Most Updated and Latest Edition 2022

Covering all Recent Updates & Qs up to June 2022 Exams

Includes Recent Updates of WHO 2018 Lung, WHO 2018 Male Genital System and WHO 2018 CNS/Hematopoietic Classifications

Complete Review of

Pathology

& Hematology for NEET & INI-CET

7th EDITION

As per the New Pattern Exams (NEXT) with many Clinical Case-Based Questions

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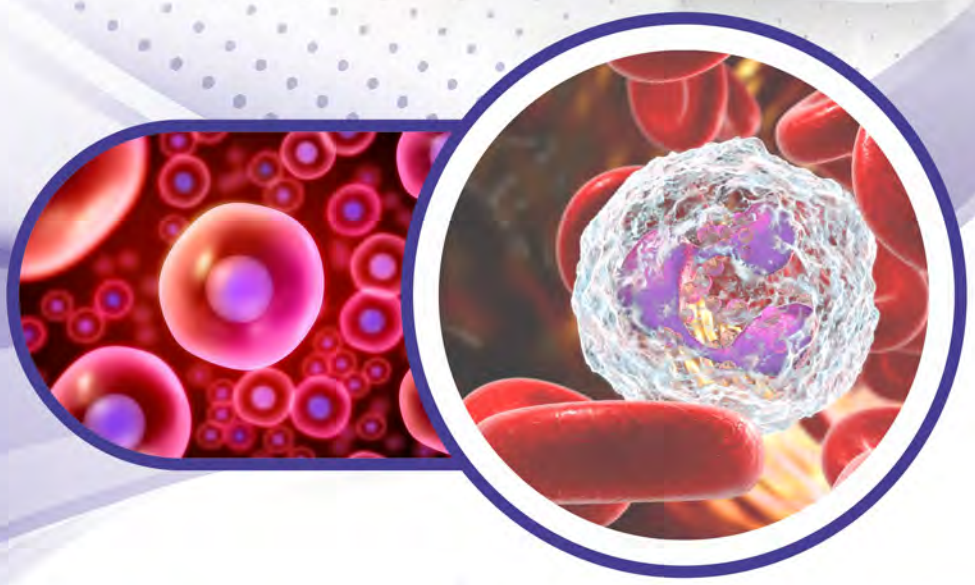

Papers Covered

- INI-CET - 2022-20
- Recent Qs (Jan) 2022 – 2010
- AIIMS June 2020 – 2010
- Expected Clinical Case-Based Qs
- Sample Video Qs
- CBME-Based Subjective Qs with Chapter References

- Written and Compiled by Leading Faculty and Subject Expert of Pathology
- Enriched with Recent/Latest Updates

Includes

2500+	300+	300+	1000+
MCQs of Recent Exams	CBQs	IBQs	Illustrations/Images

CBSPD

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Praveen Kr Gupta • Vandana Puri

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7th Edition

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Preface

"The best way to predict your future is to create it."
—Abraham Lincoln

Achieving **success in Postgraduate Medical Entrance Exams (PGMEE)** and to be able to pursue a specialty of choice in the premier medical institutes of the country has been the ultimate dream of every medical student. To make this dream a reality—**a belief in self, setting realistic goals, 'intelligent hard work', 'smart and productive studying'** and **selection of the right study material** are some of the very important factors.

To cover more than 15 subjects of medical curriculum in a limited time span is definitely not an easy task, however it's not impossible.

As, **impossible itself says I'm possible!**

It is very important to **strengthen your fundamentals and get your basics right! Pathology is the backbone of medical science.** One cannot understand clinical subjects, like **Medicine, Surgery, Pediatrics** and **Gynecology** without being well-versed with the basic pathology of diseases. By the time a student appears for any PGMEE, usually during or after internship, preclinical subjects, like **Pathology tend to fade away from the memory** as the clinical subjects largely dominate the mind.

In the recent NBE pattern examinations, **25–30 MCQs out of 300** are being asked from core pathology. Most of the MCQs asked from Medicine and Surgery also have one or two options related to Pathology, which makes contribution of **50–60 MCQs from pathology; which is almost 15–20% of any examination. In AIIMS there were over 60 Image-based Questions which re-emphasized the importance of conceptual learning with figures rather than nearly solving repeats.**

Solving recent exam questions not only requires **mastery over the repeated MCQs** but also **thorough knowledge** of topics with **special emphasis on concepts and high-yielding facts**.

For the first time Chapter-wise Clinical Pattern Qs have been added to ace your preparation from clinical point of view. Chapter-wise NEXT Pattern Qs have been added as per the changing scenario of upcoming examination.

With so many MCQ-based guidebooks flooding the market, there was a felt need for a book on Pathology which is ***student friendly, lucid, interesting, not full of big paragraphs loaded with heavy information, but which covers all topics and relevant information that can be revised in limited time and is updated with all recent facts and advancements.***

This book is useful **not only** for the students preparing for various PGMEE exams, but also for the **undergraduate students and pathology students pursuing postgraduation**, it will also help in concept building as well as **quick revision**.

Praveen Kumar Gupta

Vandana Puri

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2. CELL ADAPTATION, INJURY AND DEATH

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6. DISEASES OF THE IMMUNE SYSTEM

7. NEOPLASIA

8. DISEASES OF INFANCY AND CHILDHOOD

9. WHITE BLOOD CELLS AND RELATED DISORDERS

10. RED BLOOD CELLS AND RELATED DISORDERS

11. BLEEDING AND COAGULATION DISORDERS

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13. RESPIRATORY SYSTEM AND RELATED DISORDERS

14. GASTROINTESTINAL TRACT AND RELATED DISORDERS

15. LIVER, GALLBLADDER, PANCREAS AND RELATED DISORDERS

16. RENAL SYSTEM AND RELATED DISORDERS

17. MALE AND FEMALE GENITOURINARY TRACT

18. BREAST

19. ENDOCRINE SYSTEM AND RELATED DISORDERS

20. SKIN AND RELATED DISORDERS

21. CENTRAL NERVOUS SYSTEM AND RELATED DISORDERS

22. BLOOD BANKING AND TRANSFUSION MEDICINE

23. TUMORS OF SOFT TISSUE AND HEAD AND NECK

24. DISEASES OF MUSCLES

25. TUMORS OF BONE AND JOINTS

26. RECENT TECHNIQUES IN PATHOLOGY

27. STAINS AND FIXATIVES

CBME-Based Subjective Questions with Chapter References*

Competencies	Subjective Questions	For Answer Refer to Chapter
	PATHOLOGY	
	Topic: Introduction to Pathology	
PA1.1	Describe the role of a pathologist in diagnosis and management of disease	–
PA1 2	Enumerate common definitions and terms used in pathology	–
PA1.3	Describe the history and evolution of pathology	–
	Topic: Cell Injury and Adaptation	
PA2.1	Demonstrate knowledge of the causes, mechanisms, types and effects of cell injury and its clinical significance	CHAPTER 2
PA2.2	Describe the etiology of cell injury. Distinguish between reversible-irreversible injury: mechanisms; morphology of cell injury	CHAPTER 2
PA2.3	Intracellular accumulation of fats, proteins, carbohydrates, pigments	CHAPTER 2
PA2.4	Describe and discuss Cell death- types, mechanisms, necrosis, apoptosis (basic as contrasted with necrosis), autolysis	CHAPTER 2
PA2.5	Describe and discuss pathologic calcifications, gangrene	CHAPTER 2
PA2.6	Describe and discuss cellular adaptations: atrophy, hypertrophy, hyperplasia, metaplasia, dysplasia	CHAPTER 2
PA2.7	Describe and discuss the mechanisms of cellular aging and apoptosis	CHAPTER 2
PA2.8	Identify and describe various forms of cell injuries, their manifestations and consequences in gross and microscopic specimens	CHAPTER 2
	Topic: Amyloidosis	
PA3.1	Describe the pathogenesis and pathology of amyloidosis	CHAPTER 6
PA3.2	Identify and describe amyloidosis in a pathology specimen	CHAPTER 6
	Topic: Inflammation	
PA4.1	Define and describe the general features of acute and chronic inflammation including stimuli, vascular and cellular events	CHAPTER 3
PA4.2	Enumerate and describe the mediators of acute inflammation	CHAPTER 3
PA4.3	Define and describe chronic inflammation including causes, types, non-specific and granulomatous; and enumerate examples of each	CHAPTER 3
PA4.4	Identify and describe acute and chronic inflammation in gross and microscopic specimens	CHAPTER 3
	Topic: Healing and Repair	
PA5.1	Define and describe the process of repair and regeneration including wound healing and its types	CHAPTER 3
	Topic: Hemodynamic Disorders	
PA6.1	Define and describe edema, its types, pathogenesis and clinical correlations	CHAPTER 4
PA6.2	Define and describe hyperemia, congestion, hemorrhage	CHAPTER 4
PA6.3	Define and describe shock, its pathogenesis and its stages	CHAPTER 4
PA6.4	Define and describe normal haemostasis and the etiopathogenesis and consequences of thrombosis	CHAPTER 4
PA6.5	Define and describe embolism and its causes and common types	CHAPTER 4
PA6.6	Define and describe Ischaemia/infarction its types, etiology, morphologic changes and clinical effects	CHAPTER 4
PA6.7	Identify and describe the gross and microscopic features of infarction in a pathologic specimen	CHAPTER 4

**Important competency-based topics covered*

Contd...

Latest Exam Questions 2022

1. INI-CET May 2022 (Recall Questions)
2. Recent Questions May 2022

INI-CET MAY 2022 (RECALL QUESTIONS)

1. NK cell marker is:
a. CD 3 b. CD 68
c. CD 94 d. CD 25

2. Ectopic tissue in Meckel's diverticulum:
a. Thyroid and gastric tissue
b. Colon and pancreas
c. Gastric and pancreas
d. Gastric and colon

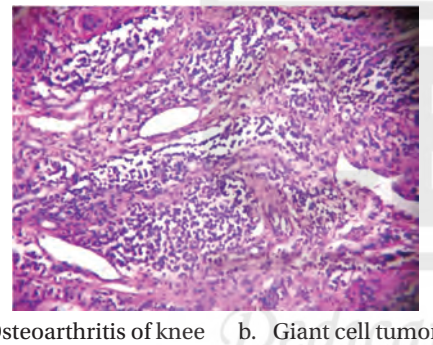
3. All are AIDS defining malignancies; except:
a. Non Hodgkin's lymphoma
b. Invasive cervical carcinoma
c. Melanoma
d. Kaposi sarcoma

4. Anemia of chronic disease are all; except:
a. Serum hepcidin high b. Serum ferritin high
c. Chronic infection d. Iron store adequate

5. Which of the following is X linked dominant?
a. Rett syndrome
b. DMD
c. Fragile X syndrome
d. Charcot Marie Tooth disorder
Red - rett
Rose- rickets
For-fragile X syndrome
Child- charcot marie

6. Ratio of T and B lymphocytes in normal healthy individual:
a. 1:1 b. 1:3
c. 4:1 d. 1:4

7. A 72-year-old male came with complaint of unilateral knee pain. X-ray examination showed reduced joint space. Pathological findings shown below is of :



a. Osteoarthritis of knee b. Giant cell tumor
c. Rheumatoid arthritis d. Lyme disease

8. Match the following :

a. Osteosarcoma	i. Giant cells
b. Choriocarcinoma	ii. Codman triangle
c. Giant cell tumor	iii. Syncytiotrophoblast
d. Ewing's sarcoma	iv. Small round blue cells

a. a – i, b- ii , c- iii, d- i
b. a- ii, b- iv, c- ii, d- i
c. a- ii, b- iii, c- i, d- iv
d. a- i, b- iv, c- iii, d- ii

9. Neurooendocrine tumors are seen in all; except:
a. MTC b. Pituitary adenoma
c. Paraganglioma d. Adrenal cortical tumor

10. Match the following:

a. Plag1	i. Neuroblastoma
b. Myc	ii. Burkitt lymphoma
c. Mycn	iii. Retinoblastoma
d. Rb	iv. Pleomorphic adenoma

a. a – iv, b- i , c- iii, d- ii
b. a- ii, b- iv, c- iii, d- i
c. a- ii, b- iii, c- i, d- iv
d. a- iv, b- ii, c- i, d- iii

11. Which is familial?
a. Retinoblastoma b. Retinitis pigmentosa
c. Myopia d. Poag

12. Blood transmission requires donor blood screening of; except:
a. Malaria b. HIV
c. Dengue d. Hep B

13. Differential effects of the same gene in different parent is:
a. Mosaicism b. Genomic epigenetics
c. Epigenetics d. Anticipation

14. A 50-60-year-old female complains of fatigue and dyspnea. O/E - HB was found to be 6 gm/dl. Diagnosis:
a. Poikilocytes
b. Microcytic hypochromic
c. Macrocyte hypochromic
d. Target cell

15. Boy with low platelet with malena and atopic dermatitis. What is the diagnostic investigation?
a. Wasp gene mutation
b. Anti platelet antibodies
c. BM evaluation

16. What is not seen in pleomorphic adenoma
a. Myoblastic
b. Keratin pearls. (Sq. Cell carcinoma)
c. Chondroid differentiation (chondromyxoid matrix)
d. Perineural invasion (rare)

17. Match the following:

a. Prealbumin	i. Fatty acid
b. Albumin	ii. Hemoglobulin
c. Haptoglobulin	iii. Heme
d. Hemopexin	iv. Thyroid

a. a – iv, b- i , c- ii, d- iii
b. a- ii, b- iv, c- ii, d- I
c. a- ii, b- iii, c- i, d- iv
d. a- iv, b- ii, c- i, d- ii

18. Banding technique used in dicentric chromosome:
a. G b. NOR
c. C d. R

19. Not a part of Innate Immunity:
a. Alpha defensins
b. B lymphocytes
c. Delta gamma T lymphocytes
d. Lectin pathway

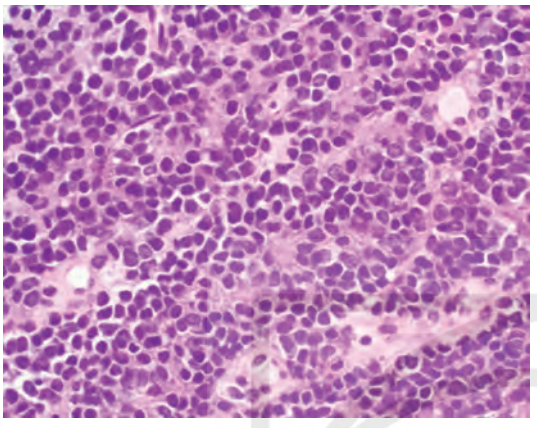
20. Toulidene stain stains:
a. Mast cell b. Plasma cells
c. Macrophages d. Nuclei

21. Cell in cell appearance seen in:
a. Necrosis b. Apoptosis
c. Necroptosis d. Entosis

Ans.

1. c
2. c
3. c
4. a
5. a,c,d
6. c
7. a
8. c
9. d
10. d
11. a,b,d
12. c
13. d
14. b
15. a
16. c
17. a
18. a
19. b
20. a
21. d

22. A 15-year-old boy with lesion in tibia and diaphyseal having periosteal reaction HPE shows:

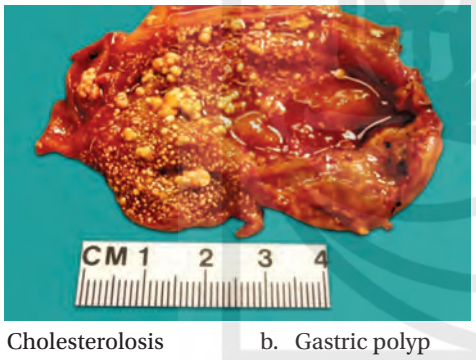


a. Ewing's sarcoma
b. Osteosarcoma
c. Metastatic
d. Neuroblastoma

23. MHC 1 bind to antigen and activated:

a. Cytotoxic
b. Helper
c. NK cell
d. Suppressor T cell

24. Image shows:



a. Cholesterolosis
b. Gastric polyp
c. Ga cancer
d. Strawberry bladder

25. Blood transmission requires donor blood screening of; except:

a. Malaria
b. HIV
c. Dengue
d. Hep B

26. Liver secretes substance A to decrease the iron absorption by reducing another substance expression. Select the correct combination:

a. Haptoglobin- DMT
b. Ceruloplasmin- DMT
c. Hepcidin- ferroportin
d. Transferrin - Transferrin R

27. What is correct about Autophagy:

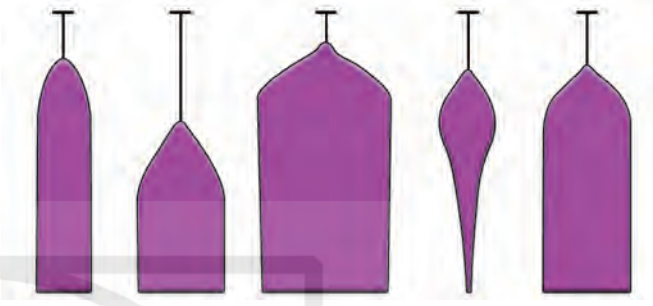
a. Combines lysosome to form autophagolysosome
b. Binds to all cell organelles
c. Combines with hydrolases
d. Internal process of a cell

RECENT QUESTIONS MAY 2022

28. Single nucleotide change resulting in stop codon is called:

a. Missense
b. Nonsense
c. Point mutation
d. Silent

29. A trauma patient was to undergo emergency laparotomy, they wanted to monitor the coagulation studies. Which investigation for graph is shown below?



a. Thrombography
b. Thromboelastography
c. Ultragraphy
d. Plethysmography

30. What will increase lifespan?

a. Regular exercise (Walking for 30 mins)
b. Decreasing stress
c. Decrease calorie by 30%
d. Meditation

31. Which is AR inheritance?

a. Cystic fibrosis
b. Huntington's disease
c. Achondroplasia
d. Treacher collins

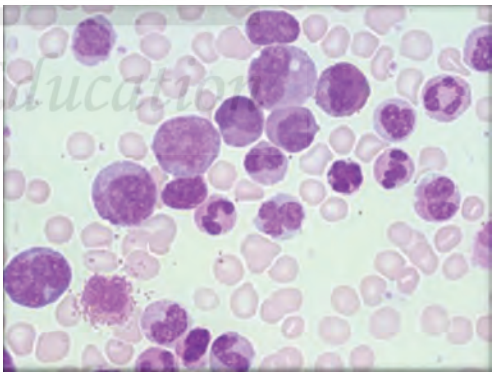
32. True about NET are all; except:

a. Seen in sepsis
b. Seen with bacteria
c. Mitochondrial DNA is seen
d. It is chromatin with antibacterial enzymes

33. Cause of hypochromic microcytic anemia with reduced RBC indices and target cells present. RBC count of 5.2*10.9/ul, MCV = 65 FC, next investigation?

a. HbA2
b. Serum ferritin
c. Serum folate
d. BM evaluation

34. 56/M c/o TLC high, platelets high, High Hb, dragging sensation in abdomen, PS with metamyelocytes, myelocytes on PS. O/e there is massive splenomegaly, mutation seen is:



a. t9,22
b. 8,14
c. 8,11
d. 11, 14

Ans.

22. a
23. a
24. a
25. c
26. c
27. a
28. b
29. b
30. c
31. a
32. c
33. a
34. a

Answers with Explanations

INI-CET MAY 2022 (RECALL QUESTIONS)

1. Ans. (c) CD94

CD94 is NKG2D . It is a receptor of NK cells.

2. Ans. (c) Gastric and pancreas

Ectopic tissue in meckel's diverticulum is Gastric thereafter its pancreatic.

3. Ans. (c) Melanoma

- Candidiasis of esophagus trachea or lungs
- Cervical Cancer (invasive)
- Coccidiomycosis
- Cryptococcosis
- Cryptosporidiosis
- Isosporiosis
- Cytomegalovirus disease
- HSV (>1 month duration)
- Disseminated histoplasmosis
- HIV encephalopathy
- Kaposi's sarcoma
- Lymphoma (CNS or Burkitt's)
- Mycobacterium avium complex
- Mycobacterium tuberculosis (pulmonary)
- Pneumocystis pneumonia
- Recurrent bacterial pneumonia
- Progressive multifocal leukoencephalopthy
- Recurrent salmonella septicemia
- Toxoplasmosis the brain
- HIV wasting syndrome

4. Ans. (a) Serum hepcidin high

5. Ans. (a) Rett syndrome; (c) Fragile X syndrome; (d) Charcot marie tooth disorder

Red - rett
Rose- rickets

6. Ans. (c) 4:1

T = 60-70%
B= 10-20%

7. Ans. (a) Osteoarthritis of knee

Dense inflammation with fibrosis is suggestive of osteoarthritis

8. Ans. (c) a- ii, b- iii, c- i, d- iv

9. Ans. (d) Adrenal cortical tumor

10. Ans. (d) a- iv, b- ii, c- i, d- iii

11. Ans. (a) Retinoblastoma, (b) Retinitis pigmentosa and (d) Poag

12. Ans. (c) Dengue

13. Ans (d) Anticipation

14. Ans. (b) Microcytic hypochromic

15. Ans. (a) Wasp gene mutation

T- thrombocytopenia
E- eczema
I- infection

16. Ans. (c) Chondroid differentiation (chondromyxoid matrix)

17. Ans. (a) a – iv, b- i , c- ii, d- iii

18. Ans. (a) G

GIT
Mucosa

19. Ans. (b) B lymphocytes

20. Ans. (a) Mast cell

21. Ans. (d) Entosis

E-cadherin mediated cell–cell adhesion between two identical cells and the activation of actin–myosin contraction.

