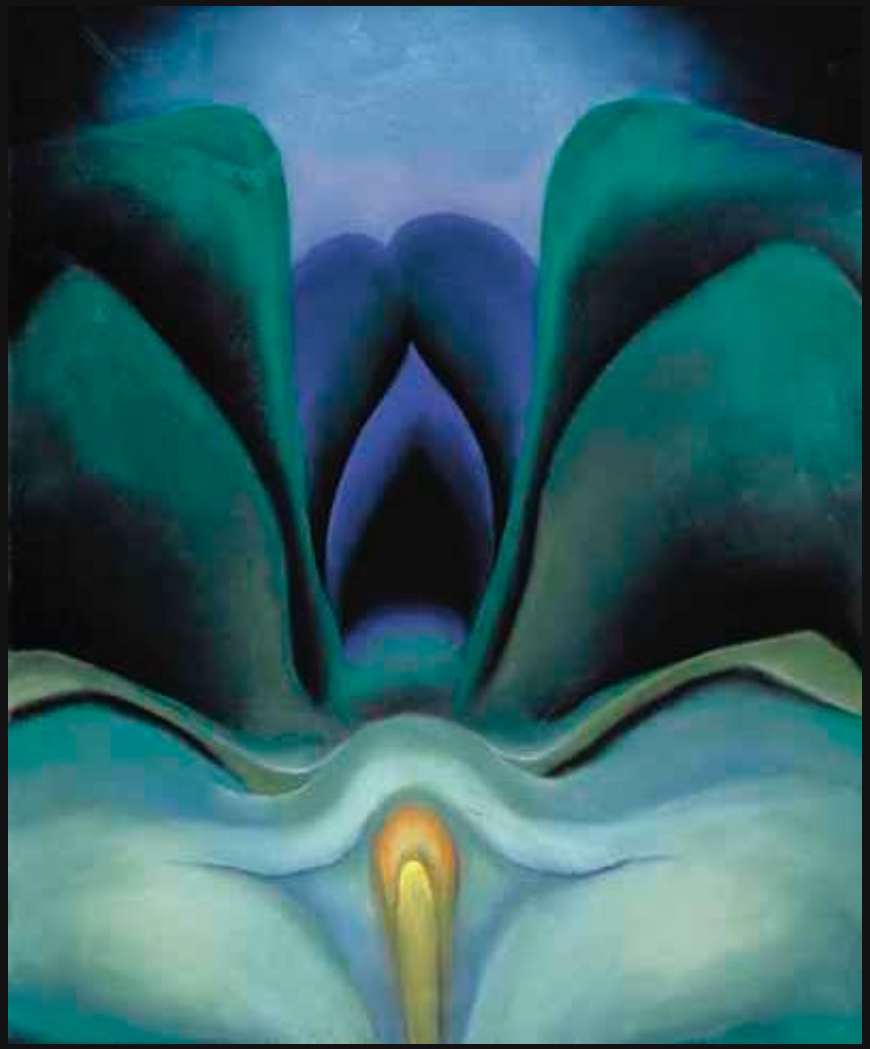


Female Reproductive System

Kristine Krafts, M.D.

Female Reproductive Learning Objectives

1. Explain what cervical dysplasia is and why it matters. Describe the incidence, peak age, cause, and most important prognostic factor for cervical carcinoma.
2. Describe what endometriosis is, how it presents, and how it affects fertility.
3. Explain what endometrial hyperplasia is and how it is related to endometrial carcinoma.
4. Describe the clinical features, risk factors, histologic features, and prognosis of leiomyoma, leiomyosarcoma, and endometrial carcinoma.

More Female Reproductive Learning Objectives

5. Compare and contrast the general incidence and mortality rate of ovarian vs. breast cancer (don't memorize numbers though).
6. Describe the typical age, risk factors, symptoms, and prognosis of ovarian carcinoma. What type of carcinoma accounts for most cases?
7. Describe why and how breast lumps are evaluated, and know in general how likely a lump is to be cancerous.

Yet More Female Repro Learning Objectives

8. Describe the incidence, peak age, risk factors, clinical features, and histology of fibroadenoma.
9. Describe the clinical presentation and risk factors for breast cancer.
10. Describe how prognosis is determined for patients with breast cancer. Explain what the T, N, and M stand for in the TNM staging system, and explain how they are used to determine the stage and relative prognosis of breast cancer (but don't memorize specific numbers from slide 58!).

Female Reproductive System Outline

- Cervix
- Uterus
- Ovaries
- Breast

Female Reproductive System Outline

- Cervix
  - Cervical carcinoma

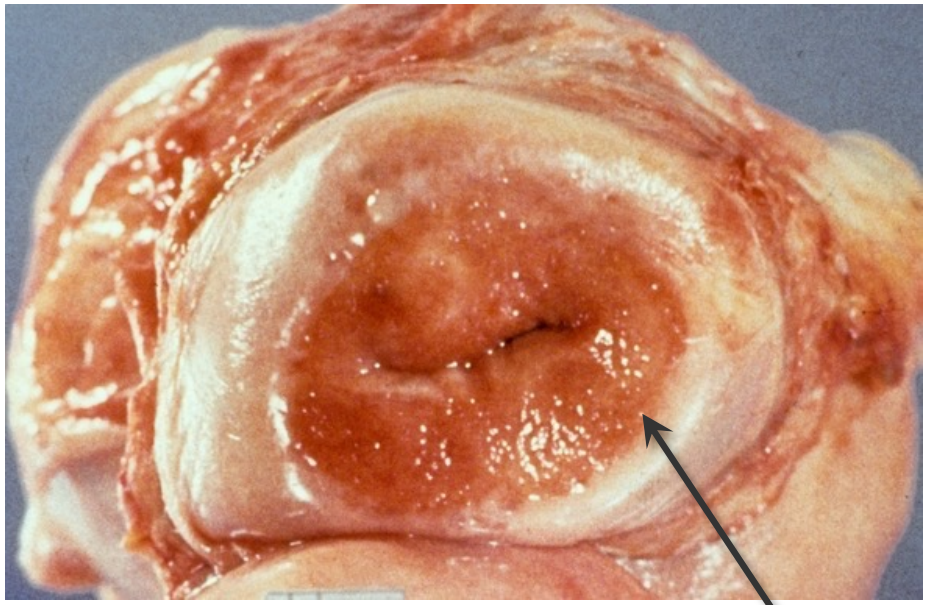
Cervical Carcinoma

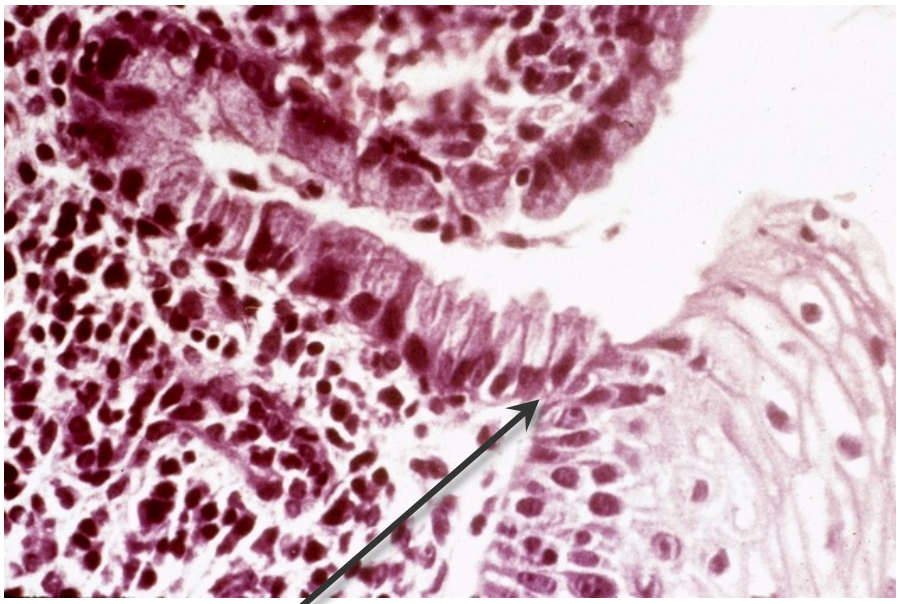
- Most are squamous cell carcinomas; a few are adenocarcinomas
- Caused by high-risk HPV (mostly 16, 18)
- Low-risk HPV (6, 11) causes condylomas
- Preceded by dysplastic epithelial changes
- Pap smears catch most cases before they become invasive

Squamous Intraepithelial Lesion (SIL)

- Used to call the dysplastic precursor lesions "cervical intraepithelial neoplasia" (CIN)
- Current term is "SIL"
- Low-grade SIL (LSIL): mild dysplasia
- High-grade SIL (HSIL): mod-severe dysplasia
- LSIL usually reverts to normal, but HSIL usually progresses to carcinoma

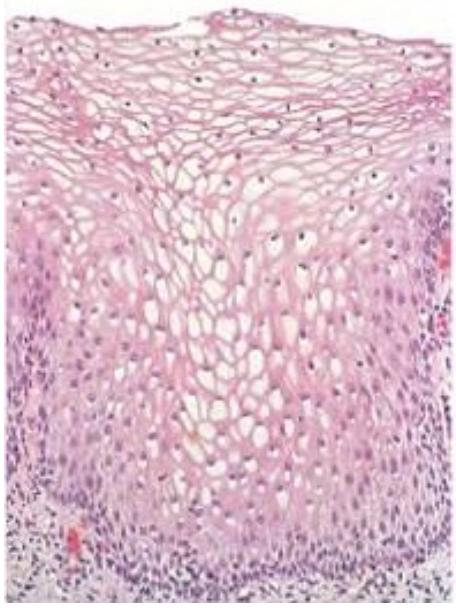
Cervical carcinoma usually arises in the transformation zone

