Smoking related lung diseases

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17 MAY 2017

UOM

As King James 1 said…

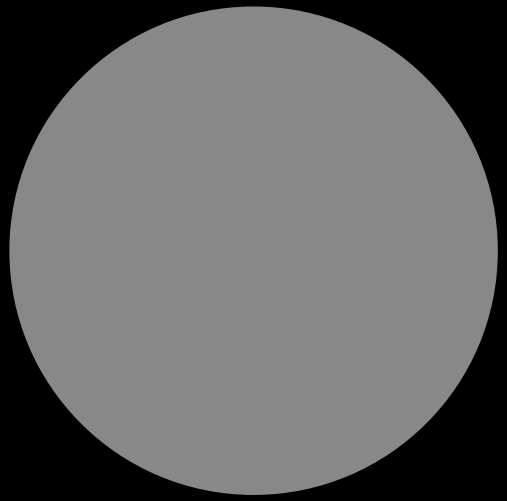
- “tobacco smoking is a custom loathsome to the eye, hateful to the nose, harmful to the brain and dangerous to the lungs “

Early 1950s

- Sir Richard Doll and Sir Austin Bradford Hill established the connection between smoking and lung cancer
- British Doctors Study (1964)
- X 2 increase in Lung cancer in smoking doctors

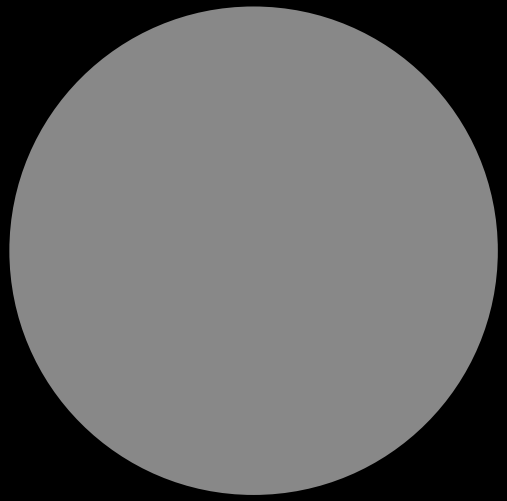
Tobacco smoke

- Nicotine
- Carcinogens
- Irritants
- Carbon Monoxide



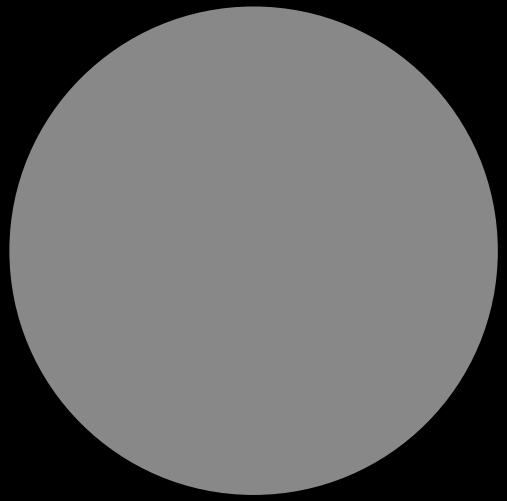
Topics

- Lung cancer and screening
- COPD
- Interstitial lung disease
- Cessation of smoking
- e- cigarettes



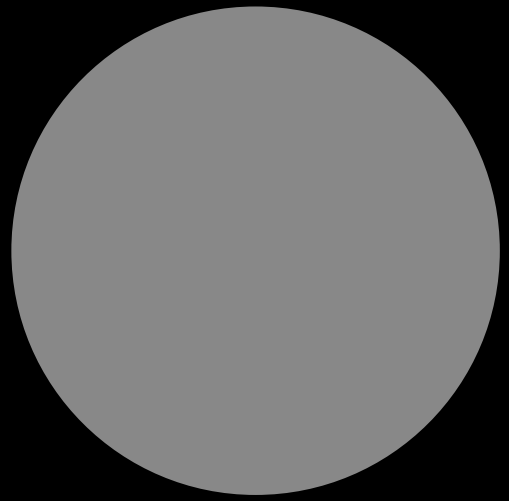
Red flags for lung cancer

- A change in smoker's cough
- Persistent cough after chest infection
- Haemoptysis
- Pleuritic pain
- Dyspnoea
- Hoarseness and stridor
- Systemic symptoms

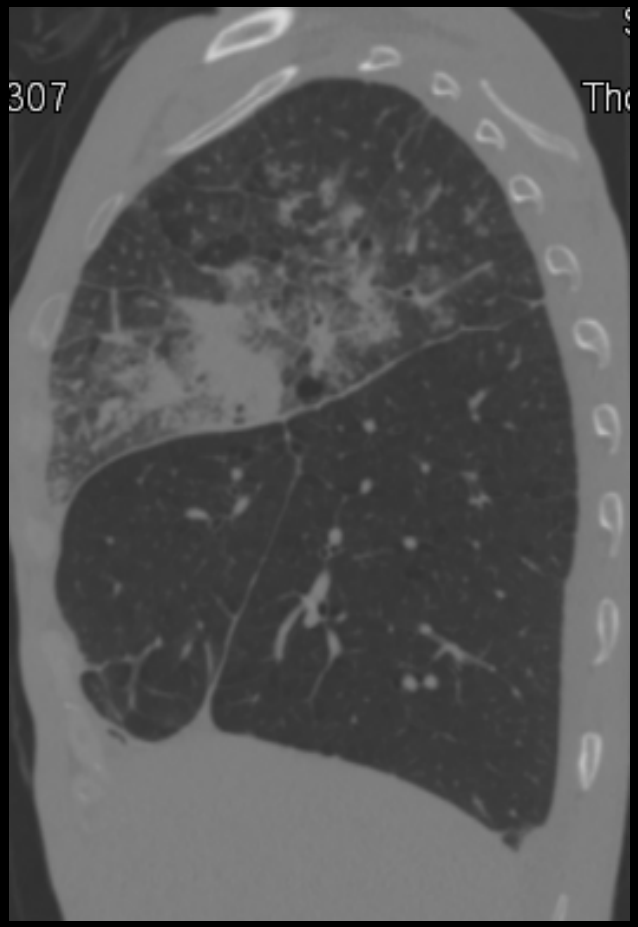


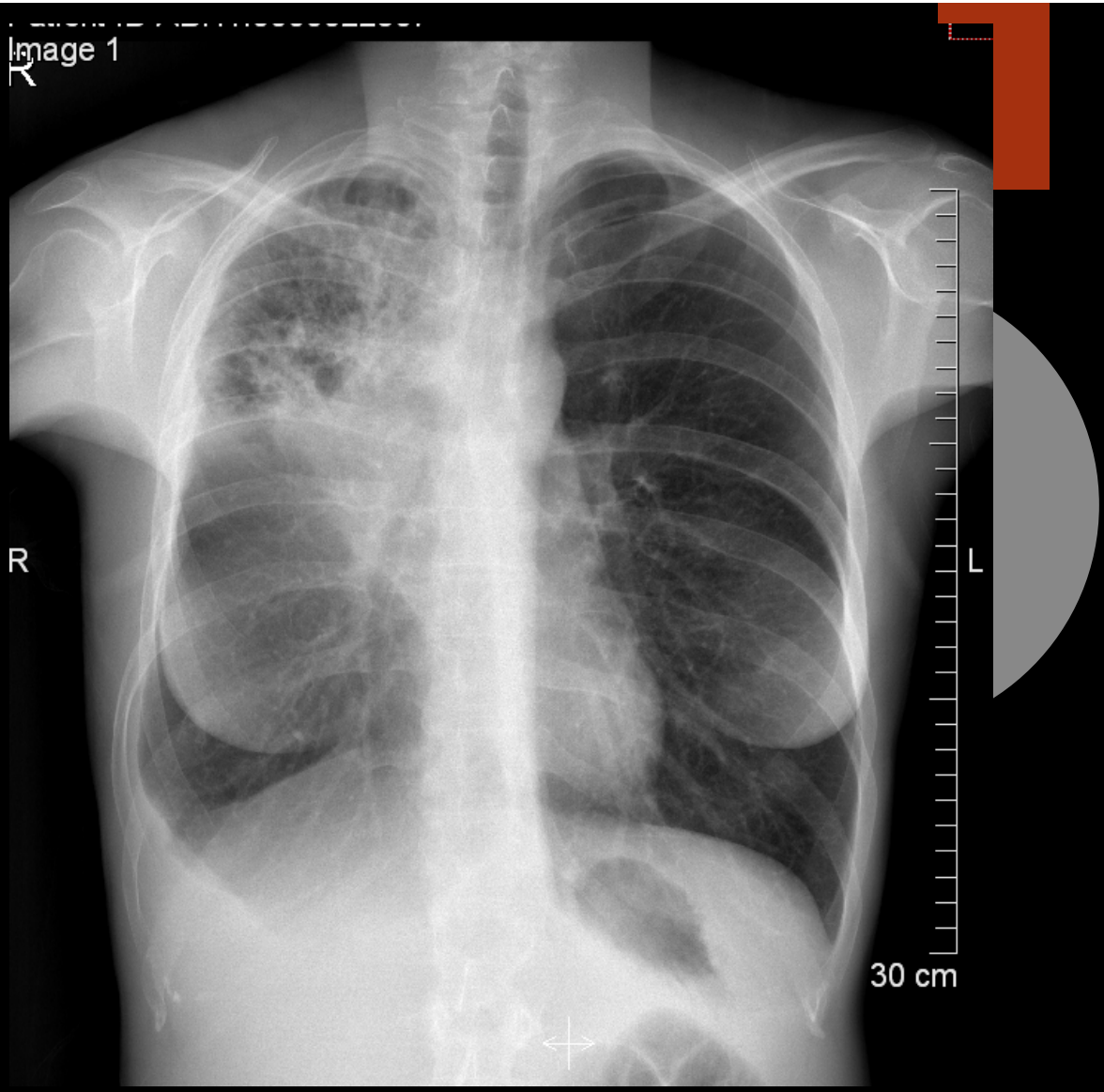
Lung Cancer

- 42 yr mum of 2 young kids
- 24 pack year
- Persistent worsening cough
- Severe R pleuritic pain
- Dyspnoea mMRC 4 and wheeze
- Systemic symptoms
- Stridulous sounds , low pitched wheezes

