

tumor

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MSc pathology

Q. Define neoplasia.

Neoplasia (new growth) is excessive and unregulated proliferation that eventually becomes autonomous (independent of physiologic growth stimuli).

Q. Define oncology.

Oncology is the study of the tumours or neoplasms (oncos in Greek means tumour).

Q. Define cancer.

cancer is the common term for malignant tumours

Q. What is clonality?

A tumour is said to be clonal when the entire population of cells within a tumour arises from a single cell that has incurred genetic change. A clonal neoplasm is therefore constituted by cells which carry the same genetic anomaly, eg, in lymphoma and leukaemia, clonality is proven by the amplification of a single rearrangement of their immunoglobulin gene

(for B cell lesions) or T cell receptor gene (for T cell lesions). The demonstration of clonality is now considered to be necessary to identify a lymphoid cell proliferation as neoplastic; however, as this is not always possible, clonality is not included in the definition of neoplasia.

Q. What are the two main components of all neoplasms?

Histologically, almost all neoplasms are composed of two main components:

1) Tumour cells that comprise the parenchyma (also called specific component).

2) Tumour stroma which is a supporting framework consisting of connective tissue and newly formed blood vessels elicited from adjacent tissues.

There is perpetual interaction between parenchyma and stroma, which directly influences the growth of the tumour.

Q. What is desmoplasia?

Hyperplasia of fibroblasts and formation of abundant collagen in the stroma as a reaction to infiltration by a cancer is labelled desmoplasia.

Q. Define a teratoma.

Teratoma is a tumour derived from a variety of cell types representing more than one germ cell layer, usually all three.

Characteristics:

- Derived from totipotent cells (cells with an ability to differentiate into any cell type),
teratomas are usually encountered in gonads. They sometimes develop in sequestered primitive cell rests elsewhere.
- Sacrococcygeal teratomas are the most common tumours in newborns, and mature cystic teratomas account for 10–20% of all ovarian neoplasms.
- Teratomas are also frequently seen in the head and neck region, mediastinum and retroperitoneum.

Q. Define a hamartoma.

Aberrant differentiation may produce a mass of disorganized but mature, specialized cells/tissue indigenous to the particular site (thought to be either an anomalous development or a neoplasm in origin), eg, hamartoma of the lung.

Neoplasms can be classified into different types based on the following features:

1. Gross or naked-eye appearance:

- Benign lesions are usually encapsulated and circumscribed and grow along Broadford's (have pushing margins).
- Malignant lesions are usually unencapsulated, ill-defined and infiltrating. They can have several different gross appearances, that is, annular (endophytic), ulcerative, fungating (exophytic or cauliflower-like), scirrhous (showing excessive fibrosis) or mucoid (containing abundant mucin).

2. Histological appearance and histogenetic/embryological considerations:

- Cell of origin, ie, epithelial or connective tissue, undifferentiated stem cells or highly specialized cells/tissue.
- Vascular/lymphatic invasion
- Capsular invasion
- Histopathological margins (infiltrating or expansile)

3. Behavioural characteristics (indolent, borderline aggressive or frankly aggressive)

4. Aetiological characteristics (tumour induced by radiation, chemical or viral carcinogens; tumour of primary or secondary origin)

5. Functional characteristics (some tumours secrete hormones or proteins with characteristic effects on the body, eg, adrenocorticotrophic hormone (ACTH), parathormone (PTH) and antidiuretic hormone (ADH) secreted by lung carcinoma and keratin produced by well-differentiated squamous cell carcinoma)

Q. Define and classify benign tumours?

Benign tumours are neoplasms, which grow as cohesive expansile masses, which do not invade, infiltrate or metastasize. They are usually encapsulated. (The capsule is made of a rim of compressed connective tissue derived largely from the native stroma.)

Nomenclature and Classification

1. Tumours of mesenchymal origin: Designated by adding suffix 'oma' to the cell of origin, eg, fibroma, lipoma (Fig. 6.1), osteoma and chondroma.
2. Tumours of epithelial origin are variously classified:
 - (a) Some based on the cell of origin, eg, squamous odontogenic tumor.
 - (b) Others based on the microscopic architecture, eg, adenoma (glandular pattern), papilloma (finger-like or warty projections), cystadenoma, (cystic masses) and papillary cyst adenoma (papillary cystic masses)
3. Mixed tumours: Divergent differentiation of a single line of parenchymal cells resulting in tumours comprised more than one cell type; usually derived from one germ cell layer, eg, pleomorphic adenoma of the salivary gland.



Lipoma (gross)

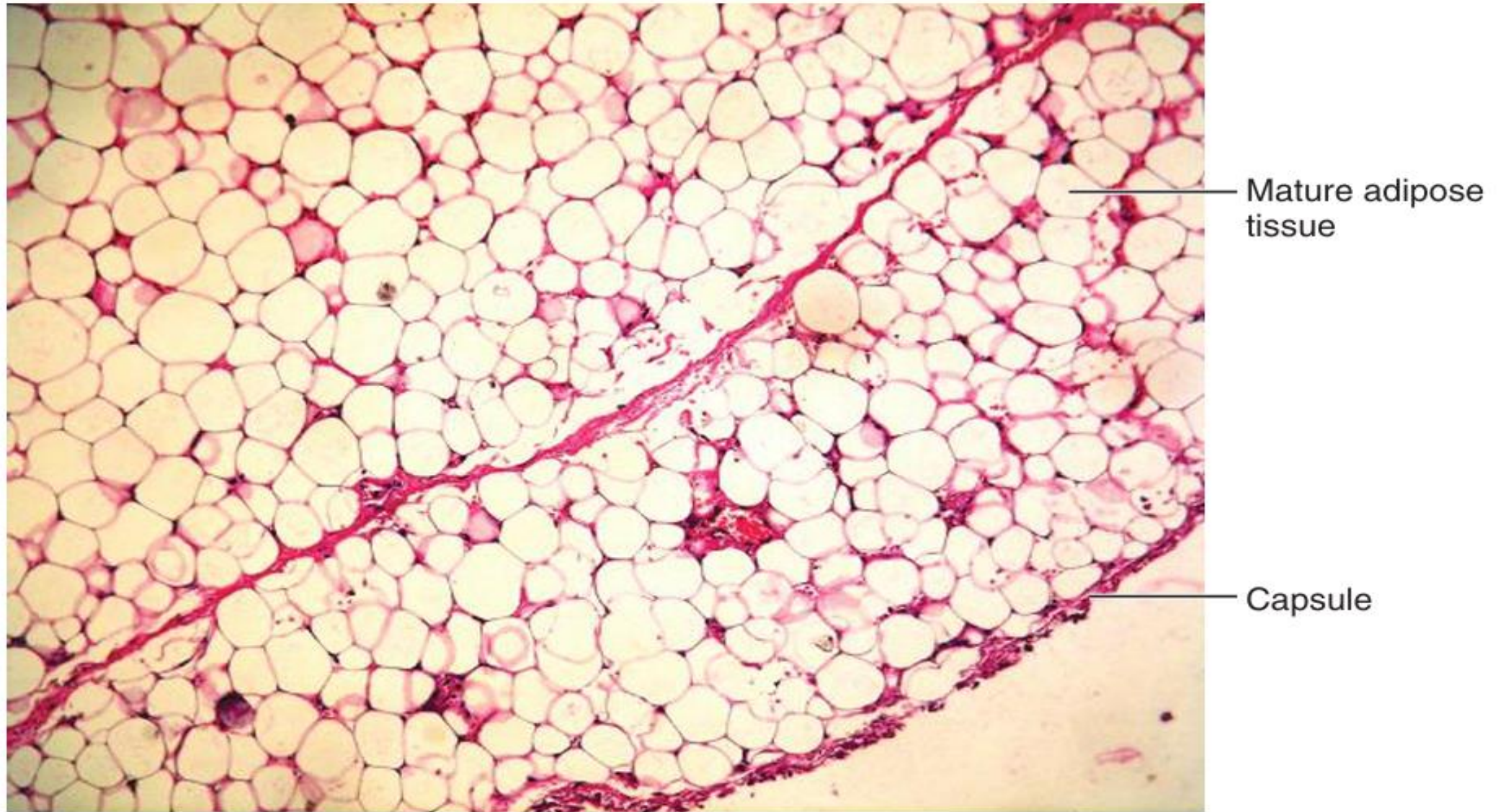


FIGURE 6.1. Lipoma composed of mature adipocytes and surrounded by a well-formed capsule indicating its benign nature (H&E; 100X).

Q. Define differentiation?

Differentiation is the extent to which neoplastic cells resemble comparable normal cells, both morphologically and functionally.

- The cells in benign tumours are almost always well differentiated and resemble their normal cells of origin. Cancers, however, vary from well differentiated to poorly differentiated.
- Well-differentiated cancers show progressive maturation or specialization of undifferentiated cells as they proliferate. Poorly differentiated or undifferentiated cancers show proliferation without differentiation or maturation.
- Well-differentiated squamous cell carcinomas of the epidermis elaborate keratin, just as well-differentiated hepatocellular carcinomas elaborate bile. Highly anaplastic undifferentiated cells, whatever is their tissue of origin, lose their resemblance to the normal cells from which they have arisen.

Q. Define anaplasia. Enumerate the morphological features indicative of anaplasia.

Anaplasia is defined as lack of differentiation; literal meaning is 'reverse differentiation'. It is a hallmark of malignant transformation.

