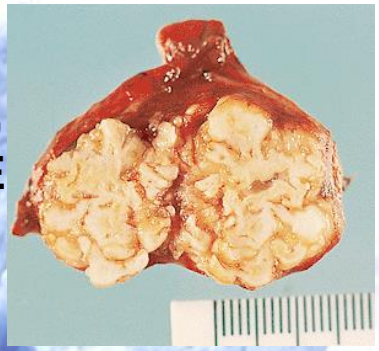
LECTURE 11

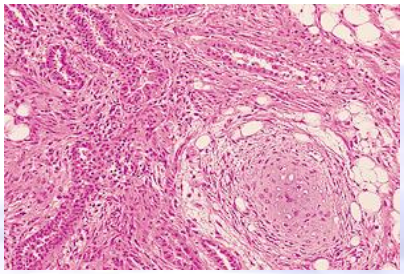
ANTONIE VAN LEEUWENHOEK
(1632-1723)

DISTURBANCES OF GROWTH AND DIFFERENTIATION

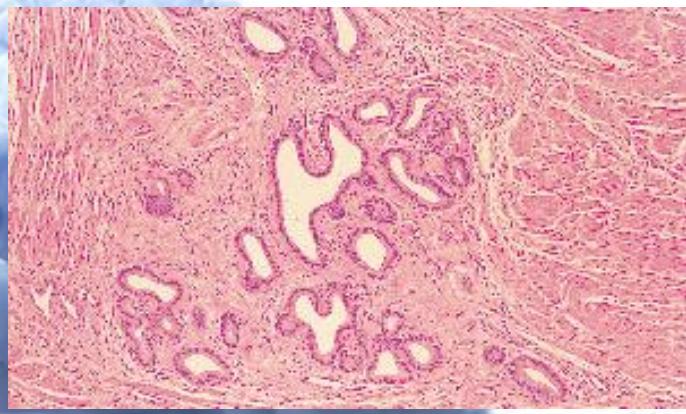
DISTURBANCES IN GROWTH

HAMARTOMAS – FOCAL, USUALLY LIMITED, HYPERPLASTIC, NOT PROPORTIONAL TO THE TISSUE PRESENT IN THE ORGAN

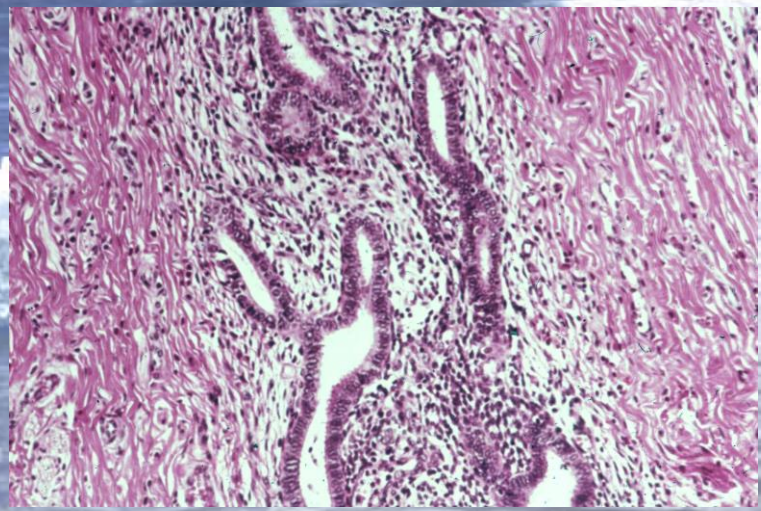




CHORISTOMAS – CHANGES SIMILAR TO HAMARTOMA, BUT THE TISSUE IS NOT NORMALLY SEEN IN THAT PART OF THE BODY



ECTOPY – TISSUE WITH PROPER APPEARANCE BUT IMPROPER PLACEMENT

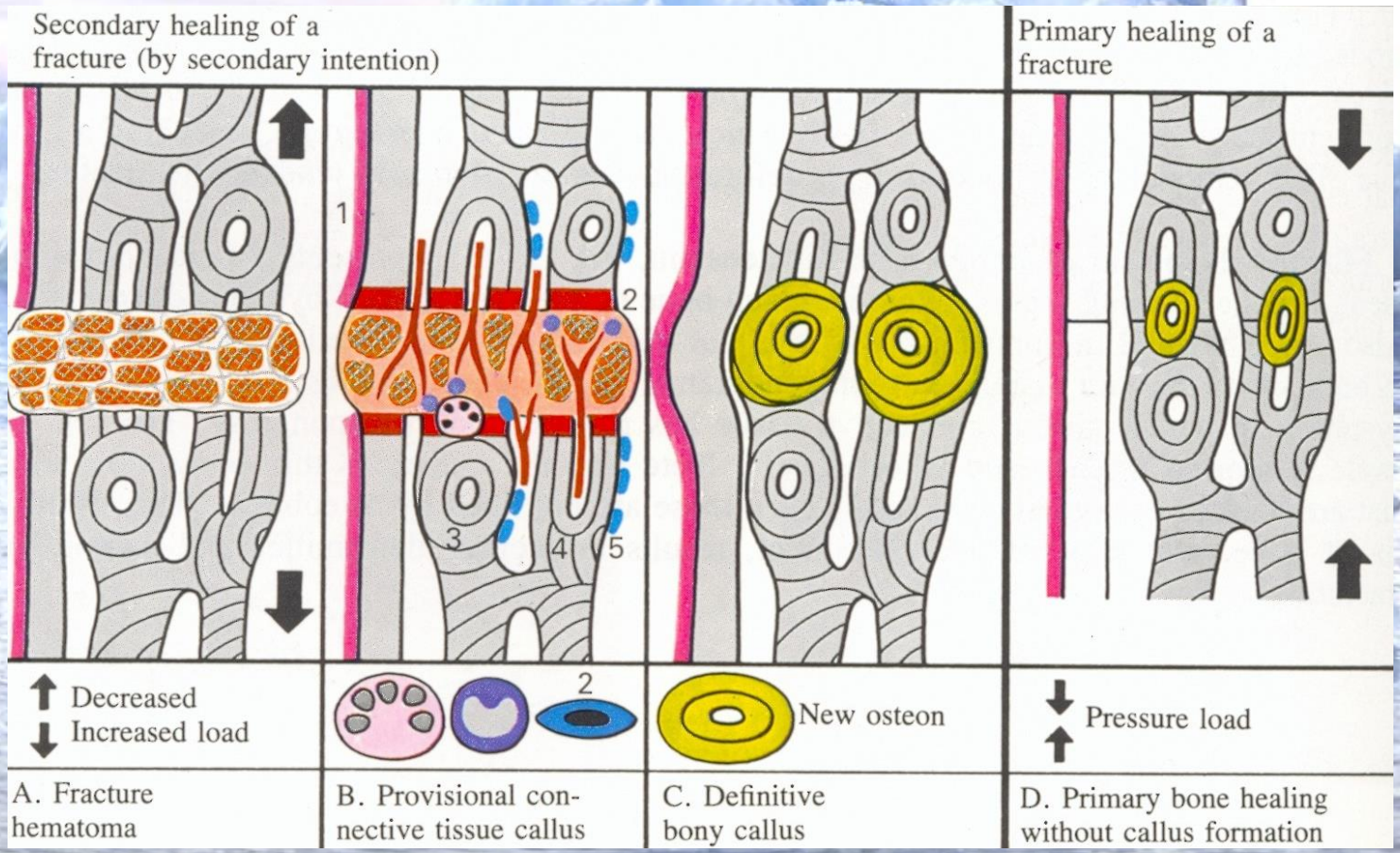


DISTURBANCES OF GROWTH AND DIFFERENTIATION

REPAIR PROCESSES

THE INJURY OF A TISSUE OF ANY KIND, INFLAMMATORY PROCESSES STIMULATE THE REPAIR PROCESSES – PROLIFERATION OF CELLS PROVOKING THE RESTORATION OF THE PROPER STRUCTURE AND FUNCTION OF THE TISSUE.

***EXAMPLE:* THE HEALING OF A BROKEN BONE**

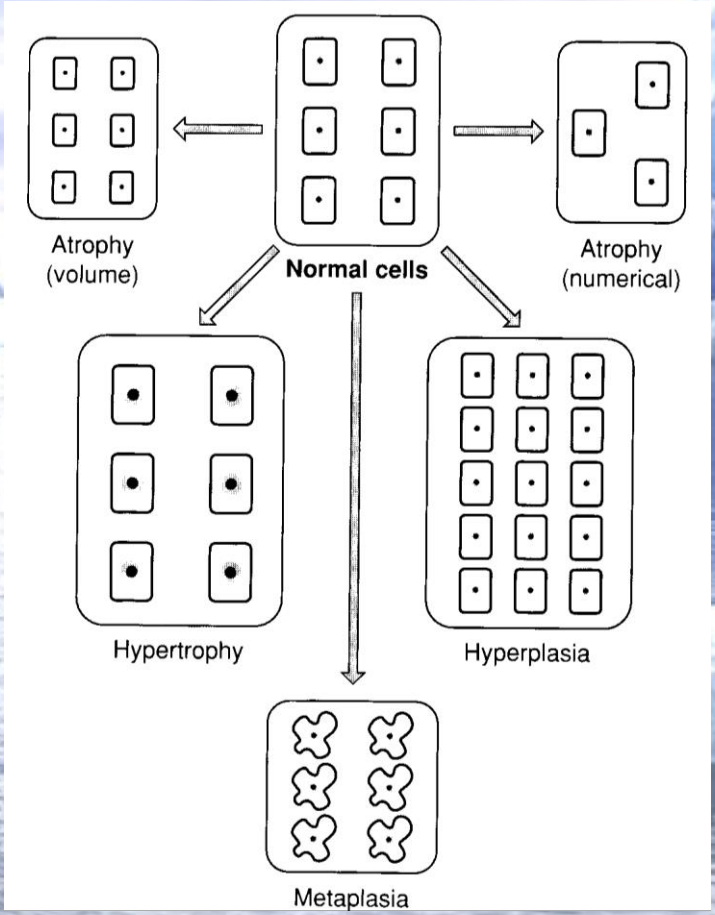


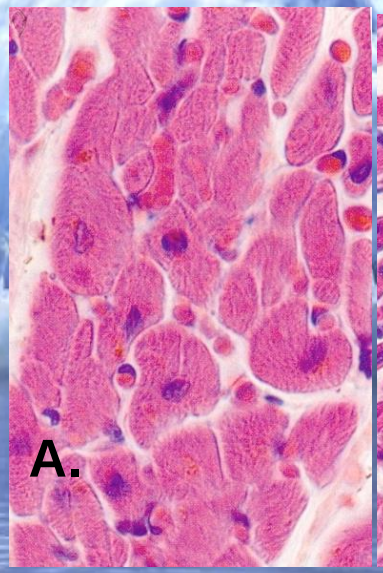
DISTURBANCES OF GROWTH AND DIFFERENTIATION

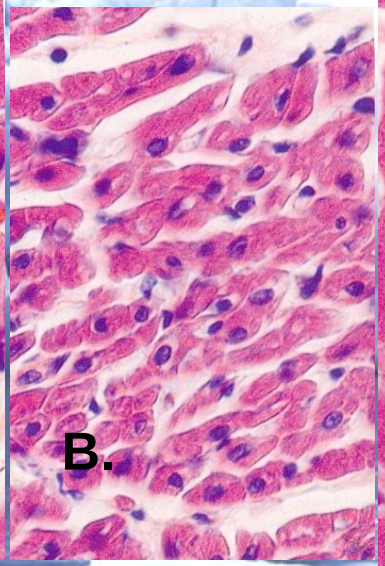
HYPERTROPHY AND ATROPHY

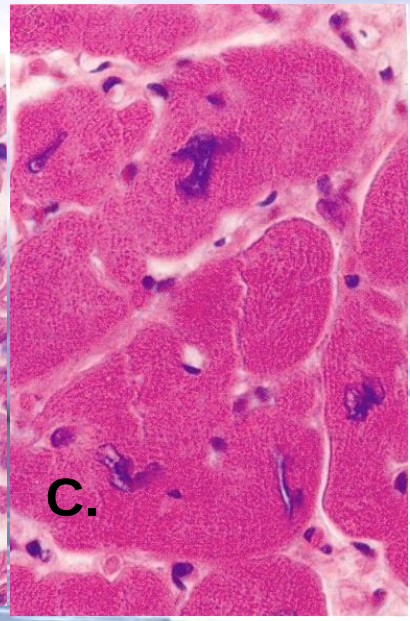
HYPERTROPHY - INCREASE IN THE SIZE OF THE CELLS AND TISSUE OR ORGAN. MOST COMMON CAUSES: OVERWORKING OR HORMONAL STIMULATION.

ATROPHY – EXAMPLE ATROPHY OF THE HEART





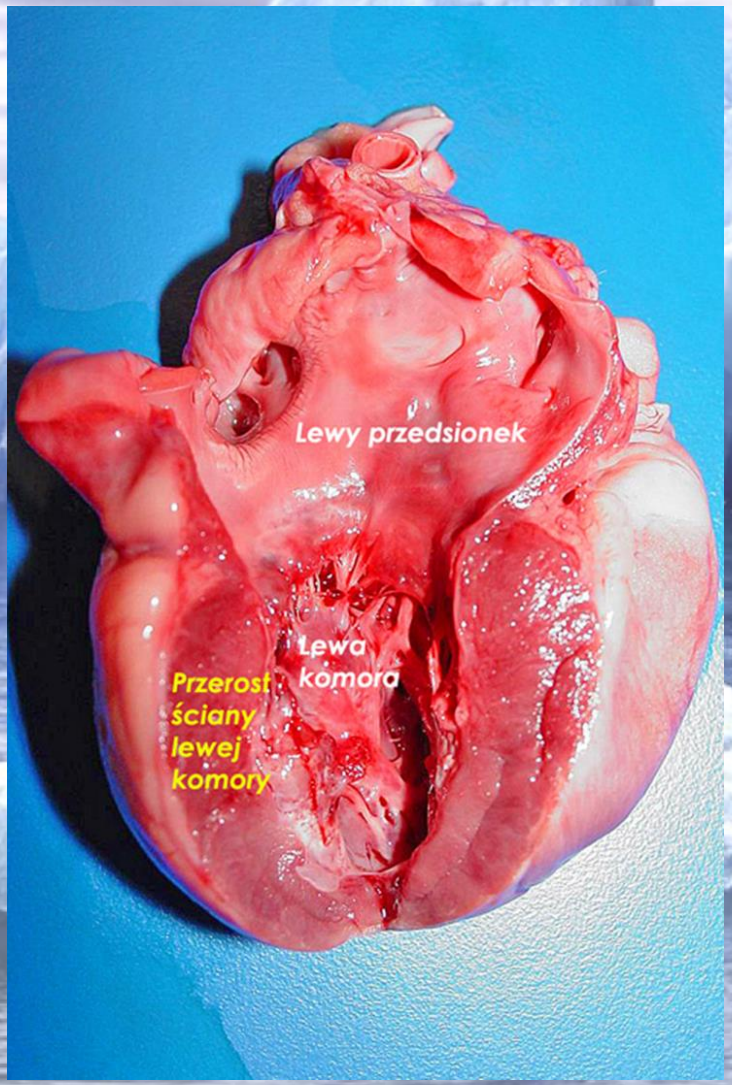




PICTURE OF THE HEART IN THREE DIFFERENT CASES

A. NORMAL MUSCLE
B. ATROPHIC MUSCLE
C. HYPERTROPHIC MUSCLE

HEART MUSCLE HYPERTROPHY

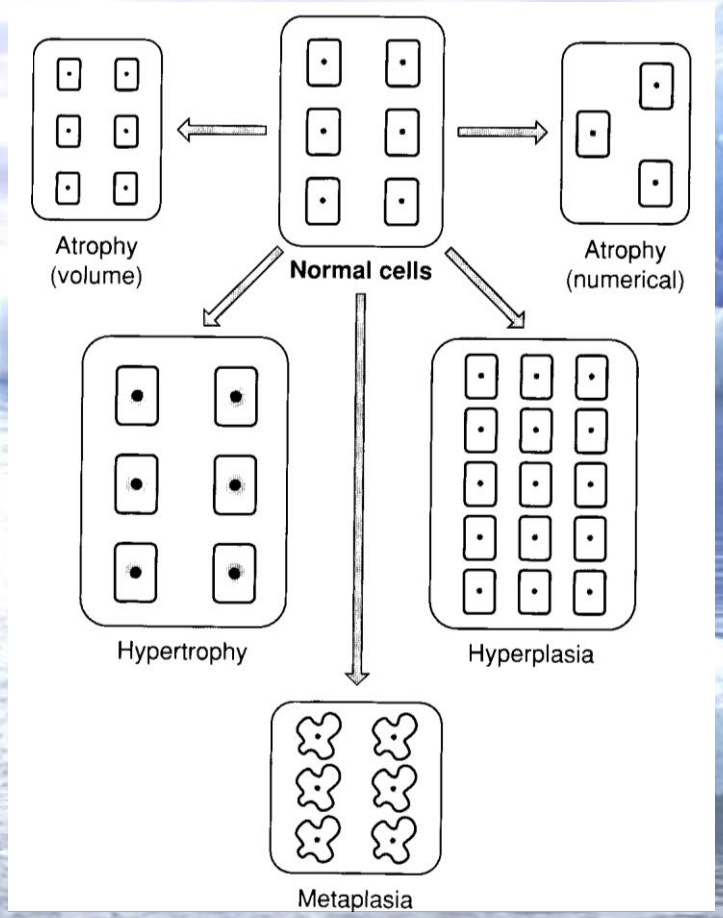


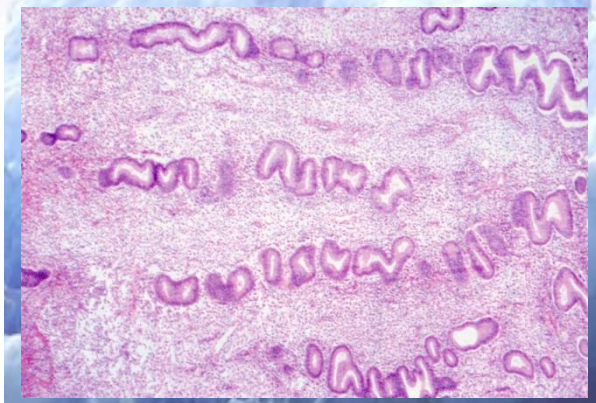
DISTURBANCES OF GROWTH AND DIFFERENTIATION