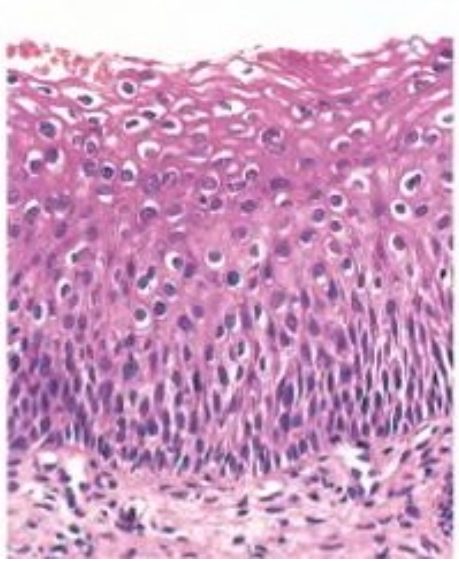


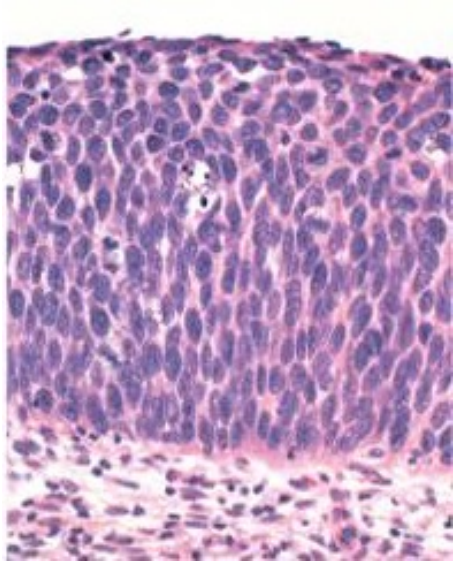


Transformation zone

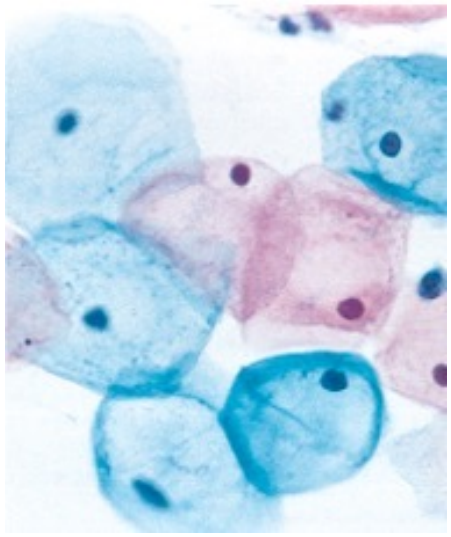
Tissue biopsy

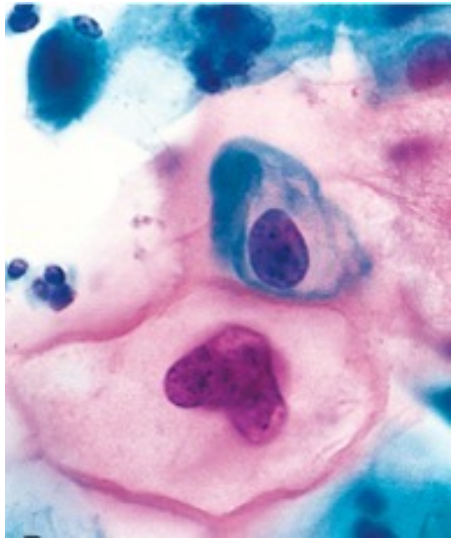


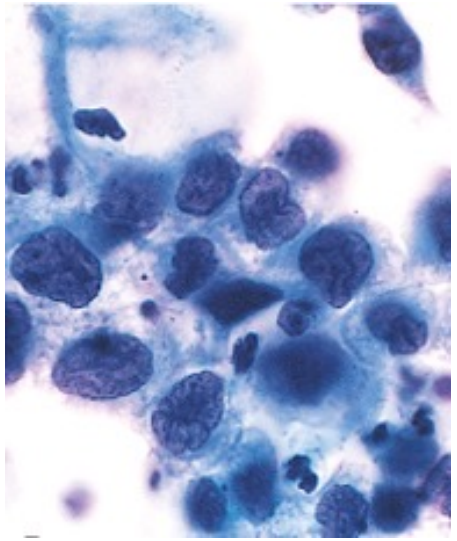




Pap smear



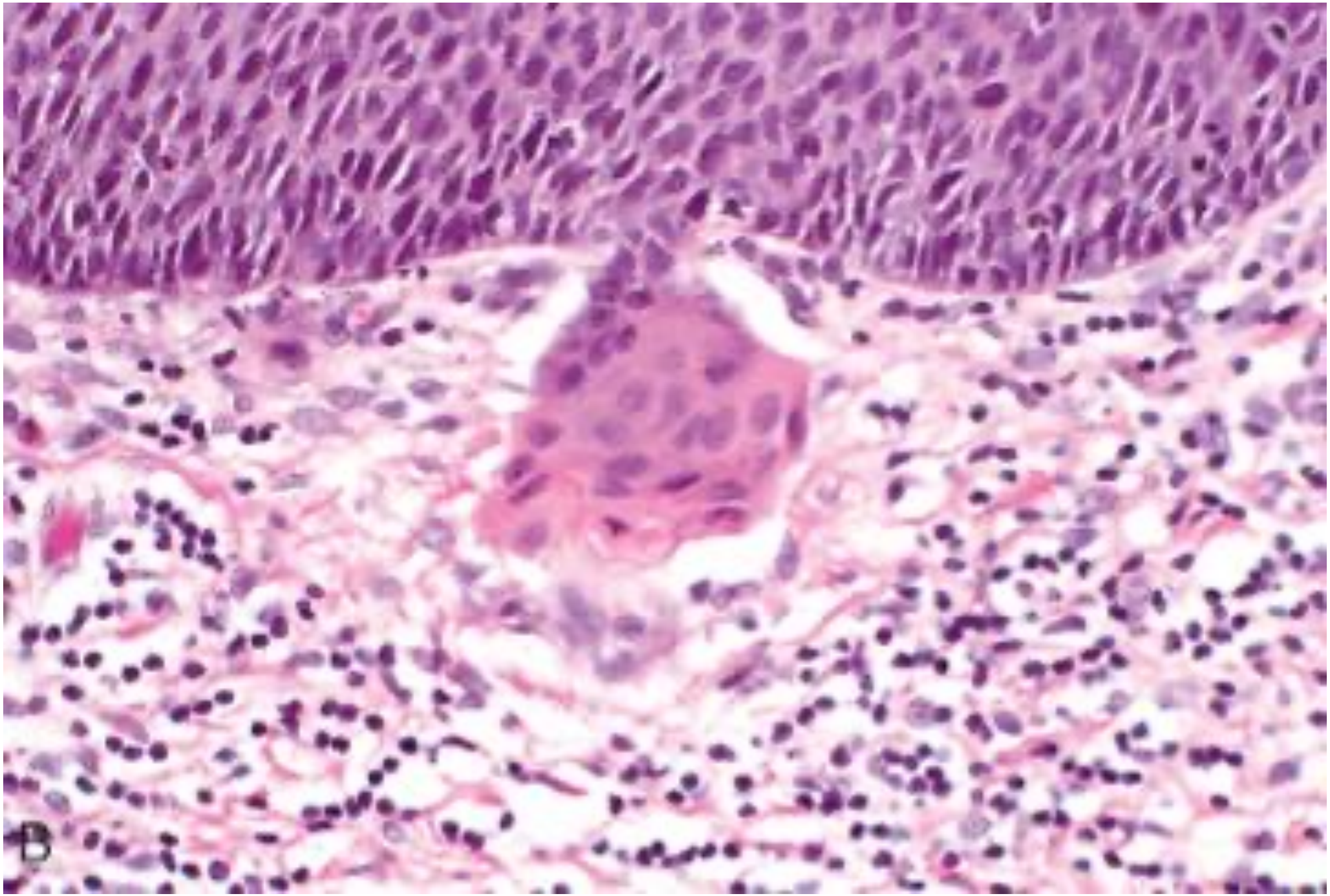




Normal

LSIL

HSIL



Invasive cervical carcinoma

Invasive Cervical Carcinoma

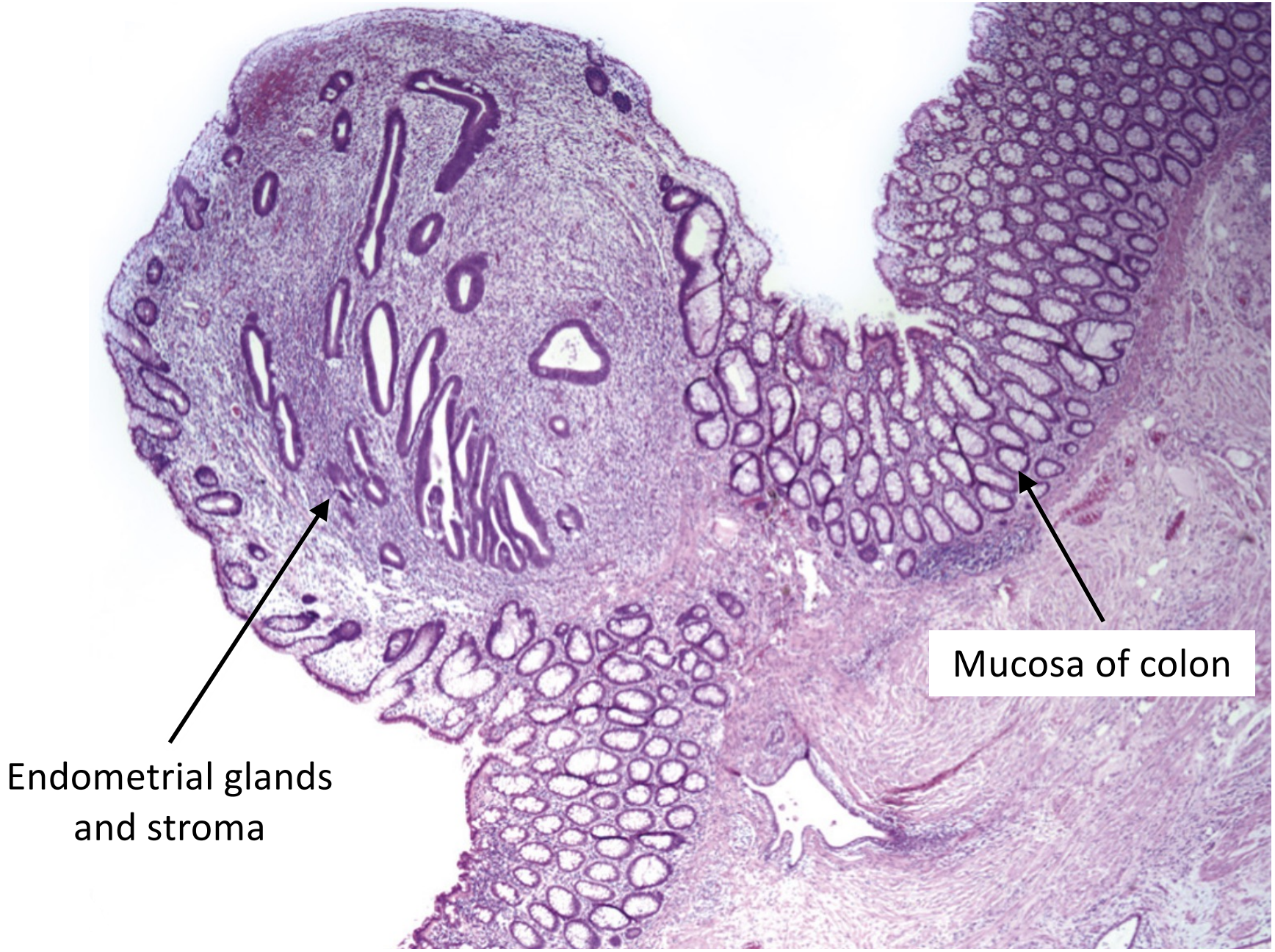
- Peak age: 45 (10-15 years after SIL develops)
- Spreads slowly
- Staging is super important for prognosis
  - Localized disease: 90% 5-year survival
  - Regional mets: 50% 5-year survival
  - Distant mets: 15% 5-year survival

