NEOPLASIA : 1

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Education is the key to unlocking the world, a passport to freedom.

-Oprah Winfrey

Neoplasia: Terminology

- Neoplasia is “new growth”
- Oncology(Greek oncos –tumor) study of tumors or neoplasms
- Cancer – common term for all malignant tumors derives from Latin for crab because a cancer “adheres to any part that it seizes upon in an obstinate manner like crab

Willis Definition:

A neoplasm is an abnormal mass of tissue the growth of which exceeds and is uncoordinated with that of normal tissue and persists in the same excessive manner after cessation of the stimuli which evoked the change.

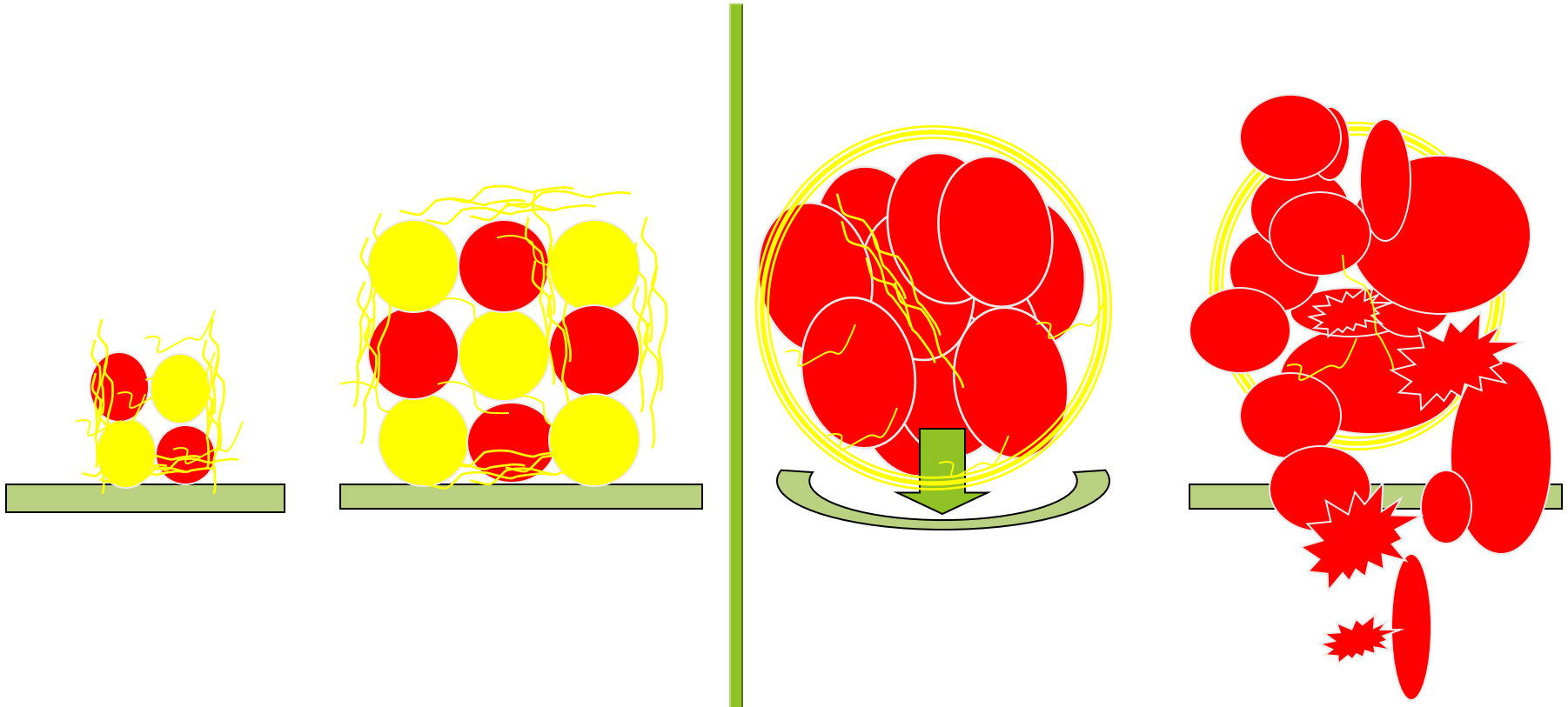
Thus neoplasia means:

An abnormal mass of tissue which differs from the normal in:

- **Growth**
- **Differentiation**
- **Function**
- **Organization**

Mechanism of Neoplasia

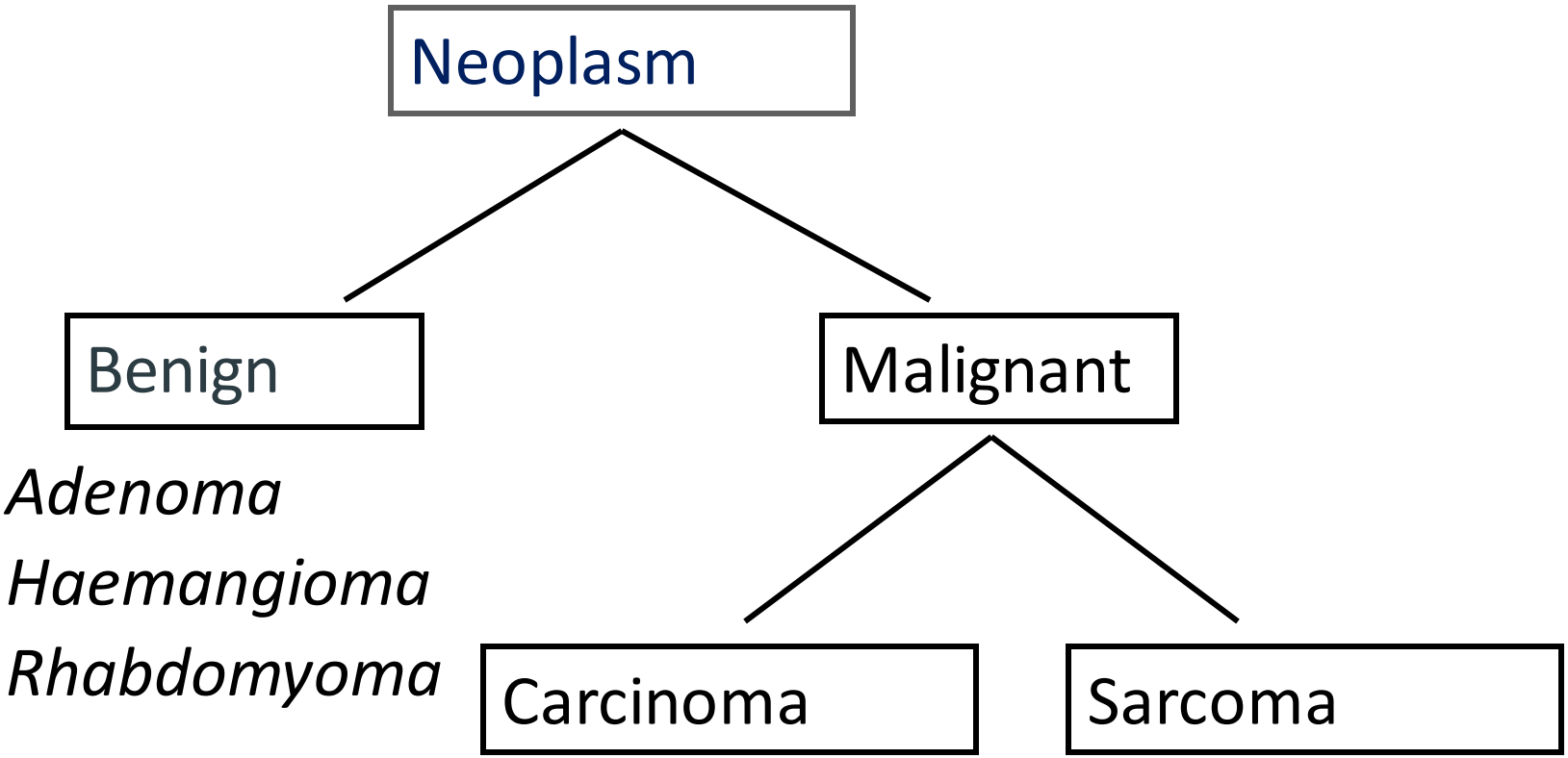
Normal Adaptation Benign Malignant



Non-Neoplastic
(Polyclonal)

Neoplastic
(Monoclonal)

Nomenclature



Nomenclature: Cell of origin + Suffix

Suffix - oma

- Fibroma
- Osteoma
- Adenoma
- Papilloma
- Chondroma

Carcinoma / Sarcoma

- Fibrosarcoma
- Osteosarcoma
  Adenocarcinoma
- Squamous cell carcinoma
- Chondrosarcoma

Mixed tumors

Pleomorphic Adenoma e.g. Mixed tumor of the salivary gland origin.

