Concepts in Pathology

SALIENT FEATURES

- Based on latest pattern of AIIMS/PGI/AIPG and other PG-MEE-exams.
- Chapter wise meticulous explanation of theory and MCQs with simplified diagrams and flow charts.
- Text and MCQ are thoroughly cross checked from standard reference books.
- Precise and updated coverage of controversial topics.
- "High yield info" covers recent advances for future MCQs.
- Hematology, gross and Histopathology diagrams are enumerated and well explained for rapid revision and understanding.
- Chapter of "Extra edge info including End of controversies" have included numerous tough and controversial high yield topics.

Devesh Mishra did his MBBS; MD Pathology (TNMC, Mumbai); Senior residency from AIIMS, New Delhi. At present he is taking pathology lectures all over India under name of "Concepts in Pathology". Every day he interacts and clears doubts with more tha 50,000 students across the country through his famous forum on Facebook named "Devesh Pathology Discussion Forum".

HIS REVIEW FROM TOPPERS OF VARIOUS EXAM ARE EVIDENCE OF HIS METICULOUS PASSIONATE APPROACH TOWARDS TEACHING PATHOLOGY

Stuti Gupta: Thanks devesh sirr... thanks for everydng... sirr ur golden words wrkd fr me... path notes formed basis of evry subject.. clear fine concepts u gave us made my life... evry day ur diff kind of motivations filled me wid new hope... u are my superhero sirr... thanks sirr i got more den i dsrv... got md anaesthesia in aiims...

Kunaal Paul: wonderful 3days of pathology session in kolkata sir.. thoroughly enjoyed your art of teaching.. a totally new integrated approach to the subject with full of authentic standard text books references... NO ADVERTISEMENT of your own book for a single time... it was as usual motivating and inspiring also... we are lucky to be born in the era to witness your awesome teaching. thank you so much sir...

Vanishri Ganakumar: Hello sir. Got AIIMS rank 9 sir. Thankyou for ur wonderful classes. This group was the ultimate source of answers for all the doubts, thankyou for ur efforts for students like us sir.

Harshita Shanbhag: got 34th RANK AIIMS... thank you for ur concepts, this paper had lots of patho :), I only had time to revise your general patho notes few days before exam... and it helped!! looking forward to jipmer sir. god bless :)

Anand Singh Brar: Respected Devesh Mishra Sir, With your guidance, I managed to achieve 19th Rank in AIIMS MD/MS entrance exam. From the depth of my heart, I would like to thank you... :) You will go down in memory as the best pathology teacher. Your grasp of pathology is perfect to say the least. As much as I enjoyed your classes, your #End-ofControversy was something to look forward to, while preparations were going on :)

Sindhu Dm: hi sir this is SINDHU DM from bhatia class bangalore.. im happy to tell you tat i got rank 9 in aiims... and it wouldnt have been possible without ur class lectures and notes which is really good... thanks a lot sir for being my teacher, the credit of my success truly goes to u :) and must say ur really an amazing teacher :)

Ram Manohar Talupula: Got 2nd rank in AIIMS... I still feel as if I am dreaming.. Thank you very much sir for your class, inspiring words and the forum. They were are really very helpful :)

Harshit Khare: Sir got rank 18 in UPPG!!! I thought, will write it in the post to give u a surprise!!! Sir thank u soooooooo much sir... No matter what I write, it will not be enough to thank u for ur constant, unending, support... Thank U so much.. I m literally at loss of words... I always wanted to make U proud.. u have always been more than a teacher to me, more like a life coach to me... and ur guideness has enabled me, to complete this journey.. U r the Best!! Hop to meet u once again... :)

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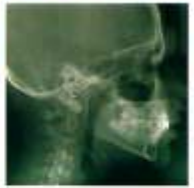
The Pathology book written by best faculty of pathology of India to crack AIIMS/PGI/AIPG/FMGE and other PGMEE.

Concepts in Pathology

2nd EDITION

- Comprehensively and Precisely Updated from Robbins 9/e; Harrison 19/e; Wintrobe's Hematology 13/e; Ackerman 10/e and Sternberg's 6/e
- Chapter-wise Concise Theory
- Image-based Information
- Live Lectures



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CONTENTS

CHAPTER 1

CELL PATHOLOGY & AGEING

- Cells can alter their **functional state** in response to modest stress to maintain the steady state.
- **More excessive physiologic stresses, or adverse pathologic stimuli (injury), result in**
  1. Adaptation
  2. Reversible injury
  3. Irreversible injury and cell death

CELLULAR ADAPTATION

- Adaptations are **reversible changes** in the size, number, phenotype, metabolic activity, or functions of cells in response to changes in their environment.
- **These changes include:**
  1. Hypertrophy (increased cell mass)
  2. Hyperplasia (increased cell number)
  3. Atrophy (decreased cell mass)
  4. Metaplasia (change from one mature cell type to another)

Hypertrophy

- Increase in size of cells but number remains same.
- Mechanisms of hypertrophy is by increased production of cellular proteins.

End of controversy

- **"Pregnant uterus"** is mainly hypertrophy and some amount of hyperplasia.
- **"Uterus hyperplasia"** is mostly pathological and precursors of **type-I endometrial adenocarcinoma.**
- **Breast tissue (during pregnancy and pubertal period) is an example of both hyperplasia and hypertrophy normally or physiologically.**
- **Lactating breast** tissue is **only hypertrophy.**

Hyperplasia

- Increase in **number** of cells; size remains same.

EDULANCHE PREVIEW

Atrophy

- Both number and size of cells are decreased.
- **Mechanisms of atrophy**
  a. Consist of a combination of decreased **protein synthesis** and increased protein degradation by **ubiquitin-proteasome pathway**.
  b. Increased **autophagy** by forming autophagy vacuoles.

Metaplasia

- A reversible **change** where one differentiated cell type (epithelial or mesenchymal) is replaced by another cell type.
- **Mechanisms of metaplasia:**
  - It is due to **re-programming of stem cells** and not because of already differentiated mature cells.

