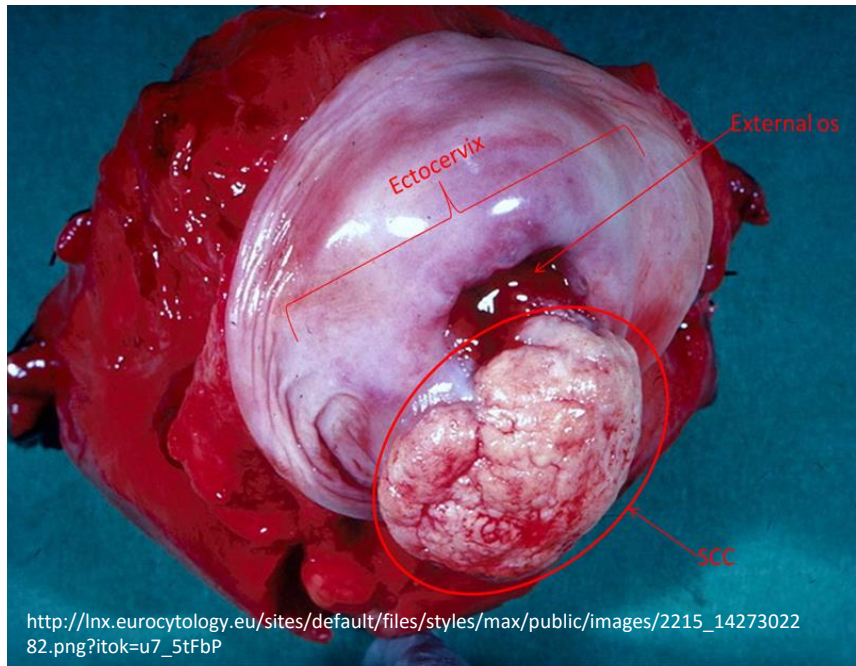
Papanicolaou smear

CERVICAL SQUAMOUS CELL CARCINOMA

Incidence:

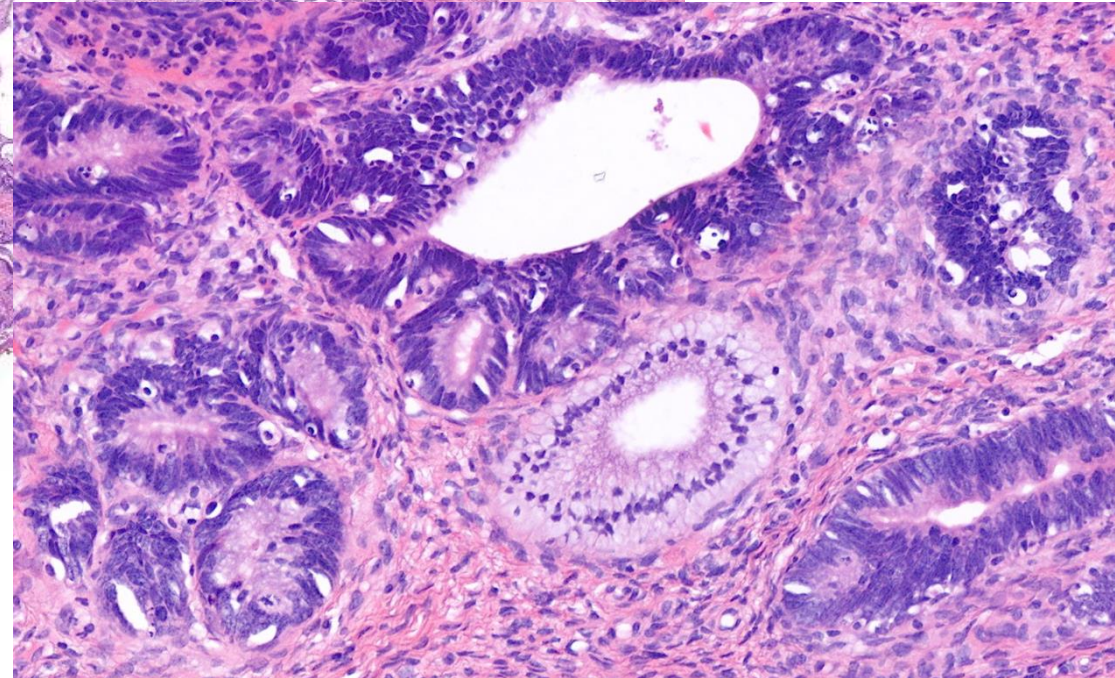
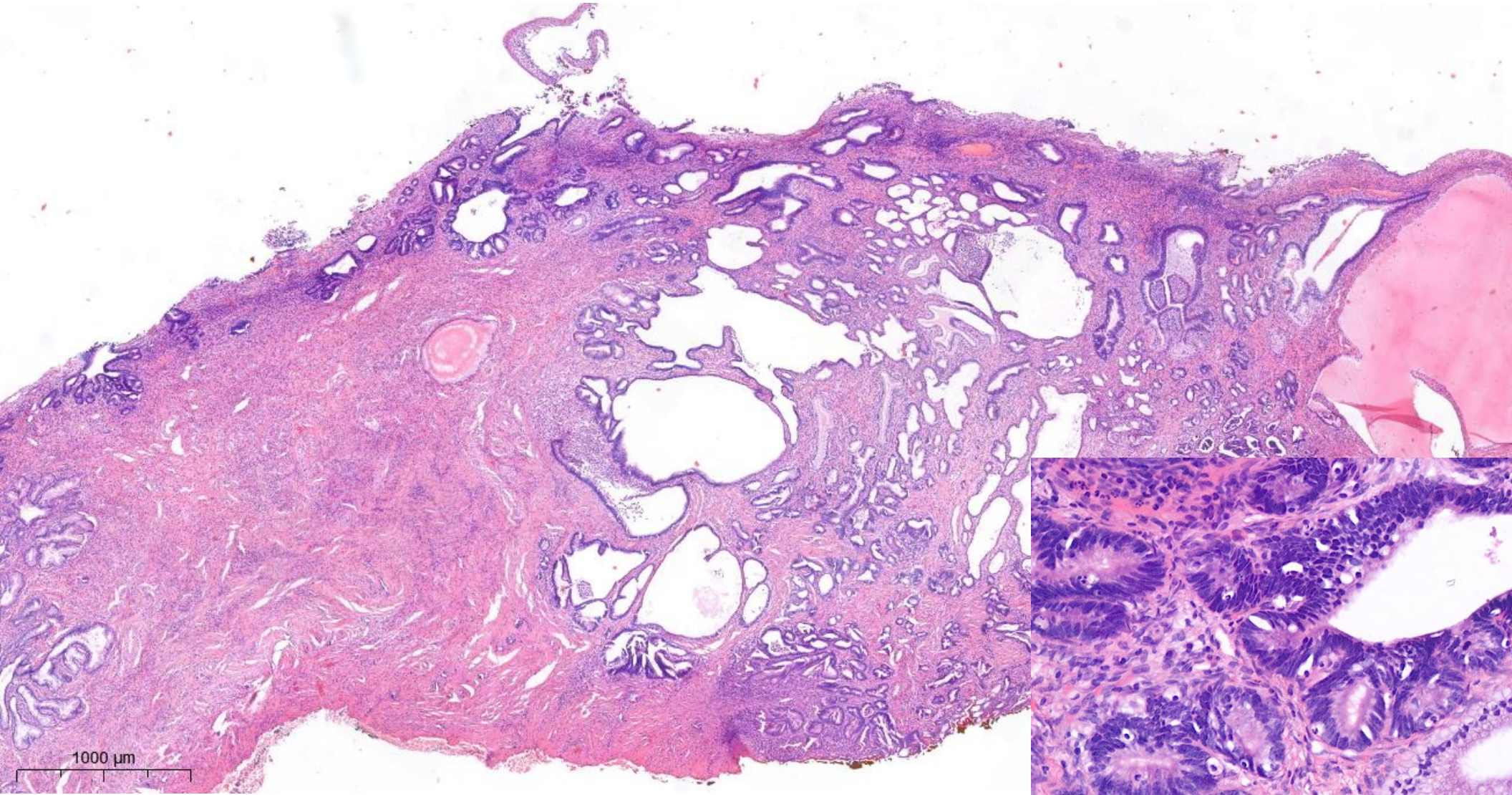
Worldwide: 1-100/100000 person

Hungary: 1000-1500 new cases/year
500 deaths/year

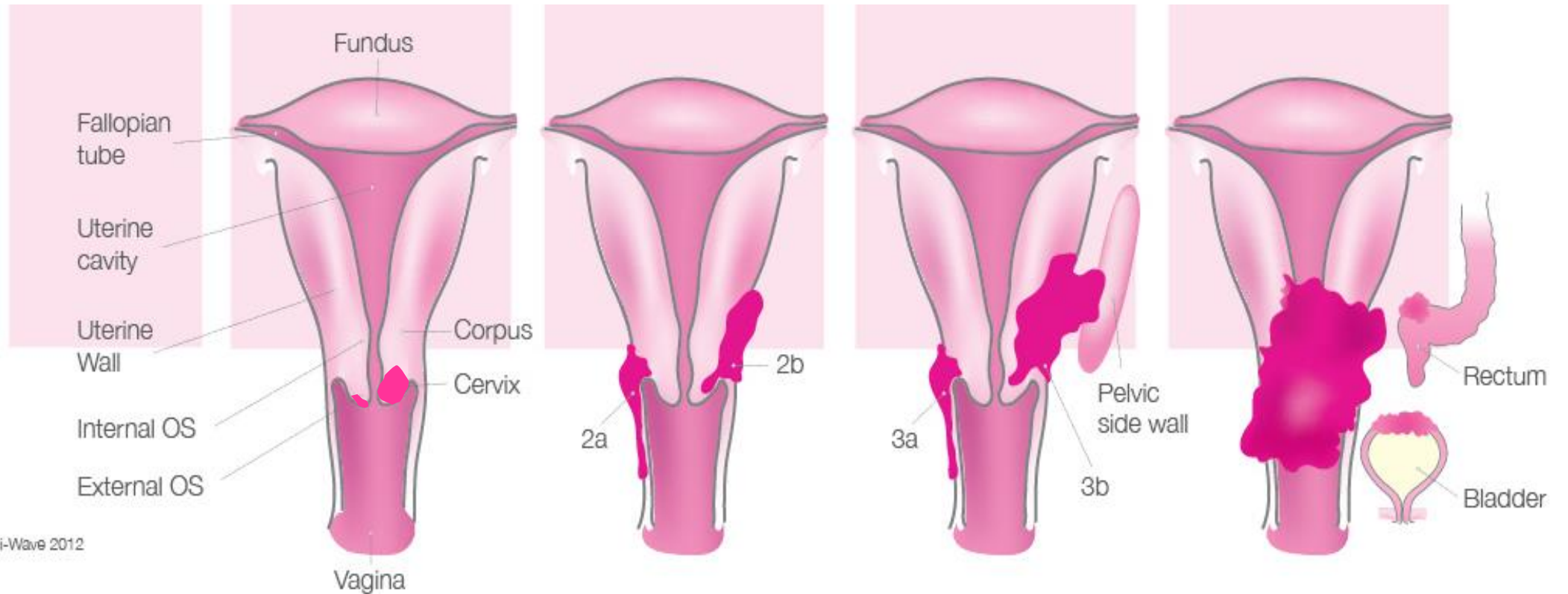


Surgical excision of the cervix with a fungating squamous cell carcinoma

CERVICAL ADENOCARCINOMA



CERVICAL CANCER – SPREAD



© Vagi-Moose & Vagi-Wave 2012

Pelvic lymph node metastasis
Distant metastasis

Prognosis, therapy: stage-dependent!

PREVENTION IS THE BEST THERAPY!

Anti-HPV vaccination:

Gardasil 9 vaccine

Screening:

Papanicolaou smear (~Pap-teszt)

Molecular HPV testing

Bethesda classification

~~(P0)
P1
P2
P3
P4
P5~~



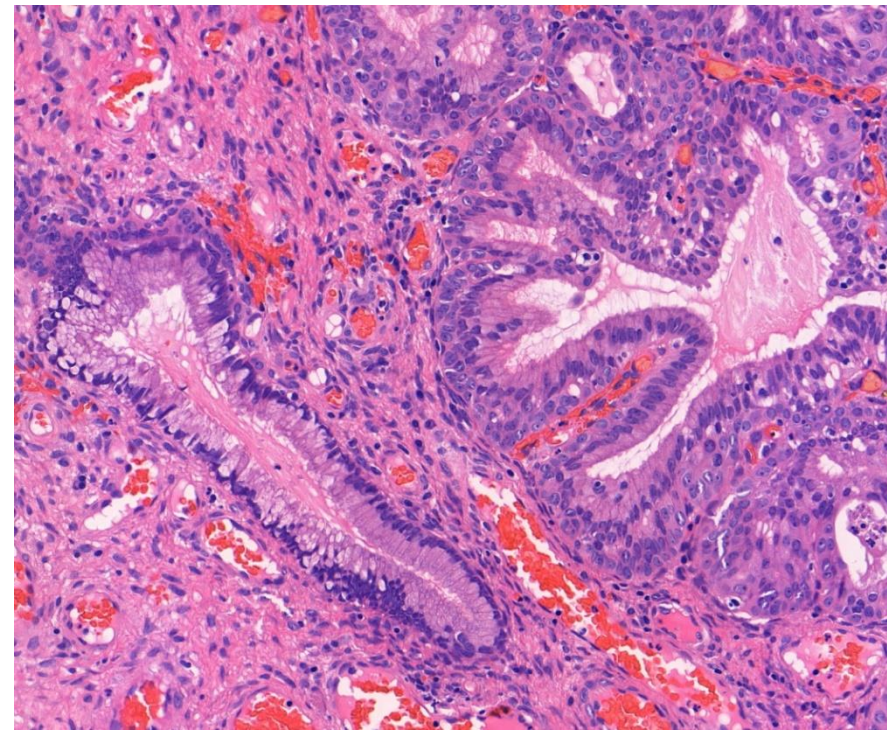
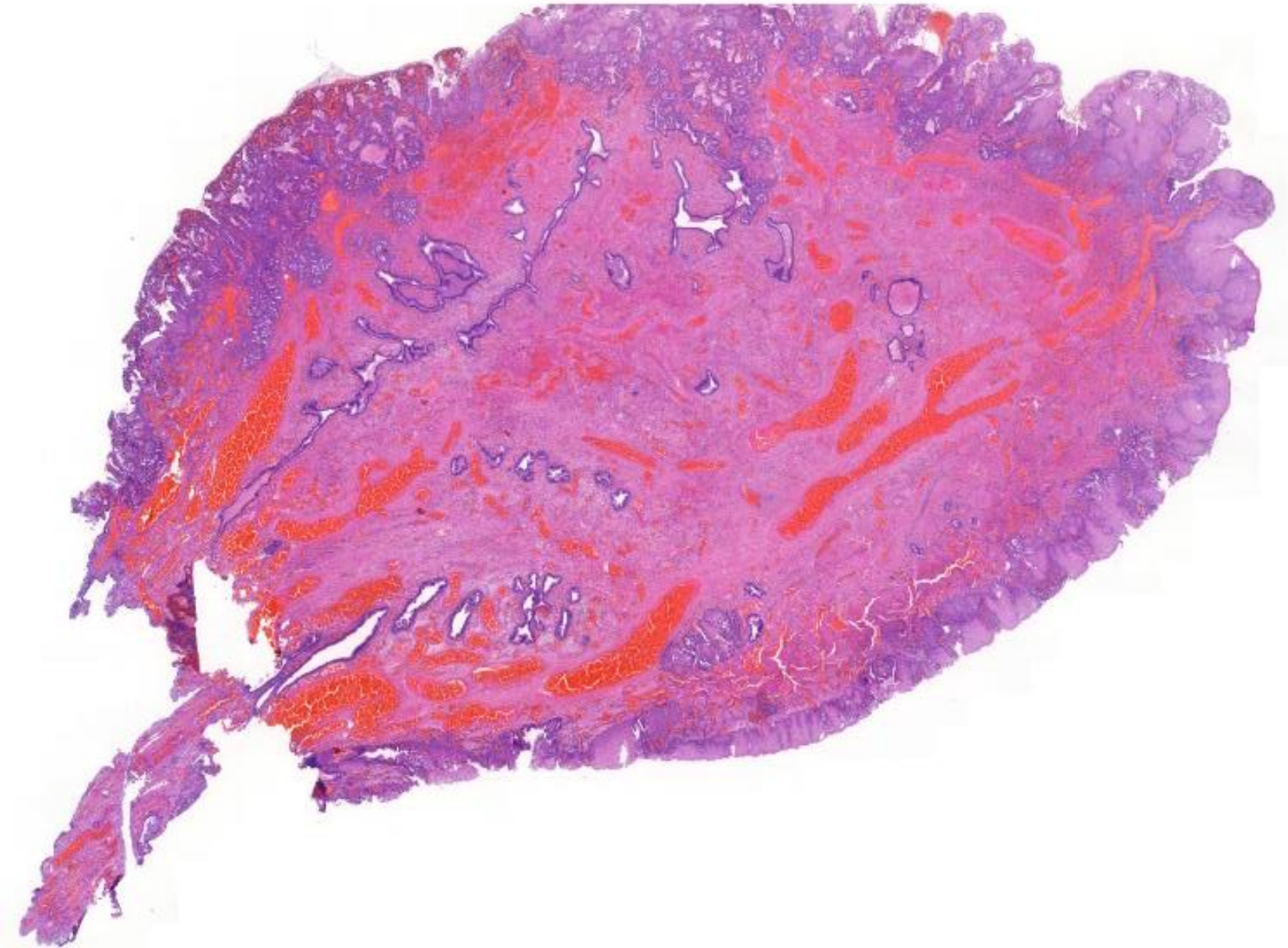
Squamous lesions

