MOLECULAR BASIS OF CANCER

MOLECULAR GENETICS OF CANCER

- Gens and molecular factors involved in pathogenesis of cancer and grouped as under:
    a. Oncogenes
    b. Anti oncogenes
    c. Mutator genes
    d. Telomerase

- **Oncogenes:-**

  -These are cancer causing genes

  -Derived from proto-oncogenes or cellular genes [c-oncs]

  -They are identified by DNA transformation

  -The mechanism involved for their activation are:

  -Change in structure of gene.

  -Change in regulation of expression of gene.

Human oncogenes and related tumors:

ONCOGENE	TYPE	TUMOUR
SIS	EXTRACELLULAR GROWTH FACTOR	SARCOMAS
hst, k 53	FGF	STOMACH CANCER,KAPOSI SARCOMA
Erb B1,her-2/neu Erb B2	TRANS MEM.GROWTH REC.FACTOR EGF-RECEPTOR	CA.LUNG , CA. BREAST
fms	•CSF-RECEPTOR •INTRACELLULAR SIGNAL TRANSDUCTION PROTEINS	LEUKEMIA
ras	•GTP BINDING	CA.LUNG ,CA.COLON
abl	•Non receptor tyrosine kinase	CML, ALL
myc	•TRANSCRIPTION	BURKIT'S LYMPHOMA
n-myc	•ACTIVATORS	NEUROBLASTOMA
CYCLIN-D	•CYCLINS	MENTAL CELL LYMPHOMA
CD K4	•CYCLIN DEPENDENT KINASE	GLIOBLASTOMA
BCL2	•APOPTOTIC INHIBITOR,ANTI	FOLLICULAR, B CELL

- ANTI ONCOGENES[TUMOR SUPPRESOR GENE]

-> they are pair of normal genes. It regulates cell growth

-> two imp.tumor suppresor genes are:

Rb gene in Retinoblastoma

p53 gene products

Imp. Tumor suppresor gene & ass.tomors

GENE	LOCATION	TUMOUR
Rb	NUCLEUS	RETINOBLASTOMA
P 53	NUCLEUS	CA. COLO-RECTUM
APC	CYTOSOL	FAMILIAL APC
WT1	NUCLEUS	WILMS TUMOR
NF1	PLASMA MEMB.	NEUROFIBROMATOSIS
BRCA1	NUCLEUS	CA. BREAST
BRCA2	NUCLEUS	CA. OVARY

- MUTATOR GENES:-

They are characterised byloss of normal surveillance function & render DNA susptible to accumulation of mutation & progression to cancer e.g)

Heriditory non-polyposis colonic ca.

Ataxia telangiectasia

- Telomerase in cancer

  - They are the terminal tips of chromosomes which progressively shorten due to repetative
  - Telomerase is the enzyme required for continued recognition of telomere in successive cell divisions.
  - Cancer cells express telomerase

- **THEORIES OF CARCINOGENESIS**

  1- The genetic theory

  2- The epigenetic theory

  3- The multisteps theory

  4- Immune surveillance theory

  5- Monoclonal hypothesis
- Of all genetic theory is popular. This theory suggest that cells become neo plastic because of alteration in the DNA
- The mutated cells transmit their characters to the next progeny of cells.

- **CLINICAL ASPECT OF NEOPLASIA**

  a. two major clinical aspects

  b. tumor host inter relation

  c. lab. Diagnosis of cancer

- **EFECT OF TUMOR ON HOST**

  a. malignant tomors production more ill effects then benign tumors. The effects are:

  b. local effects viz. compression, mechanical obliteration, tissue damage, infarction, tissue damage,infarction, ulceration

  c. cancer cachexia

  d. fever

  e. para neoplastic yndromes.

