HARRISON

EDITION 22nd

PULMONOLOGY, GENETICS

Respiratory Medicine

Approach To Respiratory System	Completed
Diagnostics In Respiratory Medicine	Completed
Disturbances Of Respiratory Function	Completed
Asthma	Completed
Hypersensitivity Pneumonitis	Completed
COPD	Completed
Sleep Related Disorders	Completed
Bronchiectasis	Completed
Disorder Of Pleura	Completed
Interstitial Lung Diseases	Completed
Occupational Lung Diseases	Completed

Approach to Respiratory System

Cardinal Symptoms

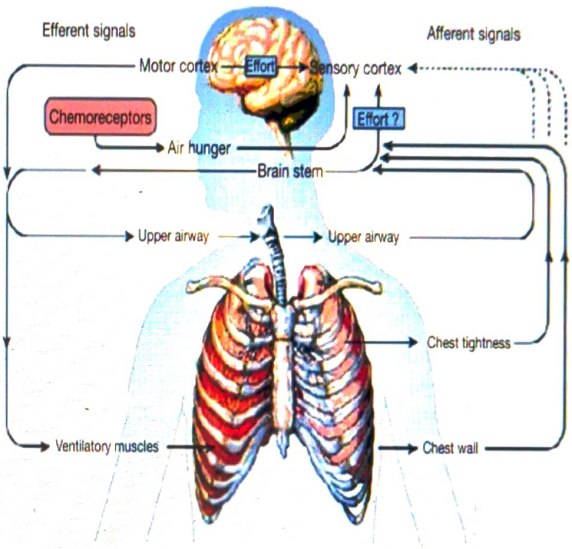
- Dyspnea
- Cough
- Sputum
- Hemoptysis
- Wheeze
- Chest Pain

TABLE 295-1 Categories of Respiratory Disease

CATEGORY	EXAMPLES
Obstructive pathophysiology—airway disease	Asthma Chronic obstructive pulmonary disease (COPD) Bronchiectasis Bronchiolitis
Restrictive pathophysiology—parenchymal disease	Idiopathic pulmonary fibrosis (IPF) Asbestosis Desquamative interstitial pneumonitis (DIP) Sarcoidosis
Restrictive pathophysiology—neuromuscular weakness	Amyotrophic lateral sclerosis (ALS) Guillain-Barré syndrome Myasthenia gravis
Restrictive pathophysiology—chest wall/pleural disease	Kyphoscoliosis Ankylosing spondylitis Chronic pleural effusions
Pulmonary vascular disease	Pulmonary embolism Pulmonary arterial hypertension (PAH) Pulmonary venoocclusive disease Vasculitis
Malignancy	Bronchogenic carcinoma (non-small-cell and small-cell lung cancer) Metastatic disease
Infectious diseases	Pneumonia Bronchitis Tracheitis

Dyspnea

- Sensation of dyspnea is an amalgam of two components.
  - Sensory input to the cerebral cortex
    - information from specialized receptors, predominantly mechanoreceptors, at various sites in the respiratory apparatus (predominantly the upper airways) and face
  - Perception of the sensation,
    - rests heavily on the interpretation of information
    - depends greatly on the psychological makeup of the person



Dyspnea

- Asthmatic often interprets breathlessness in terms of "tightness in the chest."
- The patient with COPD
  - c/o inability to take a deep, satisfying breath.
  - often less severe breathlessness than would be expected from the degree of airway obstruction,
  - possibly reflecting adaptation, either to the chronic obstructive airway disease or to CO_2 retention
- Breathing discomfort at rest that decreases with activity
  - anxiety or other psychological issues are the cause
  - Highly unlikely due to a cardiopulmonary abnormality

Dyspnea

TABLE 27-3 Common Causes of Acute and Chronic Dyspnea[a]

Acute
Pulmonary edema
Asthma
Injury to chest wall and intrathoracic structures
Spontaneous pneumothorax
Pulmonary embolism
Pneumonia
Adult respiratory distress syndrome
Pleural effusion
Pulmonary hemorrhage
Foreign body aspiration
Vocal cord dysfunction
Chronic, progressive
Chronic obstructive pulmonary disease
Left ventricular failure
Diffuse interstitial fibrosis
Asthma
Pleural effusions
Pulmonary thromboembolic disease
Pulmonary vascular disease
Psychogenic dyspnea
Anemia, severe
Postintubation tracheal stenosis
Hypersensitivity disorders

Positional Forms of Breathlessness

- **Orthopnea:**
  - Hallmark of pulmonary congestion (decreases compliance).
  - The decrease in compliance on lying flat is attributable to the fact that more of the lung is located at or below the level of the heart
- Some patients with chronic lung disease or asthma are also intolerant of lying flat.
  - attributed to the mechanical disadvantage in the recumbent position.

