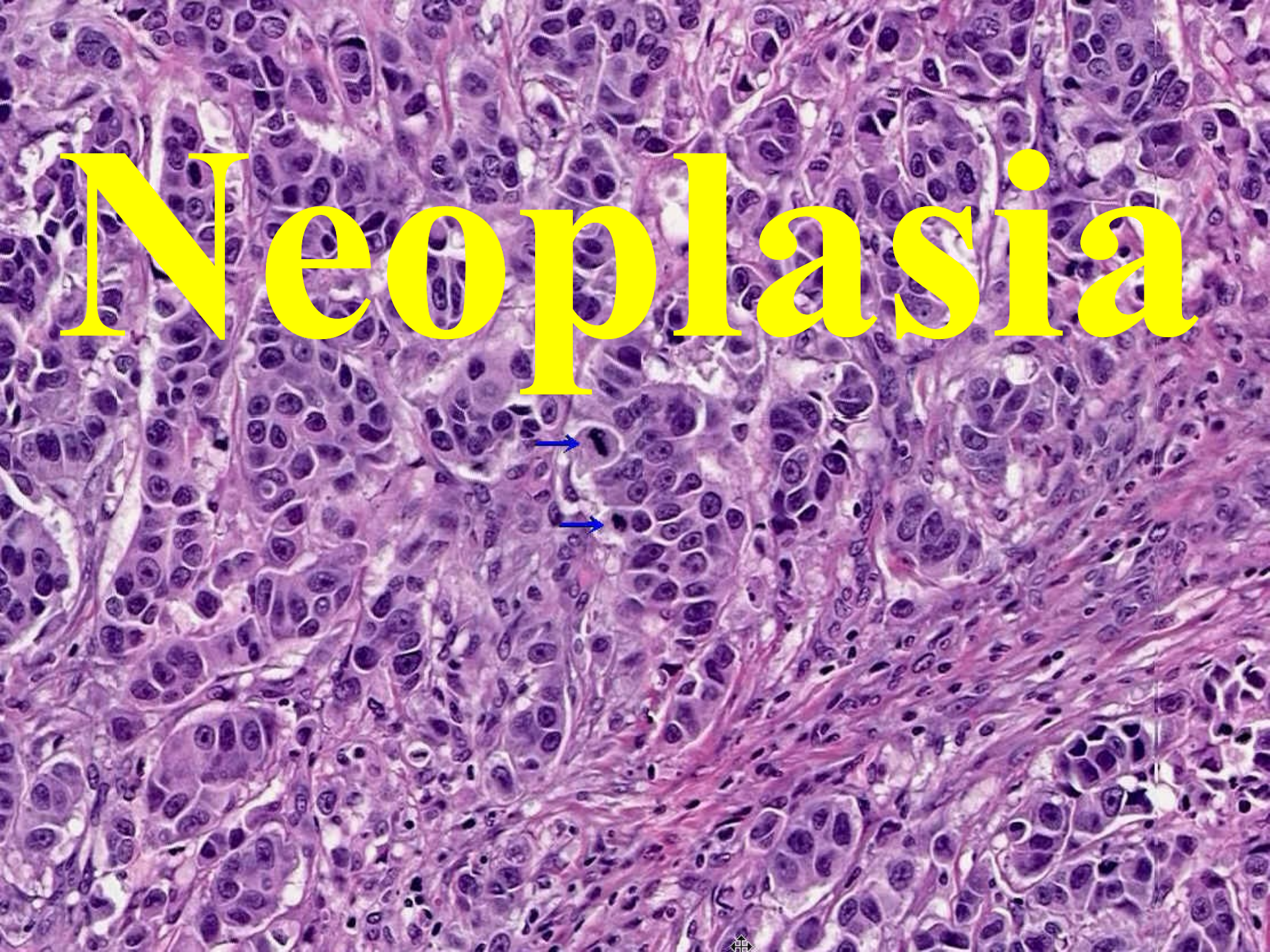
Neoplasia



Neoplasm

Definition Is a new growth

Or abnormal mass of tissue, with the excessive growth & uncoordinated with that of normal tissue & persist in the same excessive manner even after cessation of stimuli which evoke the changes

Tumor : (Greek ,swelling)

Tumor classify into

benign or malignant on the basis of:

- **Histologic and cytologic features**
- **The biological behavior of tumor**

All malignant tumor : are **Cancer**

Tumor basic component

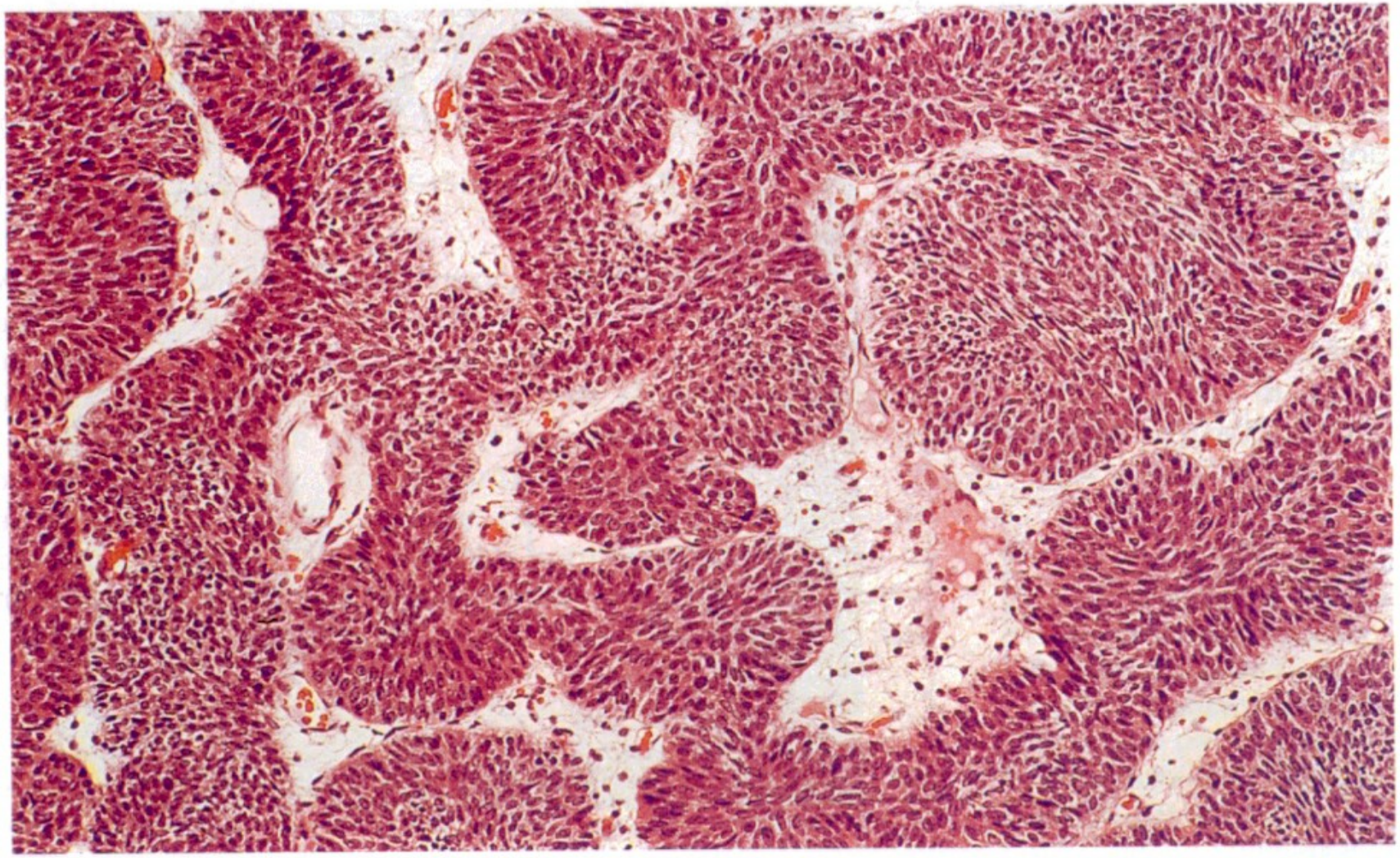
All tumor compose of

1-proliferating neoplastic cells (parenchyma).

- **The parenchyma determine the biologic behavior & this component from which the tumor derives its name**

2-supportive stroma non neoplastic (c.t & bl.v).

- **tumor growth and evolution is critically dependent on their stroma**



Nomenclature of Tumors

- **All have the suffix oma**

Depending on histogenesis (cell or tissue of origin) tumor can broadly divided into those derived from

epithelial or mesenchymal

EPITHELIAL NEOPLASMS

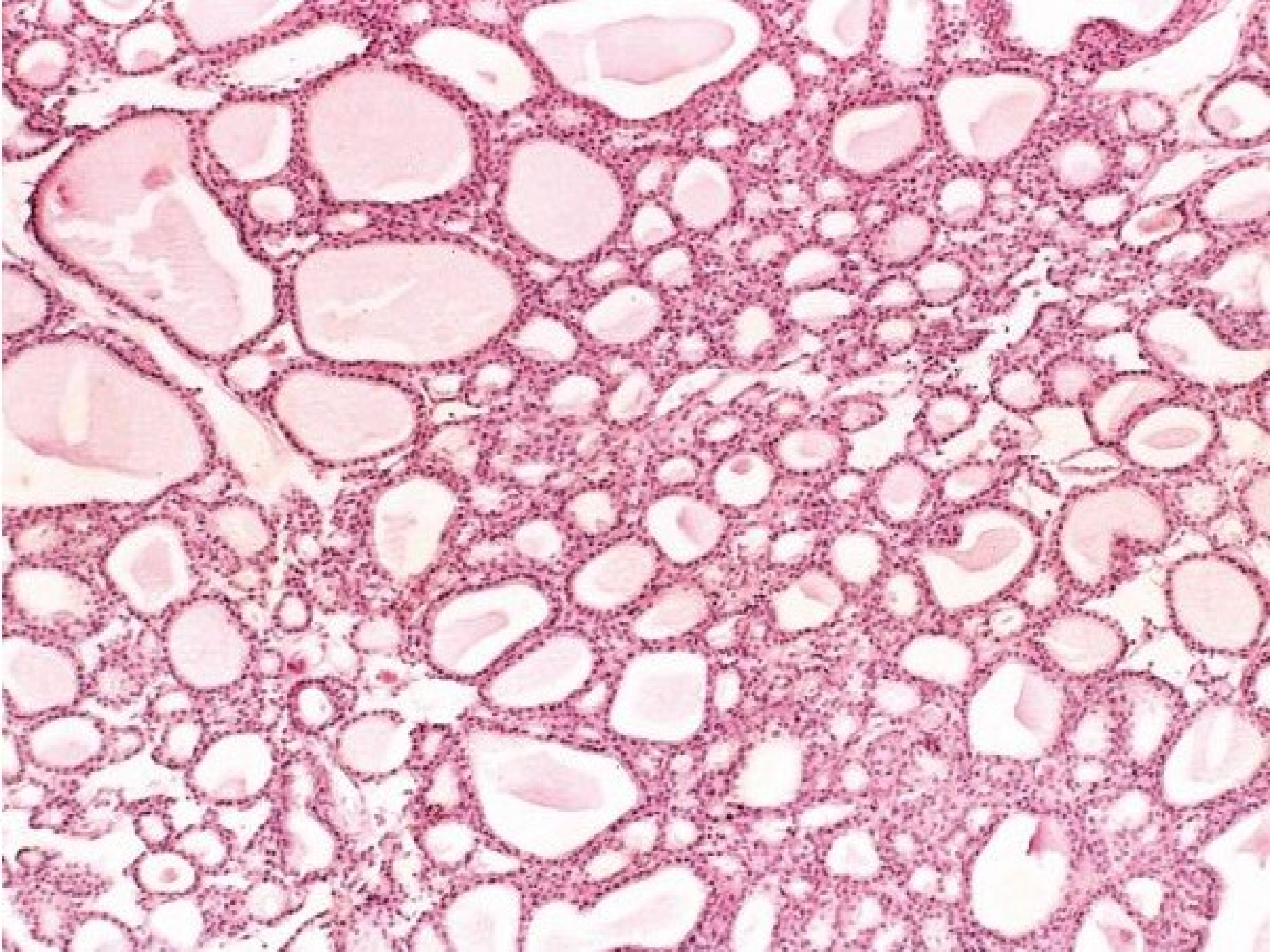
- **Adenoma** **A benign epithelial neoplasm that arises within a gland (eg, thyroid adenoma, colonic adenoma)**
- **papilloma** **(Latin, *papilla* = nipple) when arising from an epithelial surface.**