N.B. : Teratomas- tumors from totipotent cells containing parenchymal cells of all the 3 germ layers e.g. dermoid cyst

Table 7-1 Nomenclature of Tumors

Tissue of Origin	Benign	Malignant
Composed of one parenchymal cell type		
Tumors of Mesenchymal Origin		
Connective tissue and derivatives	Fibroma Lipoma Chondroma Osteoma	Fibrosarcoma Liposarcoma Chondrosarcoma Osteogenic sarcoma
Vessels and surface coverings		
Blood vessels	Hemangioma	Angiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma
Mesothelium	Benign fibrous tumor	Mesothelioma
Brain coverings	Meningioma	Invasive meningioma
Blood Cells and Related Cells		
Hematopoietic cells		Leukemias
Lymphoid tissue		Lymphomas
Muscle		
Smooth	Leiomyoma	Leiomyosarcoma
Striated	Rhabdomyoma	Rhabdomyosarcoma
Tumors of Epithelial Origin		
Stratified squamous	Squamous cell papilloma	Squamous cell carcinoma
Basal cells of skin or adnexa		Basal cell carcinoma
Tumors of Epithelial Origin (cont'd)		
Epithelial lining of glands or ducts	Adenoma Papilloma Cystadenoma	Adenocarcinoma Papillary carcinomas Cystadenocarcinoma
Respiratory passages	Bronchial adenoma	Bronchogenic carcinoma
Renal epithelium	Renal tubular adenoma	Renal cell carcinoma
Liver cells	Hepatic adenoma	Hepatocellular carcinoma
Urinary tract epithelium (transitional)	Transitional cell papilloma	Transitional cell carcinoma
Placental epithelium	Hydatidiform mole	Choriocarcinoma
Testicular epithelium (germ cells)		Seminoma Embryonal carcinoma
Tumors of Melanocytes	Nevus	Malignant melanoma
More than one neoplastic cell type—mixed tumors, usually derived from one germ cell layer		
Salivary glands	Pleomorphic adenoma (mixed tumor of salivary origin)	Malignant mixed tumor of salivary gland origin
Renal anlage		Wilms tumor
More than one neoplastic cell type derived from more than one germ cell layer—teratogenous		
Totipotential cells in gonads or in embryonic rests	Mature teratoma, dermoid cyst	Immature teratoma, teratocarcinoma

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

BENIGN TUMOURS

e.g.

- adenoma - (glandular)
- papilloma - (finger-like)
- cystadenoma - (cystic)
- papillary - (combined features Papillae & cyst) cystadenomaa
- polyp - (mucosal projection)

Exceptions: **Synovioma, Leukemia, Lymphoma, Glioma, melanoma, Hepatoma**

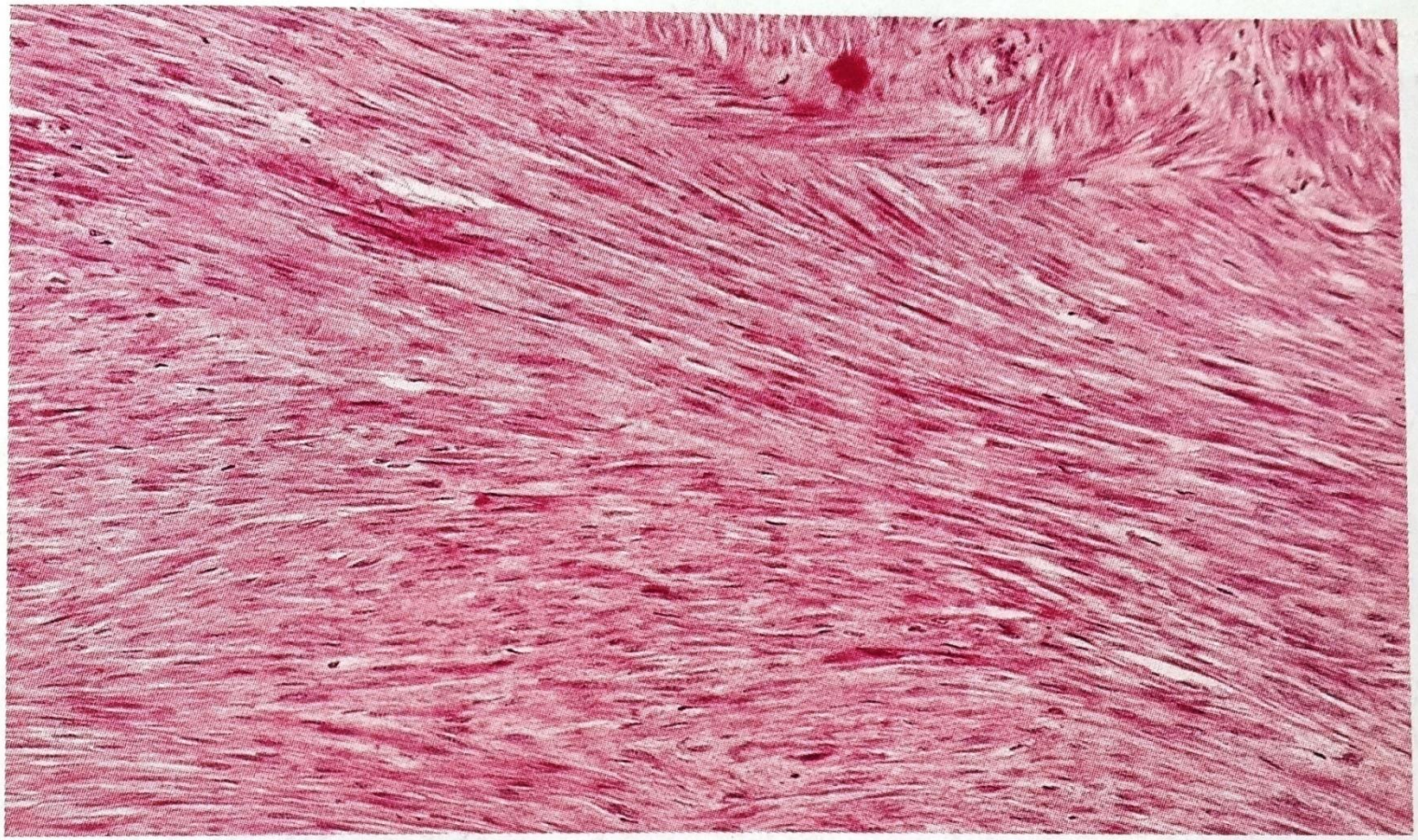


Figure 7-4 Leiomyoma of the uterus. This benign, well-differentiated tumor contains interlacing bundles of neoplastic smooth muscle cells that are virtually identical in appearance to normal smooth muscle cells in the myometrium.

