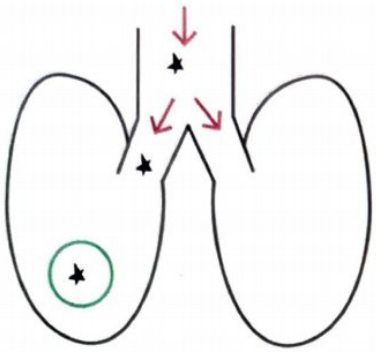
62 OBSTRUCTIVE LUNG DISORDERS

BASIC CONCEPTS

LUNG ABSCESS

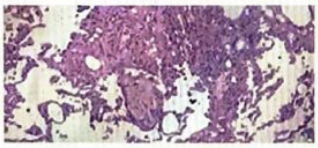


- Right bronchus is more aligned with trachea → FB impaction is more common in right lung.
- FB is the MC cause of lung Abscess → MC involves right lower lobe.
- Can also be seen due to
  - Pneumonia
  - Septicemia
  - Malignancy → improper drainage of secretion → contamination
- Pus settles down with air on top → air-fluid level on radiograph
- Food particles is the MC foreign body
- Anaerobes are MC microorganisms causing lung abscess.

Previous Year's Questions

Q. Patient with history of long-standing depressive illness comes to ER acute breathlessness. The X-ray shows diffuse infiltrates with predominance in right middle lobe and right lower robe. The patient did not survive and the following picture in the lungs was seen on autopsy. It is suggestive of?

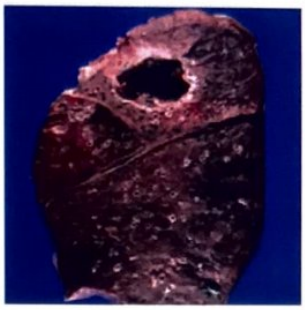
(AIIMS - Nov - 2017)



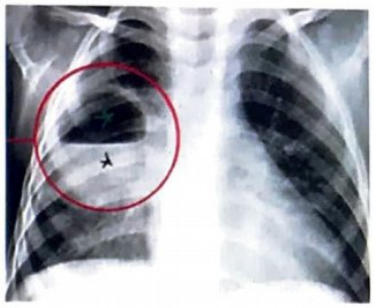
A. Severe neurosis with fungal hyphae, severe fungal pneumonia
B. Coagulation necrosis, tuberculosis
C. Vegetable matter, aspiration pneumonia.
D. Severe neurosis, severe necrotizing pneumonia.

Clinical features

- Fever
- Foul smelling sputum
- Hemoptysis



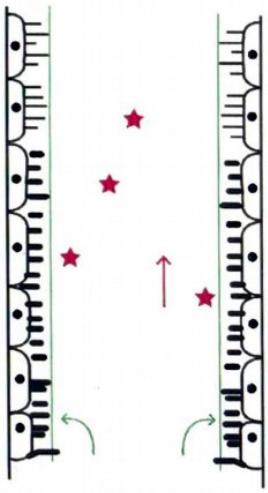
Cavitory lesios



Air-fluid level

- Other causes
  - Elderly → malignancy
  - Multiple lung abscesses → staph aureus infection

Normal Histology



- Lined by pseudo stratified ciliated columnar epithelium → nuclei are present in haphazard fashion, no true stratification
  - Except vocal cord where stratified squamous epithelium is present
- Presence of glands → secretion of mucus
  - ↓ Mucus → infections
- Dust / bacteria / Ag → attach to mucus → cilia (escalator

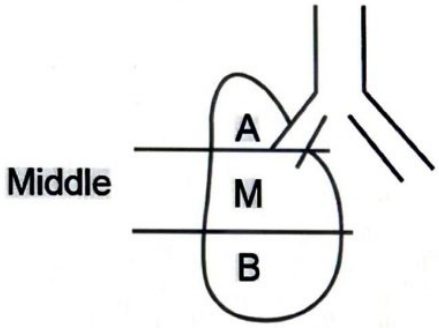
like action)
  - ↓ Ciliary activity → ↑ infections
- Acquired ciliary abnormality: Smoking
- Congenital ciliary abnormality: Defect in dynenin → Kartagener Syndrome
  - Also associated with ↓ fertility

Important Information

Kartagener Syndrome Triad
- Bronchiectasis
- Situs inversus (Dextrocardia)
- Sinusitis

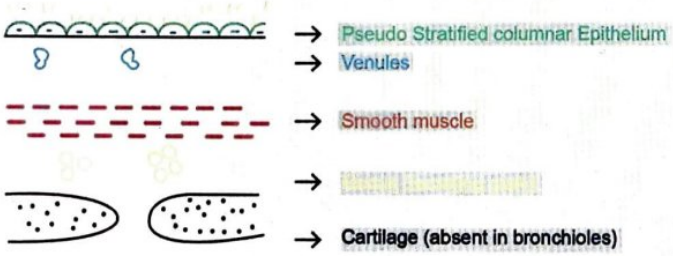
- ↓ Mucus secretion
  - Cystic fibrosis: CFTR defect → chloride channel defect → dry mucus → ↑ risk of infections

Lung physiology



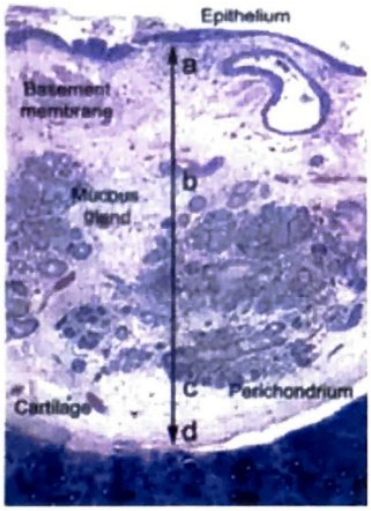
- Ventilation maximum at Base
- Perfusion maximum at Base
- Perfusion is maximum at Base
- V/p ratio is maximum at Apex
- VQ ratio: normal - 0.8 (cannot be >1)

Reid's Index



- Venules at lamina propria → provides ambient temperature to air

- Reid's Index: A/B
  - A: Thickness of mucus gland layer
  - B: Distance b/w epithelial cell & cartilage
- Normal value: 0.4 (increased in Pulmonary Bronchitis)



Reid's Index

- Smaller airway has no cartilage, ↓ glands
- Functional unit of lung: Acinus
- Between alveoli → pores of Kohn is present
  - Significance: Bacteria can travel from one alveolar sac to adjacent alveolar sac

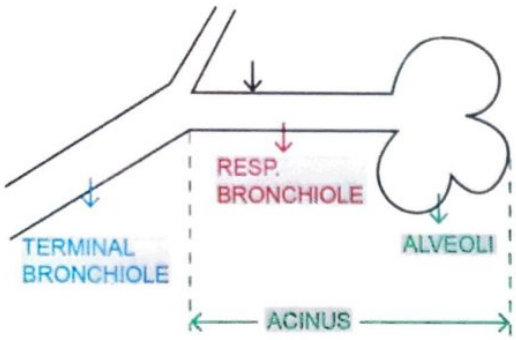
Pneumocytes
- Type 1 → contributes to majority of surface area
- Type 2
  - Present in more number
  - Secretes surfactant (DPPC) → ↓ surface tension at expiration
  - Alveolar repair

Spirometry 00:29:07

	Obstructive Disease	Restrictive Disease
FEV_1	< 80%	N/↓
FVC	N/↓	↓
FEV_1/ FVC	< 0.7	> 0.7
TLC	N/↑	↓

EMPHYSEMA

00:32:00



- Acinus involvement
- Abnormal permanent dilatation of airway beyond terminal bronchiole (acinus) → alveolar wall destruction with minimal fibrosis

Damaging factors

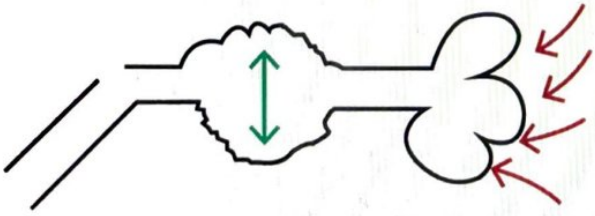
- Elastase (Neutrophils / Macrophages) → Elastin fibers damage
- Smoking associated with ↑ elastase
- Air pollution
- Pneumoconiosis

Protective Factors

- Anti-elastase activity
  - α_1 anti-trypsin (produced by liver)
  - α_1 macro globulin
- Gene for α_1 anti-trypsin: PiMM gene present on chromosome 14
- α_1 anti-trypsin deficiency
  - PiMZ gene defect (heterozygous) → ↓ α1 - anti trypsin (MC)
  - PiZZ gene defect (homozygous) → ↓↓↓ very low α1 anti-trypsin → emphysema
  - Also associated with α1 anti-trypsin misfolded proteins in liver → cirrhosis

ANATOMICAL CLASSIFICATION

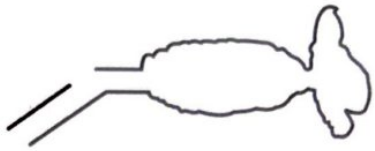
Centri-acinar emphysema



CENTRIACINAR EMPHYSEMA

- Proximal part of acinus is involved
- MC type of emphysema (associated with smoking)
- Upper lobes of lungs are affected
- MC type of emphysema seen clinically
- Alveoli are spared

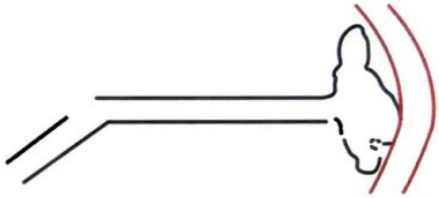
Pan Acinar Emphysema



PANACINAR EMPHYSEMA

- Complete acinus is involved
- MC associated with α1 - anti trypsin deficiency
- Base of the lung is involved
- They co-exist with cirrhosis

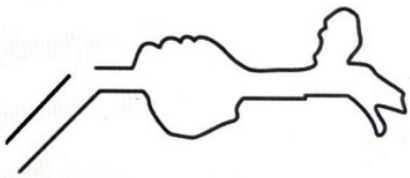
Distal Acinar Emphysema



DISTAL ACINAR EMPHYSEMA

- Seen more commonly in smoker
- Upper Lobe of lungs is involved
- Damage at the distal acinus → Bleb/bullae formation → damage at visceral pleura → air from acinus enters pleura → Spontaneous pneumothorax

Irregular Emphysema



IRREGULAR EMPHYSEMA

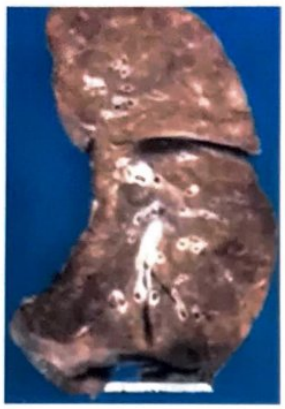
- Patchy involvement
- MC type of emphysema that is seen microscopically

Important Information

- NRF2 gene: works as sensor for oxidative molecules produced by smoking
- NRF2 → activates anti oxidative defense mechanisms
- Problem at NRF2 gene → more damage to the lungs

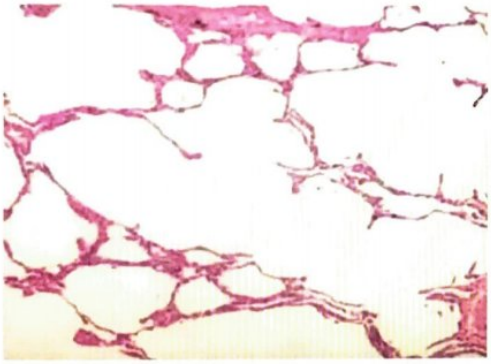
CLINICAL FEATURES

- Elderly
- Dyspnea
- Barrel chest
  - Loss of elastin fibers → loss of elastic recoil → air trapping → hyperinflation
  - CXR: flattening of diaphragm
- Weight loss
- Pink Puffers
- Long-term complication: Hypoxemia → pulmonary Hypertension → Cor pulmonale



