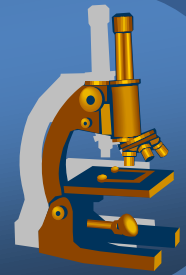
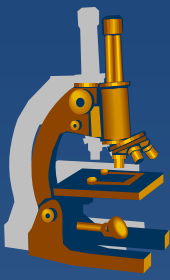


Systematic pathology

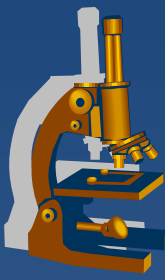


Genital system pathology

Breast pathology



Male genital tract pathology



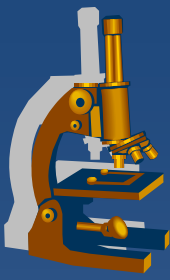
- x Prostate**
- x Penis, scrotum**
- x Testis, epididymis**

⇒ *congenital defects*

⇒ *circulatory disorders*

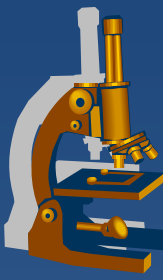
⇒ *inflammations*

⇒ *tumors*



Prostate gland

Prostate gland



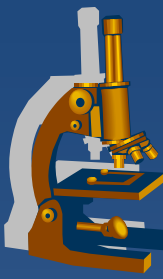
✗ inborn defects uncommon

✗ circulatory disorders:

⇒ *infarction*

- in the setting of benign hyperplasia
- regenerative + reparative processes adjacent to the infarction focus may mimic a malignant lesion (esp. in needle biopsy)

Prostate gland



x inflammations:

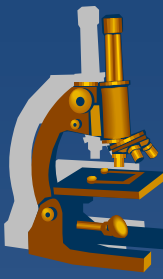
⇒ *bacterial (acute purulent or chronic)*

- systemic symptoms, dysuria, frequency, local pain
- ascendent, iatrogenic (catheterisation, surgery, ...)
- *E. coli, Klebsiella, Proteus, enterobacter...*
- tb
 - most common tb presentation in the male genital system
 - local spread or isolated metastasis of lung tb
 - diff. dg. x reactive or idiopathic granulomatous prostatitis

⇒ *abacterial*

- most common, chronic pain or asymptomatic
- *Chlamydia trachomatis, ureaplasma...*

Prostate gland



x pseudotumors, tumors:

⇒ *Benign prostatic hyperplasia*

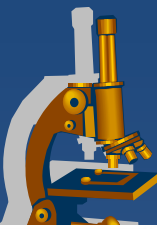
⇒ *Carcinoma*

- **Acinar**
- Ductal
- Squamous cell
- Adenosquamous
- Transitional cell
- Neuroendocrine

⇒ *Secondary tumors*

- local ca infiltration from adjacent organs (bladder, rectum)
- haematogenous metastases (lung ca, malignant melanoma, ..)

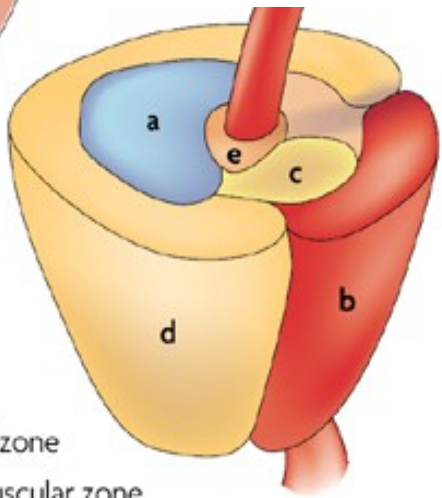
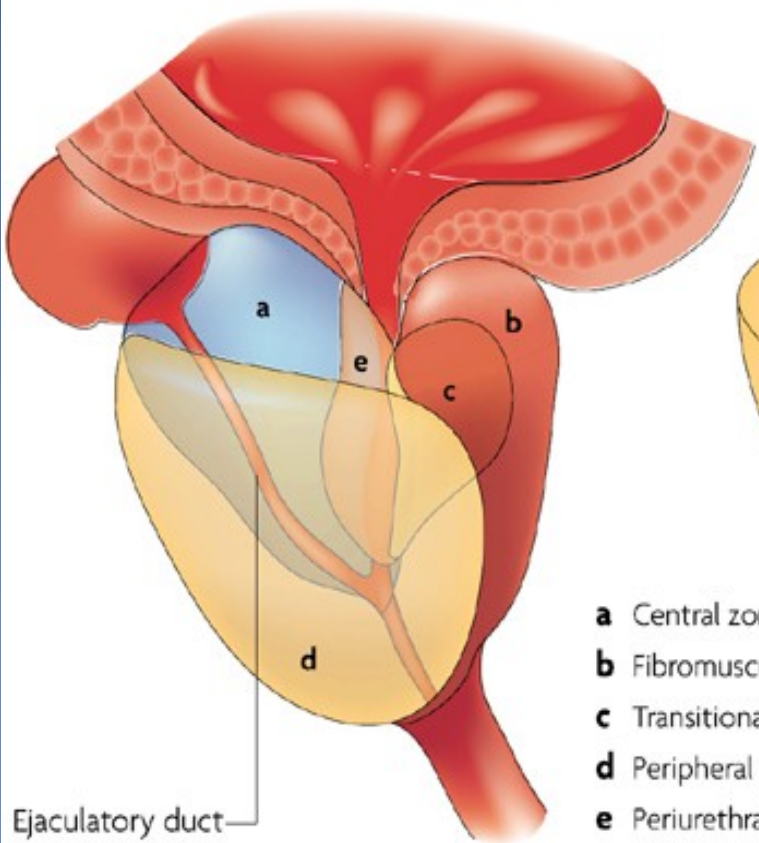
Zonal predisposition of prostate diseases



	Prostate zone		
	Peripheral	Transition	Central
Focal atrophy	Medium-high prevalence	Medium-high prevalence	Low prevalence
Acute inflammation	Low prevalence	Low prevalence	None
Chronic inflammation	Medium-high prevalence	Medium-high prevalence	Low prevalence
Benign prostatic hyperplasia	None	High prevalence	Low prevalence
High-grade PIN	Medium-high prevalence	Low prevalence	Low prevalence
Carcinoma	Medium-high prevalence	Low prevalence	None

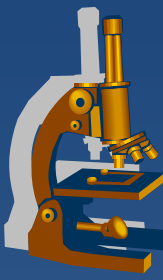
High prevalence Low prevalence
 Medium-high prevalence None

Prostate zones



- a** Central zone
- b** Fibromuscular zone
- c** Transitional zone
- d** Peripheral zone
- e** Periurethral gland region

Ejaculatory duct



Benign prostatic hyperplasia

x epidemiologic factors:

- ⇒ *age (BPH prevalence rising with age, 70% by age 60, 90% by 80)*
- ⇒ *geographic/racial (low in Asia, more common in W Europe)*

x pathogenesis:

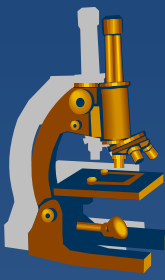
- ⇒ *not completely clear*
- ⇒ *hormonal dysbalance, dihydrotestosteron induced growth factors → stromal proliferation + ↓ death of glandular cells*

x gross nodular hyperplasia:

- ⇒ *periurethral (transition zone) mostly affected → urethral compression + obstruction → dysuria*

x consequences:

- ⇒ *lower urinary tract symptoms, acute/chronic urinary retention, cystitis*
- ⇒ *bladder hypertrophy + diverticula, hydroureter + -nephrosis, pyelonephritis*



Benign prostatic hyperplasia

x micro:

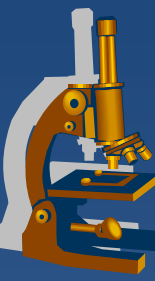
⇒ ***nodular structure***

⇒ ***glands:***

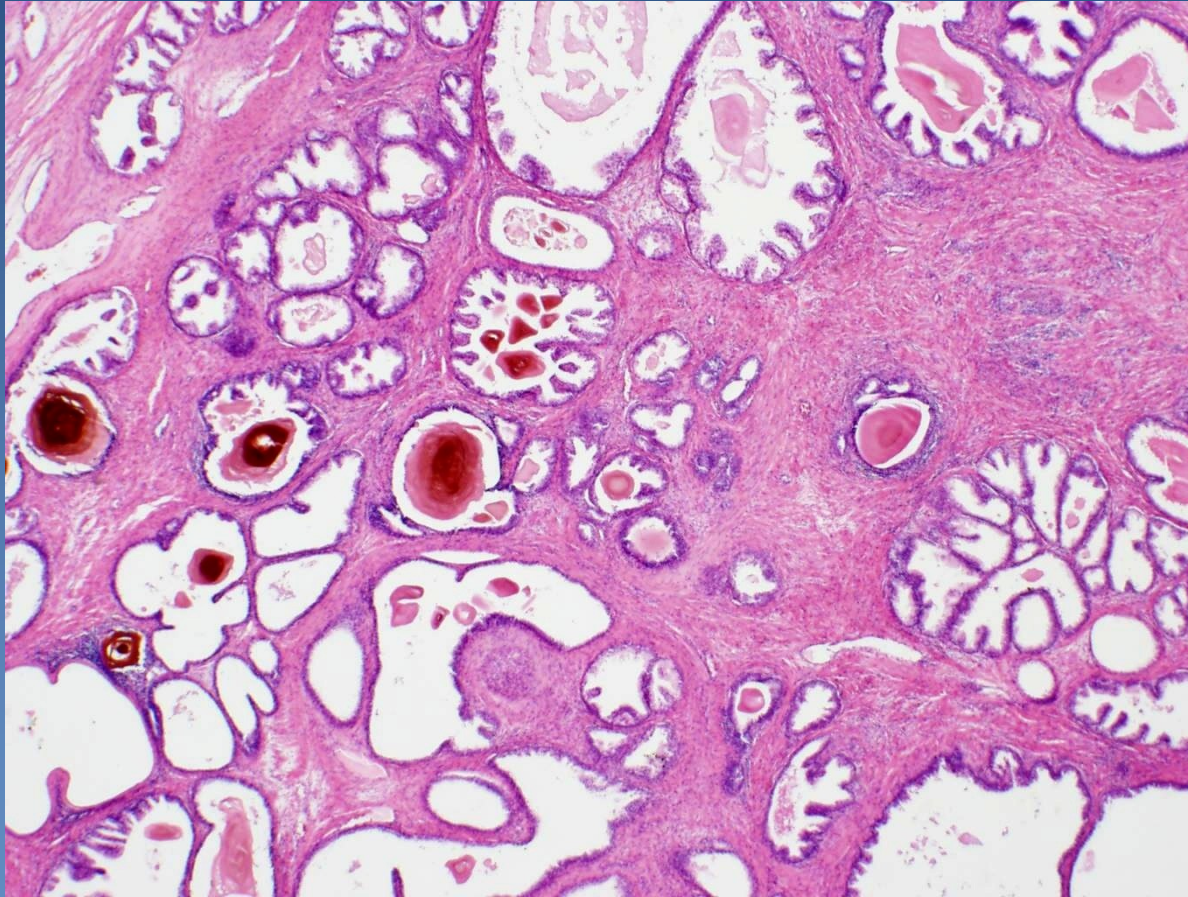
- hyperplastic, uneven size, common cystic dilatation
- bi-layered epithelium – external myoepithelial (!x invasive ca), inner secretory (sm. papillary proliferation)
- inspissated luminal secretions → corpora amylacea

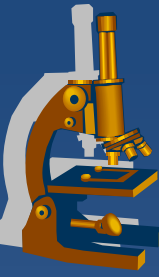
⇒ ***stroma:***

- hyperplastic, common purely stromal fibromuscular nodules
- disperse chronic inflammatory reaction

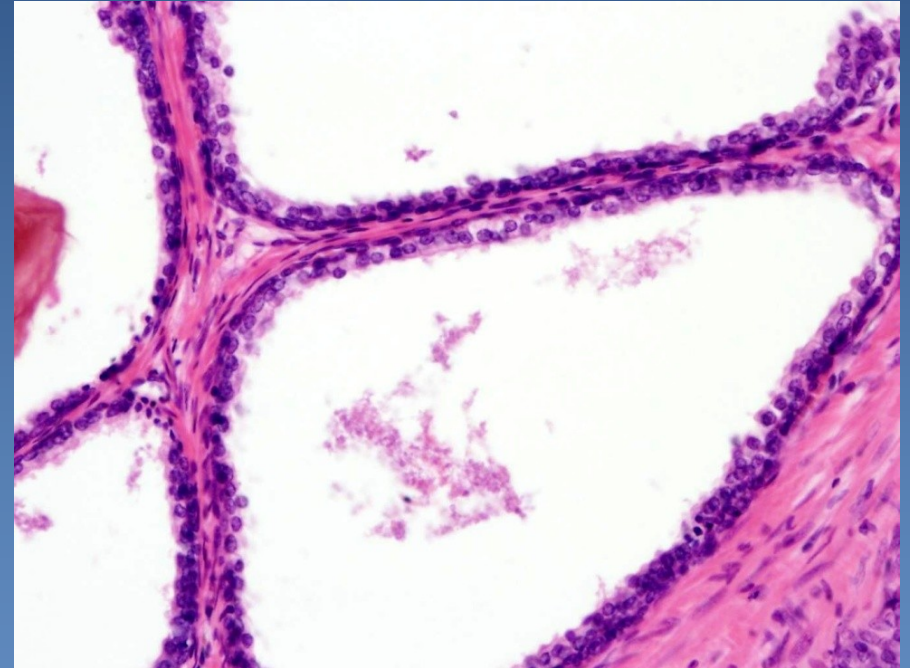
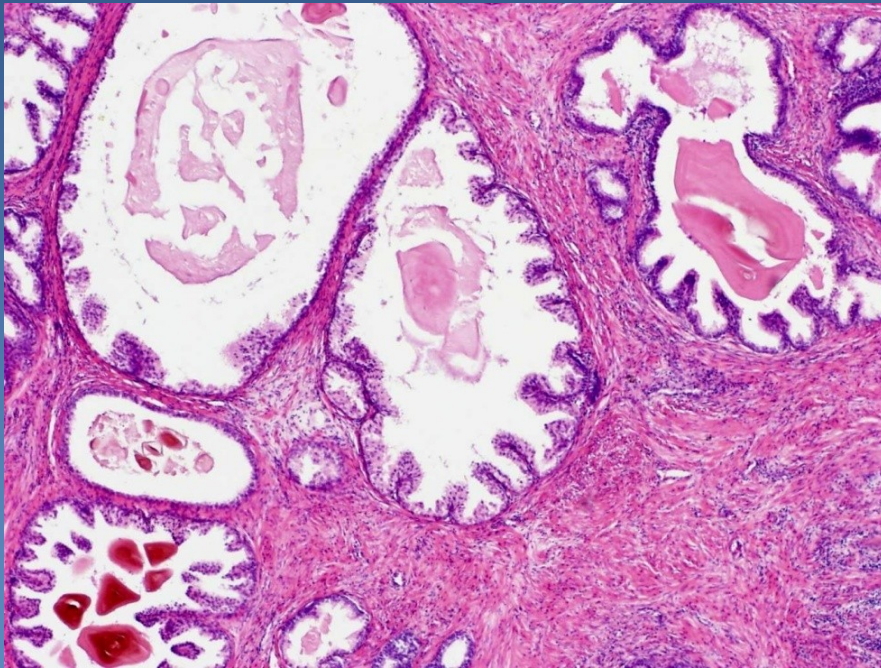


Benign prostatic hyperplasia

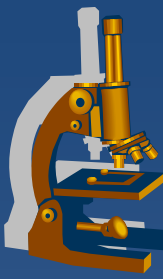




Benign prostatic hyperplasia



Prostatic adenocarcinoma

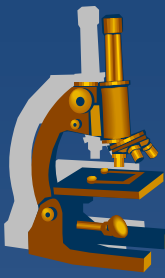


- x ↑ incidence
 - ⇒ *1st – 3rd of the most common male malignancies (prostate – lungs – colorectal)*

- x **peripheral zone of prostate, dorsal part (per rectum!)**

- x dg.:
 - ⇒ *needle biopsy (most common, by suspicion)*
 - ⇒ *transurethral resection (BHP treatment – accidental)*
 - ⇒ *suprapubic prostatic resection*

Prostatic adenocarcinoma



✘ Prostatic intraepithelial neoplasia (PIN)

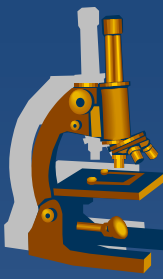
⇒ *Low-grade*

- more numerous acinar cells, without significant nuclear atypias

⇒ *High-grade*

- significant cytonuclear atypia of acinar cells (enlarged nucleus, prominent nucleolus)
- **commonly in proximity of acinar adenocarcinoma – precursor lesion**

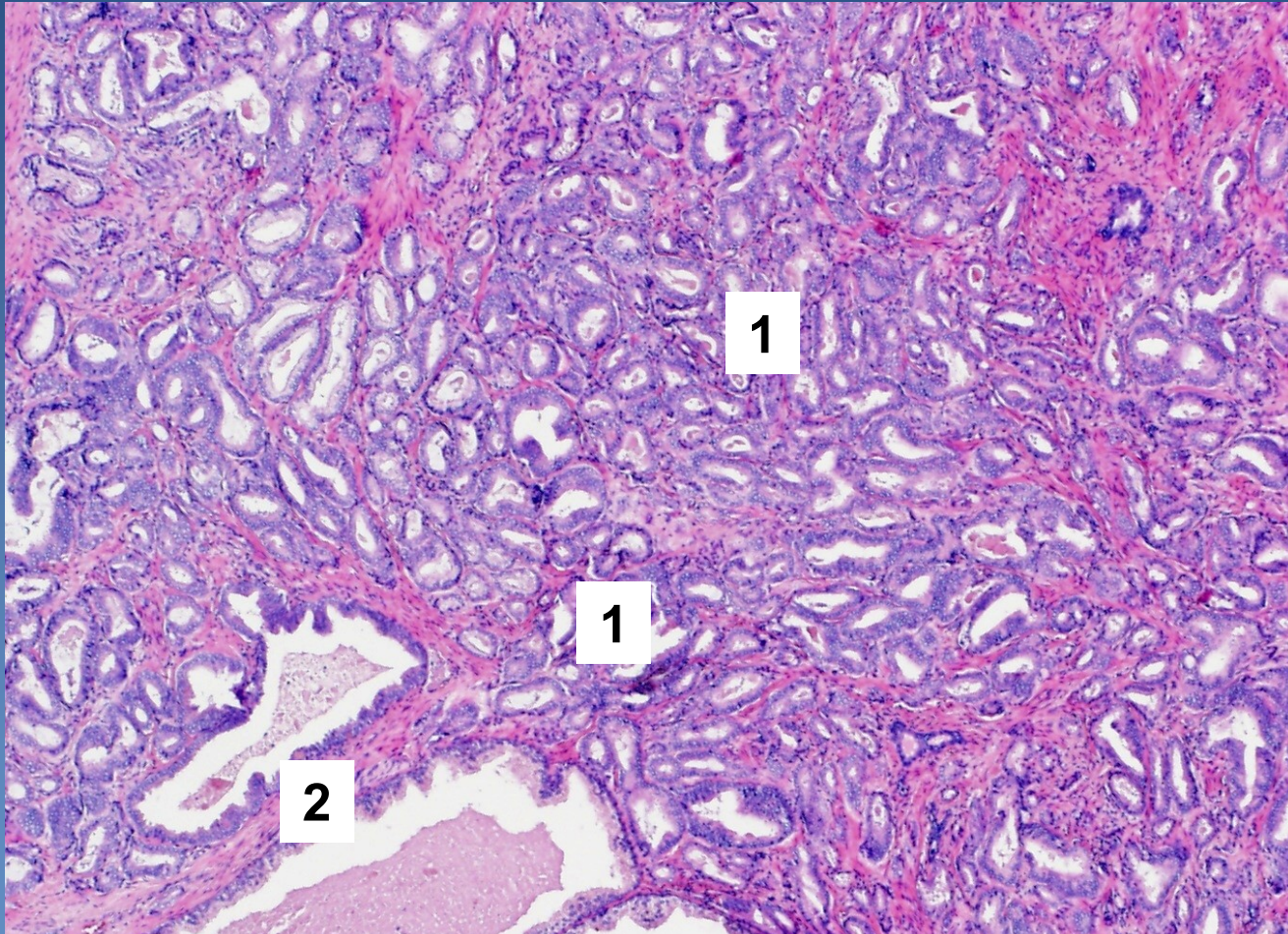
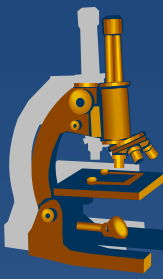
Acinar prostatic adenocarcinoma



x micro:

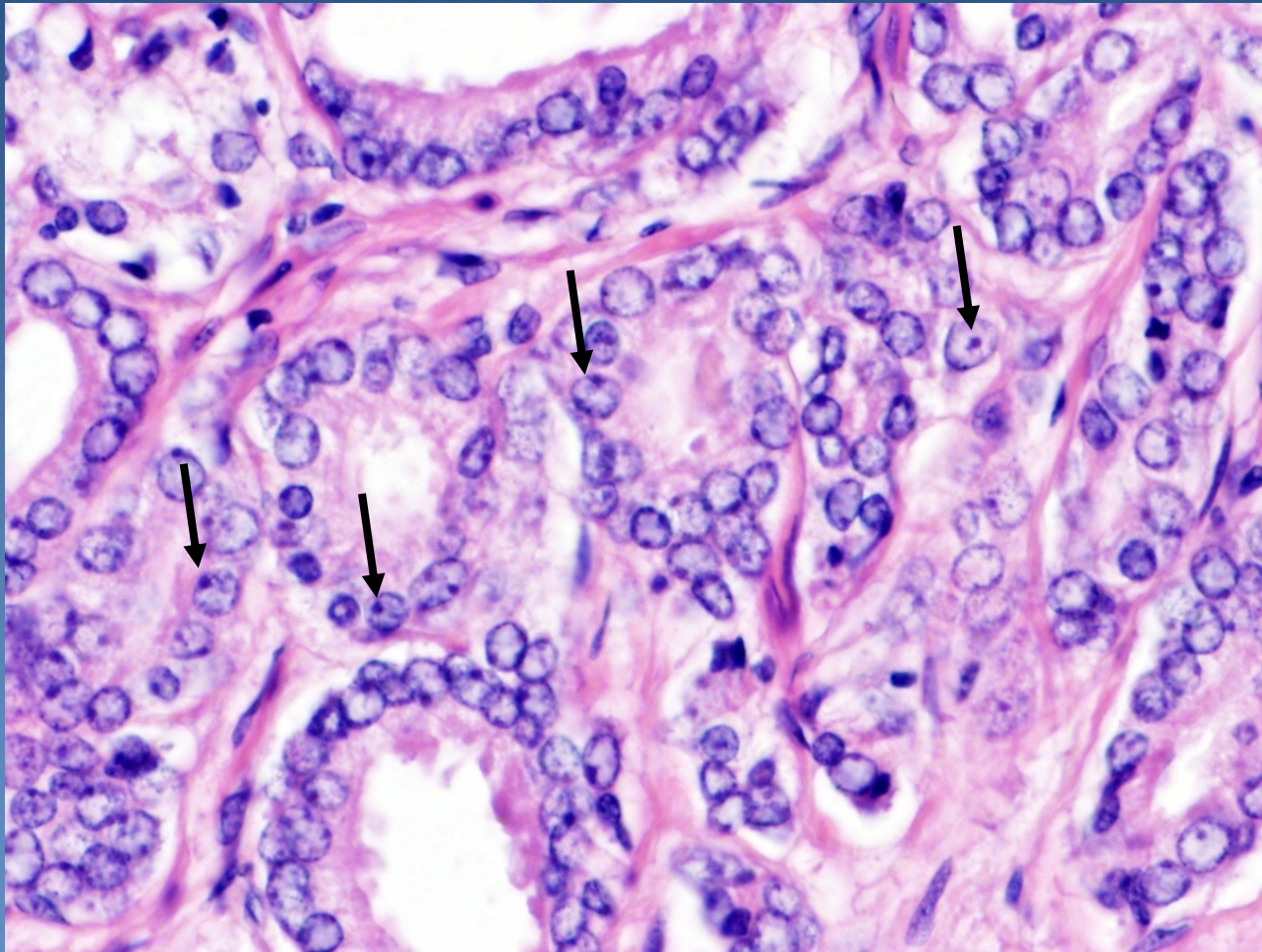
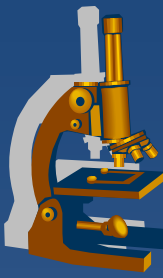
- ⇒ neoplastic cells with round nuclei and prominent nucleoli*
- ⇒ smaller crowded glands **without detectable layer of basal cells***
 - immunohistochemistry: HMW CK, p63 negative
 - neoplastic acini infiltrating between normal glands
 - intraluminal crystalloids (pale eosinophilic substance)
- ⇒ perineural and/or extraprostatic propagation possible*

Acinar prostatic adenocarcinoma



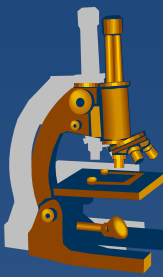
Small neoplastic acini (1) growing between prostatic glands (2)

Acinar prostatic adenocarcinoma



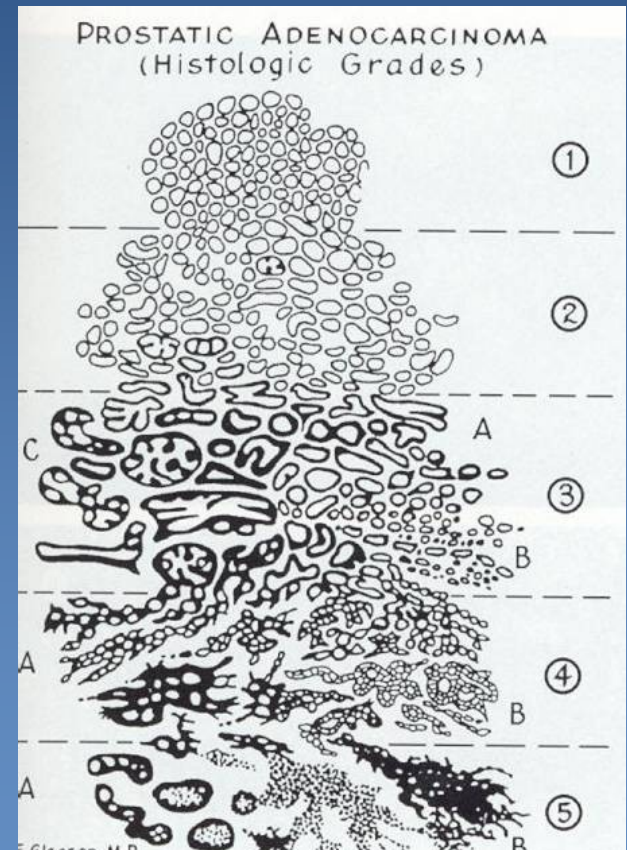
Nucleoli (arrows). Missing basal layer.

Acinar prostatic adenocarcinoma

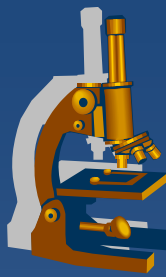


✘ Gleason histologic grading (WHO modification):

- grade of glandular differentiation, growth pattern
- **combined score - dominant + secondary pattern in 5-grade system**
- grade 1 similar to normal prostatic tissue (uncommon in ca)
- grade 5 with solid, dissociated pattern
- final combined score, commonly Gleason score 7 (4+3)

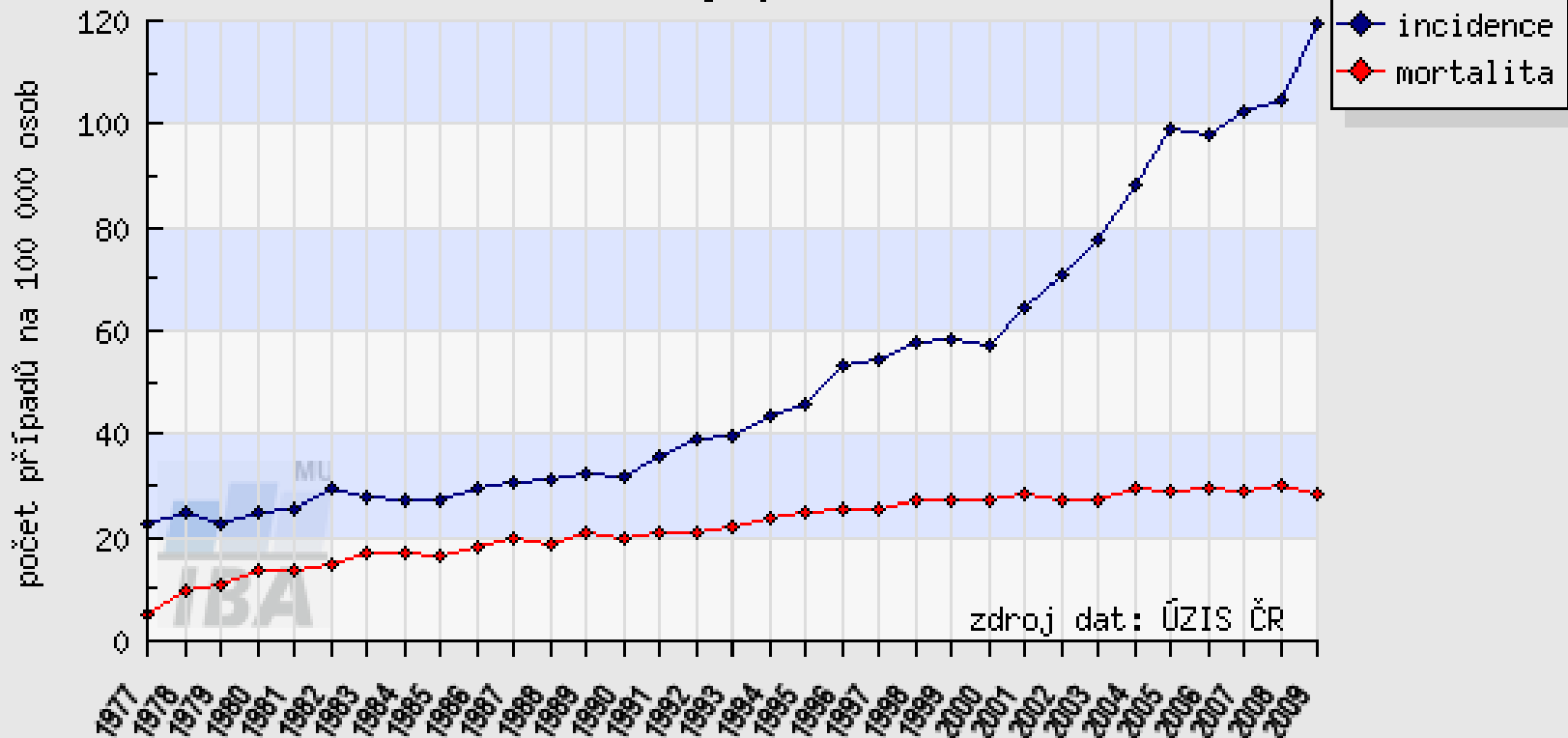


Acinar prostatic adenocarcinoma



C61 - ZN předstojné žlázy - prostaty, muži

vývoj v čase

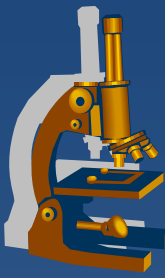


zdroj dat: ÚZIS ČR

analyzovaná data: N(inc)=85211, N(mor)=36040

<http://www.uroweb.cz>

Acinar prostatic adenocarcinoma



x spread

⇒ *local (per continuitatem)*

- into periprostatic soft tissues, seminal vesicles, urinary bladder (!x transitional cell ca, may be both in the same patient)

⇒ *via lymphatics*

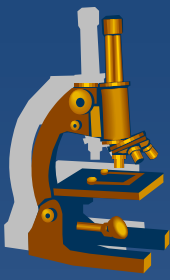
- into regional LN

⇒ *via blood*

- into bones – osteoblastic/osteosclerotic metastases (pelvis, vertebrae, ribs, long bones)
- later into liver, lungs...

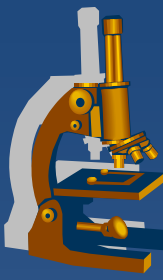
x prognosis

- ⇒ *depend on the clinical stage (TNM), Gleason score, pre-operative PSA level in serum*



Penis, scrotum

Penis, scrotum



x congenital defects

⇒ *hypospadia, epispadia*

- commonly + cryptorchidism
- in complex somatosexual disorders

⇒ *phimosis*

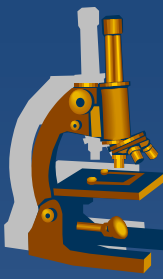
x circulatory disorders

⇒ *chronic venoous congestion*

⇒ *oedema*

⇒ *corpora cavernosa thrombosis, gangrene (uncommon)*

Penis, scrotum



x inflammations

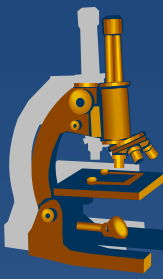
⇒ ***balanoposthitis*** (*glans + inner surface of the prepuce*)

- STD (gonorrhoea, genital herpes, lymphogranuloma venereum, syphilis ...)
- risk factors:
 - phimosis, chronic mechanical/chemical irritation
 - streptococi, staph., coliforms; candidas (DM)...

⇒ ***balanitis xerotica obliterans = lichen sclerosus***

- epithelial hyperkeratosis, atrophy, inflammatory infiltrate

Penis, scrotum



x tumors, pseudotumors:

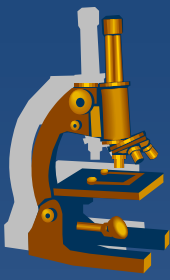
⇒ *Peyronie's disease – penile fibromatosis*

⇒ *benign epithelial tumors*

- **condyloma accuminatum**
 - HPV 6, 11

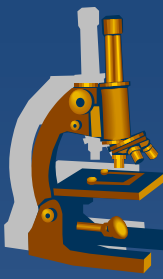
⇒ *malignant epithelial tumors*

- **carcinoma in situ**
 - Bowen's disease / erythroplasia of Queyrat on the glans
 - bowenoid papulosis (multiple, HPV 16, non-progressive)
- **invasive squamous cell carcinoma**
 - geography (Latin America, East Asia)
 - circumcision - protective factor (↓HPV, carcinogenes in smegma)
 - risk factor – smoking, occupational (mineral oil, tar)



Testis, epididymis

Testis, epididymis



x congenital defects

⇒ *cryptorchidism (undescended testis)*

x circulatory and regressive changes

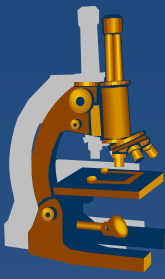
⇒ *necrosis (haemorrhagic infarction) – typical due to testicular torsion, ! emergency*

⇒ *atrophy – senile involution, vascular, hormonal...*

⇒ *intrascrotal swelling*

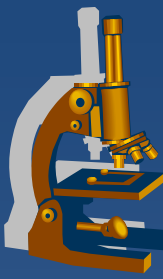
- hydrocele (serous fluid in tunica vaginalis)
- haematocele (haemorrhage into tunica vaginalis)
- varicocele (varicose veins)
- spermatocele (cystic dilatation of epididymis ducts)

Testis, epididymis inflammations



- ✗ epididymis >>> testis
- ✗ usually ascending from urinary tract and/or prostate
- ✗ caused by
 - ⇒ *gramnegative bacteria (children)*
 - ⇒ *chlamydias, gonococcus (adults)*
 - ⇒ *E. coli (older adults)*

Testis, epididymis inflammations



x Bacterial

⇒ *purulent* → *abscess, non-specific orchitis/epididymitis*

x Interstitial non-purulent orchitis

⇒ *mumps in adults*

⇒ *interstitial oedema + lymphocytes, plasma cells, macrophages*

x Granulomatous orchitis

⇒ *may be posttraumatic, v.s. autoimmune inflammation*

⇒ *non-caseating tuberculoid granulomas centered on tubules*

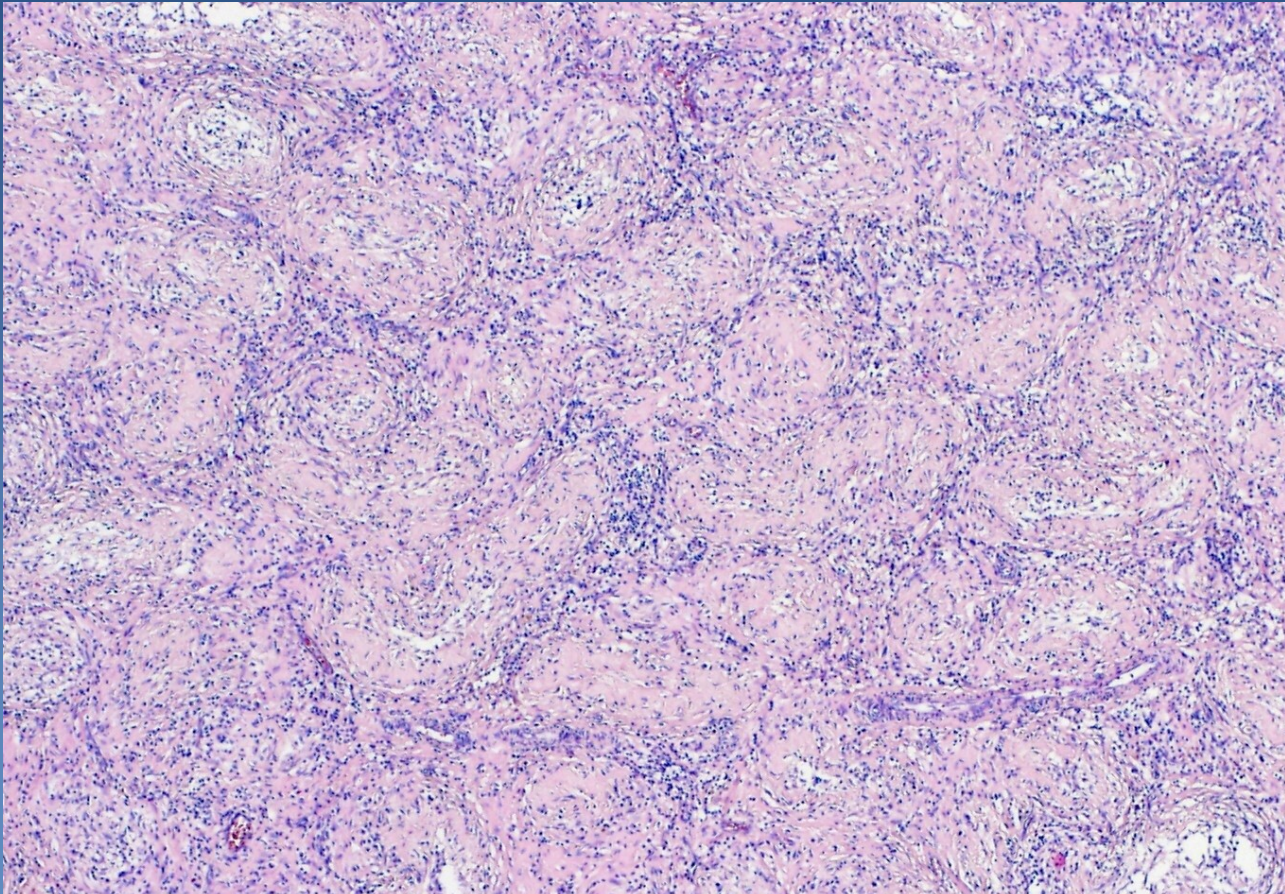
⇒ *firmer testicular mass (diff. dg. x tumor)*

x Spermatocytic granuloma

⇒ *in the head of epididymis due to rupture of tubules*

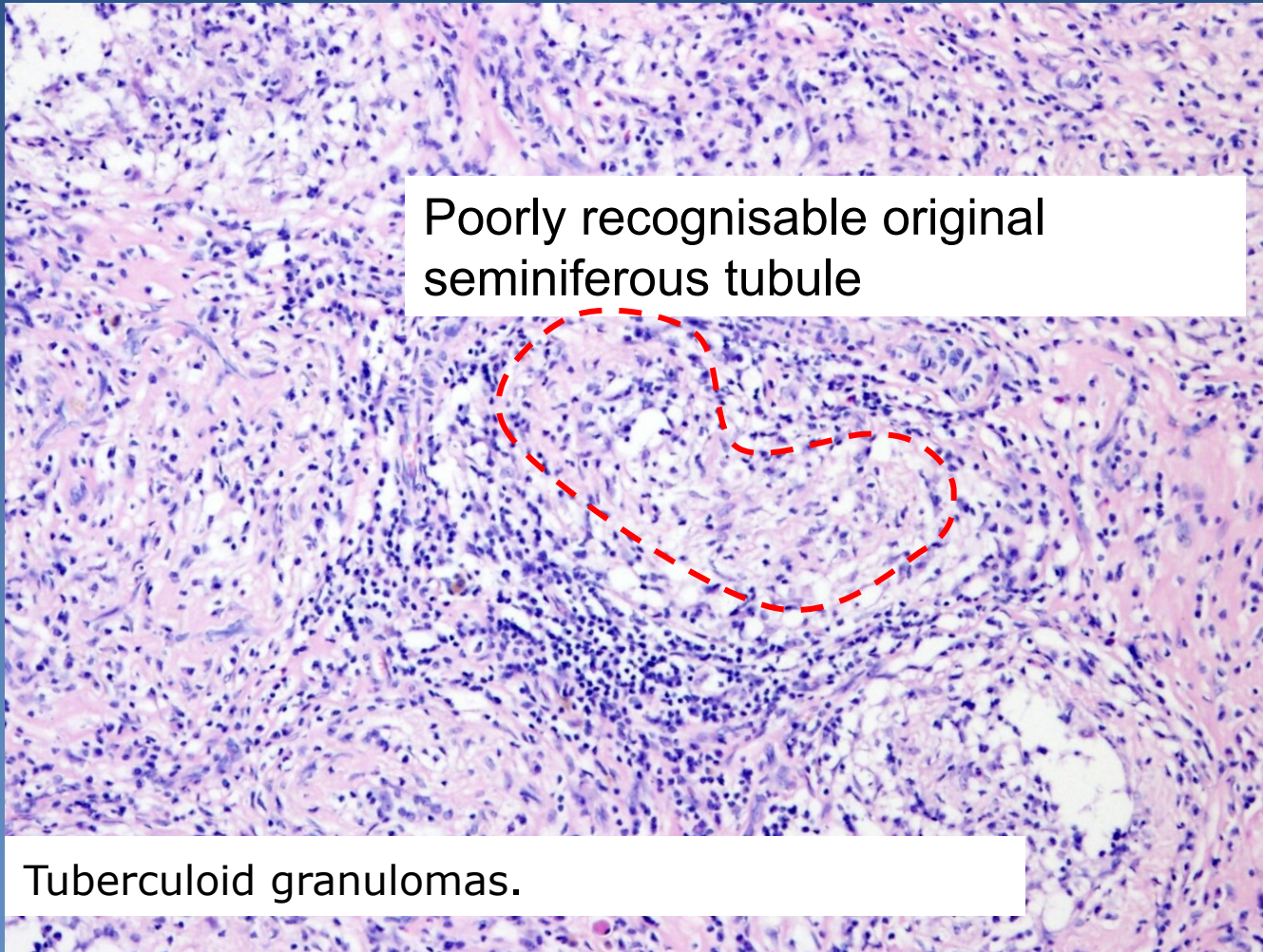
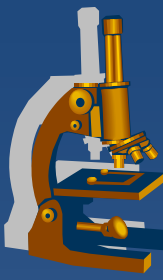
⇒ *reactive tuberculoid granulomas around spermatozoa*

Granulomatous orchitis



Tuberculoid granulomas.