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

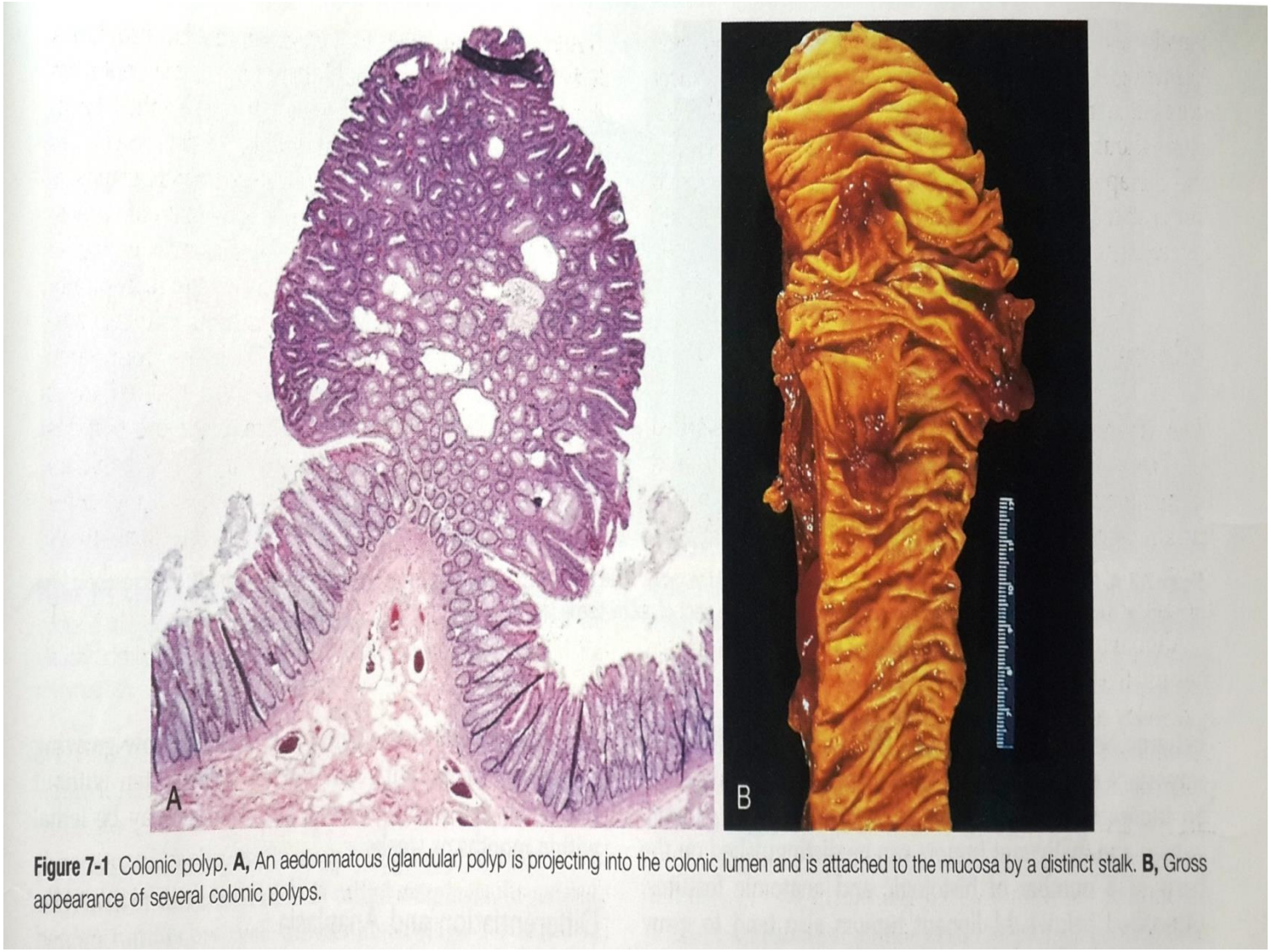


Figure 7-1 Colonic polyp. **A,** An aedonmatous (glandular) polyp is projecting into the colonic lumen and is attached to the mucosa by a distinct stalk. **B,** Gross appearance of several colonic polyps.

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

Hamartoma: not neoplastic, it is rather a malformation. Aberrant differentiation produce mass of disorganized but mature of mature (adult-type) tissue indigenous to particular site e.g. hamartoma in lung contain island of cartilage, blood vessels, bronchial type structures & lymphoid tissue

Choriostoma: Heterotrophic rest. It is normal tissue in abnormal place.

- e.g. rest of adrenal cells under kidney capsule.

  pancreatic nodular rest in mucosa of small intestine

Mixed Tumors

- "Mixed" tumors show divergent differentiation
- Examples
  - Pleomorphic adenoma – glands + fibromyxoid stroma
  - Fibroadenoma – glands + fibrous tissue
- Not to be confused with teratomas
- Teratoma: more than one germ-cell layer
  - Teratoma contains: bone, epithelium, muscle, fat, nerve….