Positional Forms of Breathlessness

- **Platypnea**
  - Due to gravity, increased blood flow worsens right-to-left shunting of blood through arteriovenous malformations at the lung bases; it may be accompanied by *orthodeoxia*
- **Trepopnea:**
  - patients with asymmetric lung disease may experience *trepopnea*—
  - dyspnea when the affected side of the chest is in the dependent position, promoting ventilation–perfusion mismatch and resultant hypoxemia.

PND

- Episode of paroxysmal nocturnal dyspnea (PND), the patient is aroused from sleep, gasping for air, and must sit up or stand to catch his or her breath; sweating may be profuse.

- Attacks occasionally recur several times a night, forcing the patient to sleep upright in a chair.

- Precipitous failure of the LV
  - Pulmonary hypervolemia caused by a surge in systemic venous return.
  - Mobilization of peripheral edema from the periphery
  - Acute increase in pulmonary blood volume increases pulmonary capillary pressures, thereby promoting pulmonary edema, while the surge in venous return imposes an additional burden on the left ventricle.

Cardiac Asthma

- Asthmatic wheezes, often audible in patients with pulmonary congestion, have given rise to the term *Cardiac asthma.*

- Wheezes are a manifestation of tracheobronchial edema and often are accompanied by overt signs of pulmonary edema.

- **Occurs due to:-**

1) Reduction in the lumen of the airways and thickening of bronchial walls by edema
2) High intrathoracic pressures, which are required to overcome the obstruction during expiration, tend to narrow the airways even further.

Cough

- Explosive expiration that protects the lungs against aspiration and promotes the movement of secretions and other airway constituents upward toward the mouth.

- Critical element in the self-clearing and protective mechanisms of the lungs—a reflex act that usually, but not invariably, arises from stimulation of the bronchial mucosa somewhere between the larynx and the second- order bronchi.

- On rare occasions the cause is remote: impacted cerumen in the external auditory canal or an inflammatory process of the pleura

Cough with Sputum

- A cough that is productive of purulent sputum is generally a reliable indication of infection in the tracheobronchial tree or lungs.
- Rust-colored sputum, was previously seen often in pneumococcal pneumonia; it is less commonly seen today due to the widespread use of antibiotics.
- The classic description of sputum in *Klebsiella* pneumonia is a resemblance to currant jelly
- Purulent sputum with a foul odor usually indicates an anaerobic infection, commonly due to streptococci or *Bacteroides* in a lung abscess.

Cough with Sputum

- Sputum that is mucoid may be a consequence of any long-standing bronchial irritant.
- Copious sputum production *(bronchorrhea)* may be a sign of adenocarcinoma in situ (AIS) or minimally invasive adenocarcinoma (MIA), previously known as bronchoalveolar carcinoma.

Chronic Cough

- Defined as lasting longer than 8 weeks
- Most common causes of chronic cough and sputum are postnasal drip, gastroesophageal reflux disease (GERD), and asthma
- In patients treated with angiotensin-converting enzyme (ACE) inhibitors, the drug is very often the cause of a chronic cough

Hemoptysis

- The coughing up of blood is termed hemoptysis.
- Material and amount produced varies from mere blood streaking of expectorated sputum to massive volumes of pure blood

- **Massive Hemoptysis:-**

Previously defined as a specific volume of expectorated blood within a particular period of time.

- ranged quite widely from **200 to 1,000 mL/ 24 h**
- ≥500 mL of expectorated blood over a 24 hour period or bleeding at a rate ≥100 mL/hour.

Massive Hemoptysis

- However, approximating the amount of hemoptysis is challenging, and frequently over- or underestimated.