- LSIL
- HSIL
- Invasive carcinoma
- ASCUS, etc.

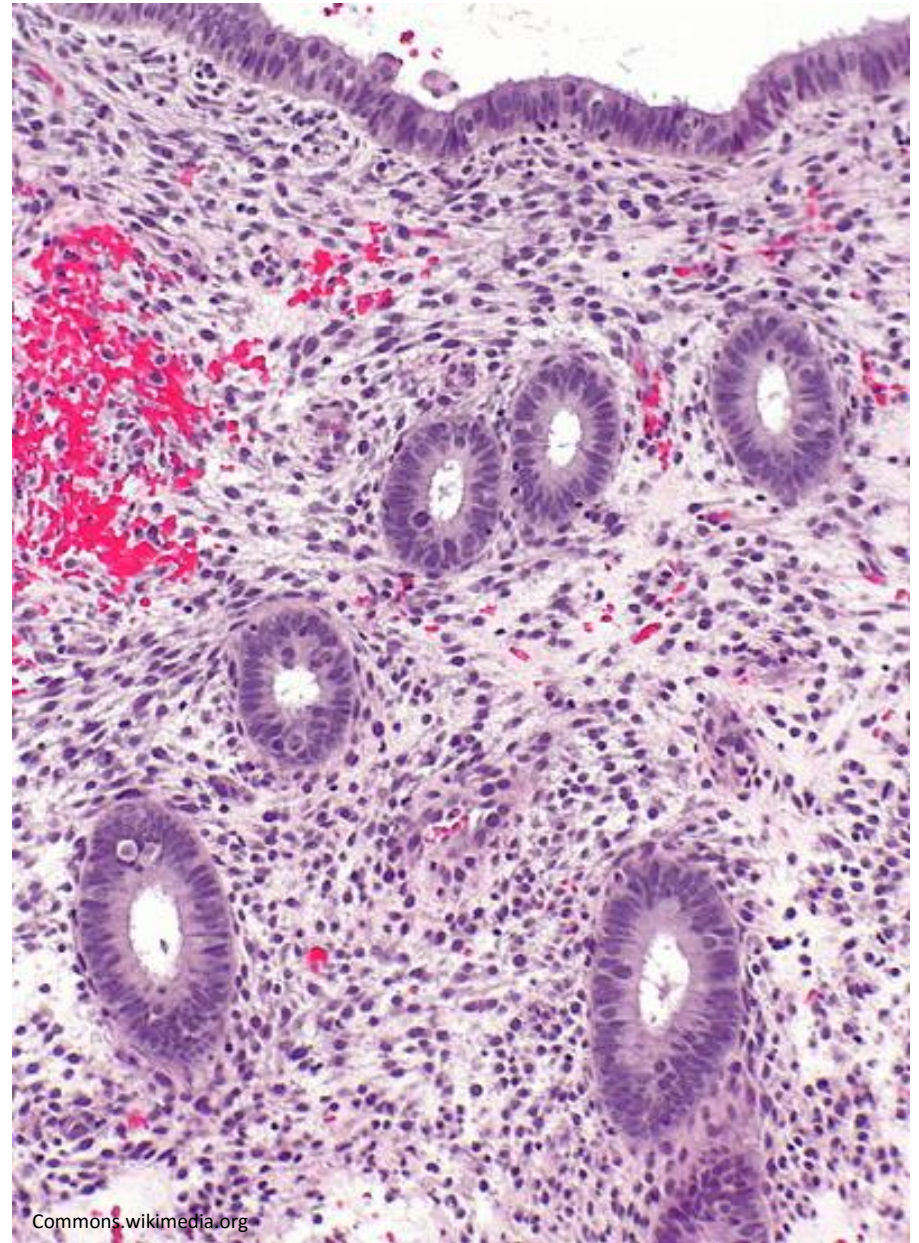
Glandular lesions

Other lesions (etc. microbes)

ENDOCERVICAL POLYP



UTERINE CORPUS



ABNORMAL UTERINE BLEEDING

Menorrhagia – heavy menstrual bleeding

Metrorrhagia – abnormal bleeding independent of menstruation

Reproductive age, perimenopause

Postmenopause

Anovulation

Dysfunctional bleeding (hormonal)

Excessive hormone effect

Submucosal leiomyoma

Adenomyosis

Pregnancy complications

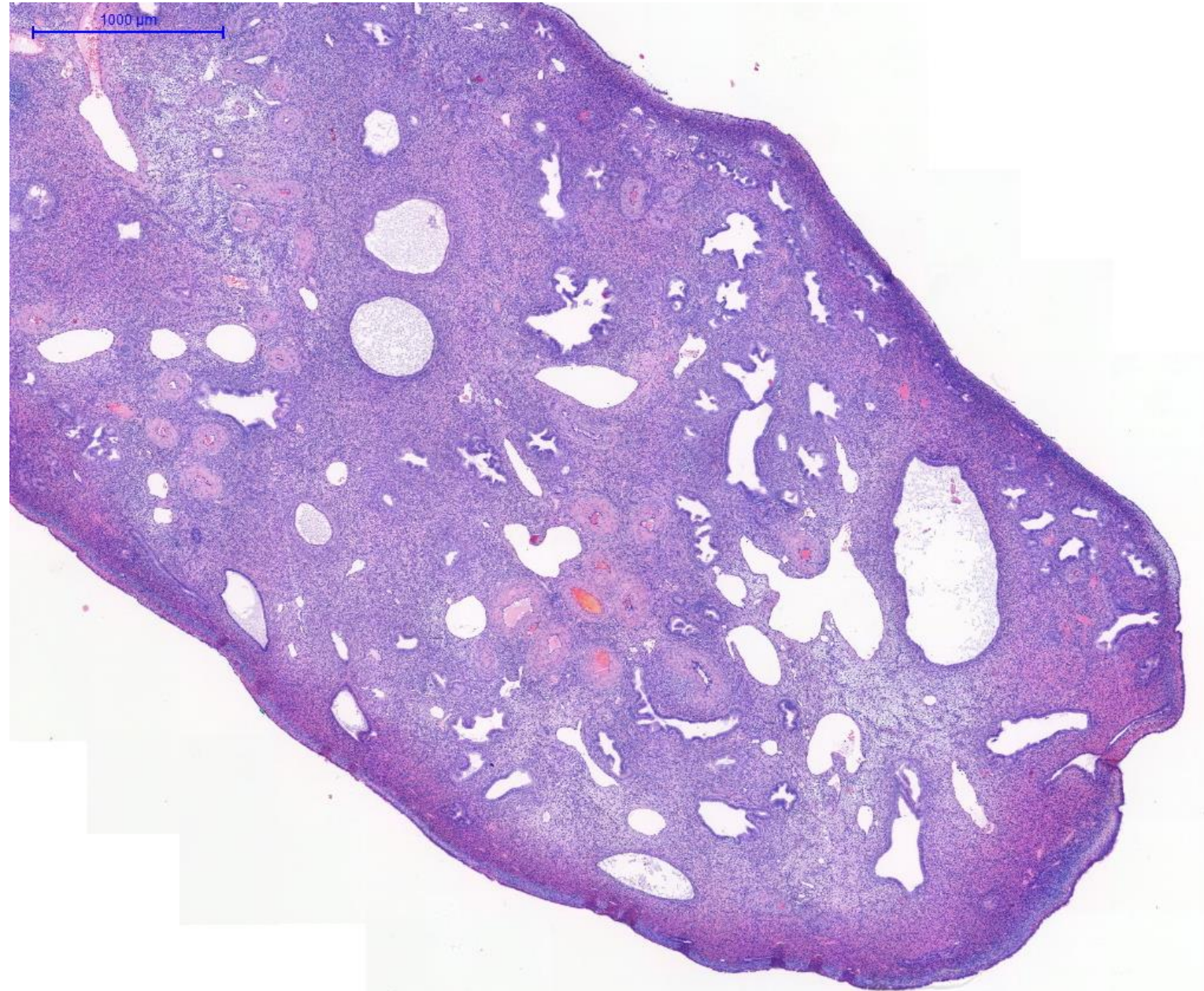
Endometrial atrophy

Endometrial/
endocervical polyp

Endometrial hyperplasia

Endometrial carcinoma

ENDOMETRIAL POLYP



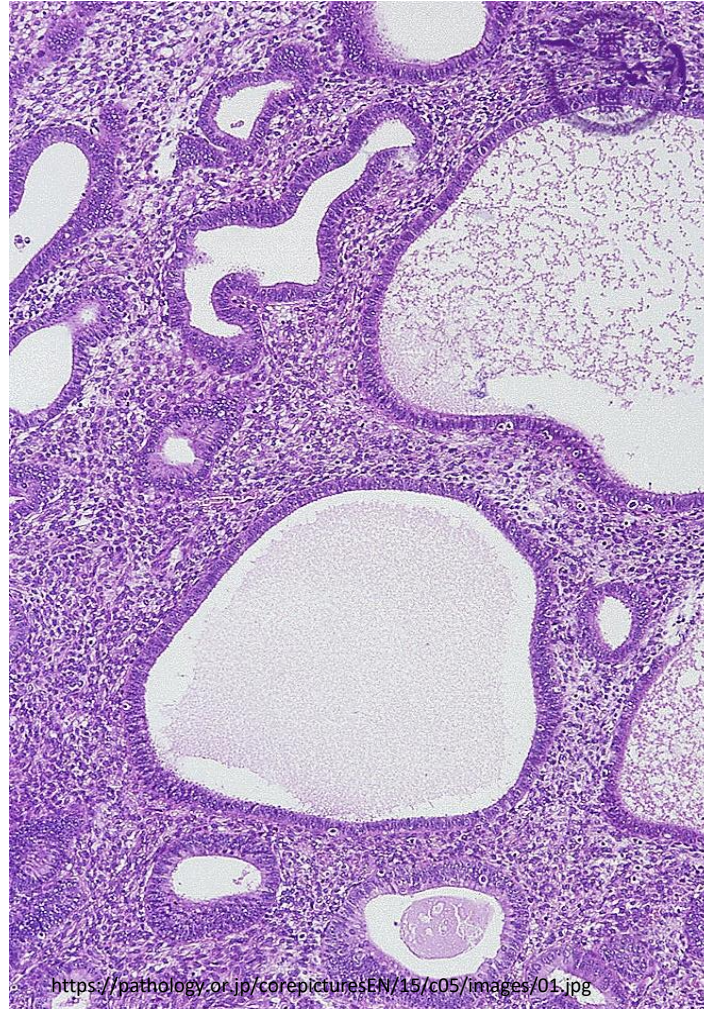
PROLIFERATIVE LESIONS OF THE ENDOMETRIUM

Disordered proliferation



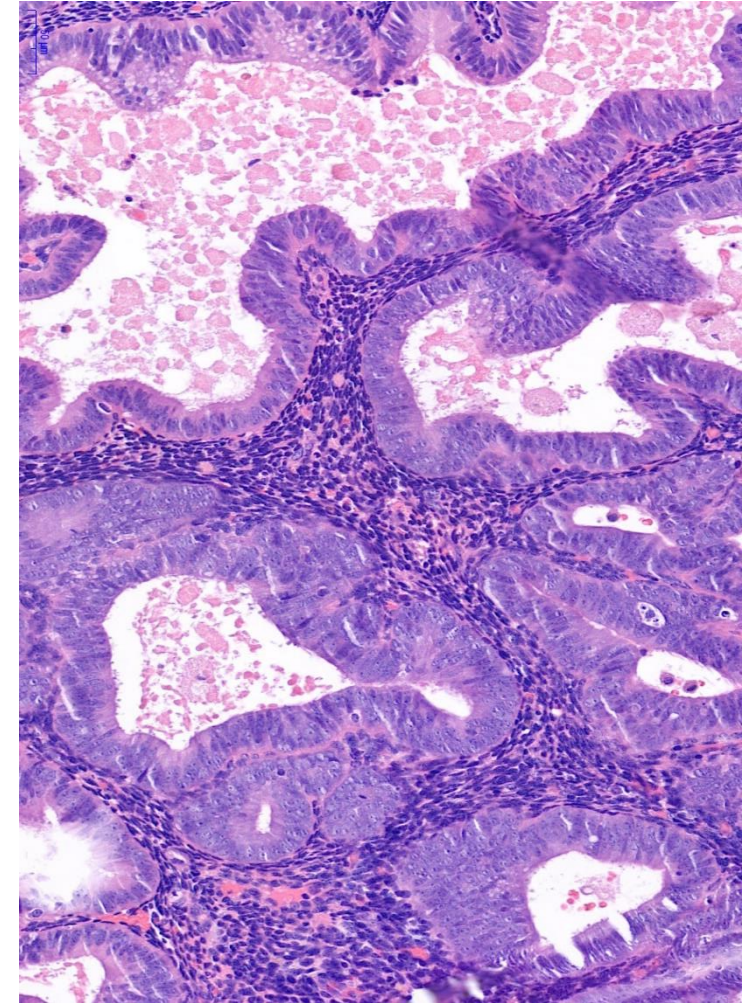
https://librepathology.org/w/images/thumb/f/f5/Disordered_proliferative_endometrium_-_intermed_mag.jpg/800px-Disordered_proliferative_endometrium_-_intermed_mag.jpg

Hyperplasia without atypia



<https://pathology.or.jp/corepicturesEN/15/c05/images/04.jpg>

Hyperplasia with atypia/Endometrial Intraepithelial Neoplasia (EIN)



ESTROGEN EXCESS

Malignant transformation: 1-3%

Malignant transformation: 20-50%!