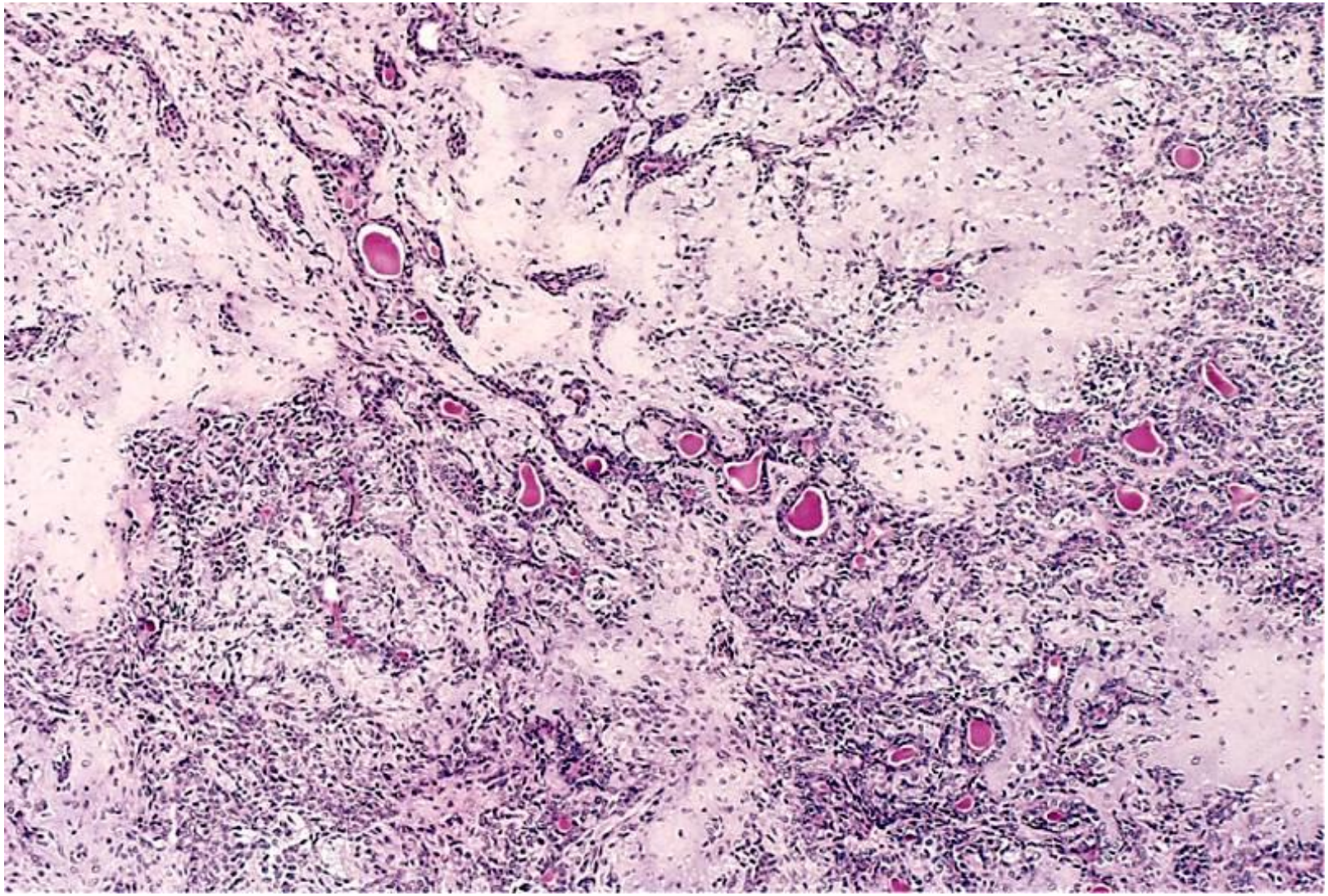


Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

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Pleomorphic adenoma

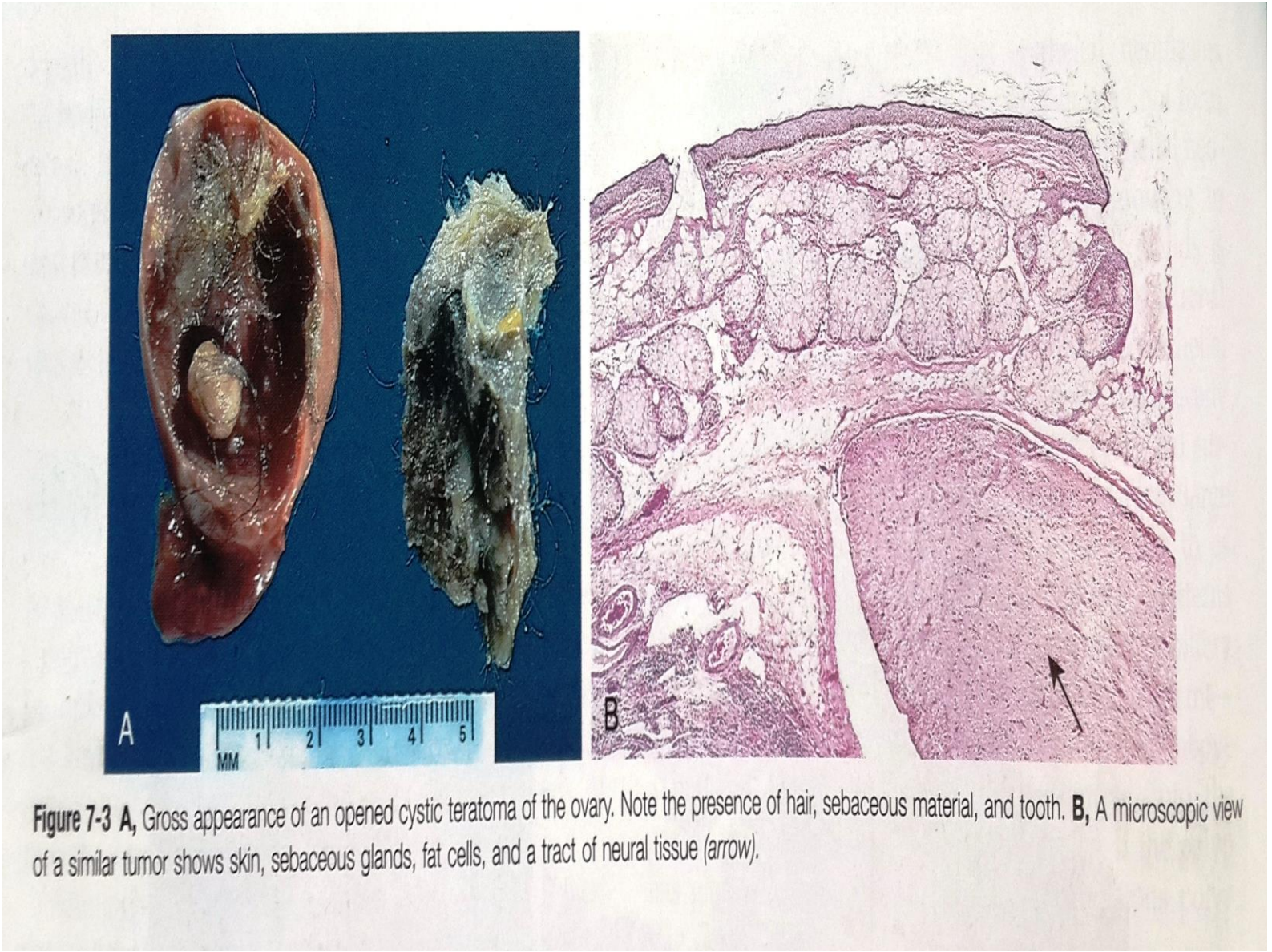


Figure 7-3 A, Gross appearance of an opened cystic teratoma of the ovary. Note the presence of hair, sebaceous material, and tooth. **B,** A microscopic view of a similar tumor shows skin, sebaceous glands, fat cells, and a tract of neural tissue *(arrow)*.

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

Structure of Neoplasm:

Two components

1. Proliferating neoplastic cells
2. Supportive stroma
   - Connective tissue
   - Blood vessels

   Variable amounts of (1) and (2) give tumours their gross features, e.g. excessive collagenous stroma (desmoplasia), schirrous tumours.

- Fast growth → less stroma
- Less stroma → more necrosis

Benign and Malignant

- How do we know benign from malignant tumor?
- Features:
  - Differentiation and Anaplasia
  - Rate of Growth
  - Local Invasion
  - Metastasis

Differentiation

- Differentiation is the extent to which tumor cells resemble their normal cells morphologically and functionally
- Generally:
  - Benign tumors are well differentiated
  - Malignant tumors can be well differentiated, moderately differentiated or poorly differentiated. They can be “undifferentiated”

Anaplasia is lack of differentiation

- Pleomorphism
- Hyperchromatic nuclei
- High nuclear to cytoplasmic ratio (N/C ratio)
- Tumor Giant cells
- Mitosis
- Loss of polarity and normal arrangement
- Loss of strcuture

Cellular Organization

Degree of loss of normal organization

- e.g. layered ~ squamous epithelium
  - loss of polarity
- e.g. glands
  - abnormal size or shape
  - loss of ability to form glands

Functional differentiation

Well differentiated tumours → normal product

Poorly differentiated tumours less likely to have specialized functional activity

Range:

- No product ---Normal---Increased

  e.g. insulin, mucin, keratin

- New or ectopic product

  e.g. PTH Lung carcinoma

  ACTH Lung carcinoma

  AFT Liver carcinoma (foetal antigen)

Dysplasia

- Not neoplstic growth
- Disordered growth and differentiation
- Show mild anaplastic features eg. Nuclear pleomorphism, hyperchromasia, mitosis….

e.g. Cervical Cancer (HPV)

Mild dysplasia

Moderate

Severe

Carcinoma in situ

-Intact basement membrane

‘PAP’ smear with metaplastic squamous cells

Figure 7-47 A normal cervicovaginal smear shows large, flattened squamous cells and groups of metaplastic cells; interspersed are neutrophils. There are no malignant cells. (Courtesy Dr. P. K. Gupta, University of Pennsylvania, Philadelphia, Pa.)

'PAP’ smear with malignant cells

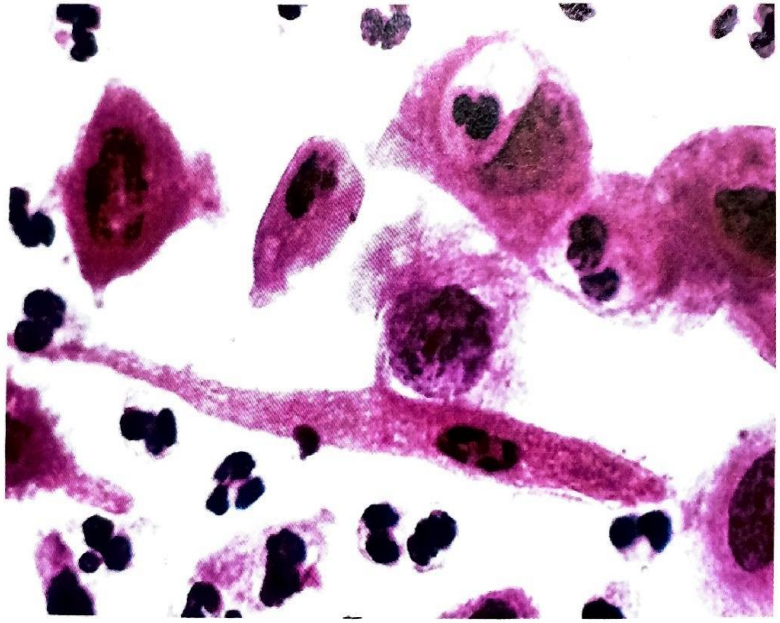


Figure 7-48 An abnormal cervicovaginal smear shows numerous malignant cells that have pleomorphic, hyperchromatic nuclei; interspersed are normal polymorphonuclear leukocytes. (Courtesy Dr. P. K. Gupta, University of Pennsylvania, Philadelphia, Pa.)