Morphological Features Indicative of Anaplasia

- **Pleomorphism** (variation in size and shape of cells)
- **Anisonucleosis** (variation in size of nuclei)
- **Abnormal nuclear morphology:**
 - **Abundant and darkly staining** (hyperchromatic) DNA
 - **Coarsely clumped chromatin or clumping of nuclear chromatin** along the nuclear membrane resulting in prominent appearing nucleoli
 - **Increased nucleocytoplasmic ratio** (normal from 1:4 to 1:6; may approach 1:1)
 - **Numerous mitoses** with abnormal, atypical, bizarre, tri, quadri and multipolar spindles (abnormal mitoses are seen in malignant tumours only)
- **Loss of polarity** (orientation of cells)
- **Presence of the tumour giant cells**

Q. Define dysplasia. Enumerate the steps in the course of progression of dysplasia to invasive cancer.

Dysplasia (disordered growth) is defined as the **loss of architectural orientation of cells** with respect to one another **and presence of pleomorphism, nuclear hyperchromatism and mitoses**. Dysplasia may sometimes (not always) progress to invasive carcinoma

Carcinoma in situ ('cancer in place') is a lesion in which the dysplastic cells show essentially **no maturation** and **grow rapidly without regulation**; however, they remain localized, and do not invade past the basement membrane into the subepithelial tissue or stroma. **Invasive carcinoma** is the **final step in this sequence of events**. It is the stage in which the malignant cells have **invaded beyond the basement membrane** and have acquired the potential to metastasize. Invasive carcinoma, if left untreated, is almost always fatal.

(Dysplasia involving the entire thickness of the epithelium)

Invasive carcinoma

(Frank invasion into the stroma by malignant cells)

Q. Differentiate between dysplasia and anaplasia.

Ans. Differences between dysplasia and anaplasia are shown in [Table 6.2](#).

TABLE 6.2. Differences between dysplasia and anaplasia		
Features	Dysplasia	Anaplasia
Definition	Lack of uniformity of individual cells with architectural distortion	Lack of morphological and functional differentiation of cells
Behaviour	A potentially precancerous condition, which may or may not progress to cancer	Anaplasia is usually a hallmark of malignant transformation
Tissue involved	Mainly epithelium	Both epithelium and mesenchyme
Cellular pleomorphism and nuclear atypia	Present, but usually low grade	High grade
Mitotic figures	Present, usually not atypical	Abnormal and atypical figures may be seen (tripolar, quadripolar and multipolar spindles)
Tumour giant cells	Absent	Present

Q. Differentiate between metaplasia and dysplasia.

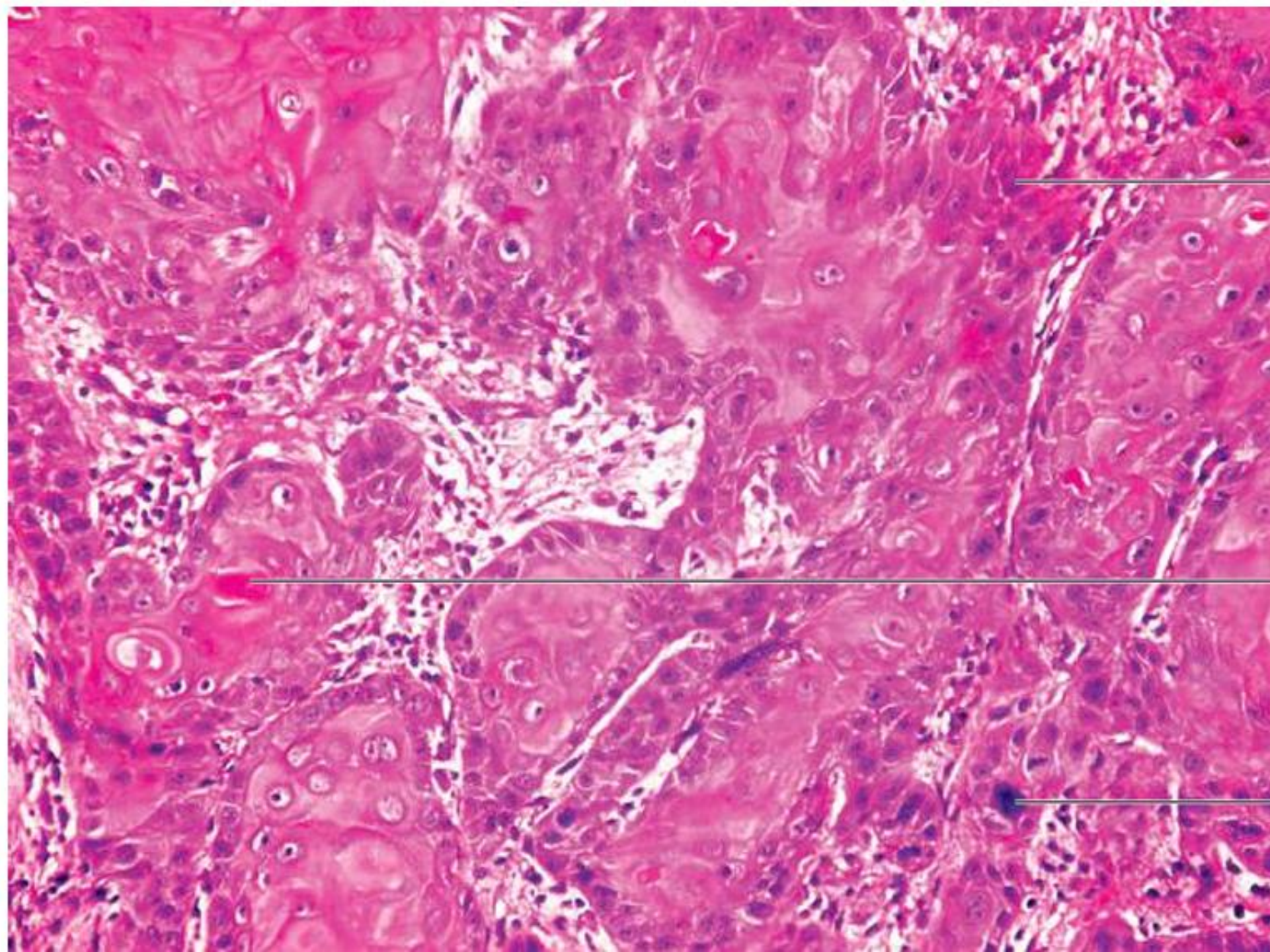
Ans. Differences between metaplasia and dysplasia are enlisted in [Table 6.3](#).

TABLE 6.3. Differences between metaplasia and dysplasia		
Features	Metaplasia	Dysplasia
Definition	Reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type	Loss of uniformity of the individual cells (mainly epithelial) as well as lack of architectural orientation with respect to one another
Cellular pleomorphism	Usually not seen	Present
Nuclear atypia	Usually not seen	Hyperchromatic and abnormally large atypical nuclei may be seen
Mitotic figures	Few	Many
Orientation with respect to one another (tissue architecture)	Maintained	Loss of ordered maturation as in dysplastic stratified squamous epithelium
Reversibility	Reversible, if triggering factors are removed	May become irreversible if it involves the whole thickness of the epithelium
Example	Columnar to squamous epithelium in respiratory tract of chronic smokers	Cervical intraepithelial neoplasia (CIN)

Q. Define and classify malignant tumours.

Malignant tumours are neoplasms which **infiltrate**, **invade** and **metastasize**. They may be

- **Mesenchymal** or connective tissue in origin, eg, **sarcomas**
- **Epithelial** in origin, eg, **carcinomas**, usually named after their parent organ or tissue of origin, eg, adenocarcinoma of intestine and squamous cell carcinoma of the cervix or oral mucosa (Fig. 6.3)
- **Poorly differentiated** or **undifferentiated** malignant tumours, eg, cancers composed of undifferentiated cells or cells of unknown origin



Malignant
squamous
cells

keratin pearls

Atypical mitosis

Q. Define metastasis. Write briefly on the various pathways of spread of the tumours.

Tumour implants discontinuous with the primary tumour, confirm the malignant nature of a tumour and are labelled metastases. All cancers metastasize with a few exceptions, eg, basal cell carcinoma (rodent ulcer) and gliomas of the central nervous system, which are locally invasive and rarely metastasize.

Pathways of Spread of the Tumours

1. **Direct seeding** of body cavities and surfaces: Penetration of a tumour into a natural open field/space, eg, pleural, pericardial, subarachnoid and synovial. Sometimes mucinous tumours of appendix and ovary (both benign and malignant) fill the peritoneal cavity with a gelatinous neoplastic mass called 'pseudomyxoma peritonei'.

2. Lymphatic spread

(a) There are numerous interconnections between lymphatic and vascular channels; so, emphasis on differentiating lymphatic and vascular dissemination may be purposeless.

(b) Functional lymphatics are absent in tumours and lymphatic vessels located at the surface are sufficient for lymphatic spread.

(c) Lymphatic spread tends to follow natural routes of lymphatic drainage and is the usual route for dissemination of epithelial malignancies, sarcomas may also use this route.

(d) Drainage of tumour cell debris and antigens may induce reactive hyperplasia and the spread of tumour cells to regional lymph nodes.

(e) A 'sentinel' lymph node is defined as the first node in the regional lymphatic chain to receive lymph flow from the primary tumour.