HIGH YIELD INFO

- **Vitamin A (retinoic acid) deficiency or excess**, both can cause **metaplasia**.
- Vitamin A deficiency induces squamous **metaplasia in respiratory epithelium**.

- **Most common** epithelial metaplasia is **columnar to squamous**, e.g. cigarette smoker's respiratory epithelium.
- Persistent stimuli can initiate malignant transformation in metaplastic epithelium.

Barrett's esophagus

- **Squamous to columnar type** of metaplasia seen in esophagus.
- **Intestinal metaplasia** (due to presence of goblet cells) is **hallmark** of Barrett's esophagus **(Image 1.1)**.

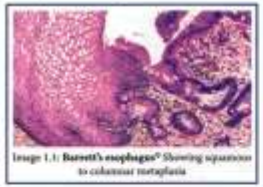


Image 1.1: **Barrett's esophagus** Showing squamous to columnar metaplasia

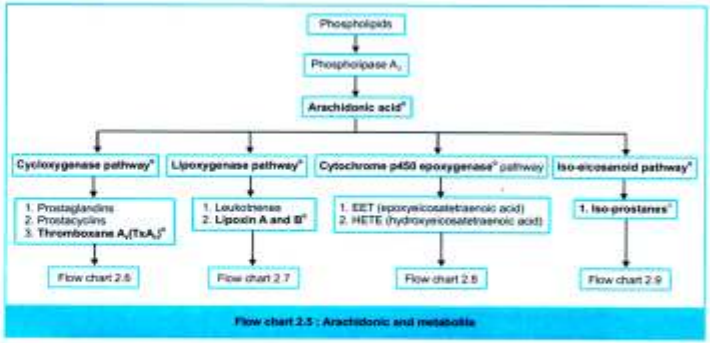
- Associated with increased risk of **esophageal adenocarcinoma**.

CELL INJURY

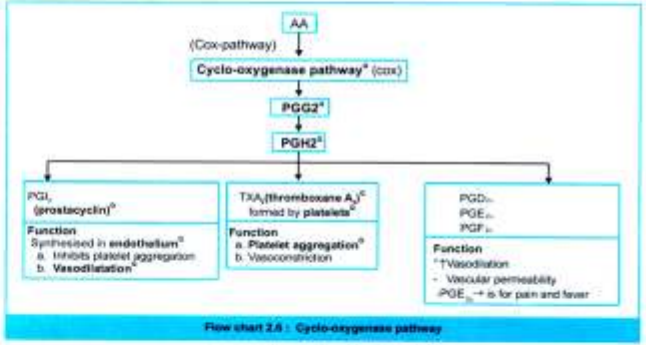
- Cellular stress beyond the level of adaptive response will results in cellular injury.
- Most common cause of cell injury is hypoxia (most common cause of **hypoxia** is ischemia)

HIGH YIELD INFO

- **Neurons** undergo irreversible damage **within 3 to 4 minutes** of ischemic change **(most susceptible tissue to ischemia)**.
- **Myocardial cells** undergo irreversible damage within **20 to 30 minutes** of ischemic change.
- **Fibroblast** is **most resistant** to ischemic damage.



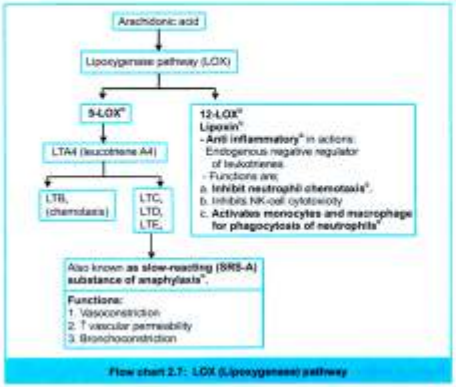
Flow chart 2.5 : Arachidonic acid metabolite



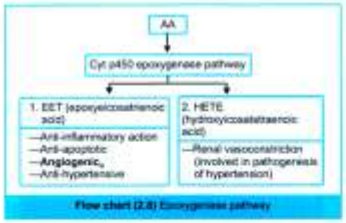
Flow chart 2.6 : Cyclo-oxygenase pathway

- It is induced by inflammatory stimuli to generate prostaglandins and thromboxanes.
- **PGD 2and PGE 2**
- It causes
  - Vasodilation
  - Increases vascular permeability
  - Potentiating edema formation.
  - **PGD 2** is a **chemoattractant for neutrophils**.
- **PGF 2-alpha**
- It causes
  - Contraction of smooth muscles (uterus and bronchus)
  - Contraction of small arterioles.
  - It is **chemoattractant for neutrophils**.
- **PGE**

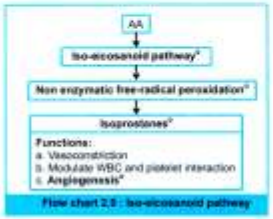
- It is for **pain and fever**[6].
- It is **hyperalgesic** and makes the skin hypersensitive to painful stimuli.
- Involved in cytokine induced fever during infections.



Flow chart 2.7: LOX (Lipoxygenase) pathway



Flow chart (2.8) Epoxygenase pathway



Flow chart 2.9 : Iso-eicosanoid pathway

- Clinical manifestations begin 6 to 9 months after birth as hemoglobin synthesis swithesis from HbF to HbA.
- **Peripheral blood will show :**
  - Marked anisocytosis.
  - Microcytic, hypochromic RBCs.
  - **Target cells (characteristic) (Image 8.6).**
  - **Basophilic stippling** is constant finding **(Image 8.7).**

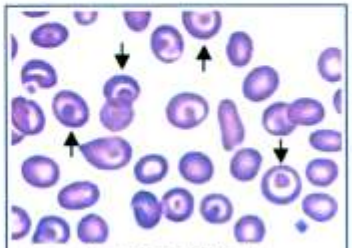


Image 8.6: Target cells (Codocytes) :
RBC with "lump" of hemoglobinized cytoplasm within the area of normal central pallor, causing them to resemble a "bull's-eye" target. It is **pathognomonic in Beta-thalassemia major**[6]. Seen in:

1) Iron deficiency anemia
2) Hypochromic anemia, homozygous and heterozygous forms of c, d, e hemoglobinopathies.