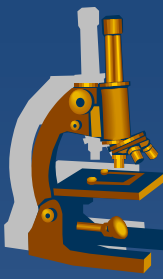
Granulomatous orchitis



Poorly recognisable original seminiferous tubule

Tuberculoid granulomas.

Testicular tumors



- × **Germinal**

 - ⇒ *from germ cell*

- × **Sex cord-stromal**

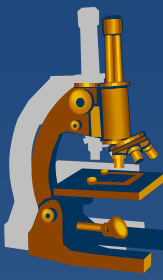
 - ⇒ *from specialized mesodermal gonadal stroma*

- × **Mixed germ cell – sex cord stromal tumors**

- × **Other primary tumors**

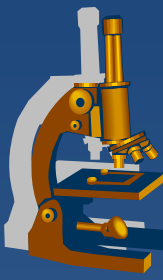
- × **Metastatic (secondary) tumors**

Testicular tumors : histopathological report



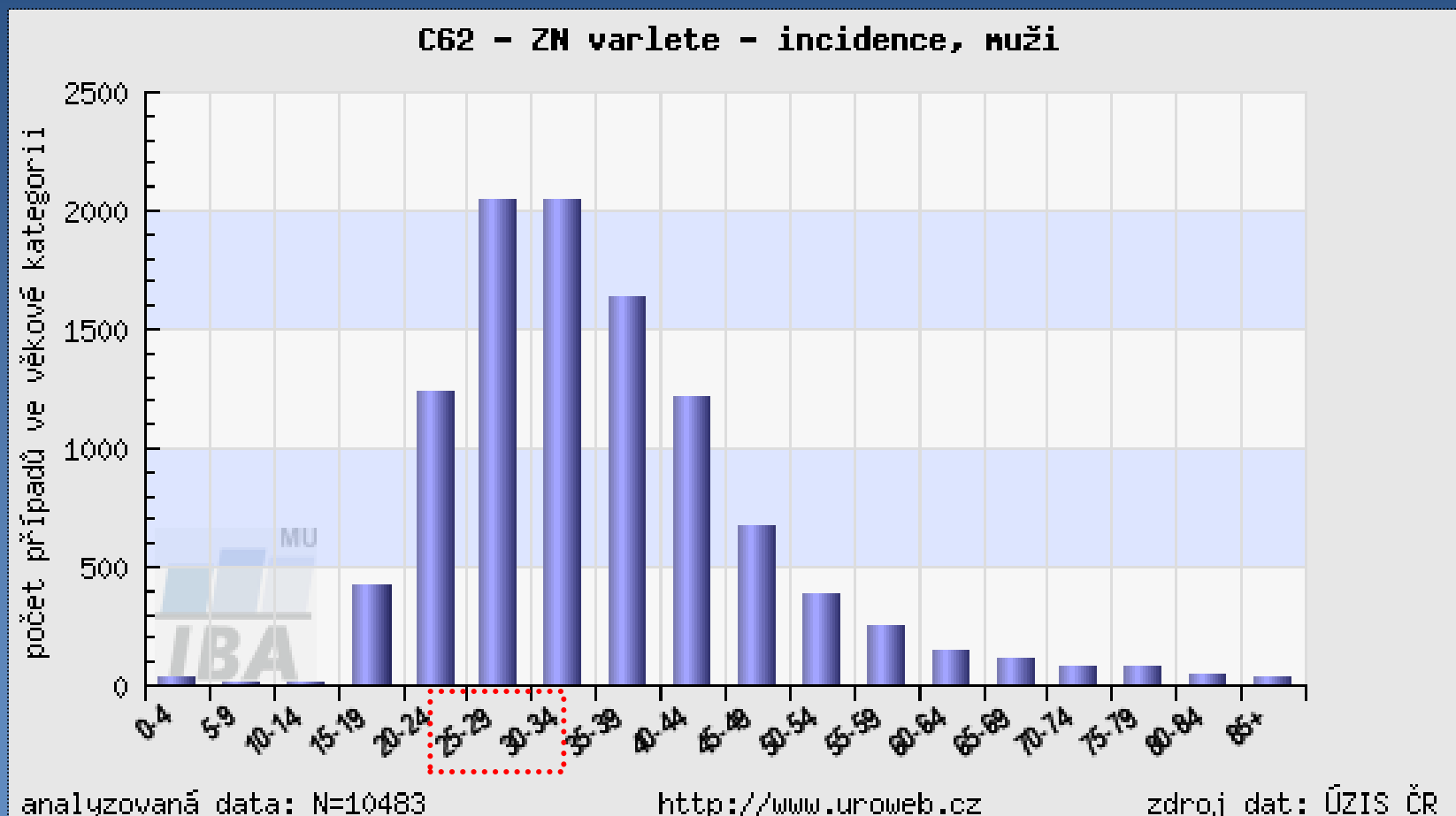
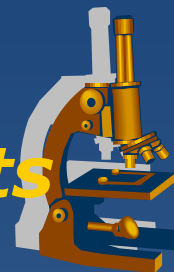
- x** gross picture (incl. size)
- x** histological type
- x** presence of vascular / lymphatic propagation
- x** tumor staging (TNM classification)
- x** presence of intratubular germ cell neoplasia (ITGCN - in situ germ cell lesion)

Germ cell tumors

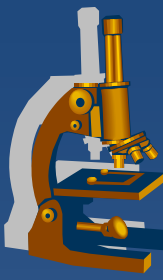


- x ~90 % of primary testicular tumors
- x cryptorchidism
 - ⇒ 3-5x ↑ risk of malignancy in undescended testis
- x oncogenic markers:
 - ⇒ α FP, hCG, PLAP, CEA, LDH
 - ⇒ detection in serum, tissues
 - ⇒ important in diagnosis, monitoring the response to therapy, patient check-up after therapy

Age structure of testicular tumors patients

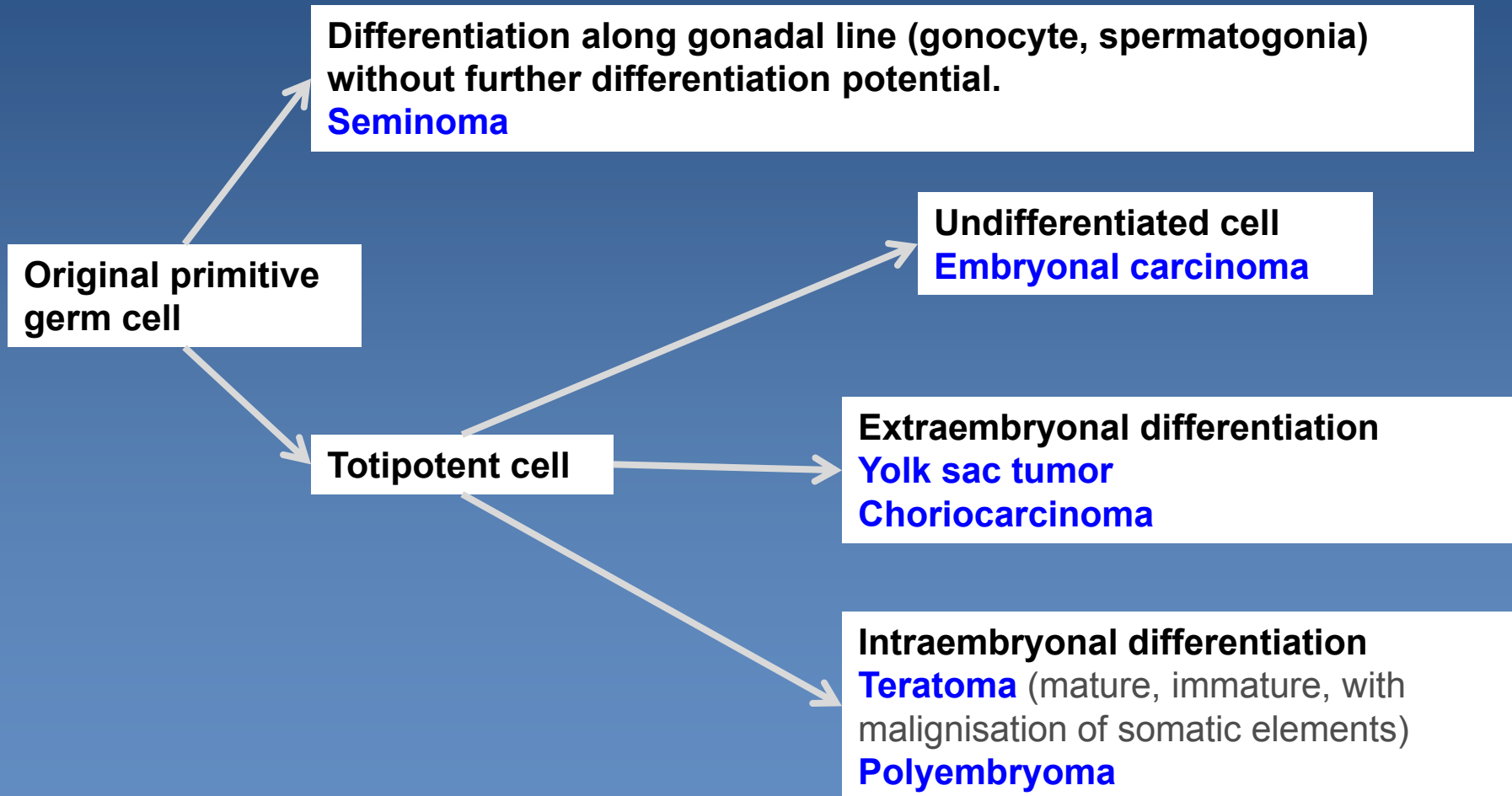
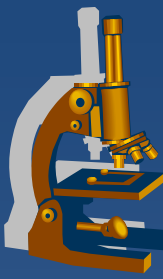


Germ cell tumors

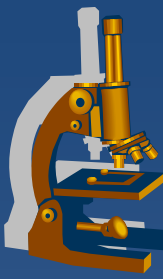


- ✘ intratubular germ cell neoplasia
 - ⇒ *ITGCN - in situ germ cell lesion*
 - ⇒ *common precursor lesion of germ cell tumors*
- ✘ basic classification:
 - ⇒ *seminoma*
 - ⇒ *non-seminomatous tumors*
- ✘ germ cell tumors of 1 histologic type – 60 %
- ✘ mixed germ cell tumors – 40 %
- ✘ metastases into LN (paraaortal LN),
via blood (most commonly into lungs)

Germ cell tumors histogenesis



Germ cell tumors classification



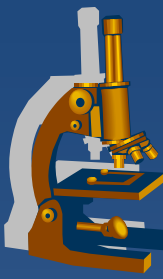
x tumors of single histologic type

⇒ ***Seminoma*** (+ variants)

⇒ ***Non-seminomatous germ cell tumors***

- **Embryonal carcinoma**
- **Yolk sac tumor**
- **Choriocarcinoma**
- **Teratomas**
 - mature
 - immature
 - with malignisation of somatic elements

Germ cell tumors classification



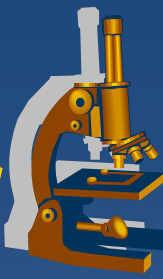
- x mixed germ cell tumors**

 - ⇒ tumors with >1 histogenetic type*

- x Spermatoctytic seminoma**

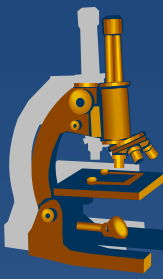
 - ⇒ separate clinical and pathological entity
(different morphology/prognosis)*

Germ cell tumors Characteristics



	age	marker	structure
Seminoma	30-50	10% HCG	solid, clear cells, lymphocytic stroma
Embryonal carcinoma	20-30	90% HCG/AFP	undiff. cells, organoid, necrosis
Yolk sac	<3	90% AFP	variable
Choriocarcinoma	20-30	100% HCG	cyto- + syncytiotrophoblast
Teratoma	no predilection	possible HCG,AFP	variable structures of >1 germ layer
Mixed tu	15-30	possible HCG,AFP	variable structures

Seminoma



x classical

⇒ *morphological variants:*

- seminoma with high mitotic rate (anaplastic), same treatment
- seminoma with syncytiotrophoblastic cells (↑ HCG)

⇒ *mostly age 25 - 45 years*

⇒ *tumor cells*

- in solid nests
- large cell, clear cytoplasm (glycogen), distinctive cellular membrane, large nuclei with 1-2 nucleoli

⇒ *fibrovascular septa*

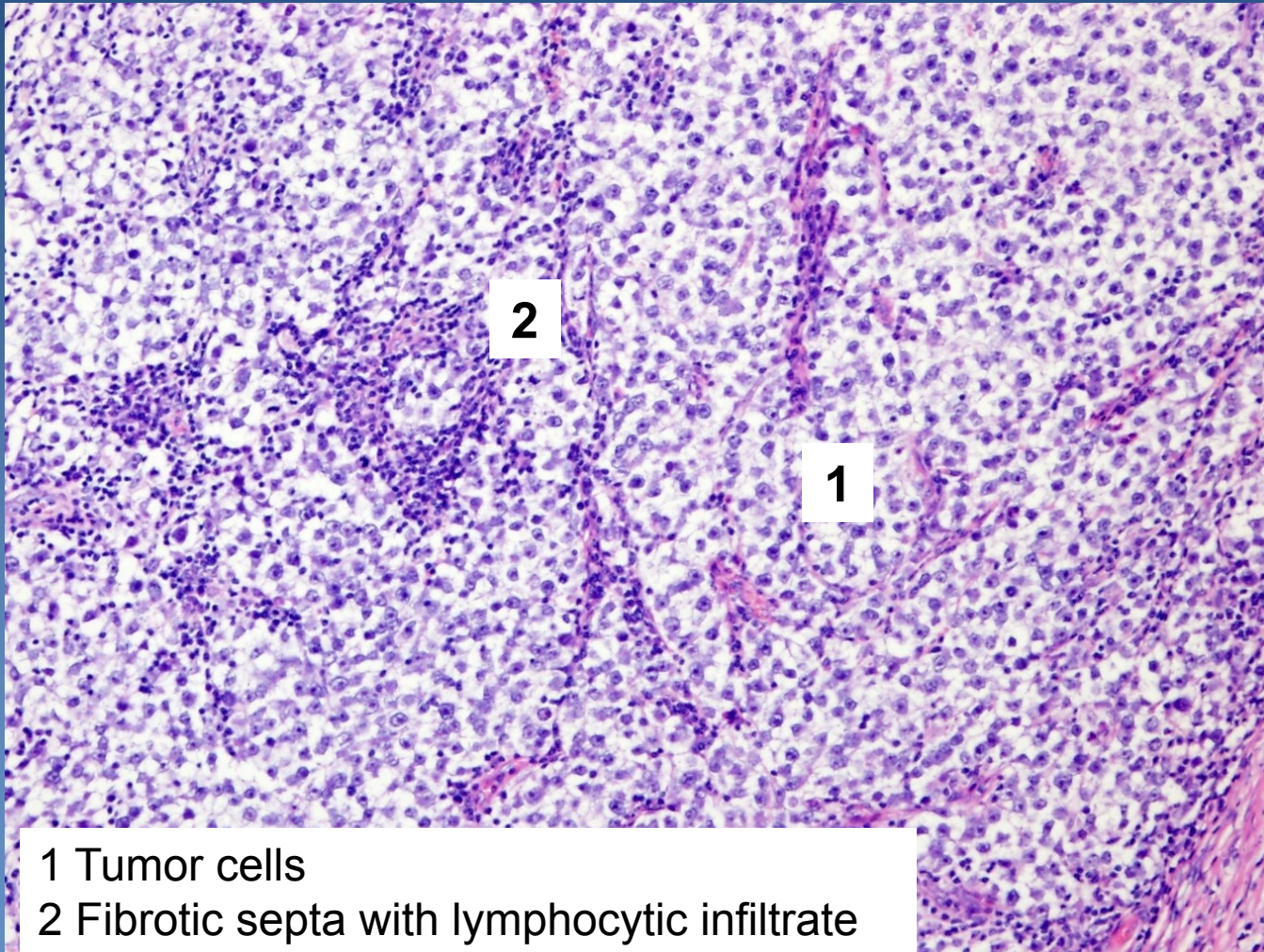
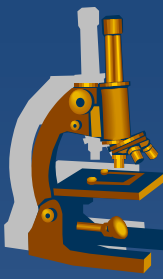
- with lymphocytic infiltrate (event. + granulomas)

⇒ *immunohistochemistry: PLAP+*

⇒ *marker – 10% HCG*

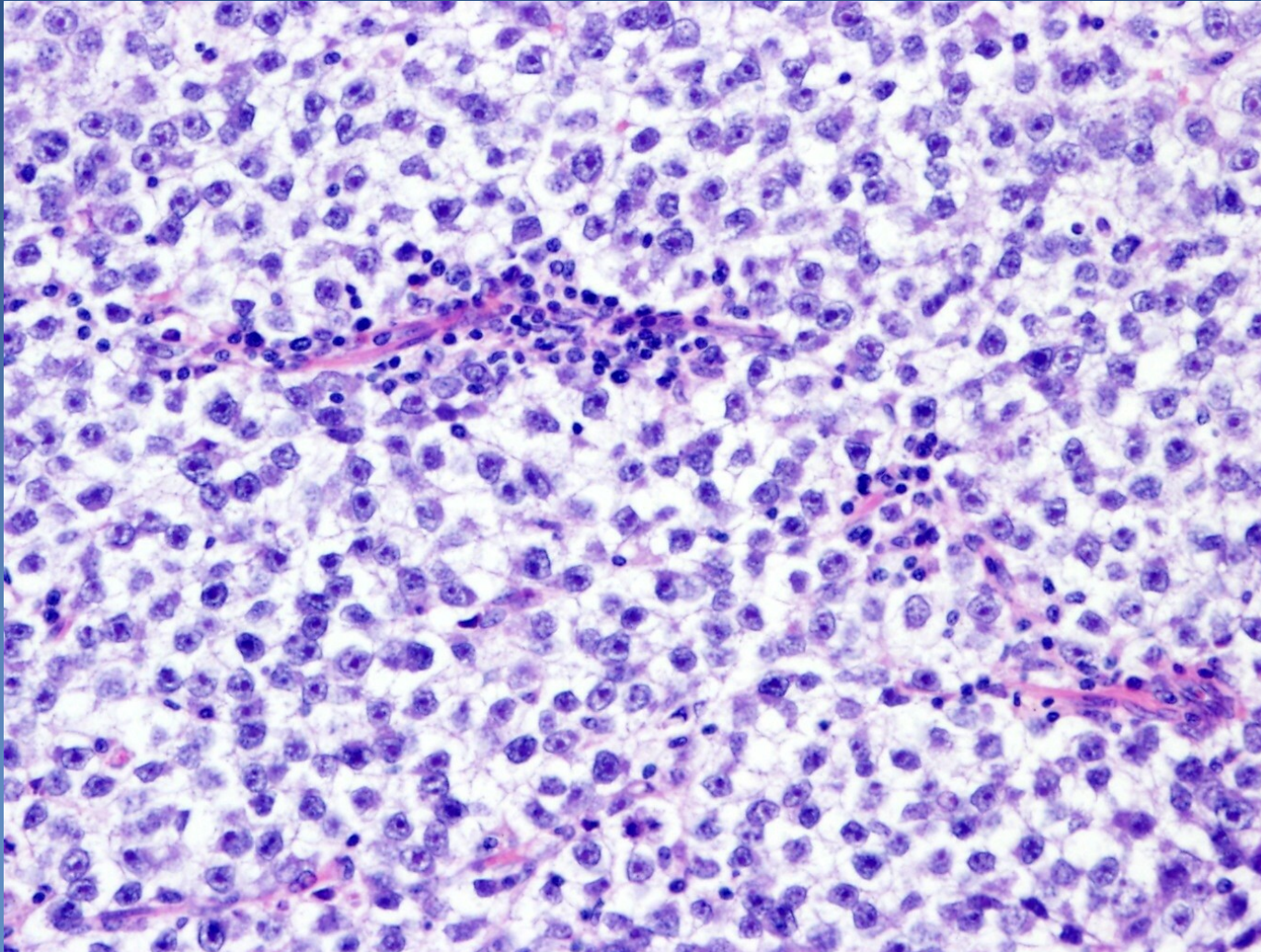
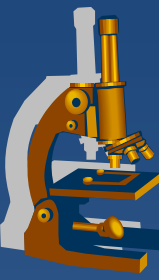
⇒ *radio- and chemosensitive (usually good prognosis)*

Seminoma

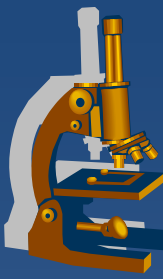


- 1 Tumor cells
- 2 Fibrotic septa with lymphocytic infiltrate

Seminoma

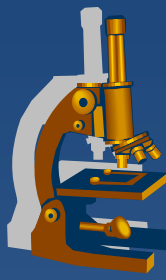


Seminoma

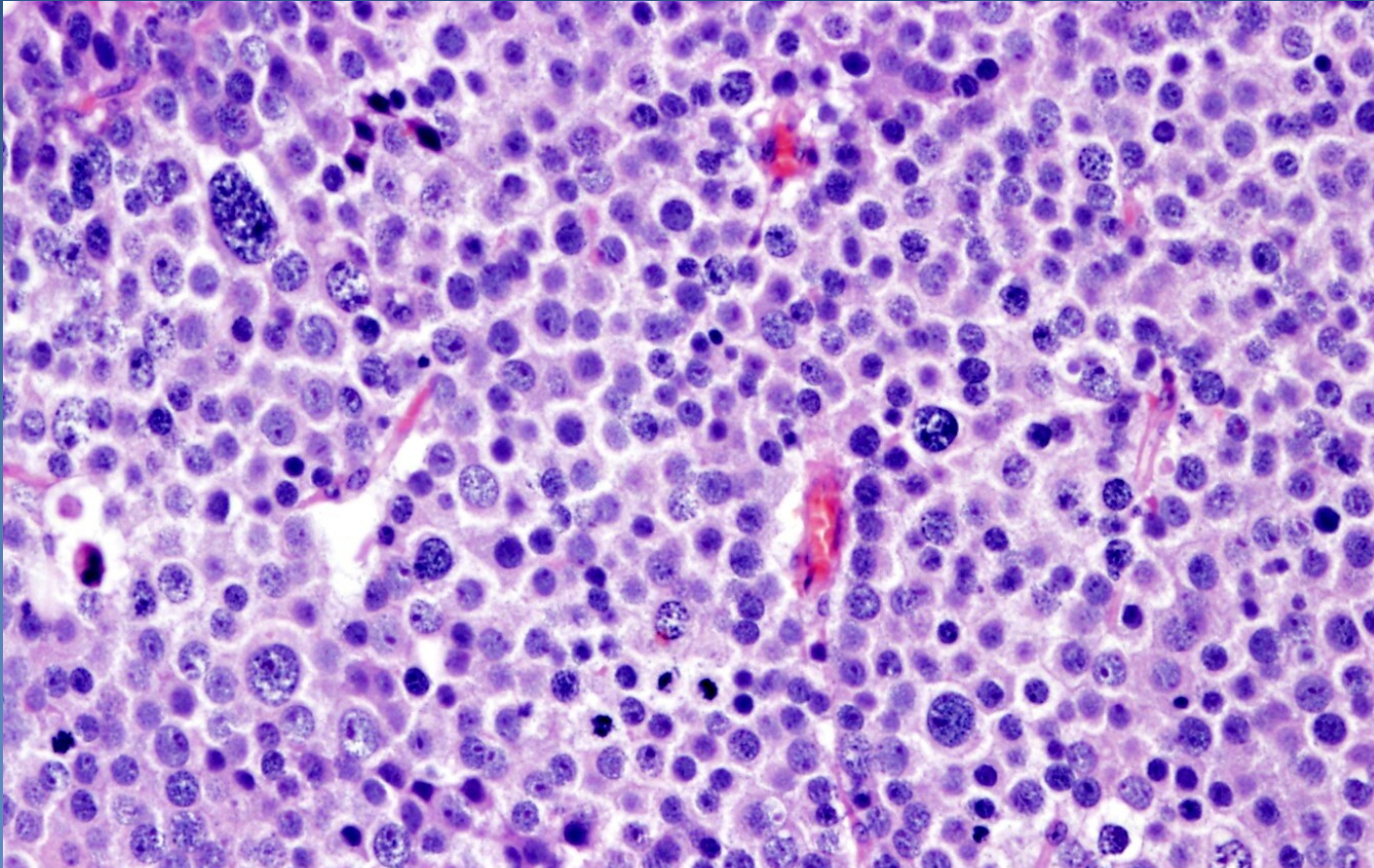


x Spermatocytic

- ⇒ *quite distinctive tumor, not a part of mixed germ cell tumors*
- ⇒ *only in the testis, older M, rare*
 - locally aggressive, no metastases
- ⇒ *tumor cells*
 - variable size (≈early stages of spermatogenesis)
 - **no glycogen**, no association with intratubular germ cell neoplasia
- ⇒ *fibrovascular septa without lymphocytic reactive infiltrate*
- ⇒ *IHC: PLAP-*

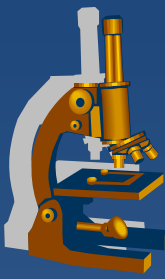


Spermatocytic seminoma



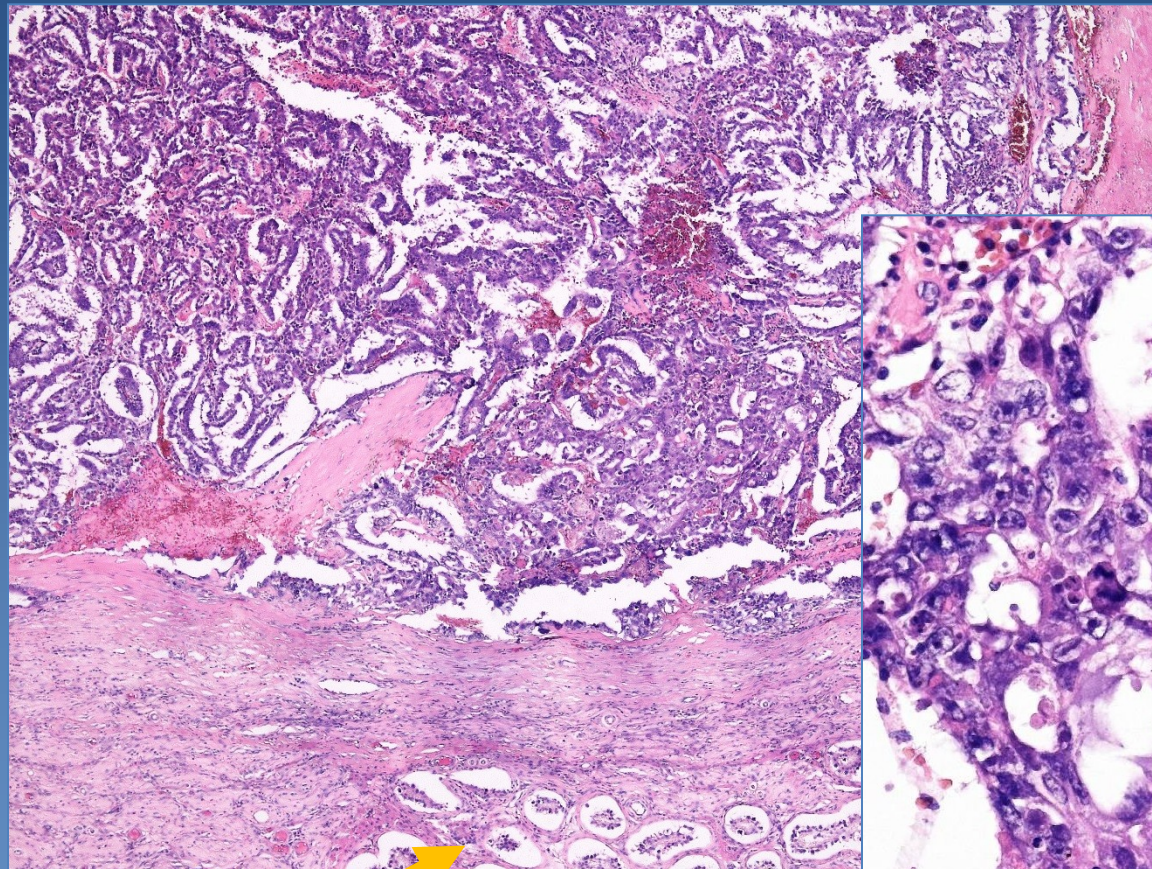
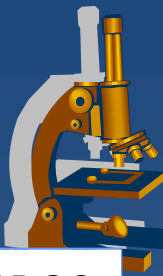
Mixture of polymorphic tumor cells (~ early stages of spermatogenesis): large cells with lacy chromatin, middle-sized cells with round nuclei, small lymphocyte-like cells.
Fibrotic septa without lymphocytic infiltrate

Embryonal carcinoma

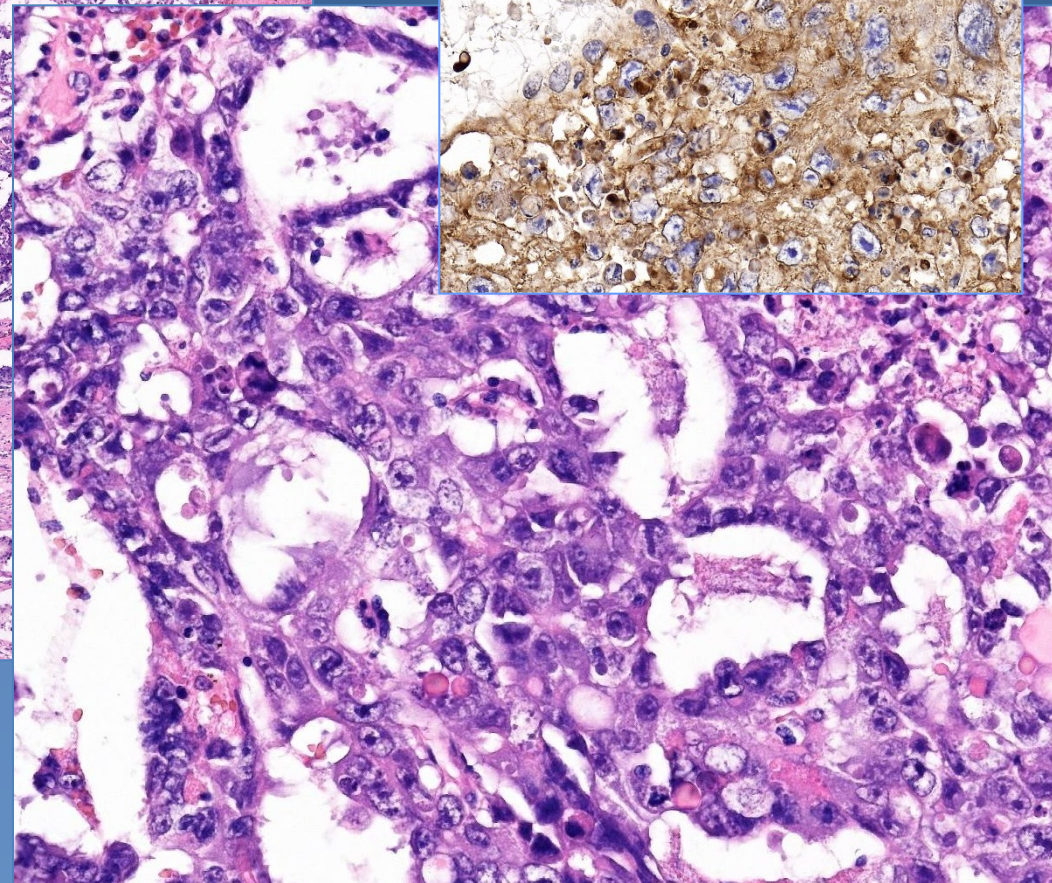
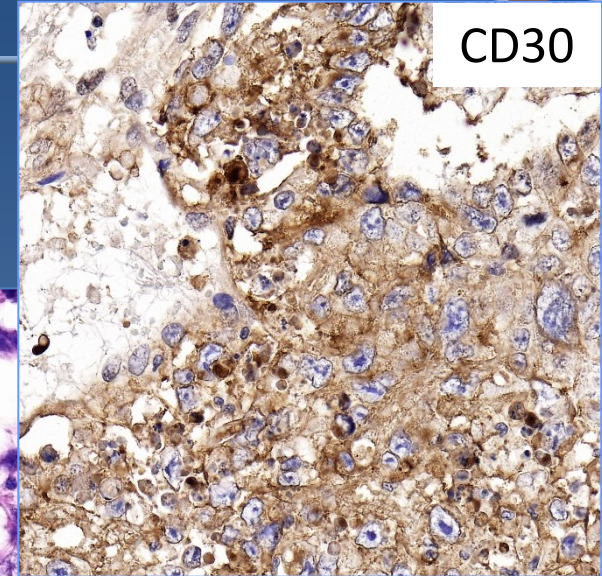


- ✗ undifferentiated tumor, cells of epithelial appearance
- ✗ commonly as part of mixed germ cell tumors
 - ⇒ *worse prognosis*
- ✗ **micro:**
 - ⇒ *solid, trabecular, abortive tubular formations*
 - ⇒ *large cells, high mitotic activity*
 - ⇒ *stroma without lymphatic reaction*

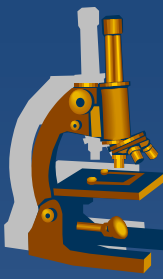
Embryonal carcinoma



Seminiferous tubules



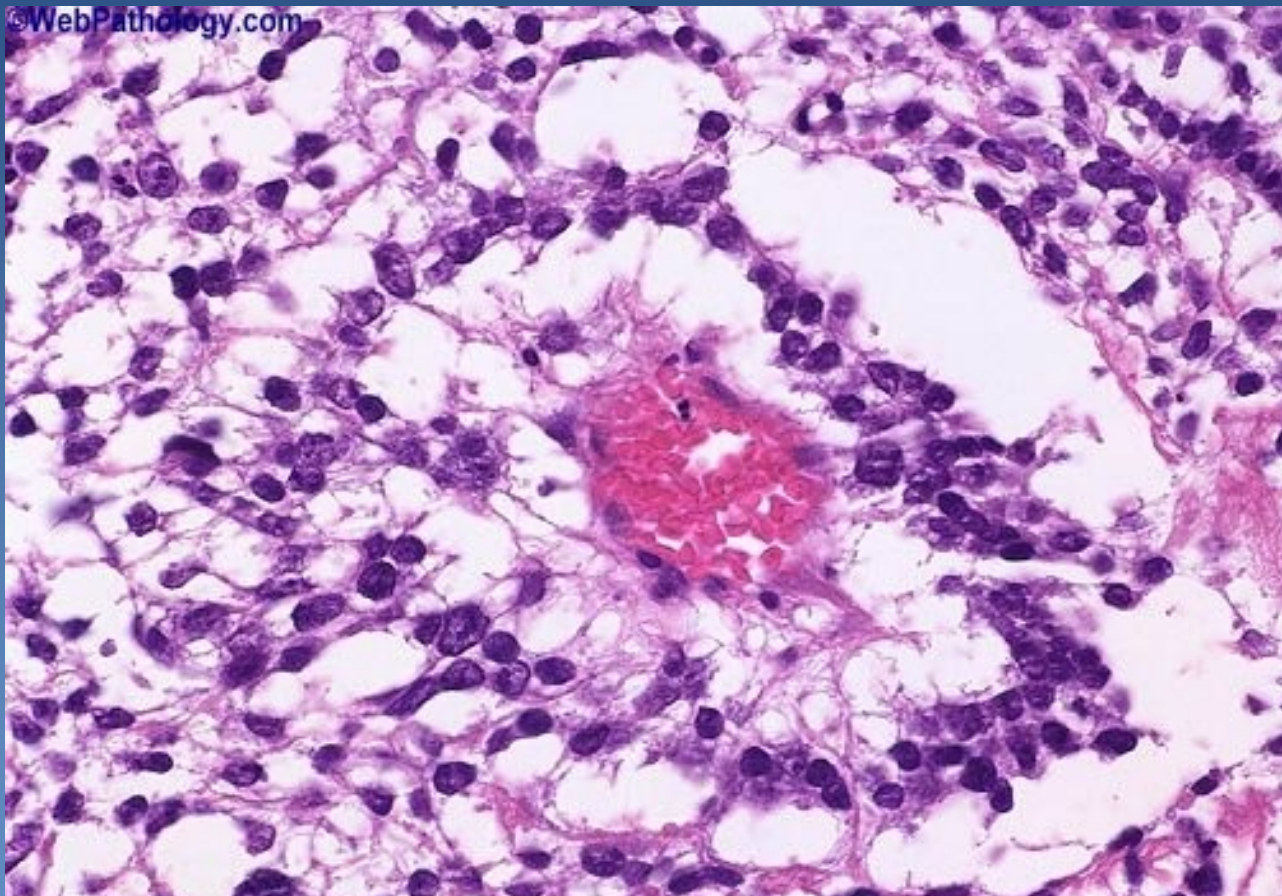
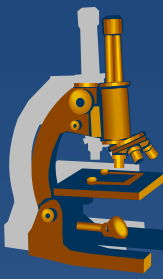
Yolk sac tumor



- ✗ ~ yolk sac structures, extraembryonal mesodermal tissues
- ✗ in pure form in infants, young (<3 yrs) children, better prognosis
- ✗ in adults a component of mixed germ cell tumors, worse prognosis
- ✗ α -fetoprotein (AFP) secretion – IHC, serum

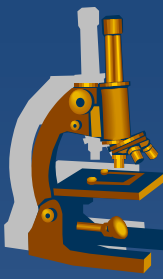
- ✗ **micro:**
 - ⇒ *microcystic, reticular, papillary formation, variable patterns*
 - ⇒ *glomeruloid structures (Schiller-Duval bodies)*
 - stalk with capillary lined on the surface by layer of tumor cells
 - ⇒ *tumor cells*
 - flat, polygonal or cuboidal

Yolk sac tumor



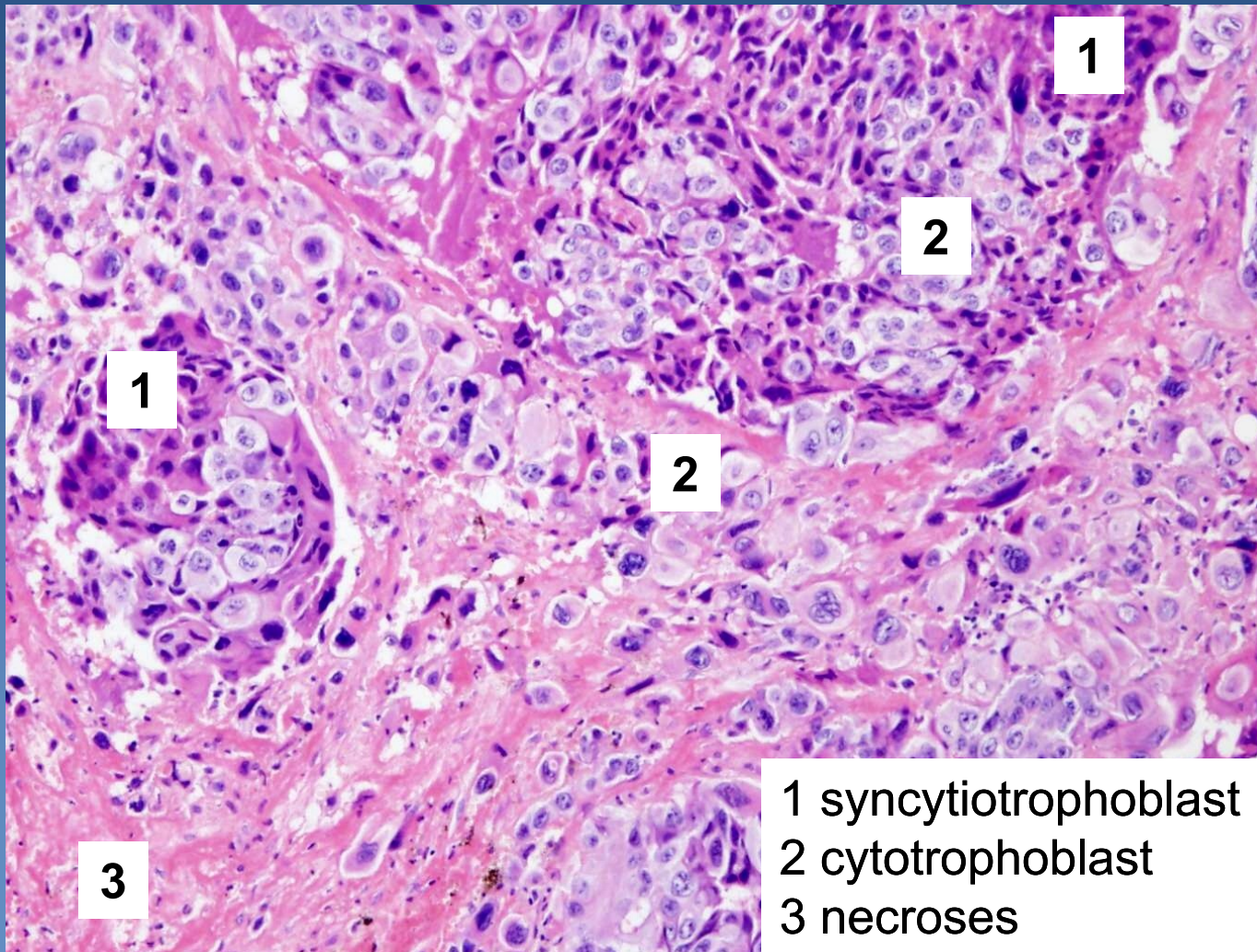
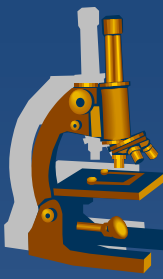
Schiller-Duval body (glomeruloid formation)