CORPUS – ENDOMETRIOID CARCINOMA

Type I

526 000 uterine cancer
cases/year

80%: endometrioid carcinomas

Mean age: 55-64 yrs

(may occur at younger age)

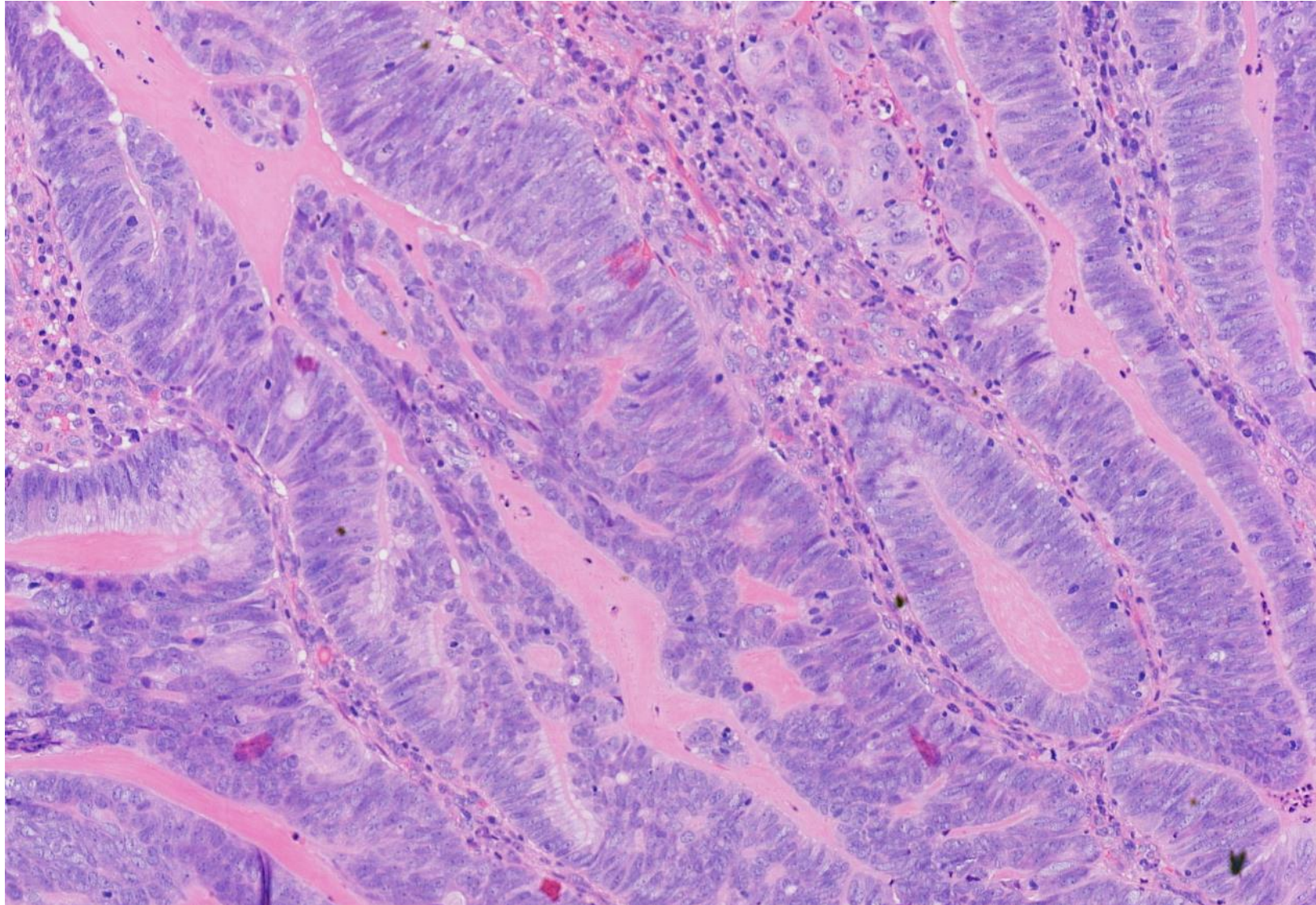
PTEN mutations

Mismatch repair mutations
(Lynch-syndrome)

Grade 1-2-3

Gland formation

Nuclear atypia



CORPUS – SEROUS CARCINOMA

Type II

~ 15% of corpus carcinomas

NO estrogen excess

Endometrial atrophy or polyp

Older women

TP53 mutations

Precursor: Serous

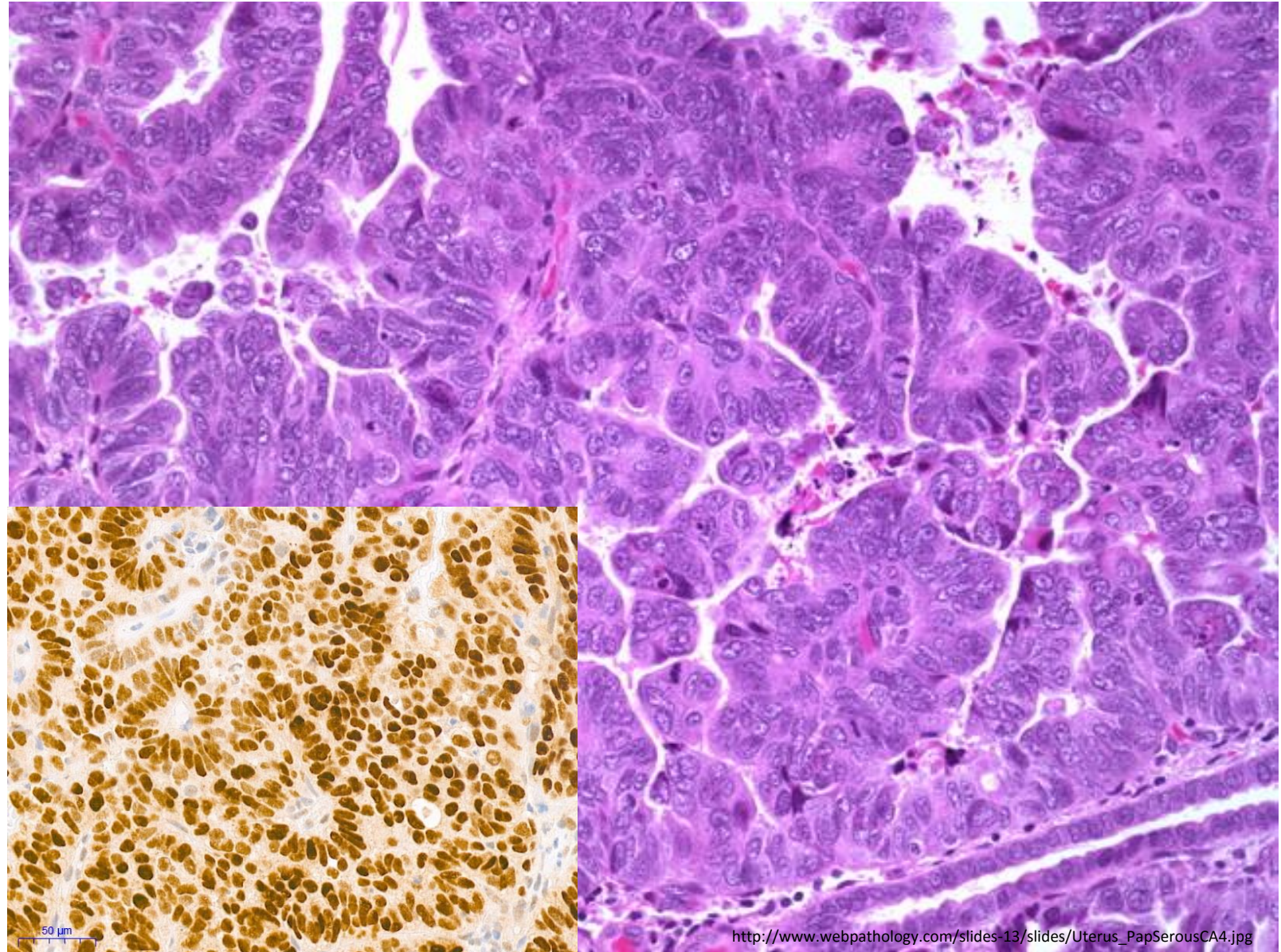
intraepithelial carcinoma (SEIC)

High grade carcinoma!