22. Ans. (a) Ewing's sarcoma

Small round blue cell

23. Ans. (a) Cytotoxic

24. Ans. (a) Cholesterolosis

25. Ans. (c) Dengue

26. Ans. (c) Hepcidin- ferroportin

27. Ans. (a) Combines lysosome to form autophagolysosome

RECENT QUESTIONS MAY 2022

28. Ans. (b) Nonsense

29. Ans. (b) Thromboelastography

30. Ans. (c) Decrease calorie by 30%

31. Ans. (a) Cystic fibrosis

32. Ans. (c) Mitochondrial DNA is seen

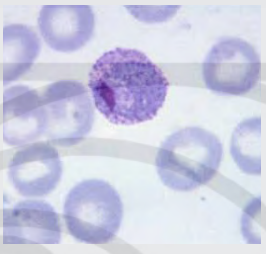
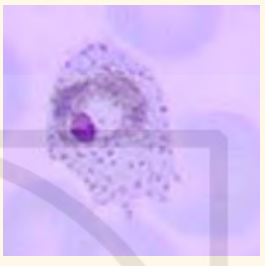
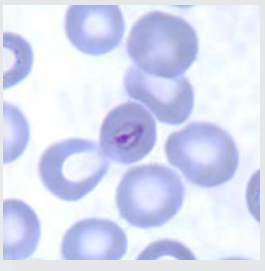
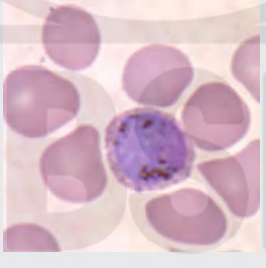
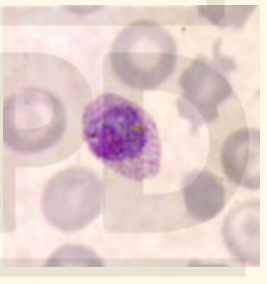
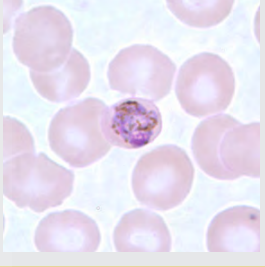
33. Ans. (a) HbA2

Annexures

Annexure 1. Important Special Stains and Fixatives

Name of stain	Elements stained
For Microorganisms	
Ziehl-Neelsen stain, Kinyoun stain	Acid-Fast Organism
May - Grünwald Giemsa Stain	Bacteria, blood elements
Gram stain	Bacteria
Toluidine Method, Steiner method	Helicobacter pylori (stained black)
Grocott's methenamine silver method, PAS	Fungi
Macchiavello stain	Rickettsia and viral inclusions
Shikata's orcein stain	Hepatitis B Antigen
Mucicarmine	Cryptococcus
Warthin – Starry method	Spirochetes
Gomori Methenamine silver	Fungus (stained black)
Calcofluor white	Acanthamoeba (stained white)
For Connective tissue and lipids	
Hematoxylin & Eosin stain (H&E)	All tissues (most commonly used stain)
Trichrome Stain	Collagen
Verhoeff - Van Gieson's stain (Best for Elastin)	Elastic fibers
Luna stain	Elastin & Mast cells
Silver Methenamine stain	Reticulin
Oil red O stain (on Fresh specimen/Frozen section) ***Sudan black (on fixed specimen)***	Fat
Mallory's PTAH stain	Muscle striations
MSB (martius scarlet blue) (1st stain to stain fibrin in various stages)	Fibrin
PAS, Silver Methenamine stain	Basement membrane
Bielschowsky (silver stain)	Neurofibrillary tangles, Senile plaques
Luxol fast blue	Myelin
Papanicolau stain	Cervical Exfoliative cytology
For Carbohydrates	
PAS	Glycogen/neutral mucin or mucoprotein
Alcian blue ***(at pH 2.5: positive for acid mucopolysaccharides)***	Differentiates Acid & neutral mucopolysaccharides
Mucicarmine stain (specific)	Acidic epithelial Mucin
Alcian blue at pH 1	Highly acidic mucins (sulphated mucins)

Annexure 19. Morphological Differentiation of Malaria Parasites

	P. falciparum	*P. vivax*	*P. ovale*	*P. malariae*
Infected red cells	Normal size,[a] Maurer's clefts[b]	Enlarged; Schuffner's dots[c]	Enlarged; oval and fimbriated; Schuffner's dots[c]	Normal or microcytic; stippling not usually seen
Ring forms (early trophozoites)	Delicate; frequently 2 or more; accole forms;[d] small chromatin dot  Falciparum Ring forms	Large, thick; usually single (occasionally 2 in cell; large chromatin dot)  Vivax Trophozoite	Thick compact rings 	Very small, compact rings 
Later trophozoites	Compact, vacuolated; sometimes 2 chromatin dots	Amoeboid; central vacuole; light blue cytoplasm	Smaller than *P. Vivax,* slightly amoeboid	Band across cell; deep blue cytoplasm
Schizonts	18-24 merozoites filling 2/3 of cell	12-24 merozoites, irregularly arranged	8-12 merozoites filling 3/4 of cell	6-12 merozoites in daisy-head around central mass of pigment
Pigment	Dark to black clumped mass	Fine granular; yellow brown	Coarse light brown	Dark, prominent at all stages
Gametocytes	Crescent of sausage-shaped; diffuse chromatin; single nucleus  Falciparum gametocyte	Spherical compact, almost fills cell; single nucleus 	Oval, fills 3/4 of cell; similar to but smaller than P. vivax 	Round; fills 1/2 to 2/3 of cell; similar to *P. vivax* but smaller, with no Schuffner's dots 

Annexure 20. Autoantibodies in Autoimmune Disease

Autoantibodies	Disease	Test sensitivity (%)
Antiacetylcholine receptor	Myasthenia gravis	>85
Antibasement membrane	Goodpasture syndrome	>90
Anticentromere	CREST syndrome Diffuse systemic sclerosis	40 <2
Antiendomysial IgA	Celiac disease	95
Antigliadin IgA	Celiac disease	80
Antihistone	Drug-induced lupus	90-95
Anti-insulin	Systemic lupus erythematosus, Type 1 diabetes	50-70 50
Anti-islet cell	Type 1 diabetes	75-80
Anti-intrinsic factor	Pernicious anemia	60
Antiparietal cell	Pernicious anemia	90
Antimicrosomal	Hashimoto thyroiditis	97
Anti-Smith (Sm)	Systemic lupus erythematosus	20-30
Anti-SS-A (Ro)	Sjögren syndrome Systemic lupus erythematosus	70-95 30-50
Anti-SS-B (La)	Sjögren syndrome	60-90
Antithyroglobulin	Systemic lupus erythematosus Hashimoto thyroiditis	10-15 85
Antitissue transglutaminase IgA	Celiac disease	98
AntiDNA topoisomerase	Diffuse systemic sclerosis	30-70
Antimitochondrial	CREST syndrome Primary biliary cirrhosis	10-20 90-100
Antimyeloperoxidase	Microscopic polyangiitis	80 (p-ANCA)
Antinuclear	Systemic lupus erythematosus Systemic sclerosis Dermatomyositis	-100 70-90 <30
Antiproteinase 3	Polymyositis MCTD Primary biliary cirrhosis Wegener granulomatosis	30-60 95-99 50 >90 (c-ANCA)
Antiribonucleoprotein	MCTD Systemic lupus erythematosus	85 30-40
Anti-TSH receptor	Graves disease	85

1

Cell as a Unit of Health and Disease

Key Points

- Human genome contains **3.2 billion DNA base pairs.**
- **The most common forms of DNA variation in the human genome** is **single-nucleotide polymorphisms.**
- **Epigenetics is heritable changes**[Q] in **gene expression, not caused by** alterations in **DNA sequence.**
- Proteins involved in tight junctions are **occludin, claudin, zonulin and catenin.**
- **All growth factors are proto-oncogenes, except TGFβ,**[Q] **which is a tumor suppressor gene.**
- **Type IV collagen is a** nonfibrillary collagen which contribute to the structures of planar **basement membranes.**
- **Bone morphogenic protein (BMP) is both mitogenic and morphogenic.**
- **Collagen I is the most abundant collagen in the body.**
- **Stem cells are characterized by two important properties: Self-renewal and asymmetric division.**
- **Transdifferentiation**[Q]**: Irreversible** conversion of cells from **one differentiated cell type to another.**
- **Shinya Yamanaka** and **Sir John Gurdon** were awarded **Nobel Prize for IPSC in 2012.**

Key Recent Updates

CRISPR–clustered regularly interspaced short palindromic repeats forms genome editing technology.

THE HUMAN GENOME

- Human genome contains **3.2 billion DNA base pairs.**Q
- **20,000 protein-encoding genes**Q, comprising only **1.5% of the genome.**Q
- Function of these **protein encoding** genes: **enzymes, structural components, and signaling molecules** and to **assemble and maintain** all cells in the body.

Noncoding DNA

- It refers to the **98.5%** of human genome that does **not encode proteins.**
- **The amount of noncoding DNA varies greatly among species,** e.g., in bacteria, only 2% of genome is noncoding DNA.
- Noncoding DNA is **also transcribed into functional noncoding RNA molecules (e.g., transfer RNA, ribosomal RNA, and regulatory RNAs).**

R9th Latest Update

ENCODE (ENCyclopedia of DNA Elements) project: 2007

- This project has systematically **mapped regions of transcription, transcription factor association, chromatin structure and histone modification.**
- **Striking conclusion: 80% of the human genome, even the noncoding regions** either **binds proteins** or **regulate gene expression.**

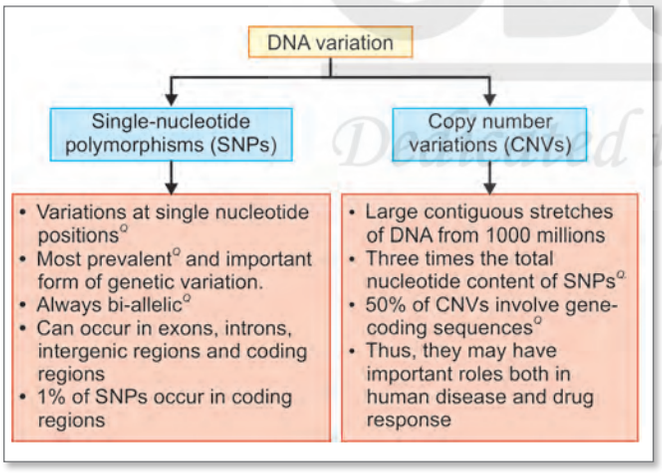
Major **classes** of functional **nonprotein-coding sequences:**

Nonprotein coding sequences	Characteristics
Promoter and enhancer regionsQ	Provide **binding sites** for transcription factors
Binding sites for factors	**Organize and maintain** higher order **chromatin structures**
Noncoding regulatory RNAs	Regulate gene expression: **miRNAs** and **long noncoding RNAs**
Mobile genetic elementsQ ***(transposons/"jumping genes")***	Segments **that move around the genome**, exhibiting **wide variation** in number and positioning; Role in gene regulation and chromatin organization
Special structural regions of DNA	Chromosome ends (**Telomeres)** and "tethers" **(centromeres)**

POLYMORPHISM

Any two individuals share greater than 99.5% of their DNA sequences.Q ***So what is the reason of genetic variations?***
The most common forms of DNA variation in the human genome is shown in Flowchart 1.

Flowchart 1: DNA variation in human genome



Role of SNPs

- SNPs located in **noncoding regions** are **regulatory elements**Q in the genome.
- They **alter gene expression**Q and have **direct influence** on **disease susceptibility.**
- Even, if any SNP has no effect on gene function **(Neutral SNP)**Q, it may be coinherited with the "actual disease causing gene," if located close to that gene → "**Linkage disequilibrium"**Q
- May act as **markers of multigenic complex diseases,** e.g., diabetes, hypertension.

Epigenetics

- ***Definition***
  - **Heritable changes**Q in **gene expression**, **not caused by** alterations in **DNA sequence.**Q
- ***Epigenetic factors***
  - Histones and histone-modifying factors
    - **H**istone methylation, **H**istone acetylation, **H**istone phosphorylation, DNA methylation, chromatin organizing factors

NEXT Pattern Questions

1. A study of peripheral blood smears shows that neutrophil nuclei of women have a Barr body, whereas those of men do not. The Barr body is an inactivated X chromosome. Which of the following forms of RNA is most likely to play a role in Barr body formation?

a. lncRNA b. mRNA
c. miRNA d. siRNA

1. Ans. (a) lncRNA

- There are forms of noncoding RNA that play a role in gene expression. Long noncoding RNA (lncRNA) segments greater than 200 nucleotides in length can bind to chromatin to restrict access of RNA polymerase to coding segments. The X chromosome transcribes XIST, an lncRNA that binds to and represses X chromosome expression. However, not all genes on the "inactive" X chromosome are switched off. The RNA transcribed from nuclear DNA that directs protein synthesis through translation is mRNA. MicroRNAs (miRNAs) are noncoding RNA sequences that inhibit the translation of mRNAs. Gene-silencing RNAs (small interfering RNAs [siRNAs]) have the same function as miRNAs, but they are produced synthetically for experimental purposes. Transfer RNA (tRNA) participates in the translation of mRNA to proteins by linking to specific amino acids.

2. At the site of a surgical incision, endothelial cells elaborate vascular endothelial growth factor. There is sprouting with migration of endothelial cells into the wound to establish new capillaries. Which of the following intracellular proteins is most important in facilitating movement of endothelial cells?

a. Actin b. Cytokeratin
c. Desmin d. Lamin

2. Ans. (a) Actin

- Actin is a microfilament involved with cell movement.
- The other possibilities listed in b to d are intermediate filaments, which are larger than actin but smaller than myosin (a thick filament interdigitating with actin, required for muscle movement). Cytokeratins form cytoskeletal elements of epithelial cells. Desmin forms the scaffold in muscle cells on which actin and myosin contract. Lamin is associated with the nuclear membrane.

3. A 62-year-old man has increasing knee pain with movement for the past 10 years. The knee joint surfaces are eroded and the joint space narrowed. There is loss of compressibility and lubrication of articular cartilaginous surfaces. Loss of which of the following extracellular matrix components has most likely occurred in this man?

a. Elastin b. Fibronectin
c. Hyaluronan d. Integrin

3. Ans. (c) Hyaluronan

- He has osteoarthritis, or degenerative joint disease, with loss of articular hyaline cartilage. Hyaluronan (hyaluronic acid) is a large mucopolysaccharide, one form of proteoglycan, which forms a hydrated, compressible gel contributing to the shock-absorbing function of joint surfaces. Elastin is a fibrillar protein that provides recoil in tissues such as skin, arterial walls, and ligaments that need to stretch and return to their original shape. Fibronectin is a form of glycoprotein that serves an adhesive function. Integrins are glycoproteins that serve as cellular receptors for extracellular matrix components; they can link to intracellular actin so that cells can alter their shape and mobility.

Multiple Choice Questions

Most Recent Questions

1. About RNAi, true is: *(INI-CET July 2021)*
a. Knock up
b. Knock in
c. Knock down
d. Knock out

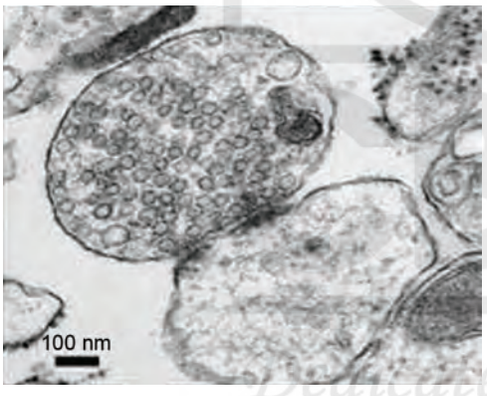
2. Methylation is responsible for all; except: *(INI-CET 2020)*
a. Gene alterations
b. Chromatin transformation
c. RNA splicing
d. DNA base excision repair

3. Integrin connects actin to which macromolecule in ECM? *(AIIMS Nov 2018)*
a. Vitronectin
b. Laminin
c. Fibronectin
d. Collagen

4. In 2018, for what contribution was the Nobel Prize given? *(AIIMS Nov 2018)*
a. Negative immune regulation in treatment of cancer
b. Apoptotic pathway
c. CRISPR-Cas9
d. Molecular mechanisms controlling circadian rhythm

5. Integrin binds to: *(AIIMS Nov 2018)*
a. Fibronectin
b. Vitronectin
c. Collagen
d. Laminin

6. The small inner circles in the given image of EM signifies which of the following? *(AIIMS May 2018)*



a. Neurotransmitter
b. Neurosecretory granules
c. Collagen fibril
d. Microtubules

7. Type 1 collagen is present in all; except: *(AIIMS May 2018)*
a. Bone
b. Cartilage
c. Ligament
d. Aponeurosis

8. Which among the following is not seen in disorder to deficiency in elastin production? *(AIIMS May 2018)*
a. Aortic dissection
b. Lens subluxation
c. Ligament hyperlaxity
d. Bone fracture

9. Which vitamin increases iron absorption? *(AIIMS May 2018)*
a. Vitamin C
b. Biotin
c. Vitamin B6
d. Vitamin E

10. Which of the following plays a role in gene editing? *(AIIMS May 2017)*
a. Gene Xper
b. CRISPR
c. Health care apps
d. Big data

11. Cell to cell permeability occurs through: *(Recent Question 2016-17)*
a. Occludin
b. Zona adherens
c. Connexins
d. Zonulin

12. Tensile strength of tendon depends on: *(Recent Question 2016-17)*
a. Fibrillin
b. Collagen
c. Fibronectin
d. Elastin

13. All of the following are intermediate filaments, except: *(Recent Question 2016)*
a. Lamin
b. Cadherin
c. Vimentin
d. Desmin

14. Tight junction consists of all; except: *(Recent Question 2016)*
a. Occludin
b. Claudin
c. Zonulin
d. Cadherin

15. Titin protein is mutated in: *(Recent Question 2016)*
a. DCM
b. HOCM
c. RCM
d. Non functional cardiomyopathy

16. Peripheral proteins in cell membrane are attached by: *(Recent Question 2016)*
a. GpI
b. Desmosome
c. Catenins
d. Cadherins

Answers with Explanations

1. Ans. (c) Knock down

2. Ans. (d) DNA base excision repair

3. Ans. (c) Fibronectin > (b) Laminin

Integrins localized in the plasma membrane are the major adhesion receptor connecting cells with components of the extracellular matrix. Integrins interact directly with laminin and mainly fibronectin present in the basal lamina and intracellularly contact actin through intermediate proteins, such as alpha-actinin, vinculin, and talin. Integrins are calcium-independent adhesion molecules.

4. Ans. (a) Negative immune regulation in treatment of cancer

The 2018 Nobel Prize in physiology or medicine was awarded to James P. Allison and Tasuku Honjo "for their discovery of cancer therapy by inhibition of negative immune regulation." Their pioneering work on the CTLA4 and PD1 immune checkpoints revealed that these pathways act as so-called "brakes" on the immune system, and showed that the inhibition of these checkpoint pathways allows T cells to more effectively eradicate cancer cells. This research laid the foundation for the clinical development of immune checkpoint inhibitors, which have dramatically improved outcomes for many people with cancer.

- James P. Allison studied a known protein that functions as a brake on the immune system. He realized the potential of releasing the brake and thereby unleashing our immune cells to attack tumors.
- Cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and programmed death 1 (PD-l) immune checkpoints are negative regulators of T-cell immune function. Inhibition of these targets, resulting in increased activation of the immune system, has led to new immunotherapies for melanoma, non-small cell lung cancer, and other cancers.
- For several types of cancer, including lung cancer, renal cancer, lymphoma, and melanoma, checkpoint therapy against PD-l has proven to be more effective and positive results have been found.
- But recent clinical studies indicate that for melanoma, the combination therapy of both CTLA-4 and PD-l is more effective.
- Thus, Allison and Honjo combined different strategies to release the brakes on the immune system with the aim of eliminating tumor cells even more efficiently.
- Their paper formed the basis of current cancer immunotherapy.
- But the original concept of cancer immunotherapy was given by William Bradley Coley (1872).

5. Ans. (d) Laminin > (a) Fibronectin

Integrins localised in the plasma membrane are the major adhesion receptors connecting cells with components of the extracellular matrix. Integrins interact directly with laminin, fibronectin present in the basal lamina and intracellularly contact actin through intermediate proteins, such as alpha-actinin, vinculin, and talin.

6. Ans. (b) Neurosecretory granules

Neurosecretion is the storage, synthesis and release of hormones from neurons. These neurohormones, produced by neurosecretory cells, are normally secreted from nerve cells in the brain that then circulate into the blood.

7. Ans. (b) Cartilage

Major types of collagens and disorders associated with them:

Type	Present in	Disorders
I	Bone[Q], cornea,[q] scar tissue, tendons, skin, artery walls, endomysium of myofibrils[Q], fibrocartilage, teeth	Osteogenesis-imperfecta[Q], Ehlers-Danlos syndrome[Q], Caffey's disease[Q]
II	Hyaline cartilage[Q], Vitreous humor[Q] of the eye.	Collagenopathy
III	Granulation tissue[Q], reticular fiber, artery walls, skin, intestines and the uterus	Ehlers-Danlos syndrome[Q]
IV	Basement membrane[Q], eye lens[Q], Glomerular basement membrane	Alport syndrome[Q] (COL4α5) Goodpasture's syndrome[Q] (COL4α3)

8. Ans. (d) Bone fracture

9. Ans. (a) Vitamin C

10. Ans. (b) CRISPR *(Ref. R 9th/p 5-6)*

CRISPR-Cas9 is a genome editing tool essential in adaptive immunity in select bacteria enabling the organisms to respond to and eliminate invading genetic material.