- Important additional clinical factors
  - riskness of bleeding,
  - ability of a patient to maintain a patent airway and expectorate blood,
  - patient's underlying physiological reserve
  - the swiftness of available therapeutic options

- **Any degree of hemoptysis causing clinical consequences such as respiratory failure from airway obstruction or hypotension is considered life-threatening hemoptysis.**

Davidson K, Shojaee S. Managing Massive Hemoptysis. Contemporary Reviews in Critical Care Medicine. CHEST 2019

Etiologies

Table 1. Differential Diagnosis of Hemoptysis

Primary vascular source	Pulmonary parenchymal source	Tracheobronchial source
Arteriovenous malformation	Tuberculosis	Bronchiectasis
Pulmonary embolism	Pneumonia	Neoplasm
Elevated pulmonary venous pressure	Lung abscess	Bronchitis
Pulmonary artery rupture	Lung contusion	Bronchoolithiasis
Pseudohemoptysis	Mycetoma ("fungus ball")	Airway trauma
Upper airway source	Idiopathic pulmonary hemosiderosis	Foreign body
Gastrointestinal source	Wegener granulomatosis	**Miscellaneous and rare causes**
Serratia marcescens (gram-negative bacterium that produces a red pigment that may be mistaken for blood)	Lupus pneumonitis	Systemic coagulopathy or thrombolytic agents
Malingering	Goodpasture syndrome	Catamenial hemoptysis (pulmonary endometriosis)

NOTE: *Diagnoses listed in approximate order of frequency.*

Adapted with permission from Weinberger SE, Lipson DA. Cough and hemoptysis. In: Fauci AS, Braunwald E, Kasper DL, et al., eds. Harrison's Principles of Internal Medicine. 17th ed. New York, NY: McGraw-Hill, 2008:227.

- Cryptogenic hemoptysis :
  - without a known cause despite extensive investigation by both CT and bronchoscopy
  - 3- 42% of patients initially presenting with hemoptysis
  - *Smoke-related hemoptysis*

- Recurrent hemoptysis :
  - repeated episodes of hemoptysis following initial treatment with either medical therapy or BAE

Imaging

- X-ray Chest
- HRCT thorax
- CECT thorax
- CT Angiography (Bronchial and Pulmonary)

Imaging – The most important initial study, beyond history and physical examination, for all patients presenting with hemoptysis is a chest radiograph

JACR Journal of the American College of Radiology

APPROPRIATE USE CRITERIA | VOLUME 17, ISSUE 5, SUPPLEMENT , S148-S159, MAY 01, 2020

ACR Appropriateness Criteria® Hemoptysis

Expert Panel on Thoracic Imaging • Kathryn M. Olsen, MD • Shawdi Manouchehr-pour, MD •

Variant 1: Massive (life-threatening) hemoptysis. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
Arteriography bronchial with embolization	Usually Appropriate	☢☢☢☢
CTA chest with IV contrast	Usually Appropriate	☢☢☢
Radiography chest	Usually Appropriate	☢
CT chest with IV contrast	Usually Appropriate	☢☢☢
CT chest without IV contrast	May Be Appropriate	☢☢☢
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢

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ACR Appropriateness Criteria® Hemoptysis

Expert Panel on Thoracic Imaging • Kathryn M. Olsen, MD • Shawdi Manouchehr-pour, MD •

Variant 2. Nonmassive (non–life-threatening) hemoptysis. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
CT chest with IV contrast	Usually Appropriate	☢☢☢
CTA chest with IV contrast	Usually Appropriate	☢☢☢
Radiography chest	Usually Appropriate	☢
Arteriography bronchial with embolization	May Be Appropriate	☢☢☢☢
CT chest without IV contrast	May Be Appropriate	☢☢☢
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢

Chest Pain

- Most characteristic pain associated with the respiratory apparatus is pleural pain.
- Originates in the parietal pleura and endo- thoracic fascia
- Visceral pleura is insensitive to pain.
- Irritation of the diaphragmatic pleura by an inflammatory process either below or above the diaphragm often causes ipsilateral shoulder pain

Pain a/w tracheitis or tracheobronchitis

- Searing pain
- Central chest pain
- Most pronounced after cough.
- Invariably, associated with evidence of upper respiratory infection.
- Cold air may be intolerable.

Pain a/w pulmonary hypertension

- The pain is substernal and is associated with dyspnea
- Usually absent at rest
- Appears during exertion.
- Often mistaken for classic angina

Musculoskeletal pain

- Also aggravated by breathing may be confused with pleuritic pain.
- Often bilateral,
- Generally intensified by changes in body position or flexing the thorax.
- It is rarely severe and incapacitating
- The affected muscles are often tender to gentle pressure.

