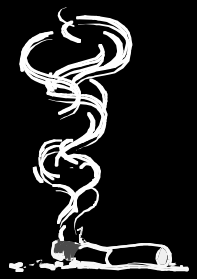
Smoking: What Happens to the Puff



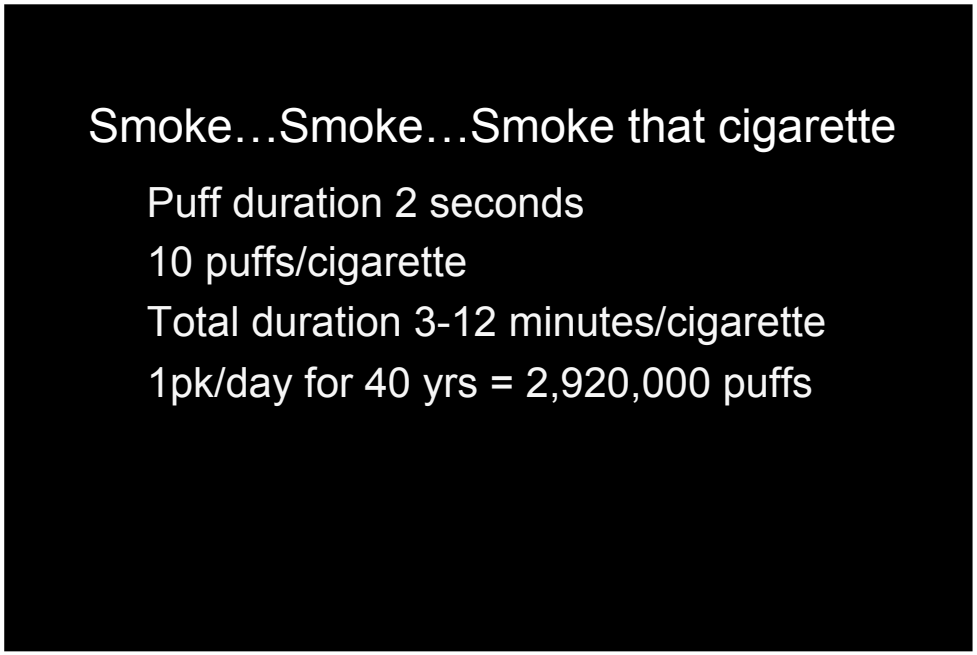
Jud W Gurney MD

Medical schools and residency training programs rarely talk about smoking. In this lecture, we will examine the habit, the puff and the respiratory consequences of smoking.

Objectives

- What are the components of the puff
- What are the four pathologic responses to the puff
- How does physiology affect the distribution of smoking related diseases

At the end of this lecture, you should be able to answer the following objectives.



The unit dose in cigarette smoking is the puff. A typical smoker accumulates nearly 3 million puffs.

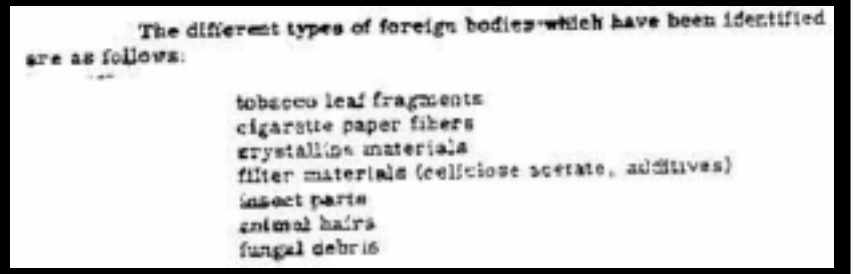
Puff

- 50 ml diluted in tidal volume 1000 ml
- Mean aerodynamic diam 0.46 mm
- Particulate concentration 10^{11}
- 50% deposited (9:1 lobule to airways)
- 1 pk/day 20 mg “tar”/cig = 6000 gm/40 yrs
- 300,000,000,000,000,000 particles

The puff contains gases and particulate material called tar. Inhaled particles are heterogeneous in size. Smaller particles deposit primarily within respiratory bronchioles. Total particulate dose is large.

from The Cigarette Papers 1959

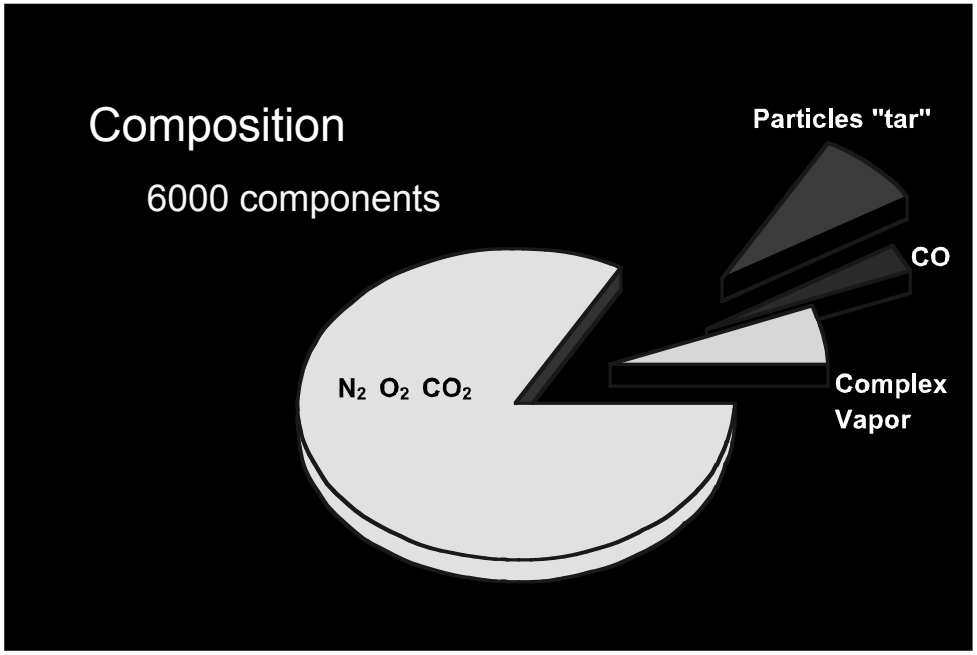
Brown & Williamson



The different types of foreign bodies which have been identified are as follows:

tobacco leaf fragments
cigarette paper fibers
crystalline materials
filter materials (cellulose acetate, additives)
insect parts
animal hairs
fungal debris

Cigarettes contain a wide variety of materials besides tobacco leaf. From the Brown & Williamson files, foreign bodies included insect parts, animal hairs, and fungal debris.

