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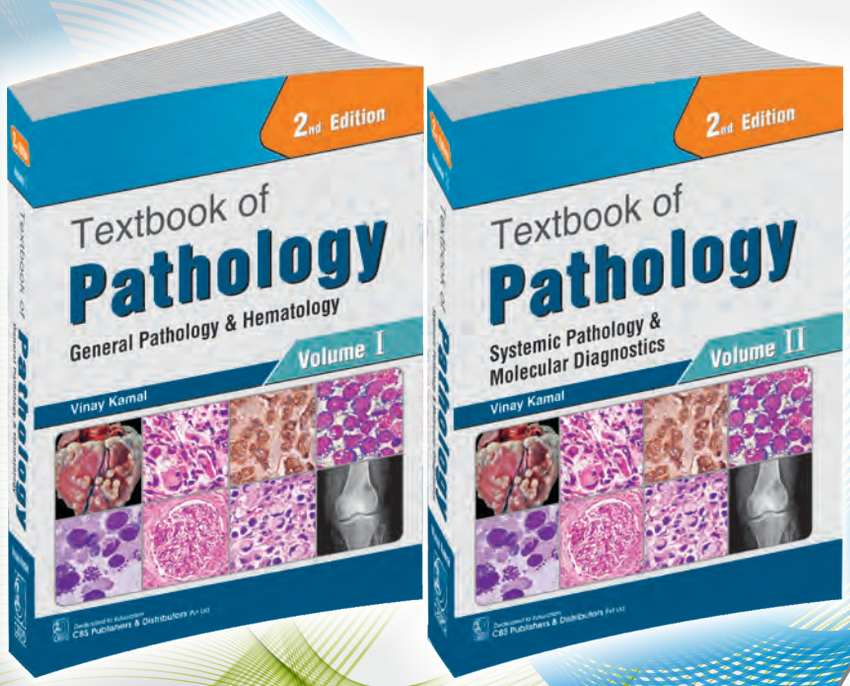
2nd Edition-2025

Textbook of Pathology

2 Volumes Set

Volume I
General Pathology & Hematology

Volume II
Systemic Pathology & Molecular Diagnostics



Author:
Vinay Kamal

Key features of the book

- Textbook of Pathology Designed for Undergraduates, Postgraduates
- 1901 High Resolution Colored Figures
- 1719 Tables for Quick Revision
- Reader-Friendly Large Font Text
- Recent Concepts in Cellular Biology of Disorders given in Boxes
- Revised WHO Classification of Tumors
- Chapters on 'Molecular Diagnostics' and 'Blood Transfusion'

About the Author

Dr Vinay Kamal has more than three-decade of teaching experience at India's premier institution, while serving as Director Professor, Department of Pathology, Maulana Azad Medical College, New Delhi.

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Textbook of

Pathology

Second Edition (Volume I & II)

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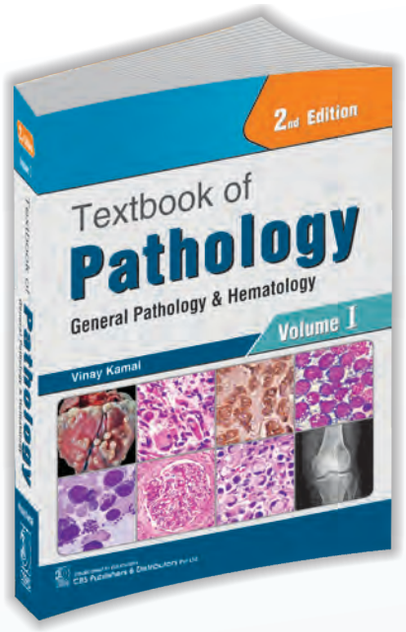
Volume I: General Pathology & Hematology
Volume II: Systemic Pathology & Molecular Diagnostics

Key Features

- Second edition of **Textbook of Pathology** by Vinay Kamal has been designed for undergraduates and postgraduates of pathology. Book has been amended as per the 'Competency-based Medical Education Curriculum'.
- Textbook contains general pathology, hematology and systemic pathology including WHO classification of tumors, blood banking and molecular diagnostic techniques in the context of modern cellular and molecular biology applied in clinical practice.
- Book has comprehensive coverage of etiopathogenesis of disease, clinical manifestations, clinicopathologic correlation and diagnostic approach. Clinical cases have been discussed after chapters.
- Book contains about 1901 figures of high resolution-colored clinical photographs, radiographs, surgical specimens, light microscopy and schematic diagrams.
- Book contains about 1719 tables for quick revision.

About the Authors

Dr. Vinay Kamal has more than three decades of teaching experience of India's premier institution as Director Professor, Department of Pathology, Maulana Azad Medical College, New Delhi. An alumnus of Post Graduate Institute of Medical Sciences, Rohtak has served the institution in various positions. He has been actively involved in academic activities across nation. Dr. Anubhav and Dr. Vigyat have been backbone in completion of book. Authors have published many articles in national and international journals.

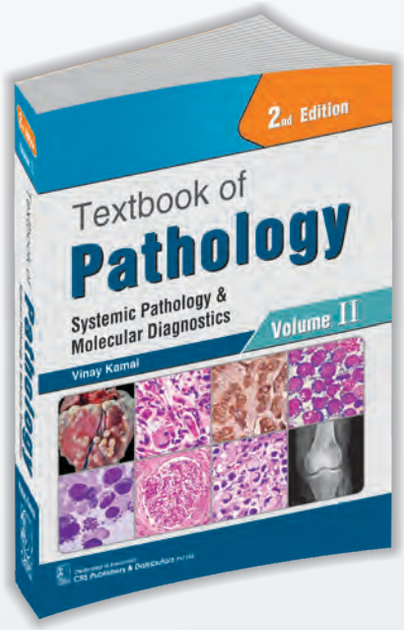


Volume I

Section I: General Pathology

Section II: Hematology

Section III: Systemic Pathology



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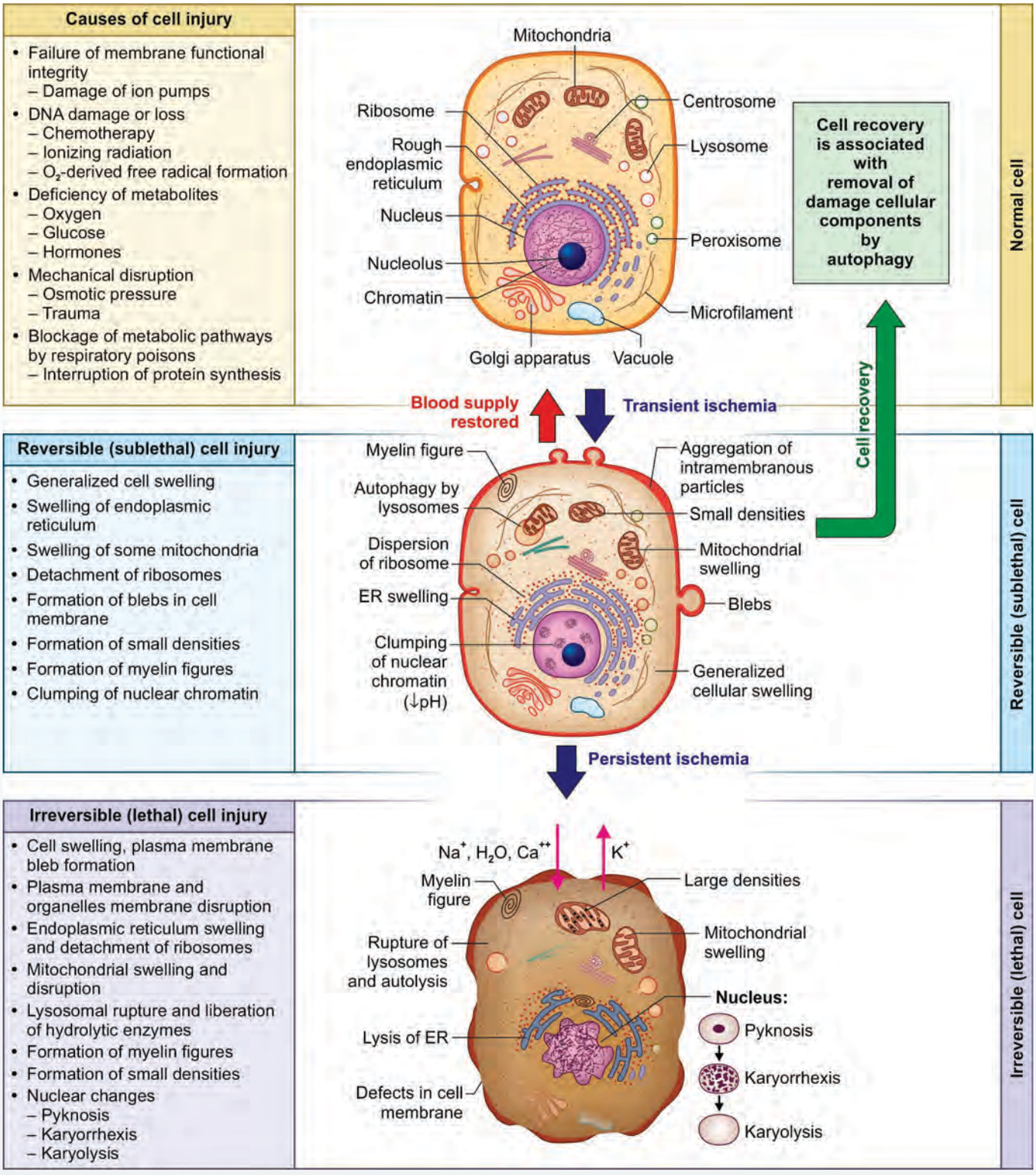
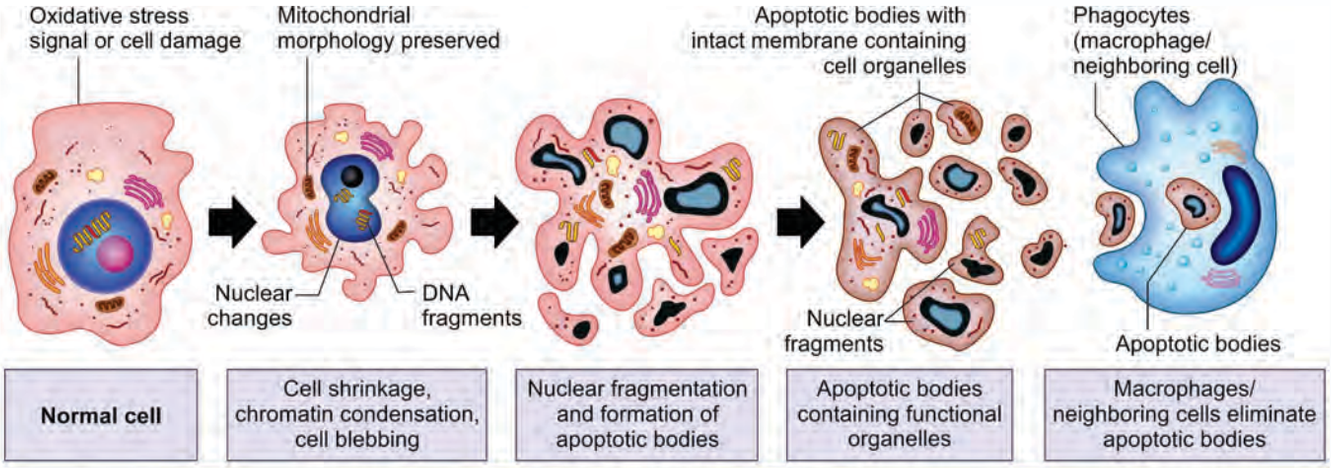
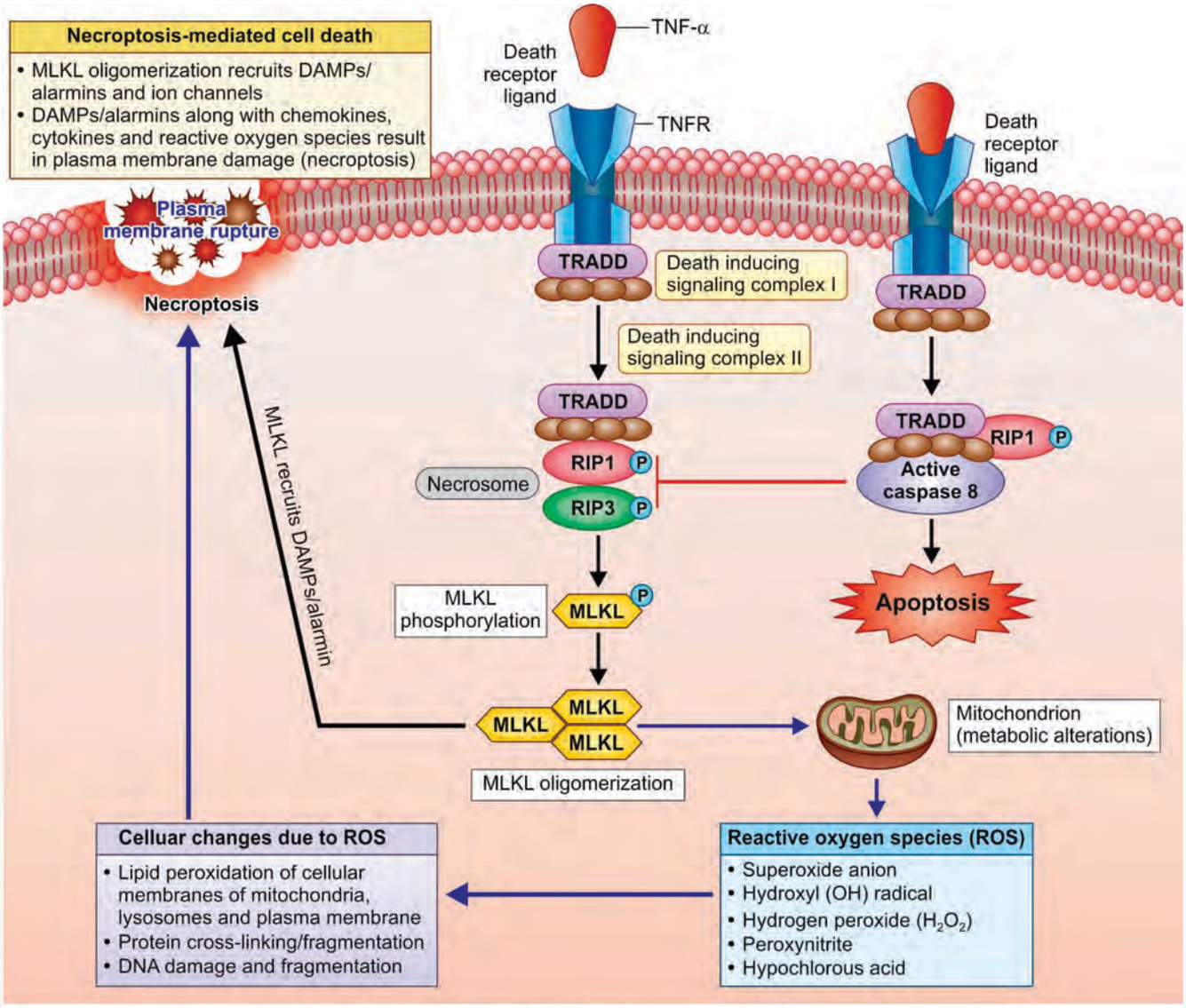


Fig. 1.15: Schematic representation of pathophysiology of reversible and irreversible cell injury. The main difference between reversible and irreversible cell injury is that the reversible cell injury can return to the normal state by altering homeostasis of the cells, whereas the irreversible cell injury cannot return to the viable state as the cell has passed the point of no return.



Apoptosis (programmed cell death)	
Induction stimuli	Oxidative stress, death receptor ligands and chemotherapy
Process	Active process executed by caspases (physiologic or pathologic processes)
Sequence of events to induce apoptosis in normal cell	***Role of TP53 (p53 protein) pathway to induce apoptosis in normal cell:*** Phosphorylated p53 protein → Activation of **BAX, PUMA** and **NOXA** → **Apoptosome** (APAF, cytochrome c, procaspase) → Activated **caspases 9 and 3** → **Apoptosis**
Sequence of events to induce apoptosis under pathologic state	***Extrinsic death receptor pathway of apoptosis:*** **FasL** → **Fas** → **FADD** (Fas activated death domain) → Activation of **caspase 8** → Activation of **caspases 3, 6, 7** → **Apoptosis** ***Intrinsic mitochondrial pathway of apoptosis:*** **BCL-2** protein → **BAX** proapoptotic protein → **Mitochondrial cytochrome c leakage/APAF-1** (apoptotic protease activating factor) → **Apoptosome** (cytochrome c + APAF-1 + caspase 9) → Activation of **caspase 9** → Activation of **caspases 3, 6, 7** → **Apoptosis** • Both extrinsic and intrinsic pathways can flow independently until the last step of DNA degradation by executioner caspases. The caspases cause proteolysis of specific substrates resulting in various morphological and biochemical characteristics in cells. • **Initiator caspases or upstream caspases like 2, 8, 9, 10, 11 and 12** • **Effector caspases or downstream caspases like 3, 6 and 7**
Cytomorphologic changes	Cell shrinkage, chromatin condensation, nucleus undergo fragmentation, plasma membrane blebbing without loss of cell integrity, organelles located in the plasma membrane blebs, and generation of apoptotic bodies.
Molecular changes	Cleavage of caspases, poly (ADP-ribose) polymerase (PARP involved in DNA repair) and nuclear fragmentation by endonucleases.
Clearance	Apoptotic bodies containing functional organelles are phagocytosed by neighboring cells and macrophages.
Laboratory diagnosis	Techniques for detection of apoptotic cells include: (a) cytomorphologic changes, (b) DNA discontinuous fragmentation ladder assay on agarose gel electrophoresis, (c) TUNEL assay, executioner caspase 3 and annexin V (IHC), (d) p53, executioner caspase 3 activation, FasR, TNF-α, and TRAIL (IHC, RT-PCR, Western blot, ELISA), and (e) cytochrome c release (ELISA).

Fig. 1.33: Schematic representation of apoptosis mediated by extrinsic (death receptor), intrinsic (mitochondrial) pathways. Both pathways can flow independently until the last step of DNA degradation by executioner caspase. Apoptosis is characterized by cell shrinkage, chromatin condensation, nuclear fragmentation by endonuclease, plasma membrane blebbing, generation and phagocytosis of apoptotic bodies by macrophages and surrounding epithelial cells and lack of inflammation.