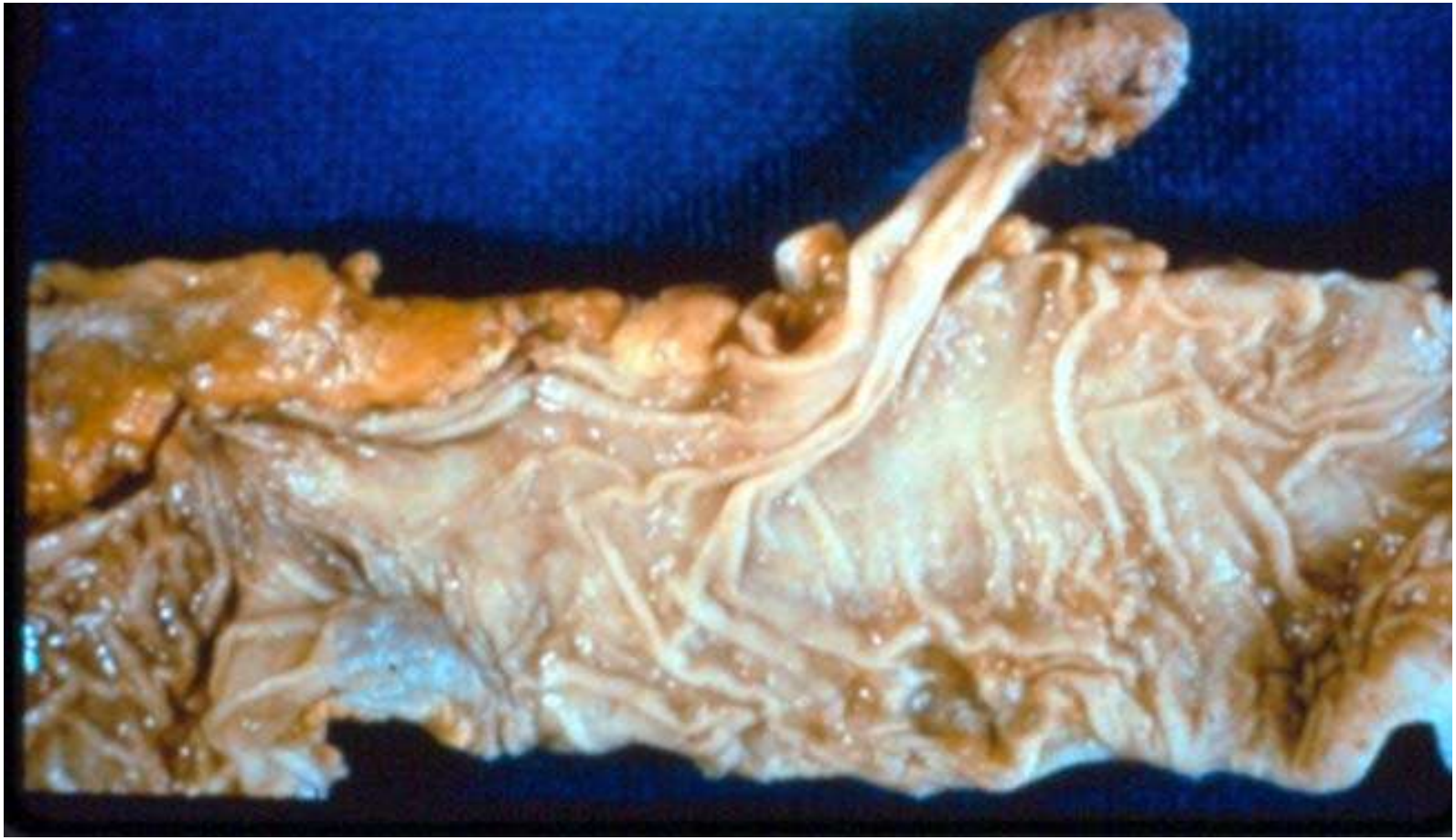


FIG PAPILLOMA OF COLON

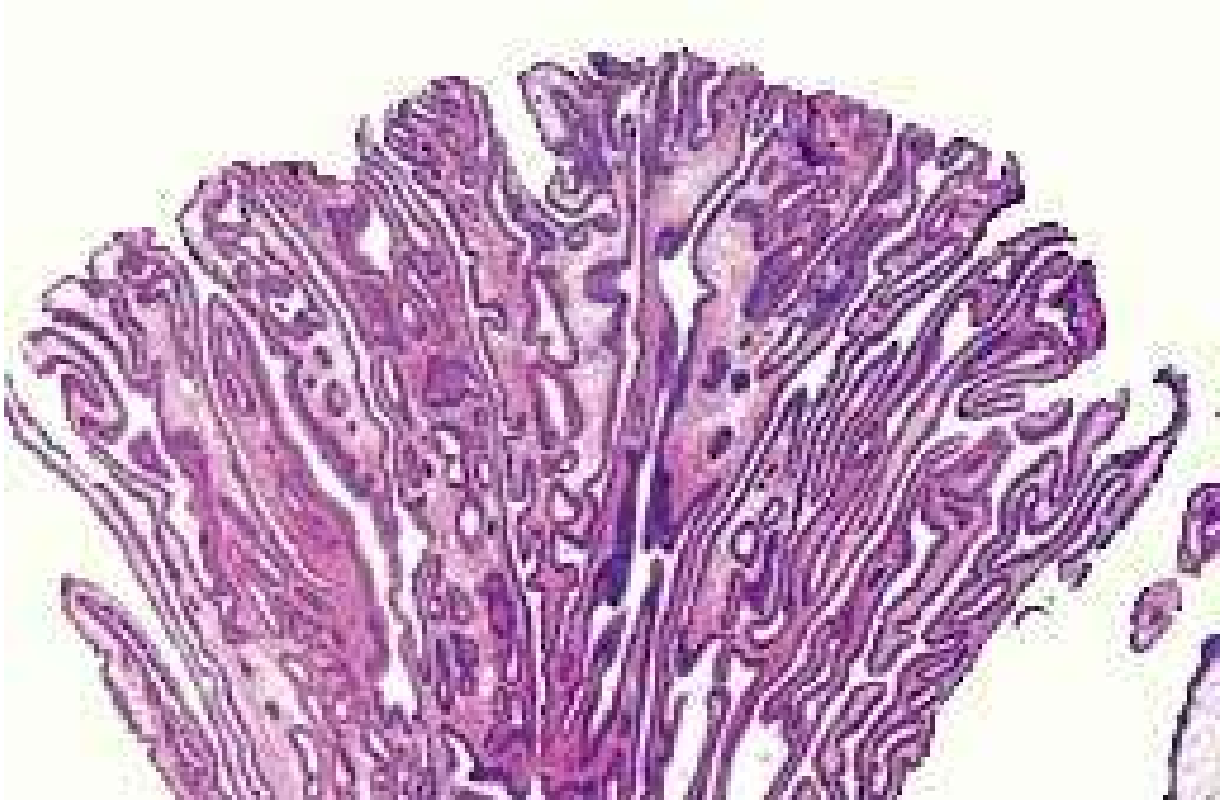


FIG 1. Papilloma of the colon with finger-like projections into the lumen

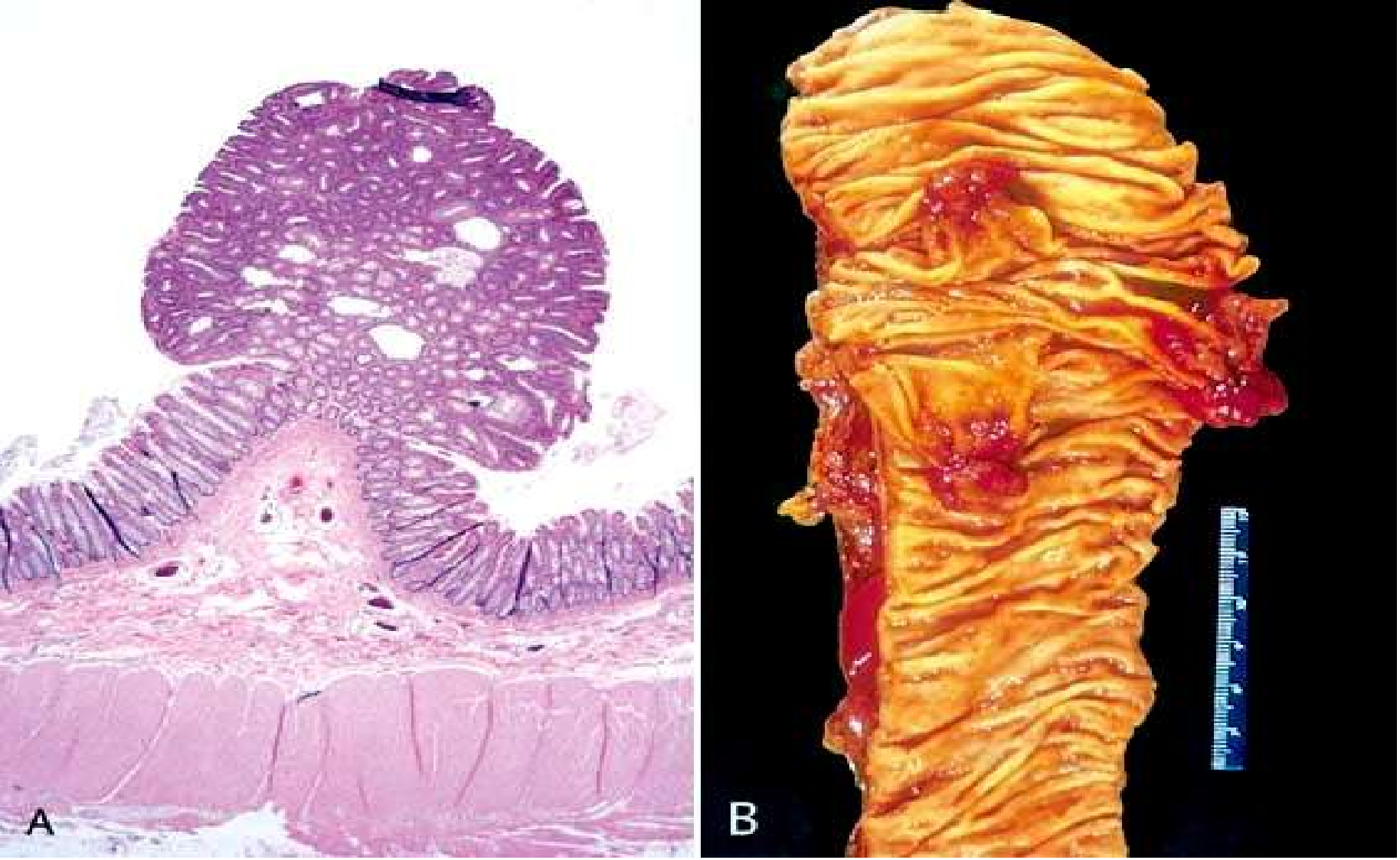


Figure 2 Colonic polyp. *A,* This benign glandular tumor (adenoma) , *B,* Gross appearance of several colonic polyps

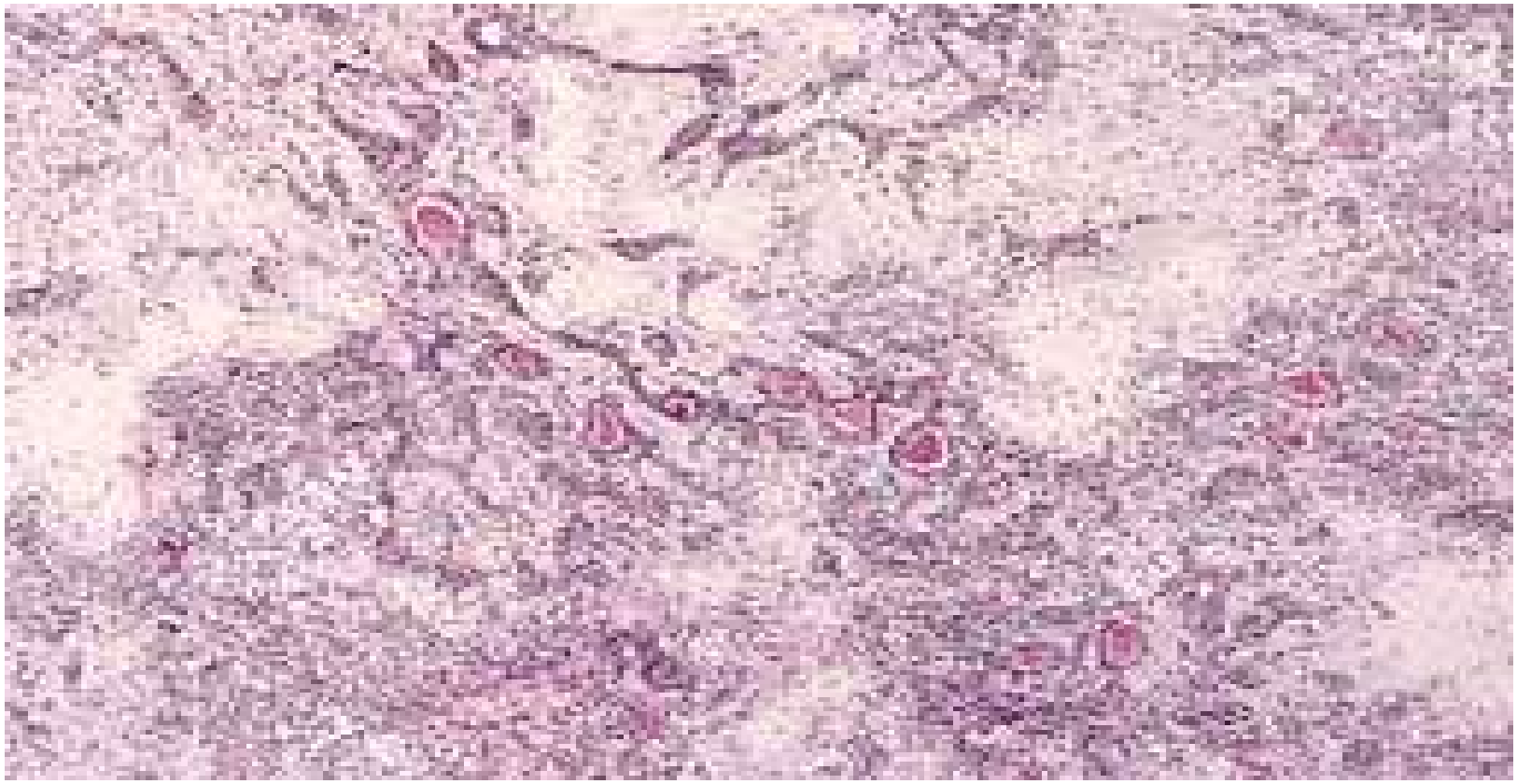


Figure 3 This mixed tumor of the parotid gland contains epithelial cells forming ducts and myxoid stroma that resembles cartilage

Figure 4 *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)*.

GROSS LIEOMYOMA

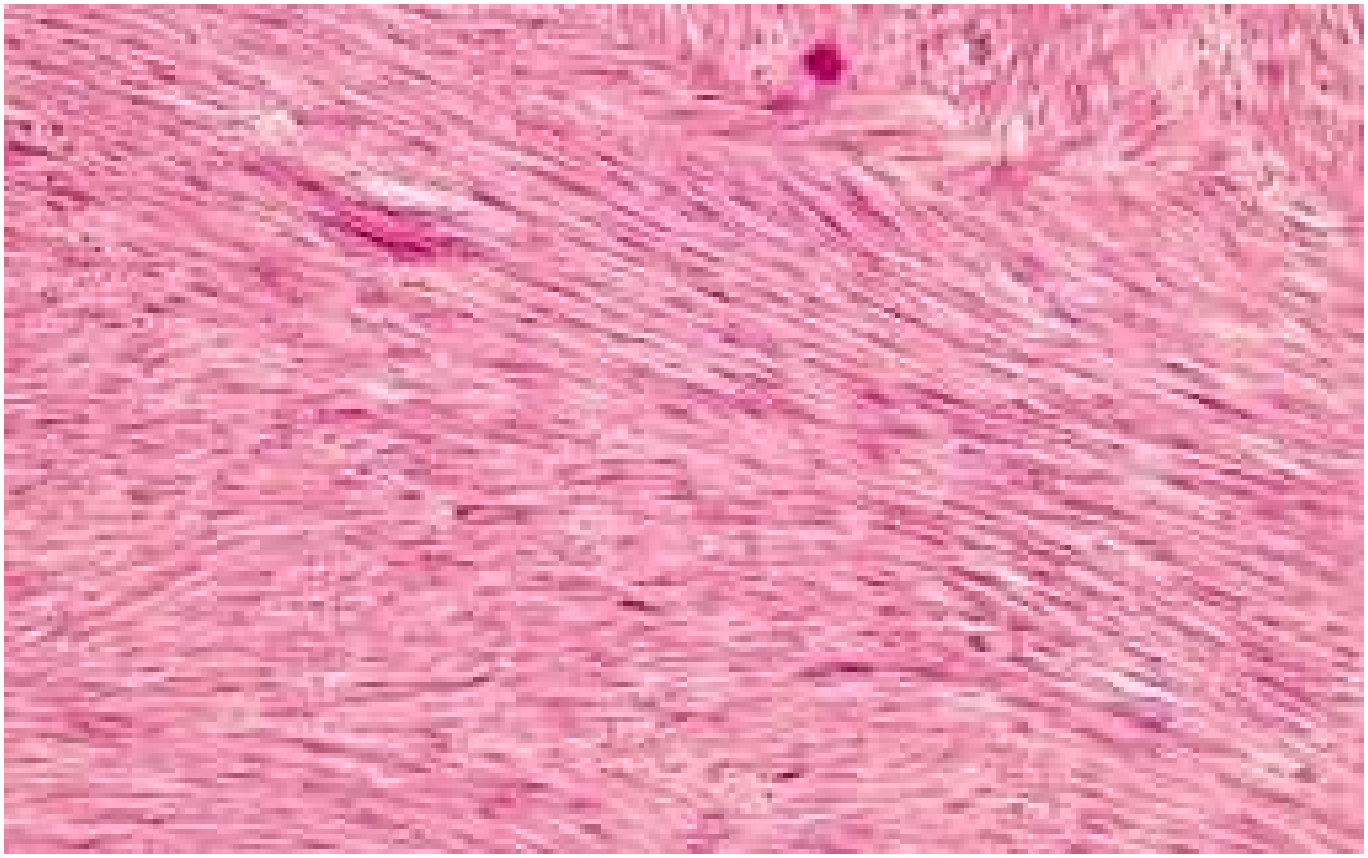
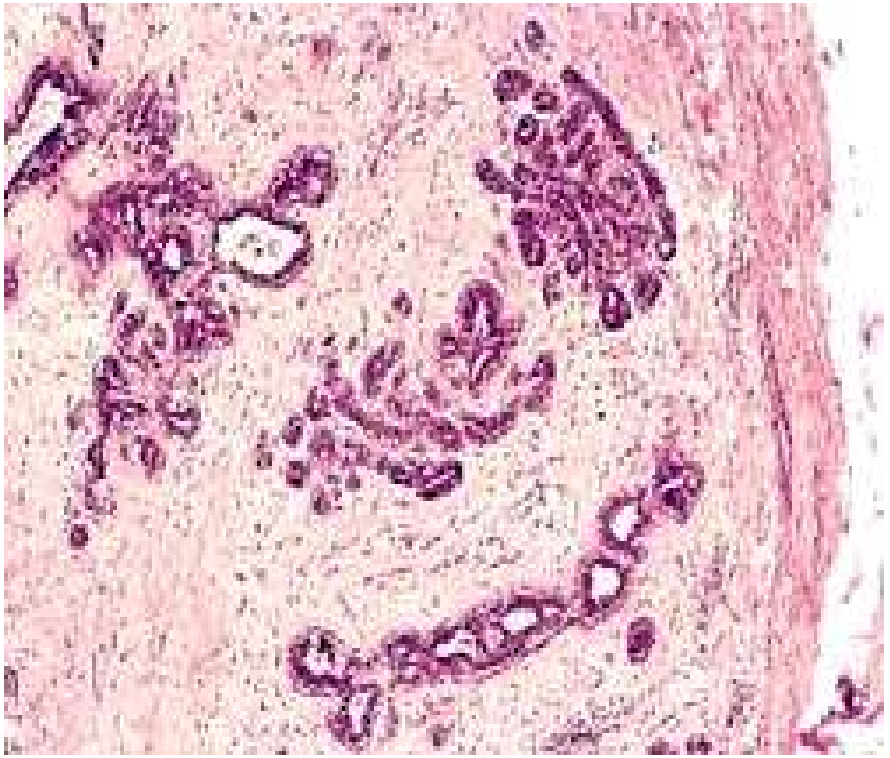


Figure 7-5 Leiomyoma of the uterus. This benign, well-differentiated tumor contains interlacing bundles of neoplastic smooth muscle cells that are virtually identical in appearance to normal smooth muscle cells in the myometrium

Figure 14 Fibroadenoma of the breast. The tan-colored, encapsulated small tumor is sharply demarcated from the whiter breast tissue.