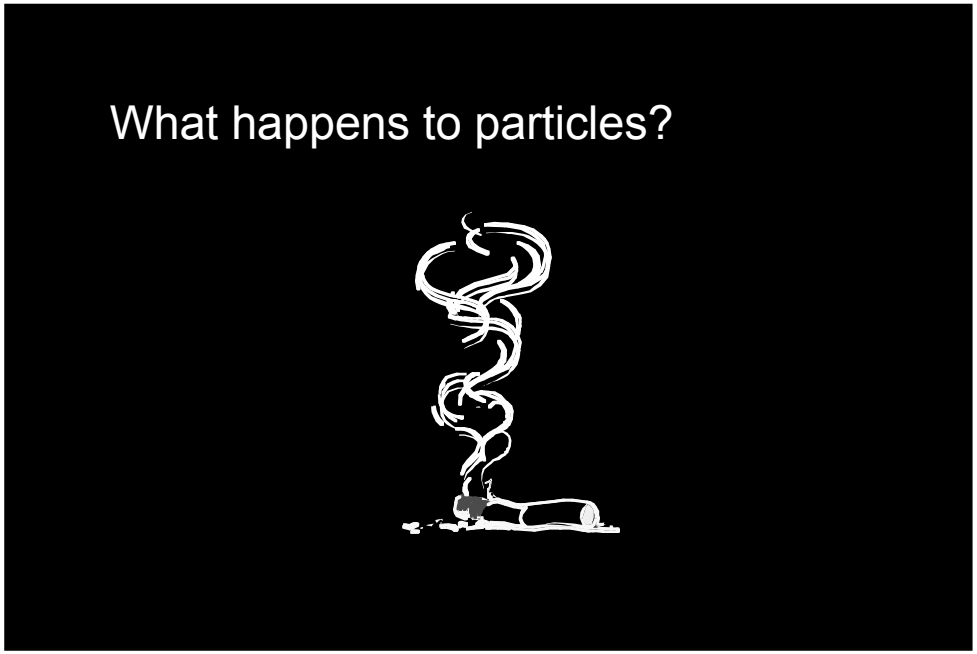


Tobacco burns at approximately 900 degrees centigrade. This combustions produces a wide variety of organic compounds, not all of which have been studied. The puff is mostly gas, including carbon monoxide, and particulate material called tar.

Components

- Plutonium, arsenic, lead, cadmium
- Hydrogen cyanide
- Formaldehyde
- Ammonia
- Methane
- Toluene
- Methanol
- Acetaldehyde
- Acetone

These well known poisons are all known constituents of the puff.



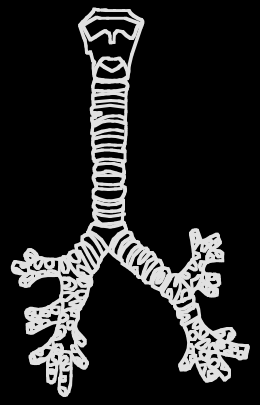
Let’s now turn our attention to what happens to the puffs constituents when inhaled.

What happens to particles?

	Central	Peripheral
Bronchus	Bifurcations	Respiratory
Volume	150 ml	4500 ml
Flow	High	None

Particles will deposit somewhere along the airways. Large particles deposit on the ciliated airways from impaction. Small particles less than 5 microns in size will suspend in air currents until they reach the respiratory bronchioles. At this point airflow markedly decreases and particles are deposited.

Central Airways



- High turbulent flow
- Deposition studied
  - Airway casts
  - Ferric oxide microspheres (1.7 - 12.2 mm)

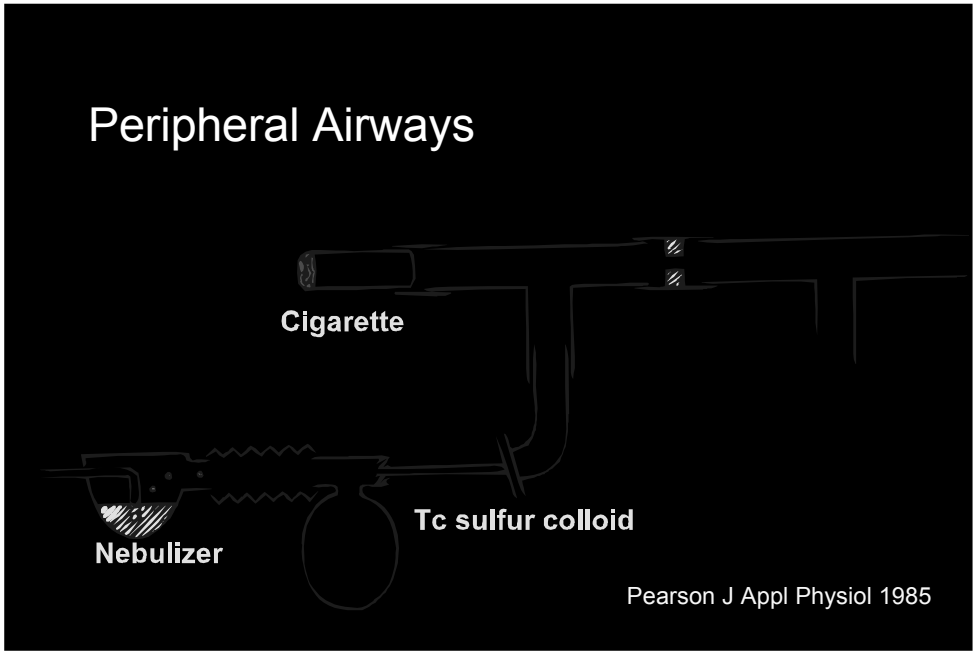
Central airway anatomy is complex. Airflow through these tubes produces complex turbulence. Particle deposition is generally studied using airway casts with varying size particles.