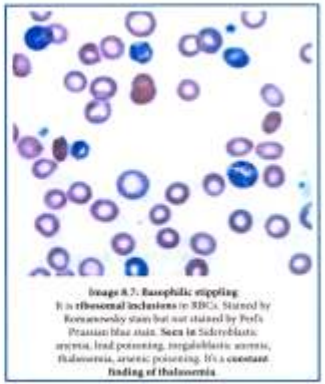


Image 8.7: Basophilic stippling
It is **ribosomal inclusions** in RBCs. Stained by Romanowsky stain but not stained by Perl's Prussian blue stain. **Seen in** Sideroblastic anemia, lead poisoning, megaloblastic anemia, thalassemia, arsenic poisoning. It's a **constant finding of thalassemia**.

4) Lymphoplasmacytic lymphoma/Waldenstrom's macroglobulinemia

- **B-Cell neoplasm**[C] affecting **60 to 70 years**.
- Characterstically secretes **monoclonal IgM**[C] to cause a hyperviscosity syndrome known as **Waldenstrom's macroglobulinemia**.
- All cases of lymphoplasmacytic lymphoma are associated with acquired **mutations in MYD88**[C].
- **Most common cytogenetic**[Q] abnormality is **deletion of chromosome 6q**[Q].
- **Heavy and light chain** synthesis is balanced so the complications of excess light chains (e.g., **amyloidosis or renal failure**) are rare.
- There is **no bone destructions**[S].
- Marrow infiltration causes anemia (cold type AIHA due to **cold agglutinin IgM**)[Q].
- **IgM secretion results** in a **hyperviscosity syndrome** causing visual impairment, neurologic problems, bleeding and cryoglobulinemia.
- **Bone marrow biopsy** shows lymphocytes, plasma cells and plasma cytoid lymphocytes along with **mast cell hyperplasia**.
- It may have **Dutcher bodies** and **Russel Bodies**.

Langerhans' cell histiocytosis

- It is a spectrum of proliferations of a special type of **immature dendritic cell**[S] known as Langerhans cell.
- It is considered as neoplastic in origin due to oncogenic mutations of **BRAF (50 to 60% of cases)**[Q].
- Proliferating **Langerhans' cells** have abundant, often **vacuolated cytoplasm** and vesicular nuclei containing **linear grooves or folds**.
- **Birbeck granules**[C] are present in cytoplasm which are pentalaminar tubules with a dilated terminal end producing a **tennis racket**[Q]**-like appearances on electron microscopy**[Q] **(Image 9.17)**.
- **Birbeck granules** contain protein **langerin (CD 207)**[S].
- **Tumor cells** express **HLA-DR, S-100**, and **CD1a**[Q].

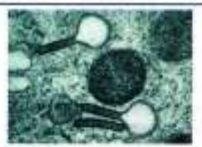


Image 9.17: **Tennis Tennis racket appearance**[Q]: racket shaped structures of **Birbeck granules**[S] (electron microscopy). Seen in Langerhans cells cytoplasm in histiocytosis x (Langerhans cell histiocytosis).

Clinicopathologic entities of LCH are:-

a) **Letterer-Siwe disease**
   - It's an **multifocal, multisystem** Langerhans' cell histiocytosis.
   - It's an **aggressive** systemic disorder occurring **before 2 years**[Q] **of age**.
   - They show cutaneous lesions due to skin infiltration by tumor cells resemble like a **seborrheic dermatitis**[S].
   - **Bone destruction** involving all the bones of body simultaneously is characteristic.

b) **Eosinophilic granuloma**
   - Also known as unifocal and multifocal unisystem Langerhans' cell histiocytosis.
   - **Most common**[Q] presentation is **calvarial defect (skull defect)**[S].

c) **Hand-Schuller Christian**
   - **Syndrome** consists of triad of **calvarial bone defects, diabetes insipidus** and **exophthalmos**.

ii) **Fibrinoid necrosis**[Q] consisting of fibrin deposition and wall necrosis known as **necrotizing arteriolitis**[S].

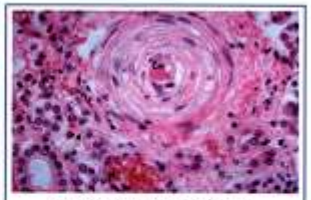


Image 10.2 : **Hyperplastic arteriosclerosis**

- Seen in malignant hypertension.
- Blood vessel will show:
  1) Onion skin appearence
  2) Hyperplastic arteriosclerosis
  3) Fibrinoid necrosis

ARTERIOSCELROSIS

- Arterial wall **thickening**[S] and **loss of elasticity**[S] is known as **arteriosclerosis**.
- **It has three patterns :-**
  - **A) Arteriolosclerosis**
    - It affects small and medium-sized arteries and arterioles.
    - Seen in **diabetes** and **hypertension** as hyperplastic and hyaline type of arteriolosclerosis.
  - **B) Monckeberg medial sclerosis**[S]
    - Characterized by **medial calcification** in muscular arteries.
    - Commonly seen after age **50 years**.
    - They are **non-obstructive**[S] and have **no clinical significance**.
  - **C) Atherosclerosis**
    - **Most common** pattern with clinical siginificance.
    - It is due to **intimal damage**.

Atherosclerosis

- It is a slowly progressive disease of large to medium-sized muscular and elastic arteries.
- Characterized by elevated **intimal-based plaques**.