Choriocarcinoma

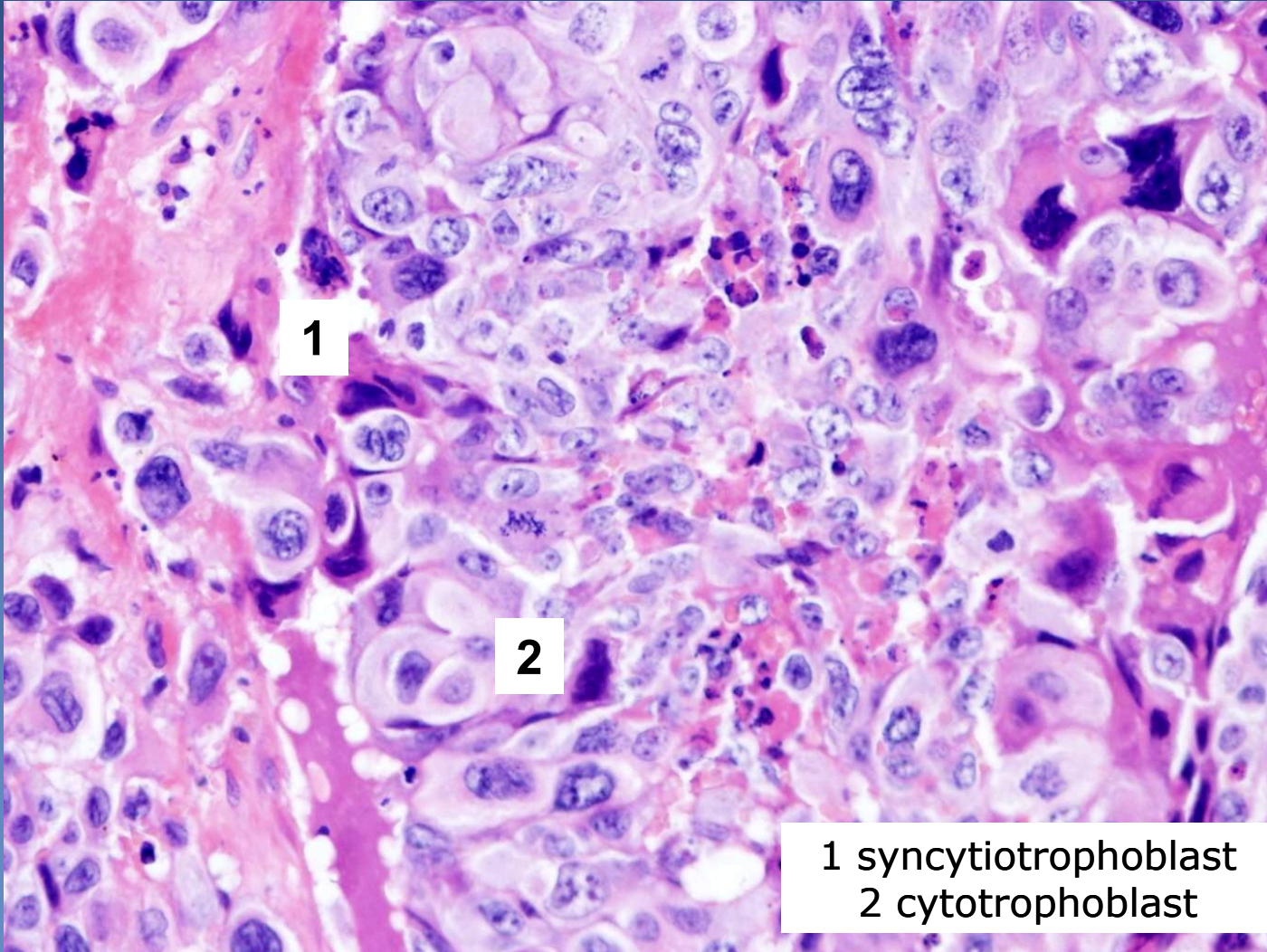
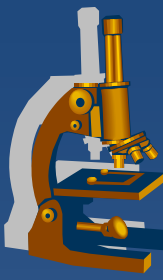


- ✗ mixture of syncytiotrophoblast, cytotrophoblast, intermediate trophoblast cells
- ✗ pure very rare, more commonly as component of mixed germ cell tumors, HCG ↑
- ✗ gross/ micro:
 - ⇒ *haemorrhagic + necrotic tumor*
 - ⇒ *variable patterns of syncytiotrophoblast with admixture of larger polygonal cells of cytotrophoblast event. + intermediate trophoblast*

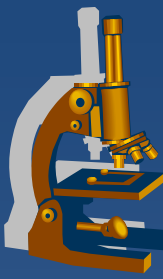
Choriocarcinoma



Choriocarcinoma



Teratoma



x intraembryonal differentiation

⇒ *terminal differentiation into 3, 2 or 1 germ layers (monodermal teratoma)*

x mature uncommon in testis (x ovary); pure in children

x histologic classification

⇒ *differentiated mature t.*

- completely matured tissues with organoid structure
- commonly cystic, containing serous fluid, mucus, keratin

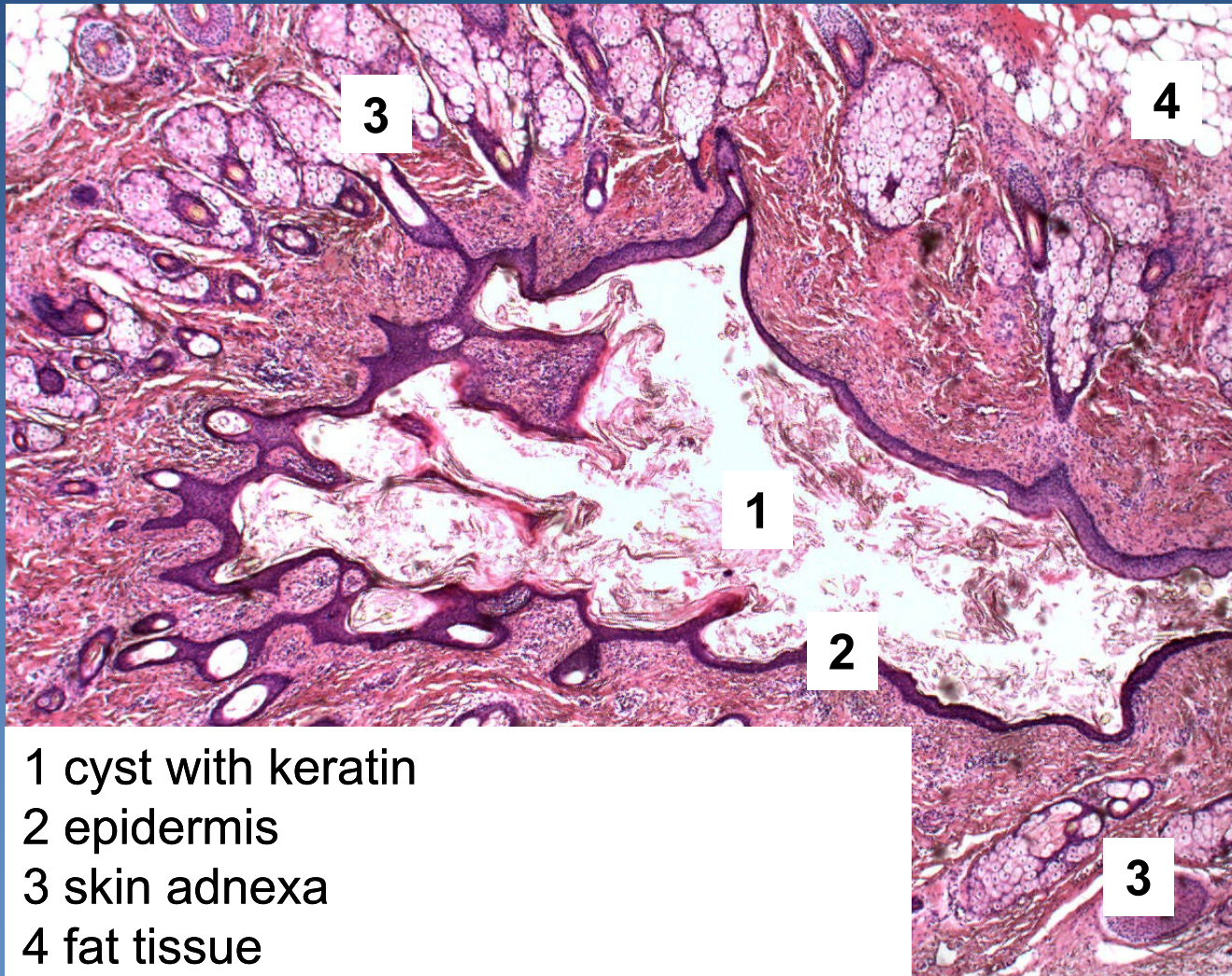
⇒ *differentiated immature t.*

- immature tissues of embryonal/fetal appearance (neuroectoderm)

⇒ *t. with somatic type malignancy*

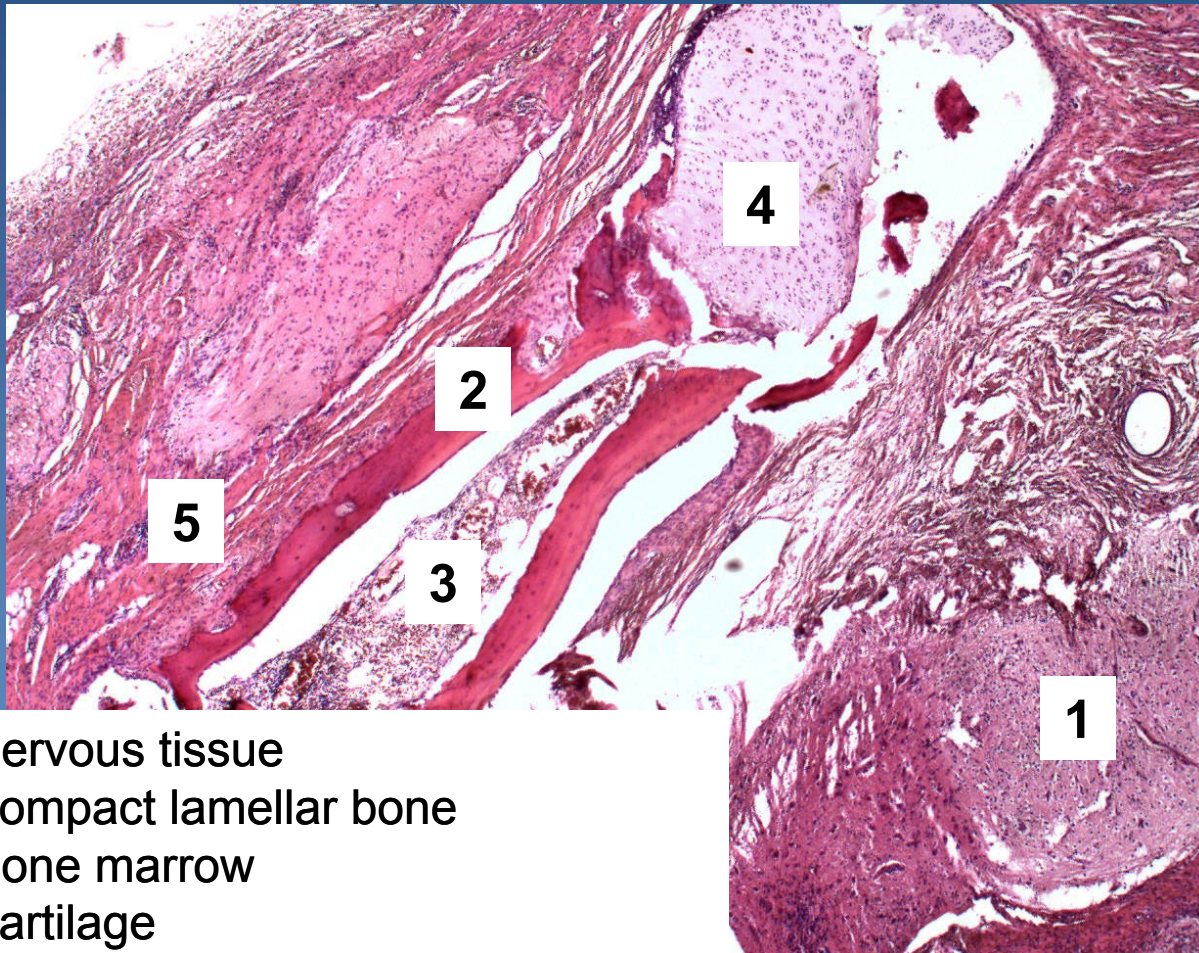
- sarcoma, carcinoma, PNET

Differentiated mature teratoma (dermoid cyst)



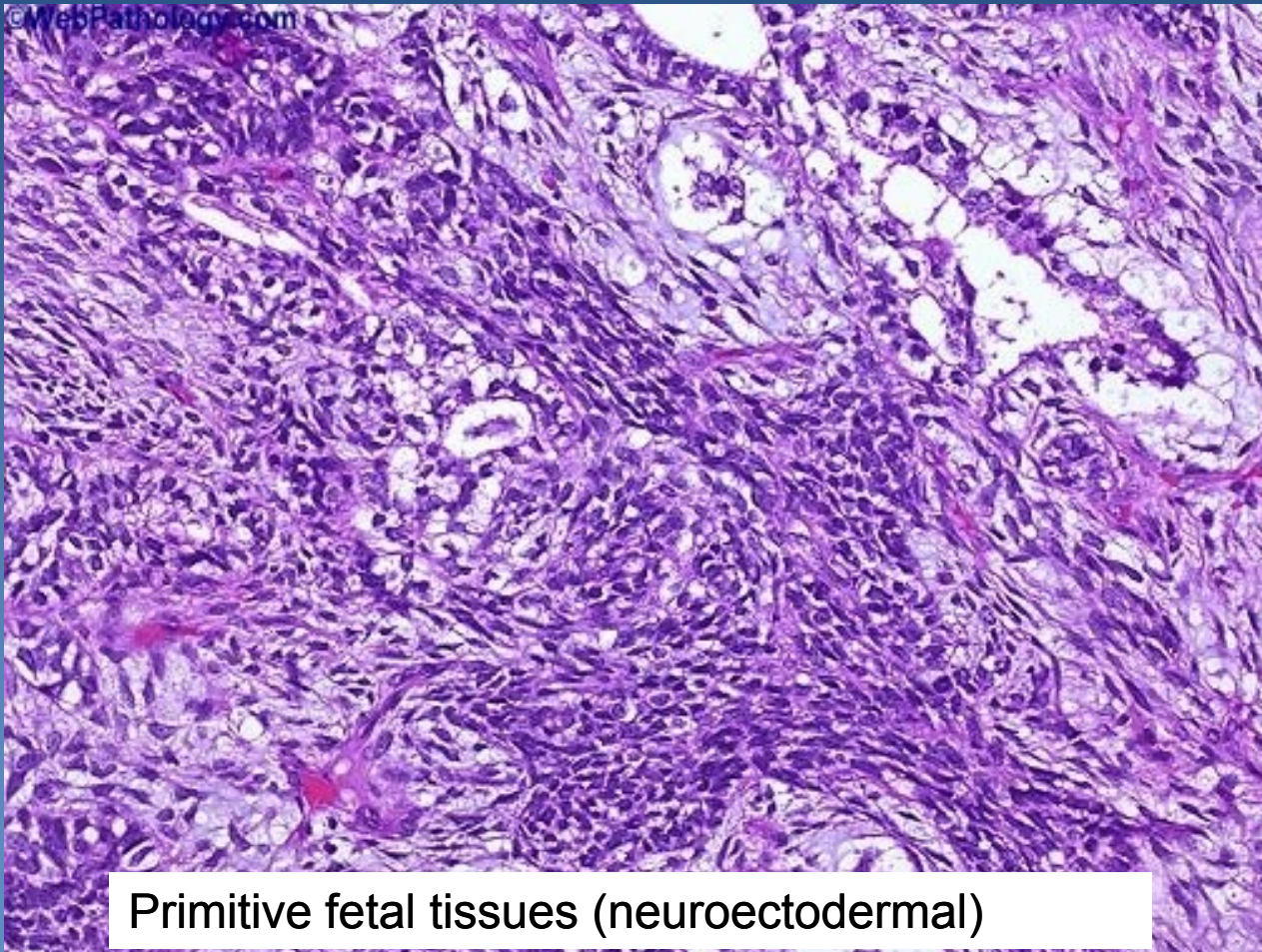
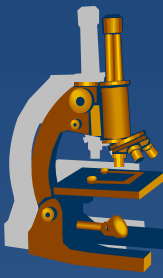
- 1 cyst with keratin
- 2 epidermis
- 3 skin adnexa
- 4 fat tissue

Differentiated mature teratoma

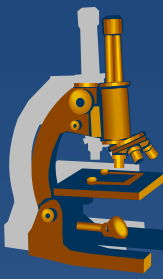


- 1 nervous tissue
- 2 compact lamellar bone
- 3 bone marrow
- 4 cartilage
- 5 striated muscle

Differentiated immature teratoma



Extragenadal germ cell tumors (EGT)

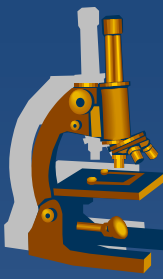


- ✗ primary germ cell tumors arising in extragonadal localisation

- ✗ more common in males

- ✗ origin unclear:
 - ⇒ *from primordial germ cells?*
 - ⇒ *faulty migration?*
 - ⇒ *faulty localisation of totipotent cells?*
 - ⇒ *ectopic germ cells in healthy people?*

Extragenital germ cell tumors (EGT)



✘ localisation:

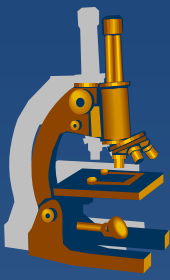
⇒ *in midline structures (pathway of germ cells descensus into gonadal blastema):*

- brain (pineal, suprasellar) sacrococcygeal, anterior mediastinum, retroperitoneum,..., thymus, prostate, stomach,.....

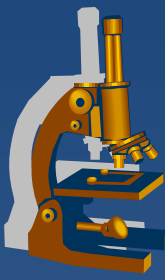
✘ seminomas, non-seminomatous

✘ pure or mixed

✘ general prognosis worse, except EGT seminoma

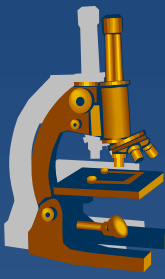


Female genital system pathology

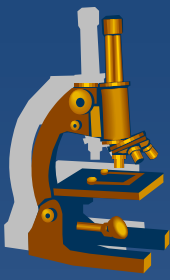


- x vulva**
- x vagina**
- x exocervix, endocervix**
- x uterine body**
 - ⇒ *endometrium*
 - ⇒ *myometrium*
- x fallopian tubes**
- x ovaries**

Pathology

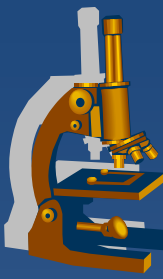


- ⇒ *inborn defects*
- ⇒ *circulatory disorders*
- ⇒ ***inflammations***
- ⇒ ***tumors***



Vulva

Vulvar inflammations



- ✘ **candida**

 - ⇒ *mycotic vulvovaginitis (DM, post-ATB)*

- ✘ **HPV**

 - ⇒ *condyloma accuminatum, vulvar intraepithelial neoplasia - dysplasia (VIN I-III)*

- ✘ **HSV, type 2, 1**

 - ⇒ *vesicles → ulcers, primoinfection + systemic signs*

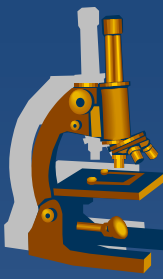
- ✘ **Neisseria gonorrhoeae**

 - ⇒ *purulent inflammation (gonorrhea) in glands – periurethral, Bartholin, ...*

- ✘ **Treponema pallidum**

 - ⇒ *lues (chancre)*

Non-neoplastic epithelial disorders

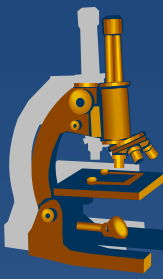


- × gross appearance of leukoplakia – white plaque
- × mostly in peri-, postmenopausal women
- × inflammatory dermatoses (psoriasis, chronic dermatitis), pre-malignant lesions (VIN, ca), disorders of unknown etiology

- × **Lichen sclerosus**
 - ⇒ *epithelial atrophy + hyperkeratosis*
 - ⇒ *superficial dermis – band of oedema + hyalinisation*
 - ⇒ *perivascular mononuclear inflammatory cell infiltrate*
 - ⇒ → → *stenosis of vaginal orifice (craurosis vulvae)*

- × **Lichen simplex chronicus – squamous cell hyperplasia**
 - ⇒ *epithelial hyperplasia + marked hyperkeratosis*
 - ⇒ *not a precancerosis*

Vulvar neoplasia



x condyloma accuminatum

⇒ *low-risk HPV (6, 11)*

⇒ *squamous cell papilloma with koilocytar epithelial transformation*

x vulvar intraepithelial neoplasia - VIN

⇒ *high-risk HPV (16)*

⇒ *VIN II, III –high risk of progression into SCC*

x carcinoma

⇒ *squamous ca (90 %)*

- **precursor lesions:**

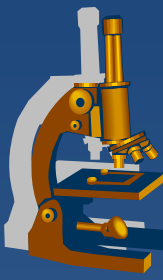
- VIN II, III

- lichen sclerosus (in older females)

⇒ *adenocarcinoma, basal cell carcinoma*

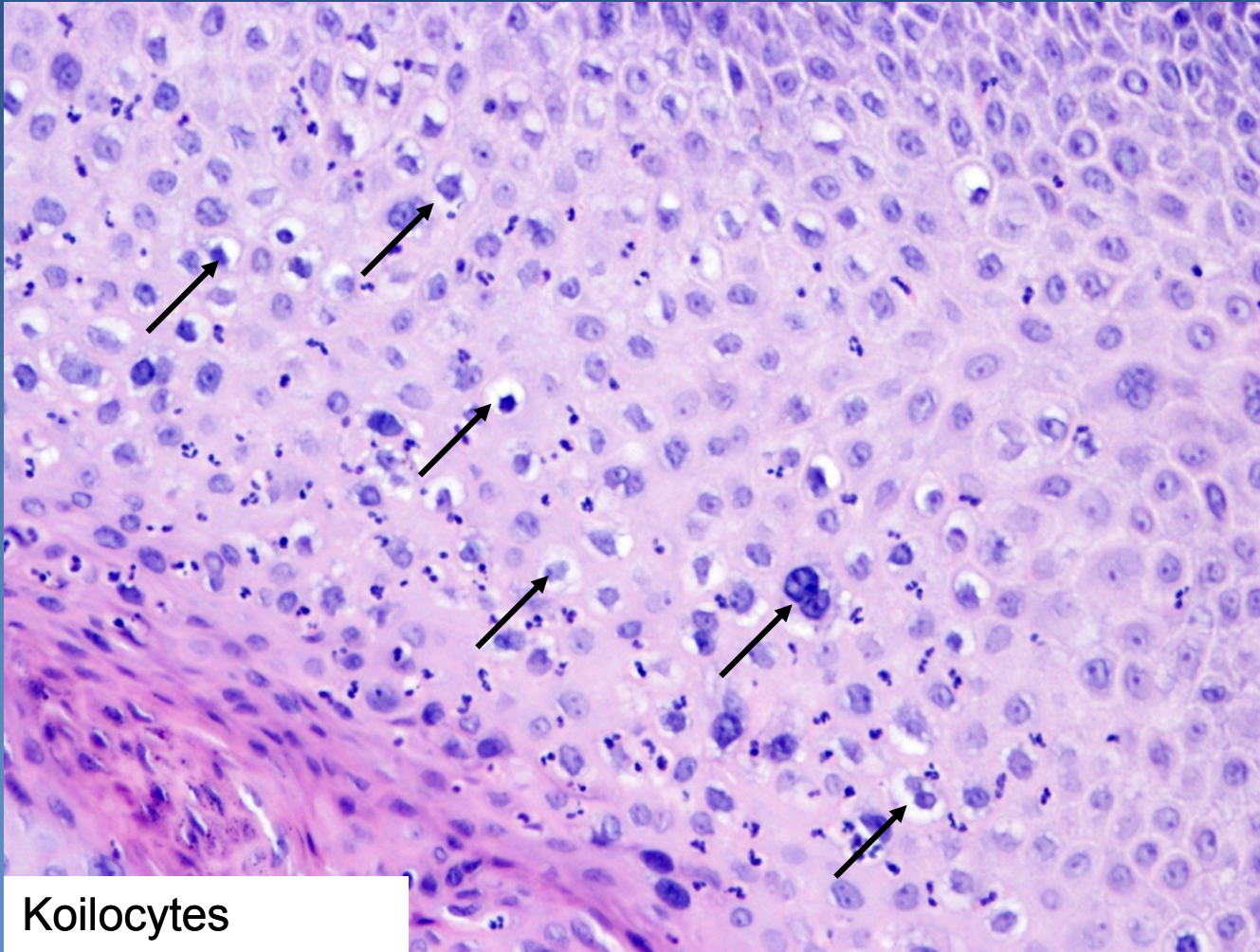
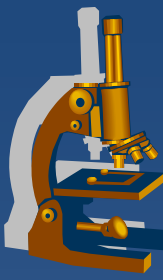
x malignant melanoma

Condyloma accuminatum

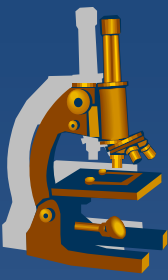


Papillomatous architecture

Condyloma accuminatum

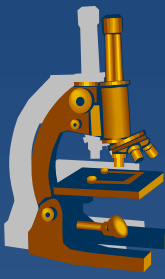


Koilocytes
(arrows)



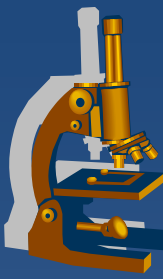
Vagina

Vaginal inflammation



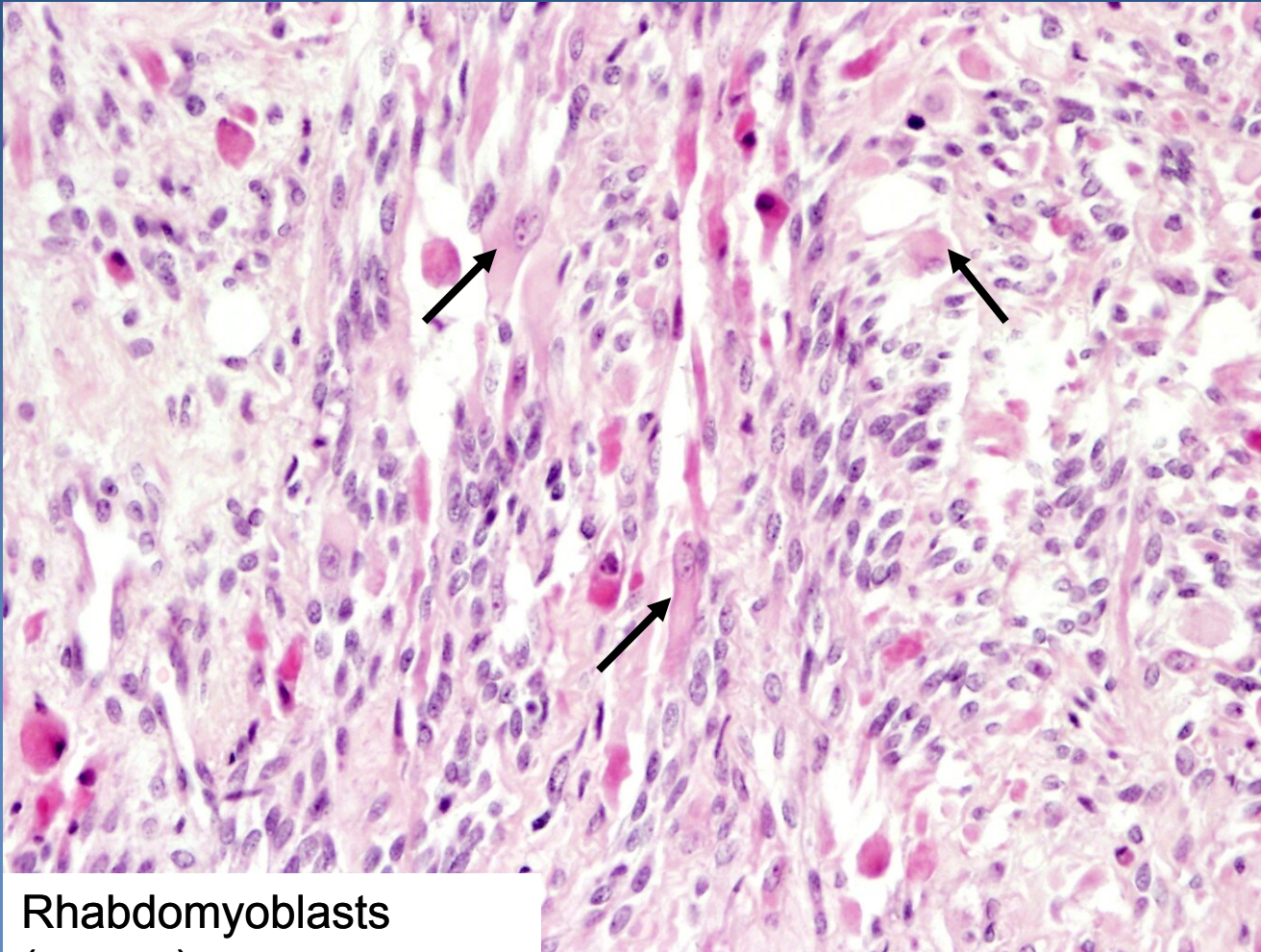
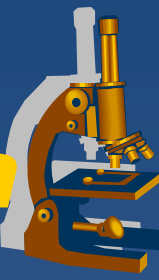
- ✘ colpitis commonly concurrent with cervicitis, catarrhal or purulent inflammation
- ✘ STD: *Trichomonas vaginalis*; *Neisseria gon.*; bacterial vaginosis (*Gardnerella* + anaerobes); candidosis, ...

Vaginal tumors and pseudotumors

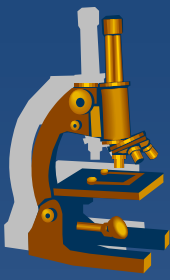


- x fibroepithelial polyps, glandular cysts**
- x HPV lesions concurrent with cervical/vulvar**
 - ⇒ *condyloma accuminatum, vaginal intraepithelial neoplasia (VaIN I-III) → squamous carcinoma*
- x embryonal rhabdomyosarcoma (sarcoma botryoides)**
 - ⇒ *gross – soft polypoid tumor protruding into vaginal lumen*
 - ⇒ *girls <5 years*

Embryonal rhabdomyosarcoma

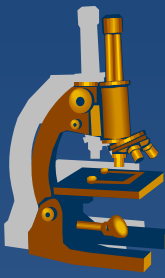


Rhabdomyoblasts
(arrows)



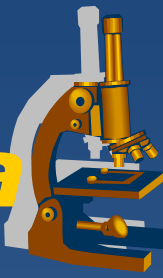
Cervix (endocervix, exocervix)

Cervicitis



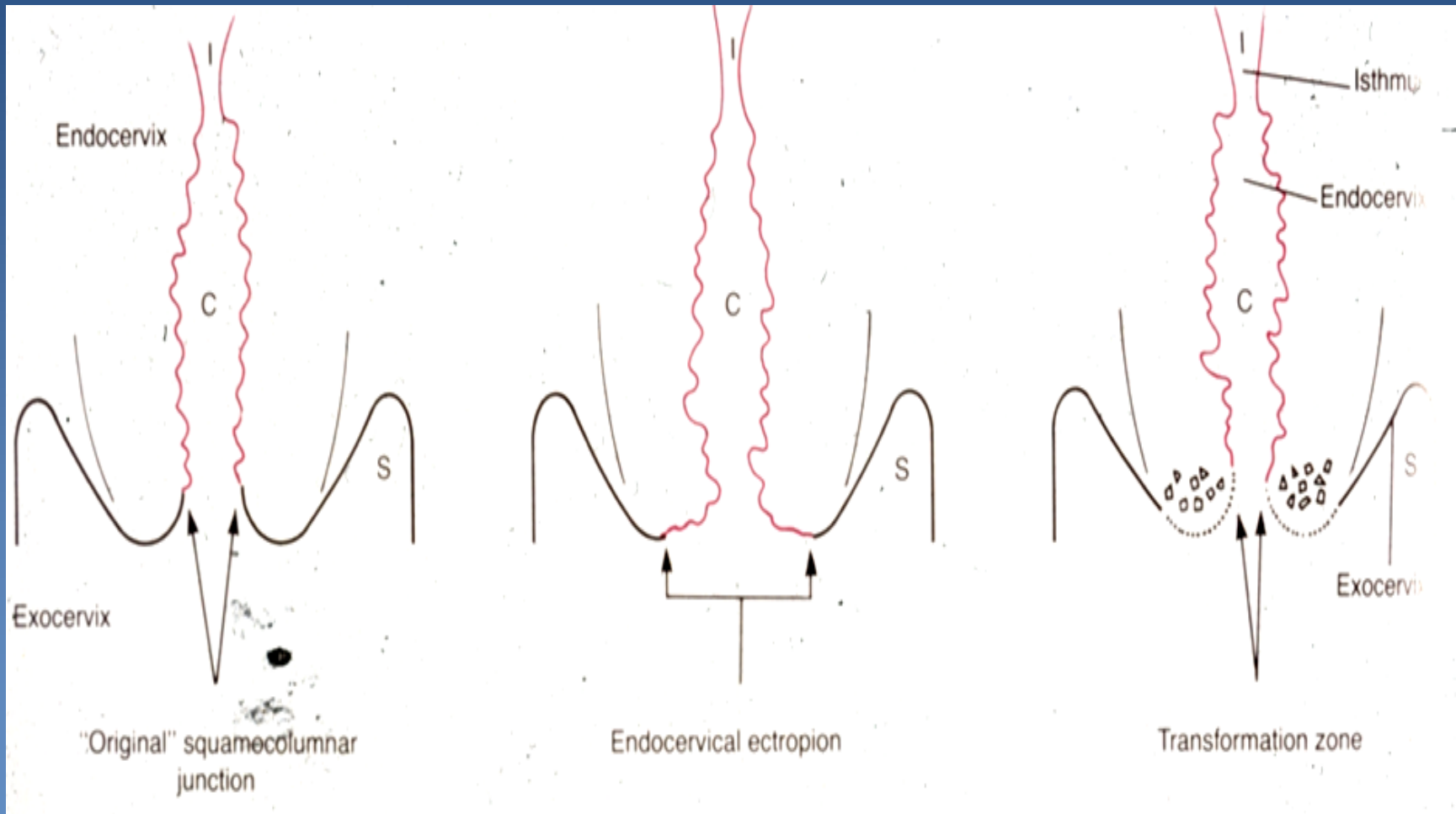
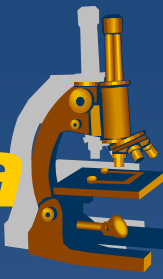
- x commonly with colpitis, non-specific
 - ⇒ *similar microbial causes*
- x chronic cervicitis may lead to mucosal hyperplasia → endocervical polyp

Cervical squamous metaplasia

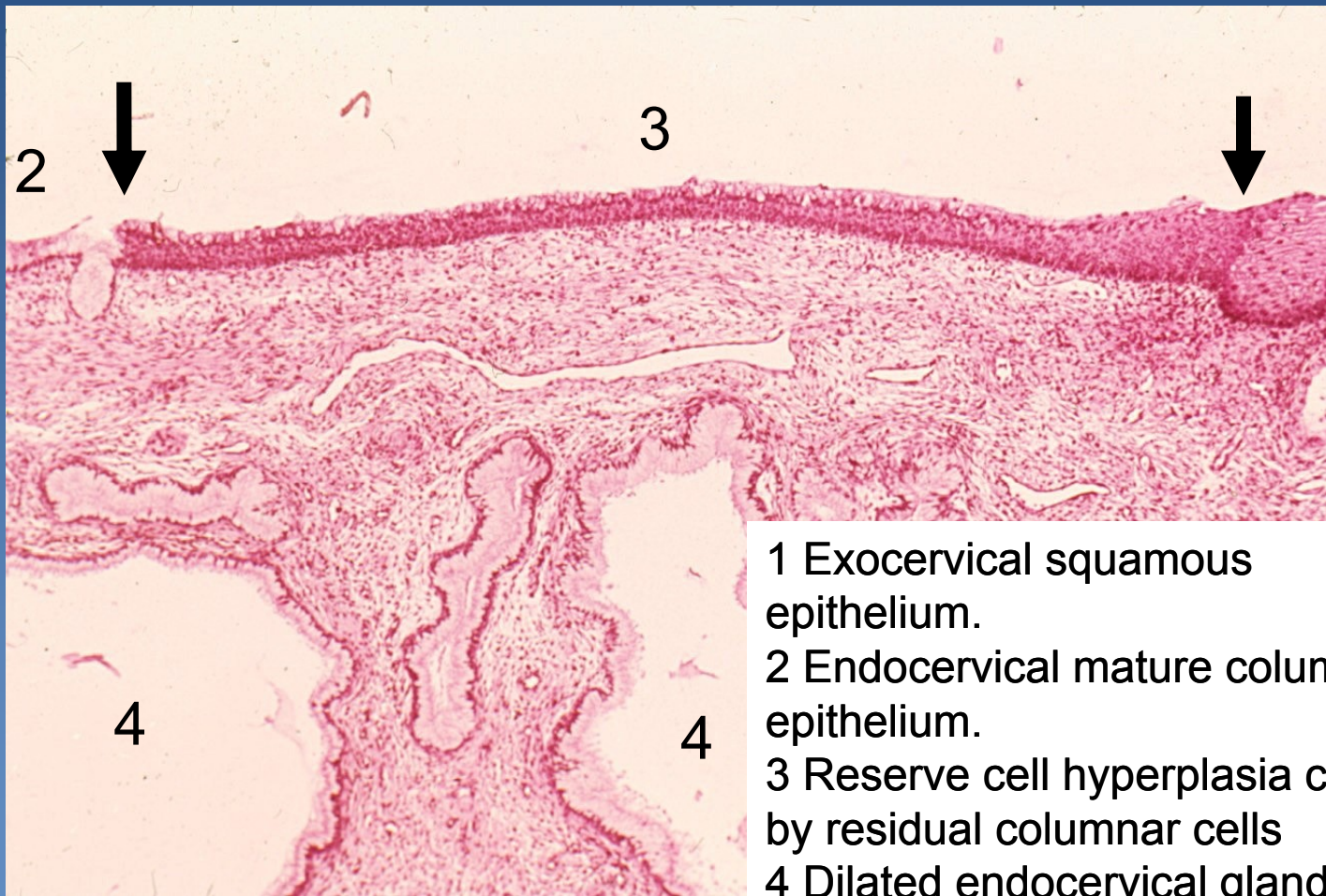
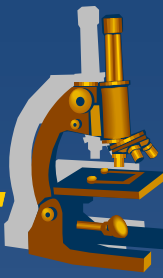


- ✘ transformation zone (squamo-columnar junction)
 - ⇒ *eversion of columnar epithelium into vagina (ectopy, ectropium)*
 - ⇒ *reserve cell hyperplasia → immature squamous metaplasia → mature metaplasia*
- ✘ closure of endocervical glands by overgrowth of squamous epithelium → *ovulation (cystic dilatation of the glands)*

Cervical squamous metaplasia



Squamous metaplasia, ovulosis.



