

NEOPLASIA

Dian Yuliartha Lestari

A series of horizontal lines in teal and white colors, located on the right side of the slide, extending from the teal bar above.

neoplasma

- Pertumbuhan sel abnormal yang terus menerus, walaupun rangsangannya telah dihentikan (autonom), tumbuh aktif melebihi kebutuhan, inkoordinasi, tanpa tujuan, dan merugikan host
- Dikategorikan menjadi 2 :
 - Benign dan Malignant
 - Tipe neoplasma berdasarkan karakteristik parenchym-nya

nomenclature

- Memiliki 2 komponen dasar :
 - Parenchyme : Adanya sel yang bertransformasi ganas
 - Supporting stroma : terdiri dari jaringan ikat fibrous dan pembuluh darah sebagai kerangka tumbuhnya sel ganas
- **BENIGN**
 -+ *oma*
- **MALIGNANT**
 - = **cancers**
 - Dibagi menjadi 2 kategori :
 - *Carcinoma* → dari sel epitel
 - *Sarcoma* → dari sel mesenchymal

- Beberapa tumor memiliki lebih dari 1 parenchym :
 - **Mixed tumor** → berkembang dari 1 germinal layer yang berdifferensiasi menjadi lebih dari 1 parenchym, contoh : Benign Mixed Salivary Gland (Pleomorphic Adenoma)
 - **Teratoma** → terdiri dari beberapa sel parenchym yg berkembang dari lebih satu germinal layer, biasanya 3 germinal layer: ectoderm, mesoderm, dan endoderm

Table 7.1

Classification of tumours.

TISSUE OF ORIGIN	BENIGN	MALIGNANT
I. TUMOURS OF ONE PARENCHYMAL CELL TYPE		
A. Epithelial Tumours		
1. Squamous epithelium	Squamous cell papilloma	Squamous cell (Epidermoid) carcinoma
2. Transitional epithelium	Transitional cell papilloma	Transitional cell carcinoma
3. Glandular epithelium	Adenoma	Adenocarcinoma
4. Basal cell layer skin	—	Basal cell carcinoma
5. Neuroectoderm	Naevus	Melanoma (Melanocarcinoma)
6. Hepatocytes	Liver cell adenoma	Hepatoma (Hepatocellular carcinoma)
7. Placenta (Chorionic epithelium)	Hydatidiform mole	Choriocarcinoma
B. Non-epithelial (Mesenchymal) Tumours		
1. Adipose tissue	Lipoma	Liposarcoma
2. Adult fibrous tissue	Fibroma	Fibrosarcoma
3. Embryonic fibrous tissue	Myxoma	Myxosarcoma
4. Cartilage	Chondroma	Chondrosarcoma
5. Bone	Osteoma	Osteosarcoma
6. Synovium	Benign synovioma	Synovial sarcoma
7. Smooth muscle	Leiomyoma	Leiomyosarcoma
8. Skeletal muscle	Rhabdomyoma	Rhabdomyosarcoma
9. Mesothelium	—	Mesothelioma
10. Blood vessels	Haemangioma	Angiosarcoma
11. Lymph vessels	Lymphangioma	Lymphangiosarcoma
12. Glomus	Glomus tumour	—
13. Meninges	Meningioma	Invasive meningioma
14. Haematopoietic cells	—	Leukaemias
15. Lymphoid tissue	Pseudolymphoma	Malignant lymphomas
16. Nerve sheath	Neurilemmoma, Neurofibroma	Neurogenic sarcoma
17. Nerve cells	Ganglioneuroma	Neuroblastoma
II. MIXED TUMOURS		
Salivary glands	Pleomorphic adenoma (mixed salivary tumour)	Malignant mixed salivary tumour
III. TUMOURS OF MORE THAN ONE GERM CELL LAYER		
Totipotent cells in gonads or in embryonal rests	Mature teratoma	Immature teratoma

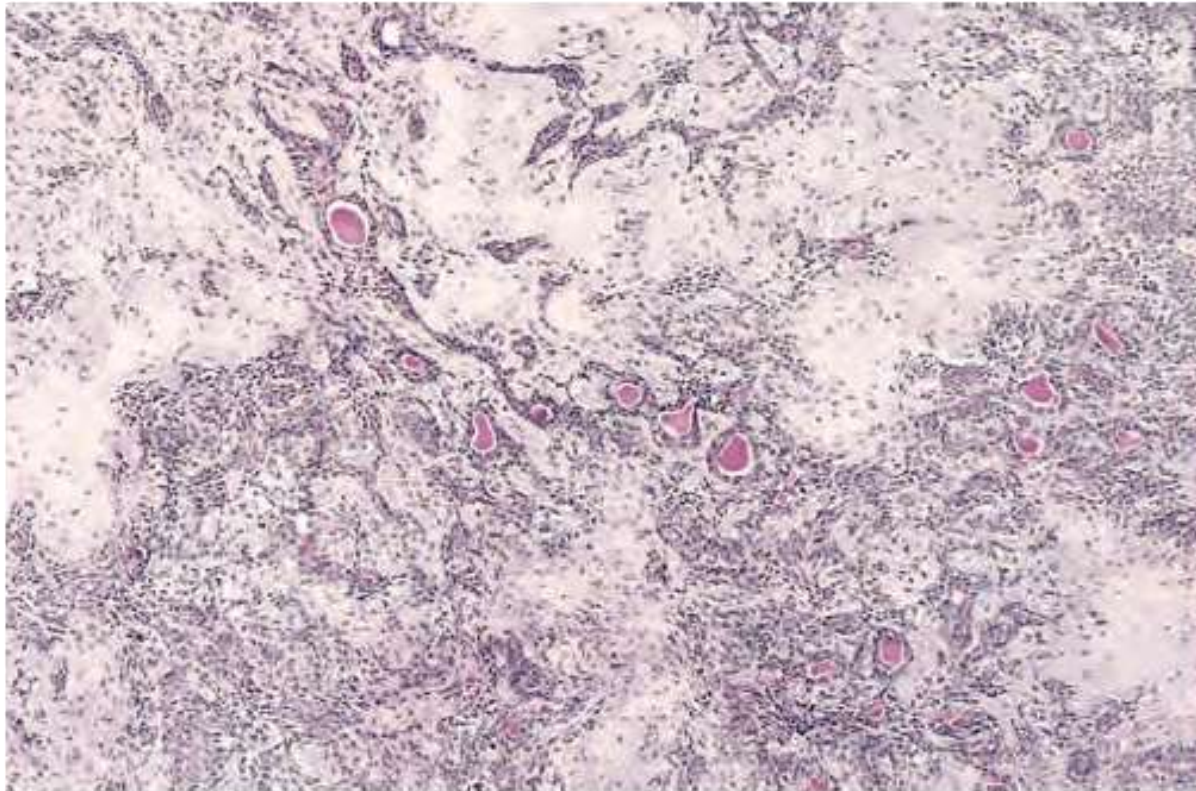


Figure 7-2 This mixed tumor of the parotid gland contains epithelial cells forming ducts and myxoid stroma that resemble cartilage. (Courtesy Dr. Trace Worrell, University of Texas Southwestern Medical School, Dallas, Texas.)



Figure 7-3 **A**, Gross appearance of an opened cystic teratoma of the ovary. Note the presence of hair, sebaceous material, and tooth. **B**, A microscopic view of a similar tumor shows skin, sebaceous glands, fat cells, and a tract of neural tissue (arrow).

- **Choriostoma** → jaringan ectopik yang non-transformed , cth: sel pancreas di bawah mucosa small bowel
- **Hamartomas** → massa terdiri dari beberapa jaringan ikat yang berkumpul di satu tempat (lung, genu)



Non neoplastik

- **Blastoma atau Embryoma** → Tumor ganas yang berasal dari sel blastema atau sel pada masa embriology (sel immatur), biasanya pada usia < 5 tahun , cth : Nephroblastoma, retinoblastoma

eponim

- Tumor diberi nama sesuai dengan penemunya:
 - Burkitt's lymphoma
 - Wilms tumor
 - Hodgkin lymphoma
 - Ewing sarcoma
 - Warthin tumor

EXCEPTIONS ! (- OMA tapi ganas)

**HEPATOMA, BASALIOMA, MELANOMA MALIGNA,
SEMINOMA, DYSGERMINOMA, LYMPHOMA,
MALIGNANT GLIOMA.**

Benign vs Malignant

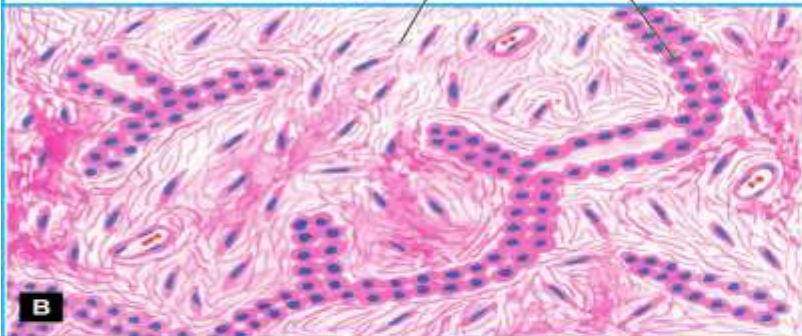
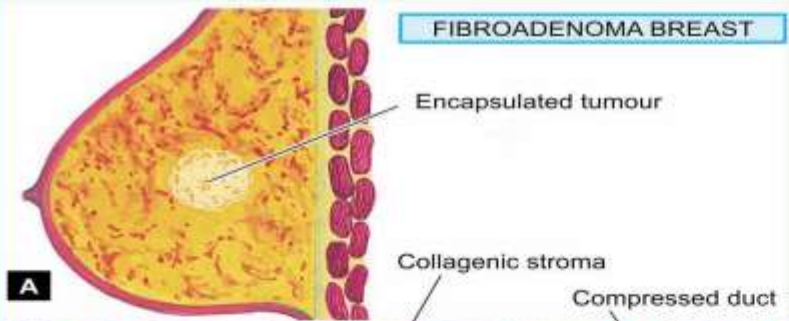
- Dibedakan berdasarkan 4 kategori:
 - Transformasi malignant
 - Differensiasi
 - Anaplasia
 - Rate of growth
 - Local invasion
 - Metastases

Table 7.2 Contrasting features of benign and malignant tumours.

FEATURE	BENIGN	MALIGNANT
I. CLINICAL AND GROSS FEATURES		
1. <i>Boundaries</i>	Encapsulated or well-circumscribed	Poorly-circumscribed and irregular
2. <i>Surrounding tissue</i>	Often compressed	Usually invaded
3. <i>Size</i>	Usually small	Often larger
4. <i>Secondary changes</i>	Occur less often	Occur more often
II. MICROSCOPIC FEATURES		
1. <i>Pattern</i>	Usually resembles the tissue of origin closely	Often poor resemblance to tissue of origin
2. <i>Basal polarity</i>	Retained	Often lost
3. <i>Pleomorphism</i>	Usually not present	Often present
4. <i>Nucleo-cytoplasmic ratio</i>	Normal	Increased
5. <i>Anisonucleosis</i>	Absent	Generally present
6. <i>Hyperchromatism</i>	Absent	Often present
7. <i>Mitoses</i>	May be present but are always typical mitoses	Mitotic figures increased and are generally atypical and abnormal
8. <i>Tumour giant cells</i>	May be present but without nuclear atypia	Present with nuclear atypia
9. <i>Chromosomal abnormalities</i>	Infrequent	Invariably present
10. <i>Function</i>	Usually well maintained	May be retained, lost or become abnormal
III. GROWTH RATE	Usually slow	Usually rapid
IV. LOCAL INVASION	Often compresses the surrounding tissues without invading or infiltrating them	Usually infiltrates and invades the adjacent tissues
V. METASTASIS	Absent	Frequently present
VI. PROGNOSIS	Local complications	Death by local and metastatic complications

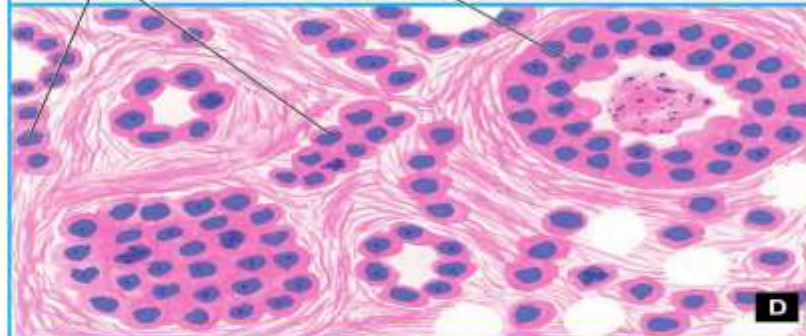
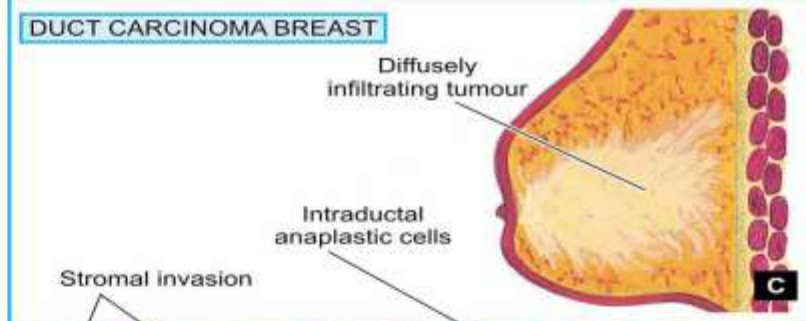
BENIGN EPITHELIAL

FIBROADENOMA BREAST



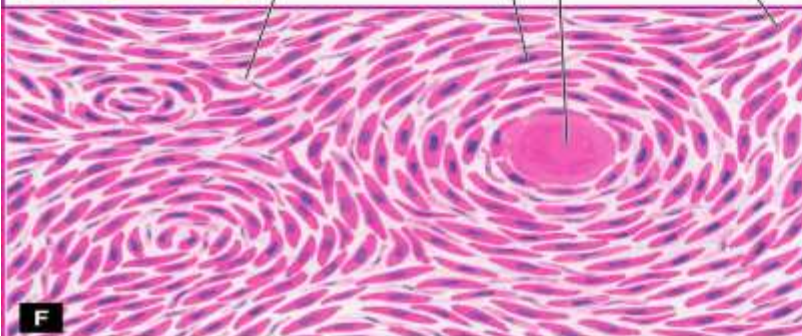
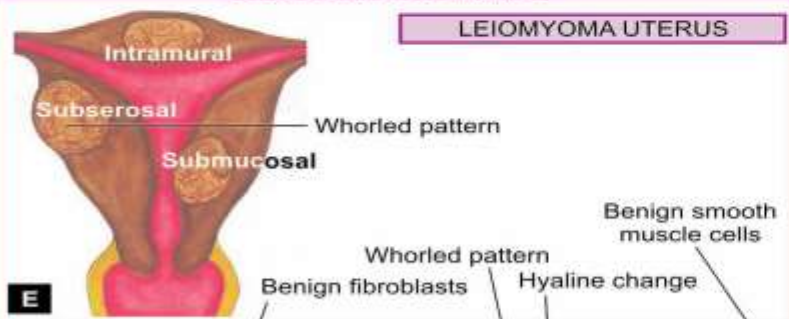
MALIGNANT EPITHELIAL