Female Reproductive System Outline

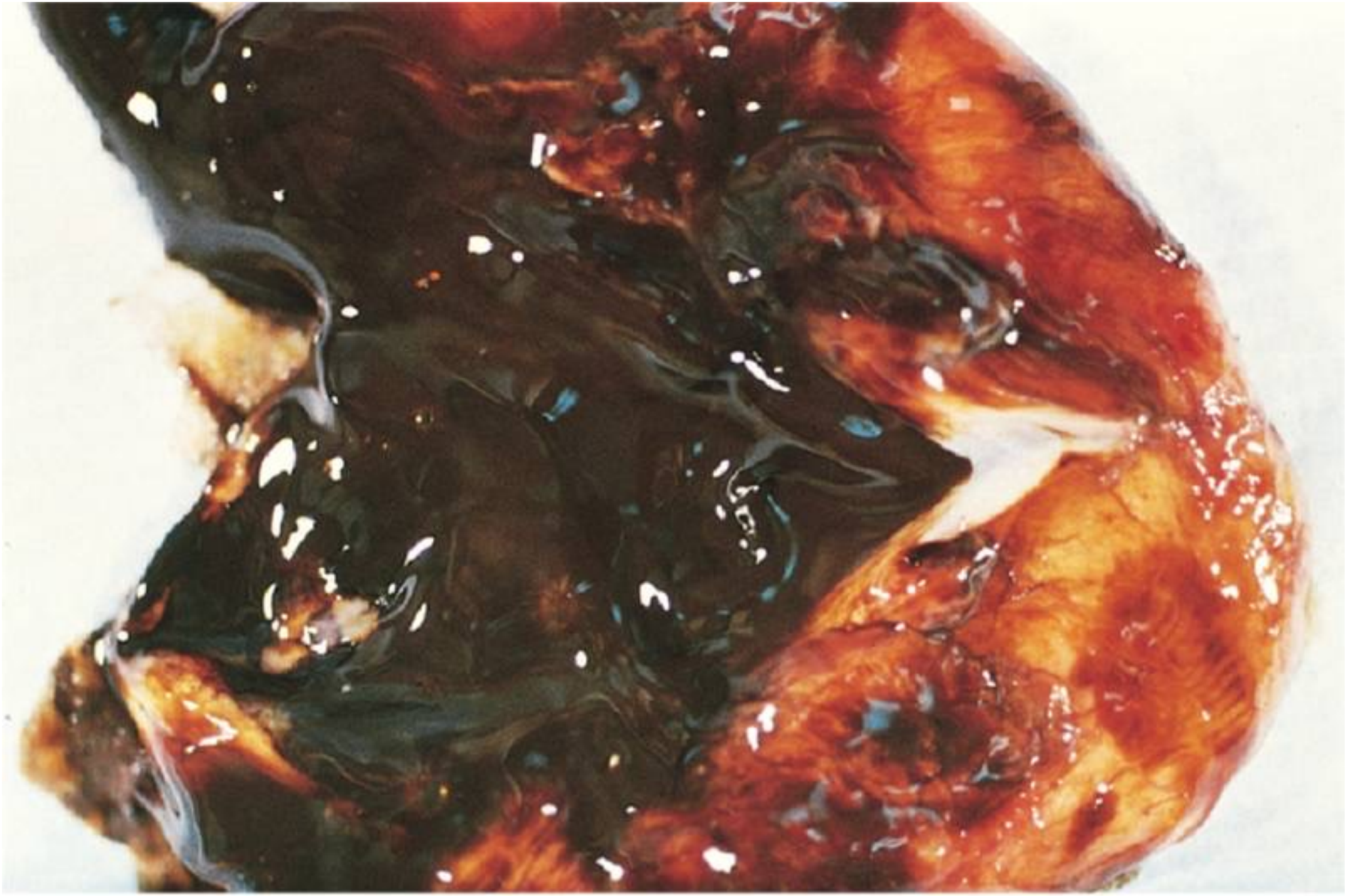
- Cervix
- Uterus
  - Endometriosis
  - Endometrial hyperplasia
  - Tumors

Endometriosis

- Ectopic endometrial glands (outside uterus)
- Ectopic endometrium undergoes cyclic bleeding
- Can cause pain, scarring, infertility



Endometriosis in colon

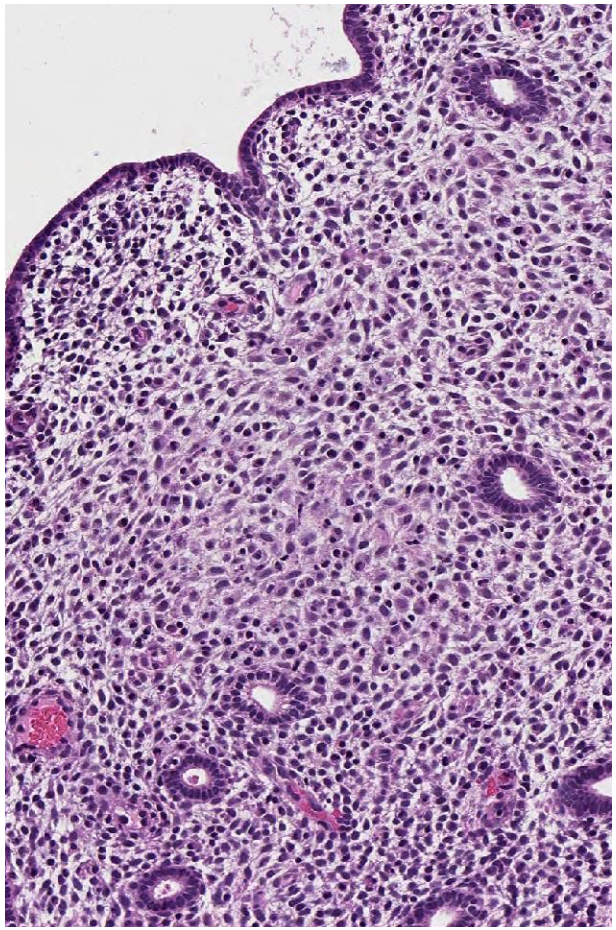


Endometriosis in ovary (“chocolate cyst”)

Endometrial Hyperplasia

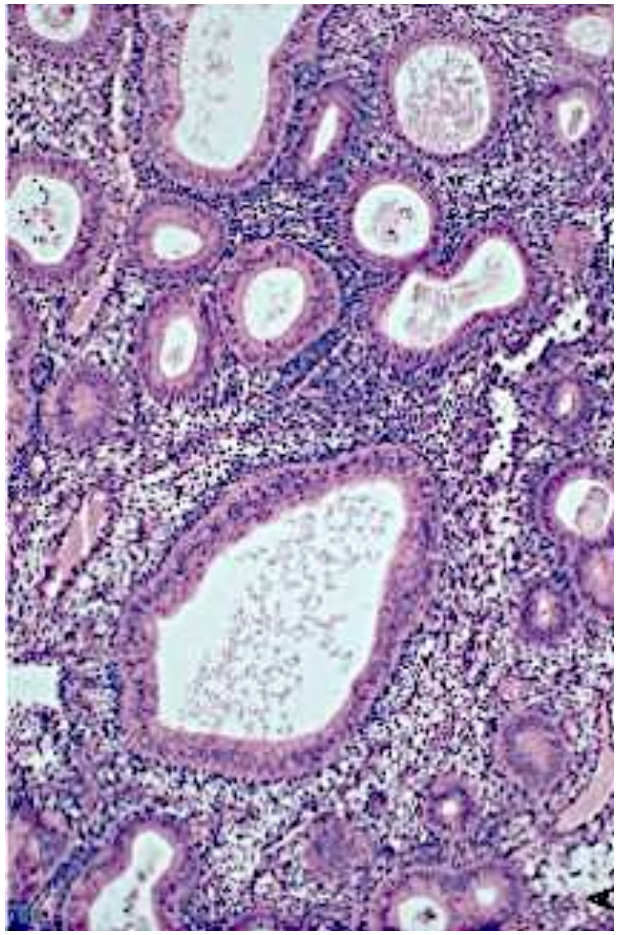
- Proliferation of endometrial glands and stroma
- Risk factors involve estrogen excess (obesity, nulliparity, estrogen replacement therapy)
- Presents with abnormal bleeding
- “Atypical hyperplasia” = increased risk of transformation into adenocarcinoma

Cute little glands



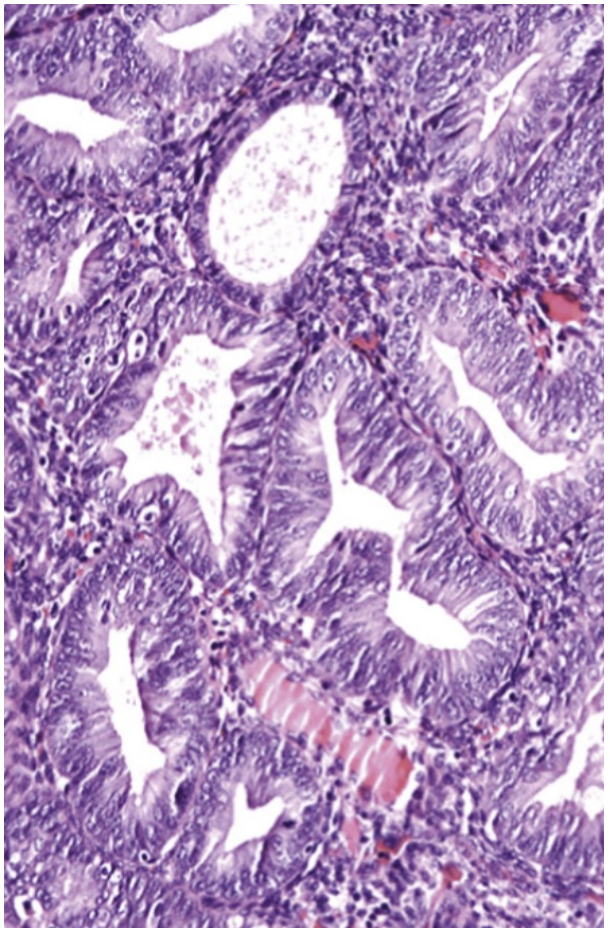
Normal
endometrium

Crowded, dilated glands



Typical
endometrial hyperplasia

Back-to-back glands
containing atypical cells



Atypical
endometrial hyperplasia

Leiomyoma (“Fibroid”)