Distribution

Lobe	Deposition %	Origin Cancer
RUL	31.4	33.5
RML	6.2	7.5
RLL	18.6	19.4
LUL	29.6	26
LLL	14.2	13.6

Schlesinger & Lippman Am Ind Hyg Assoc J 1972

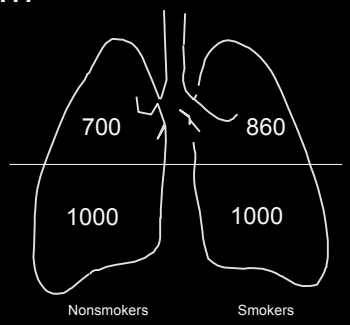
Such studies show that most particles are deposited in the upper lobe airways at bifurcation points. Note the concordance between this experimental data and the historical frequency of the origin of central lung cancers.



Studying particulate deposition in the peripheral airways is more difficult. This typical smoking apparatus adds a nebulized radionuclide particle to the puff.

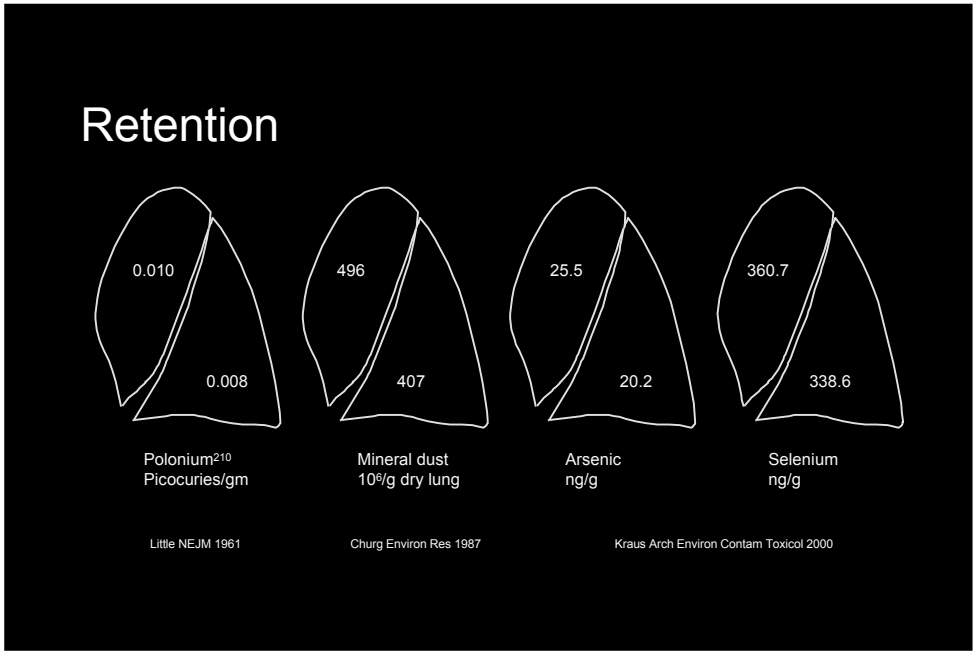
Cigarette aerosol study

- Median diam 0.78 mm
- Apex/base ratio
  - Control 0.69
  - Smoking 0.86



Pearson J Appl Physiol 1985

Small particles are deposited in the bases. This conforms to pulmonary physiology where the lower lobes are better ventilated. Compared to nonsmoking controls, smoking skews the deposition towards a more uniform deposition, however, more particles accumulate in the lower lobes.



Deposition is only one aspect of how the lung handles particles. Once deposited particles are gradually removed. The chronic retention of particulate material can be determined by autopsy examination of different elements. Even though the analyses involve different methods, the results are remarkably similar. Particles tend to accumulate over time in the upper lobes, approximately 1.25 times that of the lower lobes.

Lymphatic removal

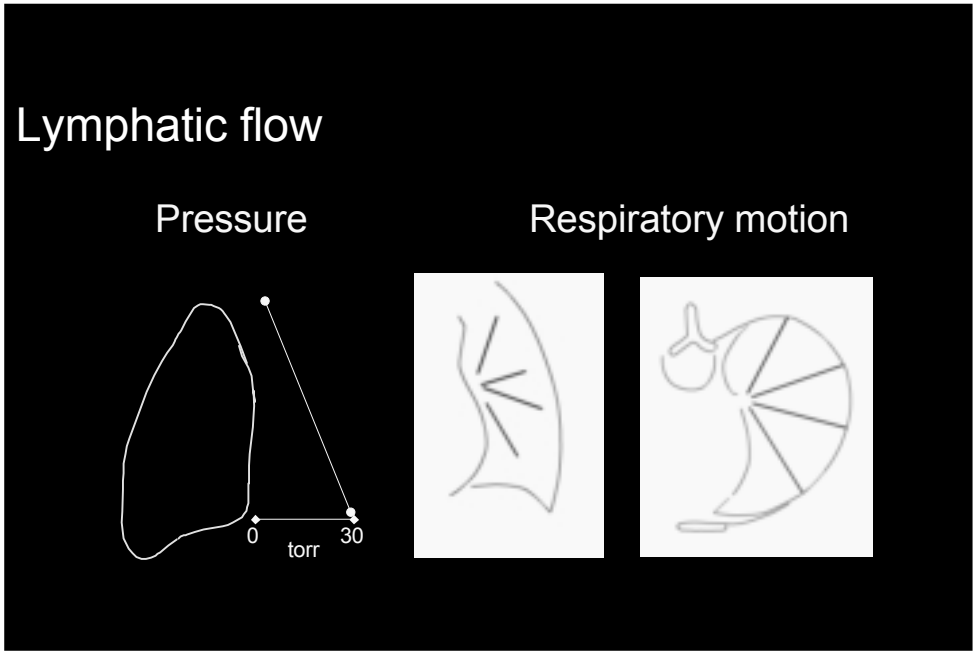
Flow:

Arterial pressure

Respiratory motion

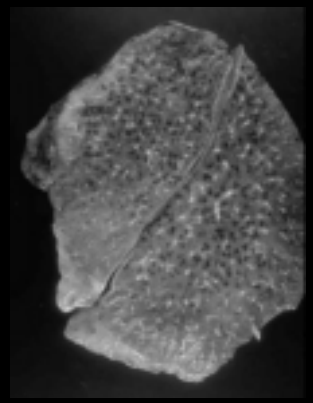
Nagaishi Functional anatomy and histology of the lung 1972

Note that the respiratory bronchiole and alveolar unit are devoid of lymphatics. The lung lymphatics are composed of two systems, one along the bronchovascular bundle and the second peripheral system along the pulmonary veins. What happens to particles that reach the respiratory bronchioles? Well they can be absorbed or engulfed by macrophages. Some are trapped forever. Those particles which can be engulfed by macrophages are removed through the lymphatics (or migrate to the terminal bronchiole and escape via the cilia). As we've seen, removal of particles is slow. Lymphatic flow is, in part, determined by arterial pressure and respiratory motion, which aids lymphatic flow.

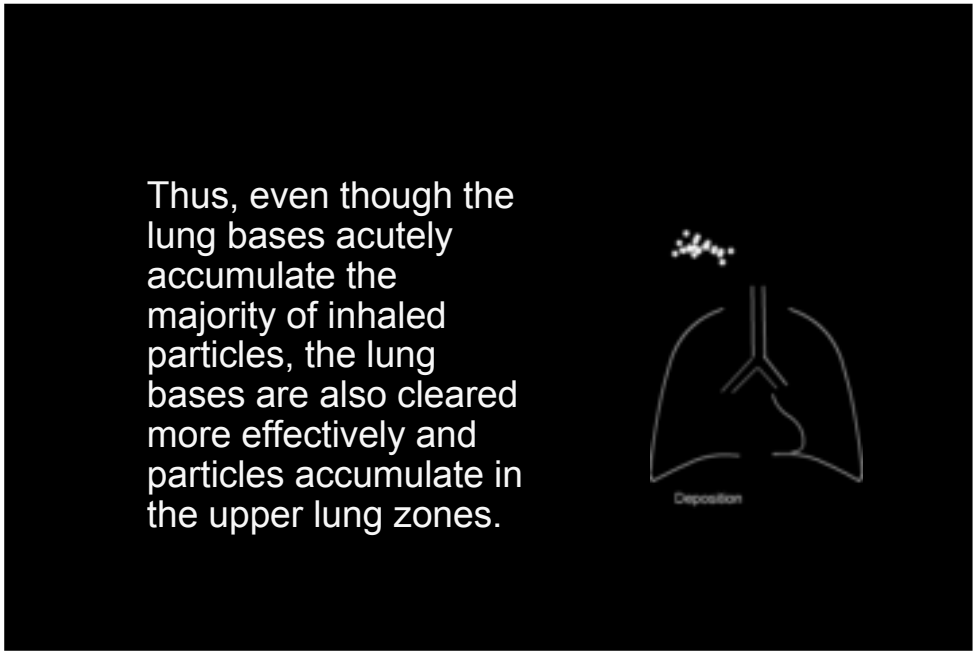


Arterial pressure is nonuniform, the low pressure pulmonary artery system is linearly affected by gravity. Normal pulmonary pressure is just sufficient to perfuse the apex of the lung, thus the driving pressure for lymphatic flow will diminish towards the lung apex. In addition, passive respiratory motion is nonuniform, the lung bases and the anterolateral portion of the lung undergoes greater degree of respiratory expansion than the apices and dorsal aspect of the lung.