Normal lung

Emphysema



Destruction of alveolar wall

CHRONIC BRONCHITIS

- Risk factor: H/O smoking

Pathogenesis

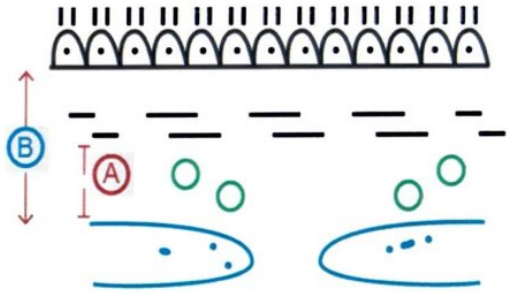
SMOKING
↓
INFLAMMATION
↙ ↘
2° INFECTION (H.Infulenza) ← ↑MUCUS PRODUCTION

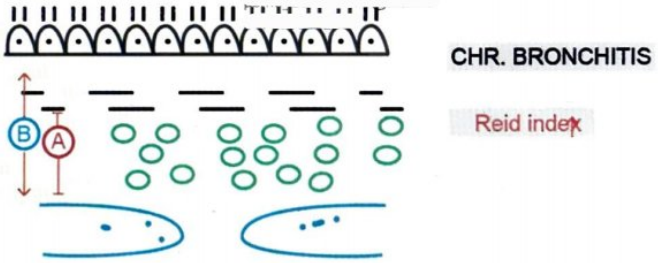
- Productive cough
- Mucus gland thickness ↑
- Airway obstruction

Clinical Features

- Productive cough (minimum duration of 3 months in 2 consecutive years)
- Fever
- Cyanosis
- ↑ Reid's index
- Hypoxemia (Blue bloaters) → Pulmonary HTN → Cor Pulmonale
- No associated amyloidosis
- Smoking → squamous metaplasia → ↑ cancer
- COPD → Emphysema + Chronic Bronchitis + Small airway disease
- Smoking → irritation of vagal afferents → ↑ Ach → Bronchospasm

$$\text{REID'S INDEX} = \frac{A}{B}$$





Treatment

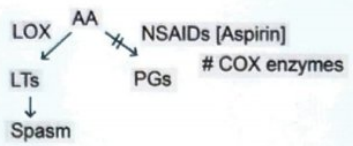
- O_2 Supplementation
- Ipratropium
- Mucolytic drugs
- Antibiotics

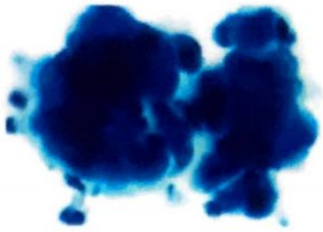
BRONCHIAL ASTHMA

01:15:20

- Reversible airway obstructive disorder

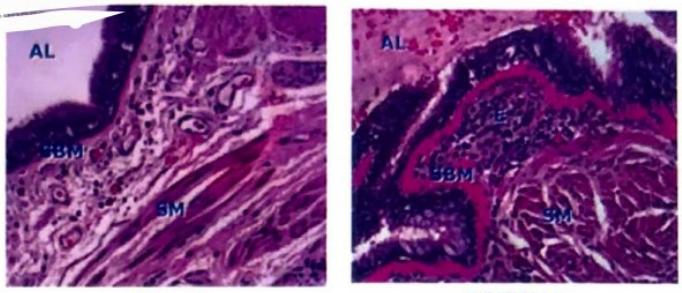
EXTRINSIC BA	INTRINSIC BA
• Type 1 HR • External antigen (House dust/pollens) • ↑↑ IgE • Childhood onset • H/O atopy	• Not due to HR • No association with External antigen • Normal IgE • Adults • No history of atopy • H/O viral infection → hyper-responsiveness • Exposure to Cold





Creola Body

AIRWAY REMODELLING



NORMAL ASTHMA

- ADAM 33 gene → responsible for proliferation of smooth muscle and fibroblasts
- YKL 40 protein correlates with severity of Asthma

Treatment
- Steroids
- Bronchodilators: Terbutaline, Salbutamol
- Montelukast

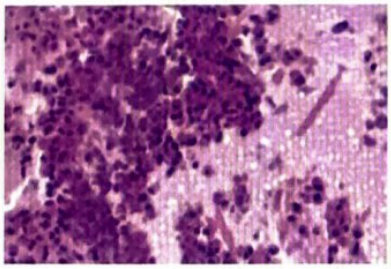
Important Information

Samter's Triad
- Aspirin intolerance
- Asthma
- Adult nasal polyps (child with nasal polyp → CF)

Clinical features
- Dyspnea
- Wheezing
- Nocturnal cough

Diagnosis
- Spirometry
- Sputum examination
  - Charcot - Leyden Crystals is composed of galectin 10
- Airway remodeling

Curschmann Spirals



Charcot - Leyden Crystals

Previous Year's Questions

Q. Which of the following is not a feature of bronchial asthma? (FMGE - Dec – 2018)
A. Thickening of bronchial wall.
B. Increase in number of goblet cells glands.
C. Hypotrophy of smooth muscle
D. Increased IgE

BRONCHIECTASIS

01:29:56

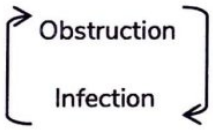
- Chronic necrotizing infection/inflammation → abnormal permanent dilatation of airways

Etiology
- Congenital risk factors
  - Kartagener Syndrome
  - Cystic Fibrosis
- Obstruction (FB or tumor) → inability to clear secretion → secondary infections
- Infections
  - TB

- Staph aureus
- ABP aspergillosis

- Miscellaneous factors
  - RA
  - GVHD

Pathogenesis



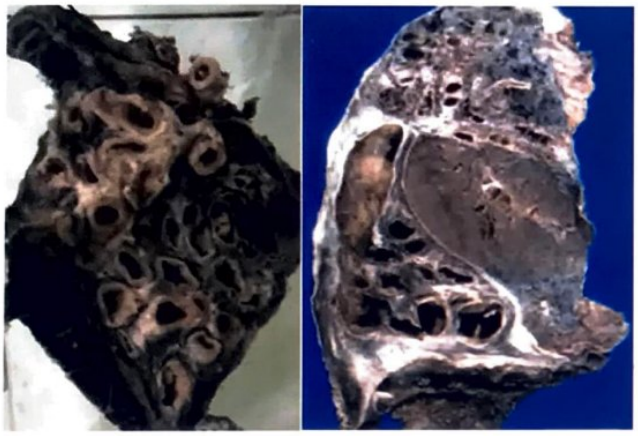
- Prolonged inflammation → wreaking of wall → dilatation of airway

Clinical features

- Bronchorrhea
- Left sided Basal involvement is more
- HRCT → Tram track appearance (honeycomb lung)
- Fever
- Dyspnea
- Associated with secondary amyloidosis
- Benign condition

Treatment

- Mucolytics
- Antibiotics
- Supportive therapy



Dilated airways across the lung

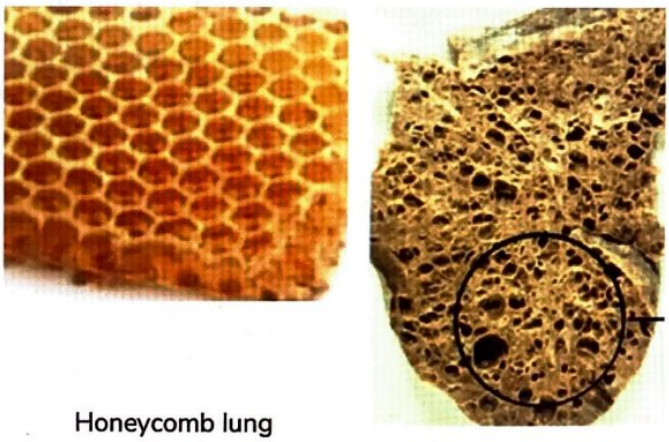
63 RESTRICTIVE LUNG DISEASE

Spirometry findings
- TLC ↓↓
- FVC ↓↓ → FEV1 (normal/↓)
- FEV1/FVC ↑↑
- Fibrosis
  - ↓ Compliance
  - ↓ Diffusion Capacity

ETIOLOGY

Extra parenchymal causes
- Chest wall disorders: obesity/kyphosis/scoliosis/ankylosing spondylitis
- Neuromuscular disorders: diaphragmatic palsy/MG/GBS/muscle dystrophy

Parenchymal causes
- Acute: ARDS
- Chronic
  - Fibrosing: IPF/NSIP/COP/ Pneumoconiosis → Irregular cystic cavities Honeycomb lung
  - Granulomatous: HP/Sarcoidosis
  - Eosinophilic: Loeffler Syndrome/Drug Allergy
  - Smoking related: Diphtheria/Respiratory Bronchiolitis



Honeycomb lung

IDIOPATHIC PULMONARY FIBROSIS (IPF)

00:08:18

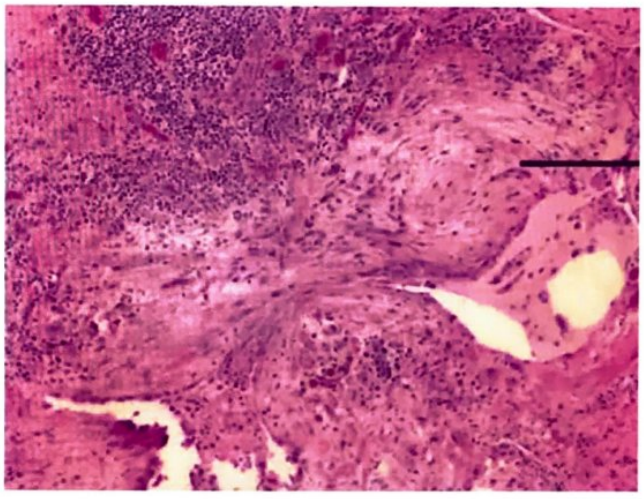
- Aka cryptogenic fibrosing alveolitis

Alveolar Epithelial Injury
Alveolitis
↓
TGF-β
↓
Fibrosis

Risk Factors
- Age: Elderly
- Genetic Factors: Telomerase/mucin/Surfactant
- Environmental factors: GERD, Tobacco exposure

Clinical features
- Male > 50yrs
- Dry cough
- Dyspnea
- Dry inspiratory crackles
- R/O previous radiation exposure and drugs
  - Methotrexate
  - Bleomycin
  - Amiodarone

Diagnosis
- It is a diagnosis of exclusion
- Surgical biopsy → usual interstitial pneumonia. Characterized by
  - Patchy interstitial fibrosis (Heterogeneous: fibroblastic foci, collagen)
  - Architectural distortion → cyst → honeycombing
  - Site of biopsy: lower lobe (sub-pleural, along interlobular septa)
- HRCT scan
- IPF → death within 3yrs from diagnosis



Fibroblastic foci (sub-pleural, along interlobular septa)

Important Information

- UIP can also be seen in hypersensitivity pneumonitis. Rheumatoid arthritis

Treatment

- Lung transplant
- TGF β inhibitor: Pirfenidone
- Tyrosine kinase inhibitor: Nintedanib (↓ fibrosis)

NON SPECIFIC INTESTITIAL PNEUMONIA (NSIP)

00:22:56

- Idiopathic
- Connective Tissue disorders (exception Rheumatoid Arthritis)

Clinical features

- Elderly female
- 6th decade of life
- Non smoker
- Dyspnea
- Dry Cough

Diagnosis

- Radiology: HRCT scan Reticular opacities
- Surgical biopsy
  - NSIP → "Homogenous/uniform appearance"
  - Presence cellular NSIP (or) Fibrosing NSIP (poor prognosis)
    → Both never seen together
  - Distinguishing factors from UIP: No fibroblastic foci/variability/honeycombing
  - No granulomatous lesion/hyaline membrane

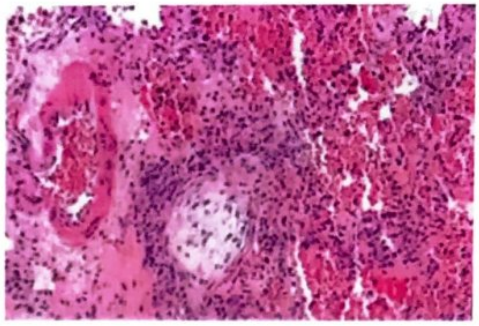
Treatment

- Steroids

CRYPTOGENIC ORGANISING PNEUMONIA (COP)