DUCT CARCINOMA BREAST



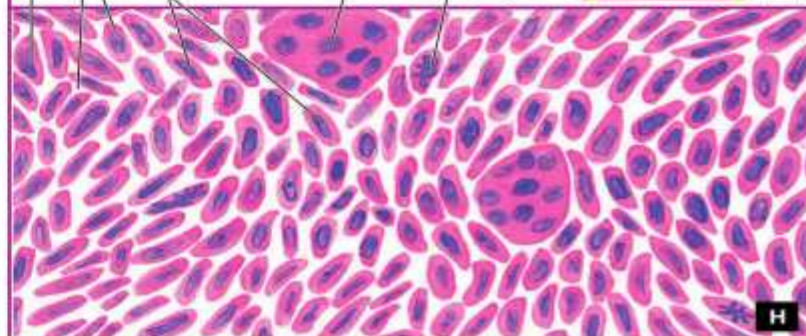
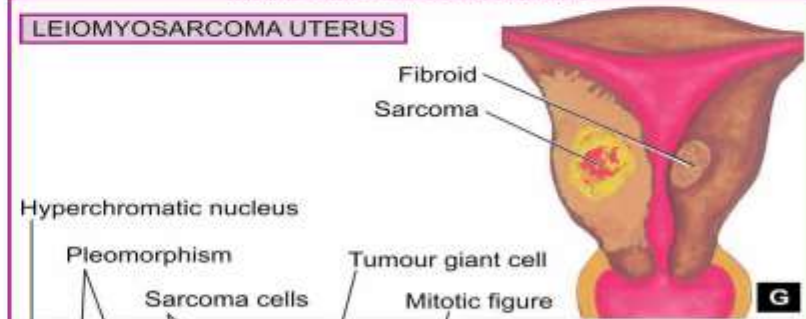
BENIGN MESENCHYMAL

LEIOMYOMA UTERUS



MALIGNANT MESENCHYMAL

LEIOMYOSARCOMA UTERUS



Differentiation

- = kemiripin sel tumor dengan sel normal.
- Benign neoplasm → sangat mirip dengan sel normal
- Malignant neoplasm → 4 kategori
 - Well differentiated
 - Moderate differentiated
 - Poorly differentiated
 - Undifferentiated
- Hilangnya differensiasi → **ANAPLASIA**
→hallmark of cancer !!

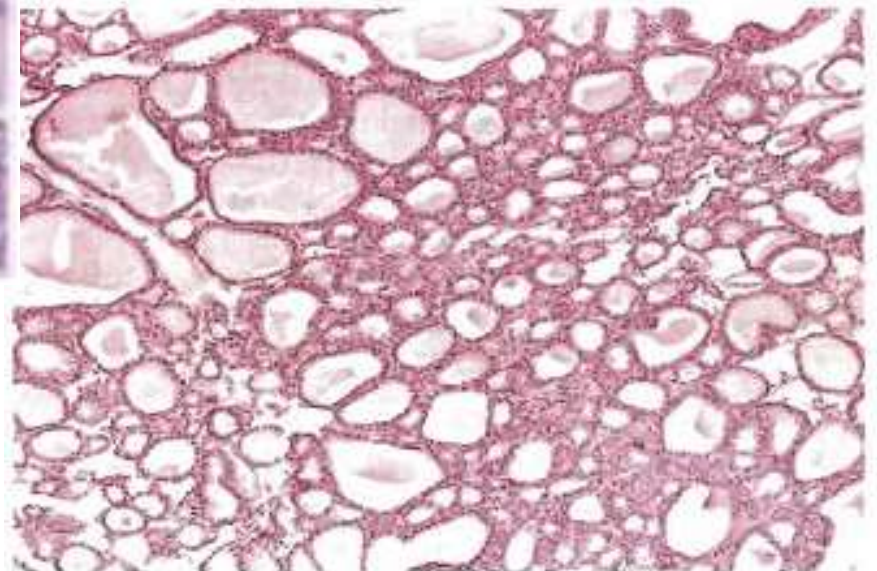
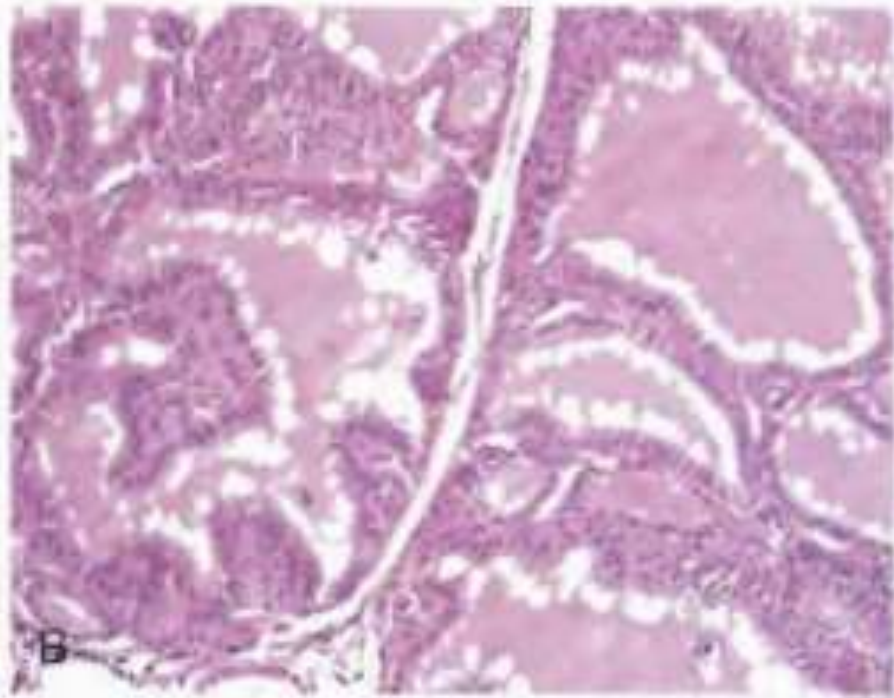


FIGURE 7-5 Benign tumor (adenoma) of the thyroid. Note the normal-looking (well-differentiated), colloid-filled thyroid follicles. (Courtesy of Dr. Trace Worrell, University of Texas Southwestern Medical School, Dallas, TX.)

ANAPLASIA

- Nuclear & cellular pleomorphisme
- Hyperchromasia
- Nuclear-cytoplasmic ratio (N/C) > 1
- Abundant mitosis (abnormal mitotic)
- Loss of polarity
- Tumor giant cell

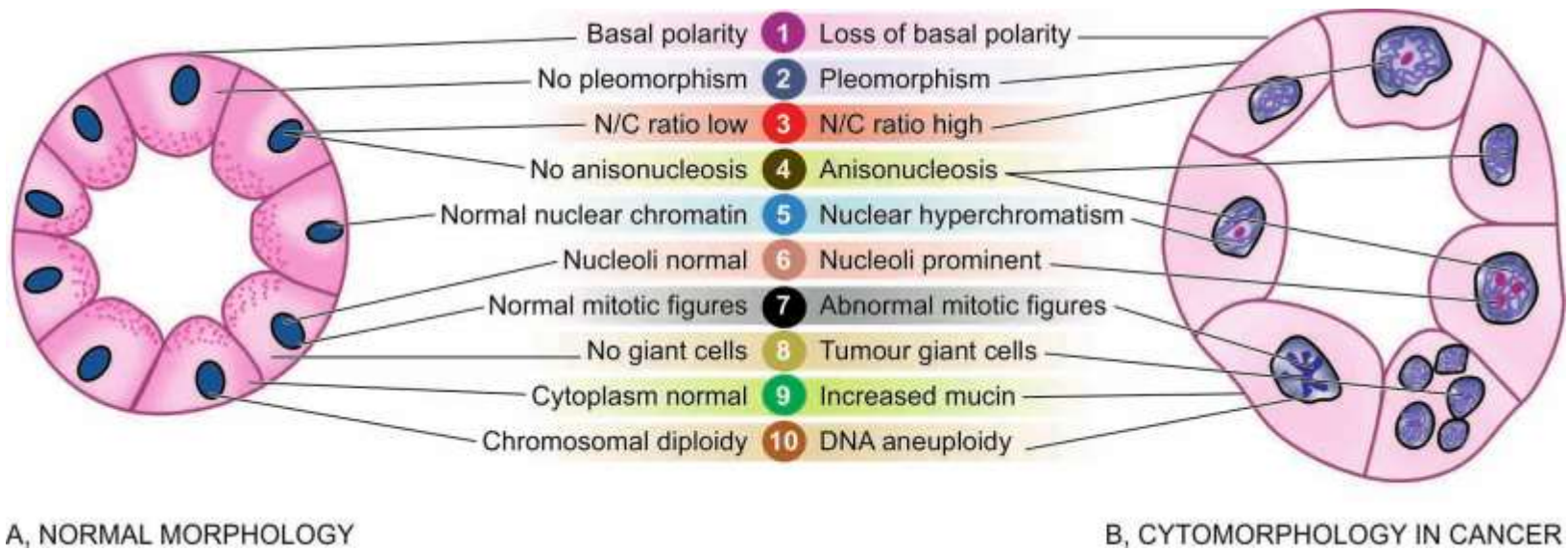


Figure 7.4 Diagrammatic representation of cytomorphologic features of neoplastic cells. Characteristics of cancer (B) are contrasted with the normal appearance of an acinus (A).

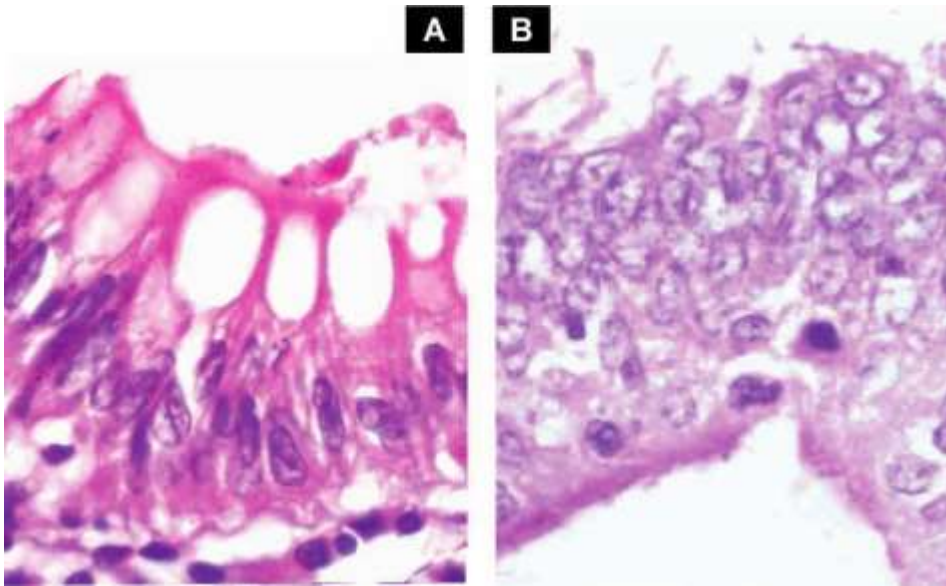
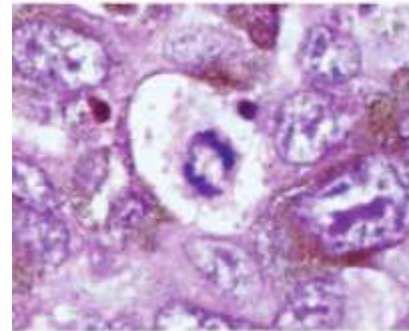
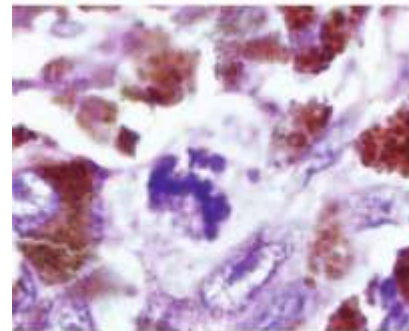
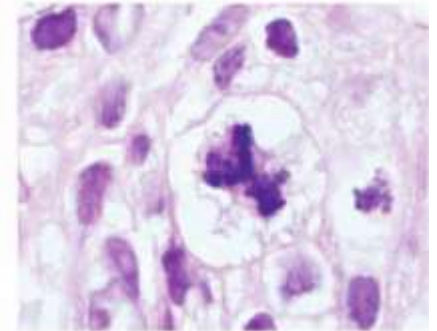


Figure 7.5 Microscopic appearance of loss of nuclear polarity (B) contrasted with normal basal polarity in columnar epithelium (A). The basement membrane is intact in both.

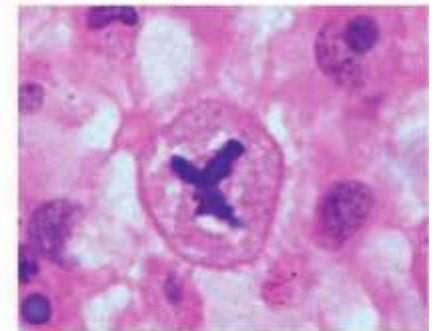
BIPOLAR MITOSIS



ABNORMAL MITOSIS



ABNORMAL MITOSIS



ABNORMAL MITOSIS

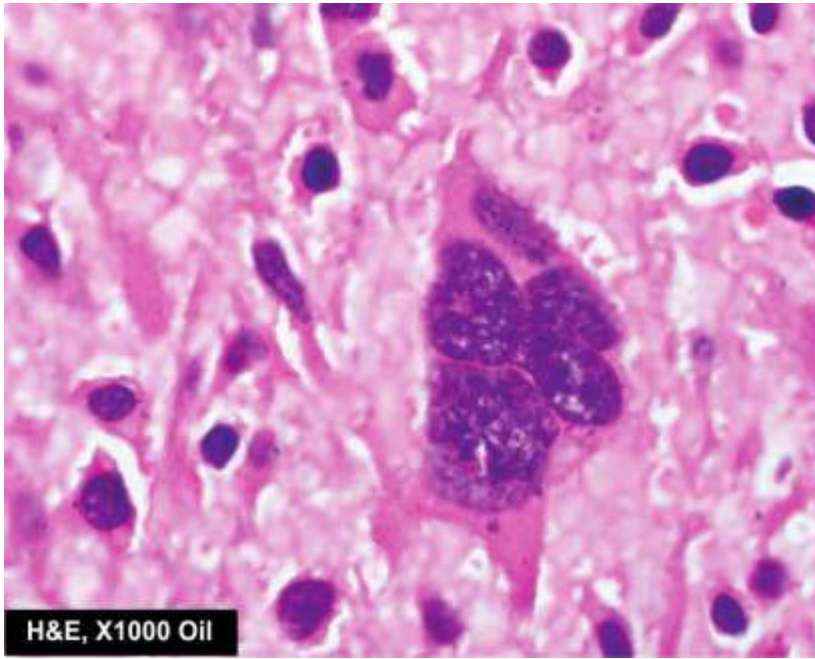


Figure 7.8 A multinucleate tumour giant cell in osteosarcoma.