Death receptor-dependent pathway of necroptosis	
• **Necroptosis** is an alternative mode of regulated kinase mediated cell death mimicking features of apoptosis and necrosis. It emerges as a backup mechanism, when apoptosis remains nonfunctional. It involves the release of intracellular 'danger signals' which results in considerable inflammation. • Necroptosis depends on receptor interacting protein kinase 3 (RIP3)-mediated phosphorylation of the pseudokinase mixed-lineage kinase domain-like (MLKL). • Necroptosis is demonstrated by immunohistochemistry and immunofluorescence employing antibodies to phosphorylated MLKL. Patients are treated with inhibitors of necroptosis such as necrostatins.	
Process	Mostly passive process, always pathological
Induction stimuli	Viruses, chemical exposure, radiation, endogenous or pathological factors
Morphologic changes	Swelling of cells and organelles, loss of plasma membrane integrity, receptor shedding, lysosomal exocytosis
Molecular changes	Acidosis, random degradation, release of cellular proteins
Clearance of necrotic cells	Necrotic cells phagocytosed by macrophages associated with significant inflammation

Fig. 1.28: Schematic representation of necroptosis. Necroptosis mimics features of necrosis and apoptosis. It involves the release of intracellular danger that results in considerable inflammation. Necroptosis requires protein RIPK3, a regulator of inflammation, cell survival and disease. Necroptosis is regulated by receptor-interacting protein kinase 1 and 3 (RIPK1, RIPK3) mediated phosphorylation of mixed-lineage kinase domain-like (MLKL). Necroptosis is demonstrated by immunohistochemistry and immunofluorescence microscopy by applying monoclonal antibody to phosphorylated MLKL.

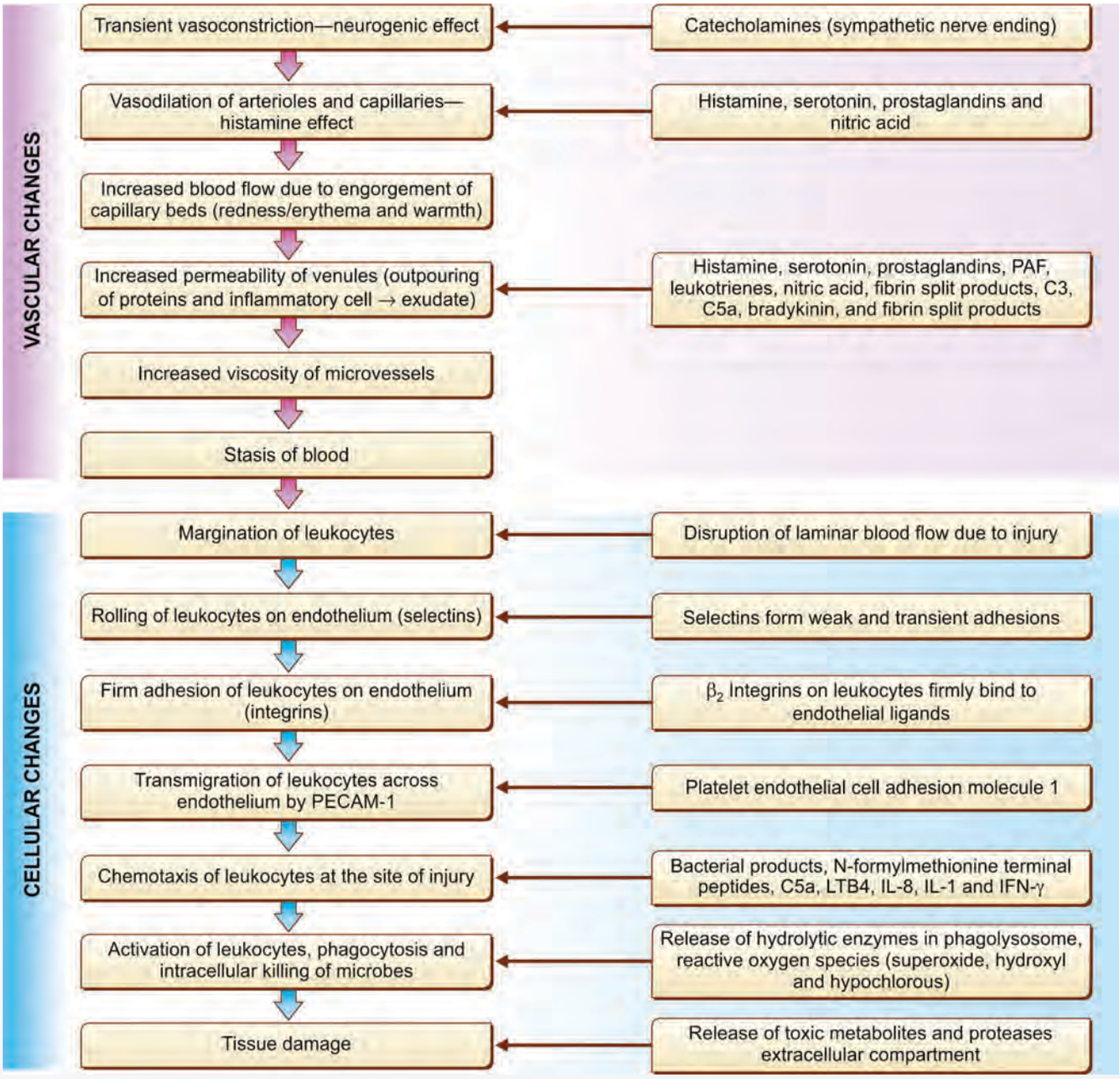


Fig. 2.3: Vascular and cellular events in acute inflammation. Vascular phase is characterized by vasodilatation and increased vascular permeability of the vascular barrier and the process is regulated by chemical mediators. Cellular phase is characterized by neutrophil margination, rolling, adhesion, and emigration to the injured site.

Table 2.8 Endothelial–leukocyte adhesion molecules and their major roles

Endothelial Molecule	Leukocyte Receptor	Major Roles
P-selectin (CD62P)	▪ Sialyl-Lewis X ▪ PSGL-1	Rolling of polymorphonuclear (PMN) cells, monocytes, lymphocytes
E-selectin (CD62E)	Sialyl-Lewis X	Rolling and adhesion of leukocytes
GlyCam-1, CD4	L-selectin (CD62L)	Rolling of PMN cells and monocytes
ICAM-1 (Ig family)	Integrins (LFA-1, Mac-1) CD11/CD18	Adhesion, arrest and transmigration of PMN cells, monocytes and lymphocytes
VCAM-1 (Ig family)	VLA-4 integrin	Adhesion of PMN cells, monocytes and lymphocytes
PECAM (CD31)	CD31	Transmigration of all leukocytes through endothelium

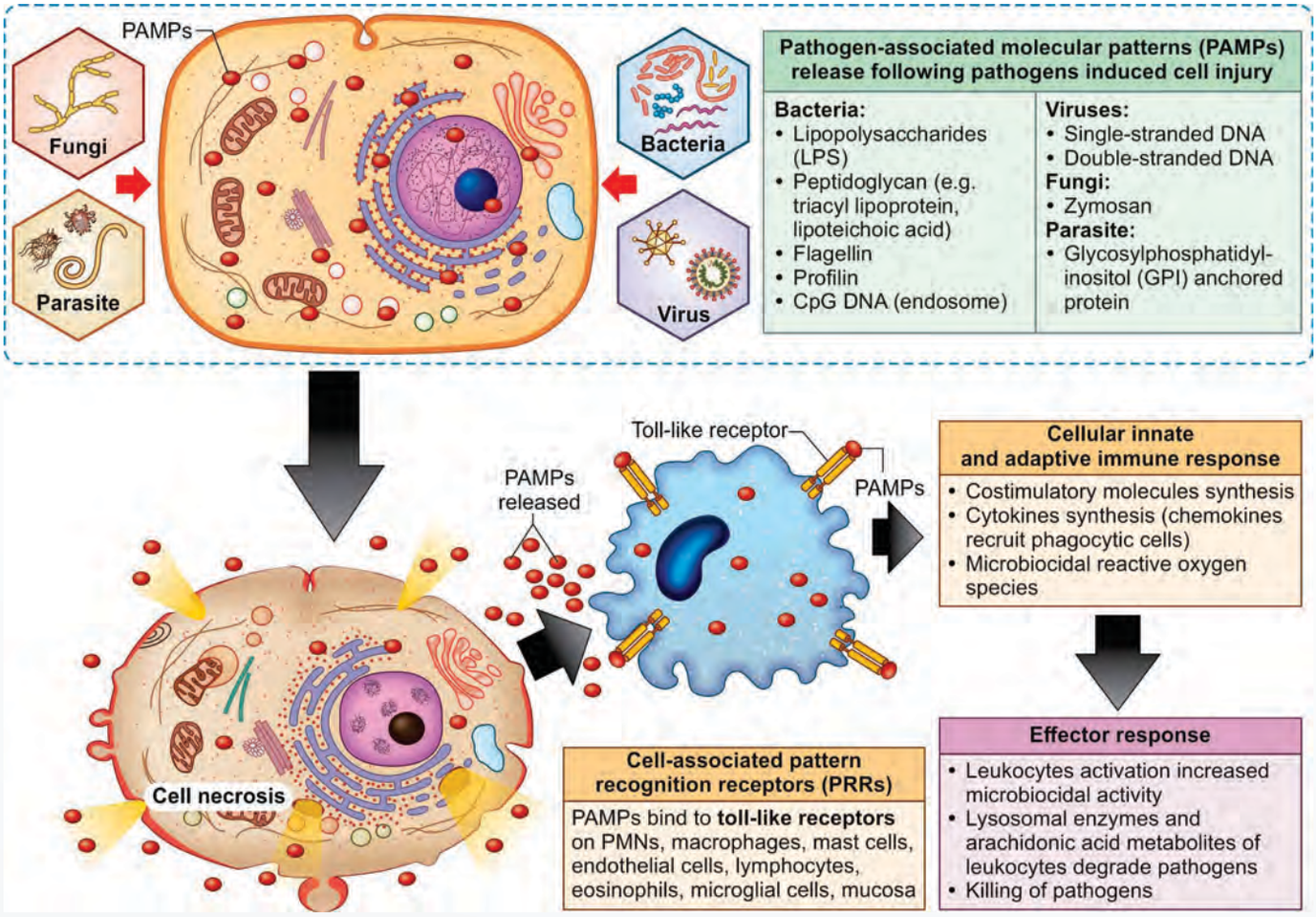


Fig. 2.11: Pathogen-associated molecular patterns. Microbes release PAMPs that bind to the family of pattern recognition receptors (PRRs), i.e. toll-like receptors and mediate innate and adaptive immune responses. Activation of toll-like receptors by specific ligands induces cytokine release and costimulatory molecules that instruct the type on immune response and direct antimicrobial response and tissue injury.

Table 2.10 Major pathogen-associated molecular patterns (PAMPs) in microbes

Pathogens	Pathogen-associated Molecular Patterns (PAMPs)	Tolle-like Receptors
Bacteria		
Gram-negative bacilli	Lipopolysaccharides (LPS), endotoxin	TLR-4
Gram-positive cocci	Peptidoglycan (e.g. triacyl lipoprotein, lipoteichoic acid)	TLR-1, TLR-2, TLR-6
Bacterial flagella	Flagellin	TLR-5
Bacterial profilin	Profilin	TLR-1
Endosome	CpG DNA (immunostimulatory cytosine-guanosine rich DNA sequence ends of DNA)	TLR-2, TLR9
Viruses		
Nucleus	▪ Single-stranded DNA ▪ Double-stranded DNA	▪ TLR-3, TLR-7, TLR-9 ▪ TLR-3
Yeast		
Fungi	Zymosan	TLR-2
Parasite		
Parasite component	Glycosylphosphatidylinositol (GPI) anchored protein	TLR-2

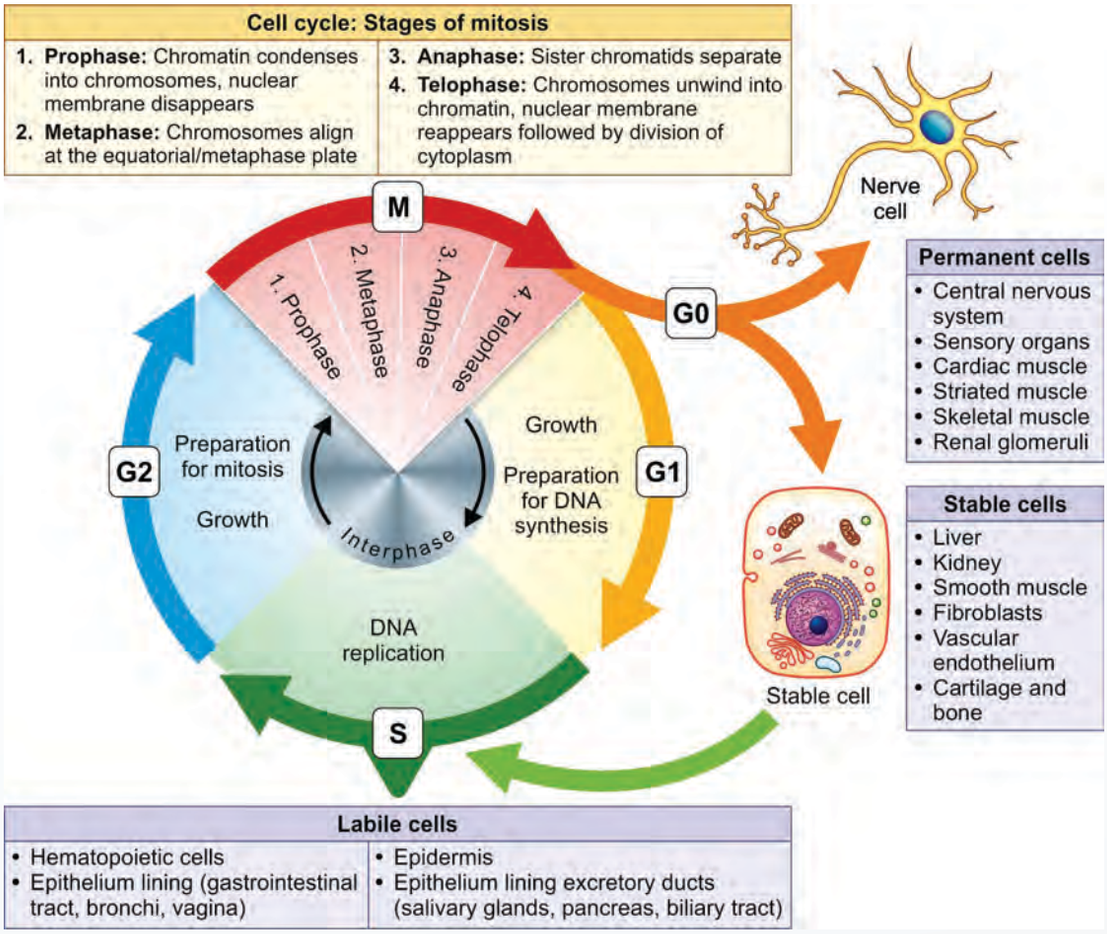
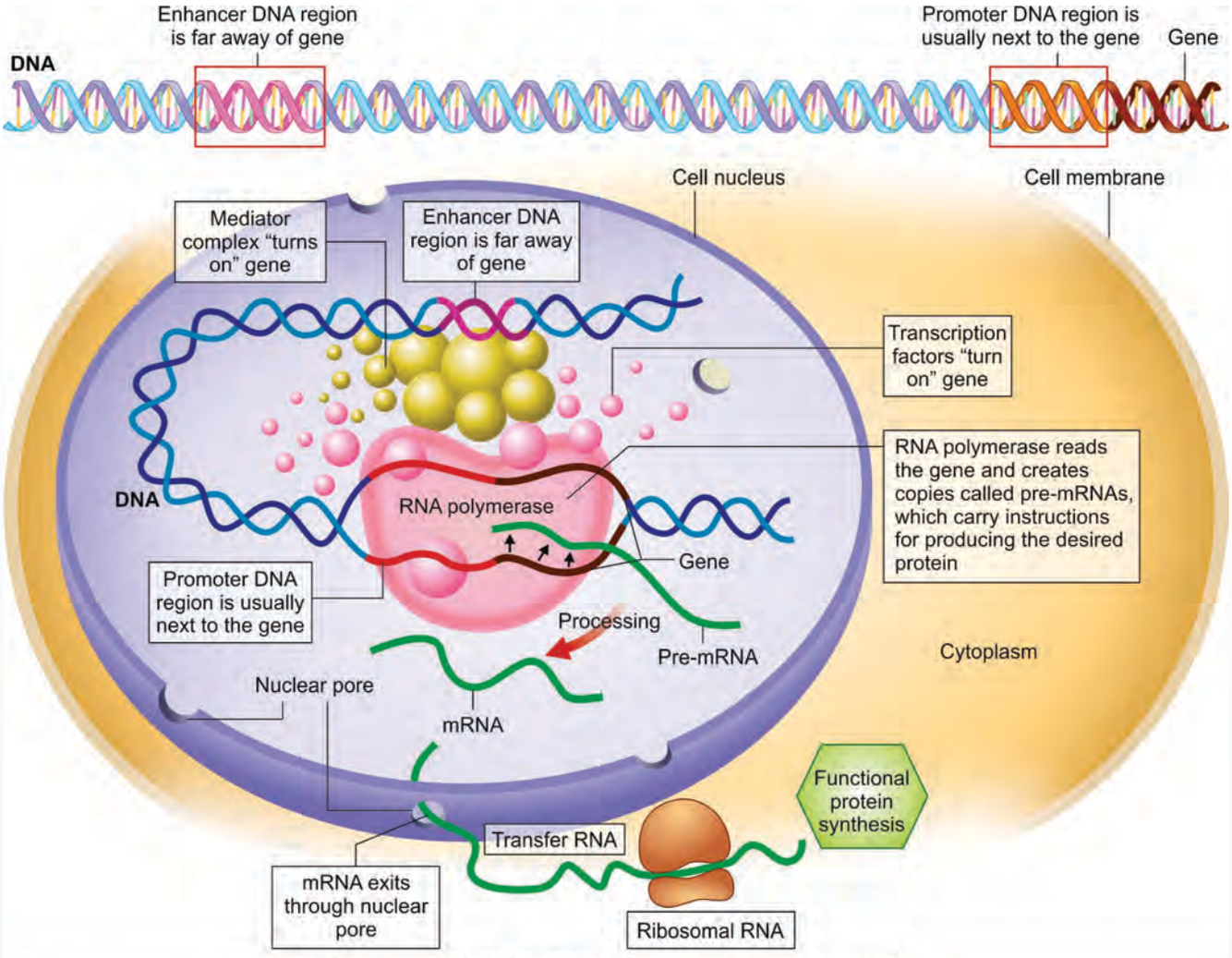


Fig. 2.54: G0, G1, G2, S and M phases of cell cycle. Location of the G1 is the restriction point. G1/S and G2/M are checkpoints of cell cycle. Cells from labile tissues such as bone marrow, epidermis, epithelial lining gastrointestinal tract, bronchi and vagina may cycle continuously.