00:28:56

- Unknown etiology
- Clinical features: cough & Dyspnea
- Diagnosis: Surgical biopsy → presence of Masson body (plug of connective present in airway)
- Treatment: Good response to steroids

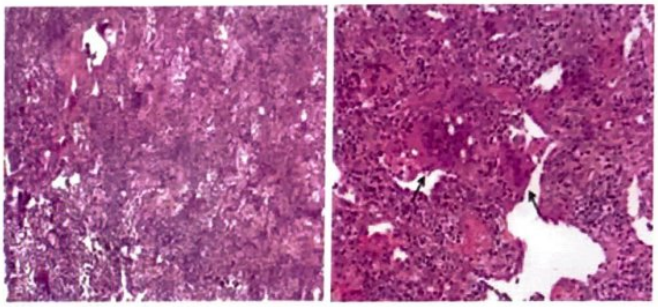


Masson body

DESQUAMATIVE INTERSTITIAL PNEUMONIA

00:31:01

- No Desquamation of pneumocytes
- Smoking → Pigmented alveolar macrophages (Smoker's macrophages)
- Mild interstitial Fibrosis
- Steroids provides good relief



Smoker's macrophage

- Respiratory bronchiolitis: Pigmented macrophages on respiratory bronchioles

PNEUMOCONIOSIS

00:34:04

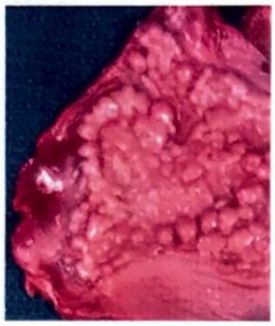
Inhalation of dust particles (1-5μ)
↓
Activation of alveolar macrophages
↓
Fibrosis
↓
Restrictive lung disorder

SILICOSIS

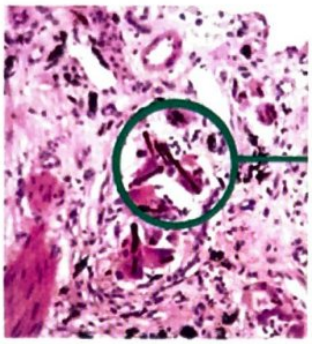
- MC pneumoconiotic disorder
- Exposure to silica/sand dust
- Upper lobe involvement
- ↑ Risk of TB/cancer
- On CXR, Egg shell calcification is seen
- Polaroid microscopy: Birefringent silica crystals

ASBESTOSIS

- Asbestos – chemical carcinogen
- Associated with fibrotic nodule formation in pleura → Pleural plaques (MC lesion)
- Interstitial fibrosis → asbestos body/ferruginous body (asbestos particle covered by proteinaceous material containing iron)
- ↑ Risk of cancer
  - Bronchogenic carcinoma (MC)
  - Malignant mesothelioma (Most Specific)



Pleural plaque



Ferruginous body

COAL WORKER'S PNEUMOCONIOSIS

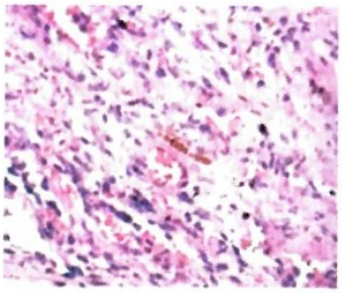
- Due to inhalation of coal dust
- Asymptomatic (anthracosis)
- Symptomatic (coal workers pneumoconiosis)
  - Cold nodule
  - Centriacinar emphysema
- Continuous exposure → Progressive Massive Fibrosis (complicated CWP)
- Black lung → prolonged exposure to coal dust
- CWP + RA → Caplan syndrome

OTHER TYPES OF PNEUMOCONIOSIS

- Byssinosis → Inhalation of cotton dust in textile industry
- Bagasosis → Inhalation of fungal contaminated sugarcane spores in farmers
  - Spray of 2 % Propionic Acid → ↓ risk of bagasosis
- Berylliosis → Exposure to beryllium in aerospace industry

Previous Year's Questions

Q. A worker was working in a factory from the past 20 years. Now presented with pleural thickening & fibrosis. Histopathology of lesion is shown in below image. Most likely diagnosis is which of the following? (AIIMS – May - 2018)



A. Asbestosis
B. Cotton fiber
C. Coal worker's disease
D. Silicosis

SARCOIDOSIS

00:48:20

- Immune dysregulation
- Presence of HLA A/B8
- Female >> Male
- Commonly seen in non-smokers

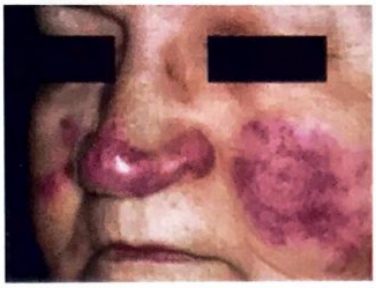
Pathogenesis

Unknown AG
↓
CD_4T activation
↓
Cytokines
(TNF α → marker in BAL fluid)
↓
Non-caseating granuloma

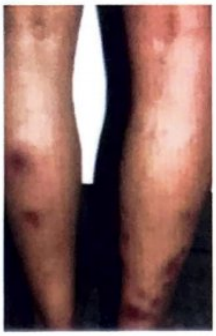
Clinical features

- Lungs
  - Dyspnea
  - Cough
  - Bilateral hilar lymphadenopathy "potato nodes"
- Skin
  - Lupus pernio
  - Erythema nodosum
  - Loffgren syndrome
    → Erythema nodosum
    → Arthralgia

→ B/L lymphadenopathy



Lupus pernio



Erythema nodosum

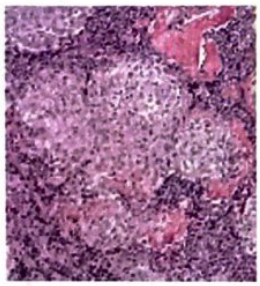
- Eyes: Uveitis (MC ophthalmologic manifestation)
- Mickulicz syndrome: Lacrimal gland/salivary gland destruction → dryness of eye and mouth
- Spleen/Liver/Bone marrow: presence of granuloma
- Endocrine: pituitary involvement
- Muscle: myalgia, fatigue

Important Information

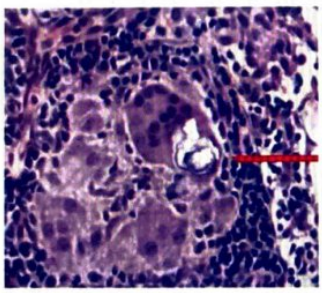
- MC cause non-infectious granulomatous hepatitis: Sarcoidosis

Diagnosis

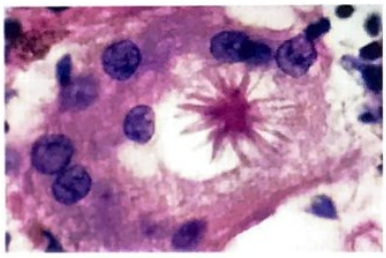
- Diagnosis by Exclusion
- ↑↑ S. ACE levels
- ↑ Activity of 1α – hydroxylase → ↑↑ Ca^{2+}
- Cutaneous anergy (↓ cell mediated immunity)
- BAL fluid
  - ↑ TNF α
  - ↑ CD_4:CD_8 T-cell ratio (5-15:1)
- LN biopsy: Non caseating granuloma
- Kveim test: Intra-cutaneous injection of spleen extract from known case of sarcoidosis → Non-caseating granuloma formation in 4-6 weeks



Naked granuloma



Schaumann body



Asteroid body

Treatment

- Spontaneous Remission
- Improvement on Steroids

HYPERSENSITIVITY PNEUMONITIS 01:06:03

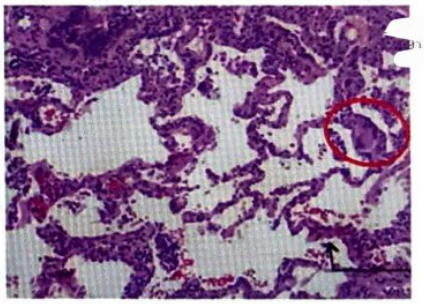
- Aka extrinsic allergic alveolitis
- Exposure to known Ag → interstitial pneumonitis & non-caseating granuloma

Acute Exposure(4-6 hrs after exposure)
↓
Immune Complex (Type 3 HR)
↓
Alveolitis

- Chronic Exposure → T-Cell activations → granuloma (Type 4 HR)
- Type 4 HR >> Type 3 HR

Clinical features

- Dyspnea
- Cyanotic manifestations
- Respiratory failure



Interstitial pneumonitis

- Farmer's lung → thermophilic actinomyctes
- Pigeon breeder's lung → bird protein
- Humidifier lung → bacteria

64 PULMONARY HYPERTENSION

Important Information

- Normal pulmonary artery pressure: 10mm Hg
- Pulmonary HTN: > 25 mmHg

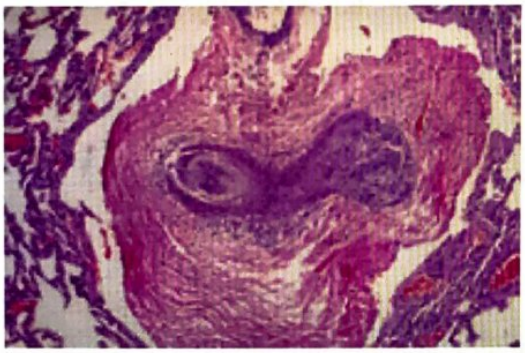
1° Pulmonary HTN 00:00:41

- Young female (20-40yrs)
- Inactivation mutation of BMPR 2 (Bone Morphogenic Protein Receptor)
- Normal gene → smooth muscle cell apoptosis
- Mutation → ↑↑ proliferation of smooth muscle cell → Pulmonary HTN

2° Pulmonary HTN

- Hypoxemia causes vasoconstriction
- Seen in high altitude/pulmonary disease
- Left ventricular Failure/mitral Stenosis
- Recurrent Pulmonary Embolism
- Obstructive sleep apnea

Microscopic appearance



Medial hypertrophy

- Medial hypertrophy (affects elastic & muscular arteries)
- Pulmonary artery atherosclerosis
  - Presence of plexiform lesion
- Right ventricular hypertrophy

Clinical features

- Dyspnea
- Fatigue
- Chest pain
- CXR → Tapering of pulmonary arteries

Treatment

- Administration of O_2
- Diuretics
- Vasodilators
  - Endothelin Antagonists
  - Prostanoids
- Lung transplantation

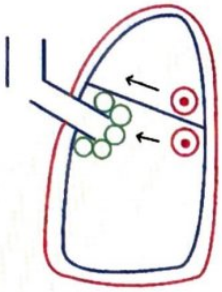
65 INFECTIVE LUNG DISORDERS

PULMONARY TUBERCULOSIS

- Causative organism: Mycobacterium tuberculosis hominis
- Mode of transmission: Droplet infection
- Obligate aerobe
- Cord factor → virulence
- LAM → inhibits phagocytosis

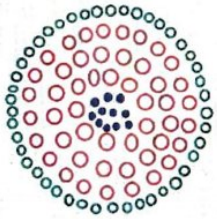
Primary pulmonary TB

- 1st entry of pathogen



Gohn's complex

- Ghon's focus: sub-pleural lesion near the inter-lobar fissure
  - 1st cell affected by Ghon's focus → alveolar macrophages
- Ghon's complex: Ghon's focus + Lymphatics + Hilar LN enlargement (occurs within 3 weeks)
- After 3 weeks: APC → TH1 cell → INF γ → macrophage activation
- Macrophage + IL-2 + TNF α → Granuloma formation → inactivation of bacilli



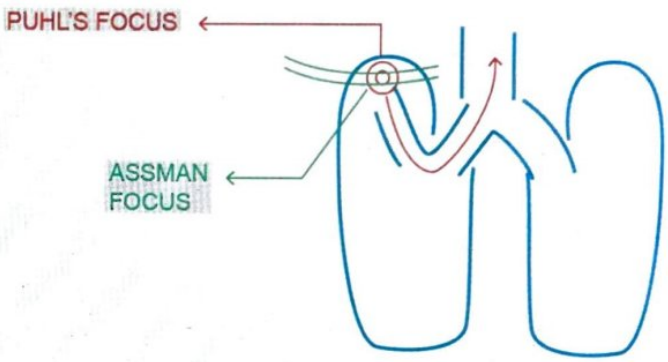
Macrophages covered by lymphocytes

- Raenke's complex: Fibro-calcified Ghon's complex
- Simon's focus: Apical lesion seen in immunocompromised individual
- In severely immunocompromised patients → dissemination of bacteria → progressive pulmonary TB