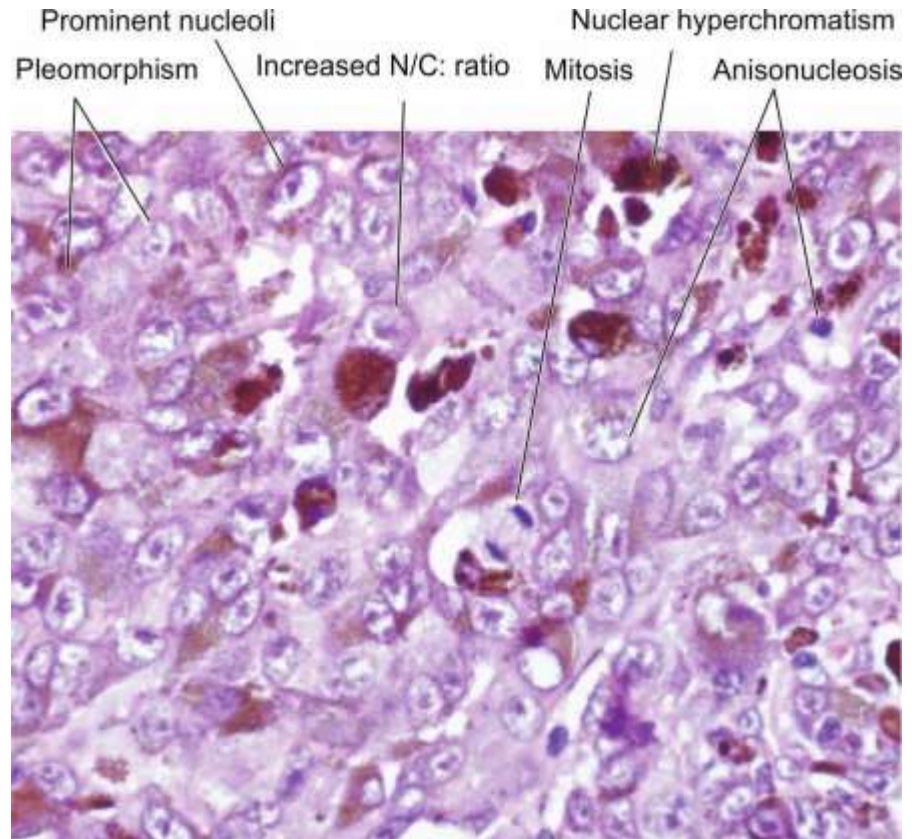


Figure 7.6 Nuclear features of malignant cells in malignant melanoma—pleomorphism, anisonucleosis, increased N/C: ratio, nuclear hyperchromatism and prominent nucleoli.

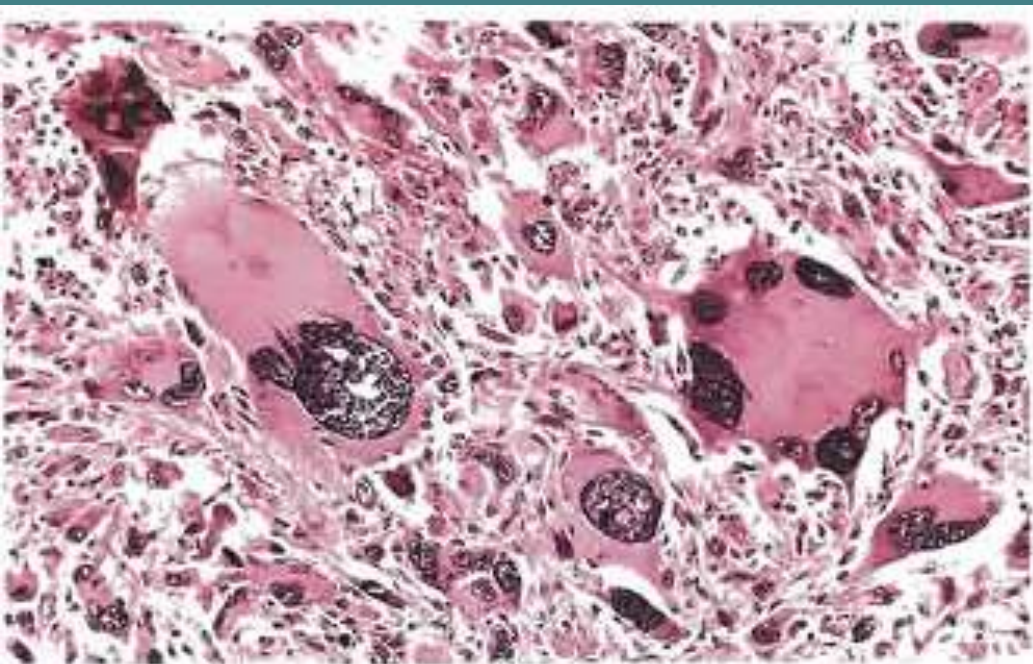


FIGURE 7-8 Anaplastic tumor of the skeletal muscle (rhabdomyosarcoma). Note the marked cellular and nuclear pleomorphism, hyperchromatic nuclei, and tumor giant cells. (Courtesy of Dr. Trace Worrell, University of Texas Southwestern Medical School, Dallas, TX.)

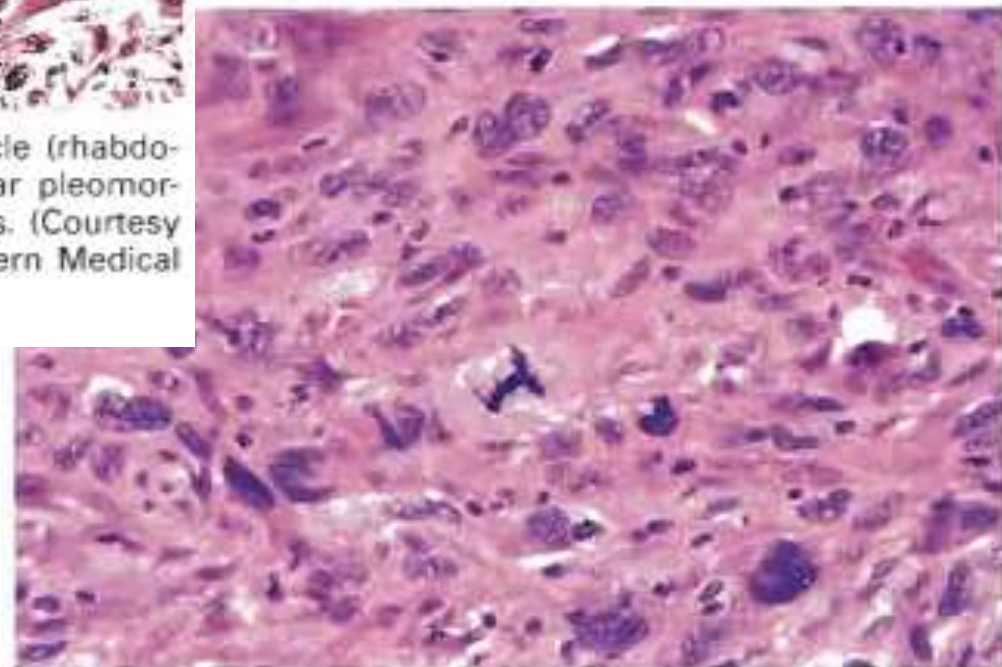


FIGURE 7-9 Anaplastic tumor showing cellular and nuclear variation in size and shape. The prominent cell in the center field has an abnormal tripolar spindle.

Dysplasia

- Disorder, non-neoplastic growth
- Biasanya pada epitel (cervix)
- Dibagi menjadi:
 - Ringan (mild)
 - Sedang (moderate)
 - Berat (severe)
- Kalau mengenai seluruh ketebalan epitel →
CARCINOMA IN SITU

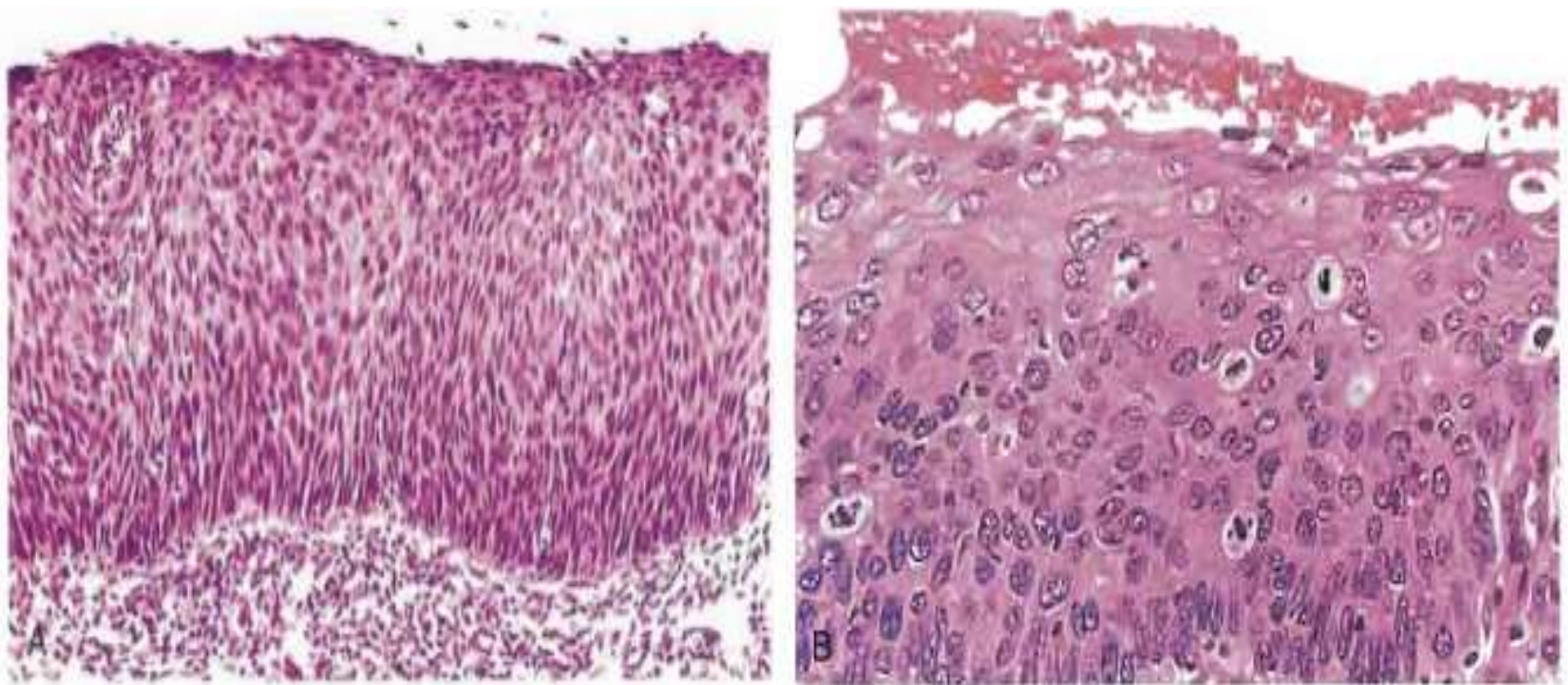


FIGURE 7-10 **A**, Carcinoma in situ. This low-power view shows that the entire thickness of the epithelium is replaced by atypical dysplastic cells. There is no orderly differentiation of squamous cells. The basement membrane is intact, and there is no tumor in the subepithelial stroma. **B**, A high-power view of another region shows failure of normal differentiation, marked nuclear and cellular pleomorphism, and numerous mitotic figures extending toward the surface. The basement membrane is not seen in this section.

Rates of Growth

- Bergantung pada 3 parameter :
 - Doubling time sel tumor
 - Jumlah sisa sel di proliferative pool (growth fraction)
 - Kecepatan sel tumor lepas dari sekitarnya
- Malignant tumor → doubling time yang cepat dan kematian sel yang rendah → daya proliferasinya tinggi

Local invasion

- **Benign**
 - Massa cohesive berbatas jelas yang dibungkus kapsul → menekan jaringan sekitar
 - Didapatkan celah antara tumor dan jaringan sekitar → terapi dapat enukleasi
- **Malignant**
 - Tumbuh invasive dan infiltratif, serta merusak jaringan sekitar
 - Tidak didapatkan kapsul dan celah (cleavage) → enukleasi susah dilakukan



FIGURE 7-12 Fibroadenoma of the breast. The tan-colored, encapsulated small tumor is sharply demarcated from the whiter breast tissue.

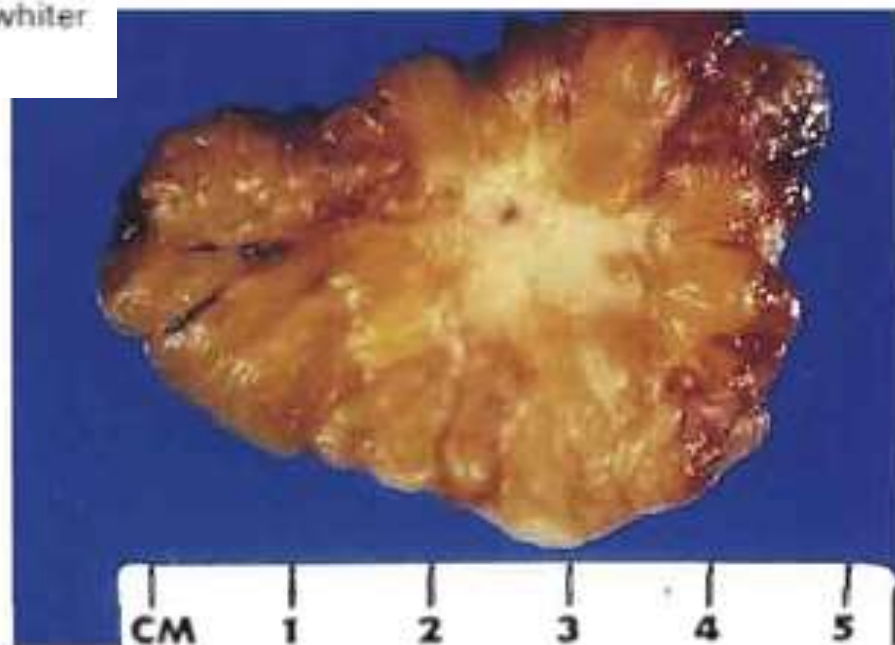


FIGURE 7-14 Cut section of an invasive ductal carcinoma of the breast. The lesion is retracted, infiltrating the surrounding breast substance, and would be stony hard on palpation.