Table 2.59 Cell cycle phases comprising G0, G1, G2 and M phases

Stage	Major Functions	
G0 phase of cell cycle		
G0 phase	Relatively inactive and nondividing stable state for cell cycle	
Interphase of cell cycle		
G1 phase	▪ Period of cell growth and preparation for DNA synthesis in the cell: G1/S checkpoint	▪ Ki-67 is expressed during active phases of cell cycle (G1/M)
S phase	▪ Period during which DNA is synthesized	▪ Ki-67 is expressed during active phases of cell cycle (G1/M)
G2 phase	▪ In G2 phase the cell grows and prepares for cell division: G2/M checkpoint	▪ Ki-67 is expressed during active phases of cell cycle (G1/M)
M phase of cell cycle		
Prophase	Chromosomes condense and mitotic spindle formed	
Prometaphase	Nuclear envelope disintegrates, spindle microtubules anchor to kinetochores	
Metaphase	Chromosomes align on metaphase plate; spindle-assembly checkpoint	
Anaphase	Sister chromatids separate, becoming individual chromosomes that migrate toward spindle poles	
Telophase	Chromosomes arrive at spindle pole. The nuclear envelope re-forms, and the condensed chromosomes relax	
Cytokinesis	Cytoplasm divides	

1. Ki-67 is expressed during active phases of cell cycle (G1/M). 2. In M phase, the cell undergoes mitosis and cytokinesis or equal division of chromosomes and cell membrane, cytoplasm and organelles between two daughter cells. 3. Proliferation of the cell is only appreciated once cytokinesis has occurred.



Gene expression: DNA replication, transcription and translation

Gene expression (DNA→RNA→Protein)	
• DNA replication	DNA→DNA copy occurs in nucleus.
• Transcription	DNA→mRNA occurs in nucleus, then mRNA moves on to ribosomes into the cytoplasm for translation.
• Translation	Protein synthesis occurs in cytoplasm (mRNA transcript is decoded into protein with the help of a ribosome and tRNA).
Human genome contains around 30,000 genes, each gene codes for one protein.	

Fig. 6.4: Gene expression involving DNA replication, transcription and translation. Gene expression is the process by which information from a gene is used in the synthesis of a functional gene product such as protein. Transcription is the process of making messenger RNA (mRNA) from a DNA template by RNA polymerase. Transcription factor is a protein that binds to DNA and regulates gene expression by promoting or suppressing transcription. Transcription factor and mediator proteins complex 'turn on' the gene and help RNA polymerase to read the gene.

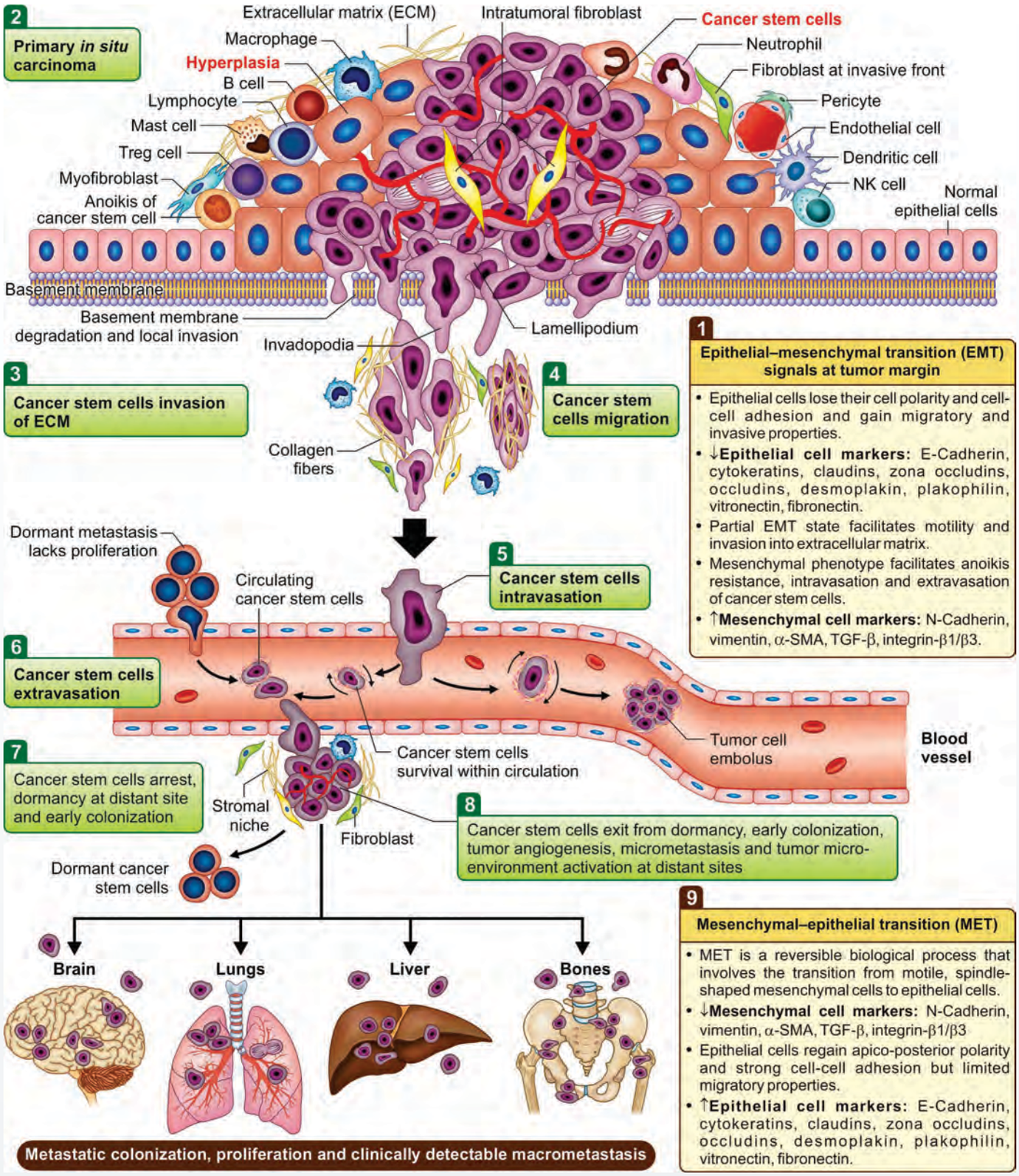


Fig. 6.81: Schematic representation of the malignant epithelial tumor invasion and metastasis. The initial transformation of normal epithelial cells to cancer stem cells results in carcinoma in situ. With reduced adhesiveness and enhanced migratory behavior, carcinoma in situ progresses to an invasive carcinoma. After enzymatic degradation of the basement membrane by secreted matrix metalloproteinases (MMPs), CSCs invade the surrounding extracellular matrix, migrate and intravasate into lymphatics and blood vessels. Circulating survived CSCs arrest in the capillaries of distant tissues/organs. There, CSCs remain in dormant state without reproliferating for considerable time. Alternatively, CSCs exist blood circulation (extravasate) proliferate and produce secondary tumors after CSC proliferation, tumor angiogenesis in tumor microenvironment and settle in distant organ(s).

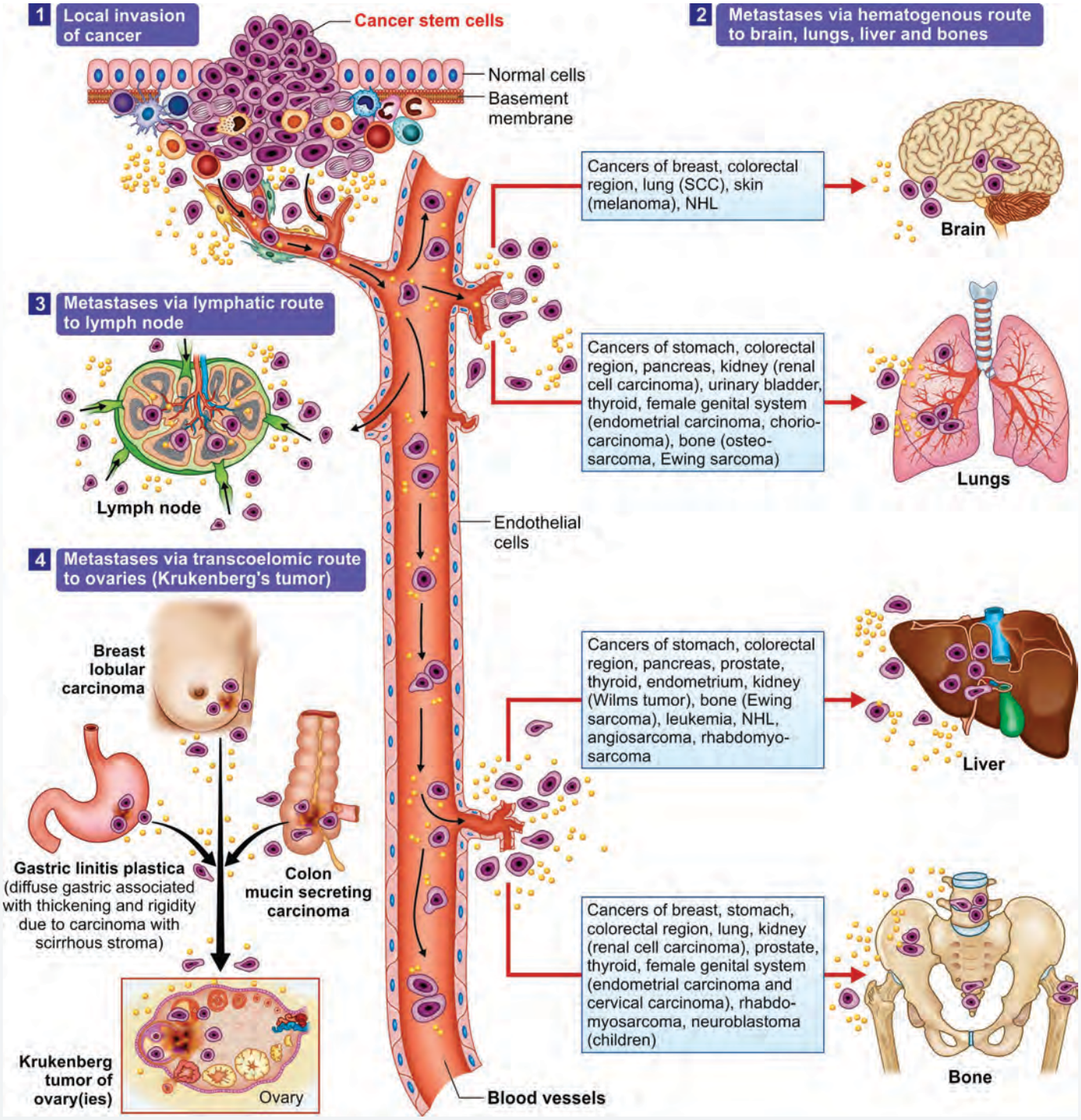
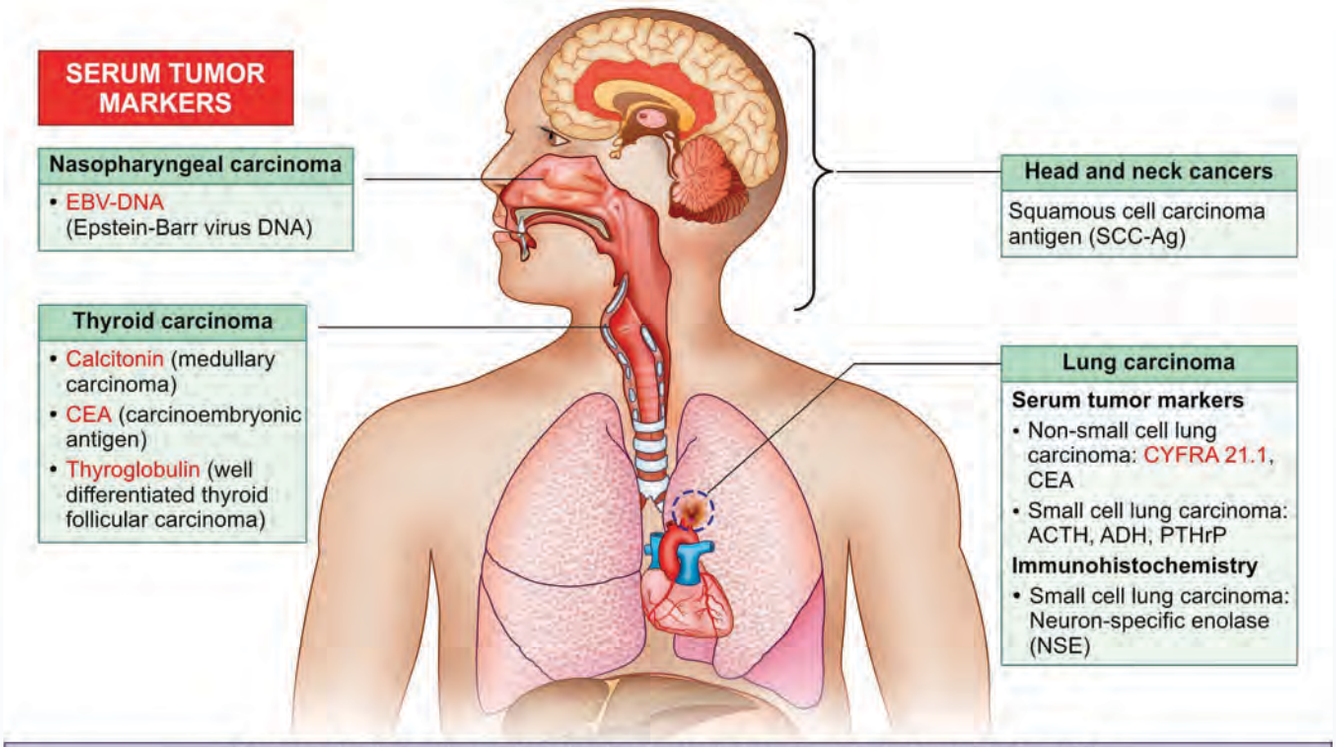


Fig. 6.61: Local invasion and metastasis of various cancers via various routes. Metastatic cascade represents a multistep process which includes CSC invasion, entry into the vasculature followed by the exit of cancer stem cells from the circulation and colonization in the distant organs.



Paraneoplastic syndrome (synthesis of ectopic hormones/substances by tumors)

Paraneoplastic neurological syndrome in small cell lung carcinoma
- Neuronal cell 'Hu antibodies'

Paraneoplastic cerebellar ataxia usually in gynecological tumors
- Purkinje cell 'Yo antibodies'

Lambert-Eaton myasthenic syndrome in small cell lung carcinoma
- Voltage-gated calcium channel antibodies

Cushing syndrome due to synthesis of ACTH-like hormone
- Small cell lung carcinoma
- Pancreatic carcinoma
- Neural tumors

Syndrome of inappropriate anti-diuretic hormone secretion (SIADH)
- Small cell lung carcinoma
- Thymoma
- Lymphomas (Hodgkin's disease, Non-Hodgkin's lymphoma)
- Prostatic carcinoma
- Gastric carcinoma
- Colon carcinoma

Ferritin (iron regulator protein)
- Hepatocellular carcinoma
- Acute leukemia
- Hodgkin's disease
- Multiple myeloma
- Hepatocellular carcinoma
- Prostatic carcinoma

Parathormone-like ectopic hormone (PTHrP) inducing hypercalcemia
- Small cell lung carcinoma
- Breast carcinoma
- Ovarian carcinoma
- Renal cell carcinoma
- Prostatic carcinoma
- Hepatocellular carcinoma
- Adult T cell leukemia

Erythropoietin-like ectopic hormone inducing polycythemia
- Renal cell carcinoma
- Cerebellar hemangioma
- Hepatocellular carcinoma

Insulin-like ectopic hormone inducing hypoglycemia
- Fibrosarcoma
- Hepatocellular carcinoma

Carcinoid syndrome due to neuroendocrine tumor
- Serotonin
- Bradykinin
- Histamine

Serotonin (5-hydroxytryptamine)
- Bronchial adenoma
- Pancreatic carcinoma
- Gastric carcinoma

Fig. 6.128: Tumor markers in cancers of head and neck, lung, mesenchymal and paraneoplastic syndromes.

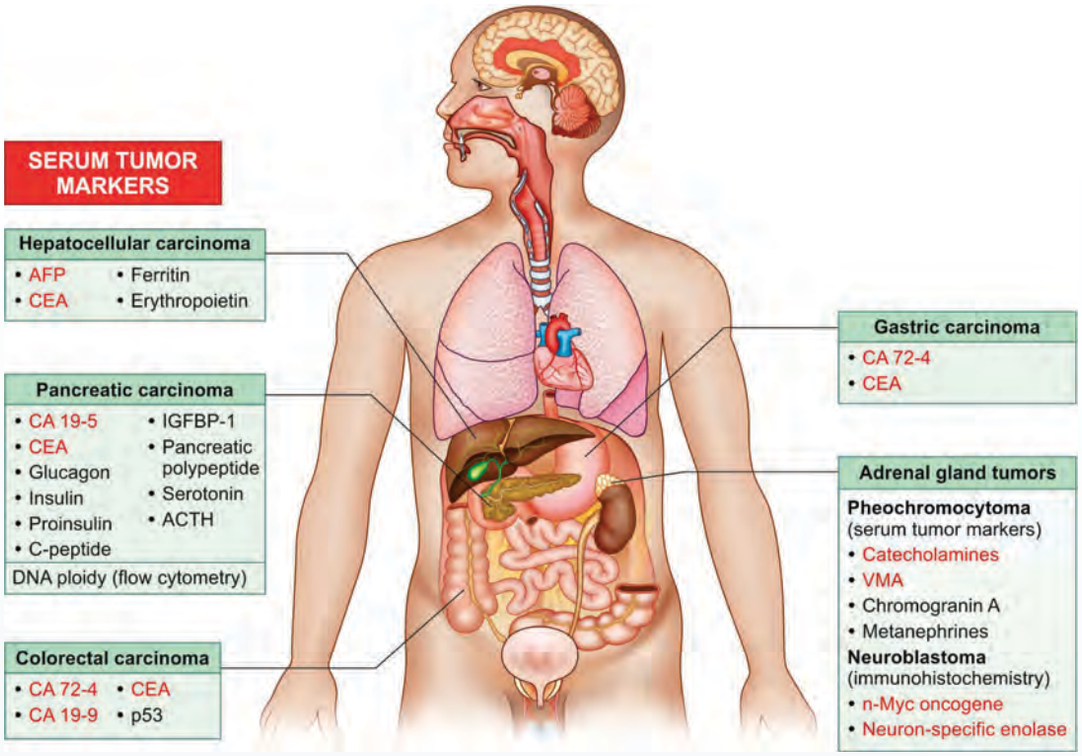


Fig. 6.129: Tumor markers in cancers of liver, pancreas, colorectal region, gastric region and adrenals.