Microscopic view of fibroadenoma of the breast seen in. The fibrous capsule (*right*) delimits the tumor from the surrounding tissue

CARCINOMA BREAST

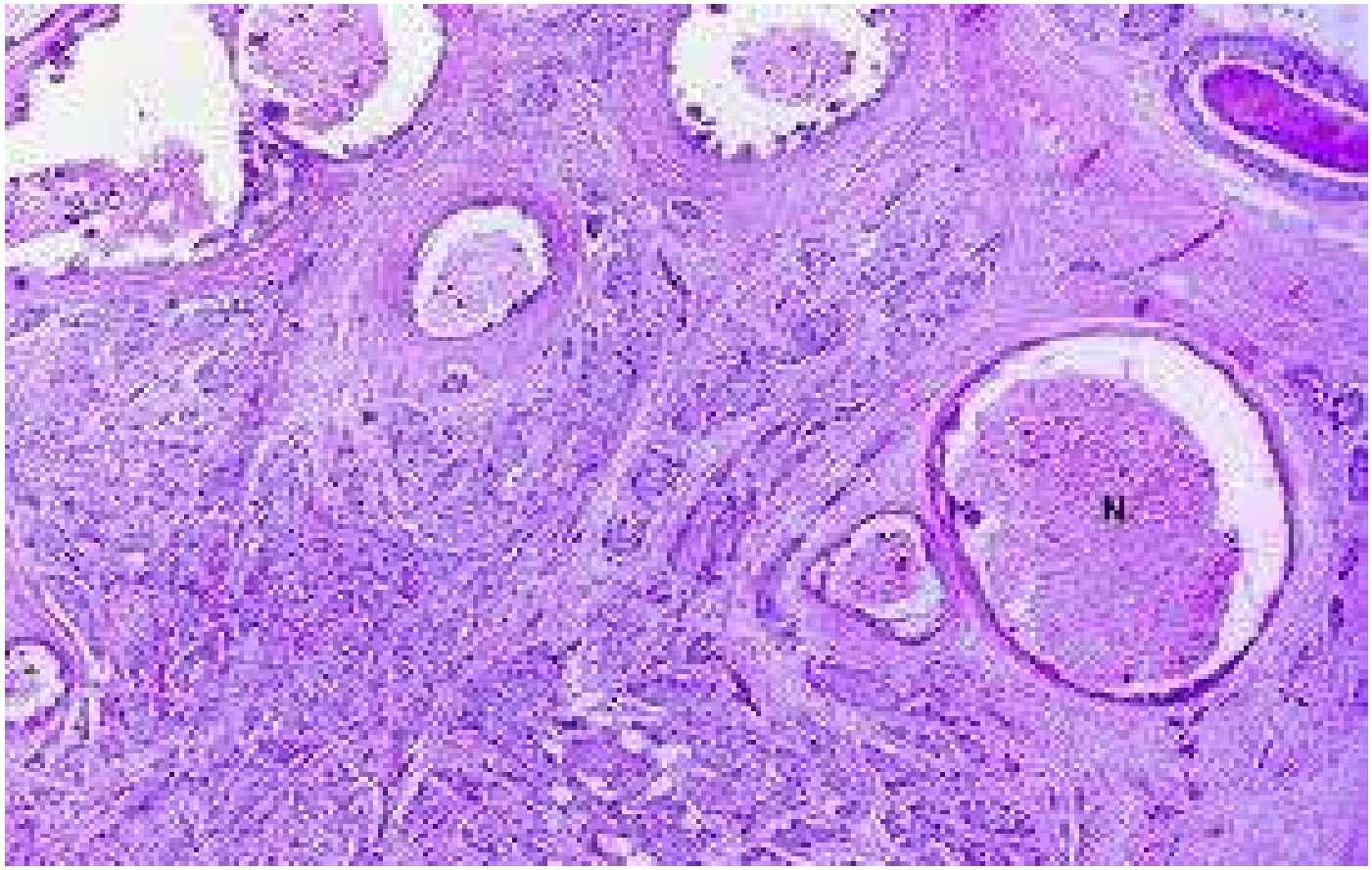


FIG 9 DUCTAL CARCINOMA BREAST

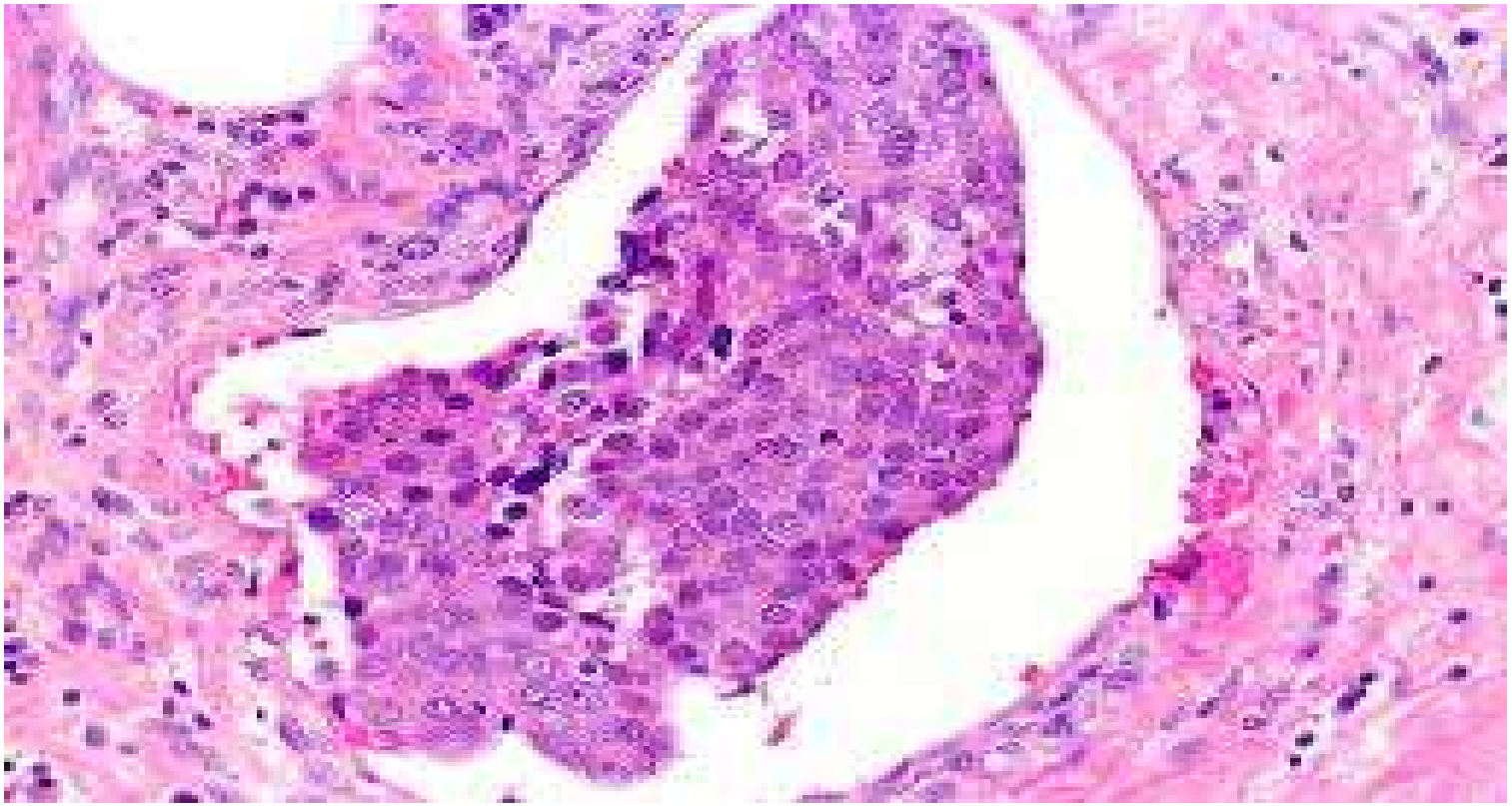
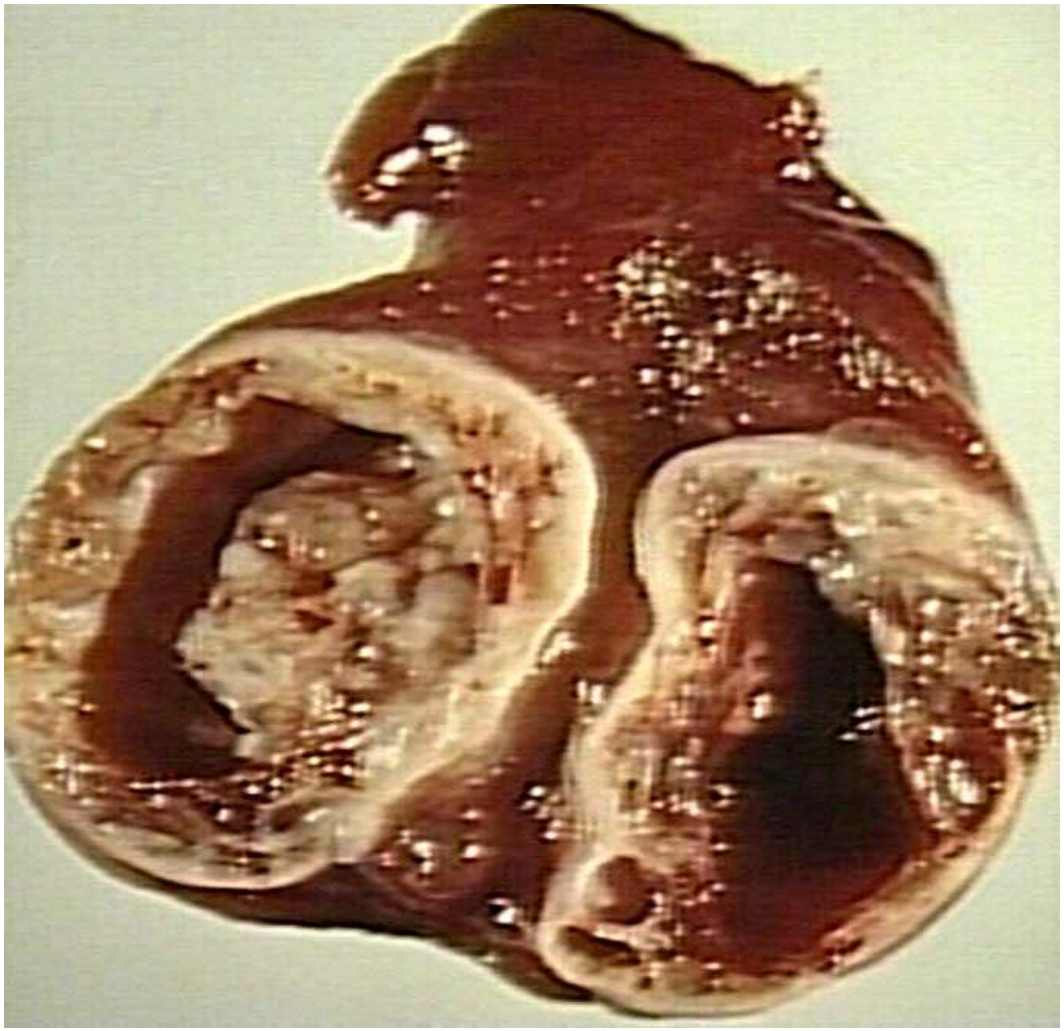