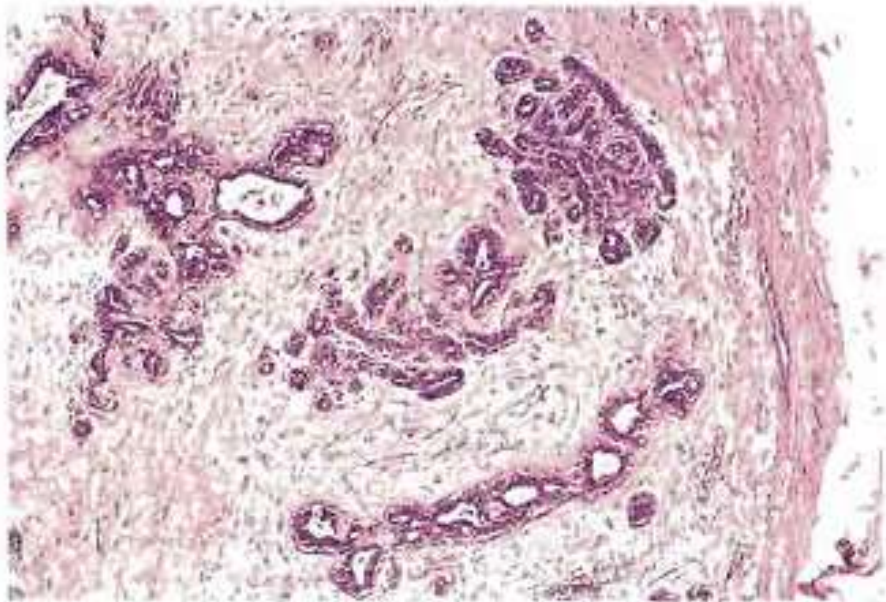


FIGURE 7-13 Microscopic view of fibroadenoma of the breast seen in Figure 7-12. The fibrous capsule (*right*) delimits the tumor from the surrounding tissue. (Courtesy of Dr. Trace Worrell, University of Texas Southwestern Medical School, Dallas, TX.)

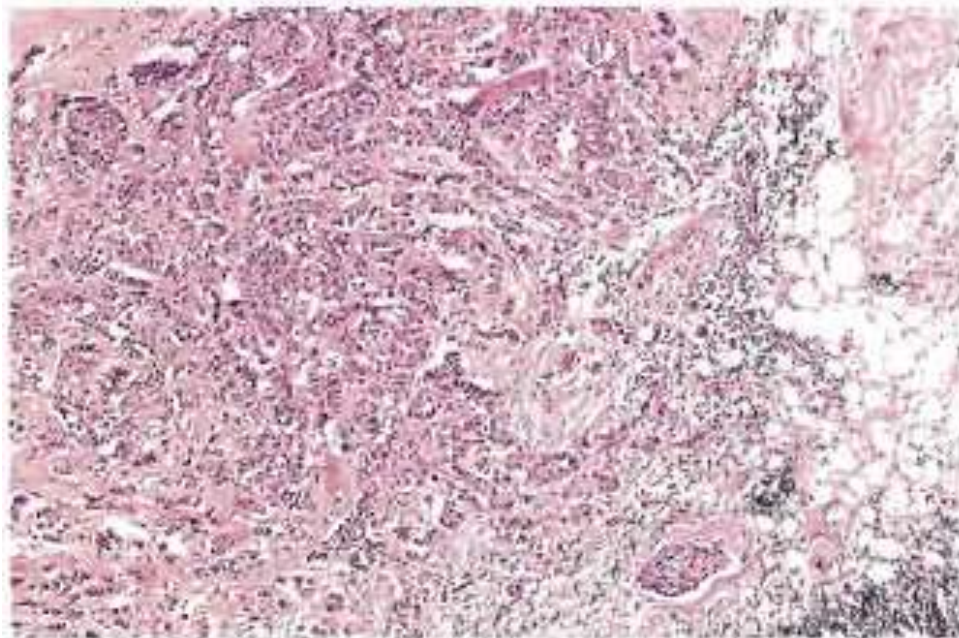


FIGURE 7-15 The microscopic view of the breast carcinoma seen in Figure 7-14 illustrates the invasion of breast stroma and fat by nests and cords of tumor cells (compare with fibroadenoma shown in Fig. 7-13). The absence of a well-defined capsule should be noted. (Courtesy of Dr. Trace Worrell, University of Texas Southwestern Medical School, Dallas, TX.)

Metastasis (Distant Spread)

- Karakteristik Malignant : Anaplasia, Invasi, Metastasis
- MALIGNANT !!!! → kecuali:
 - Brain tumor
 - Basal cell kulit
- Pathways of spread :
 - Spread into body cavities
 - Invasion of lymphatics → Carcinoma
 - Hematogenous spread → Sarcoma

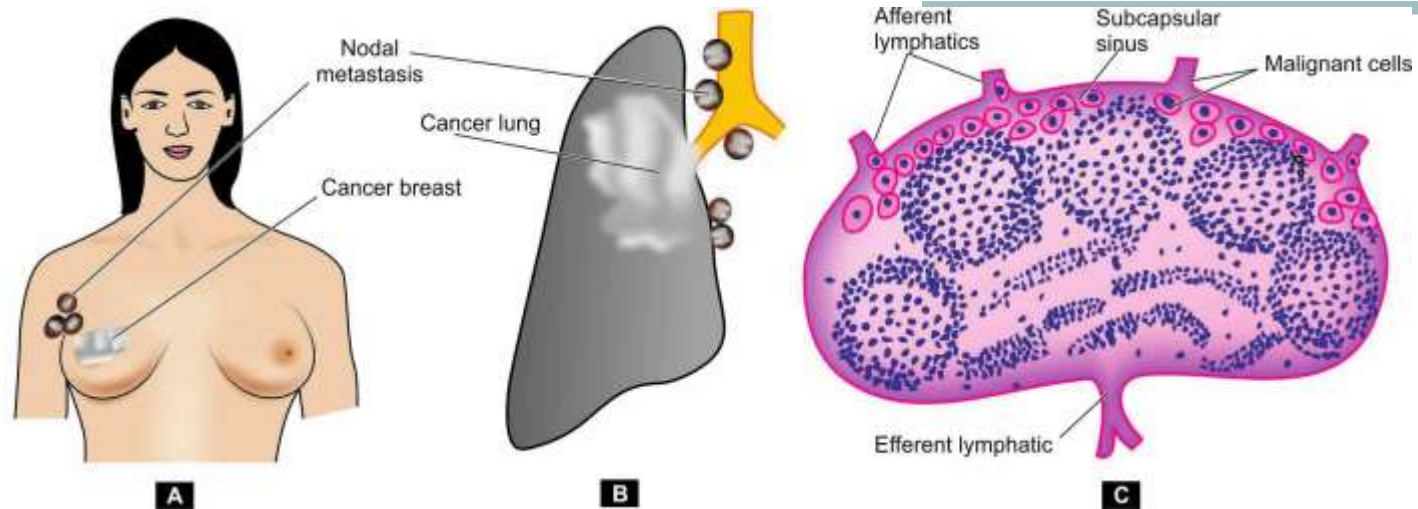


Figure 7.11 Regional nodal metastasis. A, Axillary nodes involved by carcinoma breast. B, Hilar and para-tracheal lymph nodes involved by bronchogenic carcinoma. C, Lymphatic spread begins by lodgement of tumour cells in subcapsular sinus via afferent lymphatics entering at the convex surface of the lymph node.

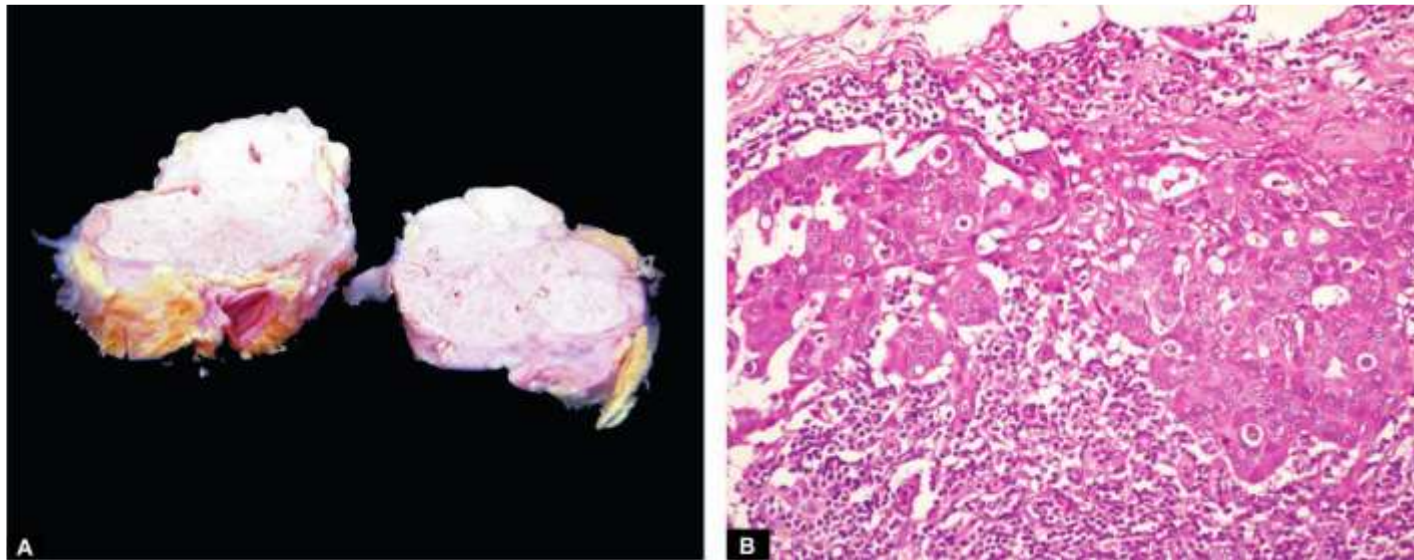


Figure 7.12 Metastatic carcinoma in lymph nodes. A, Matted mass of lymph nodes is surrounded by increased fat. Sectioned surface shows merging capsules of lymph nodes and replacement of grey brown tissue of nodes by large grey white areas of tumour. B, Masses of malignant cells are seen in the subcapsular sinus and extending into the underlying nodal tissue.

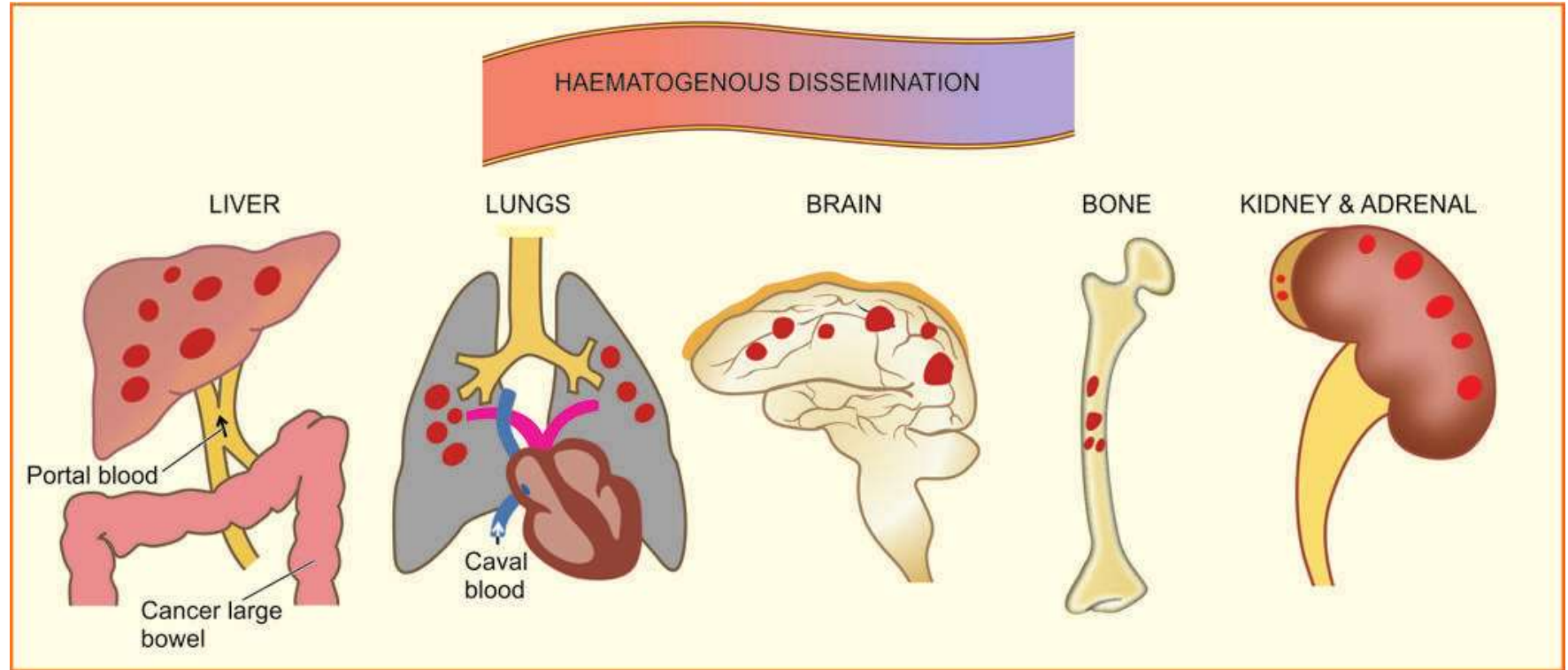


Figure 7.13 Gross appearance of haematogenous metastases at common sites.

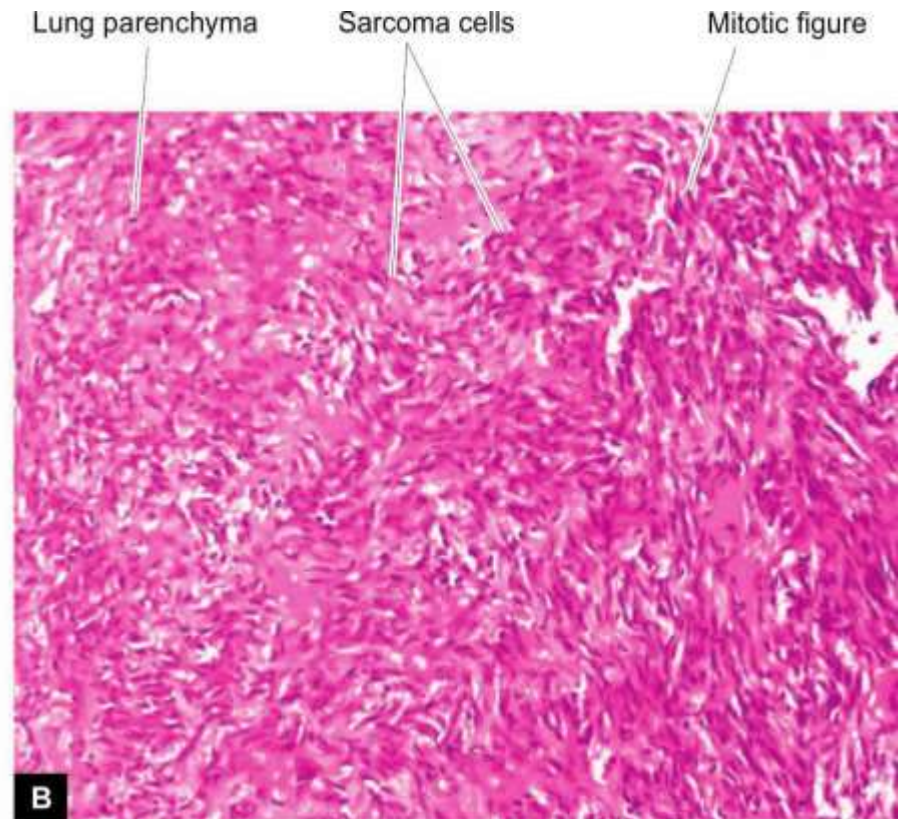
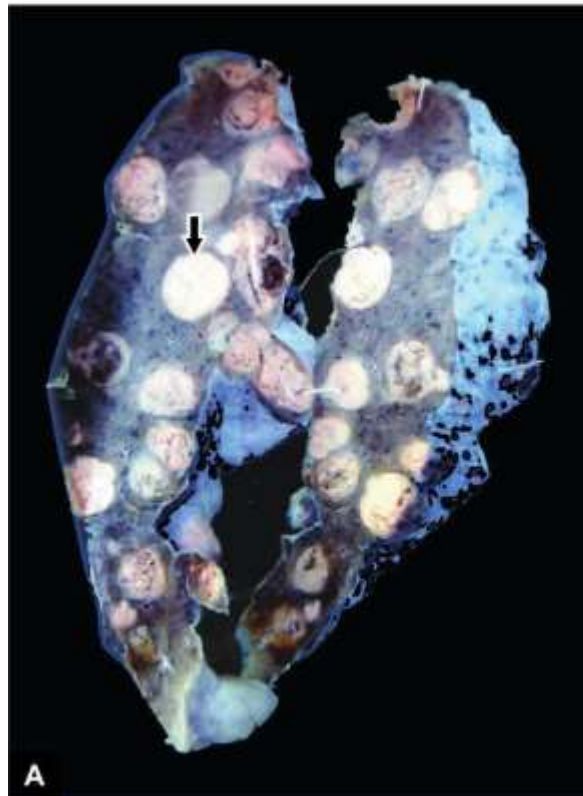


Figure 7.14 Metastatic sarcoma lung. A, Sectioned surface of the lung shows replacement of slaty-grey spongy parenchyma with multiple, firm, grey-white nodular masses, some having areas of haemorrhages and necrosis. B, Microscopic appearance of pulmonary metastatic deposits from sarcoma.