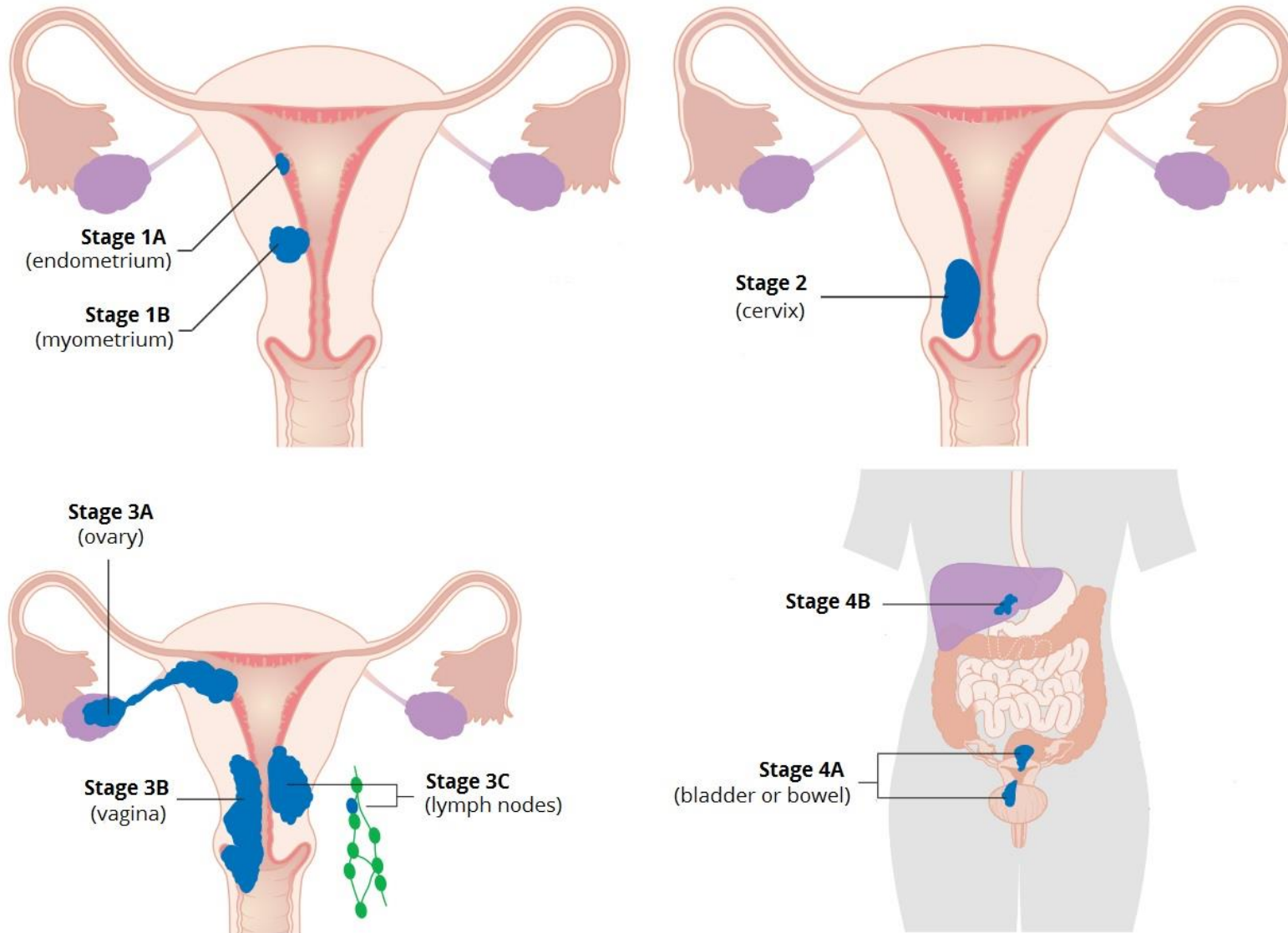
Usually advanced stage

Aggressive; poor prognosis

Aberrant p53 expression >>>



ENDOMETRIAL CARCINOMA – SPREAD



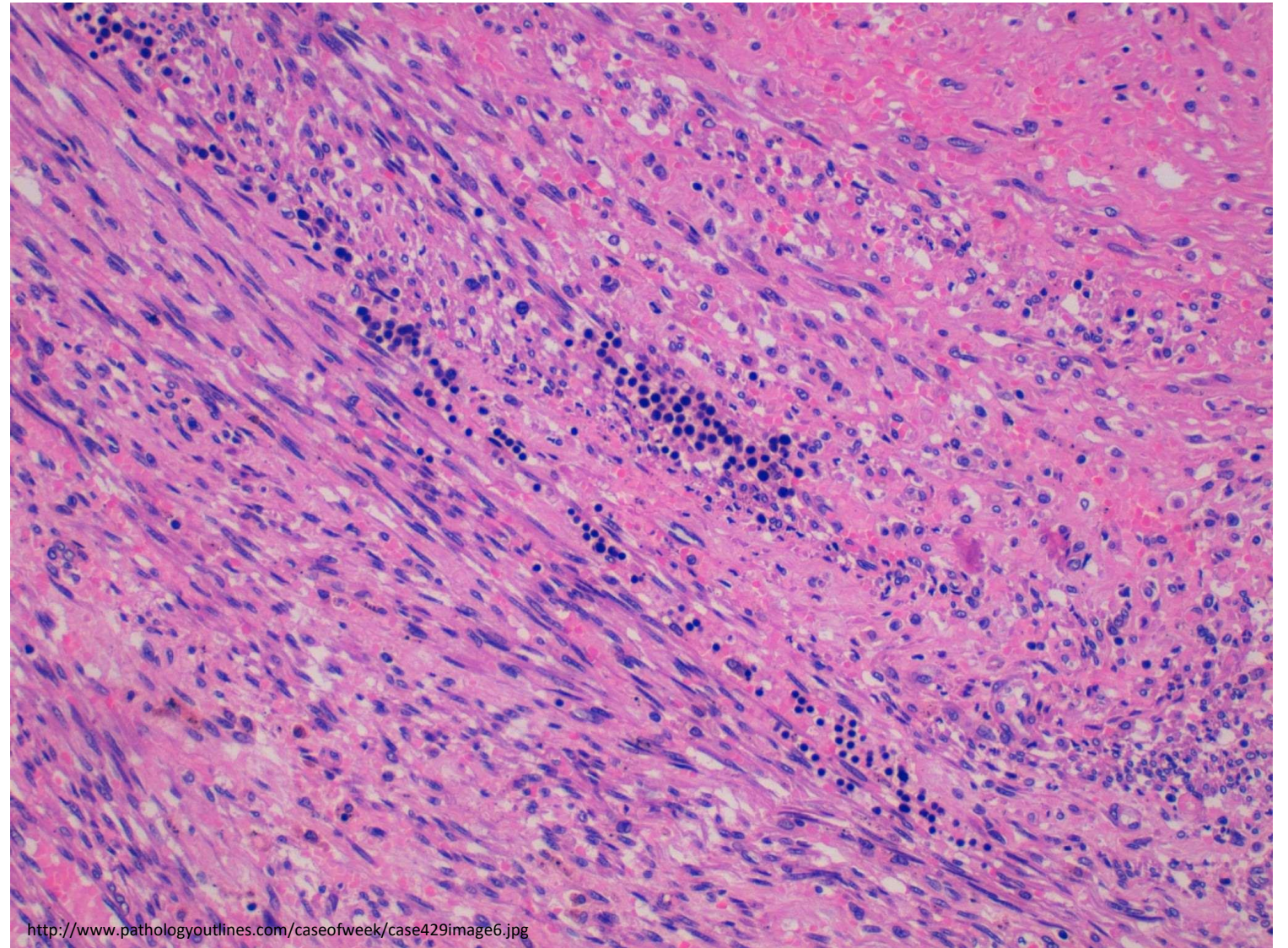
Pelvic or para-aortic
lymph nodes

Distant metastasis

**Prognosis, therapy:
stage-dependent!**

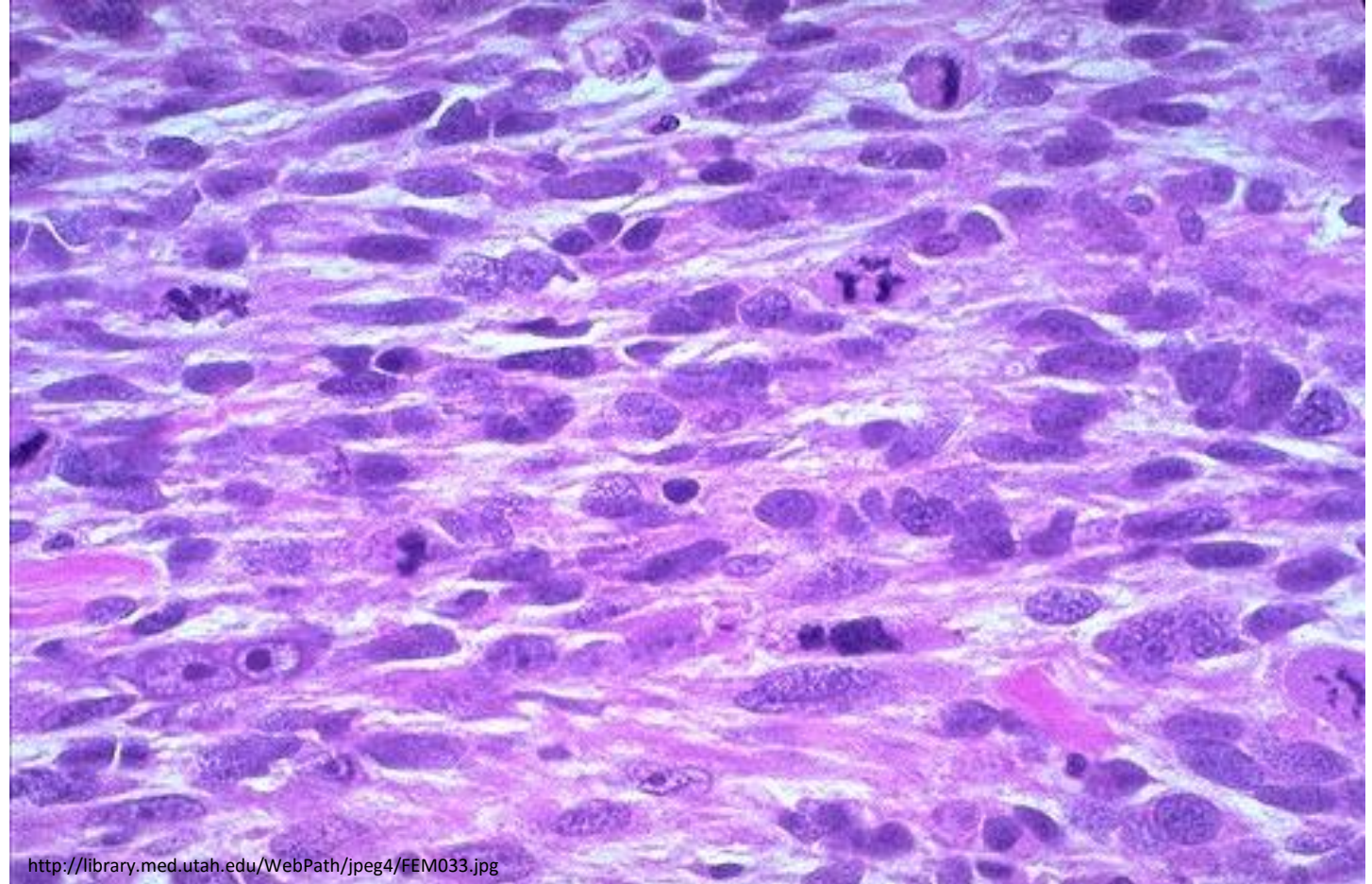
CORPUS – LEIOMYOMA

Frequent!



CORPUS – LEIOMYOSARCOMA

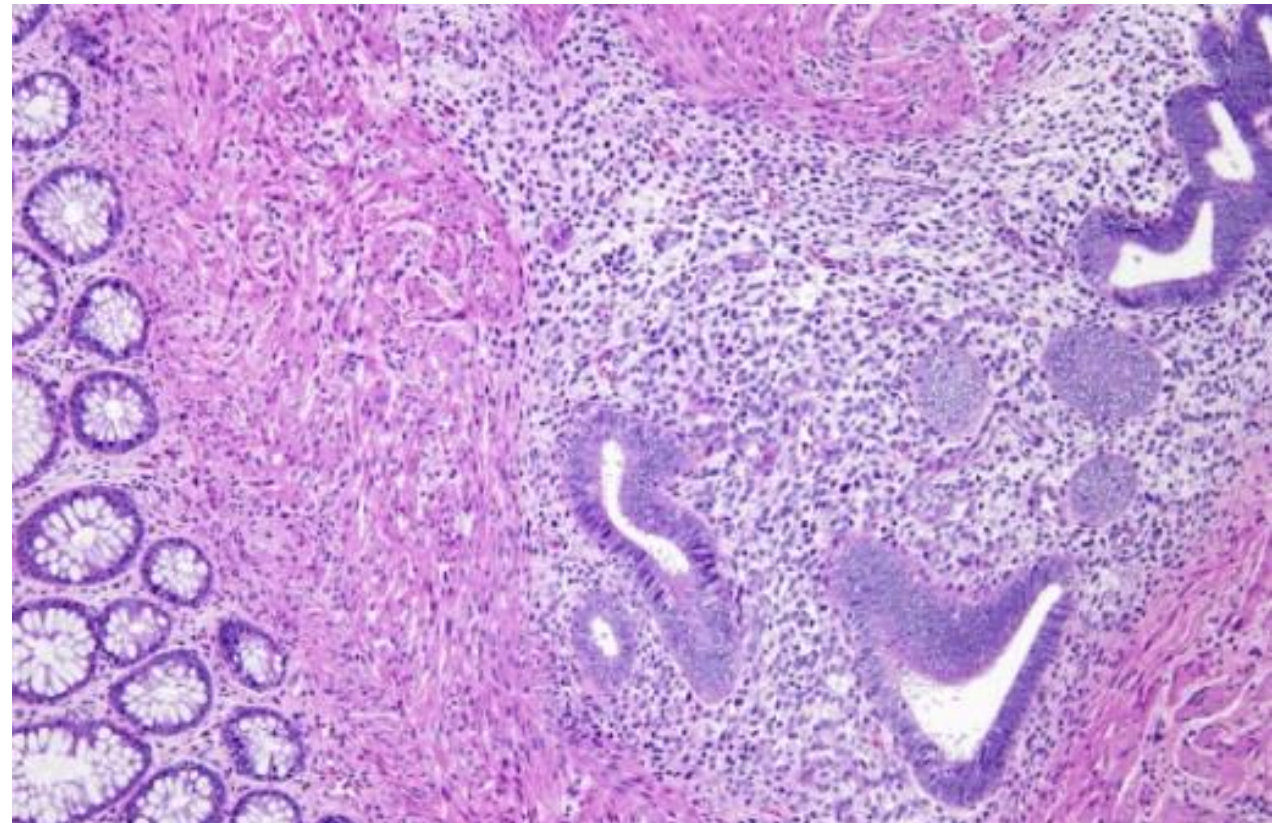
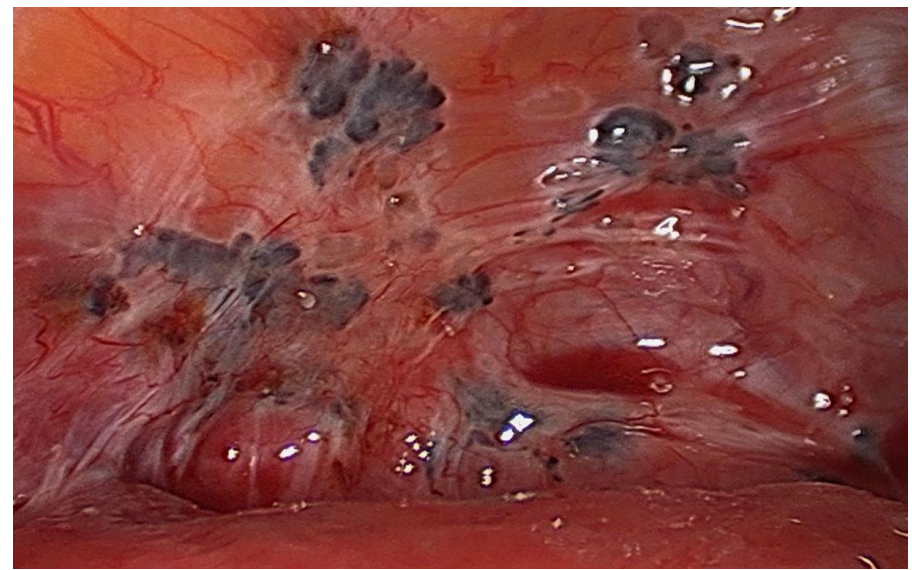
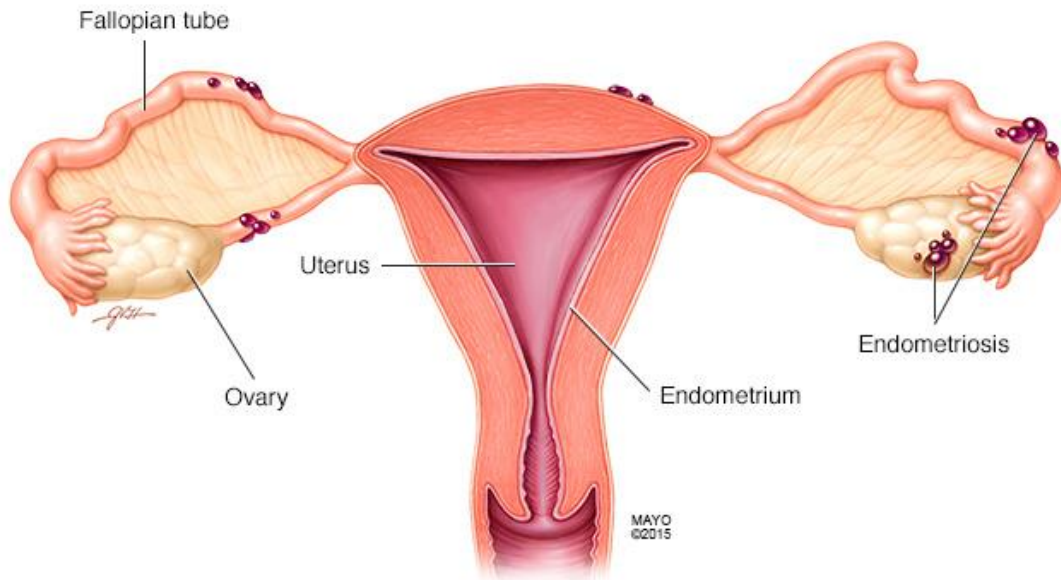
Rare



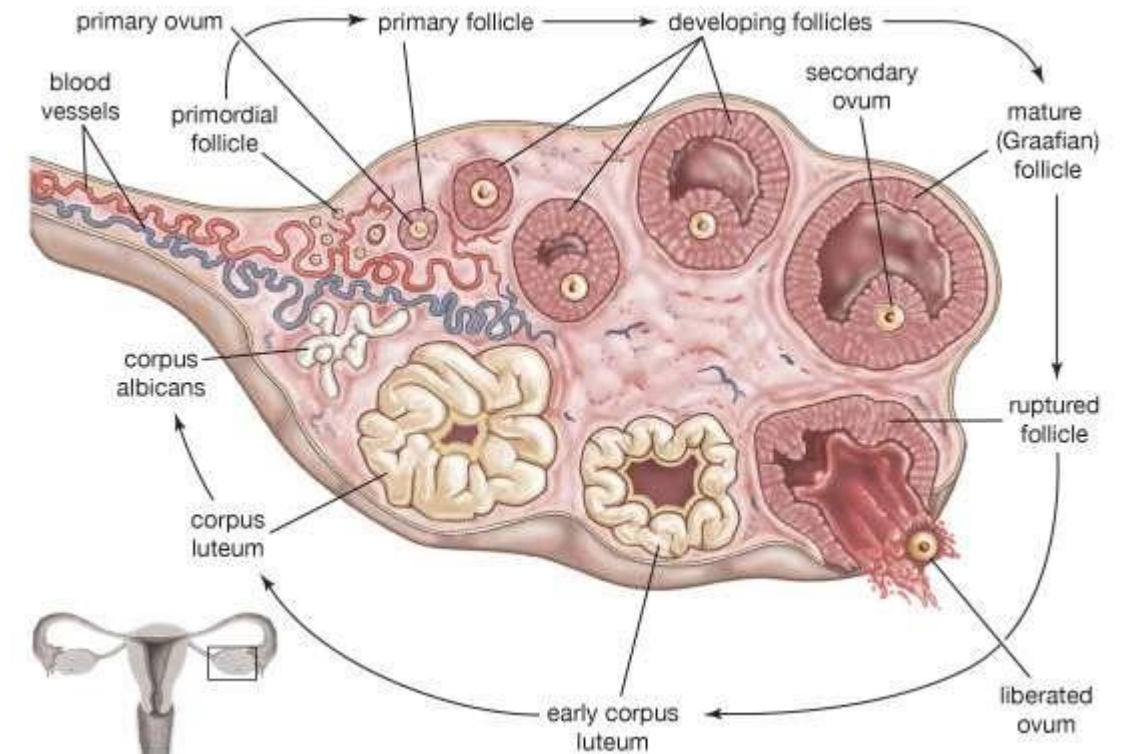
ENDOMETRIOSIS

Up to 10% of reproductive age women

- Dysmenorrhoea
- Lower abdominal pain
- Infertility
- Dysuria
- Dyspareunia
- Pain when defecating