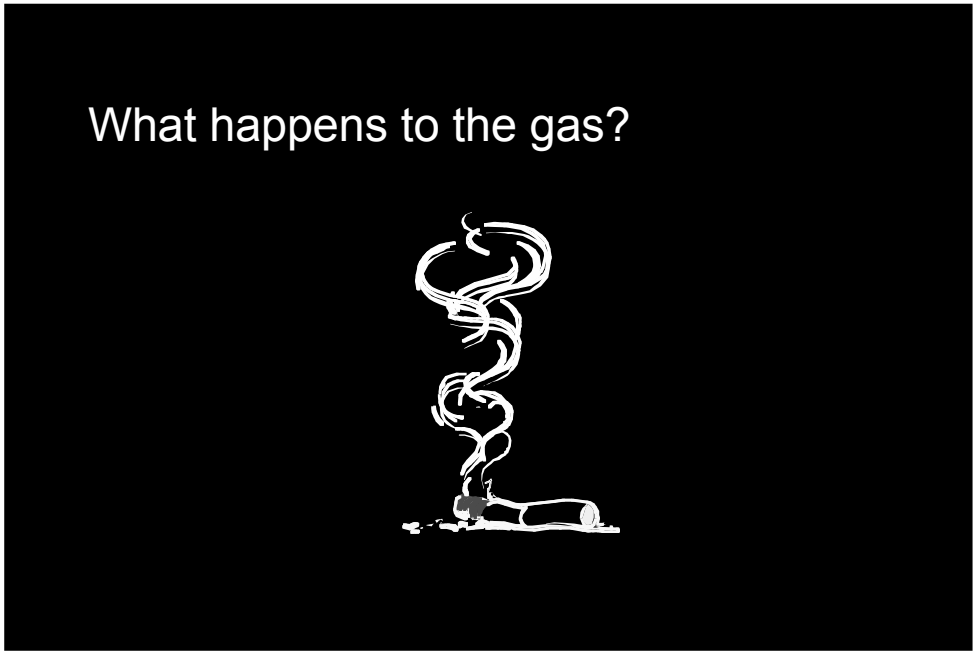
True distribution unknown



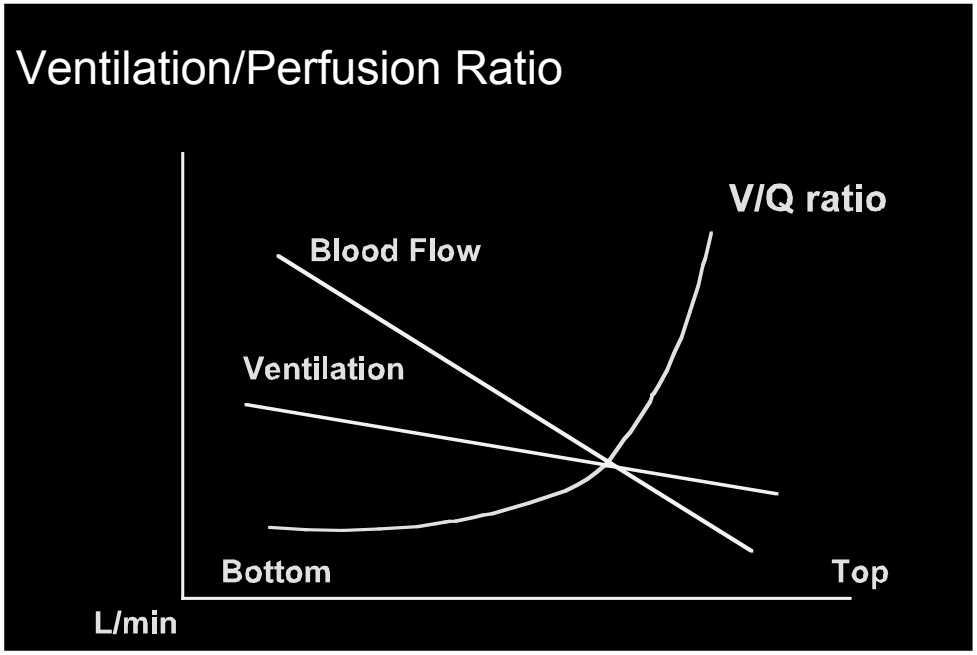
If gravity is important in the distribution of dusts and particles in the lung then the anatomical analysis used in these investigations is the incorrect method. For example, in a sagital section of the lung, the lower portion of the upper lobe and the upper portion of the lower lobe occupy the same gravitational plane, thus an analysis based on traditional anatomic boundaries will blur the true distribution of particulate material in the lung. The correct analysis will bread loaf the lung, much as we do with CT. Note that in this lung, pigmentation gradually diminish toward the base. Note the degree of pigmentation in the superior segment of the lower lobe is the same as the upper lobe.



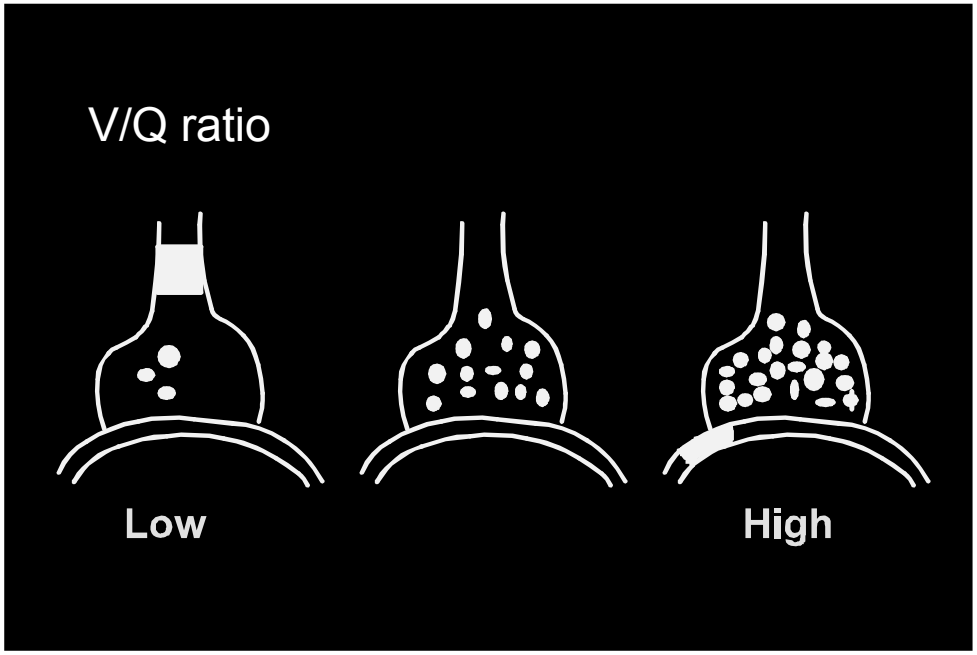
Chronically, particles tend to accumulate in the upper lung zones. This is true of most of the dust diseases, from silica and coal, and as will we see, the smoking related diseases.