Spread along body cavities

- Transcoelomic spread → menembus dinding serosa dan implantasi di sekitar
 - Ca Gaster metastasis di ovarium
 - Ca ovarium metastasis di peritoneum
 - Ca brochus metastasis di pleura
- Spread along epithelium-line surface
 - Ca ovarium metastasis di tuba-uterus
 - Ca cervix metastasis di corpus uteri

- Spread into cerebrospinal fluid
 - Ependyma dan leptomeningas metastasis di sepanjang CNS
- Implantation
 - Latrogenic → pisau bedah, jarum dll

Invasion & Metastasis

1. Detachment of tumor cells from each other
2. Attachment to matrix component
3. Degradation of ECM
4. Migration of tumor cell

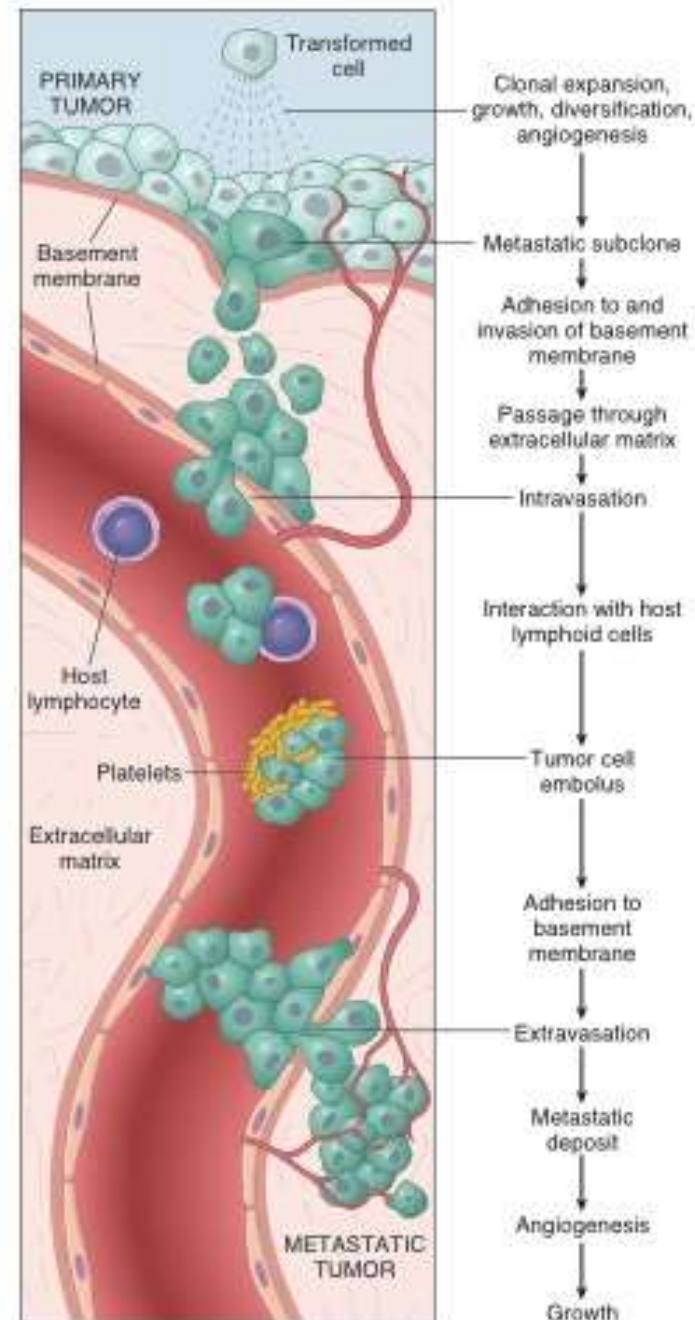
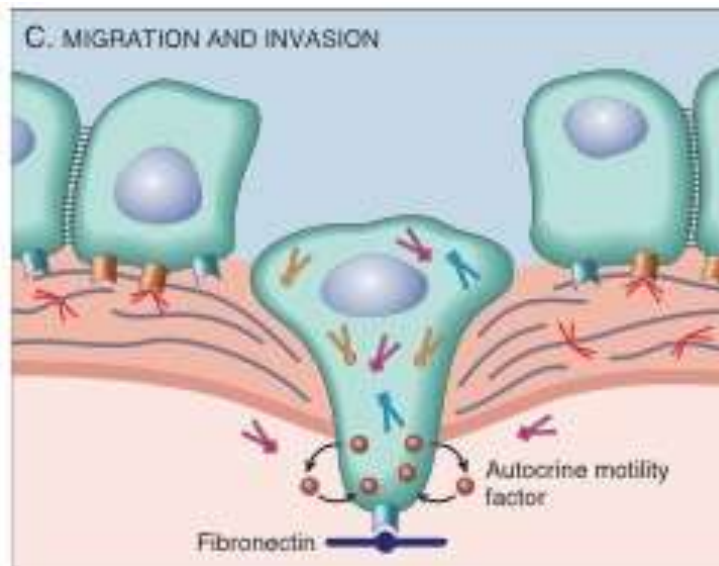
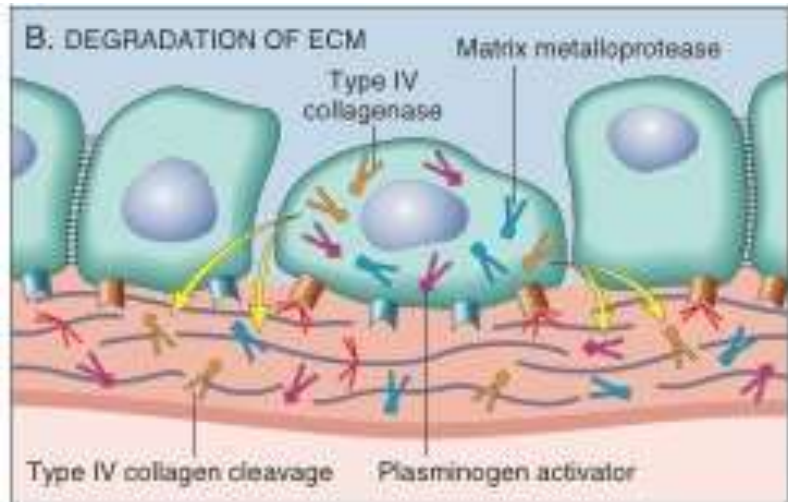
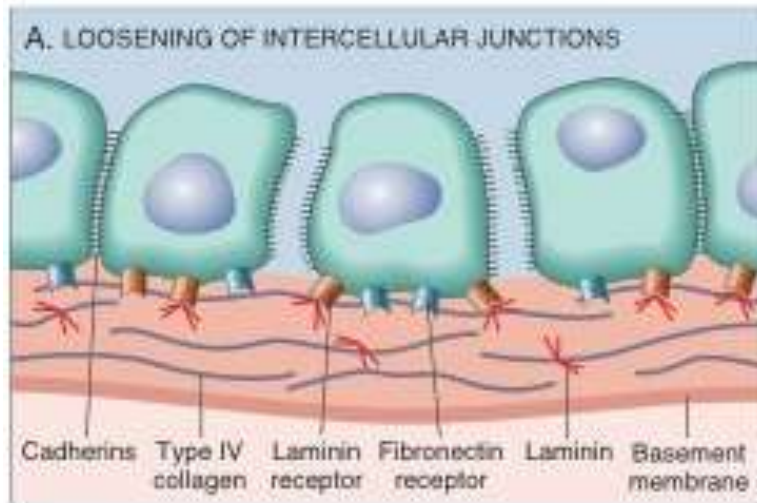


Figure 7-38 The metastatic cascade. Sequential steps involved in the hematogenous spread of a tumor.



Prognostic Indicator

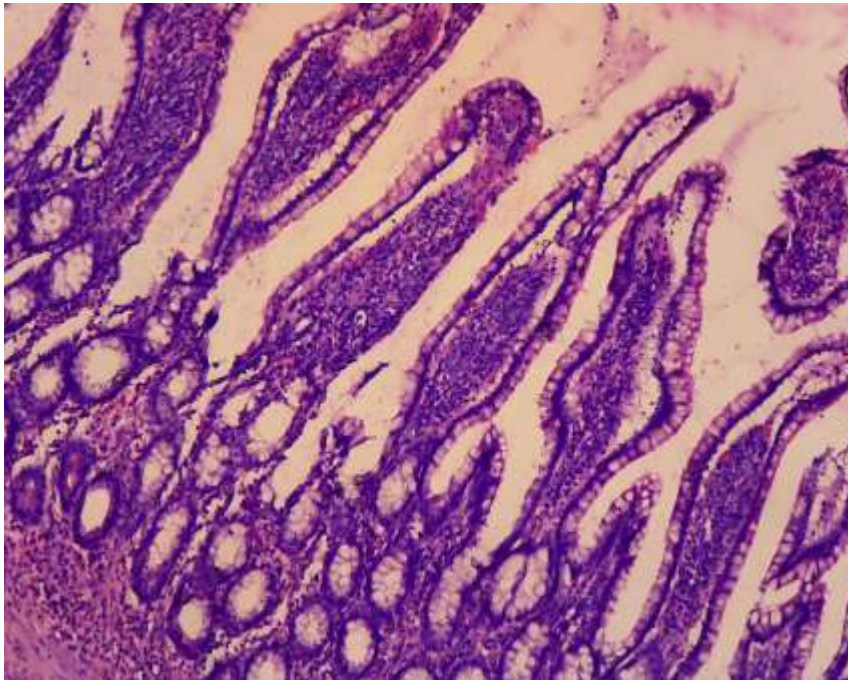
- **Clinical marker :**
 - Size, histologic grade, nodal involvement, vascular invasion
- **Molecular marker :**
 - Ki-67 → Proliferative rate
 - VEGF → angiogenesis
 - E-cadherin, MMP-9 → metastasis
 - Spesifik marker : ER, PR, CD45

GRADING dan STAGING

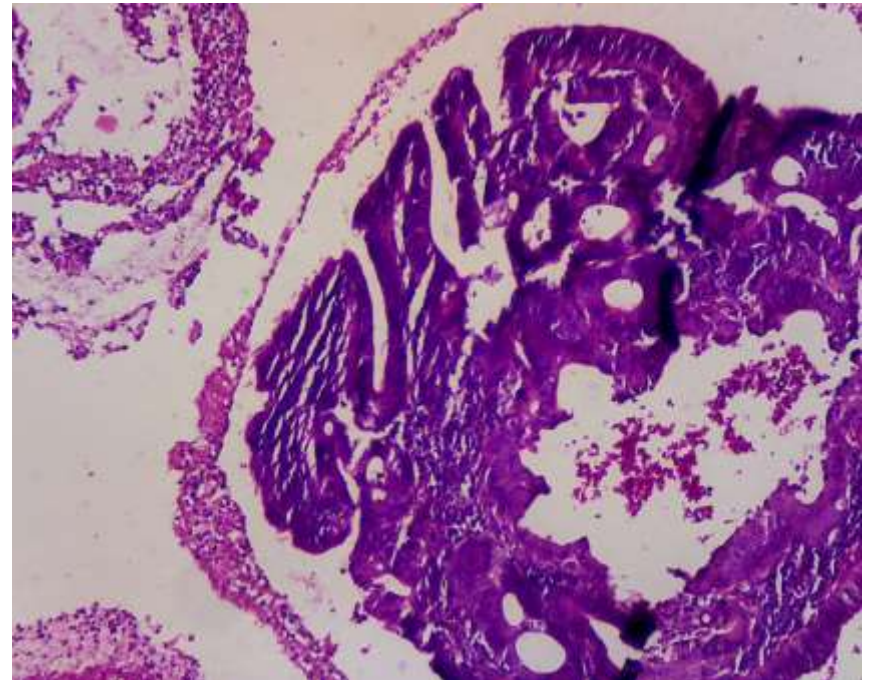
- Grading → differensiasi
 - Broder's grading :
 - Grade I : Well differentiated (25% anaplastic cell)
 - Grade II : Moderately diff (25-50%)
 - Grade III : Poorly diff (50-75%)
 - Grade IV : Undiff (> 75%)
- Staging
 - TNM
 - AJC

- **TNM**
 - T → Tumor size
 - N → nodal metastasis
 - M → distant metastasis
- **AJC (Americant Joint Comitte)**
 - Stage I-IV → Size, Nodal metastasis, dan distant metastasis)
- **Khusus :**
 - FIGO → uterus
 - Gleason → Prostat
 - DUKES → Colon