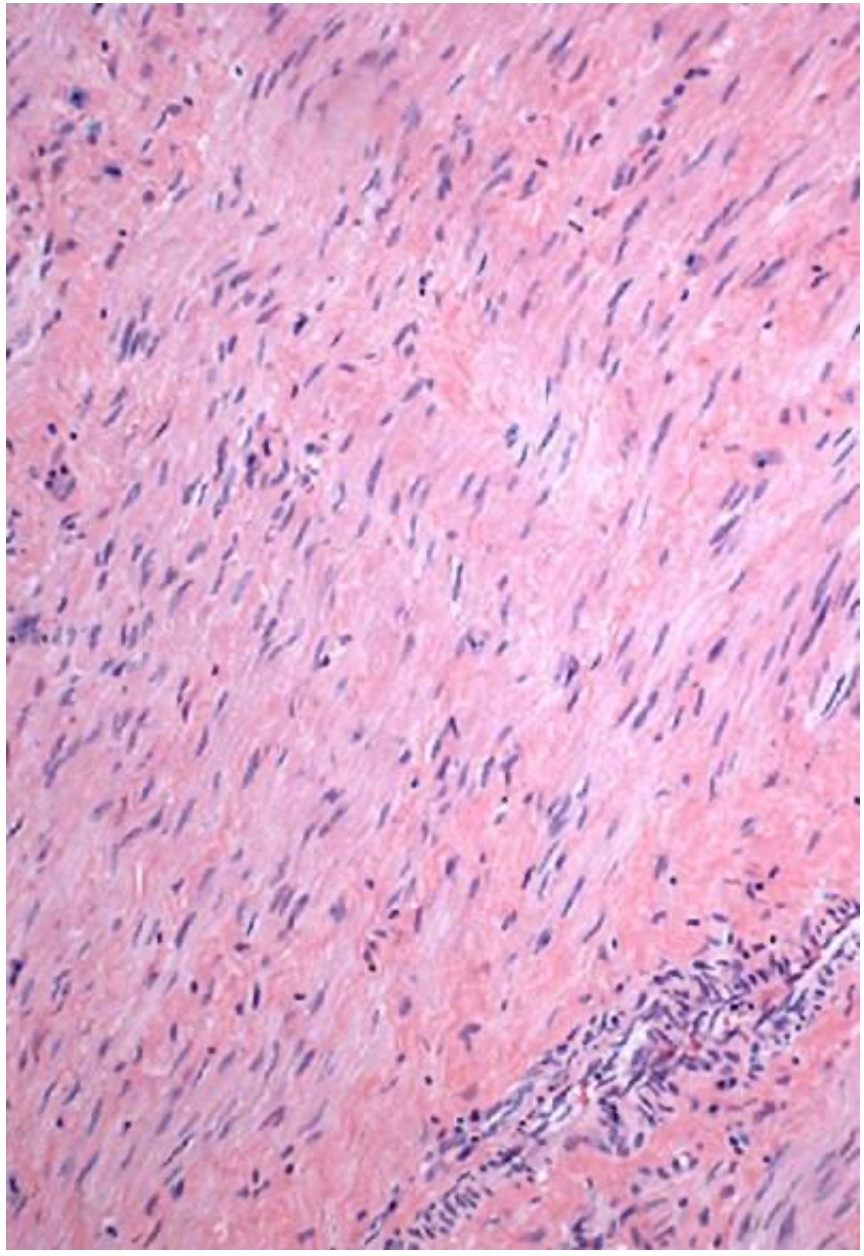
- Benign tumor of smooth muscle
- Very common!
- Stimulated by estrogen
- Can cause pain and abnormal bleeding

Leiomyosarcoma

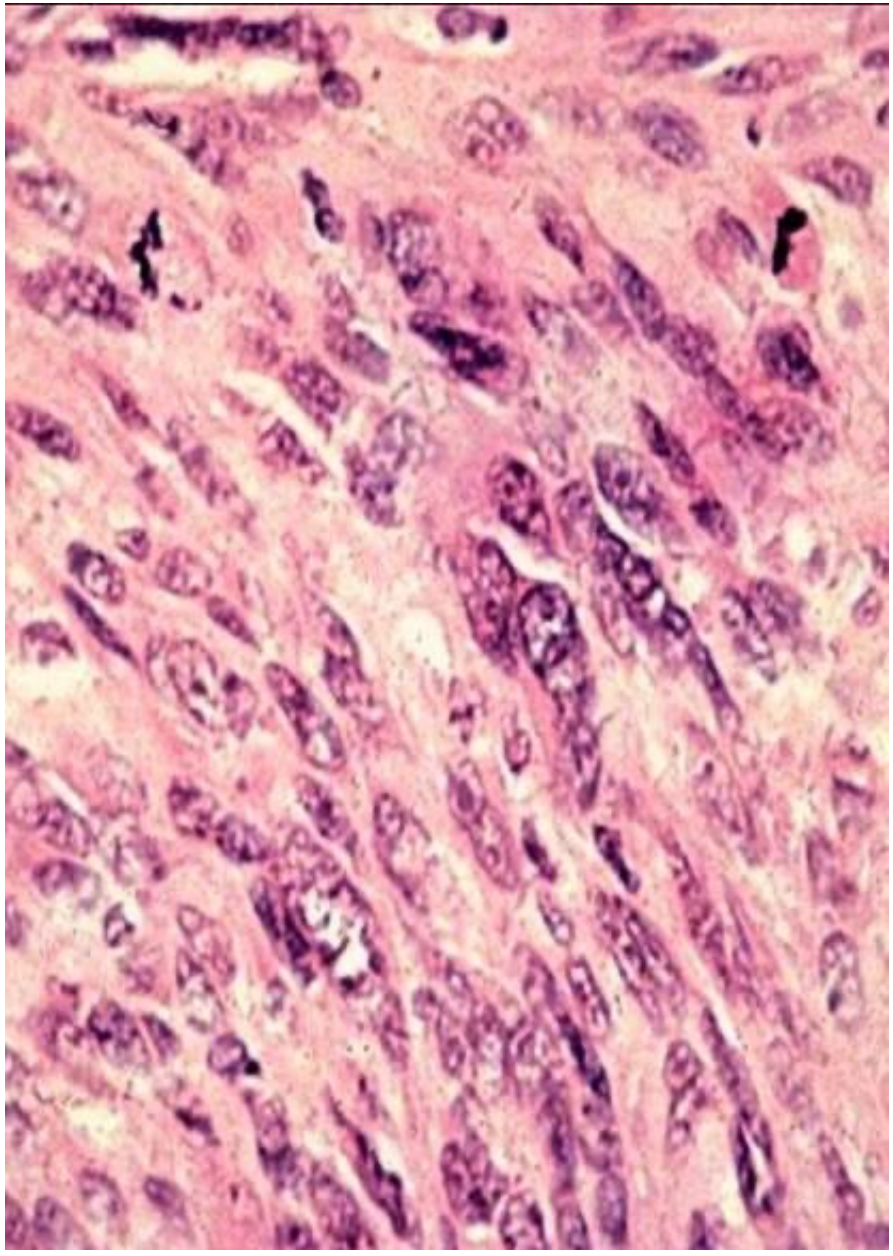
- Malignant tumor of smooth muscle
- Necrotic, with atypical cells and lots of mitoses
- Metastasizes early, often to lungs
- 5-year survival = 40%

Leiomyoma

Leiomyosarcoma



Leiomyoma



Leiomyosarcoma

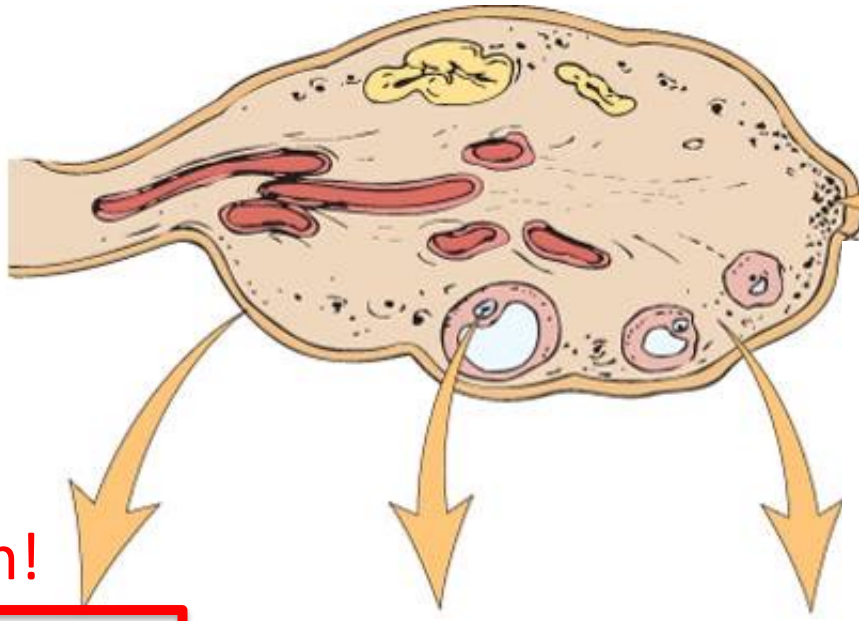
Endometrial Carcinoma

- Peak age: 55-65 (not before 40)
- Frequently preceded by atypical endometrial hyperplasia
- Risk factors involve estrogen excess
- Presents with abnormal bleeding
- Metastasizes late

Female Reproductive System Outline

- Cervix
- Uterus
- Ovaries
  - Tumors

Origin of Ovarian Tumors



Most common!

Surface epithelial tumors
- Cystadenoma
- Cystadenocarcinoma

Germ cell tumors
- Teratoma
- Dysgerminoma
- Yolk sac tumor
- Choriocarcinoma

Sex cord-stromal tumors
- Granulosa-theca cell tumor
- Sertoli-Leydig cell tumor

Cystadenoma

- Benign tumor derived from surface epithelium of the ovary
- Contains cystic spaces filled with fluid
- Typically large, occasionally bilateral