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

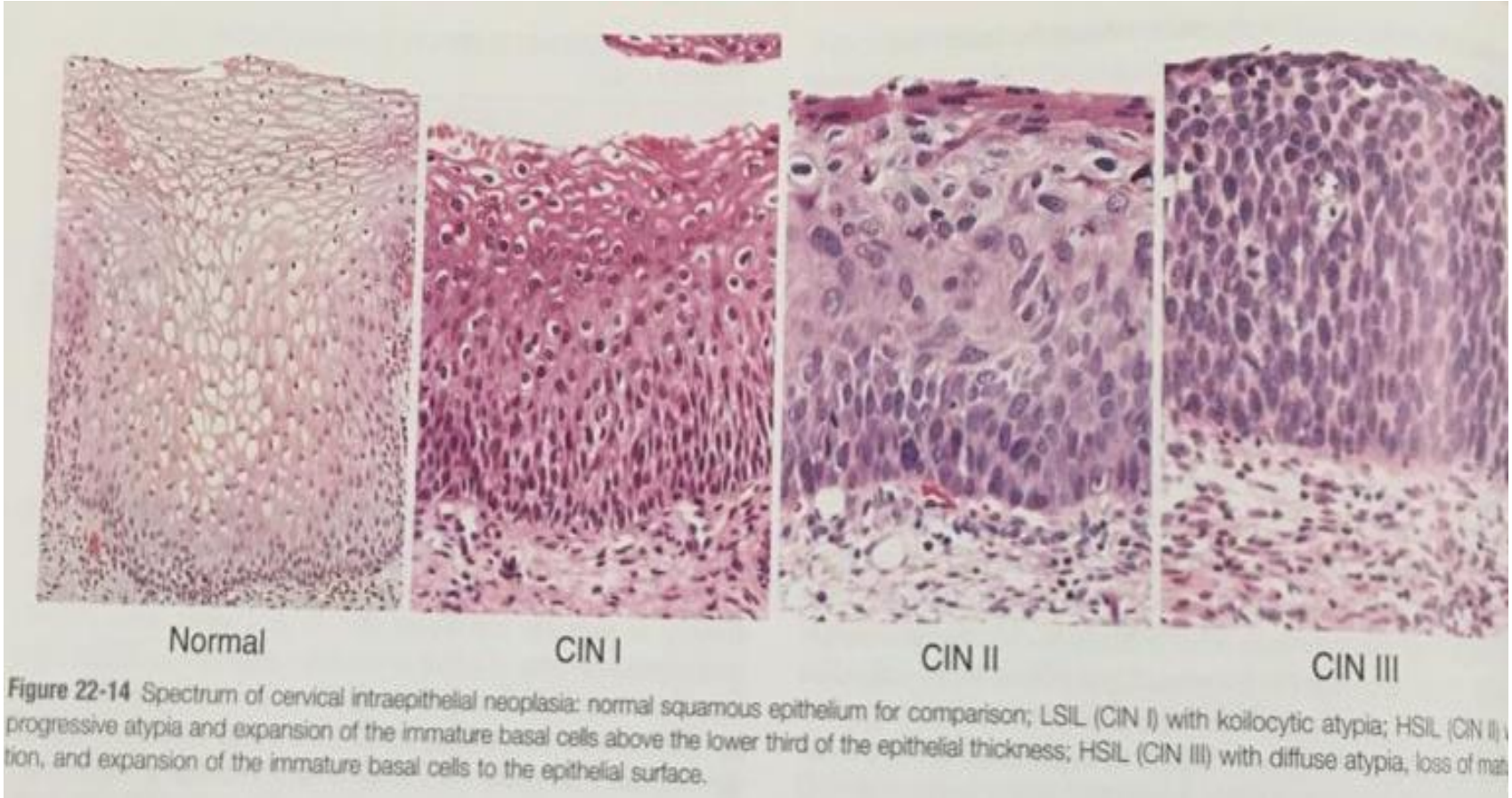


Figure 22-14 Spectrum of cervical intraepithelial neoplasia: normal squamous epithelium for comparison; LSIL (CIN I) with koilocytic atypia; HSIL (CIN II) with progressive atypia and expansion of the immature basal cells above the lower third of the epithelial thickness; HSIL (CIN III) with diffuse atypia, loss of maturation, and expansion of the immature basal cells to the epithelial surface.

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

Urinary bladder – Urothelium

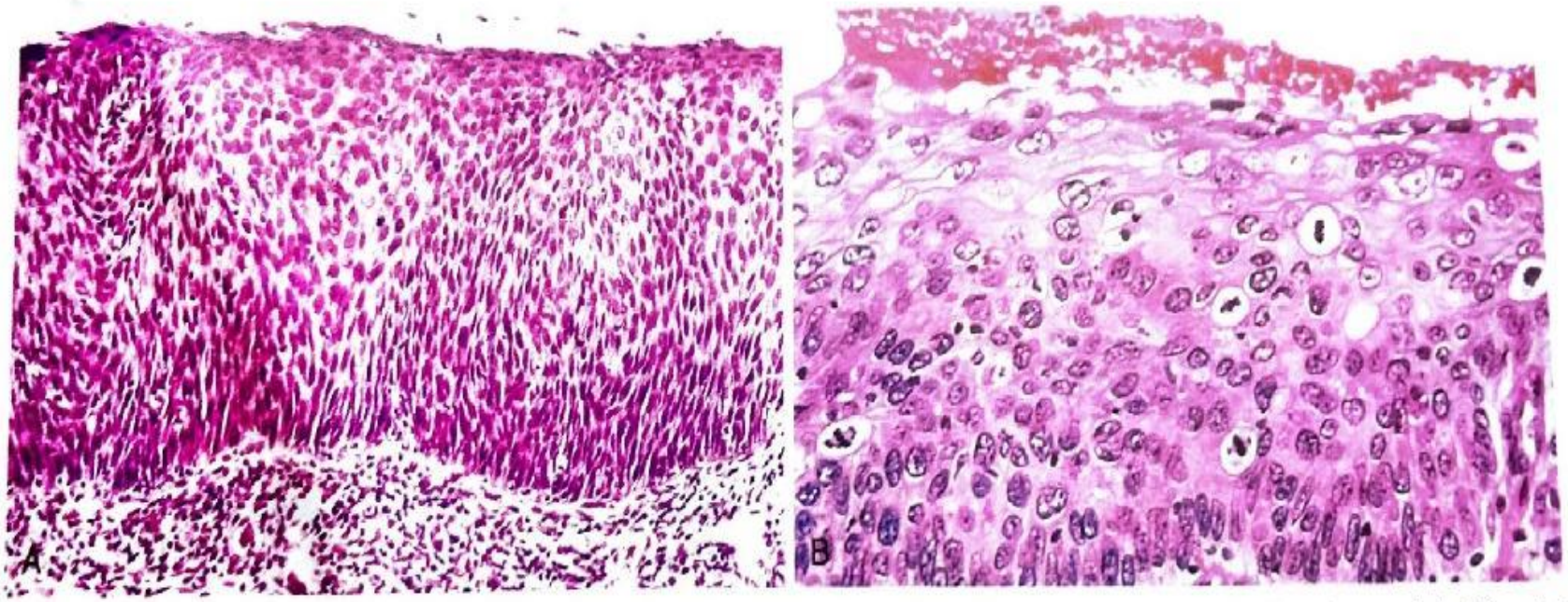


Figure 7-10 A, Carcinoma in situ. A low-power view shows that the epithelium is entirely replaced by atypical dysplastic cells. There is no orderly differentiation of squamous cells. The basement membrane is intact, and there is no tumor in the subepithelial stroma. **B,** A high-power view of another region shows failure of normal differentiation, marked nuclear and cellular pleomorphism, and numerous mitotic figures extending toward the surface.

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

Benign

- Progressive & Slow growing,
- capsulated,
- Non-invasive

  do not metastasize,

  well differentiated,

  structure typical of tissue of origin. Mitotic figures rare & normal
- suffix “oma” e.g.. Fibroma.

Malignant

- Erratic & slow to fast growing,
- non capsulated,
- Invasive & Infiltrate
- Metastasize.
- lack of differentiation with anaplasia, structure often atypical mitotic figures numerous & abnormal
- Suffix “Carcinoma” or “Sarcoma”

- Benign tumours usually closely resemble normal cells (well differentiated).
- Malignant tumours show a range of abnormal differentiation – well to undifferentiated (anaplastic)