FIG DUCTAL CARCINOMA BREAST



GROSS THYROID ADENOMA

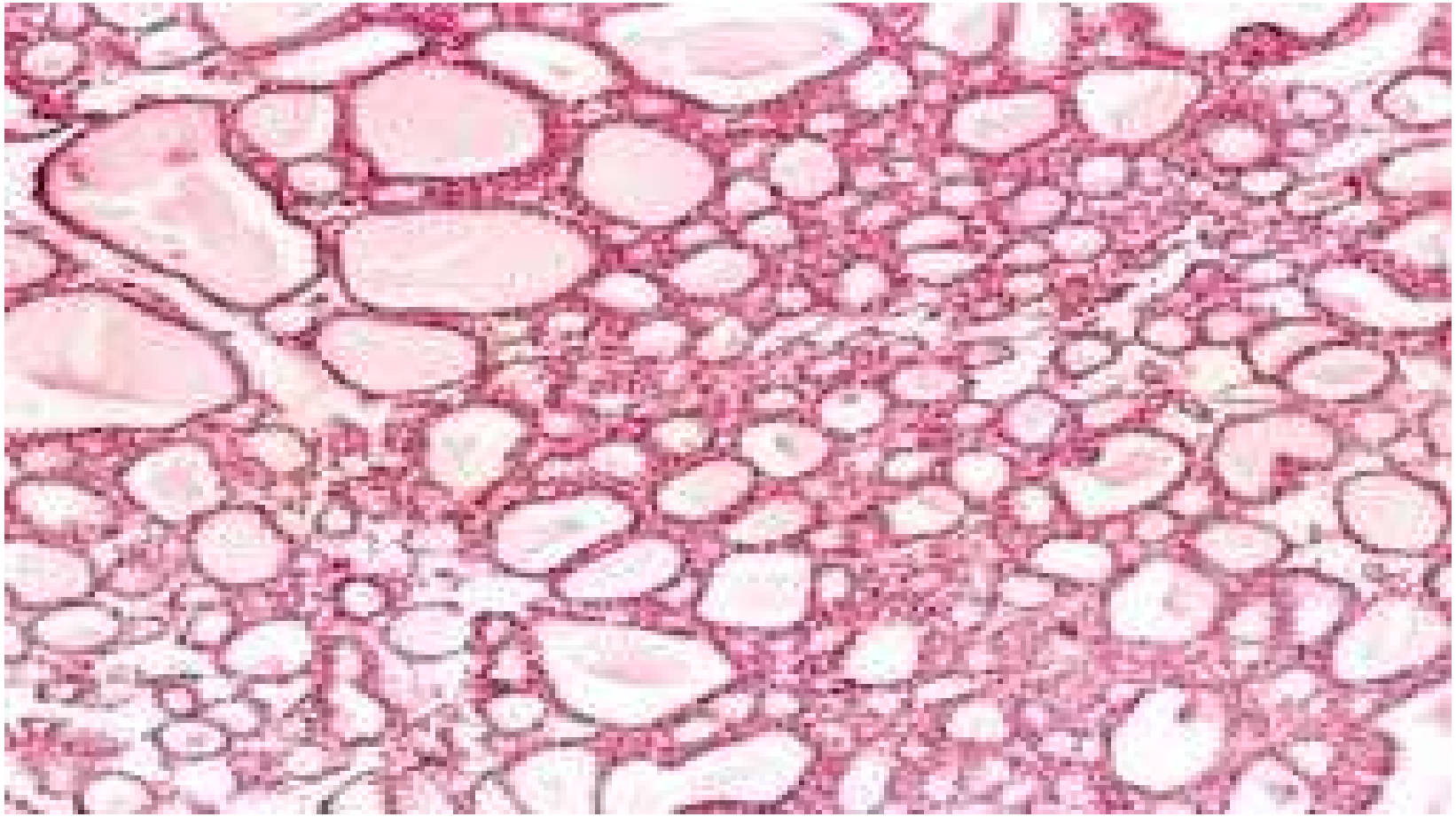
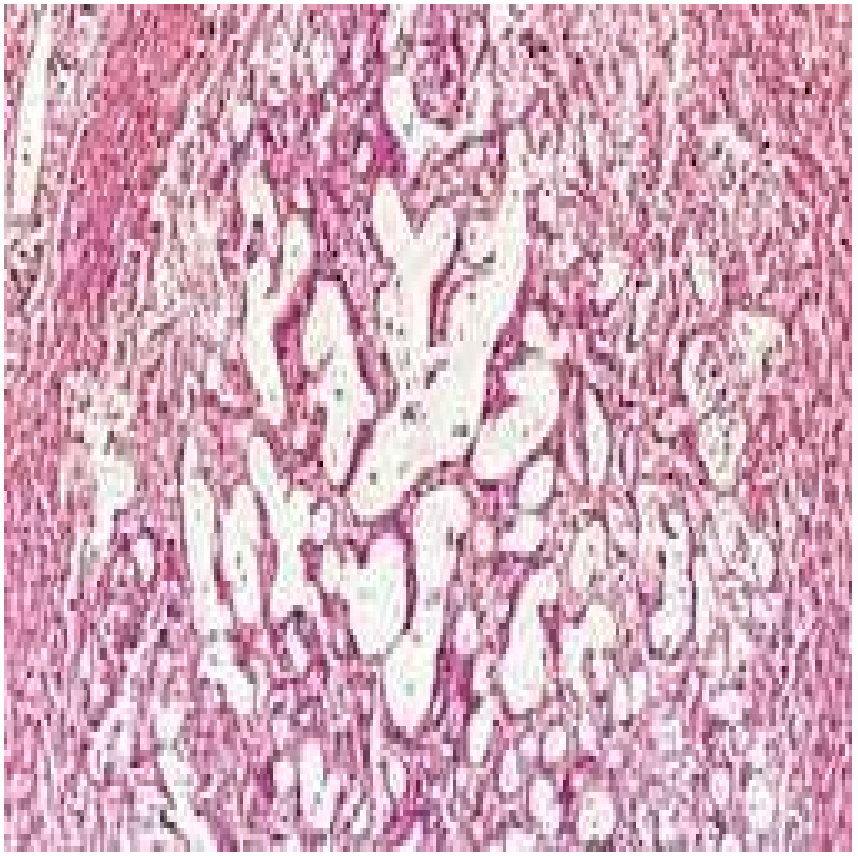


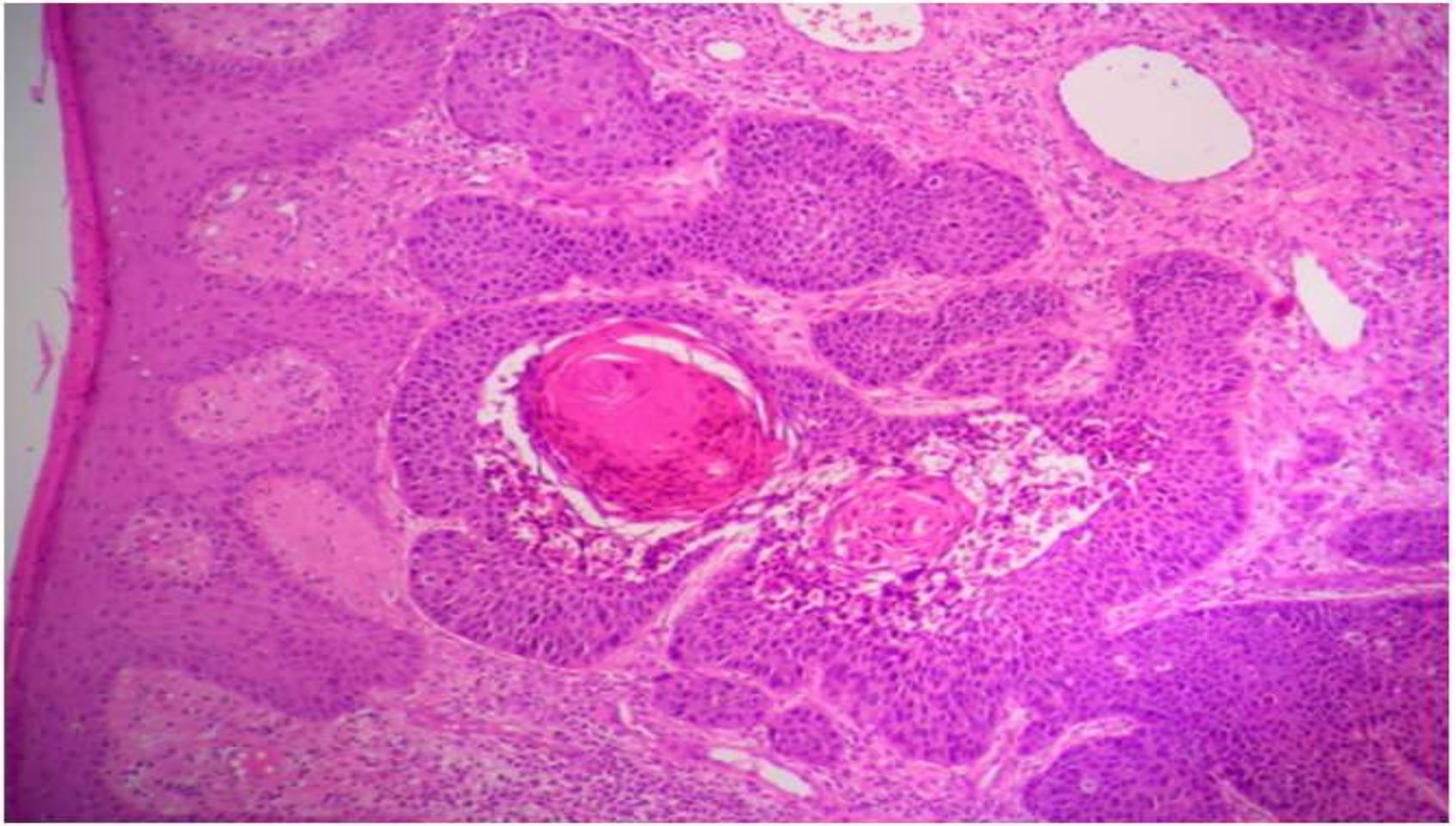
Figure 6 Benign tumor (adenoma) of the thyroid. Note the normal-looking (well-differentiated), colloid-filled thyroid follicles