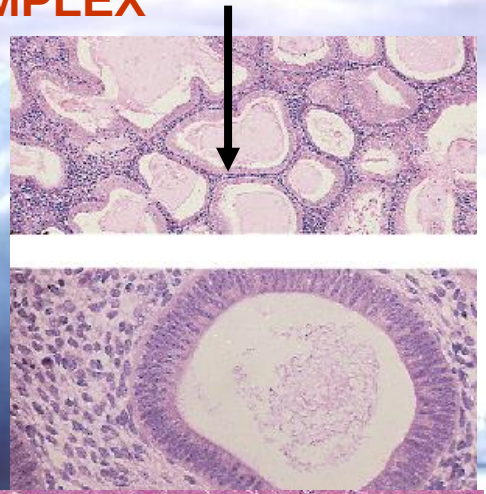
HYPERPLASIA

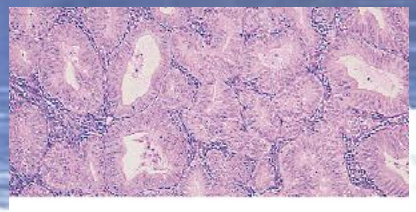
HYPERPLASIA - THE ABSOLUTE INCREASE IN THE AMOUNT OF CELLS BUT NOT THE TISSUE OR ORGAN.

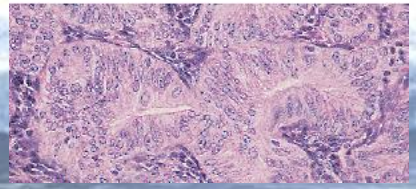
EXAMPLE : **HYPERPLASIA ENDOMETRII SIMPLEX**

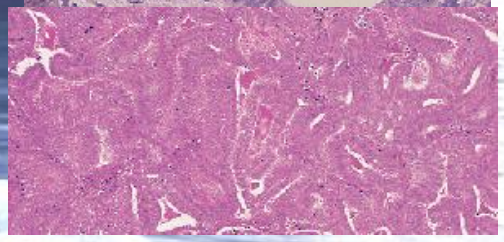


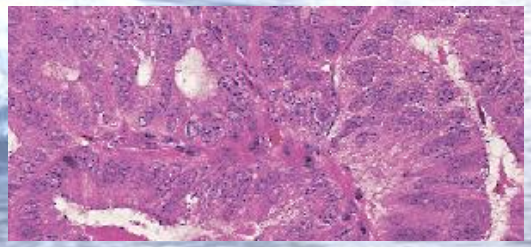




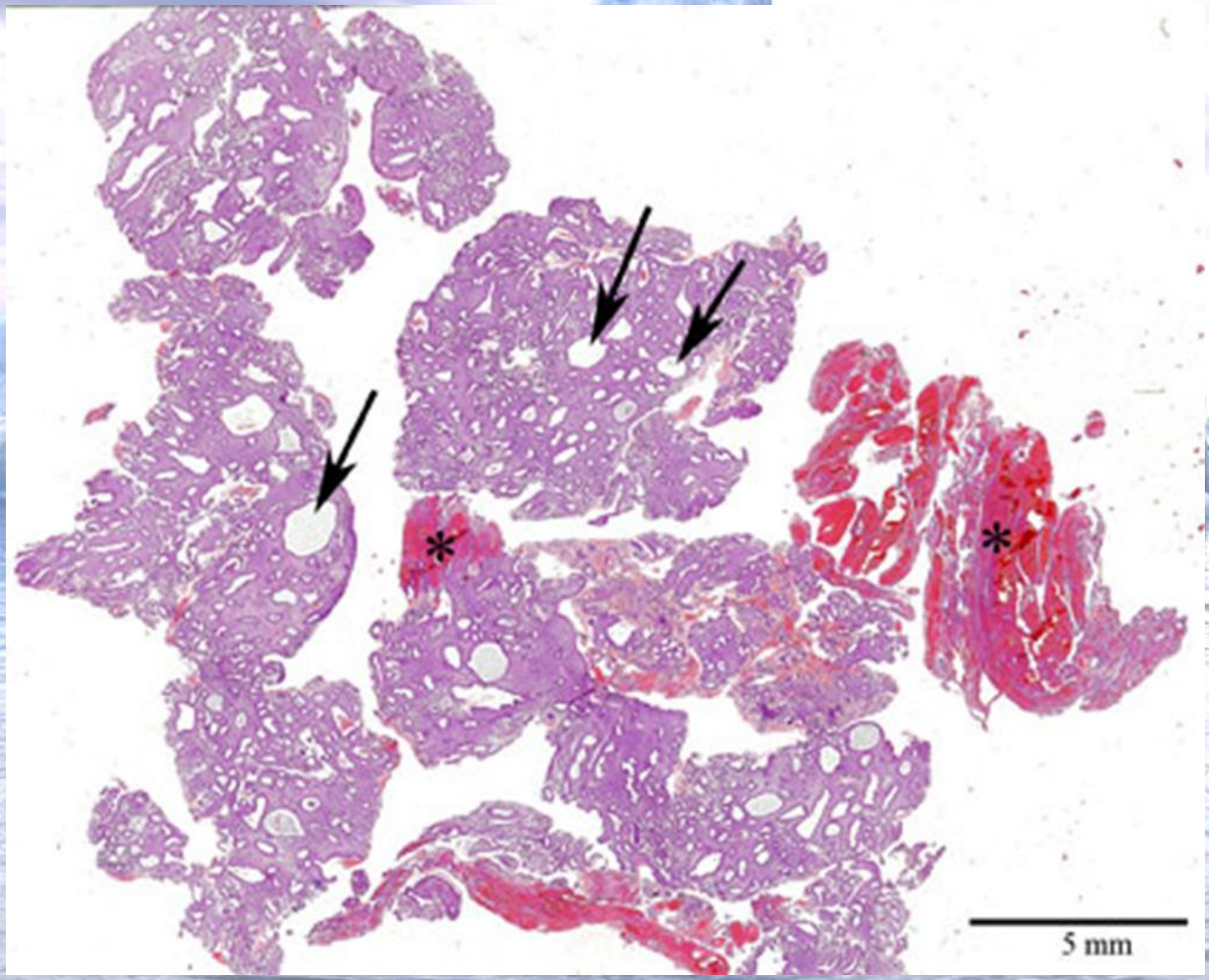








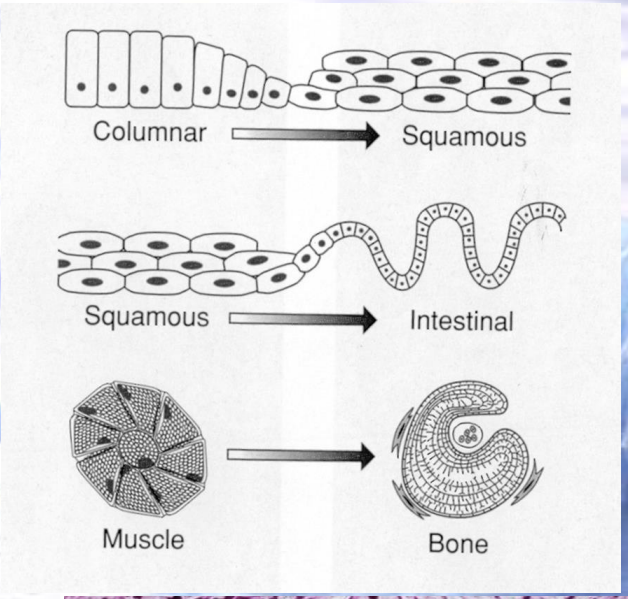
ENDOMETRIAL HYPERPLASIA

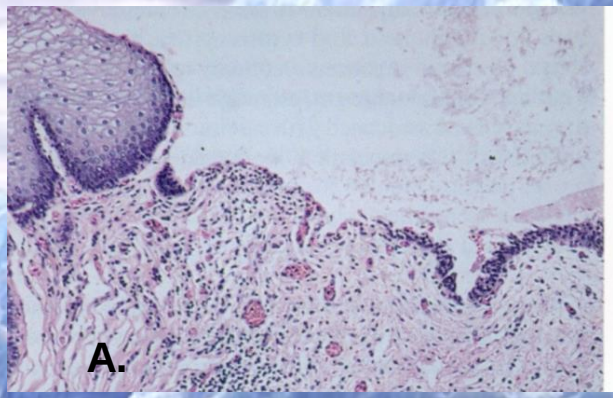


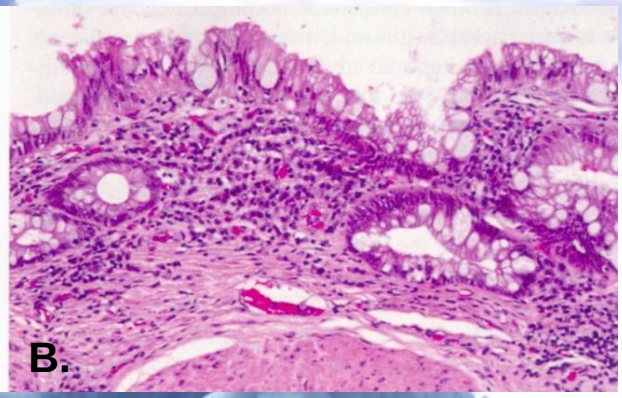
DISTURBANCES OF GROWTH AND DIFFERENTIATION

METAPLASIA

METAPLASIA- IS THE CHANGE OF ONE TYPE OF ADULT CELLS OR TISSUE INTO OTHER ADULT CELLS OR TISSUE. THIS PROCESS IS ONLY SEEN IN THE SAME GROUPS OF TISSUES eg. CONNECTIVE, EPITHELIAL.

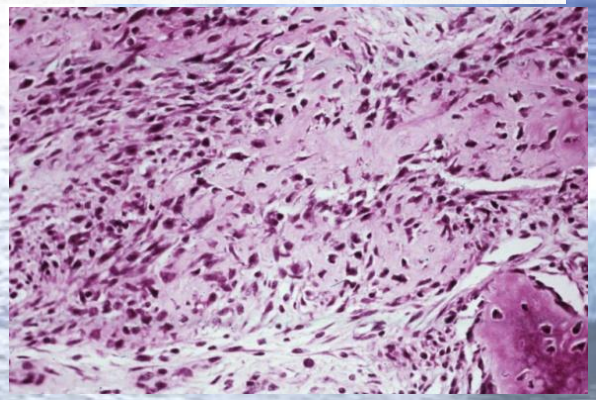






SQUAMOUS METAPLASIA (A)

INTESTINAL (B) IN MUCOSA OF BLADDER



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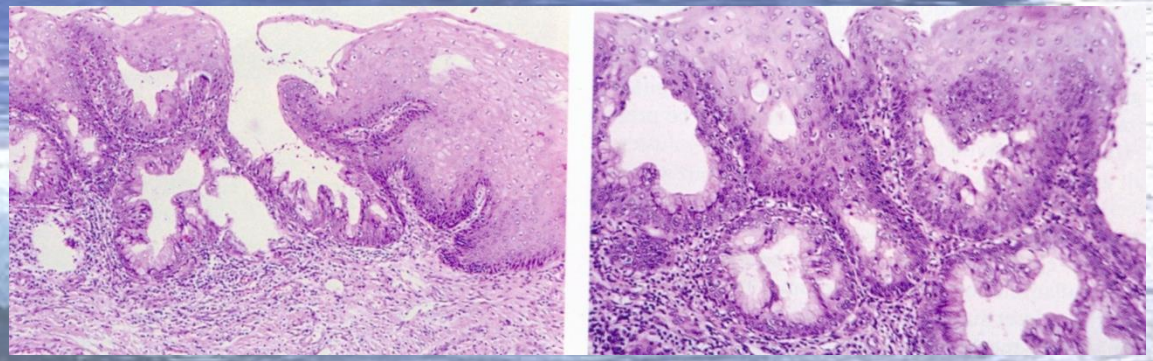


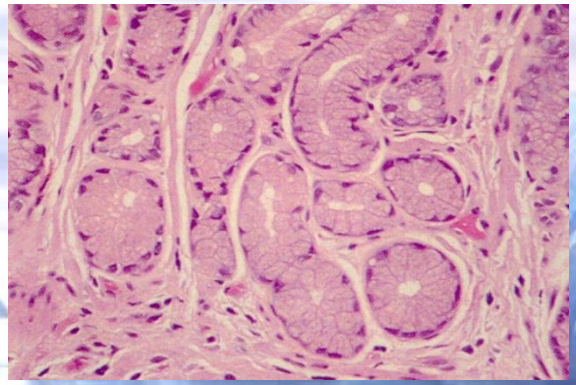
SQUAMOUS CELL EPITHELIUM IN THE TRANSITIONAL ZONE OF THE CERVIX

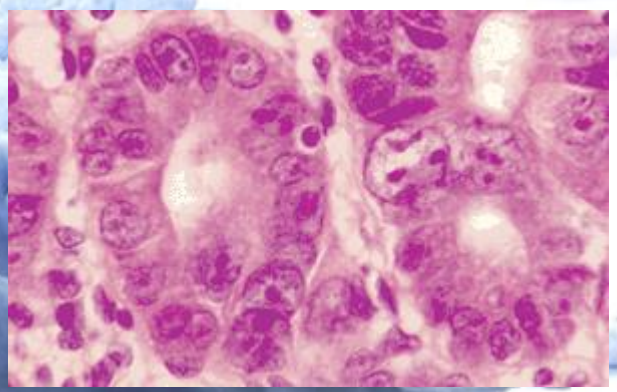
INTESTINAL METAPLASIA IN STOMACH

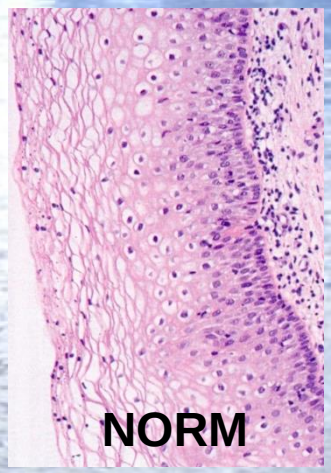
DISTURBANCES OF GROWTH AND DIFFERENTIATION

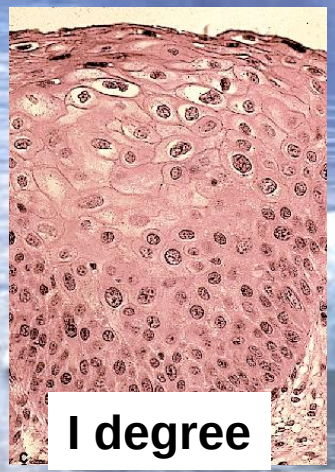
DYSPLASIA

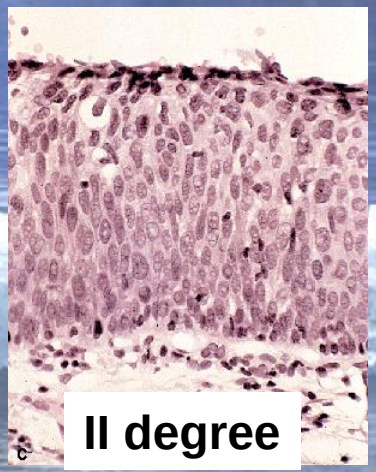
DYSPLASIA – IS THE DISTURBANCE CONCERNING MAINLY THE EPITHELIAL TISSUE, WHICH IS THE CHANGE IN THE SIZE, SHAPE OF CELLS, SIZE OF NUCLEUS, THE PROPORTION OF NUCLEUS TO CYTOPLASM (NUCLEUS PREVAILS), DISTURBANCES IN THE LAYERING STRUCTURE OF THE EPITHELIUM, INCREASE IN AMOUNT OF IMPROPER MITOTIC FIGURES (CIN, VIN etc VERSUS BENIGN DYSPLASIA)