Table 10.2 : Morphologic Changes in Myocardial Infarction

Time	Gross features	Light microscopy	Electron microscopy
a) Reversible injury 0-1/2 hrs.	None	None	Mitochondrial swelling, glycogen loss
b) Irreversible injury 1/2-4 hrs.	None	Waviness of fiber	**Mitochondrial amorphous densities**[Q], sarcolemmal disruption
4/12 hrs.	Occassional dark mottling	**Early coagulation necrosis**[Q], edema hemorrhage	–
12-24 hrs.	**Dark mottling**[Q]	• Ongoing coagulation necrosis pyknosis of nuclei • Marginal **contraction band necrosis**[Q] • Early **neutrophilic infiltrates**[Q] • Myocyte hypereosinophilia	
1-3 days	Mottling with **yellow tan infarct**[Q] centre	• Coagulation necrosis • Brisk neutrophilic infiltrates	
3-7 days	**Hyperemic border**[Q] central yellow tan softening	• Beginning disintegration of dead myofibers, dying neutrophils macrophage at infarct border	
7-10 days	Maximally yellow tan and soft, with depressed red-tan margins	• Well-developed phagocytosis of dead cells • **Early granulation tissue**[Q]	
10-14 days	Red-gray depressed infarct borders	• Well-established granulation tissue with new blood vessels and collagen cellularity	
2-8 weeks	Gray-white scar, progressive from border toward core of infarct	• Increased collagen deposition with decreased cellularity	
> 2 months	**Scarring complete**[Q]	■ Dense collagenous scar	
	Earliest[Q] : **a) Gross finding**[Q]	→ Occasional **dark mottling**[Q]	
	b) Light Microscopic finding[Q]	→ **Waviness**[Q] of fibers	
	c) Electron microscopy[Q]	→ **Mitochondrial swelling**[Q]	

Table 10.3: Cardiac biomarkers

Enzymes	Initiation time	Peak time	Return to normal
Myoglobin[Q]	**2 hrs.**[Q]	-	24 hrs.
CK-MB[Q]	2-4 hrs.	24 hrs.	**48-72 hrs.**[Q]
Tropoponin (I or T)[Q]	2-4 hrs.	48 hrs.	**7-10 days**[Q]
SGOT	Within 12 hrs.	48 hrs.	4-5 days
LDH[Q]	24 hrs.	4-5 days	**After 10 days**[Q]

- **Subacute IE**
  - They have smaller vegetations and leaflets invasion is rare.

Diagnosis

- **Blood cultures** are critically important for directing therapy **(Table 10.6)**.

Table 10.6: Duke's diagnostic criteria for infective endocarditis

A) Pathologic criteria

i) Microorganism demonstrated by **culture or histologic examination**[Q], in a vegetation or intracardiac abscess.

ii) **Histologic confirmation**[Q] of active endocarditis in vegetation or intracardiac abscess.

B) Clinical criteria

1. **Major**[Q]
   - i) **Blood cultures**[Q] positive for a characteristic organism or persistently positive for an unusual organism.
   - ii) **Echocardiographic identification**[Q] of a valve-related or implant-related mass or abscess, or partial separation of artificial valve.
   - iii) **New valvular regurgitation**[Q].
2. **Minor**[Q]
   - i) **Predisposing heart lesion**[Q] or intravenous drug use.
   - ii) **Fever**[Q]
   - iii) **Vascular lesions**[Q], including arterial petechiae subungual/splinter hemorrhages, emboli, septic infarcts, mycotic aneurysm, intracranial hemorrhage, Janeway lesions.
   - iv) **Immunological phenomena**[Q] including glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor.
   - v) **Microbiologic evidence**[Q], including a single culture positive for an unusual organism.
   - vi) **Electrocardiographic findings**[Q] consistent with but not diagnostic of endocarditis including worsening or changing of a pre-existent murmur.

Diagnosis requires

- Either pathologic or clinical criteria.
- **For clinical criteria :-**
  - a) 2 major
  - b) 1 major + 3 minor
  - c) 5 minor

Clinical features

- **Janeway lesions**
  - These are small **non-tender**[Q], erythematous or hemorrhagic macular lesions.
  - Seen on **palms and soles**[Q] due to **septic emboli**.
- **Osler nodes**
  - These are **small, tender**[Q] **subcutaneous nodules**.
  - Seen in **pulp**[Q] of the digits.
  - Persist for **hours to several days**.

CARDIOMYOPATHIES

- Three main functional and pathologic patterns are dilated, hypertrophic, and restrictive cardiomyopathies.

Dilated cardiomyopathy (DCM)

- It is characterized by gradual four chamber hypertrophy and dilation.
- It presents with systolic dysfunction and progressive congestive heart failure.
- Most commonly unknown etiology (idiopathic DCM).

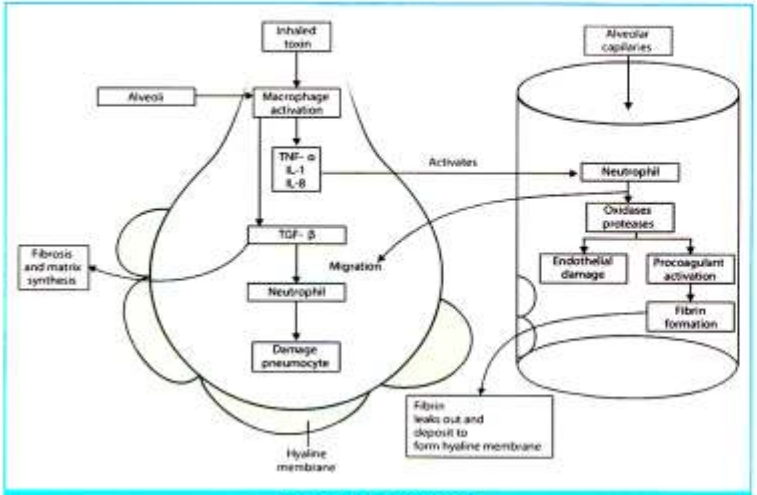


Fig 11.1 : ARDS Pathogenesis

Clinical Course

- **Dyspnea** and **tachypnea** are the **earliest presentation** of ALI, followed by cyanosis, hypoxemia and respiratory failure refractory to oxygen therapy.
- **Chest X-ray** will show diffuse bilateral infiltrates.
- There will be ventilation-perfusion mismatch and hypoxia.
- Therapy involves mechanical ventilation and treatment of the underlying cause (e.g., infection);
- Overall **mortality rate is 40%.**