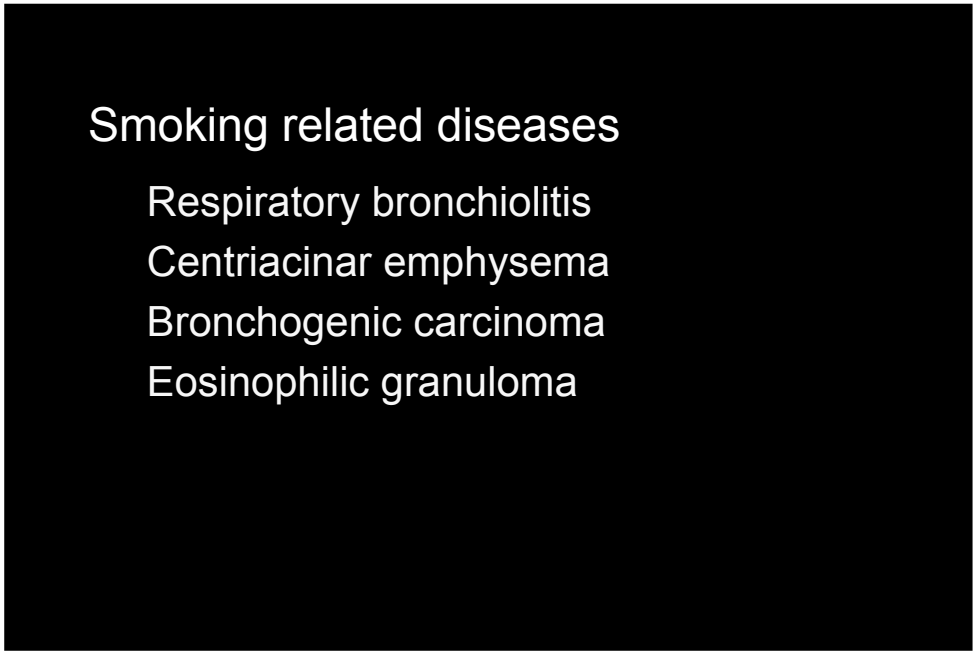
Harmful substances are also contained in the gas. Let’s quickly examine how the lung handles this gaseous component.



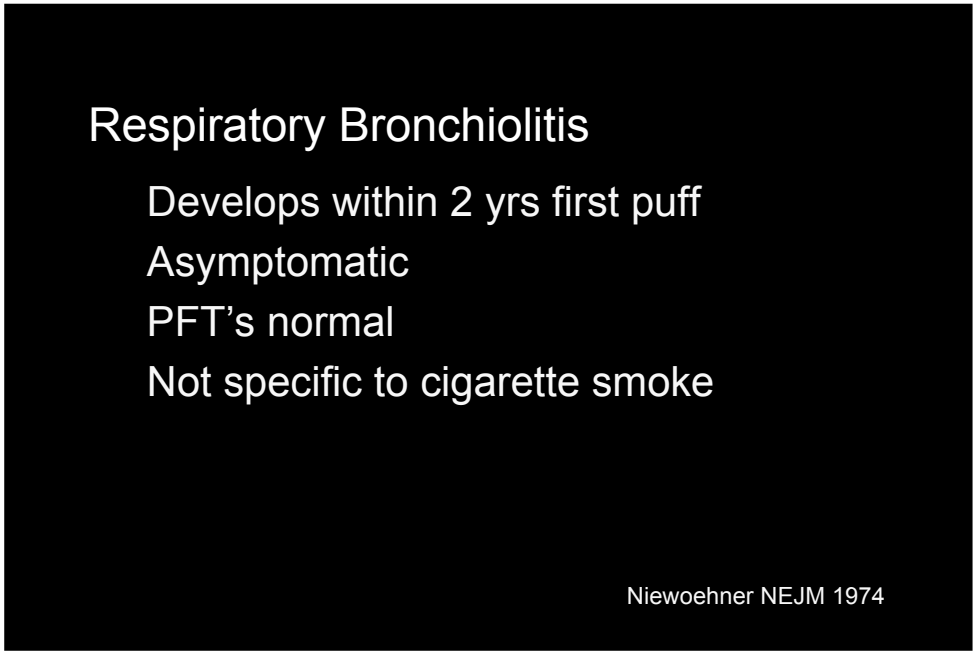
The concentration of gas in the alveolus depends on the linear relationship between blood flow and ventilation. Both are affected by gravity, higher at the base in the upright lung. Because the rate of change between blood flow and ventilation differs in the upright lung, the V/Q ratio is highest in the upper lung zones.



This diagram illustrates the extreme, no ventilation or no perfusion. As the V/Q ratio increases the concentration of inhaled gas also increases



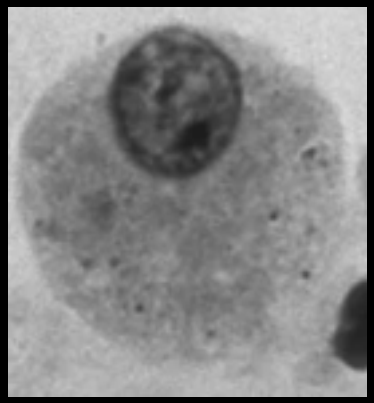
We will examine four diseases related to the harmful products in the puff.



Respiratory bronchiolitis was first described in young victims of motor vehicle accidents. This pathologic condition develops within 2 years of the first puff. The majority of patients are asymptomatic and have normal pulmonary function. This significance of this lesion is unknown. The condition is not specific to cigarette smoke but is seen with other dust pollutants.