3. Haematogenous spread

(a) Typical of sarcomas but also seen in carcinomas

(b) Arteries have thick walls, are less penetrable than veins

(c) liver and lungs;

(d) Cancers in the vicinity of vertebral column, eg, thyroid and prostate, metastasize to the vertebrae via paravertebral plexus

Vascular emboli

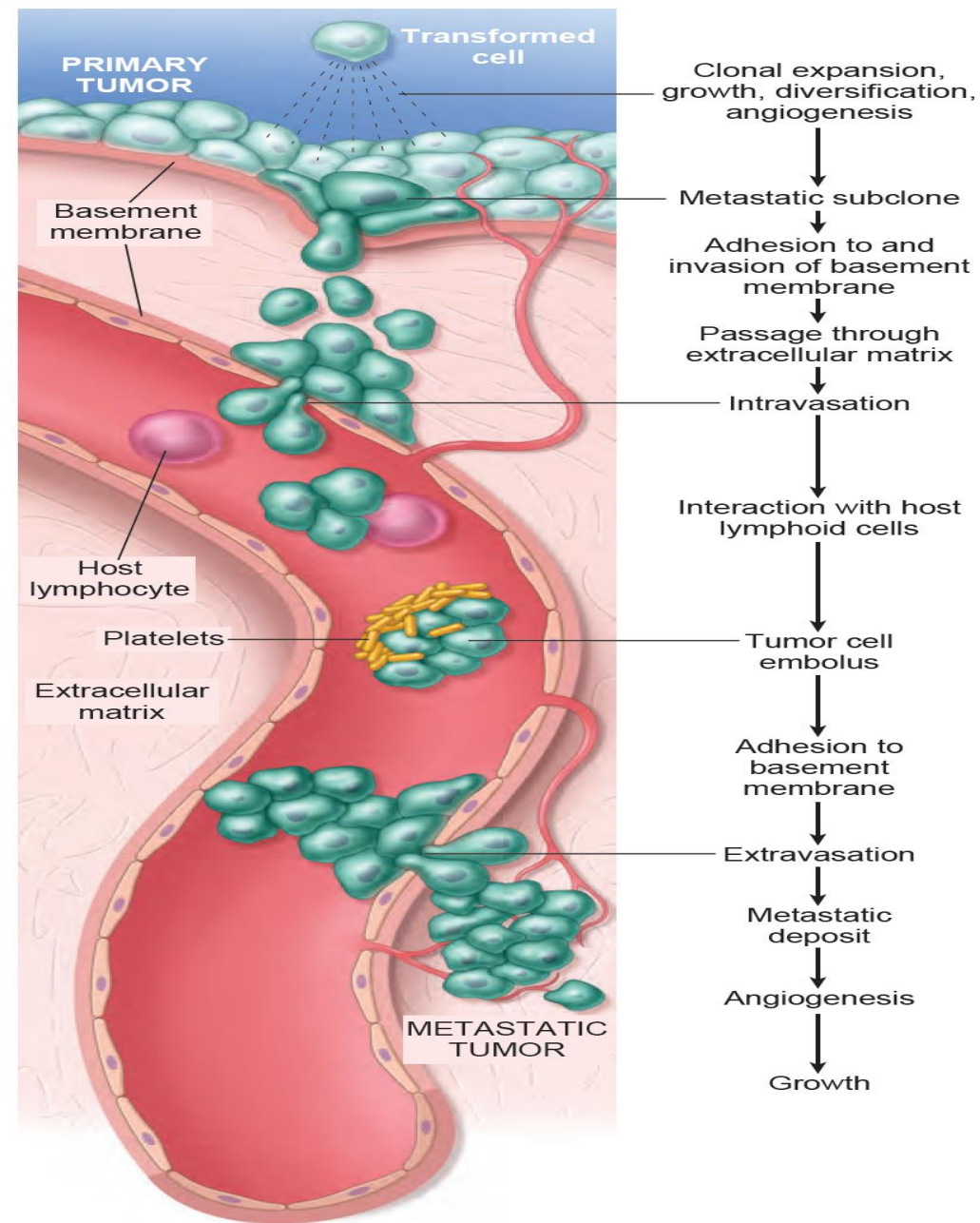


Figure 7.34 The metastatic cascade. Sequential steps involved in the hematogenous spread of a tumor.

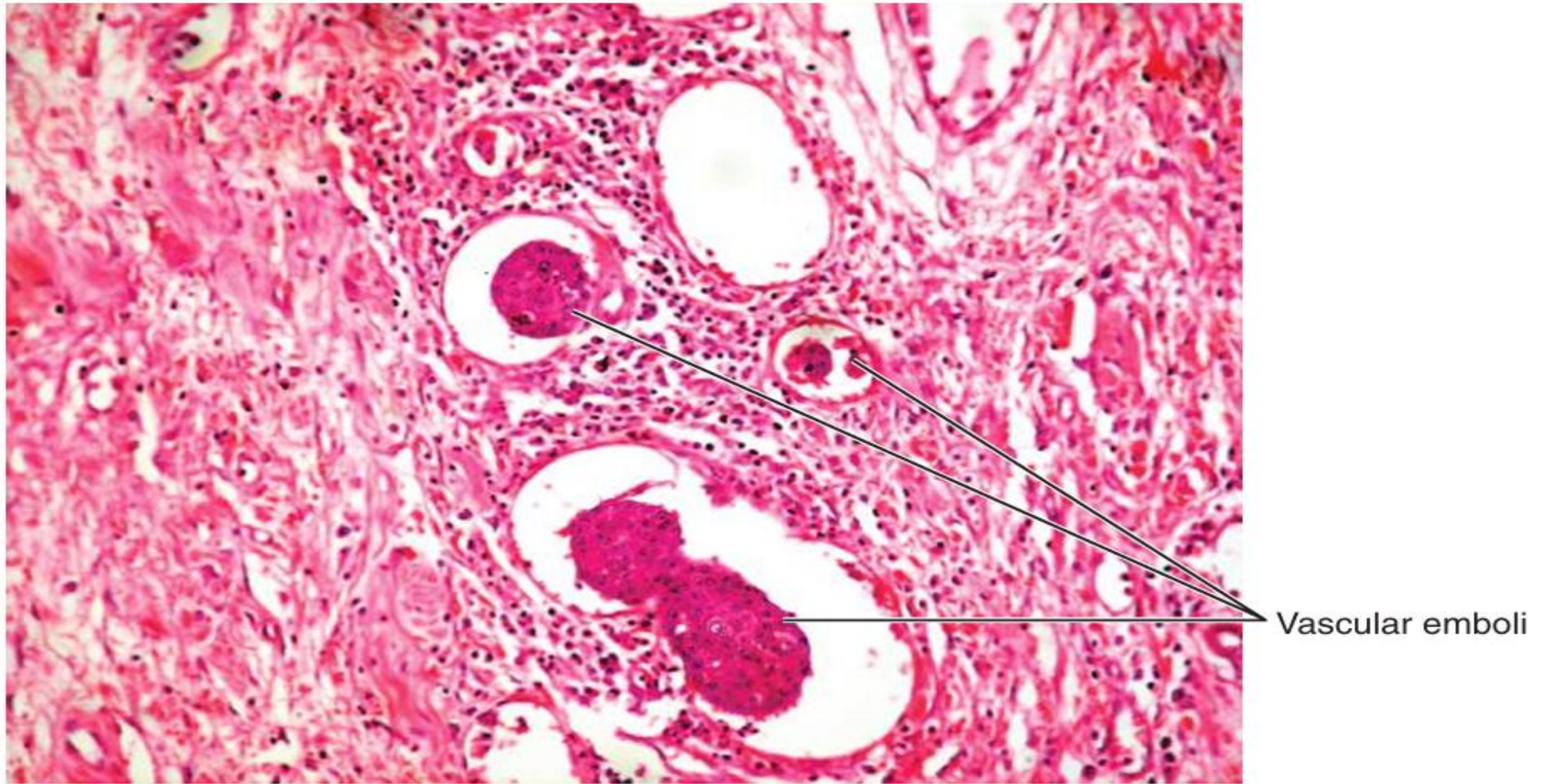


FIGURE 6.4. Section showing vascular tumour emboli (H&E; 200×).

Q. Write briefly about the biology of the tumour growth.

Ans. Rate of growth of the tumour depends on:

- **Doubling time** of tumour cells (time taken by the tumour cells to double their volume or number of cells).
- **Growth fraction** (fraction of the tumour cells that are in the replicative pool).
- **Rate at which cells are shed** and lost in the growing lesion.
- Fast-growing tumours have a high cell turnover (high rate of, both proliferation and apoptosis); the tumour growth is possible only if rate of proliferation is greater than rate of apoptosis.
- **Most anticancer drugs act on cells, which are in the growth cycle.**
- **Tumours with high growth fraction are more susceptible to radio and chemotherapy.**
- **Debulking with surgery and radiation shifts tumour cells from G0 to G1 phase.**
- Rate of growth is proportional to the level of differentiation of cells.

Q. Write briefly about the epidemiology of malignant tumours.

Cancer is a leading cause of death worldwide, accounting for a large number of deaths. Lung, stomach, liver, colon and breast cancer cause most cancer deaths each year. The frequency of different cancers differs between men and women. Most cancers can be attributed to five leading behavioural and dietary risks: high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco and alcohol use. The following are the commonest malignant tumours encountered worldwide:

Men:

Prostate (oral cavity in India), Lungs, Colon or rectum, Leukaemia and lymphoma, Liver

Women:

Breast (cervix in India), Lungs, Colon or rectum, Leukaemia and lymphoma, Ovary

Children:

Acute leukaemia

CNS tumours

Lymphomas

Neuroblastoma

Bone sarcomas

Epidemiological Factors Influencing Neoplasia

Familial and Genetic Factors (Inherited Predisposition to Cancer)

1. Autosomal dominant inherited cancer syndromes

The autosomal dominant inheritance of a single mutant gene greatly increases risk of developing a tumour. The inherited mutation is generally a point mutation occurring in a single allele of a tumour suppressor gene. Defect in the second allele occurs in the somatic cell, as a consequence of deletion or recombination. As in other autosomal dominant conditions, both incomplete penetrance and variable expressivity occur.