- Unilateral pain, along the distribution of an intercostal nerve, is characteristic of herpes zoster before the appearance of the skin eruption and is often described as an intense burning sensation.

Cyanosis

- **Cyanosis** refers to a bluish discoloration of the skin that is caused by increased amounts of reduced hemoglobin in the sub-capillary venous plexus.

- Most apparent in the lobes of the ears, the cutaneous surfaces of the lips, and the nail beds.

- In patients with dark skin, the mucus membranes and the retina are important sites to examine for cyanosis.

Cyanosis

- Concentration of reduced hemoglobin in the skin capillaries must reach about **5 g/dL** before cyanosis becomes discernible.

- In severe Anaemia, when hemoglobin concentrations are exceedingly low (on the order of **3–4 g/dL**), an insufficient amount of reduced hemoglobin remains to produce a visible discoloration.

- **Polycythemic patient** develops cyanosis at a higher arterial Oxygen saturation than does the normal individual.

Central Cyanosis
Decreased arterial oxygen saturation
Decreased atmospheric pressure—high altitude
Impaired pulmonary function
Alveolar hypoventilation
Inhomogeneity in pulmonary ventilation and perfusion (perfusion of hypoventilated alveoli)
Impaired oxygen diffusion
Anatomic shunts
Certain types of congenital heart disease
Pulmonary arteriovenous fistulas
Multiple small intrapulmonary shunts
Hemoglobin with low affinity for oxygen
Hemoglobin abnormalities
Methemoglobinemia—hereditary, acquired
Sulfhemoglobinemia—acquired
Carboxyhemoglobinemia (not true cyanosis)
Peripheral Cyanosis
Reduced cardiac output
Cold exposure
Redistribution of blood flow from extremities
Arterial obstruction
Venous obstruction

Cyanosis Due to Abnormal Pigments in Blood

- Methemoglobinemia is an occasional cause of cyanosis.
- Arterial blood examination discloses a normal PO2
- Methemoglobinemia blood is chocolate brown, and spectrophotometric examination of blood reveals the characteristic pigment

Clubbing

- Selective bulbous enlargement of the distal segments of the digits due to an increase in soft tissue
- Appears to be vasodilation of vessels in the fingertip, including formation of the arteriovenous connections.
- COPD does not cause clubbing

Clubbing

- Clubbing may be hereditary, idiopathic, or acquired

- **Associated with:-**

1. Cyanotic congenital heart disease,
2. Infective endocarditis,
3. Pulmonary conditions (lung cancer, bronchiectasis, asbestosis, sarcoidosis, lung abscess, cystic fibrosis, tuberculosis, and mesothelioma),
4. Gastrointestinal diseases (including inflammatory bowel disease and hepatic cirrhosis).

Hypertrophic osteoarthropathy

- Pain and swelling of the soft tissues over the distal ends of the long and tubular bones.

- Formation of new bone beneath the periosteum of the distal diaphyses of the long bones of the extremities

- Most common disorder associated with HOA is carcinoma of the lung.

- Small-cell carcinoma is rarely implicated; a peripheral carcinoma of the lung is slightly more common than a central one.