Patient with ovarian cystadenoma

Ovarian cystadenoma

Ovarian cystadenoma

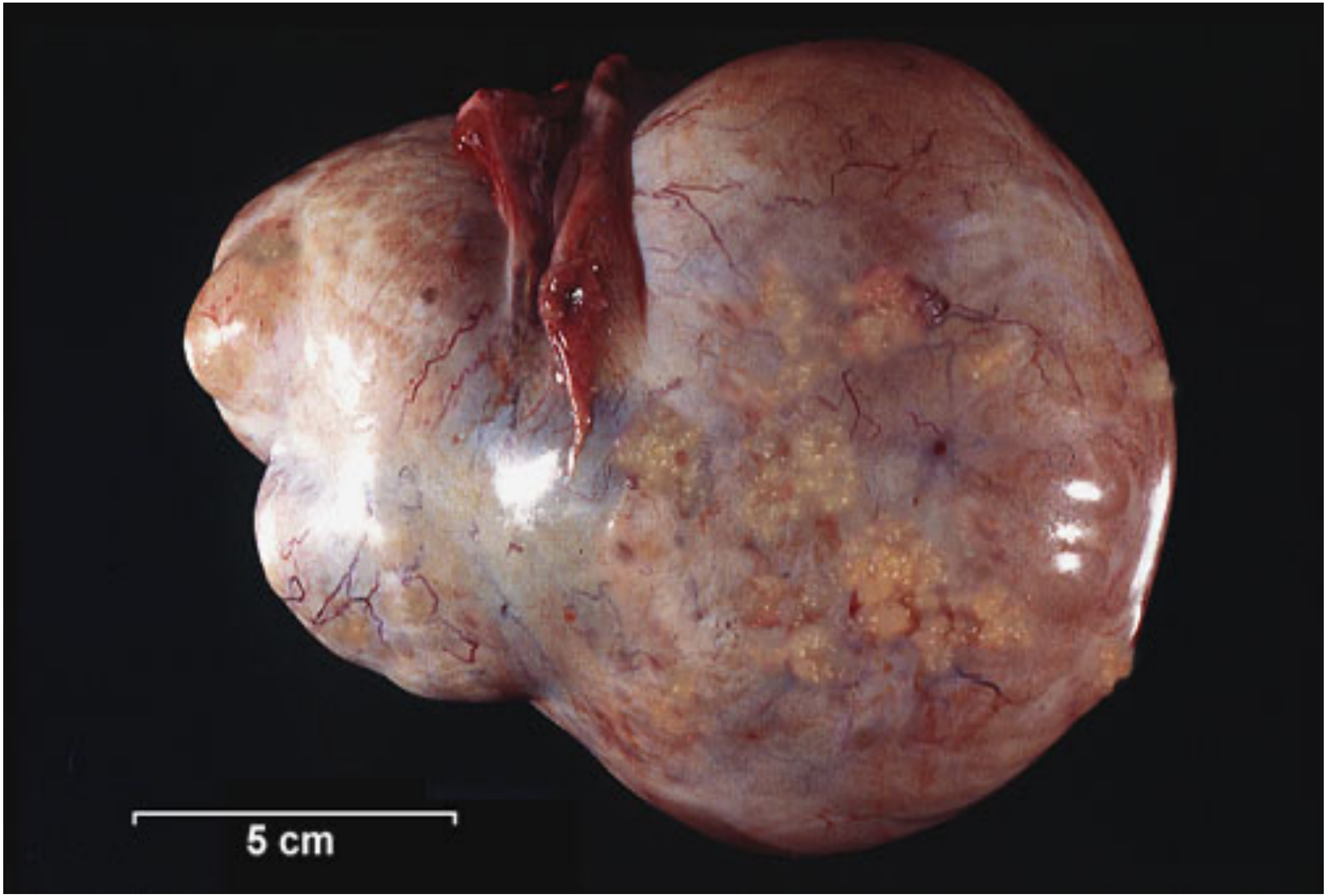
Teratoma

- Benign tumor arising from germ cells
- Sometimes called “dermoid cyst” because it’s usually cystic and lined by skin
- Usually presents as an abdominal mass
- Often contains many types of tissue such as cartilage, bone, neural tissue
- Rare cases become malignant

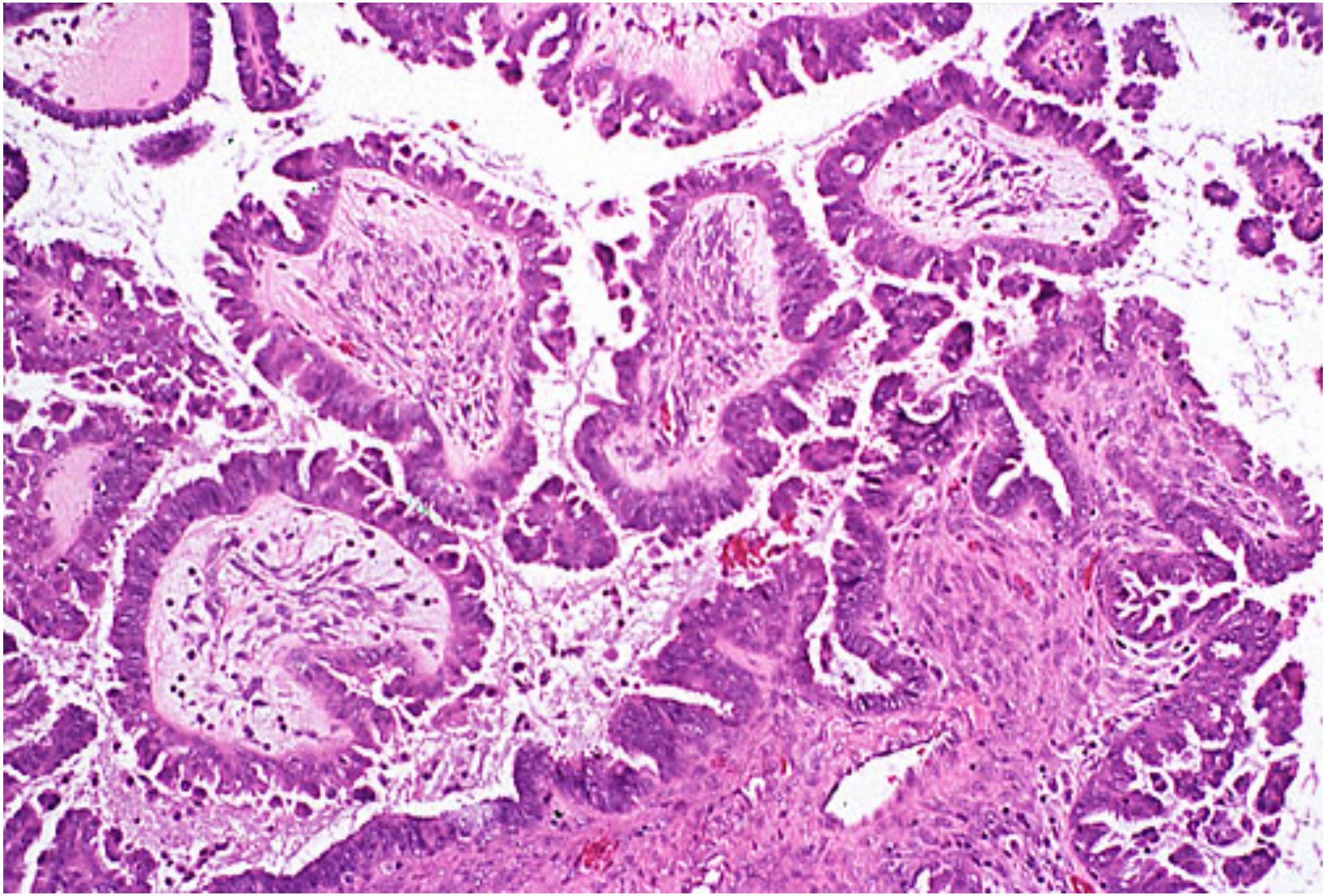
Teratoma

Ovarian Cancer

- 2023 estimates: 20,000 new cases / 13,000 deaths
- Peak age: 50
- Risk factors: estrogen excess, family history
- Symptoms: bloating, pain, more frequent/urgent urination
- Often metastatic at diagnosis
- Most are cystadenocarcinomas



Papillary cystadenocarcinoma



Papillary cystadenocarcinoma

Ovarian Cancer

- Treatment: surgery, radiation, chemotherapy
- Prognosis depends on stage
  - Cancer inside ovary: 5y survival 70%
  - Cancer outside ovary: 5y survival 13%

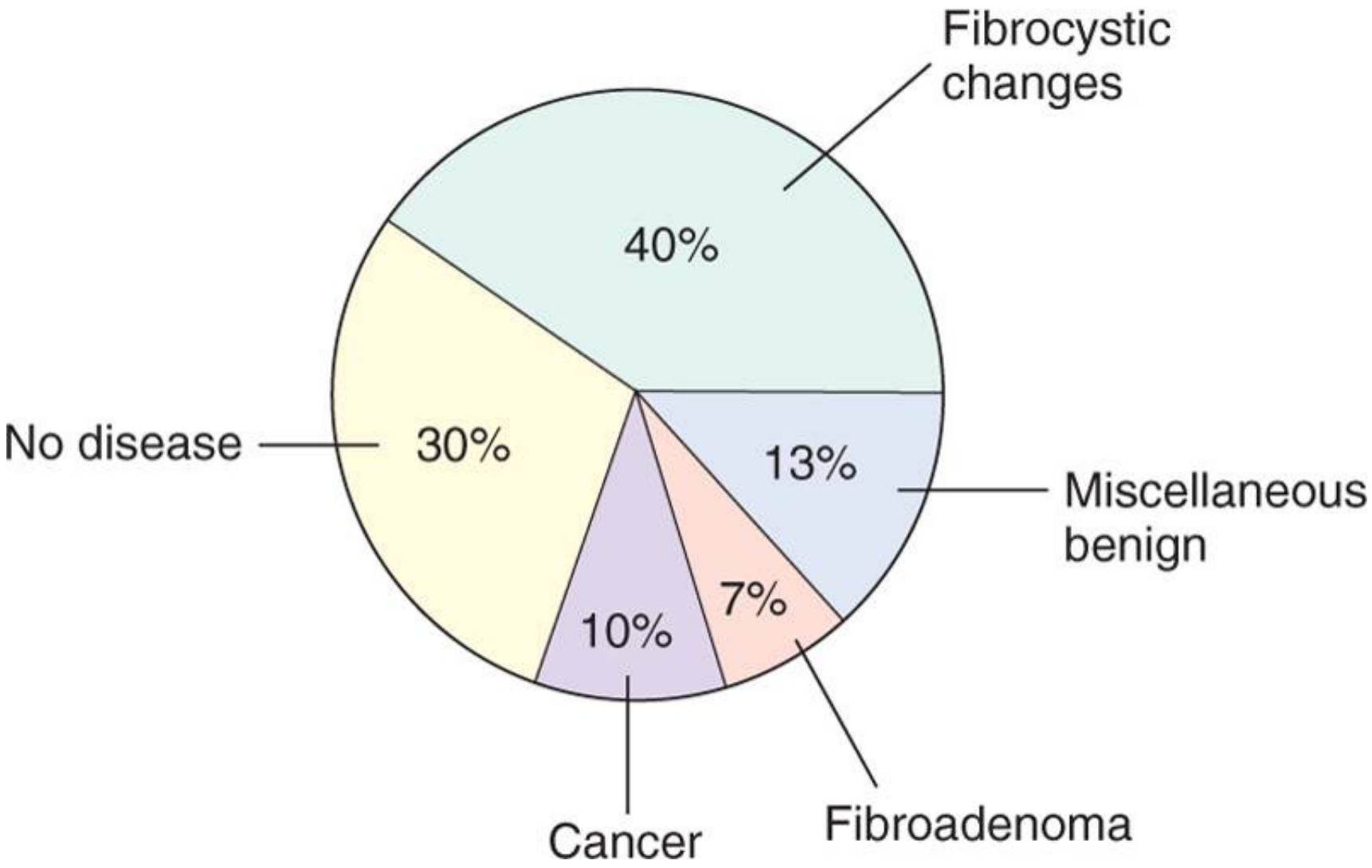
Female Reproductive System Outline

- Cervix
- Uterus
- Ovaries
- Breast
  - Fibrocystic change
  - Tumors

Breast

- Many breast diseases present as lumps
- Most lumps are NOT cancerous…
- …but a lump always needs to be evaluated
- Ultrasound, mammography, fine needle aspiration, and biopsy are the usual methods