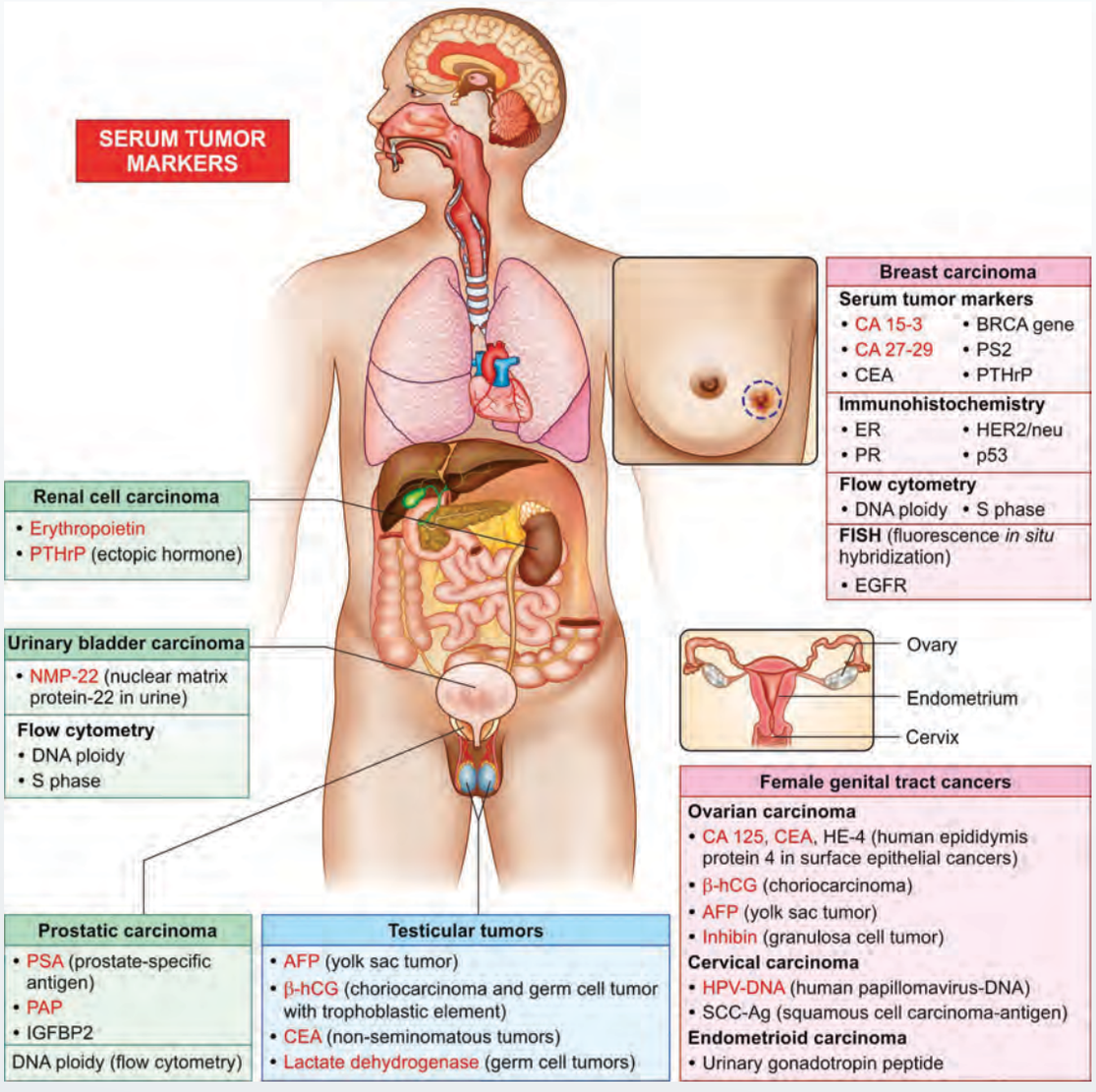


Fig. 6.130: Tumor markers in cancers of breast, kidney, urinary bladder, prostate, testes, ovaries, endometrium, and cervix.

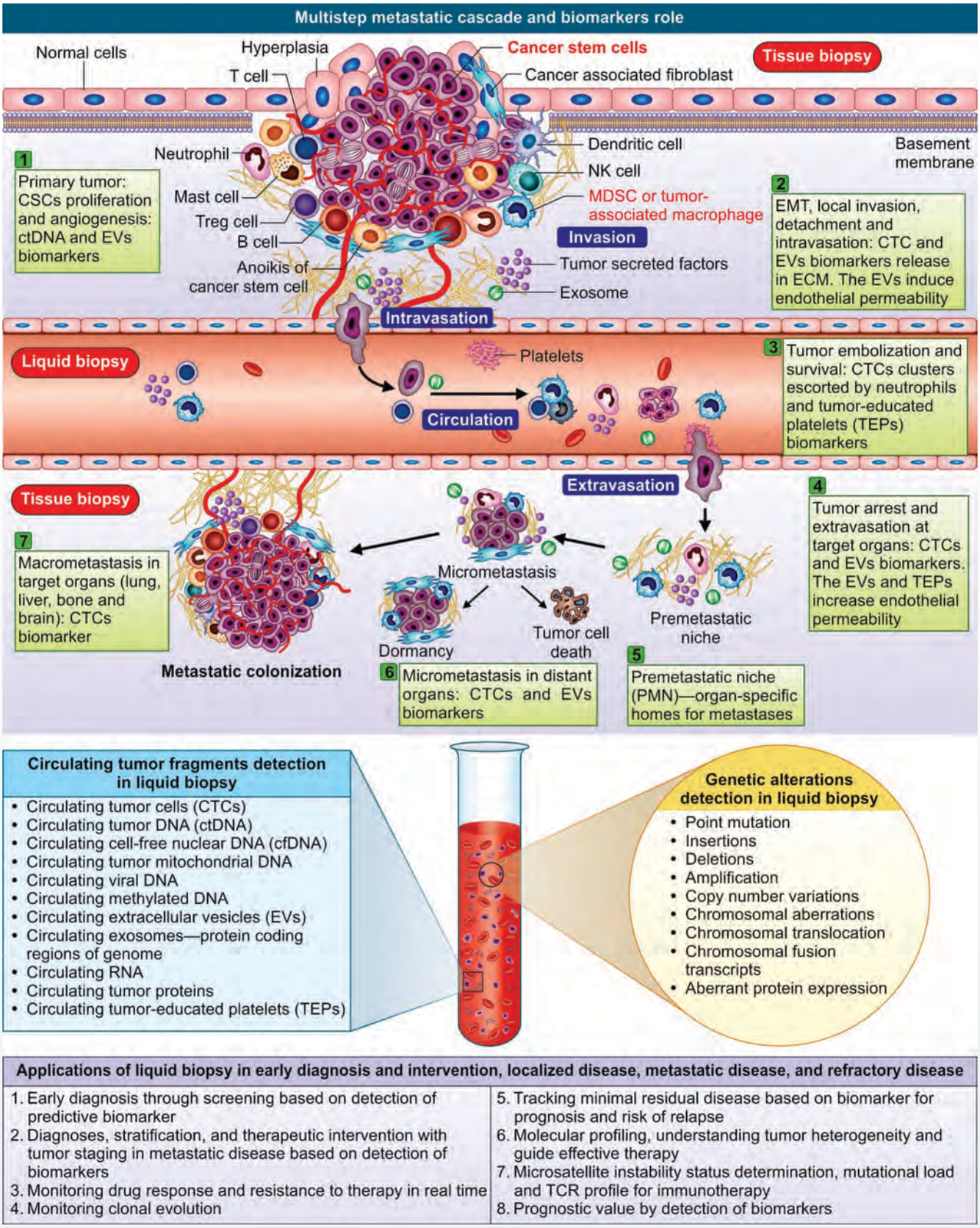


Fig. 6.136: Multistep metastatic cascade and biomarkers analysis, and clinical applications of liquid biopsy for treatment strategy in various stages of cancer. Liquid biopsy has broad potential applications for cancer diagnosis and treatment including early diagnosis through screening, study of tumor heterogeneity and clonal evolution, detection of minimum residual disease, and assessment of treatment response and development.

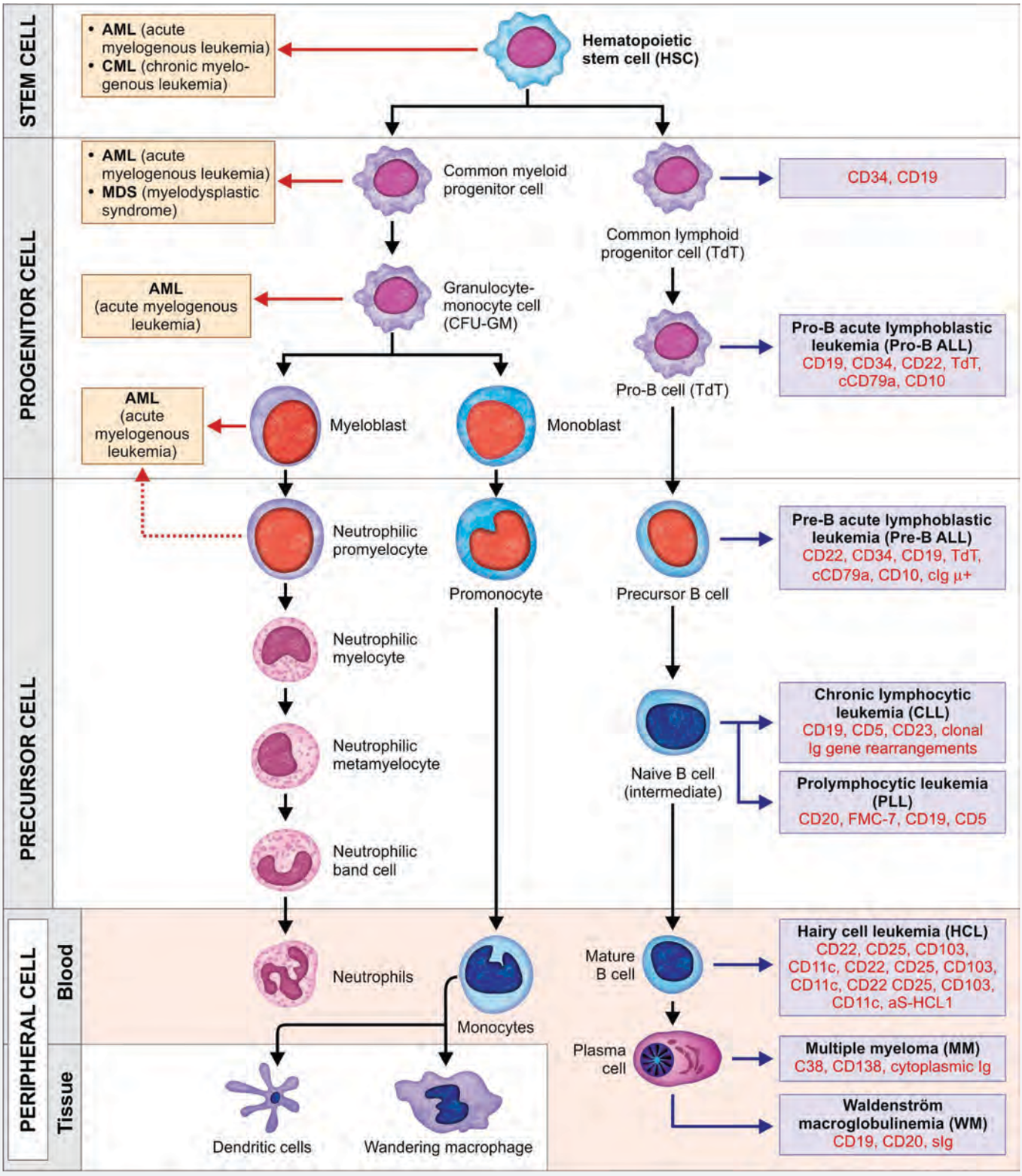


Fig. 9.9: Schematic representation of origin of acute myelogenous leukemia (AML), acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), prolymphocytic leukemia (PLL), hairy cell leukemia (HCL), multiple myeloma (MM), Waldenström heavy chain disease. AML and ALL may originate from any of the hematopoietic cells that fall within the pathways of the downward arrows. Importantly, the AML cell of origin acquires the capacity for self-renewal and maturation arrest.

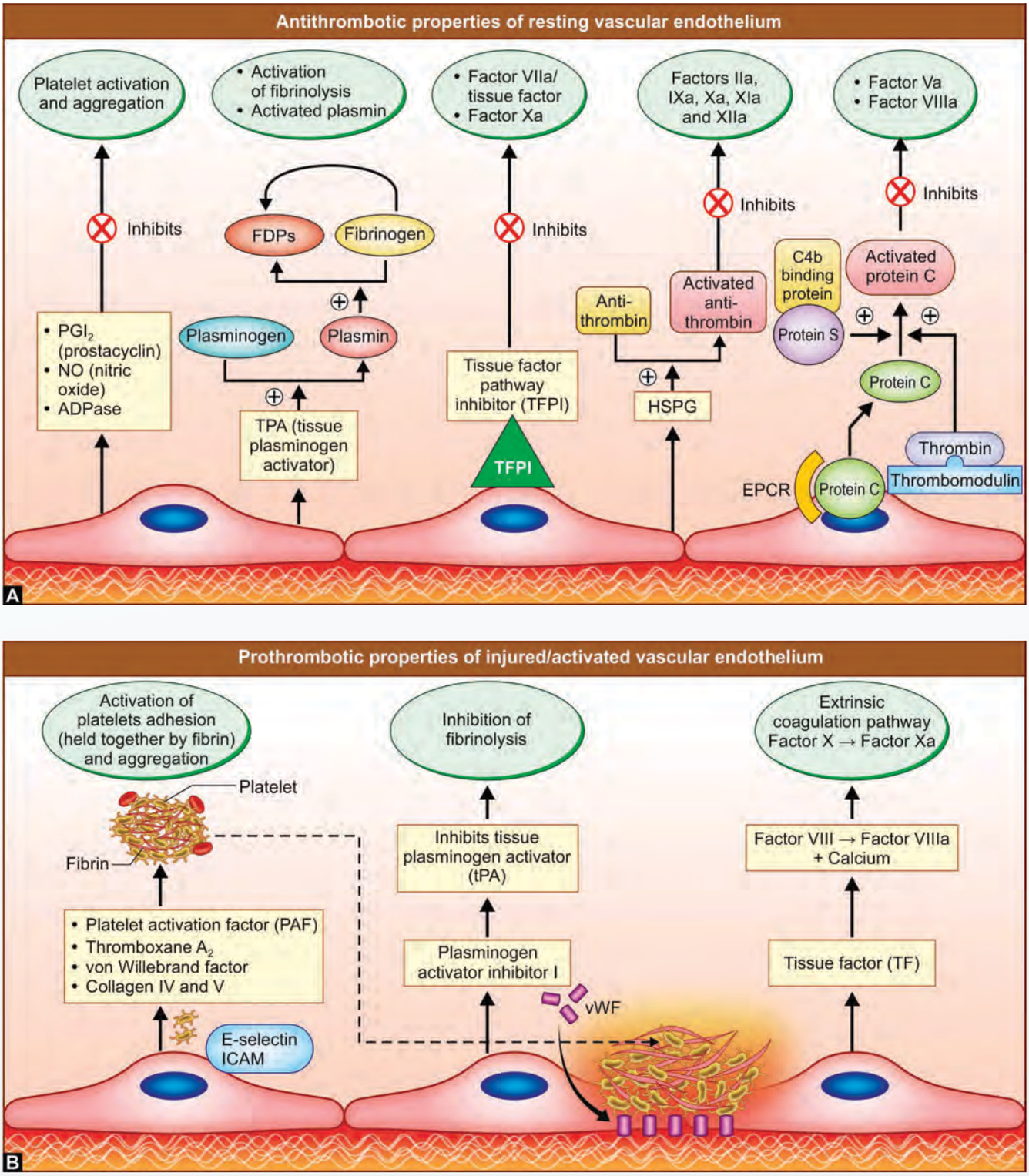


Fig. 10.1: Antithrombotic characteristics of resting vascular endothelium versus the prothrombotic effects of damaged or activated vascular endothelium. (A) Antithrombotic properties of resulting endothelium provide an environment that inhibit activation of hemostasis by secretion of substances that (1) inhibit platelet activation, e.g. PGI2 (prostacyclin), NO (nitric oxide), ADPase; (2) inhibit coagulation (heparan sulfate/GAG as a cofactor for AT III (antithrombin III), TM (thrombomodulin) for activation of protein C, which inactivates activated FVa and FVIIIa, and TFPI 1, i.e. tissue factor pathway inhibitor 1); and (3) activate fibrinolysis (tPA, i.e. tissue-type plasminogen activator, uPA, i.e. urinary type plasminogen activator). (B) Prothrombotic properties of injured activated vascular endothelium secrete substances that (1) activate platelets (TXA2, e.g. thromboxane, PAF, i.e. platelet activating factor) and bind them to the vessel wall (vWF, i.e. von Willebrand factor); (2) activate coagulation (TF, i.e. tissue factor which initiates formation of fibrin); and (3) inhibit fibrinolysis (PAI-1, i.e. plasminogen activator inhibitor 1). EPCR—endothelial protein C receptor. HSPG; heparin sulfate proteoglycans.