11. Ans. (c) Connexins *(Ref: Robbins 9th/pg 11)*

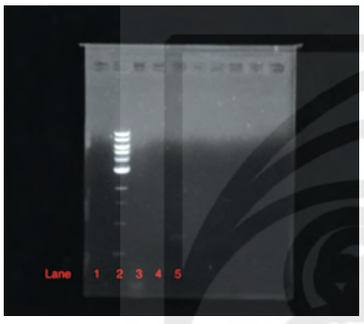
- Communicating junctions (Gap junctions) mediate the passage of chemical or electrical signals from one cell to another.
- Consists of pores called connexions and formed by hexamers of transmembrane proteins called connexins.

12. Ans. (b) Collagen *(Ref: Robbins 9th/ pg 12-13)*

Fibrous structural proteins like collagens confer tensile strength and elastins provide recoil to the tension.

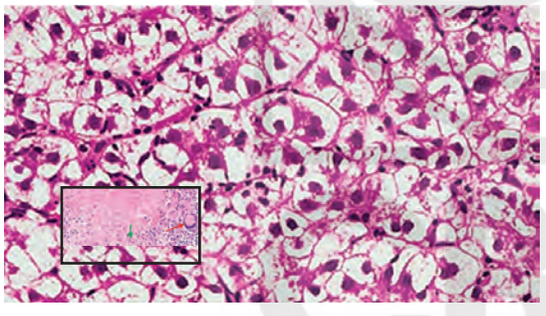
Image-Based Questions

1. A 45-year-old male had history of hepatitis B infection. On liver biopsy, multiple councilman bodies were seen. Electrophoresis was done to pick up whether he was undergoing apoptosis or necrosis. Identify the pattern in lane 2 and diagnosis.



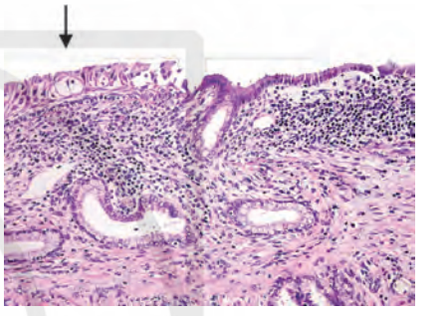
a. Step ladder pattern, apoptosis
b. Smeared pattern, necrosis
c. Step ladder pattern, necrosis
d. Smeared pattern, apoptosis

2. Earliest morphological change seen in reversible cellular injury? Inset shows normal hepatocytes as control.



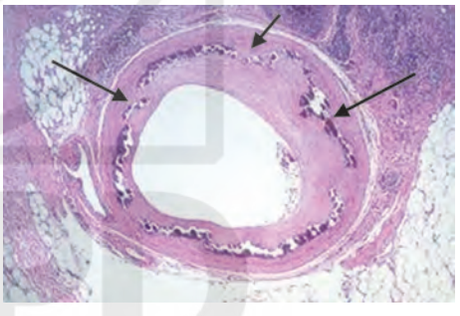
a. Hydropic change
b. Fatty change
c. Necrosis
d. None

3. A 50-year-old female comes with history of discharge per vaginum. On examination, her squamocolumnar junction of cervix appears erythematous. She underwent cervical biopsy which showed following findings. Describe the change marked by arrow.



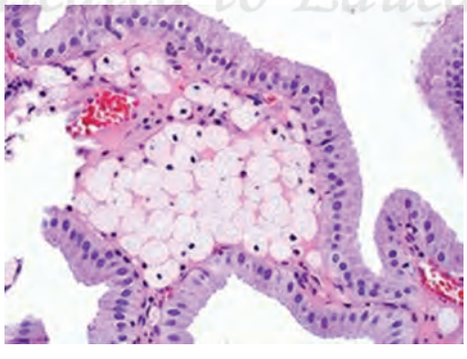
a. Squamous metaplasia
b. Columnar metaplasia
c. Transitional metaplasia
d. None

4. A 60-year-old asymptomatic female shows following change in tunica media of blood vessels. Diagnosis is:



a. Medial calcification
b. Medial fibrosis
c. Amyloidosis
d. None

5. A 50-year-old female underwent cholecystectomy. On examination, the lamina propria of gall bladder was seen infiltrated by foam cells. Diagnosis is:



a. Cholesterolosis
b. Atherosclerosis
c. Steatosis
d. None

Answers of Image-Based Questions

1. Ans. (a) Step ladder pattern, apoptosis

- This is step ladder pattern which is typically seen in apoptosis, its also called DNA laddering characterized by the activation of endogenous endonucleases with subsequent cleavage of chromatin DNA into internucleosomal fragments of roughly 180-200 base pairs (bp).
- Smear pattern is seen in necrosis.

2. Ans. (a) Hydropic change

- Cellular swelling is the first manifestation of almost all forms of injury to cells. Cellular swelling appears whenever cells are incapable of maintaining ionic and fluid homeostasis and is the result of failure of energy-dependent ion pumps in the plasma membrane. It is reversible.
- On microscopic examination, small clear vacuoles may be seen within the cytoplasm; these represent distended and pinched-off segments of the ER. This pattern of nonlethal injury is sometimes called hydropic change or vacuolar degeneration.
- This is a case of hydropic change in hepatocytes (control normal hepatocytes are seen in inset).

3. Ans. (a) Squamous metaplasia

- Here, we are seeing endocervix lined by columnar epithelium. Underlying stroma shows endocervical glands. Here, columnar epithelium is being changed to squamous epithelium suggestive of squamous metaplasia. Inciting cause for this metaplasia is chronic cervicitis.

4. Ans. (a) Medial calcification

- Medial artery calcification (MAC), also known as Mönckeberg's arteriosclerosis, is a nonobstructive condition leading to reduced arterial compliance that is commonly considered as a nonsignificant finding.
- With the H&E stain, calcium appears deep blue-purple.

5. Ans. (a) Cholesterolosis of the gallbladder

- Here, we are seeing accumulation of foam cells in lamina propria of gallbladder suggestive of cholesterolosis.

4

Hemodynamics

Key Points

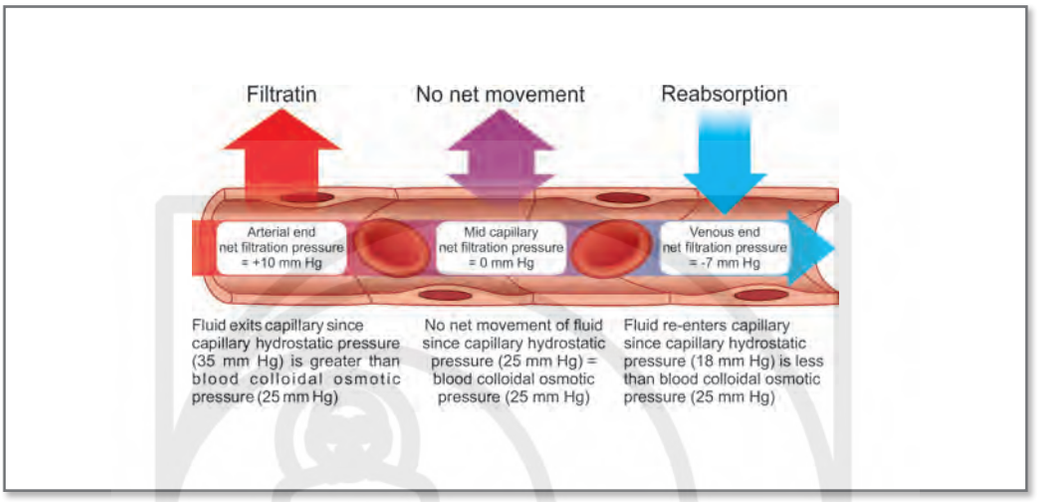
- **Hyperemia** is an **active** process.
- **Nutmeg liver** is seen in chronic passive hepatic congestion.
- Hemosiderin-laden macrophages **(heart failure cells)** are seen in chronic pulmonary congestion.
- **Line of Zahn**-distinguish antemortem clots from the bland non-laminated postmortem[Q] clots.
- Fat embolism syndrome is characterized by pulmonary insufficiency, neurologic symptoms, **anemia** and thrombocytopenia (petechial rash).
- Arterial occlusions cause **white infarcts** whereas venous occlusion cause **red Infarcts**[Q].
- Primary initiating factor in septic shock: **cytokine release**.
- Most common cytokine involved in septic shock is **TNF-**α.

Key Recent Updates

- **Procalcitonin** is marker of sepsis.
- Most common cause of septic shock is **gram positive bacteria** (PAMP).
- **Endotoxin** [lipopolysaccharide] and lipoteichoic acids are PAMPs (pathogen associated molecular patterns).

HEMODYNAMICS

- **Vascular hydrostatic pressure** is **balanced** by **plasma colloid osmotic pressure**[Q]
- Accumulation of fluid in tissues is called **edema** or body cavities is called **effusions.**[Q]
- It occurs due to either **elevated**[Q] hydrostatic pressure or **diminished**[Q] colloid osmotic pressure



The excessive interstitial fluid can be either a **transudate** or an **exudate**

Characteristic	Transudate	Exudate
Appearance	Clear, Colorless	Yellow, turbid, purulent, bloody
Specific gravity	**<1.015**[Q]	**>1.015**[Q]
Protein	<3 g/dL	>3 g/dL
LDH	<200 IU	>200 IU
Cell count	<1000/uL[Q]	**>1000/uL**[Q]
Permeability	**Normal**[Q]	**Altered**[Q]
Conditions	**Congestive heart failure**	Infections, Malignancies

HYPEREMIA AND CONGESTION

- **Increased volume of blood**[Q] within dilated vessels of tissue or organ.

Features	Hyperemia	Congestion
Process	Active process[Q]	Passive process[Q]
Cause	Arteriolar dilation	Impaired venous outflow
Edema	Absent	Present[Q]
Colour of the tissues	Red color[Q]	Blue red color[Q] (deoxyhemoglobin)
Seen in	Inflammation[Q]	Right heart failure

Acute pulmonary congestion:
- **Engorged alveolar capillaries**[Q]
- Alveolar **septal edema**[Q]
- **Focal intraalveolar hemorrhage**[Q]

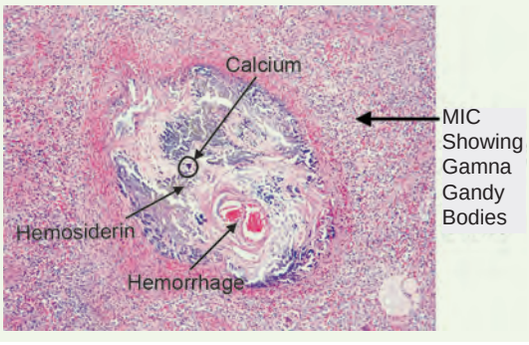
Acute hepatic congestion:
- **Centrilobular** hepatocytes: **ischemic necrosis**[Q]
- **Periportal** hepatocytes - **fatty change**[Q]

Chronic pulmonary congestion:
- Septa are **thickened and fibrotic**[Q]
- **Hemosiderin-laden macrophages (heart failure cells)**[Q] **(Figs 1A and B)**

Chronic passive hepatic congestion:
- ***Nutmeg liver***[Q]: centrilobular regions are red-brown against surrounding zones of uncongested tan liver **(Figs 2A and B)**
- Initially **centrilobular necrosis and hemosiderin laden macrophages.**[Q]
- **Later: hepatic fibrosis called cardiac cirrhosis.**[Q]

High Yield Facts

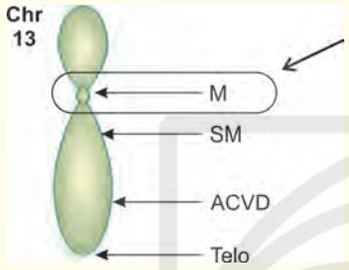
- CVC liver—**Nutmeg liver**
- CVC spleen shown **Gamna Gandy Bodies**. (organized hemorrhage with dystrophic calcification and hemosiderin pigment in spleen)



Multiple Choice Questions

Most Recent Questions

1. Which mutation is the arrow mark pointing to? ***(INI-CET Nov 2021)***



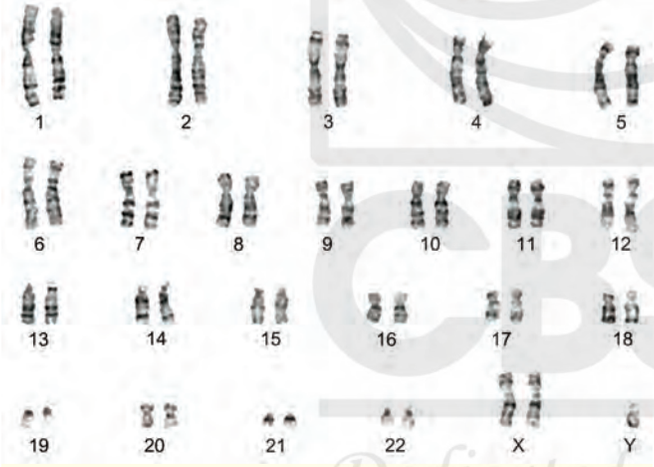
a. Acrocentric
b. Submetacentric
c. Telocentric
d. Metacentric

2. Which of the following is an RNA-based sequencing technique? ***(INI CET July 2021)***

a. RT PCR
b. Sanger
c. Western blot
d. G banding

3. The Karyotype of an individual showed the following picture. Which of the following clinical features may be seen? ***(INI CET July 2021)***

a. Webbed neck
b. Gynecomastia and thin limbs
c. Polydactyly
d. Flat occiput



4. A 25-year-old man presents for a routine physical examination. The patient is tall (6 ft, 5 in) and on examination, he was found to have an early diastolic murmur. Which of the following is the mode of inheritance by which the disease is likely to be transmitted? ***(Recent Question 2020)***

a. AD
b. AR
c. XLR
d. XLD

5. Which of the following is the correct statement related to Huntington's Chorea? ***(Recent Question 2020)***

a. It is a tri-nucleotide expansion mutation related disorder
b. There are abnormal repeats of CUG
c. Loss of function mutation
d. Abnormality is seen due to mutation in Chromosome 6

6. Maltese cross appearance in urinary sediment is seen in which of the following diseases other than nephrotic syndrome? ***(AIIMS Nov 2019)***

a. Felty syndrome
b. Fanconi Syndrome
c. Fabry disease
d. Friedreich's ataxia

7. Which of the following is an autosomal recessive disorder? ***(Recent Question 2019)***

a. Albinism
b. Huntington's syndrome
c. Marfan's syndrome
d. Neurofibromatosis-1

8. Biopsy of an 8-year-old child with leg swelling was showing small round blue tumor cells consistent with diagnosis of Ewing's sarcoma. What will be the best method to detect translocation t (11,22) in this malignancy?

a. Conventional karyotyping
b. Next generation sequencing
c. FISH
d. PCR

9. Abnormality in elastin protein can lead to all; except:

a. Fractures
b. Aortic aneurysm
c. Joint laxity
d. Subluxation of lens

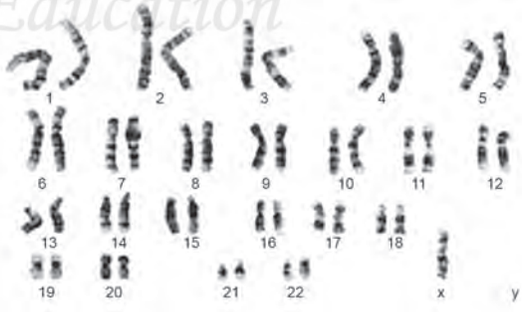
10. Which chromosome is responsible for the production of MIF? ***(Recent Question 2018)***

a. Chromosome 16
b. Chromosome 22
c. X Chromosome
d. Y Chromosome

11. Which of the following is/are true about Turner syndrome?

a. Most common viable aneuploidy
b. Long stature
c. High hair line
d. Narrow chest
e. Mental retardation present

12. Karyotype of a male patient shows the following, what is the clinical abnormality that is expected? ***(Recent Question 2016)***



a. Turner syndrome
b. Kallmam syndrome
c. Androgen insensitivity syndrome
d. Down syndrome

Answers with Explanations

1. Ans. (d) Metacentric

2. Ans. (a) RT PCR

Sequencing Technique

- Sequence the entire chromosome/gene
  There are 2 ways:
  1. Sanger sequencing (old)
  2. NGS: Next generation sequencing (New)
     - Entire human chromosome can be sequenced
     - Done as human genome project (HGP)

3. Ans. (b) Gynecomastia and thin limbs

Not herbal retard, but lowers IG ↑risk of DM, extrogonadal germ cell tumors

"K-L-N-E-F-E-L-T-S" syndrome

- **K**aryotype, most common is 47, XXX[Q], 47 ixq, y
- **L**ong stature with long leg[Q]
- **In**fertility[Q], **In**cidence:1 in 1000 men
- **N**on-disjunction of **paternal**[Q] sex chromosomes
- **E**unuchoid[Q] body proportions
- **F**SH elevated[Q], scanty **F**acial and axillary hair
- **E**stradiol/testosterone ratio elevation → Gynecomastia[Q]
- **L**H elevated, **L**eukemias (increased risk for AML)[Q] and breast tumors, **L**earning disability
- **T**estosterone reduced, small **T**estes and penis[Q]
- **S**econdary sexual characters absent

4. Ans. (a) AD

Marfan's syndrome is an inherited disorder that affects connective tissue—the fibers that support and anchor the organs and other structures in the body.

Marfan's syndrome most commonly affects the heart, eyes, blood vessels and skeleton.

- Above condition signifies marfan's syndrome.
- Marfan's syndrome, an autosomal dominant disease with genetic defect in fibrillin which is a connective tissue protein required for elastic tissue formation.

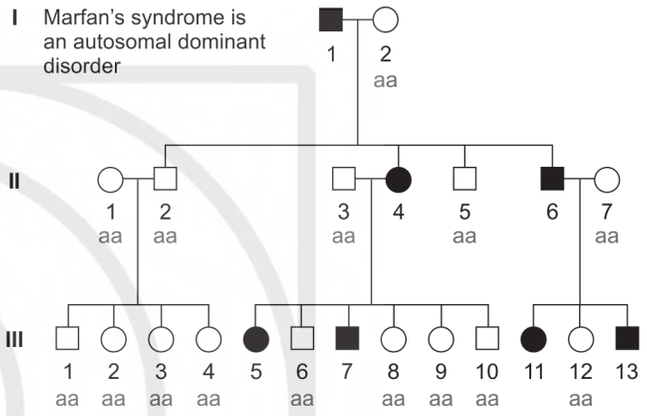
Marfan's syndrome features may include:

- Tall and slender build.
- Disproportionately long arms, legs and fingers.
- A breastbone that protrudes outward or dips inward.
- A high, arched palate and crowded teeth.
- Heart murmurs.
- Extreme nearsightedness.
- An abnormally curved spine.
- Flat feet.

The damage caused by Marfan's syndrome can be mild or severe.

Genetics of Marfan's Syndrome

It is an autosomal dominant disorder as it affects both sexes and appears in every generation as seen in pedigree.



5. Ans. (a) It is a tri-nucleotide expansion mutation related disorder

- This disease is an autosomal dominant, fatal, progressive degeneration and atrophy of the striatum (caudate nucleus and putamen) and frontal cortex with neuronal depletion and gliosis.
- It is characterized by the delay of clinical abnormalities until 30–40 years of age; course extends 15–20 years, beginning with athetoid movements, followed by progressive deterioration leading to hypertonicity, fecal and urine incontinence, anorexia and weight loss, and eventually dementia and death.
- Cholinergic and GABA-ergic neurons are especially affected.
- Huntington disease is marked by increased numbers (more than the normal 1 1 to 34) of CAG trinucleotide repeats within the HD (Huntingtin) gene on the short arm of chromosome 4.
- Paternal transmission results in an increased number of CAG repeats and correspondingly earlier onset of disease manifestations in successive generations.
- This disease may be related to a failure in the up-regulation of transcription of brain derived neurotrophic factor (BDNF), a pro survival factor for the neurons of the striatum.
- The transcription of BDNF is apparently decreased in the presence of the Huntingtin gene with increased numbers of CAG repeats.

6. Ans. (c) Fabry disease

- Fabry disease is an inherited disorder that results from the buildup of a particular type of fat, called globotriaosylceramide, in the body's cells.

9

White Blood Cells and Related Disorders

Key Points

- Hematopoiesis starts between 3 and 4th week of intrauterine life in yolk sac.
- Leukopenia is abnormally **low WBC (TLC <4000/uL), while leukocytosis is increase in the count of WBCs (>11,000/uL).**
- **Leukemia** refers to hematological neoplasms with involvement of **bone marrow and peripheral blood lymphoma** refers to **discrete tissue masses**Q usually involving lymph node, spleen and liver.
- ALL is the **most common cancer among children.**
- **The most common leukemia** among adults in the **Western world is CLL.**
- The most common site for extranodal lymphoma is stomach.
- **Follicular lymphoma is the most common** form of **indolent (low grade) NHL** in the West.
- **DLBCL is the most common** form of **NHL in India.**
- Burkitt's lymphoma shows **"starry sky" pattern.**
- Diagnostic hallmark of Hodgkin's lymphoma is Reed-Sternberg cells.
- Cut off for blast counts in AML is <20%, if AML is associated with cytogenetic abnormalities like t(15;17), t(8;21), inv(16).
- **BCR-ABL gene**Q (210 kDa in size) is hallmark of CML.

Key Recent Updates

- CSF3R mutation is seen in CNL.
- Provisional response to TKI is added in accelerated phase of CML.

HEMATOPOIESIS

Formation of blood components happens during embryonic stage and throughout adult life.