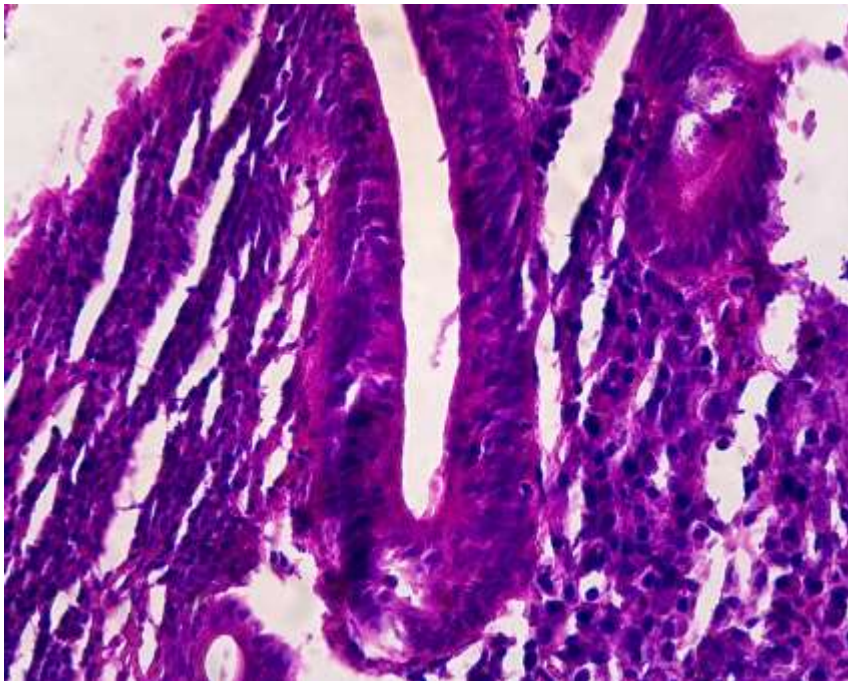
Usus normal



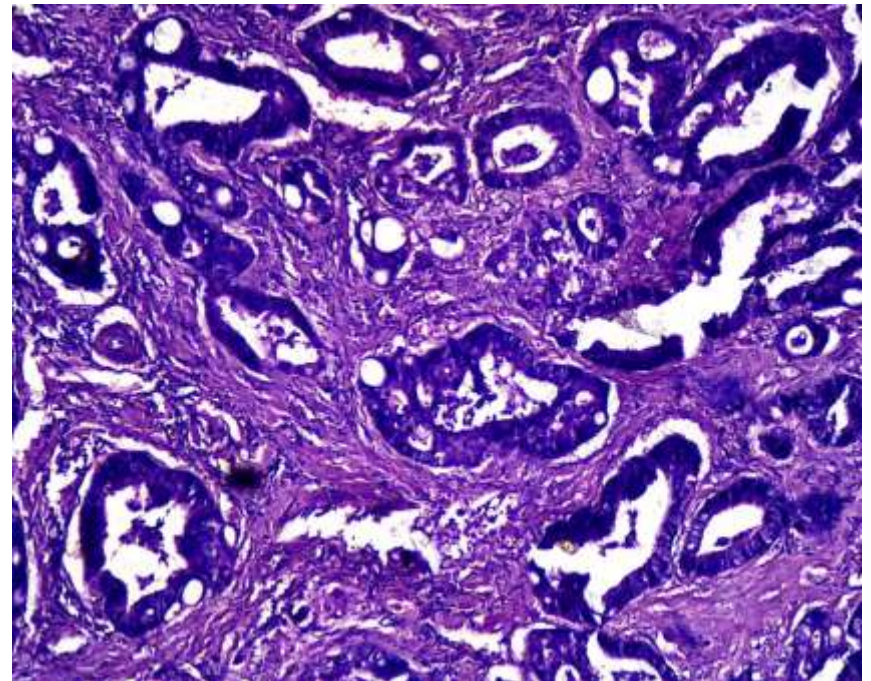
Displasia berat



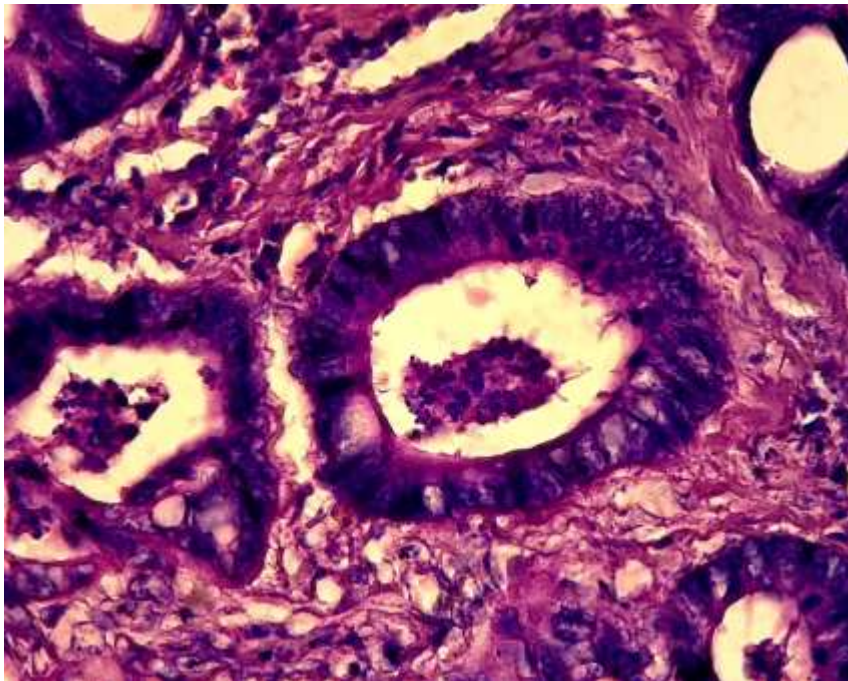
Displasia berat



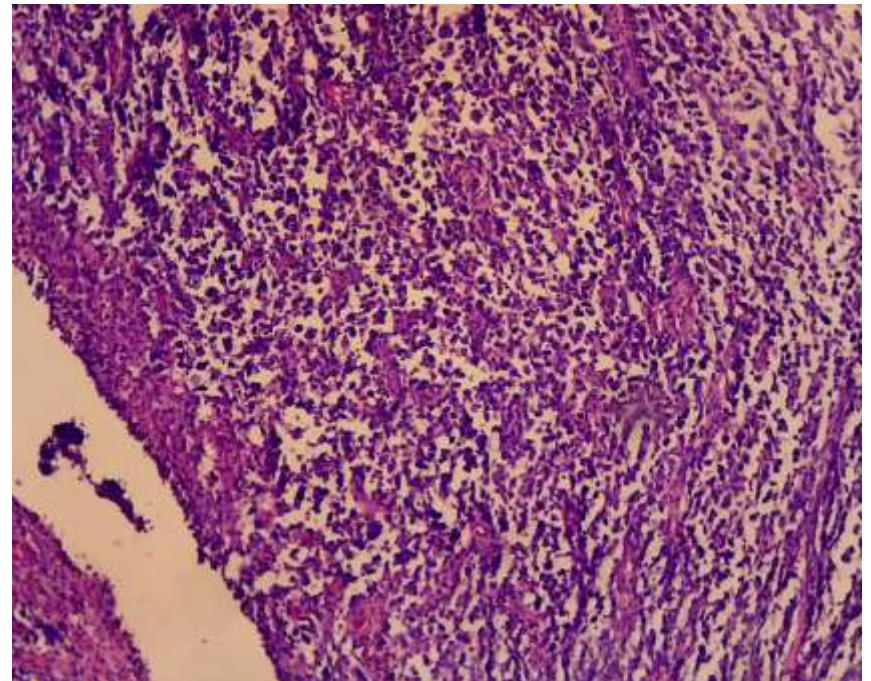
Adeno ca well diff



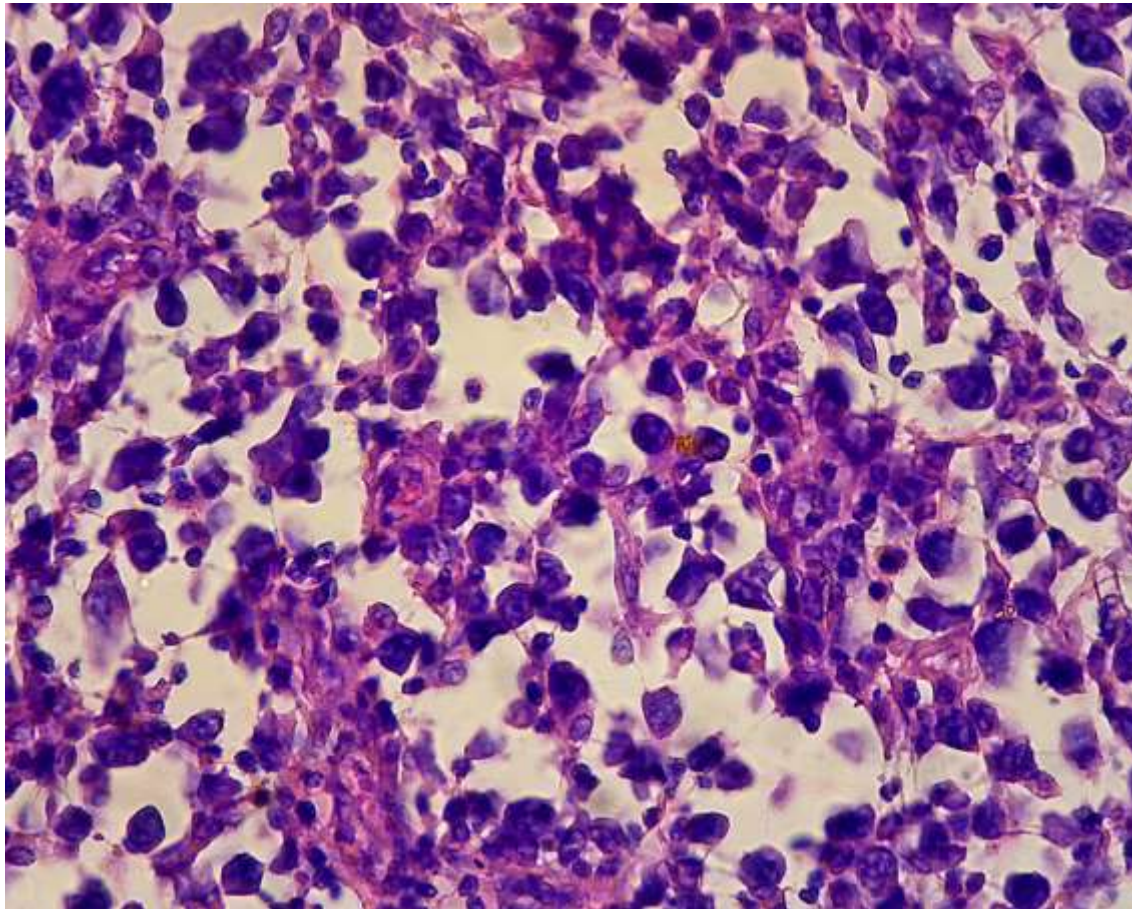
Adeno ca well diff



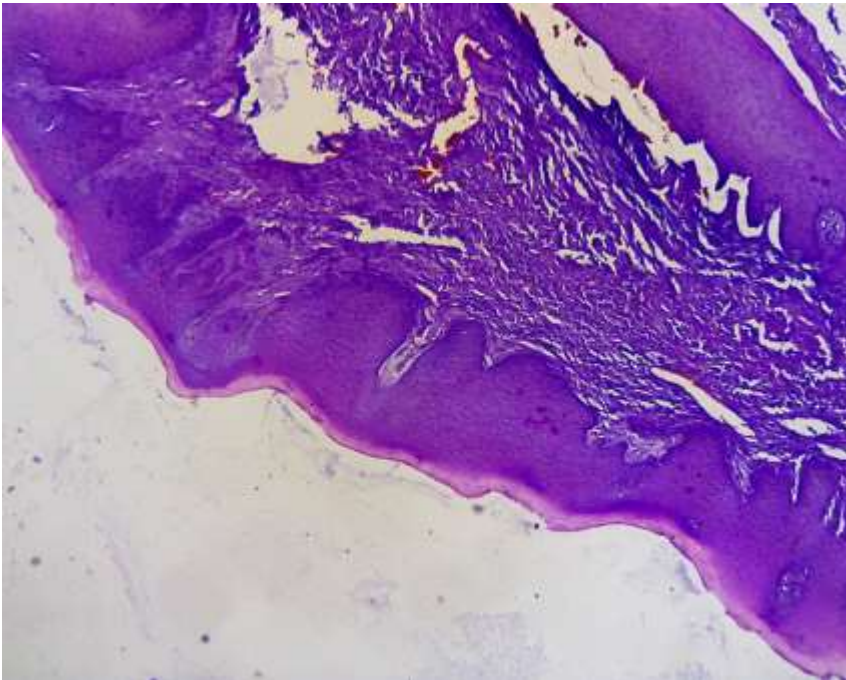
Adeno ca poorly diff



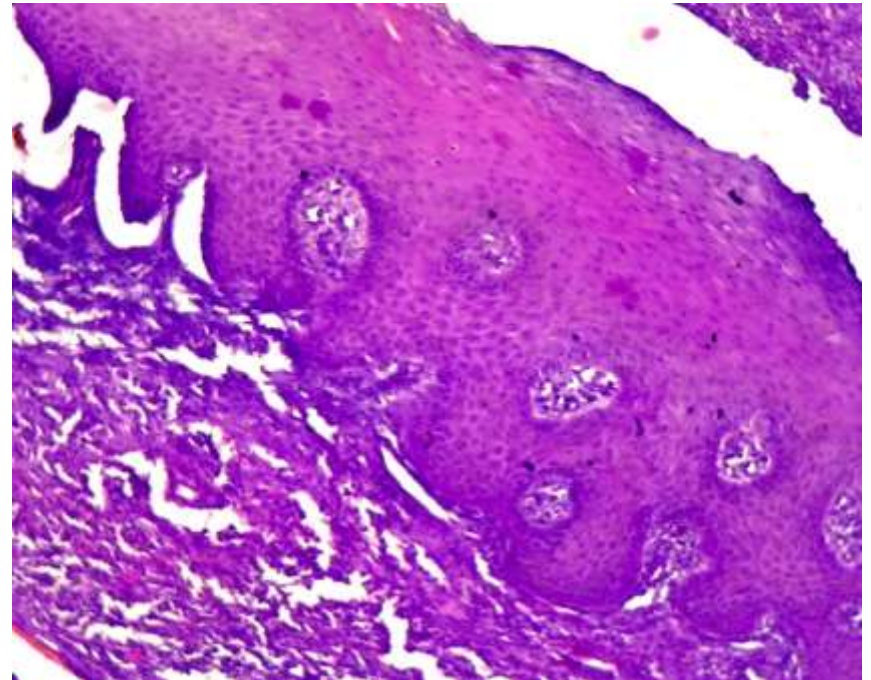
- Adeno ca poorly diff