OVARY

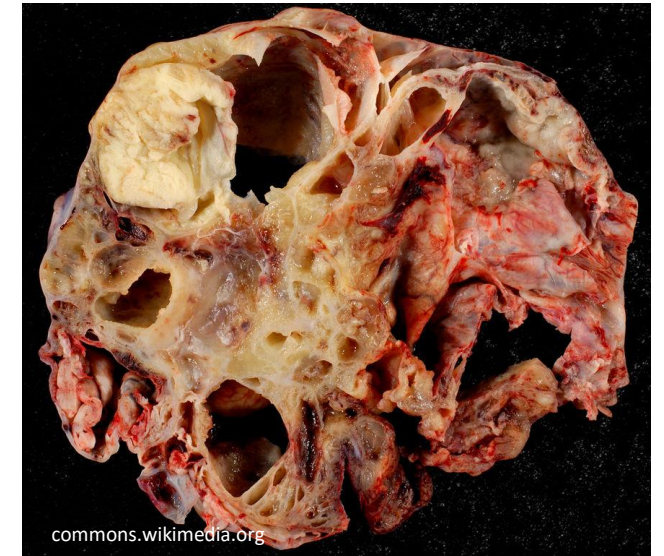


OVARIAN CYSTS

Non-neoplastic cysts

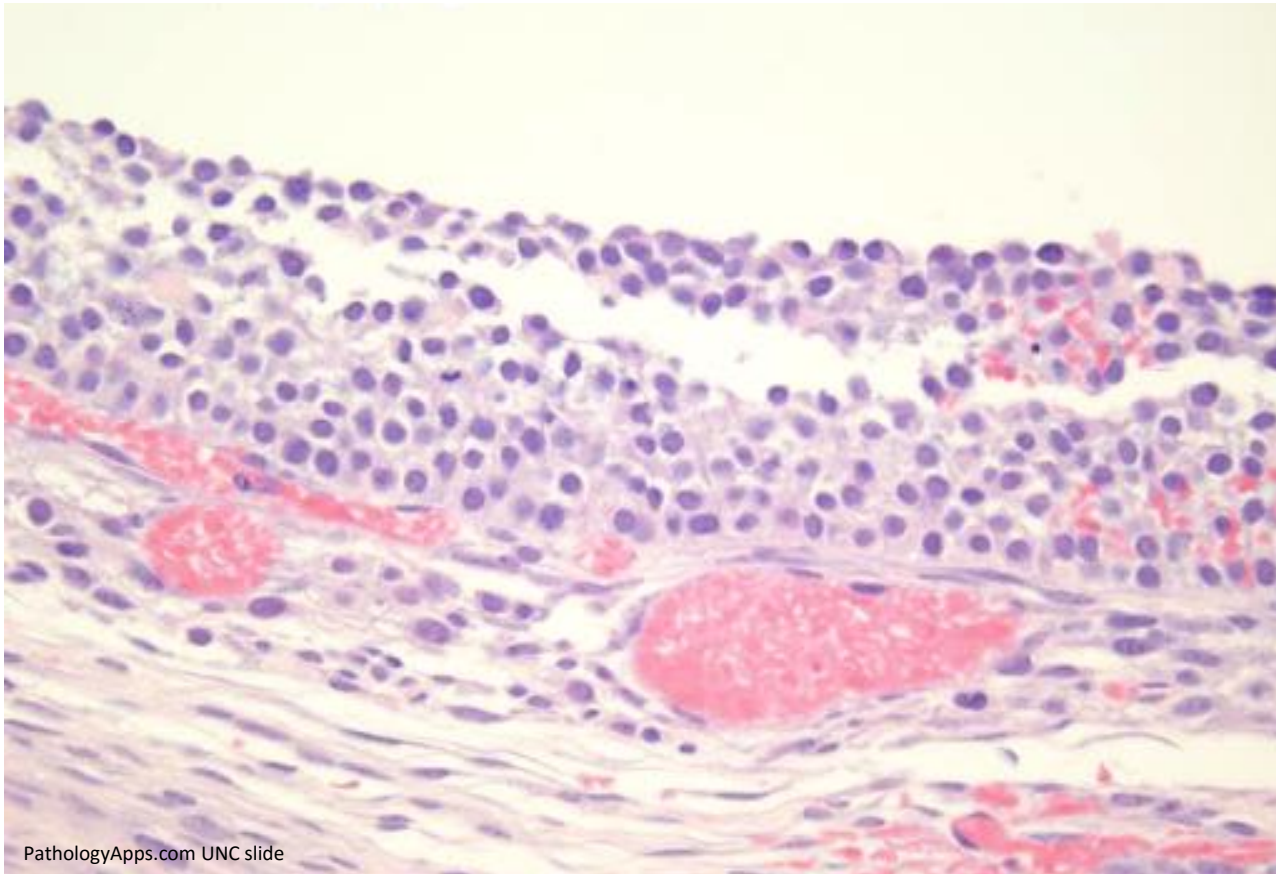
- Follicularis cyst
- Corpus luteum cyst
- Parovarian/paratubal cysts
- Endometriotic cyst

Cystic ovarian tumors

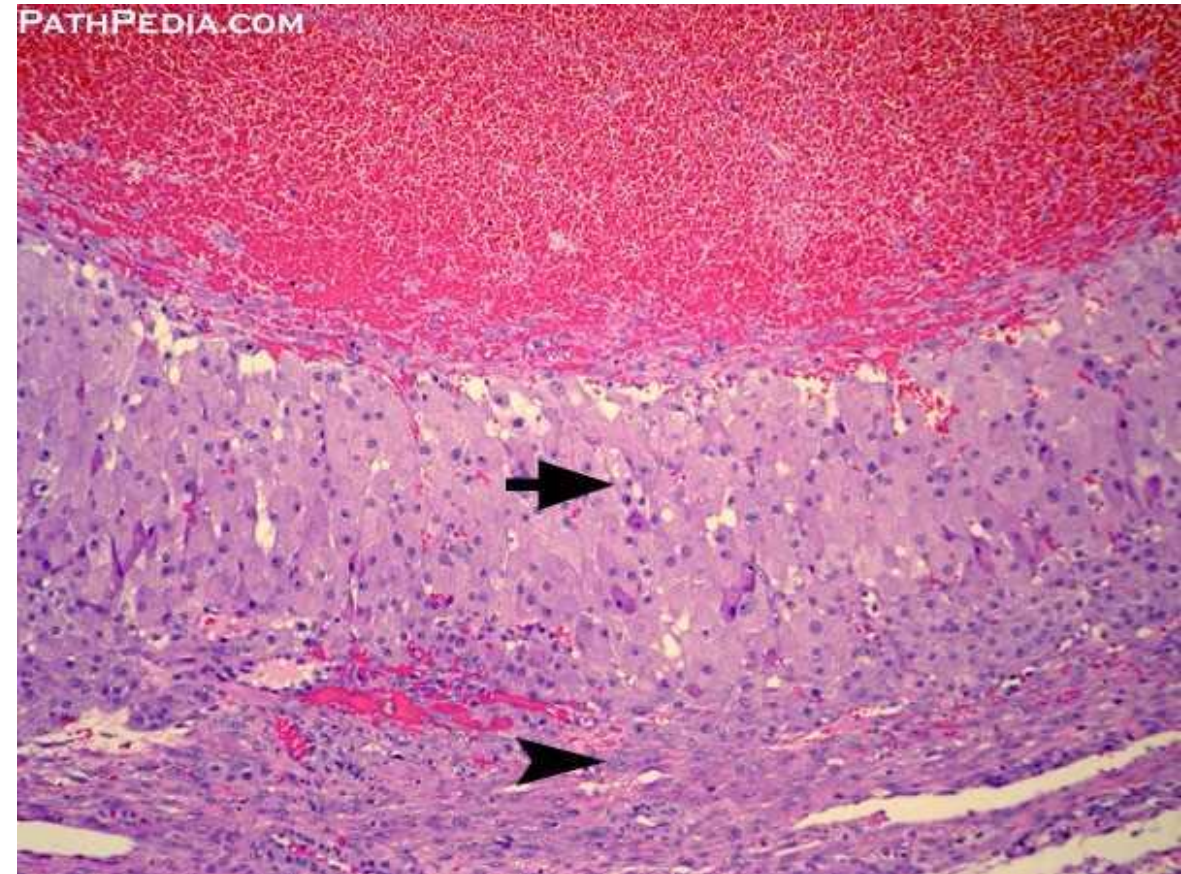


OVARIAN CYSTS

Follicular cyst



Corpus luteum cyst

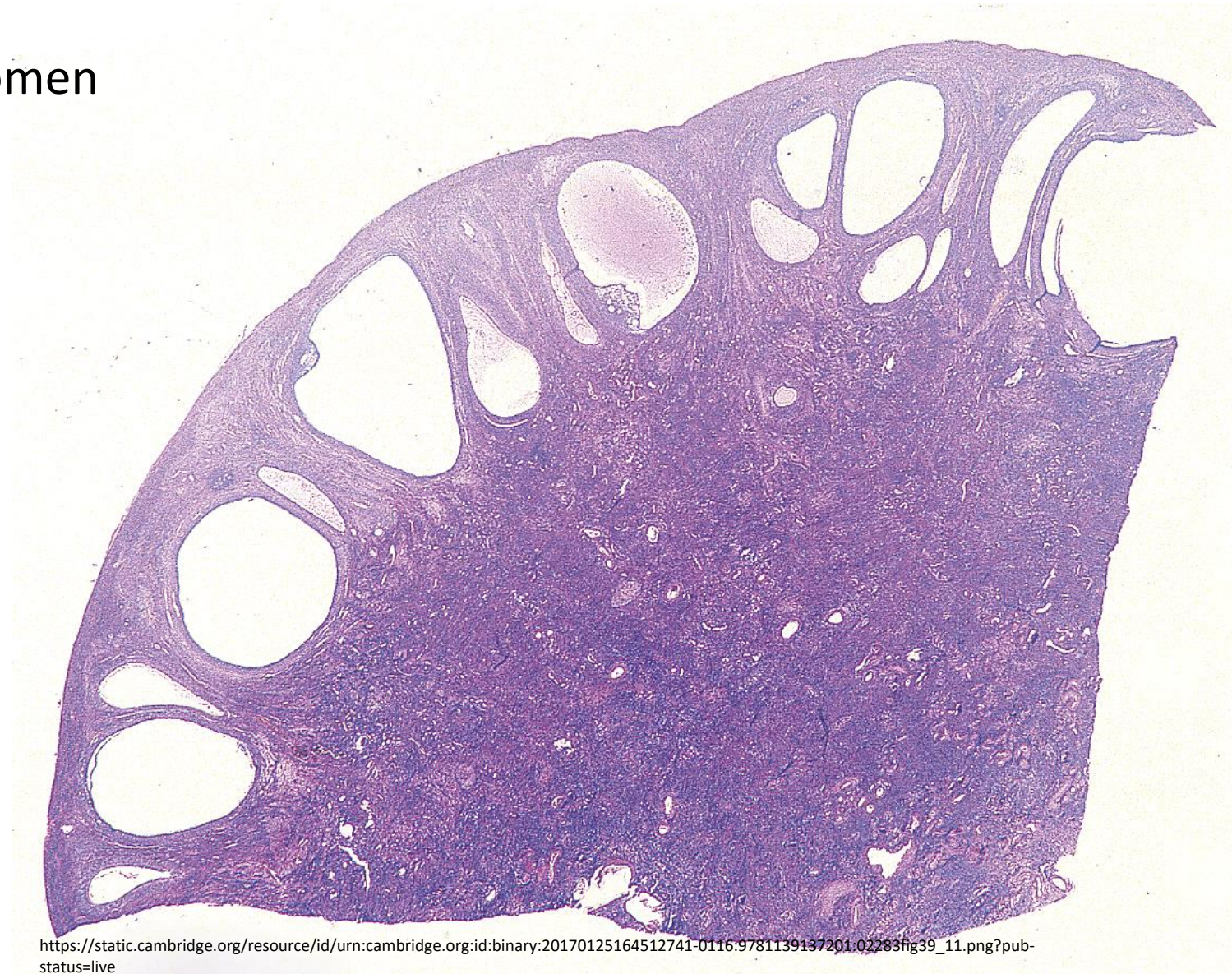
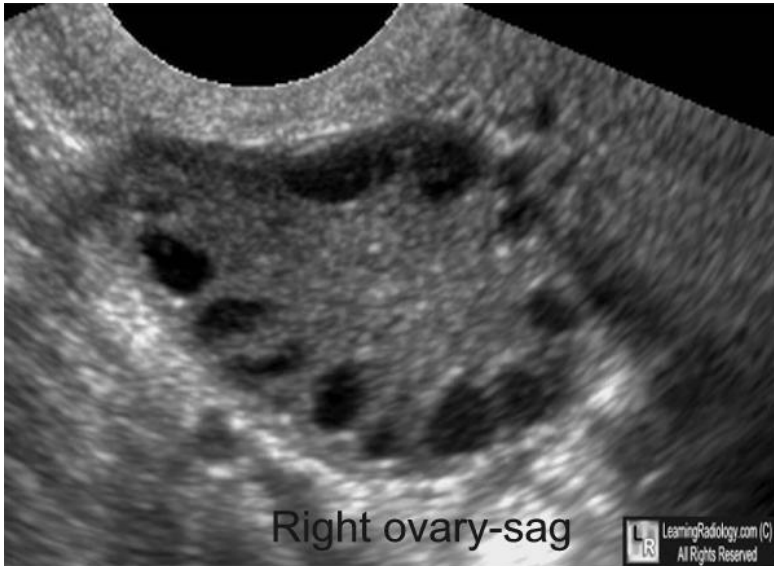


POLYCYSTIC OVARY SYNDROME (PCOS)

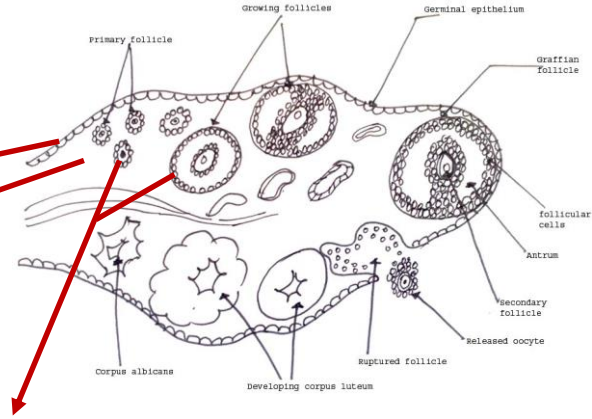
Complex endocrine condition

Up to 10% of reproductive age women

- Chronic anovulation
- Oligo-amenorrhea
- Hyperandrogenism
- Estrogen excess!
- Infertility
- Obesity
- Insulin resistance