- ***Definitive hematopoiesis:***
  - Forms multipotent hematopoietic stem cells (HSCs) in 4th week of intrauterine life around aorta, gonads and mesonephros.
- ***Sites at different ages:***

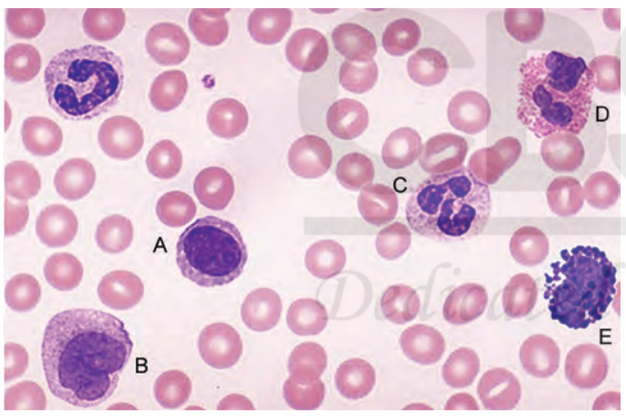
Age group	Site of Hematopoiesis
Embryo[Q]	Till the **3rd week** in **yolk sac;**[Q] Up to **3rd month** in **liver**[Q]
Fetus	**4th** month onward: Bone marrow[Q]
Birth	Bone marrow[Q]
Child	Bone marrow: **throughout the skeleton**[Q]
Adult	Bone marrow: **Flat bone** (Vertebra, ribs, sternum, pelvis)[Q], proximal epiphysis of humerus and femur

Properties of Hematopoietic Stem Cells

- **Pluripotency**[Q] - Ability of a single HSC to generate all mature blood cells
- Capacity for **self-renewal**[Q]
- **Not** seen usually in **peripheral blood**[Q]
- Under conditions of **stress**, e.g., severe anemia or acute inflammation, HSCs are **mobilized from bone marrow** and appear in the **peripheral blood.**[Q]

Morphology of Bone Marrow

	Light Microscopy
Normal ratio of **Myeloid: Erythroid** = **3–4:1**[Q]	• Thin-walled **sinusoids**[Q] lined by **single layer of endothelial cells**
Normal ratio of **marrow cells: fat cells = 1:1**[Q]	• Clusters of **hematopoietic** and **fat cells** within the interstitium
Normal cellularity (%) = **100 – Age**[Q] • Decreases with age • At 10 years = 100 – 10 = 90% cellularity • At 30 years = 100 – 30 = 70% cellularity	• **Megakaryocytes** lie **next to sinusoids**[Q] where they release platelets. • Red cell precursors (**erythroblasts**) surround macrophages (so-called **nurse cells**)[Q].



A-Lymphocyte B-Monocyte C-Neutrophil
D-Eosinophil E-Basophil

High Yield Facts

- **Agranulocytosis: Clinically significant reduction in neutrophils** making one susceptible to bacterial and fungal infections.[Q]
- **Drugs are** the most common cause of **agranulocytosis**[Q].
- Serious infection increases when ANC <500/mm³.

DISORDERS OF WHITE BLOOD CELLS

- Quantitative defects
  - Leukopenia
  - Leukocytosis
- Qualitative defects

Leukopenia

- ***Definition:***
  - An abnormally **low white cell count** (leukopenia; **TLC <4000/μL)**[Q]

Clinical Case-Based Questions

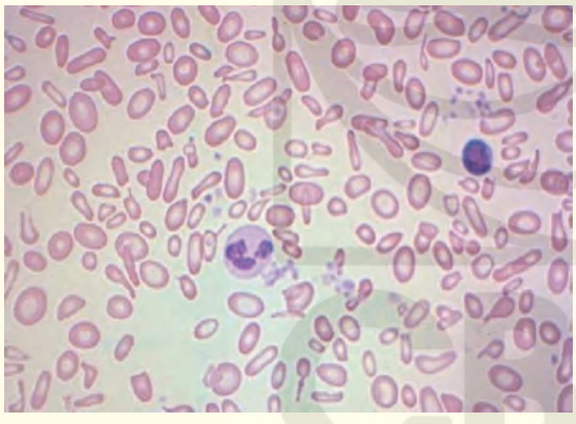
1 CBQ

A 12-year-old boy is brought to the casualty after an automobile accident. Physical examination shows bleeding from multiple wounds, and a CBC reveals a normocytic, normochromic anemia. Which of the following indices is most helpful in defining this patient's anemia as normocytic?

a. Hemoglobin
b. Mean corpuscular hemoglobin concentration
c. Mean corpuscular volume
d. Red blood cell count

2 CBQ

A 20-year-old female patient presented to the physician with the complaint of easy fatiguability and tiredness. Her menstrual cycle is normal and regular every month. On the advice of the doctor, she undergoes peripheral smear examination (image is shown below). Based on the above findings, what do you expect in this patient?



a. Hyperbilirubinemia
b. Increased serum ferritin
c. Low iron level
d. Vitamin B_{12} deficiency

3 CBQ

A 49-year-old woman presents with signs of anemia and states that every morning her urine is dark red color. Laboratory studies find anemia, leukopenia, and thrombocytopenia. A bone marrow biopsy is unremarkable, and no morphologic abnormalities of blood cells are seen on the peripheral smear. A Coombs' test is negative, but a Ham test and sucrose lysis test on erythrocytes is positive. Which one of the following is most likely to be decreased or absent on the red blood cells from this woman?

a. AIRE
b. CD 22
c. CD 59
d. Kell antigen

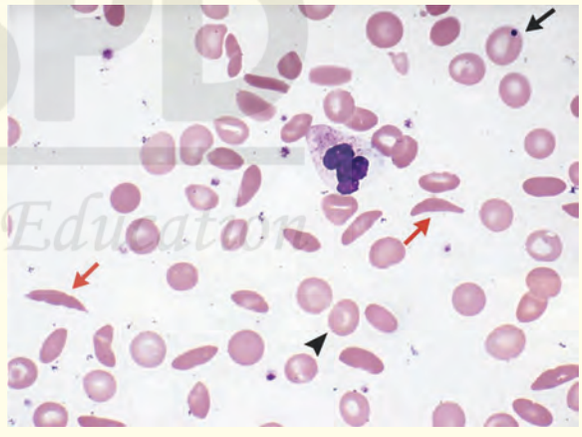
4 CBQ

A 35-year-old white woman went to her physician complaining of headache, dizziness, and nausea. The head-aches had been increasing in severity over the past 6 months. This was coincident with her shifting into an older house built about 1900. She had been renovating the house, including stripping paint from the woodwork. Her CBC results showed a mild hypochromic, microcytic anemia, with polychromasia and basophilic stippling noted. Which of the following tests would be most useful in confirming the cause of her anemia?

a. Serum lead level
b. Serum iron level and TIBC
c. Absolute reticulocyte count
d. Prussian blue staining of the bone marrow to detect iron stores in macrophages

5 CBQ

A 13-year-old boy has the sudden onset of severe abdominal pain and cramping accompanied by chest pain, nonproductive cough, and fever. On physical examination, his temperature is 39°C, pulse is 110/min, respirations are 22/min, and blood pressure is 80/50 mm Hg. He has diffuse abdominal tenderness, but no masses or organomegaly. Laboratory studies show a hematocrit of 18%. The peripheral blood smear is shown in the figure. A chest radiograph shows bilateral pulmonary infiltrates. Which of the following is the most likely mechanism for initiation of his pulmonary problems?



a. Defects in the alternative pathway of complement activation
b. Extensive RBC adhesion to endothelium
c. Formation of autoantibodies to alveolar basement membrane
d. Intravascular antibody-induced hemolysis

Answers of Clinical Case-Based Questions

1. Ans. (c) Mean corpuscular volume

(Ref: Robbins 10th Ed pg 636)

MCV is the index used to measure the volume of a red blood cell. It categorizes RBCs by size. Cells with normal size are called normocytic, smaller cells are termed microcytic, and larger cells are referred to as macrocytic. Mean corpuscular hemoglobin concentration (choice b) measures hemoglobin content.

2. Ans. (c) Low iron level

The blood smear reveals microcytic, hypochromic erythrocytes, characteristic of iron deficiency anemia caused by inadequate uptake or, more often, excessive loss of iron. Women who have menorrhagia, especially those who consume restricted diets, are especially prone to iron deficiency anemia. Iron stores of the body are reduced, as evidenced by reduced levels of serum ferritin (not increased ferritin, choice b) and low iron saturation (iron/total iron binding capacity). None of the other laboratory findings would be expected in a patient with iron deficiency anemia.

3. Ans. (c) CD 59

Ham test and sucrose lysis test are two tests that are used to diagnose individuals with paroxysmal nocturnal hemoglobinuria (PNH). In this disorder complement-regulating surface proteins, including CD55 (decay-accelerating factor), CD59 are decreased or absent on all blood cells, including red blood cells.

4. Ans. (a) Serum lead level

Anemia, when present in lead poisoning, is most often normocytic and normochromic; however, with chronic exposure to lead, a microcytic, hypochromic clinical picture may be seen. Lead inhibits pyrimidine nucleotidase, an enzyme involved in the breakdown of ribosomal ribonucleic acid (RNA) in reticulocytes. This causes undegraded ribosomes to aggregate, forming basophilic stippling.

5. Ans. (b) Extensive RBC adhesion to endothelium

The crescent-shaped RBCs (sickled RBCs) are characteristic of hemoglobin SS. The sickled RBCs are susceptible to hemolysis (mainly vascular, in the spleen), but they also can cause microvascular occlusions anywhere in the body, most commonly bone, lungs, liver, and brain, leading to ischemia and severe pain. Vascular occlusions in the lungs are often accompanied by infection and lead to "acute chest syndrome." Abdominal pain and back pain are common and severe, requiring prompt and effective analgesia. The cell membranes of reversibly sickled cells are abnormally "sticky," and they adhere to capillary endothelium, especially in lungs. Adhesion of RBCs to endothelium retards blood flow, creates hypoxia, and precipitates local sickling and vascular occlusion.

6. Ans. (b) False increase due to reticulocytosis

Limitations: Reticulocytes have higher G6PD activity compared to mature RBCs. Reticulocytosis typically occurs as a response to an acute hemolytic episode and will falsely increase the patient's G6PD activity over baseline values.

7. Ans. (c) Impaired utilization of iron from storage sites

Anemia of chronic disease arises in association with chronic inflammatory diseases (e.g., tuberculosis and rheumatoid arthritis) and malignant conditions. Chronic disease leads to ineffective use of iron from macrophage stores in the bone marrow, resulting in a functional iron deficiency, although storage iron is normal or even increased. The anemia of chronic disease is mild to moderate, and the red cells are often microcytic. Serum iron levels tend to be reduced. However, in contrast to iron deficiency anemia, total iron binding capacity also tends to be decreased (as is the serum albumin level). The other choices are not related to anemia of chronic disease.

11

Bleeding and Coagulation Disorders

Key Points

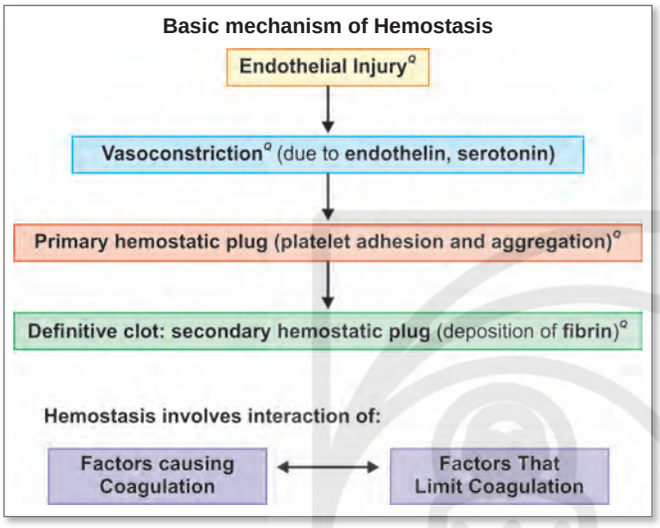
- **Hemoglobin** can be first visualized at **polychromatic (Intermediate) erythroblast**[Q] stage.
- **Platelet adhesion** refers to attachment of vWF on endothelium with **GpIb/IX** on platelets.
- **Platelet aggregation** refers to attachment of **GpIIb/IIIa** on platelets that bridges adjacent platelets.
- **Primary hemostatic plug** consists of: **Platelets, Fibrinogen, Entrapped RBCs and WBCs**.
- **All clotting factors** are synthesized by liver, except factor VIII, from endothelium.
- Vitamin K–dependent factors are F- **II, VII, IX**, and **X**[Q] and anticoagulant **proteins C, S and Z**.
- **Thrombomodulin** synthesized from liver **inhibits** activation of **factor V and VIII**.
- **ITP** results from platelet destruction by platelet-specific **(GpIb/IX; GpIIb/IIIa) autoantibodies**.
- **Von Willebrand disease can be diagnosed by decreased Ristocetin cofactor assay**[Q]**/Ristocetin induced platelet aggregation**.
- **D-dimer test** is **more specific**[Q] for detection of **FDPs** in diagnosis of **DIC**.
- **Factor V Leiden is the most common inherited thrombophillia**.

Key Recent Updates

Thromboelastography is used to assess viscoelastic changes in clotting used to assess hypo- and hypercoagulable states and to guide hemostatic therapies with fresh-frozen plasma, with platelet concentrates as well as with coagulation factor concentrates.

HEMOSTASIS

Process of formation of a **blood clot**[Q], which **prevents or limits** bleeding.



High Yield Facts

- **1st response** to endothelial injury is **vasoconstriction**
- Endothelial injury **activates extrinsic pathway** by releasing **tissue factor**

Formation of Primary Hemostatic Plug

Platelet Plug Formation: 2 Processes

- ***Platelet adhesion:***
  - vWF on **endothelium**[Q] with Gp Ib/IX on **platelets**[Q]
- ***Platelet aggregation:***
  - Gp IIb/IIIa on **platelets**[Q] **that bridges adjacent platelets**[Q]

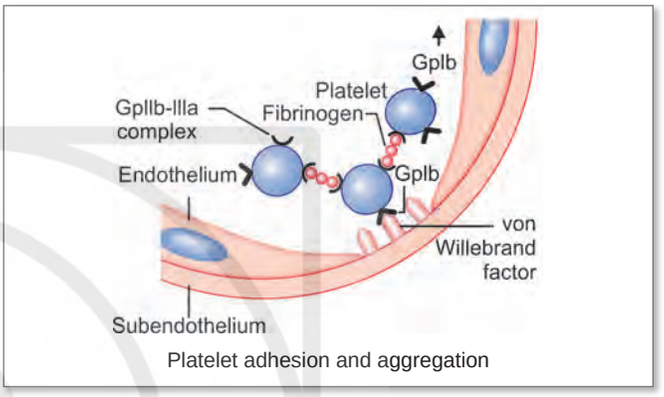
PLATELET: Disc shaped anucleate[Q] **cell fragments shed from megakaryocytes**

α-Granules contains:
- **P-selectin (adhesion molecule)**
- **Fibrinogen**[Q]
- **Coagulation factors: V**[Q]**, VIII**[Q]**, vWF**[Q]
- **Platelet factor 4**[Q] (a heparin binding chemokine)
- Platelet derived growth factor **(PDGF)**
- Transforming growth factorβ **(TGF-β)**

Dense (or δ) granules contain: **("DENSE")**
- a**DEN**osine diphosphate **(ADP)**[Q]
- Serotonin[Q]
- Epinephrine[Q]
- Ionized calcium[Q]

High Yield Facts

- Platelets life span is 7–10 days
- Amyloidosis causes pinch purpura
- Solar purpura is senile
- Gloves and stock syndrome is caused by Parvo B_{19}, CMV
- F VIII and IX are x-linked while other are AR



Platelet adhesion and aggregation

Mnemonic

"B comes before G and Ib comes before IIb"	
Disease	**Deficient Gp**
Bernard Soulier syndrome	**Ib**/IX
Glanzmann thrombasthenia	**IIb**/IIIa

Formation of Secondary Hemostatic Plug

Coagulation Cascade

Series of **amplifying**[Q] **enzymatic reactions** that leads to the deposition of an **insoluble fibrin clot**.[Q]

Each reaction step involves:
- **Enzyme** (an **activated coagulation factor**)
- **Substrate** (an **inactive proenzyme** form of a coagulation factor)
- **Cofactor** (a reaction accelerator)

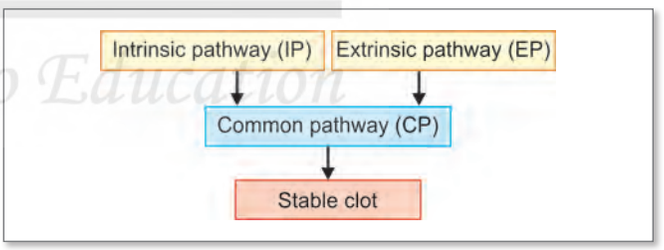
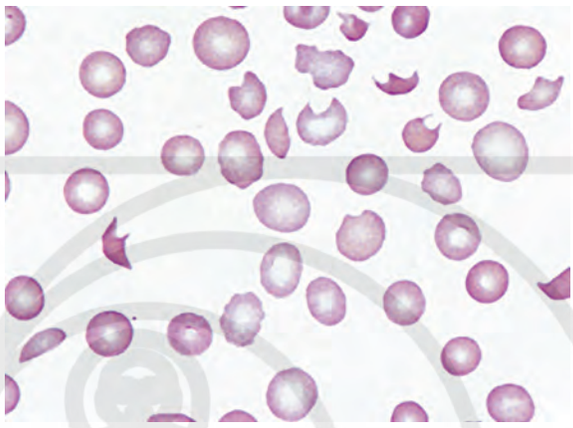


Image-Based Question

1. Identify the defect in RBC morphology.



a. Sickle cell
b. Bilte cells
c. Schistocytes
d. Elliptocytes

Answer of Image-Based Question

1. Ans. (c) Schistocytes

- The given smear shows helmet cells with spiculated ends in a case of microangiopathic hemolytic anemia.

Multiple Choice Questions

Most Recent Questions

1. In an Endothelial injury a tissue factor is released. This tissue factor combines with which of the following (marked A based)? *(INI-CET July 2021)*

a. Factor 7 b. Factor 8
c. vWF d. Factor 12

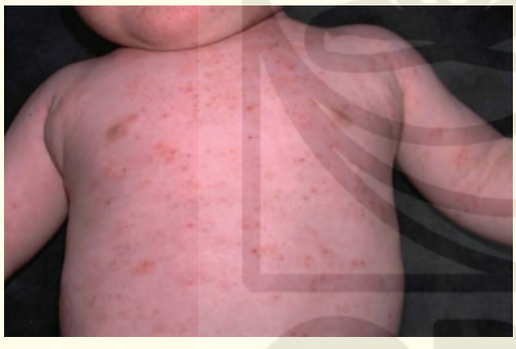
2. Which clotting factor deficiency will not affect clotting in vivo? *(INI-CET Nov 2020)*

a. 5 b. 7
c. 9 d. 12

3. Rapid assessment of entire coagulation pathway in emergency? *(INI-CET Nov 2020)*

a. PT b. APTT
c. CT d. Thromboelastography

4. A 5-year-old male child presented to the clinic with history of recurrent infections. On examination the child had rashes as shown below. Routine blood investigations revealed the patient had low platelets. Which of the following is the probable diagnosis in the kid? *(Recent Question 2020)*



a. Job Syndrome
b. Wiskott-Aldrich syndrome
c. Henoch-Schonlein purpura
d. Bruton's agammaglobulinemia

5. Which of the following produces vWF? *(AIIMS Nov 2019)*

a. Endothelial cells b. Platelets
c. Neutrophils d. Macrophages

6. Which of the following regarding BM biopsy needle and for procedure not true? *(AIIMS Nov 2019)*

a. Can be done in prone or lateral position
b. To find out infiltrative and granulomatous disorders
c. Breath holding not necessary
d. Platelet count of 40,000 is a contraindication

7. For detection of intrinsic pathway of coagulation which one is used? *(AIIMS May 2019)*

a. APTT b. PT
c. BT d. CT

8. From the following which is not hemostatic agent? *(AIIMS May 2019)*

a. Zeolite b. Chitosan
c. Boric acid d. Kaolin

9. Arrange the following clotting factor in sequence that they follow in coagulation cascade? *(AIIMS May 2019)*

1. 13 2. 12
3. 10 4. 5
5. 9

Select the correct answer using the code below:

a. $2 \rightarrow 3 \rightarrow 4 \rightarrow 1 \rightarrow 5$
b. $2 \rightarrow 5 \rightarrow 3 \rightarrow 4 \rightarrow 1$
c. $1 \rightarrow 2 \rightarrow 5 \rightarrow 3 \rightarrow 4$
d. $2 \rightarrow 3 \rightarrow 5 \rightarrow 4 \rightarrow 1$

10. What is the choice of treatment for idiopathic thrombocytopenia purpura (ITP)? *(Recent Question 2019)*

a. Blood transfusion
b. Spontaneous recovery
c. IV infusion
d. Splenectomy

11. Glanzmann thrombasthenia is due to: *(Recent Question 2019)*

a. Decreased GPIb
b. Decreased GPIIb/IIIa
c. Anti-GPIIb/IIIa antibodies
d. Inhibition or deficiency of ADAMTS 13

DISORDERS OF PRIMARY HEMOSTASIS

12. Glanzmann thrombasthenia is due to defect in: *(Recent Question 2019)*

a. Gp IIb/IIIa
b. Gp Ib-IX
c. CD68
d. Von Willebrand factor

13. Bleeding time increased in which of the following conditions? *(Recent Question 2018)*

a. Von Willebrand disease
b. Hemophilia A
c. DIC
d. Both a & c

14. Which of the following is true regarding Bernard-Soulier syndrome? *(Recent Question 2018)*

a. It is due to defect in platelet adhesion
b. It is due to defect in platelet aggregation
c. It is due to defect in platelet receptor GpIb-IX
d. Both a and c

15. Earliest event of vascular trauma is: *(Recent Question 2016)*

a. Vasoconstriction b. Platelet adhesion
c. Platelet aggregation d. Vasodilatation

16. Which of the following is a qualitative defect of platelet? *(Recent Question 2016)*

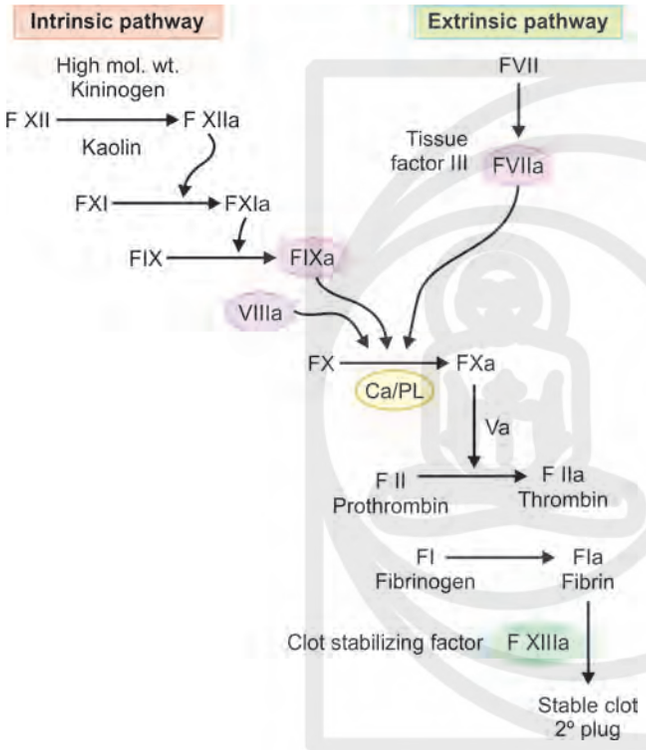
a. VWD
b. Hemophillia A
c. Hemophillia C
d. Glanzmann thrombasthenia

Answers with Explanations

1. Ans. (a) Factor 7

Bleeding Pathway and Disorders

Secondary plug



2. Ans. (d) 12

3. Ans. (d) Thromboelastography

4. Ans. (b) Wiskott-Aldrich syndrome

- Immunodeficiency with thrombocytopenia and eczema (Wiskott-Aldrich syndrome)
- This syndrome is an X-linked disorder.
- Characteristics include eczema, thrombocytopenia, recurrent infections, and poor antibody response to polysaccharide antigens. Total immunoglobulins most often are normal.