Obstructive and Restrictive Pulmonary Diseases

- Chronic, non-infectious, diffuse pulmonary disease is physiologically classified as-
  - **a) Obstructive disease**
    - Increased resistance to airflow (at any level from trachea to alveoli)
  - **b) Restrictive disease**
    - Reduced expansion of lung parenchyma with decreased total lung capacity.
    - It is of two categories:-
      - i) **Chest wall disorders** (e.g. neuromuscular disease, obesity, pleural disease etc.)
      - ii) Chronic interstitial and infiltrative diseases

Obstructive Pulmonary Diseases

- There are four disorders in this category-
  - a) Emphysema
  - b) Chronic bronchitis

Image 11.2 : Ghon's focus: Subpleural fibrocaseous lesion (Consolidation) of lung parenchyma. Microscopically contains epithelioid granulomatous inflammation.

2. **Ghon's complex (Image 11.3)**
   - Consists of subpleural **Ghon's focus** and involved **lymph nodes.**
   - Ghon's complex found below clavicle.

Image 11.3 : Ghon's complex: Ghon's focus along with lymphatics and lymph node involvement is called as Ghon's complex.

3. **Ranke's complex (Image 11.4)**
   - **Ghon's focus** alson with **fibrosis and calcification.**

Clinical features

- Classically present with **easy fatigability, ptosis,** and **diplopia.**
- Symptoms worsen with repeated stimulation.
- **Nerve conduction test** will be **normal.**
- **Most sensitive test[1]** is **single fiber electromyography[2].**
- **Most specific[1]** test is **antibodies to acetylcholine receptors[2].**

2) **Lambert-Eaton Myasthenic Syndrome**
   - It is an **autoimmune disorder** caused by antibodies that block acetylcholine release by **inhibiting a presynaptic calcium channel[2].**
   - **Most cases (more than 50%)** are **paraneoplastic[2]** and are classically associated with **small cell lung carcinoma.**
   - Patients without cancer often have other autoimmune disorders such as **vitiligo or thyroid disease.**
   - In contrast to myasthenia gravis, rapid **repetitive stimulation increases muscle response.**

Extra edge image based info: (Image 16.5), (Image 16.6), (Image 16.7)

Image 16.6 : Congenital Nemaline rod myopathy:
Electron microscopic showing Z- band (made of **actinin**)[3]

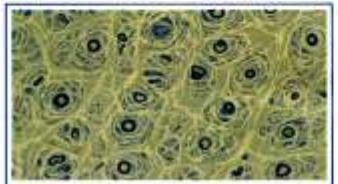


Image 16.5 : Onion bulb neuropathy :
It occurs due to segmental myelination and demyelination seen in:
1) CIDP (chronic inflammatory demyelinating polyneuropathy)
2) Charcot Marie Tooth disease
3) Refsums disease, Dejerine Sottas syndrome,
Adrenoleukodystrophy.

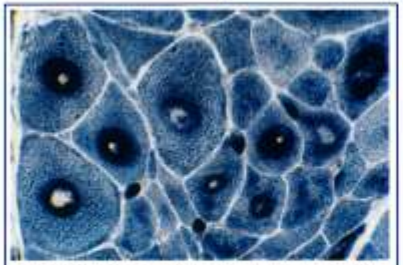


Image 16.7: Target fibers: Target fibers can be seen in **neurogenic atrophy[1]** and **Motor neuron Disease[2].** They appear as a centrally located dark staining patch on **Gomori's modified trichrome[3]** best demonstrated by NADH-TR preparations. Classically, there is a pale core with no NADH-TR activity, ensured by a darkly stained ring and surrounded by a more normal staining peripheral zone. Substantial variation in fiber diameter with atrophic and hypertrophic fibers typical for neurogenic atrophy is also present in this specimen.

- Zona **glomerulosa** (outermost) - **Mineralocorticoid** secretions.
- Zona **fasciculata** (middle) - **Glucocorticoid** secretions.
- Zona **reticularis** (innermost) - **Androgen (sex steroid)** secretions.

Hypoadrenalism

1) **Addison's disease (primary chronic adrenocortical insufficiency) -**
   - Destruction of **more than 90%** of the **adrenal cortex** produces this clinical picture.
   - **Causes are -**
     - **Most common causes :-**
       a) In world is **autoimmune adrenalitis** (idiopathic adrenitis/atrophy).
       b) In India is **tuberculosis.**
     - Others includes amyloidosis, hemochromatosis, metastatic carcinoma.
   - **Morphology -** cortex is atrophic with chronic inflammatory cells.
   - **Clinical features -** weakness, fatigability, anorexia, nausea and vomiting, weight loss, hypotension, **hyperpigmentation** (from elevated **proopiomelanocortin** peptides).
   - **Autoimmune Addison's disease** is divided into two types :-
     - **Type I**
       i) It will have hypoparathyroidism and mucocutaneous candidaissis.
       ii) Defect in suppresser T-cell function.
     - **Type II (Schmidt's syndrome)**
       i) Associated with **HLA-A1 and B8.**
       ii) Addison's disease
       iii) Autoimmune thyroid disease and insulindependent diabetes mellitus.

2) **Primary acute adrenocortical insufficiency -**
   - **Causes are :-**
     - Due to **rapid withdrawal** of steroids - **most common cause.**
     - Crisis in patients with Addison's disease.
     - Precipitated by stress.
     - Massive hemorrhage.
     - Neonates - massive hemorrhage following prolonged or difficult delivery due to hypoxia or trauma.
     - **Waterhouse-Friderichsen syndrome :-**
       i) Hemorrhagic distruction of the adrenals due to bacterial infection.
       ii) **Starts in medulla** and then involves cortex.
       iii) Presents with rapidly progressive shock and hypotension.
       iv) **Meningococcemia (septicemia)** is most common cause.
       v) Others include - Pneumococci, staphylococci, Hemophilus influenzae.
       vi) Widespread petechiae, purpura, hemorrhages throughout body, particularly skin and mucosal surfces.
     - Grossly-adrenals are hemorrhagic and necrotic with sacs of blood clots.