Examples are as follows:

(a) Retinoblastoma (RB): Approximately 40% of retinoblastomas (RBs) are inherited. Carriers of a mutant RB tumour suppressor gene have a 10,000-fold increased risk of developing RB, usually bilateral. They also have a greatly increased risk of developing a second cancer, usually osteogenic sarcoma.

(b) Familial polyposis coli (FAP):

Presents with polypoid adenomas at birth and shows 100% conversion to familial polyposis coli by age of 50 years.- The genetic defect in FAP is a germline mutation in the adenomatous polyp

(c) Multiple endocrine neoplasia (MEN) syndromes:- The term MEN

encompasses several distinct autosomal dominant syndromes

featuring both benign and malignant tumours derived from endocrine and nonendocrine tissue.- There are two major forms of MEN—type 1 and type 2—which are distinguished based on the genes involved and hormones secreted **MEN 1**—adenomas of pituitary, parathyroid and pancreas;

MEN 2—medullary carcinoma thyroid, pheochromocytoma and parathyroid tumours.-

(d) Neurofibromatosis (NF) or von Recklinghausen disease:- NF is an autosomal dominant disorder that affects bones, nervous system, soft tissue and skin.

(e) Li-Fraumeni syndrome: Results from germline mutation of P53

2. Defective DNA repair syndromes

Human syndromes with DNA repair deficiencies cause genomic instability which is the driving force behind cancer development. There are four categories of DNA repair genes:

(a) Mismatch repair genes

(b) Base excision repair genes

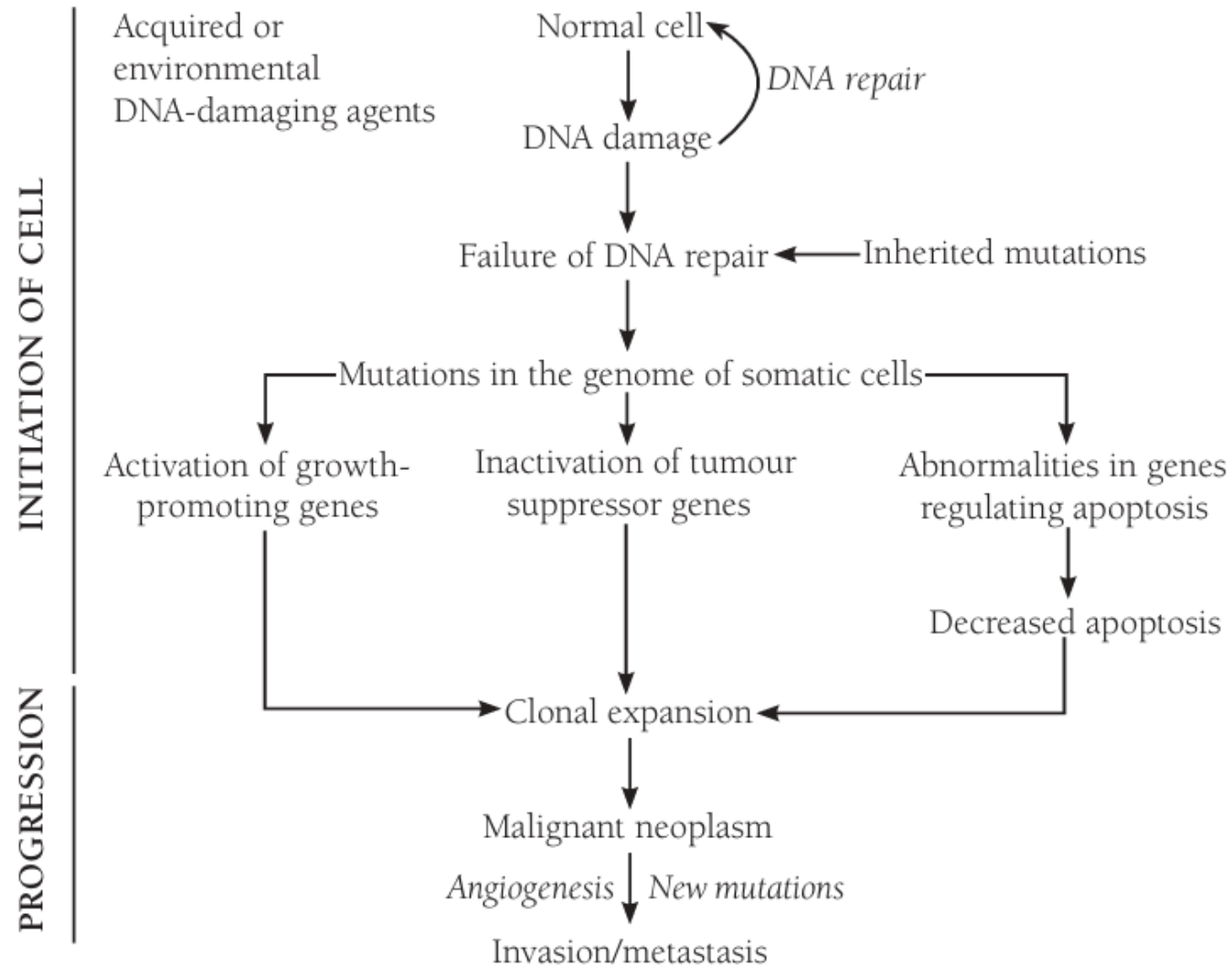
(c) Nucleotide excision repair genes

(d) Double strand break repair genes

Mostly autosomal recessive in inheritance, common examples of DNA repair defects include xeroderma pigmentosa, ataxia telangiectasia and Bloom syndrome. Xeroderma pigmentosa manifests with extreme sensitivity to UV

Q. Enumerate the steps involved in carcinogenesis.

Ans. Carcinogenesis is a multistep process ([Flowchart 6.2](#)).



FLOWCHART 6.2. Steps involved in carcinogenesis.

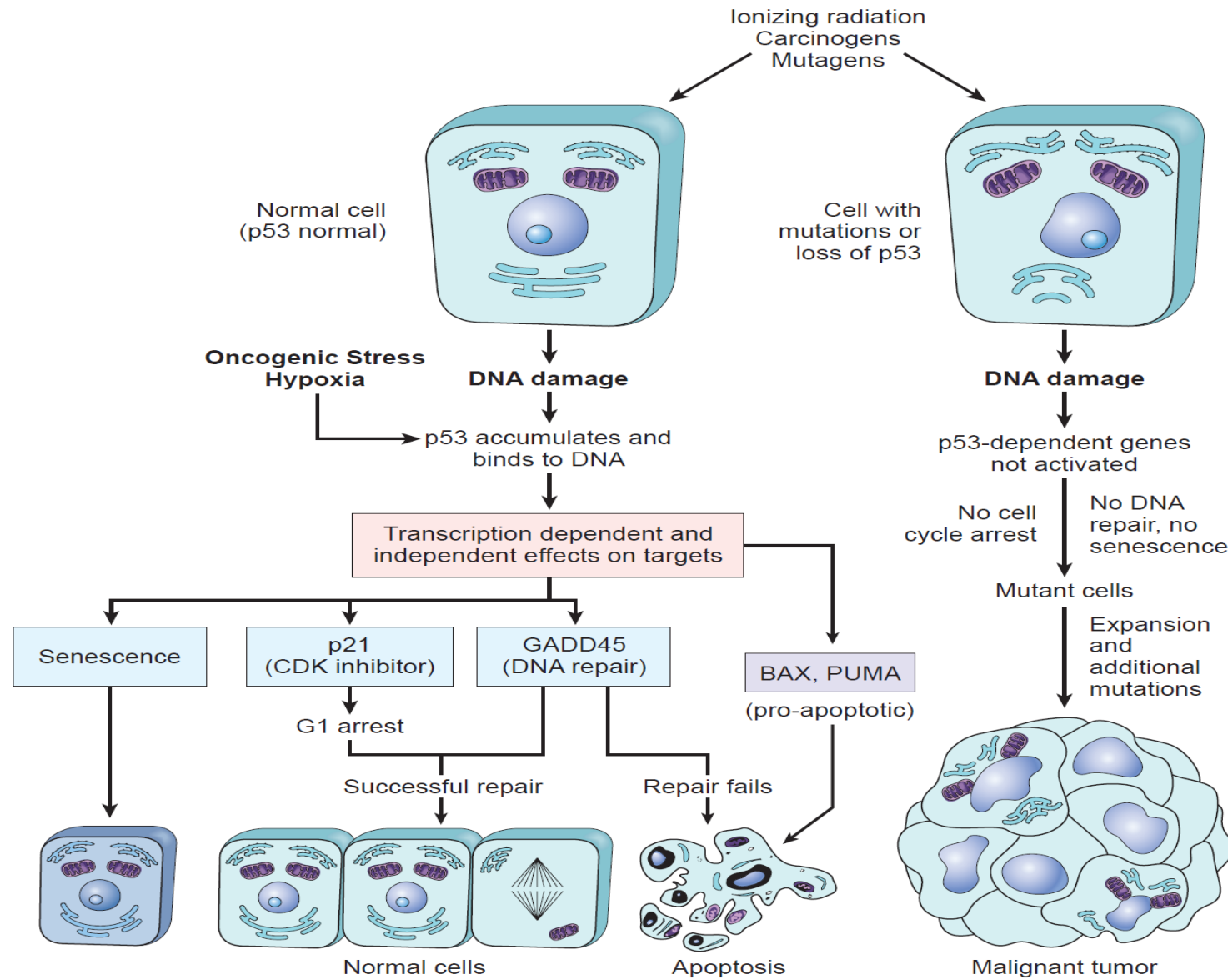


Figure 7.27 The role of p53 in maintaining the integrity of the genome. Activation of normal p53 by DNA-damaging agents or by hypoxia leads to cell cycle arrest in G₁ and induction of DNA repair by transcriptional upregulation of the cyclin-dependent kinase inhibitor *CDKN1A* (encoding the cyclin-dependent kinase inhibitor p21) and *GADD45* genes. Successful repair of DNA allows cells to proceed with the cell cycle; if DNA repair fails, p53 triggers either apoptosis or senescence. In cells with loss or mutations of the p53 gene, DNA damage does not induce cell cycle arrest or DNA repair, and genetically damaged cells proliferate, giving rise eventually to malignant neoplasms.