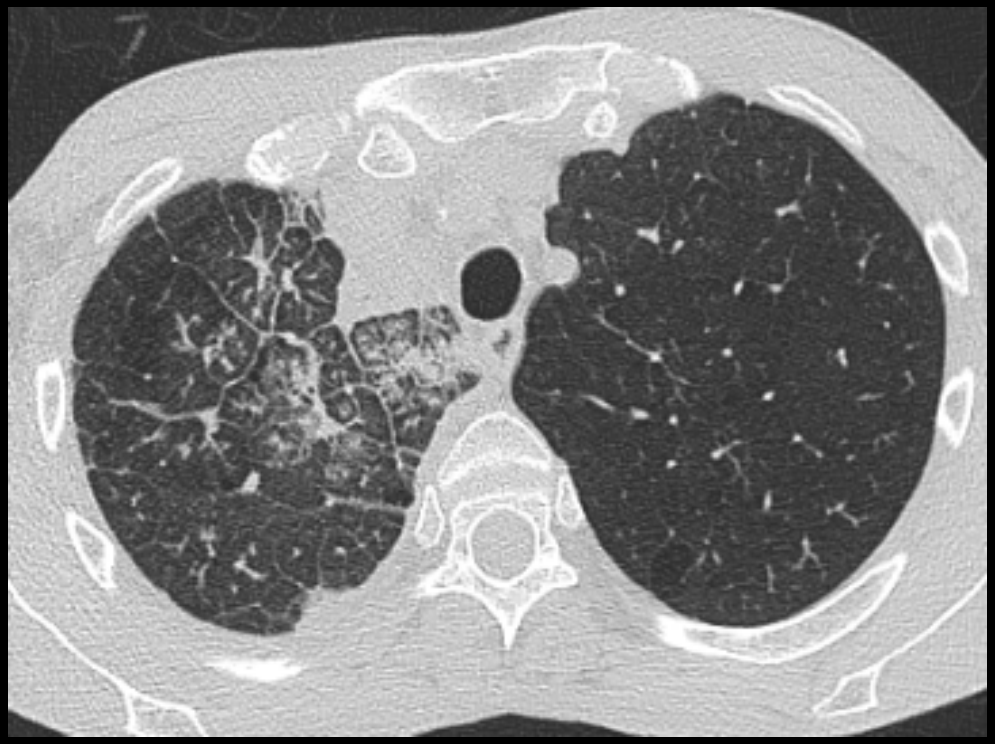


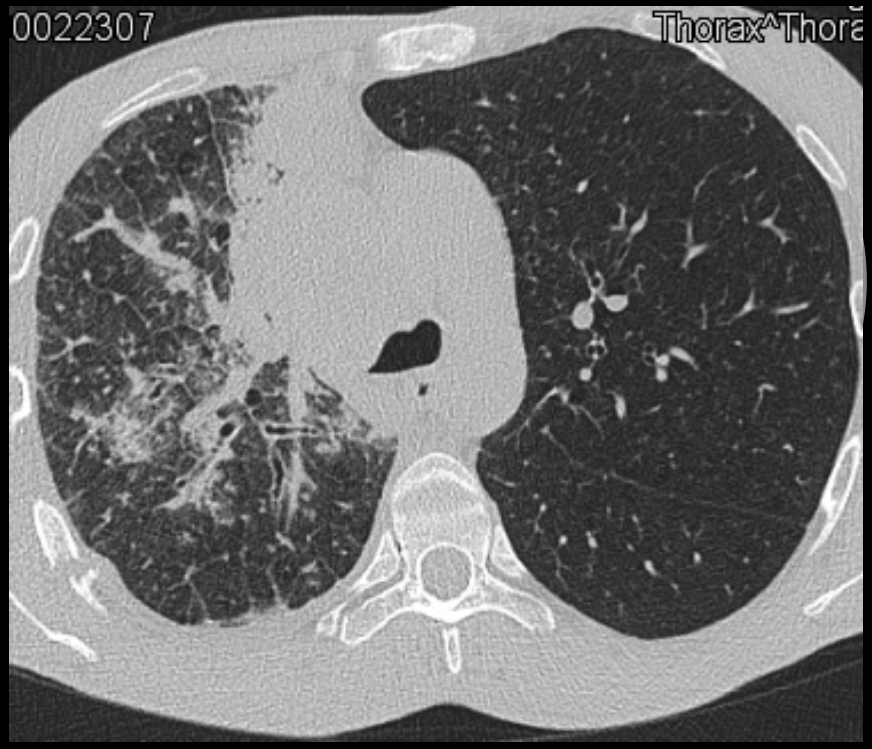
Ca bronchus

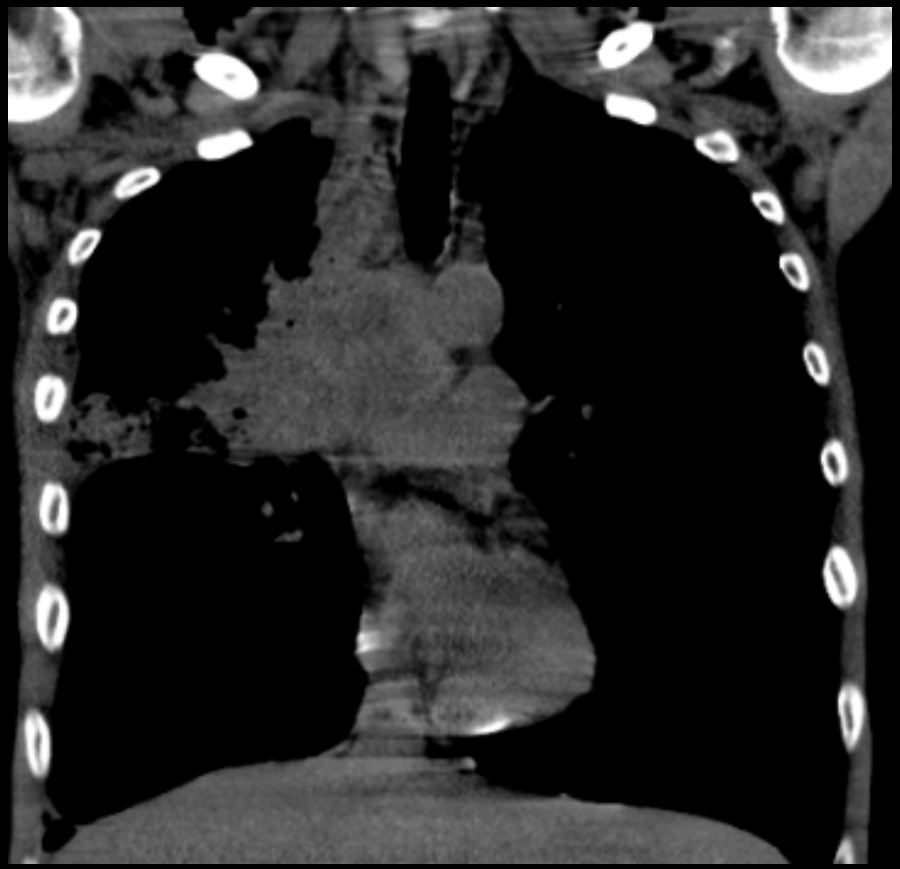




Small cell Ca bronchus





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Lung cancer –further management

- Bronchoscopy- tumour invading lower trachea on R. RUL bronchus obliterated and RMB very narrowed by tumour.
- Histopathology : Small cell carcinoma

- Referred to oncologist, chemotherapy. Good initial response

TNM classification

- Anatomical delineation of disease
- Determines operability and prognosis
- International comparisons of disease patterns and treatment results

Histopathology

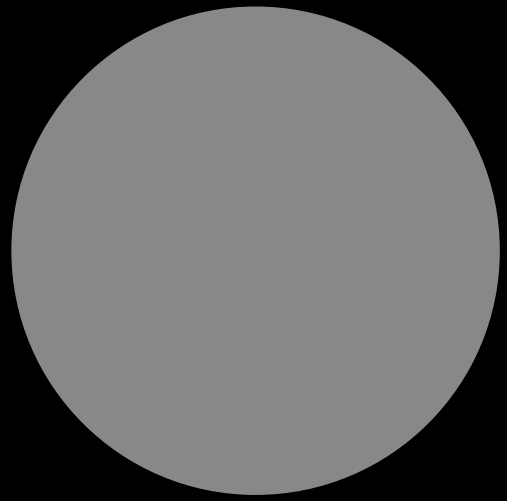
NSCLC – 75 %

Adenocarcinoma

Large cell carcinoma

Squamous cell ca

SMALL CELL carcinoma- 20 %



New Treatments for advanced NSCLC

- An explosion !
- Targeted treatment- aiming at tumour mutations- EGFR, ALK, ROS1, KRAS in adenocarcinomas
- Immunotherapy- checkpoint inhibitors eg PD L 1

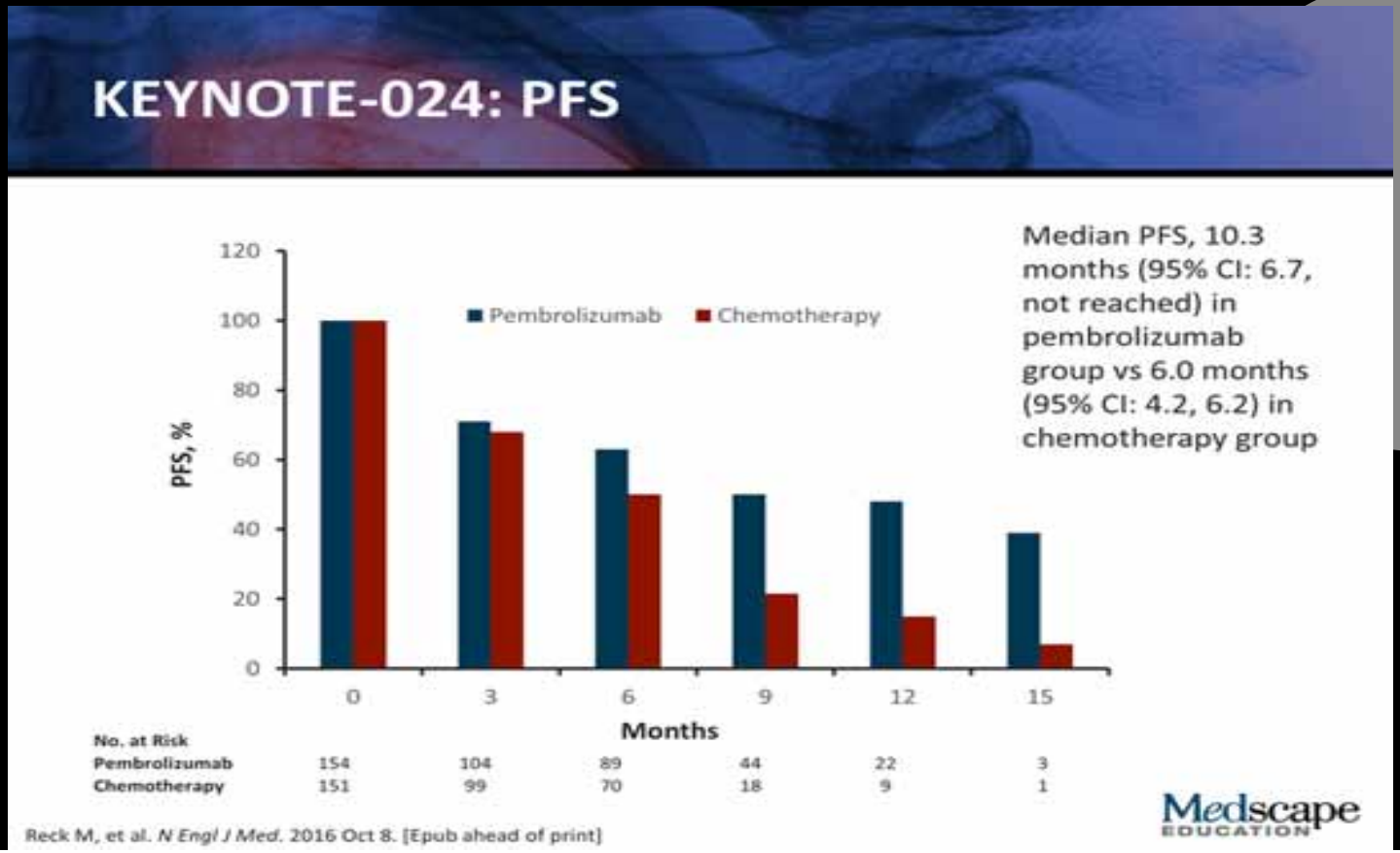
EGFR Inhibitors

- EGFR- cell surface protein involved in cell growth
- Gene mutation in some NSCC tumours XS EGFR and tumour cell proliferation
- EGFR inhibitors (TKI inhibition) block this signalling and tumour growth
- Women, Orientals,non- smokers
- ERLOTINIB , gefitinib, afatinib