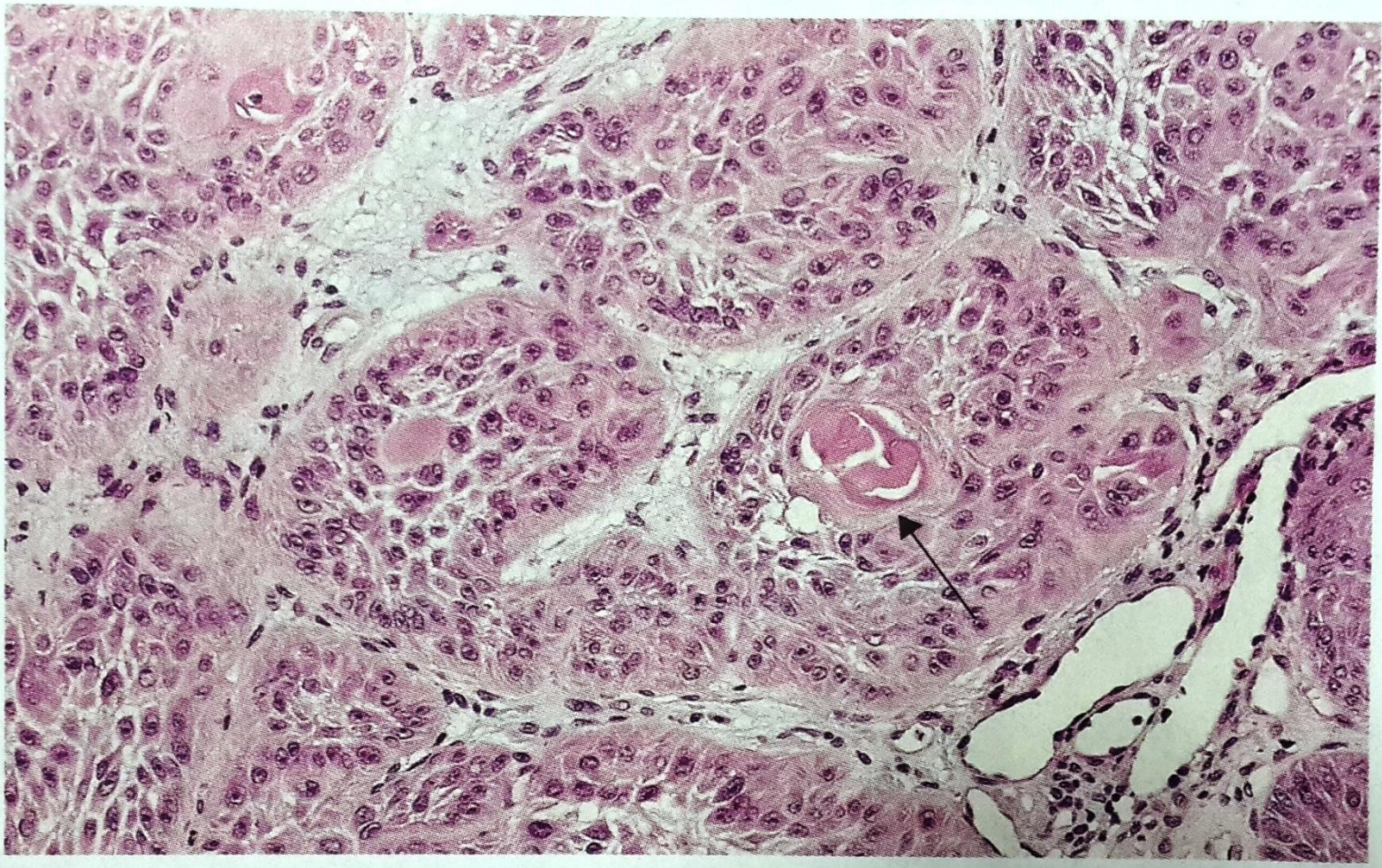


Figure 7-7 Well-differentiated squamous cell carcinoma of the skin. The tumor cells are strikingly similar to normal squamous epithelial cells, with intercellular bridges and nests of keratin pearls *(arrow)*. (Courtesy Dr. Trace Worrell, University of Texas Southwestern Medical School, Dallas, Texas.)

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

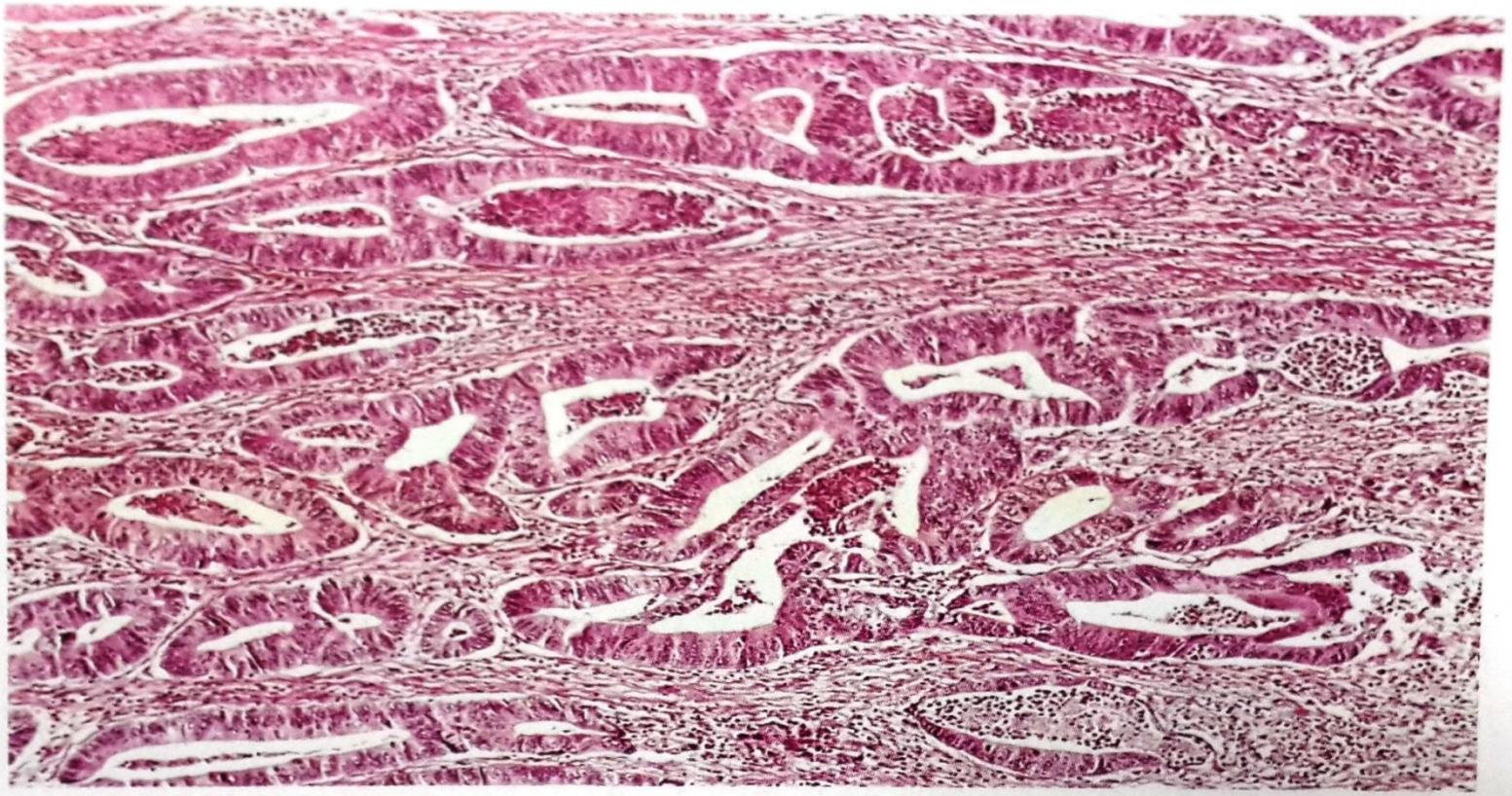
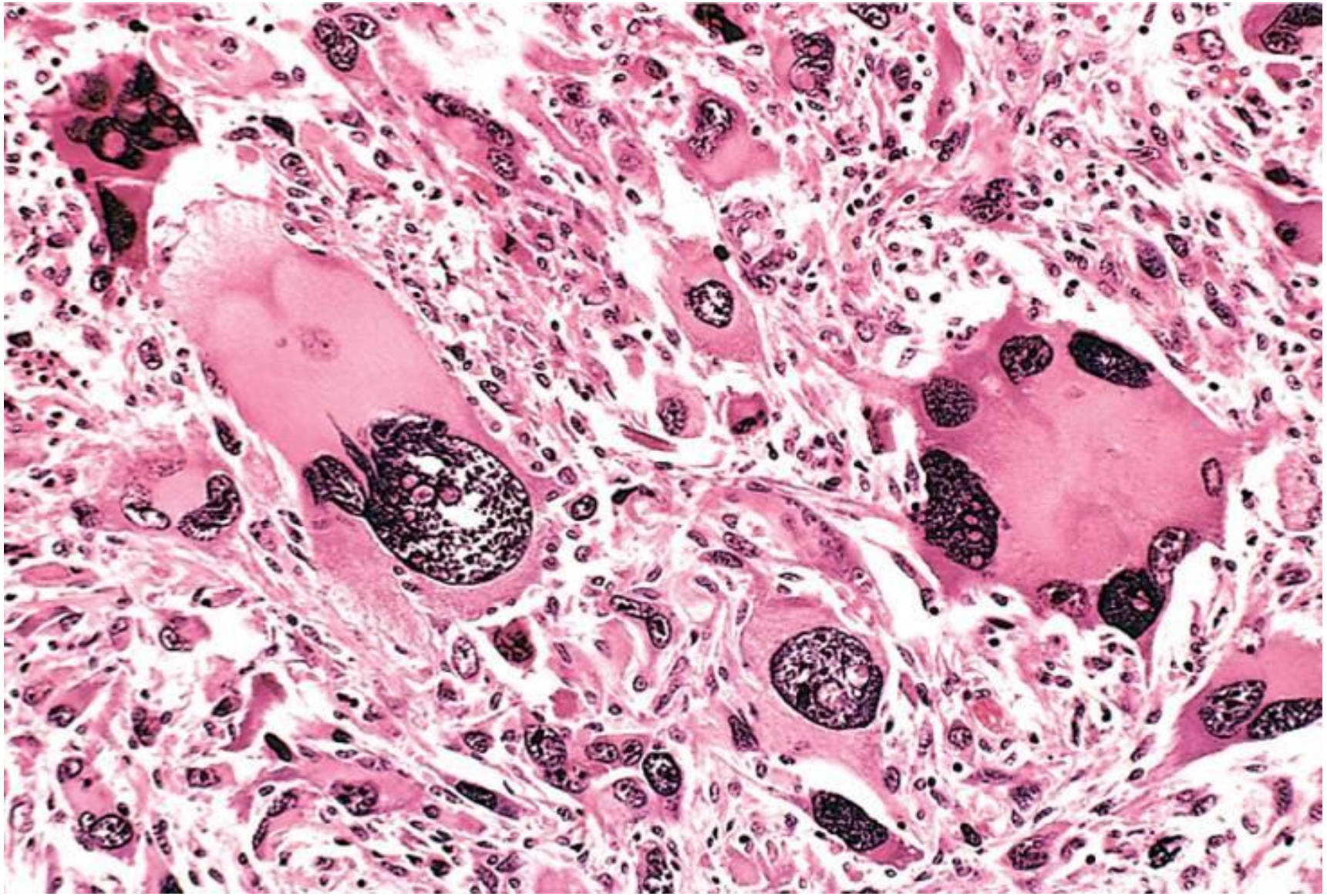