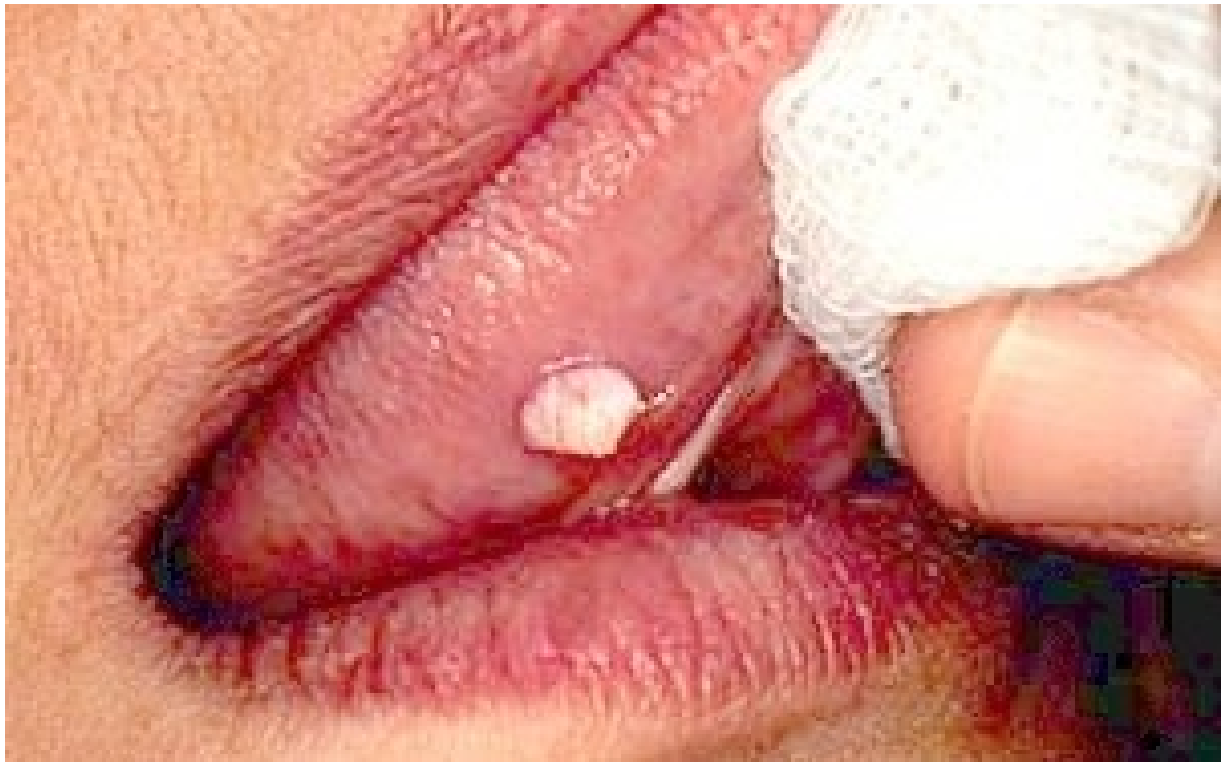
  Papillomas may arise from squamous, glandular, or transitional epithelium .
- **Carcinoma** **Malignant epithelial neoplasms**

  adenocarcinomas if derived from glandular epithelium;

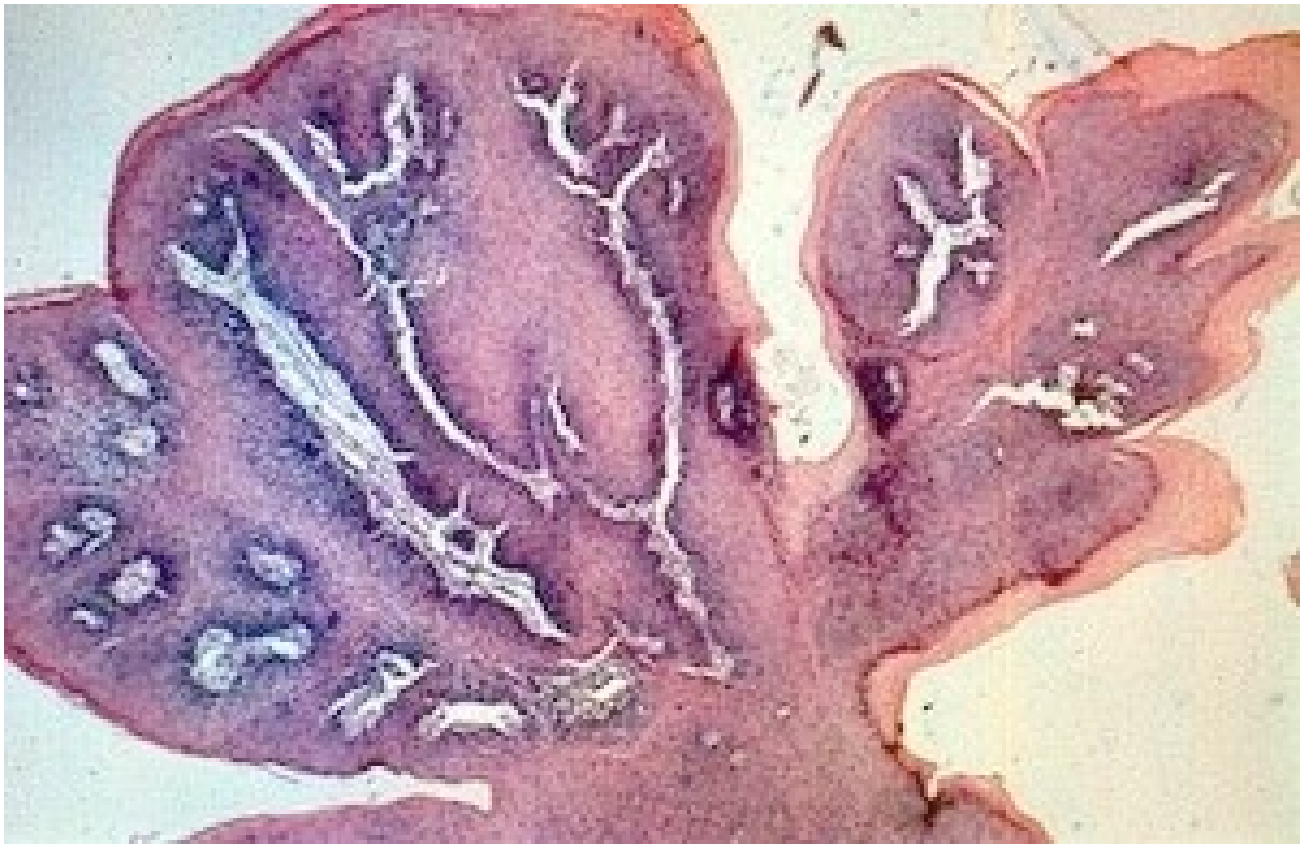
  squamous carcinoma

  transitional cell carcinoma

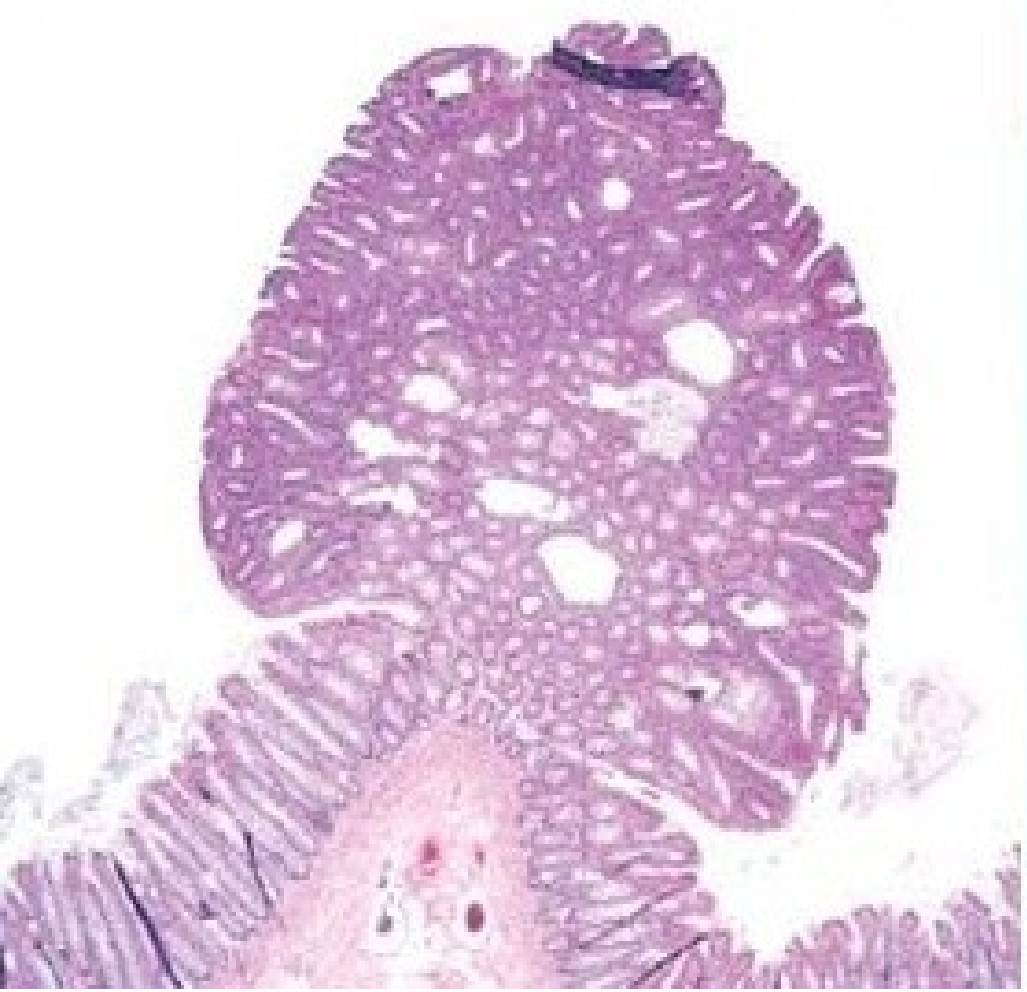


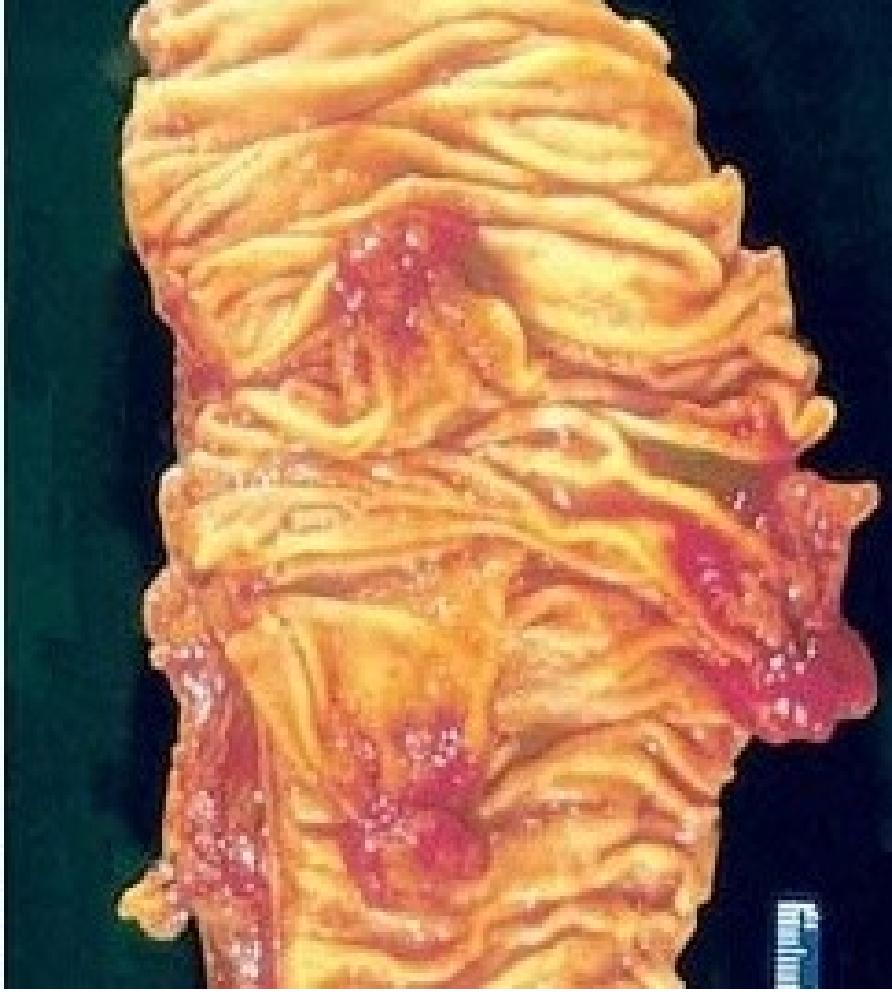


Papilloma of the tongue



Microscopical appearance of squamous papilloma





MESENCHYMAL NEOPLASMS

- **Benign mesenchymal neoplasms are named after the cell of origin followed by the suffix *-oma***
- **E.g fibroma, lipoma, leiomyoma**
- **Malignant mesenchymal neoplasms are named after the cell of origin, to which is added the suffix *-sarcoma.* liposarcomas**

Mixed tumors

- **Tumors with mixed differentiation**
  - e.g. **pleomorphic adenoma of salivary gland**
  - **carcinosarcoma**

- The names of some malignant neoplasms are formed by adding the suffix *-oma* to the cell of origin, eg,
- plasmacytoma (plasma cell),
- melanoma (melanocyte),
- Neoplasms of blood-forming organs are called leukemias and lymphomas (mass forming)

some confusing terminology

Aberrant differentiation (not true neoplasms)

- **Hamartoma** :**is disorganized mass of tissue (malformation) compose of mature cell normally present in that tissue in haphazard arrangment**

  e,g Hamartoma of lung (contain bronchial cell,bl.v., cartilage,lymphoid tissue)

choristoma

- (ectopic normal tissue in abn.location)

  e.g arrest of adrenal cell under kidney capsule or small nodule containing pancreatic tissue found in submucosa of the stomach.

Character of benign & malig.neoplasm

Differentiation by following feature

1.Differentiation & anaplasia.