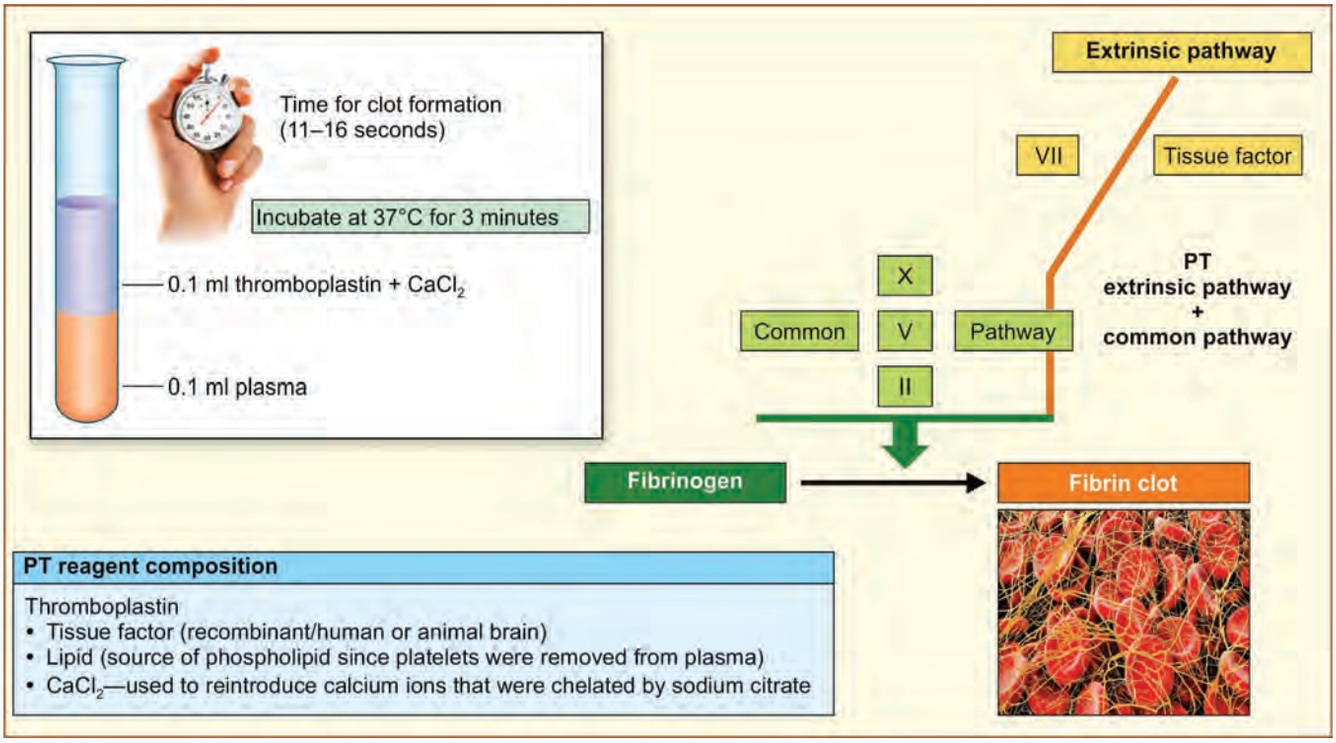


Fig. 11.11: Procedure of one stage prothrombin time

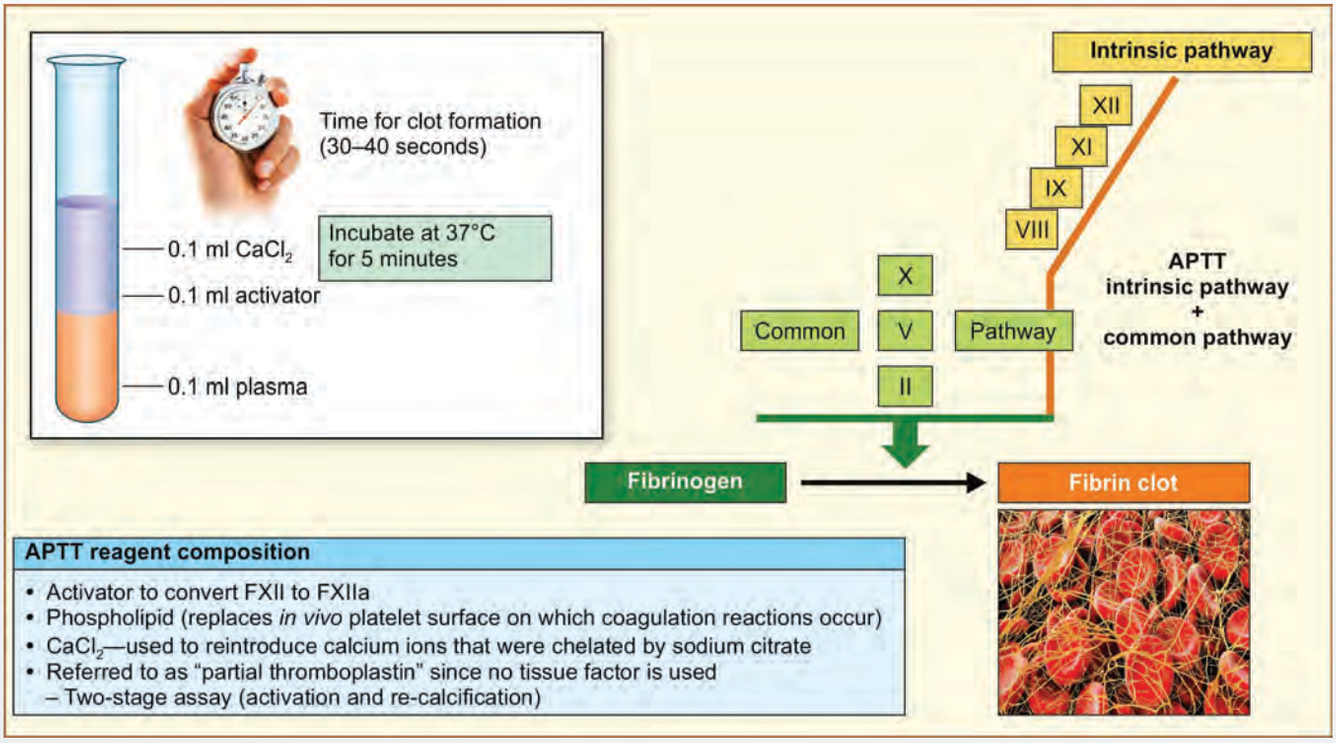


Fig. 11.12: Procedure of activated partial thromboplastin time (APTT).

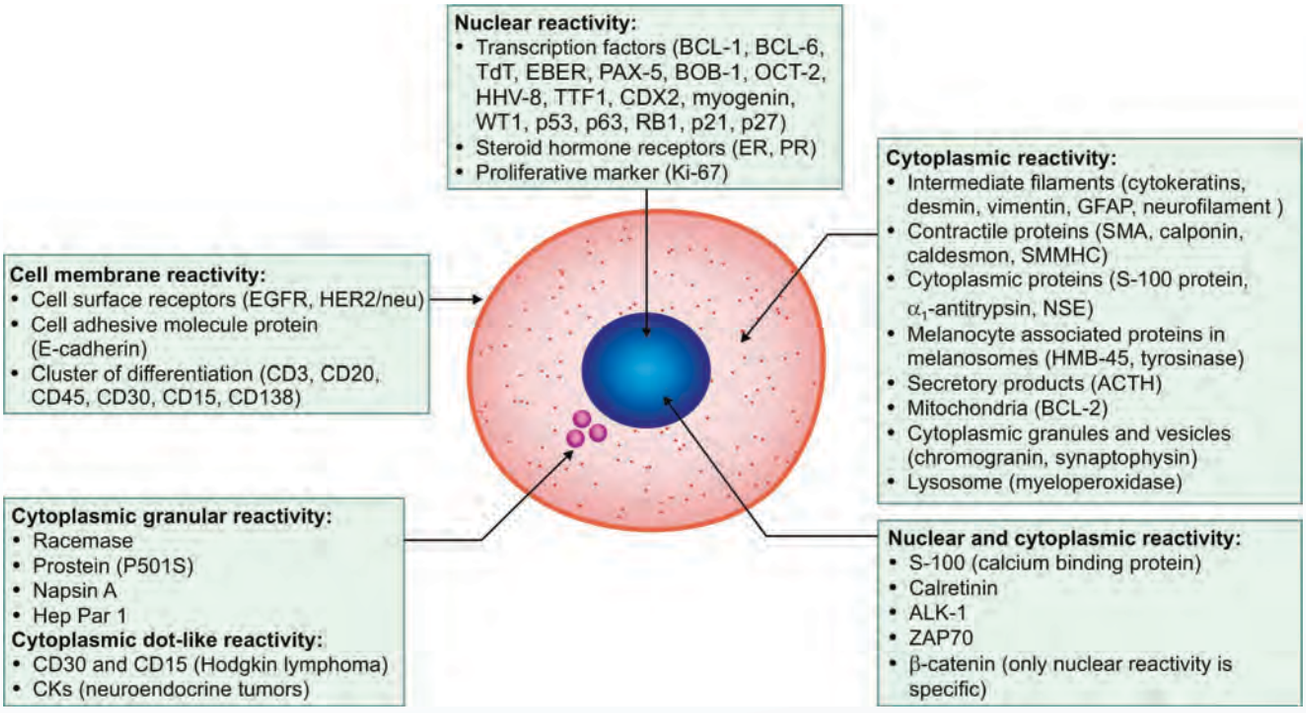
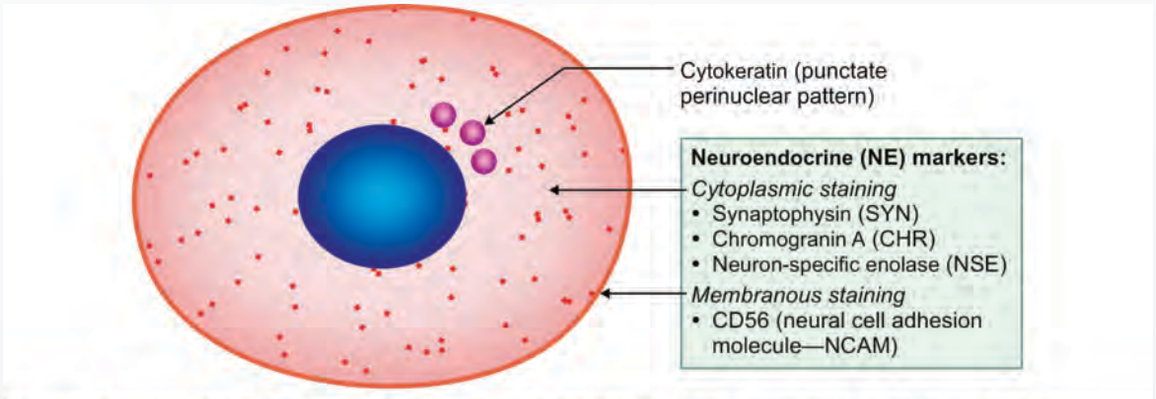


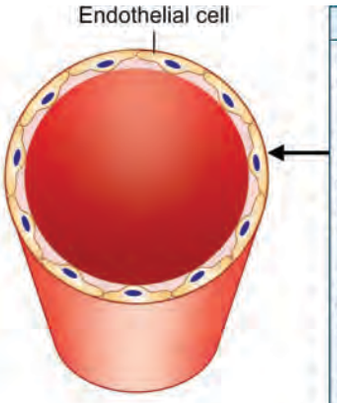
Fig. 14.9: Primers on location of antigens in the cells demonstrated by immunohistochemical markers.



Immunohistochemical markers of neuroendocrine (NE) and neuroectodermal neoplasms

- Carcinoid tumors (SYN, CHR, NSE, CD56, CK, TTF1)
- Medullary carcinoma of thyroid (SYN, CHR, NSE, CD56, CK, TTF1, calcitonin, CEA, amyloid)
- Pancreatic endocrine neoplasm (SYN, CHR, NSE, CD56, CK)
- Pheochromocytoma (SYN, CHR, NSE, CD56, CK, S-100 protein)
- Paraganglioma (SYN, CHR, NSE, CD56, S-100 protein)
- Small cell neuroendocrine carcinoma (SYN, CHR, NSE, CD56, TTF1)
- Merkel cell carcinoma (SYN, CHR, NSE, CD56, CK, neurofilament, Merkel cell polyomavirus)
- Pituitary neoplasms (SYN, CHR, NSE, CD56, CK, GH, ACTH, TSH, LH, FSH)
- Parathyroid neoplasms (SYN, CHR, NSE, CD56, CK, parathormone)
- Neuroblastoma (SYN, CHR, NSE, CD56, S-100 protein)
- PNET/Ewing sarcoma (NSE, CK, CD99, PAS)

Fig. 14.12: Flow chart represents panel of immunohistochemical markers of neuroendocrine and neuroectodermal neoplasms.



Vascular differentiation IHC markers

CD31 (PECAM1)
- More sensitive and specific for blood vessel and lymphatic
- Most angiosarcomas
- Kaposi sarcoma

CD34 (hematopoietic progenitor cell antigen)
- Less sensitive and specific for blood vessel
- Angiosarcoma (50%)

D2–40 (podoplanin)
- Novel specific marker for lymphatic endothelial cells
- Kaposi sarcoma
- Most angiosarcoma
- Lymphangioma

Factor VIII vWF
- Epithelioid hemangioblastoma
- Some angiosarcoma

Ulex europaeus 1
- More sensitive marker for endothelial cells
- Vascular tumors

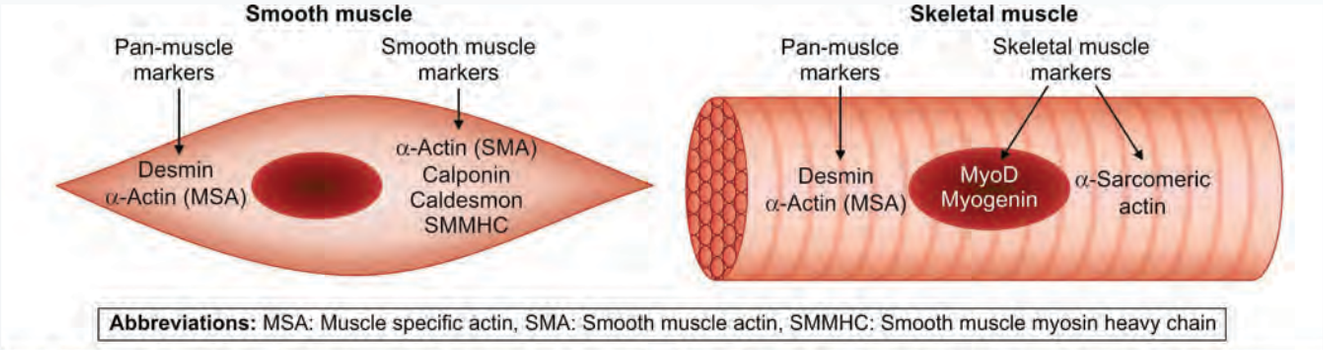
CD141 (thrombomodulin)
- Marker for endothelial cells of blood vessels and lymphatic channels
- Variable expression in angiosarcoma

Fli-1 immunohistochemical marker
- Marker for endothelial cells of blood vessels and lymphatic channels
- Angiosarcoma

CD34+ marker for nonvascular tumors
- Solitary fibrous tumor (SFT)
- Dermatofibrosarcoma protuberans (DFSP)
- Gastrointestinal stromal tumor (GIST)
- Epithelioid sarcoma
- Nerve sheath tumors
- Granulocytic sarcoma, and other

Applications of vascular differentiation IHC markers
- To demonstrate vascular nature of a poorly differentiated neoplasm such as:
  - Kaposi sarcoma
  - Angiosarcoma
  - Epithelioid hemangioendothelioma
  - Hemangiopericytoma
- To highlight blood vessels and lymphatic to demonstrate:
  - Lymphovascular invasion in various malignant tumors

Fig. 14.10: Vascular endothelial immunomarkers.



Abbreviations: MSA: Muscle specific actin, SMA: Smooth muscle actin, SMMHC: Smooth muscle myosin heavy chain

IHC markers for smooth muscle differentiation

Desmin (intermediate filament)
- Universal pan-muscle marker for smooth muscle and striated muscle and also expressed variable in myofibroblasts
- Leiomyoma
- Leiomyosarcoma (70%)
- Rhabdomyosarcoma
- Also expressed in various epithelial neoplasms, e.g. renal cell carcinoma (clear cell variant), endometrioid carcinoma, thyroid carcinoma, mesothelioma, salivary gland carcinoma, sweat gland carcinoma and spindle cell carcinoma of any site

Muscle specific actin (MSA)
- Pan-muscle marker for smooth muscle and striated muscle

Smooth muscle actin (also known as actin)
- Expressed in smooth muscle, but absent in striated muscle
- Smooth muscle tumors (e.g. leiomyoma, leiomyosarcoma)
- Myoblastic tumors like lesion (nodular fasciitis)

Contractile apparatus associated proteins
- Expressed in smooth muscle, but absent in skeletal muscle.
- Smooth muscle myosin heavy chain (SMMHC)
- Calponin (contractile apparatus associated proteins encoded by CALD-1 gene) expressed in smooth muscle, leiomyoma, leiomyosarcoma, , myofibroblasts, myofibroblastic tumors and myoepithelial cells
- Caldesmon (encoded by CALD-1 gene) expressed in normal smooth muscle, leiomyoma and leiomyosarcoma

IHC markers for skeletal muscle differentiation

Desmin (intermediate filament)
- Universal pan-muscle marker for smooth as well as striated muscle (antibody clone D33)
- Expression of desmin variable in myofibroblasts
- Leiomyoma
- Leiomyosarcoma (70%)
- Rhabdomyosarcoma
- Also expressed in various epithelial neoplasms, e.g. renal cell carcinoma (clear cell variant), endometrioid carcinoma, thyroid carcinoma, mesothelioma, salivary gland carcinoma, sweat gland carcinoma and spindle cell carcinoma of any site

Muscle specific actin (MSA)
- Like desmin, muscle specific antigen is pan-muscle marker for smooth muscle and striated muscle. HHF-35 antibody recognizes epitope common to α-skeletal, α-cardiac and γ-smooth muscle actin

MyoD1 and myogenin (transcriptional factors)
- Expressed in striated muscle but absent in smooth muscle
- Expressed in leiomyosarcoma but absent in leiomyoma
- Embryonal rhabdomyosarcoma shows focal positivity staining pattern
- Alveolar rhabdomyosarcoma shows diffuse positivity staining pattern

Fig. 14.11: Immunomarkers for smooth muscle and skeletal muscle differentiation.