- 1 Exocervical squamous epithelium.
- 2 Endocervical mature columnar epithelium.
- 3 Reserve cell hyperplasia covered by residual columnar cells
- 4 Dilated endocervical glands

Cervical preneoplastic changes + intraepithelial lesion



- ✘ LR (low-risk) HPV (6,11) →→→ *koilocytic atypia* of squamous cells
 - ⇒ *replication + cytopathic viral effect, productive infection*
 - ⇒ *nuclear atypia, cytoplasmic perinuclear halo*
- ✘ Cervical dysplasia – intraepithelial neoplasia associated with **HR (high-risk) HPV**:
 - ⇒ **HR HPV:**
 - 16, 18, 31, 33, 35
 - ⇒ *deregulation of the cell cycle, ↑ proliferation, ↓ or arrested maturation*

Cervical preneoplastic changes



x risk factors

⇒ HPV

- early sexual activity (<16 years of age)
- number of sexual partners

⇒ other STD (HSV, chlamydia)

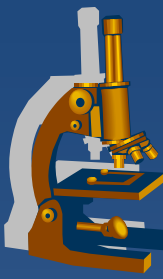
⇒ cigarette smoking

⇒ early age of first pregnancy

⇒ combined oral contraceptives

⇒ immunosuppression

Cervical intraepithelial neoplasia



× Older classification

⇒ *CIN I (mild dysplasia):*

- koilocytic atypia + changes in the lower third of epithelium:
 - anisokaryosis
 - nuclear enlargement, hyperchromasia
 - loss of cell polarity
 - nuclear superposition

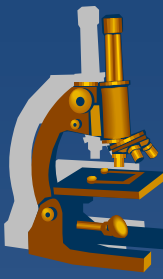
⇒ *CIN II (moderate dysplasia):*

- changes in the lower 2/3 of epithelial thickness, progressive atypia, expansion of the immature basal cells

⇒ *CIN III (severe dysplasia):*

- changes in the whole epithelium, diffuse atypia, almost complete loss of maturation

Cervical intraepithelial lesion



✘ 2 categories, according to the risk of progression and clinical management:

⇒ ***LSIL (low-grade squamous intraepithelial lesion)***

= ***CIN I, exophytic or flat condylomatous lesion***

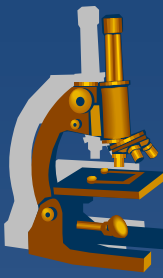
- mostly self-limited (viral clearance), productive infection, lower rate of progression

⇒ ***HSIL (high-grade squamous intraepithelial lesion)***

= ***CIN II/III + ca in situ***

- majority persists or progresses to carcinoma

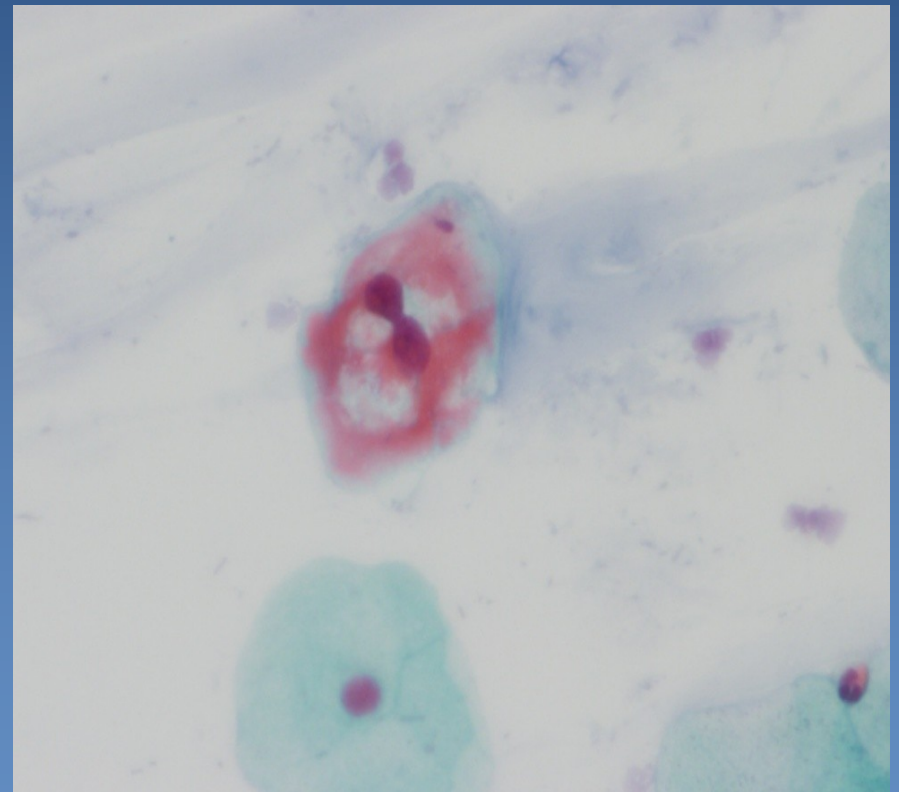
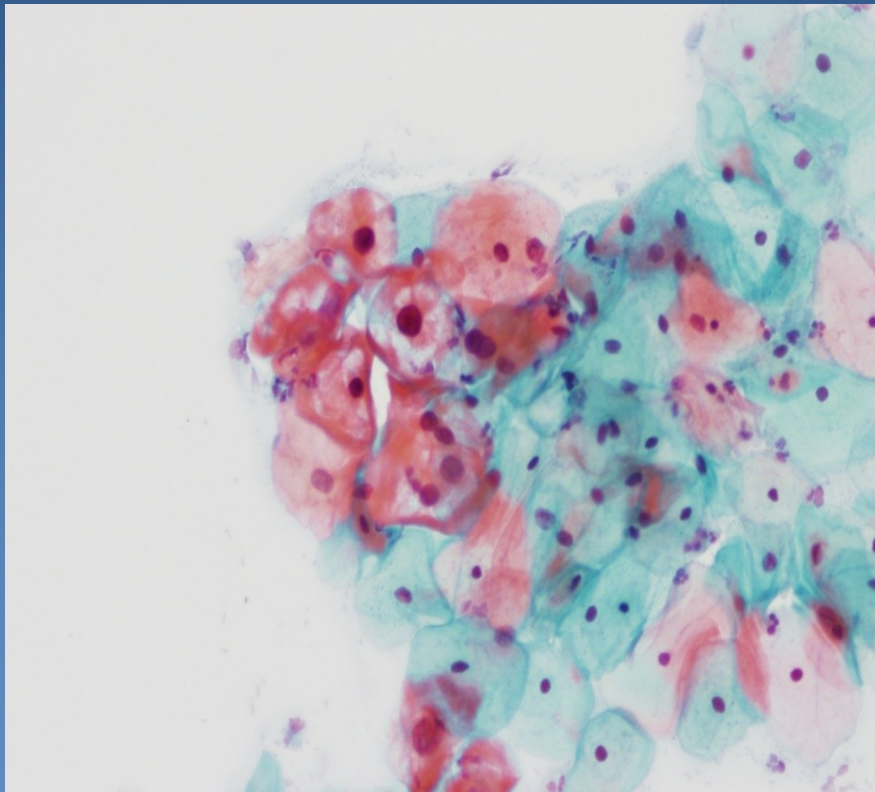
Cervical cytology: LSIL



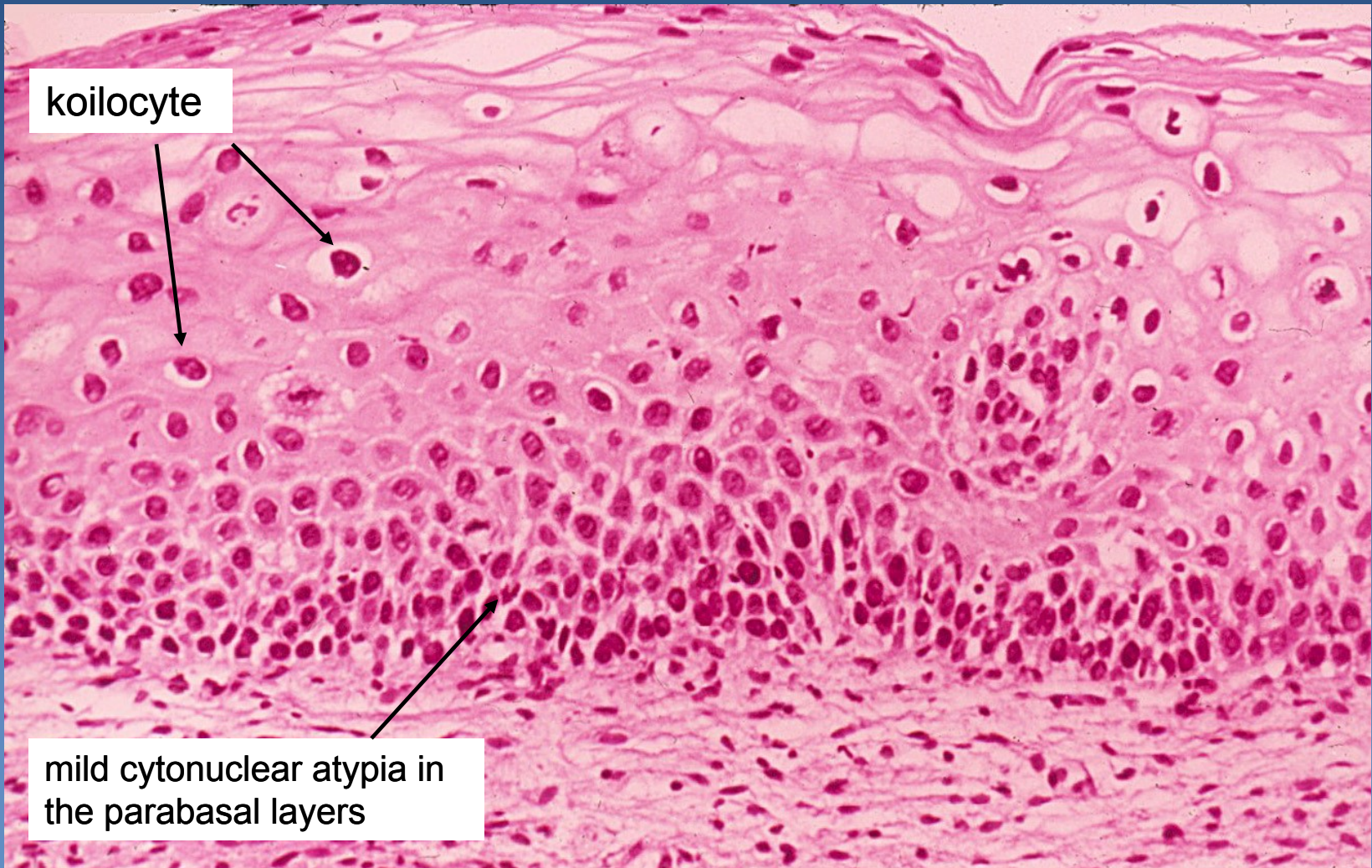
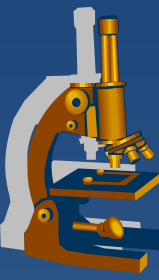
screening of cervical carcinoma

cytology (Bethesda System) + colposcopy

koilocytes with dyskaryotic nuclei



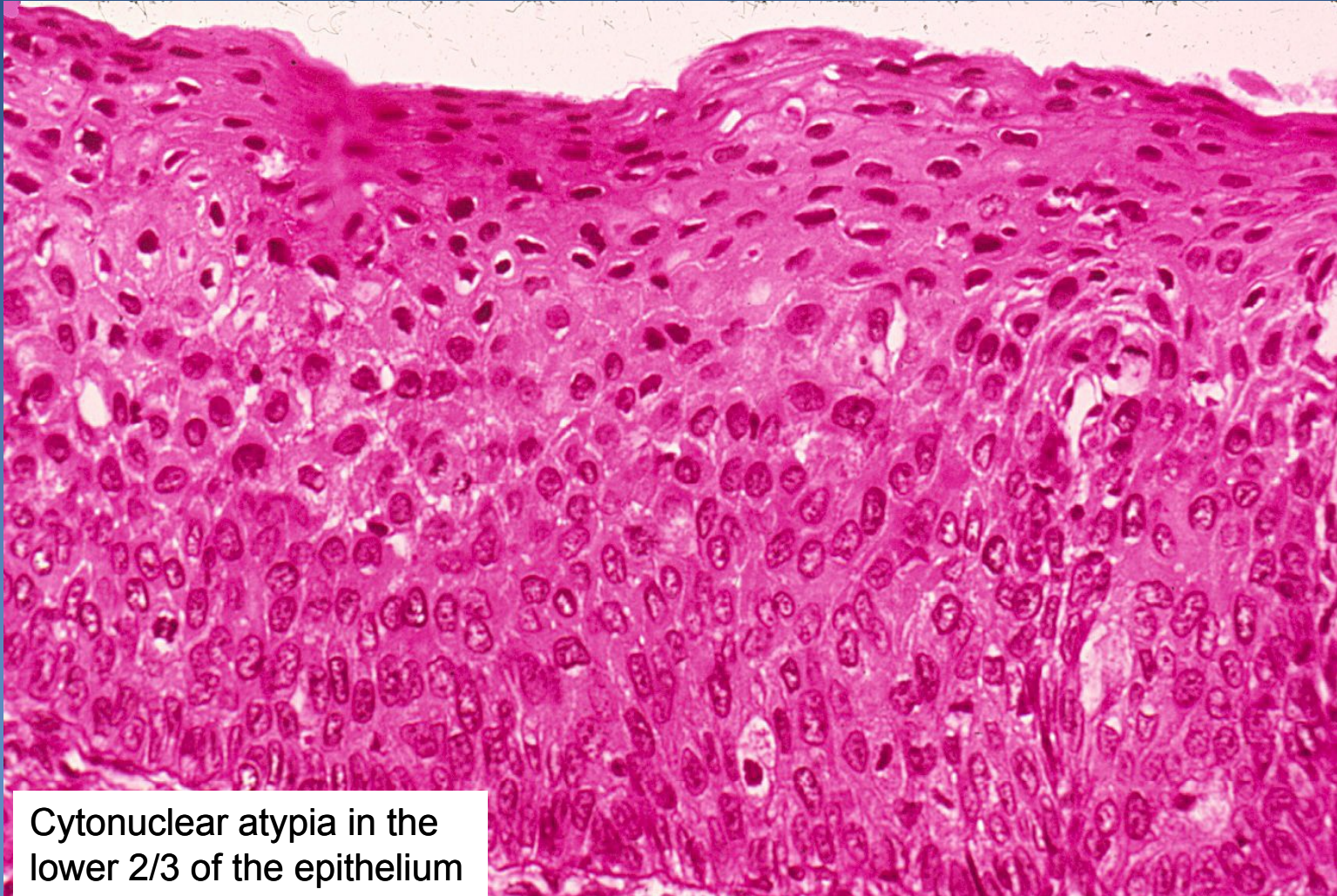
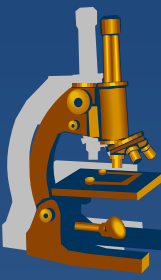
Cervical intraepithelial lesion LSIL (CIN I)



koilocyte

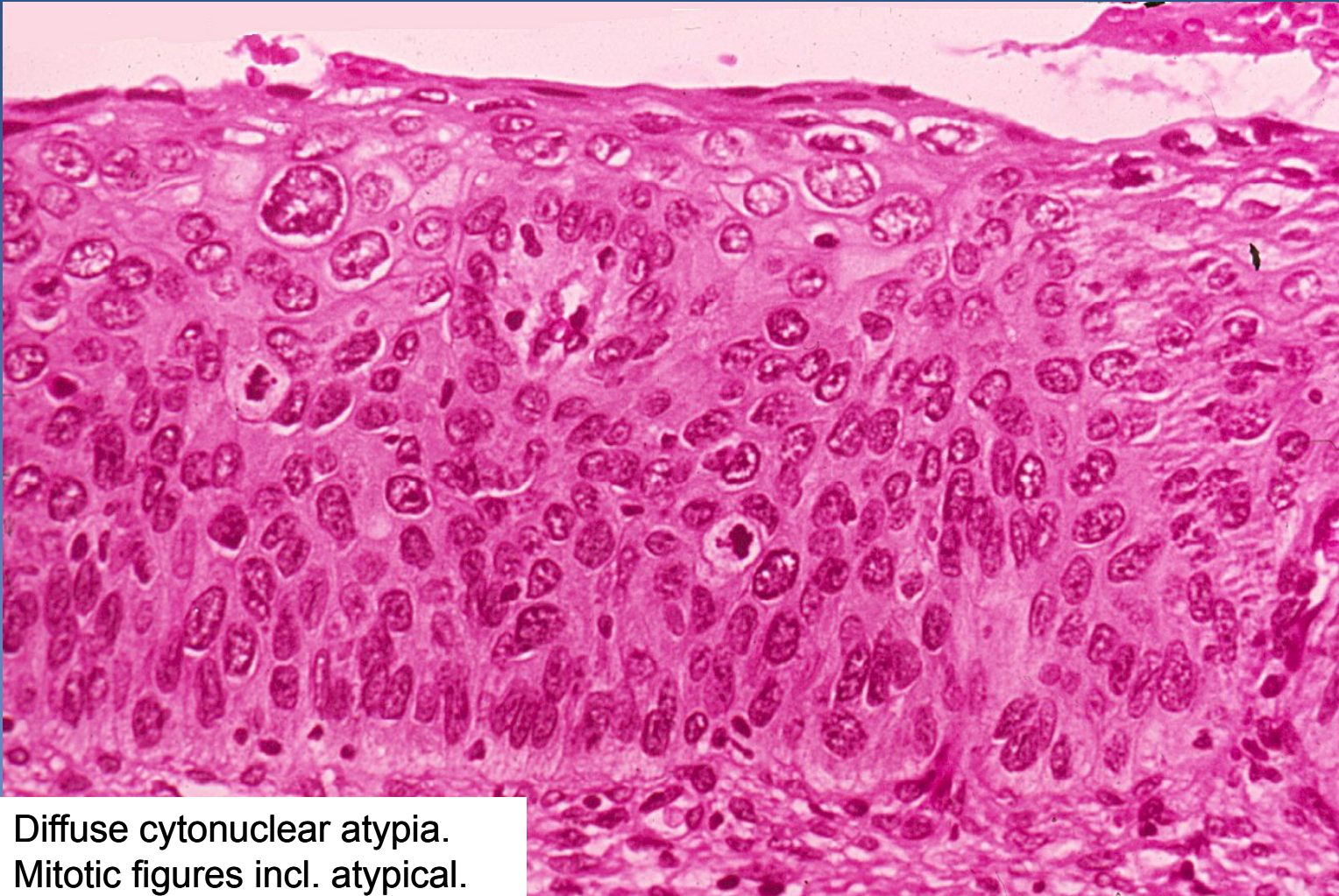
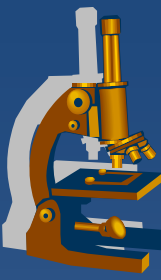
mild cytonuclear atypia in
the parabasal layers

Cervical intraepithelial lesion HSIL (CIN II)



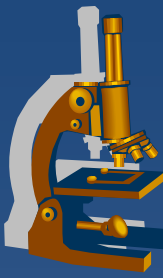
Cytonuclear atypia in the lower 2/3 of the epithelium

Cervical intraepithelial lesion HSIL (CIN III)

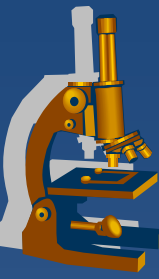


Diffuse cytonuclear atypia.
Mitotic figures incl. atypical.

Invasive cervical squamous cell carcinoma



- ✘ almost always by HSIL progression
- ✘ mostly starts in the transformation zone
- ✘ growth:
 - ⇒ *local progression*
 - size + depth of the invasive component
 - direct invasion into adjacent organs, fistulae
 - regional LN metastases
 - ⇒ *distant metastases via blood (lung, liver, bone marrow)*
- ✘ ↑ incidence, but mostly lower stages (if screened), ↓ mortality



Other cervical carcinomas

- x Adenocarcinoma**

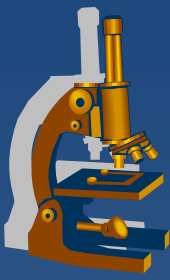
 - ⇒ *cervical glandular intraepithelial lesion*

 - ⇒ *adenocarcinoma in situ*

 - ⇒ *! diff. dg. x endometrial ca*

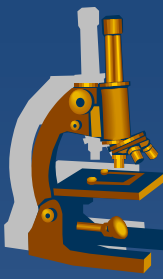
- x Adenosquamous carcinoma**

- x Neuroendocrine cervical carcinoma**



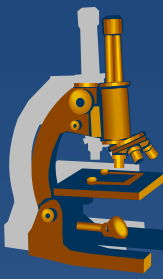
Uterine corpus

Endometritis



- ✘ rather uncommon
- ✘ acute inflammation mostly in association with
 - ⇒ *pregnancy (delivery, abortion)*
 - ⇒ *instrumentation (curetage,...)*
 - ⇒ *long-term IUD in situ (actinomycosis)*
- ✘ chronic inflammation (+ acute exacerbation)
 - ⇒ *chlamydia, chronic gonorrhoea*
 - ⇒ *tb (miliary, or per continuitatem from the fallopian tubes)*

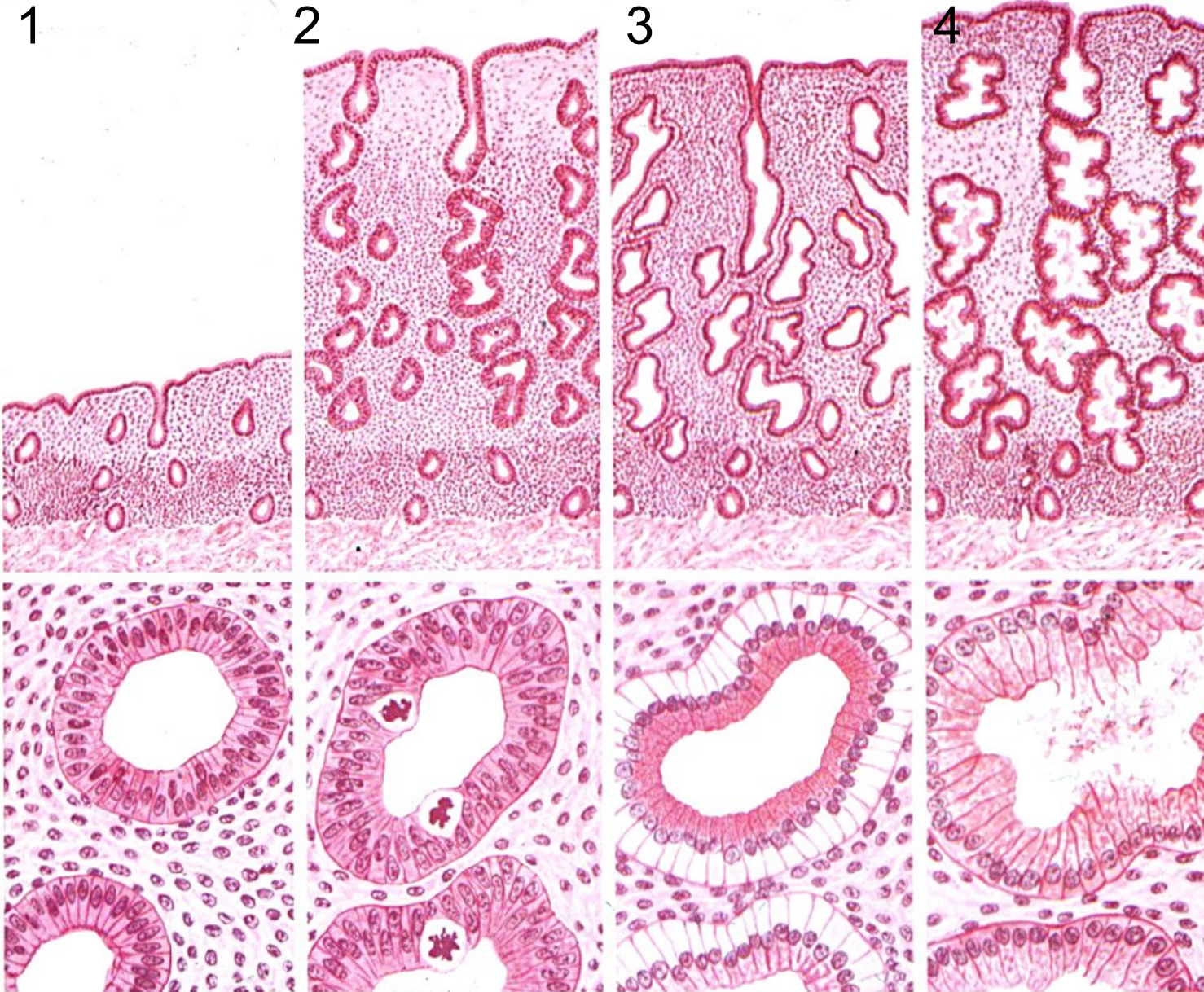
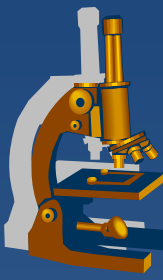
Endometriosis



- ✘ foci of functional endometrium (glands + stroma) in an ectopic localisation
 - ⇒ *ovaria, cavum Douglasi, fallopian tubes, peritoneum, bladder, umbilical skin, ... lung, bones ...)*
 - ⇒ *cyclical changes during MC*
 - haemorrhagic (chocolate) cysts, hemosiderin pigmentation
 - ⇒ *pain, pelvic inflammatory disease + adhesions, infertility*
 - ⇒ *possible source of endometrioid adenocarcinoma*

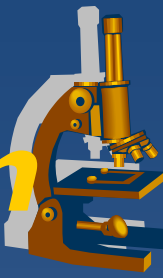
- ⇒ *adenomyosis:*
 - endometrial diverticula (outpouching of basalis into myometrium, mostly no functional hormonal changes)

Endometrium, menstrual cycle



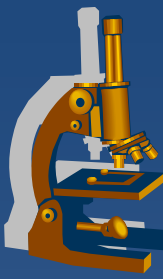
- 1 Early proliferation
- 2 Late proliferation
- 3 Early secretion
- 4 Late secretion

Dysfunctional endometrium



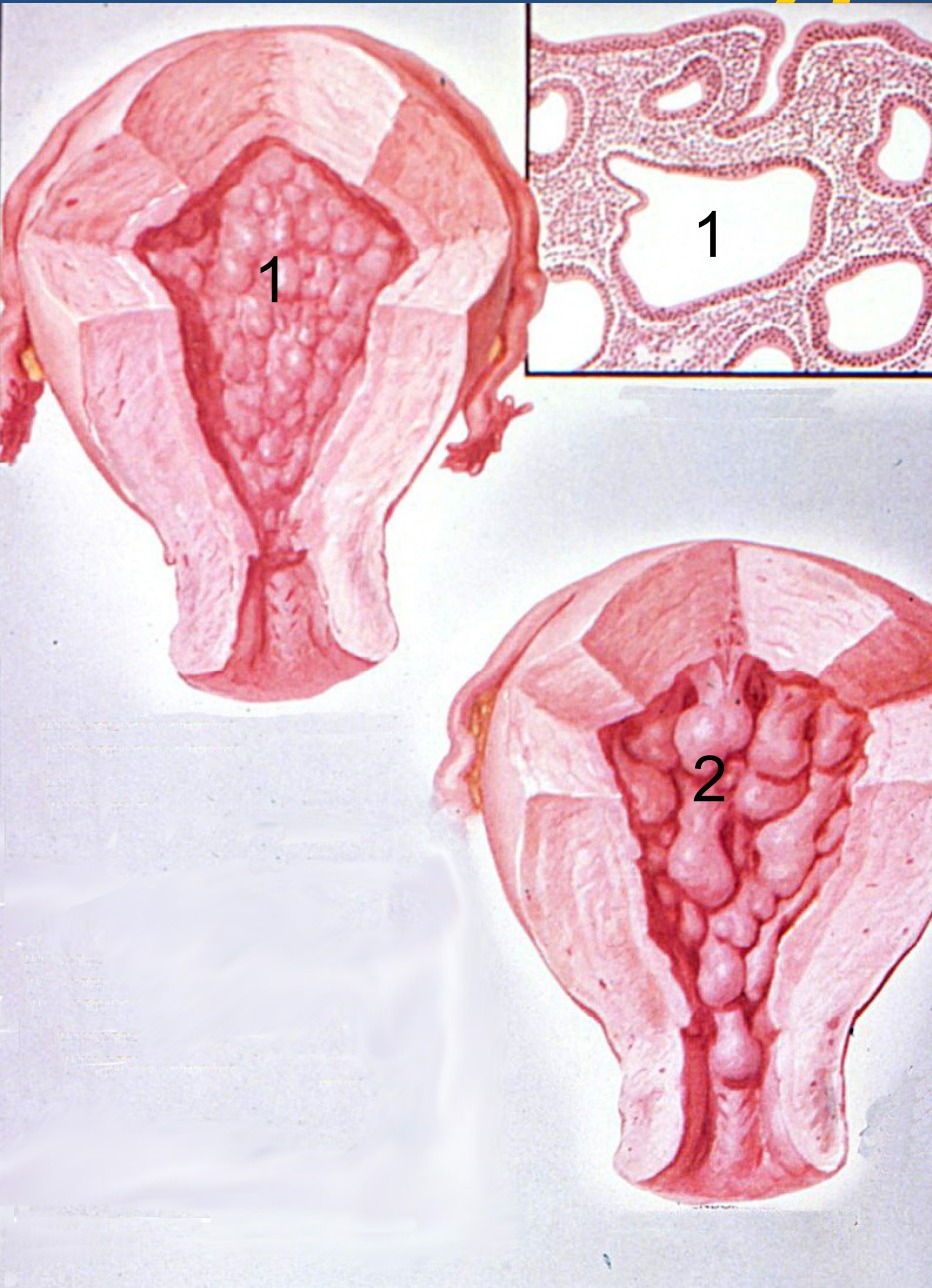
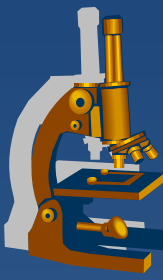
- × Usual clinical presentation – **abnormal bleeding**
- × **Hormonal dysbalance, variable origin**
- × **Non-secretory** ← abnormal estrogenic stimulation
 - ⇒ ↓ **E** → hypoproliferative → atrophic endometrium
 - ⇒ ↑ **E** → hyperproliferative → hyperplastic endometrium (anovulatory cycle)
 - ⇒ *unopposed* ↑ **E by missing progestogenes** → **hyperplastic endometrium**
- × **Secretory** ← abnormal progestogenes
 - ⇒ ↓ **P** → hyposecretory endometrium (luteal phase insufficiency)
 - ⇒ ↑ **P** exogenous (contraception) - stroma-glandular dissociation – pseudo-decidualized stroma + atrophic glands
 - ⇒ ↑ **P** → hypersecretory endometrium (similar to gestational); Arias-Stella phenomenon (!GEU)
- × **Irregular, mixed** ← E+P dysbalance
 - ⇒ **irregular shedding** – mixed secretory + menstrual + proliferative

Endometrial hyperplasia



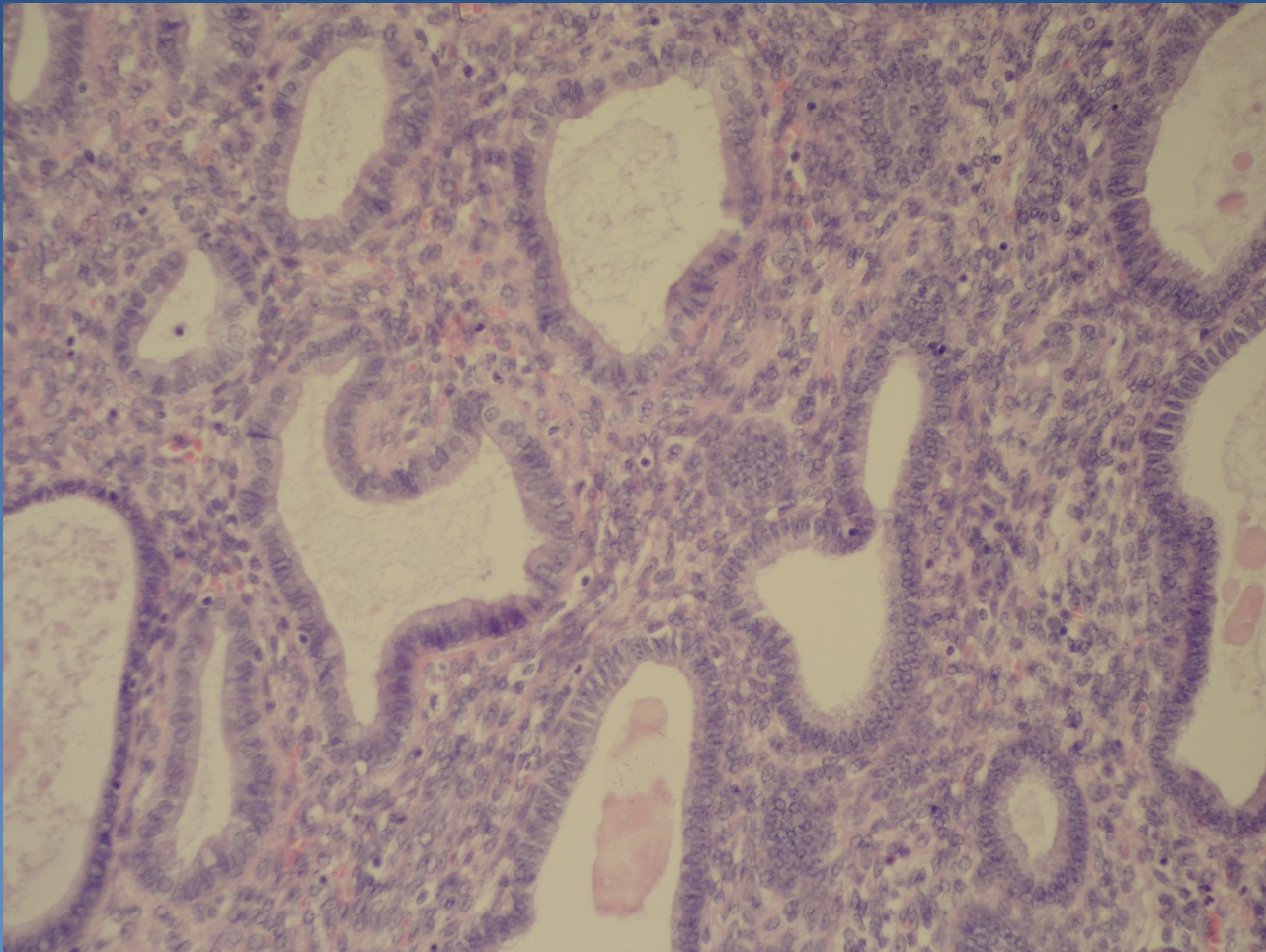
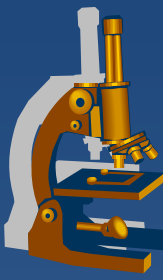
- × **increased glandular proliferation** - ↑ gland-to-stroma ratio
- × **classification according to architecture, cytological atypia**
- × **simple** – dilated irregular glands, epithelial stratification, „swiss cheese“
 - ⇒ **without atypia**, almost no progression to adenocarcinoma,
 - ⇒ **with atypia** → cytologic atypia present, **low progression**, rare
- × **complex** – irregular branching crowded glands, ↓ stroma (back-to-back)
 - ⇒ **without atypia**
 - ⇒ **with atypia** → round nuclei + nucleoli, commonly monoclonal – neoplastic – **high grade of progression**, commonly (1/4-1/2) concurrent ca present;

Endometrial hyperplasia



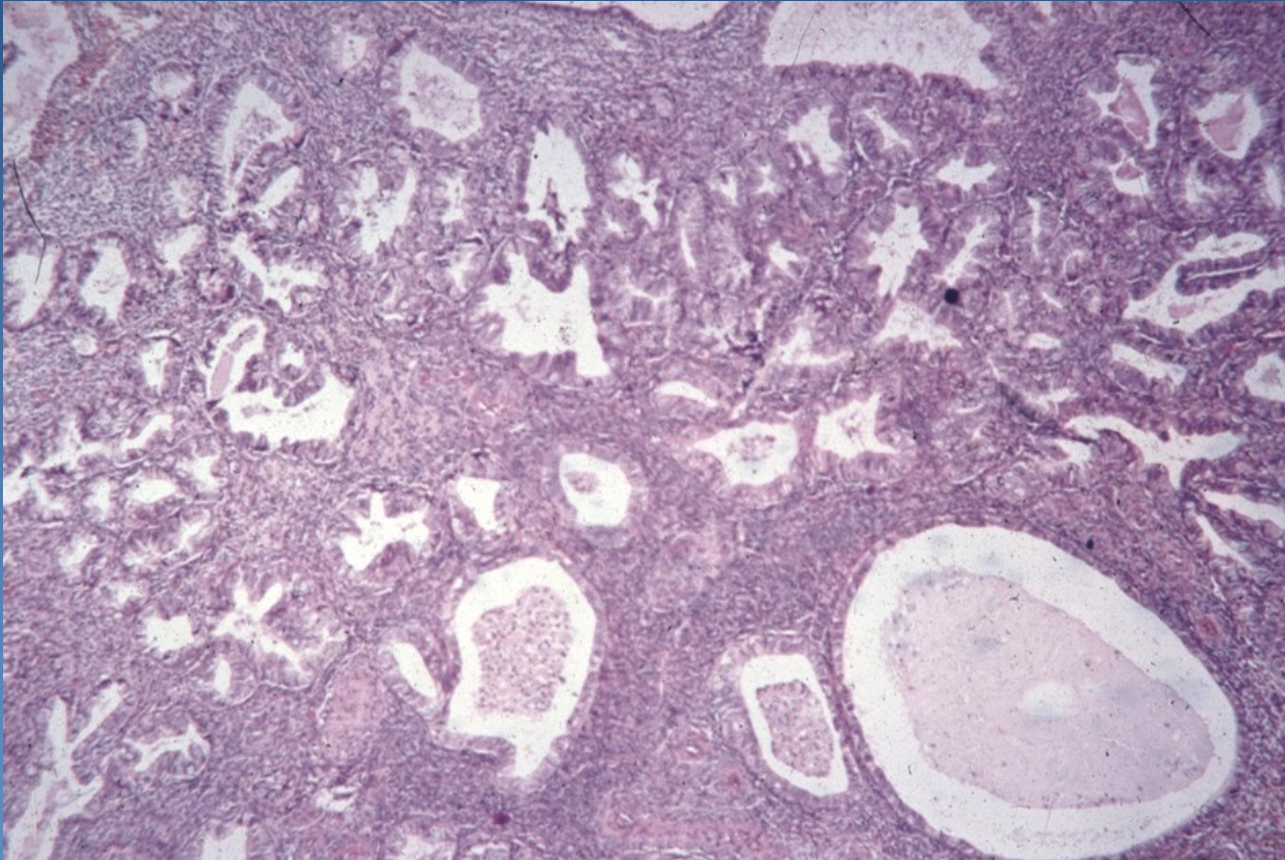
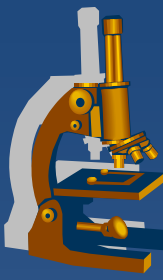
- 1 Endometrial hyperplasia
- 2 Polypous endometrial hyperplasia

Simple hyperplasia

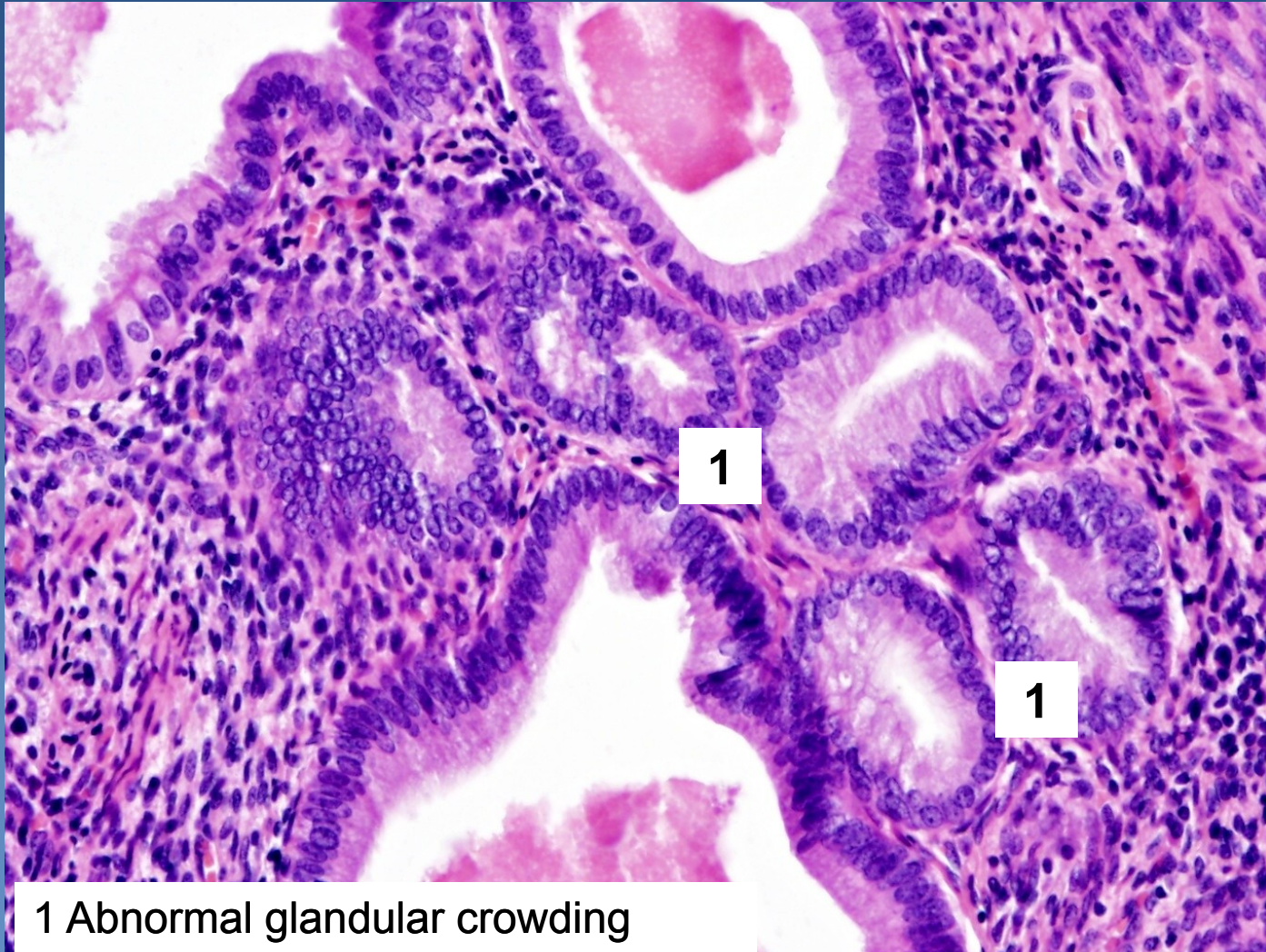
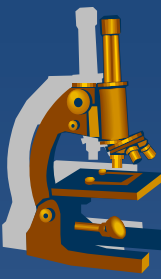


Cystic transformation of endometrial glands
Stromal hyperplasia

Complex hyperplasia

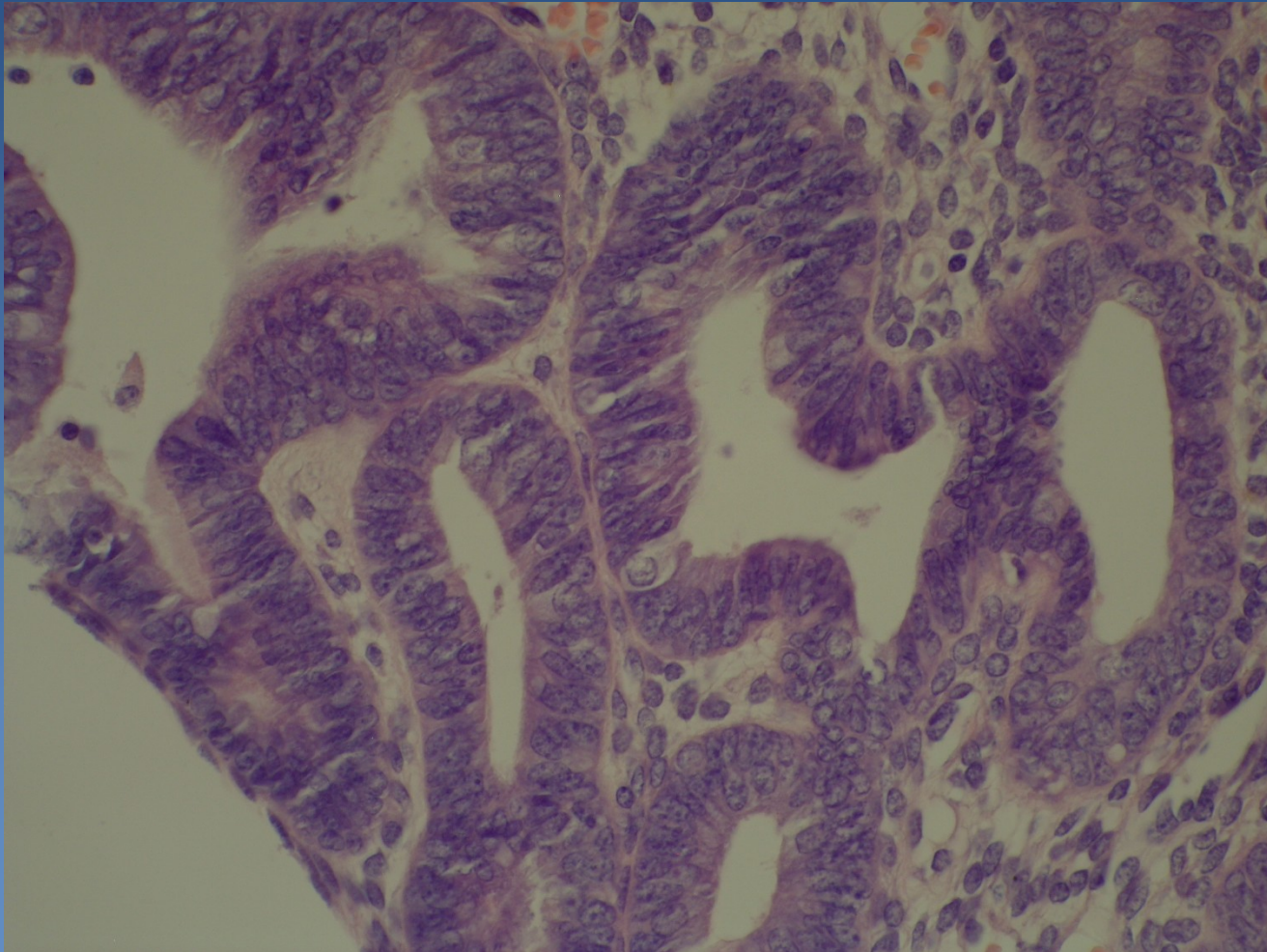
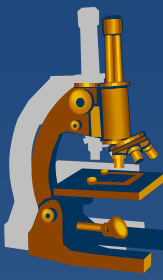