3) **Secondary adrenocortical insufficiency -**
   - Due to disorders of **hypothalamus or pituitary** resulting in decreased levels of ACTH, e.g. infections, infarctions, irradiations, exogenous corticosteroids and metastatic cancers.
   - **No hyperpigmentation** due to low melanotropic hormones level **(hyperpigmentation is seen in Addison's disease).**

Hyperadrenalism

- **There are three patterns :-**
  1. Glucocorticoid excess - **Cushing's syndrome**
  2. Mineralocorticoid excess - **Hyperaldosternoism**
  3. Androgen excess - **Adrenogenital syndrome**

BONE

1. **Which of the changes occur in bone growth?**
   a) Increased acid phosphatase *(AIIMS Dec. 97)*
   b) Increased urinary calcium
   c) Increased bone nucleotidase
   d) Increased osteocalcin

2. **Osteoblasts produce-** *(JIPMER 79, Delhi 92)*
   a) Collagen
   b) Calcium
   c) Pyrophosphate
   d) Monosodium urate

3. **Bone resorption markers are all except-** *(AIIMS May 08)*
   a) Tartarate resistant acid phosphatase
   b) Osteocalcin
   c) Cross-linked N-telopeptides
   d) Urine total free deoxypyridionoline

4. **Rate of newly synthesized osteoid mineralization can be best estimated by-** *(AI 09)*
   a) Tetracycline labeling
   b) Alizarin red stain
   c) Calcein stain
   d) von Kossa stain

5. **Marker of bone formation are all except-**
   a) Osteocalcin *(AIIMS Nov. 11)*
   b) alkaline phosphatase
   c) Procollagen residue
   d) Hydroxyproline

ARTHRITIS

6. **Which of the following statements about rheumatoid factor is true?** *(AI 12)*
   a) It is an IgM antibody directed against IgG
   b) It is an IgG antibody directed against IgM
   c) It is more specific than anti-CCP antibodies
   d) It is positive in all cases of juvenile rheumatoid

7. **Which of the following joint is characteristically involved in RA?** *(AIIMS Sep. 96; Recent exam 2015)*
   a) Spine
   b) Sacroiliac joint
   c) Metacarpophalangeal joint and proximal interphalangeal joint
   d) Wrist joint

ARTHRITIS

8. **Characteristic feature of Still's disease-** *(AIIMS Dec. 97, Sep. 96)*
   a) Prominent kidney involvement
   b) Rashes
   c) Positive rheumatoid factor
   d) Neutropenia

9. **Rheumatoid factor is directed against-** *(AI 13, 14)*
   a) IgG
   b) IgD
   c) IgM
   d) IgA

10. **Which one of the following is not a characteristic feature** *(AI 15, 14)*
    a) Sacroiliitis
    b) Metacarpophalangeal joint involvement
    c) Symmetrical arthritis
    d) Positive rheumatoid factor

11. **Rheumatoid factor is-** *(AI 08)*
    a) Antibody
    b) Mucopolysaccharide
    c) Fatty acid
    d) Glycoprotein

12. **Whic of the following is not a seronegative spondyloarthropathy?** *(AI 13, 14)*
    a) Psoriatic arthritis
    b) Ankylosing spondylitis
    c) Rheumatoid arthritis
    d) Reiter's arthritis

13. **"Tophus" is the pathognomonic lesion of which of the following condition?** *(AIIMS May 05)*
    a) Multiple myeloma
    b) Cystinosis
    c) Gout
    d) Eale's disease

14. **Tophi in gout found in all regions except-**
    a) Joint capsule *(PGI Nov. 14)*
    b) Skin
    c) Muscle
    d) Articular cartilage
    e) Synovial membrane

METABOLIC BONE DISORDERS

15. **Osteoporosis is caused by all, except-** *(AIIMS June 98)*
    a) Corticosteroid
    b) Estradiol
    c) Methotrexate
    d) Chronic heparin therapy

16. **All are causes of osteoporosis-** *(AIIMS Sep. 96)*
    a) Old age
    b) Chronic heparin therapy
    c) Hypothyroidism
    d) Thyroxtoxicosis

17. **Paget's disease involves which of the following bone?** *(PGI May 14)*
    a) Pelvis
    b) Vertebrae
    c) Skull
    d) Phalanges
    e) Toes

19. **Histological features of chronic hepatitis -**
    a) Fibrosis of porta hepatitis *(PGI May 13, Nov 14)*
    b) Architechtural changes
    c) Bridging necrosis
    d) Ballooning degenerations

FATTY LIVER

20. **Periportal fatty infiltration of liver is seen with -**
    a) Alcoholism *(DNB Dec 07)*
    b) Viral hepatitis
    c) Malnutrition
    d) Tetracycline

21. **A 40 yrs old obese lady with diabetes mellitus; hypertriglyceridemia; RUQ pain and recurrent jaundice.What will be seen in liver pathology-**
    a) NASH *(Recent exam 15, AIIMS May 14)*
    b) Microvesicular hepatosis
    c) Peliosis hepatitis
    d) Autoimmune hepatitis

22. **On stopping alcohol, all the following changes are reversible except -** *(DNB Dec 10)*
    a) Hepatitis
    b) Cirrhosis
    c) Microvesicular fatty change
    d) Macrovesicular fatty change

23. **Increased IgA level is seen in?**
    a) Alcoholic hepatitis *(Recent exam 15, JIPMER 14)*
    b) Biliary cirrhosis
    c) Gilbert's syndrome
    d) Autoimmune hepatitis

24. **Which one of the following diseases characterisitcally causes fatty change in liver -** *(AI 05)*
    a) Hepatitis B virus infection
    b) Wilson's disease
    c) hepatitis C virus infection
    d) Chronic alcoholism