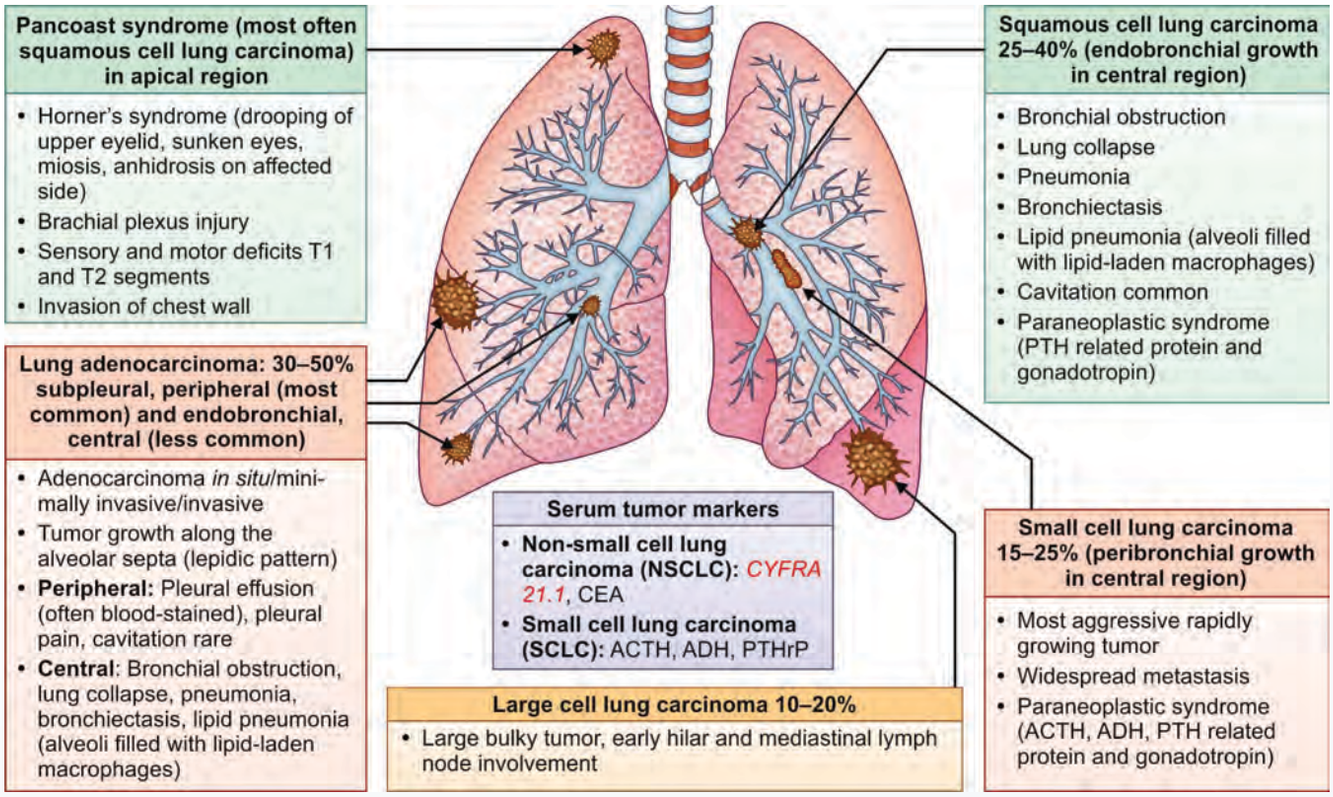
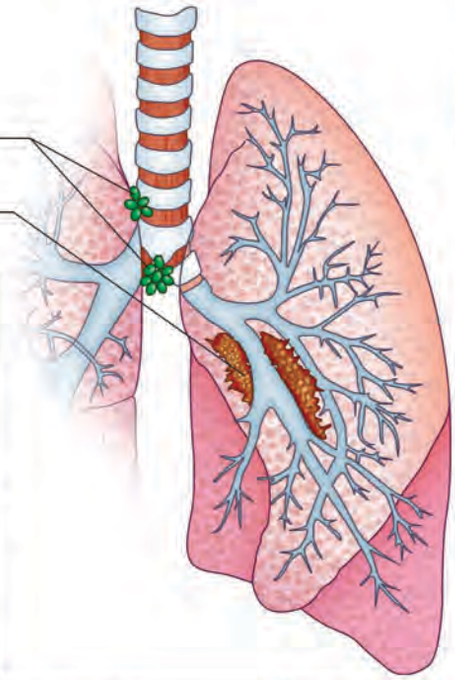


Fig. 18.47: Histologic variants of primary lung cancers. Clinical features of lung cancer depend on site of lesion, invasion of neighboring structures and extent of metastases.

Table 18.45 Cell of origin and histologic variants of lung carcinomas

Cell of Origin of Lung Carcinoma	Histologic Variants of Lung Carcinoma
Neuroendocrine cells (also known as Kulchitsky cells) in bronchopulmonary region	Small cell lung carcinoma
Basal cells in major bronchi (lobar or segmental)	Squamous cell lung carcinoma
Mucous cells in terminal bronchioles	Lung adenocarcinoma
Clara cell in terminal bronchoalveolar region	Bronchoalveolar carcinoma, histologic variant of adenocarcinoma



Small cell lung carcinoma 15–25% (peribronchial growth in central region)

- Most aggressive rapidly growing tumor
- Not associated with smoking
- Very early metastases to mediastinum or distal area of lung
- Widespread metastasis
- Paraneoplastic syndrome (ACTH, ADH, PTH-related protein and gonadotropin)
- Treatment (chemotherapy) but surgical resectability is poor

Paraneoplastic syndrome in small cell lung carcinoma

- **Lambert-Eaton myasthenic syndrome:** IgG autoantibodies against calcium channel in motor nerve terminals, weakness of pelvic girdles, proximal limbs and trunk (acetylcholine not released)
- **Peripheral neuropathy:** IgG autoantibodies against anterior and lateral horns of CNS
- **Cerebellar degeneration:** IgG autoantibodies against cerebellum leading to ataxia, vertigo and dysarthria
- **Corticotropic-like effects:** Facial edema, decreased serum potassium and alkalosis
- **ADH-like effects:** Increased urine osmolality, low serum potassium and weakness
- **Parathormone-like effects:** Increased serum calcium
- **Gonadotropic-like effects:** Gynecomastia and testicular atrophy

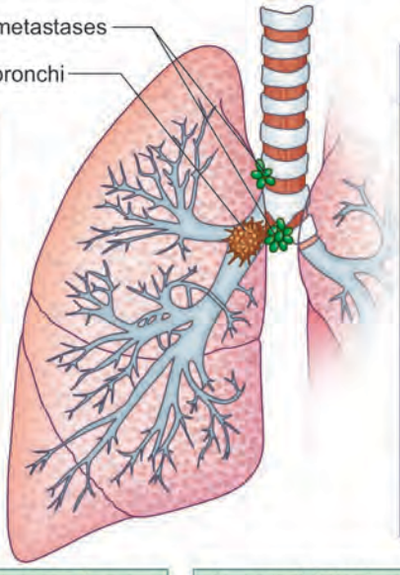
Gene mutations in small cell lung carcinoma

Oncogene	c-Myc oncogene
Tumor suppressor gene	RB gene (80–100%)
	p53 gene (50–80%)
Anti-apoptotic gene	BCL-2 gene (90%)

Immunohistochemistry of small cell lung carcinoma

Markers	Expression
Chromogranin	Positive
Synaptophysin	Positive
Leu7 (CD57)	Positive
Nonspecific esterase (specific marker)	Positive
CD56	Positive

Fig. 18.49: Small cell lung carcinoma shows risk factors, gene mutations, clinical manifestations, immunohistochemistry and metastases.



Risk factors of squamous cell lung carcinoma

- Cigarette smoking (squamous and small cell lung carcinoma)
- Asbestosis [adenocarcinoma (most common) and squamous cell lung carcinoma]
- Ionizing radiation (squamous and small cell lung carcinoma, adeno-carcinoma)
- Uranium miners (lung cancer after 17 years)
- Metals (nickel, chromium, arsenic, cadmium exposure result in lung cancer)

Clinical features of squamous cell lung carcinoma

- Cough (75% cases)
- Hemoptysis (<50% cases)
- Dyspnea (pleural effusion, phrenic nerve invasion)
- Hoarseness of voice (recurrent laryngeal nerve involvement)
- Superior vena cava syndrome
- Cardiac tamponade
- Paraneoplastic syndrome (PTH-related protein causing increased serum calcium; gonadotropin leading to gynecomastia and testicular atrophy)
- Lung manifestations (bronchial obstruction, collapse, pneumonia, bronchiectasis and lipid pneumonia)

Gene mutations in squamous cell lung carcinoma

Genes	Examples	Frequency
Oncogenes	EGFR	80%
	HER2/neu	30%
Tumor suppressor genes	p53 gene	60–80%
	RB gene	15%

Immunohistochemistry of squamous cell lung carcinoma

Markers	Expression
Cytokeratins	Positive
Carcinoembryonic antigen (CEA)	Positive
Epithelial membrane antigen (EMA)	Positive
Cytoplasmic and intranuclear surfactant	Positive

Fig. 18.52: Squamous cell lung carcinoma shows risk factors, gene mutations, clinical manifestations, immunohistochemistry and metastases.

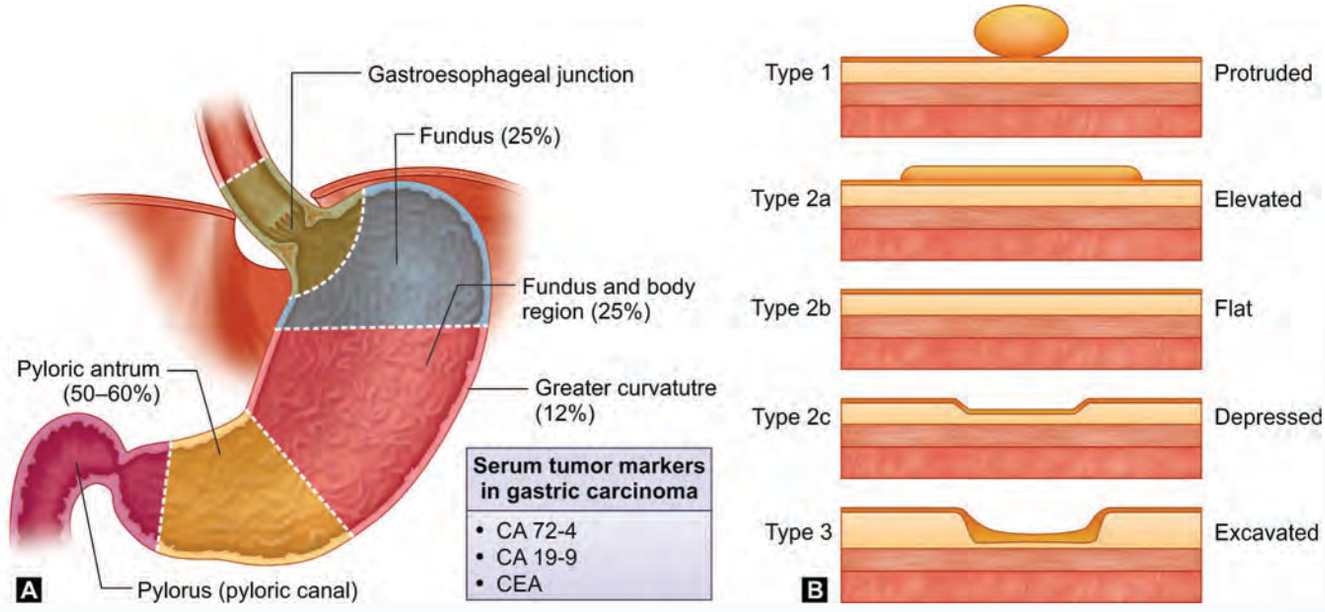
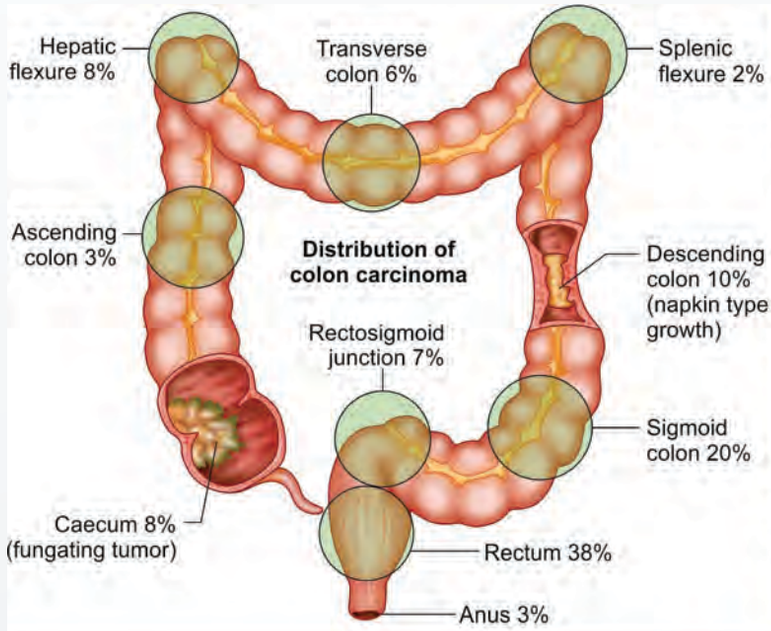


Fig. 20.18: (A) Distribution of gastric carcinoma including serum tumor markers. (B) Endoscopic classification of early gastric cancer (ECG) is defined as involvement of mucosa and submucosa, irrespective of lymph node status. Advanced gastric carcinoma involves muscular coat and beyond.



Risk factors: Colorectal carcinoma

- Age >50 years
- High fat, low fiber diet
- Ulcerative colitis and Crohn's disease
- Familial adenomatous polyposis (FAP)
- Hereditary nonpolyposis colorectal cancer (HNPCC)
- Adenomas (villous, tubular and tubulovillous)
- Peutz-Jeghers syndrome
- Family history of colorectal cancer

Immunohistochemistry: Colorectal carcinoma

Tumor markers	Expression
• Carcinoembryonic antigen (CEA)	Positive
• CK20	Positive
• CDX2 (transcription factor)	Positive
• SAT2 (transcription factor)	Positive
• p53	Positive
• β-Catenin	Positive
• CK7	Focally positive

Serum tumor markers used to detect colorectal carcinoma

Category	*Tumor marker*	*Cancers*	*Category*	*Tumor markers*	*Cancers*
Oncofetal proteins	Carcinoembryonic antigen (CEA)	• **Colon carcinoma** • NSGCT of testis • Gastric carcinoma • Pancreatic carcinoma • Lung carcinoma • Breast carcinoma	Mucins and glycoproteins	CA 19-9	• **Colon carcinoma** • Pancreatic carcinoma
				CA 72-4	• **Colon carcinoma** • Gastric carcinoma

Fig. 20.67: Colorectal carcinoma. Figure shows distribution, risk factors, serum tumor markers and immunohistochemistry.

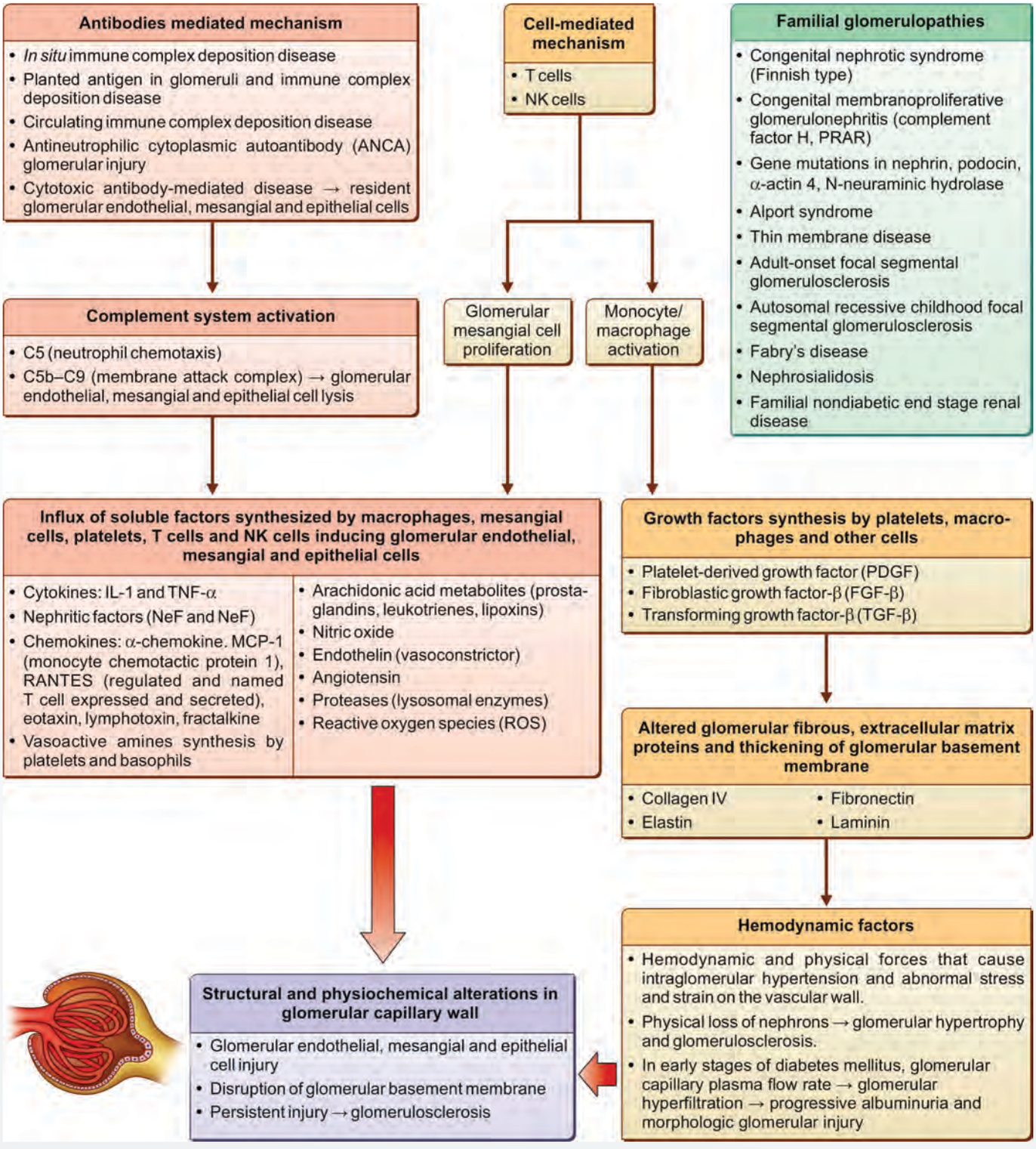


Fig. 22.13: Schematic representation of pathogenesis of glomerulonephritis.