Figure A liver studded with metastatic cancer



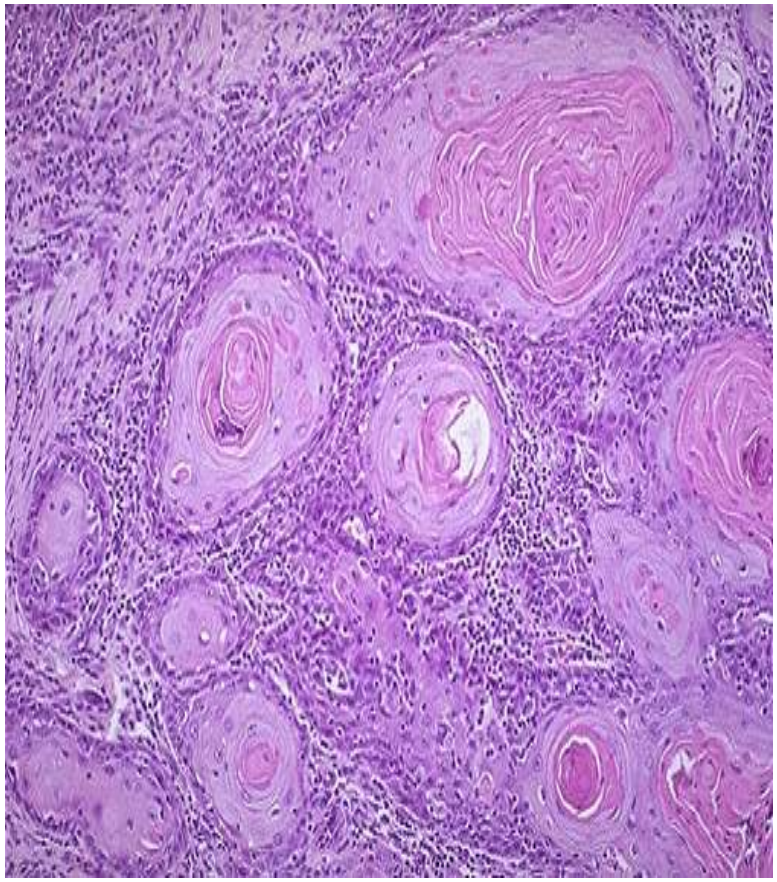
Microscopic view of liver metastasis

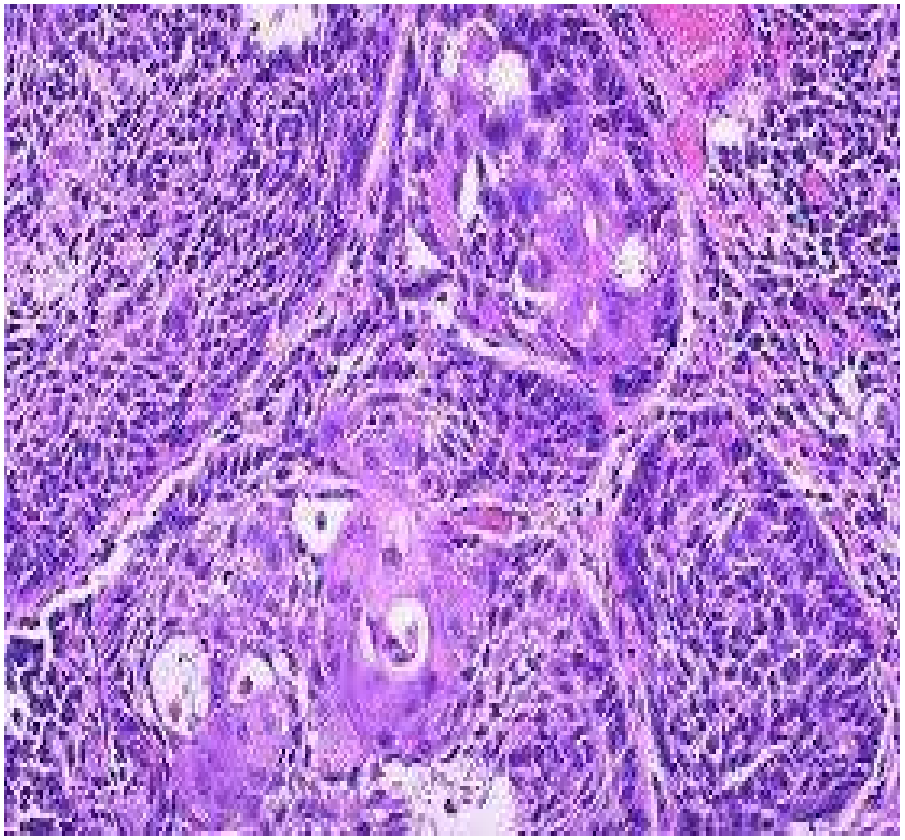
FIG 14 SQUAMOUS CELL PAPILLOMA



MICROSCOPIC STRUCTURE OF SQUAMOUS CELL PAPILLOMA

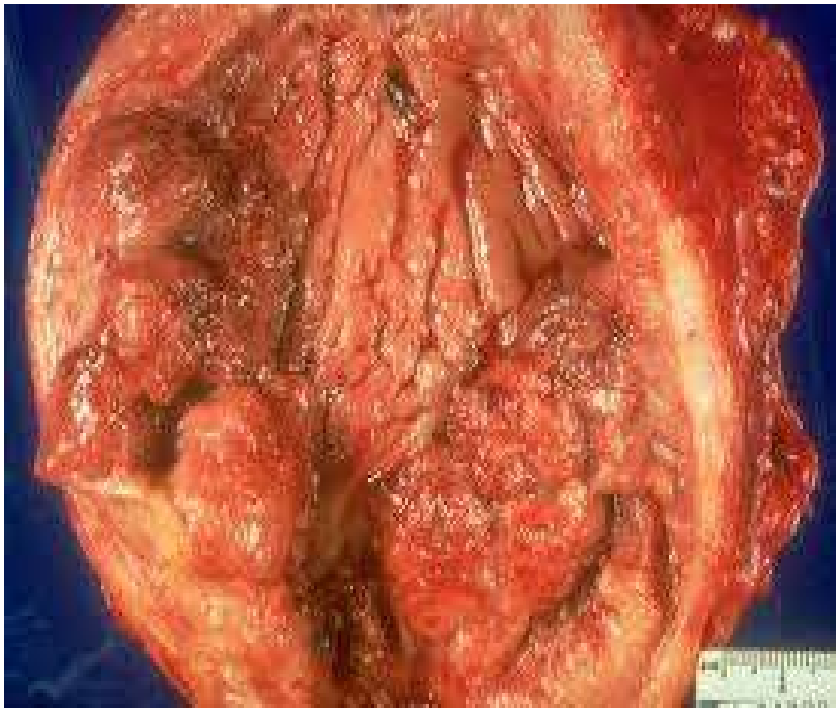
SQUAMOUS CELL CARCINOMA OF SKIN

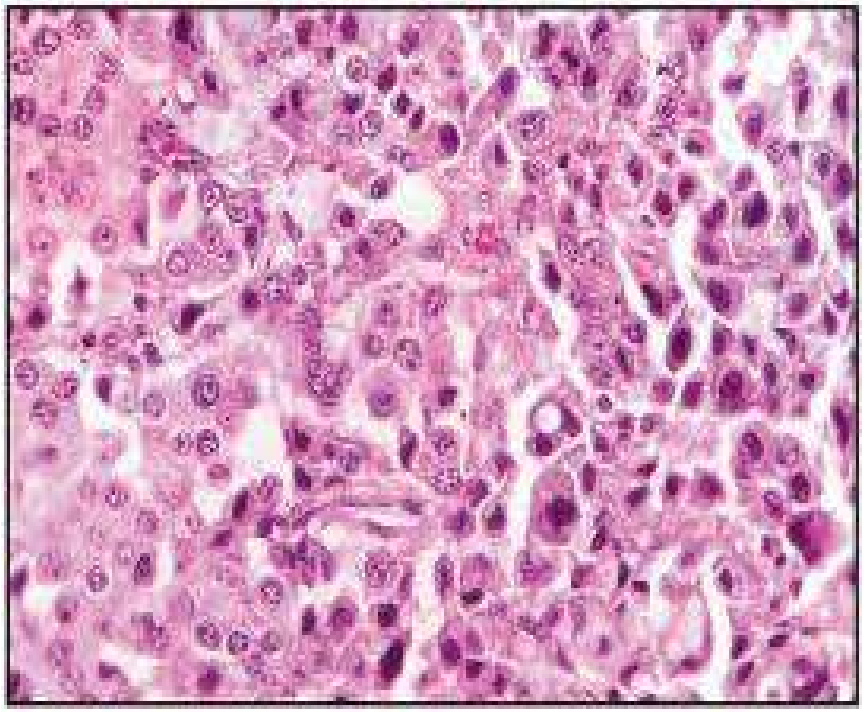




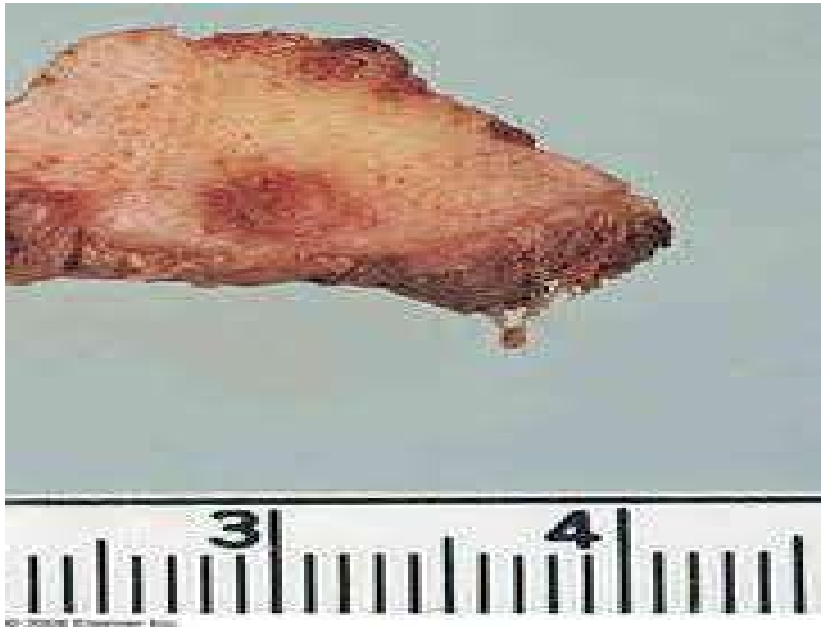
MICROSCOPIC PICTURE OF SQUAMOUS CELL CARCINOMA