25. **Mega-Mitochondria is a characteristic feature of-**
    a) Alcoholic liver injury *(Recent exam 13, Jipmer 14)*
    b) Viral hepatis
    c) Peliosis Hepatitis
    d) None

26. **Pathological manifestation of chronic alcoholism include all of the following except -** *(AI 15, 14)*
    a) Piecemeal necrosis
    b) Ballooning degeneration
    c) Microvesicular fatty changes
    d) Central hyaline sclerosis

27. **A 49 yr old male presents with symptoms that developed following a long weekend of binge drinking. His serum reveals GGT level of 65 IU/L. A liver biopsy reveals fatty change (steatosis) of numerous hepatocytes. This patient's liver abnormality is most likely the result of -** *(Recent exam 2013, JIPMER 2015)*
    a) Decreased free fatty acid delivery to liver
    b) Decreased production of triglycerides
    c) Increased mitochondrial oxidation of fatty acids
    d) Increased NADH production

28. **Macrovesicular fatty liver is seen in -** *(AI 96)*
    a) Protein-energy malnutrition
    b) Viral hepatitis
    c) Acute fatty liver of pregnancy
    d) Reye's syndrome

29. **Mallory bodies contain -** *(AI 13, 14)*
    a) Vimentin
    b) Cytokeratins
    c) Desmin
    d) Collagen

30. **Which does not cause microvesicular steatosis -**
    a) Alcoholic fatty liver *(AI 13, 14)*
    b) Tetracycline toxicity
    c) Acute fatty liver of pregnancy
    d) Reye's syndrome

31. **Mallory hyaline is characteristic feature of -**
    a) Hepatocellular carcinoma *(DNB June 11)*
    b) Primary biliary cirrhosis
    c) Alcoholic liver disease
    d) Wilson'ss disease

32. **Microvesicular fatty liver is caused by -** *(AI 97)*
    a) DM
    b) Valproate
    c) Starvation
    d) IBD

33. **A 4 yr old girl presents with severe vomiting after viral fever of 6 days. She develops cerebral edema later on. What would be the liver biopsy findings?** *(AIIMS May 2014)*
    a) Centrizonal haemorrhagic necrosis
    b) Marked microvesicular steatosis
    c) Ring granuloma
    d) NASH

34. **All of the following conditions may show mallory hyaline changes except -** *(AI 97)*
    a) Wilson disease
    b) Indian's childhood cirrhosis
    c) Primary biliary cirrhosis
    d) Hepatitis E

35. **Mallory's hyaline is seen in -** *(DNB Dec 07)*
    a) Hepatitis C infection
    b) Amebic liver abscess
    c) Indian childhood cirrhosis
    d) Autoimmune hepatitis

36. **Mallory hyaline bodies are present in all of the following except -** *(DNB Nov 14)*
    a) Primary biliary cirrhosis
    b) Secondary biliary cirrhosis

13. **Ans. is 'c' i.e., IL-2** *[Ref: Robbin's 9th/e p. 191 & 8th/e p. 188]*

14. **Ans. is 'c' i.e., NK cells** *[Ref: Robbin's 9th/e p. 191 & 8th/e p. 188]*

15. Ans. is 'b' i.e., II

Type II Hypersensitivity

- a/k/a - antibody-dependent cell-mediated cytotoxicity (ADCC).
- Cells exhibiting the foreign antigen are tagged with antibodies (IgG or IgM).
- These tagged cells are then recognised by natural killer cells (NK) and macrophages (recognised via IgG bound (via the Fc region) to the effector cell surface receptor, CD16 (FcγRIII)), which in turn kill these tagged cells.

16. **Ans. is 'c' i.e., They are MHC restricted cytotoxic cells** *[Ref: Robbin's 9th/e p. 191 & 8th/e p. 188]*

Natural killer cells:

- Also known as "Large granular lymphocytes" as they are larger than small lymphocytes and contain abundant azurophilic granules.
- They are approximately 5 to 10% of peripheral blood lymphocytes.
- NK cells differentiate and mature in bone marrow, lymph nodes, spleen, tonsils, and thymus.
- They are "First line of defense" against viral infections and tumor cells.
- NK cell cytotoxicity is neither MHC restricted nor antibody dependent.
- NK cells are identified by
  a) CD16 (Fc receptor for IgG)
  b) CD56

17. **Ans. is 'b' i.e., Cells which are not able to expres MHCI** *[Ref: Robbin's 9th/e p. 191 & 8th/e p. 188]*
- Functional activity of NK cells is regulated by balance between signals from:
  a) Activating (NKG2D family)
     - NKG2D receptors recognize surface molecules induced by various kinds of stress like infection and DNA damage.
  b) Inhibitory receptors (MHC I).
     - NK cell inhibitory receptors recognize class I MHC molecules expressed on all healthy cells.
     - This preventNK cells from killing normal cells.
     - Viral infections or neoplastic transformation enhances expression of ligands for activating receptorsand reduces expression of class I MHC molecules which favors cytotoxicity by NK cells.

18. **Ans. is 'c' i.e., NK cells** *[Ref: Ananthanarayan 7th/e p. 1 25; Ref: Robbin's 9th/e p. 191 & 8th/e p. 188]*

19. Ans. is 'b' i.e., CD16, CD56 *[Ref: Robbin's 9th/e p. 191 & 8th/e p. 188]*

20. Ans. is 'c' i.e., Effective against virus infected cells

21. **Ans. is 'a' i.e., Mature dendritic cells** *[Ref: Robbin's 9th/e p. 192 & 8th/e p. 187]*
- Most potent and effective antigen presenting cells in the body is Mature dendritic cells.