TUMORS OF THE OVARY



Surface epithelial

- Serous
- Mucinous
- Endometrioid
- Brenner (urothelial)
- Clear cell

Sex cord/stroma

- Fibroma
- Thecoma
- Granulosa cell
- Sertoli-Leydig-cell

Germ cell

- Teratoma
- Dysgerminoma
- Yolk sac
- Embryonal carcinoma
- Choriocarcinoma

Other

- Leiomyoma
- Carcinoid (NET-G1)
- Lymphoma (Burkitt)
- Metastasis

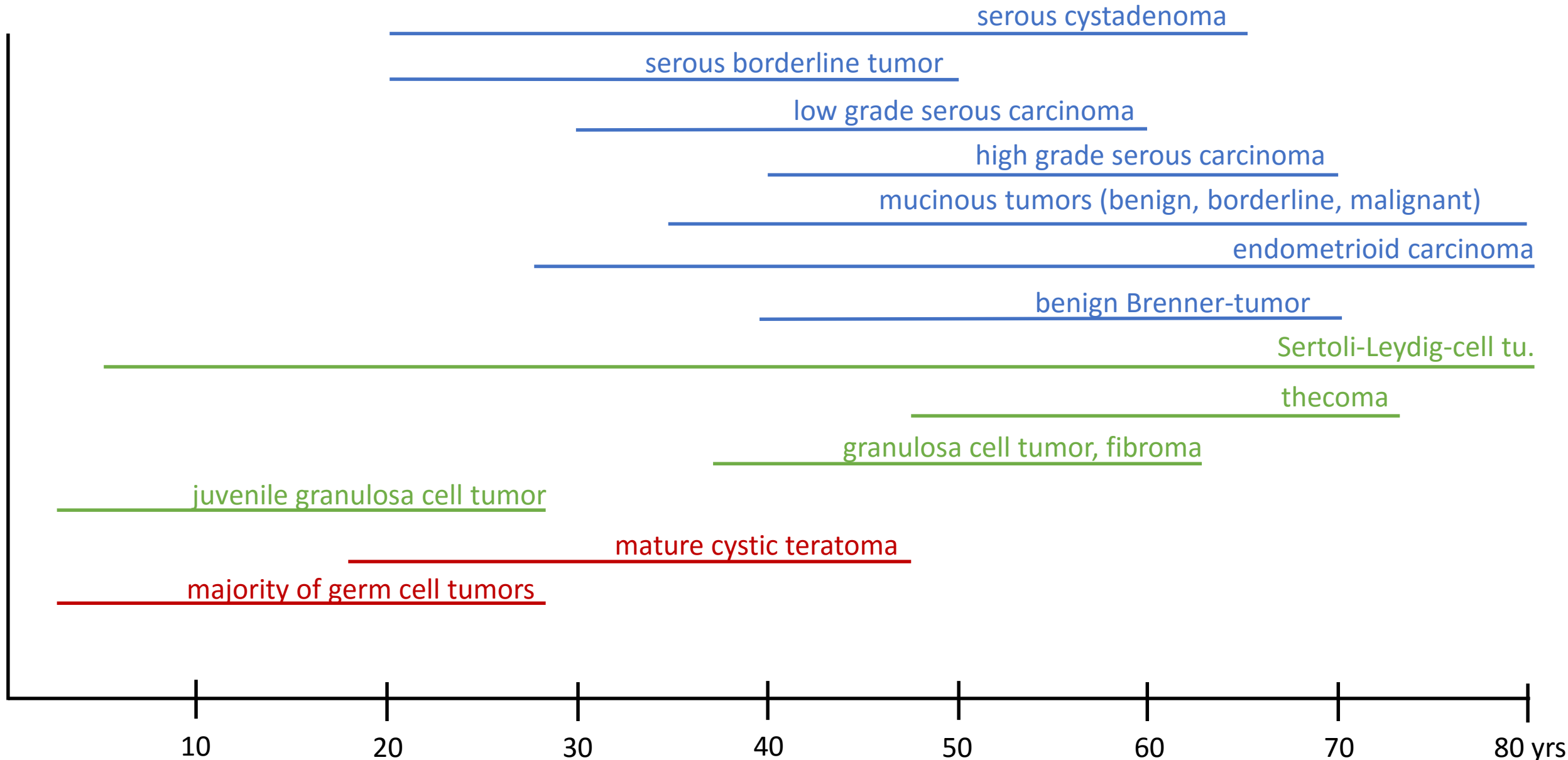


BENIGN

BORDELIN

MALIGNANT (CARCINOMA)

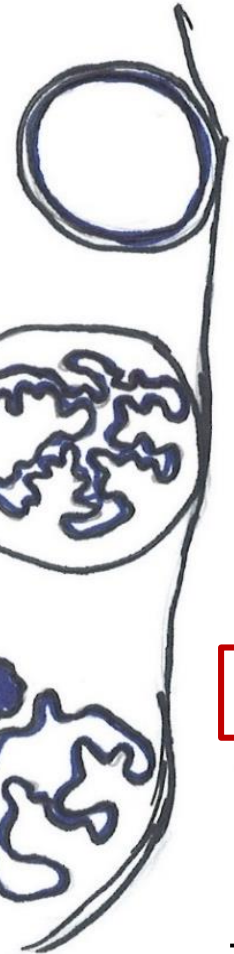
TUMORS OF THE OVARY – AGE DISTRIBUTION



TUMORS OF THE OVARY – CLINICAL PRESENTATION

- Often vague or nonspecific symptoms
- Abdominal mass
- Abdominal or pelvic pain, abdominal complaints
- Abdominal distension (ascites!)
- Symptoms of estrogen or androgen production (amenorrhea, virilization, precocity, abnormal uterine bleeding)
- Lymphadenopathy
- Weight loss

SEROUS TUMORS – 1.

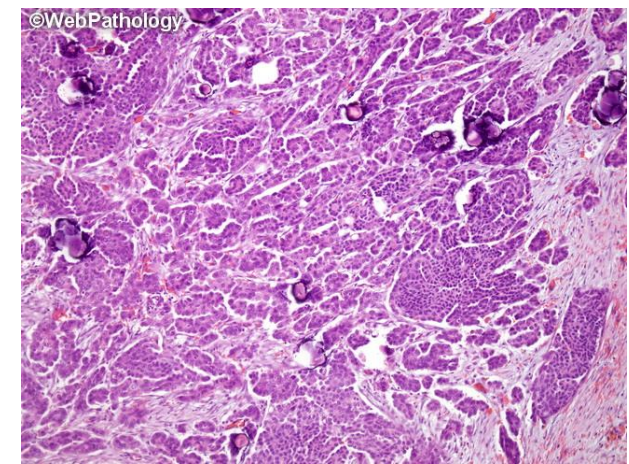
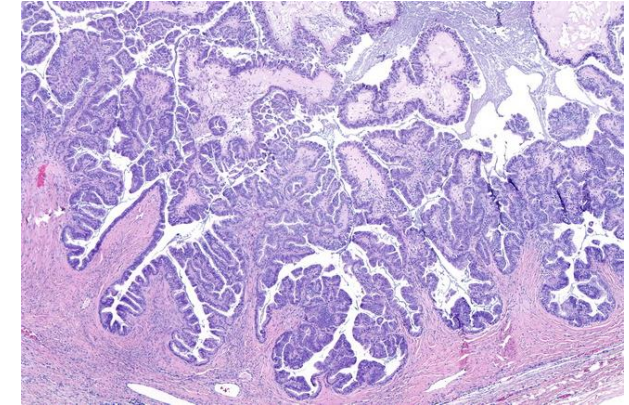
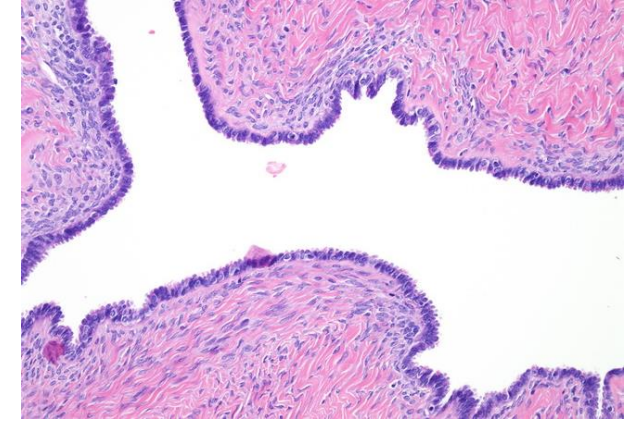


Benign (60%)
Serous cystadenoma
(or cystadenofibroma)

Borderline (15%)
Serous bordeline tumor

KRAS, BRAF mutations

Malignant (Type I) 1-2%
Low-grade serous carcinoma

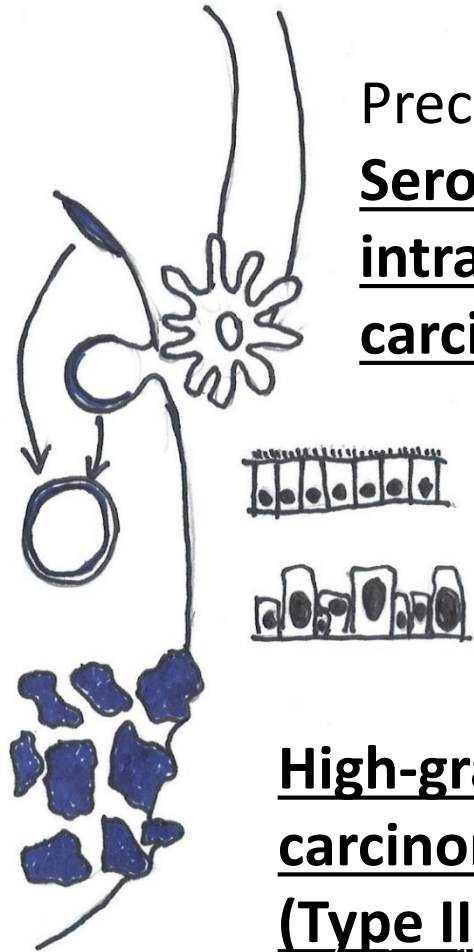


SEROUS TUMORS – High-grade serous carcinoma

Almost half of ovarian malignant tumors
Often bilateral

Precursor:

Serous tubal
intraepithelial
carcinoma (STIC)



High-grade serous
carcinoma
(Type II)