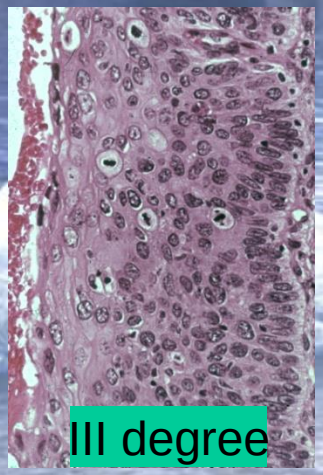


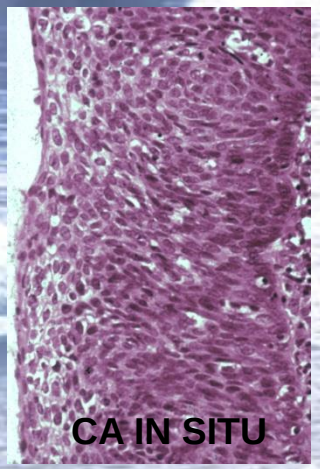




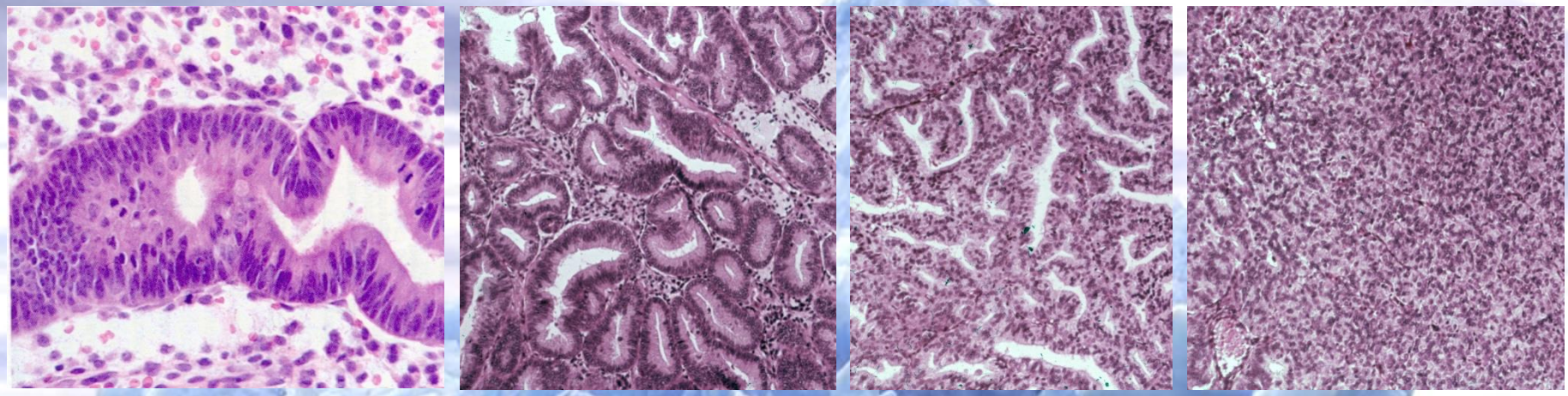




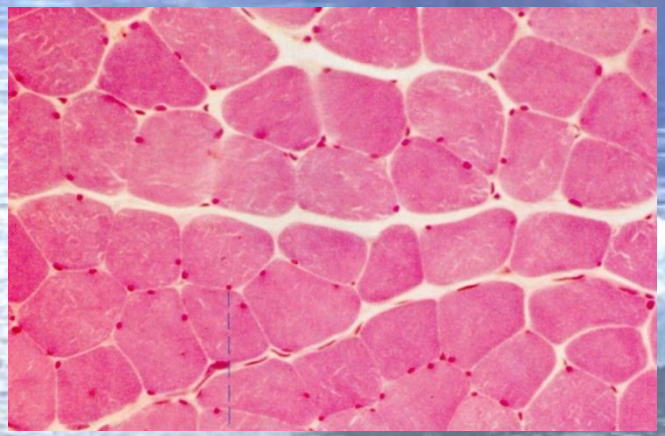




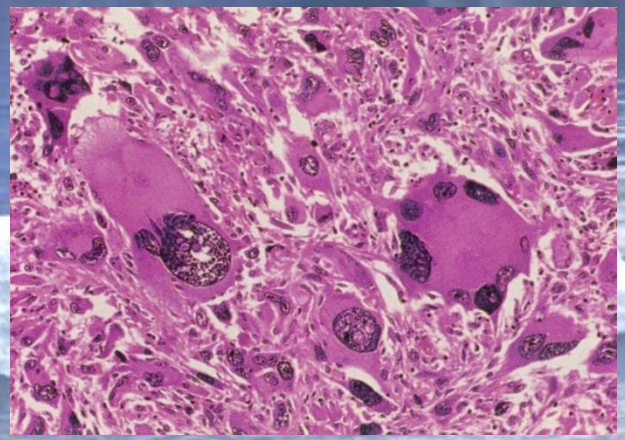
DISTURBANCES OF GROWTH AND DIFFERENTIATION–
ANAPLASIA, DEDIFFERENTIATION



DEDIFFERENTIATION OF ENDOMETRIUM



SKELETAL MUSCLE



RHABDOMYOSARCOMA

ANAPLASIA

NEOPLASMA

NEOPLASMS

TUMORS

CANCER

CARCINOMA

DEFINITION OF NEOPLASM

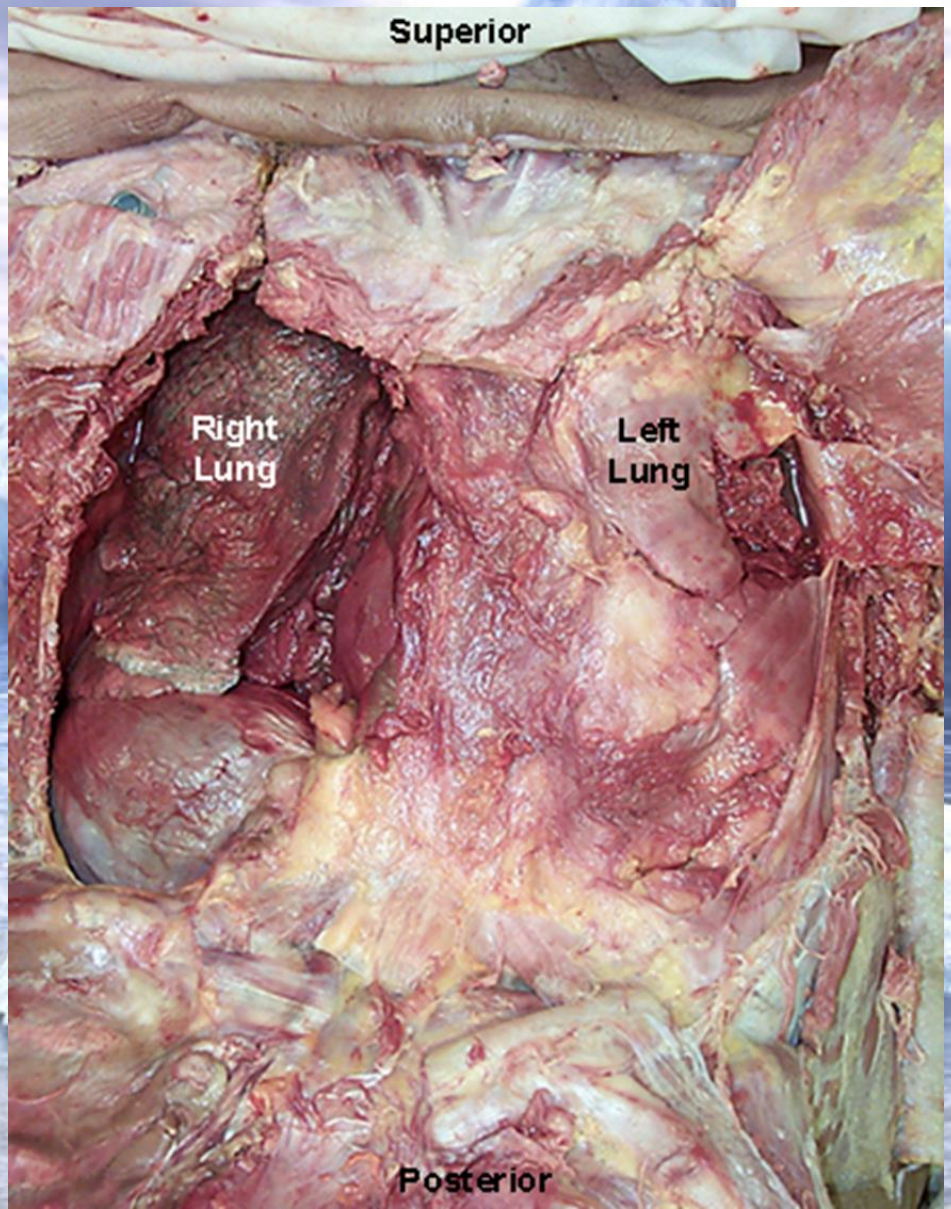
„NEOPLASM IS A FIXED, ABNORMAL, AND A RELATIVELY AUTONOMICAL PROLIFERATION OF CELLS BEING THE RESULT OF A CONSTANT CELL DEFECT TRANSFERRED ONTO DAUGHTER CELLS. THIS DEFECT CAUSED BY A SINGLE OR MULTIPLE AGENTS, ONCE PROVOKED REMAINS INDEPENDENT”

***USING ABOVE DEFINITION WE MUST ACCEPT CERTAIN RESTRICTIONS*:**

1. ATYPICAL PROLIFERATION OF CELLS CAN PRODUCE A TISSUE VERY SIMILAR TO THE PROPER ONE

2. IN VERY RARE CASES THE DEFECT OF A CELL IS NOT CONSTANT, SELF-REGRESSION OF TUMORS HAPPENS

LUNG CARCINOMA



TAXONOMY AND NOMENCLATURE

THERE ARE MANY TERMS AND DESCRIPTIONS USED TO DESCRIBE THE NEOPLASTIC PROCESS - MANY ARE USED IMPROPERLY.

THERE EXISTS A SERIES OF NEOPLASTIC CLASSIFICATIONS, SOME OF WHICH ARE RARELY USED AND IMPRACTICAL.

1. CLASSIFICATION ASSOCIATED WITH ETIOLOGY

2. CLASSIFICATION ASSOCIATED WITH EMBRYOGENESIS

3. CLASSIFICATION ASSOCIATED WITH THE LOCALISATION ON THE BODY OR IN THE ORGAN

4. CLASSIFICATION ASSOCIATED WITH FUNCTION

5. HISTOGENETIC CLASSIFICATION (CYTOGENETIC):
VERY USEFUL, BASIC, BASED ON THE TYPE OF CELL AND STRUCTURE COMPARED TO THE PROPER TISSUE

6. CLASSIFICATION ASSOCIATED WITH BIOLOGICAL ACTIVITY OF NEOPLASM
ONE OF THE BASIC CLASSIFICATIONS, SOMETIMES ARBITRARILY DIVIDES NEOPLASMS INTO TWO BASIC GROUPS: BENIGN NEOPLASMS AND MALIGNANT NEOPLASMS

SOME DIFFERENCES BETWEEN MALIGNANT AND BENIGN TUMORS

TYPE OF NEOPLASM	BENIGN	MALIGNANT
GROWTH	SLOW	QUICK
MITOSIS	FEW	MANY
NUCLEAR CHROMATIN	NORMAL	INCREASED
DIFFERENTIATION	GOOD	BAD
LOCAL GROWTH	EXPANSIVE	INVASIVE
CAPSULE	PRESENT	LACKING
DESTRUCTION OF TISSUE	SMALL	SIGNIFICANT
VESSEL INFILTRATION	ABSENT	FREQUENT
METASTASES	ABSENT	FREQUENT
SUCCESSION	USUALLY SMALL	SIGNIFICANT

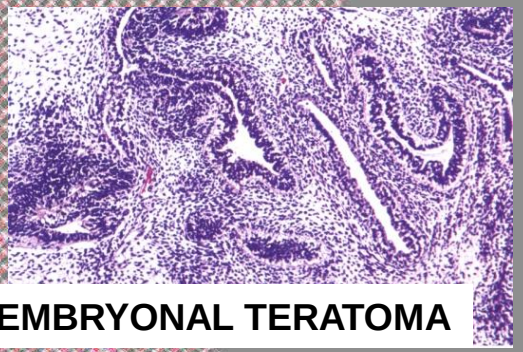
*MANY TUMORS SHOW A LACK OF ONE OR MORE OF ABOVE FEATURES

EXAMPLES OF NOMENCLATURE

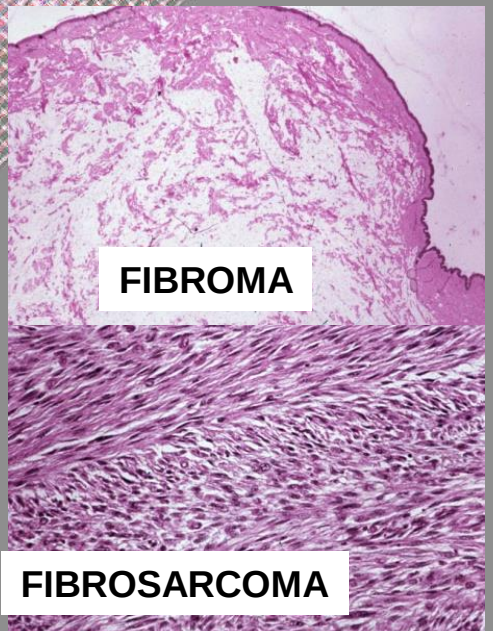
Table 7–1. NOMENCLATURE OF TUMORS

TISSUE OF ORIGIN	BENIGN	MALIGNANT
I. Composed of One Parenchymal Cell Type		
A. Mesenchymal tumors		
1. Connective tissue and derivatives	Fibroma	Fibrosarcoma
	Lipoma	Liposarcoma
	Chondroma	Chondrosarcoma
	Osteoma	Osteogenic sarcoma
2. Endothelial and related tissues		
Blood vessels	Hemangioma	Angiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma
Synovium		Synovial sarcoma
Mesothelium		Mesothelioma
Brain coverings	Meningioma	Invasive meningioma
3. Blood cells and related cells		
Hematopoietic cells		Leukemias
Lymphoid tissue		Malignant lymphomas
4. Muscle		
Smooth	Leiomyoma	Leiomyosarcoma
Striated	Rhabdomyoma	Rhabdomyosarcoma
B. Epithelial tumors		
1. Stratified squamous	Squamous cell papilloma	Squamous cell or epidermoid carcinoma
2. Basal cells of skin or adnexa		Basal cell carcinoma
3. Epithelial lining		
Glands or ducts	Adenoma	Adenocarcinoma
	Papilloma	Papillary carcinoma
	Cystadenoma	Cystadenocarcinoma
4. Respiratory passages		Bronchogenic carcinoma
		Bronchial "adenoma" (carcinoid)
5. Neuroectoderm	Nevus	Malignant melanoma
6. Renal epithelium	Renal tubular adenoma	Renal cell carcinoma
7. Liver cells	Liver cell adenoma	Hepatocellular carcinoma
8. Urinary tract epithelium (transitional)	Transitional cell papilloma	Transitional cell carcinoma
9. Placental epithelium (trophoblast)	Hydatidiform mole	Choriocarcinoma
10. Testicular epithelium (germ cells)		Seminoma
		Embryonal carcinoma
II. More Than One Neoplastic Cell Type—Mixed Tumors		
1. Salivary glands	Pleomorphic adenoma (mixed tumor of salivary origin)	Malignant mixed tumor of salivary gland origin
2. Breast	Fibroadenoma	Malignant cystosarcoma phyllodes
3. Renal anlage		Wilms' tumor
III. More Than One Neoplastic Cell Type Derived From More Than One Germ Layer—Teratogenous		
1. Totipotential cells in gonads or in embryonic rests	Mature teratoma, dermoid cyst	Immature teratoma, teratocarcinom