Primary TB

Secondary Pulmonary TB

00:12:55



- Occurs due to
  - Reactivation (MC) → ↓ immunity
  - Reinfection
- Apical Lesion is seen → due to maximum ventilation perfusion ratio

Apical lesion	
Delayed hypersensitivity	**Immunosuppression**

• Caseation
• Cavitation
• Hemoptysis
• No hilar lymphadenopathy
	• Lymphatic spread → lung → military pulmonary TB
	• Hematogenous
	• Aerogenous
	  ○ Endobronchial TB
	  ○ Laryngeal TB

Important Information

- MC blood vessel to bleed in Tuberculosis: Bronchial artery

- In secondary pulmonary TB
  - Supra-clavicular lesion → Puhl's focus
  - Infra-clavicular lesion → Assman focus

Secondary pulmonary TB

Clinical features
- Cough (> 2 weeks)
- Weight loss
- Low grade fever with rise in the evening
- Night sweats
- Hemoptysis
  - Uncommon Pulmonary artery involvement → Rasmussen's aneurysm

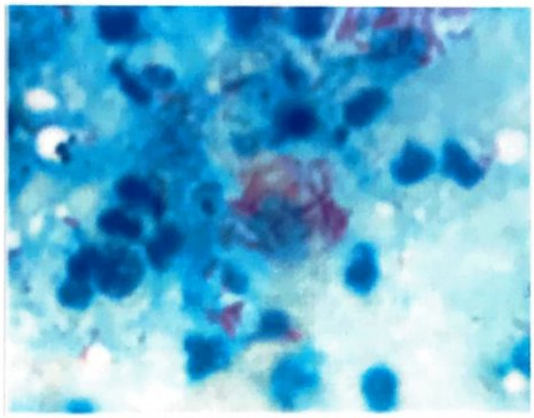
Refer Table 65.1

Millet-like foci (Miliary TB)

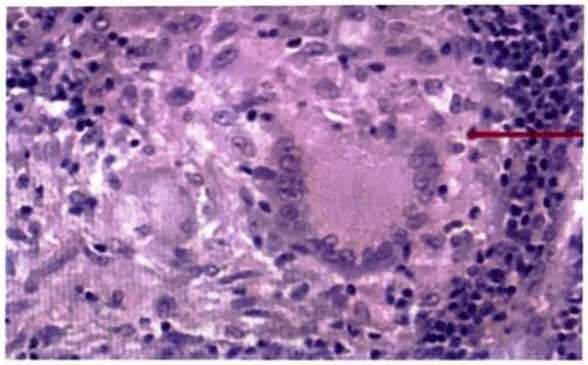
Diagnosis

00:34:15

- ↑↑ ESR
- Lymphocytosis
- Sputum Examination (Petroff's method/NALC method)
  - Early morning sample is preferred
  - Stain: ZN stain → acid fast bacilli
  - Culture
    - → LJ media
    - → BACTEC method (faster growth)
  - PCR: mycobacterial NA → CBNAAT
- Chest X-ray: pleural effusion
  - Straw colored fluid in pleural tap
  - ↑↑ ADA



Acid fast bacilli



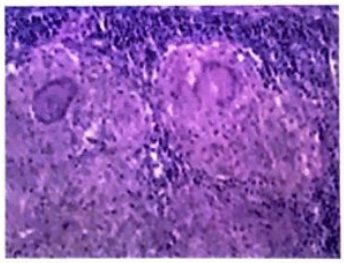
Langhans cell

Caseous necrosis

Treatment
- ATT
  - MDR-TB: Resistance to isoniazid/rifampicin
  - XDR–TB: Resistance 1st line ATT/1 Injectable fluoroquinolone/aminoglycosides

Previous Year's Questions

Q. A 11 years old boy came with history of cough for 15 days. On examination he was found to have cervical lymphadenopathy. The lymph node biopsy is shown below. Which of the following is the most appropriate diagnosis? (NEET - Jan - 2020)



A. Tuberculosis
B. Leprosy
C. Sarcoidosis
D. Syphilis

PNEUMONIA

00:42:12

- Infection of lung parenchyma

Refer Table 65.2

Laennec Stages of Typical Pneumonia

- Congestion (1-2 days): Vascular engorgement & presence of alveoli containing bacteria & WBCs
- Red hepatisation (3-4 days): Alveoli with RBCs & ↑ fluid → change in consistency
- Grey hepatisation (5-8 days): Lysis of RBC, massive fibrin deposition
- Resolution (>8 days): Causative organisms are removed by Phagocytic cells

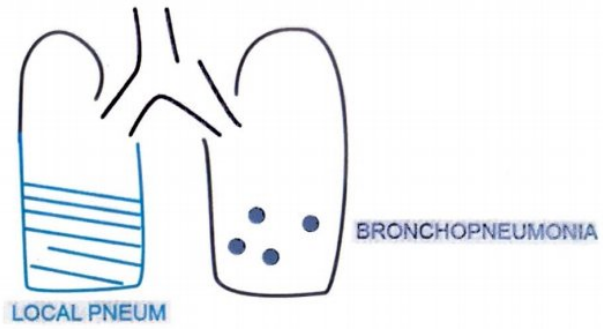
Previous Year's Questions

Q. A non-smoker patient has the presence of alveolar exudate. He presented with flu like symptoms which were followed by radiological evidence of consolidation in the lung. Which of the following is the likely organism is seen? (JIPMER - Nov - 2017)

A. Streptococcus pneumoniae
B. Staph aureus
C. Pseudomonas aeruginosa
D. klebsiella pneumonia

Types of Typical Pneumonia

- Lobar pneumonia: Extensive involvement of lung tissue, can be seen on chest X-ray
- Bronchopneumonia: Patchy involvement. Seen in children and elderly.
  - B/L involvement
  - Basal lobe is usually involved



Typical Pneumonia - Causative Organisms 00:54:58

Streptococcus pneumonia	• CAP (community Acquired Pneumonia) • Rusty Sputum
Staphylococcus aureus	• 2° pneumonia • Abscess formation
Klebsiella pneumonia	• Alcoholic → Aspiration • Red currant Jelly sputum
H.Influenzae	• Exacerbation of COPD • H/O Epiglottitis • type 'b' → Hib vaccine (offers protection)
Pseudomonas Aeruginosa	• ↓ immunity • Burns • Cystic Fibrosis • Nosocomial Pneumonia (VAP) → greenish pus

Atypical Pneumonia - Causative Organisms

Refer Table 65.3

Table 65.1

Organs affected by TB	
LN	2nd MC organ affected → Scrofula → Matted LN
CNS	Rich focus; TB meningitis (basal cistern, cobweb appearance)
Heart	Chronic constrictive pericarditis
Bone	Vertebral column involved → Potts spine → cold abscess
Kidney	TB pyelonephritis → sterile pyuria
Adrenal gland	Chronic adrenal insufficiency
Genital tract	Infertility; epididymis affected (In TB, epididymis → testicular tissue)
Liver	Simmond's focus
Pulmonary vein	Weigart Focus
Ear	Otitis media → multiple tympanic membrane perforations
Eye	Phlectenular conjunctivitis (Type 4 HR)
GIT	Ileum (ulcers/subacuteintestinal obstruction)

Table 65.2

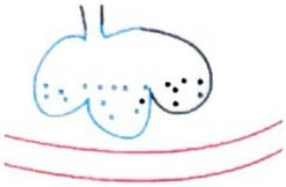
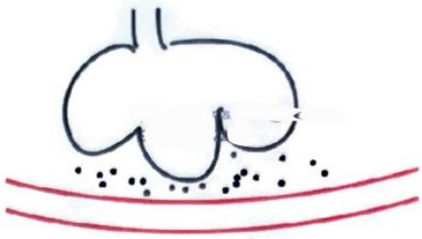
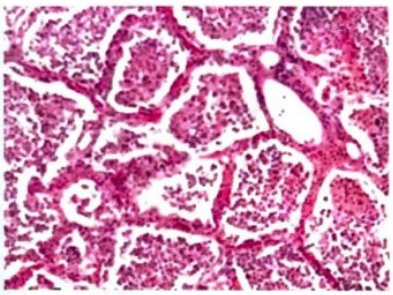
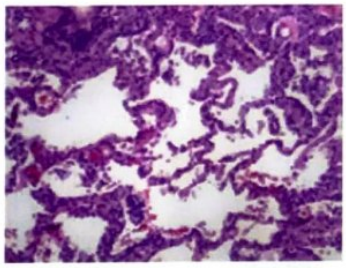
Typical Pneumonia	Atypical Pneumonia
	
• Aka air space pneumonia • Presence of alveolar exudate (most characteristic) • Neutrophilic infiltration	• Aka interstitial pneumonia • Interstitial tissue inflammation (most characteristic) • Mononuclear infiltration
 Alveolar exudate	 Alveolar septal involvement
Clinical features • High grade Fever • Chills/rigors • Productive Cough • Pleuritis • Dyspnea	**Clinical features** • Low grade fever • Dry cough • Less severe dyspnea • Malaise • Aka walking pneumonia

Table 65.3

Mycoplasma Pneumonia		• MC cause of atypical pneumonia • Cold AIHA • Hostel, military barracks → closed spaces
Chlamydia		• 2nd MC cause
Pneumocystis Jiroveci		• Fungal infection • Immunosuppression → AIDS • Silver stain is used
Coxiella Burnetii		• 'Q' fever
Legionella		• ICU → humidified air exposure • In normal individuals → Pontiac fever • Involvement of GIT/CNS is seen
Viruses	Influenza Type A	• MC viral atypical pneumonia • 2° infection → staph aureus
	RSV	• Children are affected • Bronchiolitis
	Measles	• ↓ Immunosuppression • Warthin–Finkeldey cells • Koplik spot
	CMV	• Post-transplant (kidney) • Immunosuppression • Presence of Owl-Eye Inclusions

66 ADULT RESPIRATORY DISTRESS SYNDROME

- Aka stiff lung / shock lung / hyaline membrane disease/ non-cardiac pulmonary edema
- Acute Respiratory Failure (< 7 days) + B/L Pulmonary opacities
- Diffuse alveolar damage (most characteristic feature)

Etiology 00:02:14

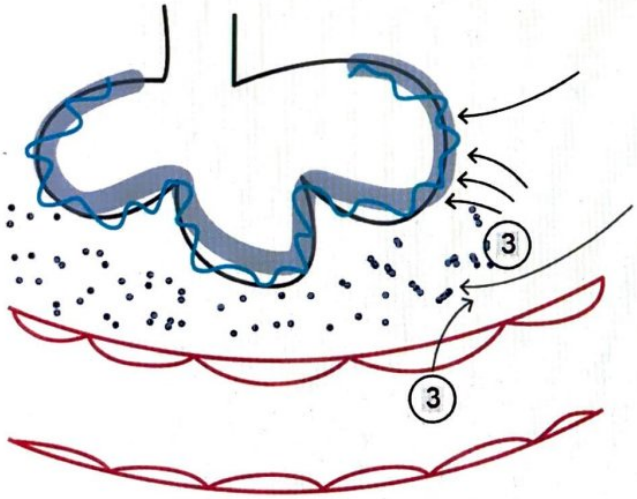
- Direct Lung Injury
  - Pneumonia (Viral)/gastric aspiration/inhaled gas
- Indirect Lung Injury
  - Gram –ve Septicemia/Mechanical trauma
  - TRALI/DIC/Fat embolism
  - Pancreatitis/drugs/burns
- MC cause of adult ARDS: Pneumonia

Pathogenesis

Endothelial Cell Injury

IL-8 → Neutrophils → Damage to alveolar epithelial cells (Type 1 > type 2) → ↓ Surfactant → Alveolar collapse