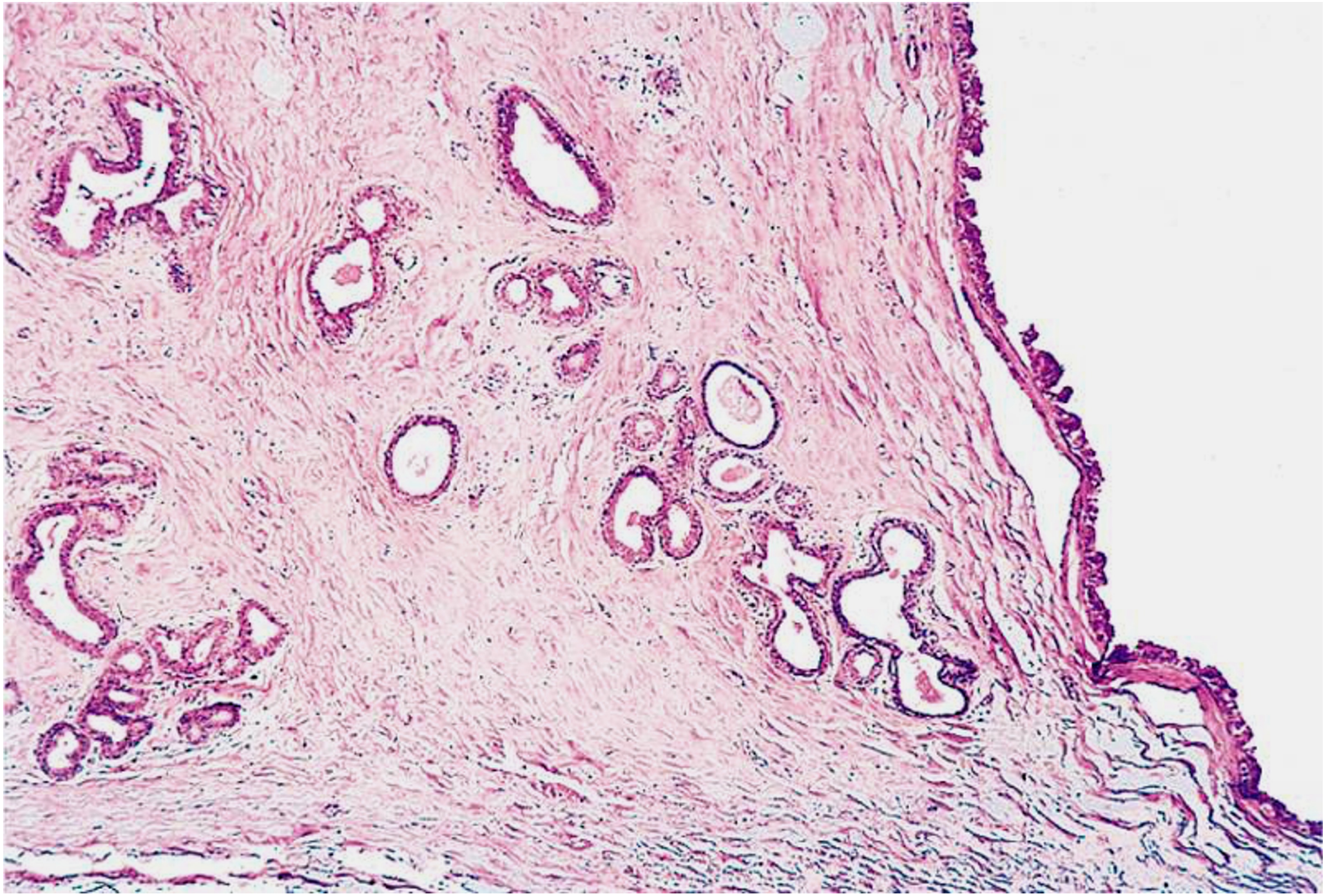
Most breast lumps are not cancerous



Fibrocystic Change

- “Lumpy bumpy” breast tissue containing cysts and fibrous tissue
- Very common
- Most cases are NOT associated with increased cancer risk

Fibrocystic change

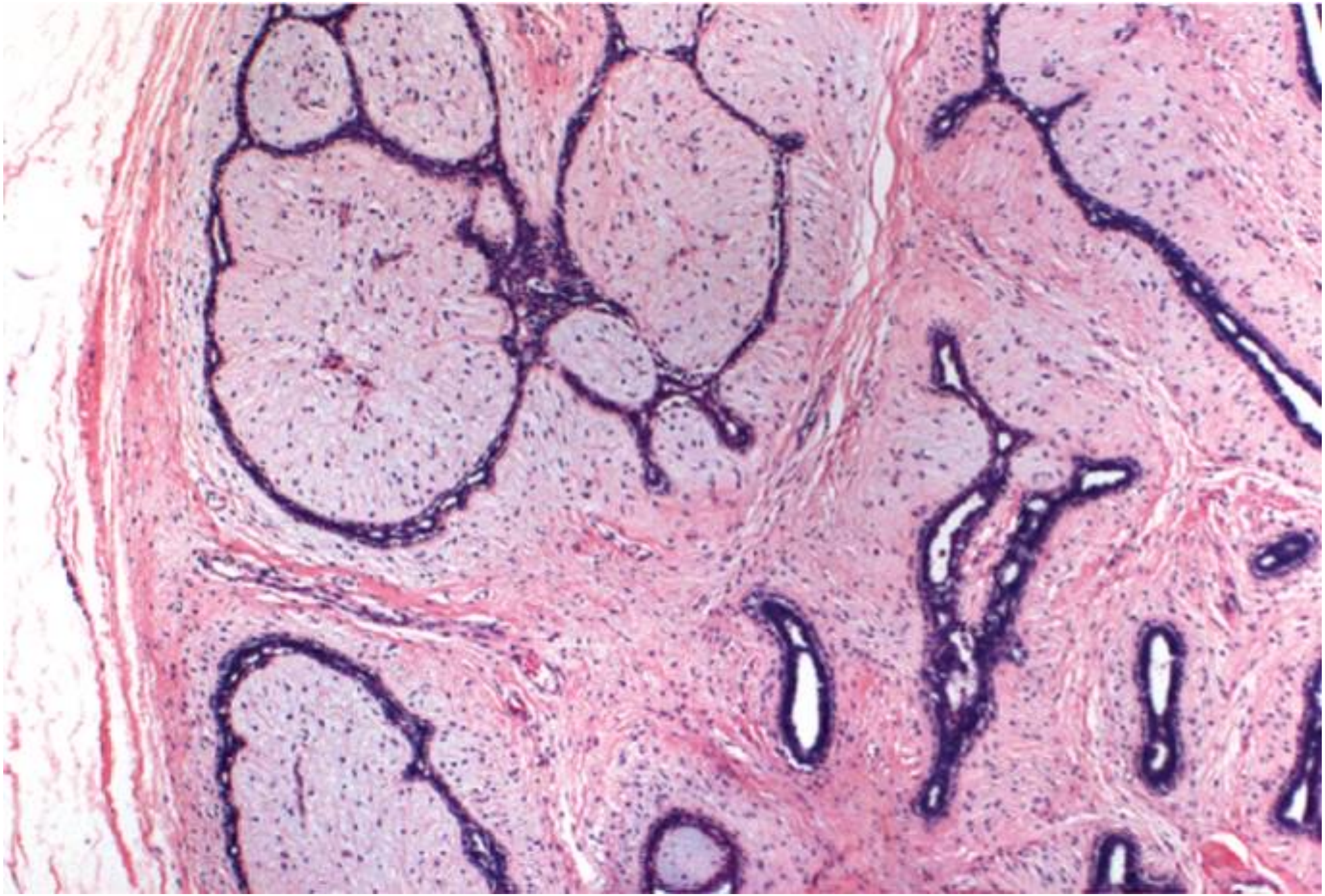


Fibrocystic change

Fibroadenoma

- Most common benign breast tumor
- Stimulated by estrogen
- Peak incidence: 20s
- Solitary, discrete, moveable mass
- Fibrous tissue with compressed ducts and lobules

Fibroadenoma



Fibroadenoma

Breast Carcinoma

- 2023 estimates: 300,000 new cases / 44,000 deaths
- Really common! Incidence: 1 in 8 women!
- Usually presents as a lump
- Risk factors: age (75% of patients are >50), estrogen excess, alcohol consumption, high-fat diet, family history (less than 10% of all cases)

Breast Carcinoma Family History

- Worry if first degree relative with breast cancer
- Most have BRCA-1 or BRCA-2 mutations
- Tumor suppressor genes; help repair DNA
- Genetic testing difficult
- Most carriers get cancer by age 70

Breast Carcinoma Clinical Findings

If discovered by palpation:

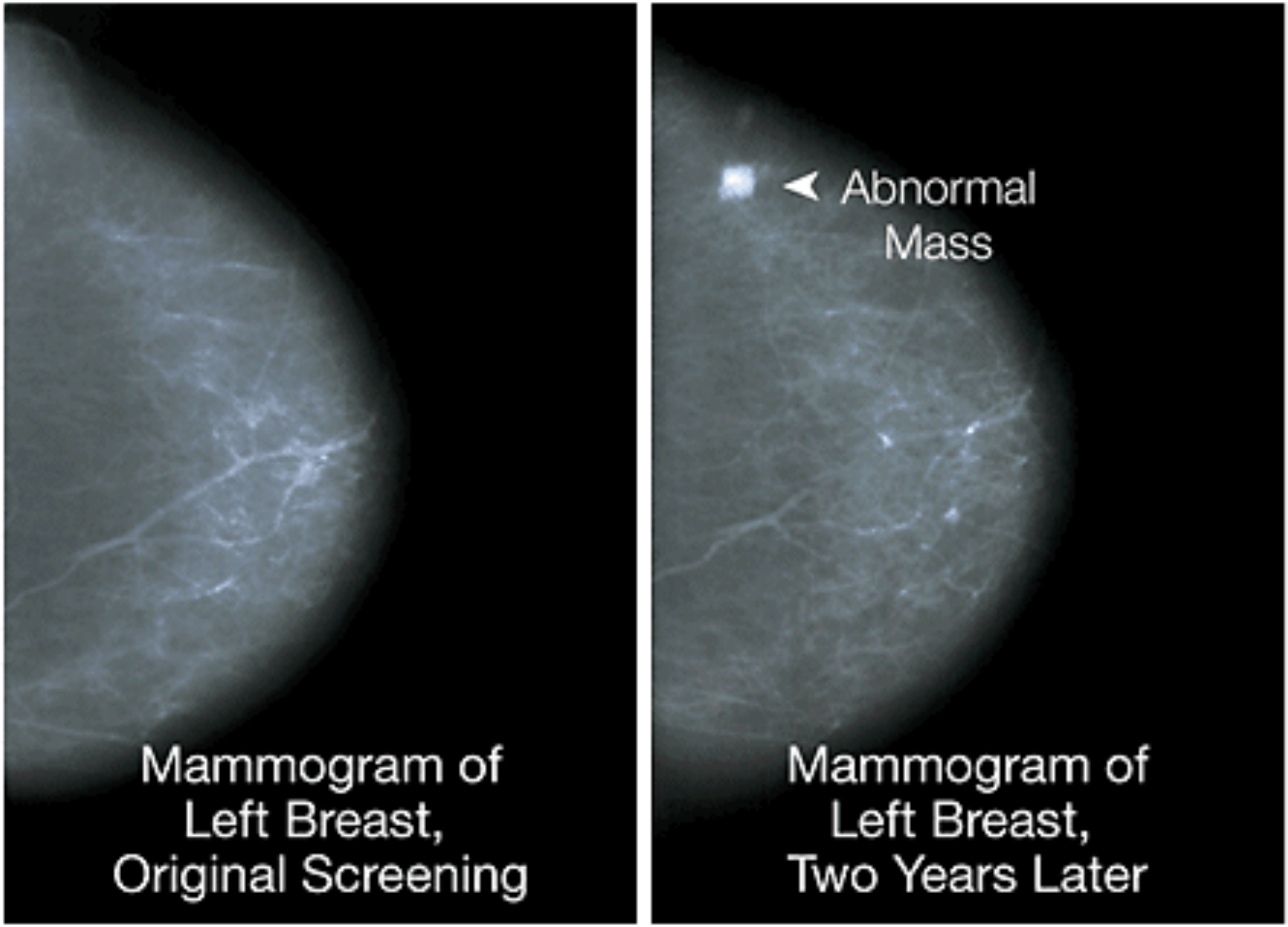
- Solitary, painless, moveable mass
- 2-3 cm in diameter
- Axillary nodes positive in 50% of patients