ADULT TERATOMA



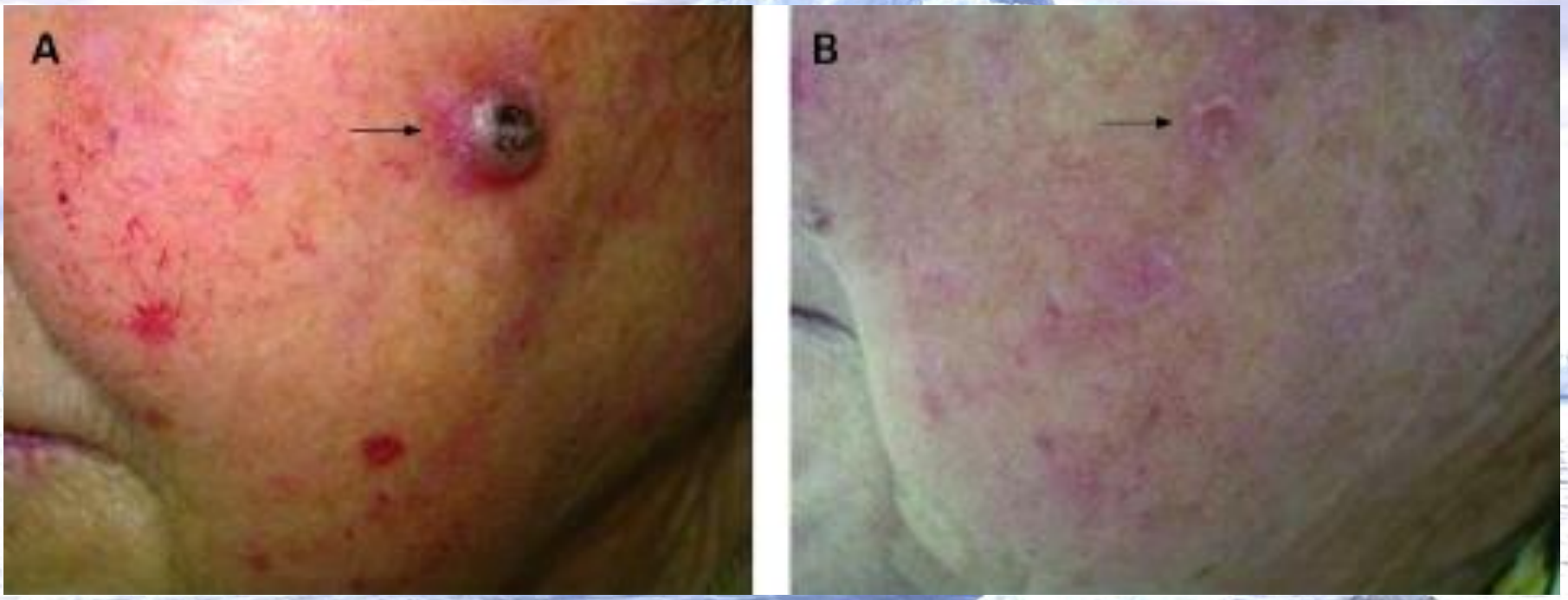
EMBRYONAL TERATOMA



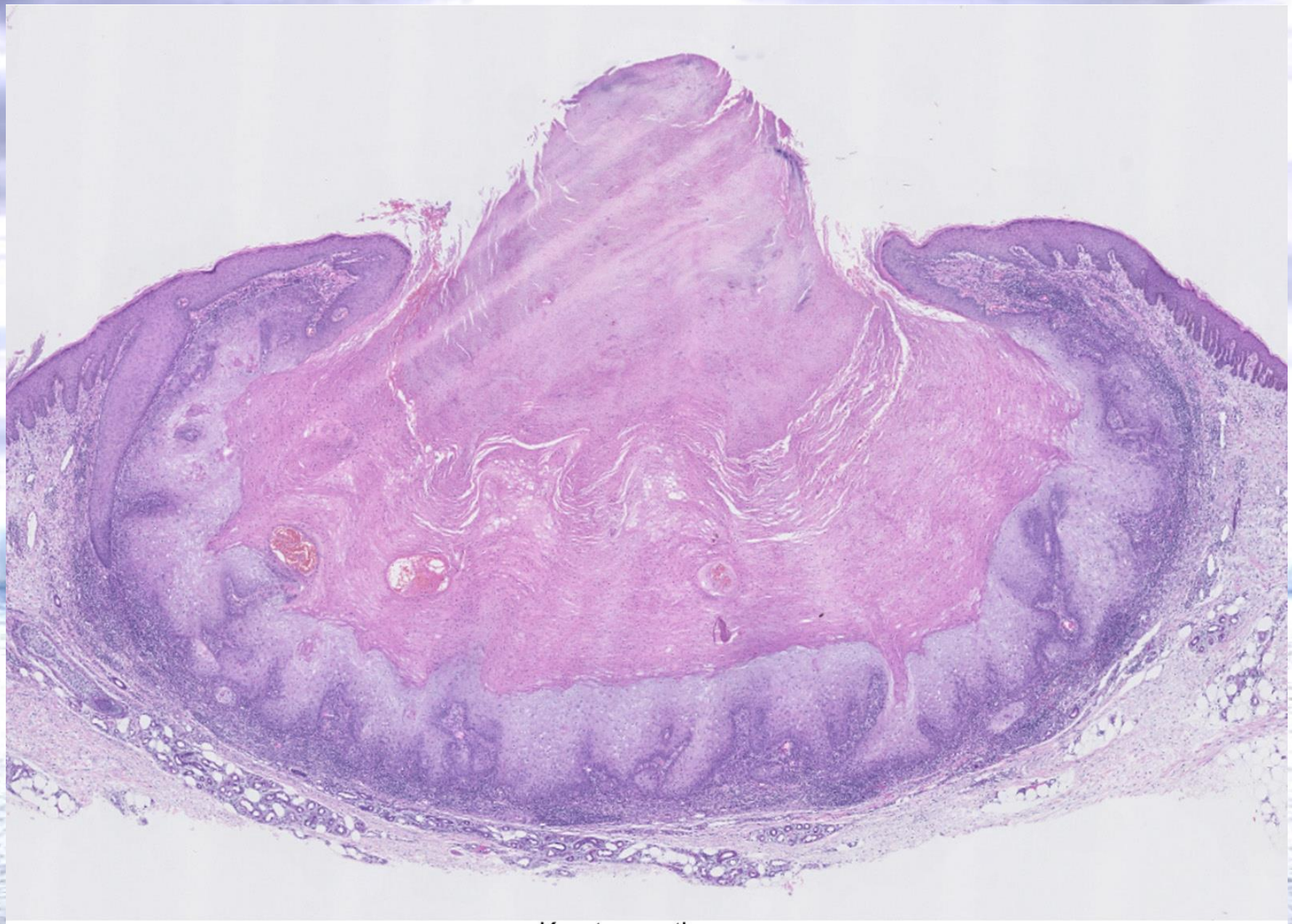
FIBROMA

FIBROSARCOMA

KERATOACANTHOMA



before (A) and after topical treatment (B)



Keratoacanthoma:
central crater filled with keratin (H&E, ×1)

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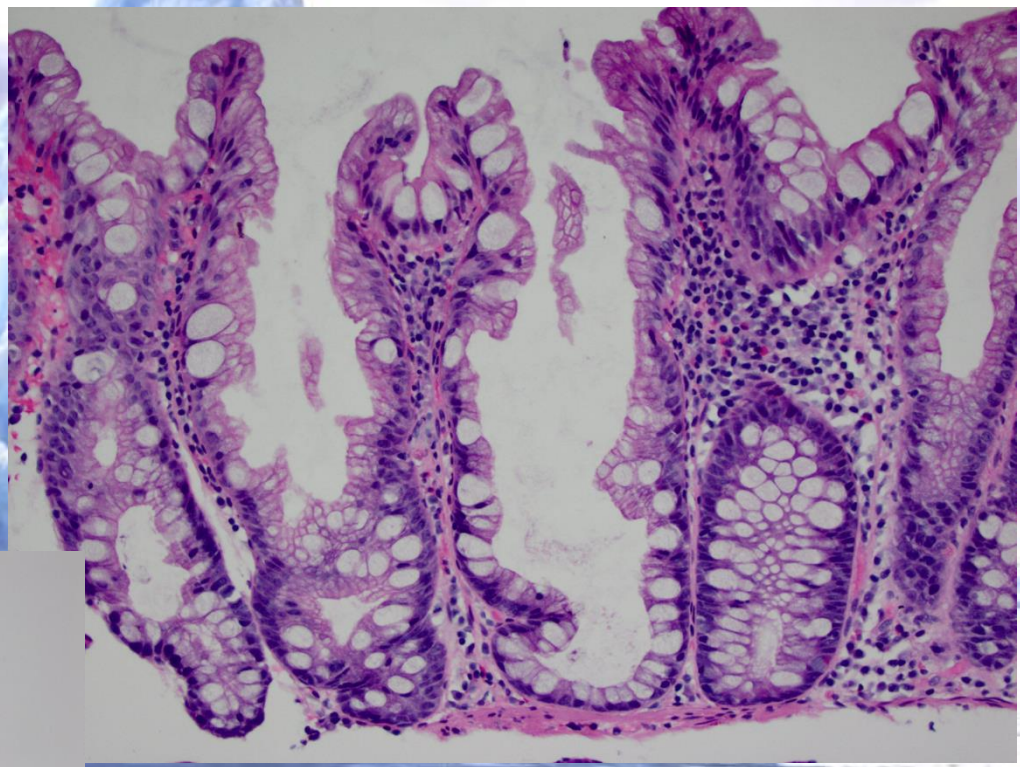
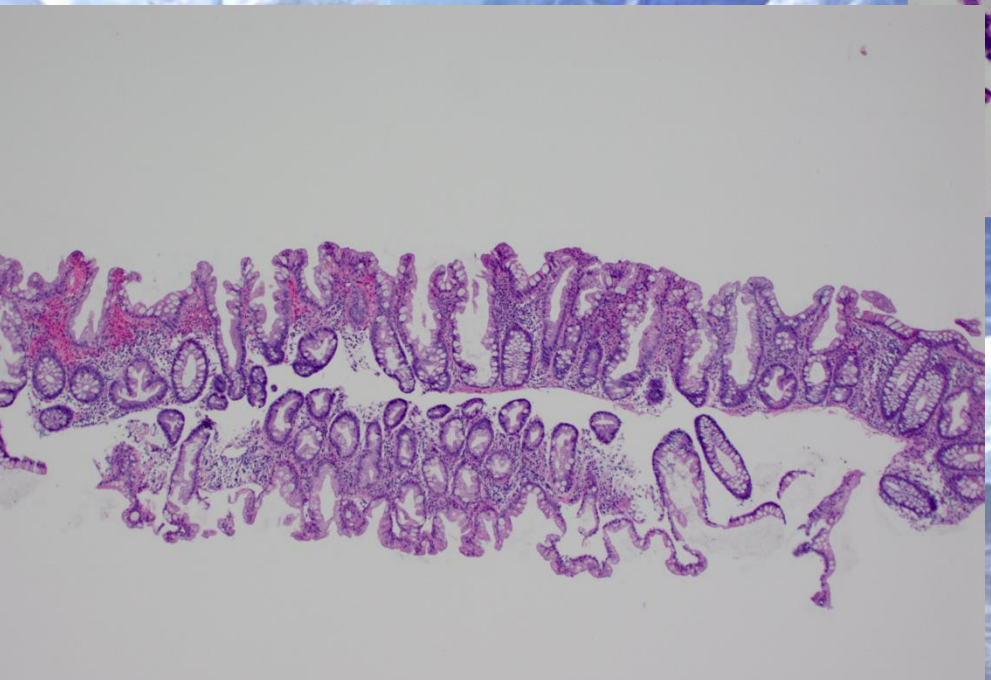
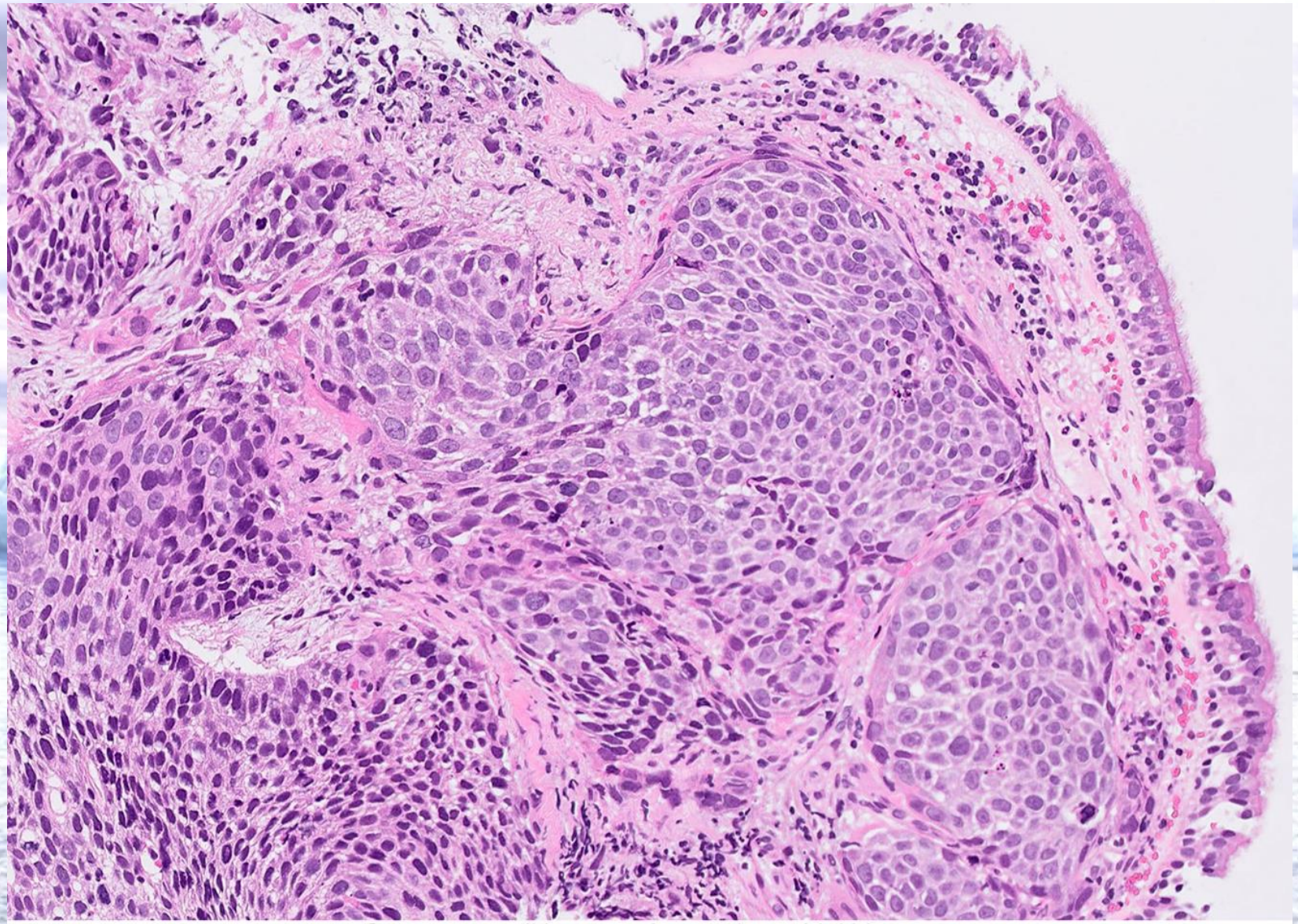
SESSILE SERRATED ADENOMA







Squamous cell lung carcinoma, bronchial biopsy:
sheets of large polygonal cells with intercellular bridges (H&E, ×20)