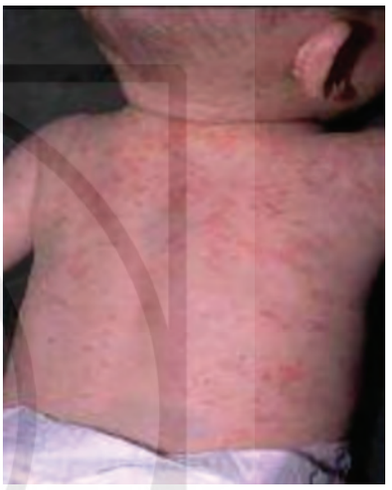
Wiskott–Aldrich syndrome (WAS) is a rare X-linked recessive disease characterized by eczema, thrombocytopenia (low platelet count), immune deficiency, and bloody diarrhea (secondary to the thrombocytopenia)

Wiskott-Aldrich Syndrome (WAS)

X-Linked Recessive

- It is caused by mutations in the gene encoding Wiskott-Aldrich syndrome protein (WASP), which is located at XP11.23.
- WASP is involved in cytoskeleton dependent responses including cell migration and signal transduction.

Wiskott-Aldrich syndrome Triad: (WA-TER) Thrombocytopenia Eczema Recurrent bacterial infections. Serum IgM level is Low, Serum IgG is Normal, Serum IgA & IgE are elevated.



5. Ans. (a) Endothelial cells

- VWF is a large multimeric glycoprotein present in blood plasma and produced constitutively as ultra-large VWF in endothelium.
- Von Willebrand Factor's primary function is binding to other proteins, in particular factor VIII, and it is important in platelet adhesion to wound sites. It is not an enzyme and, thus, has no catalytic activity.
- Endothelial cells contain intracellular stores known as Weibel Palade Bodies which contain vWF and P-selectin.

Functions of von Willebrand factor:

- Prolongs the half-life of factor VIII by stabilizing it (half-life of Factor VIII – 2.4 hours when free and 12 hours when bound to vWF in the circulation).
- Adhesion of platelets to subendothelium.
  - vWF is produced by endothelial cells and to some extent by megakaryocytes.
  - Ristocetin induces multivalent vWF multimer to bind platelet glycoprotein Ib-IX and forms interplatelet bridges.
  - Von Willebrand disease – Most common inherited bleeding disorder of humans
  - Type 1 and 3 are due to quantitative defects in vWF
  - Type 2 is due to qualitative defects in vWF

6. Ans. (d) Platelet count of 40,000 is a contraindication

Indications of Bone Marrow Biopsy:

- To accurately assess marrow cellularity
- To diagnose
  - Aplastic anemia

BLOOD VESSELS

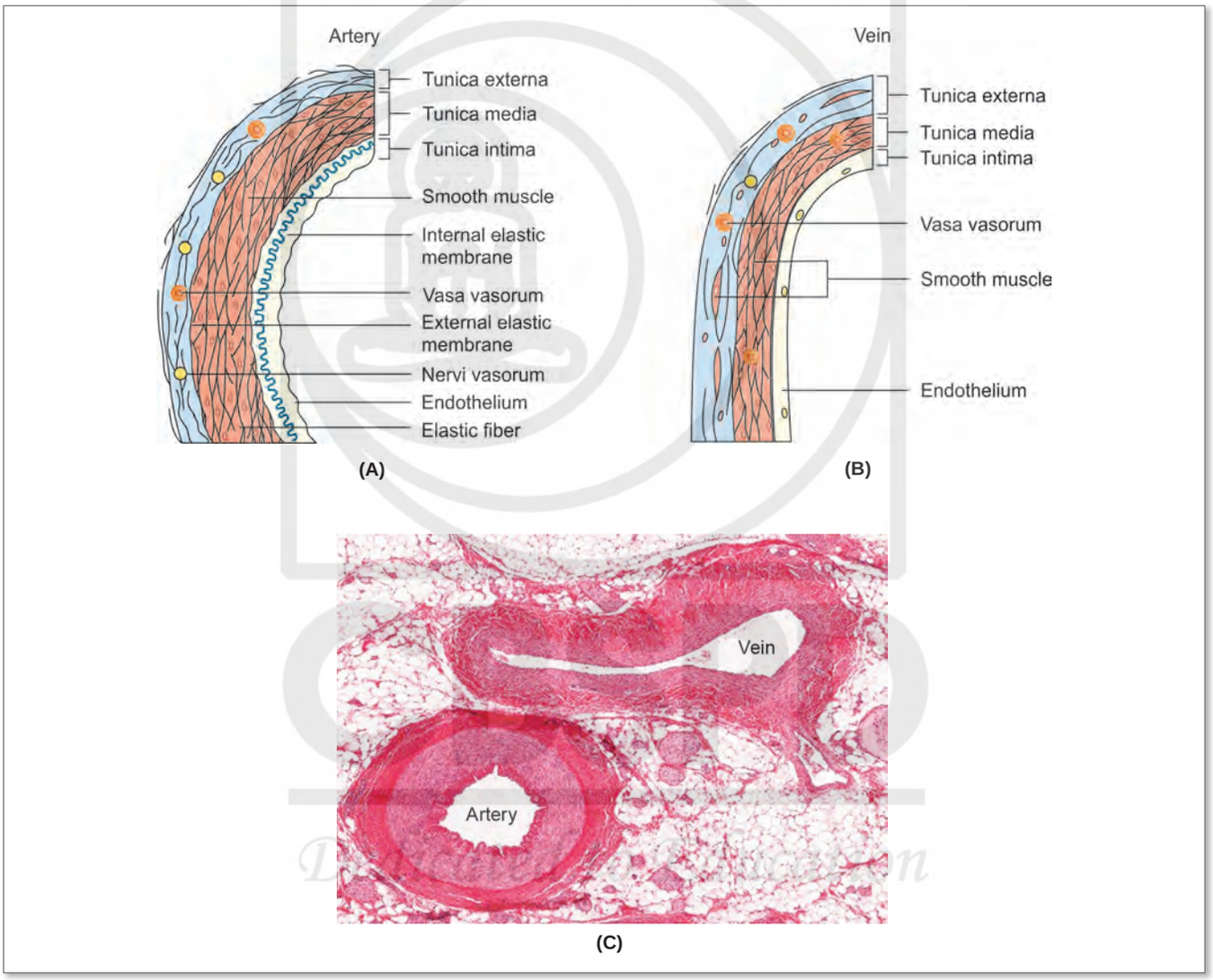
BLOOD VESSELS: OVERVIEW

The basic histological layers of the blood vessels (particularly arteries) are:

- Tunica intima (Innermost layer)-single layer of **endothelial cells**[Q]
- Internal elastic lamina
- Tunica media (Middle layer)- constituents depends on the type of artery as explained below:
- External elastic lamina
- Tunica adventitia (Outermost layer)-loose connective tissue containing nerve fibers and the **vasa vasorum**[Q]

High Yield Facts

- All vessels **except capillaries**[Q] have three-layered architecture consisting of an **intima, media, and adventitia**.
- There are 3 types of capillaries-**continuous, fenestrated and sinusoidal**



Arteries are divided into three types			
	Large or Elastic Arteries	***Medium or Muscular Arteries***	***Small Arteries (0.2 mm) Arterioles (20-100 µm)***
Type of vessel	Aorta and major branches **Pulmonary arteries**	Smaller branches of aorta (coronary and renal)	• Within tissues and organs.
Characteristic feature	Tunica media is **rich in elastin fibers**[Q]	Tunica media is rich in **smooth muscle cells**[Q]	**Resistance vessels** is other name of arterioles

Vascular anomalies

Developmental/ Berry/ Saccular Aneurysms

Cause
- Structural abnormality of the involved vessel
- Absence of smooth muscle and intimal elastic lamina[Q]

Features
- 90%- found **near major arterial branch points**[Q] in the anterior circulation of brain

Arteriovenous Fistulas

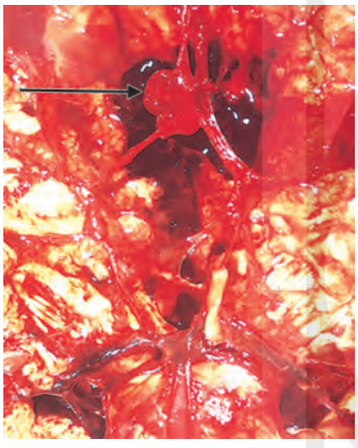
Cause
- Direct connections between arteries and veins

Features
- **Bypass the intervening capillary bed.**[Q]

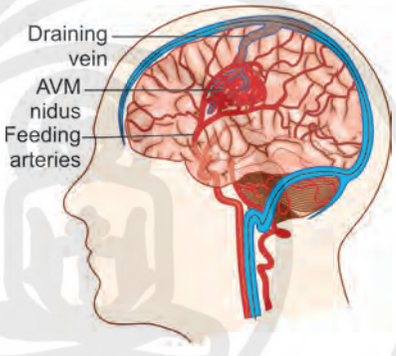
Fibromuscular Dysplasia (FMD)

Cause
- Focally thickened segments of vessel wall
- Medial and intimal hyperplasia and fibrosis

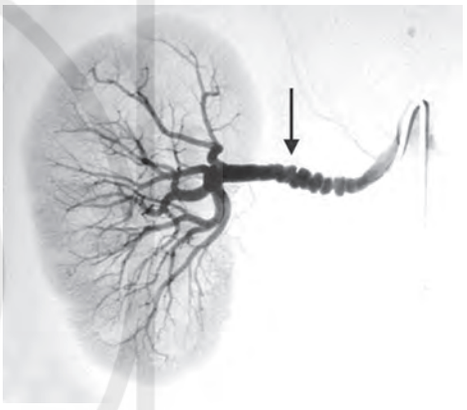
Features
- Most frequent in **young women**[Q]
- Immediately adjacent vessel segments have **markedly attenuated media**[Q] **-leading to aneurysms**[Q]



Berry aneurysm



A-V fistula



MRA or arteriography: string or beads appearance S/o FMD

High Yield Facts

Fibromuscular dysplasia
- Cause of **renovascular hypertension** in **young females** [Q]
- **No association with oral contraceptives or increased estrogen expression.**[Q]
- On angiography, the vessels have a "**string of beads**"[Q] appearance (due to **markedly attenuated media**[Q])

VESSEL SCLEROSIS

Denotes **arterial wall thickening** and **loss of elasticity**

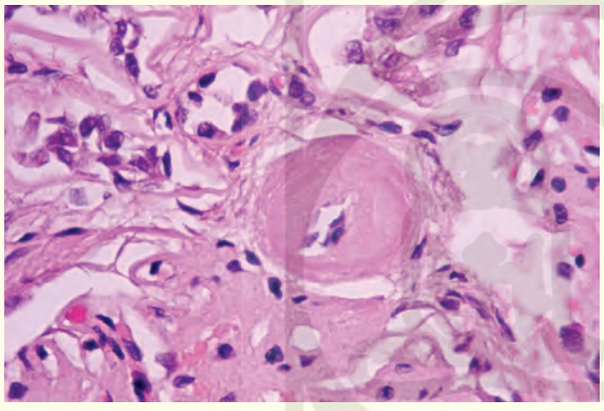
Type of vessel sclerosis

Arteriosclerosis (vessel lumen becomes narrow)		**Monckeberg medial sclerosis** (vessel lumen is normal)	**Atherosclerosis** (vessel lumen becomes narrow)
Hyaline	Hyperplastic		
• Homogeneous pink hyaline arteriolar wall thickening • Plasma protein leakage with increased smooth muscle cell synthesis. • Seen in: Benign hypertension (HT) : Diabtes mellitus (DM)	• Smooth muscle proliferation leads to concentric laminated arteriolar thickening **(Onion skinning)** • Associated with **fibrinoid necrosis & necrotizing arteriolitis** (Vessel wall necrosis) • Seen in: Malignant HT.	• Calcification of media of blood vessels typically involving internal elastic membrane. • Do not encroach on vessel lumen. • Age > 50 yrs • Not clinically significant	• Most frequent • Clinically important • Characterized by atheroma/ plaque consisting of raised focal lesion

Clinical Case-Based Questions

1 CBQ

A 65-year-old female patient undergoes routine examination and found to have Hb of 9.2 g/dL and 2+ protein in urine. General examination revealed hypertension. Renal biopsy was performed for proteinuria. Vascular changes are present in biopsy image of which is shown below. The Congo red stain is negative. What is the vascular changes?



a. Hyaline arteriosclerosis
b. Malignant arteriosclerosis
c. Necrotizing arteritis
d. Fibrosed vessel

2 CBQ

A 65-year-old man having familial history of diabetes. He diagnosed as diabetic 6 years back, and having uncontrolled sugar level along with systemic hypertension suddenly dies of congestive heart failure. The luminal surface of the abdominal aorta is shown in the image. Which of the following pathologic changes would you expect to see on microscopic examination?

a. Acute inflammation of the vessel wall
b. Bacterial colonies in the vessel wall
c. Cystic medial necrosis
d. Lipid deposition and smooth muscle cell hyperplasia

3 CBQ

A 68-year-old male patient on routine laboratory investigations found to have high cholesterol level. Relevant history shows he has abnormal lipid profile since many years which must have lead to generation of atherosclerosis in blood vessels. Fatty streaks lead to increased attachment of monocytes to endothelium and migration to subendothelium, transform themselves into foam cells. Which of the following substances is most likely to be responsible for the transformation of macrophages?

a. C-reactive protein
b. Homocysteine
c. Lp(a)
d. Oxidized LDL

4 CBQ

A 59-year-old male patient presents with abdominal pain, history taking revealed he has hypertension since long duration and also smokes since very long time. Radiological investigations were performed which show pulsating mid line mass possibly aneurysm. Which of the following statements are true regarding its generation?

a. Abnormal transforming growth factor beta signaling
b. Inflammation leading to collagen degradation and alteration
c. Weakening of vascular wall due to loss of smooth muscle cell or generation of noncollagen extracellular matrix
d. All of the above

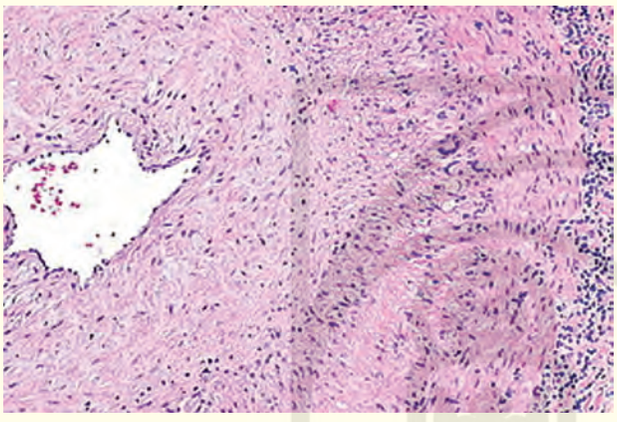
5 CBQ

A 65-year-old patient diagnosed as having hyperlipidemia on screening tests or a routine physical and laboratory investigations. Laboratory studies show total serum cholesterol of 350 mg/dL, LDL of 280 mg/dL, HDL of 37 mg/dL, and triglycerides of 380 mg/dL. This patient is symptomatic, however, is most at risk of developing an aneurysm in which of the following anatomic locations?

a. Abdominal aorta
b. Ascending aorta
c. Coronary artery
d. Renal artery

6 CBQ

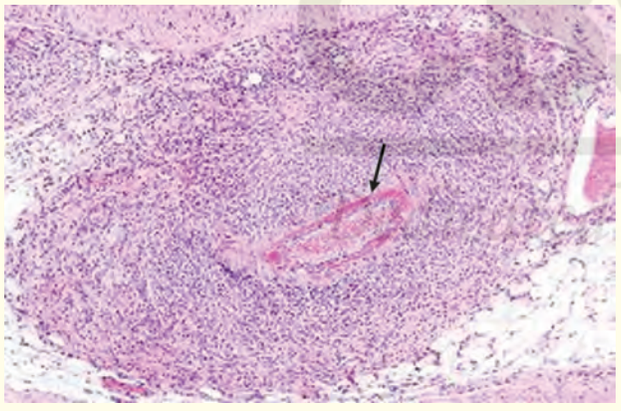
A 55-year-old male patient presented with vague symptoms of mild fever, fatigue but with intense unilateral throbbing headache on the left lateral side of scalp, while eating pain is on mandible also and blood vessels are palpable when pain is intense. A small vascular biopsy was performed and histopathological image of which is shown below. Based on the above findings what is your probable diagnosis?



a. Takayasu arteritis
b. Giant cell arteritis
c. Leucocytoclastic vasculitis
d. Wegener's granulomatosis

7 CBQ

A 45-year-old male patient presented to the emergency with chest pain, proper history taking revealed infrequently symptoms of bloody stools, abdominal pain and sometimes uncontrolled hypertension. He is a positive for HBsAg. MI is properly managed and biopsy of the vessels shows thrombosis with fibrinoid necrosis as shown below. Based on the above findings what is your probable diagnosis?



a. Atherosclerosis
b. Polyarteritis nodosa
c. Aortic dissection
d. Kawasaki disease

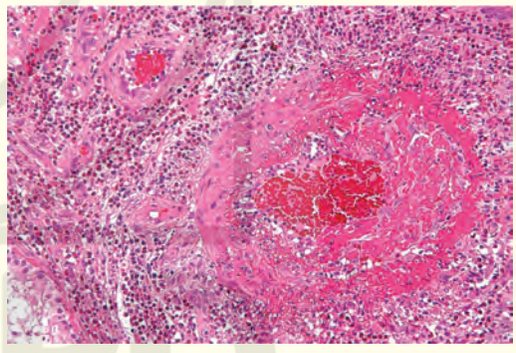
8 CBQ

A 2-year-old male baby presented with redness of eye, erythema of hand and feet along with cervical lymph node enlargement. He also complains of presence of fever. Based on the above clinical findings, all of the following statements are true regarding the disease except:

a. It results from delayed type hypersensitivity response
b. Histopathological examination will reveal dense transmural inflammatory infiltrate
c. Pathological changes are systemic and significantly affect kidney and liver
d. Immunoglobulin and aspirin therapy improve the symptoms

9 CBQ

A 58-year-old male patient presented with weakness, hematuria and other vague symptoms. Proper clinical examination shows presence of palpable purpura. Laboratory investigations performed show presence of proteinuria (2+) and MPO-ANCA positivity. Histopathological examination of the vessel shows fibrinoid necrosis without granuloma as shown below. Based on the above histopathological findings, what is your probable diagnosis?



a. Giant cell arteritis
b. Kawasaki disease
c. Polyarteritis nodosa
d. Microscopic polyangitis

10 CBQ

A 28-year-old man with a history of recent occurrence of respiratory distress after some strenuous exercise. Physical examination reveals mild hypertension (blood pressure = 150/100 mm Hg), bilateral wheezing, and numerous purpuric skin lesions on the feet. Laboratory investigations performed show presence of raised TLC (15300/µL) and eosinophilia, serum creatinine is elevated to 3.5 mg/dL. The serum ANCA test is positive. Urinalysis shows 3+ proteinuria and RBCs. A renal biopsy demonstrates vasculitis accompanied by eosinophilia. Based on the above findings what is your probable diagnosis?

a. Churg-Strauss disease
b. Henoch-Schönlein purpura
c. Wegener's granulomatosis
d. Polyarteritis nodosa

Answers of Clinical Case-Based Questions

1. Ans. (a) Hyaline arteriosclerosis

(Ref: Robbins 10th Ed pg. 493)

(a) Hyaline arteriolosclerosis: Arterioles show homogeneous, pink hyaline thickening with associated luminal narrowing. These changes reflect both plasma protein leakage across injured ECs and increased SMC matrix synthesis in response to the chronic hemodynamic pressures of hypertension.