Complex hyperplasia



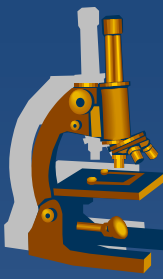
1 Abnormal glandular crowding

Complex hyperplasia with atypia



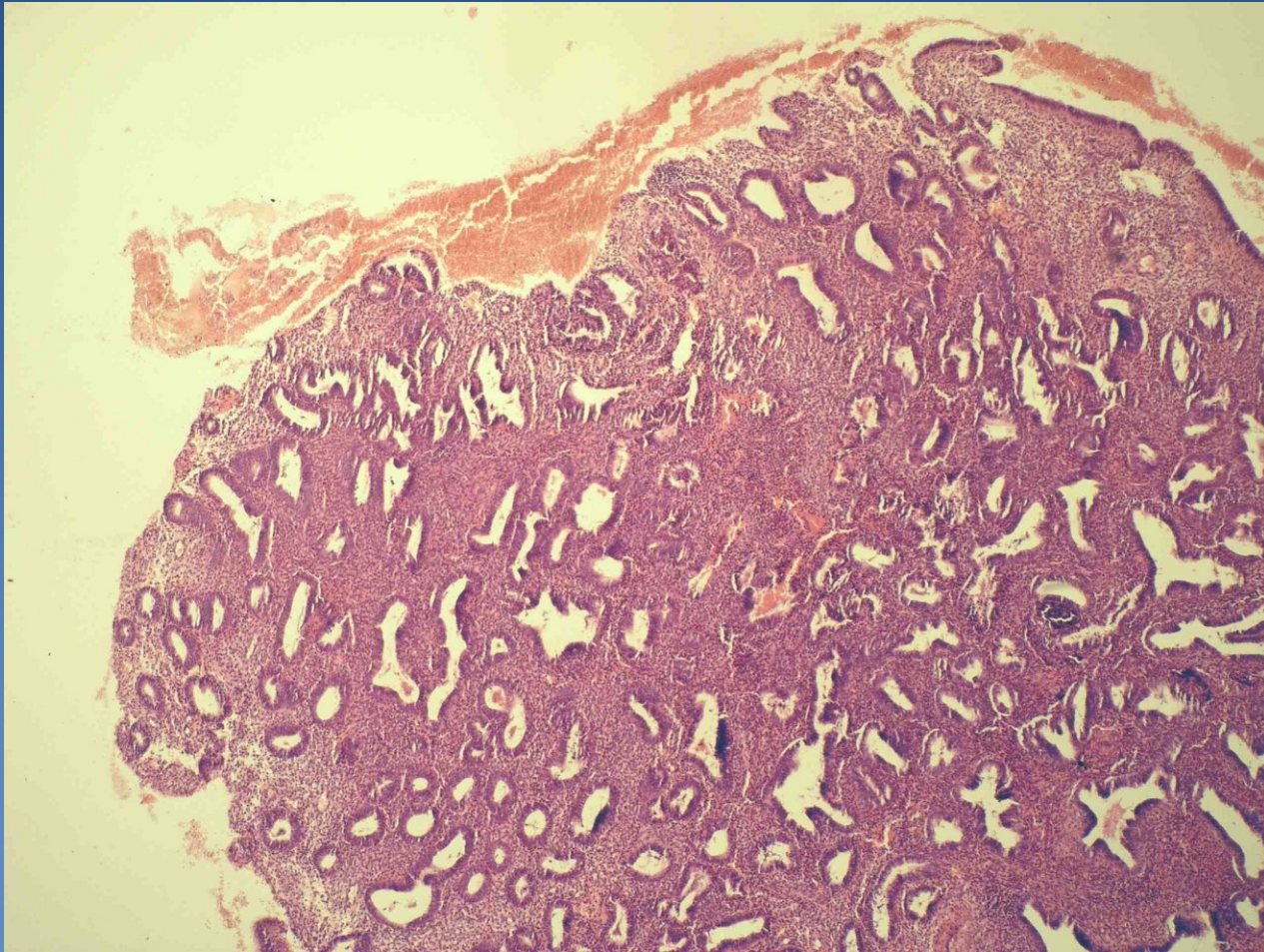
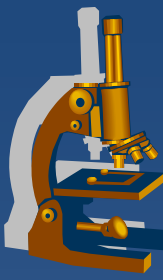
Stratification of epithelial cells, vesicular nuclei, visible nucleoli

Endometrial polyp

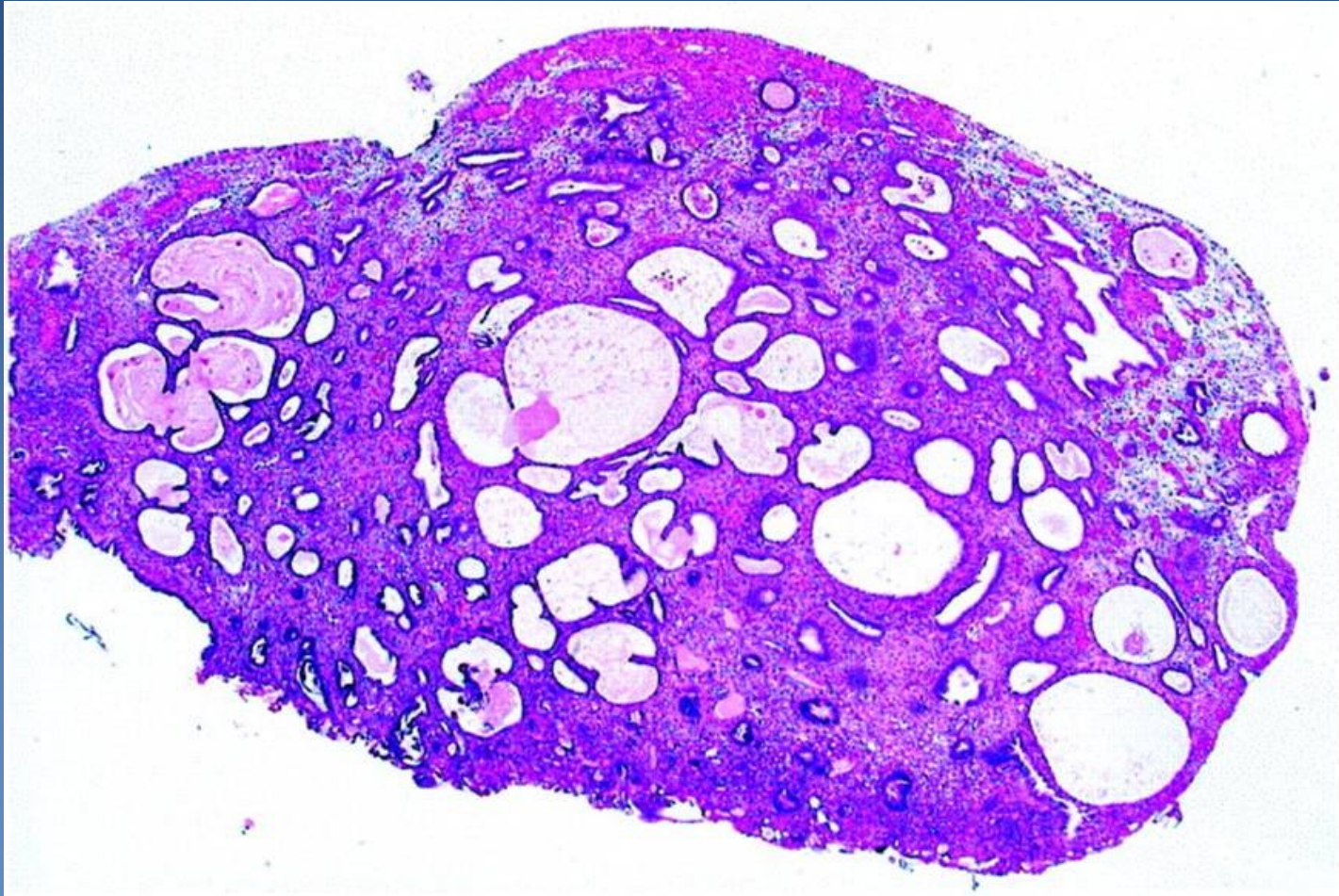
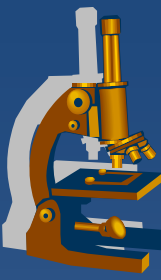


- ✗ sessile/pedunculated, solitary/multiple exophytic endometrial focus
 - ⇒ abnormal bleeding common
 - ⇒ functional/hyperplastic/atrophic endometrium
 - ⇒ stromal fibrosis, thick-walled arteries
 - ⇒ may be in association with endometrial hyperplasia, possible progression to atypical hyperplasia → adenocarcinoma

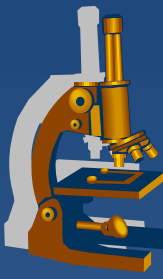
Endometrial polyp - hyperplastic



Endometrial polyp – cystic atrophic

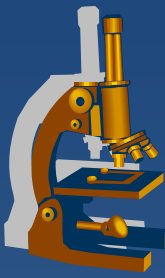


Endometrial adenocarcinoma



- ✗ Most common malignant tumor of female genital
 - ⇒ 2. cervical ca, 3. ovarian tumors
- ✗ **Abnormal bleeding**
- ✗ **type I: perimenopause**
 - ⇒ *Risk factors:*
 - ⇒ *unopposed estrogenic stimulation – endo-/exogenous*
 - ⇒ *DM, obesity, early menarche - late menopause*
 - ⇒ *precursor **atypical endometrial hyperplasia***
 - ⇒ *better prognosis, lymphatic spread possible*

Endometrial adenocarcinoma



× histologic forms:

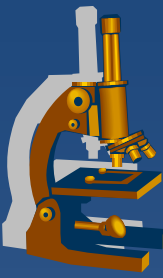
⇒ *type I*

- **endometrioid adenocarcinoma**
- mucinous
- tubal (ciliated)
- squamous cell
- adenosquamous

⇒ *bez souvislosti s estrogeny, při mutaci p53 (→ velmi agresivní průběh)*

- **serózní papilární karcinom**
- **světlobuněčný karcinom**

Endometrial adenocarcinoma



x Type II

⇒ ***postmenopausal***

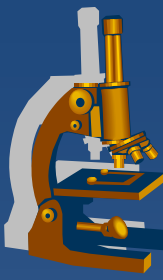
⇒ ***without estrogenic stimulation, p53 mutation (→ aggressive; intraperitoneal, lymphatic spread)***

⇒ ***in the setting of atrophic endometrium***

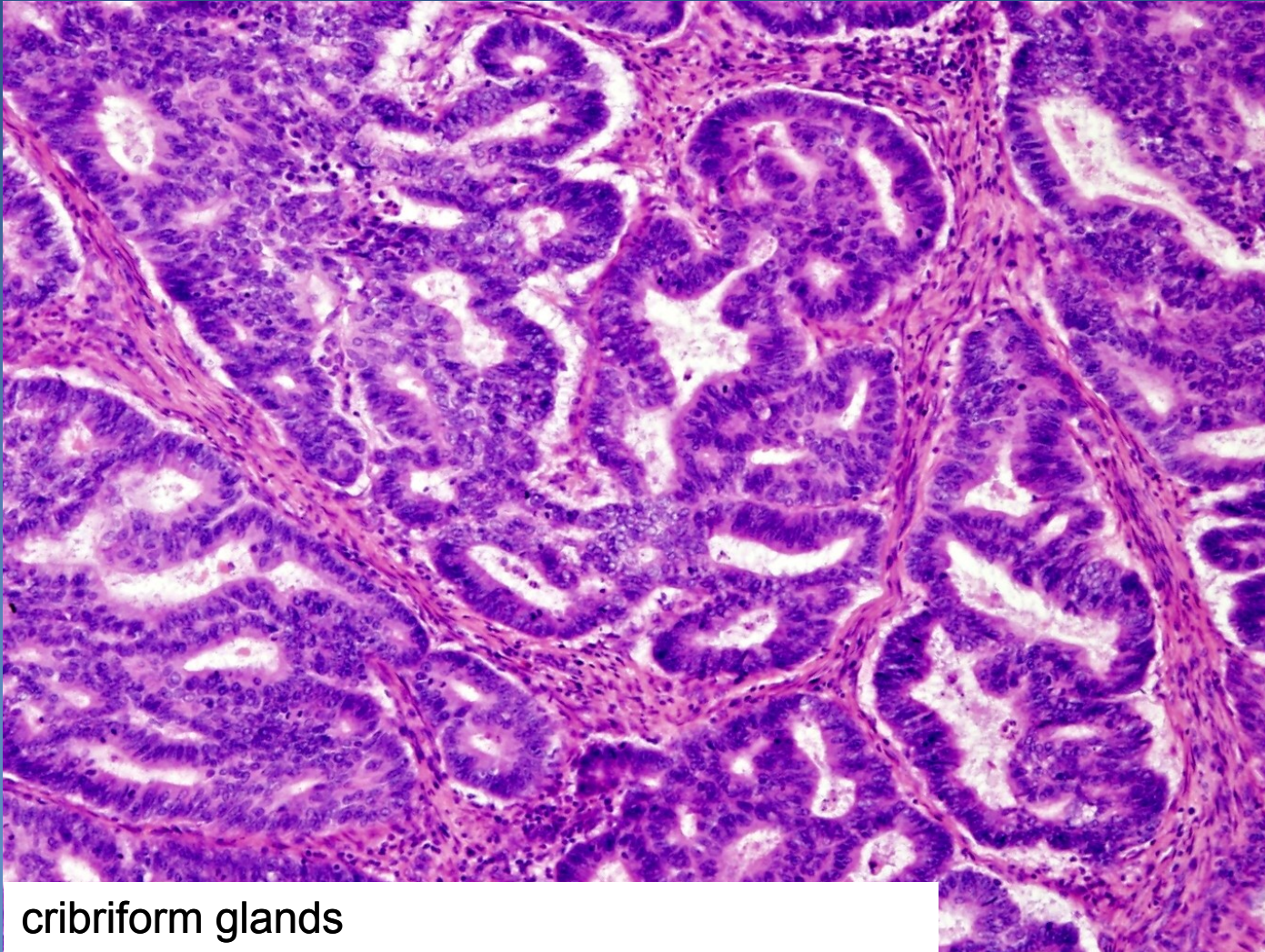
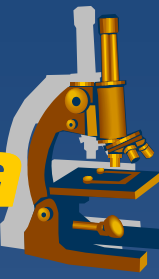
⇒ ***poorly differentiated (serous, clear cell)***

⇒ ***undifferentiated (metaplastic carcinoma)***

Endometrial adenocarcinoma

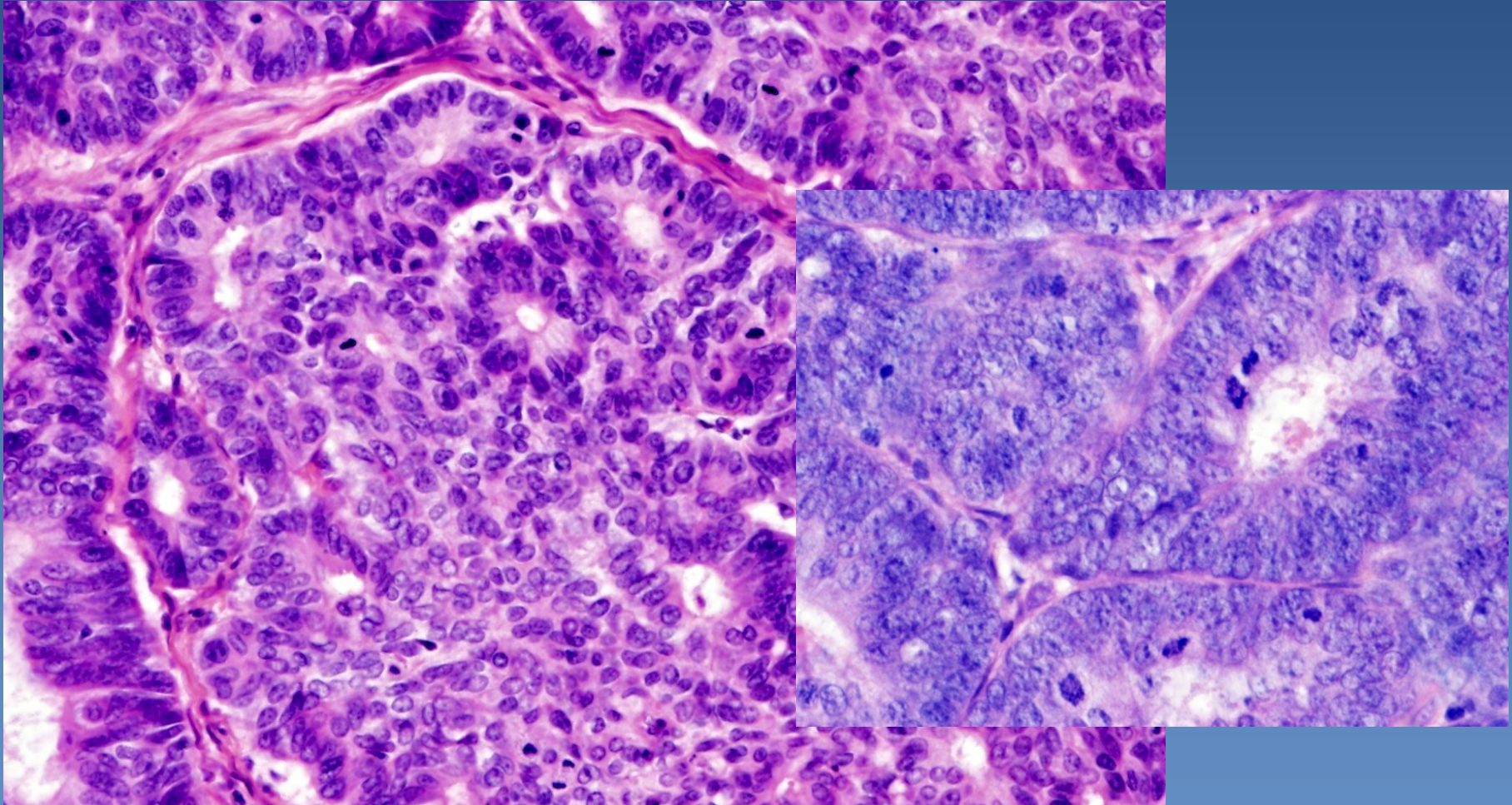
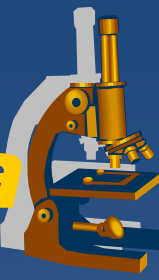


Endometrioid adenocarcinoma



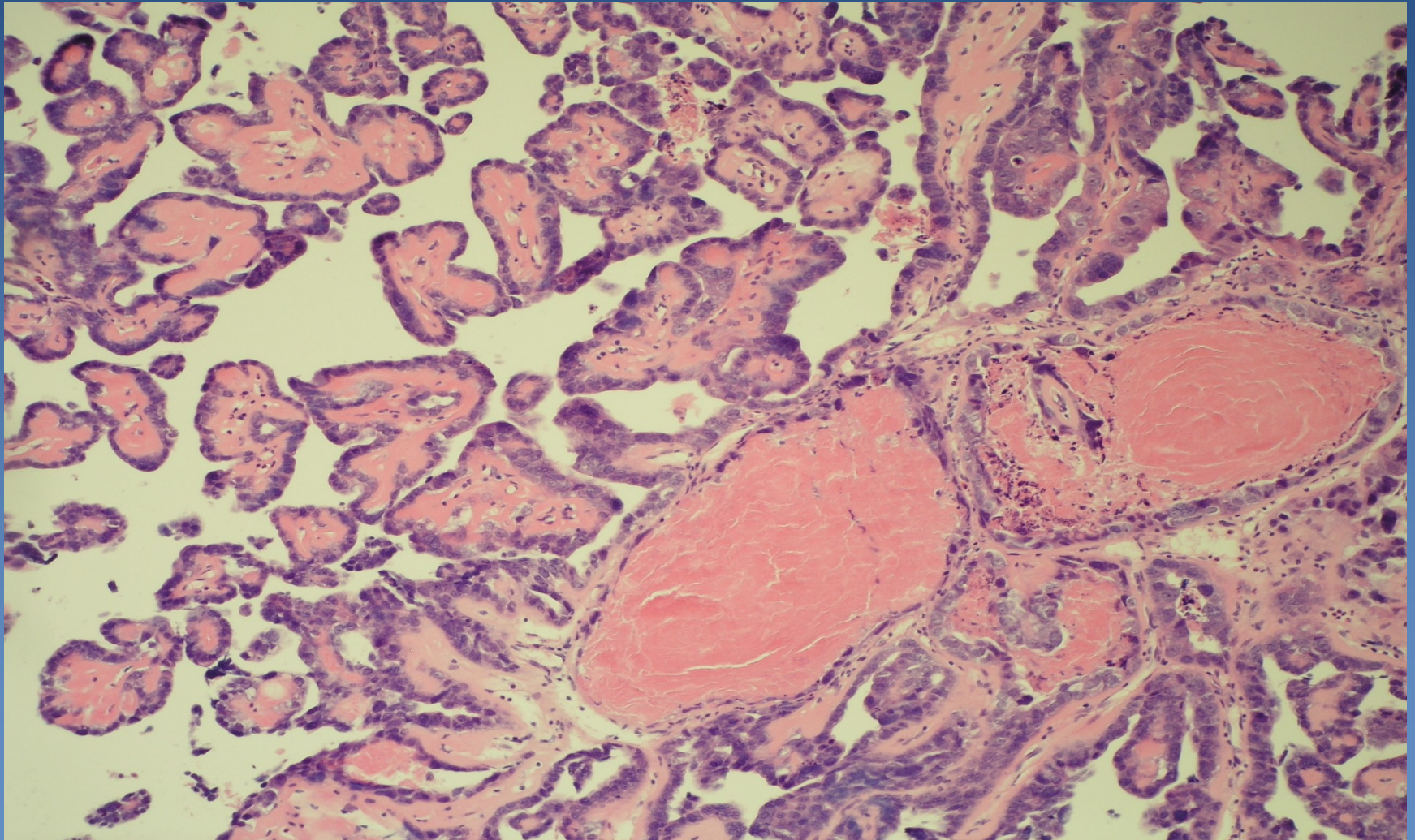
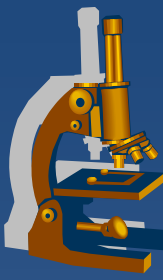
cribriform glands

Endometrioid adenocarcinoma

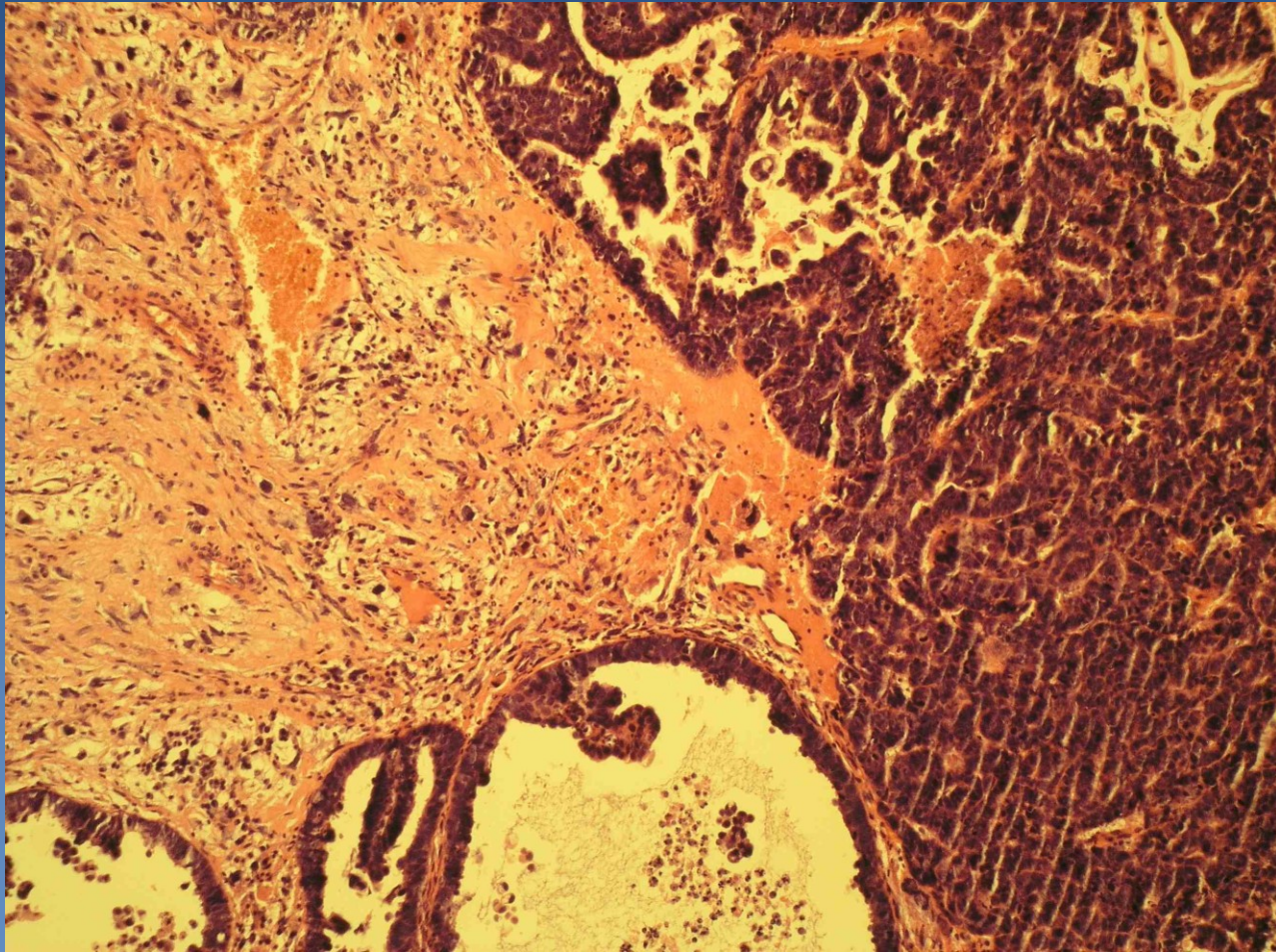
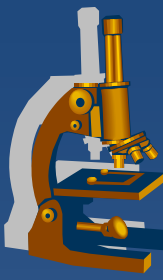


Epithelial stratification, cellular atypias, mitotic activity

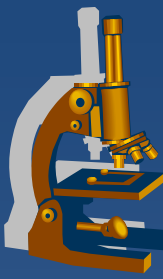
Serous adenocarcinoma



Metaplastic carcinoma



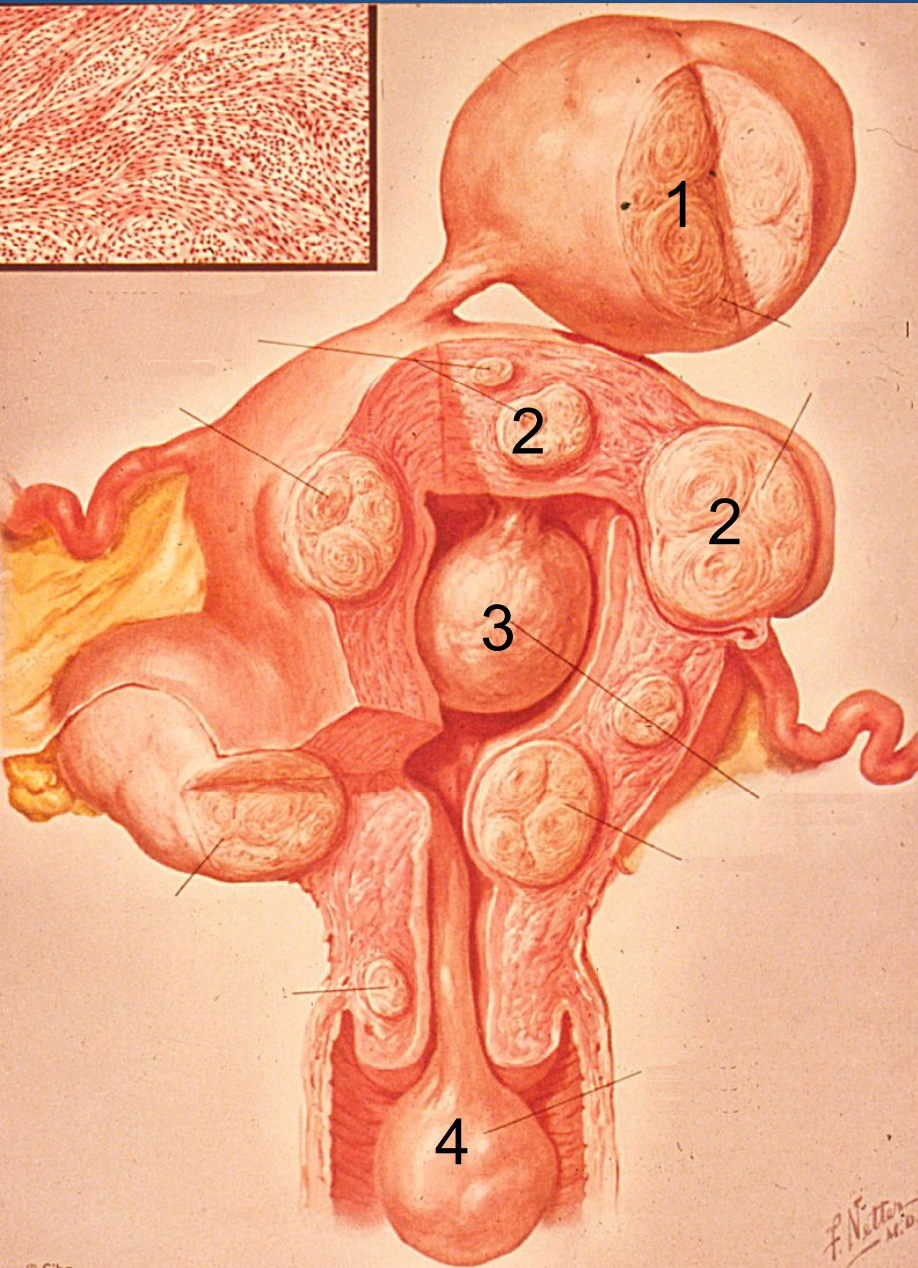
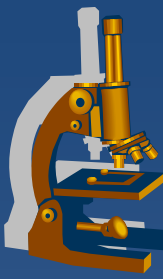
Mesenchymal tumors



x Leiomyoma

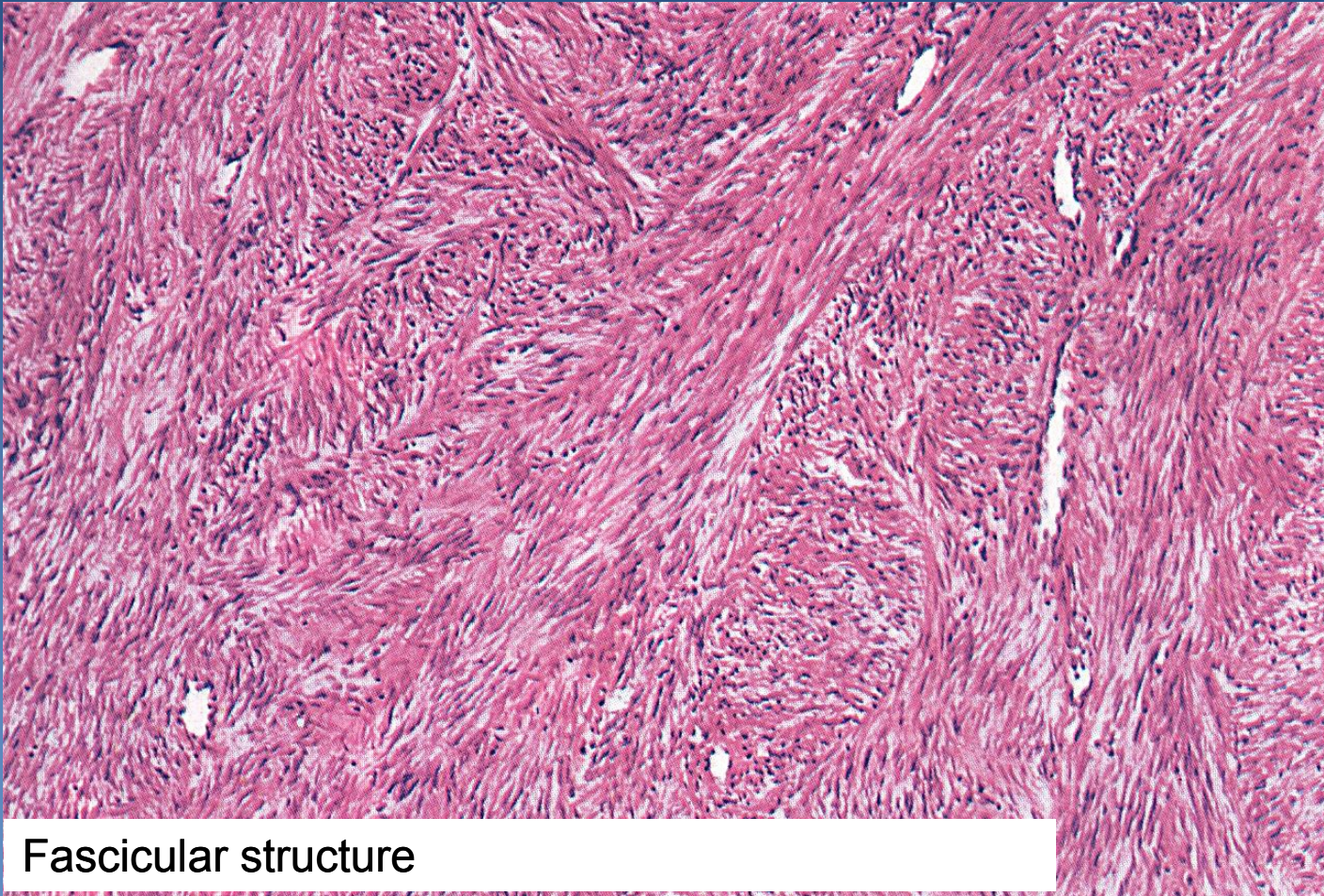
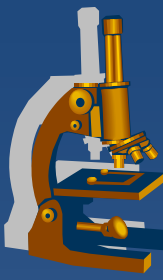
- ⇒ *most common benign female tumor (usual in later reproductive age)*
- ⇒ *size: mm - cca 20 cm*
- ⇒ *symptoms due to localisation/topography (bleeding, infertility, compression of adjacent organs)*
- ⇒ *uterus myomatosus (multiple leiomyomas)*
- ⇒ *common regressive changes (oedema, fibrosis, hyalinisation, calcification)*

Uterine leiomyomas



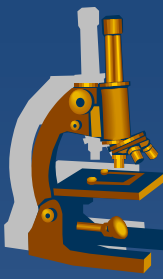
- 1 Subserous leiomyoma
- 2 Intramural myoma
- 3 Submucosal myoma
- 4 „Nascent“ submucosal myoma

Leiomyoma



Fascicular structure

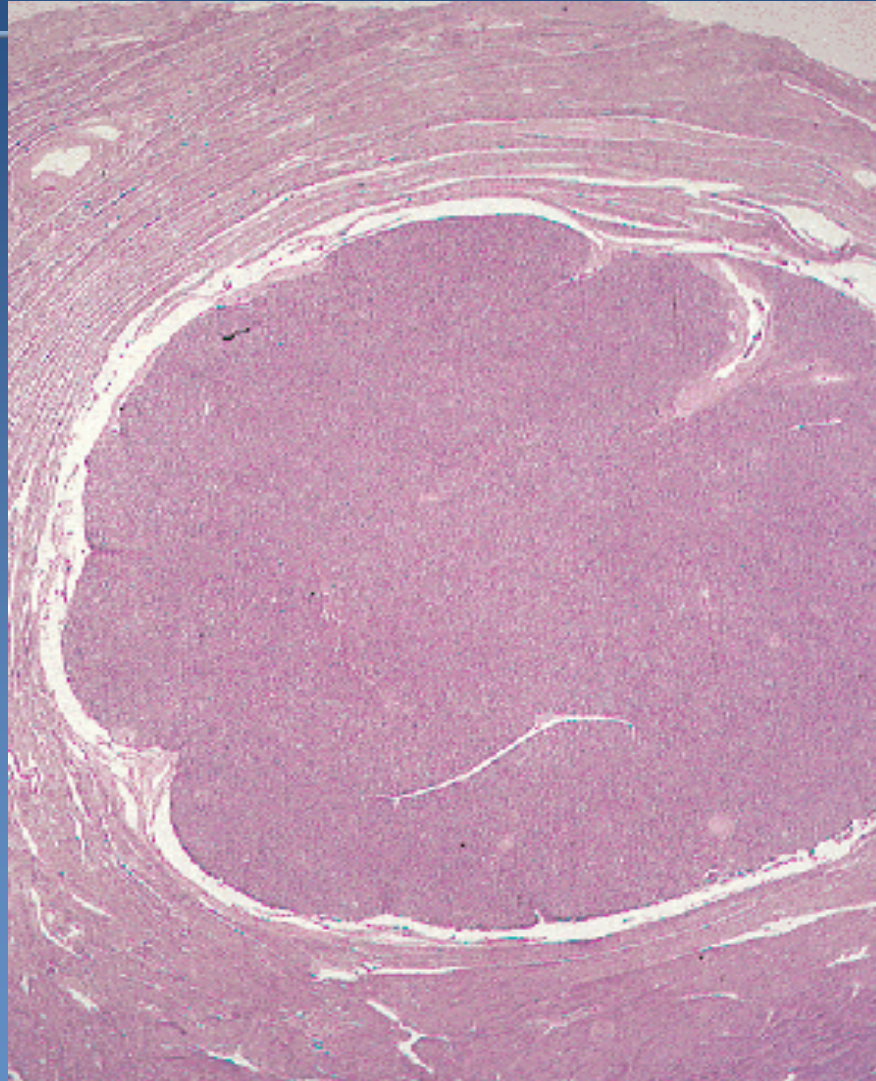
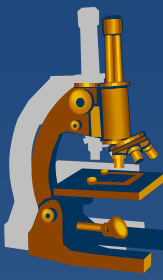
Mesenchymal tumors



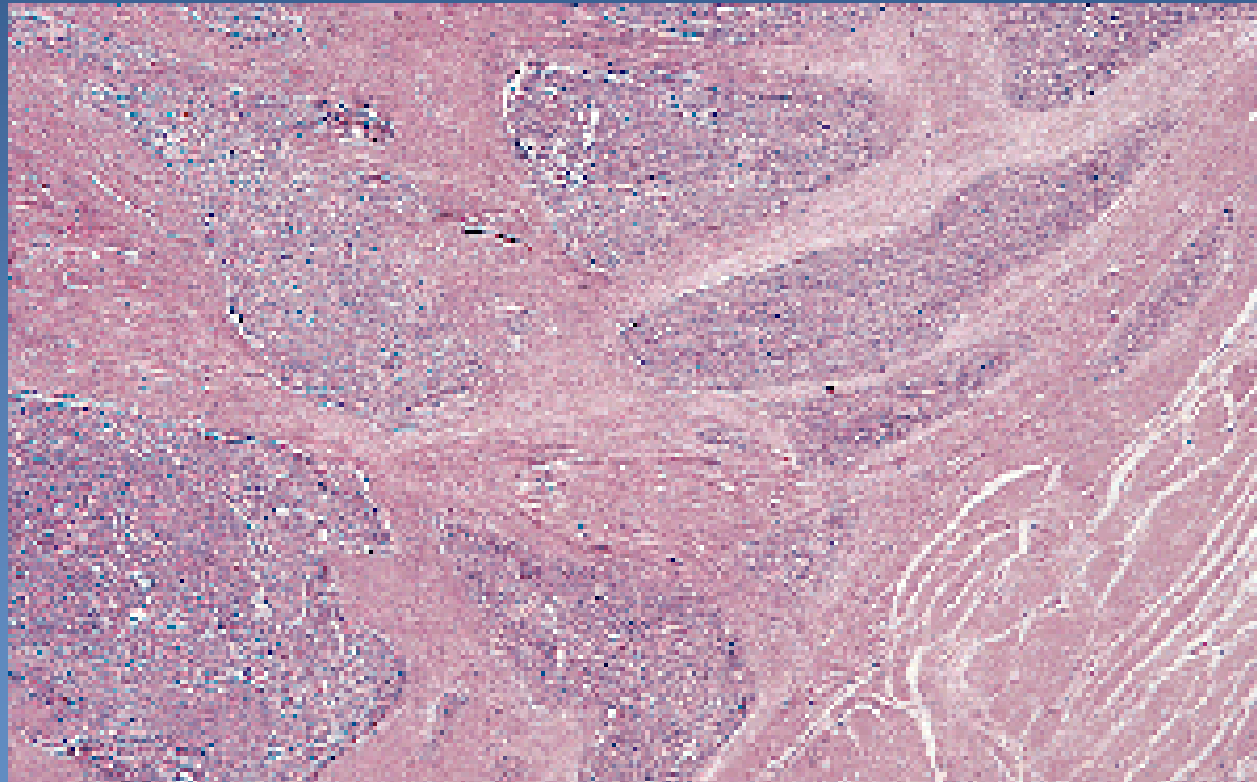
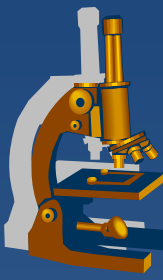
x Stromal tumors

- ⇒ *origin from endometrial stroma*
- ⇒ *Stromal nodule (benign)*
- ⇒ *Stromal sarcoma*
 - Low-grade
 - High-grade

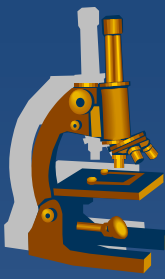
Stromal nodule



LG stromal sarcoma

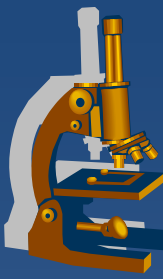


Pathology of pregnancy



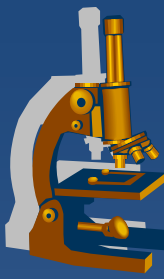
- ✗ ectopic pregnancy
- ✗ spontaneous abortion (placental disorders incl. placentation abnormalities, vascular lesions, inflammation – ascending, hematogenous; umbilical cord pathology)
- ✗ pre-eclampsia – systemic endothelial dysfunction; hypertension + oedema + proteinuria, hypercoagulative state; may → eclampsia (CNS – convulsion, coma)
- ✗ **Gestational trophoblastic disease**

Gestational trophoblastic disease



- x** proliferation of gestational trophoblast with progressive malignant potential or frankly malignant
- x** hydatidiform mole
 - ⇒ *partial, complete - benign;*
 - ⇒ *invasive – uncertain biol. potential*
 - ⇒ *from abnormal conception*
 - ⇒ *abnormal placenta with villous hydrops and variable degree of trophoblastic proliferation*
- x** trophoblastic tumors – choriocarcinoma, etc.