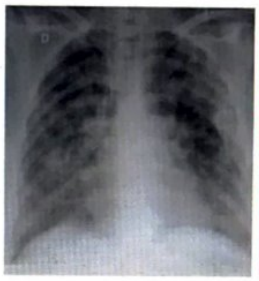
Alveolar interstitial space (exudative fluid) → Fibrin deposition/necrotic cells → Hyaline membrane → Stiff lung



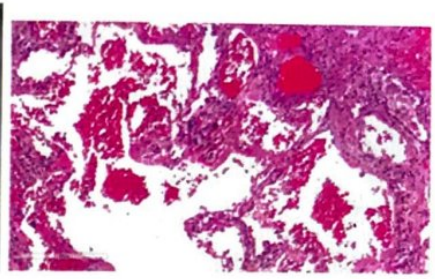
Clinical Features 00:12:22

- Respiratory Distress
- Hypoxemia
- Inflammatory pulmonary edema (exudative fluid)

Diagnosis



White out lung



Hyaline membrane

- CXR: white out lung
- Microscopic appearance
  - Diffuse alveolar damage
  - Hyaline membrane (fibrin + dead epithelial cells)
- PCWP: < 18 mmHg (NCPE)
- Macrophages → TGF β → fibrin

Treatment

- O_2 inhalation → Refractory
- Treat the Primary cause
- PEEP (Positive End Expiratory pressure)
- Steroids

67 LUNG TUMORS

BRONCHOGENIC CARCINOMA

RISK FACTORS

00:00:27

- Smoking
  - Female >> male
  - CYP1A1 polymorphism → ↑ risk of cancer
- Industrial Hazards: Asbestos
  - 15-20yrs exposure: bronchogenic carcinoma
  - 40yrs exposure: malignant mesothelioma
- Air pollution
- Genetic risk factors
  - p53/p16 mutation → ↑ risk for squamous cell carcinoma
  - Rb/myc mutation → ↑ risk for small cell lung cancer
  - EgFR/KRAS mutation → ↑ risk for adenocarcinoma of lung

Important Information

- Asbestos → atypical adenomatous hyperplasia → adenocarcinoma in-situ → MIA

Clinical features

- Cough
- Weight loss
- Dyspnea
- Hemoptysis
- Pleuritic pain
- Atelectasis
- Obstructive pneumonia
- RLN involvement → Hoarseness of voice
- Shoulder pain → involvement of C8/T1/T2
- Pancoast tumor: Tumor in apical lobe → compression of sympathetic plexus → Horner syndrome
  - Miosis
  - Anhydrosis
  - Ptosis
  - Enopthalmos
  - Loss of ciliospinal reflex

Diagnosis

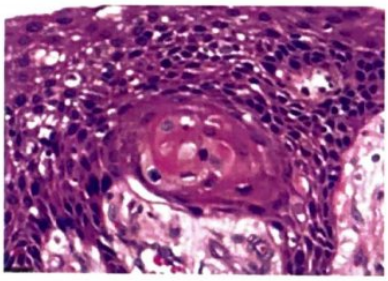
- Sputum examination → less sensitive
- PET-CT scan → Used to find extent of disease
- Bronchoscopy + Biopsy → IOC
  - HPE
  - Immunohistochemistry
  - Molecular testing

WHO 2015 Classification (Epithelial Tumors)

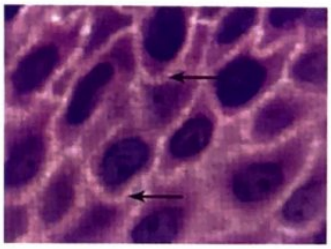
- Squamous Cell Cancer: keratinizing/non-keratinizing/Basaloid
- Adenocarcinoma: Lepidic/Acinar/Papillary/Solid
- Large Cell Cancer
- Neuroendocrine Carcinoma: DIPNECH/carcinoid tumor
  - Small cell/large cell carcinoma
  - DIPNECH: Diffuse Idiopathic Pulmonary Neuro-endocrine Cell Hyperplasia
- Mixed Carcinoma: Adenosquamous Carcinoma, combined small cell Carcinoma
- Others: Sarcomatoid/giant cell cancer/spindle cell Cancer
- NUT Carcinoma
  - $NUTM_1$ Gene → BRD4 (Chromosome 19p) – 70%
  - Chromosome 15q14 → BRD3 (Chromosome 9q) – 6%
  - Unknown gene - 24%

SQUAMOUS CELL CARCINOMA

00:19:19



Keratin pearl

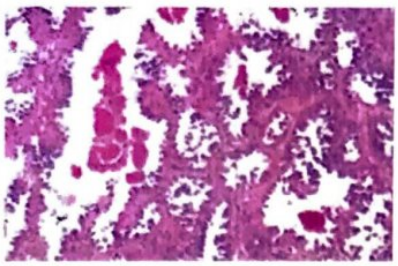


Intercellular keratin bridge

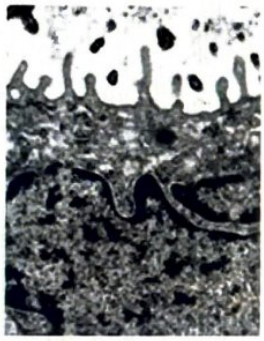
- IHC: p63/p40 +ve
- Seen in smokers
- Better prognosis (early detection due to larger proximal

airway involvement)
- Development of local cavitation
- Lipoid pneumonia
- Hypercalcemia (paraneoplastic syndrome)

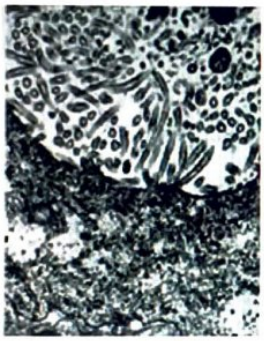
ADENOCARCINOMA



- Presence of gland & mucin
- IHC markers: TTF-1, NAPSIN-A
- Overall MC Lung cancer globally
- Non-smokers can also be affected
- Mucin glands → Thrombophlebitis
- Clubbing (hypertrophic pulmonary osteo-arthropathy)
- Smaller/periphery airways are involved
- Origin: Bronchiole-alveolar cell



Adenocarcinoma

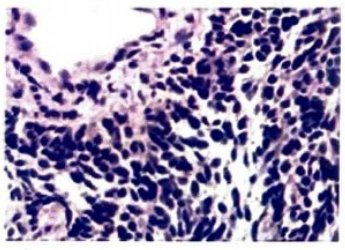


Malignant mesothelioma

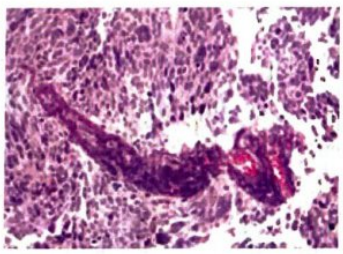
- On Electron microscopy
  - Adenocarcinoma has small, non-branching microvilli
  - Malignant has long, slender, branching microvilli

SMALL CELL CARCINOMA

00:28:09



Nuclear molding



Azzopardi effect

- Neuroendocrine carcinoma
- Presence of Neuro-secretory granules seen under electron microscopy
- IHC markers: Synaptophysin/CD-57/BCL-2/Chromogranin
- Involvement of larger airways is seen
- Highly aggressive in nature (poor prognosis)
- Neurosecretory granules → secrete active substances (ACTH → cushing syndrome, calcitonin → hypocalcemia)
- It can also be responsible for causing SVC syndrome

Microscopic appearance

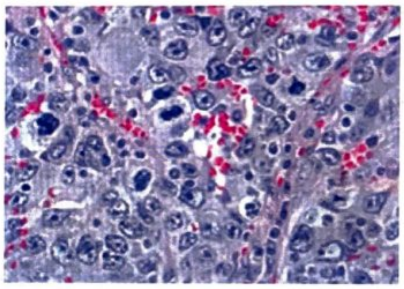
- Cells have small cytoplasm with majority being occupied by the nucleus → cells deform each other → nuclear molding
- Chromatin is finely dispersed → salt & pepper chromatin
- ↑ Mitosis
- Damage to cells → leakage of nuclear contents → staining of vascular endothelial cells (Azzopardi effect)

Important Information

- Small cell lung cancer is associated with Lambert Eaton Syndrome → antibodies produced against pre-synaptic calcium channel

LARGE CELL CANCER

00:34:24



- It is a diagnosis of exclusion
- Paraneoplastic syndrome: cells secrete estrogen → gynecomastia

Metastasis

- MC organ affected in lung cancer: adrenal gland
- MC organ affected in Small cell cancer: CNS

Treatment

- SCLC: Radiation/chemotherapy
- NSCLC: Specific therapy. Examples
  - Squamous cell carcinoma: immune checkpoint inhibitor therapy
  - Adenocarcinoma: Pemetrexed
- Patient with EgFR mutation will have better prognosis than those with K-RAS mutation

Previous Year's Questions

Q. Which is the most common tumor associated with superior vena cave syndrome? (FMGE - Dec - 2017)

A. Lung cancer
B. Lymphoma
C. Metastasis
D. Thyroid cancer

PLEURAL TUMORS

00:39:17

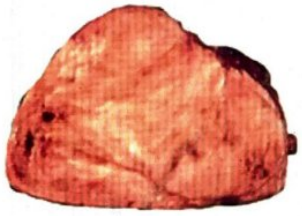
- Secondary tumor (metastasis) >>> primary tumor

Primary tumor	Secondary tumor
• Solitary fibrous tumor • Malignant mesothelioma	• MC cause of metastasis: Lung cancer • 2nd MC cause: Breast cancer • Ipsilateral involvement of pleura to lung/breast cancer

SOLITARY FIBROUS TUMOR

00:41:04

- Aka Benign Mesothelioma
- Asbestos exposure is not a risk factor
- Genetics: Chromosome 12 inversion → NAB-2 STAT 6 fusion gene



Dense fibrous tumor

- Gross appearance: Dense fibrous tumor
- Microscopic appearance: Presence of spindle cells resembling fibroblasts

	SFT	MM
CD34	⊕	⊖
Keratin	⊖	⊕

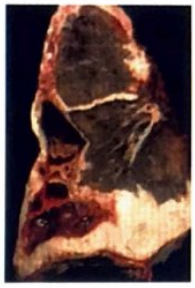
MALIGNANT MESOTHELIOMA

Risk Factors

- Asbestos exposure (Amphibole)
- Incubation period: 25-45yrs
- Radiation
- No association with smoking

Clinical Features

- Age group: 50-60yrs
- Chest pain
- Difficulty in breathing
- Pleural effusion
- Right Lung >>> Left Lung
- Involvement of Lung & Hilar lymph nodes are also seen.