2.Growth rate

3.Local invasion

4.metastasis

Differentiation

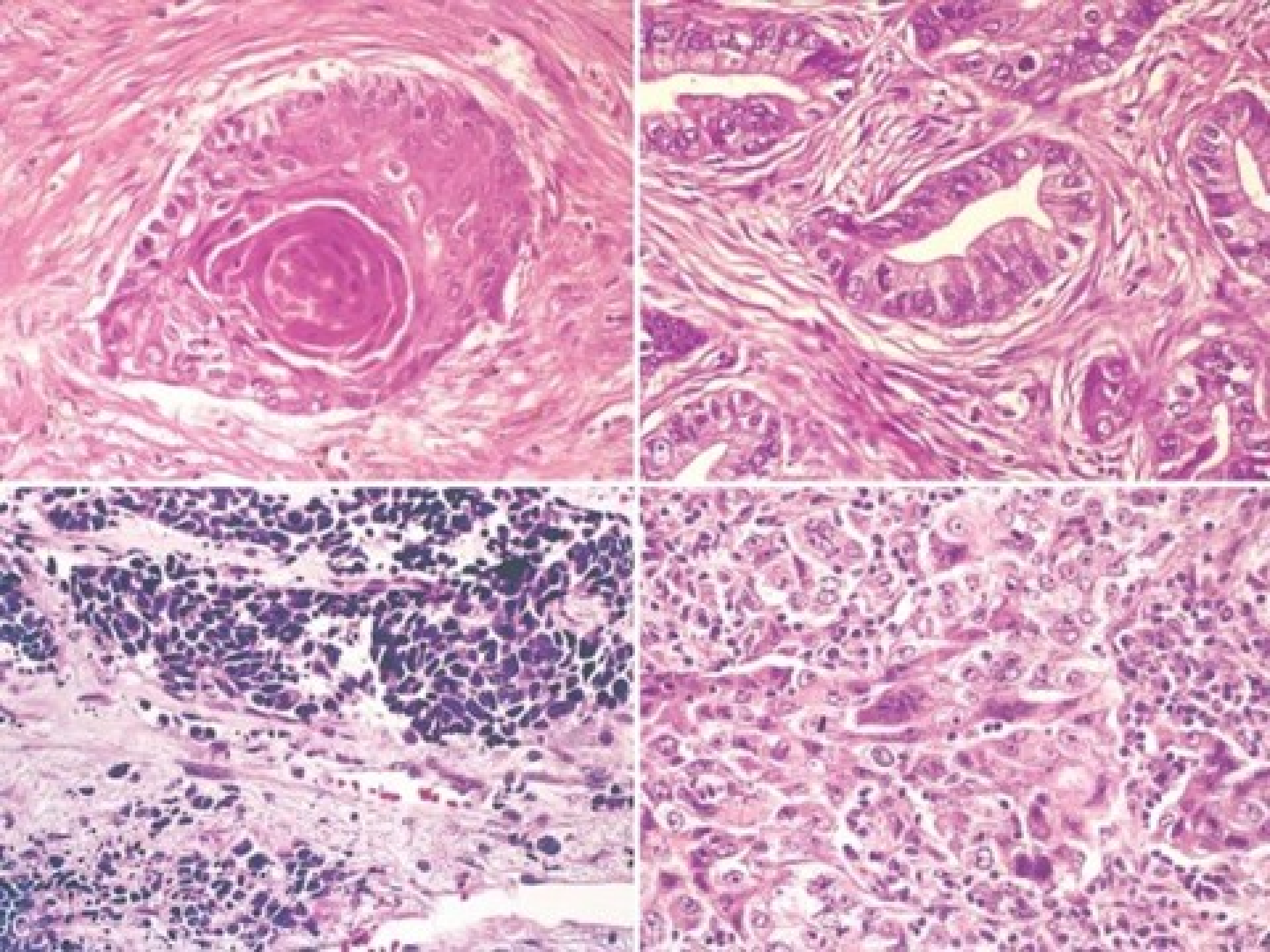
Differentiation refers to the extent to which neoplastic parenchymal cells resemble the corresponding normal parenchymal cells, both morphologically and functionally

- **Well differentiated** Resembles mature cells of tissue of origin
- **Poorly differentiated** neoplasm
  - Composed of primitive cells with little diffrerentiation.
  - **In general all benign t.are well diff.**

In contrast malig.t. range from well to poorly diff.

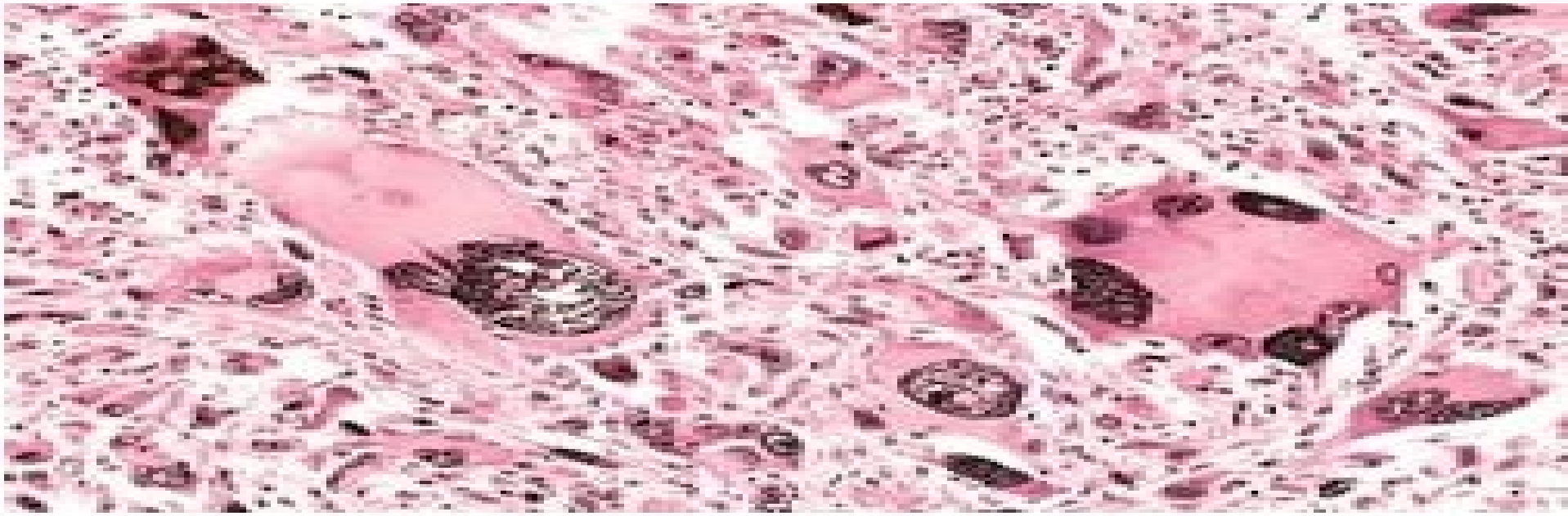
- **Differentiation determine the tumor grade**
- **Lack of differentiation (Undifferentiated tumor) are "anaplastic" tumor**

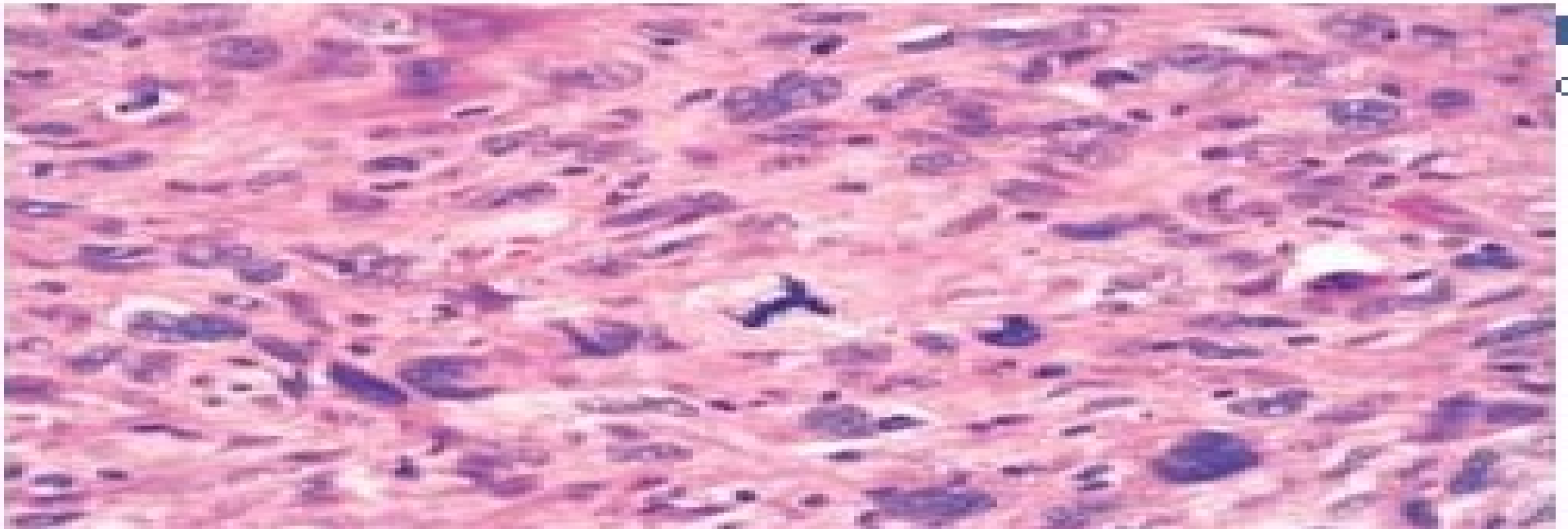
- **The degree of anaplasia correlate with aggressiveness of the tumor (biologic behavior)**
  - **Poorly differentiated malignant tumors usually have worse prognosis**

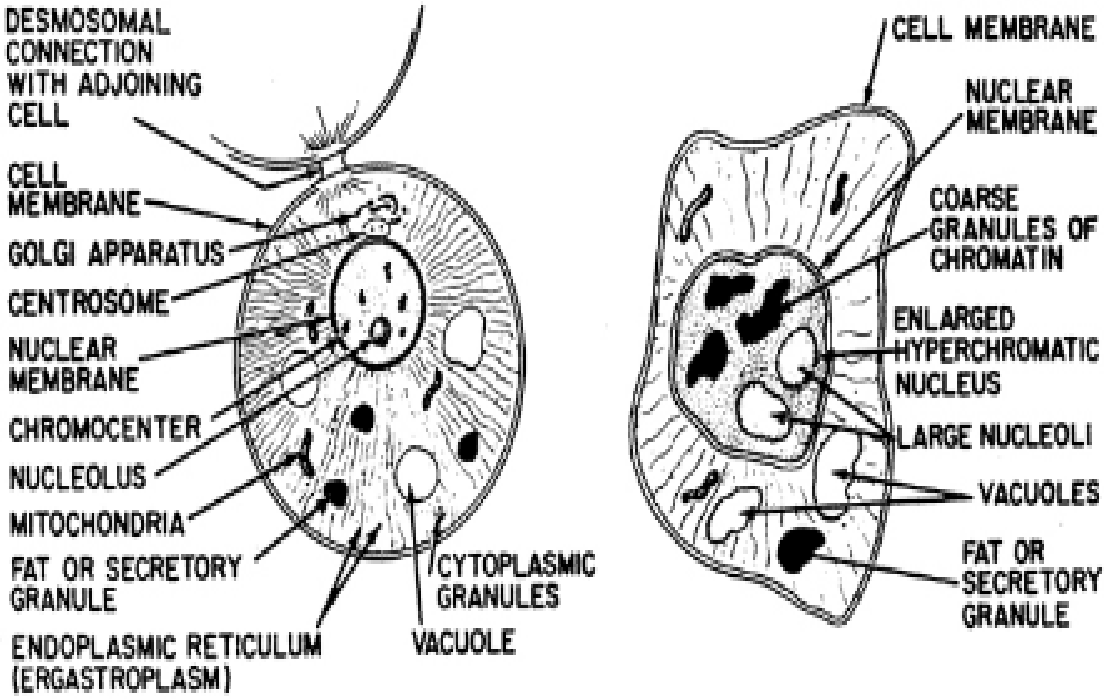


"ANAPLASIA"

- **Pleomorphism : tumor cell display variation in both (cytologic abn,)**
  - **Size**
  - **Shape (Bizzar tumor giant cell)**
- **Abnormal nuclear morphology**
  - **Hyperchromasia**
  - **High nuclear cytoplasmic ratio**
  - **Chromatin clumping**
  - **Prominent nucleoli**
  - **nuclear-to-cytoplasm ratio may approach 1 : 1 instead of the normal 1 : 4 or 1 : 6 the**
- **Mitoses**
  - Mitotic rate
  - Type of mitoses (atypical)
- **Loss of polarity**
- **Presence of necrosis**







***(left)* and a malignant cell (*right*).** The differences detailed in Table 7-3, pertain to cell configuration; nuclear size, shade, and texture; nucleolar size and shape; and the cell-to-cell relationship. The last is symbolized by the desmosome present on the benign cell and absent on the malignant cell to emphasize the reduced adhesiveness among cancer cells.