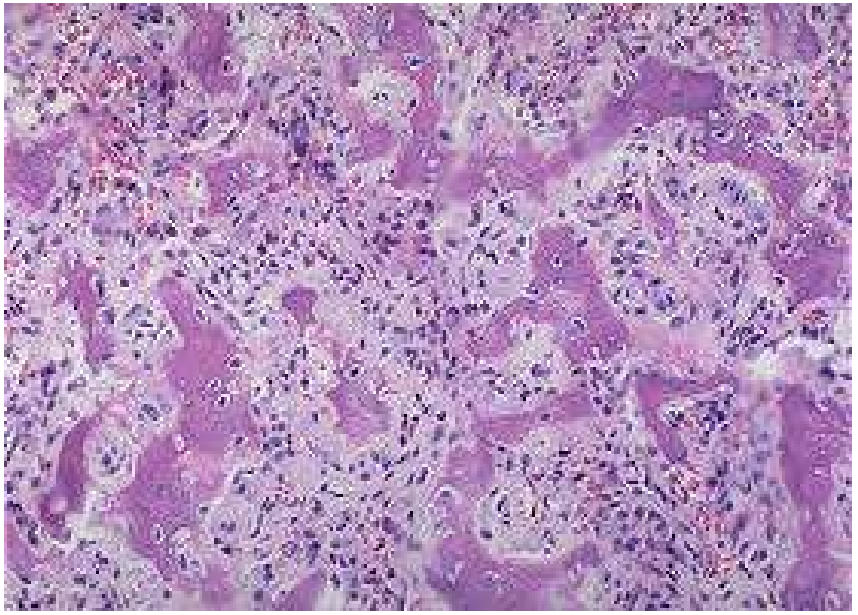
GROSS AND MICROSCOPIC STRUCTURE OF TRANSITION CELL PAPILLOMA OF BLADDER



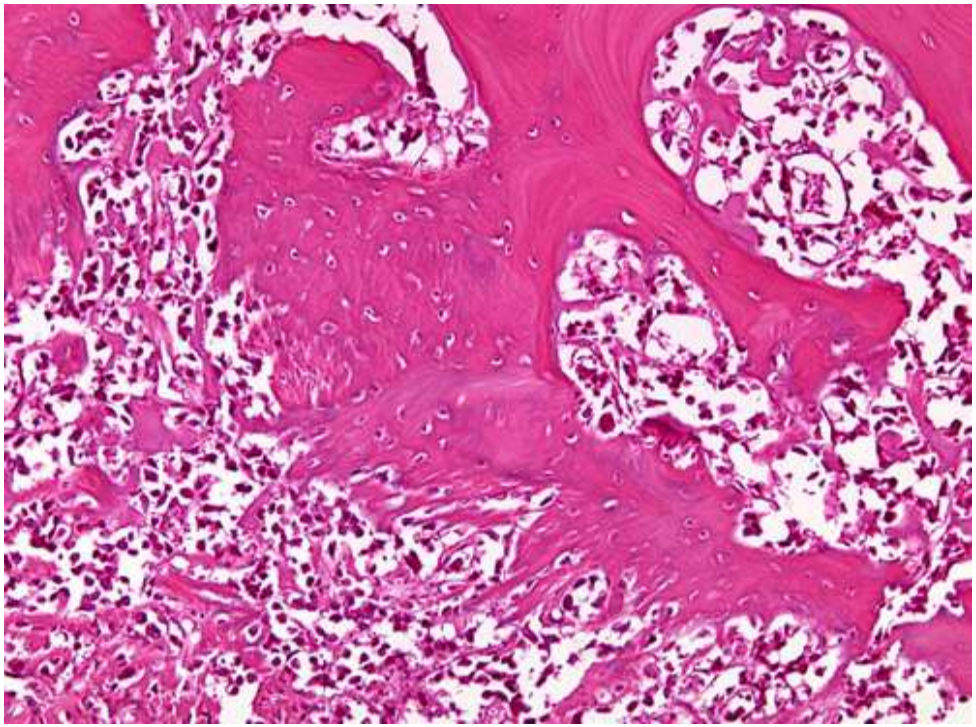


GROSS AND MICROSCOPIC STRUCTURE OF TRANSITIONAL CELL CARCINOMA OF BLADDER

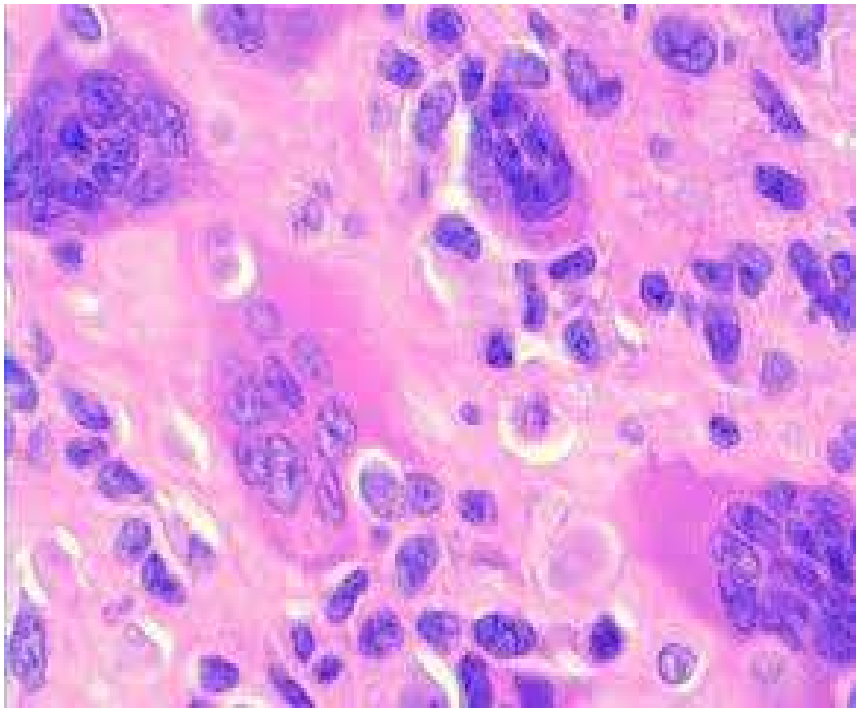




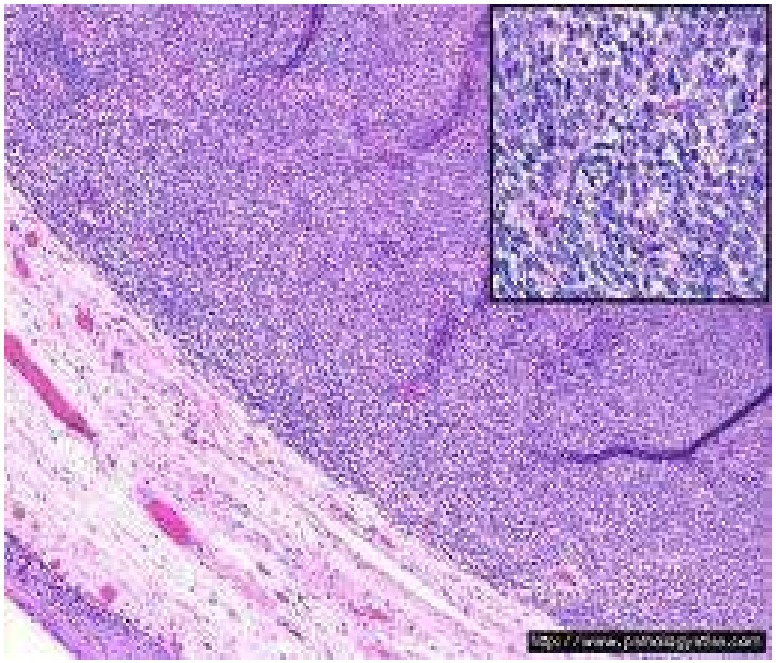
GROSS AND MICROSCOPIC STRUCTURE OF OSTEOID OSTEOMA



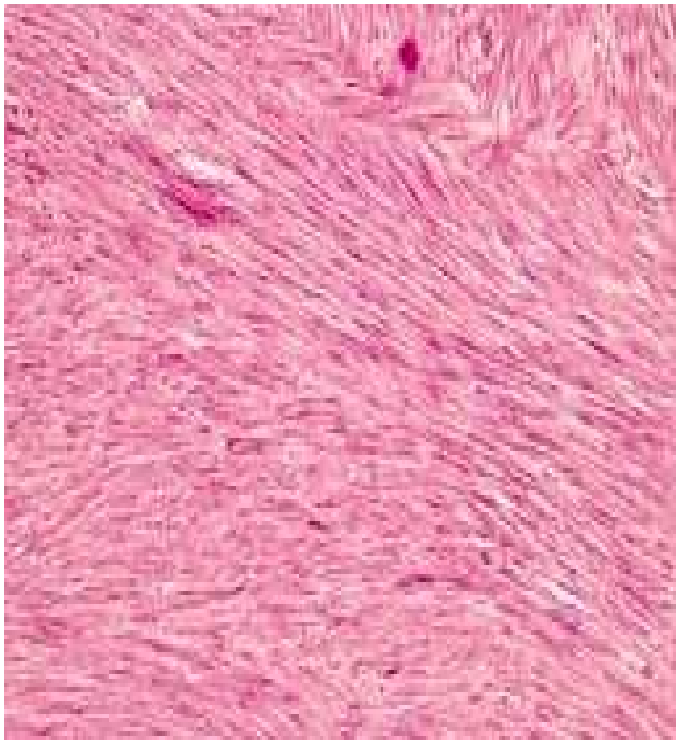
GROSS AND MICROSCOPIC FEATURES OF OSTEOGENIC SARCOMA



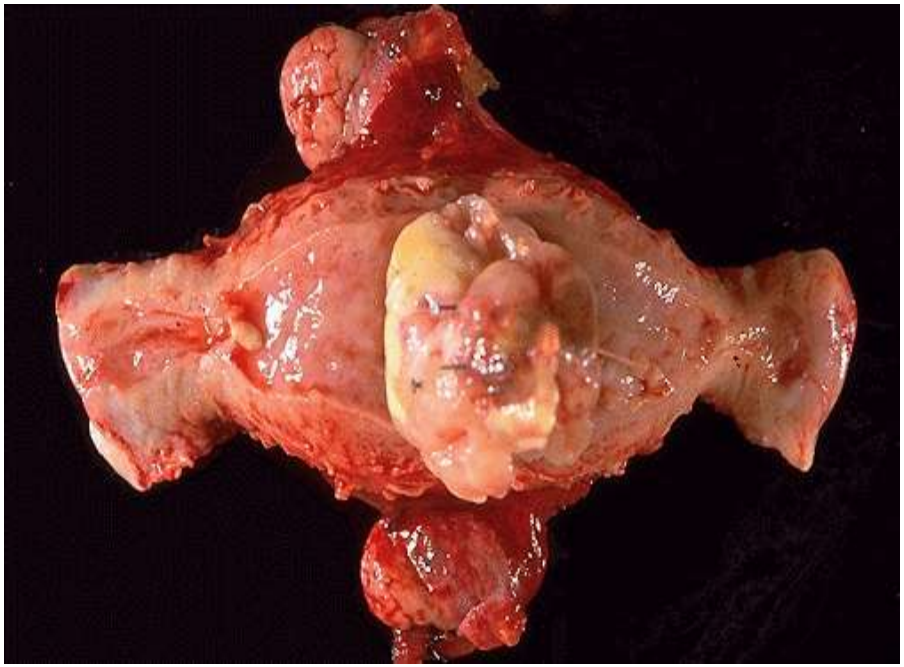
GROSS AND MICROSCOPIC FEATURES OF SYNOVIOMA