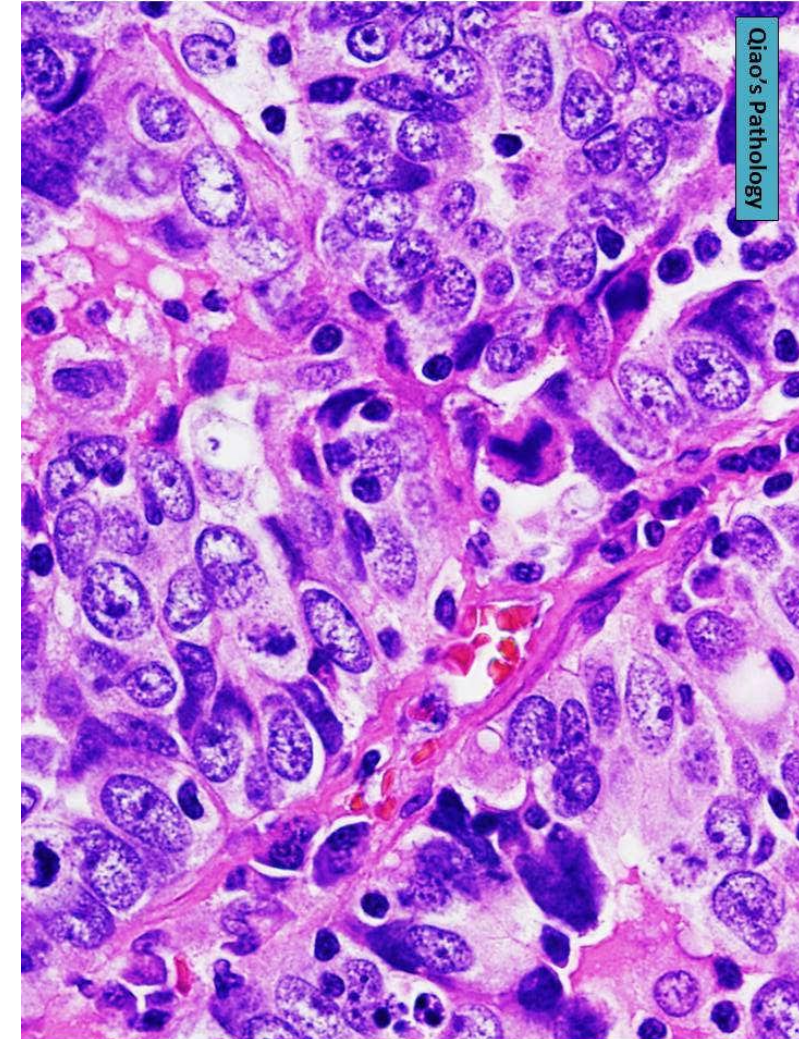
ovary

Fallopian tube

peritoneum



**TP53 mutations
chromosomal instability**

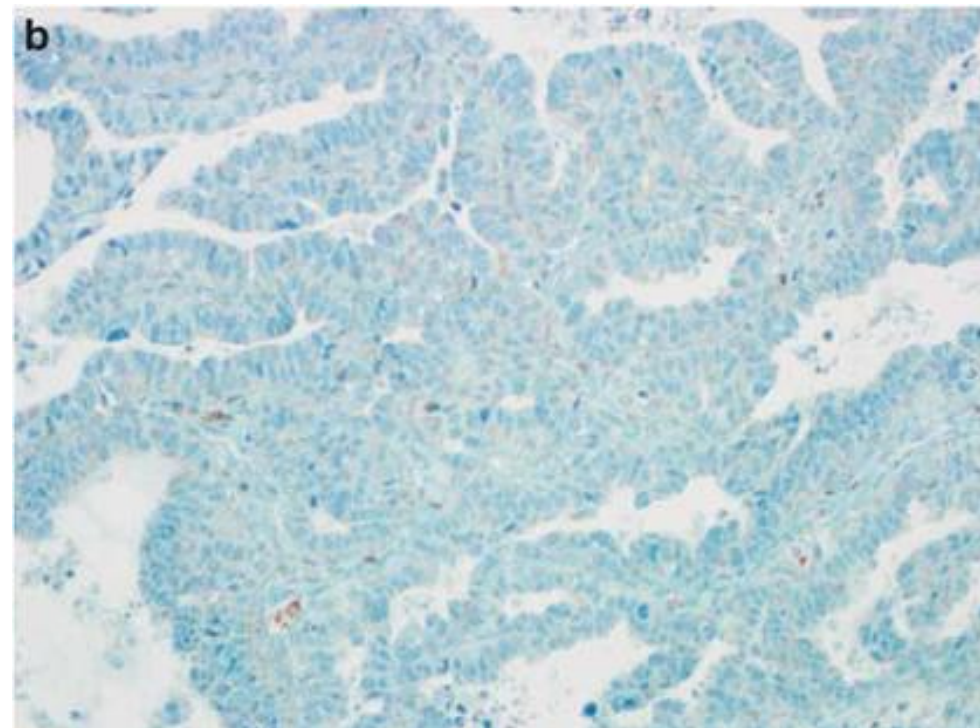
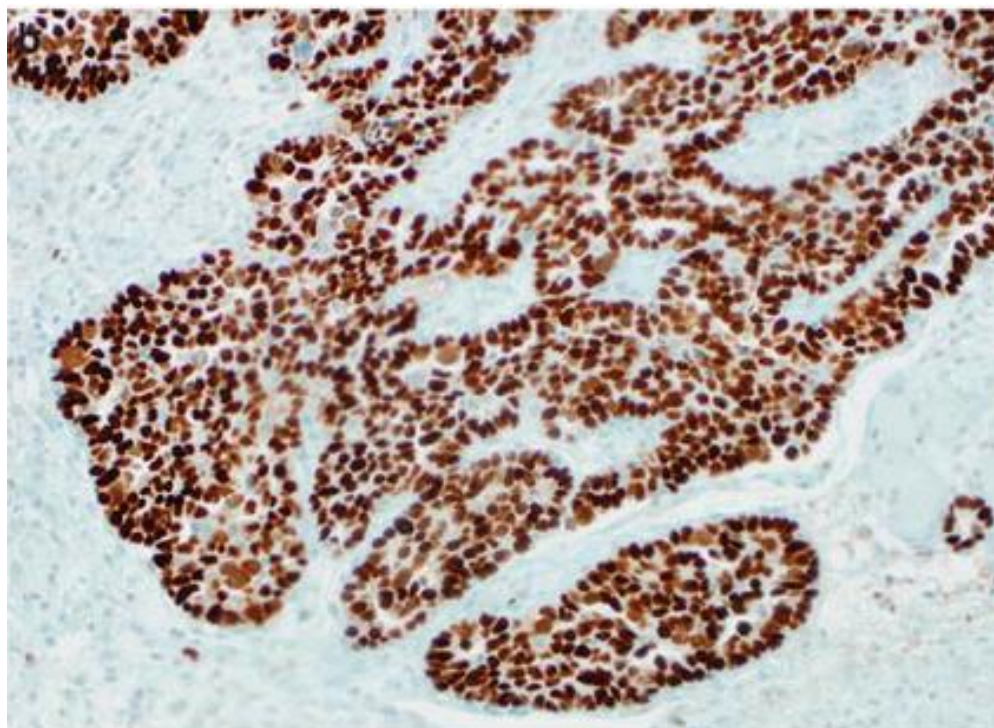


SEROUS TUMORS – High-grade serous carcinoma

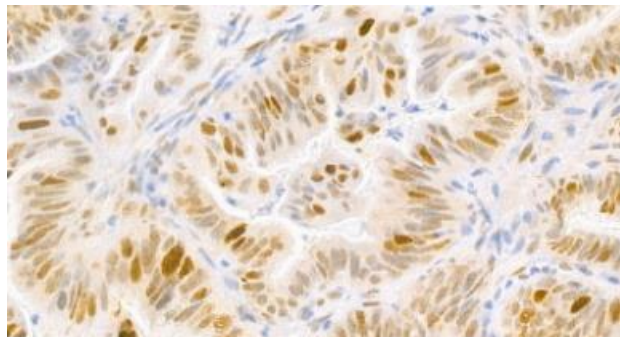
**TP53 mutation >> aberrant p53 expression
„ALL or NOTHING!”**

>>> missense mutation

>>> nonsense mutation



Wild type p53 expression:
>>> Not HGSC!!!



MUCINOUS TUMORS OF THE OVARY

80% benign:

mucinous cystadenoma



PATHPEDIA.COM

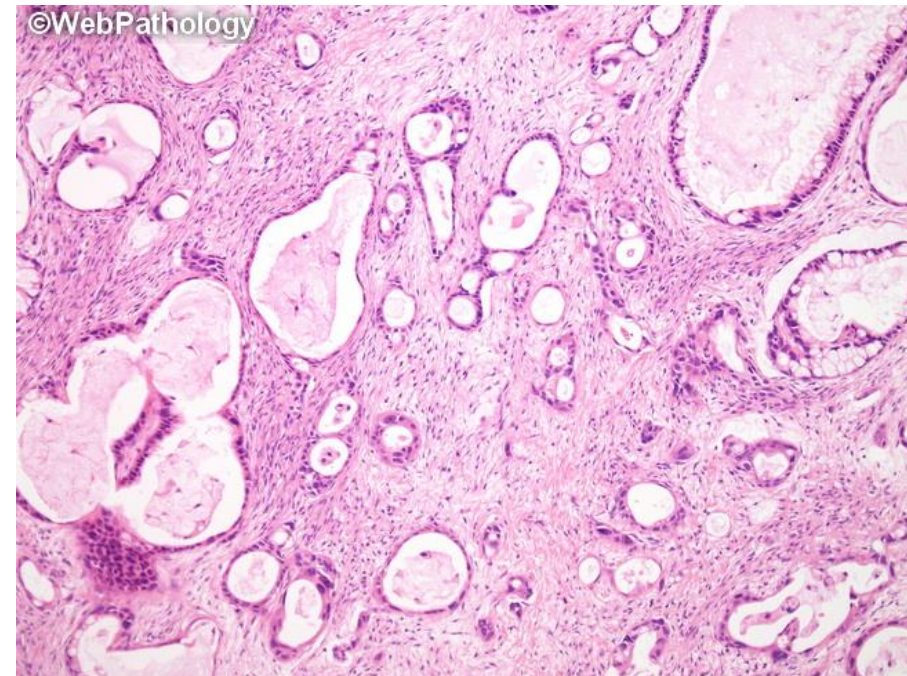
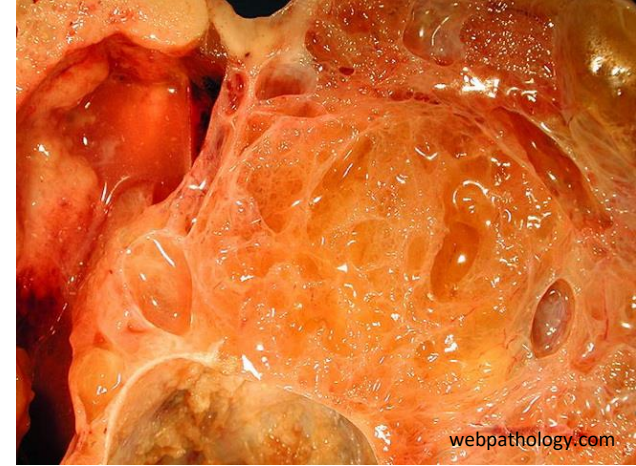


(10%: mucinous
borderline tumor)

KRAS mutations

10% malignant:

mucinous carcinoma



DIFFERENTIAL DIAGNOSIS!!!

Primary mucinous borderline tumor/carcinoma

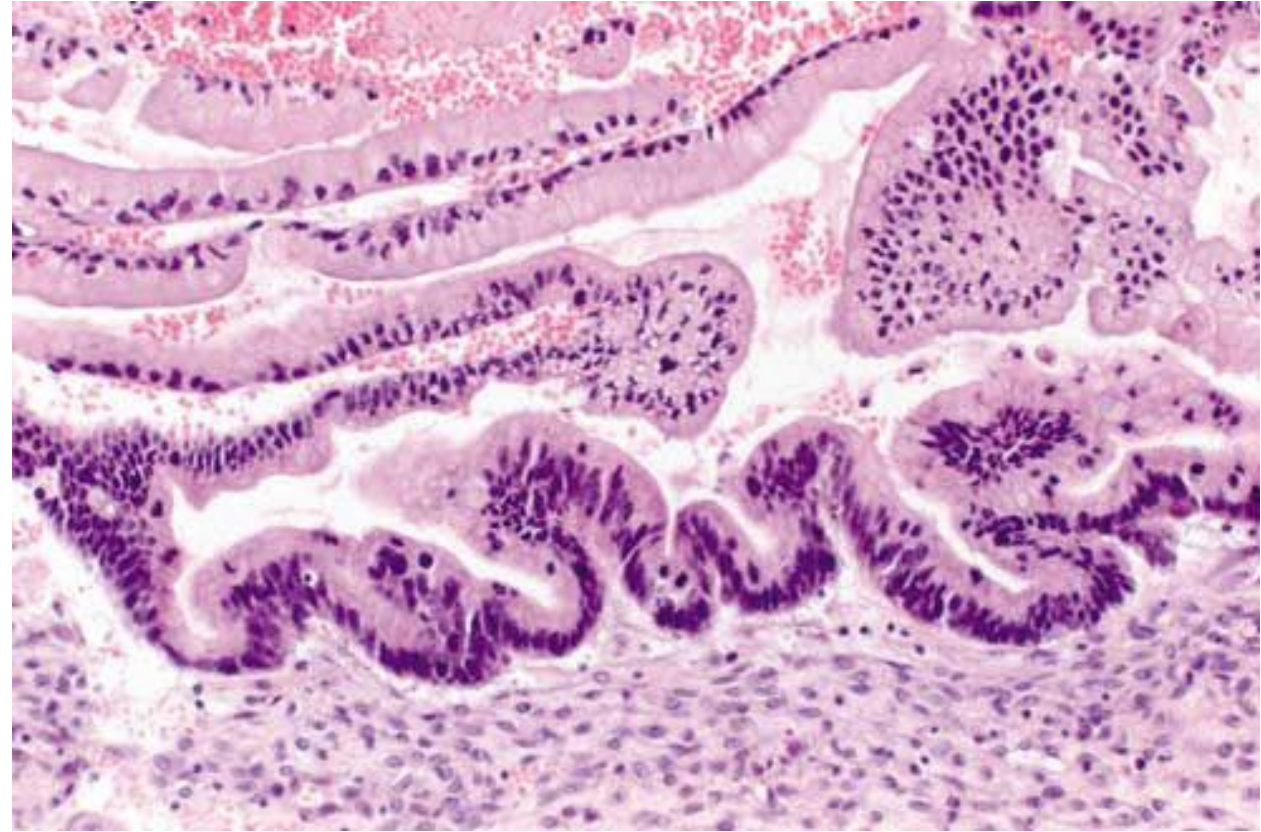
or

Metastasis?

- **pancreatic**
- **biliary**
- **gastric**
- **colorectal**

Suspect:

- **bilaterality**
- **smaller size (<10 cm)**
- **ovarian surface involvement**
- **lymphovascular invasion**



<https://media.nature.com/m685/nature-assets/modpathol/journal/v18/n2s/images/3800312f10.jpg>

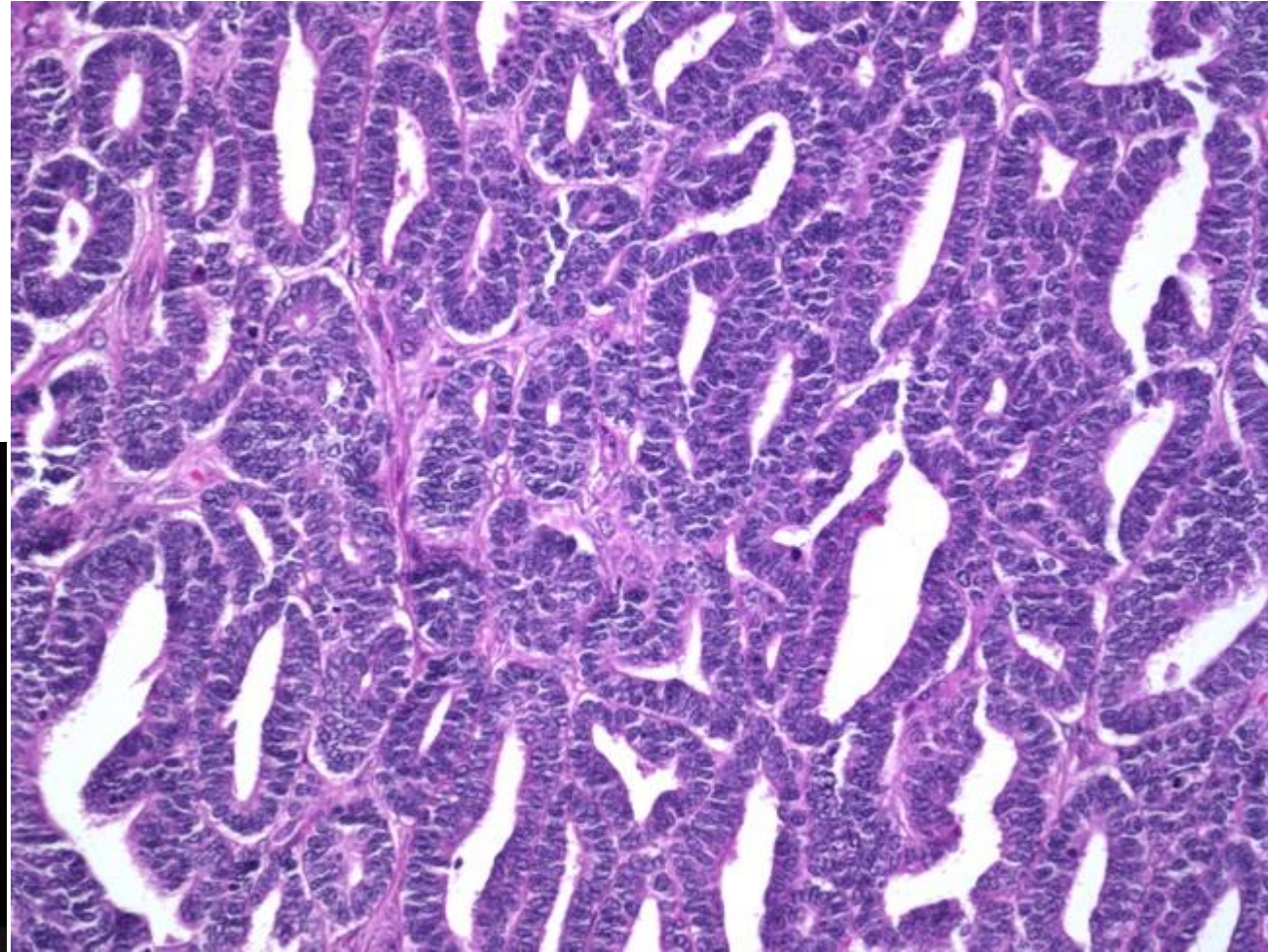
Ovarian metastasis of pancreatic adenocarcinoma!