Hydatidiform mole



x Complete

- ⇒ „empty“ (aneuclear) egg fertilised by 1 normal sperm with duplication of haploid genome (23,X → 46,XX), or 2 normal sperm - 46,XX or 46,XY; paternal genome only
- ⇒ **gross:**
 - grape-like formations
- ⇒ **micro:**
 - cystic chorionic villi – extensive stromal oedema, central cistern – empty space
 - circumferential trophoblastic proliferation, atypias

x Partial

- ⇒ normal egg fertilised by 1 diploid sperm (46,XY) or 2 haploid sperm → triploid 69,XXX or 69,XXY
- ⇒ **gross:**
 - mixture of smaller grape-like villi, parts of embryo possible
- ⇒ **micro:**
 - mixture of oedematous and fibrotic villi
 - less marked trophoblastic proliferation



Hydatidiform mole

- complete

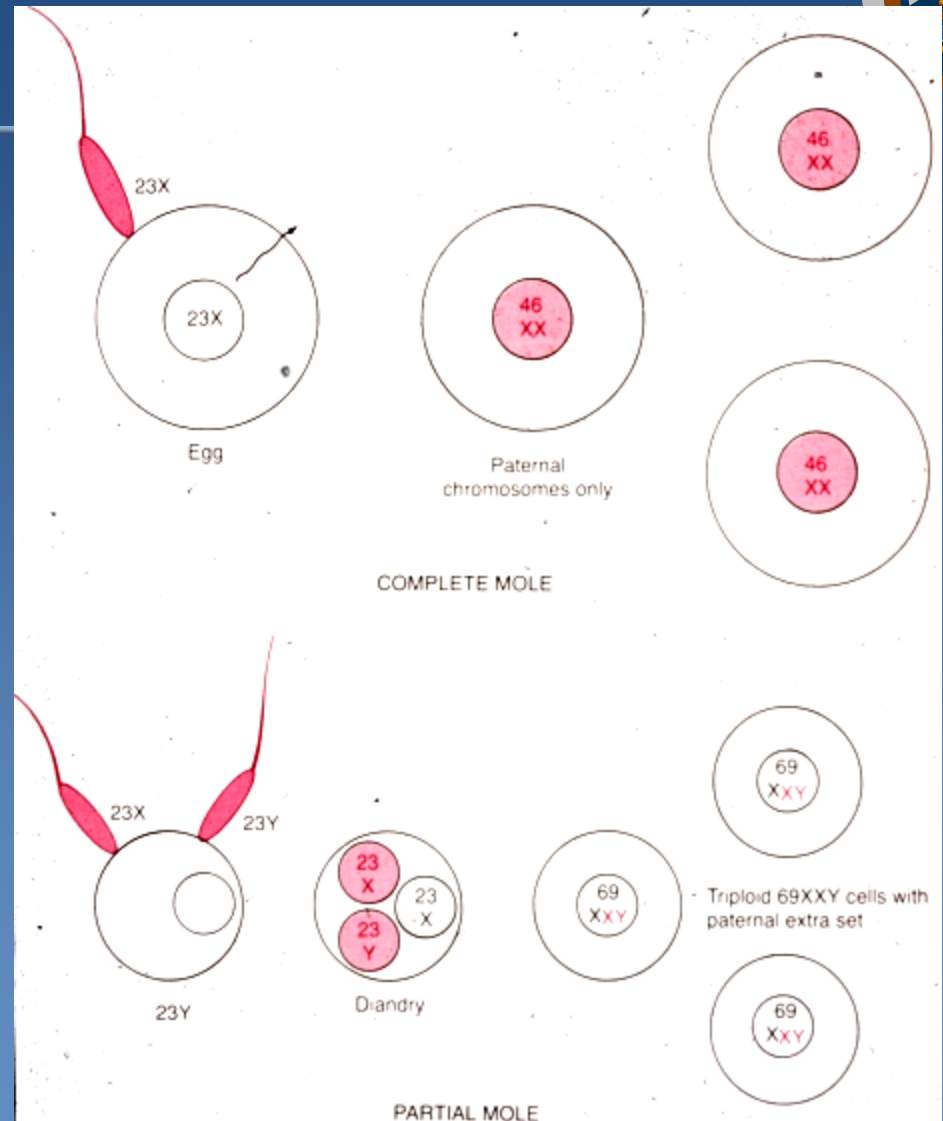
may persist or recur
10% → invasive m.
2,5% → chorioca

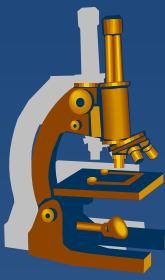
-partial

no progression,
may persist or recur

- invasive

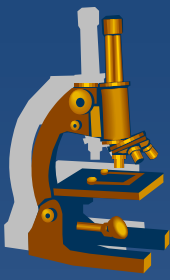
invasion of
myometrium by villi, risk of
perforation
locally destructive,
embolisation of villi into distant
organs (lungs)





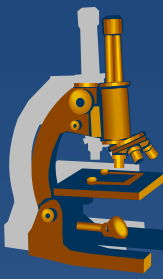
Gestational choriocarcinoma

- ✗ subsequent to molar pregnancy (50%), abortion (25%), normal gestation (22,5%), ectopic pregnancy (2,5%)
- ✗ atypical syncytio- and cytotrophoblast, no villi, minimal stroma, no angiogenesis; foci of haemorrhage, necrosis present
- ✗ early haematogenous spread (lung, vagina, brain, liver...)
- ✗ highly elevated HCG
- ✗ chemosensitive (x germ cell tumor – low response to therapy, bad prognosis)



Fallopian tubes

Salpingitis

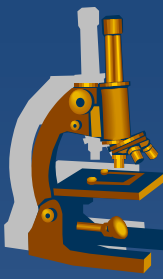


- ✗ mostly ascending inflammation from uterus
- ✗ possible secondary (appendicitis)

- ✗ risk of mucosal adhesions
 - ⇒ *infertility*
 - ⇒ *ectopic tubal pregnancy*

- ✗ part of pelvic inflammatory disease („adnextumor“)
 - ⇒ *inflammatory pseudotumor with abscessi*
 - ⇒ *pyosalpinx*

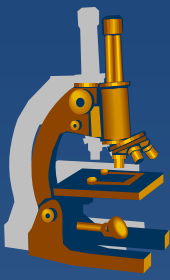
Tumors



- ✘ paratubal cysts

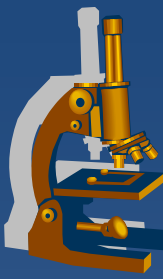
- ✘ intraepithelial serous adenocarcinoma
(possible precursor of ovarian adenoca),
invasive adenocarcinoma

- ✘ pseudotumors
 - ⇒ *inflammatory pseudotumor*
 - ⇒ *endometriosis*



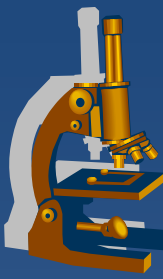
Ovary

Ovarian inflammation



- ✘ part of pelvic inflammatory disease (salpingo-oophoritis), tubo-ovarian abscess „adnextumor“
- ✘ common bacterial infections
- ✘ actinomycosis

Ovarian cysts



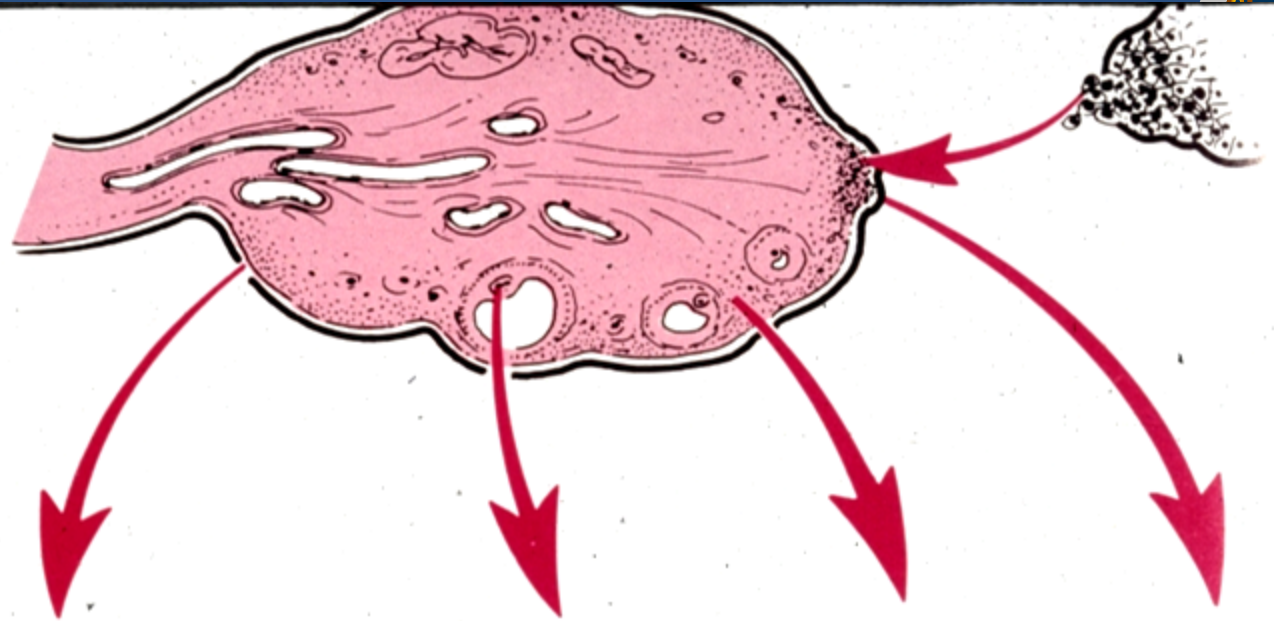
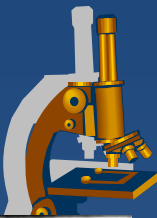
× non-neoplastic

- ⇒ inclusion c. (*mesothelial, epithelial*)
- ⇒ functional c. (*follicular, luteal, polycystic ovary syndrome, ovarian hyperstimulation syndrome*)
- ⇒ endometriosis

× neoplastic

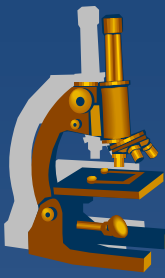
- ⇒ surface epithelial tumors,
- ⇒ germ cell tumors
- ⇒ sex-cord stromal tumors
- ⇒ metastatic tumors
- ⇒ *others*

Ovarian tumors

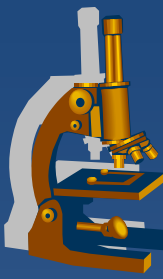


Origin	Surface epithelial cells (common epithelial tumors)	Germ cell	Sex cord–stroma	Metastasis to ovaries
Frequency	65–70%	15–20%	5–10%	5%
Age group affected	20 + years	0–25 + years	All ages	Variable
Types	<ul style="list-style-type: none"> • Serous tumor • Mucinous tumor • Endometrioid tumor • Clear cell tumor • Brenner tumor • Unclassifiable 	<ul style="list-style-type: none"> • Teratoma • Dysgerminoma • Endodermal sinus tumor • Choriocarcinoma 	<ul style="list-style-type: none"> • Fibroma • Granulosa–theca cell tumor • Sertoli–Leydig cell tumor 	

Germ cell tumors

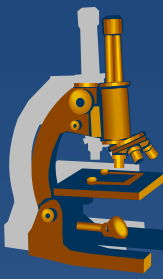


- x counterpart to germ cell testicular tumors
- x **dysgerminoma** – ovarian „seminoma“
- x most common female germ cell tumor:
 - ⇒ *benign mature (differentiated) teratoma, usually in the form of dermoid cyst*



Dermoid cyst – mature cystic teratoma

Sex cord-stromal tumors



x Granulosa-theca cell tumors

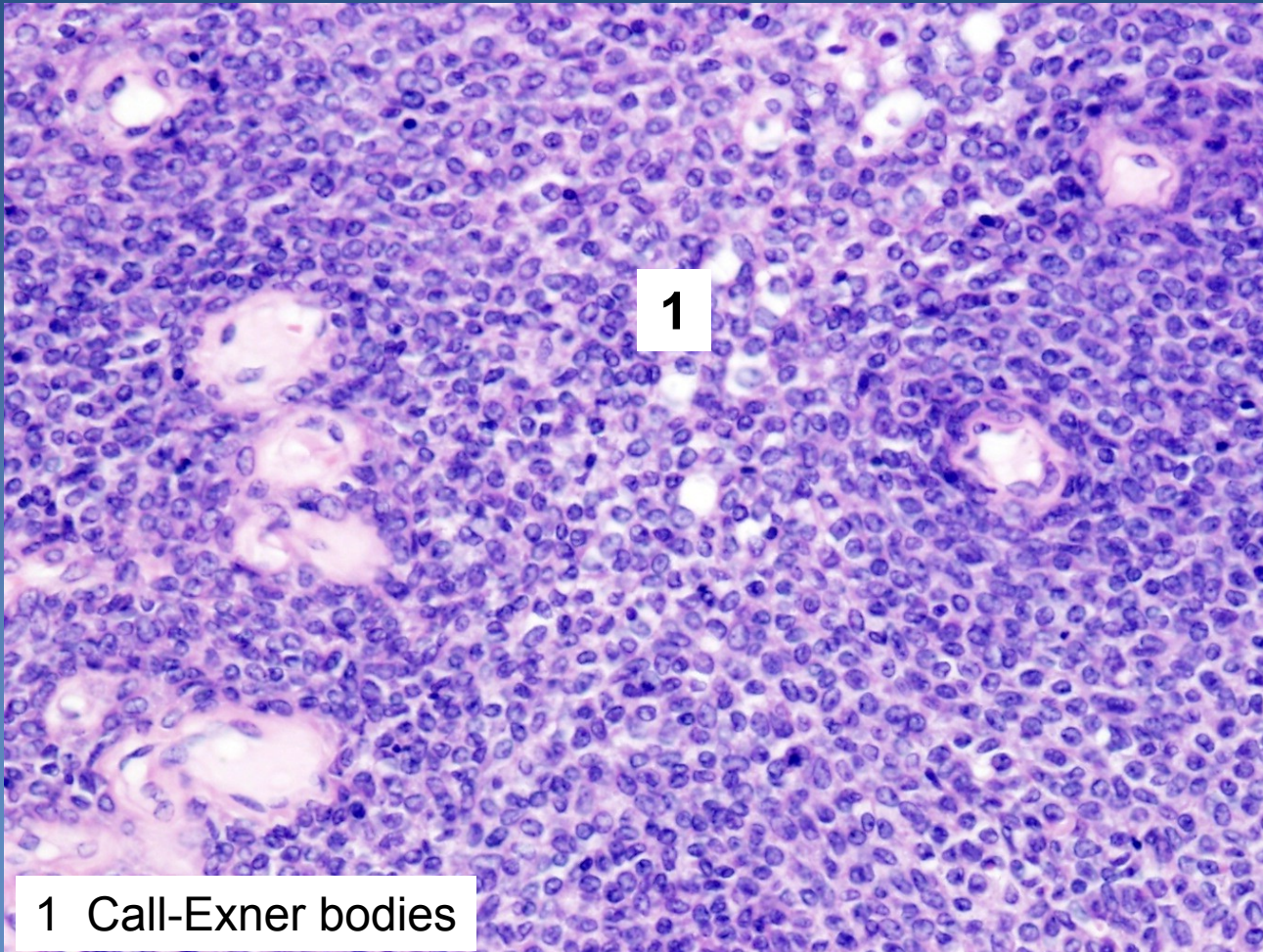
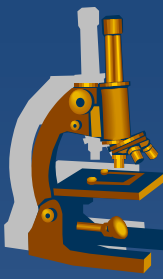
- **granulosa cell tumor (adult type)** – Call-Exner bodies; malignant potential, estrogen production
- **granulosa cell tumor (juvenile type)**
- **thecoma**
- **fibrothecoma**
- *fibroma*
- *fibrosarcoma*

x Sertoli-Leydig cell tumors

x Steroid cell tumors

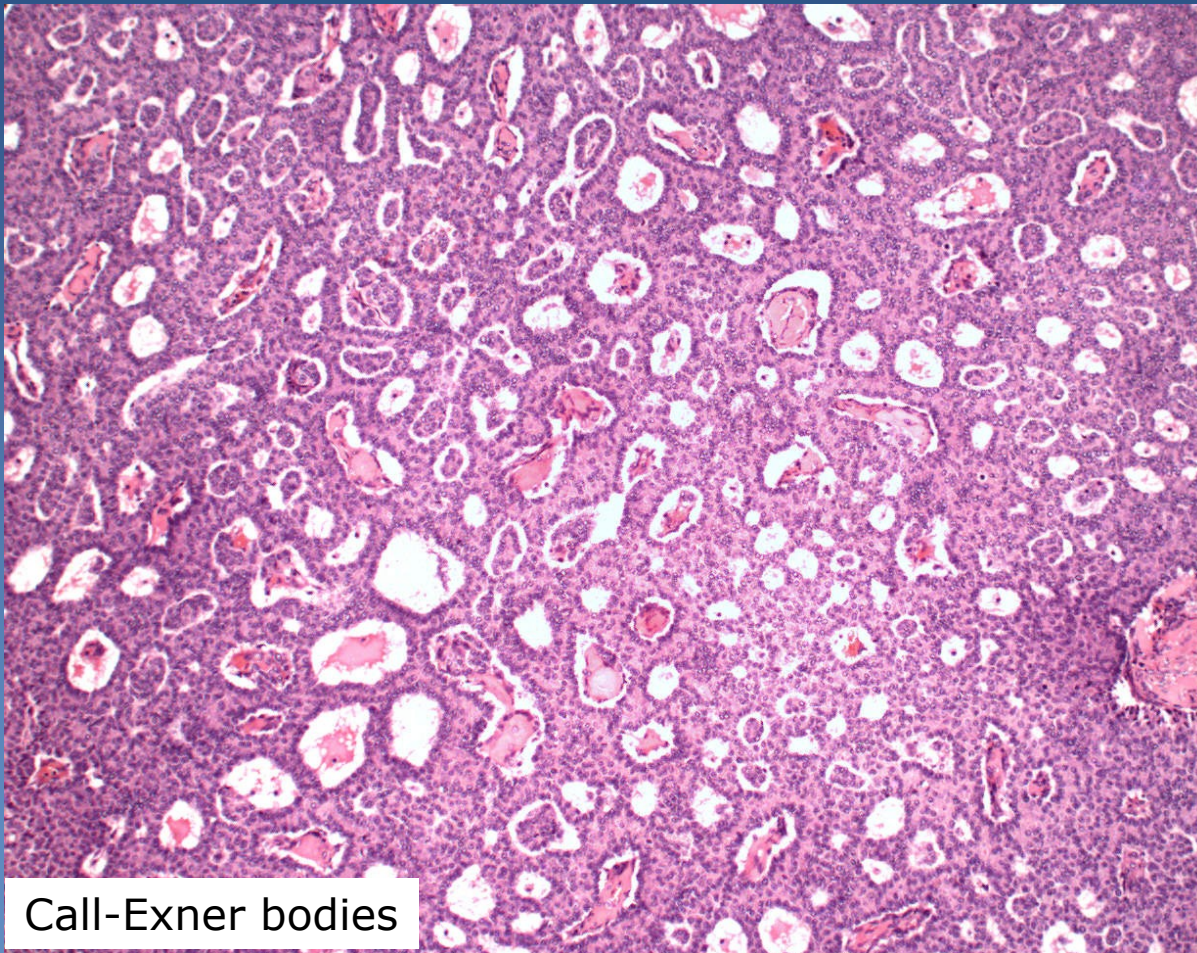
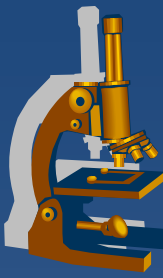
- resemble steroid hormone-secreting cells
- possible androgenic secretion

Granulosa cell tumor

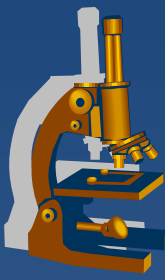


1 Call-Exner bodies

Granulosa cell tumor



Call-Exner bodies



Other tumors

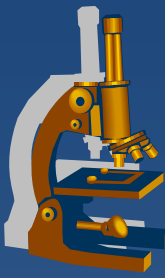
- x Mixed germ cell sex cord-stromal tumors**
- x Primary ovarian mesothelioma, adenomatoid tumor**
- x Soft tissue tumors not specific to the ovary**
- x Malignant lymphomas**

....

x Secondary ovarian tumors

- ⇒ *Krukenberg tumor (metastatic mucinous adenocarcinoma)*
- ⇒ *pseudomyxoma peritonei,...*

Surface epithelial-stromal tumors

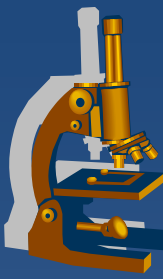


- ✗ Coelomic epithelium (mesothelium with the ability of transformation into Müllerian epithelium) → hyperplasia and metaplasia of the surface epithelium → neoplastic transformation

Biologic potential

- ✗ Benign
 - ⇒ *commonly in form of cystadenoma*
- ✗ Low malignant potential
 - ⇒ *borderline malignancy – moderate atypias, mitotic activity, architectonic changes (multilayering, irregular papillary budding), ! no invasion, but non-invasive peritoneal implants possible*
- ✗ Malignant

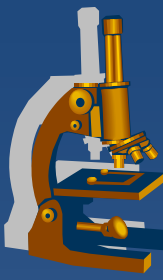
Surface epithelial-stromal tumors



Epithelial type

- x Serous*
- x Mucinous, endocervical-like and intestinal-type*
- x Endometrioid*
- x Clear cell tumors*
- x Transitional cell tumors*
- x Mixed tumors of müllerian epithelium*

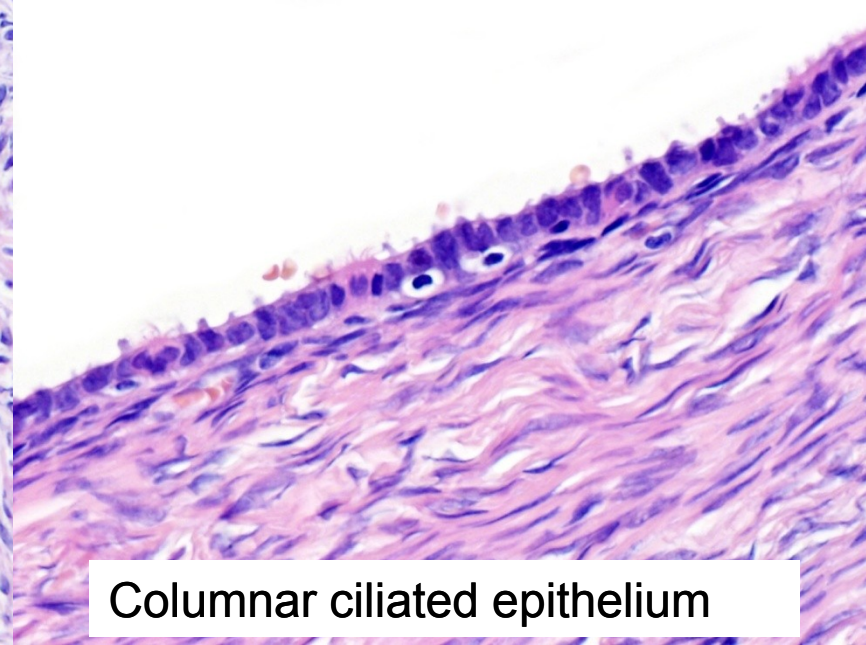
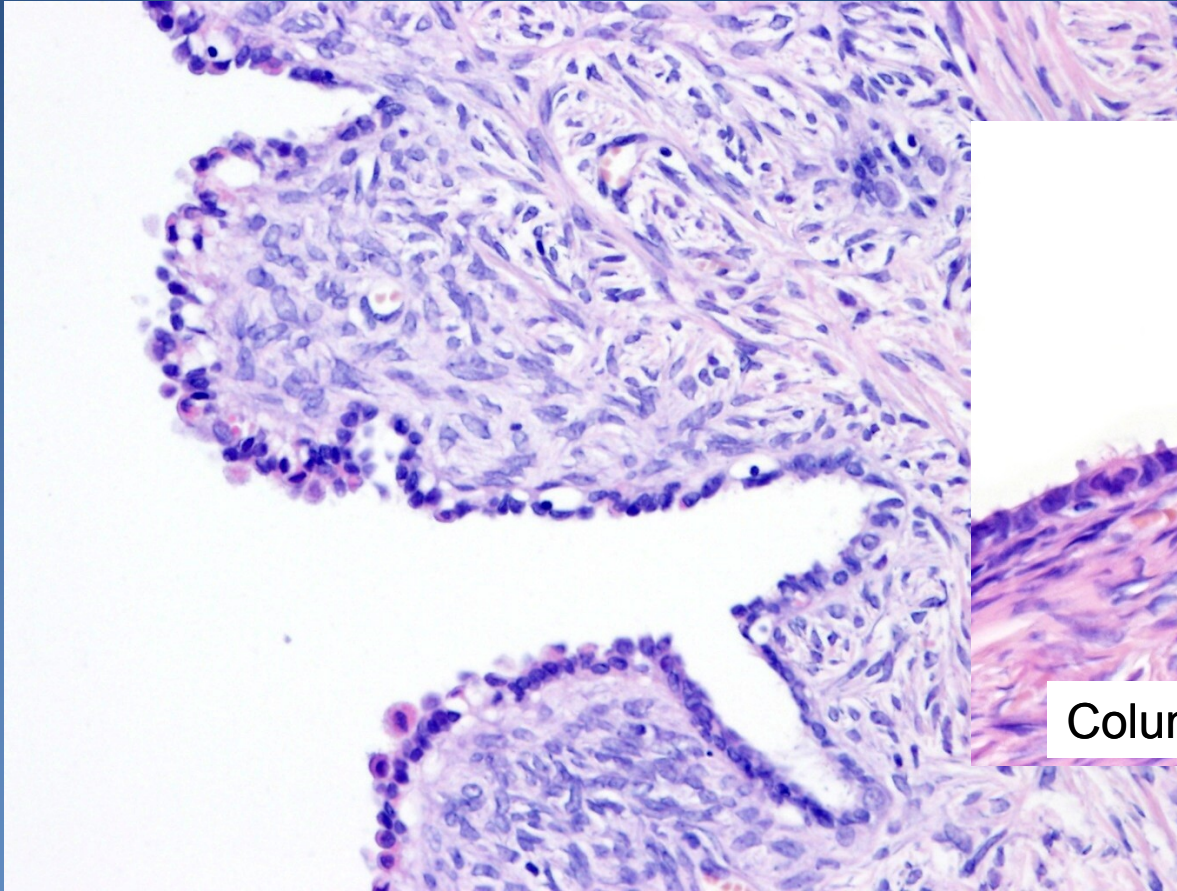
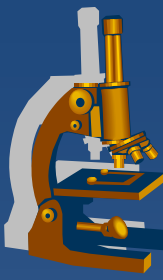
Surface epithelial-stromal tumors



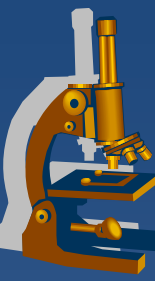
Form of growth

- ✗ Cystic
- ✗ Papillary incl. inverted
- ✗ Solid
- ✗ Increased amount of neoplastic stroma, mixed tumor (adenofibroma, adenosarcoma, etc.)

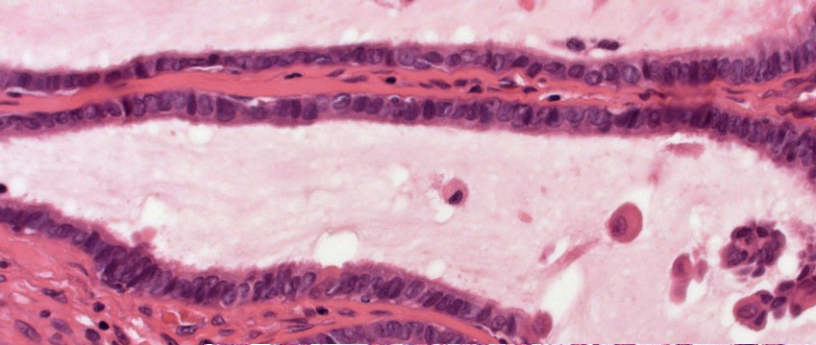
Serous cystadenoma (*cystadenofibroma*)



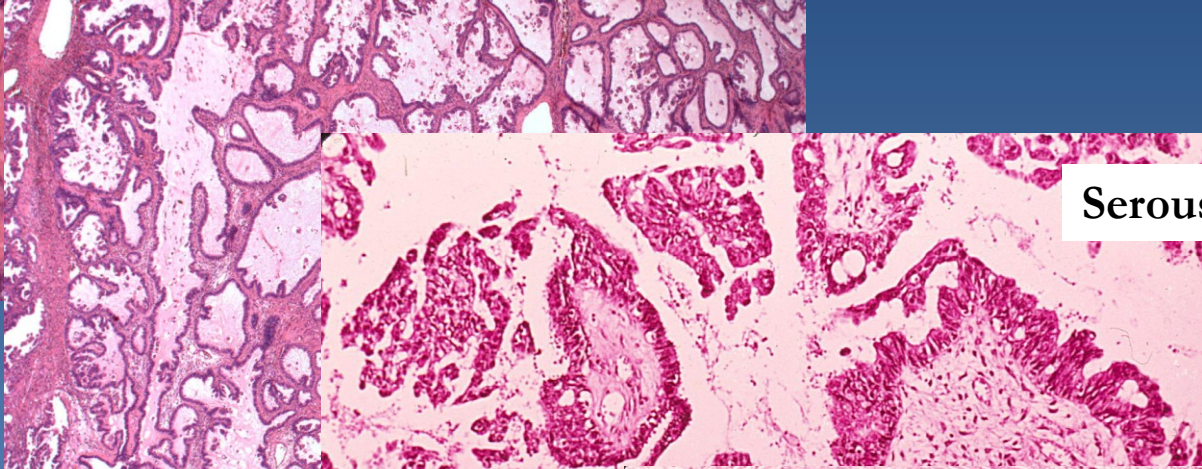
Columnar ciliated epithelium



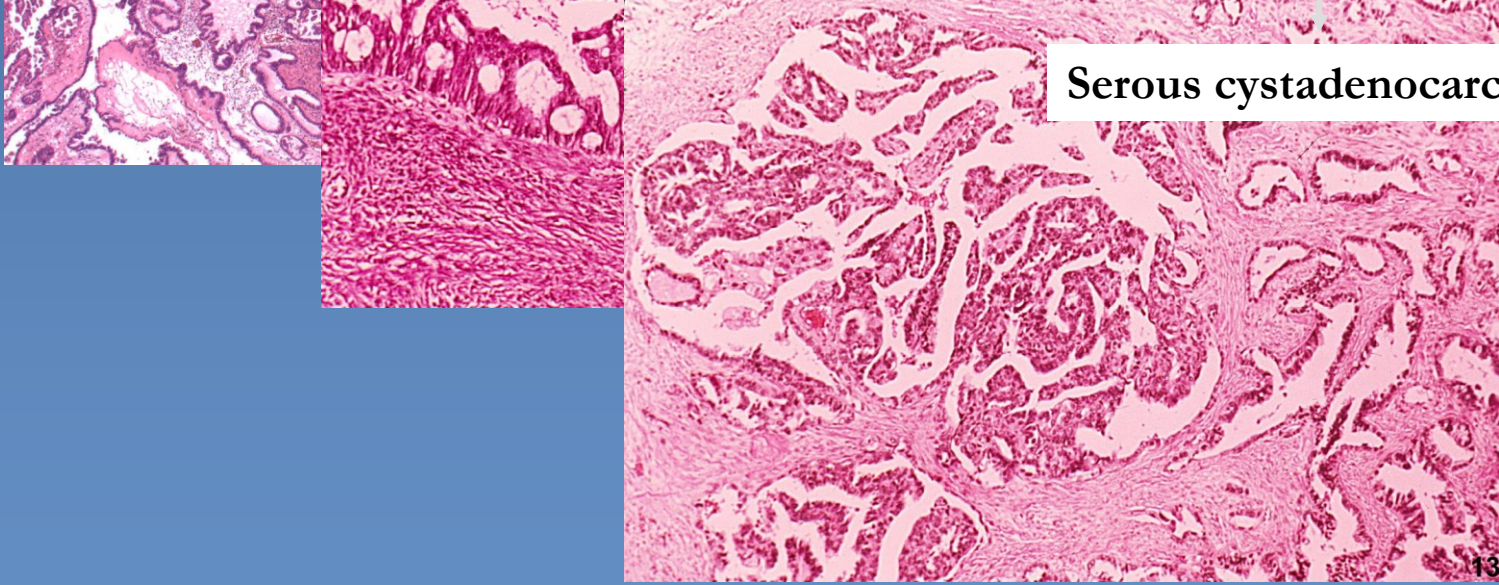
Serous cystadenoma



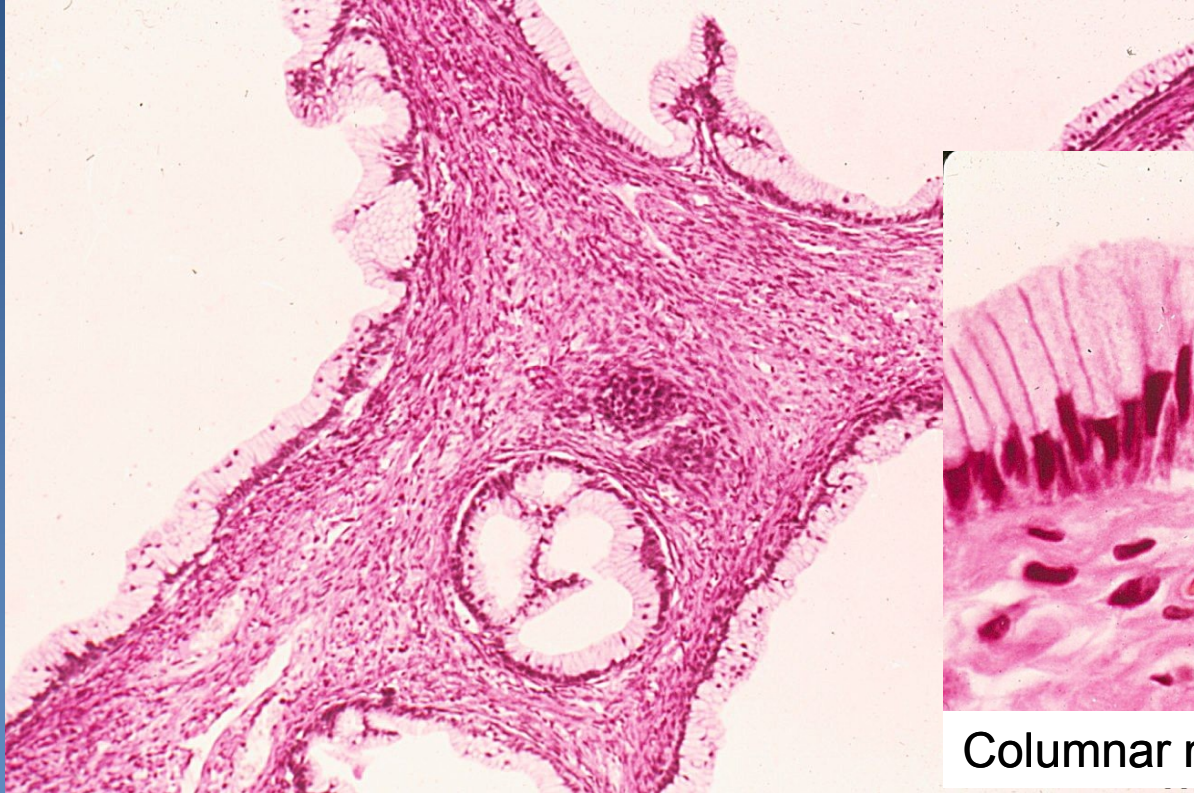
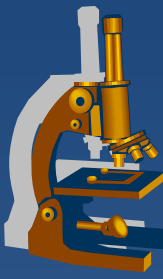
Serous borderline tumor



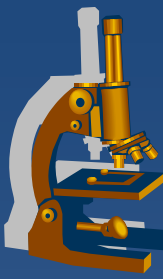
Serous cystadenocarcinoma



Mucinous cystadenoma



Columnar mucinous epithelium



Mucinous cystadenoma

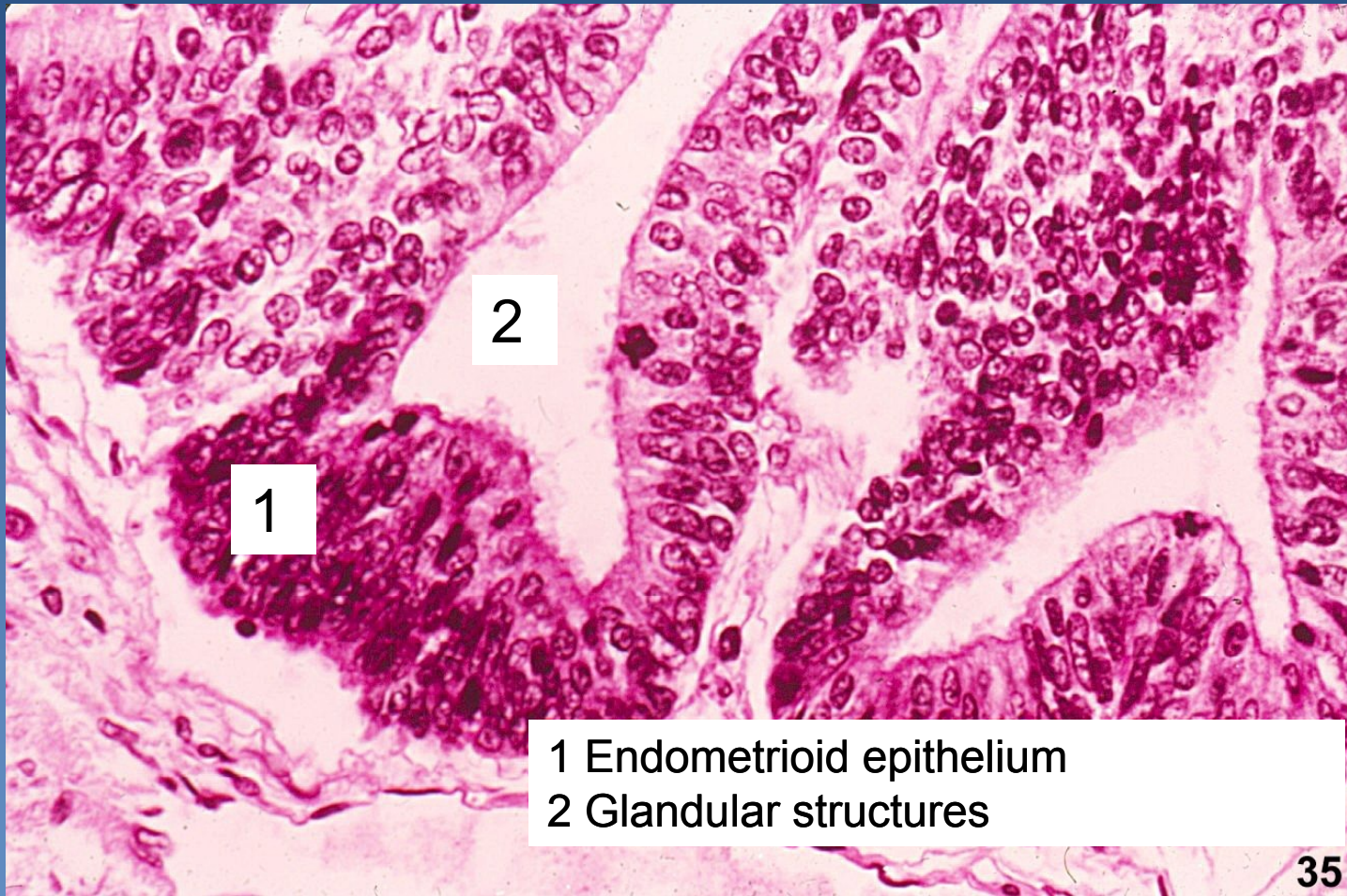
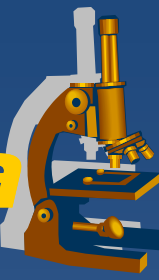


Mucinous borderline tumor

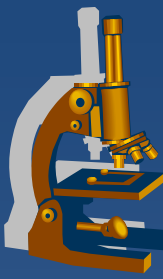


Mucinous cystadenocarcinoma

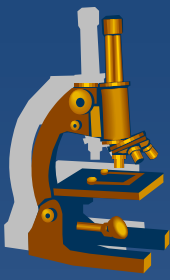
Endometrioid adenocarcinoma



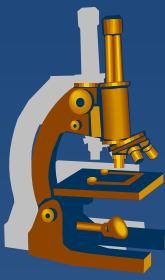
Surface epithelial-stromal tumors



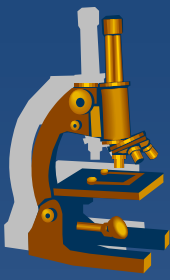
- ✘ Serous adenocarcinoma
 - ⇒ 60-80%, 30-50% bilateral
 - ⇒ usually smaller size, rapid growth
 - ⇒ common psammoma bodies
- ✘ Mucinous adenocarcinoma
 - ⇒ 5-15%, 10-20% bilateral
 - ⇒ large size, slow growth
- ✘ Endometrioid adenocarcinoma
 - ⇒ 10-30%, 10-30% bilateral
 - ⇒ slow growth, haemorrhagic content
 - ⇒ squamous metaplasia common



Pathology of the breast



- x Skin
- x **Nipple and areola**
- x **Mammary gland**
- x Soft tissues
 - ⇒ *inborn defects*
 - ⇒ *circulatory disorders*
 - ⇒ ***inflammations***
 - ⇒ ***non-neoplastic lesions***
 - ⇒ ***tumors***



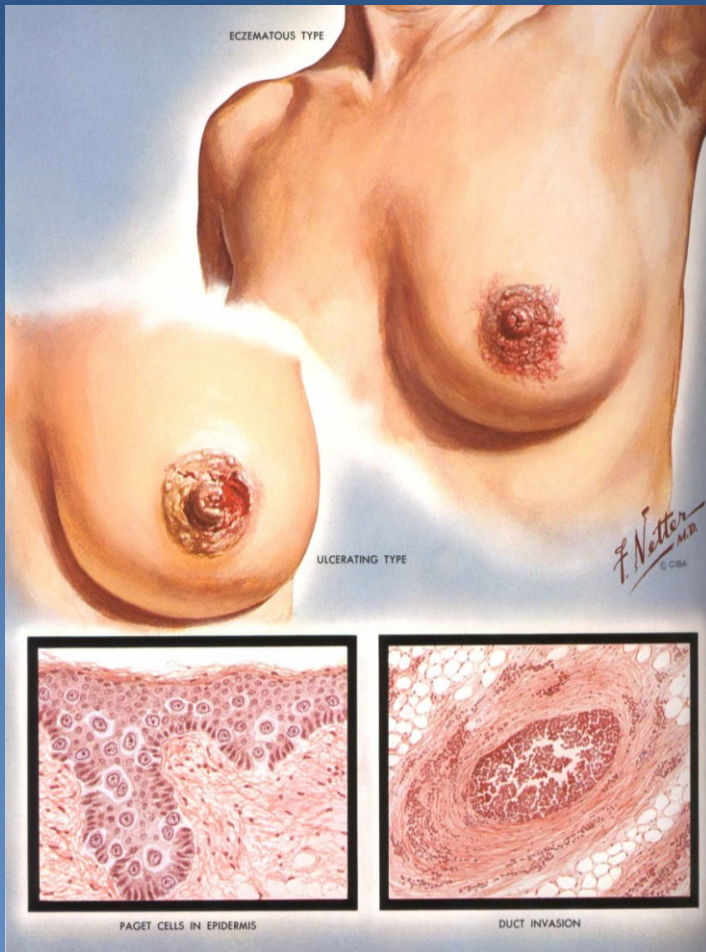
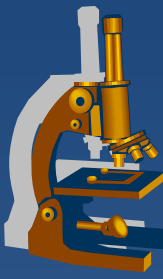
Nipple and areola