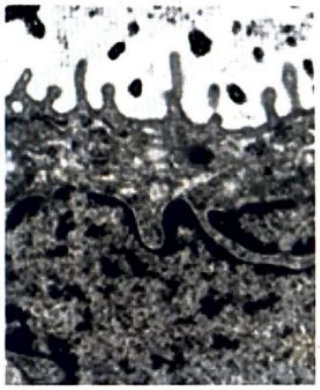
Lung encased by cancer

Variants

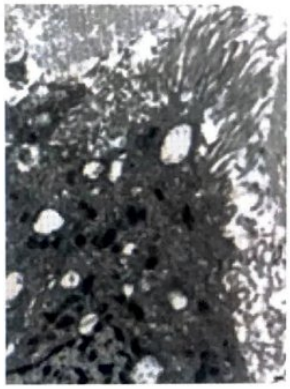
- Epithelioid type (MC)
- Sarcomatoid type
- Mixed / biphasic type

EPITHELIOD TYPE

- Tumor cells → forms papillary & tubular structures
- Resembles adenocarcinoma of lung
- Distinguished from Adenocarcinoma of Lung by Electron microscopy
  - Adenocarcinoma: Short & Non-branching microvilli
  - Mesothelioma: Long, thin, branching microvilli



Adenocarcinoma



Mesothelioma

IHC Markers	Adenocarcinoma	Mesothelioma
Calretinin (Marker of choice)	-	++
WT_1	-	++
CK5/6	-	++
MOC 31	++	-

Important Information

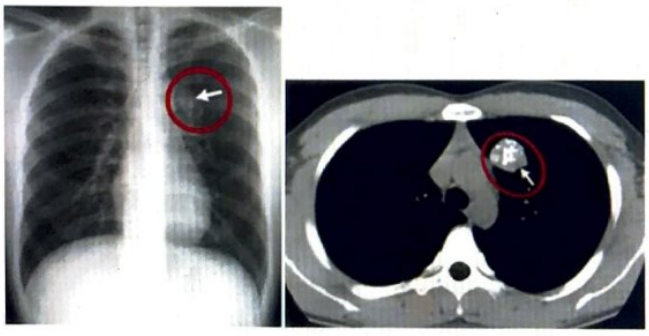
Malignant Mesothelioma

- Deletion of tumor Suppressor genes CDKN2A/INK4a on chromosome 9p
- It can be confirmed by FISH technique

PULMONARY HAMARTOMA

00:56:24

- True Neoplasm
- Nodules of Mesenchymal Tissue/Entrapped Respiratory Epithelium
  - Mesenchymal Tissue
    - → Connective tissue
    - → Fat
    - → Cartilage (predominant)
    - → Smooth muscles
    - → Genetics: t(3;12)
- Radiological finding: Pop-corn calcification
- Treatment: Surgical Excision



Pop-corn calcification

INFLAMMATORY MYOFIBROBLASTIC TUMOR

- Seen in pediatric population
- Genetics: ALK gene activation present on chromosome 2p23
- Gross appearance: Peripheral firm mass calcium deposition

Clinical features

- Fever
- Cough
- Chest pain
- Hemoptysis

Microscopic appearance

- Presence of spindle shaped cells (fibroblasts or myofibroblasts)
- Infiltration of lymphocytes & plasma cells
- Presence of peripheral Fibrosis

CLINICAL QUESTIONS

Q. A 60-year-old man, a heavy smoker, presents for treatment to stop smoking. On physical examination, he is thin and has a red complexion. He has cough with expectoration and a barrel-shaped chest. He has pursed his lips to facilitate his breathing and is sitting leaning forward. A diagnosis of emphysema is made. Which of the following is the most likely histological finding in the lungs?

A. Hypertrophy of smooth muscle of bronchus with proliferation of eosinophils
B. Leakage of protein-rich fluid into alveolar spaces with Diffuse alveolar damage
C. Destruction of alveolar walls with Dilation of air spaces
D. Hyperplasia of bronchial submucosal glands which secretes mucus

Solution

- Emphysema is an example of COPD.
- Due to the destruction of alveolar walls there is a lack of elastic recoil which causes trapping of air in alveoli, and, thus, on expiration obstruction of airflow occurs.
- In COPD, FEV1 is decreased, whereas FVC is normal or increased; therefore, patients with COPD have a decreased FEV1: FVC ratio.

Reference

- Robbins 10/e p 681

78 VASCULITIS

- Inflammation of blood vessels
- Inflammation + Edema (neutrophilic infiltration) → narrowing of lumen → Tissue ischemia and necrosis

LARGE VESSEL VASCULITIS

TEMPORAL ARTERITIS

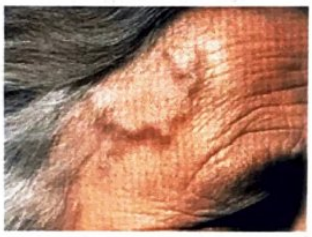
- MC vasculitis is adults (>50yrs)
- T-cell mediated damage → granuloma
- Superficial Temporal artery (terminal branch of ECA) is involved

Clinical features 00:03:13

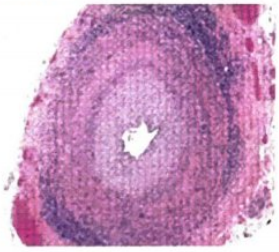
- Headache (MC symptom)
- Jaw claudication (most specific)
- Fever
- Malaise
- Polymyalgia Rheumatica → pain in Shoulder & Pelvic girdle
- Sudden onset blindness

Diagnosis

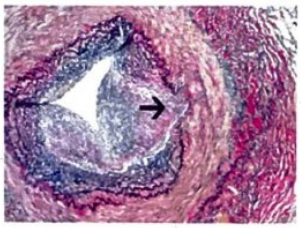
- ↑↑ TLC
- ↑↑ ESR
- Temporal Artery Biopsy
  - Presence of granuloma
  - Internal elastic lamina fragmentation
  - Minimum size of tissue should be at least 1cm
  - Absence of granuloma does not rule out the diagnosis → patchy involvement



Inflamed temporal artery



Reduction in lumen size



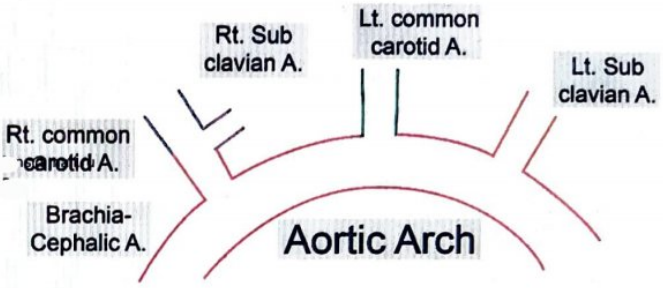
Fragmentation of internal elastic lamina (Van Gieson stain)

Treatment

- Steroids

TAKAYASU ARTERITIS 00:08:53

- Age of presentation: < 50yrs
- Involvement of aorta & subclavian vessel



- Aka aortic arch syndrome/pulseless disease/non-specific aorto-arteritis
- Involvement of Pulmonary Artery → PAH, cough & dyspnea
  - Renal Artery → activation of RAAS → Reno-vascular HTN
  - Cardiac vessels → MI

Important Information

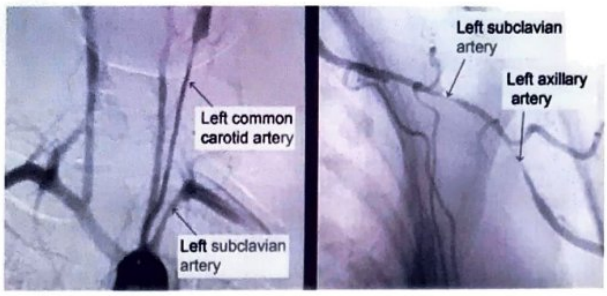
Reno-vascular HTN

- MC cause for young adults in India: Takayasu arteritis
- MC cause for young adults in USA: Fibromuscular dysplasia

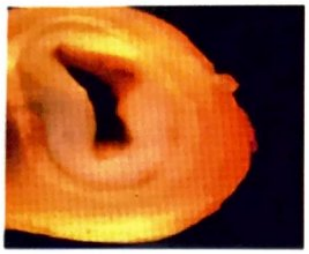
Clinical features

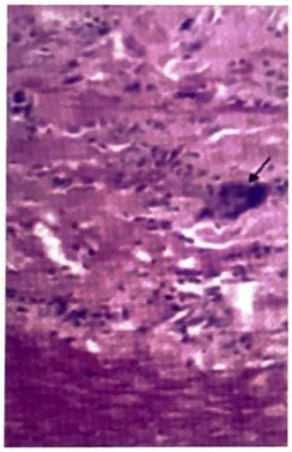
- Fever
- Malaise
- Feeble pulse
- ICA involvement → sudden onset of blindness

Diagnosis



Narrowing of lumen





Giant cells

- Angiogram → extreme Narrowing of affected vessel
- Granulomatous inflammation → giant cells

Treatment

- Steroids
- Poor prognosis

MEDIUM SIZED VESSEL VASCULITIS

00:16:12

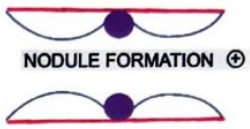
POLYARTERITIS NODOSA

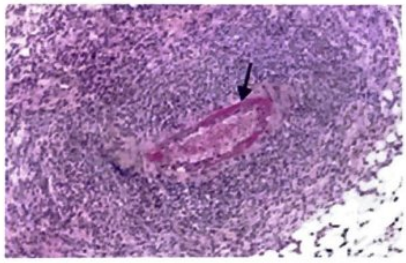
- Seen in Young Adults
- Presence of Immune complex formation → type 3 HR → Fibrinoid necrosis
- Associated with hepatitis-B infection → HBSAg + Ab → IC → organs

Clinical features

- Lungs are spared
- Kidney: Aneurysm/inflammation → HTN
- Small blood vessels are not affected → no glomerulonephritis
- GIT → abdominal pain, melena
- Skin → rash, ulcerative lesion
- Nerve → mononeuritis multiplex (MC systemic cause is DM)
- Joints → pain, difficulty in movement

Diagnosis





Fibrinoid necrosis

- Biopsy
  - Early Phase → Fibrinoid necrosis, Transmural inflammation
  - Late Phase → Fibrosis
  - Presence of nodule formation → string of pearl appearance
- MC cause of death → Renal Failure

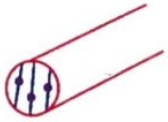
Previous Year's Questions

Q. ANCA negative vasculitis amongst the following is? (JIPMER Nov 2017)

A. Wegner granulomatosis
B. Churg Strauss syndrome
C. Polyarteritis nodosa
D. Microscopic polyangiitis

BUERGER'S DISEASE

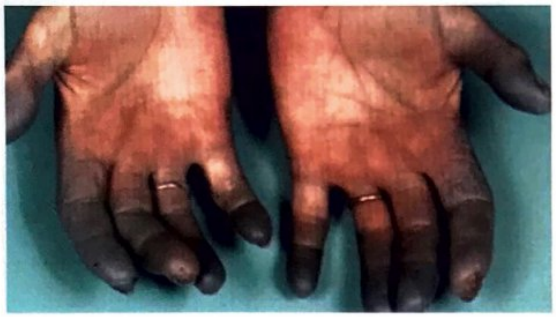
00:24:37



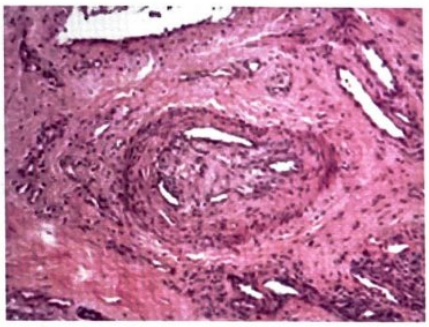
Thromboangitis obliterans

- Aka Thrombangitis Obliterans
- Seen in young male → smoker

- Genetics: HLAB 5/A9 → ↑↑ risk of Buerger's disease; HLAB12 → Protective
- Involvement of Arteries > veins > Nerves
  - Lymphatics not involved
  - Arteries involved: tibial artery, radial artery



Raynaud's phenomenon
- Tibial Artery involvement
  - ↓ Blood → Raynaud's phenomenon
  - Instep claudication



Rest pain (nerves are affected)

Microscopic appearance
- Micro-abscess formation
- Granulomatous inflammation

Treatment
- Quit smoking
- Vasodilator therapy
- Surgery

KAWASAKI DISEASE

00:33:12

- Kids < 4yrs age group
- Aka mucocutaneous LN syndrome

Clinical features

Fever +	• Conjunctivitis (non-exudative) • Rash • Edema of hands and feet • Adenopathy (unilateral; cervical) • Mucosal involvement (ulcer, strawberry tongue)

Pathophysiology

H/O viral infection
↓
T cell activation/anti-EC ab +
↓
Clinical Features

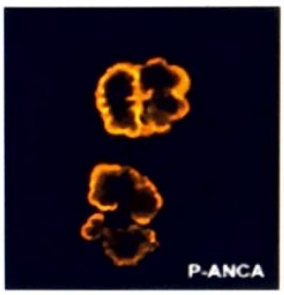
- Coronary artery vasculitis → myocardial infarction
- Diagnosis: ↑ P/C → ↑ risk of MI
- Treatment: IV Ig + aspirin

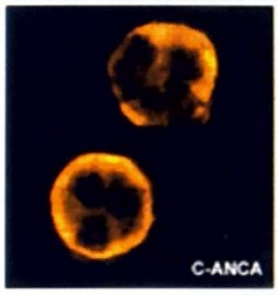
SMALL VESSEL VASCULITIS

00:39:13

ANCA: Anti-neutrophilic Cytoplasmic Ab

MPO [Ag]	Proteinase-3
↓	↓
P-ANCA	C-ANCA
↓	↓
Now k/a MPO-ANCA	Now k/a PR-3 ANCA





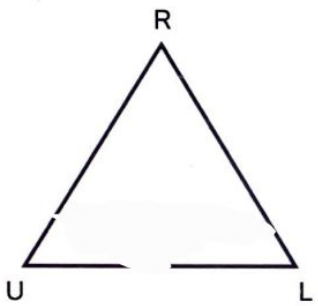
Conditions associated
- microscopic polyangiitis
- Churg-strauss syndrome
- Good pasture syndrome
- Ulcerative colitis (against nuclear envelop Ag)