22. **Ans. is 'b' i.e., Antigen presenting cells** *[Ref: Robbin's 9th/e p. 192 & 8th/e p. 187]*

23. **Ans. is 'b' i.e., Dendritic cells** *[Ref: Harrison 18th/e p. 2654-2655]*

A) Professional APCs

- Types of APCs which express MHC class II molecules are called professional antigen-presentingcells.
  1) Dendritic cells (Des)
  2) Immature dendritic cells (immature dendritic cells within the epidermis are called Langerhanscells.)
  3) Macrophages
  4) B-cells

182. **Ans. is 'b' i.e., ANA** *[Ref: Robbin's 9th/e p. 219 & 8th/e p. 215]*

183. **Ans. is 'c' i.e., both (a) and (b)** *[Ref: Robbin's 9th/e p. 225 & 8th/e p. 217-21 8]*

184. **Ans. is 'c' i.e., Class IV** *[Ref: Robbin's 9th/e p. 224 & 8th/e p. 21]*

185. **Ans. is 'a' i.e., SLE** *[Ref: Robbin's 9th/e p. 225 & 8th/e p. 219]*

186. **Ans. is 'd' i.e., Antibodies to double-stranded DNA** *[Ref: Robbin's 9th/e p. 218-219 & 8th/e p. 214-215]*

187. **Ans. is 'a' i.e., Systemic sclerosis** *[Ref: Robbin's 9th/e p. 250 & 8th/e p. 215 (table 6.9)]*

188. **Ans. is 'c' i.e., Diffuse proliferative** *[Ref: Robbin's 9th/e p. 224 & 8th/e p. 217; Davidson's 20th/e p. 499]*

189. **Ans. is 'd' i.e., Systemic sclerosis** *[Ref: www.springerlink.com]*

190. **Ans. is 'a' i.e., SLE; 'b' i.e., Systemic sclerosis & 'c' i.e., Morphea**

[Ref: Robbin's 9th/e p. 219 & 8th/e p. 215]

191. **Ans. is 'c' i.e., Lymphocytes** *[Ref: Robbin's 9th/e p. 222 & 7th/e p. 236]*

192. **Ans. is 'b' i.e. Lymphocytes** *[Ref: Robbin's 9th/e p. 227 & 7th/e p. 222]*

193. **Ans. is 'a' i.e., Amyloidosis** *[Ref: Robbin's 9th/e p. 261 & 7th/e p. 254]*

194. **Ans. is 'b' i.e., Immune complexes** *[Ref: Science of laboratory diagnosis p. 466]*
- **Raji assay** is used to identify circulating immune complexes.

195. **Ans. is 'd' i.e., Heart** *[Ref: Harrison 17th/e p. 2147; Robbin's 9th/e p. 261 & 8th/e p. 253]*

196. **Ans. is 'a' i.e., Enteric fever** *[Ref: Robbin's 9th/e p. 260 & 8th/e p. 252-253]*

197. **Ans. is 'd' i.e., Unknown** *[Ref: Robbin's 9th/e p. 258 & 8th/e p. 251]*

198. **Ans. is 'b' i.e., Primary amyloidosis ; 'c' i.e., Multiple myeloma** *[Ref: Robbin's 9th/e p.. 259 & 8th/e p. 252]*

199. **Ans. is 'c' i.e., Brilliant pink color** *[Ref: Robbin's 9th/e p. 257 & 8th/e p. 249]*

200. **Ans. is 'a' i.e., Intracellular accumulation of fibrillar protein** *[Ref: Robbin's 9th/e p.257-259 & 8th/e p. 249, 255]*

201. **Ans. is 'b' i.e., Chronic inflammatory states** *[Ref: Robbin's 9th/e p. 259 & 7th/e p. 260]*

202. **Ans. is 'a' i.e., Knee joint** *[Ref: Robbin's 9th/e p. 259 & 8th/e p. 253]*

203. **Ans. is 'd' i.e., Green birefringence of stained amyloid when viewed by polarizing microscope** *[Ref: Robbin's 9th/e p. 257 & 8th/e p. 249]*

204. **Ans. is 'd' i.e., Medullary carcinoma thyroid** *[Ref: Robbin's 9th/e p. 259 & 8th/e p. 252]*

205. **Ans. is 'a' i.e., Rectal biopsy** *[Ref: Robbin's 9th/e p. 262 & 8th/e p. 255]*

206. **Ans. is 'c' i.e., Amyloidosis** *[Ref: Robbin's 9th/e p. 261 & 8th/e p. 254]*

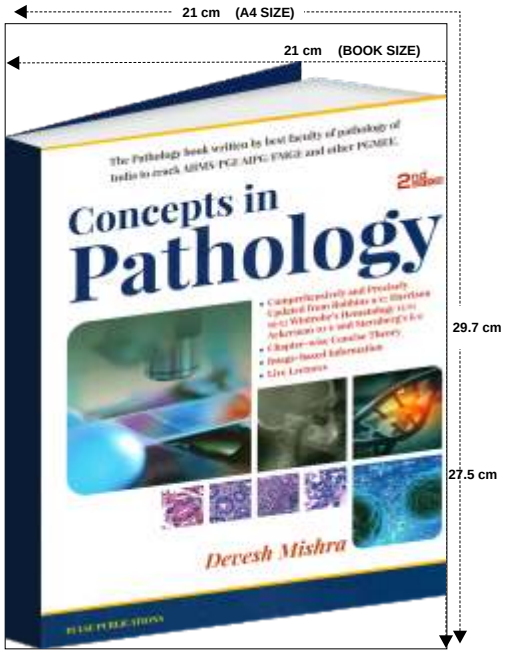
207. **Ans. is 'b' i.e., Amyloidosis** *[Ref: Robbin's 9th/e p. 262 & 8th/e p. 255]*

208. **Ans. is 'a' i.e., Medullary carcinoma thyroid** *[Ref: Chandrasoma Taylor 3rd/e p. 30]*

209. **Ans. is 'd' i.e., Diffuse amyloidosis** *[Ref: Patho Robbin's 9th/e p. 262 & 8th/e p. 254]*

Amyloidosis of Spleen:

- One of the two patterns are seen :
  a) Sago spleen:
     - It is localized deposits involving splenic follicles.
     - Grossly it is giving rise to tapioca-like granules appearance.
  b) Lardaceous spleen: (Mnemonic-La "RED" aceous)
     - Diffuse deposit in the red pulp.



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