Dysplasia

- ***Dysplasia*** **is a term that means disordered growth.**
- **Dysplasia often occurs in metaplastic epithelium**
- **Dysplasia is encountered in epithelia**
- **Dysplastic cells exhibit considerable pleomorphism and often contain large hyperchromatic nuclei with a high nuclear to-cytoplasmic ratio.**
- **The architecture of the tissue may be disorder**

Dysplasia

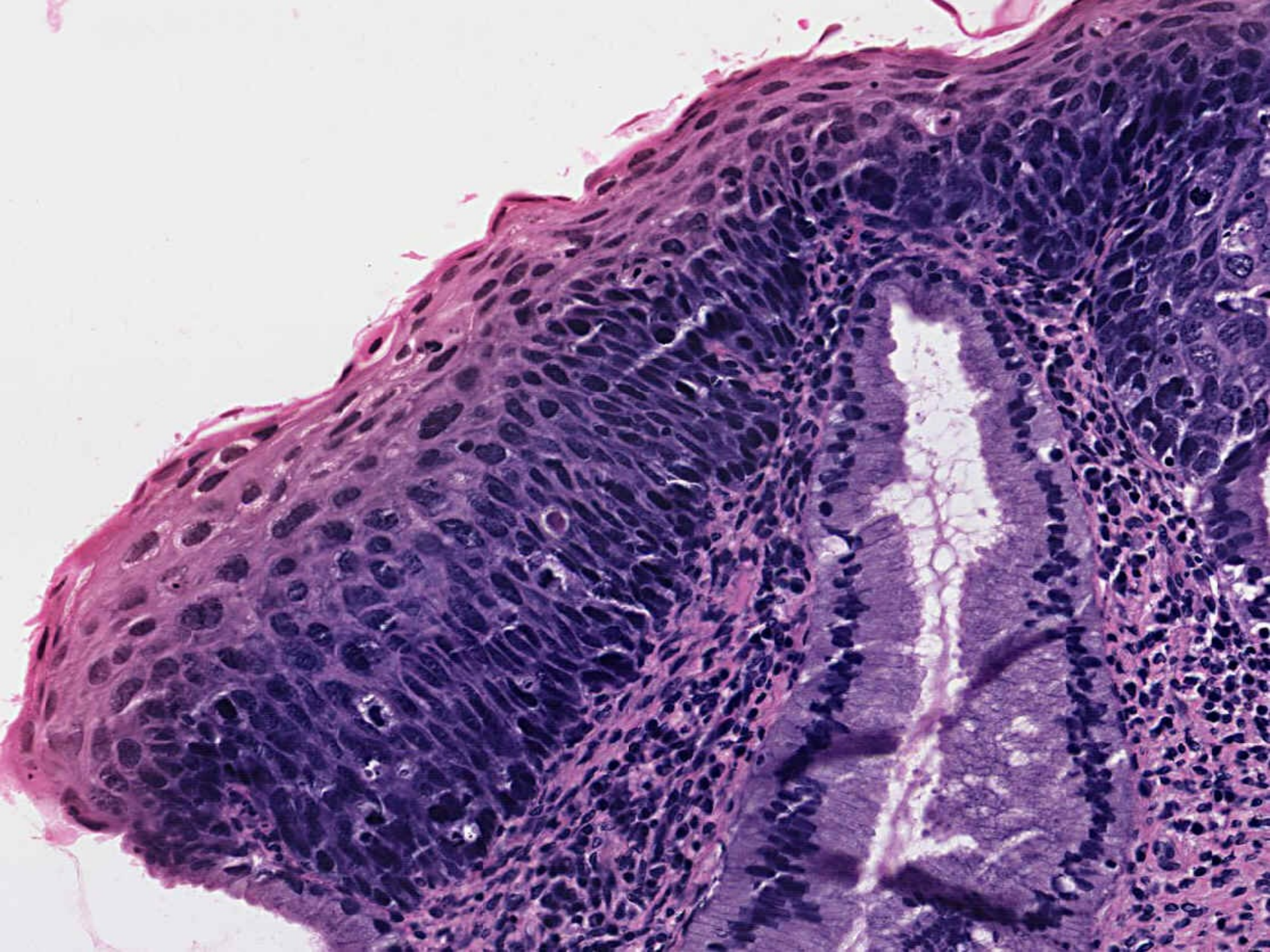
Malignant transformation is a multistep process

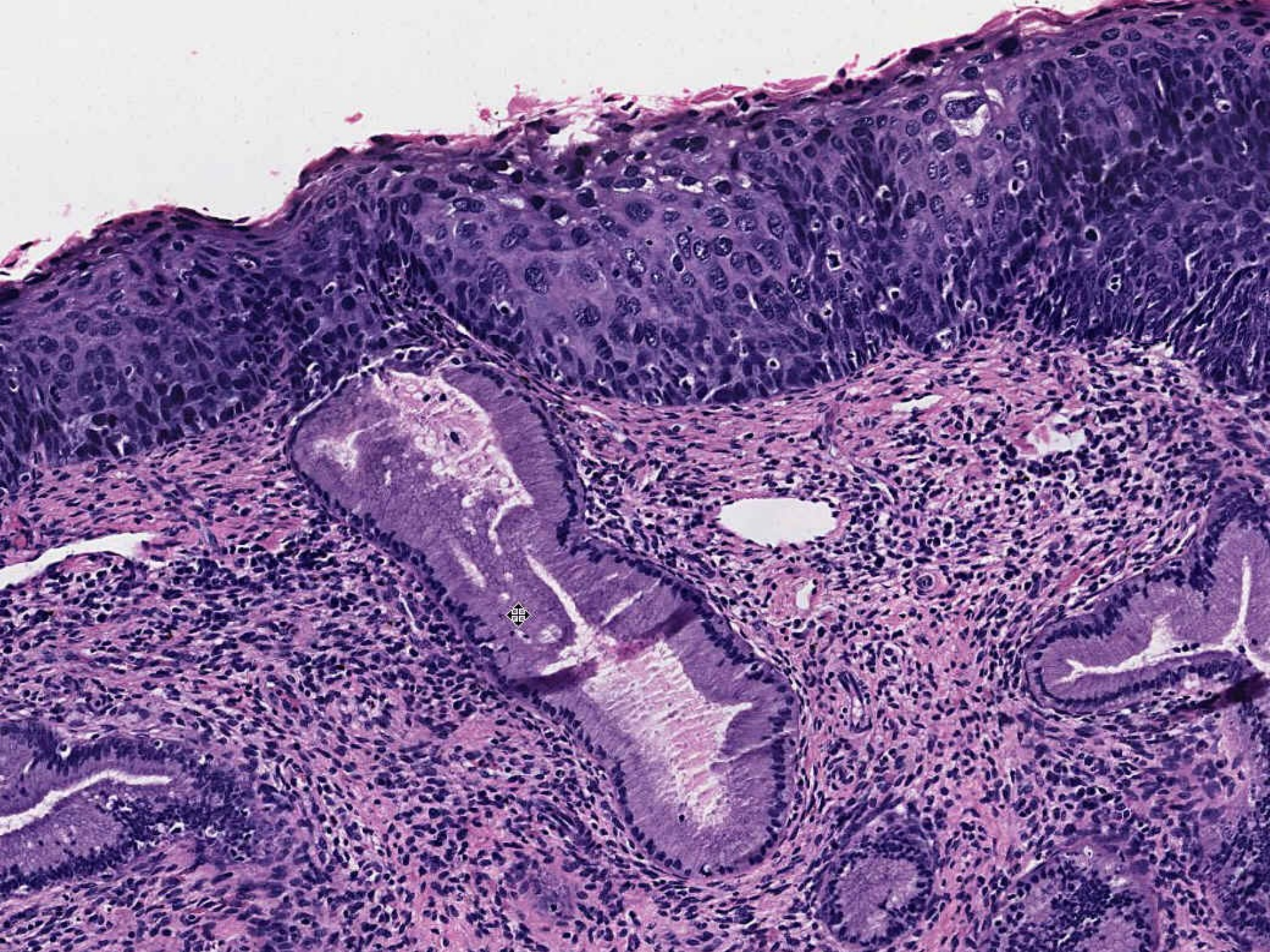
- **In dysplasia some but not all of the features of malignancy are present, microscopically**
- **Dysplasia may develop into malignancy**
  - **Uterine cervix**
  - **Colon polyps**
- **Graded as low-grade or high-grade**
- **Dysplasia may NOT develop into malignancy**
- **HIGH grade often classified with carcinoma-in-situ**

High-grade dysplasia :

- **The abnormal dysplastic cells involve whole thickness of epith.**
- **The lesion remains confined by the basement membrane ,it is pre-invasive or called (carcinoma in situ)**
- ***Dysplasia does not necessarily progress to cancer*.**

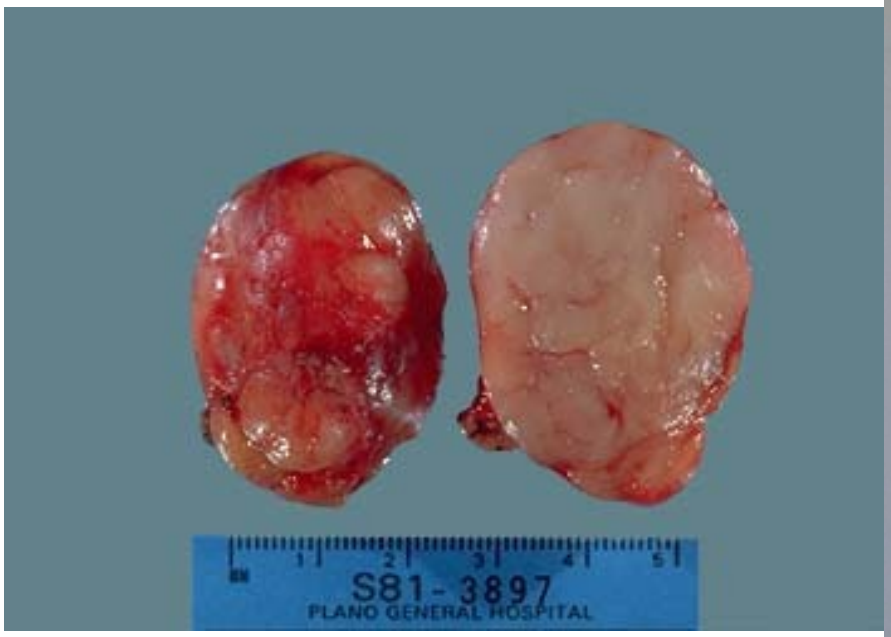
Mild to moderate changes that do not involve the entire thickness of epithelium may be reversible, after removal of the inciting agent





Growth rate

- **Benign : slowly growing**
- **Malig. : rapid growth**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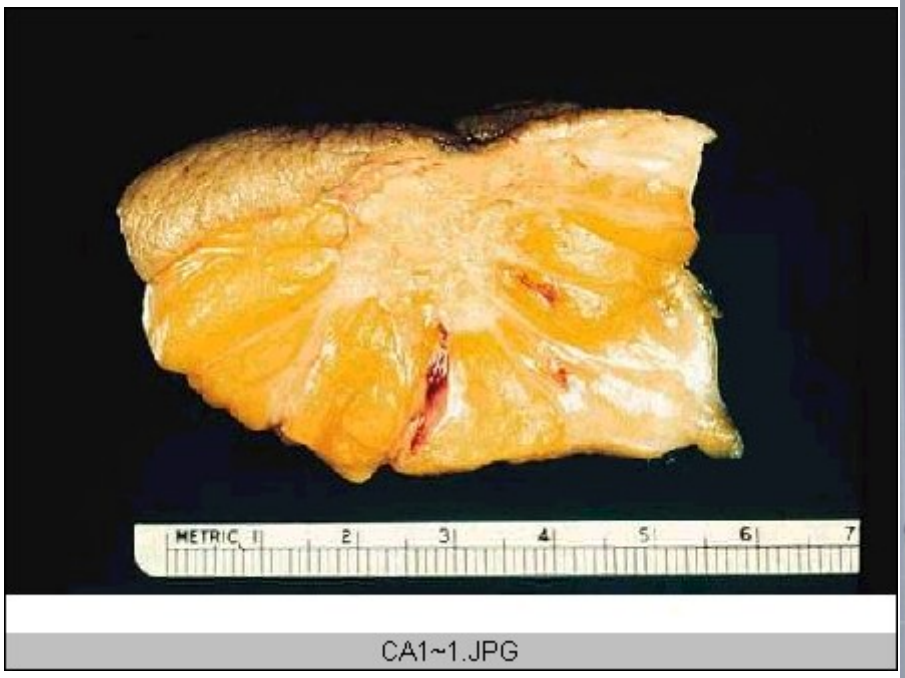
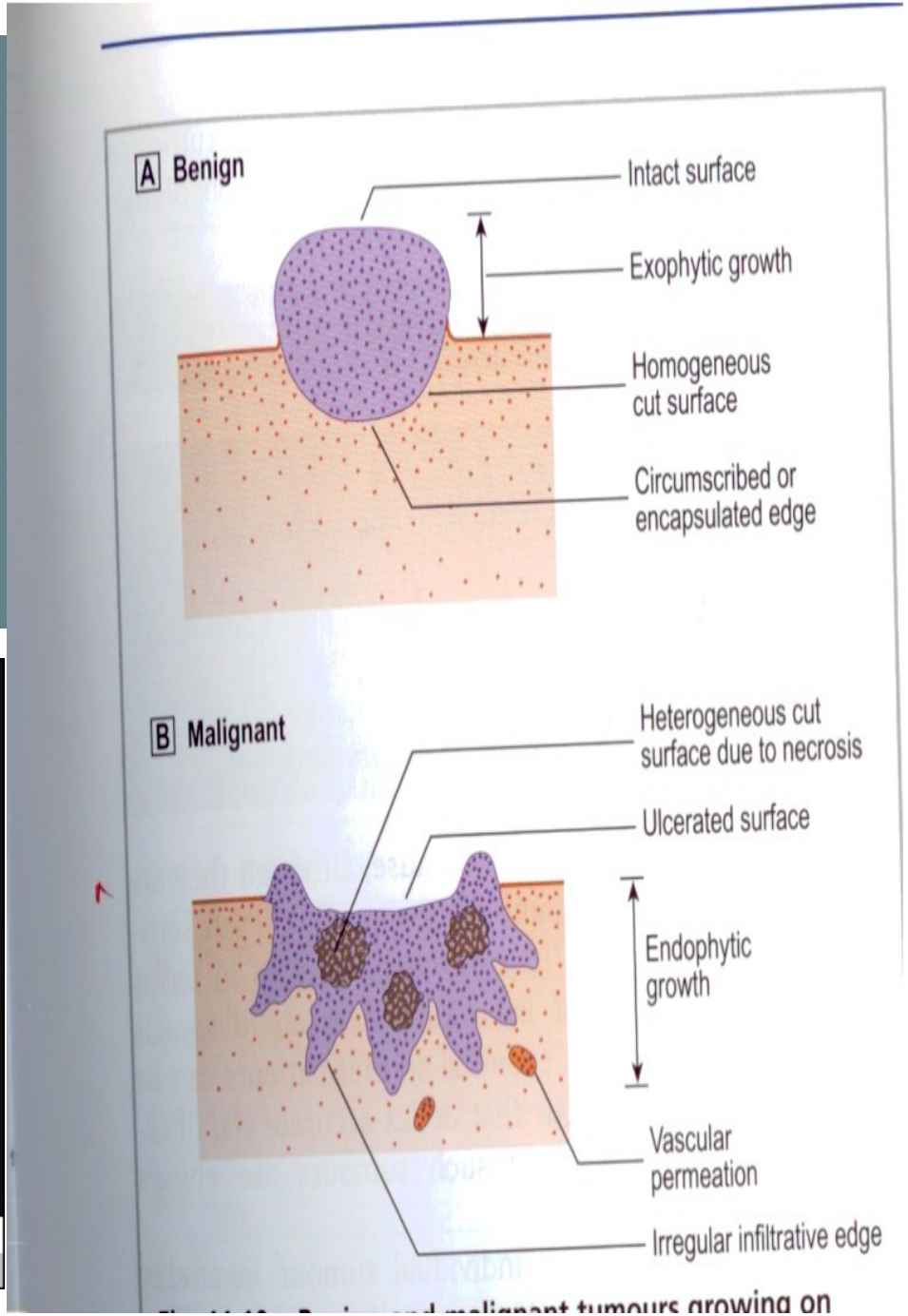
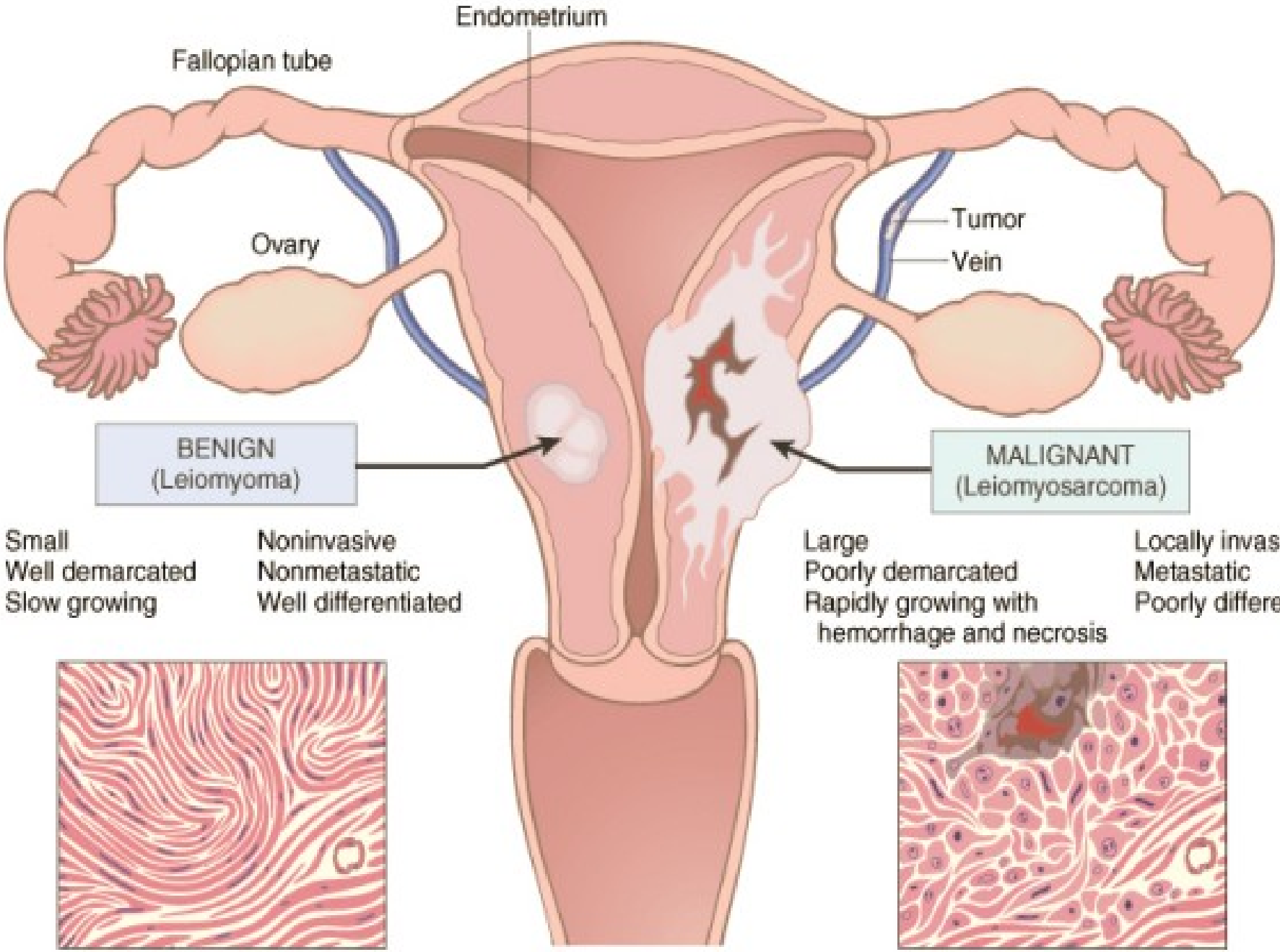
PLANO GENERAL HOSPITAL