Pathology

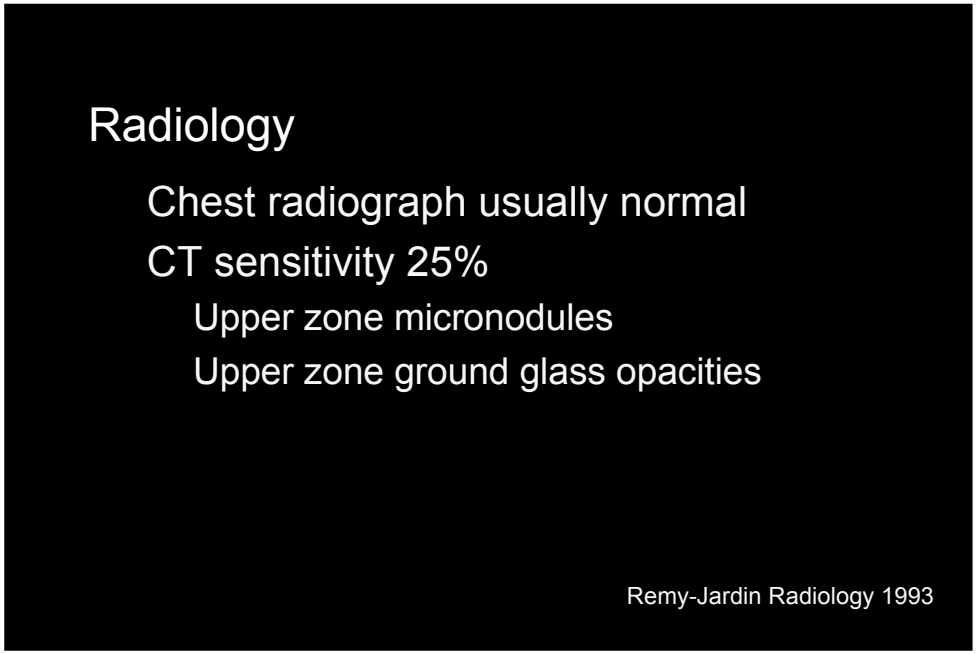
- Pigmented macrophages
- Centered on respiratory bronchioles



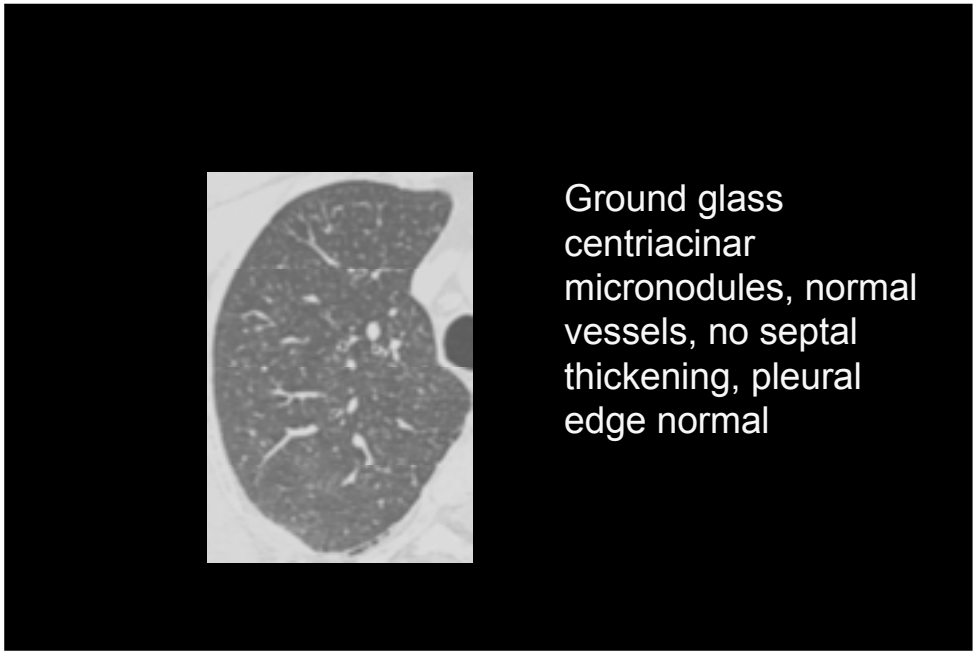
The hallmark is the pulmonary macrophage. This one is stuffed with particulate yellowish-brown material.

‘Clustered dirty macrophages associated with epithelial hyperplasia that extends into adjacent alveolar walls in a stellate fashion”

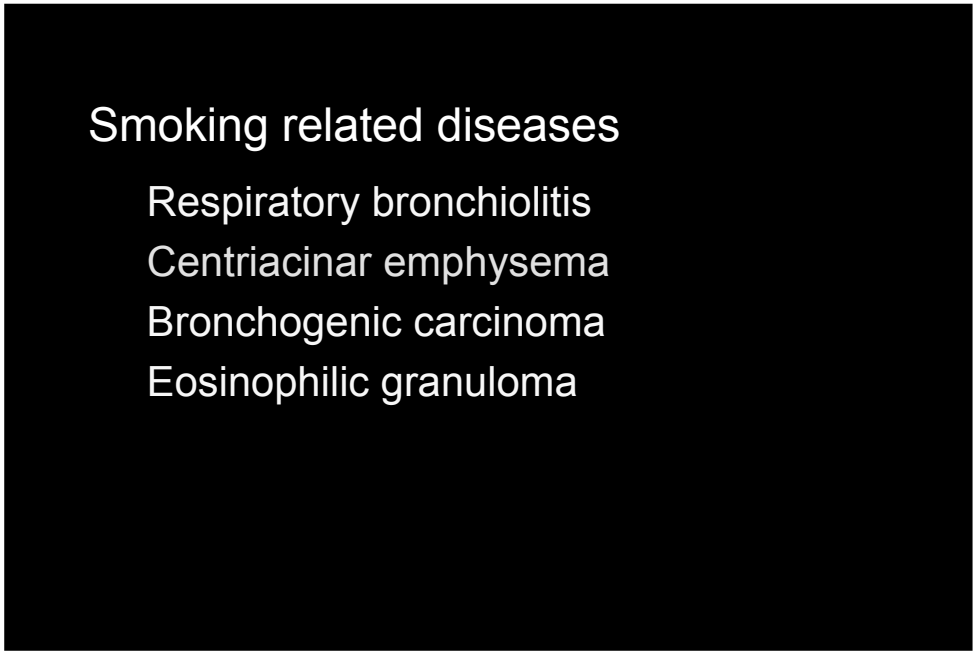
In this example, macrophages are clustered in the wall of the respiratory bronchiole, the adjacent arteriole is on the left



Chest x-rays are typically normal. Even though all smokers have respiratory bronchiolitis, even HRCT is insensitive for this condition.