3. Familial cancers

Cancers with a high frequency of occurrence within a family are called familial cancers, eg, carcinomas of breast, colon, uterus, ovary, stomach and some sarcomas. Familial cancers have the following features:

(a) Early age of onset

(b) Multiple primary cancers in a single individual (such as bilateral breast cancer)

(c) No clearly identifiable pattern of transmission
Racial and Geographic Factors

Environmental and Cultural Factors

1. **Cigarette smoking** is known to be associated with oral cancer, carcinoma of larynx, pharynx, oesophagus, lungs, pancreas and urinary bladder.
2. **Alcohol abuse** causes cancers of oropharynx, larynx, oesophagus and liver. Alcohol and smoking together increase the incidence of cancer of the upper airways and digestive tract.
3. **Industrial and environmental carcinogens** include UV rays, smog, arsenic, asbestos, benzene, vinyl chloride and b-naphthylamine.
4. **Diet:** Following factors predispose to malignancies:
 - (a) Overweight individuals
 - (b) Deficiency of vitamin A, tocopherols, selenium and zinc
 - (c) Diet rich in animal fats; low in fibre content
5. **Age:** Most cancers are seen after fifth decade; some cancers may be seen in childhood.
6. **Sex:** Males are more commonly affected, except in carcinoma breast, gall bladder, thyroid and hypopharynx.

Predisposing factors for specific malignancies:

- **Carcinoma of cervix:** Young age at first coitus, high frequency of sexual intercourse, multiplicity of partners and multiparity contribute to increasing probability of carcinoma cervix.
- **Penile carcinoma:** Rare in Jews and Muslims (because they are customarily circumcised); common in other communities.
- **Cancer of cheek and tongue:** Associated with betel nut and tobacco chewing.

Interactions between Genetic and Nongenetic Factors

Inherited variations (polymorphisms) in enzymes that metabolize procarcinogens to carcinogens can determine the susceptibility to cancer, eg, polymorphisms in gene coding for P-450 confers inherited susceptibility to lung cancer in smokers.

Nonhereditary Predisposing Conditions

- **Chronic inflammation and cancer:**
- An increased risk of cancer has been noted in chronic inflammatory conditions, eg, ulcerative colitis, Helicobacter pylori gastritis and viral hepatitis.

• Inflammation increases expression of cyclooxygenase-2 (COX-2), which induces conversion of arachidonic acid into prostaglandins, which in turn are found to be increased in cancers, eg, colonic cancer. The role of COX-2 inhibitors in cancer treatment and the potential association between cancer and chronic inflammation is being explored.

• Chronic inflammation is associated with repair and proliferation, thus increasing the tissue stem cell pool, which is vulnerable and susceptible to transformation,

• Precancerous conditions: Certain non-neoplastic and benign disorders have a well-defined association with cancer. Increased incidence of cancer in precancerous lesions is mostly attributed to continuous regenerative cell replication. These lesions include:

- Actinic or solar keratosis • Barrett oesophagus • Leukoplakia of oral cavity, vulva and penis
- Chronic atrophic gastritis • Paget disease of bone
- Multiple villous adenomas of colon • Neurofibromatosis
- Long-standing ulcerative colitis • Cirrhosis of liver • Chronic bronchitis (heavy smokers)
- Chronic irritation of the oral cavity • Old burn scar (Marjolin ulcer)

Q. Write in detail on the molecular basis of cancer.

Carcinogenesis is initiated by nonlethal genetic damage to a cell (mutation), which could be:

(a) inherited in germ line or (b) acquired (due to chemicals, radiation and viruses). Occurrence of a mutation is followed by clonal expansion of the mutated cell. Mutations that result in development of malignancy are called 'driver mutations'. The first driver mutation is called an 'initiating mutation'.

There are four main classes of regulatory genes:

1. Proto-oncogenes

- Dominant
- Cause 'gain of function' (excessively increase one or more of the normal functions of the encoded gene product)
- Can transform cells despite the presence of a normal counterpart

2. Tumour suppressor genes

- Recessive
- Mutations in these genes cause a 'loss of function'
- Both normal alleles of tumour suppressor genes must be damaged to transform cell

3. Genes regulating apoptosis and cancer

- Apoptosis in a normal cell is guided by cell death receptor CD95.
- BAD, BID, BAX and TP53 are proapoptotic.
- Bcl-2 and Bcl-X are antiapoptotic.
- Mutant form of Bcl-2 gene is seen in B cell lymphomas, carcinoma breast, thyroid and prostate.
- CD95 is depleted in hepatocellular carcinoma.

4. DNA repair genes

- Defects in DNA repair genes predispose to mutations (mutator phenotype).
- Both alleles of DNA repair genes must be inactivated to induce genomic instability (recessive inheritance).

Q. Write briefly on chemical carcinogenesis.

Ans. Induction of cancer by chemicals depends on:

- Dose, duration and mode of administration of the chemical
- Individual susceptibility
- Associated predisposing factors

Stages of Chemical Carcinogenesis

• **Initiation**: results from exposure of cells to sufficient dose of the carcinogen. The

change induced is sudden and irreversible, and has memory. Initiation alone, however,

is not sufficient for tumour formation.

• **Promotion**: entails proliferation and clonal expansion of the altered and initiated cell.

Promoters include phorbol esters, phenols, hormones, artificial sweeteners and phenobarbital. The cellular changes resulting from the application of promoters do not affect DNA directly, and are reversible.

1. Direct-acting carcinogens—Do not require metabolic activation and include:

(a) Alkylating agents

(i) Anticancer drugs, eg, cyclophosphamide, chlorambucil, busulfan, melphalan and nitrosoureas

(ii) β -propiolactone

(iii) Dimethyl sulphate

(iv) Diepoxybutane

(b) Acylating agents

(i) 1-acetyl imidazole

(ii) Dimethyl carbamyl chloride

2. Indirect-acting procarcinogens—Require metabolic activation and include:

(a) Polycyclic aromatic hydrocarbons (found in tobacco, smoke, fossil, fuel, soot, tar, mineral oils and smoked animal foods)

(i) Anthracenes (cause lung and skin cancer)

(ii) Benzopyrene (cause cancer of oral cavity)

(iii) Methylcholanthrene (associated with sarcomas)

(b) Aromatic amines and azo dyes

(i) β naphthylamine (associated with carcinoma of urinary bladder)

(ii) Benzidine (role in pathogenesis of hepatocellular carcinoma)

(iii) Azo dyes like butter yellow, scarlet red (role in pathogenesis of hepatocellular carcinoma)

(c) Naturally occurring products

- (i) Aflatoxin B1 (role in pathogenesis of hepatocellular carcinoma)
- (ii) Cycasin (role in hepatobiliary tumours)
- (iii) Safrole (carcinogenic and genotoxic)
- (iv) Betel nuts (oral cancer)

(d) Miscellaneous

- (i) Nitrosamines and amides (role in pathogenesis of gastric carcinoma)
- (ii) Vinyl chloride monomer (implicated in the pathogenesis of angiosarcoma of liver)
- (iii) Asbestosis (may lead to bronchogenic carcinoma and mesothelioma)
- (iv) Nickel, lead, cobalt and chromium (cause epidermal hyperplasia and basalcell carcinoma)

Q. Write briefly on microbial carcinogenesis.

Ans. Carcinogenic microbiological agents mainly include oncogenic DNA and RNA viruses as well as bacteria like *Helicobacter pylori*.

1. Oncogenic DNA viruses: Genomes of oncogenic DNA viruses integrate into and forms stable associations with host genome, eg, E6 proteins of high-risk HPV types complex with p53 to enhance its degradation. Oncogenic DNA viruses include:

(a) Human papilloma virus (HPV): HPV has more than 100 distinct subtypes of which types 1, 2, 4 and 7 cause benign squamous papillomas or warts. Squamous cell carcinomas (SCCs) of cervix and anogenital region, as well as, oral and laryngeal cancers are associated with HPV 16, 18, 31, 33, 35 and 51 and their precursor lesions; whereas, HPV 6 and 11 cause genital lesions with low-malignant potential.