METRIC
CA1~1.JPG


A Benign
Intact surface
Exophytic growth
Homogeneous cut surface
Circumscribed or encapsulated edge
B Malignant
Heterogeneous cut surface due to necrosis
Ulcerated surface
Endophytic growth
Vascular permeation
Irregular infiltrative edge


Endometrium
Fallopian tube
Ovary
Tumor
Vein
BENIGN
(Leiomyoma)
MALIGNANT
(Leiomyosarcoma)
Small
Well demarcated
Slow growing
Noninvasive
Nonmetastatic
Well differentiated
Large
Poorly demarcated
Rapidly growing with
hemorrhage and necrosis
Locally invasive
Metastatic
Poorly differentiated

Features of Malignant Tumors

- Cellular features
- Local **invasion**
  - Capsule
  - Basement membrane
- Metastasis
  - Unequivocal sign of malignancy
  - Seeding of body cavities
  - Lymphatic
  - Hematogenous

Invasion

- **Invasiveness is the most reliable feature differentiate malig.from benign t.**
- Some cancer are in **pre-invasive** stage called **(ca.in situ)** e.g ca.in situ of cervix without invasion to basement memb.
- **Metastasis** tumor implant discontinues with the primary tumor .
- It is unequivocal mark that the tumor malig with the exception B.C.C. of skin & C.N.S. glioma, both locally invasive but not give rise for distant metastasis

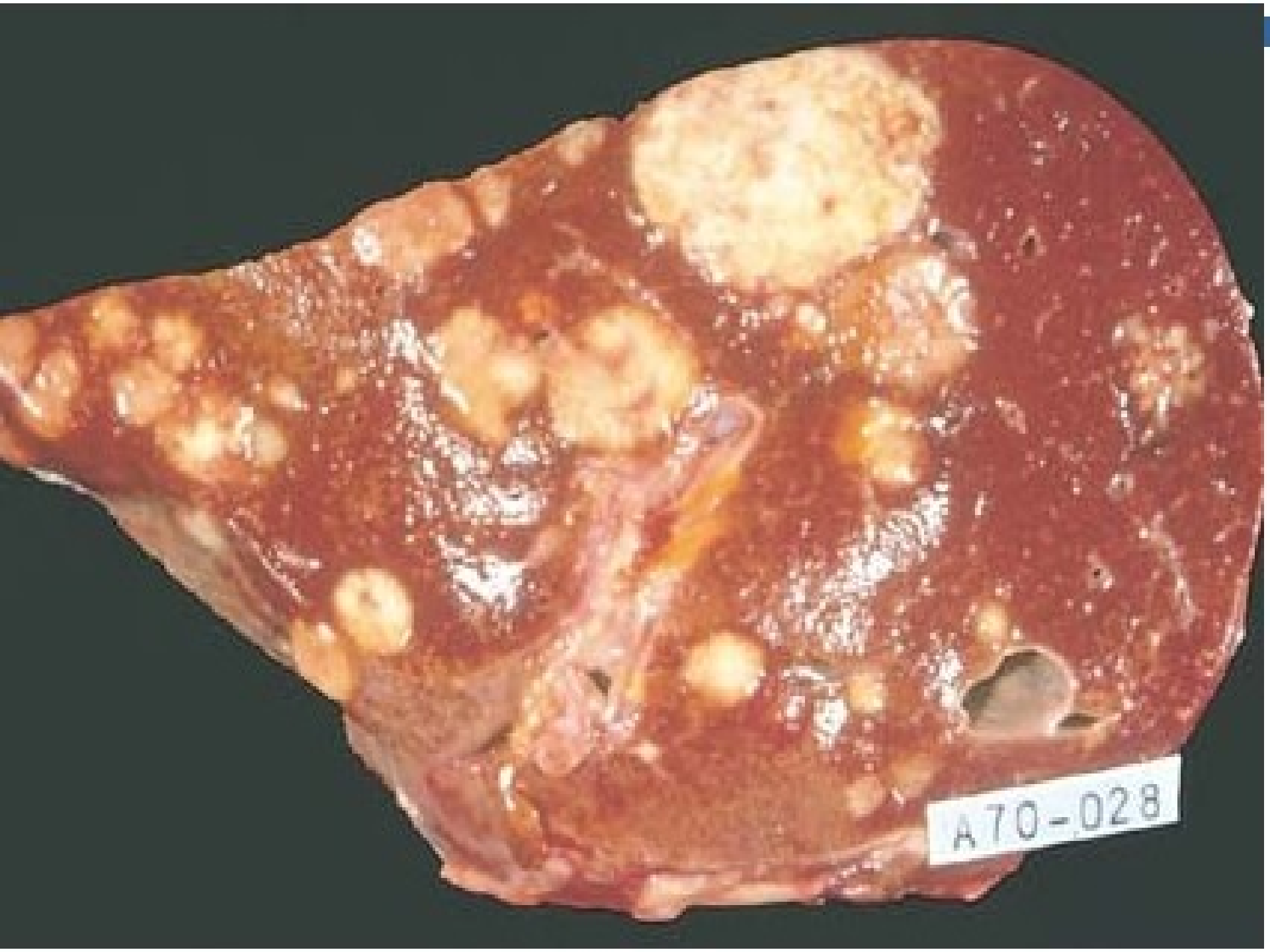
- **Benign t.:slowly growing tumor remain localized,** amenable to local surgical removal
- **Malignant: spread distant**

Table 11.1 Principal characteristics of benign and malignant tumours

Feature	Benign	Malignant
Growth rate	Slow	Relatively rapid
Mitotic activity	Low	High
Histological resemblance to normal tissue	Good	Variable, often poor
Nuclear morphology	Often normal	Usually hyperchromatic, irregular outline, multiple nucleoli and pleomorphic
Invasion	No	Yes
Metastases	Never	Frequent
Border	Often circumscribed or encapsulated	Often poorly defined or irregular
Necrosis	Rare	Common
Ulceration	Rare	Common on skin or mucosal surfaces
Direction of growth on skin or mucosal surfaces	Often exophytic	Often endophytic

Spread of malig.tumor

1. Direct seeding of body cavities or surface (pleural,peritoneum)
2. Lymphatic ,ca breast-axillary lymph.node
3. Hematogenous ,this pathway is typical for sarcoma but also for carcinoma liver,lung are frequently involved by secondary hematogenous dissemination.
4. certain cancer has propensity for invasion of vein e.g-renal cell carcinoma .


A70-028

Cancer epidemiology

- Cancer incidence
- Geographic & env.variables
- Occupational cancer

neoplasia

- **Age**
  - Most cancers occur in persons ≥ 55 years
  - Childhood cancers
    - Leukemias & CNS neoplasms
    - Bone & soft tissue sarcoma.
    - Lymphoma

- **Acquired causes or predispositions**
- **Hereditary form or predisposition (5%-10%of all human cancer) which can be divided into three categories**

Genetic inherited predispostion of cancer

can be divided into three categories :

1- Familial cancer syndromes

Example :

- **BRCA1&BRCA2 ca.breast, ovary**

Feature cc.familial cancer:

1-early age at onset

2-tumor arise in two or more close relatives

3-some time multiple & bilateral tumor

Inherited cancer synd

2. Inherited as A.D mutation (point mutation) in t.supp.gene e.g

- RB-Familial retinoblastoma ,40% inherited
- APC- (familial adenomatous polyposis) FAP of colon,germ line mutation of APC
- NF-Neurofibromatosis type 1& 2
- MEN(multiple endocrine neoplasia) syndromes
- MSH2&MSH6-hereditary non polyposis colonic cancer(HNPCC),inherit defective copy of mismatch repair gene
- P53 :various t.

Aut.Recessive syndromes

3. Inherited defect of DNA repair genes

example :

- **Xeroderma pigmentosa** (photosensitive)
- **Fanconi anemia**
- **Ataxic telangiectasia**

Acquired pre-neoplastic disorder

1. **Persist regenerative activity** 80% of hepatocellular ca.arise in cirrhotic liver & HBV play imp.role
2. **hyperplastic** Endometrial hyperplasia &end .ca.
3. **dysplastic proliferation**

- leukoplakia of oral cavity ,vulva
- Cervical dysplasia &ca.cx
- Smoking – sq.metaplasia,dysplasia- ca.bronchus

4- **chronic atrophic gastritis**

5- **Chr.infl.dis.& cancer** (ulcerative colitis crohns dis.) ,.Helicobacter pylori gastritis ,viral hepatitis ,chr.pancreatitis)

Molecular Basis of Cancer

NON-lethal genetic damage(or **mutation)** may be

- **Acquired by the action of environmental agents,** caused by exogenous agents such as chemicals, radiation, or viruses
- or it may be **inherited in the germ line**.
- Not all mutations, are “environmentally” induced. Some may be spontaneous , falling into the category of bad luck.

Molecular Basis of Cancer….cont.

- ***tumors are monoclonal formed by the clonal expansion of a single precursor cell that has incurred genetic damage.***
- **Carcinogenesis is a multistep process**

.