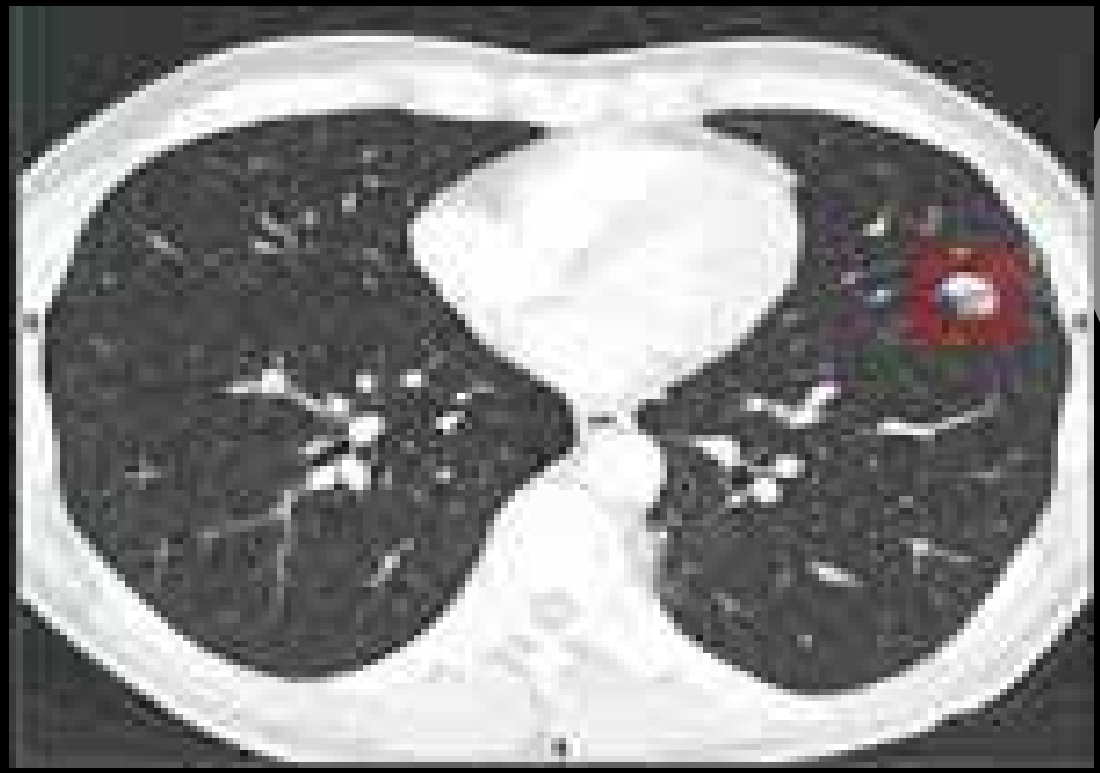
Immune checkpoint inhibition

- Immune system uses checkpoints (eg PD-1 protein on T cells) to prevent damage to normal cells
- Cancer cells can hijack this inhibitory system to prevent immune cells from attacking them
- Immune checkpoint inhibitors restore the anti tumour potential of these immune cells
- Pembrolizumab prolongs overall survival X 4 at 18 months in recent trials
- Side effects and COST are problematic

KEYNOTE study- pembrolizumab



Low dose HRCT screening



LDCT lung cancer screening

US preventive services task force, 50 000 recruits

- Age 55 – 80 yrs
- 30 pack year
- Current smoker or gave up < 15 yrs ago
- Based on findings of NLST 2011

National Lung Screening Trial - USA

- 16 % reduction lung cancer deaths
- 6.7 % reduction all cause mortality
- Incidental pick ups : Emphysema, Lung fibrosis, bronchiectasis, coronary A calcification
- 320 persons screened for one neoplasm

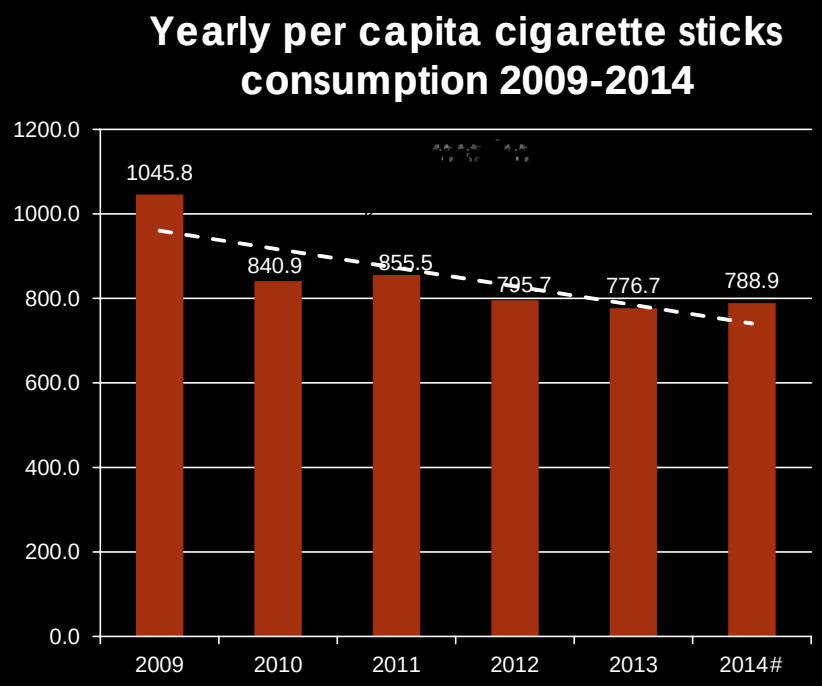
NLST USA 2011

- Many false positives- resolved by follow-up scans
- 1.9 % biopsied
- 6 deaths
- Overdiagnosis : 10 % pick ups would not have developed clinical disease in their residual lifetime
- Radiation exposure
- Cost

Other lung cancer LDCT screening projects

- Nelson Dutch- Belgian 7915 recruits
- UK Lung Cancer RCT (2 % pick up rate)
- Considered cost effective
- Annual screening best

NCD Surveys Cigs



Mauritius NCD survey 2015

- Overall 19.3 % of 18-74 yr old smoked
- 38 % men, 3.9 % women
- Stunning 50 % smokers in males 19 – 24 yrs
- Smoking rate really falls by half from age 55 onwards

Smoking cessation

- Counselling- brief advice from doctor- 5 % stop
- BABEX trial (New Delhi , low income groups) Thorax Feb 2017
- Doctor/ trained field worker : 15 min counsel and yogic breathing exercises
- 2 .5 % quit rate at 6 months vs 0.5 % for 1 min advice

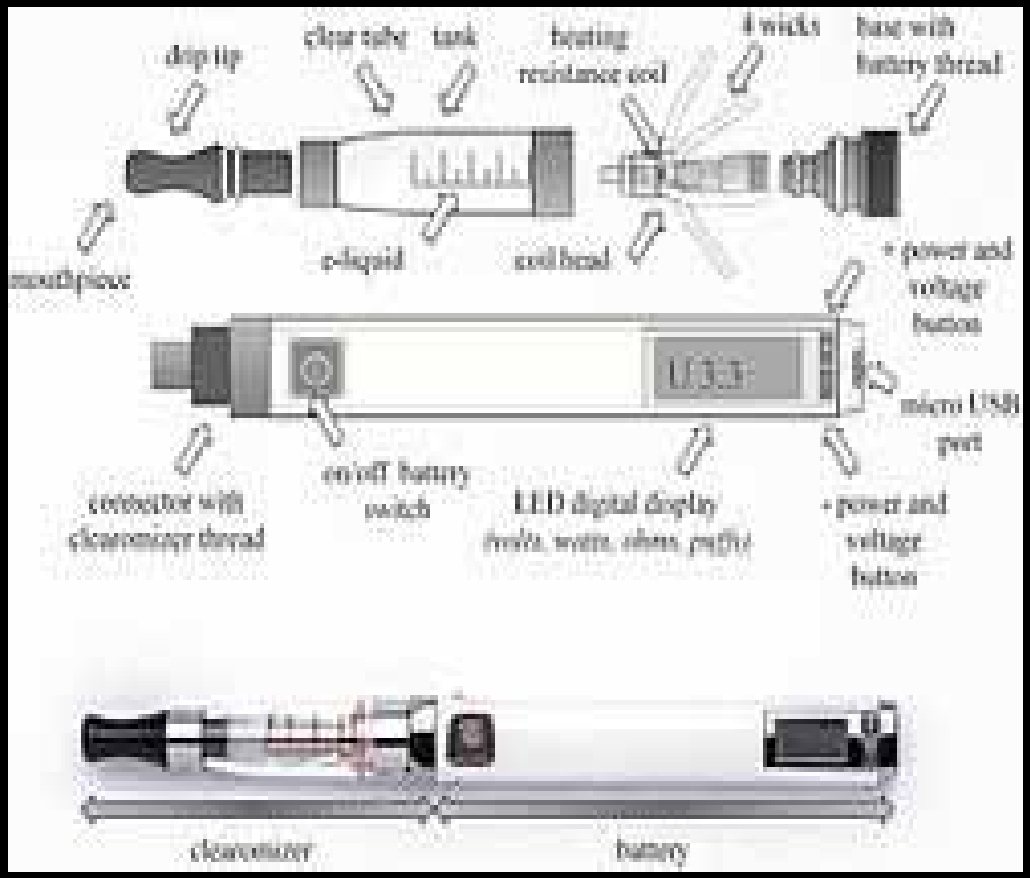
Smoking cessation

- Softly, softly approach
- Acknowledge it's difficult to stop
- Point out financial savings...for the children !
- Success stories from ex- smokers
- Immediate health benefits – cardiac is best target.

Smoking cessation- pharmacology

- CONTROLLERS- Nicotine patch, bupropion, varenicline
- RELIEVERS – Nicotine gum, nasal spray
- But MOTIVATION is primordial

e- cigarette


drip tip
clear tube
tank
heating resistance coil
4 wicks
base with battery thread
mouthpiece
e-liquid
coil head
+ power and voltage button
micro USB port
connector with clearomizer thread
on/off battery switch
LED digital display
volts, watts, ohms, puffs
+ power and voltage button
clearomizer
battery

Fashionable !

Electronic Nicotine Delivery Systems - ENDS

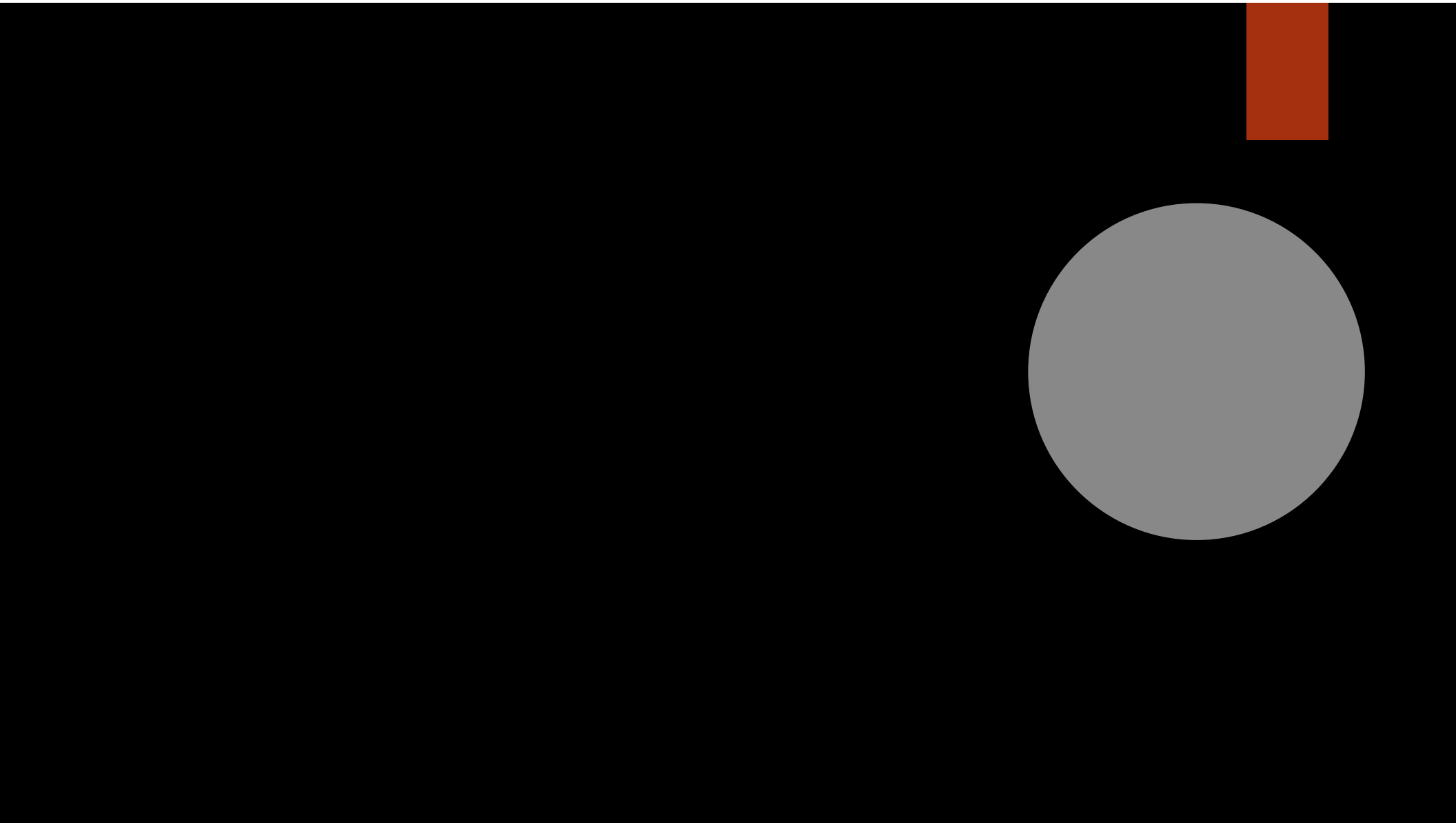
- " Vaping "
- Propylene glycol and glycerine, 8000 flavours !!!
- 2003, China, Mr. Hon Lin
- Cigalikes, eGos, MODs
- Very popular
- Used to come off real cigarettes or as a substitute – no carcinogenic tar inhalation- only nicotine