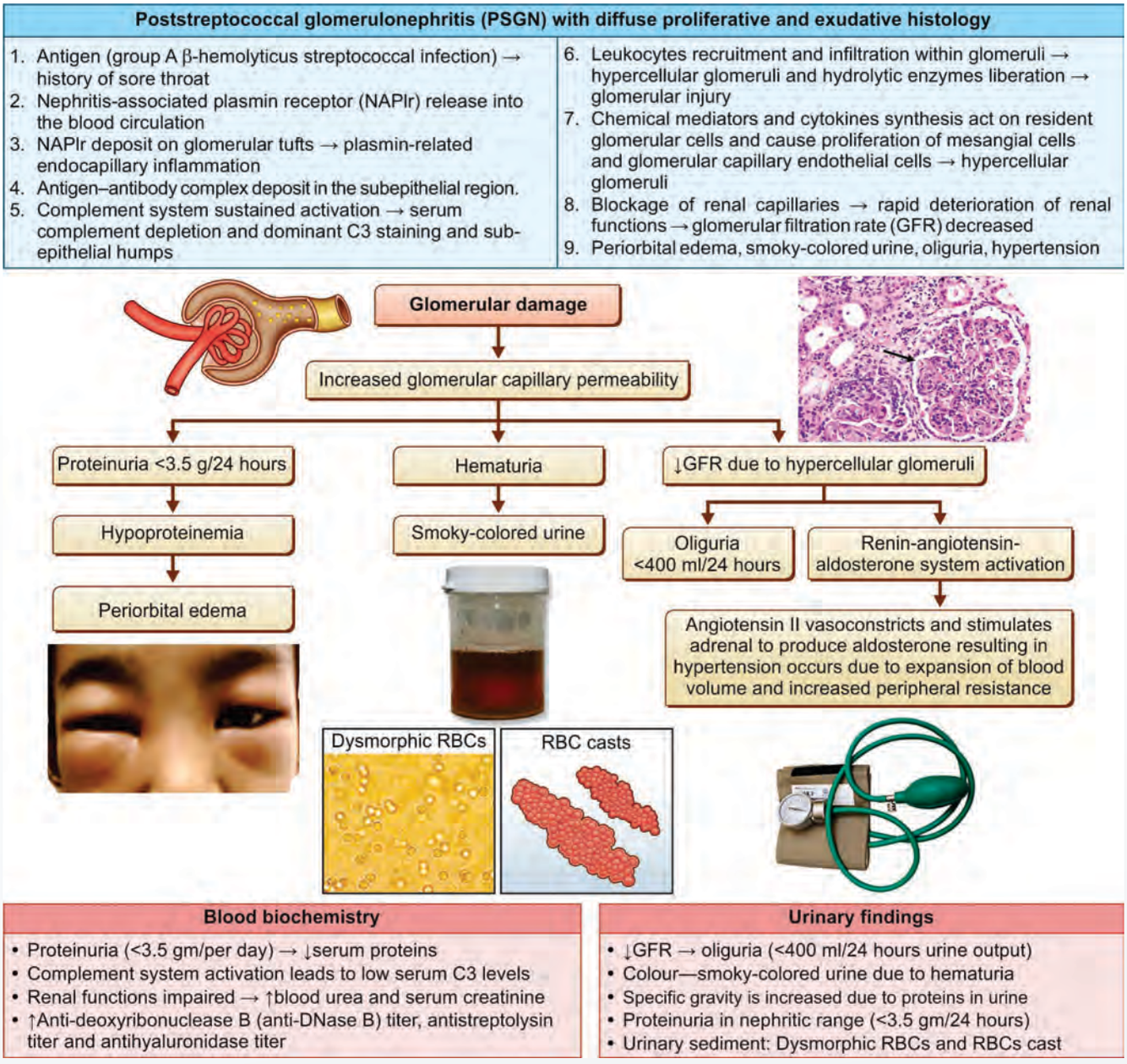


Fig. 22.20: Schematic diagram of pathophysiology of poststreptococcal glomerulonephritis (PSGN). PSGN most often affects children. Patients present with edema (often pronounced facial and orbital edema) especially in the morning, hypertension (due to decreased glomerular filtration rate and activation of renin-angiotensin-aldosterone system), proteinuria in nephritic range, macroscopic hematuria, generalized weakness or anorexia.

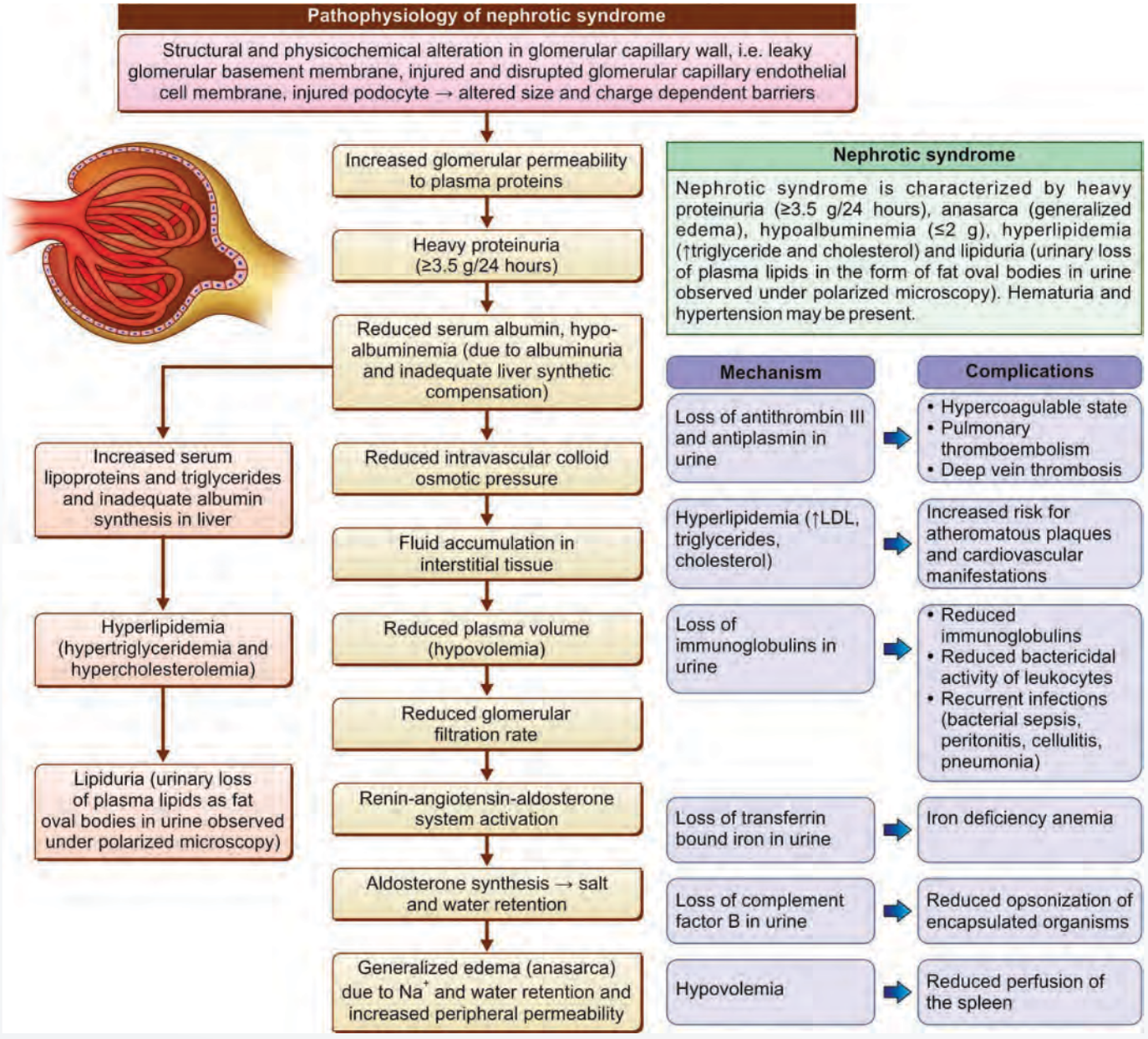


Fig. 22.28: Schematic representation of pathophysiology of nephrotic syndrome. The nephrotic syndrome is characterized by generalized edema, massive proteinuria (≥3.5 gm per day), hypoalbuminemia, hyperlipidemia and hypercholesterolemia. Hematuria, hypertension or azotemia may or may not be present. Nephrotic syndrome can be caused by primary diseases such as minimal change disease, focal segmental glomerulosclerosis, membranous glomerulonephritis; and systemic diseases (diabetes mellitus and systemic lupus erythematosus).

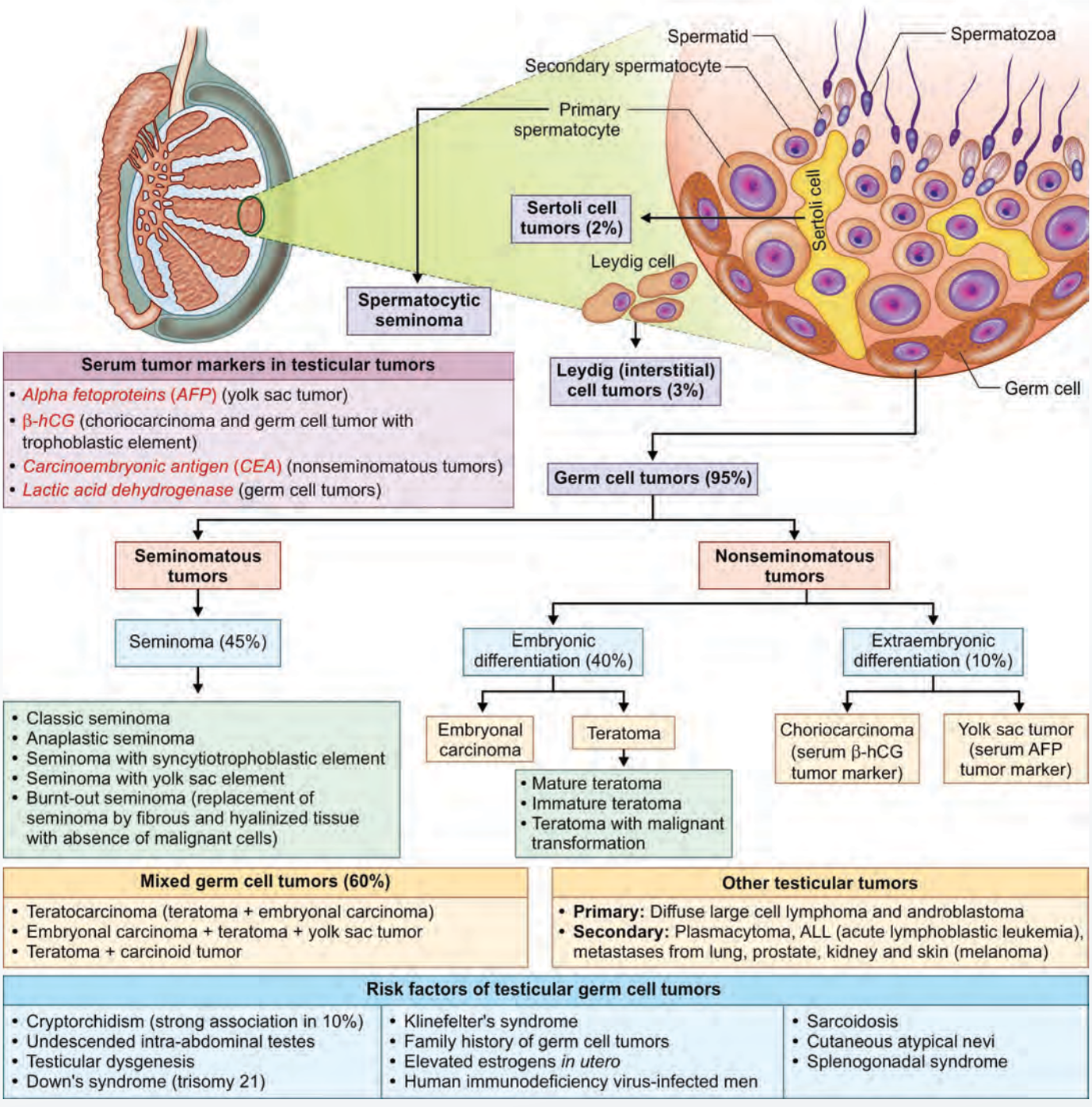


Fig. 23.15: Classification of testicular tumors.

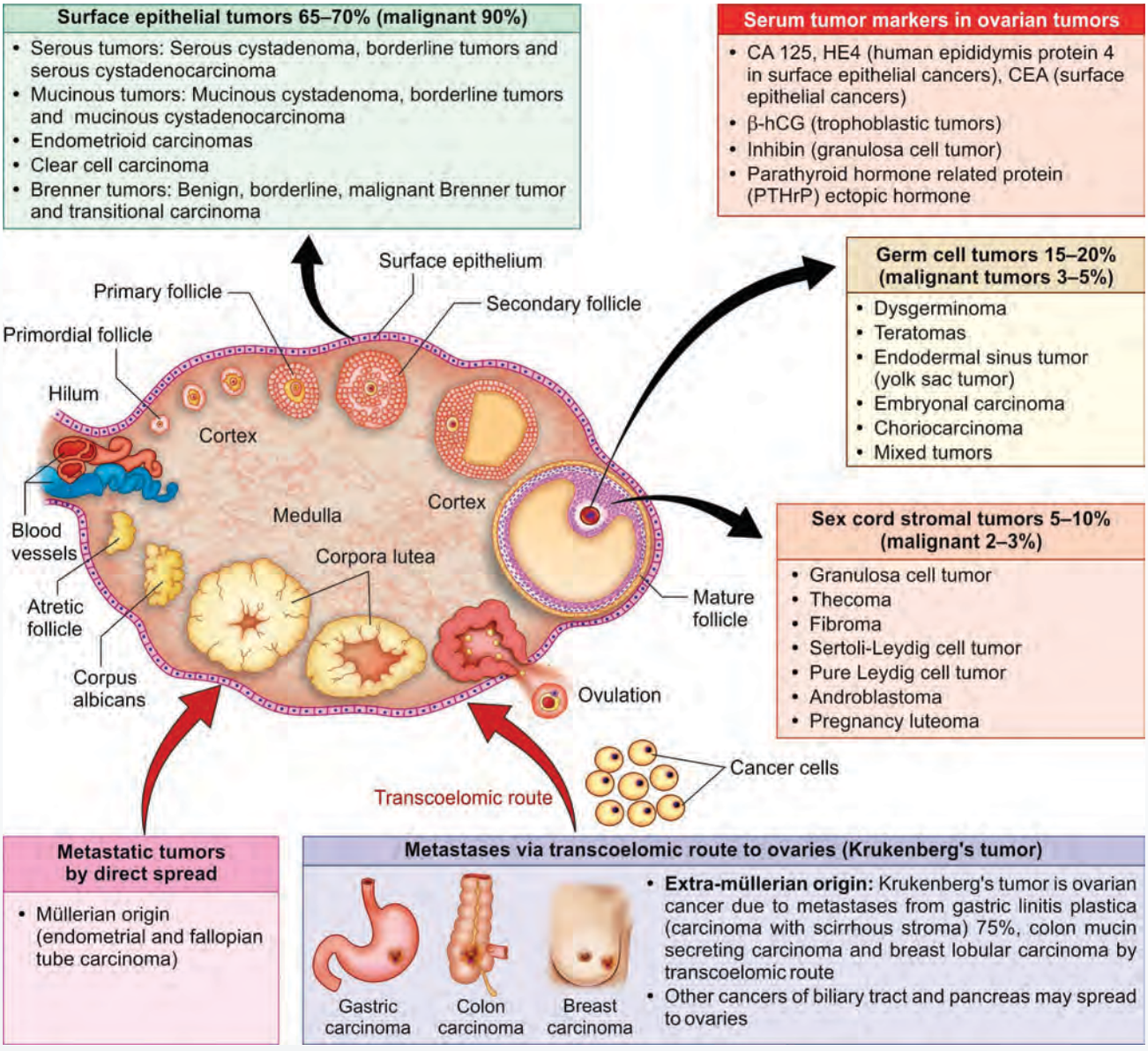


Fig. 24.70: Classification of ovarian tumors.

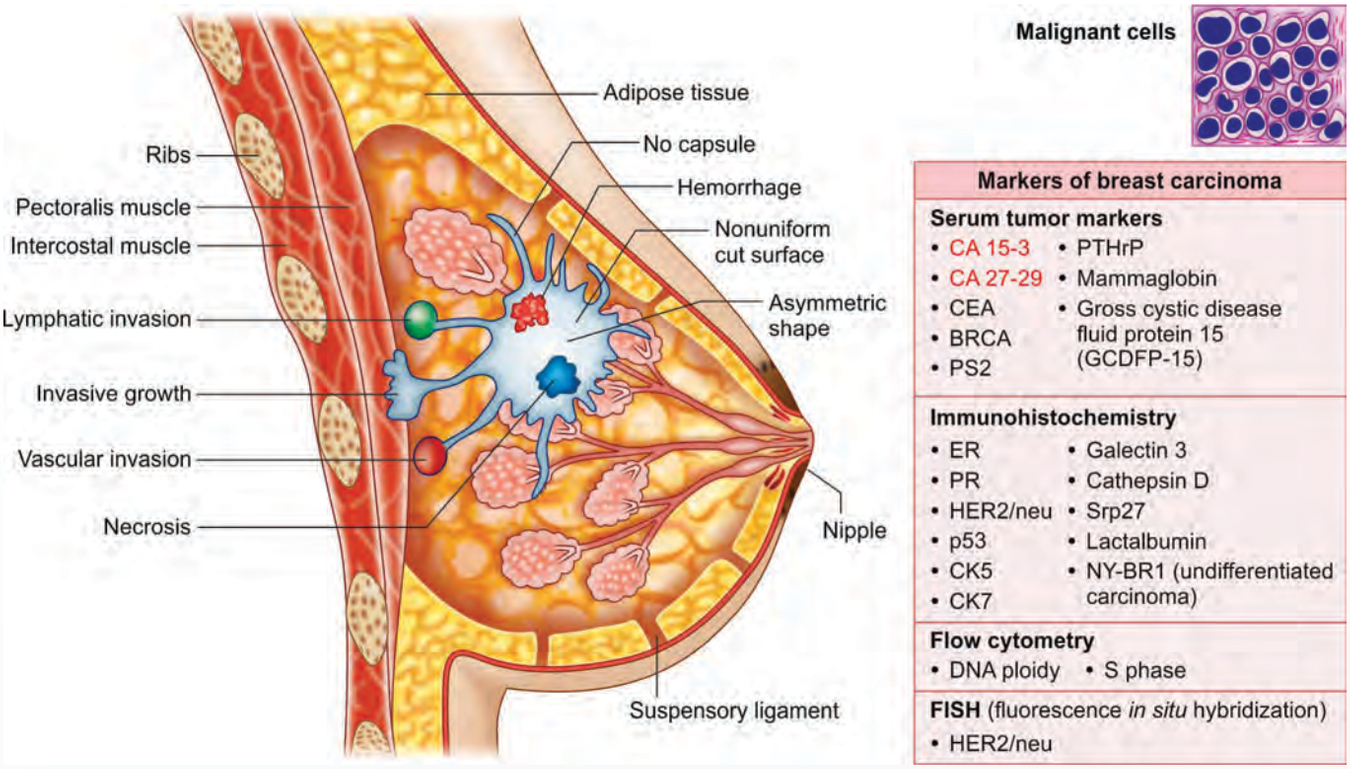


Fig. 25.26: Breast carcinoma shows invasive duct carcinoma with infiltrating margins and areas of hemorrhage and necrosis.