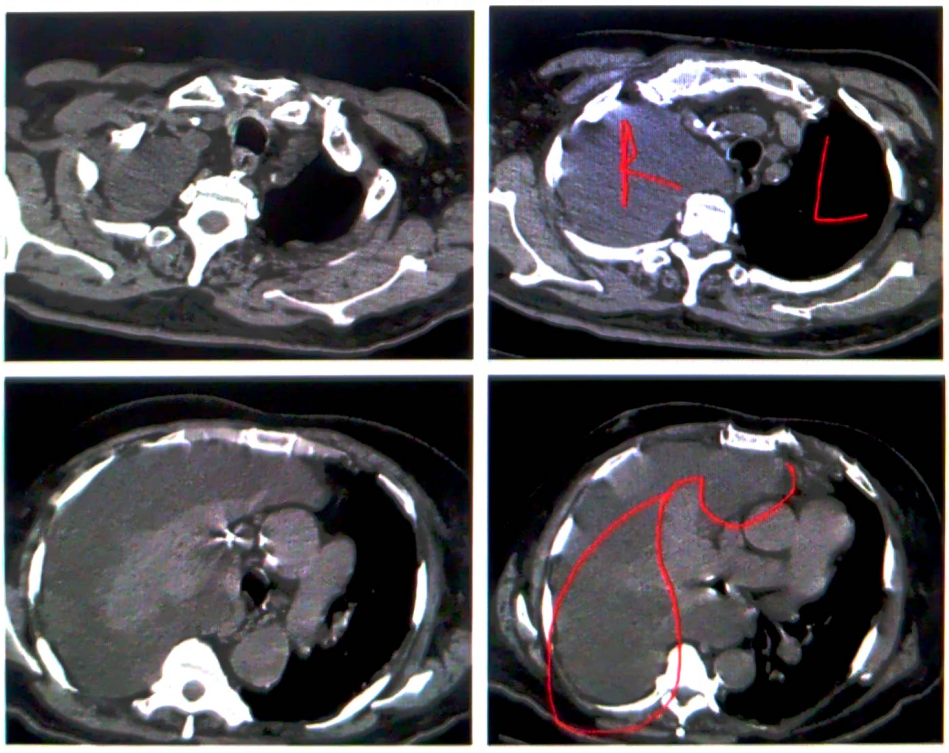
Diagnostics in Respiratory Medicine

Case 1

- 47 years old male

- **Presented with Chief complaints of :-**

1. Increased breathlessness since 01 Month, insidious and progressive, progressed from grade 1 mMRC to grade III mMRC
2. Cough with expectoration, scanty in amount and whitish in colour since 1 month.
3. History of LOA and LOW since 1 month
4. History of Low grade fever on and off since 1 month



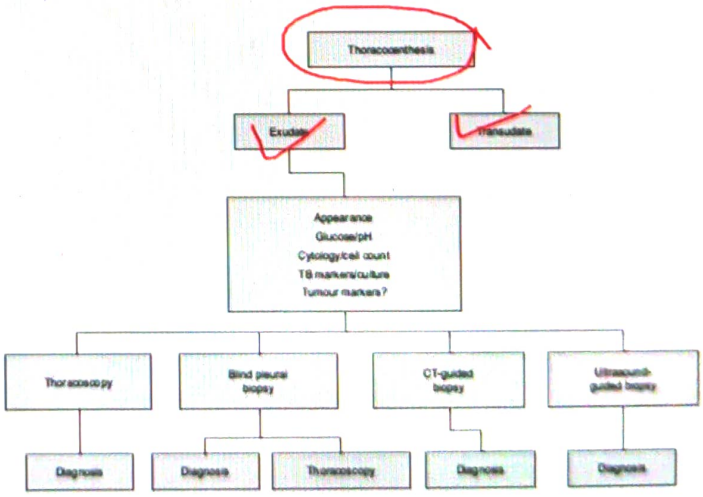
Q. What should be done next

a. Thoracoscopy
b. Thoracentesis
c. Closed pleural biopsy
d. Thoracotomy

Answer :- B (Thoracentesis)

Commonest Pleural Disease is Pleural Effusion

- 40% pleural effusions remain undiagnosed after initial pleural tap
- Obtaining pleural tissue is the *'Next Step'*.
- Etiology of ~ 20% of pleural effusions remain unclear even after pleural biopsy



Curr Opin Pulm Med 14:331–336

Eur Respir Rev 2010; 19: 117, 213–216

PLEURAL FLUID Analysis.			
SUGAR	108	LIPASE	<10.
PROTEIN	4.81	AMYLASE	<30
LDH	592	GRAM STAIN	NEG
ADA	9.5	AFB STAIN	NEG
TLC	900	FUNGAL STAIN	NEG
CHOLESTEROL	76.8	GENXPERT	NEG
TG	36.10	PYO C/S	NEG
BNP	2000		
PCV	4.2		

Pleural Fluid for Cell Block:

Pleural fluid cell block hemorrhagic and shows predominantly polymorphs, few lymphocytes, occasional mesothelial cells. No definite atypical/ malignant cells seen.