HPV genome is present in episomal (nonintegrated) form in benign warts and preneoplastic lesions. In cancers, the viral genome appears to be integrated into

the host DNA. HPV proteins have the following effects on the cell cycle:

- E6 and E7 block p53 and RB cell-cycle suppression pathways, respectively.
- E6 proteins of high-risk HPV type complex with p53 to enhance its degradation. E6 proteins of low-risk HPV types have low affinity for p53 and do not affect its stability.
- Increased p53 degradation causes a block in apoptosis (p53 increases activity of BAX, which is proapoptotic).
- E7 from high-risk types binds to RB protein, releasing sequestered E2F from the RB-E2F complex, triggering entry of cells in the S phase.
- E7 from low-risk types has a lower affinity for RB protein, and is slow in transforming cells.

- (b) Epstein–Barr virus (EBV): EBV is implicated in the pathogenesis of
- (i) African form of Burkitt lymphoma
 - (ii) B-cell lymphoma in immunosuppressed individuals
 - (iii) Hodgkin lymphoma
 - (iv) Nasopharyngeal carcinoma
 - (v) Gastric carcinoma
 - (vi) NK cell lymphoma

Mechanism of EBV-induced oncogenesis is shown in Flowchart 6.8.

EBV attaches to/infects cells of oropharynx and B lymphocytes via CD21

Linear genome of EBV circularizes to form an episome in B cells

(c) **Hepatitis viruses**: 70–80% hepatocellular carcinoma is due to HBV and HCV. Effects of HBV are mainly indirect; it causes chronic liver cell injury, and regenerative hyperplasia (increased pool of cycling cells are at risk for genetic changes). HBV also encodes a regulatory element called HBX protein, which disrupts normal growth control of infected liver cells by transcriptional activation of an insulin-like growth factor II and receptors for insulin-like growth factor I. It also binds to P53 and interferes with its growth-suppressing activities.

Q. Write briefly on laboratory diagnosis of cancer.

The modalities for laboratory diagnosis of cancer include:

1. Cytology

The main techniques used for cytological diagnosis are:

(a) Fine needle aspiration cytology (FNAC)

(b) Exfoliative cytology: Due to loss of cohesiveness, neoplastic cells are continuously shed from tumours into the surrounding space. These are called exfoliated cells and can be examined in the following preparations:

(i) Papanicolaou smears (for carcinoma cervix)

(ii) Sputum and bronchial washings (for bronchogenic carcinoma)

(iii) Pleural, pericardial and peritoneal fluid (for local cancers)

(iv) Urine (for urothelial malignancies)

(v) Cerebrospinal fluid (for CNS tumours)

(vi) Gastric secretions (for gastric carcinoma)

Diagnostic reliability of exfoliative cytology varies between 80% and 97%.

2. Histopathology: Histopathological diagnosis entails microscopy supported by clinical and investigative data. Formalin fixation is required for routine histopathology and glutaraldehyde fixation is required for electron microscopy. Frozen sectioning aids in rapid/intraoperative diagnosis.

3. Histochemistry/cytochemistry (special stains): These are diagnostic tools for identifying chemical composition of cells for the purpose of tumour diagnosis and classification

4. Immunohistochemistry/immunocytochemistry:

Immunohistochemistry (IHC) is an immunological method of recognizing a cell based on recognition of specific components called 'antigens'. 'Specific antibodies' against antigens are raised by hybridoma technique and labelled monoclonal antibodies. Antigen–antibody complexes on the slides (histological sections or cytology smears) are made visible for microscopic identification by labels (fluorochromes or enzyme systems).

Uses

- Categorization of undifferentiated neoplasms
- Specific typing of leukaemias/lymphomas
- Determination of site of origin of a metastatic tumour
- Detection of molecules that have prognostic or therapeutic significance, eg, ER–PR receptors in carcinoma breast
- Expression of protein products of oncogenes
- Differentiating benign from malignant lesions

5. Tumour markers: These are substances found in blood, urine, body fluids or tissue,

the levels of which might be elevated in association with a cancer.

Tumour markers may

be used to help diagnose cancer, predict a patient's response to cancer therapy

AFP (a-fetoprotein)

PSA (prostate-specific antigen)

HCG (human chorionic gonadotropin)

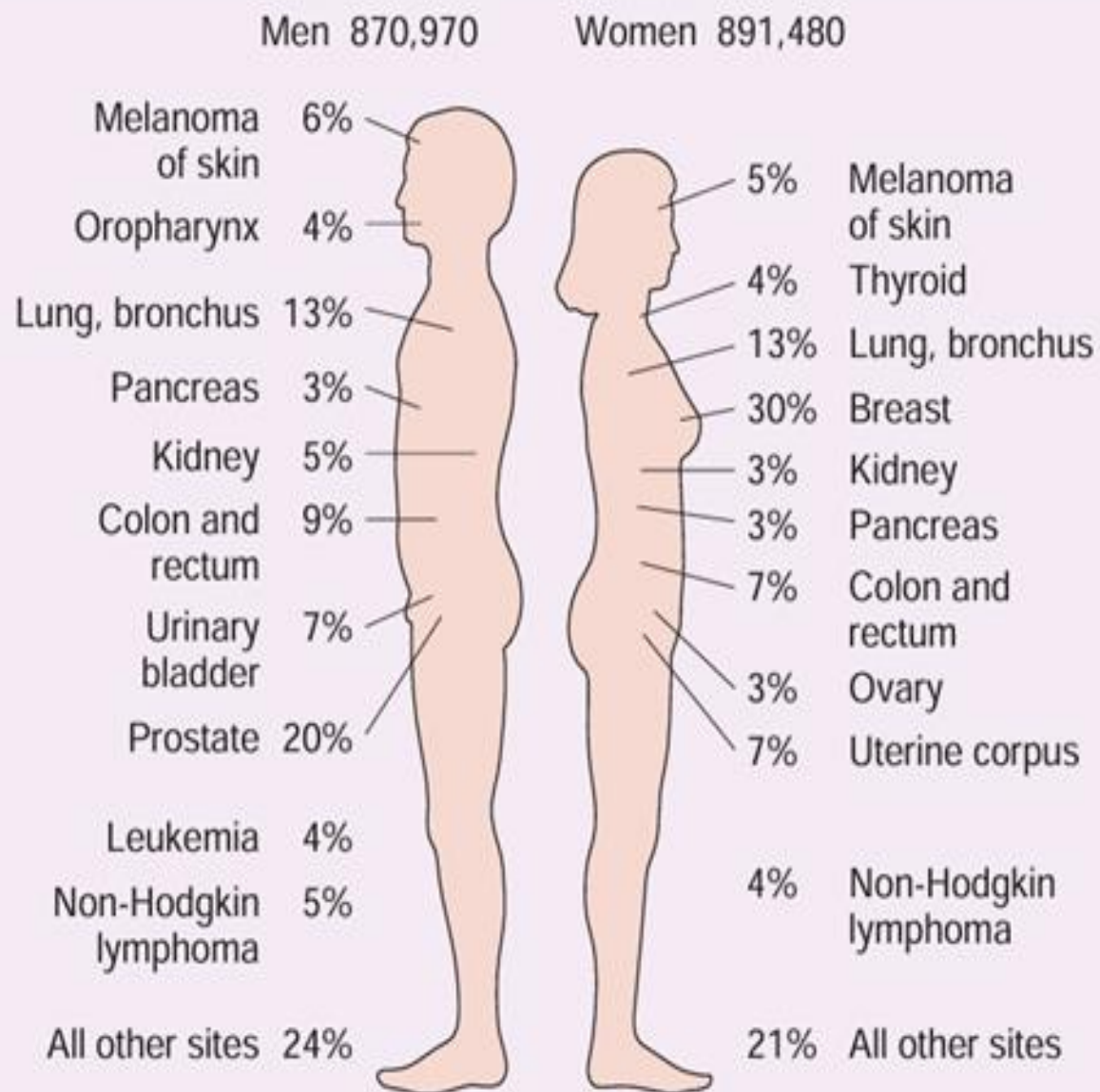
Calcitonin

Vanillylmandelic acid (VMA)