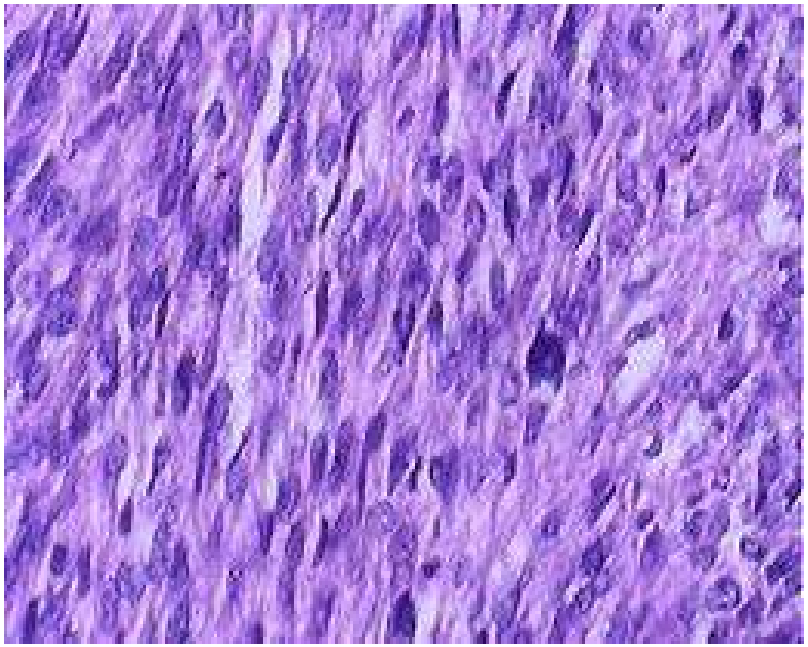


GROSS AND MICROSCOPIC FEATURES OF SYNOVIAL SARCOMA

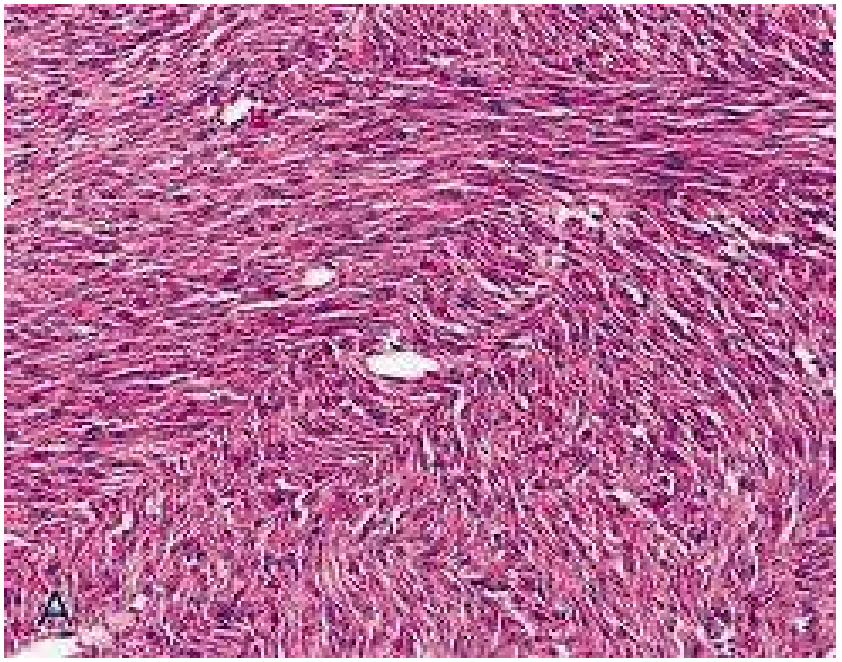


GROSS AND MICROSCOPIC FEATURES OF LIEOMYOMA

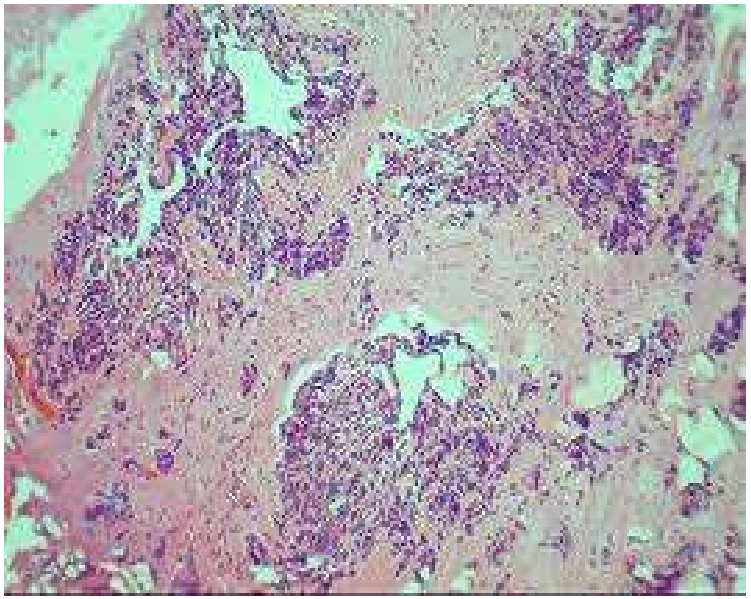




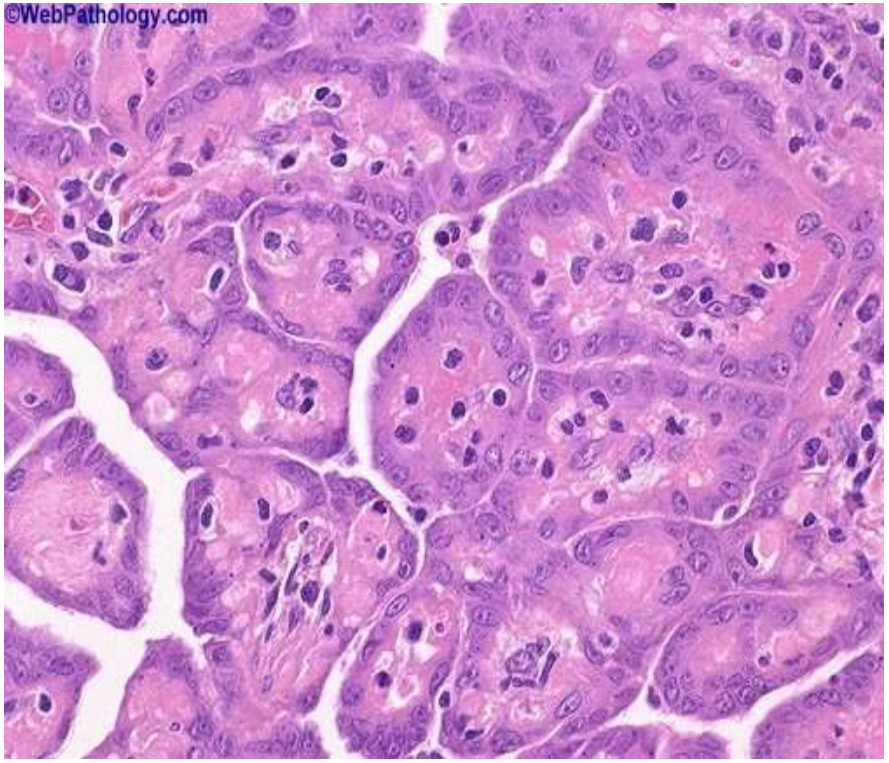
GROSS AND MICROSCOPIC FEATURES OF LIEOMYOSARCOMA



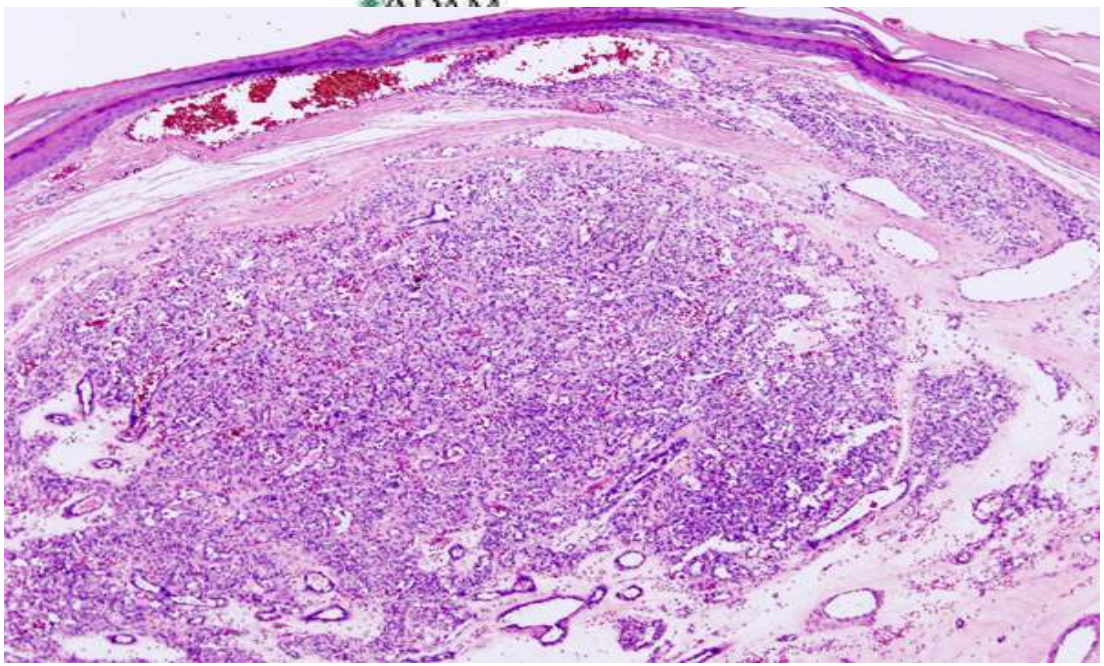
GROSS AND MICROSCOPIC FEATURES OF RABHDOMYOMA OF HEART



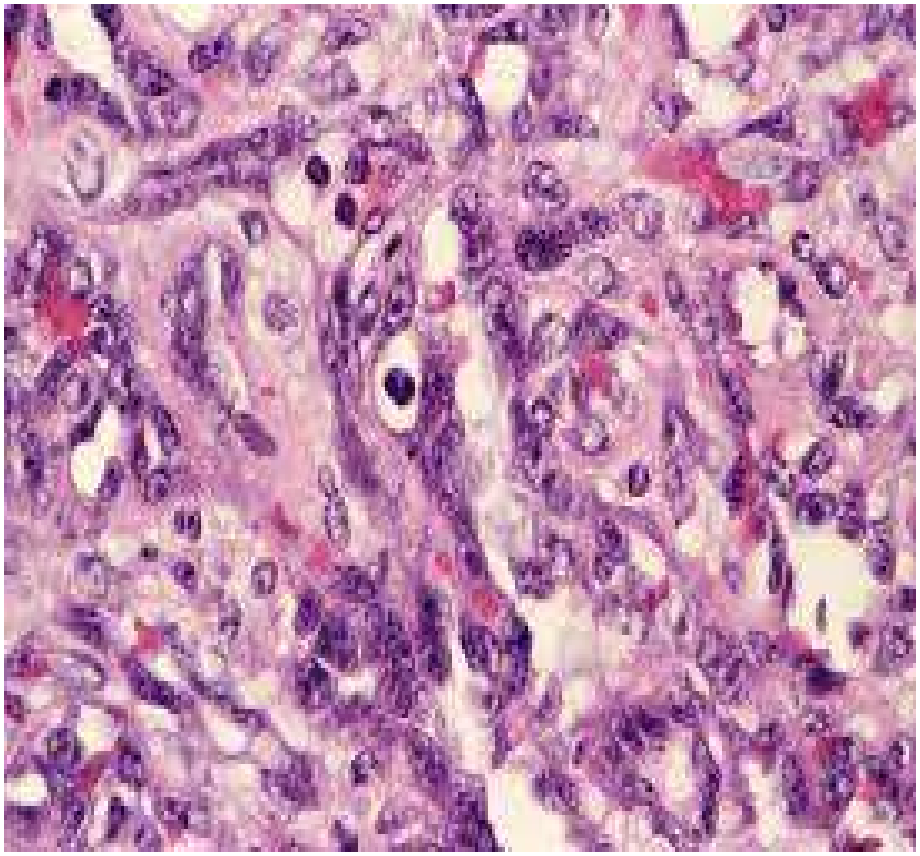
GROSS AND MICROSCOPIC FEATURES OF RHABDOMYO SARCOMA