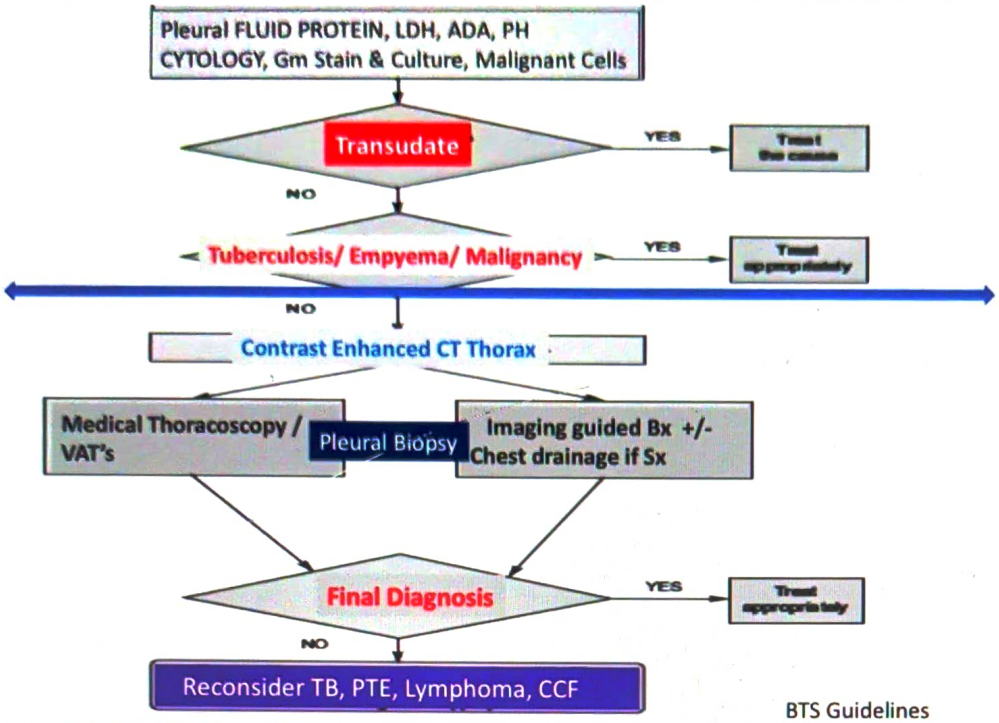
Pleural fluid for Cytology:

Neutrophilic effusion.

Q. What should be done next

a. Thoracoscopy
b. Thoracentesis
c. Closed pleural biopsy
d. Thoracotomy

Answer :- A (Thoracoscopy)



BTS Guidelines

Current diagnostic Algorithm

Closed Pleural biopsy

- Percutaneous sampling of the parietal pleural lining.

- Procedure can be performed either "blindly" (typically with an Abrams needle) or by using imaging guidance such as CT or ultrasound.

Medical thoracoscopy

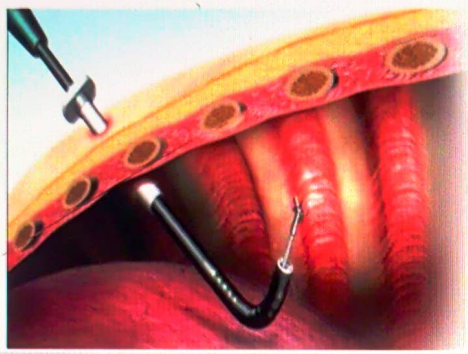
- MT also termed "local anesthetic thoracoscopy" and "pleuroscopy"

- Minimally invasive single- port endoscopic technique using rigid and semi-rigid thoracoscopies that offers direct visualization of pleural surfaces, as well as channels to perform diagnostic and therapeutic procedures

- Patients typically receive moderate sedation and breathe spontaneously throughout the procedure, without positive pressure ventilation

Medical thoracoscopy

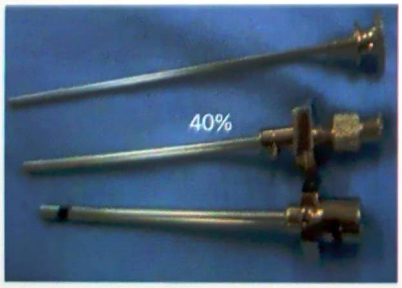
- The advantage of medical thoracoscopy is direct visualisation of both the pleural surfaces
- Enables to take biopsy under vision