e cigarettes

- No proper controlled studies of long term outcomes- efficacy and dangers
- Concern that never would have been smokers get tempted because of perception of safety and get hooked
- " Normalisation " of smoking
- Second hand nicotine inhalation

e cigarettes- official views

- UK bodies more in favour- Cochrane review, Public Health England, Royal College of Physicians " 95 % less harmful than smoking "
- WHO- against
- USA – most professional bodies do not favour their use – except for FDA – says less harmful than combustible cigs.
- Mauritius – SLO studying recommendation to make it illegal



COPD Definition

- Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

Prevalence

Prevalence of COPD

- Estimated 384 million COPD cases in 2010.
- Estimated global prevalence of 11.7% (95% CI 8.4%–15.0%).
- Three million deaths annually.
- With increasing prevalence of smoking in developing countries, and aging populations in high-income countries, the prevalence of COPD is expected to rise over the next 30 years.
- By 2030 predicted 4.5 million COPD related deaths annually.

Diagnosis and Initial Assessment

OVERALL KEY POINTS (1 of 2):

- COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease.
- Spirometry is required to make the diagnosis; the presence of a post-bronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation.
- The goals of COPD assessment are to determine the level of airflow limitation, the impact of disease on the patient's health status, and the risk of future events (such as exacerbations, hospital admissions, or death), in order to guide therapy.

Choice of thresholds

- COPD Assessment Test (CAT™)
- Chronic Respiratory Questionnaire (CCQ®)
- St George's Respiratory Questionnaire (SGRQ)
- Chronic Respiratory Questionnaire (CRQ)
- Modified Medical Research Council (mMRC) questionnaire

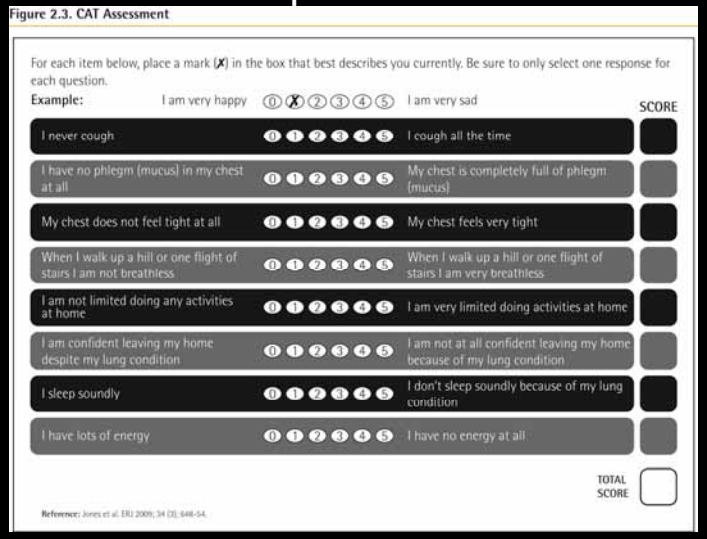


Figure 2.3. CAT Assessment

For each item below, place a mark (✗) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy 0 ✗ 2 3 4 5 I am very sad — SCORE

I never cough	0 1 2 3 4 5	I cough all the time
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition
I have lots of energy	0 1 2 3 4 5	I have no energy at all

TOTAL SCORE

Reference: Jones et al. ERJ 2009; 34 (3): 648–54.

Table 2.5. Modified MRC dyspnea scale[1]

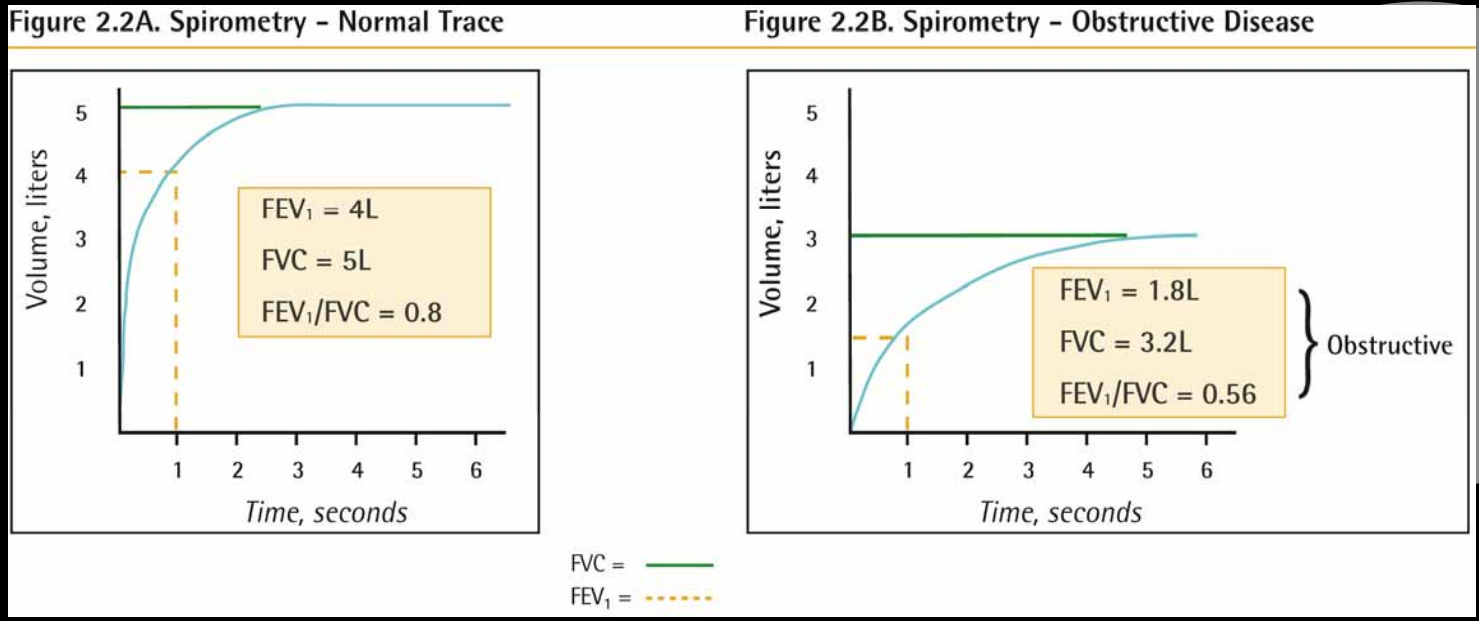
PLEASE TICK IN THE BOX THAT APPLIES TO YOU (ONE BOX ONLY) (Grades 0–4)	
mMRC Grade 0. I only get breathless with strenuous exercise.	❑
mMRC Grade 1. I get short of breath when hurrying on the level or walking up a slight hill.	❑
mMRC Grade 2. I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	❑
mMRC Grade 3. I stop for breath after walking about 100 meters or after a few minutes on the level.	❑
mMRC Grade 4. I am too breathless to leave the house or I am breathless when dressing or undressing.	❑

[1] Fletcher CM. BMJ 1960; 2: 1662.

Assessment of Exacerbation Risk

- COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy.
- Classified as:
  - Mild (treated with SABDs only)
  - Moderate (treated with SABDs plus antibiotics and/or oral corticosteroids) or
  - Severe (patient requires hospitalization or visits the emergency room). Severe exacerbations may also be associated with acute respiratory failure.
- Blood eosinophil count may also predict exacerbation rates (in patients treated with LABA without ICS).