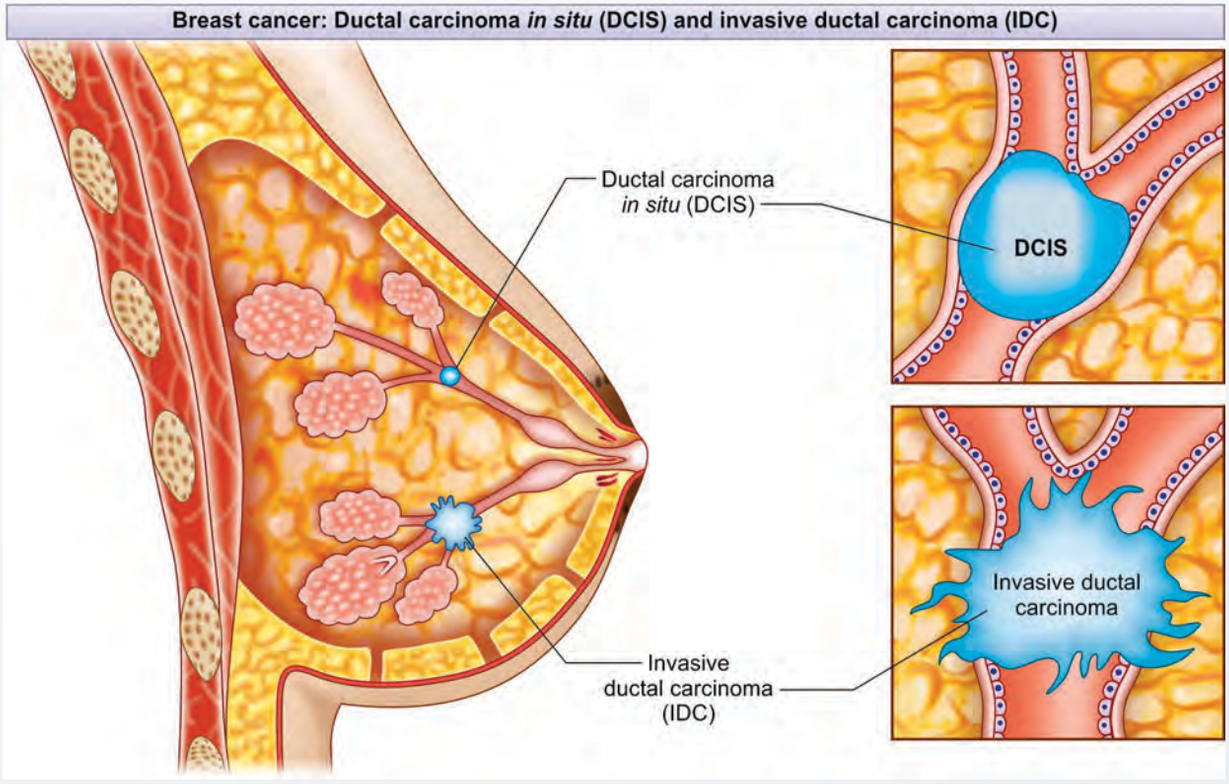


Fig. 25.27: Breast cancer—it shows ductal carcinoma in situ in lower inset and invasive ductal carcinoma with infiltrating margins in upper inset.

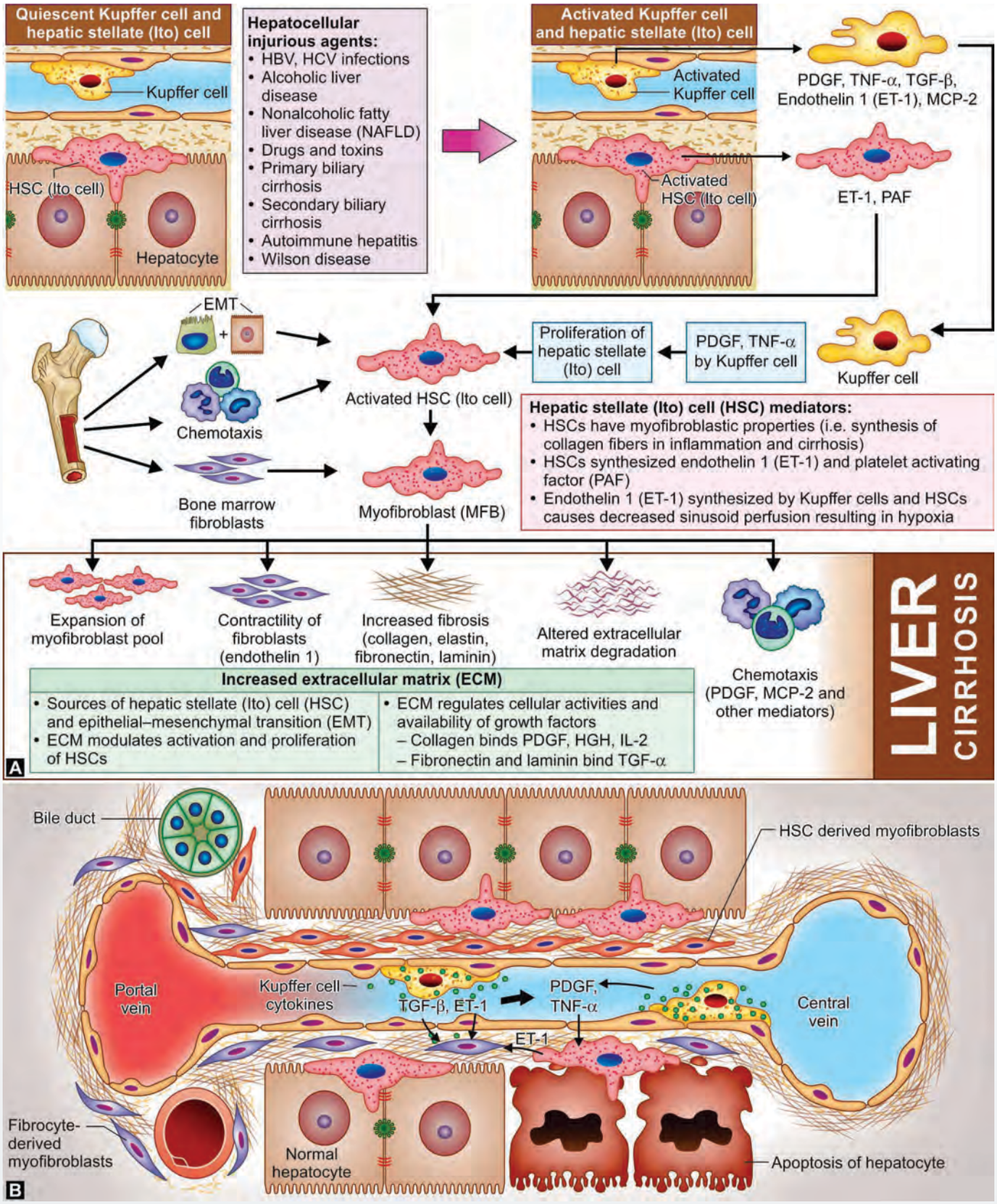


Fig. 21.42: (A) Normal liver morphology, (B) pathogenesis of cirrhosis. Kupffer cell activation and platelet activating factor synthesized by endothelial cells produce cytokines leading to influx of PMNs cells. Endothelial cells synthesize endothelins, which stimulate myofibroblast like Ito cells to synthesize collagen. Contraction of Ito stellate cells results in decreased sinusoidal perfusion and thus cause hypoxia.

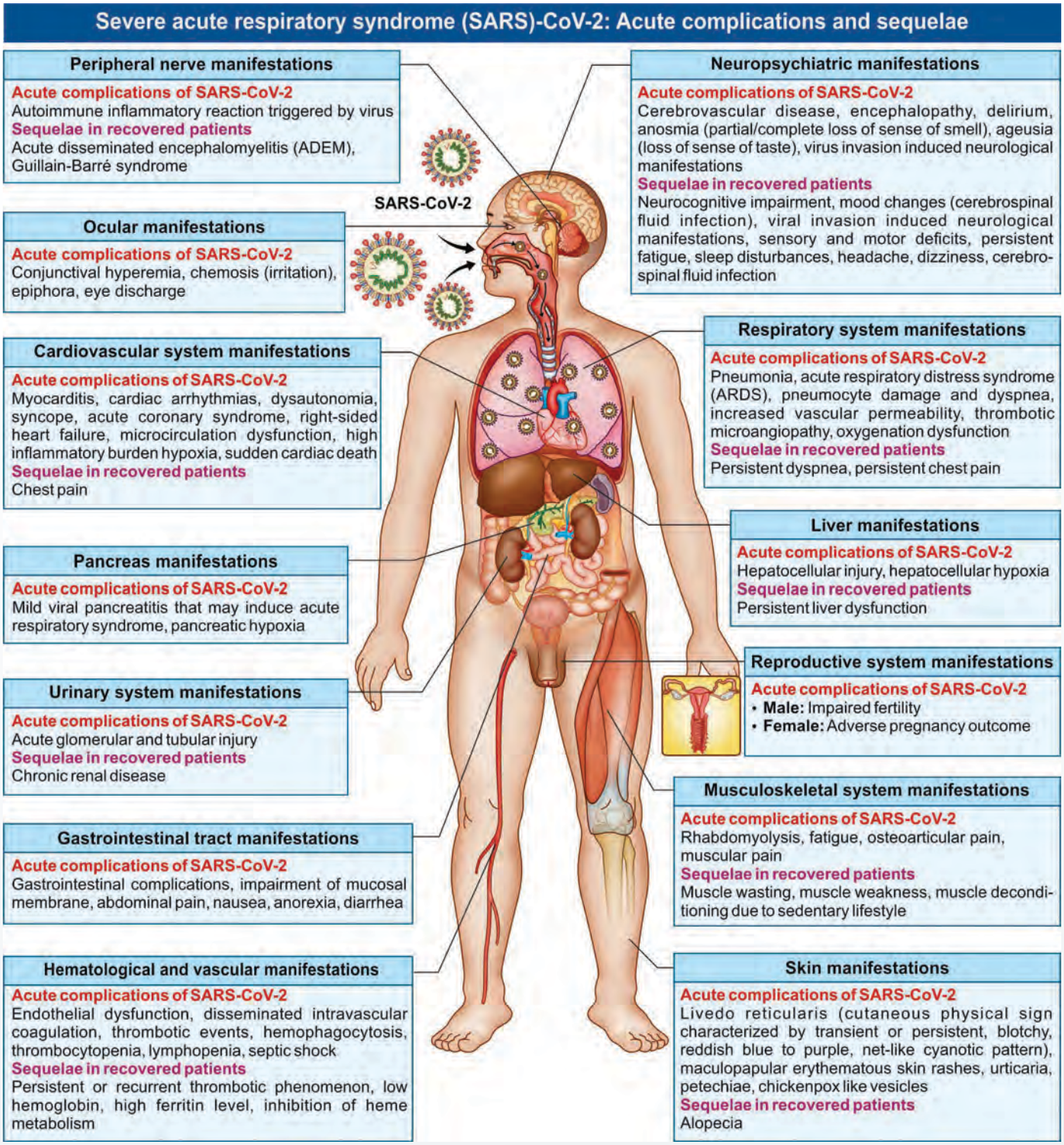


Fig. 7.43: SARS-CoV-2 acute complications and sequelae in COVID-19 survivors.

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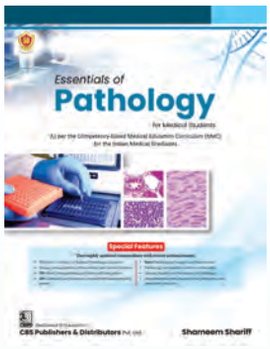

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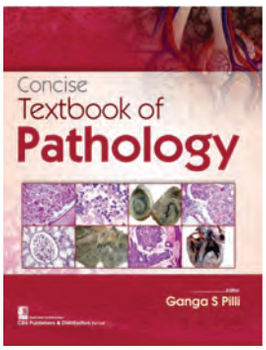

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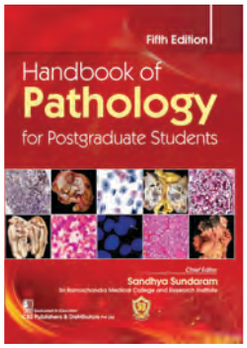

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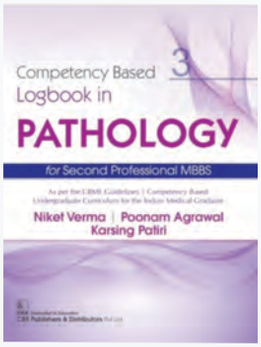

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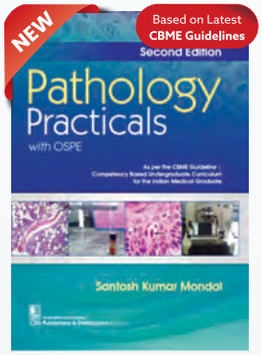

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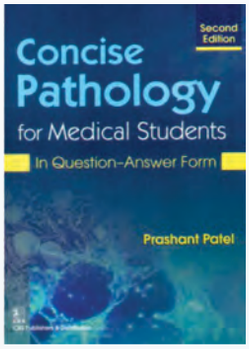

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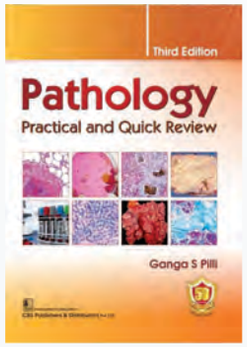

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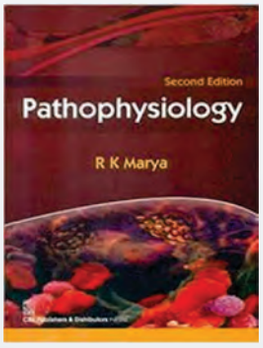

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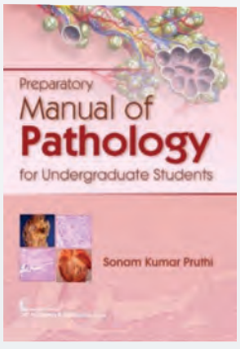

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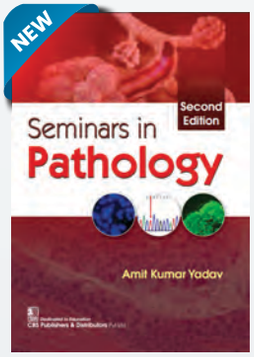

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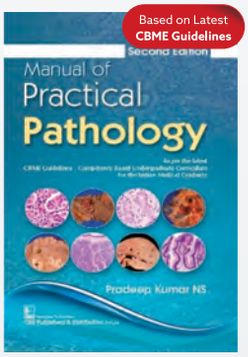

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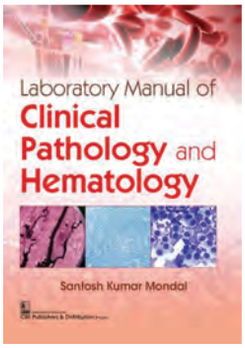

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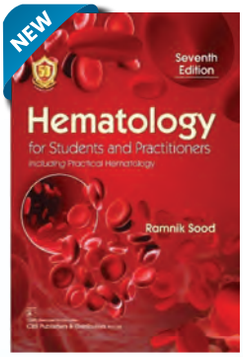

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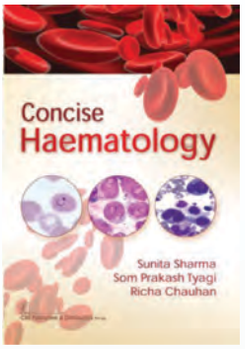

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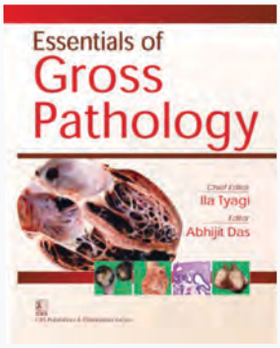

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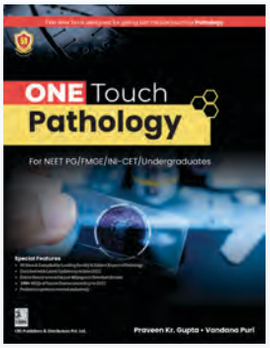

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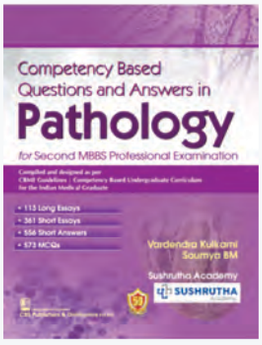

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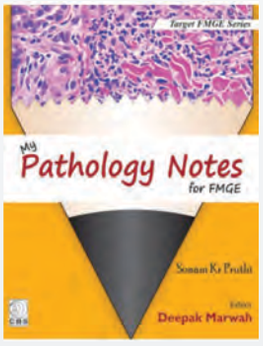

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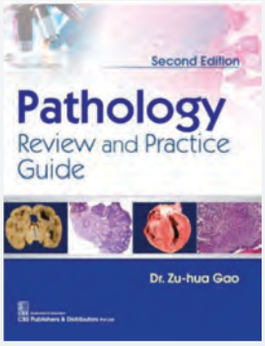

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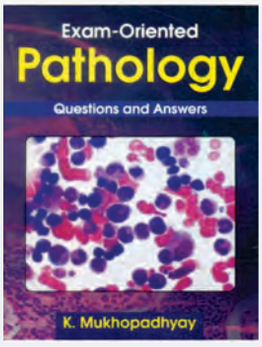

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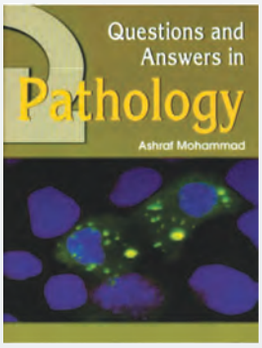

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