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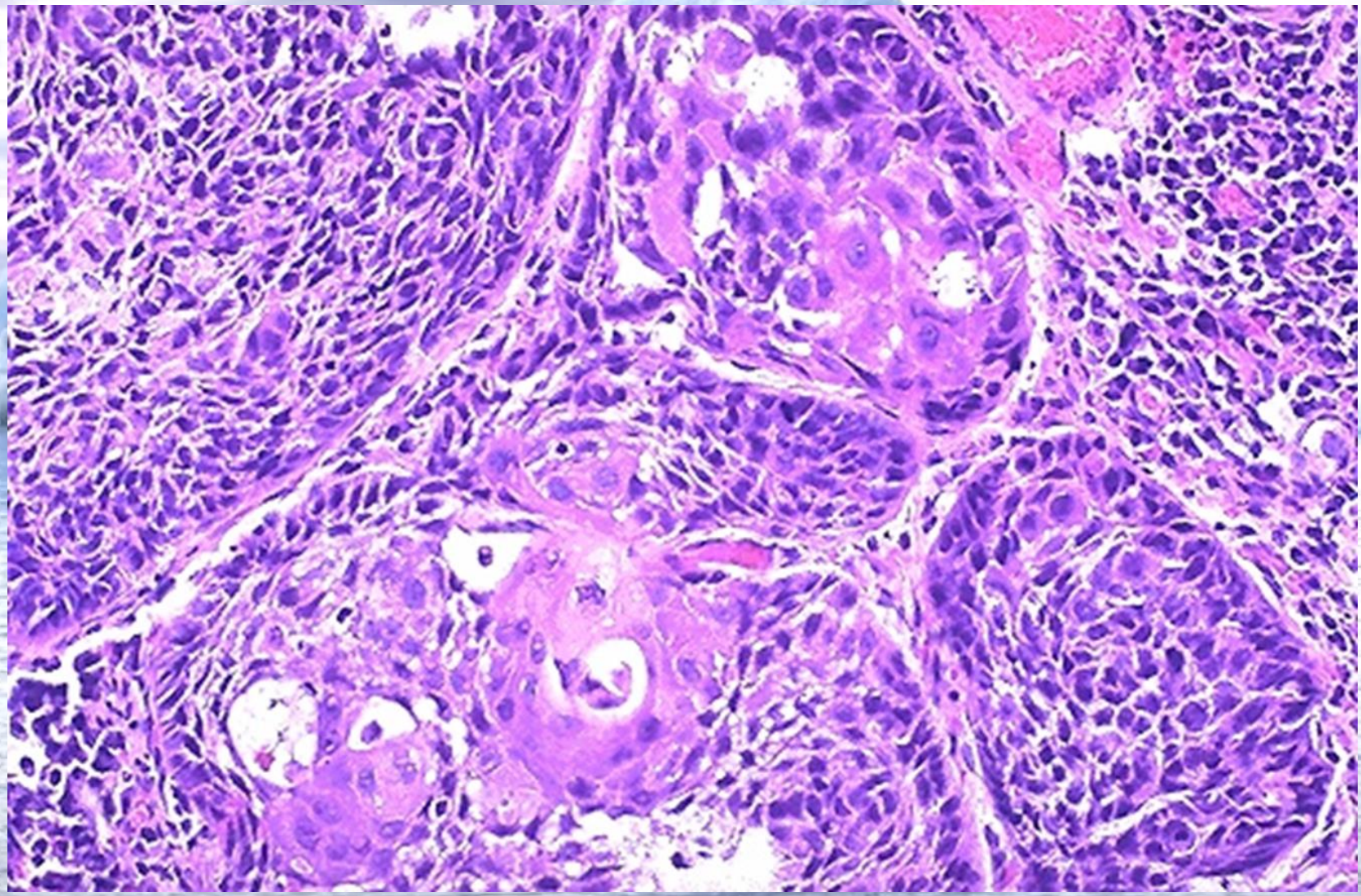
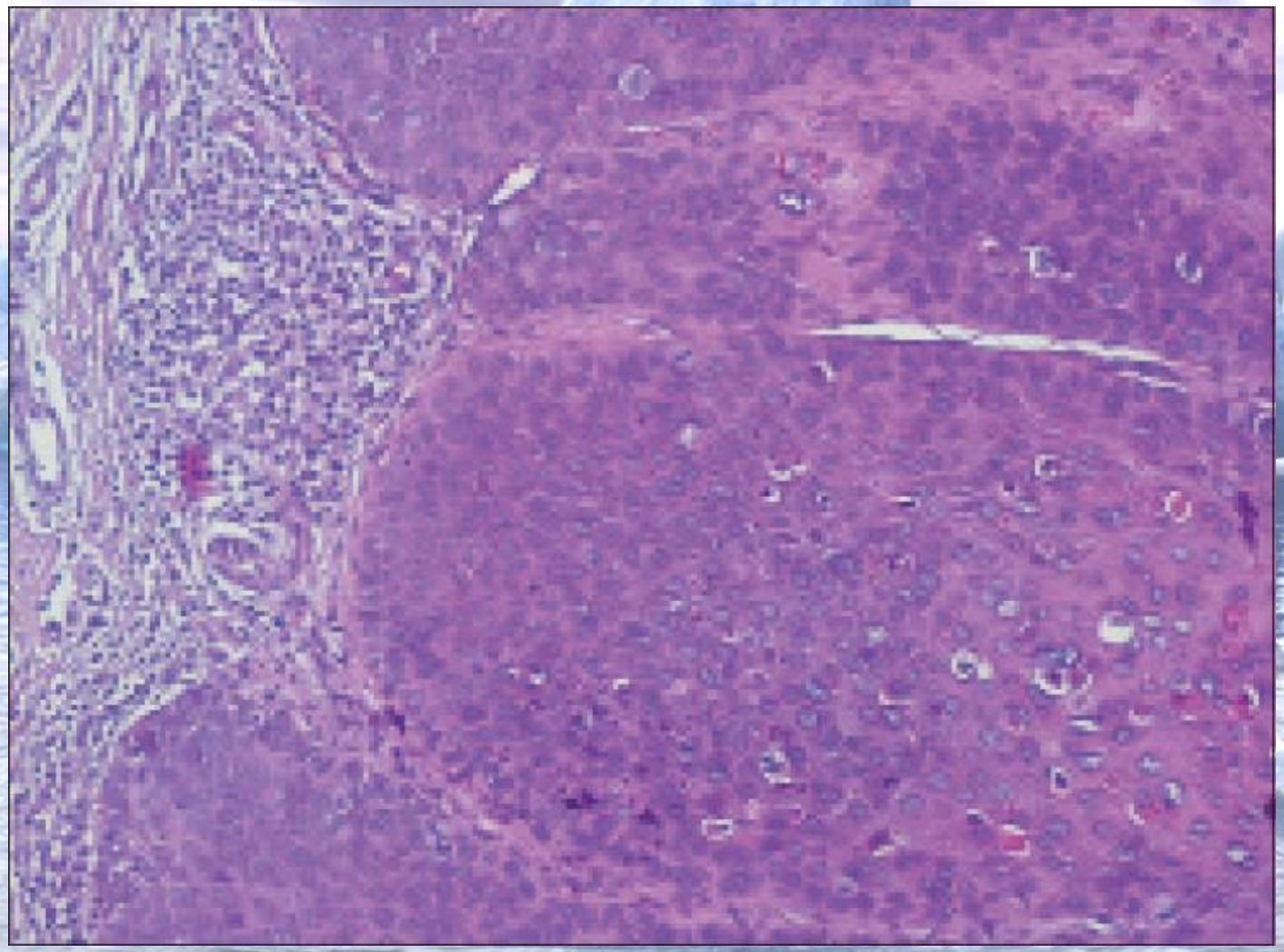
SCC - LUNG