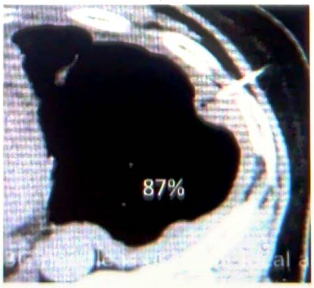




	MT	VATS
Indication	Dx of Pleural disease – do not touch the lung or visceral pleura	Rx + Lung biopsy
Anaesthesia	LA / Sedation	GA
Intubation	No	Yes (Double lumen)
Procedure Site	Suite / Room	OT
Ports of entry	Single	Multiple (2 - 3)
Invasiveness	+	++
Safety	++	++
Cost	+	+++

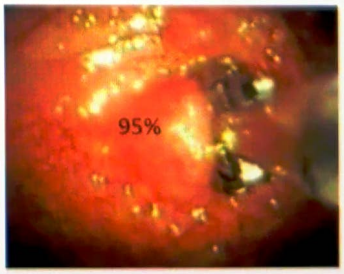
Obtaining Pleural Tissue : *Size of Meat Matters !*





No Lesion = No diagnosis in ~70%



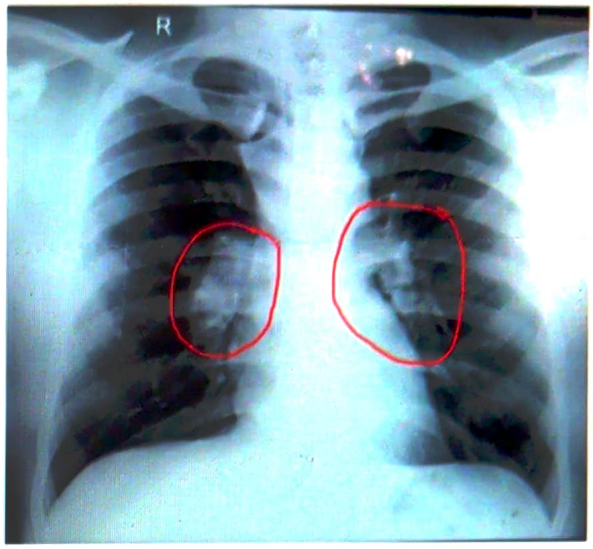


Highest Yield with Thoracoscopy

Kirsch C, et al. Chest 1997; 112:702–706

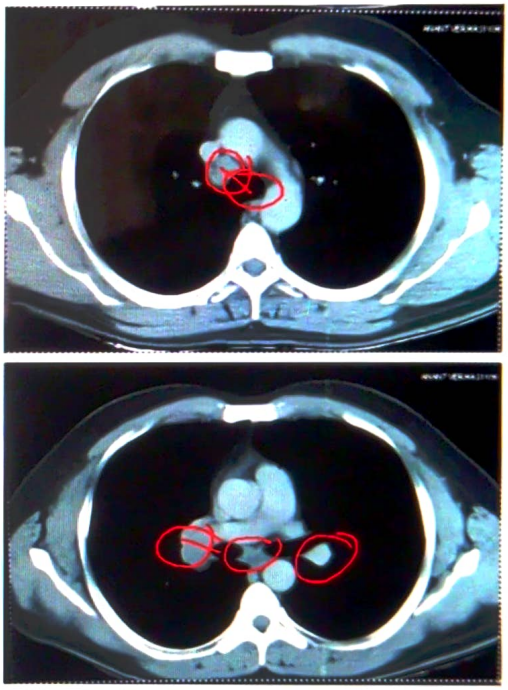
Case 2

- 31 year old male
- Software professional
- Never smoker
- No prior illness
- C/O:
  - Malaise and easy fatigability X 2 months
  - Mild arthralgias
- No fever or respiratory complaints
- O/E: General and systemic exam – NAD
- Was carrying a recent chest radiograph



On further evaluation..

- Mantoux – 0 mm
- S. ACE – 65 IU/mL
- S. Calcium – 9.4 mg/dL
- Urine 24 hour calcium – 97 mg/day (normal)
- Spirometry – normal



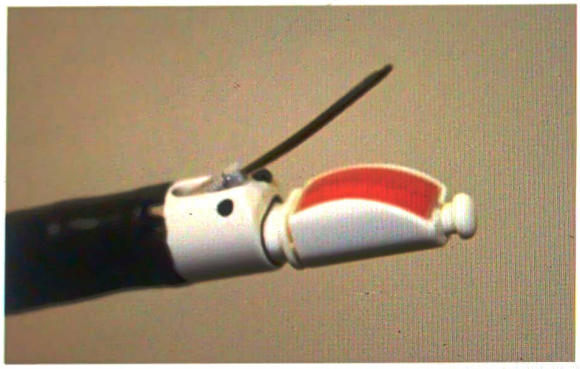
Q. What should be done next

a. CT guided biospy
b. Mediastinoscopy
c. EBUS guided lymph node sampling
d. Flexible Bronchoscopy