(b) Hyperplastic arteriolosclerosis: This lesion occurs in severe hypertension; vessels exhibit concentric, laminated ("onion-skin") thickening of the walls with luminal narrowing

(c) No necrosis seen on the histopathology

(d) Fibrosed vessel will have occluded lumen

2. Ans. (d) Lipid deposition and smooth muscle cell hyperplasia

(Ref: Robbins 10th Ed. pg 499)

(a) Atherosclerosis is a disease of large- and medium-sized elastic and muscular arteries that result in the progressive accumulation within the intima of inflammatory cells, hyperplastic smooth muscle cells, lipids, and connective tissue. The resulting characteristic lesion, the lipid plaque (atheroma), contains pools of extracellular lipid and numerous lipid-laden macrophages (foam cells).

(a) It is not an acute inflammatory condition.

(b & c) It is not an acute infectious process related changes.

3. Ans. (d) Oxidized LDL

(Ref: Robbins 10th Ed. pg 496-498)

(a) C-reactive protein is a marker for inflammation, which can increase with more active atheroma and thrombus formation and predicts a greater likelihood of acute coronary syndromes.

(b) Homocysteine levels promote atherogenesis through endothelial dysfunction.

(c) Lp(a), an altered form of LDL that contains the apo B-100 portion of LDL linked to apo A, promotes lipid accumulation and smooth muscle cell proliferation.

(d) Oxidized LDL can be taken up by a special "scavenger" pathway in macrophages; it also promotes monocyte chemotaxis and adherence. Macrophages taking up the lipid become foam cells that begin to form the fatty streak.

4. Ans. (d) All of the above

(Ref: Robbins 10th Ed. pg 505)

(a) Abnormal transforming growth factor-β (TGF-β) signaling: Excessive TGF-β activity alters vascular wall remodeling, primarily of the ascending aorta, leading ultimately to diminished ECM content and integrity with aneurysmal dilation.

(b) The balance of collagen degradation and synthesis is altered by inflammation and associated proteases. Inflammatory cells in the setting of an aortitis or associated with atherosclerosis can be found throughout the aortic wall.

The vascular wall is weakened through loss of SMCs or the inappropriate synthesis of noncollagenous or nonelastic ECM. Ischemia of the inner media occurs when there is atherosclerotic thickening of the intima, increasing the distance that oxygen and nutrients must diffuse.

5. Ans. (a) Abdominal aorta

(Ref: Robbins 10th Ed pg 506)

The two most important causes of aortic aneurysms are atherosclerosis and hypertension; atherosclerosis is a greater factor in abdominal aortic aneurysm (AAA), while hypertension is the most common etiology associated with ascending aortic aneurysms.

6. Ans. (b) Giant cell arteritis

(a) Takayasu arteritis is usually seen in less than 50 years of age.

(b) Involved arterial segments develop intimal thickening (with occasional thromboses) that reduces the luminal diameter. Classic lesions exhibit medial granulomatous inflammation centered on the internal elastic membrane with elastic lamina fragmentation; there is an infiltrate of T cells (CD4+ > CD8+) and macrophages. Although multinucleated giant cells are seen in approximately 75% of adequately biopsied specimens.

Temporal arteritis is rare before age 50. Symptoms may be only vague and constitutional—fever, fatigue, weight loss—or may involve facial pain or headache, most intense along the course of the superficial temporal artery, which can be painful to palpation. Ocular symptoms (associated with involvement of the ophthalmic artery) abruptly appear in about 50% of patients; these range from diplopia to complete vision loss.

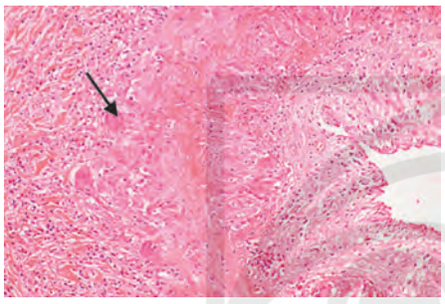
7. Ans. (b) Polyarteritis nodosa

(Ref: Robbins 10th Ed pg 513)

(b) PAN is a systemic vasculitis of small- or medium-sized muscular arteries that typically affect renal and visceral vessels but spare the pulmonary circulation. There is no association with ANCAs, but a third of patients with PAN have chronic hepatitis B. PAN is associated with segmental transmural necrotizing inflammation of small- to medium-sized arteries, often with superimposed aneurysms and/or thrombosis. Kidney, heart, liver, and gastrointestinal tract vessels are involved in descending order of frequency.

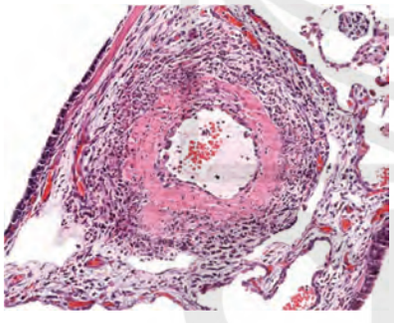
Image-Based Questions

1. A 45-year-old male presented with pulseless disease. On examination, following histopathological finding will be seen:



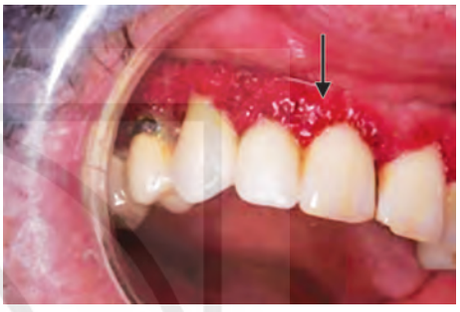
a. Granulomatous vasculitis
b. Fibrinoid necrosis
c. Leukocytoclastic vasculitis
d. Thromboangitis obliterans

2. A patient is a known case of polyarteritis nodosa. On examination of biopsy, accumulation of amorphous, basic, proteinaceous material in the vessel wall was seen. This finding is suggestive of:



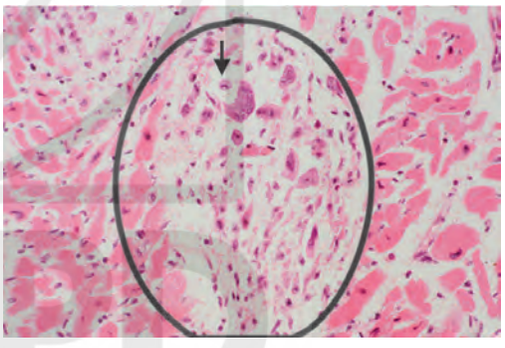
a. Fibrinoid necrosis
b. Leukocytoclastic vasculitis
c. Hyaline arteriosclerosis
d. Caseous necrosis

3. A 34-year-old male patient presented with following clinical feature. What is the diagnosis?



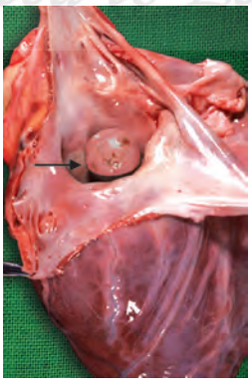
a. Kawasaki disease
b. PAN
c. MicroPAN
d. Wegener's granulomatosis

4. A 15-year-old boy presented with pancarditis, on myocardial biopsy, following finding was seen. What is the diagnosis?



a. Aschoff nodule
b. TB
c. FB giant cells
d. None

5. A 25-year-old male presented with growth in left atrium. What is the diagnosis?



a. Rhabdomyoma
b. Myxoma
c. Metastasis
d. Papillary elastosis

Answers of Image-Based Questions

1. Ans. (a) Granulomatous vasculitis

- Here we can see epithelioid cells and giant cells s/o granulomatous vasculitis
- Granulomatous vasculitis is seen in: Giant cell (temporal) arteritis, Takayasu arteritis, Wegener's granulomatosis, Churg-Strauss syndrome, Buerger's disease

2. Ans. (a) Fibrinoid necrosis

- Fibrinoid necrosis is a form of necrosis, or tissue death, in which there is accumulation of amorphous, basic, proteinaceous material in the tissue matrix with a staining pattern reminiscent of fibrin.
- How to differentiate from hyaline arteriosclerosis? Please remember in fibrinoid necrosis, pink material has fibrin like quality as opposed to glassy homogenous hyaline in hyaline arteriosclerosis. (refer to image 2)

3. Ans. (d) Wegener's granulomatosis

- This is strawberry gums, seen in wegener's granulomatosis

4. Ans. (a) Aschoff nodule

Here one can see collection of foci of swollen eosinophilic collagen surrounded by : Lymphocytes (primary T cells), Occasional plasma cells, Aschoff giant cells[Q] (macrophages of rheumatic fever)[Q] and Antischkow cells (cells with caterpillar like chromatin marked with an arrow)

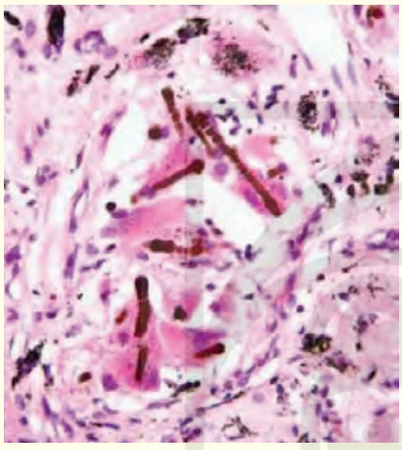
5. Ans. (b) Myxoma

The left atrium has been opened to reveal the most common primary cardiac neoplasm-an atrial myxoma. These benign masses are most often attached to the atrial wall. They can produce a "ball valve" effect by intermittently occluding the atrioventricular valve orifice.

Multiple Choice Questions

Most Recent Questions

1. Patient with clinical features of asbestosis and image of ferruginous bodies was given. Which industry does he work in? *(INI-CET Nov 2021)*

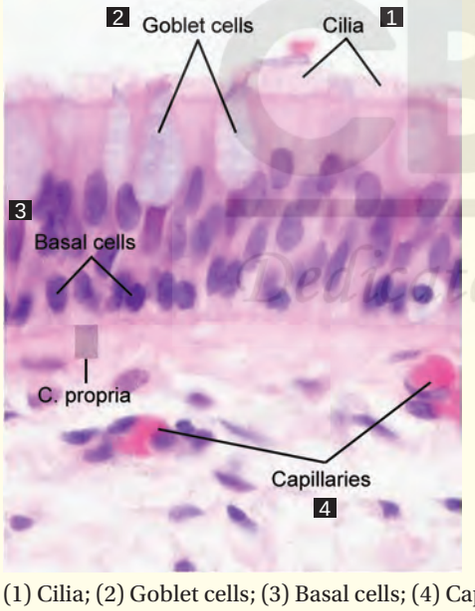


a. Asbestos industry
b. Silica industry
c. Cotton
d. Coal water: Module, nodule

2. Patient with low grade fever and cough. Caseous necrosis seen on CXR. Mechanism? *(INI-CET Nov 2021)*

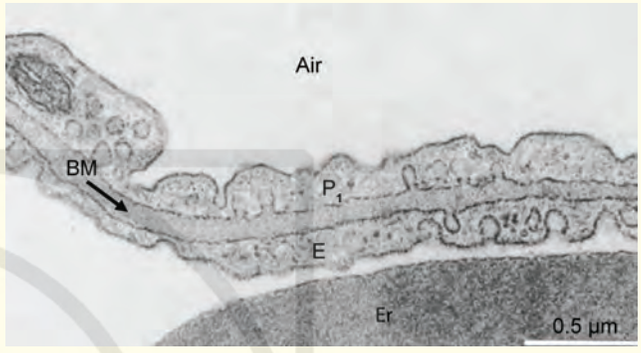
a. Epithelioid cells, giant cells, macrophage
b. Enzymatic degradation
c. Fibrinoid necrosis
d. Sudden cut off blood supply
e. Hypersensitivity with neuro

3. Marking is not correct: *(INI-CET Nov 2021)*



a. (1) Cilia; (2) Goblet cells; (3) Basal cells; (4) Capillaries
b. (1) Goblet cells; (2) Cilia; (3) Basal cells; (4) Capillaries
c. (1) Basal cells; (2) Cilia; (3) Goblet cells; (4) Capillaries
d. (1) Capillaries; (2) Cilia; (3) Goblet cells; (4) Basal cells

4. Electron microscopic picture of an alveolus with capillary and question was in Covid-19 disease which of the following is expanded? *(INI-CET July 2021)*



5. Match the following: *(INI-CET Nov 2020)*

Column A	Column B
a. Silicosis	1. CRAZY pavement
b. Mesothelioma	2. Malignant pleural effusion without mediastinal shift
c. Caplan syndrome	3. Initially demonstrated in coal workers
d. Asbestosis	4. Basal lobes involved

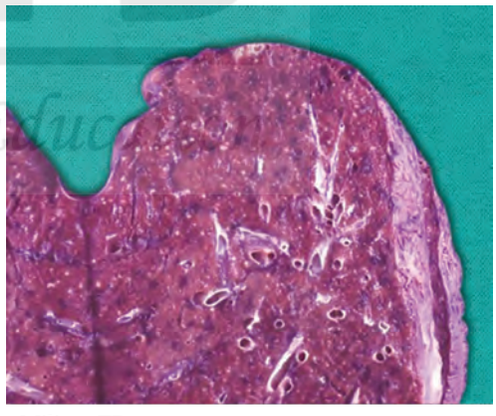
6. Most common cause of lung injury in COVID-19 infection: *(INI-CET Nov 2020)*

a. Pulmonary infarction
b. Diffuse alveolar damage
c. Endothelial injury
d. Fibrin clots

7. Alpha-1 antitrypsin works by: *(Recent Question 2019)*

a. Inhibition of trypsin
b. Inhibition of trypsinogen
c. Inhibition of elastase
d. Inhibition of chymotrypsin

8. Section of lung showing what? *(Recent Question 2018)*



a. Miliary TB
b. Pneumoconiosis
c. Bronchiectasis
d. Pneumonia

9. Whole blood is used in diagnosis of TB in: *(Recent Question 2018)*

a. Gamma-interferon assay
b. Gene expert
c. BACTEC test
d. Blood culture

RESPIRATORY SYSTEM AND ITS CONGENITAL MALFORMATIONS

10. Ciliocytophthoria is seen in: *(AIIMS Nov 2019)*

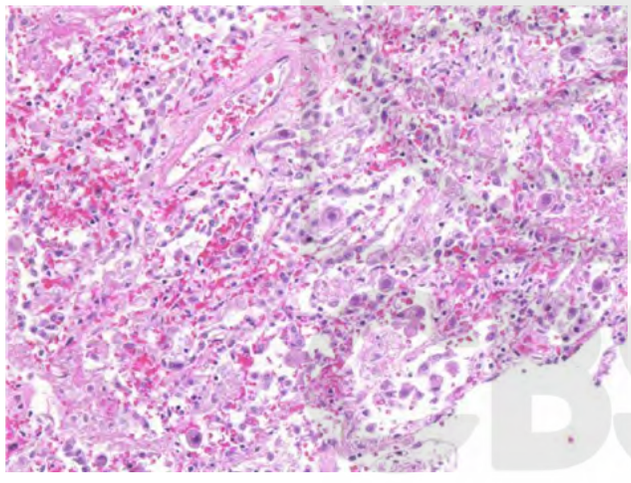
a. Kartagener
b. Situs inversus
c. Acute respiratory infection
d. Cystic fibrosis

11. Kartagener's syndrome cause of infertility is:

a. Oligospermia
b. Asthenospermia
c. Undescended testis
d. Epididymis obstruction

ARDS AND PNEUMONIA

12. A middle-aged immunocompromised male came with fever and breathlessness. HRCT showed a middle lobe lesion with infiltration in the lung as shown in image. Most likely diagnosis is: *(AIIMS May 2018)*

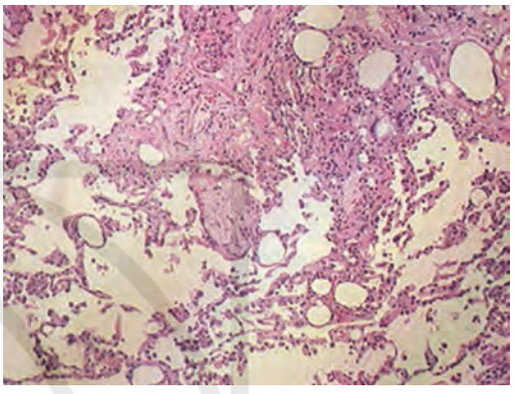


a. Tuberculous pneumonia
b. Cryptogenic organizing pneumonia
c. Small cell carcinoma lung
d. CMV pneumonia

13. What is false about ARDS? *(Recent Question 2016)*

a. Mucus plug in alveoli
b. Interstitial edema
c. Hyaline membrane present
d. Interstitial infiltrates by cells

14. Patient with h/o long-standing depressive illness came to emergency with acute breathlessness. The X-ray shows diffuse infiltrates with predominance in right middle lobe and right lower lobe. The patient did not survive and the following picture in the lungs was seen on autopsy? *(AIIMS Nov 2017)*



a. Severe necrosis with fungal hyphae, severe fungal pneumonia
b. Coagulation necrosis, tuberculosis
c. Vegetable matter; aspiration pneumonia
d. Severe necrosis; severe necrotizing pneumonia

15. The following are true regarding hyaline membrane disease; except:

a. Basic abnormality is deficiency of surfactant
b. Prenatal diagnosis by low amniotic fluid L/S ratio
c. Intratracheal surfactant helps
d. Occurs in babies born post-dates

16. Etiology of ARDS are all; except: *(Recent question 2015)*

a. Multiple transfusion
b. Sepsis
c. Aspiration of gastric contents
d. Fat embolism

17. Characteristic feature of best sputum sample is/are:

a. Presence of leukocytes
b. Respiratory epithelium
c. Neutrophils
d. Mucus with inflammatory cells
e. Presence of alveolar macrophages

18. Heart Failure cells are: *(Recent Question 2014, 2013)*

a. Lipofuscin granules in cardiac cells
b. Pigmented alveolar macrophages
c. Pigmented pancreatic acinar cells
d. Pigment cells seen in liver

19. Terminal stage of pneumonia is: *(Recent Question 2014)*

a. Congestion
b. Red hepatization
c. Gray hepatization
d. Resolution

Answers with Explanations

1. Ans. (a) Asbestos industry

2. Ans. (a) Epithelioid cells, giant cells, macrophage

3. Ans. (a) (1) Cilia; (2) Goblet cells; (3) Basal cells; (4) Capillaries

4. Ans. (E)

5. Ans. a1, b2, c3, d4

6. Ans. (b) Diffuse alveolar damage

7. Ans. (c) Inhibition of elastase

- Alpha-1 antitrypsin (A1AT) functions is to protect the lungs from neutrophil elastase, an enzyme that can disrupt connective tissue. α1-anti-trypsin, normally present in serum, tissue fluids, and macrophages, is a major inhibitor of proteases (particularly elastase) secreted by neutrophils during inflammation. α1-anti-trypsin is encoded by a gene in the proteinase inhibitor (Pi) locus on chromosome14.

8. Ans. (a) Miliary TB

This is a "miliary pattern" of granulomas because there are a multitude of small tan granulomas about 2–4 mm in size, scattered throughout the lung parenchyma. The miliary pattern gets its name from the resemblance of the granulomas to millet seeds.

- Miliary TB can occur when TB lung lesions erode pulmonary veins or when extrapulmonary TB lesions erode systemic veins.
- This results in hematogenous dissemination of tubercle bacilli producing myriads of 1–2 mm lesions throughout the body in susceptible hosts.
- Miliary spread limited to the lungs can occur following erosion of pulmonary arteries by TB lung lesions.

9. Ans. (a) Gamma-interferon assay

Tuberculosis: It is the classic granulomatous infection. The disease is divided into primary and secondary (or reactivation) tuberculosis.

- **Primary tuberculosis:** The disease is acquired from the initial exposure to *M. tuberculosis*, most commonly as a result of inhaling infected aerosols generated when a person with cavitary tuberculosis coughs.