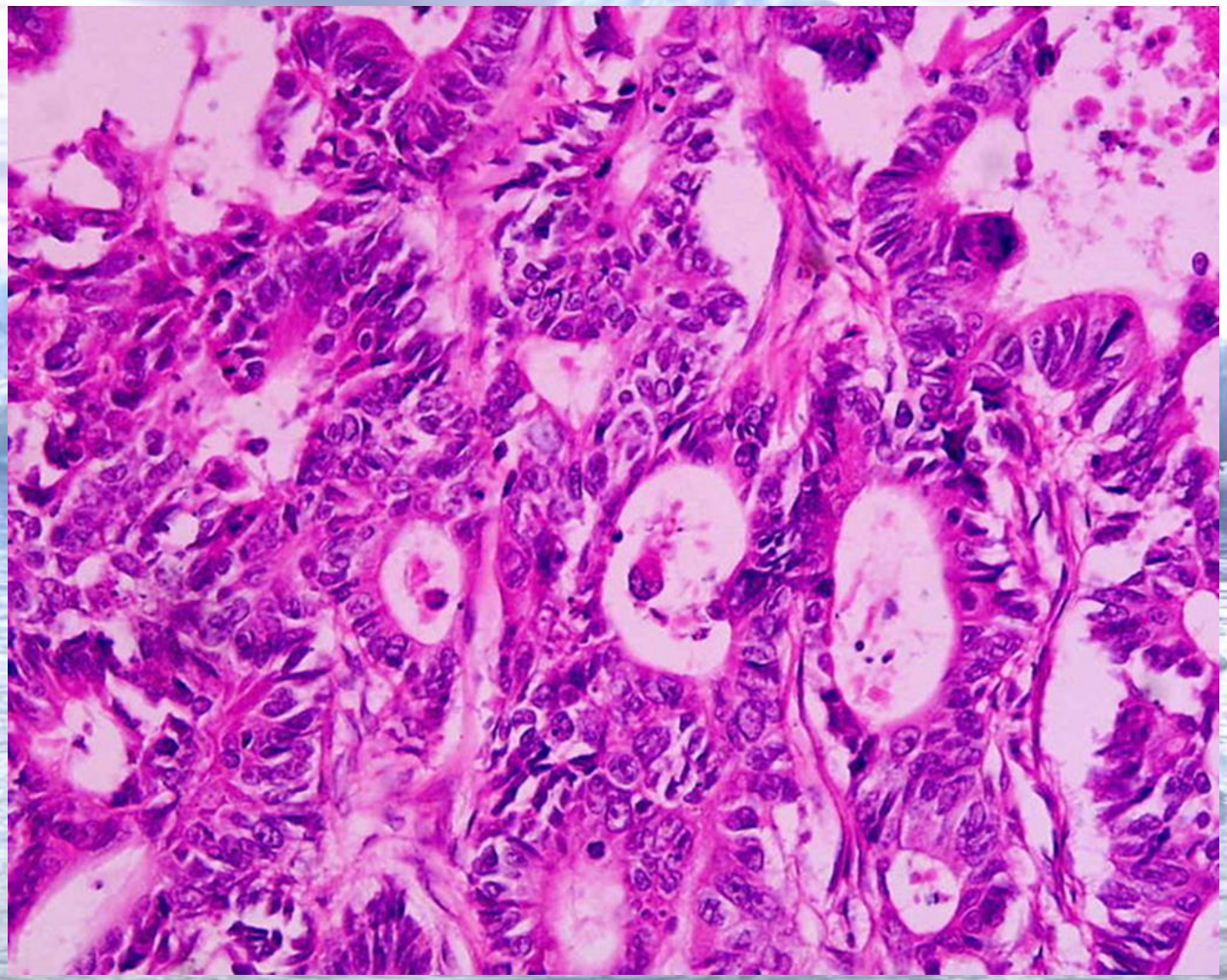


VERRUCOUS CARCINOMA

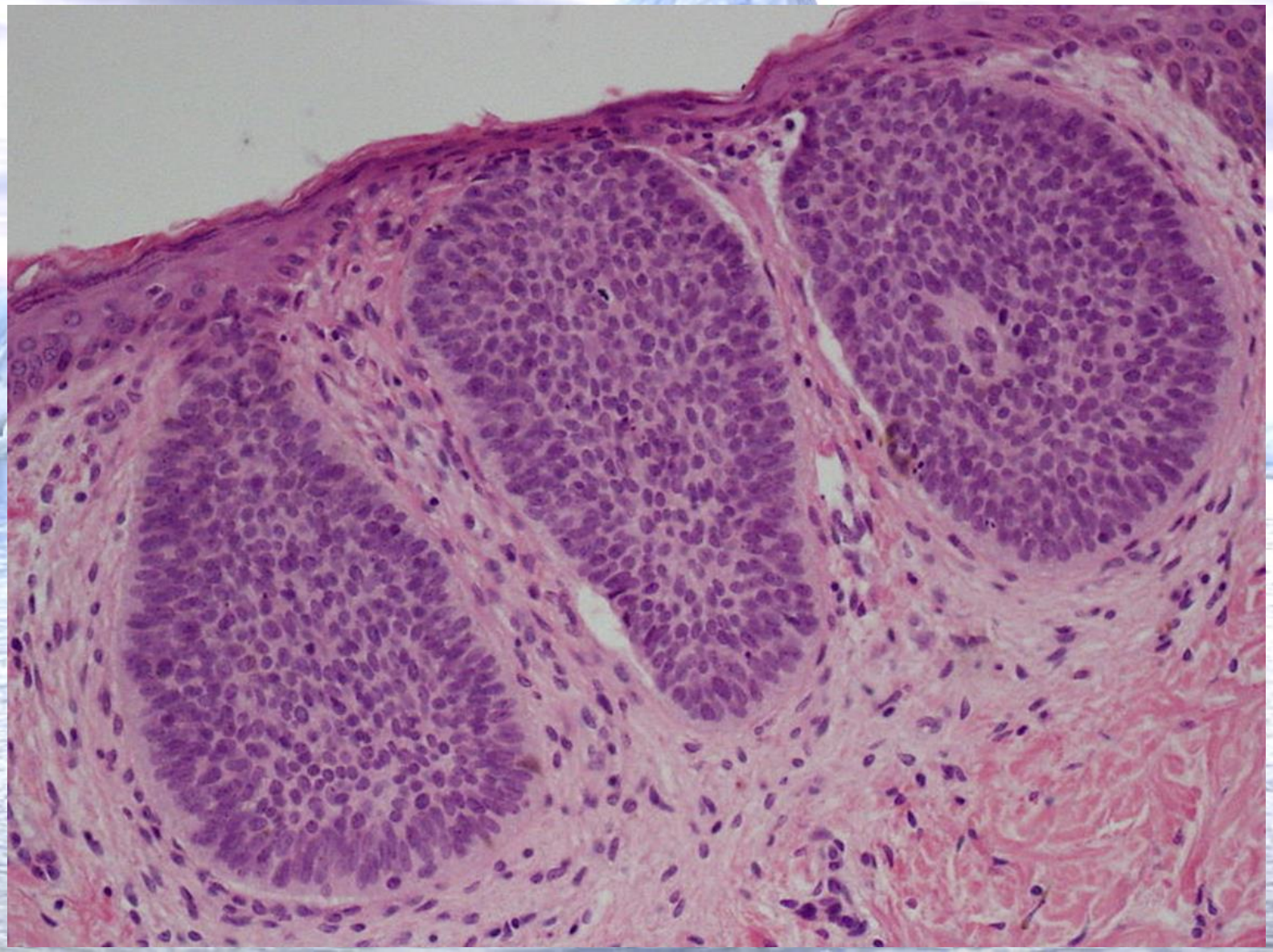
VERRUCOUS CARCINOMA



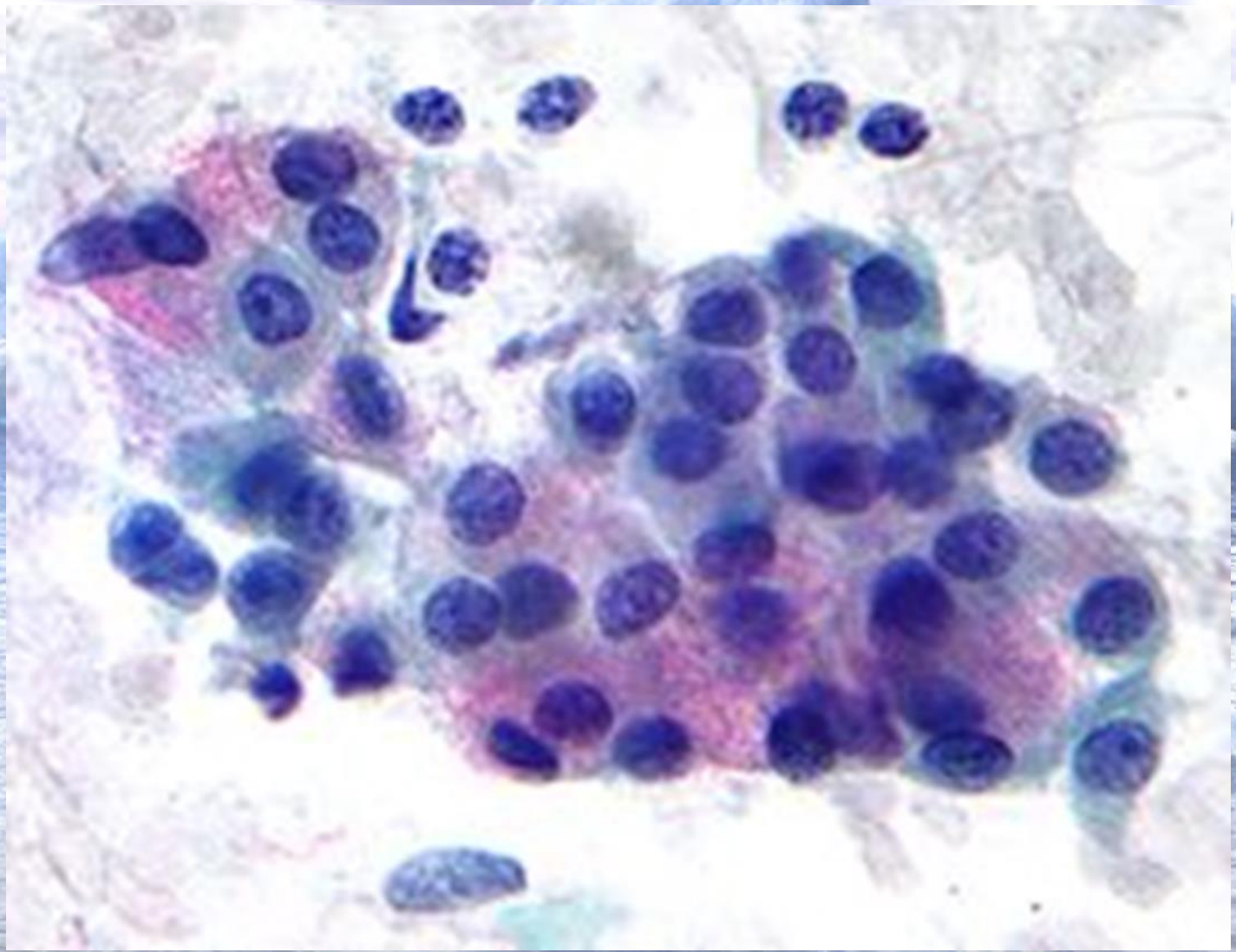
ADENOCARCINOMA



BASAL CELL CARCINOMA



CYTOLOGICAL SMEAR – CARCINOMA CELLS



GALLBLADDER CARCINOMA

GRADING AND STAGING OF TUMORS

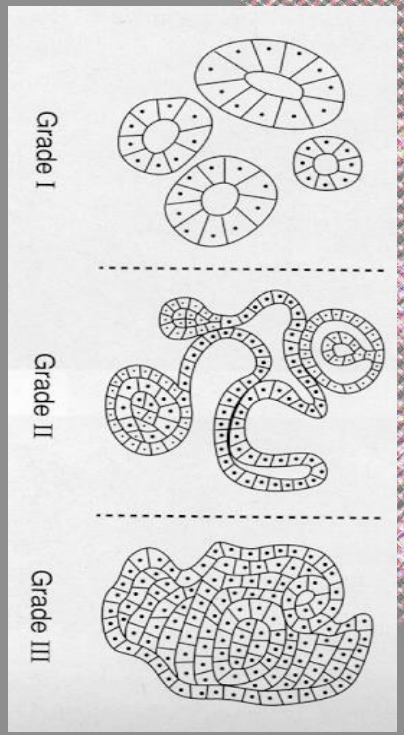
TODAY GRADING IS A VERY USEFUL CRITERION OF MALIGNANCY WITH A CAPITAL IMPACT ON PROGNOSIS. FROM MORPHOLOGICAL CHARACTERISTICS USED TO GRADE THE MALIGNANCY, FOLLOWING POINTS MUST BE MENTIONED:

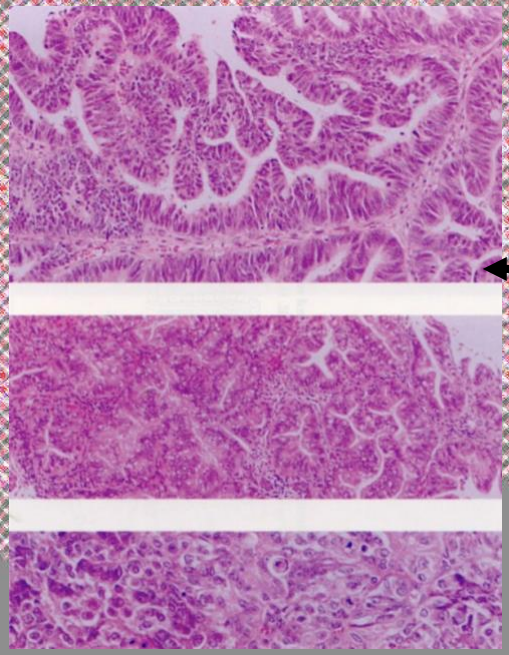
1. HISTOFORMATIVE ABILITY – THE ABILITY TO MAKE THE ARCHITECTURAL FORM OF TISSUE OF ORIGIN

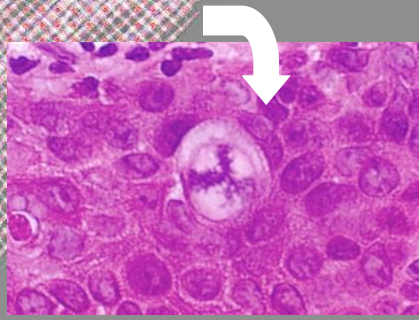
2. AMOUNT OF IMPROPER MITOSES

3. CELLULAR AND NUCLEAR PLEOMORPHISM

4. PRESENCE OF MULTINUCLEATED CELLS







GRADING OF HISTOLOGICAL MALIGNANCY OF ADENOCARCINOMA

STAGES OF ADVANCE OF TUMORS (eng. STAGING)

USED TO ASSESS THE PHASE OF NEOPLASTIC DISEASE. IT DETERMINES THE THERAPY AND HAS THE BIGGEST DIAGNOSTIC SIGNIFICANCE:

THE CLASSIFICATION TNM (*TUMOR, LYMPH NODES, DISTANT METASTASES)*

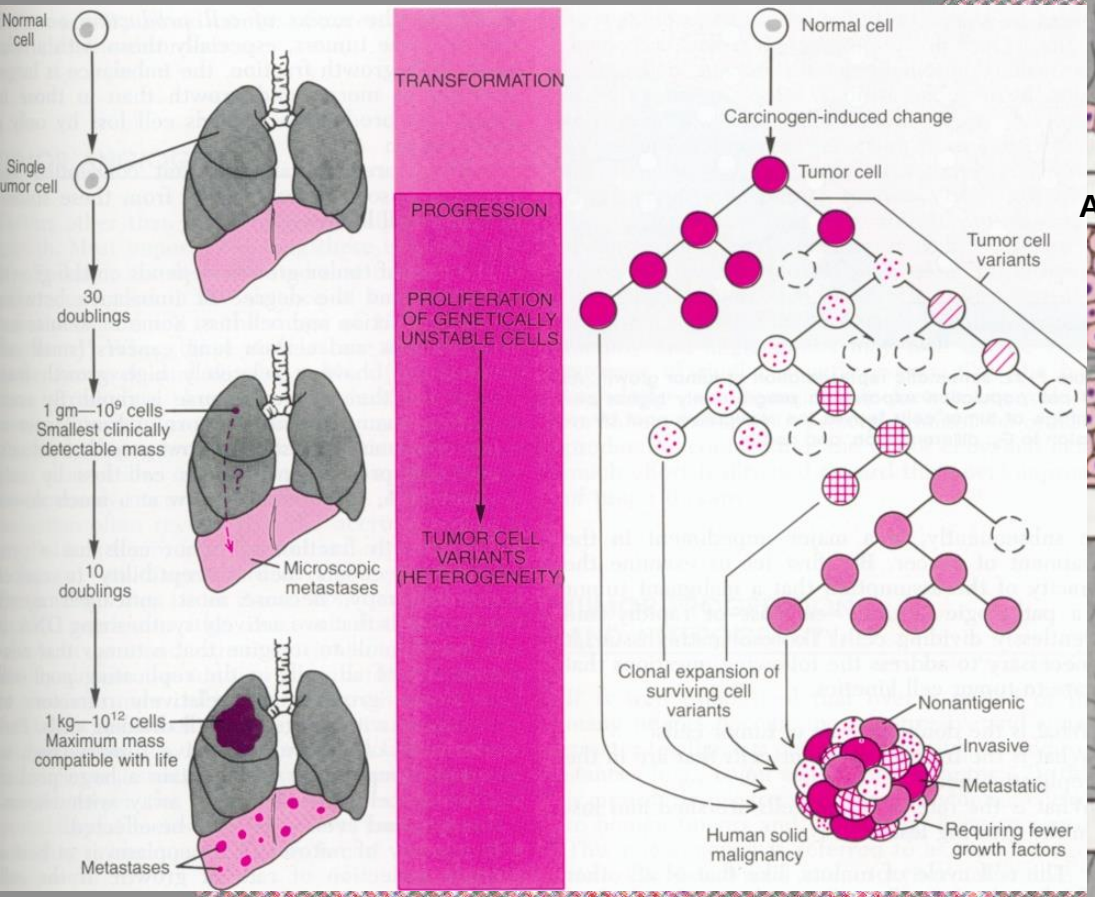
CLINICAL CLASSIFICATION OF TNM (expl. TUMORS OF LIPS AND ORAL CAVITY); cTNM vs. pTNM

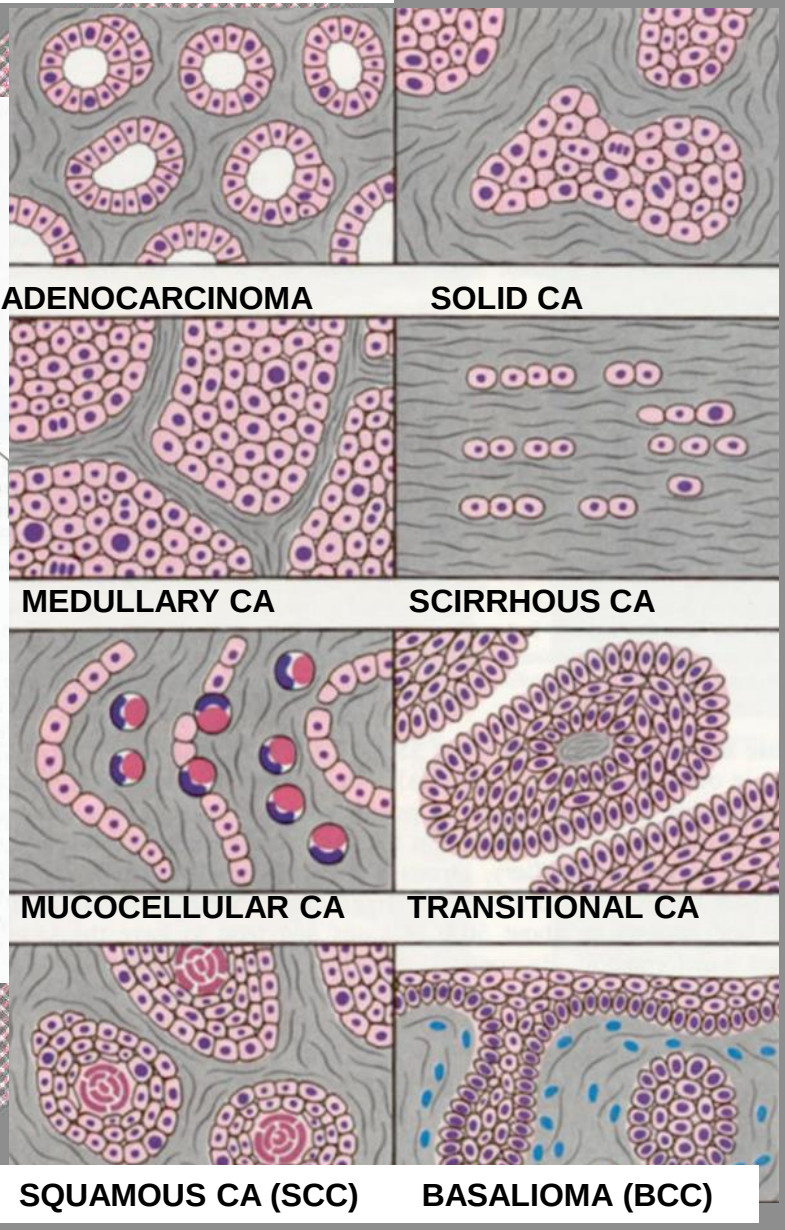
T – PRIMARY TUMOR
TX – PRIMARY TUMOR CANNOT BE ASSESSED
T0 – PRIMARY TUMOR CANNOT BE CONFIRMED
Tis – PRE-INVASIVE CARCINOMA
T1 – TUMOR UP TO 2 cm IN DIAMETER
T2 – TUMOR 2 – 4 cm IN DIAMETER
T3 – TUMOR OVER 4 cm ON DIAMETER

N/Pn – CLASSIFICATION OF LYMPH NODES
N/Pnx – LYMPH NODES CANNOT BE ASSESSED
N/Pn0 – METASTASIS IN THE LYMPH NODES IS NOT DETERMINED
N/Pn1 – METASTASIS IN ONE LYMPH NODE ON SAME SIDE THAT TUMOR IS LOCATED UP TO 3cm IN DIAMETER
N/Pn2 – BILATERAL METASTASES OR ONE SIDED 6 cm IN DIAMETER
N/Pn3 – METASTASES OVER 6 cm IN DIAMETER

M – DISTANT METASTASIS
MX – DISTANT METASTASIS CANNOT BE ASSESSED
M0 – DISTANT METASTASIS IS NOT DETERMINED
M1 – DISTANT METASTASIS DETERMINED