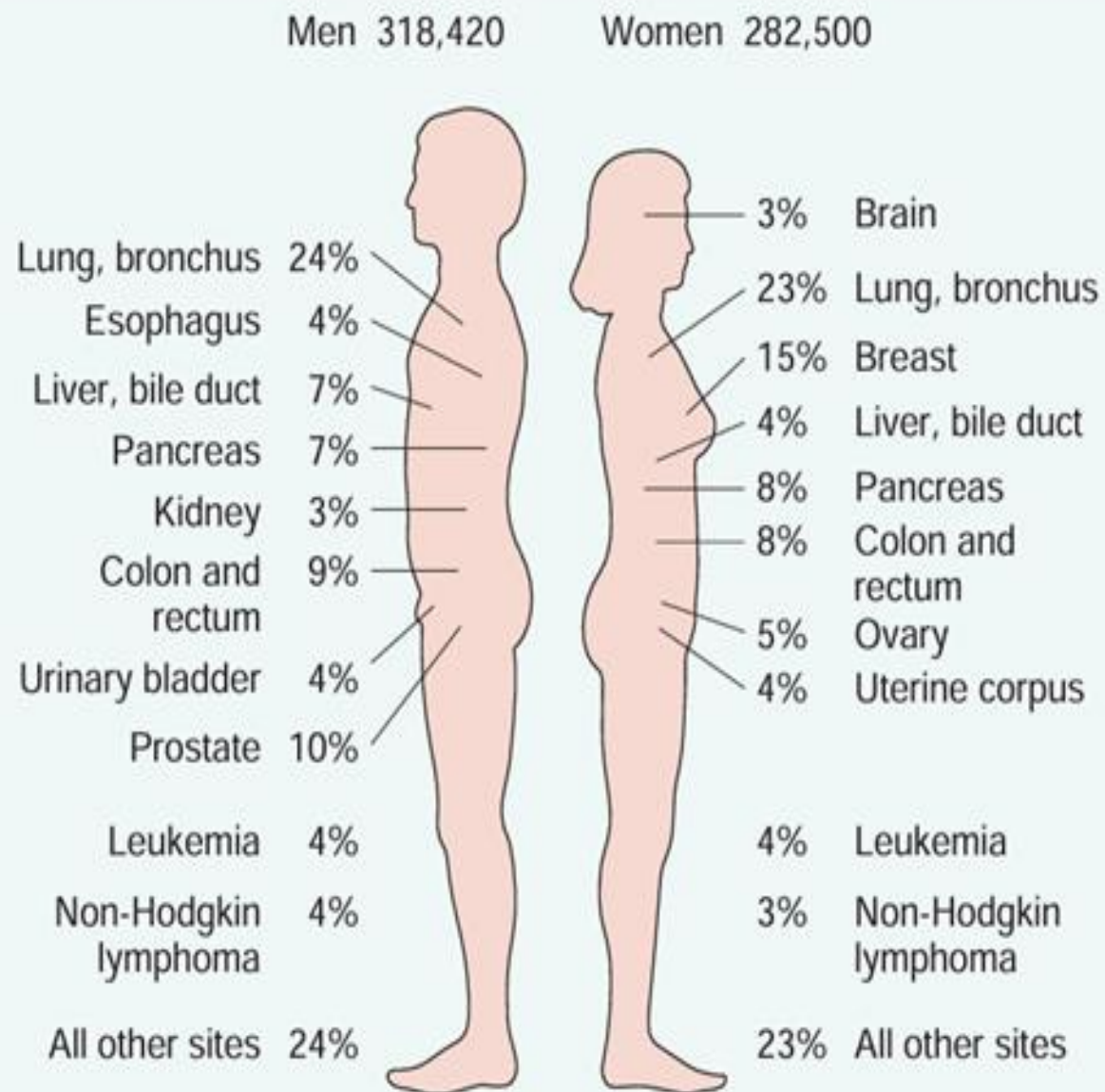
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A. 2019 ESTIMATED CANCER INCIDENCE BY SITE AND SEX



B. 2019 ESTIMATED CANCER DEATHS BY SITE AND SEX



Laboratory Diagnosis of Cancer: Histologic and Cytologic Methods.

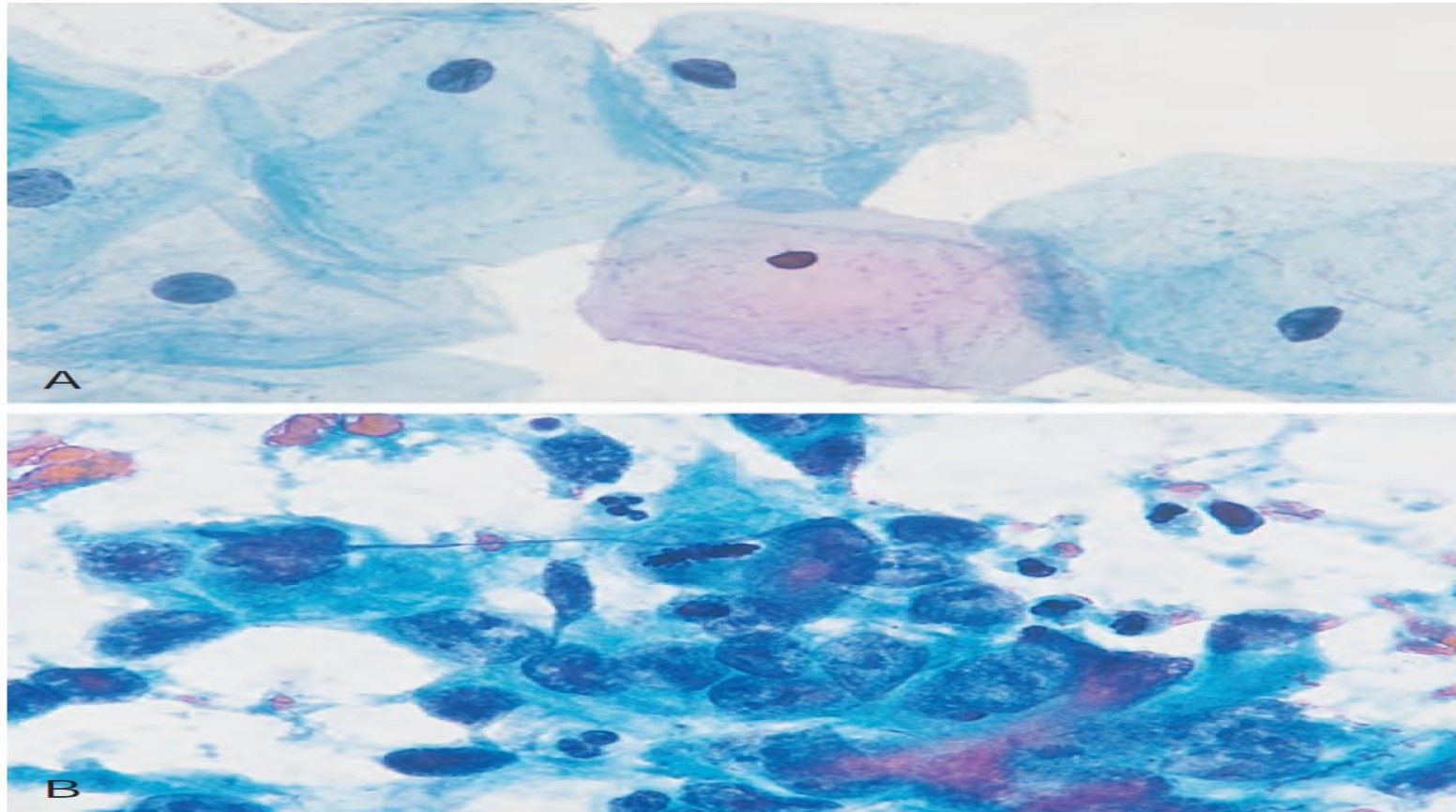


Figure 7.44 Cytology of cervical smears. (A) Normal cervicovaginal smear shows large, flattened squamous cells and groups of metaplastic cells; interspersed are neutrophils. There are no malignant cells. (B) Abnormal cervicovaginal smear shows numerous malignant cells that have pleomorphic, hyperchromatic nuclei; interspersed are normal polymorphonuclear leukocytes. (Courtesy Dr. P. K. Gupta, University of Pennsylvania, Philadelphia, Pa.)

Immunohistochemistry.