Pathology

- The Ghon's complex is the first lesion of primary tuberculosis and consists of a peripheral parenchymal granuloma, often in the upper lobes.
- When it is associated with an enlarged mediastinal lymph node, a Ranke complex is formed.
- Microscopically, a granuloma with central caseous necrosis shows varying degrees of fibrosis.
  - Apical scarring with the appearance of a fibronodular patch or ill-defined reticular shadow in the upper lung fields on chest X-ray is known as "**Simon's focus**".
  - Purl's lesion: Lesion at the apex of lung in chronic cases.
  - **Assmann's focus:** Typically, apical (site of highest oxygen tension)
  - **TB Simon's focus:** Early hematogenous seeding in apex of lungs.
  - **Ghon's complex:** Parenchymal subpleural lesion + draining lymphatics + enlarged caseous lymph nodes in primary tuberculosis.
  - **Ranke complex:** Healed lesions in lung parenchyma and hilar lymph nodes undergoing calcification due to TB.
  - **Rich focus:** Tuberculous caseous foci in brain, meninges and spinal cord.
- **Secondary tuberculosis:** This stage represents either reactivation of primary pulmonary tuberculosis or a new infection in a host previously sensitized by primary tuberculosis.
- A cellular immune response occurs after a latent interval and leads to formation of many granulomas and extensive tissue necrosis.
- The apical and posterior segments of the upper lobes are most commonly involved.
- A diffuse, fibrotic, poorly defined lesion develops. Some erode into a bronchus creates a tuberculous cavity.
- Tuberculous cavities range in size from under 1 cm in diameter to large cystic areas.
- The tuberculous cavity often communicates freely with a bronchus, and spreads the infection within the lung.
- Secondary tuberculosis is associated with a number of **complications:**
- Miliary tuberculosis refers to the presence of multiple, small (size of millet seeds), tuberculous granulomas in many organs.
- Hemoptysis
- Bronchopleural fistula occurs when a subpleural cavity ruptures into the pleural space. In turn, tuberculous empyema and pneumothorax result.
- Tuberculous laryngitis
- Intestinal tuberculosis.

Testing for Latent Tuberculosis Infection

- The goal of testing for LTBI is to identify individuals who are at increased risk for the development of active TB; these individuals would benefit most from treatment of LTBI (also termed preventive therapy or prophylaxis).

14

Gastrointestinal Tract and Related Disorders

Key Points

- Esophagus does not have serosa.
- Most common fungal organism causing esophageal infections is Candida.
- Barrett's esophagus is characterized by intestinal metaplasia within the esophageal squamous mucosa.
- Most common esophageal cancer in India is squamous cell carcinoma.
- Most important risk factor for adenocarcinoma is Barrett's esophagus.
- Ulcers occurring in the proximal duodenum and associated with severe burns or trauma are called curling ulcers.
- Hallmark of Crohn's disease: Noncaseating granulomas.
- Most common site of carcinoid tumor: Tracheobronchial tree followed by ileum, followed by rectum.
- At least 100 polyps are necessary for diagnosing classic FAP.
- Squamous cell carcinoma is the most common tumor of anal canal.

Key Recent Updates

- Dysbiosis is seen in pseudomembranous colitis.
- Combination of strong crypt CG3 staining and loss of DAS 1 stain is seen in 45% UC. Hence, these are new markers of UC.

The GI tract contains four layers:

1. **Mucosa:** Consisting of lining epithelium, **lamina propria** and muscularis mucosae
2. **Submucosa:** Mucous secreting glands, **Meissner's plexus**
3. **Muscularis propia** (inner circular layer, outer longitudinal layer): **Auerbach's plexus** in between these two layers.
4. **Adventitia or Serosa**

CONGENITAL ABNORMALITIES[Q]

Diverticulum

Meckel's Diverticulum

Most common true diverticulum which occurs in the **ileum**. (antimesenteric side)

True diverticulum is defined by the presence **of all three layers** of the bowel wall.[Q]

- Due to failed involution of the **vitelline duct**[Q]
- **Common site** of gastric ectopia, can cause **occult bleeding.**[Q]

Mnemonic

Meckel's diverticulum Rule of 2s

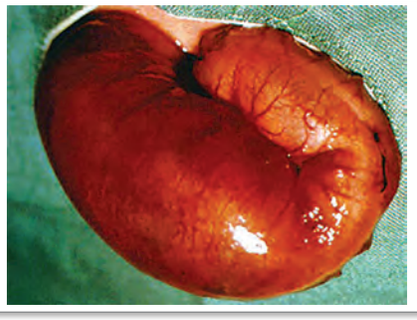
- Occur in **2%** population
- **Within 2 feet of** ileocecal valve
- **2 inches** long
- 2 times more common in males
- Symptomatic by **age 2**

Acquired Diverticulum

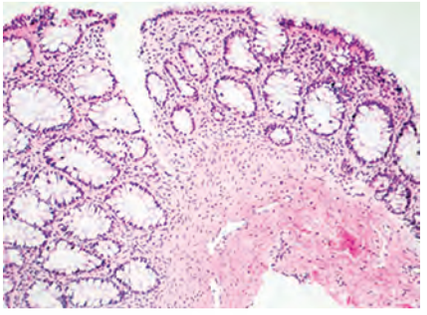
Most common in sigmoid colon

Hirschsprung Disease (Congenital Aganglionic Megacolon[Q])

- Normal migration of **neural crest cells from cecum to rectum is arrested prematurely**.
- Distal intestinal segment lacks **both the Meissner's submucosal and the Auerbach's myenteric plexus.**[Q]
- **Proximal to aganglionic segment, colon undergoes progressive dilation**[Q].
- Defect always **begins in the rectum,**[Q] but extends proximally for variable lengths.
- **Aganglionic region** may have a grossly **normal or contracted appearance**[Q].
- In contrast, **the normally** innervated proximal colon may undergo **progressive dilation (megacolon)**[Q].
- Heterozygous **loss of function mutations** in **RET gene causes most of** familial cases and 15% of sporadic cases[Q].



Megacolon



Aganglionosis of the colon (Hirschsprung disease)

Omphalocele

- Abdominal viscera herniating into a ventral membranous sac.

Gastroschisis

- Herniation of **all layers**[Q] of the abdominal wall from peritoneum to skin.

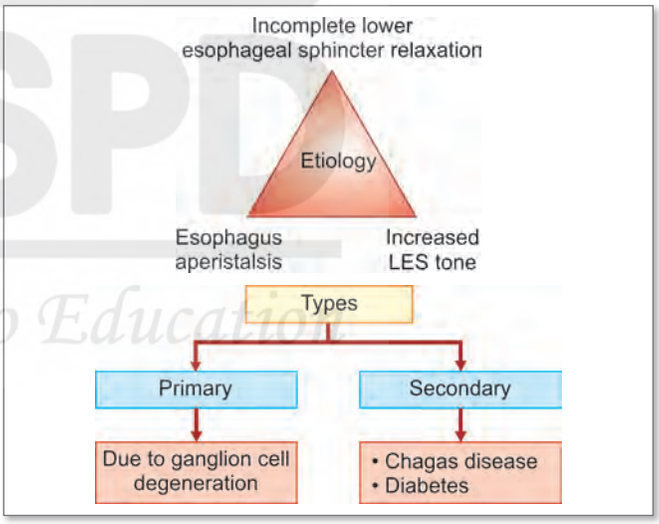
Ectopia

- **Most frequent site** of ectopic gastric mucosa is the **upper third portion of the esophagus**.

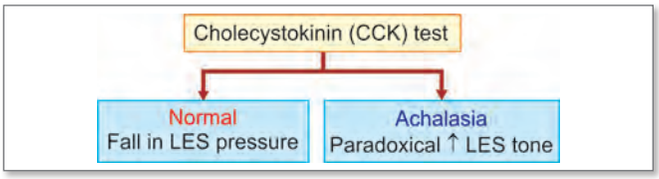
ESOPHAGUS

ACHALASIA CARDIA

- Occurs due to selective **loss of function of inhibitory neurons** like those secreting vasoactive intestinal peptide and nitric oxide, which causes relaxation of LES, whereas cholinergic innervation is intact



Screening Test



High Yield Facts

- Achlasia differs from Hirschsprung disease since dilated esophagus contains less ganglion cells, whereas dilated colon contains normal ganglion cells proximal to constricted aganglionic segment in Hirschsprungs.
- Inlet patch:[Q] Ectopic gastric mucosa is the upper third portion of the esophagus.

Diagnosis

- Barium swallow shows **bird beak appearance** of the esophagus.
- Method of choice: Manometry[Q]

LACERATIONS

Mallory-Weiss Tear	Boerhaave syndrome
• Longitudinal **mucosal** tears • These tears usually **cross the gastroesophageal junction** • Associated with **severe retching or vomiting**[Q] • Secondary to acute alcohol intoxication • Generally require **surgical intervention**[Q]	• **Transmural** tearing[Q] • Most common location: **left posterolateral part 3–5 cm above the gastroesophageal junction** • **Require surgical intervention**

ESOPHAGITIS

- Inflammation of the esophageal mucosa is known as esophagitis.
- **Most common cause**[Q]: Reflux of gastric contents into the lower esophagus due to **transient lower esophageal sphincter relaxation**[Q]
- **Gold standard** for the diagnosis of reflux esophagitis **is 24 hours pH study**[Q].

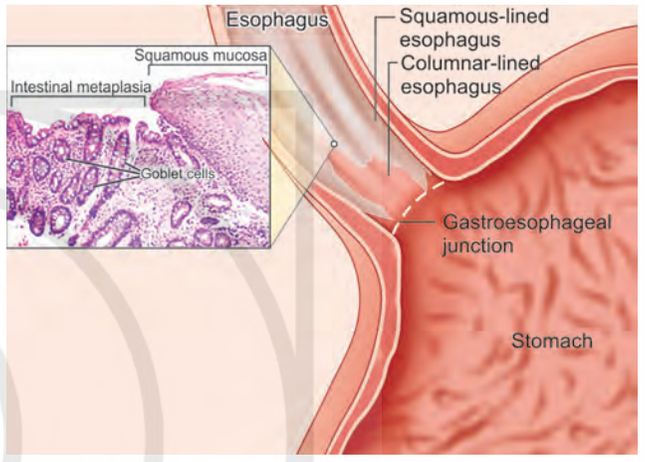
High Yield Facts

Esophageal infection

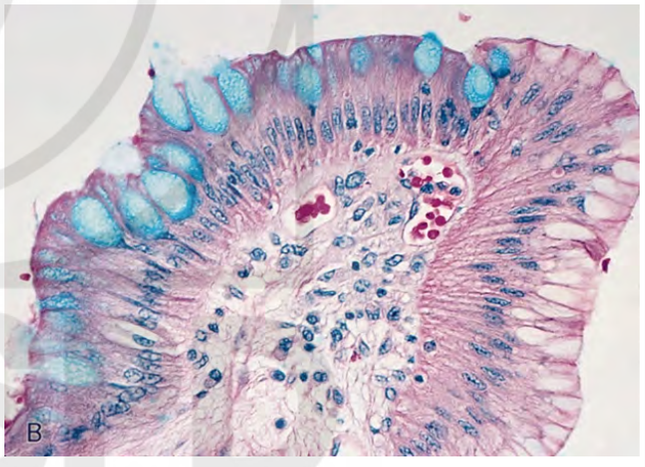
- **Herpes viruses** typically cause **punched-out ulcers**[Q].
- **CMV** causes **shallower ulcerations**[Q] with nuclear and cytoplasmic inclusions **within capillary endothelium and stromal cells**[Q].
- **M.C fungal** organism causing esophageal infections is **Candida**[Q] followed by mucormycosis and aspergillus.

BARRETT'S ESOPHAGUS

- Characterized by **intestinal metaplasia** within the esophageal squamous mucosa.[Q]
- Occurs due to **chronic gastroesophageal reflux disease** (GERD).[Q]
- Risk of **dysplasia correlates with length of esophagus affected. Long segment has the higher risk**[Q].
- Confers an **increased risk of esophageal adenocarcinoma**.[Q]
- Classified as long segment (if >3 cm is involved) or short segment (if <3 cm is involved).
- Diagnosis: Endoscopy and biopsy.
- Microscopically, **lower** esophageal squamous epithelium is replaced by columnar epithelium.
- **Definite diagnosis is made only when columnar mucosa contains the intestinal goblet cells, which show distinct mucous vacuoles that stain pale blue by hematoxylin and eosin.**[Q]



Barrett's esophagus



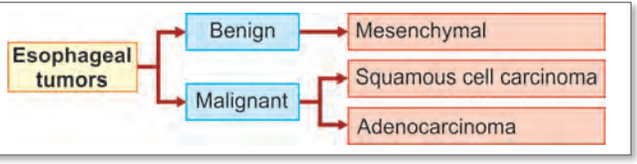
Alcian blue positivity in Barrett's esophagus

Latest Update

Dysplasia is detected in 0.2–2% of persons with Barrett's esophagus each year

- **Barrett's ulcer is the ulcer in the columnar lined portion of Barrett's esophagus.**[Q]

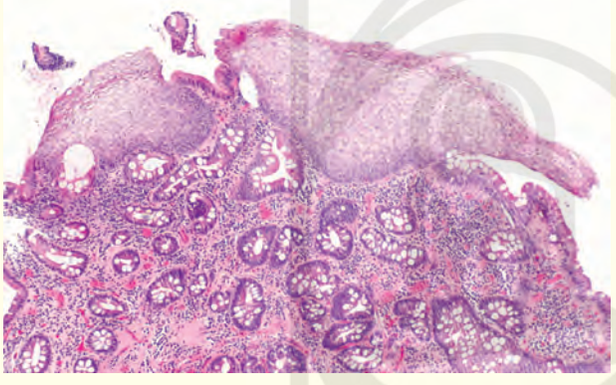
ESOPHAGEAL TUMORS



Clinical Case-Based Questions

1 CBQ

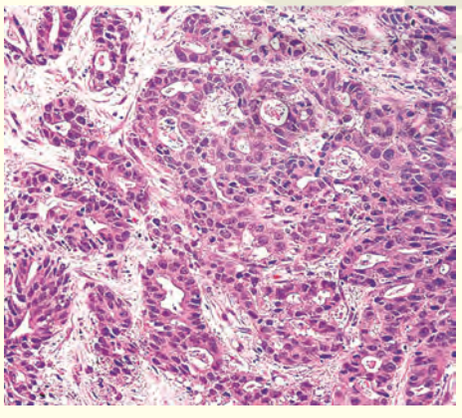
A 48-year-old male patient presented to the OPD with complaints of increasing difficulty swallowing during the past 4 months. Physical examination is unremarkable. Upper gastrointestinal endoscopy shows areas of erythematous mucosa 3 cm. A biopsy is taken erythematous lesion and histopathological image is shown below. Which of the following complications is most likely to occur as a consequence of this patient's condition?



a. Achalasia
b. Adenocarcinoma
c. Lacerations (Mallory-Weiss syndrome)
d. Squamous cell carcinoma

2 CBQ

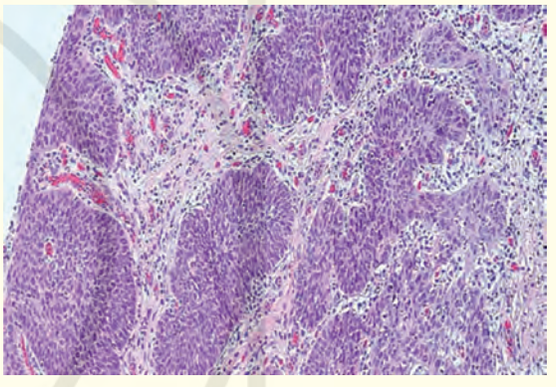
A 69-year-old woman presents with difficulty swallowing and weight loss over the past few months. Barium swallow and other radiological investigation revealed irregular narrowing of the lower third of the esophagus. A biopsy was taken and histopathological image of which is shown below. Which of the following is the most likely diagnosis?



a. Adenocarcinoma
b. Esophageal stricture
c. Leiomyosarcoma
d. Squamous cell carcinoma

3 CBQ

A 68-year-old male patient presented to the OPD with complaints of difficulty in food intake which is gradually increasing since 6 months. Endoscopy was performed shows a polypoidal mass protruding into the lumen in middle third of esophagus. Punch biopsy from the mass was taken and histopathological examination was performed, image of which is shown below. Based on the above findings, what is your probable diagnosis?



a. Adenocarcinoma
b. Squamous cell carcinoma
c. Leiomyoma
d. Lymphoma

4 CBQ

A 3-year-old boy is rushed to the casualty room in acute distress. The child has vague chest pain and difficulty in swallowing. He refuses to drink water. Physical examination shows drooling and salivation. Vital signs are normal. The mother states that she saw the boy ingesting a liquid used to clear drains. If this chemical was a strong acid, which of the following histopathologic findings would be expected in the esophagus of this child?

a. Apoptosis
b. Coagulative necrosis
c. Hyaline sclerosis
d. Liquefactive necrosis

5 CBQ

A 54-year-old woman with long-standing rheumatoid arthritis complaints of weakness and fatigue. She states that her stools have recently become black after taking a new nonsteroidal anti-inflammatory drug (NSAID). Gastroscopy shows numerous superficial, bleeding mucosal defects. Which of the following is the most likely diagnosis?

a. Acute erosive gastritis
b. Early gastric cancer
c. Helicobacter pylori gastritis
d. Ménétrier disease

Answers of Clinical Case-Based Questions

1. Ans. (b) Adenocarcinoma

(Ref: Robbins 10th Ed pg 762)

(a) Achalasia refers to the failure of the lower esophageal sphincter to relax, which gives rise to dilation of the proximal portion of the esophagus.

(b) The biopsy specimen shows squamous epithelium along with columnar metaplasia typical of Barrett esophagus. Patients with a focus of Barrett esophagus have a higher risk of developing adenocarcinoma than the general population.

(c) Mallory-Weiss syndrome is associated with vertical lacerations in the esophagus that may occur with severe vomiting and retching.

(d) Squamous cell carcinomas occur in the midesophagus, but they do not arise in association with Barrett esophagus. Instead, they are linked to smoking and alcohol consumption.

2. Ans. (a) Adenocarcinoma

(Ref: Robbins 10th Ed pg 763)

(a) Histopathological image shows markedly atypical cuboidal cells lining irregular shaped gland-like structures. Adenocarcinoma originates in the glandular metaplasia of Barrett esophagus. Endoscopic surveillance for adenocarcinoma is now commonly done in patients with Barrett esophagus, particularly those with dysplasia. Tumors tend to grow into the lumen of the esophagus. The affected region of the esophagus is typically indurated and ulcerated, causing pain and bleeding.

(b) It will not show malignant looking gland. It's infiltration in lamina propria.

(c) It will show spindle shaped cells, which is absent here.

(d) It will show malignant squamous cells with occasional keratin Pearl formation which is absent here

3. Ans. (b) Squamous cell carcinoma

(Ref: Robbins 10th Ed pg 764)

(a) Adenocarcinoma shows glands lined by atypical (malignant) cells with infiltration in the lamina propria.

(b) Squamous cell carcinomas occur in the middle third of the esophagus. Over months to years they grow into tumor masses that may be polypoid, or exophytic, and protrude into and obstruct the lumen. Most squamous cell carcinomas are moderately to well differentiated and have squamoid appearance.

(c) It will show spindle shaped cells, which is absent here.

(d) It will shows diffuse infiltration of atypical lymphocytes in the lamina propria.

4. Ans. (b) Coagulative necrosis

(a & c) Doesn't caused by acid or alkali.

(b) Chemical injury to the esophagus usually reflects accidental poisoning in children, attempted suicide in adults, or contact with medication. Ingestion of strong acids produces an immediate coagulative necrosis in the esophagus, which results in a protective eschar that limits injury and further chemical penetration.

(d) By contrast, ingestion of strong alkaline solutions is accompanied by liquefactive necrosis, with inflammation and saponification of membrane lipids. Alkaline solutions are particularly insidious because they are generally odorless and tasteless and, therefore, easily swallowed before protective reflexes come into play.

5. Ans. (a) Acute erosive gastritis

(a) Acute hemorrhagic gastritis is characterized by necrosis of the mucosa and is commonly associated with the intake of aspirin, other NSAIDs, alcohol, or ischemic injury. The factor common to all forms of acute hemorrhagic gastritis is thought to be the breakdown of the mucosal barrier, which permits acid-induced injury. Mucosal injury causes bleeding from superfi cial erosions. Defects in the mucosa may extend into the deeper tissues to form an ulcer. The necrosis is accompanied by an acute inflammatory response and hemorrhage, which may be severe enough to result in exsanguination and hypovolemic shock.

(b, c, d) The other choices are not associated with the use of NSAIDs.

6. Ans. (d) *Helicobacter pylori* infection

(a) Achlorhydria is incorrect because the formation of peptic ulcers requires at least some gastric acid secretion.