Figure 7-6 Malignant tumor (adenocarcinoma) of the colon. Note that compared with the well-formed and normal-looking glands characteristic of a benign tumor (Fig. 7-5), the cancerous glands are irregular in shape and size and do not resemble the normal colonic glands. This tumor is considered differentiated because gland formation is seen. The malignant glands have invaded the muscular layer of the colon. (Courtesy Dr. Trace Worrell, University of Texas Southwestern Medical School, Dallas, Texas.)

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017



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Rhabdmyosarcoma

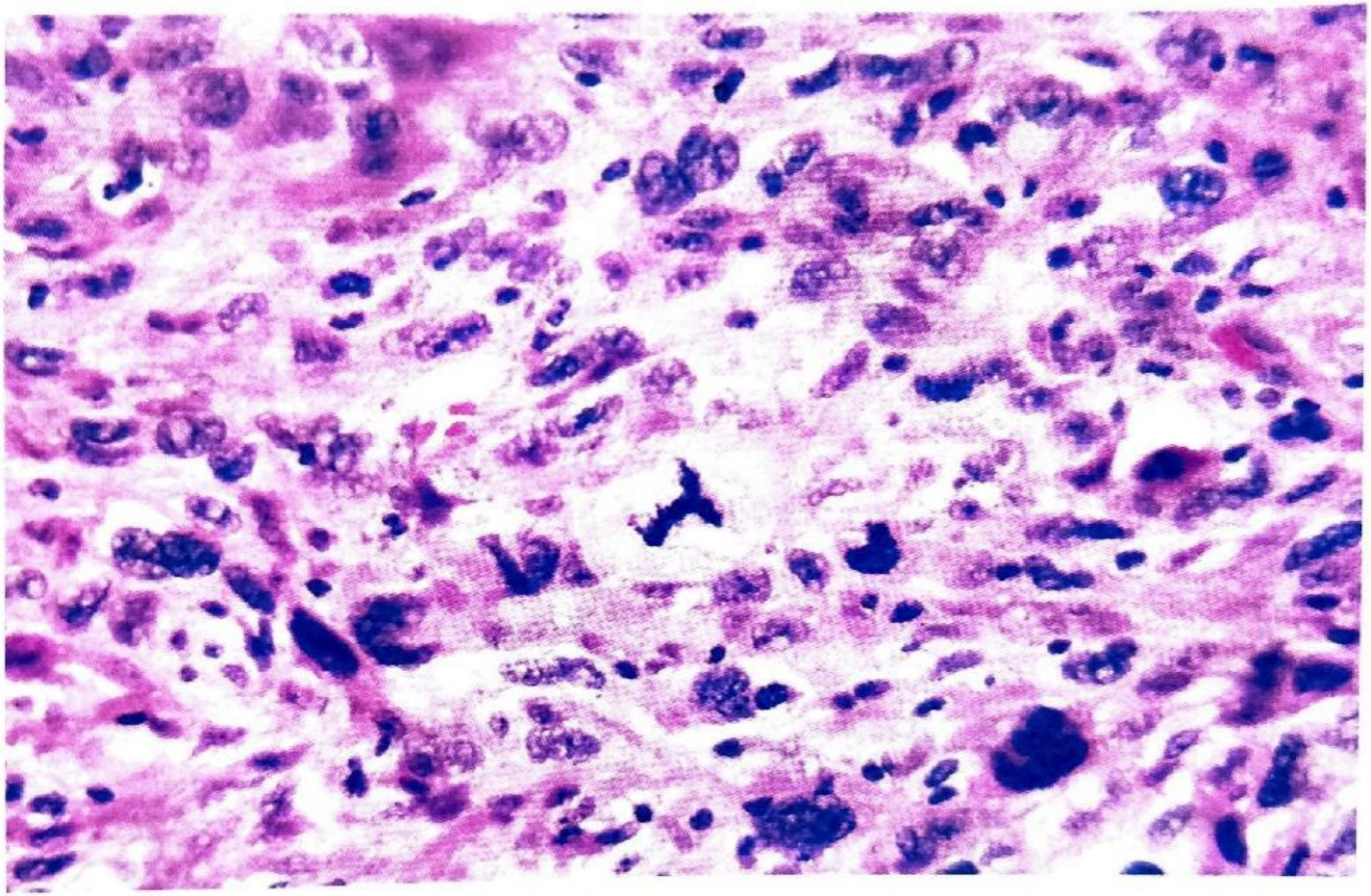

Figure 7-8 Anaplastic tumor showing cellular and nuclear variation in size and shape. The prominent cell in the center field has an abnormal tripolar spindle.