Conditions associated
- Wegener granulomatosis

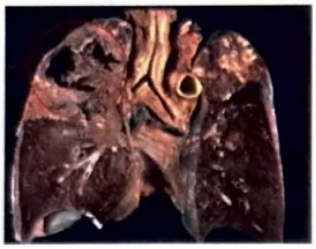
WEGENER GRANULOMATOSIS / GRANULOMATOSIS WITH POLYANGIITIS

- Characterized by presence of Necrotizing granuloma in URT, Lungs

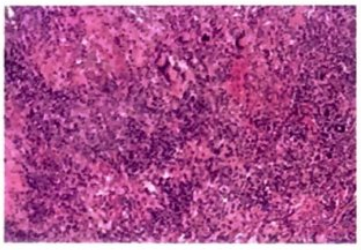
Rule of organ involvement



- Renal: Focal GN → Crescentic GN (RPGN) → renal failure
- URT
  - E - Otitis media
  - N - Septal perforation/saddle nose
  - T - strawberry gums/Sub-glottic Stenosis
- Lungs
  - Pneumonitis
  - Cavitatory lesions
  - Cough
  - Hemoptysis



Cavitatory lesion



Granulomatous inflammation

Diagnosis
- C-ANCA/PR-3 ANCA
- Biopsy
  - In kidney: Crescentic GN (RPGN)
  - In URT: necrotizing granuloma

Treatment
- Immunosuppressive therapy
- Cause of Death → Renal Failure

MICROSCOPIC POLYANGIITIS 00:52:52
- Neutrophilic inflammation → capillaries/venules (MC)/arterioles
- Aka hypersensitivity vasculitis / leukocytoclastic vasculitis
- Fragmented neutrophils are present around affected vessel

	PAN	MPA
small vessels	⊖	⊕
Lungs	⊖	⊕
Kidneys	⊕	⊕
Necrotizing gn	⊖	⊕
P-ANCA / MPO -ANCA	⊖	⊕

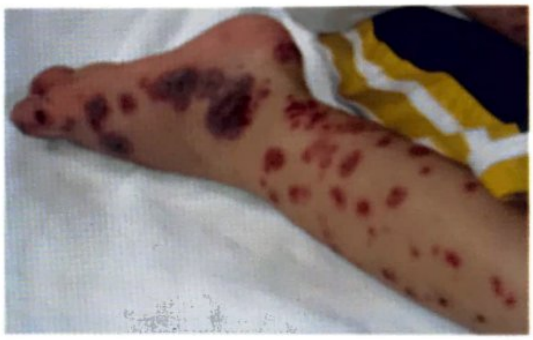
Microscopic appearance
- MPA: Same stage of inflammation
- PAN: early & late stage of inflammation co-exist
- No granuloma formation

Treatment
- Immunosuppressive therapy

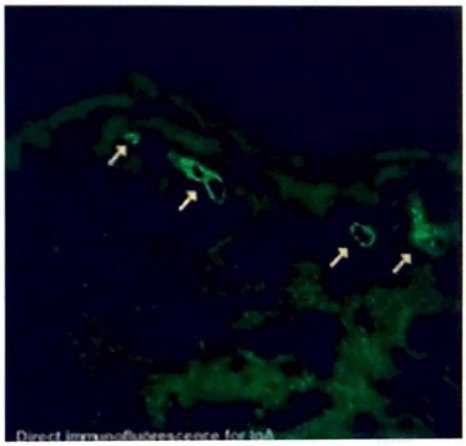
HENOCH-SCHONLEIN PURPURA
- MC vasculitis in pediatric age group
- Type 3 HR
- H/O URTI → ↑↑ IgA

Clinical features
- Kidney: Hematuria (microscopic)
- Skin
  - Rash on extensor surface, buttocks
  - Vasculitis → resembles purpura
  - P/C → Normal (non-thrombocytopenic purpura/anaphylactoid purpura)
- GIT: Abdominal pain
- Joints: joint pain/swelling

Diagnosis
- Normal platelet count
- Normal complement levels
- Skin biopsy → IgA Ab deposition at dermal papillae



Purpuric lesion

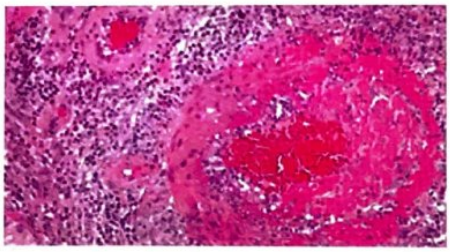


IgA Ab at dermal papillae

ALLERGIC GRANULOMATOSIS WITH POLYANGITIS

01:05:12

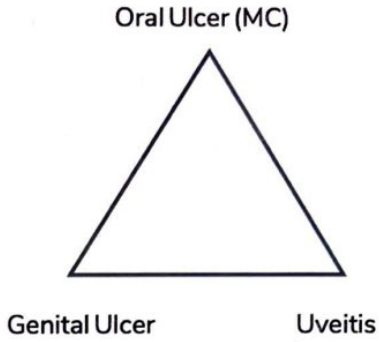
- Aka Churg-Strauss Syndrome
- Necrotizing Granulomatous inflammation → MPO-ANCA ⊕
- ↑↑ Eosinophils → Asthma/Allergic Rhinitis/Atopy
- Blood vessel inflammation
  - GIT: abdominal pain/discomfort
  - Skin: Rash
  - Heart: Cardiomyopathy (cause of death)



Large no of eosinophils

BEHCET'S DISEASE

- Aka Oculo-oral genital Syndrome
- Small vessel vasculitis
- TH_{17} → neutrophilic infiltration
- Associated with HLA B-5/B-51
- Presence of anti-EC Ab present → α-enolase
- Diagnosis by pathergy test



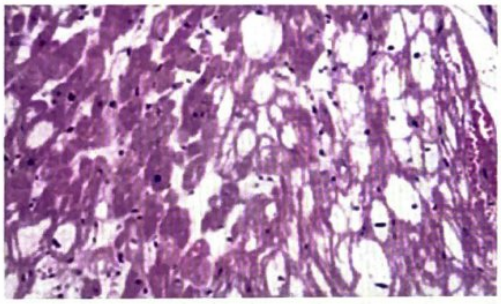
79 ISCHEMIC HEART DISEASE

- ↓ ATP → immediate change
- Loss of contractibility → < 2min
- ATP becomes
  - 50% of normal value within 10min
  - 10% of normal value within 40min
- Irreversible injury → 20min

Types of Ischemic heart disease

- Angina
  - Stable angina: fixed CA obstruction, symptomatic only during physical activity
  - Prinzmetal angina: coronary vasospasm → symptomatic
  - Unstable /pre-infarction angina: rupture of atherosclerotic plaque → MI
- MI
- Chronic IHD (HF)
- SCD → death within 1hr of cardiac symptoms onset

MYOCARDIAL INFARCTION



- Irreversible cardiac tissue injury
- Sub-lethal ischemia → associated with myocyte vacuolization
- Poor contractility (but myocytes are viable)

Ulceration/rupture/hemorrhage of atherosclerotic plaque
↓
↓ Blood supply
↓
Infarction

Subtypes of infarction

- Sub-endocardial MI
- Transmural MI
- Multifocal MI

Clinical features 00:05:29

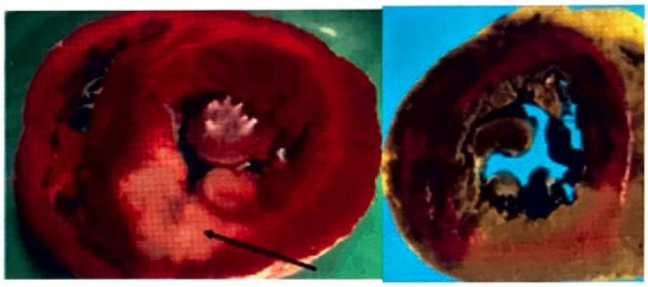
- Constricting/squeezing type of chest pain
- Levine Sign: Clenched Fist on chest
- MC type of MI: Anterior wall MI

Diagnosis

- ECG
- Blood sample
  - 1st enzyme to be elevated → HFABP
  - Myoglobin
  - CK-MB
  - Cardiac troponin
    - → Troponin T
    - → Troponin I → most sensitive/specific, marker of choice for re-infarction

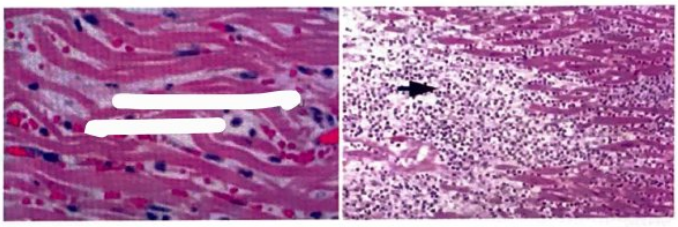
LDH

- Last enzyme to increase
- Normal: LDH1 (Heart) <<< LDH2 (blood)
- Flipping of LDH: LDH1 (Heart) >>> LDH2 (blood) → MI
- Reacts with Triphenyl Tetrazolium Chloride → brick red color



Biopsy

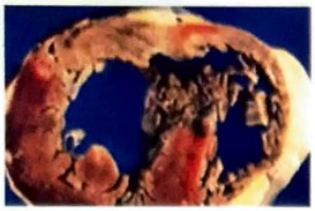
Refer Table 79.1



Waviness | Coagulative necrosis

Previous Year's Questions

Q. Gross section of myocardium following myocardial infarction is shown. What could be the duration following MI? (JIPMER Nov 2018)

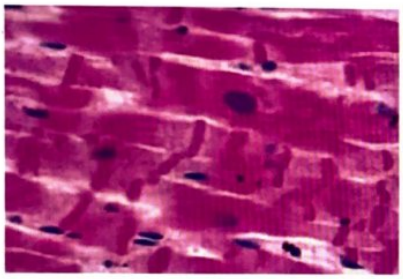


A. Immediate MI
B. 2 days
C. 2 weeks
D. Postmortem artefact

REPERFUSION INJURY

00:15:24

- Thrombolysis → influx of WBC/Free radicals/Ca^{2+}
- Patient worsens after thrombolytic therapy
- Viable myocyte exposure to calcium → Contraction Bands



Contraction bands in reperfusion injury

COMPLICATIONS

- Arrhythmias
- ↓HR
- Ventricular fibrillation → SCD
  - Death can occur within 1hr
- Cardiac failure

Cardiac rupture syndrome

- Occurs within intermediate time between loss of strength (↓ blood supply) & collagen deposition
- Seen after 3-7 days after MI
- Affects anterior wall of LV/Inter ventricular septum/mitral valve
- MC cardiac rupture: Ventricular wall rupture

Autoimmune pericarditis

- Aka Dressler syndrome
- Neo Antigens exposure → after 2-3 weeks after MI
- Neo Ag → Immune system activation → pericarditis
- Presents with chest pain (troponins differentiates it from reinfarction)

Ventricular Aneurysm

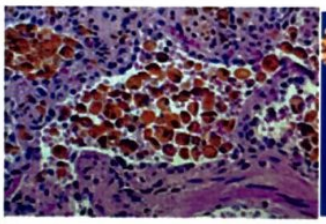
- Ventricular wall weakness → aneurysm
- Likely to form clot → thrombo-embolic manifestations

Chronic Ischemic Heart Disease

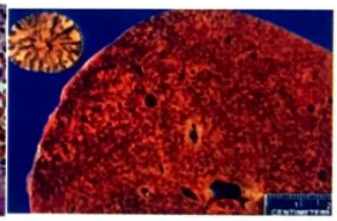
00:22:38

LVF	RVF

• Lungs: MC organ affected
  ○ Acute → dyspnea, PE
  ○ Chronic → "heart-failure" cells
• Kidney → RAAS activation, Azotemia
• CNS → Ischemic encephalopathy
	• MC cause: LVF
	• Cor pulmonale
	• Congestive hepatomegaly → nutmeg liver/cardiac cirrhosis
	• Congestive splenomegaly → GG body