Spirometry



ABCD Assessment Tool

Figure 2.4. The refined ABCD assessment tool

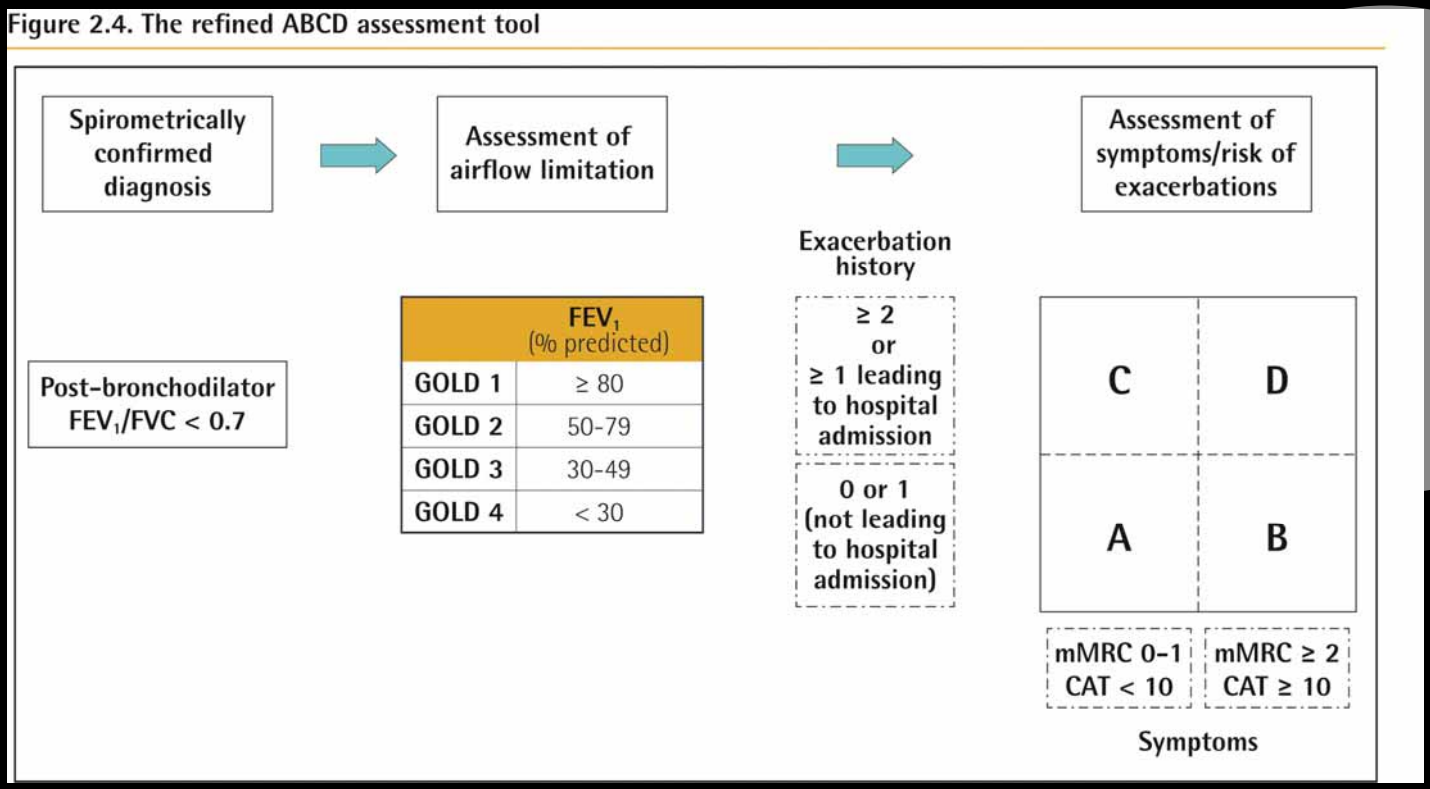
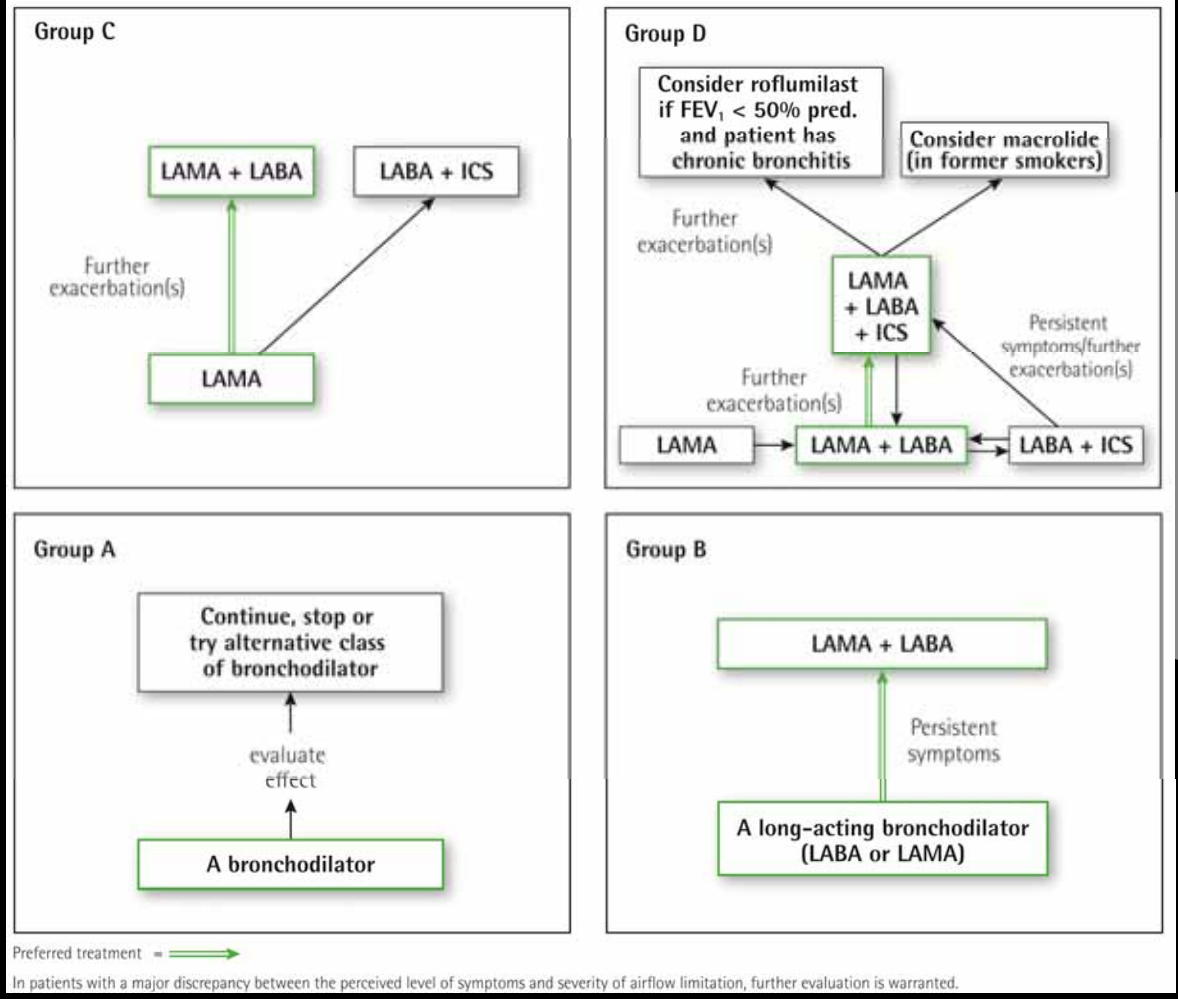


Figure 4.1. Pharmacologic treatment algorithms by GOLD Grade [highlighted boxes and arrows indicate preferred treatment pathways]



Preferred treatment =

In patients with a major discrepancy between the perceived level of symptoms and severity of airflow limitation, further evaluation is warranted.

Pharmacologic Therapy

Table 3.3. Commonly used maintenance medications in COPD*

Drug	Inhaler (mcg)	Solution for nebulizer (mg/ml)	Oral	Vials for injection (mg)	Duration of action (hours)
Beta$_2$-agonists					
Short-acting					
Fenoterol	100-200 (MDI)	1	2.5 mg (pill), 0.05% (syrup)		4-6
Levalbuterol	45-90 (MDI)	0.1, 0.21, 0.25, 0.42			6-8
Salbutamol (albuterol)	90, 100, 200 (MDI & DPI)†	1, 2, 2.5, 5 mg/ml	2, 4, 5 mg (pill), 8 mg (extended release tablet) 0.024%/0.4 mg (syrup)	0.1, 0.5 mg	4-6, 12 (extended release)
Terbutaline	500 (DPI)		2.5, 5 mg (pill)	0.2, 0.25, 1 mg	4-6
Long-acting					
Arformoterol		0.0075†			12
Formoterol	4.5-9 (DPI)	0.01†			12
Indacaterol	75-300 (DPI)				24
Olodaterol	2.5, 5 (SMI)				24
Salmeterol	25-50 (MDI & DPI)				12
Anticholinergics					
Short-acting					
Ipratropium bromide	20, 40 (MDI)	0.2			6-8
Oxitropium bromide	100 (MDI)				7-9
Long-acting					
Aclidinium bromide	400 (DPI), 400 (MDI)				12
Glycopyrronium bromide	15.6 & 50 (DPI)†		1 mg (solution)	0.2 mg	12-24
Tiotropium	18 (DPI), 2.5 & 5 (SMI)				24
Umeclidinium	62.5 (DPI)				24
Combination of short-acting beta$_2$-agonist plus anticholinergic in one device					
Fenoterol/ipratropium	50/20 (SMI)	1.25, 0.5 mg in 4ml			6-8
Salbutamol/ipratropium	100/20 (SMI), 75/15 (MDI)	0.5, 2.5 mg in 3ml			6-8

Combination Inhalers LABA / LAMA

- GSK - umeclidinium + vilanterol (OD)
- Boehringer – Tiotropium + olodaterol (OD)
- Astra Zeneca – formoterol + glycopyrronium
- Novartis- indacaterol + glycopyrronium

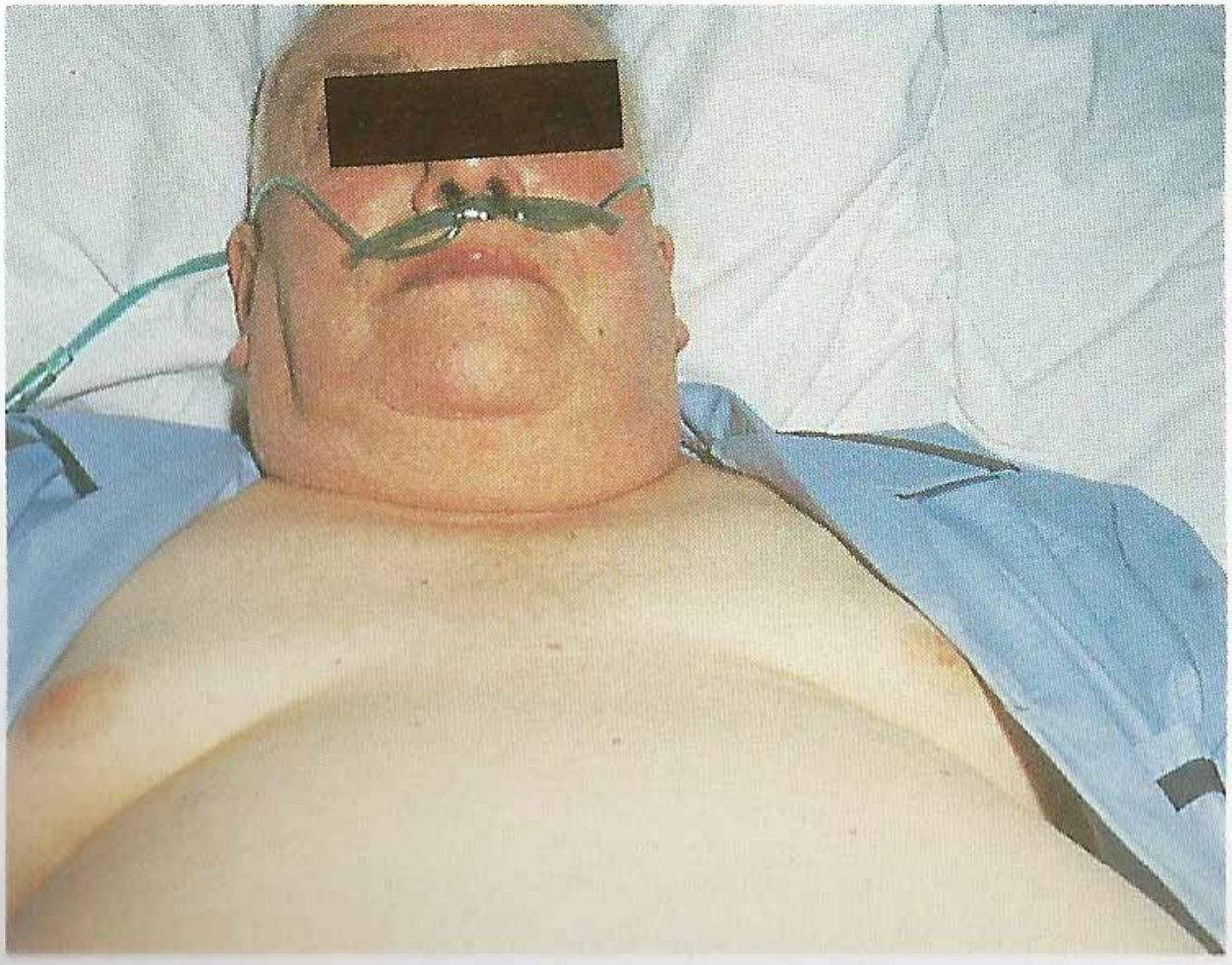


Fig. 9.35 The 'blue bloater' is obese, polycythaemic, and in respiratory and right heart failure.