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

Uterus : Leiomyoma and Sarcoma

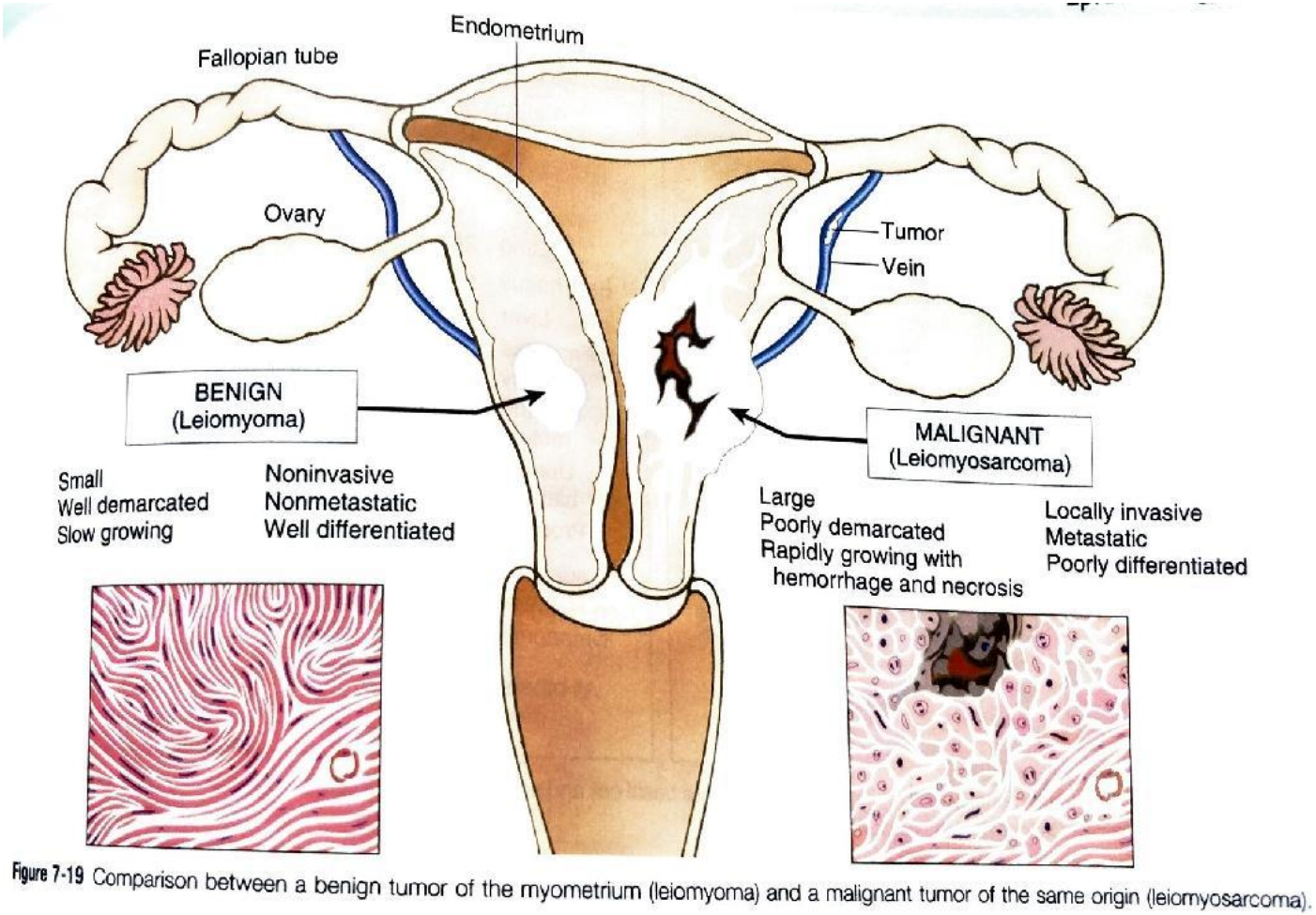

Figure 7-19 Comparison between a benign tumor of the myometrium (leiomyoma) and a malignant tumor of the same origin (leiomyosarcoma).

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

Rate of Growth

Concept:

Benign tumours grow slowly

Cancers grow rapidly

Exceptions – many

e.g. fast growing benign tumours

hormone dependence

blood supply

Range of malignant tumour progression

- Years to weeks
- Cell cycle time- 3 days
- 30 population doubling takes 90 days to produce 10^9 cells
- Spontaneous remission, e.g. renal cell carcinoma

Rate of Growth depends on

Three Factors:

- Doubling time of tumor cells
- Fraction of tumor cells in replicative pool
- Rate at which cells are shed & lost in the growing lesion

Invasion

Benign tumours are NOT invasive because of…

- Expansile probing margins
- Localized growth, readily palpable
- Do not have the capacity to infiltrate
- Encapsulation expect Haemangioma, leiomyoma

Therefore benign tumours…

- If resected do not recur
- If incompletely removed then only local recurrence occurs.

Mechanism of invasion

- Physical pressure- compression atrophy & destruction of abutting normal cells.
- Reduced adhesiveness & cohesiveness of cancer cells.
- Motility of tumor cells-the cells are capable of locomotion & cytoplasmic processes can be seen protruding from the cells.
- Loss of contact inhibition- loss of cessation of cell division and mobility on contact with other cells.
- Release of destructive enzymes- collagenases, lysosomal enzymes, plasminogen activator.

Malignant tumours are INVASIVE because of…

- Progressive growth
- Infiltration ~ poor line of demarcation
- Invasion *(importance of surgical margins)*
- Destruction of adjacent tissue
- Metastatic spread
- Death if not treated

Tumor invasion

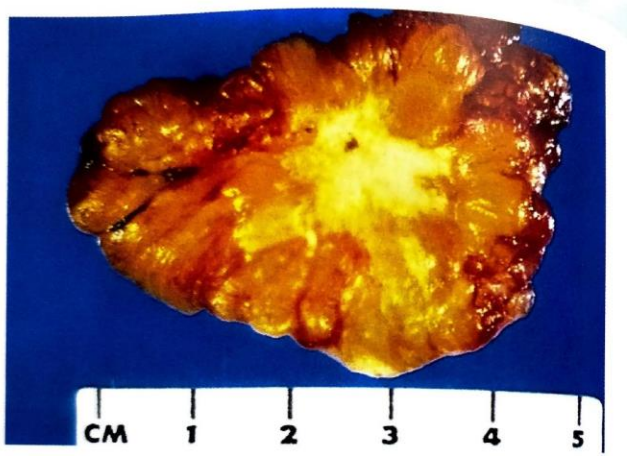

Figure 7-13 Cut section of an invasive ductal carcinoma of the breast. The lesion is retracted, infiltrating the surrounding breast substance, and would be stony hard on palpation. (Courtesy Dr. Trace Worrell, University of Texas Southwestern Medical School, Dallas, Texas.)

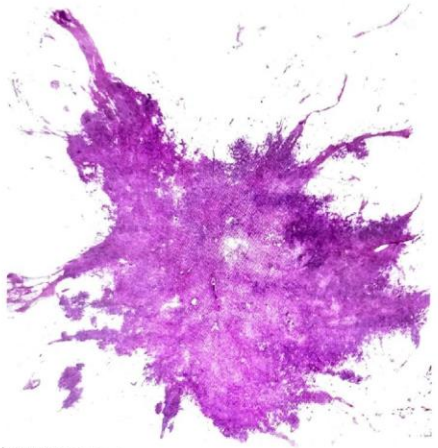

Figure 7-14 Low power microscopic view of invasive breast cancer. Note the irregular infiltrative borders without a well-defined capsule and intense stromal reaction. (Courtesy Dr. Susan Lester, Brigham and Women's Hospital, Boston, Mass.)

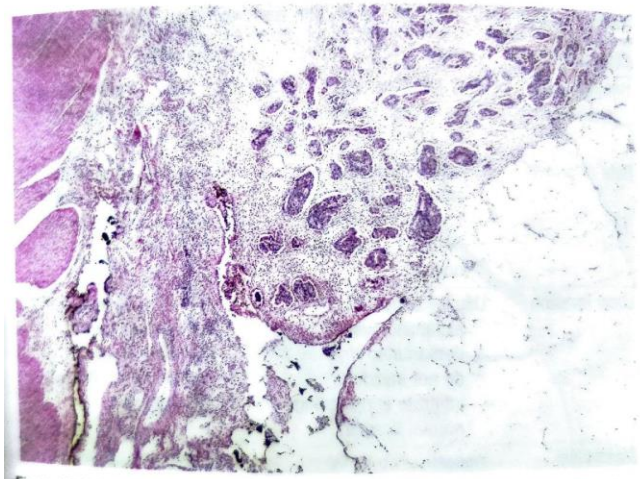

Figure 7-15 Colon carcinoma invading pericolonic adipose tissue. (Courtesy Dr. Shuji Ogino, Dana Farber Cancer Institute, Boston, Mass.)

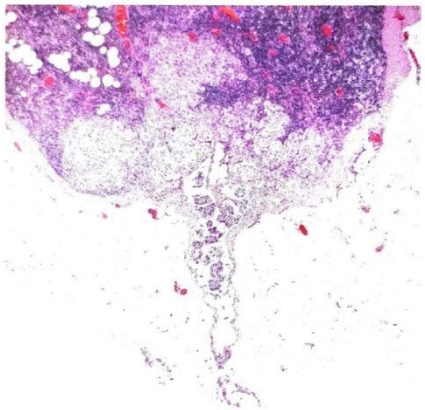

Figure 7-16 Axillary lymph node with metastatic breast carcinoma. Note the aggregates of tumor cells within the substance of the node and the dilated lymphatic channel. (Courtesy Dr. Susan Lester, Brigham and Women's Hospital, Boston, Mass.)

Figure courtesy reference : Robbins & Cotran, Pathologic Basis of Disease, South Asia Edition, 2017

Malignant tumors

Feature	Sarcoma	Carcinoma
Origin	Arise from mesenchymal tissue	Arise from epithelial tissue
Mass size	Usually larger since harder to detect them in deep tissue!!!	Usually smaller since easier to detect on surface
Time of diagnosis	Takes longer period to diagnose	Takes shorter period of time to diagnose from onset
Route of Metastasis	Goes directly to vascular system/ Blood vessels	Goes through lymphatics first – longer route to vascular system
Prognosis	Worse prognosis	Good/worse

Epidemiology of cancer

- Environmental factors
  (e.g. smoking, alcohol consumption, diet, obesity, reproductive history)
- Age
- Acquired predisposing conditions
- Genetic predisposition