Heart failure cells



Nutmeg liver

Table 79.1

< 4hrs	• "waviness" of fibers → caused by intercellular edema
4-12hrs	• coagulative necrosis starts
12-24hrs	• coagulative necrosis + neutrophilic infiltration, dark mottling is seen
1-3 days	• Brisk neutrophilic infiltration; coagulative necrosis → Infarct (yellow border)
3-7days	• Macrophage infiltration → Hyperemic border
7-10 days	• Deposition of Granulation tissue • Collagen deposition • Max yellow tan or red-brown appearance
4-6 weeks	• ↑ Collagen deposition • Scar formation → white

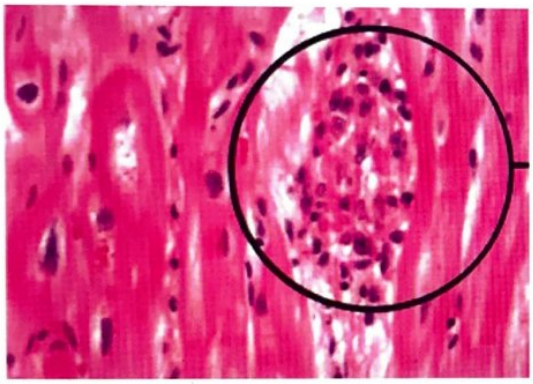
80 RHEUMATIC FEVER & INFECTIVE ENDOCARDITIS

RHEUMATIC FEVER

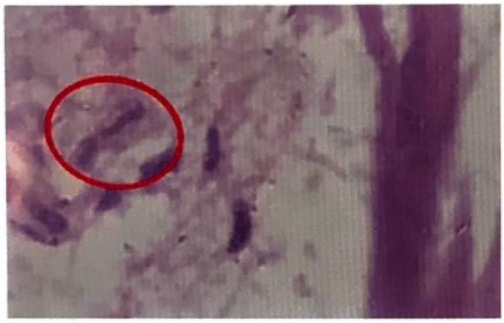
- H/O Group A β Hemolytic Streptococcus infection → Sore throat/pharyngitis
- Seen in 3% of children
- Associated with exposure to 'M' protein → immune system activation → Ab formation
- 'M' protein is similar to GP present in joints/heart/CNS/Skin
- Example of type 2 HR

Pancarditis

- Pericarditis → Bread & Butter Pericarditis (Serofibrinous exudate)
- Myocarditis → cardiac failure
- Presence of Aschoff body is seen around blood vessels
- Aschoff body: fibrinoid necrosis surrounded by eosinophilic collagen, macrophages, plasma cells
- Plump macrophages → Anitschkow cell



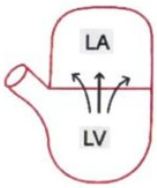
Aschoff body



Anitschkow cell

Important Information

- Anitschkow Cell can also be seen in
  - H/O Chemotherapy
  - Aphthous Stomatitis
  - Iron Deficiency Anemia



- Endocarditis: involvement of MV >> AV >> TV >> PV
- Acute: MR → McCallum plaque (located in left atrium; seen with MR)
- Chronic: MS → Button-hole/fish mouth stenosis
- Deposition of platelet/fibrin on apposed mitral valve → cardiac vegetation
- Small, sterile, firm, present along line of closure
- Marantic endocarditis: Small/sterile/firm/LOC/Emboli
  - Associated with AML-M_3/Carcinoma pancreas

Diagnosis

- Throat culture → ↑↑ anti-streptococcal Ab (Evidence of group A streptococcal infection)
- Major Criteria
  - Carditis → clinical/sub-clinical
  - Arthritis → migratory polyarthritis/mono-arthritis/polyarthralgia
  - Chorea
  - Erythema marginatum
  - Subcutaneous nodules
- Minor Criteria
  - Fever
  - Arthralgia (major criteria in high prevalence population)
  - ↑ESR (>30mm in 1hr)
  - ↑PR Interval (can be considered only when carditis is absent clinical/subclnical)
  - ↑CRP
- Initial ARF: 2 major or 1 major & 2 minor

- Recurrent ARF: 2 major or 1 major & 2 minor or 3 minor

Previous Year's Questions

Q. A 30-year-old male presented with severe dyspnea. His investigations showed mitral stenosis with left atrial enlargement. The histopathology report from his mitral valve is shown below. What is the likely diagnosis of these patients? (AIIMS Nov 2017)

A. Sarcoidosis
B. Fungal granuloma
C. Tuberculous
D. Rheumatic Heart disease

INFECTIVE ENDOCARDITIS

00:16:53

Normal individuals

- Normal Endothelial Lining – anti thrombotic in nature
- Temporary Bacteremia
- Activity of Immune System

Risk Factors

- Damage to Endothelial Lining → RHD/Congenital heart defect/artificial valve
- Prolonged bacterial Presence → Septicemia
- Immunosuppression → DM, Steroids

Acute IE

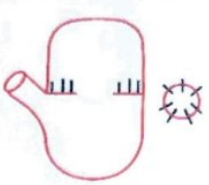
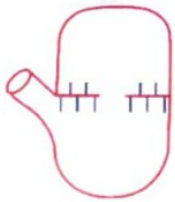
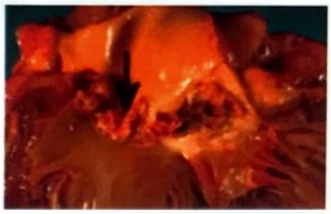
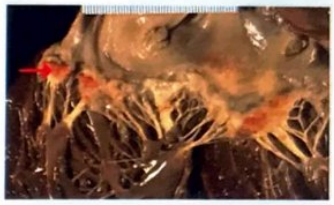
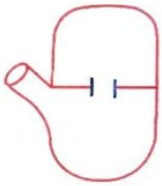
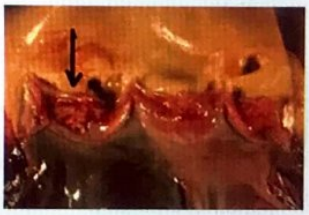
- Causative organism: staph aureus/streptococcus
- Nosocomial infection → Staphylococcus Aureus
- Damage to previously healthy valve

Sub-Acute IE

- Causative organism: Streptococcus viridians
- Previously damaged valve → infection by less virulent organism
- IV drug abusers → Staph aureus (TV affected)
- Valve surgery
  - < 2 months: staph epidermidis
  - 2 months: streptococcus
- HACEK bacteria → haemophilius/actinobacter/cardiobacterium/eikenella/kingella species

Clinical Features

- Fever
- Retinal Hemorrhage → Roth Spots
- Osler nodes → painful lesion in pulp of digits
- Janeway lesion → painless lesions in palm
- Murmurs (Changes from valve to valve) → characteristic

Infective endocarditis	Libman sack endocarditis (SLE)
	
• Large/bulky vegetation • non-sterile • Embolization can occur • Ring abscess is seen	• Lower surface is affected more • Small/sterile • No embolization
	
RHD	**NBTE (Marantic endocarditis)**
	
• Small/Sterile • Present along line of closure • No embolization	• Small/Sterile • Present along line of closure • High risk of embolization • Associated with AML-M3, Pancreatic cancer
	

Diagnosis by Modified Duke's Criteria

- Blood Culture → 1hr apart, 3 different sites
- Echocardiography

Previous Year's Questions

Q. Irregular, bulky and friable vegetation in cardiac valve is a finding of which of the following disorders?
(NEET Jan 2020)

A. Infective endocarditis
B. Rheumatic endocarditis
C. Libman sack endocarditis
D. Nonbacterial endocarditis

81 CARDIAC TUMORS

- Primary cardiac tumors
- Secondary cardiac tumors
  - Most common
  - MC metastasis: Bronchogenic carcinoma
  - Associated with involvement of Pericardium

	Malignant	Benign
In Adult	Angiosarcoma	Myxoma
In children	Rhabdomyosarcoma	Rhabdomyoma

MYXOMA

00:02:36

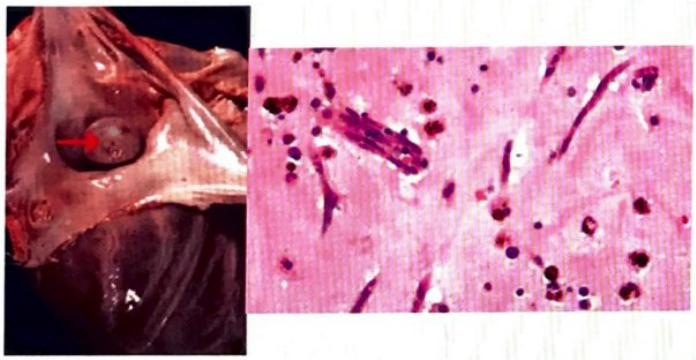
- MC primary benign cardiac tumor seen in adult
- Site of Origin
  - Mesenchymal stem cells
  - Atrium (LA >> RA): Fossa ovalis

Clinical features

- On atrial contraction, the pedunculated mass hits the surface of the valve → tumor plop sound
- Ball valve mechanism of obstruction
- IL-6: Causes weight loss, fever
- Embolism

Microscopic finding

- Lepidic cells in acidic myxoid matrix



Types

- Sporadic: Single, MC (90%)
- Familial: Bilateral (10%)
  - Associated with Carney syndrome

Important Information

Carney syndrome Triad

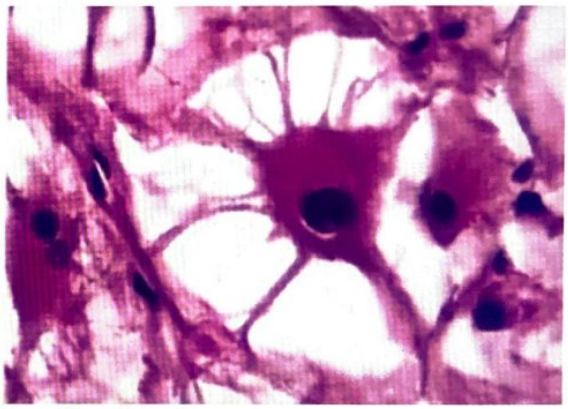
- Myxoma (cardiac & extra-cardiac site)
- Skin pigmentation
- Endocrine over-activity

- Other Associations
  - Mccune Albright syndrome ($GNAS_1$ gene mutation)
  - $PRKAR_1$ gene mutation

RHABDOMYOMA

00:07:52

- MC primary cardiac benign tumor in children
- Site of Origin: ventricles (RV = LV)
- Associated with TSC_1 & TSC_2 genes mutation
- Microscopic examination: Spider cells are seen (contains glycogen)



Spider Cells

Previous Year's Questions

Q. Most common tumor in a female diagnosed with tuberous sclerosis. (JIPMER 2018)

A. Rhabdomyosarcoma
B. Angiomyolipoma
C. Pulmonary lymphangio-leiomyomatosis
D. Optic Glioma

CLINICAL QUESTIONS

A 70-year-old man Rohan with advanced visceral cancer dies of extensive myocardial infarction. Autopsy also reveals sterile non-destructive vegetations along the mitral leaflet edges. The pathogenesis of this patient's vegetations is most similar to that of:

A. Hypercalcemia of malignancy
B. Distant metastases
C. Trousseau syndrome
D. Raynaud's phenomenon

Solution:

- The pathogenesis of non-bacterial thrombotic endocarditis (NBTE) often involves a condition of hypercoagulability that is the result of the procoagulant effects of the circulating cancer products;
- The resulting heart valve vegetation can also be referred to as endocarditis marantic.
- The pathophysiology of NBTE is similar to that of Trousseau's syndrome (migratory thrombophlebitis), which can also be induced by disseminated cancers such as mucinous adenocarcinoma of the pancreas and adenocarcinoma of the lungs, possibly related to the procoagulant effect of circulating mucin.
- Cancer metastases in the heart usually affect the pericardium or myocardium.
- Valve metastases are less common and would likely have shown invasive features on histological examination.

Reference:

- ***Robbins 10/e p564***