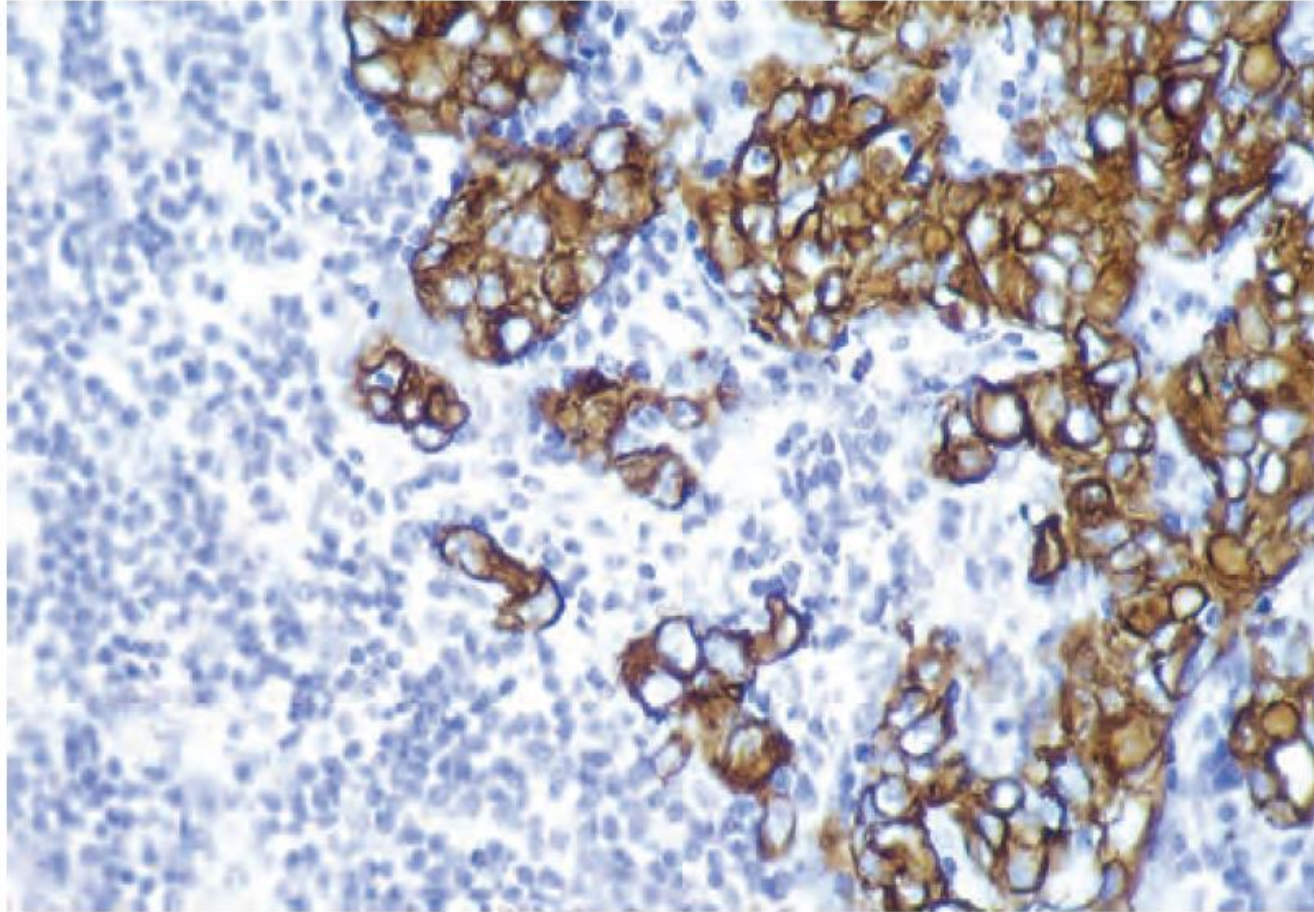
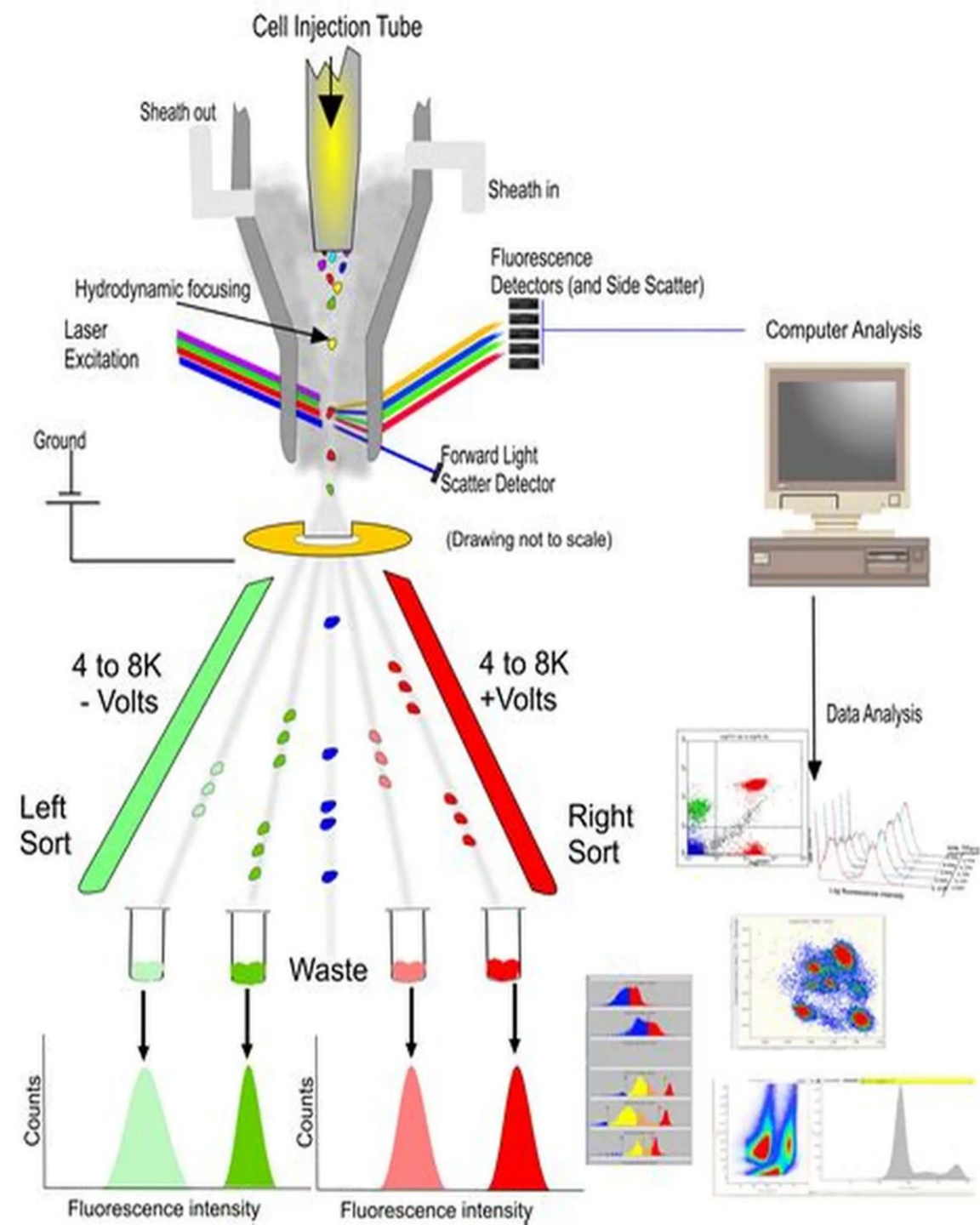
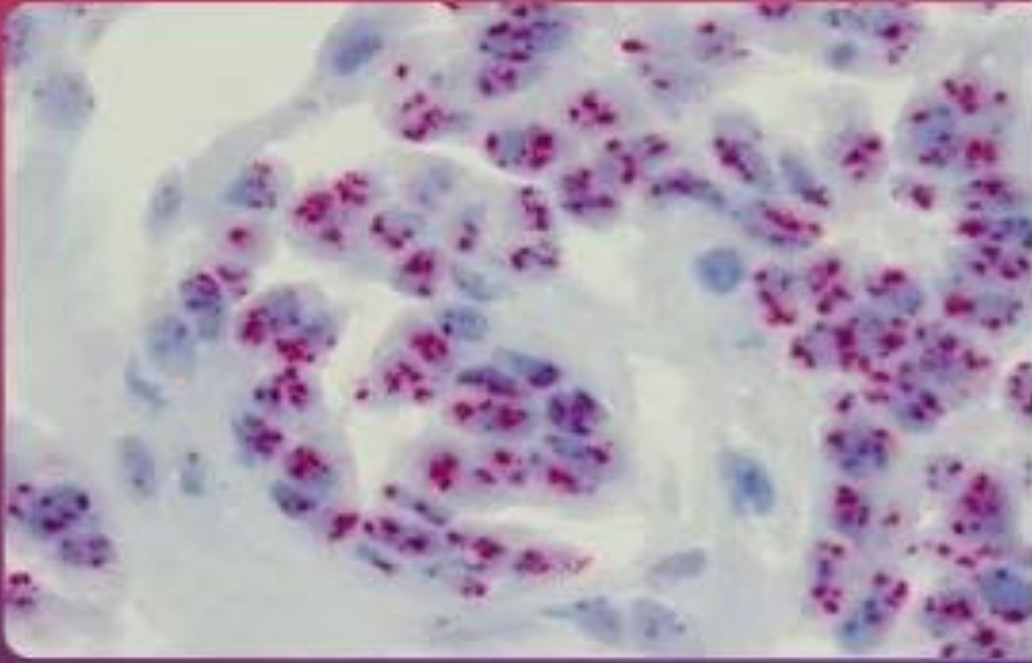


Figure 7.45 Anticytokeratin immunoperoxidase stain of a tumor of epithelial origin (carcinoma). (Courtesy Dr. Melissa Upton, University of Washington, Seattle, Wash.)

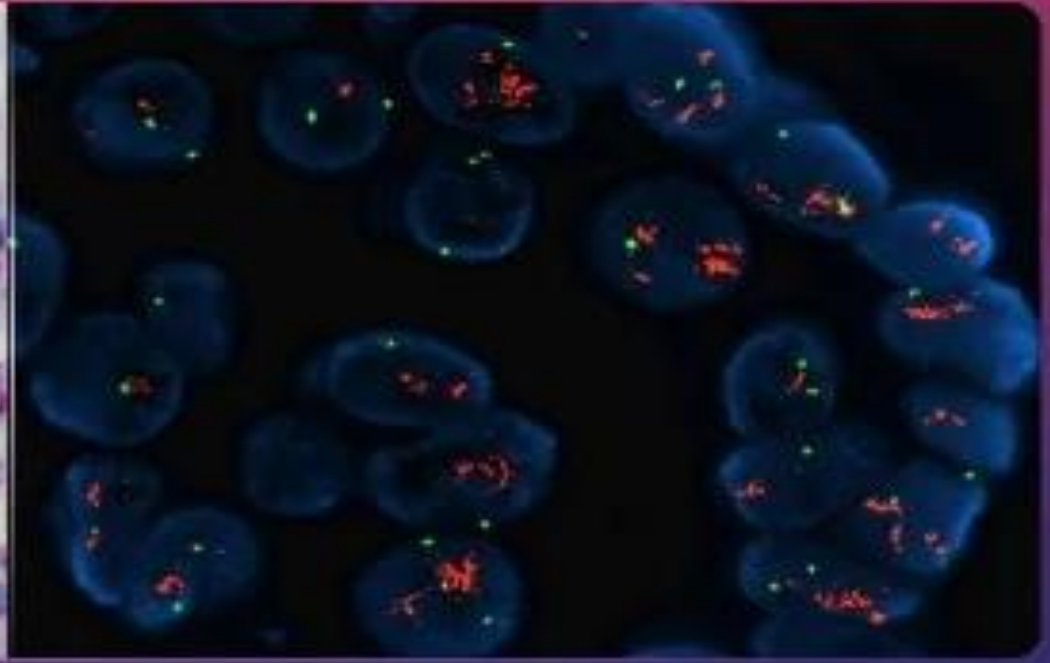
- Flow Cytometry



- Molecular Diagnostics and Cytogenetics



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