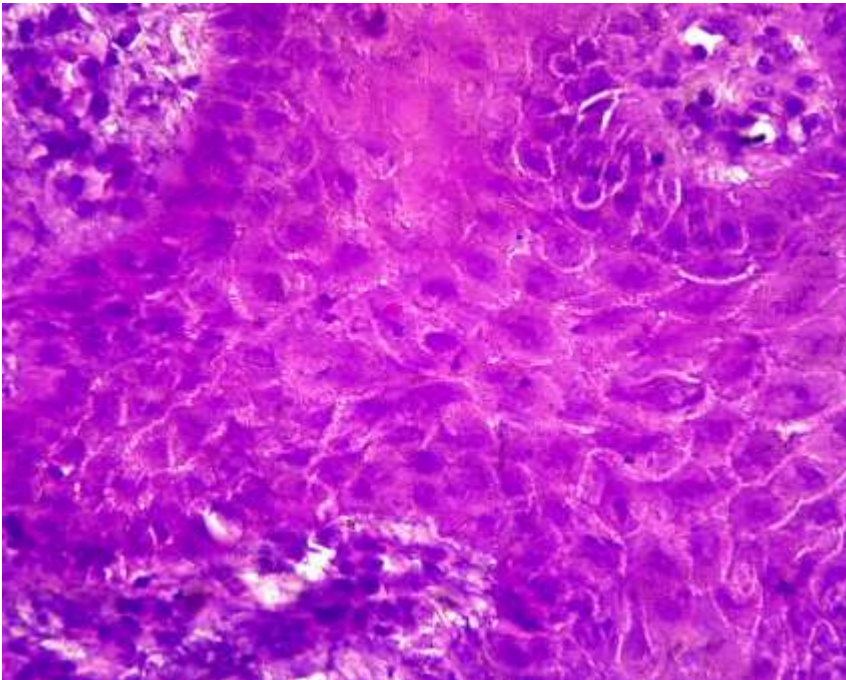
Squamous papilloma



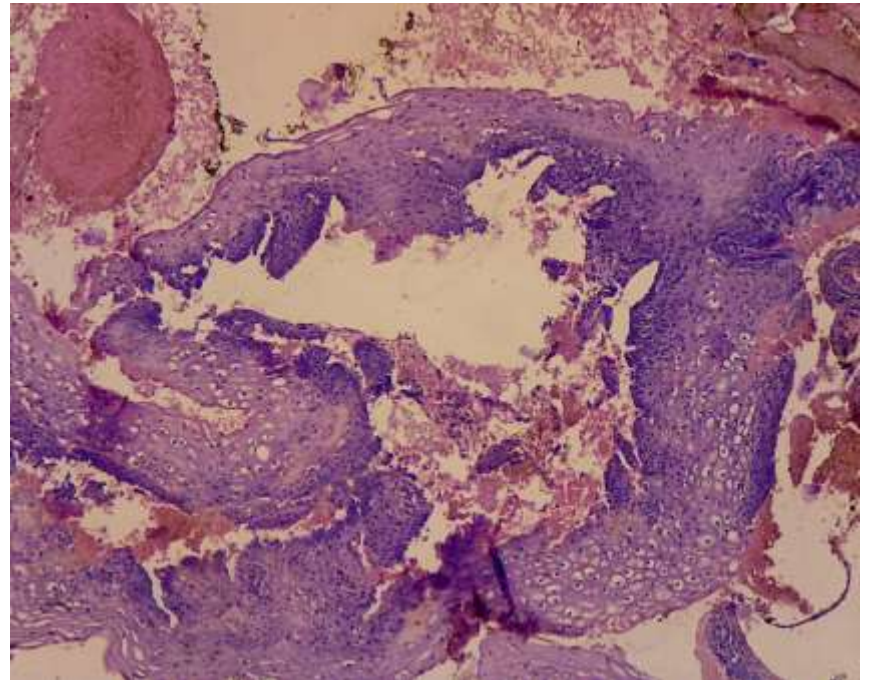
Squamous papilloma



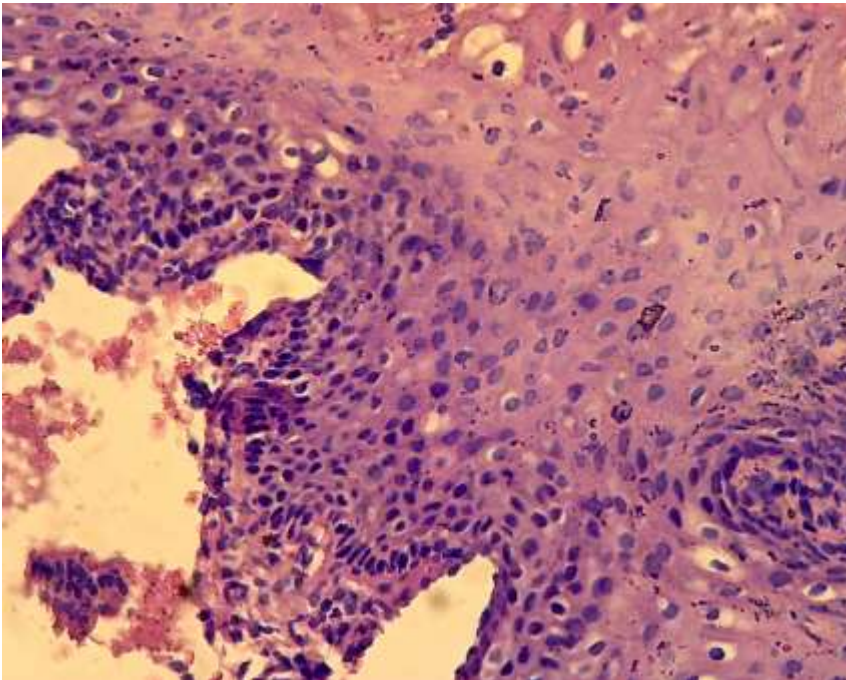
Squamous papilloma



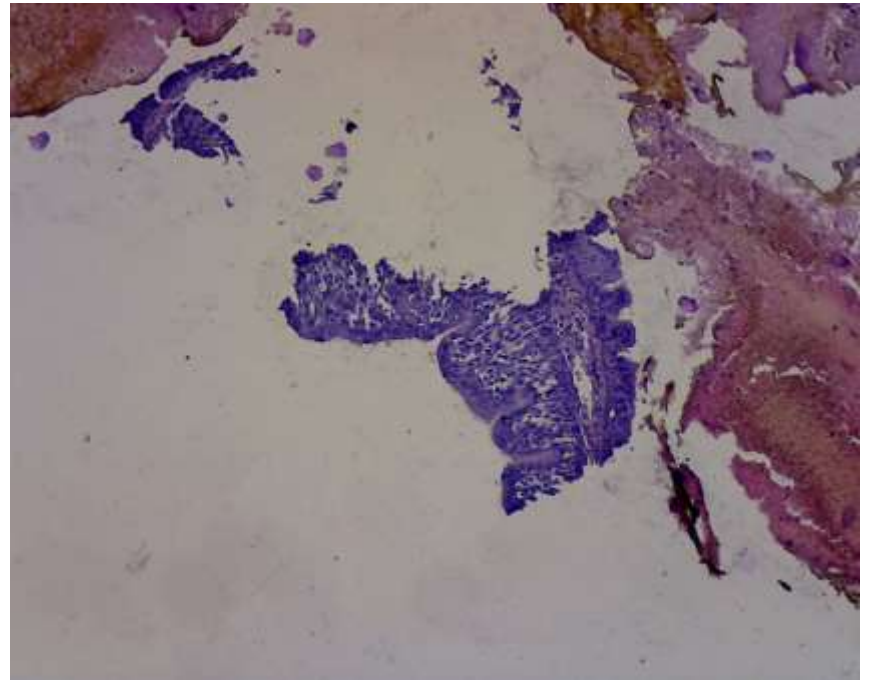
Koilocytosis (CIN 1)



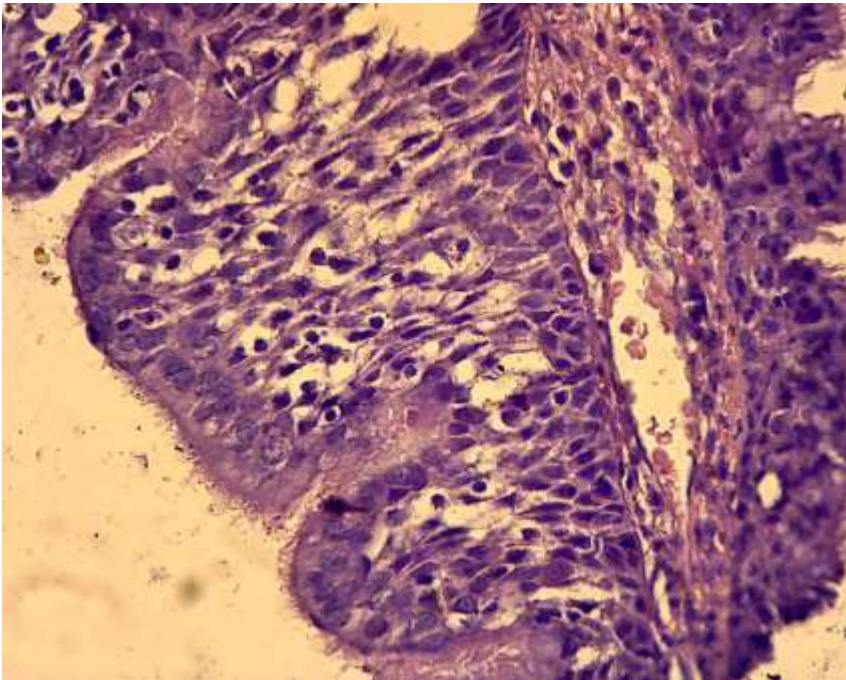
Koilositos (CIN 1)



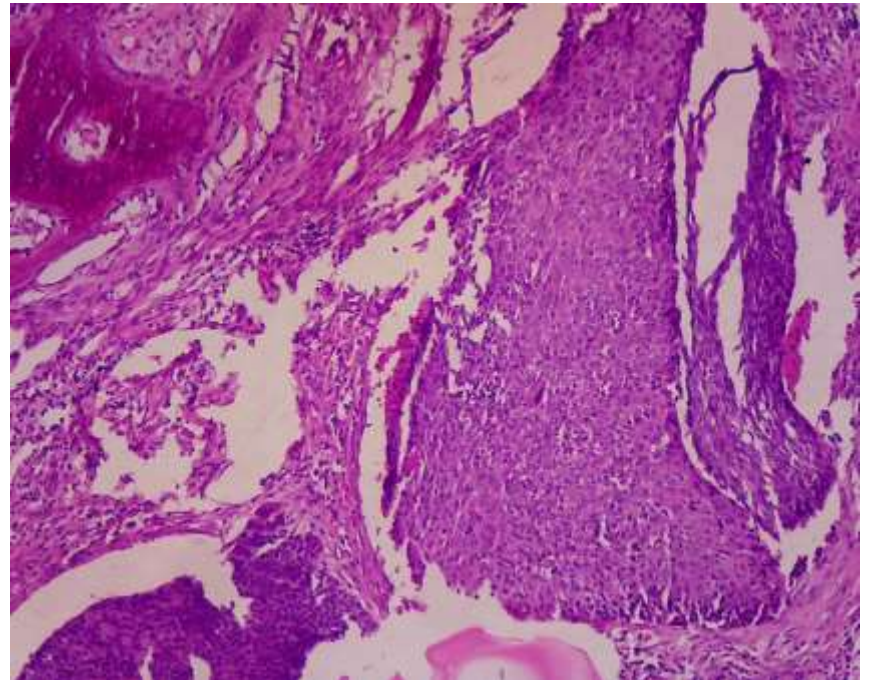
HSIL (displasia berat)



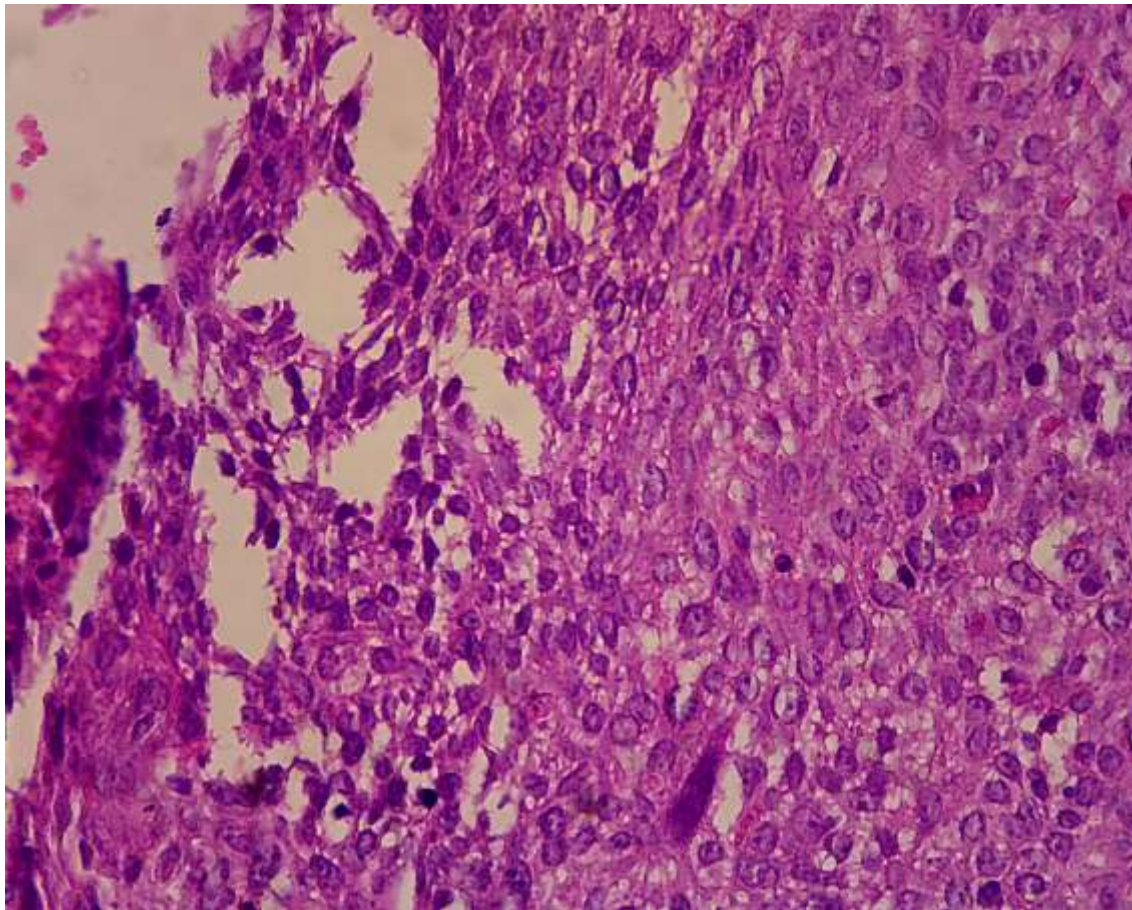
HSIL (displasia berat)