Paget's carcinoma of the nipple

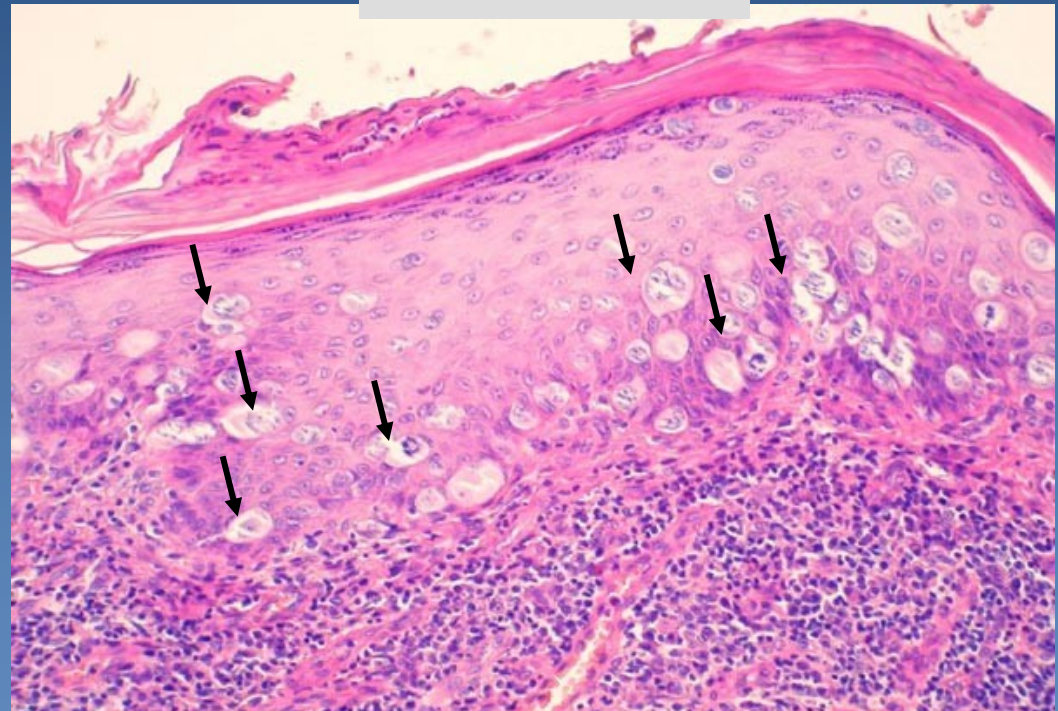


- ✘ **single neoplastic cells dispersed in the squamous cell epithelium** of the nipple
- ✘ usually concurrent with DCIS (ductal carcinoma in situ) or invasive breast carcinoma
- ✘ gross: eczema-like (erythema, oozing/ ulcerated lesion)

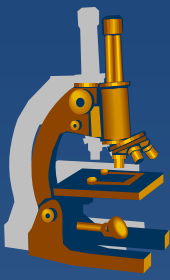
Paget's carcinoma of the nipple



www.mamma.cz

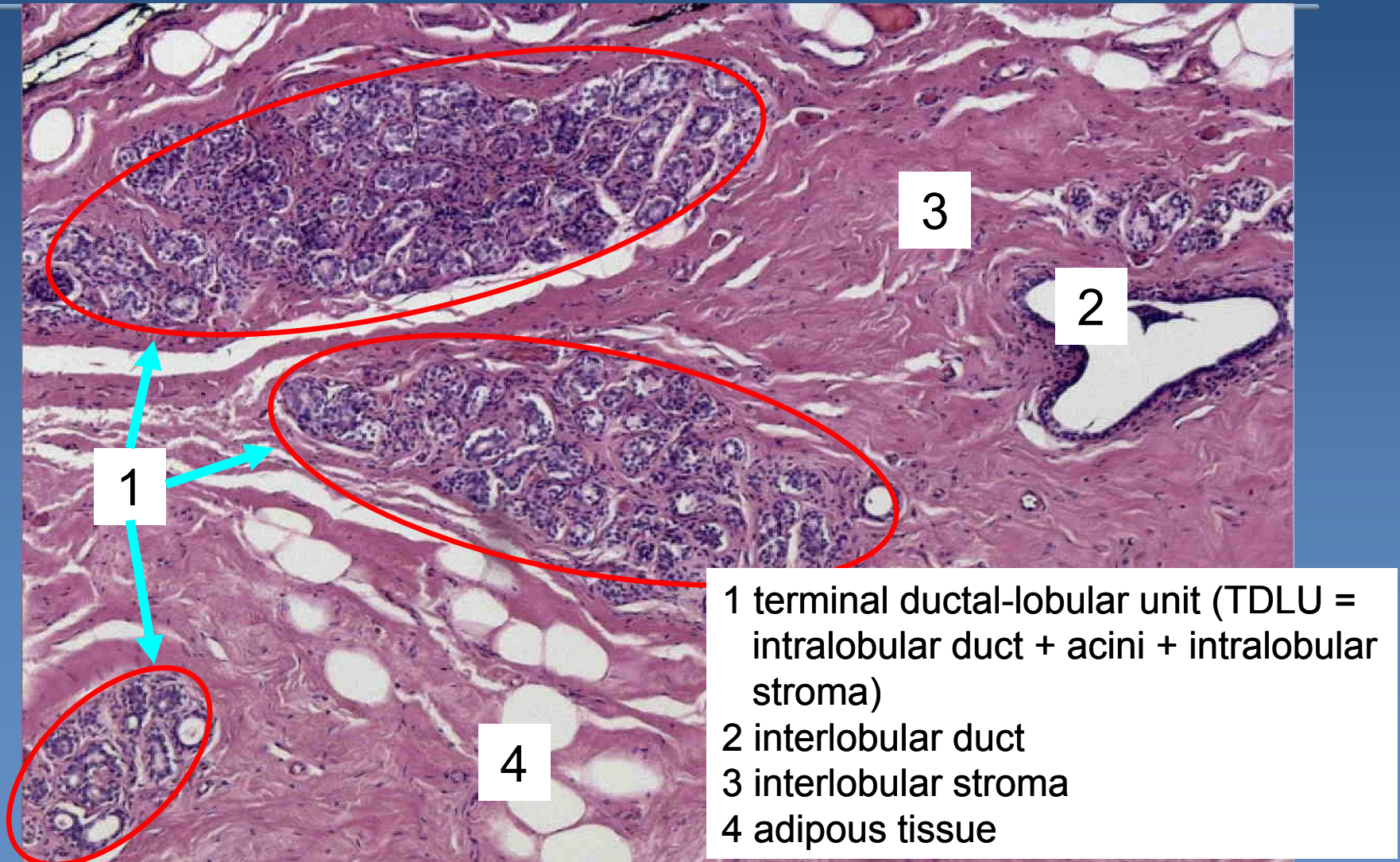
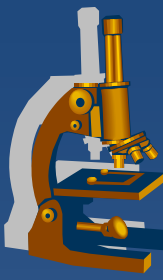


Single neoplastic cells (arrows) dispersed in squamous cell epithelium



Mammary gland

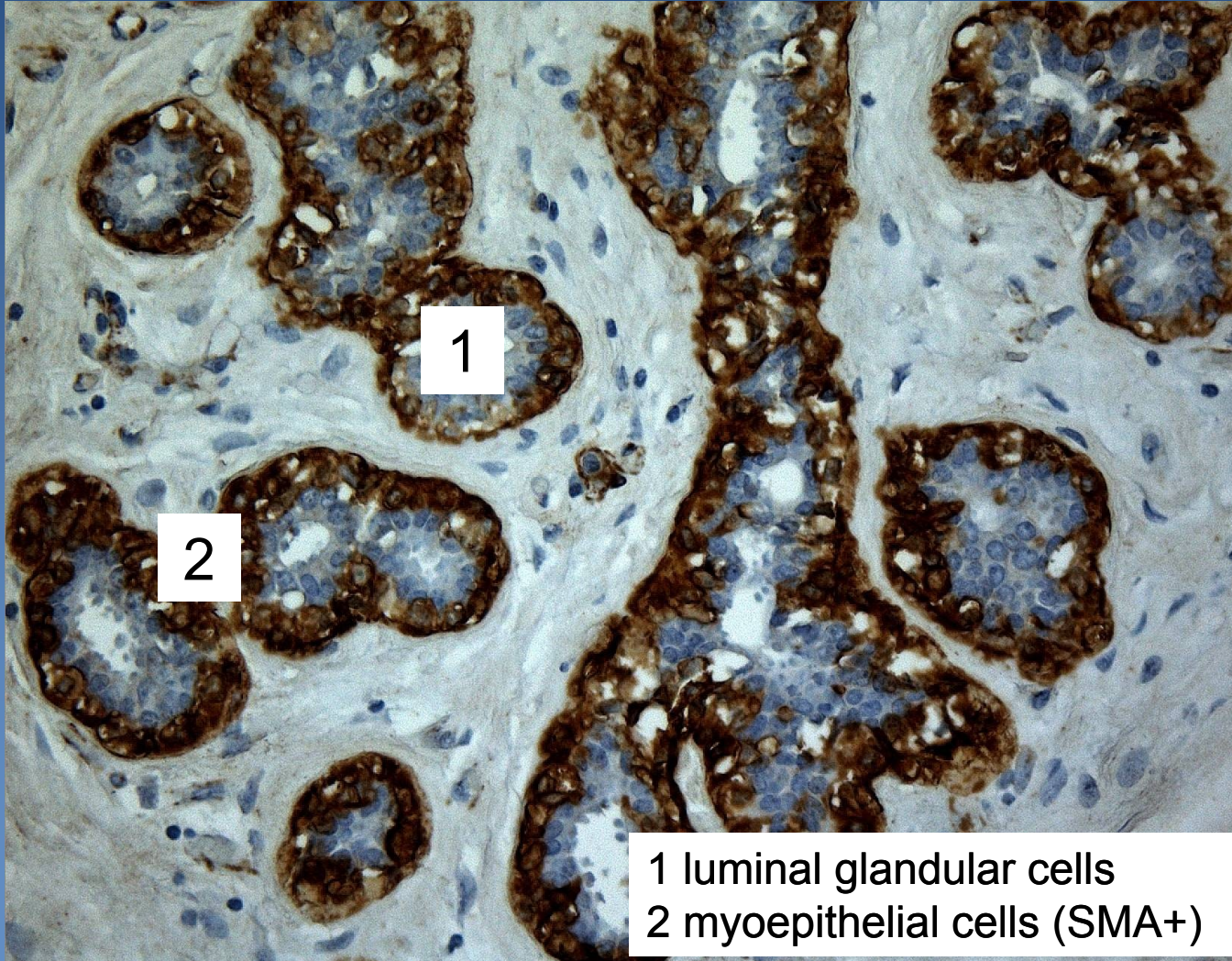
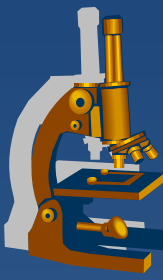
Fertile mammary gland - histology



- 1 terminal ductal-lobular unit (TDLU = intralobular duct + acini + intralobular stroma)
- 2 interlobular duct
- 3 interlobular stroma
- 4 adipous tissue

TDLU

IHC anti-SMA



1 luminal glandular cells
2 myoepithelial cells (SMA+)

Mammary gland



x selected inflammations:

⇒ *Acute pyogenic mastitis*

- during first weeks of breastfeeding
- nipple fissures + infection (i.e. *Staphylococcus aureus*) → purulent inflammation / abscess formation

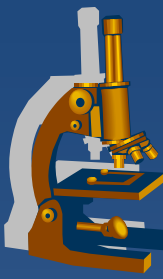
⇒ *Periductal mastitis*

- strongly associated with smoking
- squamous metaplasia in the distal parts of ducts → keratin plug → cystic dilatation / duct rupture → chronic /granulomatous periductal inflammation

⇒ *Lymphocytic (diabetic) mastopathy*

- type I. DM, autoimmune thyreoiditis
- periductal + perilobular sclerosis + dense lymphocytic infiltrate

Benign epithelial lesions



x benign alterations in ducts and lobules

x common lesions

⇒ *palpable irregularities (lumps, granularity), +/- tender*

⇒ *etiology:*

- hormone dependent
- inflammation-associated

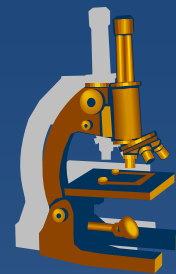
⇒ *diff. dg.: malignant tumors*

Benign epithelial lesions



- x** classification according to the risk of developing subsequent breast carcinoma
- x** non-proliferative breast changes – fibrocystic change
 - ⇒ *cysts +/- apocrine metaplasia*
 - ⇒ *fibrosis*
 - ⇒ *adenosis*

Benign epithelial lesions



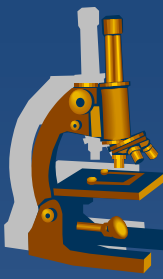
- ✗ proliferative breast disease without atypia
 - ⇒ proliferation of ductal epithelium +/-stroma
 - ⇒ usually in combination
 - ⇒ calcification common (mammography)
 - ⇒ epithelial hyperplasia (usual ductal hyperplasia – simple, florid)
 - ⇒ sclerosing adenosis
 - ⇒ papillomatosis
 - ⇒ complex sclerosing lesion

Benign epithelial lesions



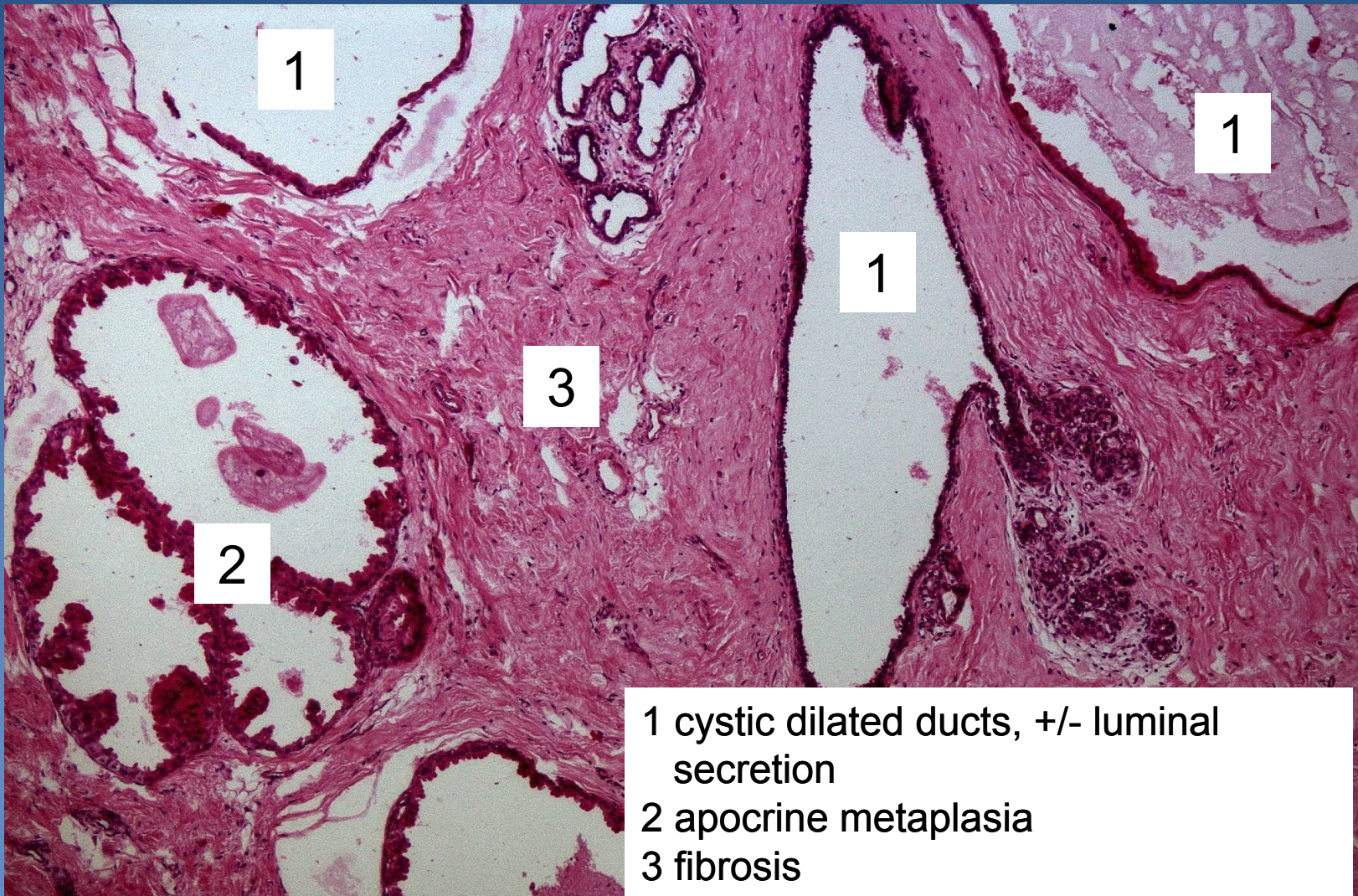
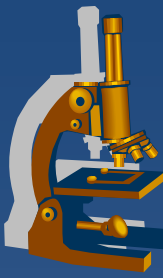
- x** proliferative breast disease with atypia
 - ⇒ *atypical ductal hyperplasia*
 - ⇒ *atypical lobular hyperplasia*

Fibrocystic change



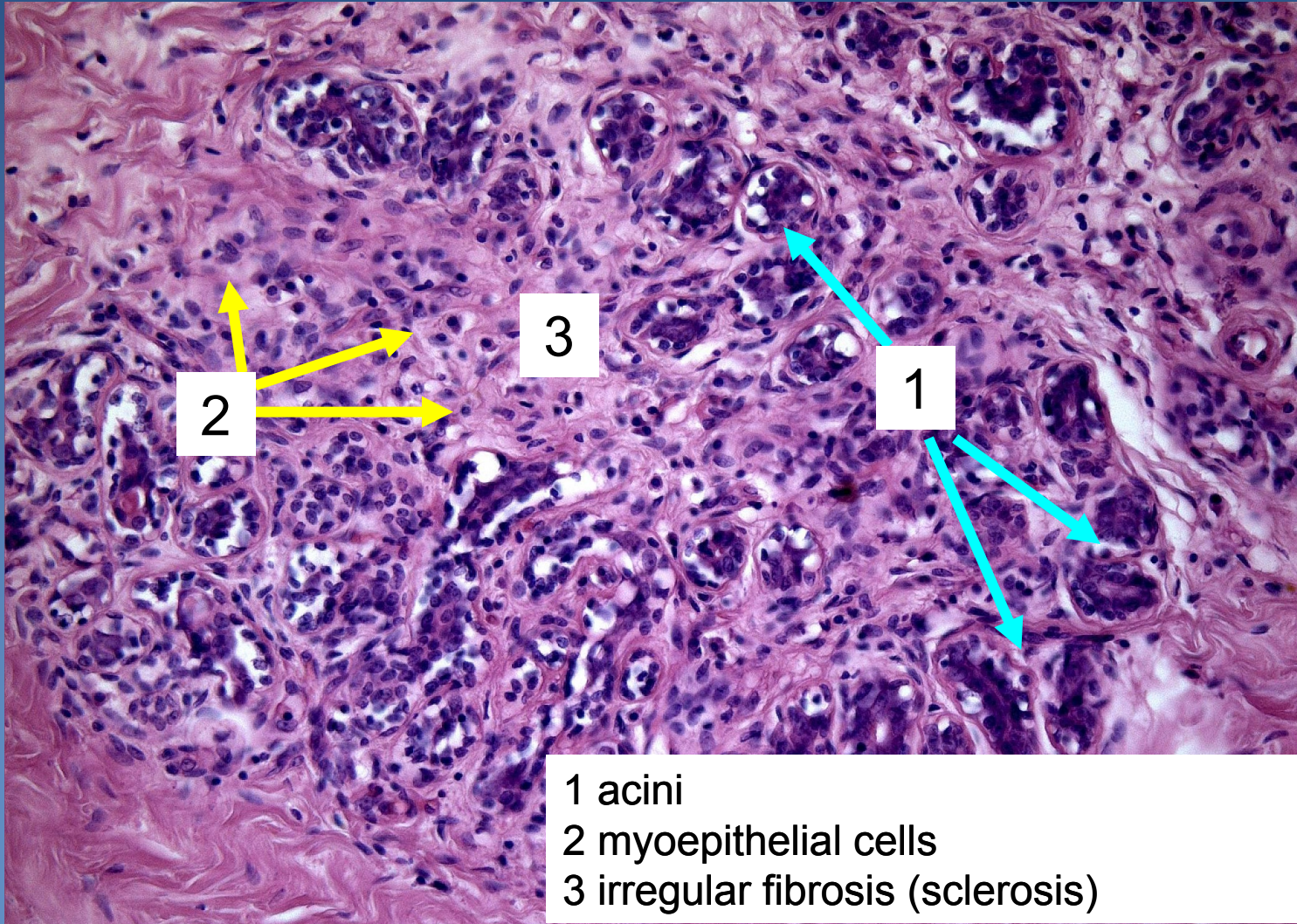
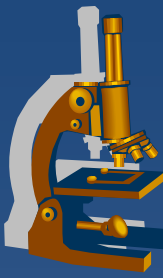
- x palpable „lumpy“ firmer tissue**
- x micro:**
 - ⇒ *extensive fibrosis*
 - ⇒ *+ cysts (apocrine metaplasia)*
 - ⇒ *+ adenosis (lobulocentric proliferative lesion = increased number of acini in a lobule, preserved lobular architectonics)*
 - ⇒ *commonly + ductal and/or lobular hyperplasia*
- x no increased risk of malignant transformation** (unless atypical epithelial hyperplasia present)

Fibrocystic change

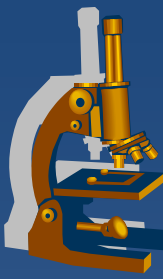


- 1 cystic dilated ducts, +/- luminal secretion
- 2 apocrine metaplasia
- 3 fibrosis

Sclerosing adenosis

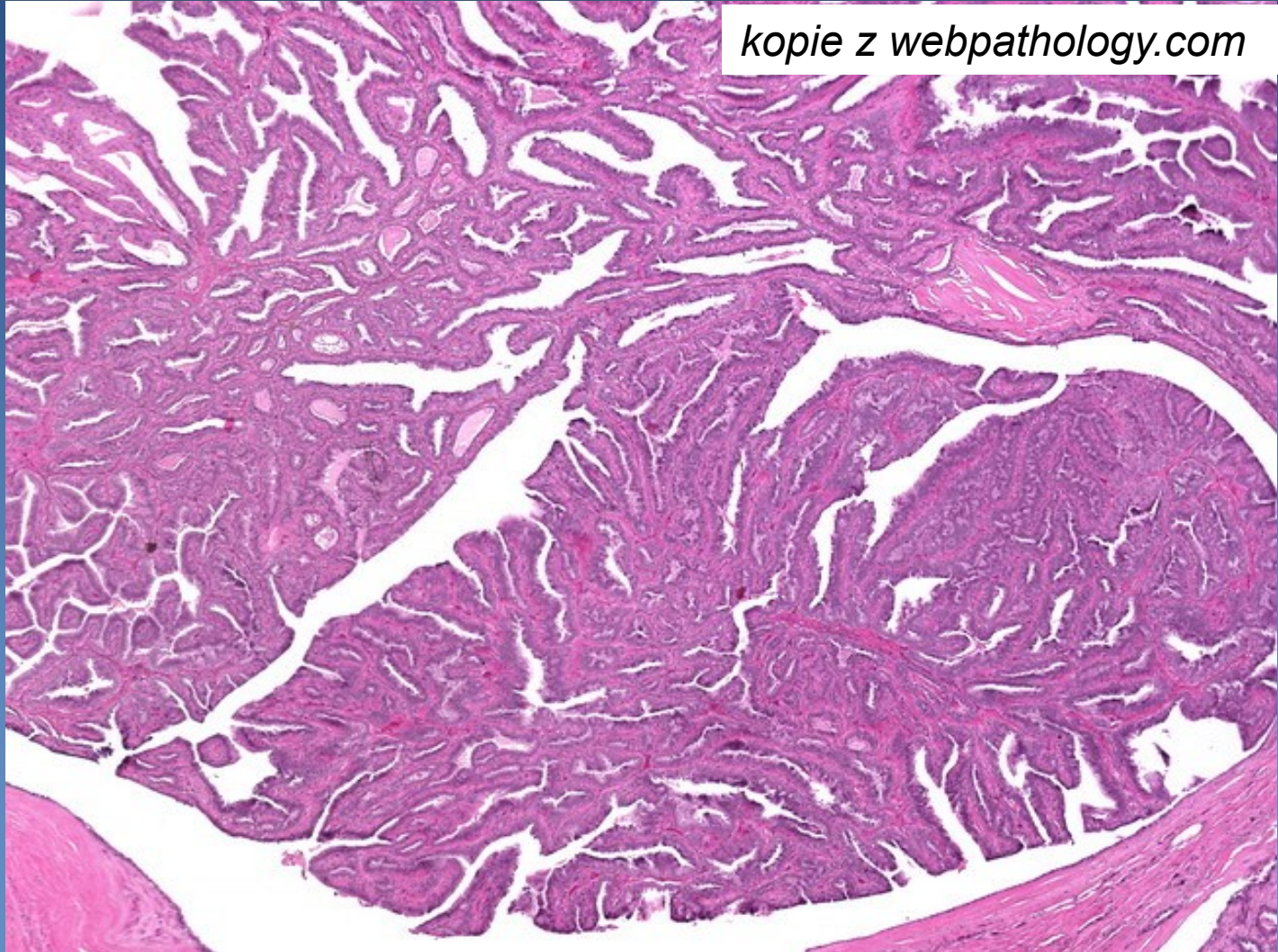
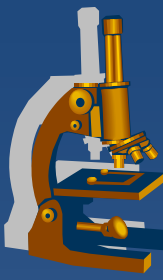


Benign epithelial tumors

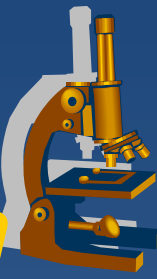


- x** rather uncommon
- x** important in diff. dg. of malignant tumors
- x** selected entities:
 - ⇒ *Intraductal, intracystic papilloma*
 - ⇒ *Lactational adenoma (?exaggerated focal response)*
 - ⇒ *Tubular adenoma*
 - ⇒ *Ductal adenoma*

Intraductal papilloma



Proliferative breast disease with atypia / in situ neoplasia



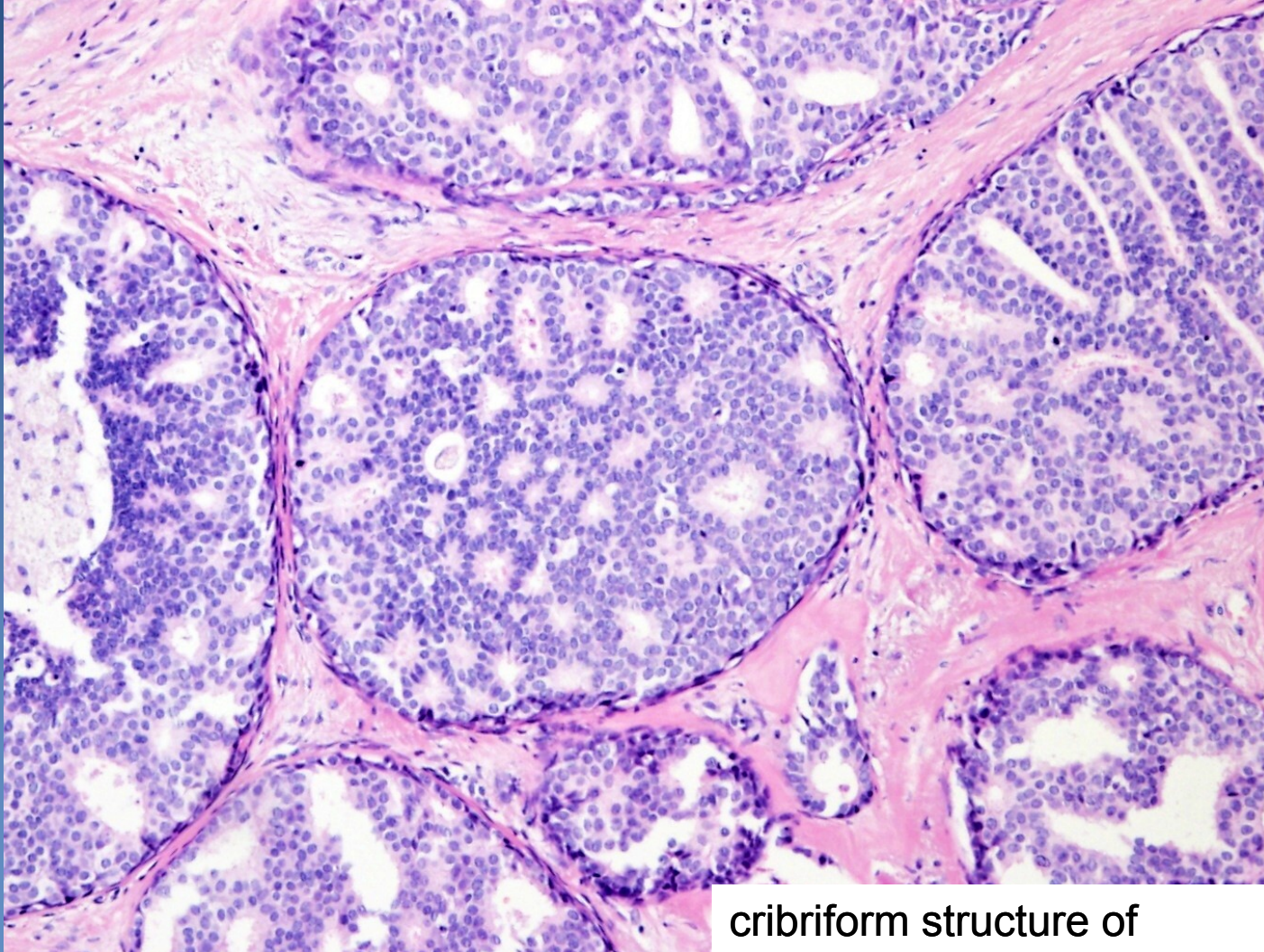
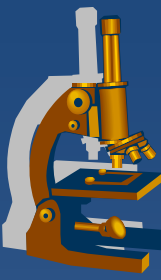
- x** relatively common
- x** potential progression into invasive carcinoma – precursor lesion
 - ⇒ ***Atypical ductal hyperplasia (ADH)***
 - ⇒ ***Atypical lobular hyperplasia (ALH)***
 - ⇒ ***Ductal carcinoma in situ (DCIS)***
 - non- high grade
 - high grade
 - ⇒ ***Lobular carcinoma in situ (LCIS)***

Proliferative epithelial lesions and in situ neoplasia



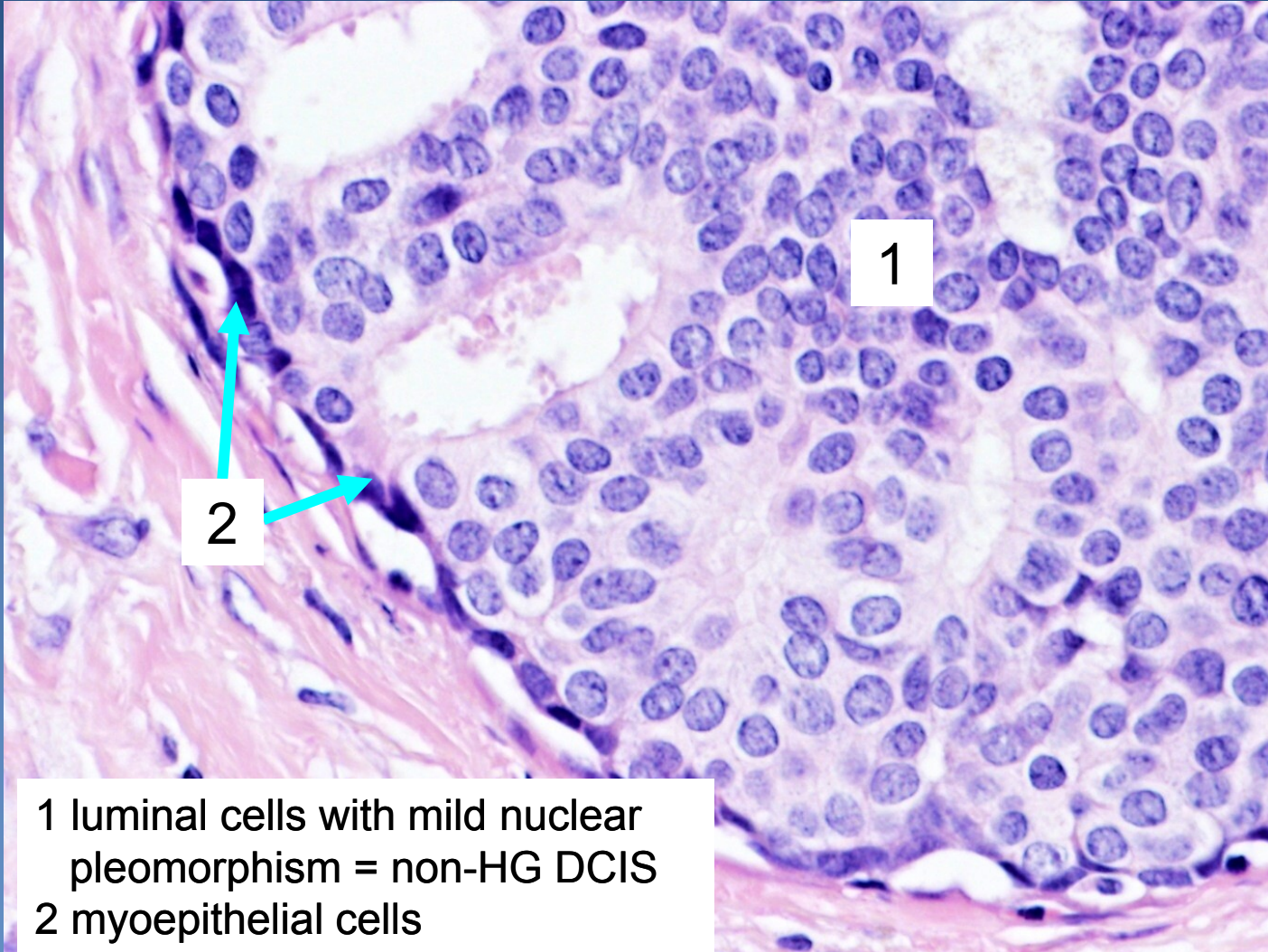
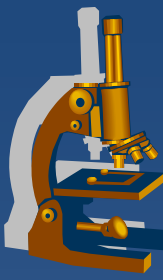
Diagnosis	Morphology
<ul style="list-style-type: none"> • Focal fibrosis • Cysts • Florid adenosis • Sclerosing adenosis 	<ul style="list-style-type: none"> • focal increase of TDLU stroma • dilated ducts • increased number of acini • increased number of acini + TDLU fibrosis
<ul style="list-style-type: none"> • Ductal hyperplasia • Lobular hyperplasia • Ductal papillomatosis • Fibroadenomatoid hyperplasia 	<ul style="list-style-type: none"> • ductal epithelium proliferation • acinar epithelium proliferation • epithelial proliferation in dilated ducts • ductal epithelial + TDLU stromal proliferation
<ul style="list-style-type: none"> • Atypical ductal hyperplasia • Atypická lobulární hyperplázie 	<ul style="list-style-type: none"> • ductal epithelium proliferation + atypias • acinar epithelium proliferation + atypias
<ul style="list-style-type: none"> • DCIS, non-high grade • LCIS 	<ul style="list-style-type: none"> • intraductal ca in situ with mild nuclear pleomorphism • lobular ca in situ
<ul style="list-style-type: none"> • DCIS, high grade 	<ul style="list-style-type: none"> • intraductal ca in situ with severe nuclear atypias

DCIS



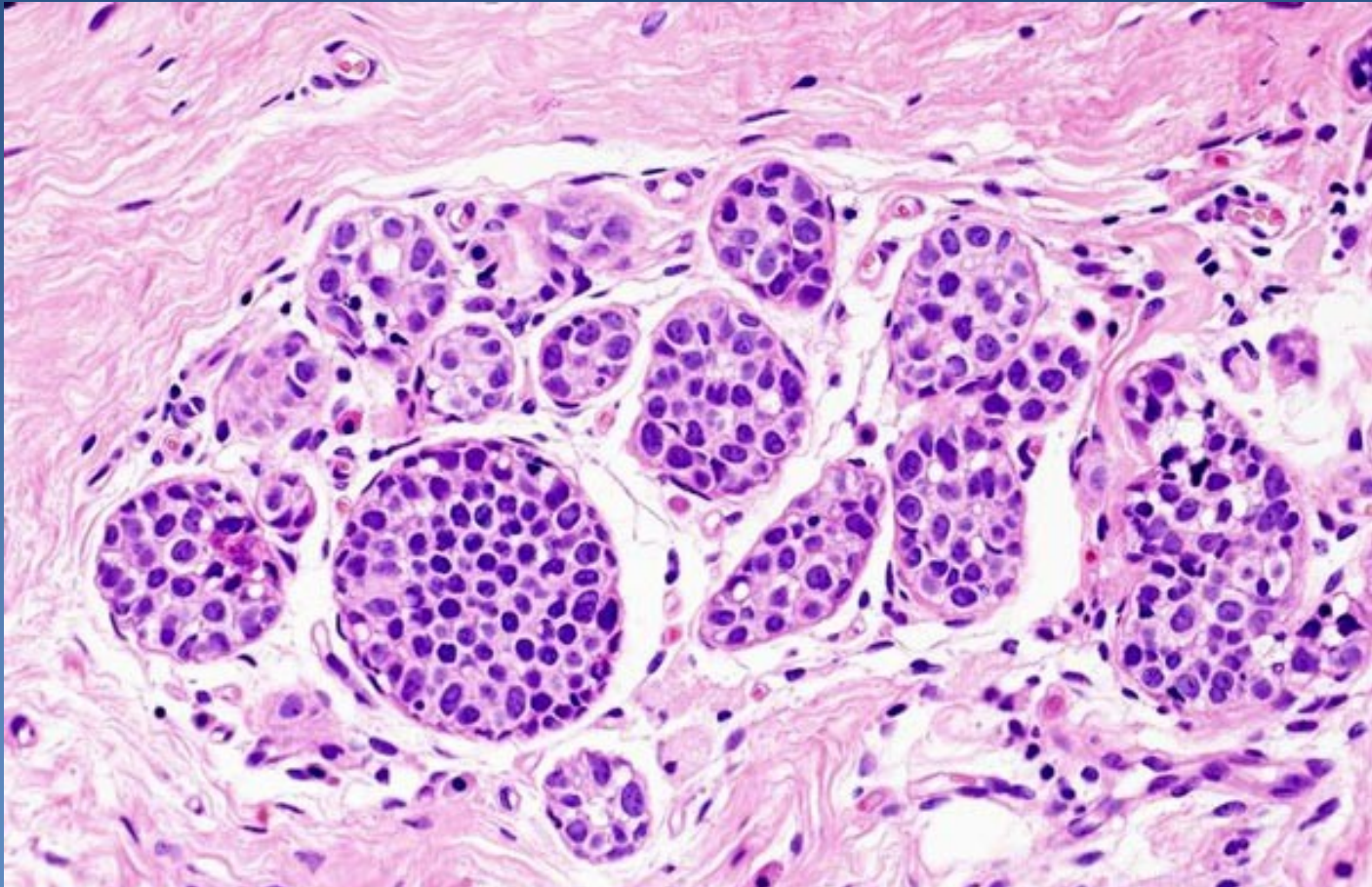
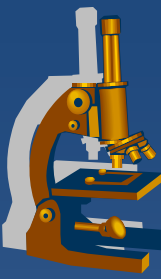
cribriform structure of
DCIS

DCIS



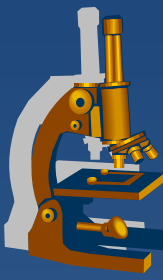
1 luminal cells with mild nuclear pleomorphism = non-HG DCIS
2 myoepithelial cells

LCIS



Expanded acini filled by mildly pleomorphic cells, intact basement membrane

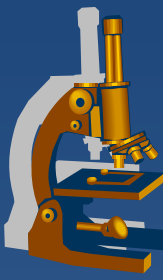
Malignant epithelial tumors



Breast carcinoma

- x commonest** malignancy in females in high-income countries
- x rising incidence**
- x falling mortality**
 - ⇒ *screening + better diagnostics*
 - ⇒ *known modifiable risk factors*
 - ⇒ *more effective therapy*
- x metastases**
 - ⇒ *lymphatic spread – regional LN (mostly axillary)*
 - ⇒ *hematogenous spread (bones, lung, liver, brain...)*

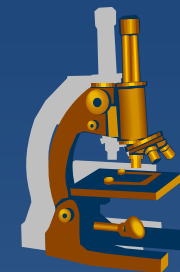
Malignant epithelial tumors



- x Sporadic carcinomas** ($\approx 95\%$)
 - \Rightarrow *accidental sequential mutations*
 - \Rightarrow *mostly perimenopausal/postmenopausal, old age (50-75)*