If discovered by mammography:

- 1 cm in diameter
- Axillary nodes positive in 15% of patients

As disease progresses:

- Fixation to chest wall
- Adherence to overlying skin
- Peau d’orange


Abnormal
Mass
Mammogram of
Left Breast,
Original Screening
Mammogram of
Left Breast,
Two Years Later

Advanced breast carcinoma: fixation to skin

Peau d’orange

Breast Carcinoma Histologic Types

Non-invasive

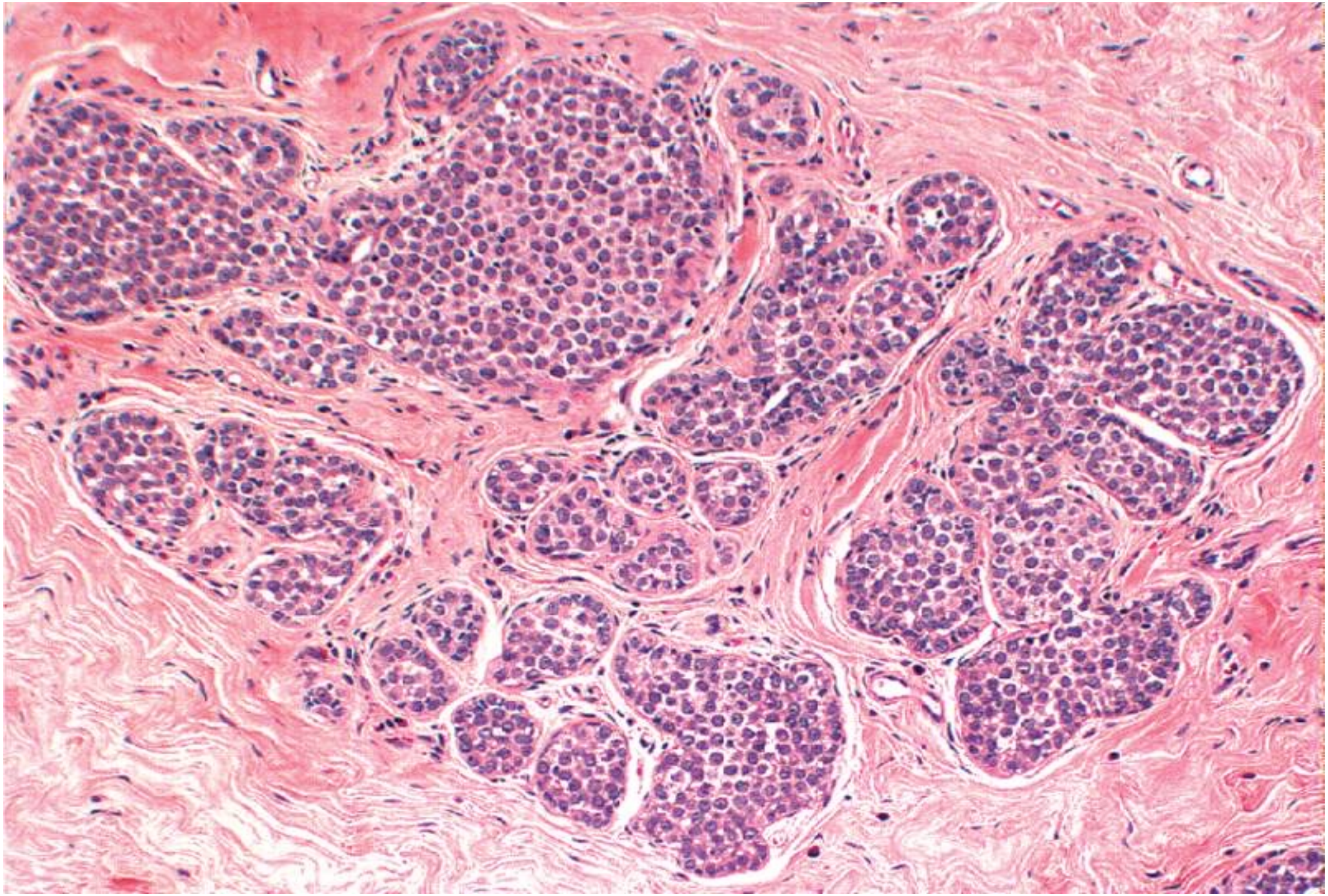
- Ductal carcinoma in situ (DCIS)
- Lobular carcinoma in situ (LCIS)

Invasive

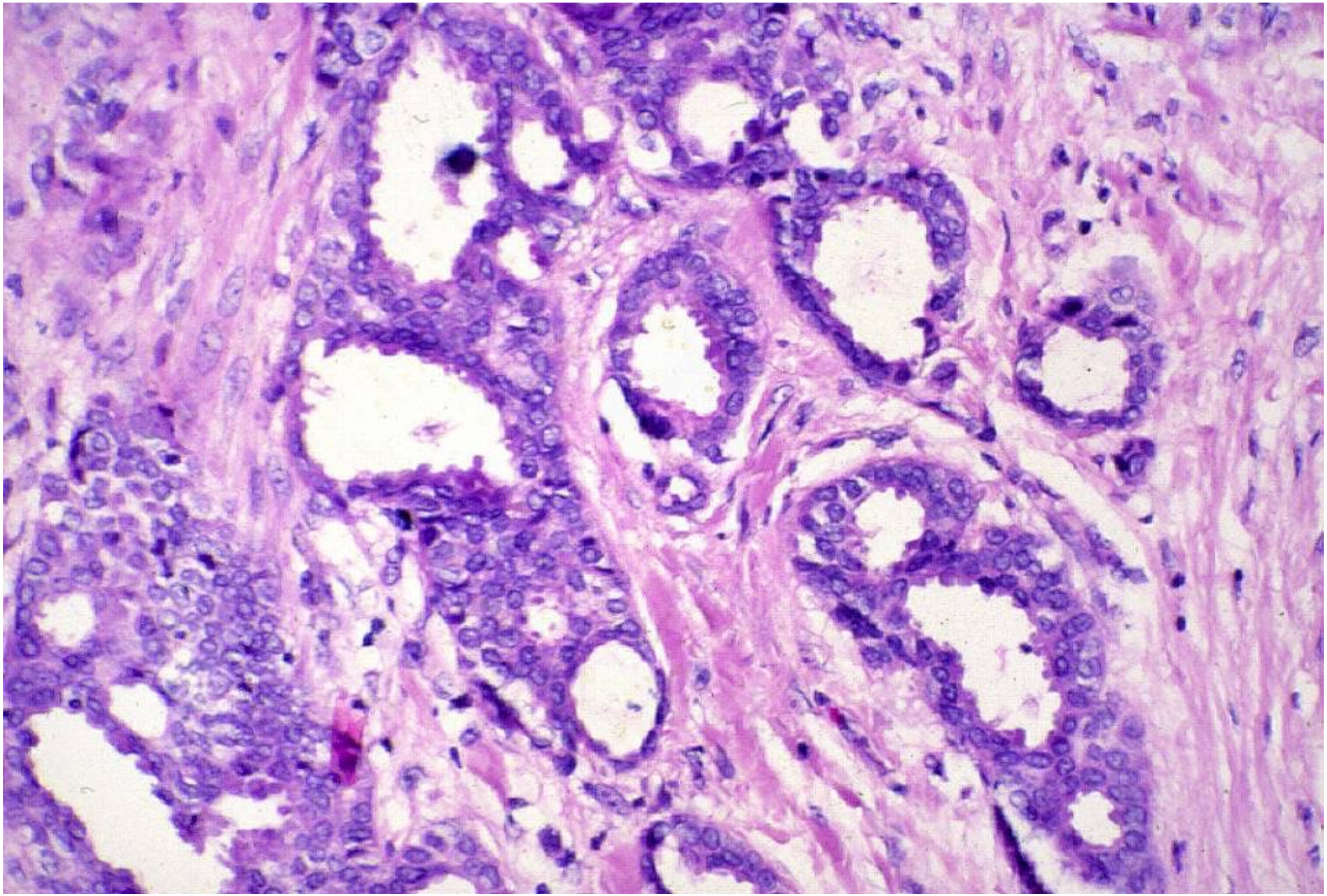
- Ductal
- Lobular
- Inflammatory
- …and a bunch of other rare types