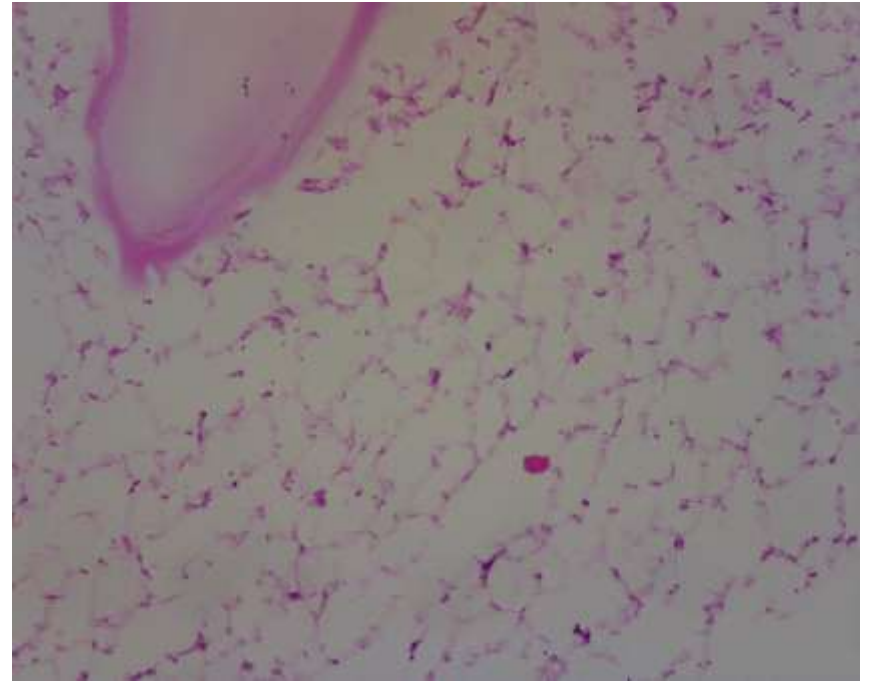
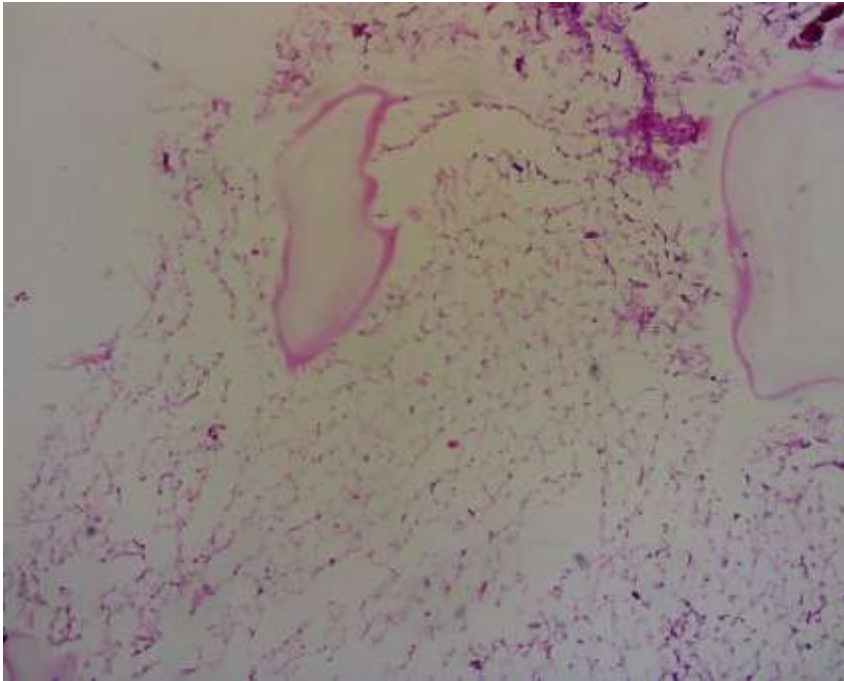
SCC well diff



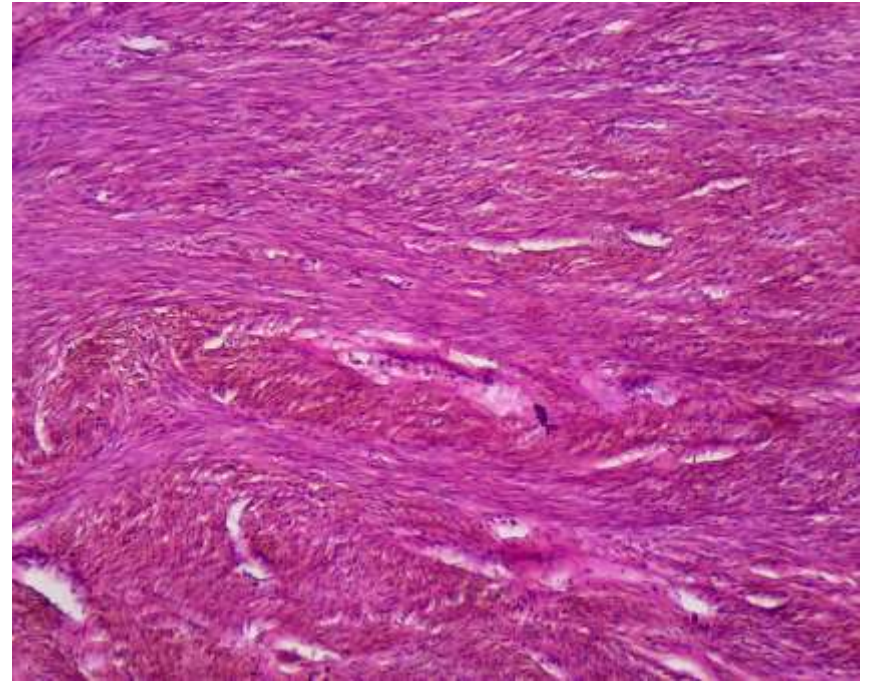
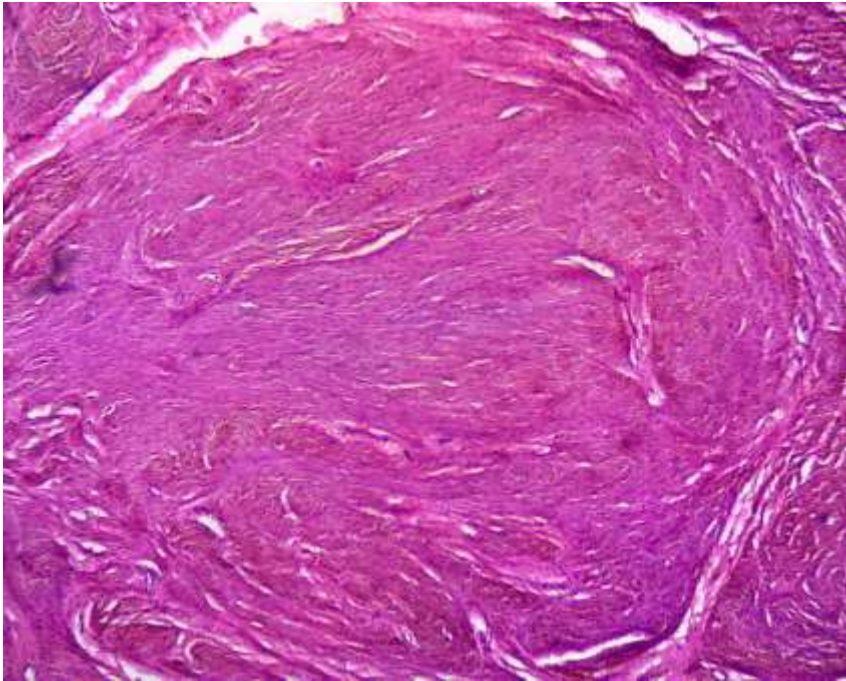
SCC Well diff



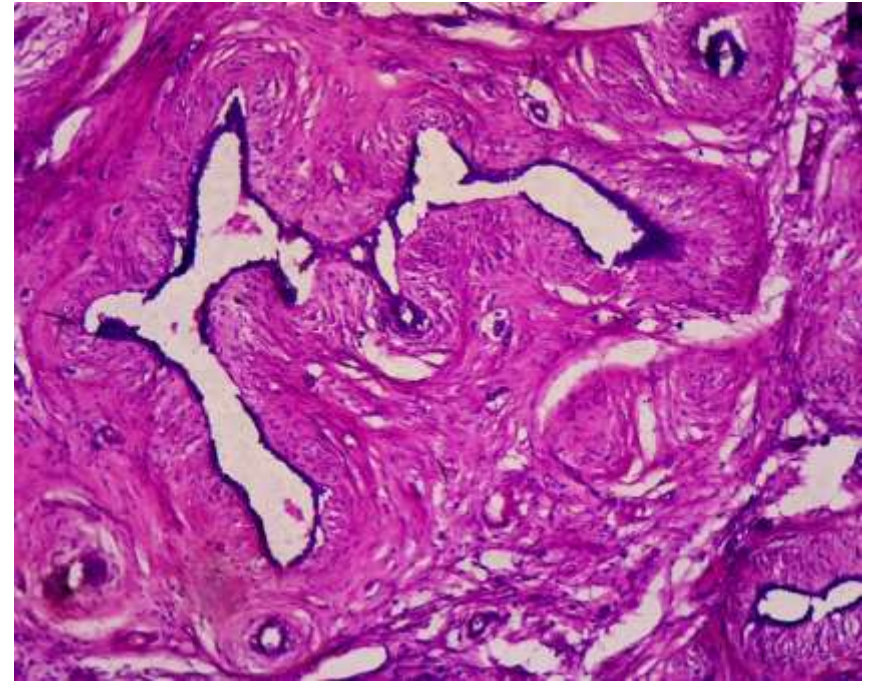
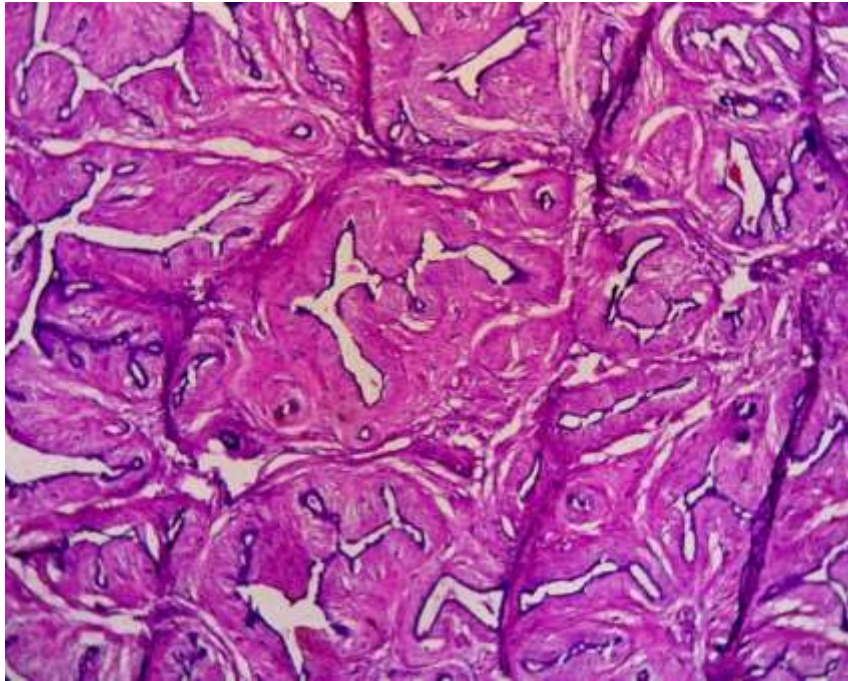
Lipoma



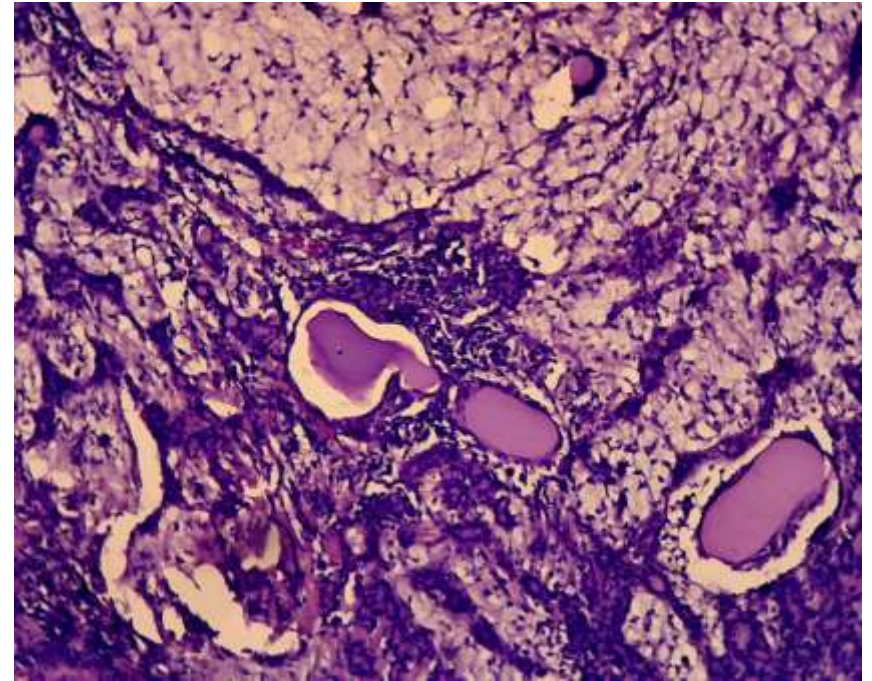
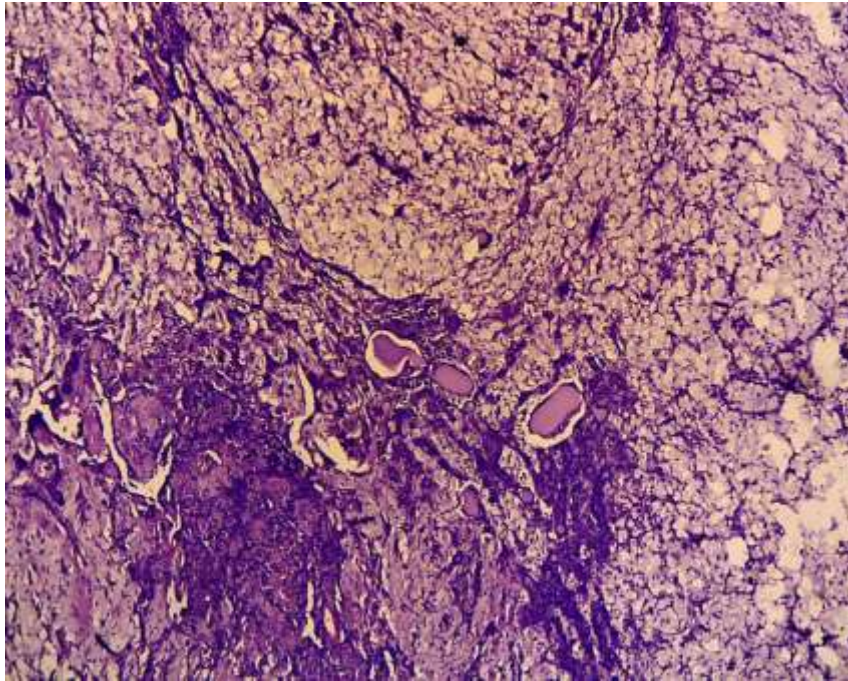
Leiomyoma



FAM



Pleomorphic Adenoma



Referensi :

- Kumar, Abbas, Aster. 2015. Robbins and Cotran Pathologic Basis of Disease, 9th edition. Elsevier
- Kumar, Abbas, Aster. 2018. Robbins Basic Pathology, 10th edition. Elsevier
- Ivan Damjanov, 2015. Text book of Pathology, 7th edition. Jaypee Brothers Medical Publisher
- Herrington, Simon. 2017. Muir Buku Ajar Patologi, Edisi 15. EGC