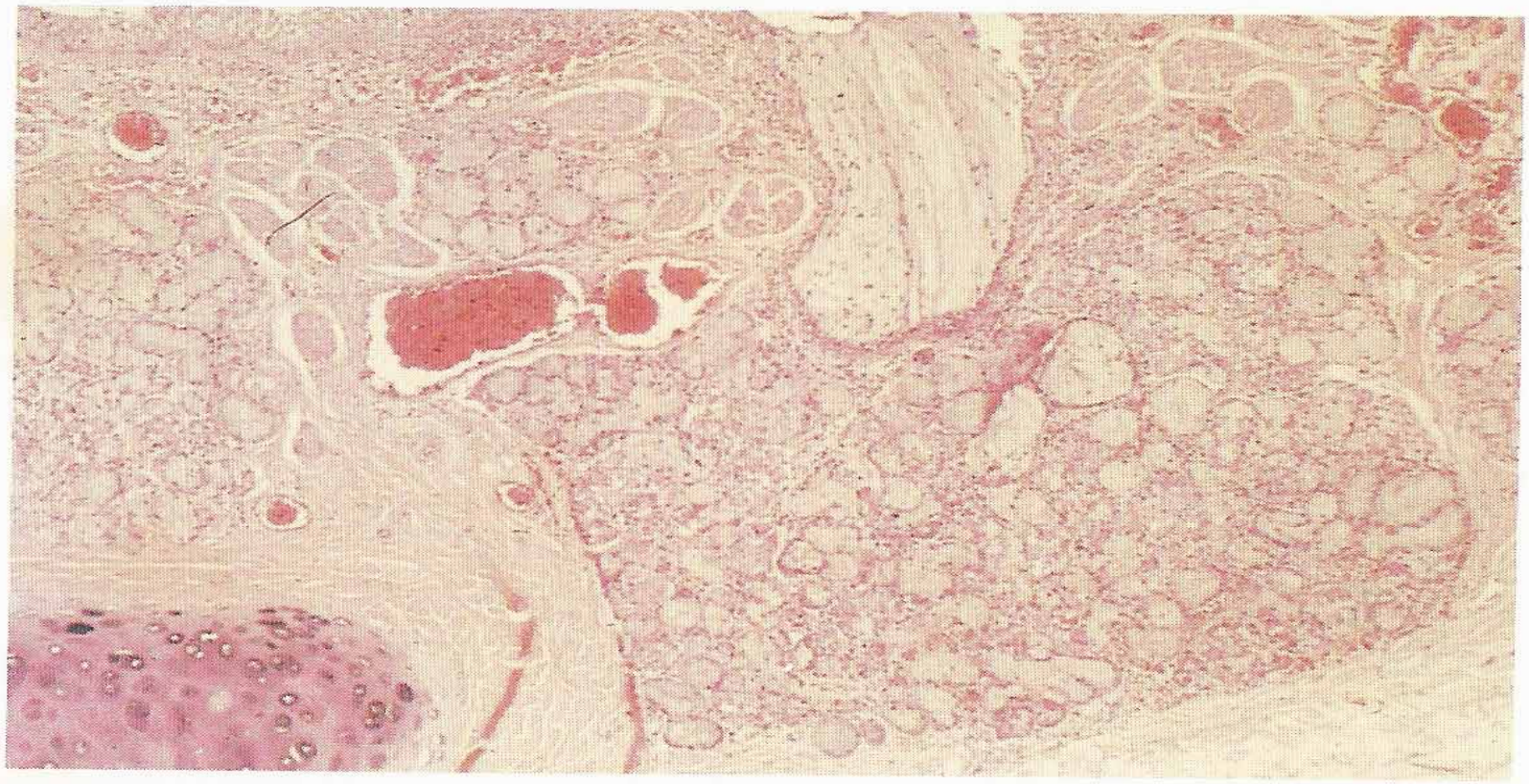


Fig. 9.15 Chronic bronchitis. There is marked glandular hyperplasia with mucus plugging of a gland. Haematoxylin and eosin stain.

Fig. 9.14 Chronic bronchitis. This cross-section of a bronchus shows marked hyperplasia of mucus-producing glands. Haematoxylin and eosin stain.

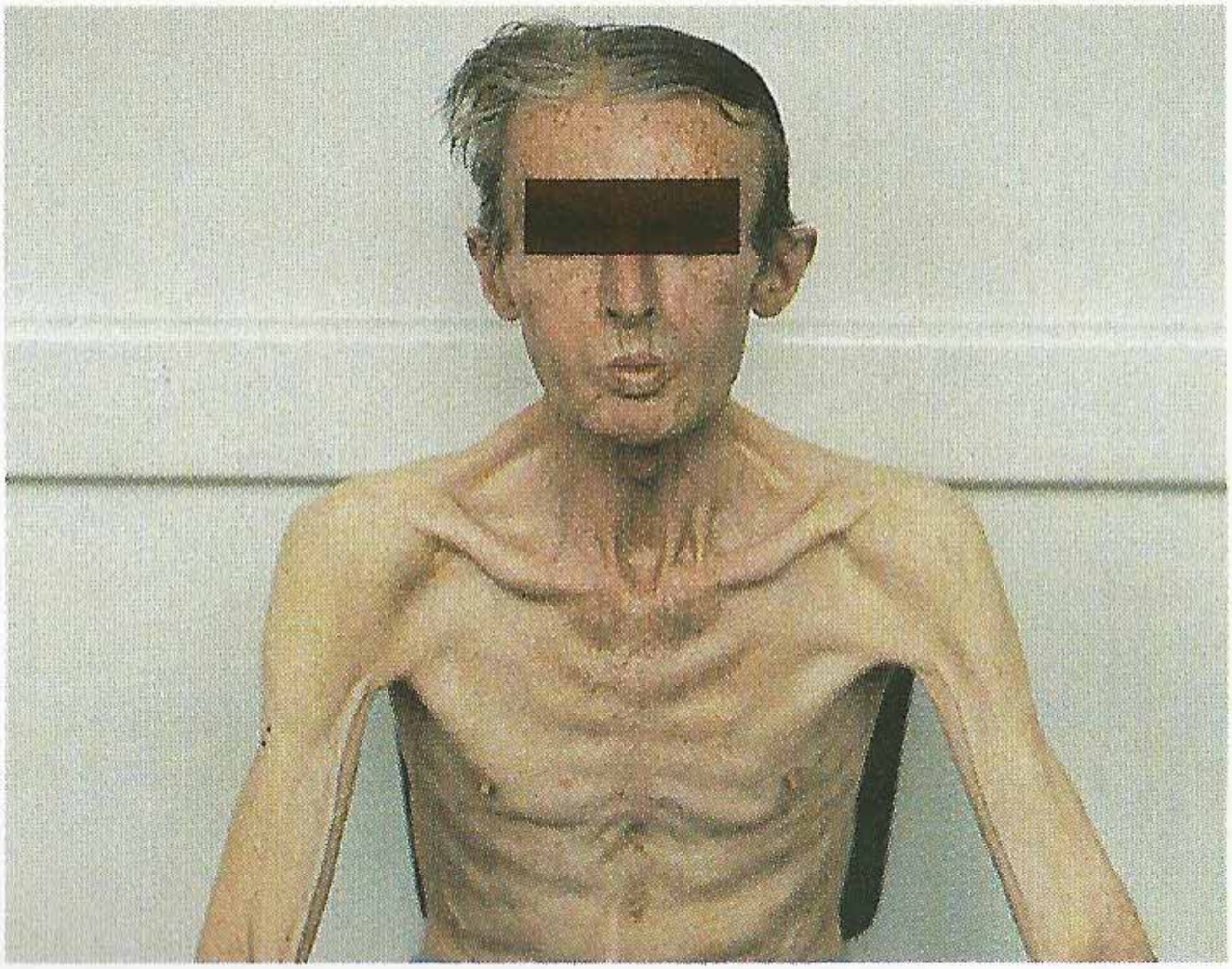
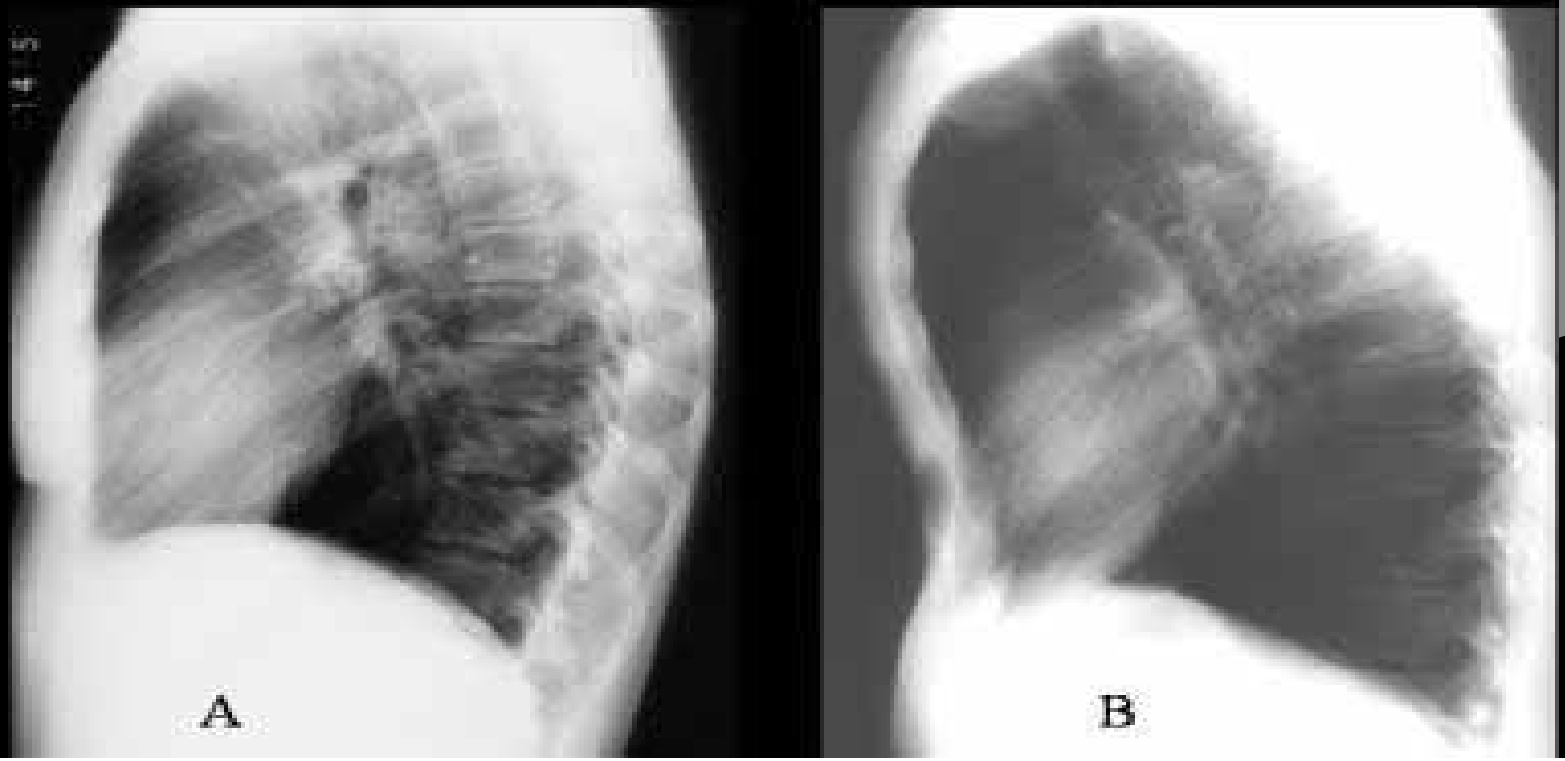


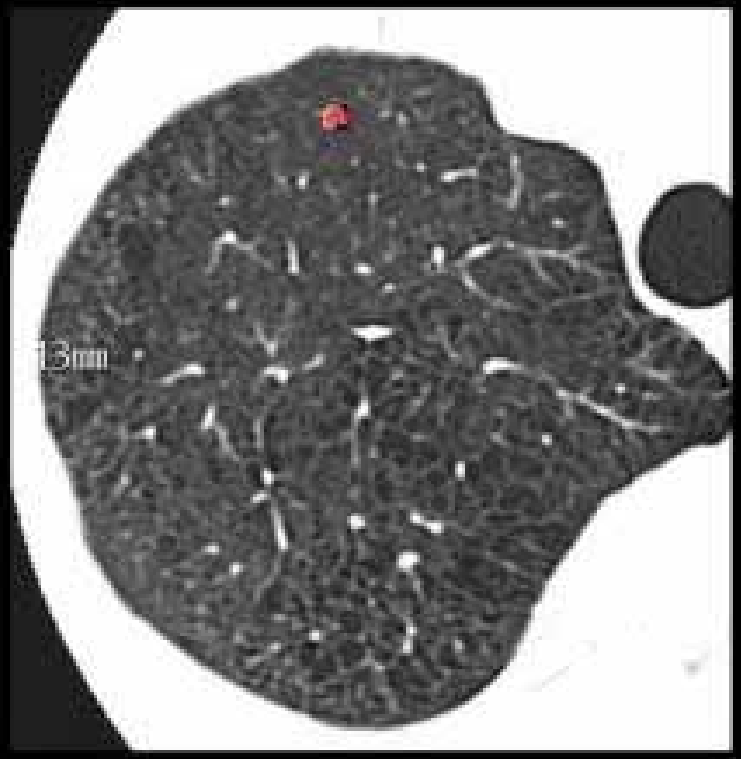
Fig. 9.36 The 'pink puffer' is thin and breathless and adopts a typical 'hands on knees' posture to provide maximum mechanical advantage for his respiratory muscles.