Breast Carcinoma Prognostic Factors

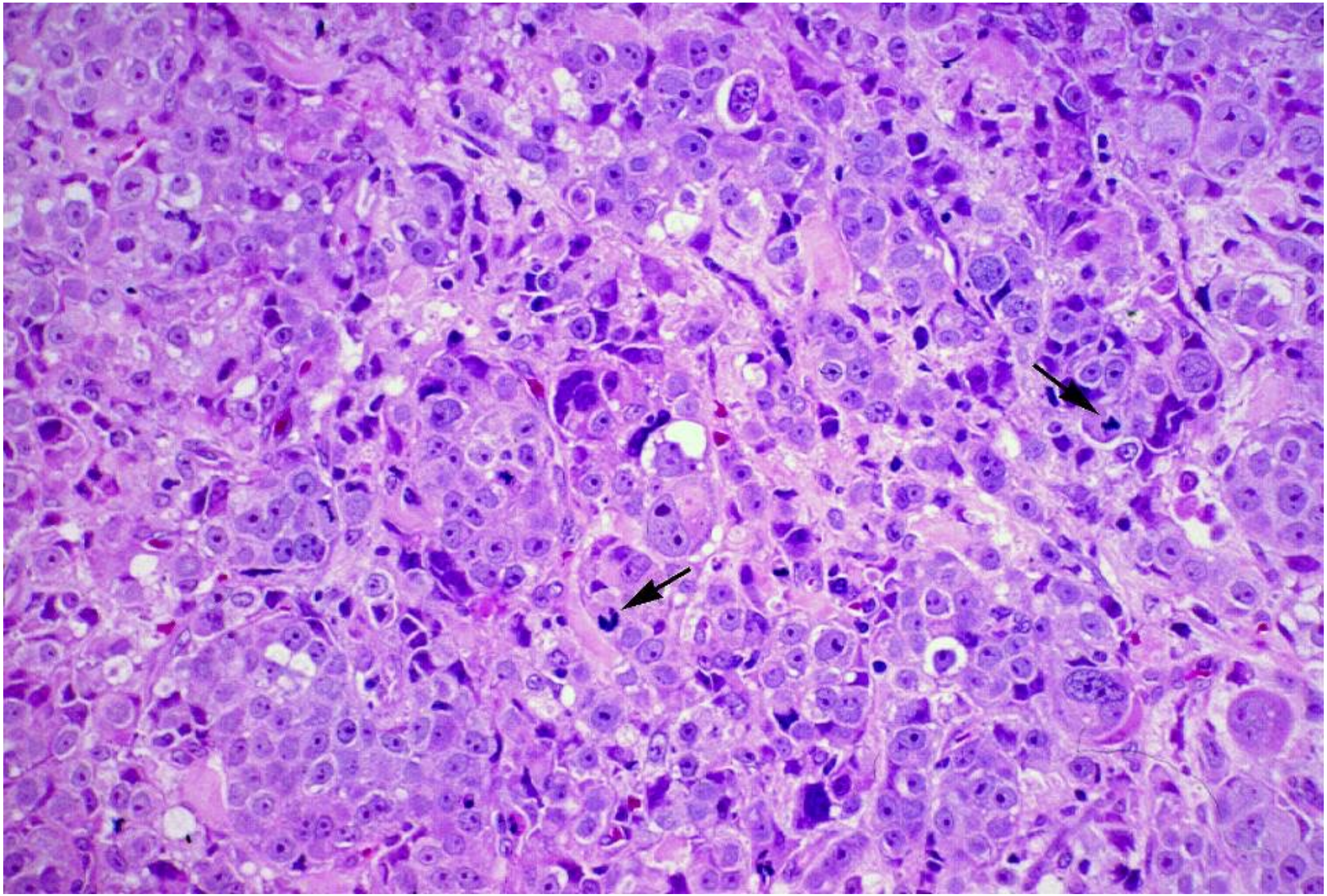
- Stage
- Grade
- Type (inflammatory is worst)



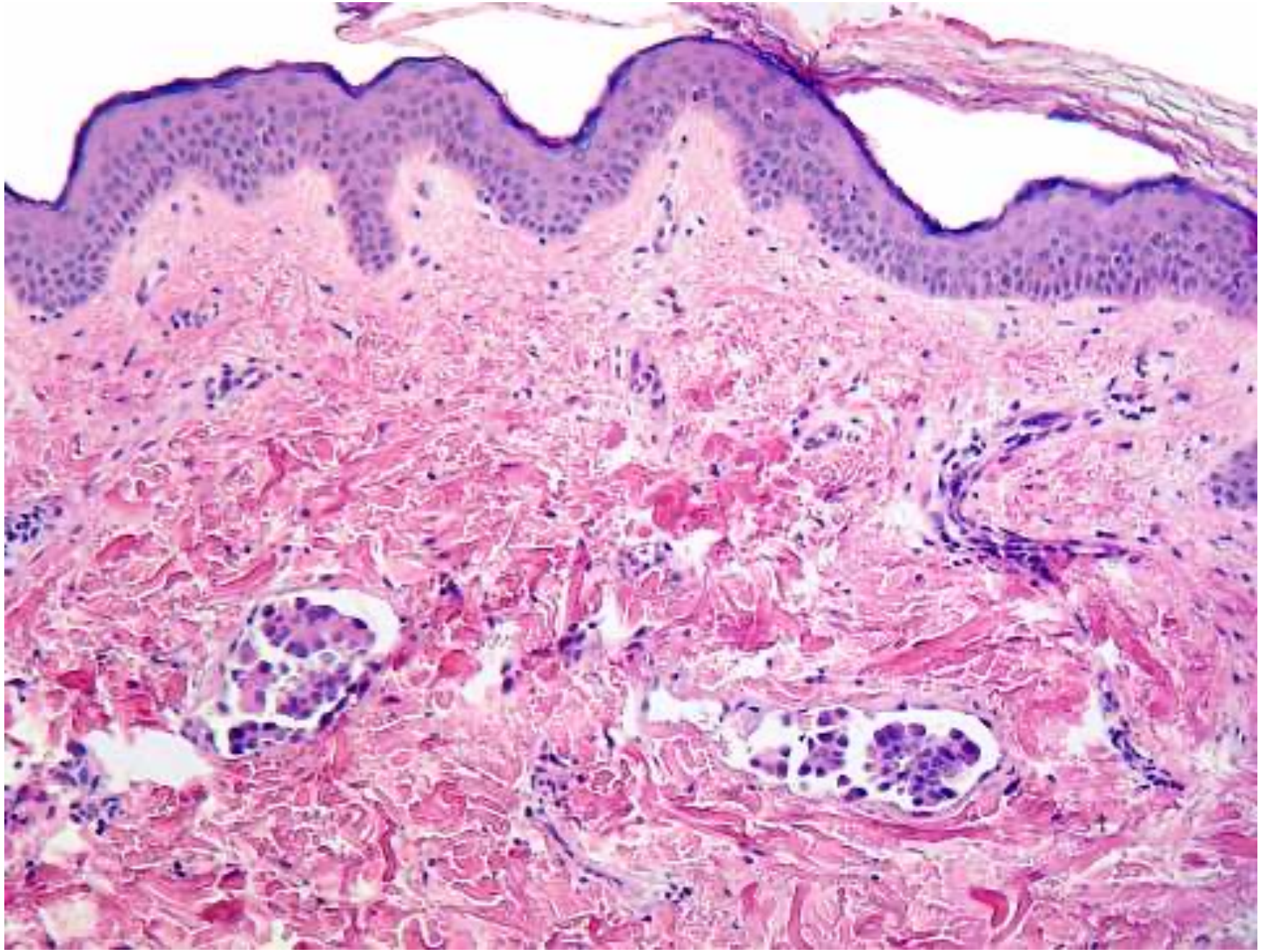
Lobular carcinoma in situ



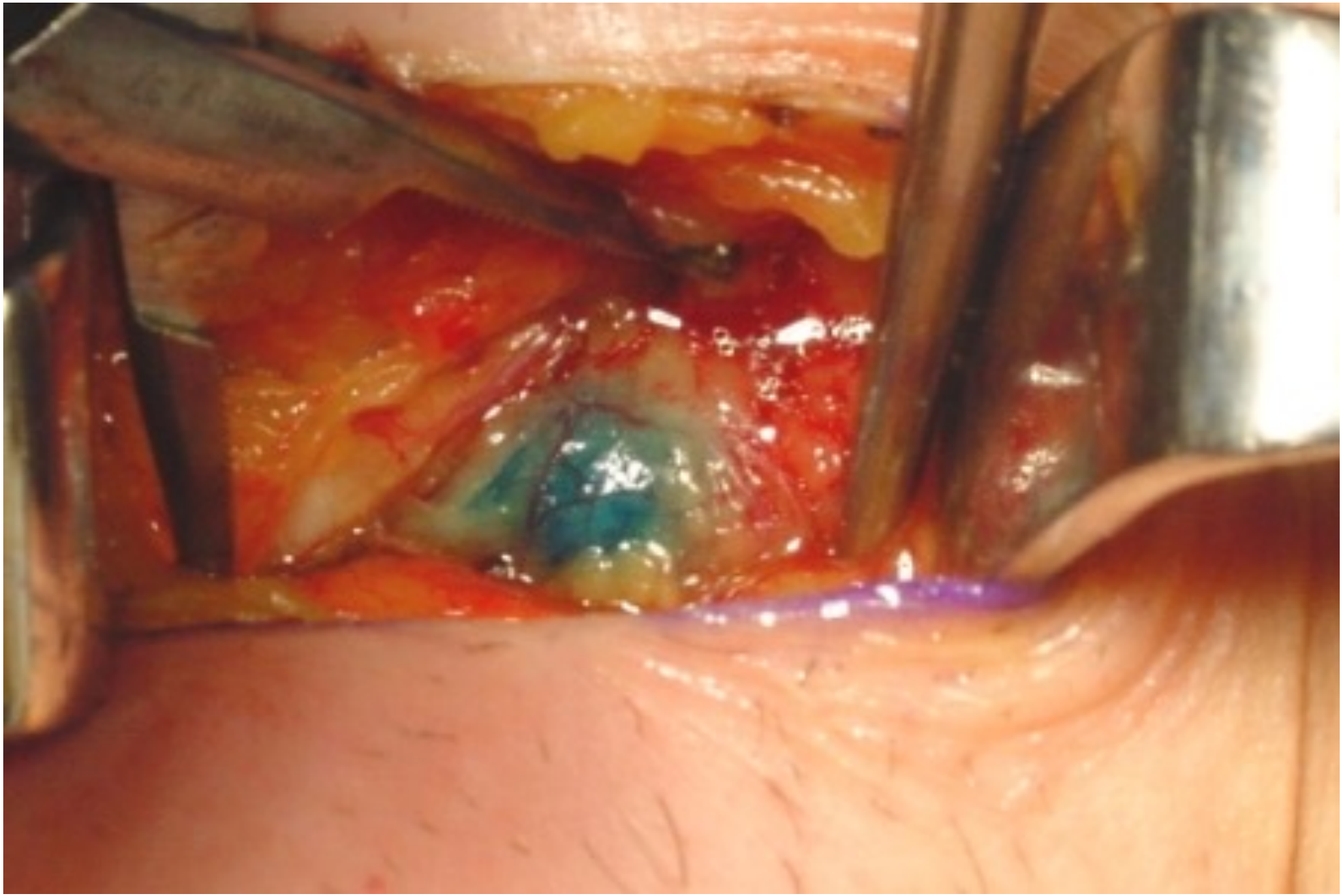
Low-grade invasive ductal carcinoma



High-grade invasive ductal carcinoma



Inflammatory breast carcinoma



Sentinel node biopsy

TNM* staging system for breast cancer

Stage	T	N	M	5-year survival
Stage 0	DCIS	0	M0	92%
Stage I	<2 cm	0	M0	87%
Stage II	<5 cm	<3	M0	75%
	>5 cm	0	M0	
Stage III	<5 cm	4+	M0	46%
	>5 cm	1+	M0	
	Any T	10+	M0	
	Any T	Any N	skin or chest wall	
Stage IV	Any T	Any N	M1	13%

* Tumor (size), nodes (# positive), metastases

Don’t memorize the numbers in this table! See learning objectives!