- **The process which result in transformation of normal cell to neoplastic cell by causing permanent genetic alteration.**
- **No single gene mutation is sufficient to cause cancer**
- **Occur by accumulation of genetic lesions that result in tumor progression**

MOLECULAR BASIS of CANCER

- **Four classes of normal regulatory genes**
  - **PROTO-oncogenes**
  - **Growth inhibitor gene (cancer suppressor gene)**
  - **DNA repair genes**
  - **Apoptosis genes**

TRANSFORMATION & PROGRESSION

- Self-sufficiency in growth signals
- Insensitivity to growth-inhibiting signals
- Evasion of apoptosis
- Defects in DNA repair: “Spell checker”
- Limitless replicative potential: Telomerase
- Angiogenesis
- Invasive ability
- Metastatic ability

ESSENTIAL ALTERATIONS FOR MALIGNANT TRANSFORMATION

- ***Self-sufficiency in growth signals***: Tumors have the capacity to proliferate without external stimuli, usually as a consequence of oncogene activation.
- ***Insensitivity to growth-inhibitory signals***: Tumors may not respond to molecules that are inhibitory to the proliferation of normal cells such as transforming growth factor β (TGF-β) and direct inhibitors of cyclin-dependent kinases (CDKIs). •

- ***Evasion of apoptosis***: Tumors may be resistant to programmed cell death, as a consequence of inactivation of *p53* or activation of anti-apoptotic genes.
- ***Limitless replicative potential***: Tumor cells have unrestricted proliferative capacity, avoiding cellular senescence and mitotic catastrophe.

LIMITLESS REPLICATIVE POTENTIAL

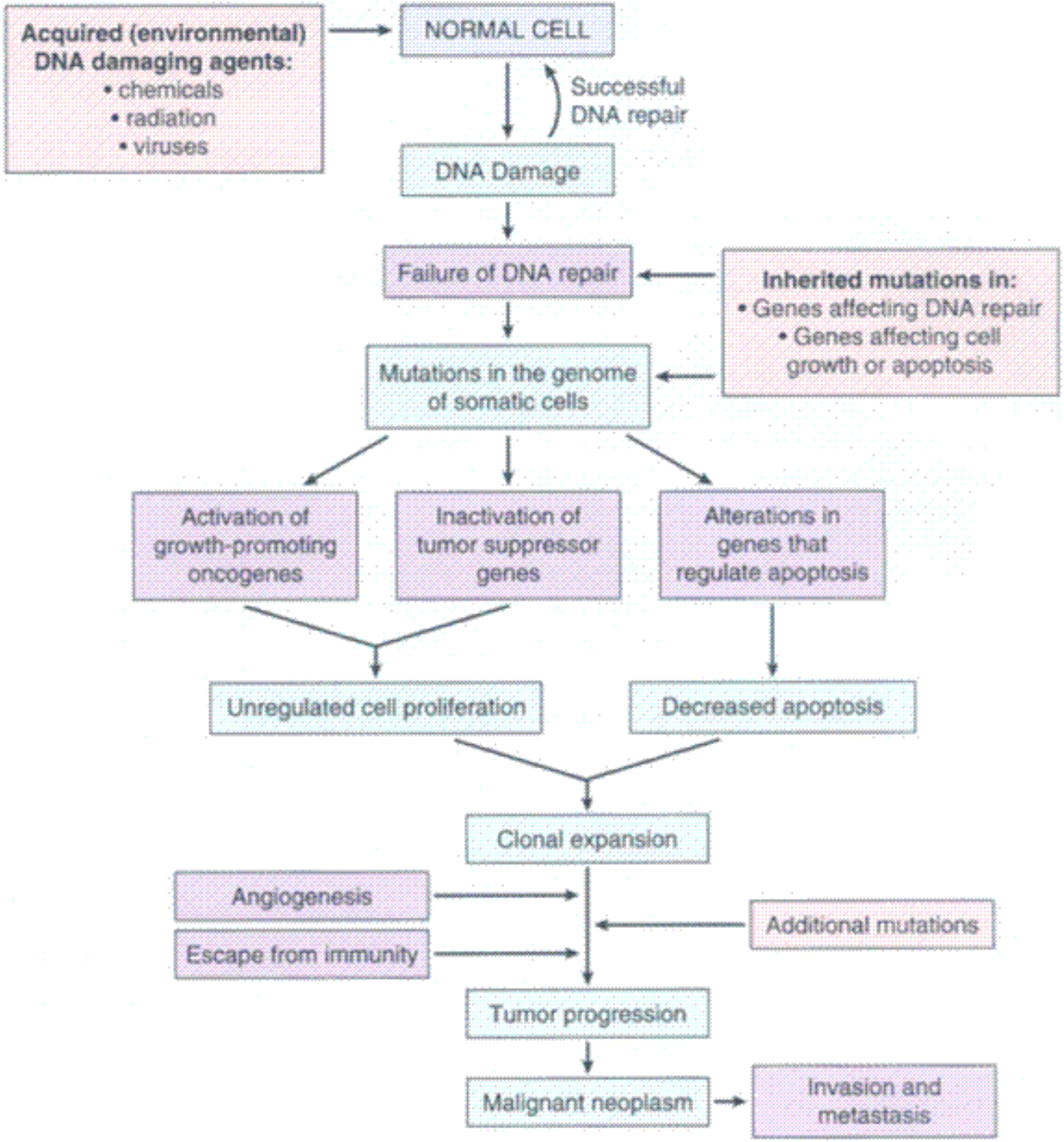
- **TELOMERES determine the limited number of duplications**
- **TELOMERASE, present in >90% of human cancers, changes telomeres so they will have UNLIMITED replicative potential**

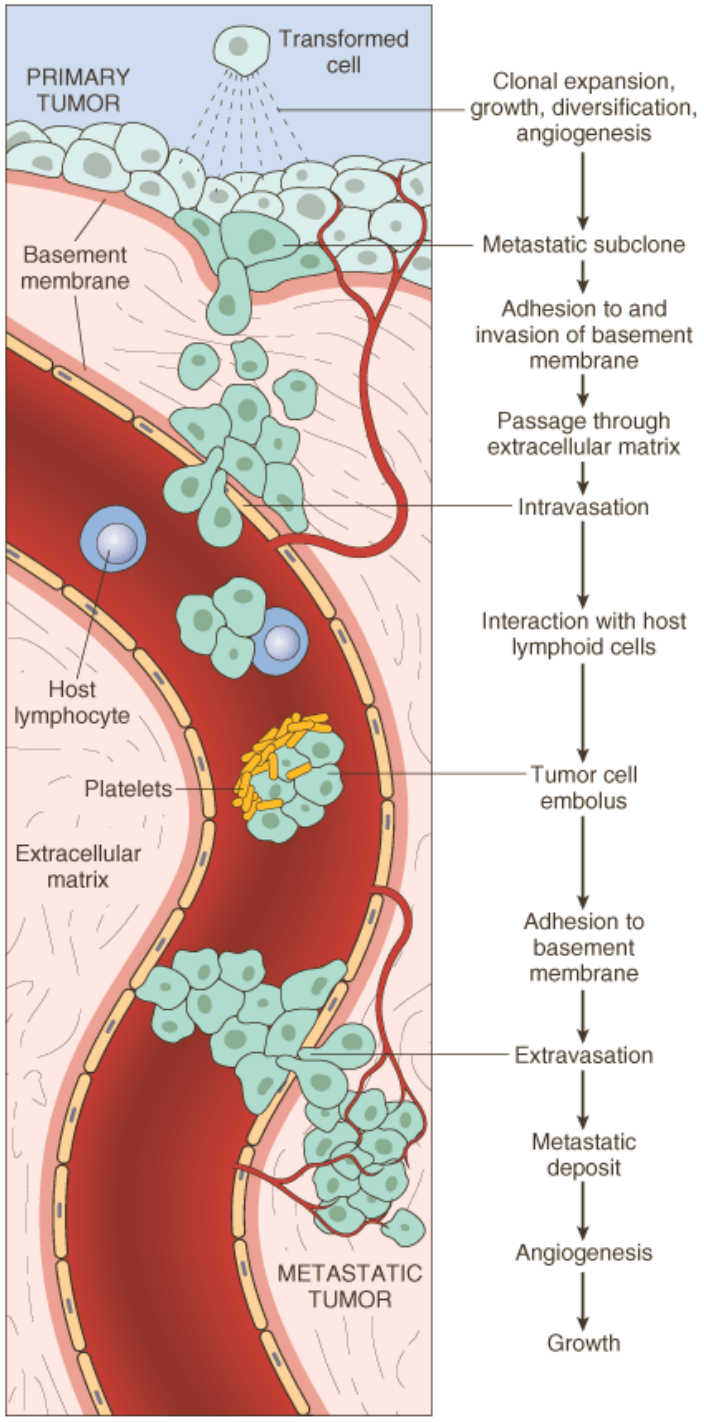
- ***Sustained angiogenesis*:** Tumor cells, like normal cells, are not able to grow without formation of a vascular supply to bring nutrients and oxygen and remove waste products. Hence, tumors must induce angiogenesis.

TUMOR ANGIOGENESIS

- **Activation of VEGF and FGF-b**
- **Tumor size is regulated (allowed) by angiogenesis/anti-angiogenesis balance**

- ***Ability to invade and metastasize*:** Tumor metastases are the cause of the vast majority of cancer deaths and depend on processes that are intrinsic to the cell or are initiated by signals from the tissue environment.
- ***Defects in DNA repair*:** Tumors may fail to repair DNA damage caused by carcinogens during unregulated cellular proliferation, leading to genomic instability


Acquired (environmental) DNA damaging agents:
• chemicals
• radiation
• viruses
NORMAL CELL
Successful DNA repair
DNA Damage
Failure of DNA repair
Inherited mutations in:
• Genes affecting DNA repair
• Genes affecting cell growth or apoptosis
Mutations in the genome of somatic cells
Activation of growth-promoting oncogenes
Inactivation of tumor suppressor genes
Alterations in genes that regulate apoptosis
Unregulated cell proliferation
Decreased apoptosis
Clonal expansion
Angiogenesis
Escape from immunity
Additional mutations
Tumor progression
Malignant neoplasm
Invasion and metastasis



TRANSFORMATION→
GROWTH→
BM INVASION→
ANGIOGENESIS→
INTRAVASATION→
EMBOLIZATION→
ADHESION→
EXTRAVASATION→
METASTATIC GROWTH→
etc.

Invasion Factors

- **Detachment** ("loosening up") of the tumor cells from each other
- **Attachment** to matrix components
- **Degradation** of ECM, e.g., collagenase, etc.
- **Migration** of tumor cells

Invasion Factors

- 1st step:E-cadherin (keep n.cell together),-it will bind to B-catenin .-lead to B catenin sequestation .in malig.cell E cadherin is lost .
- 2ns step degradation of b.m &ECM by proteolytic enzy (MMP-9&cathepsin –D) which cleave type IV collgen.

Oncogenes

- Gene promote autonomous cell growth in cancer cell in the absence of normal mitogenic signals.
- Their normal counterpart are protooncogenes which involve in physiologic regulation of cell proliferation& differentiation

ONCOGENES

- **Are MUTATIONS of NORMAL genes (PROTO-oncogenes)**
  - **Growth Factors**
  - **Growth Factor Receptors**
  - **Signal Transduction Proteins (RAS)**
  - **Nuclear Regulatory Proteins**
  - **Cell Cycle Regulators**

oncogens & their function

Neoplastic cell prolif. self stimulation mediated by :

1-Over-expression of GF

2 - Receptor for epidermal growth factor HER2 –or ERBB2 located at cell surface

3- signal transducer

Ras oncogen act on intracellular signaling (signal transducer)

e.g: pancreatic adenoca ,cholangioca, ca.colon shows point mutation

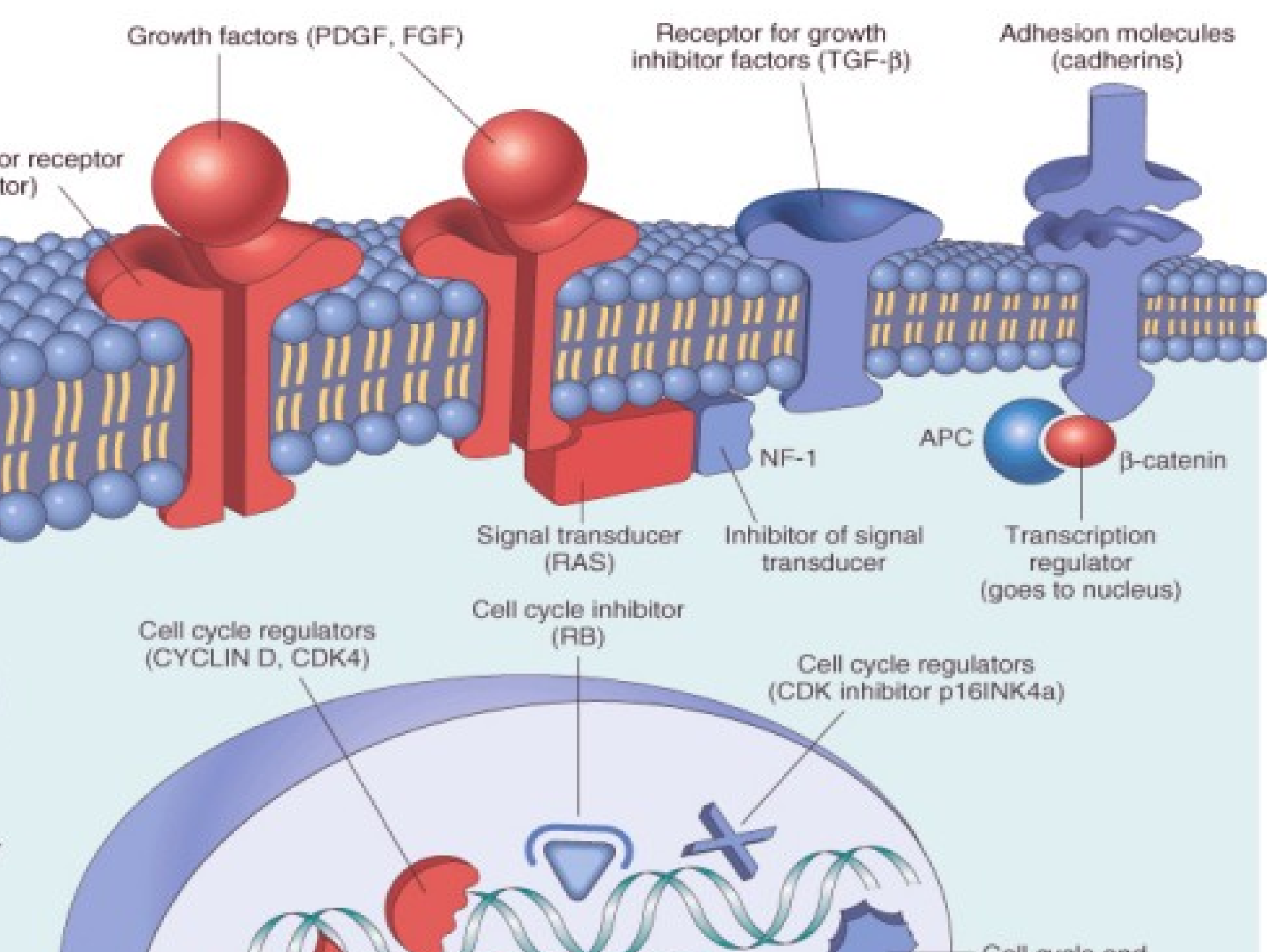
4- DNA Binding nuclear protein

myc oncogen :stimulate direct DNA synthesis

translocation t8:14 in Burkitt lymphoma.