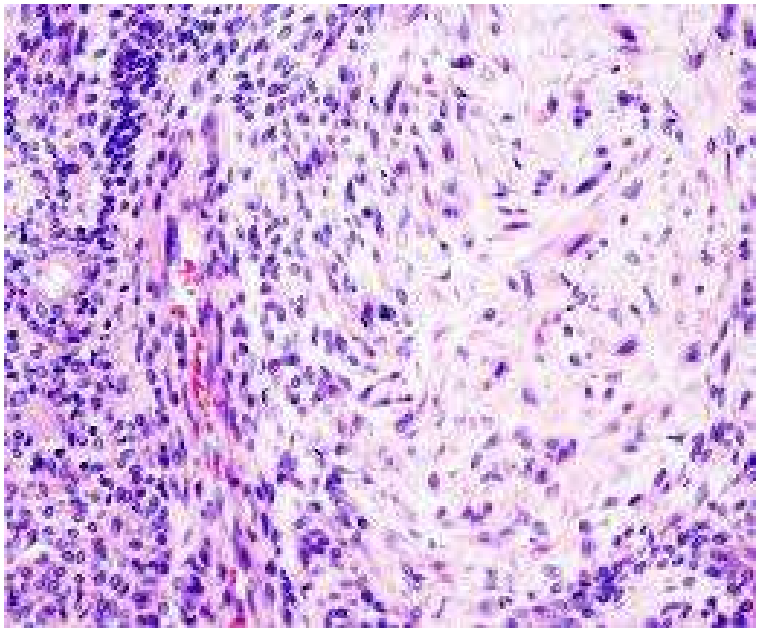
GROSS AND MICROSCOPIC PICTURES OF MESOTHELIOMA OF LUNG



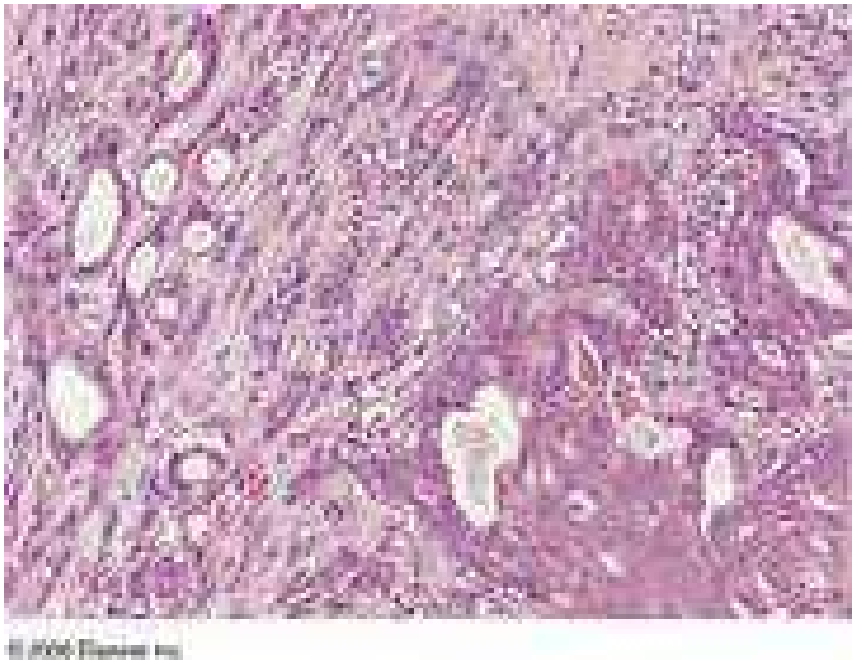
GROSS AND MICROSCOPIC PICTURES OF HEMANGIOMA



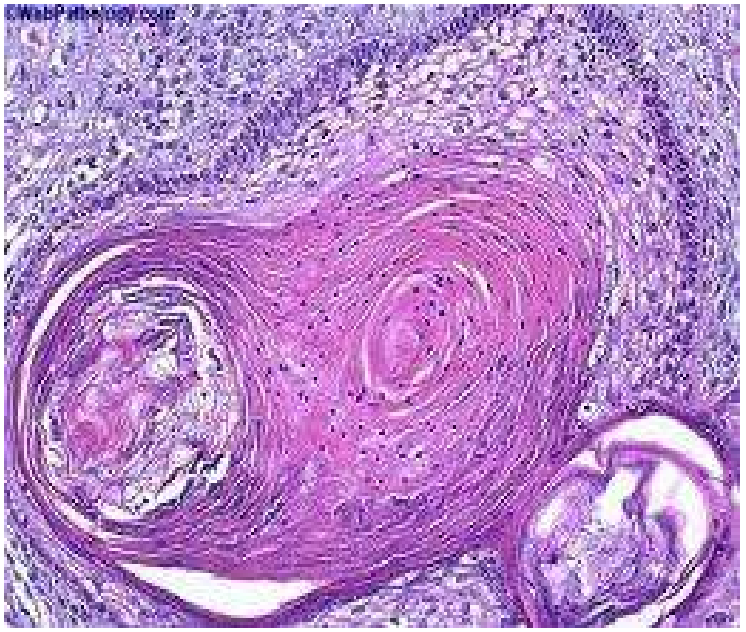
GROSS AND MICROSCOPIC FEATURES OF ANGIOSARCOMA



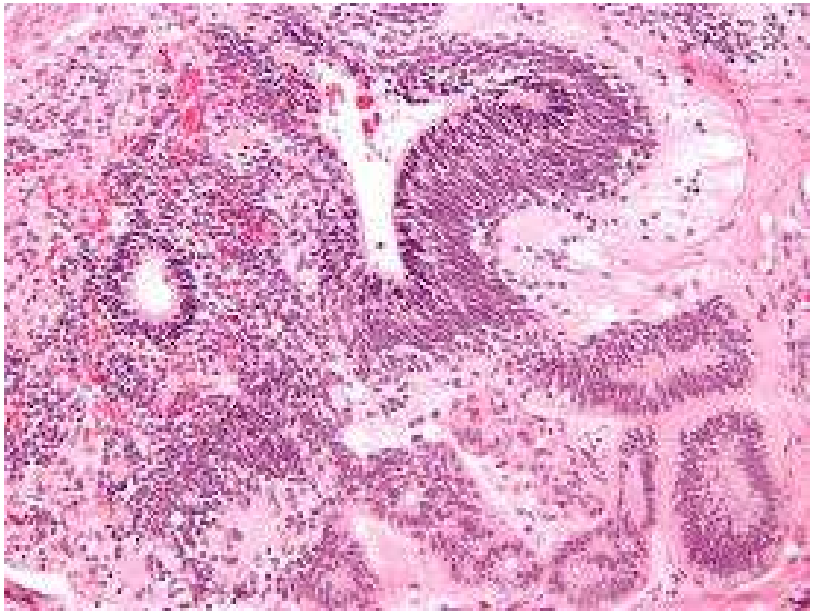
GROSS AND MICROSCOPIC PICTURES OF PLEOMORPHIC ADENOMA



GROSS AND MICROSCOPIC PICTURE OF MIXED SALIVARY GLAND TUMOR



GROSS AND MICROSCOPIC PICTURES OF MATURE TERATOMA



GROSS AND MICROSCOPIC PICTURES OF IMMATURE TERATOMA

Evidence base

Modern Pathology (2008) 21, 1156–1167

NAME OF AUTHAR	ARTICLE NAME AN LEVEL OF EVIDENCE	ABSTRACT	METHOD	CONCLUSION
Bora Gurel1, Tsuyoshi Iwata1, Cheryl M Koh1, Robert B Jenkins2, Fusheng Lan2, Chi Van Dang3, Jessica L Hicks1, James Morgan1, Toby C Cornish1, Siobhan Sutcliffe4, William B Isaacs5,6,7, Jun Luo5,7 and Angelo M De Marzo1,5,6,7,8	Nuclear MYC protein overexpression is an early alteration in human prostate Carcinogenesis MEDIUM LEVEL OF EVIDENCE	The MYC onco-protein is a transcription factor that regulates cell proliferation, metabolism, protein synthesis, mitochondrial function and stem cell renewal. A region on chromosome 8q24 encompassing the MYC locus is amplified in prostate cancer, but this occurs mostly in advanced disease suggesting that MYC alterations occur late in prostate cancer. In contrast, MYC mRNA is elevated in most prostate cancers, even those of relatively low stage and grade (eg Gleason score 6) suggesting that MYC plays a role in initiation. However, since MYC protein levels are tightly regulated, elevated MYC	Materials and methods Antibodies The anti-MYC rabbit monoclonal antibody used for both western blotting and immunohistochemistry was obtained from Epitomics (Burlingame, CA, USA, Clone Y69). Tissues and Tissue Microarray Construction	Discussion In this study, we show that overexpression of MYC protein in prostate cancer is a remarkably frequent event. Unlike previous studies that reported that MYC protein is overexpressed nearly exclusively in the cytoplasm in prostate cancer cells,7,24 we found MYC protein primarily in the nuclei of all expressing cells tested. The specificity of the staining was supported by genetically defined control experiments. Although it has been known for many years that MYC mRNA is

1.Which of the following is malignant tumour?

a.Squamous cell papilloma

b.Leiomyosarcoma

c.Hemangioma

d.Fibroadenoma of breast

2. A 76-year-old man farmer presents with a 2-cm mass on the left side of his forehead. A biopsy reveals squamous cell carcinoma. Which one of the following causes the formation of pyrimidine dimers in DNA and is associated with the formation of squamous cell carcinoma?

a. Aflatoxin B1

b. Vinyl chloride

c. UVC

d. UVB

e. Epstein-Barr virus

2. A 17-year-old man presents with a lesion on his face that measures approximately 1.5 cm in its greatest dimension. He has a history of numerous similar skin lesions that have occurred mainly in sun-exposed areas. The present lesion is biopsied and reveals an invasive squamous cell carcinoma. This patient most probably has one type of a group of inherited diseases associated with unstable DNA and increased incidence of carcinoma.

Which of the following is the most likely diagnosis?

a. Xeroderma pigmentosa

b. Wiskott-Aldrich syndrome

c. Familial polyposis

d. Sturge-Weber syndrome

e. Multiple endocrine neoplasia type I

4. A 56-year-old man presents with a 25-pound weight loss over the past 6 months. He says that he has no appetite for food and over the past several weeks has also developed an “ache” in his stomach region. Gastroscopy finds a fungating mass involving the distal portion of the lesser curvature of his stomach. Biopsies from this mass reveal infiltrating groups of highly atypical cells forming glandular structures. The malignant cells extend through the muscularis mucosa into the submucosa, but they do not extend into the muscularis externa. This type of malignancy is most frequent in which one of the following geographic locations?

a. Canada

b. France

c. Japan

d. United Kingdom

e. United States

5. A 57-year-old man presents with signs of fatigue that are the result of anemia. Workup reveals that his anemia is the result of bleeding from a colon cancer located in the sigmoid colon. The lesion is resected and at the time of surgery no metastatic disease is found. Which of the following markers would be most useful for future follow-up of this patient for the evaluation of possible metastatic disease from his colon cancer?

a. α fetoprotein (AFP)

b. Carcinoembryonic antigen (CEA)

c. Chloroacetate esterase (CAE)

d. Human chorionic gonadotropin (hCG)

e. Prostate-specific antigen (PSA)

1.Which of the following is malignant tumour?

Answer -b.Leiomyosarcoma

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Answer-d. UVB

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Answer-c. Japan

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Answer-b. Carcinoembryonic antigen (CEA)