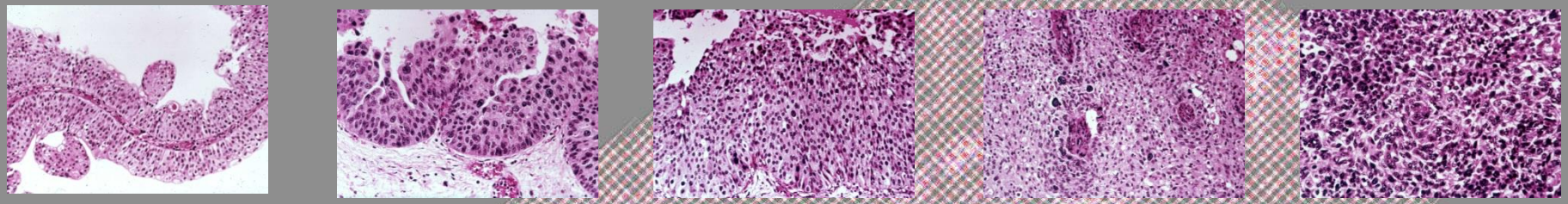
TUMOR GROWTH



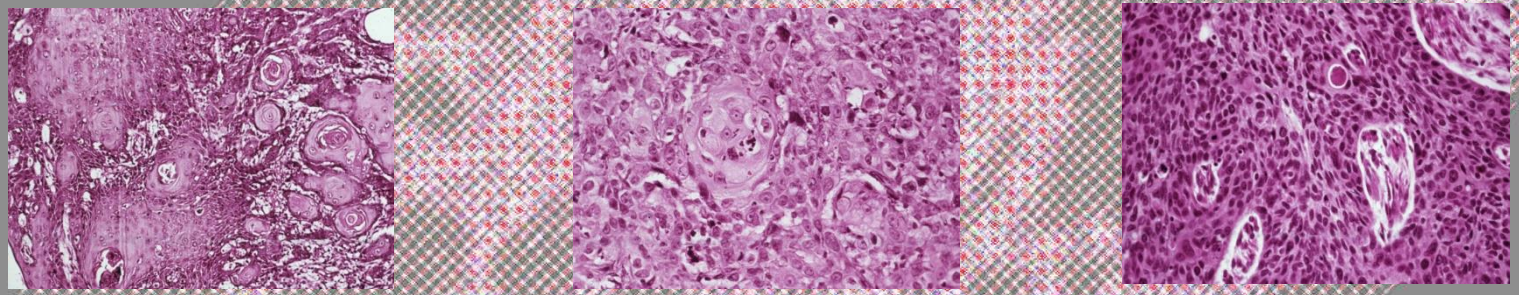


TYPES OF GROWTH IN DIFFERENT TUMORS

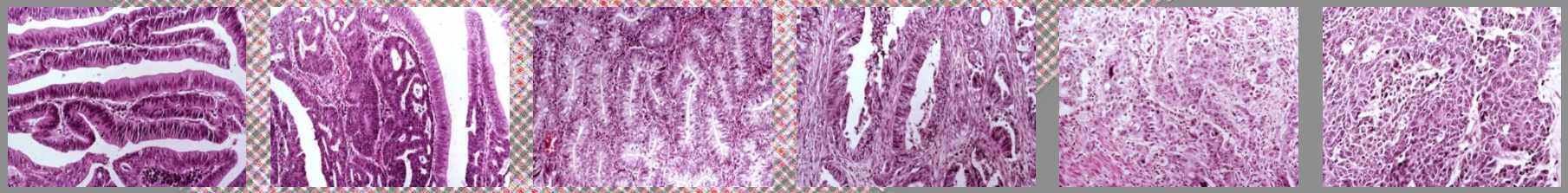
DIFFERENTIATION OF TUMORS



DEDIFFERENTIATION IN TUMORS OF TRANSITIONAL EPITHELIUM FROM PAPILLOMA TO UNDIFFERENTIATED CARCINOMA

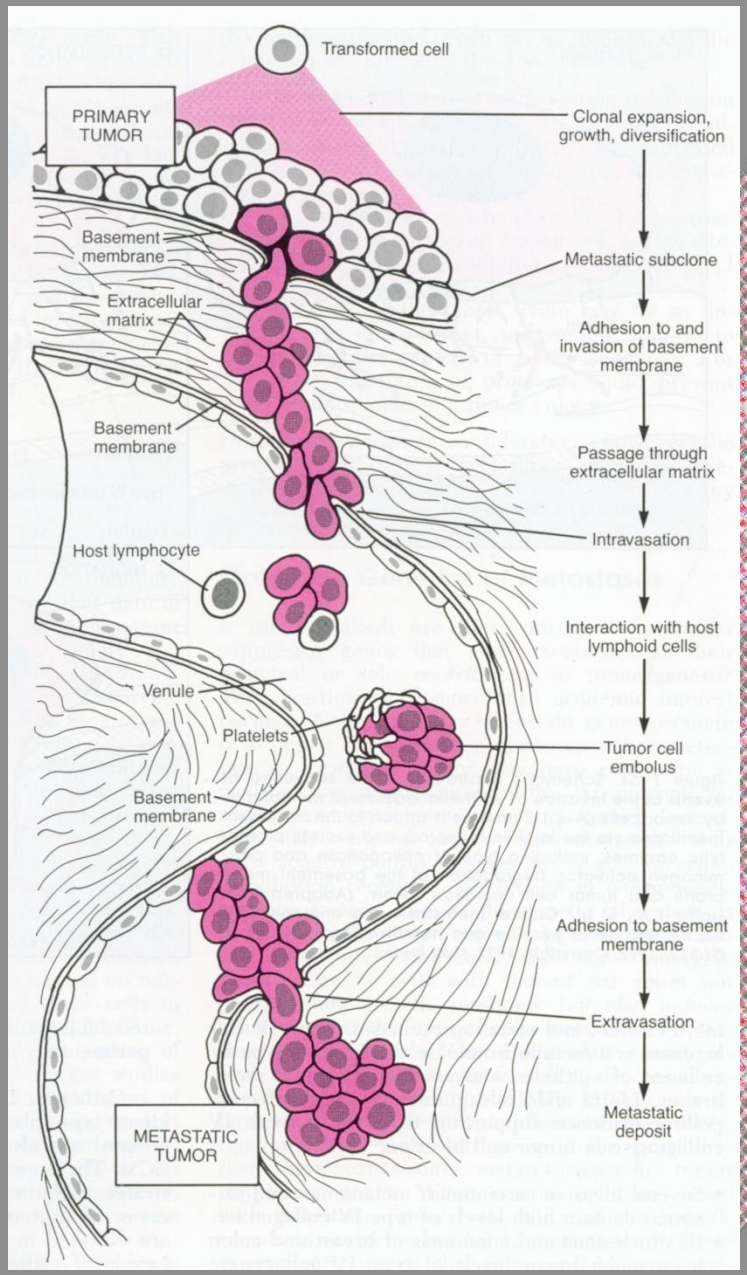


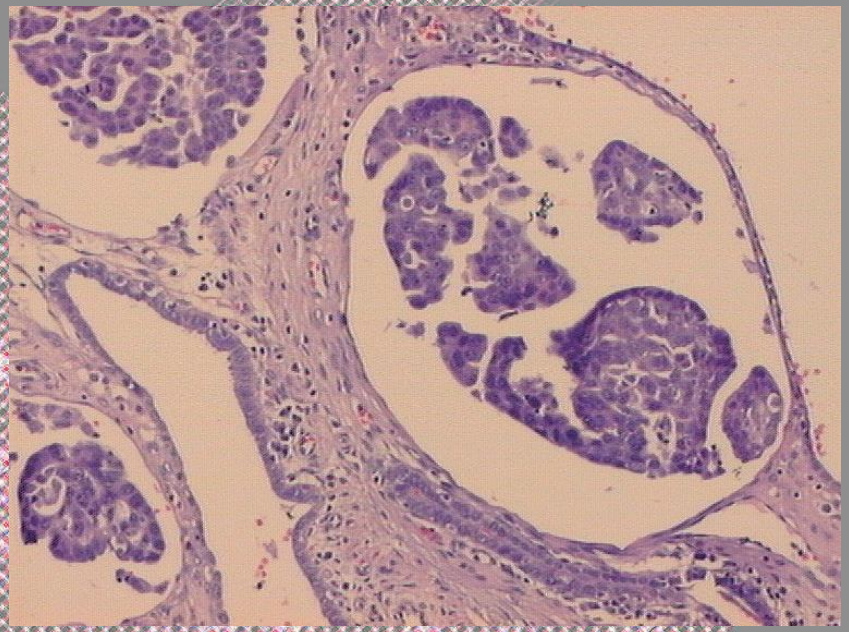
DEDIFFERENTIATION IN SQUAMOUS CELL CARCINOMA



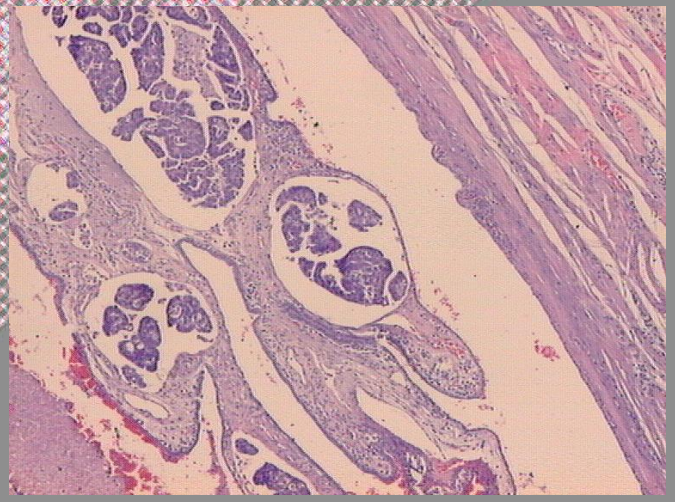
DEDIFFERENTIATION OF GLANDULAR CARCINOMA (ADENOCARCINOMA) OF THE LARGE INTESTINE

VASCULAR INFILTRATION

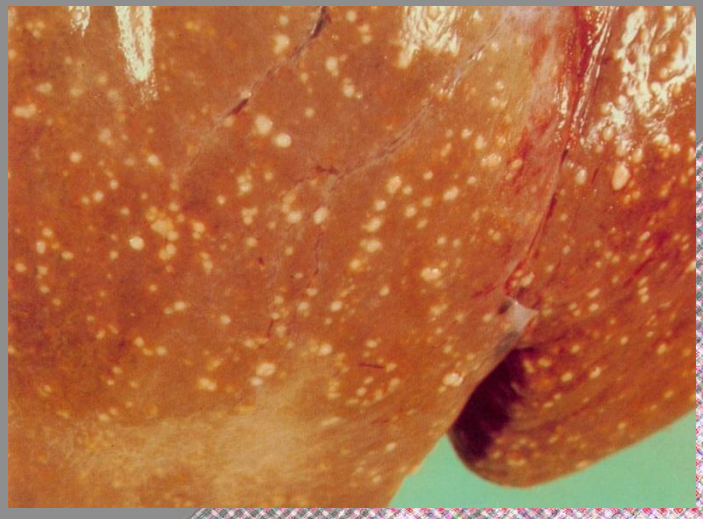




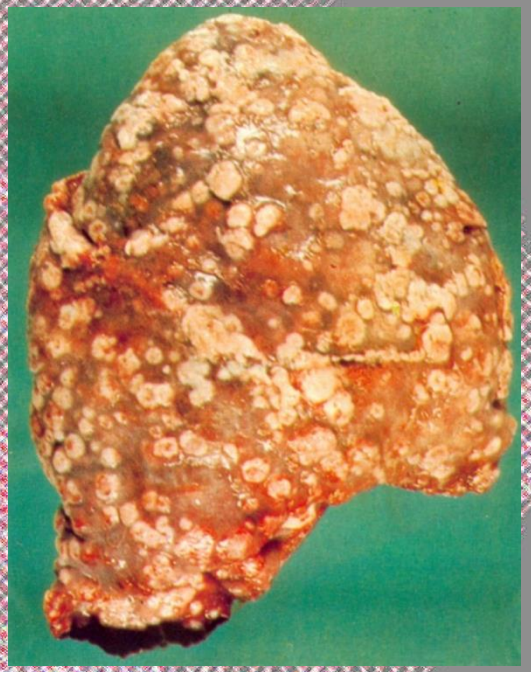
INFILTRATION OF THE LYMPHATIC VESSELS IN MUCOSA OF THE FALLOPIAN TUBE DUE TO ADENOCARCINOMA OF THE FALLOPIAN TUBE



METASTASIS

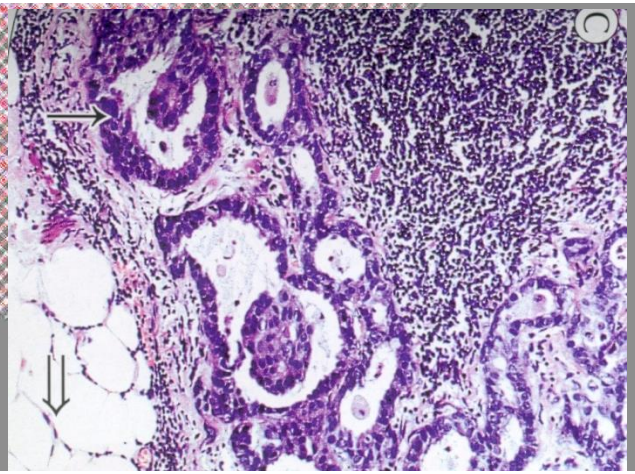


METASTASES OF BREAST CANCER TO THE LIVER



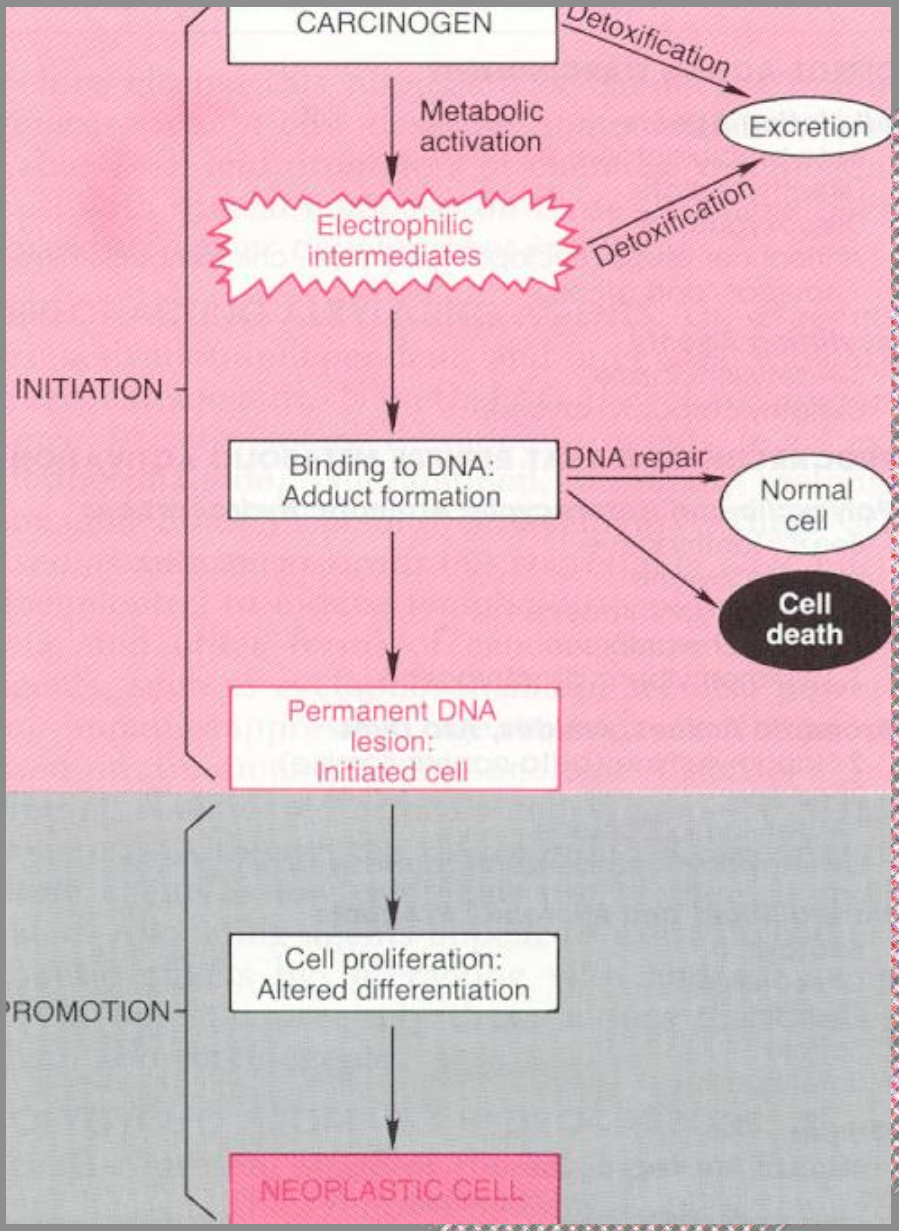
MULTIPLE METASTASES OF STOMACH CANCER TO THE LUNG

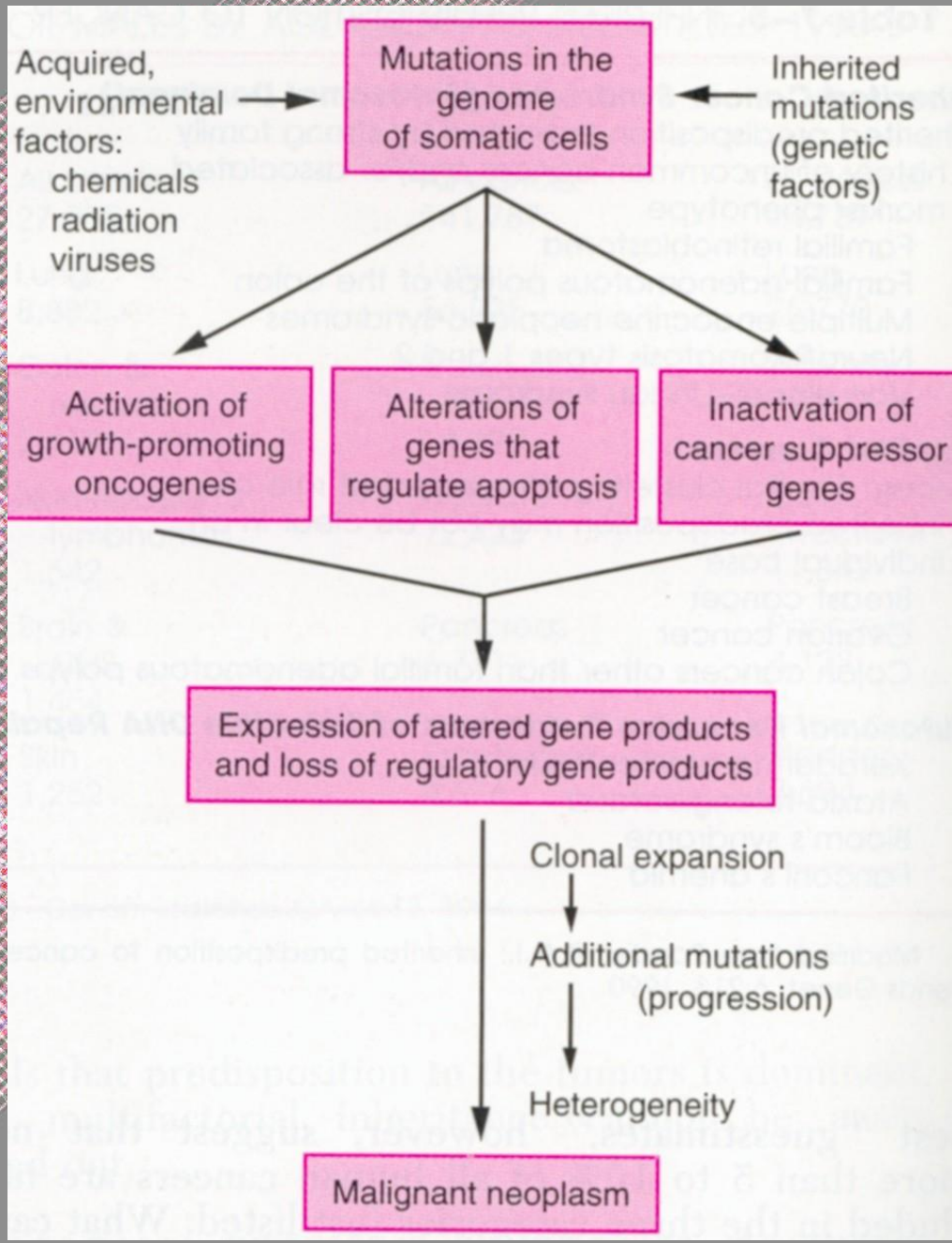
SINGLE METASTASIS OF CANCER OF THE LARGE INTESTINE IN THE LIVER WITH A CHARACTERISTIC UMBILICAL SHAPE