Frontal chest radiograms (PA). A. Normal patient. B. COPD patient .

Lateral radiograms. A: normal patient. B: COPD patient showing enlargement of the retrosternal space and diaphragm retification.



Centriacinar emphysema. The element in red shows the size of a normal acinus.



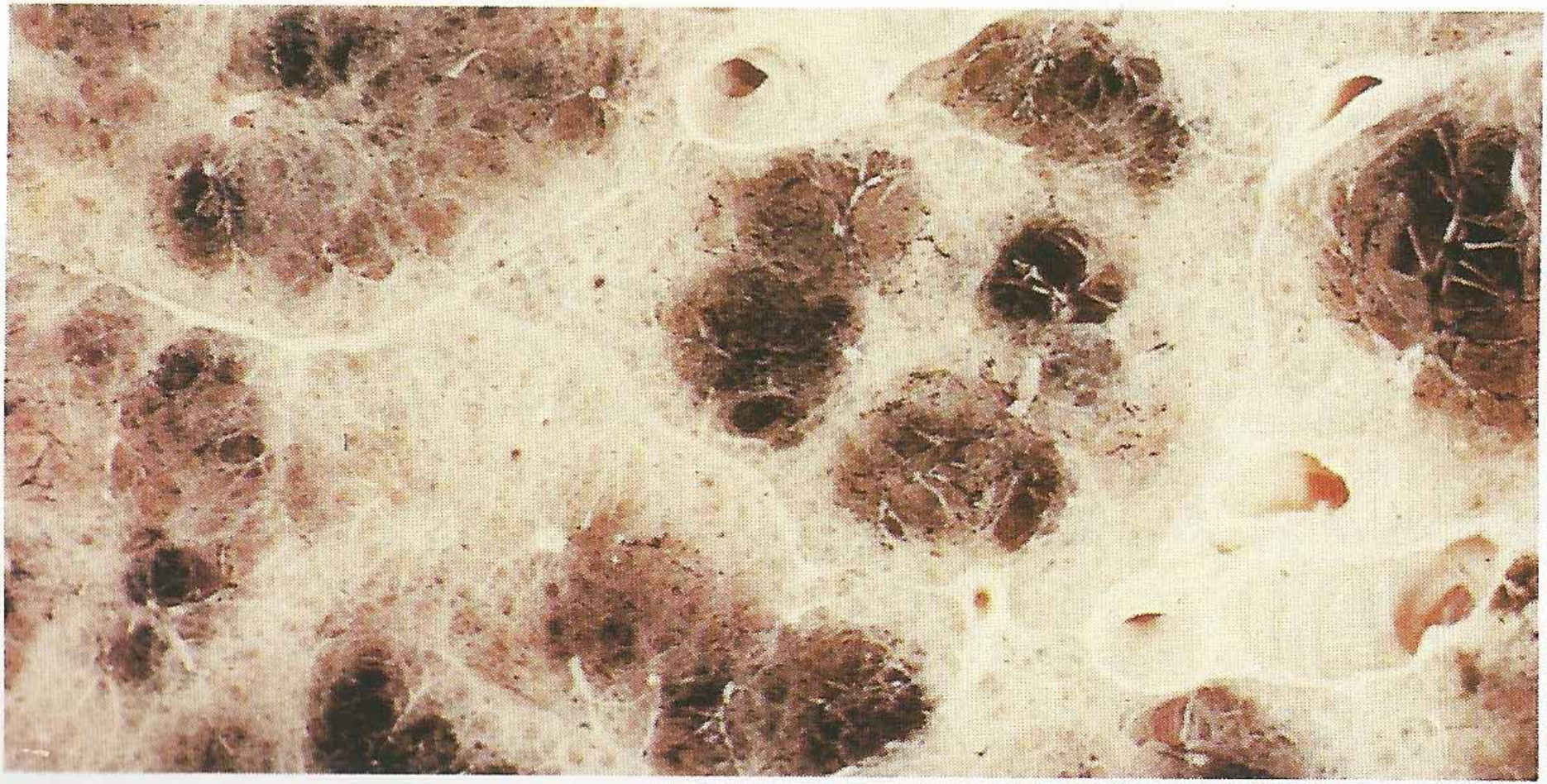


Fig. 9.23 Lung slice showing centriacinar emphysema. Barium sulphate preparation. By courtesy of Dr B.E. Heard

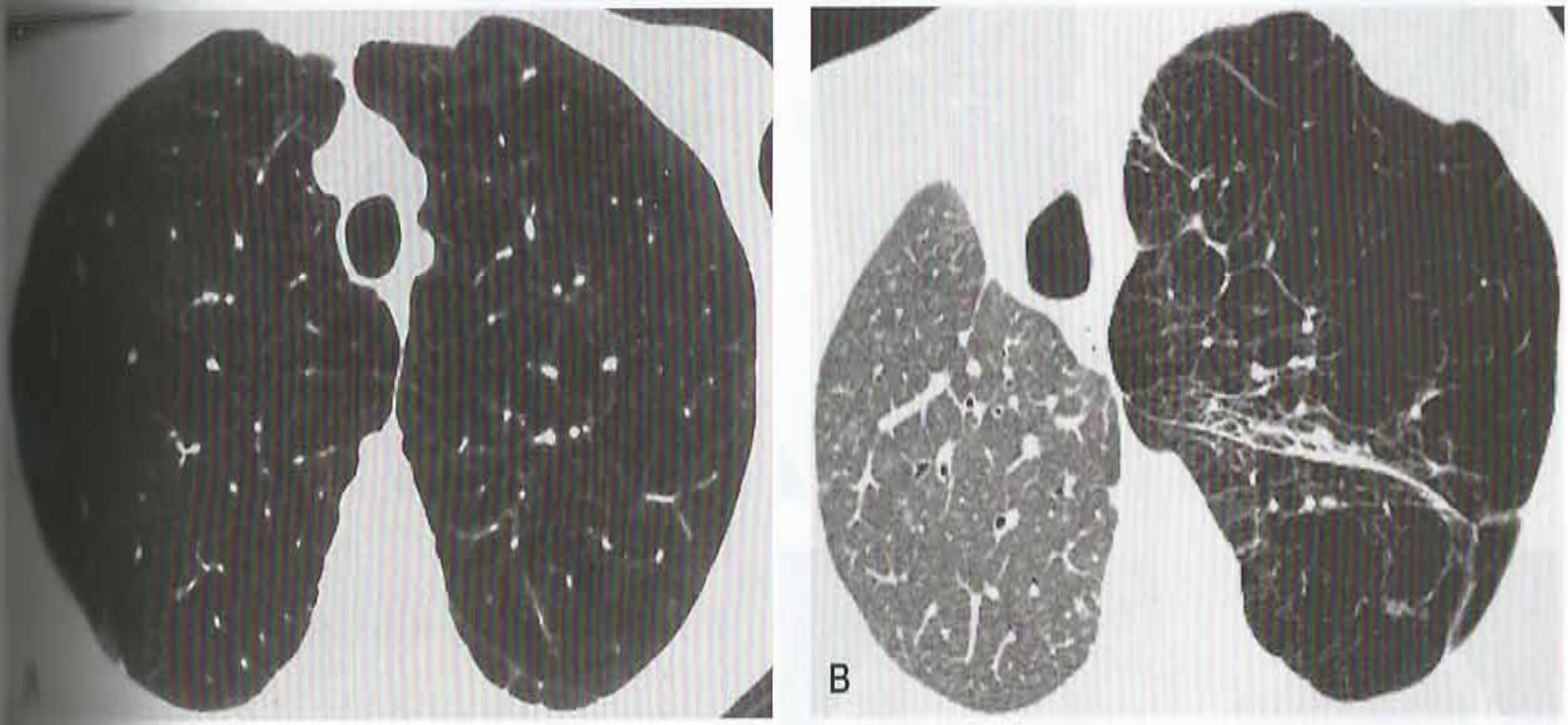


FIGURE 6-20 Panlobular emphysema in two patients. **A:** On HRCT, lung volumes are increased, the lungs appear lucent, and the size of pulmonary vessels is reduced. Focal lucencies, as seen in patients with CLE, are not visible. **B:** Panlobular emphysema in a patient who has had a right lung transplantation. The right lung is normal in appearance and attenuation. The emphysematous left lung is abnormally lucent, increased in volume, and contains fewer and smaller visible vessels.