5- cell cycle protein (regulator) Cyclin & CDK

6- Inhibitor of apoptosis (bcl-2).


Growth factors (PDGF, FGF)
Receptor for growth inhibitor factors (TGF-β)
Adhesion molecules (cadherins)
or receptor tor)
NF-1
APC
β-catenin
Signal transducer (RAS)
Inhibitor of signal transducer
Transcription regulator (goes to nucleus)
Cell cycle inhibitor (RB)
Cell cycle regulators (CYCLIN D, CDK4)
Cell cycle regulators (CDK inhibitor p16INK4a)

Most common type of nonrandom karyotypic changes in tumor cell

- **e.g of balanced translocation**

1-philadelphia chromosome in C.M.L.represent transl.bet.chr.9&22

2- Burkitts lymphoma in 90% transl.bet chr 8 &14

- **e.g of deletion**

–solid t. of non hematopoietic origin –embryonal t.of childhood (retinoblastoma, wilms t)

Loss of some normal cancer suppressor genes located on chr.13 &11 in case of wilms t.

- **Gene amplification**

e.g neuroblastoma the amplified gene is oncogen called N-myc ,or in case of ca.breast.

Tumor suppressor gene & their function

- **P53 : nuclear protein**
- **TGFB: potent inhibitor for proliferation**
  mutation seen in ca.colon
- **APC Inhibitor for transcription regulator**
  individual born with one mutant allel develop hundreds to thousands of adenomatous polyp in the colon in10-20 yr.
- **RB gene :** in nucleus **,cell cycle inhibitor (retinoblastoma,osteosarcoma)**
- **WT1 : location in nucleus**
- **NF1&NF2 : in plasma membrane ,inhibitor for signal transducer**
- **BRCA 1& BRCA 2 (DNA repair)**

P53 gene
The Guardian of the Genome

- The most common mutated gene in human cancer
- It is DNA binding protein ,regulate DNA repair & prevent DNA transcription error

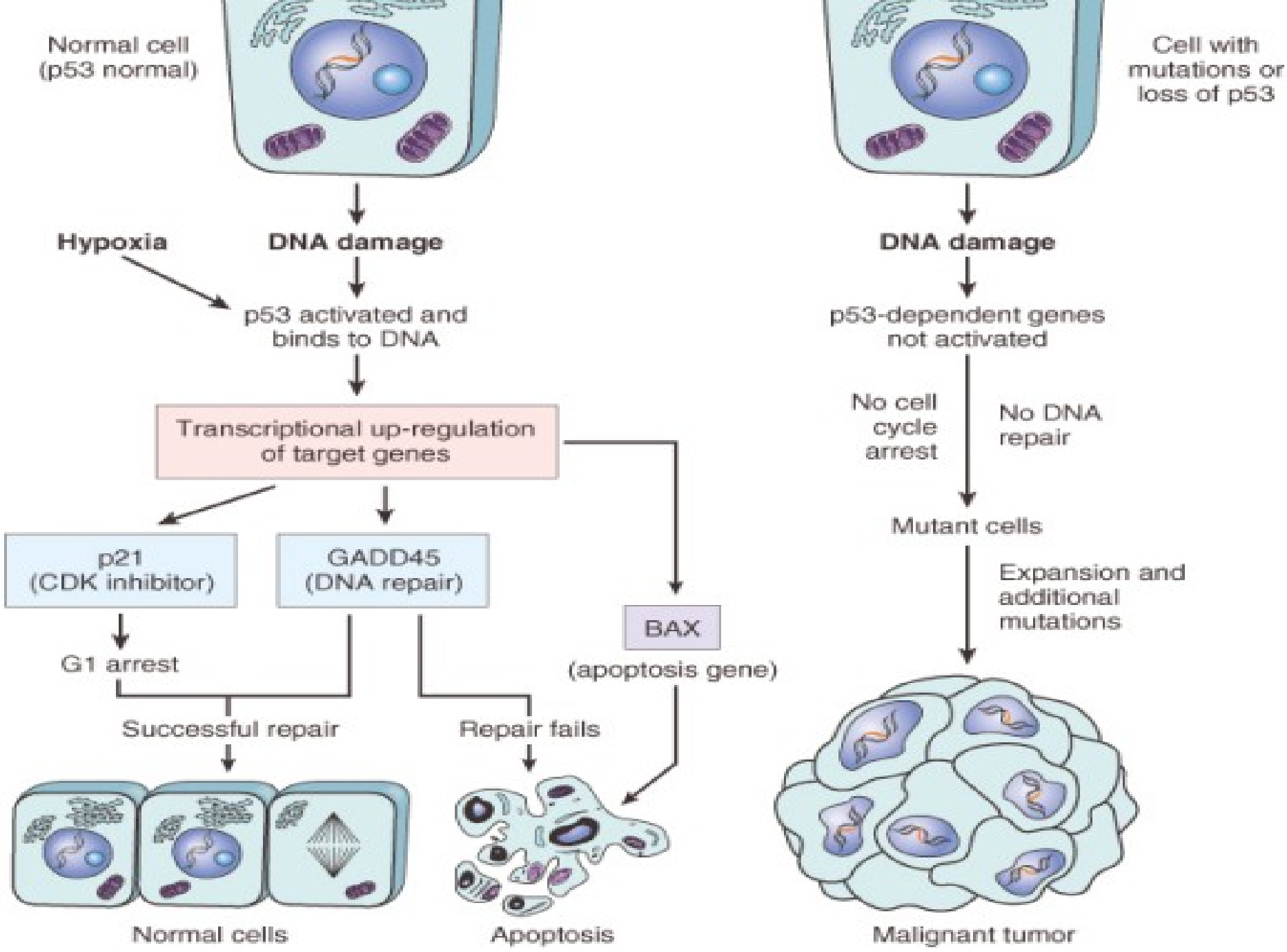
Function in normal cell (regulate cell proliferation) through

1-Activation of temporal cell cycle arrest (**quiescence**) through p21

2- permanent cell cycle arrest (**senescence**)

3-promotes cell death through BAX gene which inhibits BCL2 (Apoptotic inhibiting gene)

4- help in repair process (through GADD 45)


Normal cell
(p53 normal)
Cell with
mutations or
loss of p53
Hypoxia
DNA damage
DNA damage
p53 activated and
binds to DNA
p53-dependent genes
not activated
Transcriptional up-regulation
of target genes
No cell
cycle
arrest
No DNA
repair
p21
(CDK inhibitor)
GADD45
(DNA repair)
Mutant cells
Expansion and
additional
mutations
BAX
(apoptosis gene)
G1 arrest
Successful repair
Repair fails
Normal cells
Apoptosis
Malignant tumor

P53 & RAS

p53

- Activates DNA repair proteins
- Sentinel of G1/S transition
- Initiates apoptosis
- Mutated in more than 50% of all human cancers

RAS

- H, N, K, etc., varieties
- Single most common abnormality of dominant oncogenes in human tumors
- Present in about 1/3 of all human

Tumor (really "GROWTH") suppressor genes

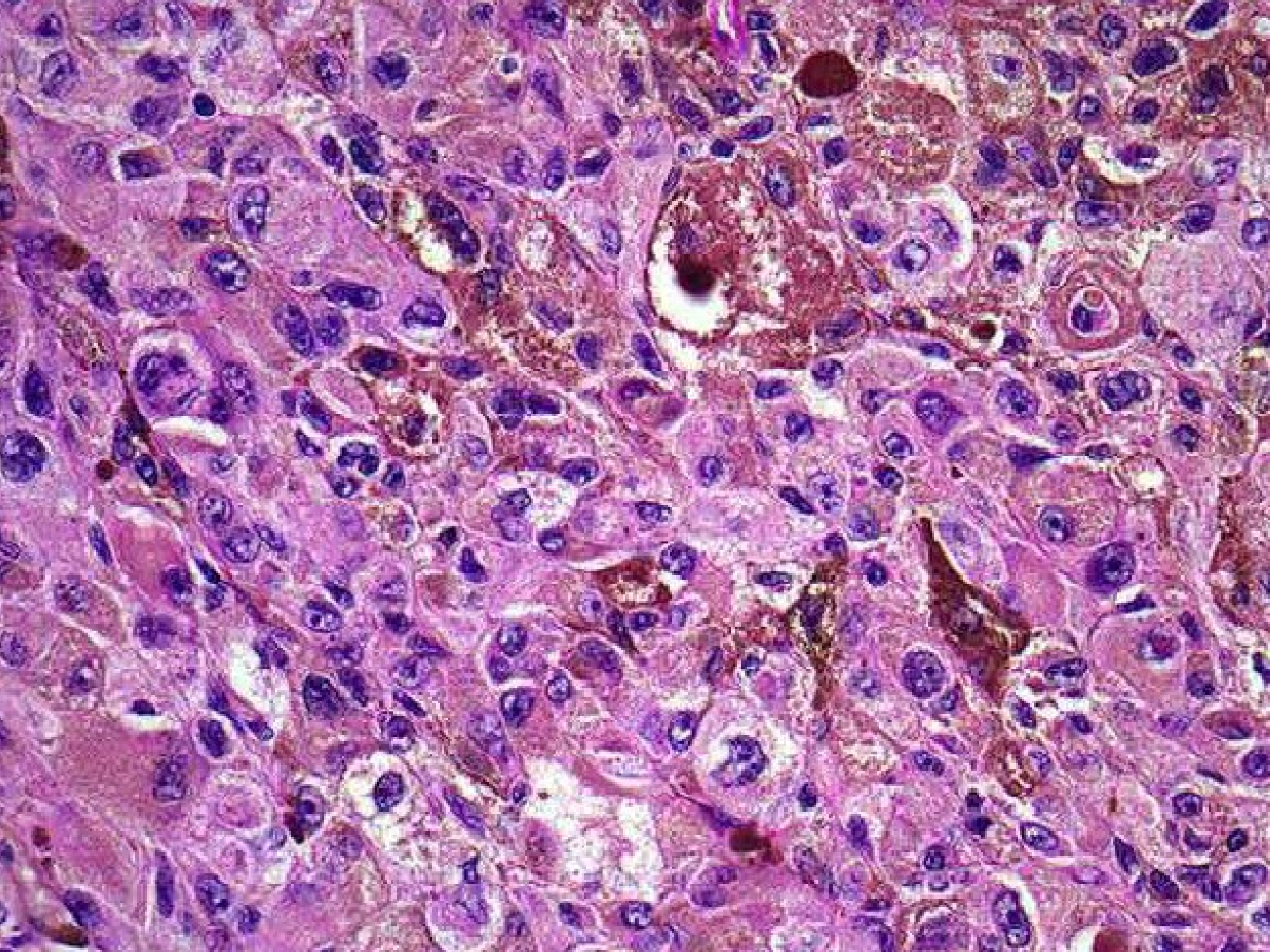
- TGF-β → COLON
- E-cadherin → STOMACH
- NF-1,2 → NEURAL TUMORS
- APC/β-cadherin → GI, MELANOMA
- SMADs → GI
- RB → RETINOBLASTOMA
- P53 → EVERYTHING!!
- WT-1 → WILMS TUMOR
- p16 (INK4a) → GI, BREAST (MM if inherited)
- BRCA-1,2 → BREAST
- KLF6 → PROSTATE