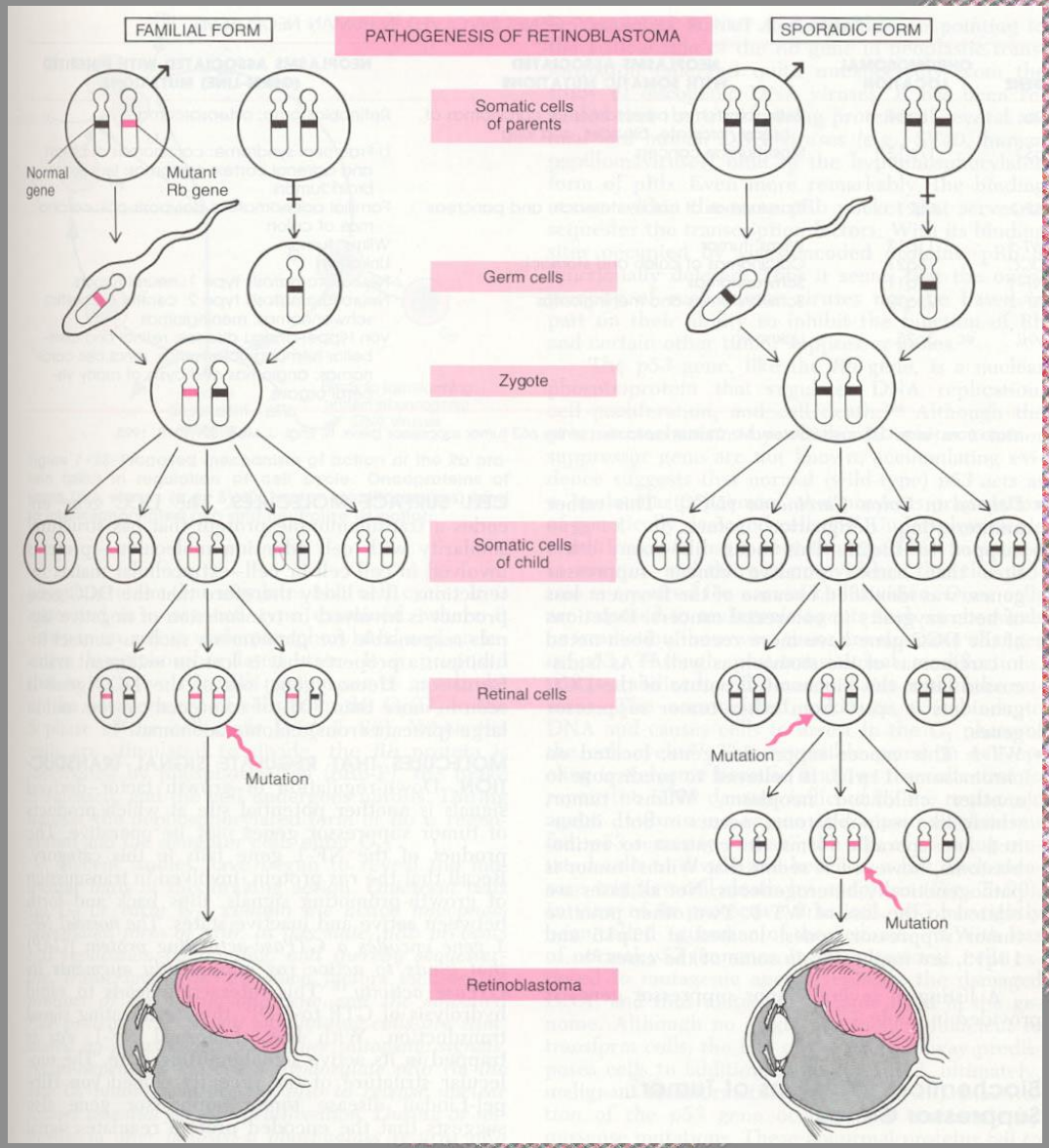
OVARIAN CANCER METASTASIS IN THE LYMPH NODE

PATHOMECHANISM OF TUMORS

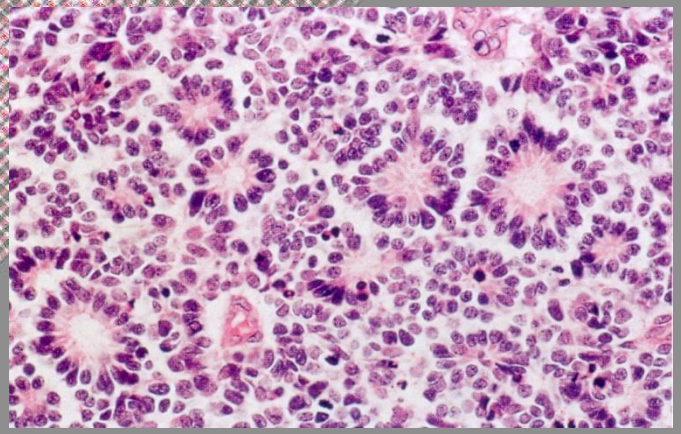




FAMILIAL CARCINOMA



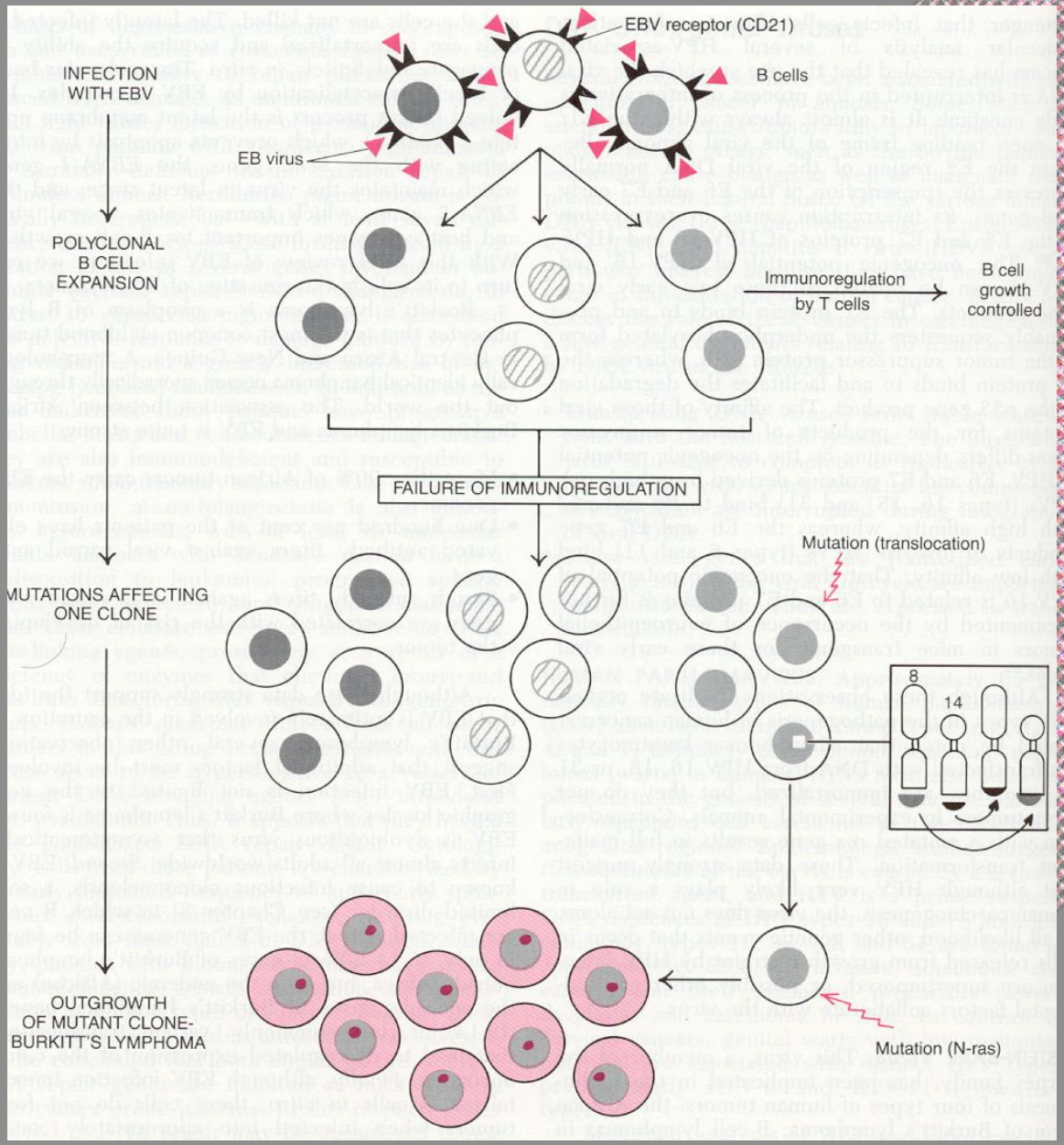
„CAT'S EYE" IN THE COURSE OF RETINOBLASTOMA -leukocoria



RETINOBLASTOMA

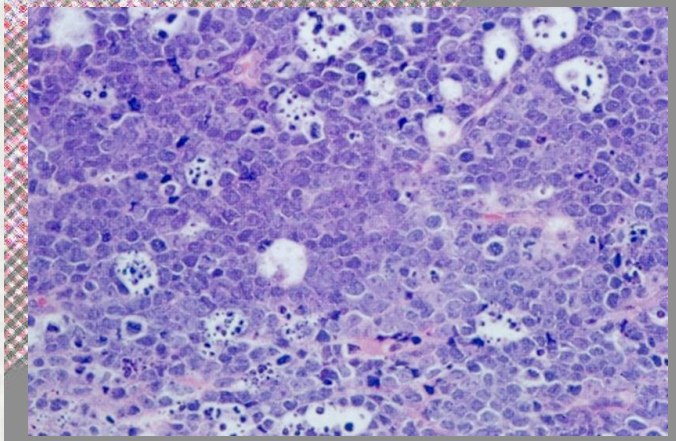
Figure 2. Bilateral leukocoria

VIRAL CARCINOGENESIS



LYMPHOMA BURKITT

IN THE ORAL CAVITY



LYMPHOMA BURKITT MICROSCOPICAL PICTURE „STARRY SKY"

CHEMICAL CARCINOGENESIS

CHEMICAL CARCINOGENSIS – HEPATOCARCINOMA INDUCED IN A RAT BY THE ADMINISTRATION OF 2-ACETYLAMINOFLUORENE

Table 7–8. MAJOR CHEMICAL CARCINOGENS

DIRECT-ACTING CARCINOGENS

Alkylating Agents
- Beta-propiolactone
- Dimethyl sulfate
- Diepoxybutane
- Anticancer drugs (cyclophosphamide, chlorambucil, nitrosoureas, and others)

Acylating Agents
- 1-Acetyl-imidazole
- Dimethylcarbamyl chloride

PROCARCINOGENS THAT REQUIRE METABOLIC ACTIVATION

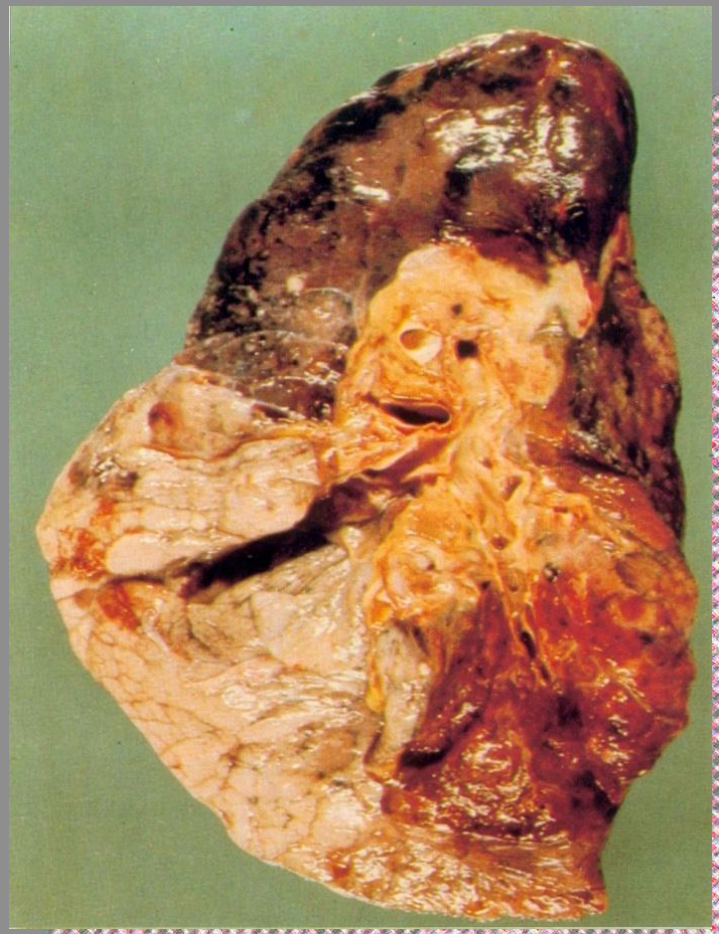
Polycyclic and Heterocyclic Aromatic Hydrocarbons
- Benz(a)anthracene
- Benzo(a)pyrene
- Dibenz(a,h)anthracene
- 3-Methylcholanthrene
- 7,12-Dimethylbenz(a)anthracene

Aromatic Amines, Amides, Azo Dyes
- 2-Naphthylamine (beta-naphthylamine)
- Benzidine
- 2-Acetylaminofluorene
- Dimethylaminoazobenzene (butter yellow)

Natural Plant and Microbial Products
- Aflatoxin B_1
- Griseofulvin
- Cycasin
- Safrole
- Betel nuts

Others
- Nitrosamine and amides
- Vinyl chloride, nickel, chromium
- Insecticides, fungicides
- Polychlorinated biphenyls

CHEMICAL CARCINOMA

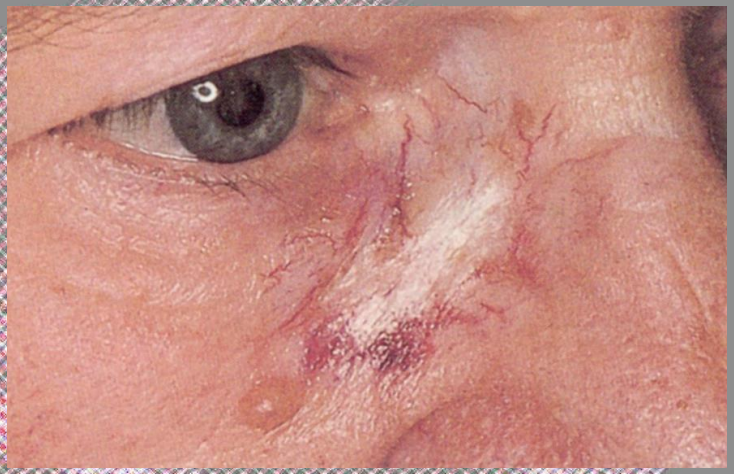


BRONCHIAL CARCINOMA

IS ONE OF THE MOST COMMON MALIGNANT TUMORS IN PEOPLE, WHOSE ETIOPATHOGENESIS IS CONNECTED WITH CHEMICAL CARCINOGENESIS (PRODUCTS FOUND IN CIGARETTES)

RADIOACTIVE CARCINOGENESIS

ATROPHY OF SKIN DUE TO CHRONIC EXPOSITION TO ULTRAVIOLET



PAVEMENT EPITHELIUM: CARCINOMA IN A SCAR AFTER X-RAY IRRADIATION OF BASAL CELL CARCINOMA

MULTIFOCAL PAVEMENT EPITHELIUM ON A RADIOLOGISTS' HAND

PRECANCEROUS STATES

PATHOLOGICAL STATES, NOT NEOPLASTIC: HIGH DISPOSITION TO MALIGNANT TRANSFORMATION (ESPECIALLY CANCER).

ACTINIC KERATOSIS

CORNU CUTANEUM – WARTY HORN

VULVAR LICHEN SCLEROSUS ET ATROPHICUS

PIGMENTED XERODERMA


THANK YOU