Answer :- C (EBUS guided lymph node sampling)

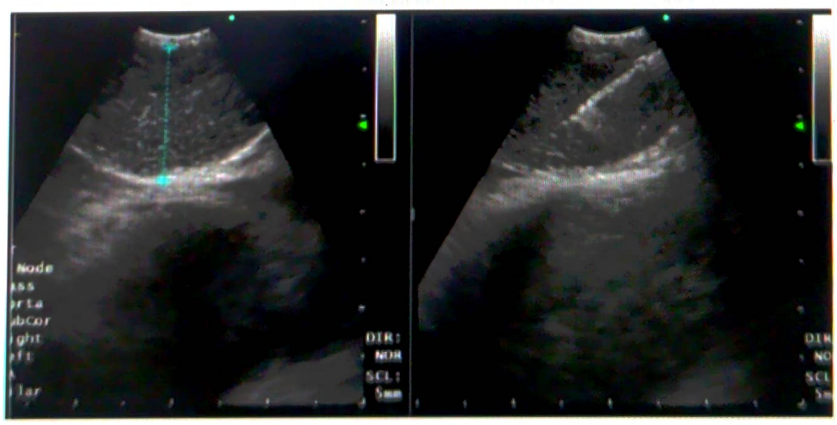
EBUS

Endobronchial ultrasonography (EBUS) is a diagnostic modality in which a miniature ultrasonic probe is introduced into the tracheobronchial lumen to provide the sonographic images of the peribronchial tissue

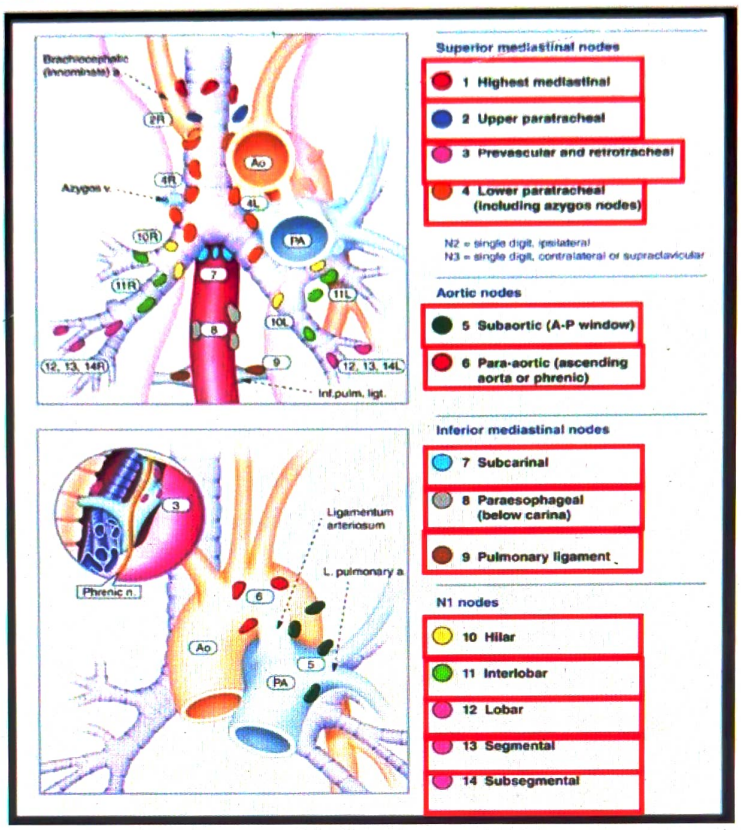


CONVEX-PROBE EBUS

EBUS sonographic vision of lymph node



IASLC Medisatinal LN Map



Stations accessed by EBUS/EUS

- **EBUS**
  - 2 R, 2 L, 3P, 4 R, 4 L, 7, 10 R, 10 L, 11R (superior and inferior) and 11 L lymph nodes
  - Station 5 and 6 cannot be accessed (May be accessed by transvascular approach)

- **EUS/EUS-B-FNA**
  - 2 L, 4 L,7, 8 and 9