(d) Peptic ulcer disease refers to breaks in the mucosa of the stomach and small intestine, principally the proximal duodenum, which are produced by the action of gastric secretions. The pathogenesis of peptic ulcer disease is believed to involve an underlying chronic gastritis caused by *H. pylori*. This pathogen has been isolated from the gastric antrum of virtually all patients with duodenal ulcers and from about 75% of those with gastric ulcers. H. pylori gastritis is the most common type of gastritis in the United States and is characterized by prominent chronic inflammation of the antrum and body of the stomach. The inflammatory infiltrate includes large numbers of plasma cells, often in clusters or sheets, within the superficial lamina propria. These are accompanied by increased numbers of lymphocytes, macrophages, and neutrophils within the lamina propria. Neutrophils infiltrate across the basement membrane and accumulate in the lumens of gastric glands, or pits, to create pit abscesses. In addition to peptic ulcer disease, *H. pylori* gastritis is a

R10th Latest Update

Molecular serum markers of liver fibrosis

Marker	Function
Liver function	
ALT	Metabolic enzymes in the liver
AST	Metabolic enzymes in the liver
ECM formation	
PHINP	Propeptide of collagen type III
PINP	Propeptide of collagen type I
Type IV collagen	Basement membrane formation
P4NP 7S	N-terminal propeptides of type IV collagen 7S domain
PVCP	Propeptide of collagen type V
HA	Component of ECM
YKL-40	Glycoprotein involved in ECM turnover
MFAP	Glycoprotein involved in ECM turnover
Fibrinolytic process	**Neo-epitope**
MMP-1/MMP-13	Degrades fibrotic matrix
MMP-2	Degrades basal membranes and fibrotic matrix
MMP-9	Degrades basal membranes
TIMP-1	Inhibits MMP-1 activity

Marker	Function
ECM degradation	
CO3-610	Collagen type III fragment generated by MMP-9
CO6-MMP	Collagen type VI fragment generated by MMP-2,9
CO1-764	Collagen type I fragment generated by MMP-2,9,13
C4M	Collagen type IV fragment generated by MMP-9
Cytokines	
TGF-β	Growth factor stimulates production of ECM by HSC
CTGF	Potent profibrogenic factor
PDGF	Growth factor stimulates proliferation of HSC
TNF-α	Inflammatory cytokine involved in fibrogenesis
IL-4, 6, 8, 18	Inflammatory cytokine involved in fibrogenesis

R10th Latest Update

Laboratory Evaluation of Liver Disease

Test Category	Blood Measurement*
Hepatocyte integrity	Cytosolic hepatocellular enzymes 1. *Serum aspartate aminotransferase* (AST) 2. *Serum alanine aminotransferase* (ALT) 3. Serum lactate dehydrogenase (LDH)
Biliary excretory function	Substances normally secreted in bile† • *Serum bilirubin* • Urine bilirubin • Serum bile acids • Plasma membrane enzymes (from damage to bile canaliculus) *Serum alkaline phosphatase* *Serum, γ-glutamyl transpeptidase* (*GGT*)
Hepatocyte function	Proteins secreted into the blood • *Serum albumin* • *Prothrombin time* (PT) • *Partial thromboplastin time* (PTT) Hepatocyte metabolism • Serum ammonia • Aminopyrine breath test (hepatic demethylation)

R10th Latest Update

World Health Organization Criteria for the Metabolic Syndrome

One of	Diabetes mellitus *or* Impaired glucose tolerance *or* Impaired fasting glucose *or* Insulin resistance
and two of:	• **Blood pressure:** ≥140/90 mm Hg • **Dyslipidemia:** Triglycerides (TG). ≥1.695 mmol/L and high-density lipoprotein cholesterol (HDL-C) ≤0.9 mmol/L (male), ≤1 mmol/L (female) • **Central obesity:** Waist-hip ratio >0.90 (male); >0.85 (female), or body mass index >30 kg/m² • **Microalbuminuria:** Urinay albumin excretion rate of ≥20 µg/min and albumin-to-creatinine ≥30 mg/g

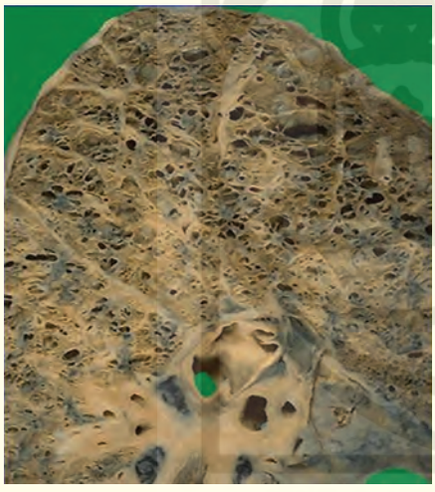
Multiple Choice Questions

Most Recent Questions

1. A patient presented with cirrhosis. On liver biopsy showed eosinophilic material cytokeratin positive. This is most likely composed of: ***(Recent Question 2021)***

a. Actin
b. Microtubule
c. Intermediate
d. Fibronectin

2. A 35-year-old woman with a long history of dyspnea, chronic cough, sputum production, and wheezing dies of respiratory failure following a bout of pneumonia. She was not a smoker or alcoholic. The lung (respiratory system) at autopsy is shown in the image. Which of the following underlying conditions was most likely associated with the pathologic changes shown here? ***(Recent Question 2020)***



a. Mutation in dynein arms
b. Cystic fibrosis
c. Alpha 1 antitrypsin deficiency
d. Antibodies against type 4 Collagen

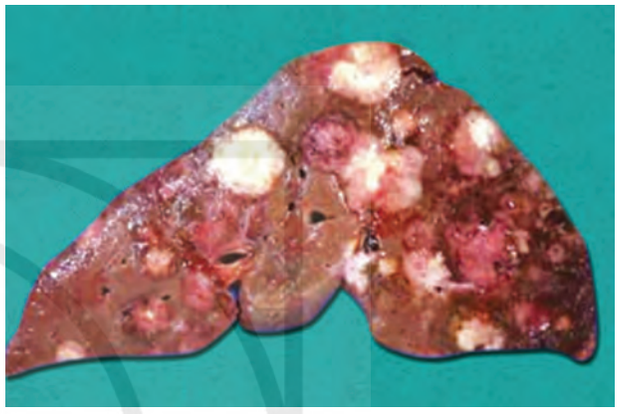
3. A 23-year-old male presented to the clinic with history of Fatigue and tiredness. On investigation he was found to have Hb values of 9 gm%, MCV of 101, FL. Peripheral smear examination showed macrocytic hematology (RBCs) and hypersegmented neutrophils. Which of the following is the most likely etiology? ***(Recent Question 2020)***

a. Lead poisoning
b. Iron deficiency anemia
c. Chronic alcoholism
d. Hemolytic anemia

4. Which form of cholesterol is present in gallstones? ***(Recent Question 2019)***

a. Amorphous cholesterol monohydrate
b. Amorphous cholesterol dihydrate
c. Crystalline cholesterol dihydrate
d. Crystalline cholesterol monohydrate

5. A lady died suddenly with pulmonary thromboembolism. A specimen of liver was given. Most likely finding is: ***(Recent Question 2018)***



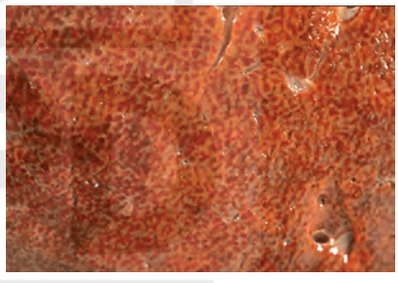
a. Multifocal hepatic adenomas
b. Liver metastasis
c. Invasive angio carcinoma
d. Metastasis from PE

STRUCTURE OF LIVER

6. In obstructive jaundice, which of the following enzyme is elevated? ***(Recent Question 2016-17)***

a. GGT
b. AST
c. ALT
d. LDH

7. The given figure shows which of the following? ***(AIIMS Nov 2015)***



a. Amyloidosis: grey areas are viable; white areas are necrotic
b. Nutmeg liver: red areas are viable pericentralareas; white areas are periportal necrotic areas
c. Nutmeg liver: Red areas are pericental necrotic areas, white areas are viable fibrotic periportal area
d. Amyloidosis - necrotic white periportal viable grey pericentral areas

8. Absent urobilinogen in urine with icterus indicates? ***(AIIMS Nov 2015)***

a. Perihepatic obstruction
b. Hemolysis
c. Hepatitis
d. Liver failure

Answers with Explanations

1. Ans. (c) Intermediate

2. Ans. (c) Alpha 1 antitrypsin deficiency

- Pathogenesis of the most significant event in emphysema, the destruction of the alveolar walls, is related to deficiency of serum α-1-antitrypsin (α1-protease inhibitor)
- The normal function of α1-AT is to inhibit proteases and hence, its name α1-protease inhibitor.
- The proteases (mainly elastases) are derived from neutrophils. Neutrophil Elastase has the capability of digesting lung parenchyma but is inhibited from doing so by anti-Elastase effect of α1-AT
- The α1-AT deficiency develops in adults and causes pulmonary emphysema in smokers as well as in non-smokers, though smokers become symptomatic about 15 years earlier than non-smokers.

3. Ans. (c) Chronic alcoholism

- MCV – 101fl is suggestive of macrocytosis
- Most commonly (especially when the increase in size is mild, and just above normal range) the cause is bone marrow dysplasia secondary to alcohol abuse and chronic alcoholism, Poor absorption of vitamin B12 in the digestive tract can also cause macrocytosis.
- Macrocytosis is frequently linked to alcoholism, with or without liver disease. In fact, it is purported to be one of the most common causes of non megaloblastic macrocytosis.
- In cases of macrocytosis related to alcoholism the elevated MCV may be due to the direct effect of the alcohol, liver disease and/or folate deficiency.

4. Ans. (d) Crystalline cholesterol monohydrate

- Gallstones are hardened deposits of digestive fluid that can form in your gallbladder.
- The most common type of gallstone, called cholesterol gallstone, often appears yellow in color.
- These gallstones are composed mainly of un dissolved cholesterol.
- Precipitation of solid cholesterol crystals from supersaturated bile has an essential role in cholesterol gallstone formation.
- Cholesterol stones account for more than 90% of all gallstones in Western industrialized countries.
- Cholesterol gallstones usually contain >50% cholesterol monohydrate plus an admixture of calcium salts, bile pigments, proteins, and fatty acids.
- When bile is concentrated in the gallbladder, it can become supersaturated with these substances, which then precipitate from the solutions microscopic crystals.
- The crystals are trapped in gallbladder mucus, producing gallbladder sludge.

5. Ans. (d) Metastasis from PE

- A liver metastasis is a malignant tumor in the liver that has spread from another organ affected by cancer. The liver is a common site for metastatic disease because of its rich, dual blood supply (the liver receives blood via the hepatic artery and portal vein).
- Metastatic tumors in the liver are 20 times more common than primary tumors. In 50% of all cases the primary tumor is of the gastrointestinal tract, other common sites include the breast, ovaries, bronchus and kidney.
- Tumor emboli entering the sinusoids through the liver blood supply appear to be physically obstructed by the Kupffer cells, but if tumor emboli are larger, they tend to become lodged in the portal venous branches.

Features

- Hepatomegaly—with a nodular free edge of liver
- Tenderness
- Cachexia
- Ascites
- Jaundice
- Pyrexia—up to 10% of patients
- Alkaline Phosphatase (ALP) and gamma-glutamyl transpeptidase (GGT) elevated
- Ultrasound scan and CT scan - multiple filling defects.

Diagnosis

- Hemoglobin decrease
- **Liver function test:** ALP elevated, bilirubin elevated, albumin decrease
- Carcinoembryonic antigen for colorectal secondaries
- Ultrasound scan
- CT scan
- Biopsy under ultrasound control

Treatment

- Treatment consists of surgery (hepatectomy), chemotherapy and/or therapies specifically aimed at the liver like radio frequency ablation, transcatheter arterial chemoembolization, selective internal radiation therapy and irreversible electroporation.
- For most patients no effective treatment exists because both lobes are usually involved making surgical resection impossible.
- Younger patients with metastases from colorectal cancer confined to one lobe of the liver and up to 4 in number may be treated by partial hepatectomy.
- In selected cases, chemotherapy may be given systemically or via hepatic artery.
- In some tumors, notably those arising from the colon and rectum, apparently solitary metastases or metastases to one or other lobes may be resected.
- A careful search for other metastases is required including local recurrence of the original primary tumor (e.g., via colonoscopy) and dissemination elsewhere (e.g., via CT of the thorax).
- Five-year survival rates of 30–40% have been reported following resection.

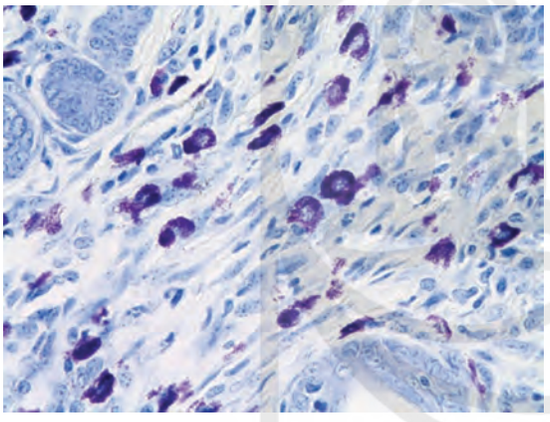
Multiple Choice Questions

Most Recent Questions

1. Fixative used in PAP smear: *(INI-CET July 2021)*
a. 95% ethanol
b. Formalin
c. Ethanol
d. Air drying

2. Staining of lipid is best with: *(INI-CET Nov 2020)*
a. Frozen section
b. Liquid paraffin
c. Formalin fixed
d. IHC

3. Toluidine blue staining is used for identification of: *(AIIMS May 2018)*



a. Mast cell
b. Fibroblast
c. Melanocyte
d. Macrophages

4. Special stain for acidic mucin: *(AIIMS May 2018)*
a. PAS
b. Alcian blue
c. GMS
d. Masson trichrome

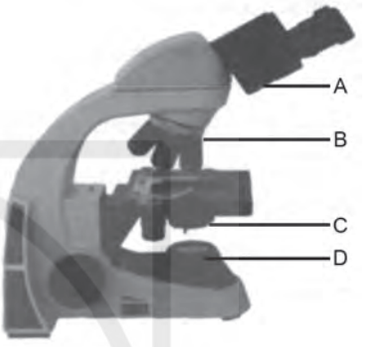
STAINS AND FIXATIVES

5. Match the following viral intracellular bodies with respect to the disease: *(AIIMS Nov 2019)*

Column A	Column B
a. HPV	1. Henderson-Paterson bodies
b. CMV	2. Decoy cells
c. Molluscum contagiosum	3. Owl eye inclusion
d. Polyomavirus	4. Koilocyte

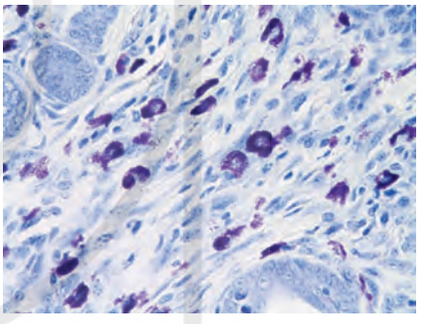
6. Which of the following stain is used for Acidic mucin? *(AIIMS May 2018)*
a. Alcian blue
b. PAS
c. Masson's trichrome stain
d. PTAH

7. Which of the following labels corresponds to the condenser of the microscope? *(AIIMS May 2018)*



a. C
b. B
c. D
d. A

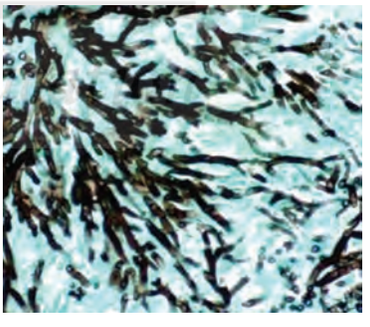
8. Toluidine blue staining is used for identification of: *(AIIMS May 2018)*



a. Mast cell
b. Fibroblast
c. Melanocyte
d. Macrophages

9. Best method for HbA1c estimation is: *(AIIMS May 2018)*
a. Affinity chromatography
b. Ion exchange chromatography
c. Electrophoresis
d. HPLC

10. Gomori methenamine silver stain for fungus is shown below. Most likely diagnosis is: *(AIIMS Nov 2017)*



a. Acute angle branching with septate hyphae - Aspergillus
b. Right angle branching and aseptate hyphae- Mucor
c. Acute angle branching with septate hyphae - Mucor
d. Right angle branching and aseptate hyphae- Aspergillus

Answers with Explanations

1. Ans. (a) 95% ethanol

Cytological Fixation and Fixatives

- Solution of ether + 95% ethanol---------? X not preferred
- _____ is now employed as a flxative by most laboratories, with excellent results (PAP smear)

2. Ans. (a) Frozen section

3. Ans. (a) Mast cell

(It gives them a red purple color)

- Toluidine blue stains the mast cells. Their cytoplasm contains metachromatic granules composed of heparin and histamine. It stains the mast cells violet with blue background.
- Melanocytes are stained by S100, HMB45, Melan-A/ MART-l, MITF, and Tyrosinase.
- Macrophages can be stained by MITF, SOX 10, CD31, CD68, and lysozyme.
- Fibroblast are identified by using fibroblast surface antigen (SFA), Vimentin, heat shock protein 47 (HSP47), and fibroblast-specific protein I (FSPl).

4. Ans. (b) Alcian blue

- Acidic mucosubstances (Sialo and sulfo mucins) are stained by the Alcian blue.
- Neutral mucosubstances are stained by PAS reaction.

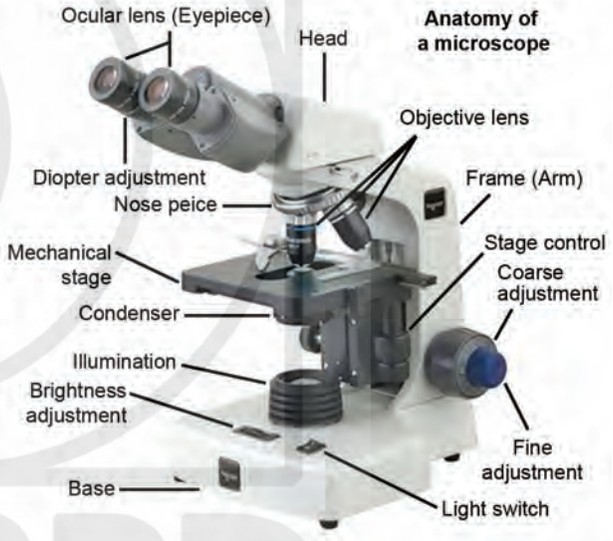
5. Ans. (a) 4, (b) 3, (c) 1, (d) 2

Viral Inclusion Bodies

Intracyto-plasmic			Henderson-Peterson bodies (Molluscum Contagiosum)
			Negri bodies (Rabies)
			Guarnieri bodies (Smallpox)
			Paschen bodies (Smallpox)
			Bollinger bodies (Fowl pox)
			Borrel bodies (Fowl pox)
Intranuclear	Acidophilic	Cowdry type A	Varicella zoster virus
			Herpes simplex virus
			Yellow fever virus
		Cowdry type B	Polio virus
	Basophilic	Cowdry type B	Adeno virus
			Cytomegalo virus

6. Ans. (a) Alcian blue

7. Ans. (a) C



8. Ans. (a) Mast cell

Toluidine blue (also known as tolonium chloride) is an acidophilic metachromatic dye that selectively stains acidic tissue components (sulfates, carboxylates, and phosphate radicals), has an affinity for nucleic acids, and therefore, binds to nuclear material of tissues with a high DNA and RNA content. Mast cell granules stain purple in color due to the presence of heparin and histamine.

9. Ans. (d) HPLC

Four basic types of methods are used most commonly to measure HbA1c: immunoassay, ion-exchange high-performance liquid chromatography (HPLC), boronate affinity HPLC, and enzymatic assays. The gold standard is HPLC method.

10. Ans. (a) Acute angle branching with septate hyphae - Aspergillus

Mucor- Broad base with obtuse branching
Aspergillus- Acute branching, Septate hyphae with narrow base

Complete Review of

Pathology

& Hematology for NEET & INI-CET

From the Authors' Desk

"Give them Quality. That's the best kind of advertising in the world."

We firmly believe in the above-mentioned quote that Quality does not need constant advertisement; it will be acknowledged anyhow. We are extremely grateful to you all for an overwhelming response for the 7th edition of the book, Complete Review of Pathology.

Join **Author's** Discussion Group

Pathology by **Dr Praveen**

Dr Vandana Pathology Study circle

Students' Reviews

Ahana Hom Chowdhury
Maharishi Markandeshwar Institute of Medical Sciences and Research, Ambala, Haryana

Annexures are not uncommon; they are given in all books BUT all these annexures given in this book are of prime importance and many sure-shot questions can be expected to appear from them. The book covers a plethora of topics. CVs GIT and RENAL are par excellence. It has been updated with Robbins 10th edition with LOTS AND LOTS OF IMAGE-BASED QUESTIONS, and histology slides. High yield facts boxes are useful when you are turning pages for revision, Flowcharts nicely depict the process.

Shoaib Ahmed Khan
Netaji Subhash Chandra Bose Medical College, Jabalpur

The language of the book is easy as compared to other books. Everything in the book is summed up in a short and easy way. After each chapter, there are MCQs & NEXT-pattern questions which are also image-based. There are many images related to the topic given to understand each and every topic easily.

Vishnu Balgi
Karnataka Institute of Medical Sciences, Hubli

Review of Pathology and Hematology by Dr Praveen Gupta and Dr Vandana Puri indeed is the master kid of Robbins Pathology. Concepts cover all the key points and is presented in an appealing manner. The stress on MCQs is what I liked most. As pathology is vast and most of us don't know what to read and focus upon. This book has just solved that issue.

Alan S Moses
Madurai Medical College, Madurai

It is crisp and concise.... it does not have unnecessary details but helped me refer to the entire Robbins easily... the questions are also nice to practice... the mnemonics are also easy to remember.

Garvit Goel
LMR Medical College, Meerut

The wow factor of the book is that it summarises the chapter in a nutshell. MCQs for practice and their explanations are presented in this book in excellent way. Image-based questions for the NEXT pattern are a quite an interesting part.

Pranay
RUHS College of Medical Sciences, Jaipur

The book is very conceptual. Concepts and all the topics are crispy and short and easy to grasp. It covered full pathology in a manner in which it can be learned and revised easily

Rahul Manoharlal Sodhai
GMC, Latur

This book is amazing. What I found difficult while studying pathology is remembering gross and microscopic features. But this book made it easier. It involves all the important points that must be remembered, and which are asked in MCQs. It helped me a lot while revising the pathology as it is a very vast subject.

Raushan Kumar
IGIMS Medical College, Patna

The language is so coherent and simple. It's kind of a very easy-to-understand book. It requires minimal effort to understand and all the required content along with loads of questions required for practice are given in a single place.

Shivam Chaudhary
AIIMS, Jodhpur

It has well-illustrated diagrams and contains concise information on all important topics which helped me to consolidate most of the topics in a very comprehensive way. It also contains all the recent updates which are must to know for future exams.

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