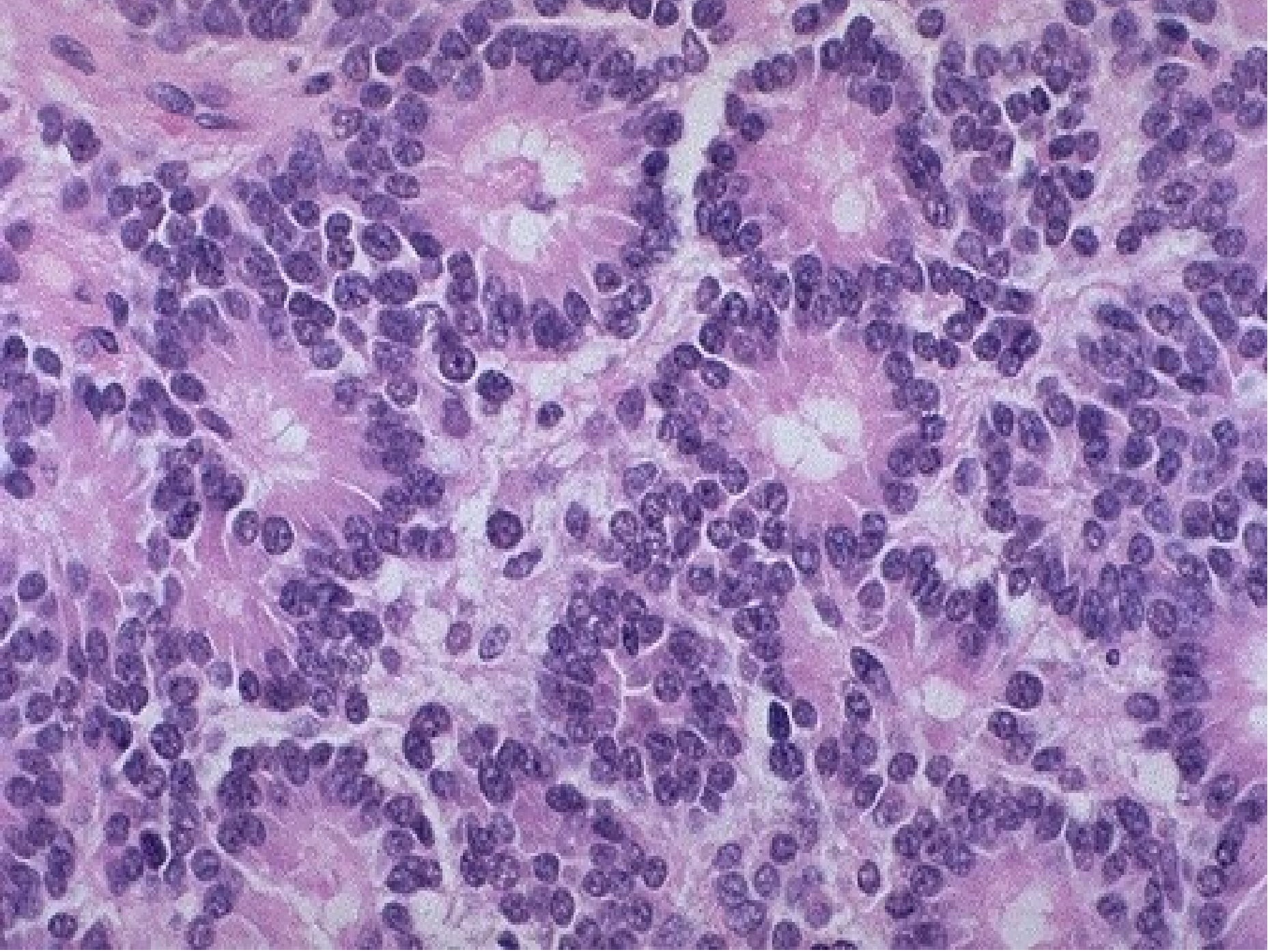
Two hit hypothesis,LOH & cancer•

- **No.of syndromes result from germ line mutation in various t.supp.gene .**

Example :

- **Li-Fraumeni synd.(inherited predispos to ca.) due to germ line mutation of p53.**
- **Familial polyposis coli synd : APC gene mutation ,also cause m.m.& ov.ca**
- **Hereditary wilms t.**
- **Von Hipple Lindau synd.**





Acquired Carcinogenic agent

1-chemical carcinogen

2-radiant energy

3-Microbial agent(bact,virus.parasite)

Chemical carcinogen

multistep process through four stages

- **Initiation & promotion sequences**
- **Progression: stage in which tumor growth become autonomus (independent of carcinogen or the promoter result from acc.mutation result in immotalize cell)**
- **Cancer: the end result of entire sequence**

Initiation

- **Is the event that induce lesion in cell genome (DNA)**

  Result from exposure of cell to

- **appropriate dose** of carcinogenic agent .
- **Initiator is mutagenic**
- **Initiated cell** (**altered ,transformed cell**) render it susceptible to give rise of tumor

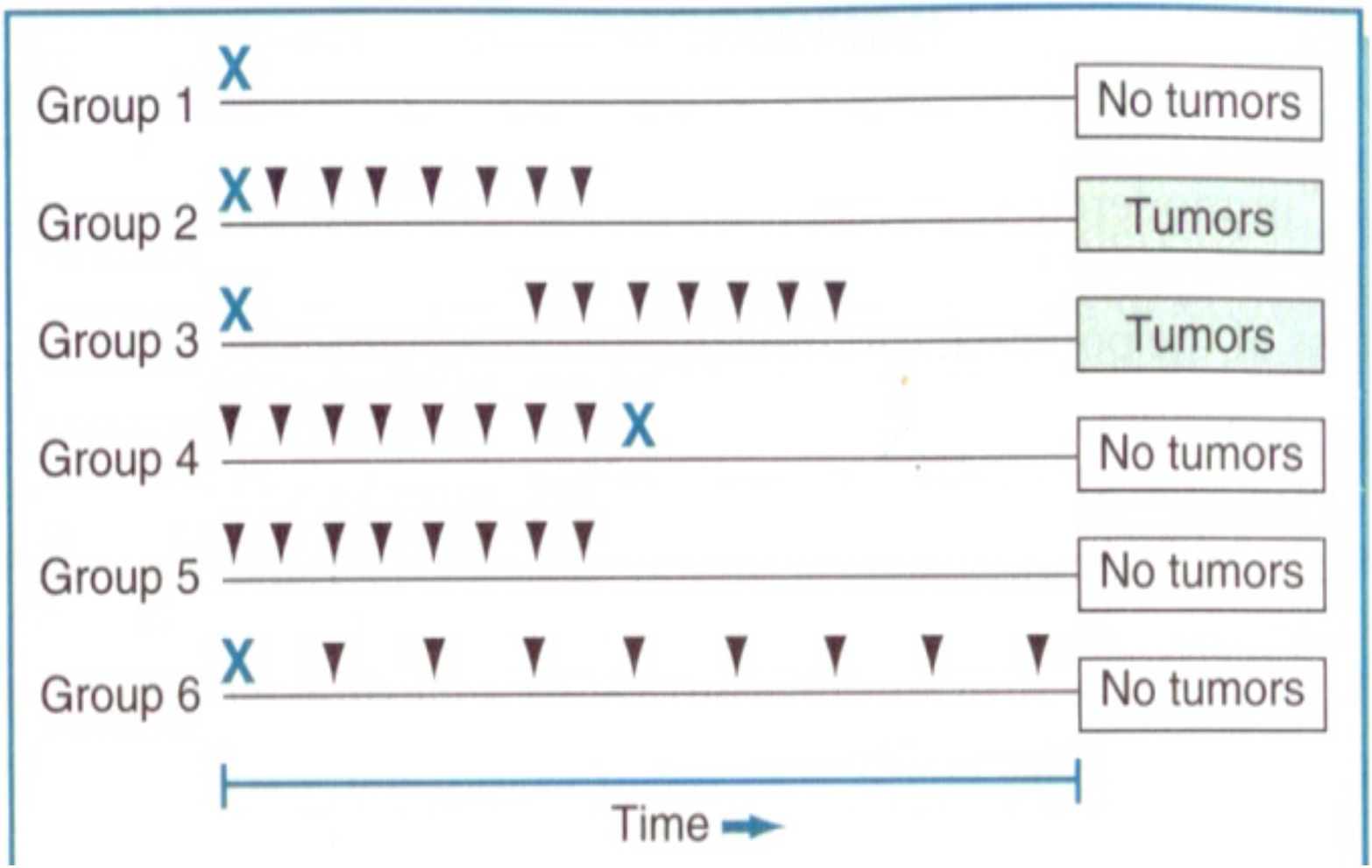
- **Initiation alone is not sufficient for tumor formation.**
- **It give rise of tumor only after promotor application**
- **initiation is rapid & irreversible**
- **the initiating carcinogen produce permanent changes in DNA of the target cell**

Promotion

Is the event lead to clonal proliferation of the initiated transformed cell .

- **promotion can induce changes in the initiated cell but they are not tumorogenic by themselves**
- **tumor does not result when promotion applied before rather than after the initiating agent .**

- **promotion is reversible changes (not affect DNA directly)**
- **promotion is dose-threshold" dependent concentration of promoter below which neoplasia will not occur.**
- **The altered cell remain dependent on the continue presence of promoter stimuli which may be (exogenous chemical ,physical or endogenous like hormonal stimulation in breast,endometrium ,prostate).**


Group 1
X
No tumors
Group 2
X
Tumors
Group 3
X
Tumors
Group 4
X
No tumors
Group 5
No tumors
Group 6
X
No tumors
Time

Major chemical carcinogens

- **Some chemical agent possess the capability of both (initiation & promotion) called**
- **complete carcinogen like Alkyalting agent ,anticancer drug ,busulphan cyclophosphamide,chlorambucil.**
- **Incomplete carcinogen capable of producing t. only after initiation**

carcinogenic initiators Examples

- **Alkylating agents like cyclophosphamide.**
- **(PCAH) polycyclic aromatic hydrocarbons**

  found in smoked foods,cigarette smoke (have broad range of target organs)produce cancer at site of application

  They are metabolized at cytochrome p450 which will oxidases to electrophilic epoxides which in turn react with cellular protein & nucleic acid
- **Nitrosamines in pickled foods. gut ca.**
- **Preserved food contain nitrites which react with other dietary component to form nitrosamines which activated by hydroxylation to form reactive ion .**

- **Aromatic amines or azo dyes used in food coloring .**
- **Vinyl choride-liver angiosarcoma**
- **beta-naphthylamine-use in rubber industry–bladder** ca.
- **microbial product**

  Fungi : aflatoxin b1 (produce by some strain of aspergillus flavus)

  cause hepatic cancer

  Act as initiator

Examples of promoters

- hormones such as estrogen,
- drugs such as diethylstibesterol,
- chemicals such as cyclamates used as sweeteners
- Chemical act as both initiator & Promoter
- (cigarette smoking & Asbestoses)

Viruses & Human cancer

- **HPV** (DNA virus).
- **HCV(RNA) & HBV(DNA) :predipose to HCC.**
- **HHV 8 (DNA virus)& kaposi sarcoma**
- **EBV (DNA virus)**
- **HTLV-1 virus: (RNA retrovirus)-T cell leukemia –lymphoma.**

(HPV)

- Anogenital cancer
- Sq.c.c. of cervix (HPVhigh risk gp. (16-18,31,33,35,51)
- benign wart low risk gp.(HPV 6-11)

The oncogenic potential of HPV is related to E6 & E7 viral protein which bind to P53 & RB gene respectively so they overcome cell cycle inhibitor

Role of EBV

- Infectious mononucleosis
- Oral hairy leukoplakia (in AIDS)
- Nasopharyngeal carcinoma
- African Burkitt's lymphoma
- Non-Hodgkin's lymphomas in AIDS

Effect of tumor on the host

I- Local effect according to tumor location

- **Pressure effect** e.g pituitary adenoma when increase in size
- **ulceration &obstruction e.g ca.colon**
- **secondary infection &bleeding**

e.g malena in ca.colon or hematurea in bladder ca

systemic effect

Cancer cachexia

It is waisting syndrome: **cc by** loss of body fat .anemia

- there are several factors contribute to malnutrition in cancer pat.

1-high prot.& fat turnover ,hypermetabolism anorexia ,reduced food intake,,

2-**Cachectin (TNF)** - produced by tumor cell &macrophages & it is a mediator of wasting syndrome

other soluble factor produced by tumor cell .

3- **PIF** proteolysis inducing factor which involved in abn.metabolism by increase catabolism of muscle & adipose tissue,

4- Impair immune defenses –prone to infection .

paraneoplastic syndrome

- **It is clinical syndrome with symptom complexes occur in cancer pat, (10% of advanced malig)**
- **Result from synthesis of bioactive sub. by tumor cells**.

symptom may be

1- endocrinopathies :elaboration of hormon from tumor cell which are not of endocrine origin

(ectopic hr.production)

Example:

- Insulin release of by fibrosarcoma
- Erythrpoitein hr.production by renal cell.ca.
- Parathyroid like hr-sq.c.ca of lung

2-Neuromyopathic paraneoplastic synd-Myasthenia Gravis. like synd.in small ell ca.of lung

3- cutaneous :Acanthosis nigrican cc by grey black patches of hyperkeratotic skin

4- Vascular & hematological changes.

- DIC (hypercoagulability)-release of PAF&procoagulant from tumor cell.

Tumor marker

Biochemical indicator of presence of tumor

- **Aid in DX**
- **Determine response to therapy**
- **Indicate relapse in follow up**

Hormones :

- **HCG :Trophoblastic t,Non seminoma testicular t.**
- **Calcitonine : Medullary ca.of thyroid**
- **Catecholamine : pheochromocytoma**
- **Ectopic hr.: paraneoplastic synd.**

Tumor marker cont.…

Isoenzy.:

- PAP:prostatic ca.
- NSE : small cell ca.of lung,neuroblastoma

Specific protein :

- Immunoglobulins : multiple myloma
- Prostatic specific Ag.:ca.prostate

Tumor marker cont….

Mucins

- **CA-125 : ovary ca.**
- **CA-19-9 : colon, pancreas ca.**
- **CA-15.3 : Breast ca.**

Oncofetal Ag.:

- **(AFP)Alpha fetoprotein: liver ca,testicular t.**
- **CEA : ca. pancreas,colon,lung,stomach**

New molecular marker :

- **P53,APC,RAS in stool& serum ca.colon**

Lab.Dx of cancer

1- Biopsy
2- Cytology
3- FNA
4- Immunocytochemistry
(by specific monoclonal Antibody for identification of cell product or surface marker)
5- flow cytometry : widely used in the classification of leukemias and lymphomas
6- Molecular methods – PCR, ISH, sequenation

Immunohistochemistry

1-categorization of undiff.malig.t

(To determine line of differentiation)

2-categorization of leukemia/lymphoma

3- determination the site of origin of metastatic tumor

like thyroglobulin marker for tumor of thyroid origin

e.g Desmin –specific for muscle

4- Detection of molecule that of prognostic & therapeutic significance

like ER,PR,erb B2 in ca.breast