ENDOMETRIOID TUMORS OF THE OVARY

- Endometrioid carcinoma (majority)
- 20-25% of primary ovarian carcinomas
- May develop from endometriosis
- Synchronous uterine endometrioid carcinoma in 15-30%
- Usually low-grade tumors



<http://www.pathologyoutlines.com/imgau/ovary/OvaryBilatEndoCaAyhan10.jpg>



http://www.webpathology.com/slides-13/slides/Uterus_Adenocarcinoma_WellDiff_PolycysticOvarianDisease.jpg

SPREAD OF OVARIAN TUMORS, PROGNOSIS

Most important prognostic factor: stage

Borderline tumors:

- Stage I tumor (confined to one ovary): 100% 5-year survival
- Peritoneal (non-invasive) implants: 95% 5-year survival

Low grade serous carcinoma:

- Stage I: good prognosis
- Advanced tumors: 50% 10-year survival

High grade serous carcinoma:

- Poor prognosis
- Mostly advanced stage tumors

OVARIAN CARCINOMA – RISK MODIFYING FACTORS

RISK FACTORS

- Early menarche, late menopause
- Nulliparity, older age at first birth
- Family history
- Inherited BRCA1/2 mutations (> high-grade serous carcinoma)
- Hereditary non-polypous colon carcinoma (Lynch-syndrome, mismatch repair mutations > endometrioid carcinoma)
- Endometriosis (> endometrioid and clear carcinoma)

PROTECTIVE FACTORS

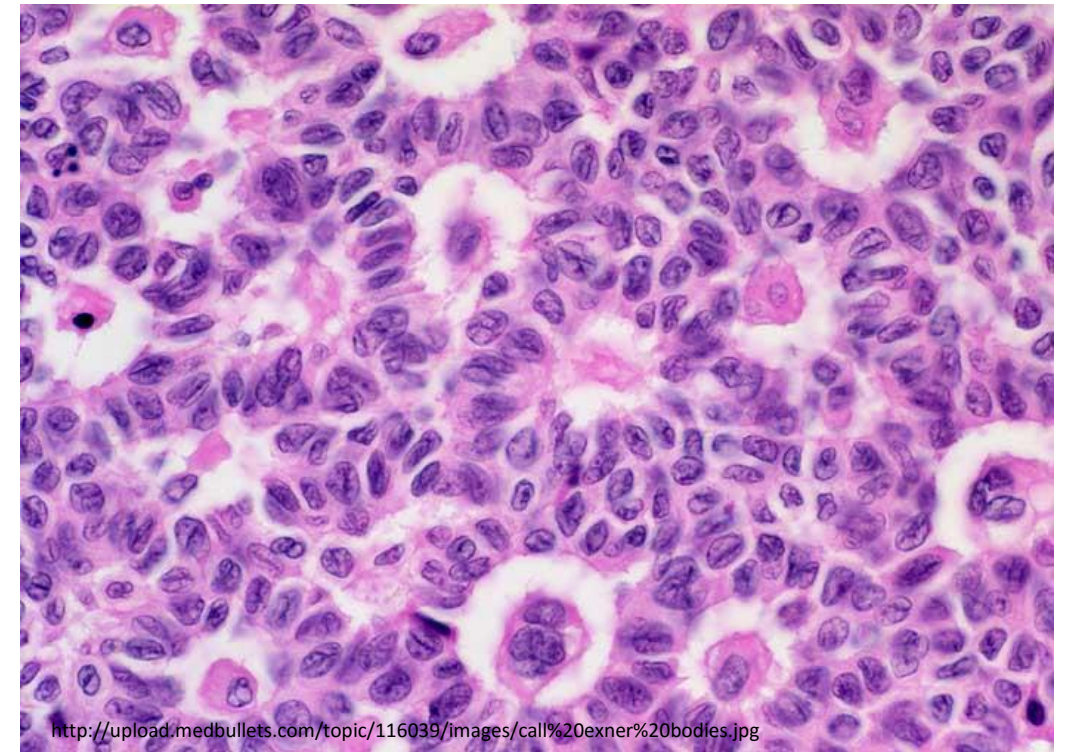
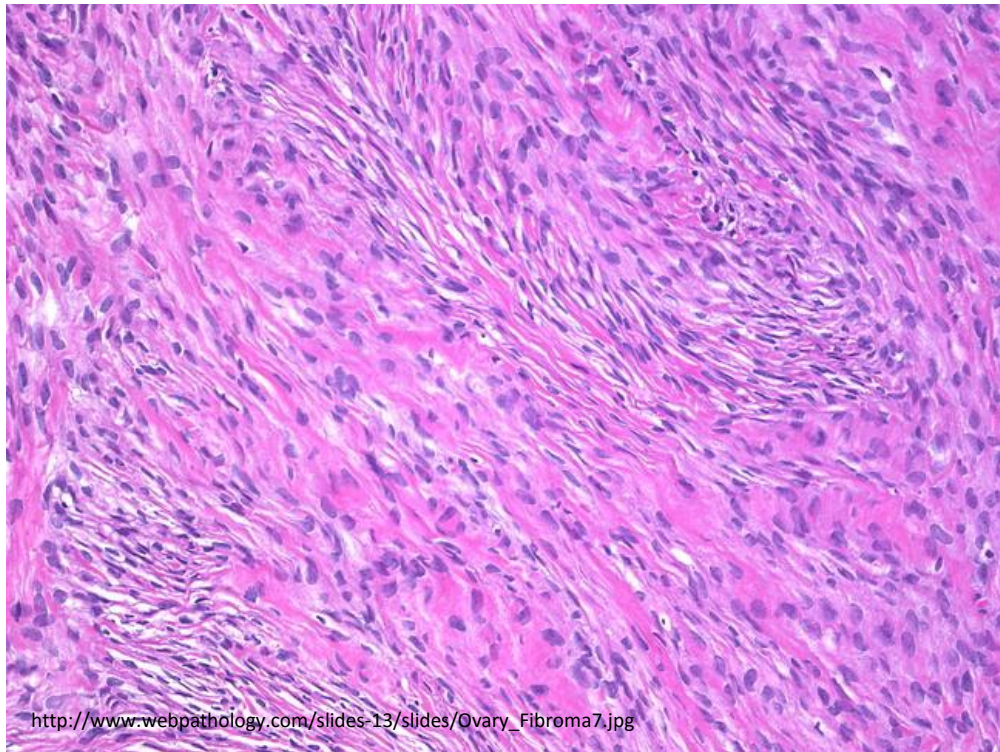
- Oral hormonal anticoncipients (long-term)
- Multiple births
- Tubal ligation

SEX CORD/STROMA TUMORS

Fibroma



Adult granulosa cell tumor

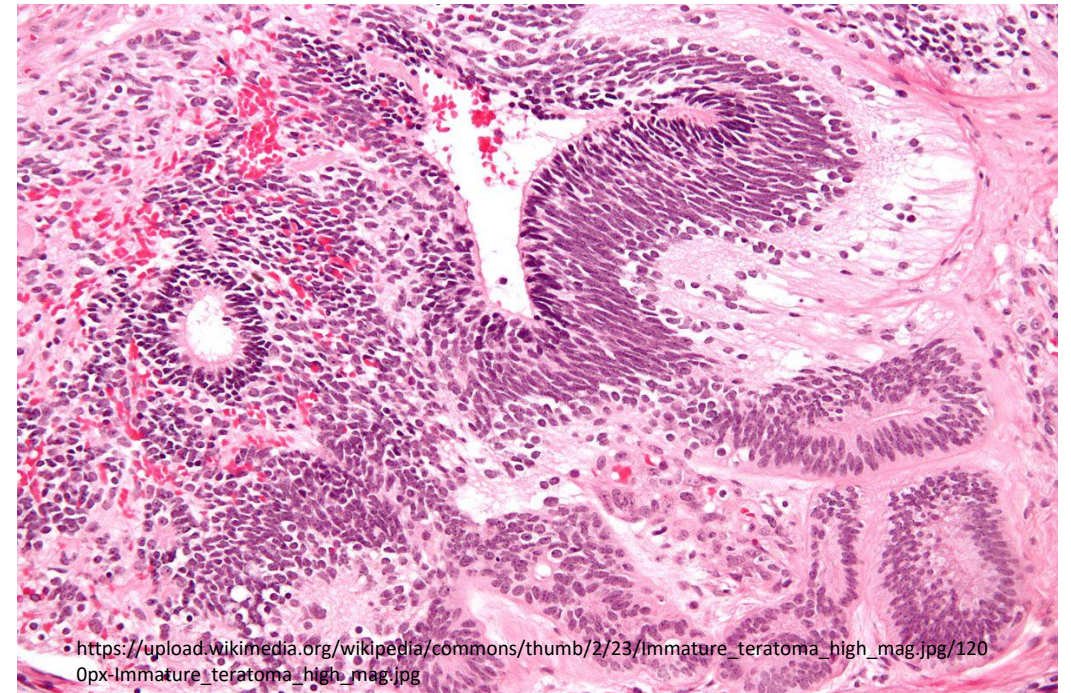
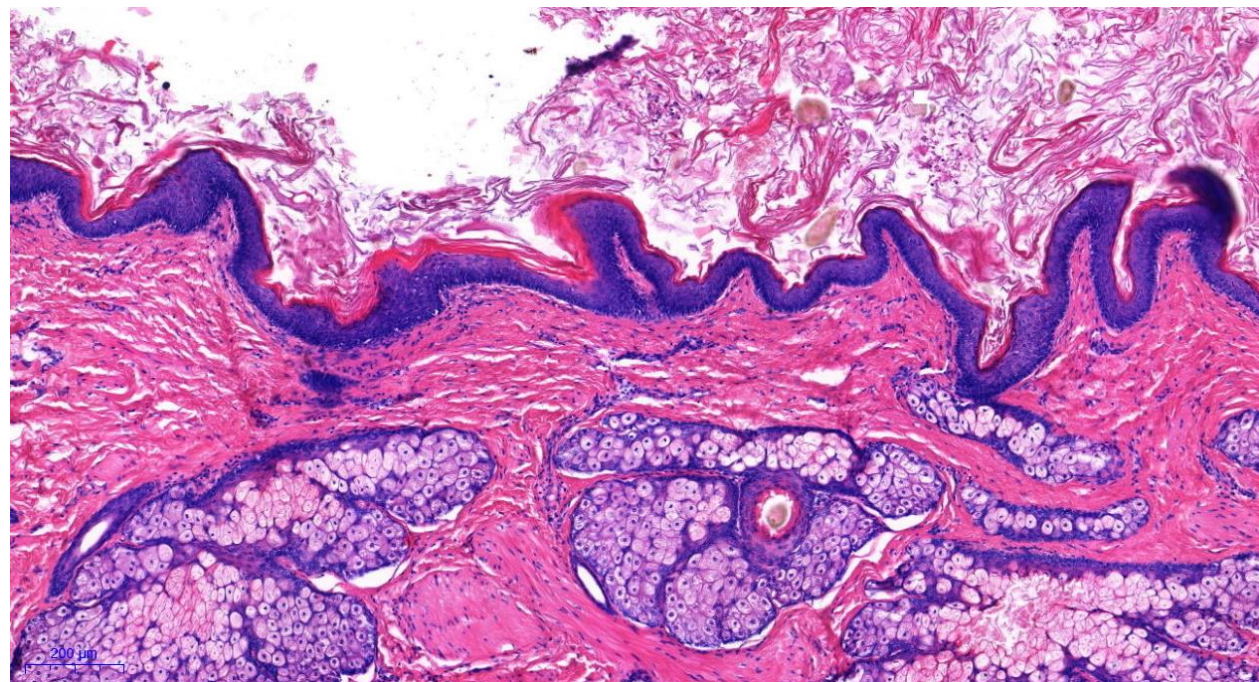


GERM CELL TUMORS

Mature cystic teratoma (dermoid cyst)



Immature teratoma



METASTASIS

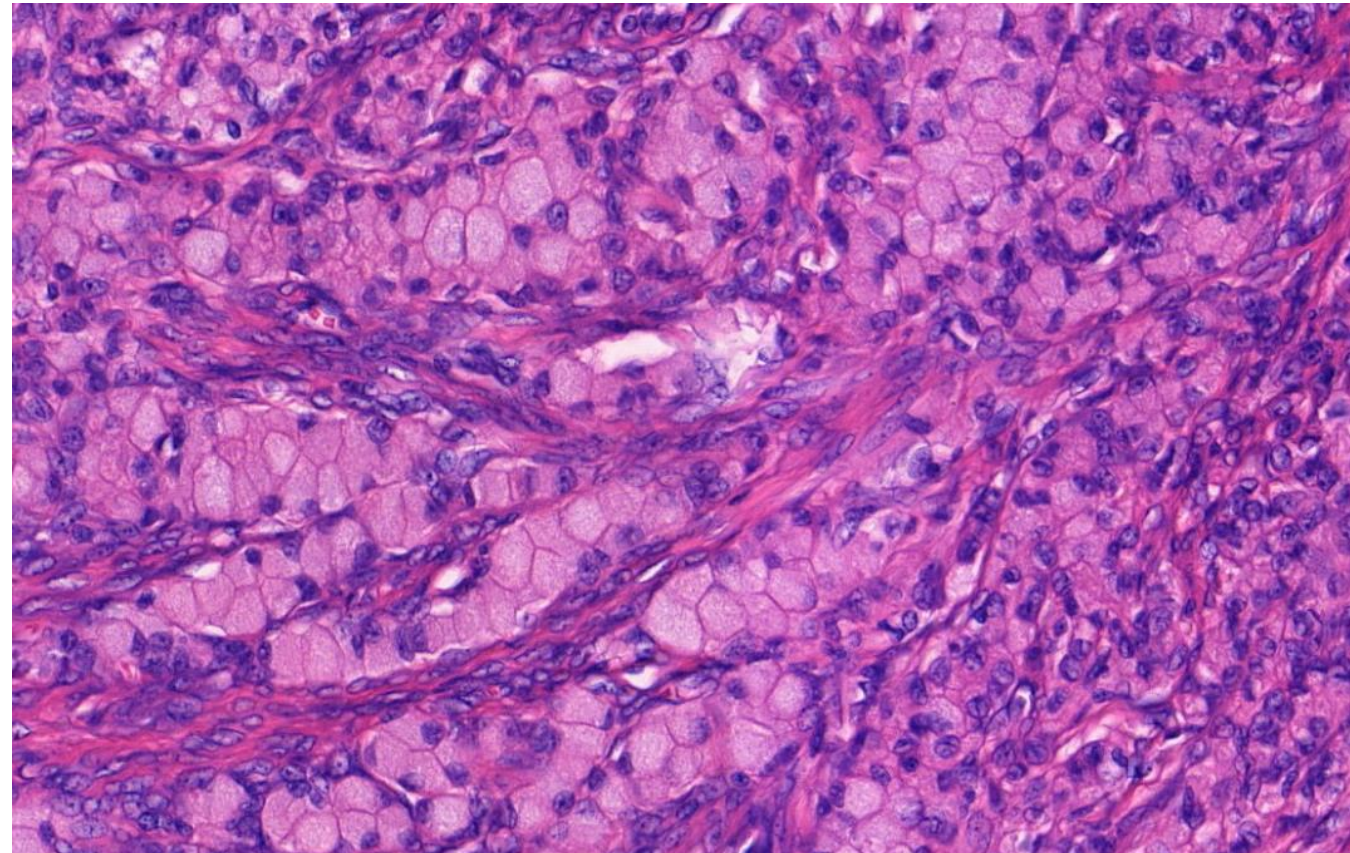
Ovarian metastasis (usually bilateral)

Metastasis of signet ring cell carcinoma:

Krukenberg-tumor

- gastric adenocarcinoma
- colorectal carcinoma
- breast carcinoma (invasive lobular carcinoma)

- pancreatic adenocarcinoma
- cholangiocarcinoma
- cervical adenocarcinoma



The image features two vertical strips of histological sections on the left and right sides, showing the structure of the respiratory tract. The sections are stained with hematoxylin and eosin (H&E), highlighting the nuclei in purple and the cytoplasm/extracellular matrix in pink. The sections show the mucosal lining, including the epithelium and underlying connective tissue, with visible airway lumens. The central area of the slide is a plain white background.

THANK YOU FOR YOUR ATTENTION!