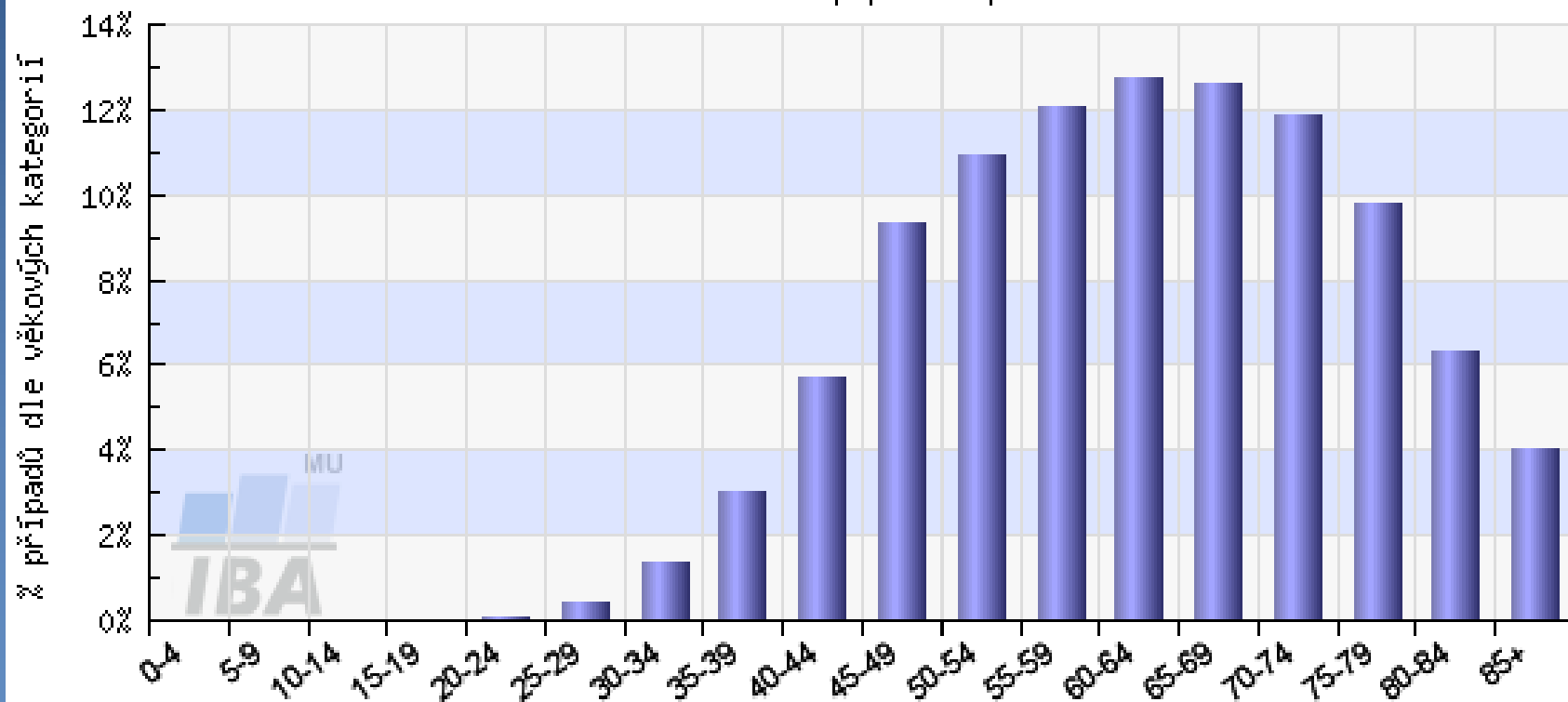
- x Familial carcinomas** ($\approx 5\%$)
 - \Rightarrow *hereditary mutations in some TSG (BRCA1, BRCA2...)*
 - \Rightarrow *typical in young females (after age of 20)*
 - \Rightarrow *possible multicentric, bilateral \rightarrow prophylactic mastectomy*
 - \Rightarrow *\uparrow risk of ovarian carcinomas*

Age incidence



C50 - ZN prsu - Incidence, ženy

věková struktura populace pacientů

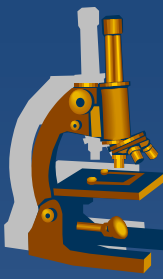


Analyzovaná data: N=142275

<http://www.svod.cz>

Zdroj dat: ÚZIS ČR

WHO classification of carcinomas



✘ Invasive ca, no special type (NST) = ductal ca, NOS

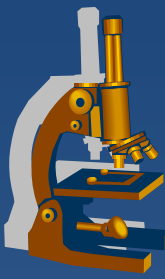
✘ Invasive lobular carcinoma

- ✘ Tubular ca
- ✘ Invasive cribriform ca
- ✘ Medullary ca
- ✘ Mucin producing ca
- ✘ Neuroendocrine tumors
- ✘ Invasive papillary ca
- ✘ Invasive micropapillary ca

- ✘ Apocrine ca
- ✘ Metaplastic ca
- ✘ Lipid-rich ca
- ✘ Secretory ca
- ✘ Onkocytic ca
- ✘ Adenoid-cystic carcinoma
- ✘ Acinic cell ca
- ✘ Glycogen-rich clear cell ca
- ✘ Sebaceous ca
- ✘ Inflammatory ca

- ✘ Bilateral carcinoma

Invasive ductal carcinoma



✘ most common

✘ gross:

⇒ *firm lesion, irregular border*

✘ micro:

⇒ *cohesive (E-cadherin+) tumor cells*

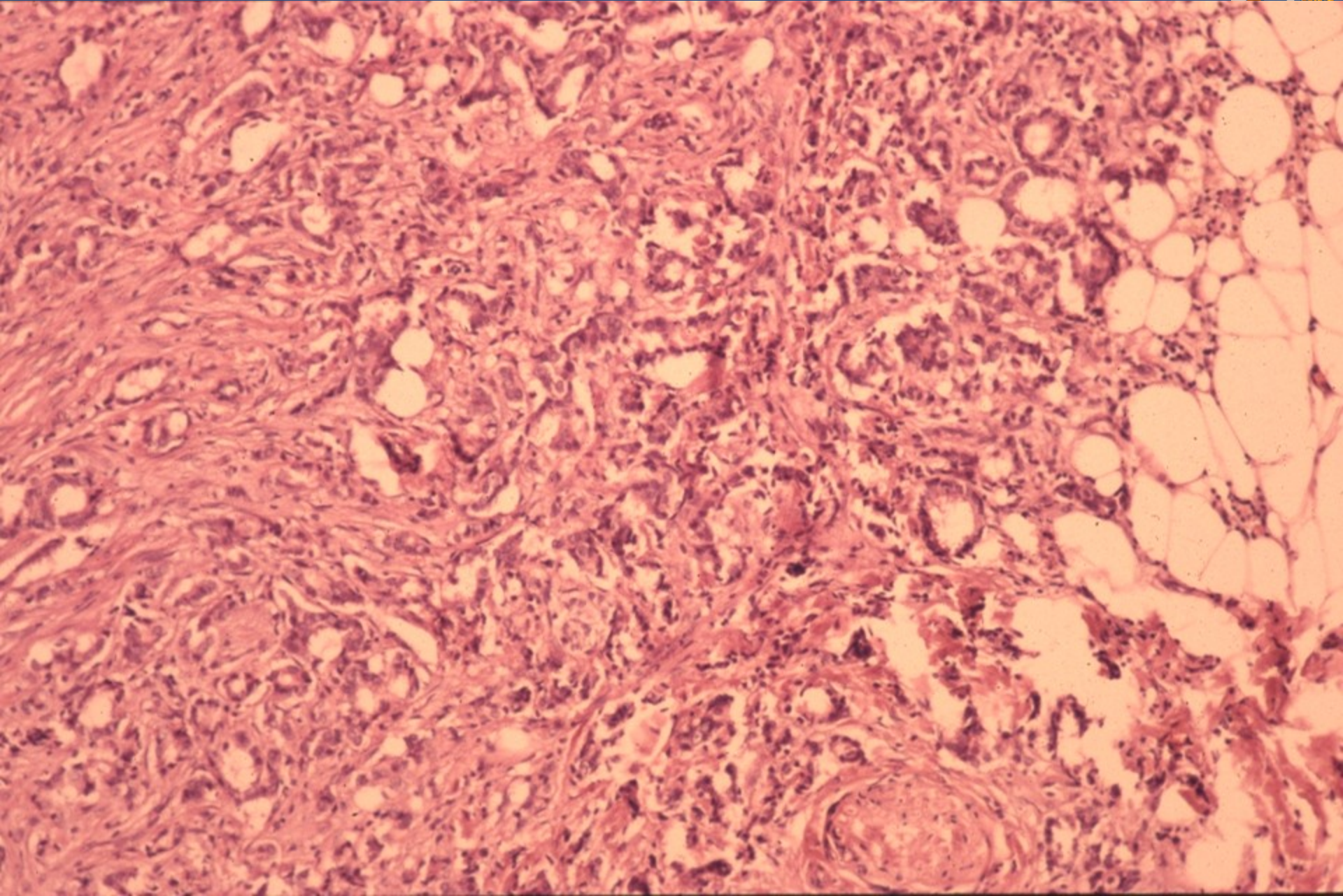
- tubules, trabeculae, solid clusters
- variable grade of nuclear pleomorphism, mitotic activity (gr. I-III)

⇒ *loss of outer myoepithelial cell layer (p63-, SMA-)*

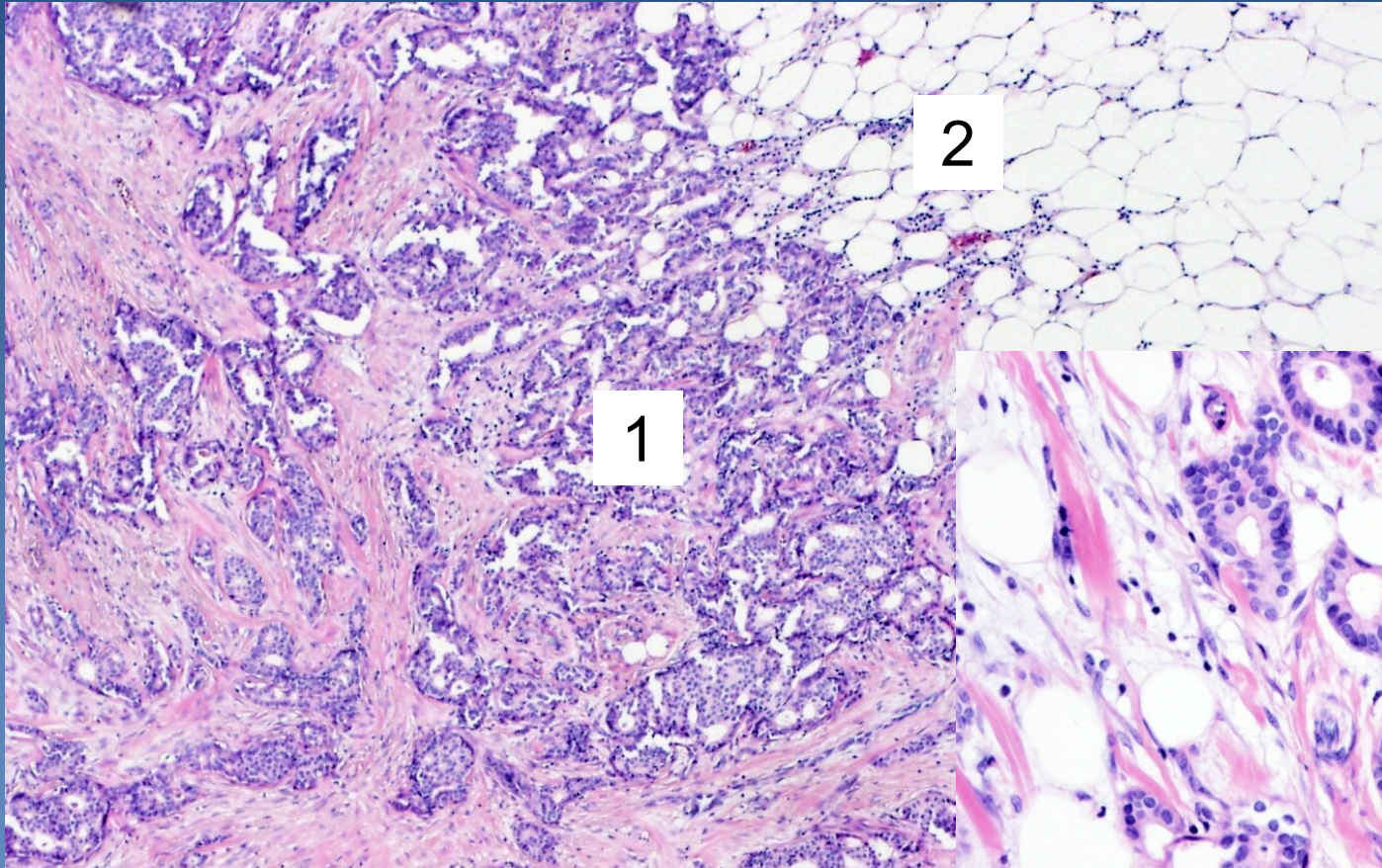
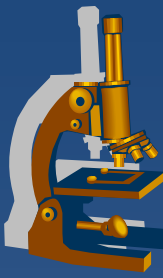
⇒ *dense fibrotic stroma, desmoplasia*

⇒ *infiltrative growth, commonly adjacent DCIS*

Invasive ductal carcinoma

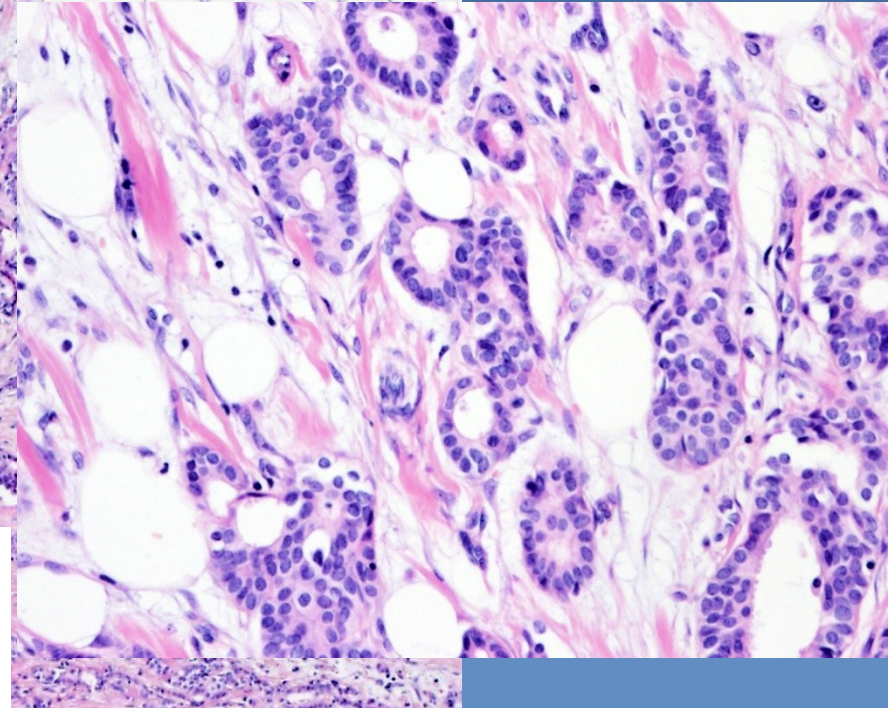


Invasive ductal carcinoma



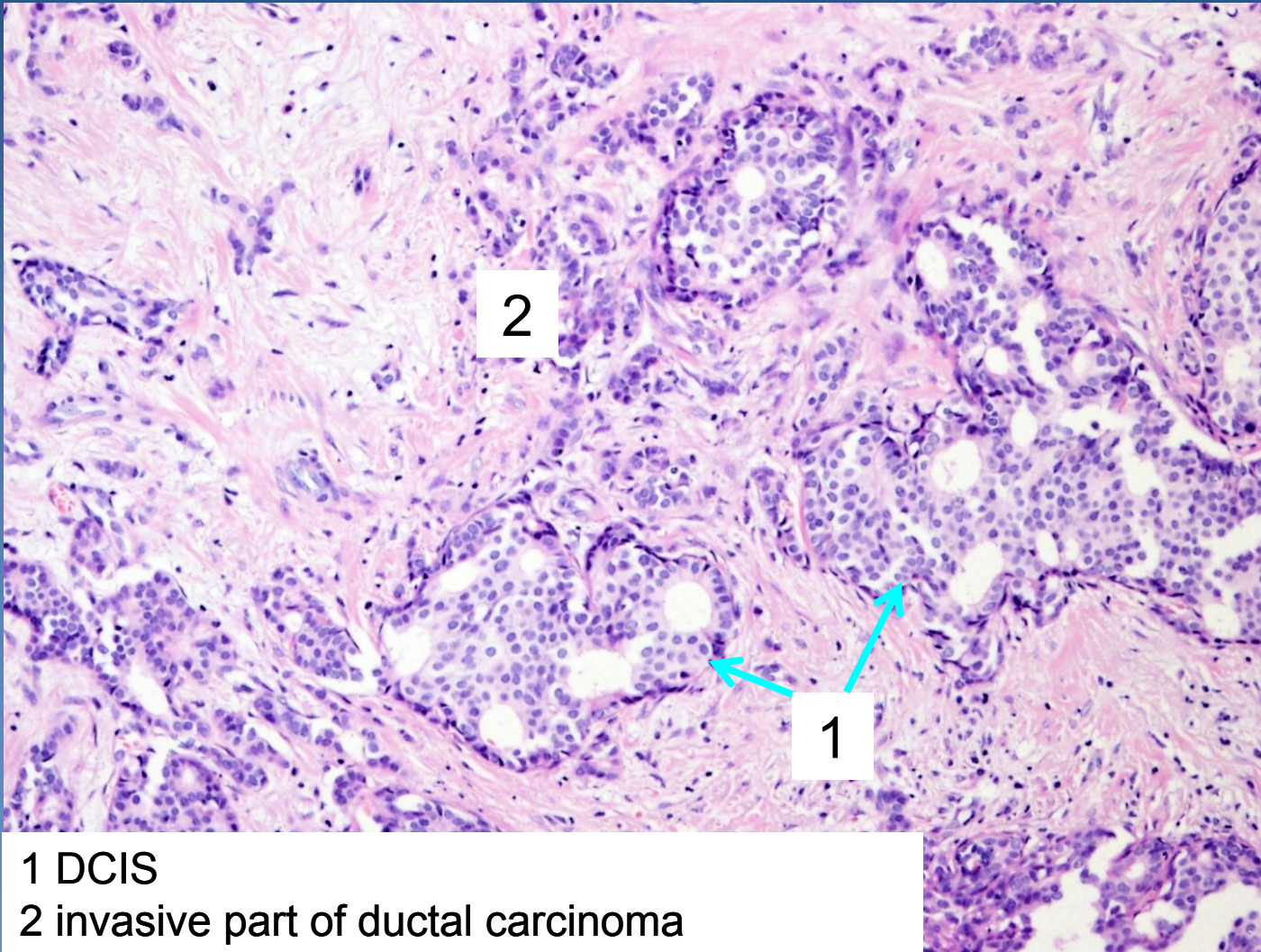
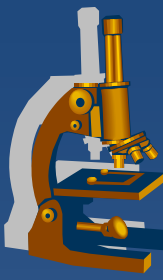
2

1



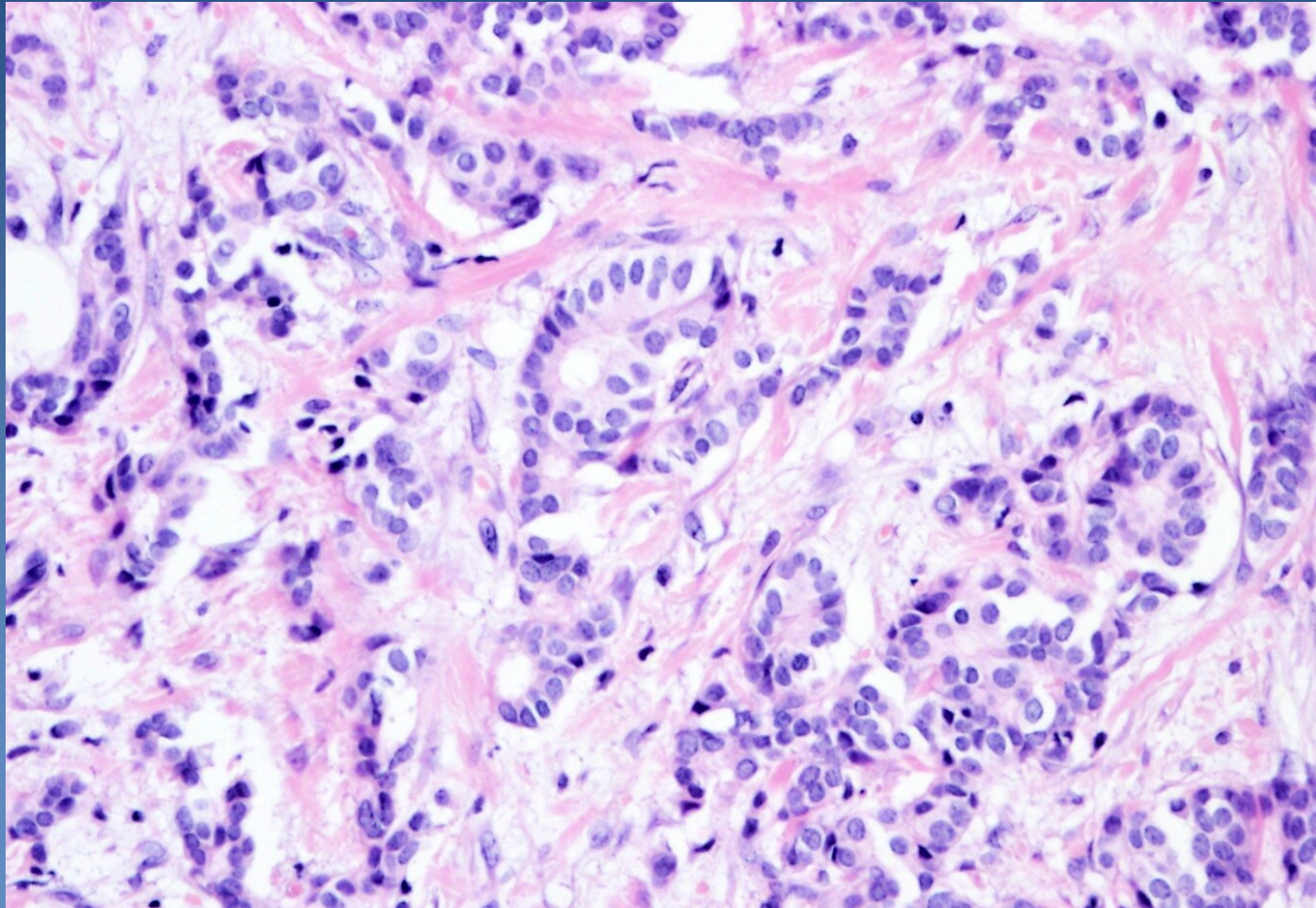
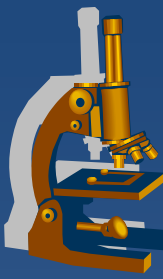
1 kohezivní nádorový infiltrát s ojedinělými tubuly
2 infiltrace tukové tkáně

Invasive ductal carcinoma



1 DCIS
2 invasive part of ductal carcinoma

Invasive ductal carcinoma



Tumorous infiltrate with irregular small tubules

Invasive lobular carcinoma



✘ častěji roste multicentricky

✘ mikro:

⇒ *nádorové buňky ztratily soudržnost (E-cadherin-)*

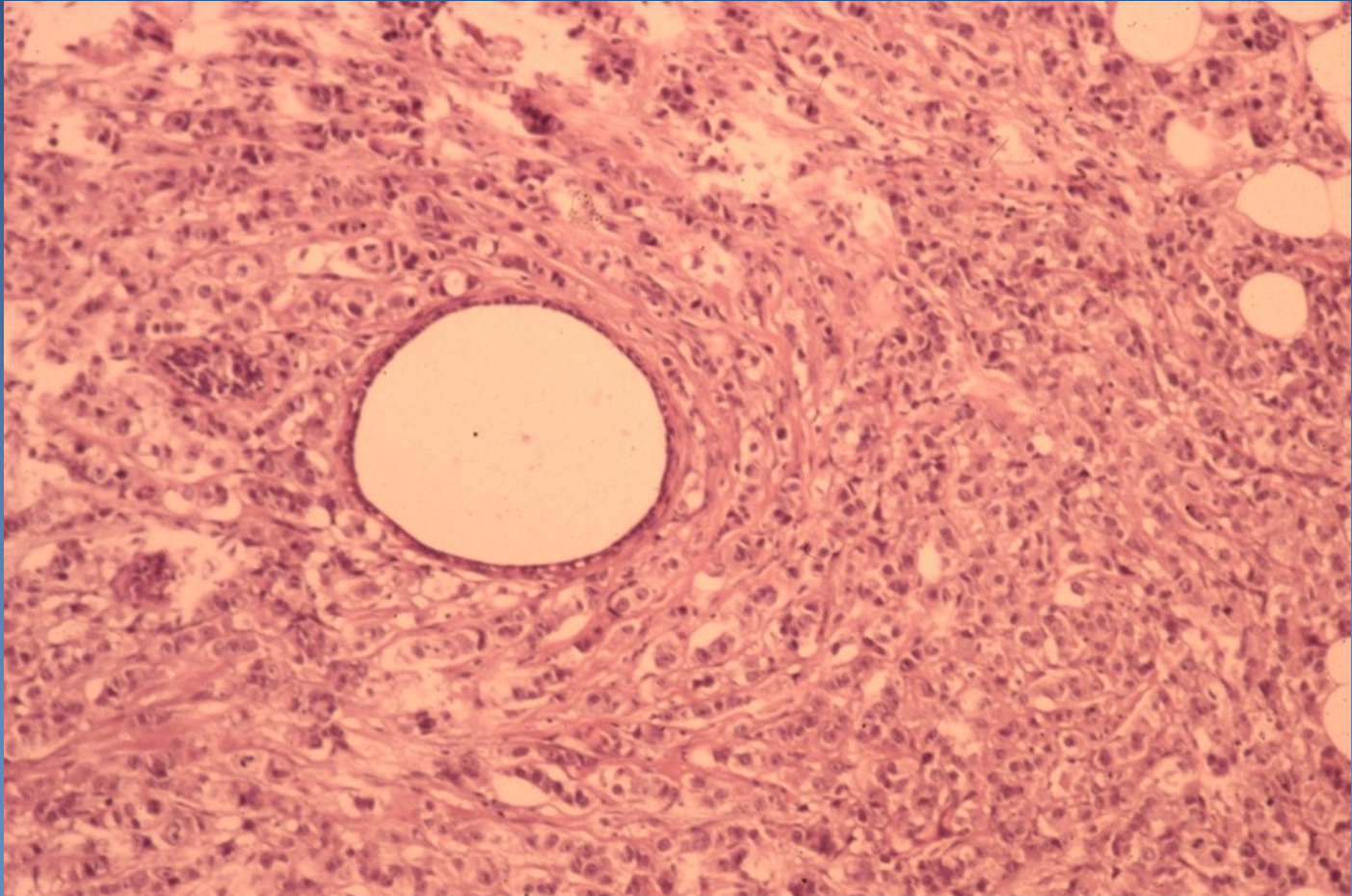
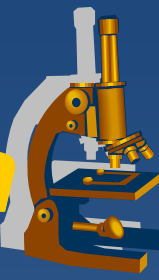
- řadí se do různě dlouhých pruhů – „husí pochod“, „indiánské péro“
- pruhy nádorových buněk jsou uspořádány naznačeně koncentricky kolem dilatovaného vývodu
- buňky mají jádra se světlejším chromatinem

⇒ *chybí myoepiteliální vrstva (SMA-)*

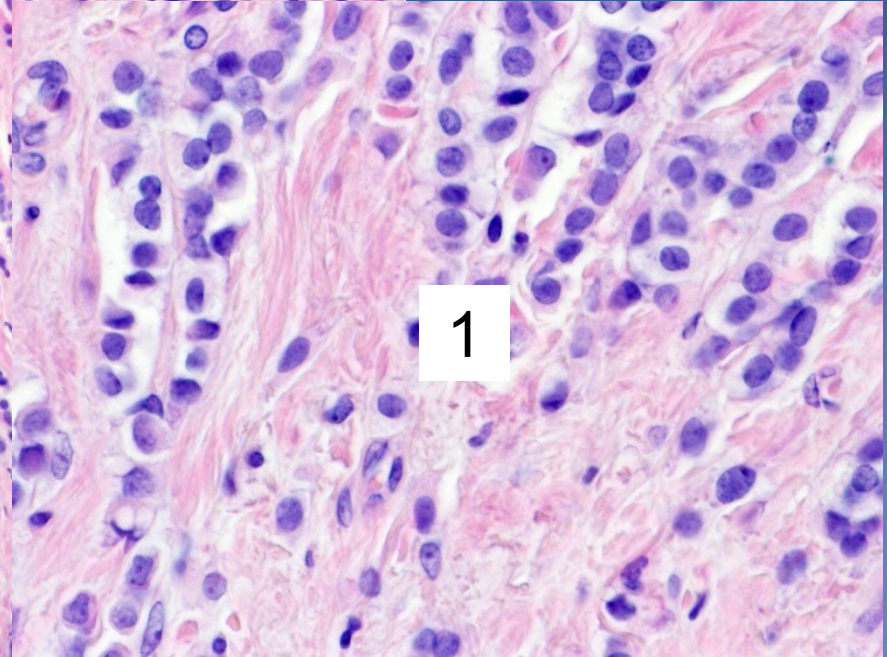
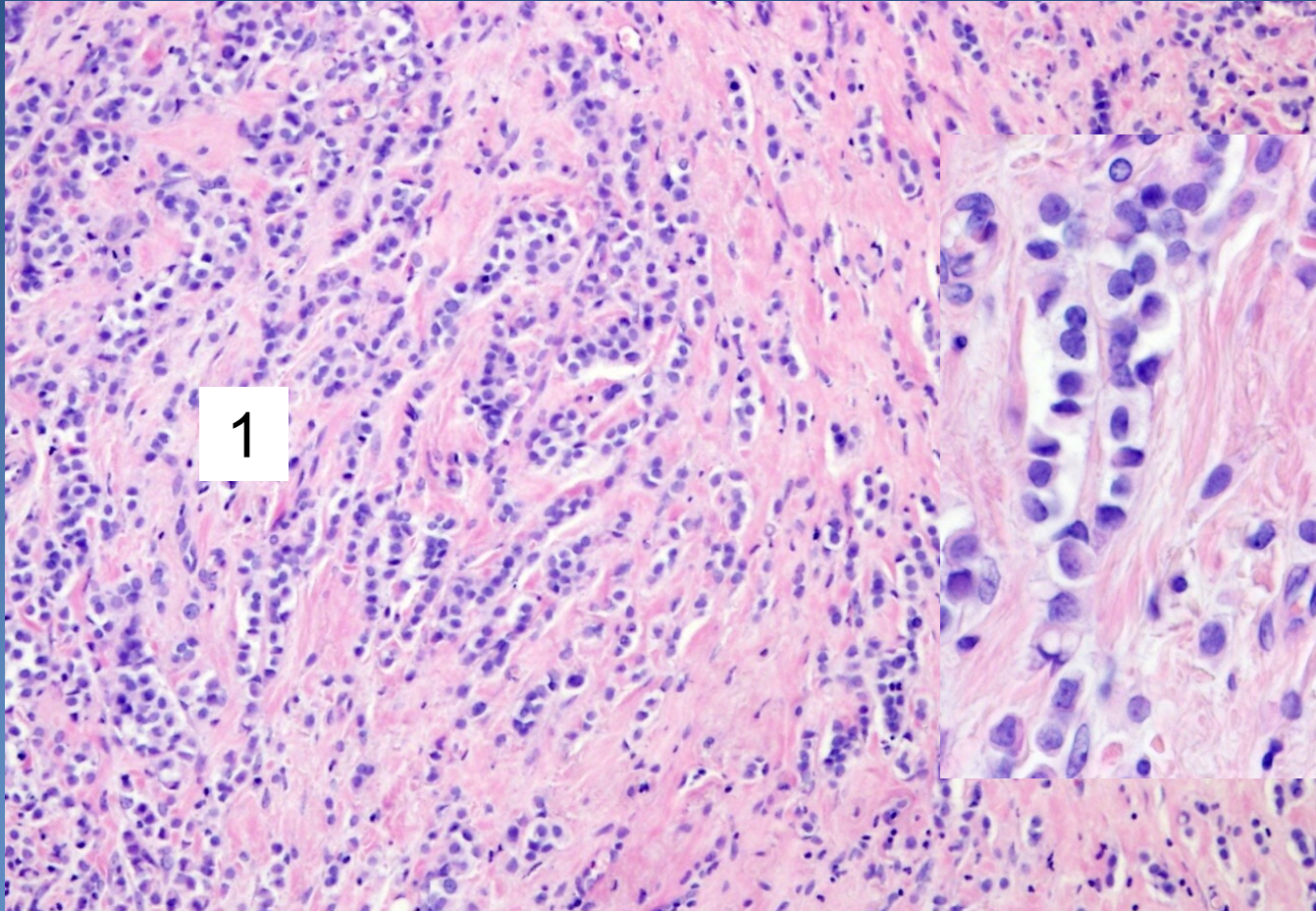
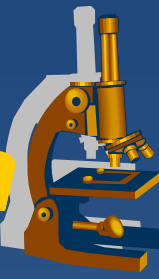
⇒ *stroma denzní, vazivové*

⇒ *infiltrativní růst, často v blízkosti LCIS*

Invasive lobular carcinoma

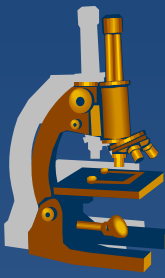


Invasive lobular carcinoma



1 dyscohesive tumor cells in single file (Indian file)

Myoepithelial lesions



- ✗ myoepithelial cells proliferation, (sm. + luminal cells)
- ✗ uncommon
- ✗ classification:
 - ⇒ *Adenomyoepithelial hyperplasia*
 - ⇒ *Adenomyoepithelioma*
 - ⇒ *Myoepithelioma*
 - ⇒ *Myoepithelial carcinoma*

Mesenchymal tumors



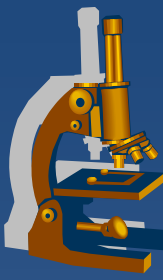
x rare in the breast

x i.e.:

⇒ *haemangiomas, leiomyoma, lipoma, schwannoma*

⇒ *angiosarcoma, leiomyosarcoma, liposarcoma*

Fibroepithelial (mixed) tumors



- x** very common

- x** **Fibroadenoma (FA)**

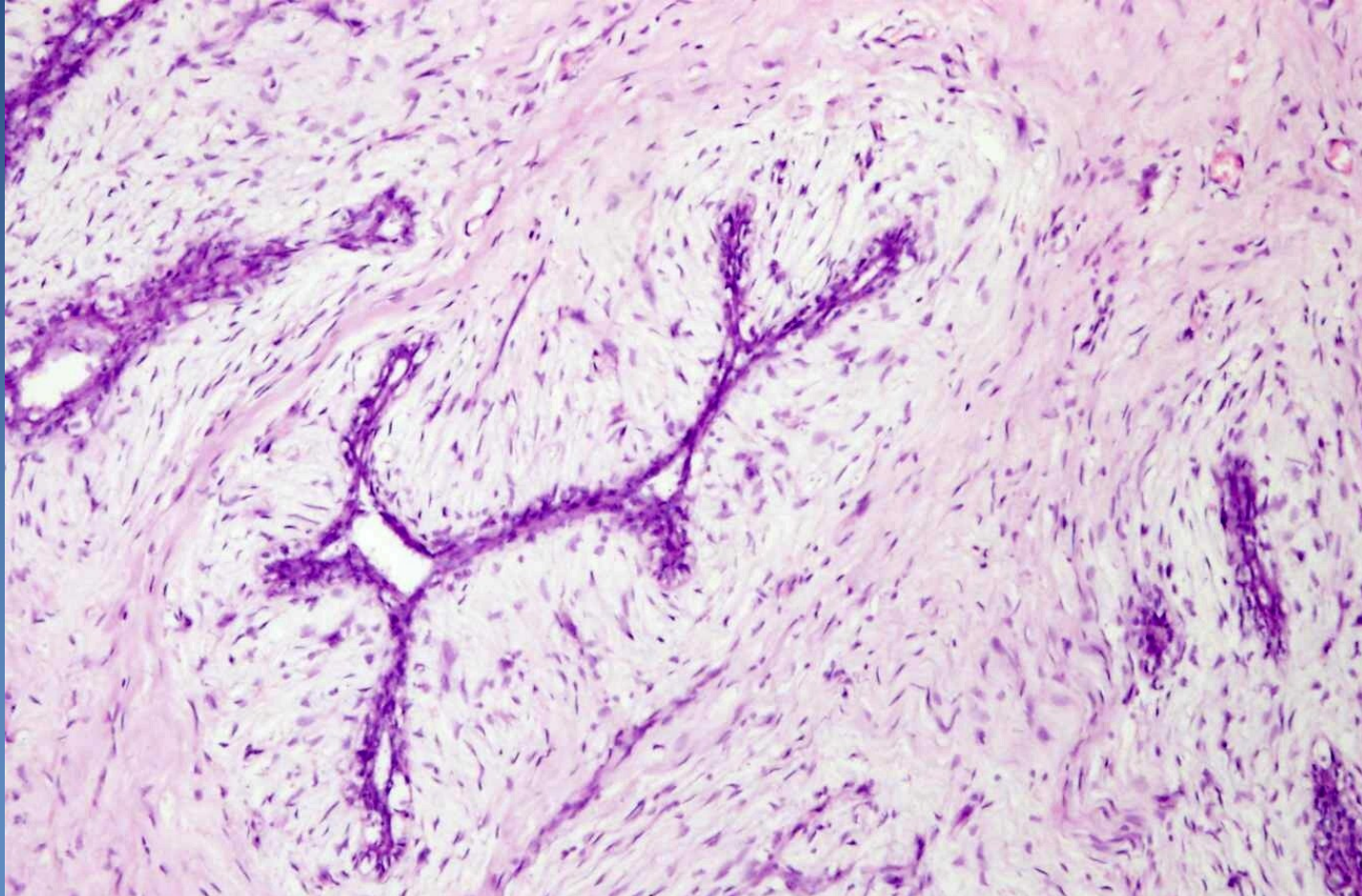
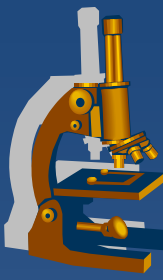
 - ⇒ *most common breast tumor in young females*

 - ⇒ *benign, circumscribed, mobile, rubbery*

 - ⇒ *proliferating ducts + increased amount of stroma (edematous or hyalinised)*

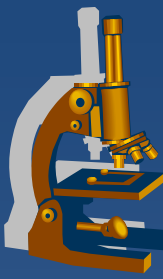
 - ⇒ *pericanalicular, intracanalicular growth*

Fibroadenoma



Slit-like newly formed ducts compressed by edematous stroma

Fibroepithelial (mixed) tumors



x Phyllodes tumor

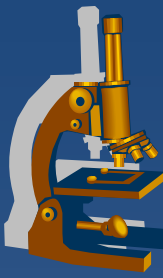
⇒ *rare (<1% of all breast tumors)*

⇒ *gross – leaflike structure and cysts (cystosarcoma phyllodes)*

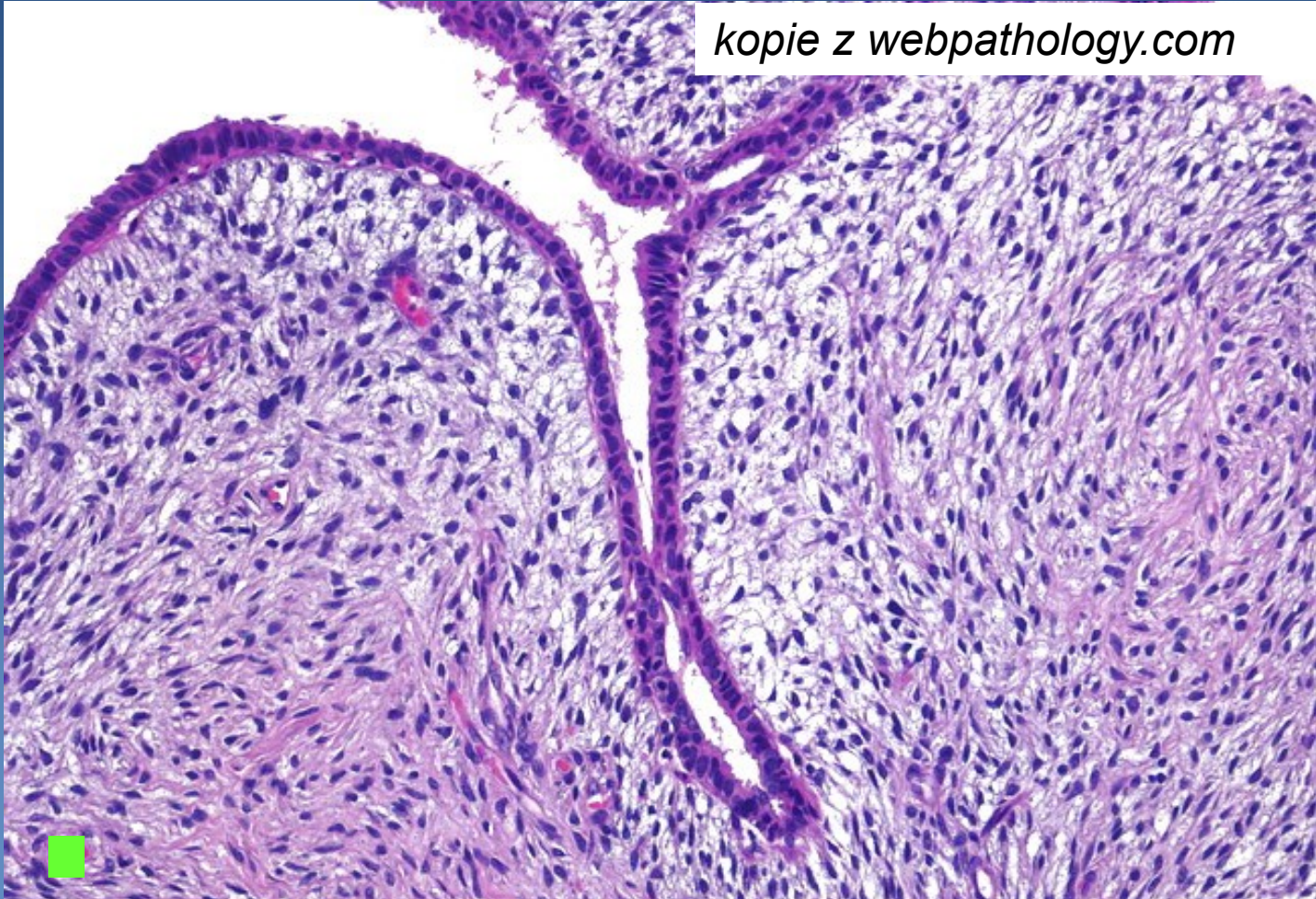
⇒ *micro similar to FA, increased stromal cellularity*

- *stromal component benign / with atypias / malignant (sarcoma)*
- *biologic behaviour:*
 - *benign*
 - *broderline*
 - *malignant*

Phyllodes tumor



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Hypercellular stroma compressing ducts

Male breast pathology



x gynecomastia

⇒ *most common*

- up to 30% adult males, commonly bilateral

⇒ *enlarged subareolar gland*

⇒ *hyperthyroidism, liver cirrhosis, CHRI, chronic respiratory failura, hypogonadism, hormone therapy.*

x carcinoma

⇒ *rare, hereditary risk possible (BRCA2)*

⇒ *worse general prognosis (usually late dg.)*