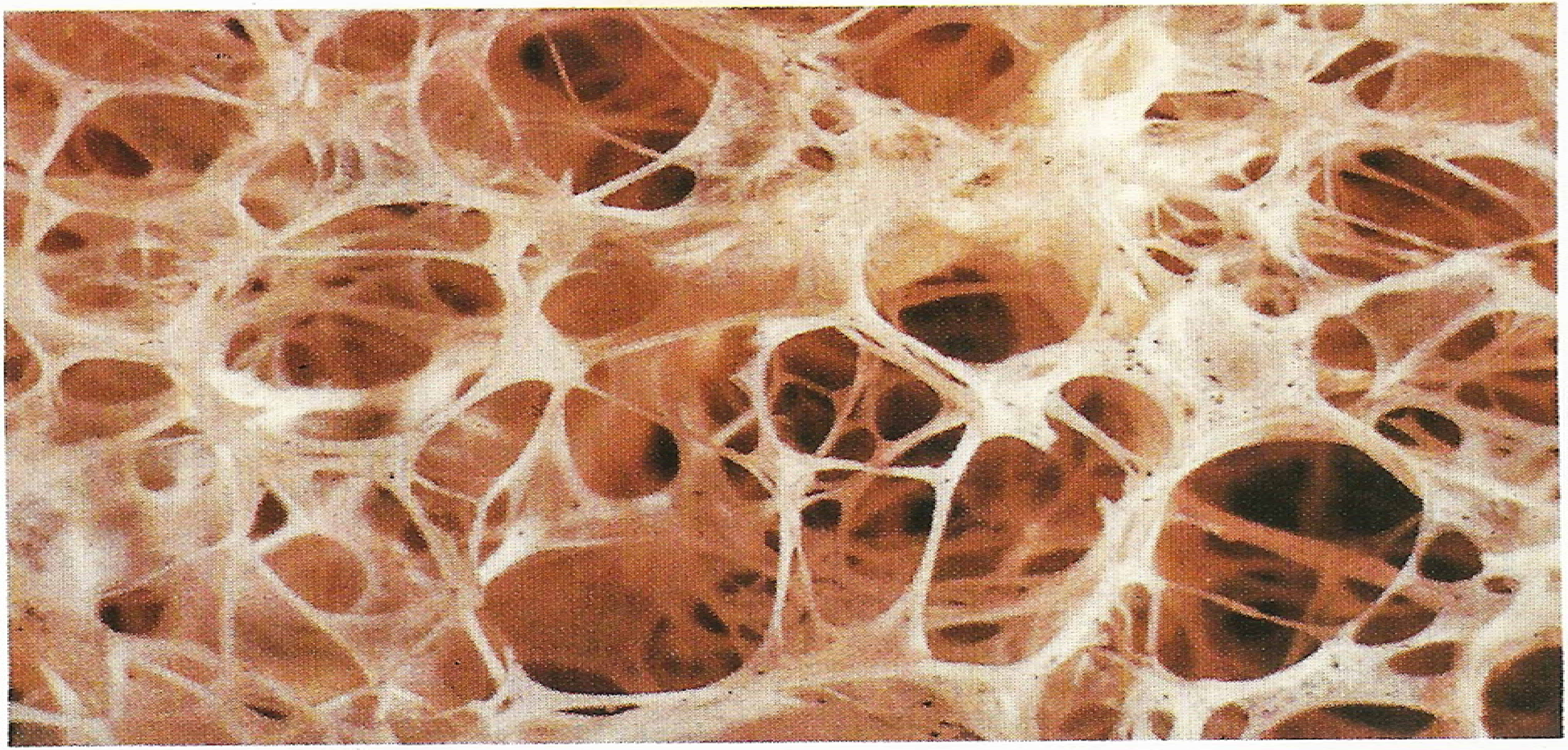
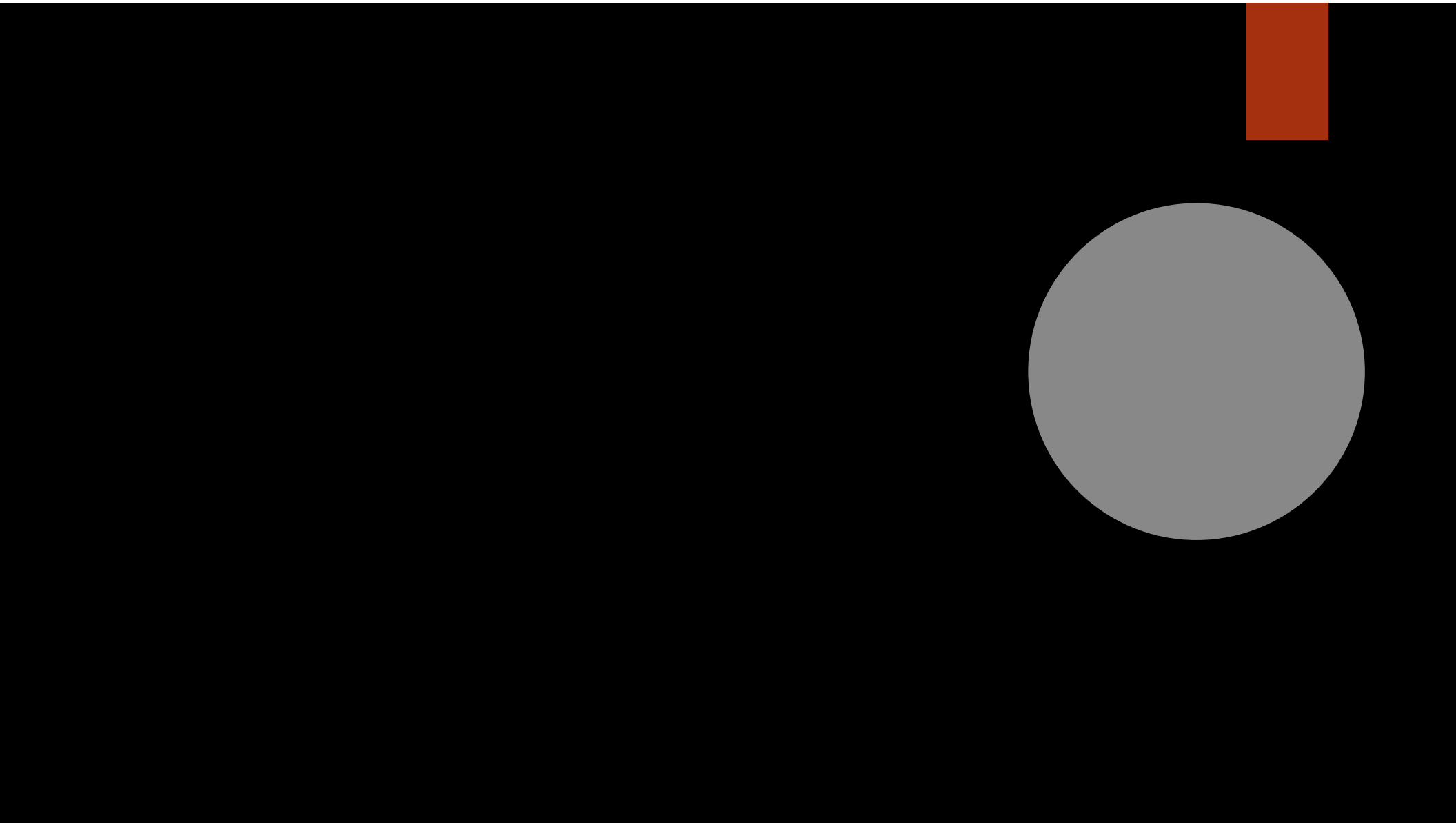
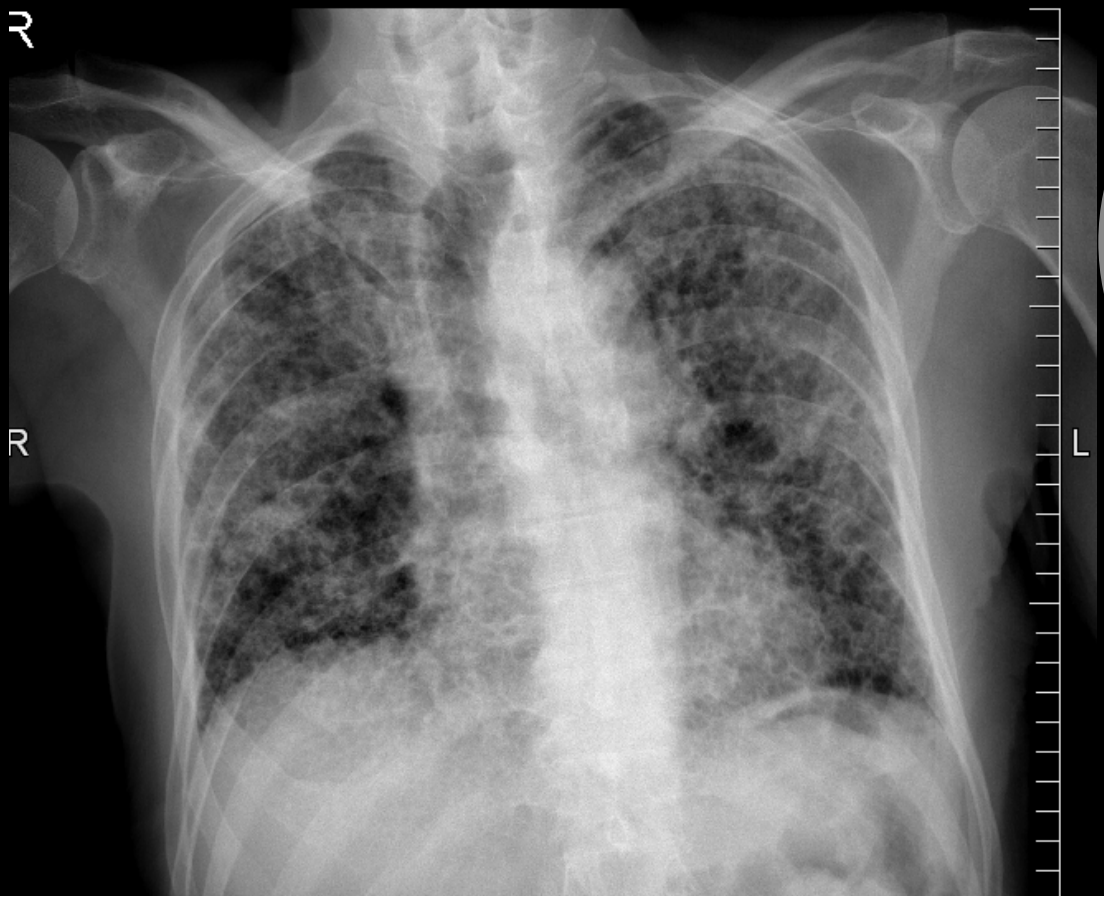


Fig. 9.24 Lung slice showing panacinar emphysema. Barium sulphate preparation. By courtesy of Dr B.E. Heard.

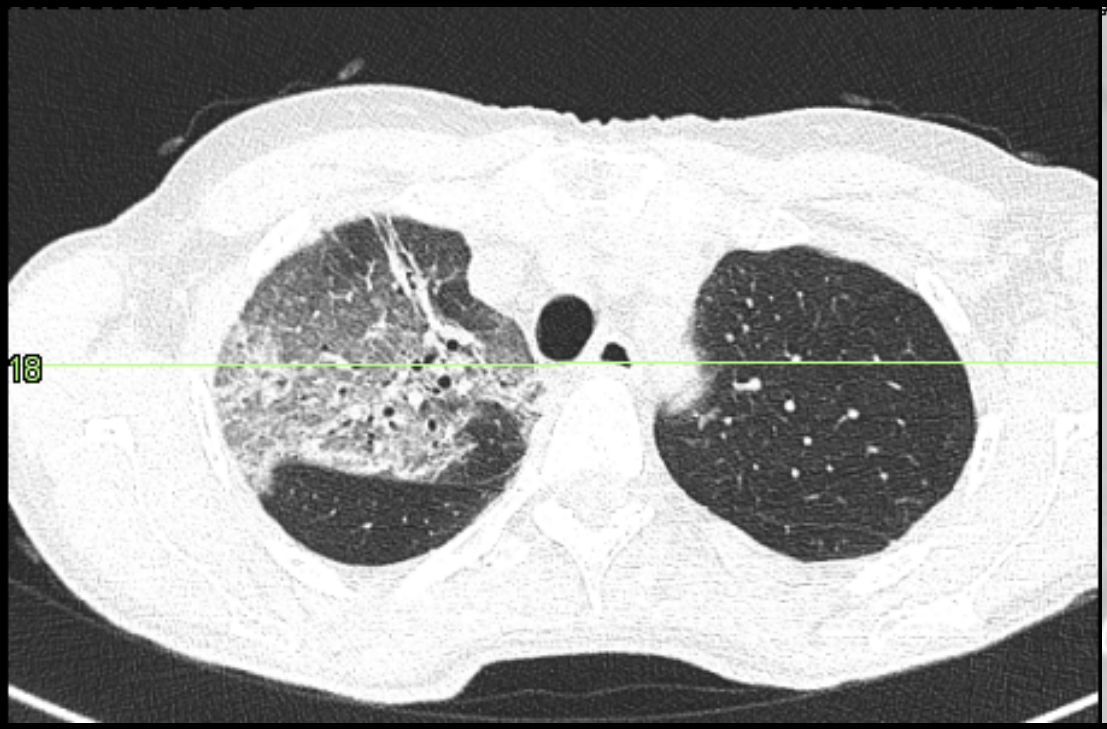
RLL Pneumonia

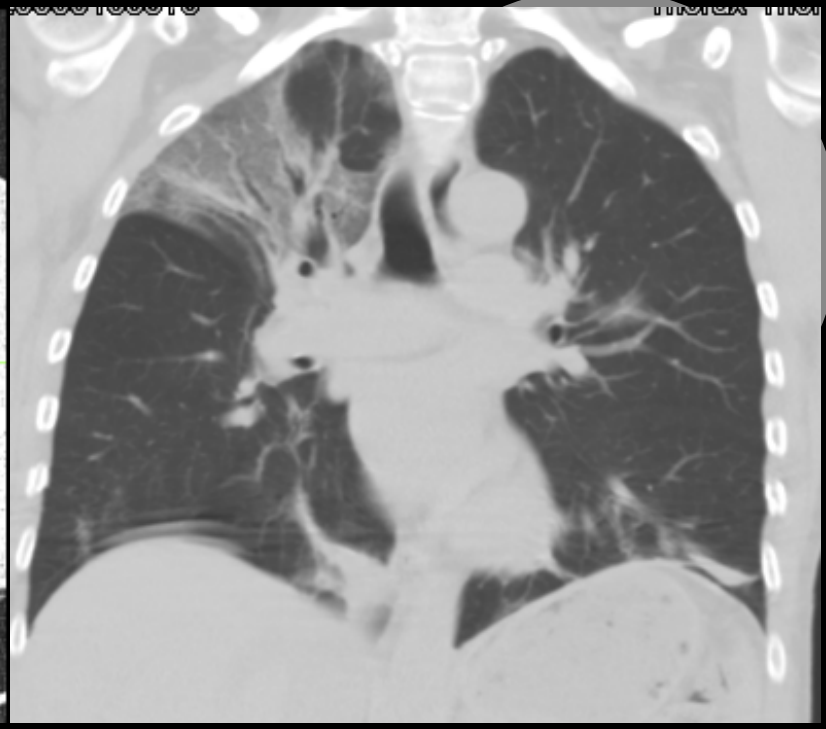


Idiopathic Pulmonary Fibrosis



RB-ILD





RB-ILD