The nodules have a centriacinar distribution. A perilymphatic distribution would demonstrate beading of the vessels, involvement of the subplueral lung, fissures, and septa.



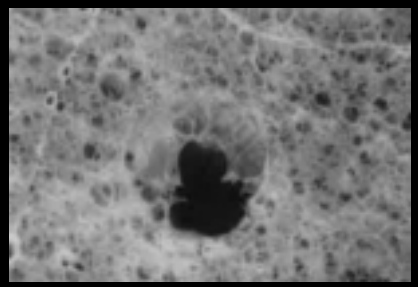
Let’s now turn to centriacinar emphysema and compare and contrast this disease with respiratory bronchiolitis.

Centriacinar emphysema

- Long term smokers
- Dose and time dependent
- 100% (> 40 pk/yrs)
- Average age @ diagnosis 64
- Usually asymptomatic < 30% destruction

This common disorder is dose and time dependent. A large portion of the lung must be destroyed before symptoms occur. Most patients with emphysema are asymptomatic.

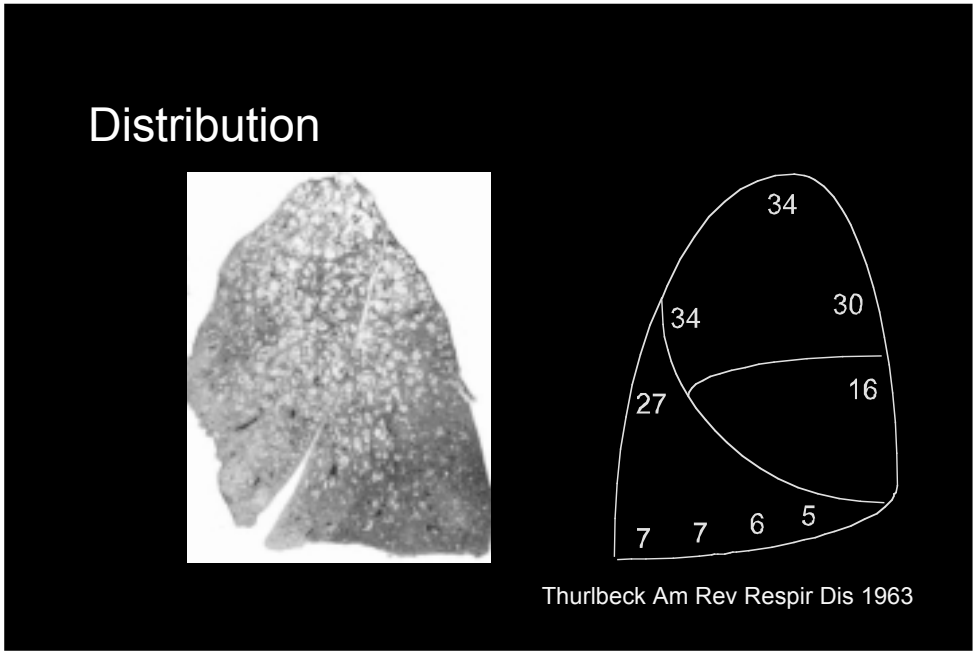
Pathology



Centered in respiratory bronchioles

"Permanent enlargement of any part of the acinus, accompanied by destruction of respiratory tissue"

Centriacinar emphysema is the dilatation and destruction of the respiratory bronchiole. In this pathologic example of a portion of the secondary pulmonary lobule, septa are visible along the top and left side of the illustration. The smaller holes are normal alveolar sacs.

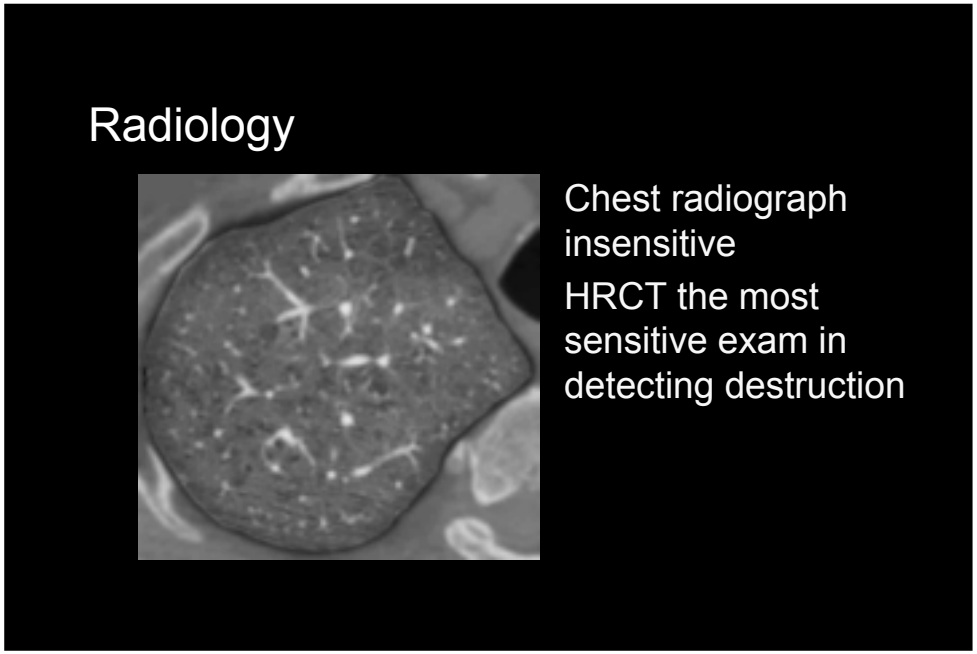


Again this is a disease of the upper lung zones. Note the vertical distribution equally involving the upper and lower lobes at any given level.

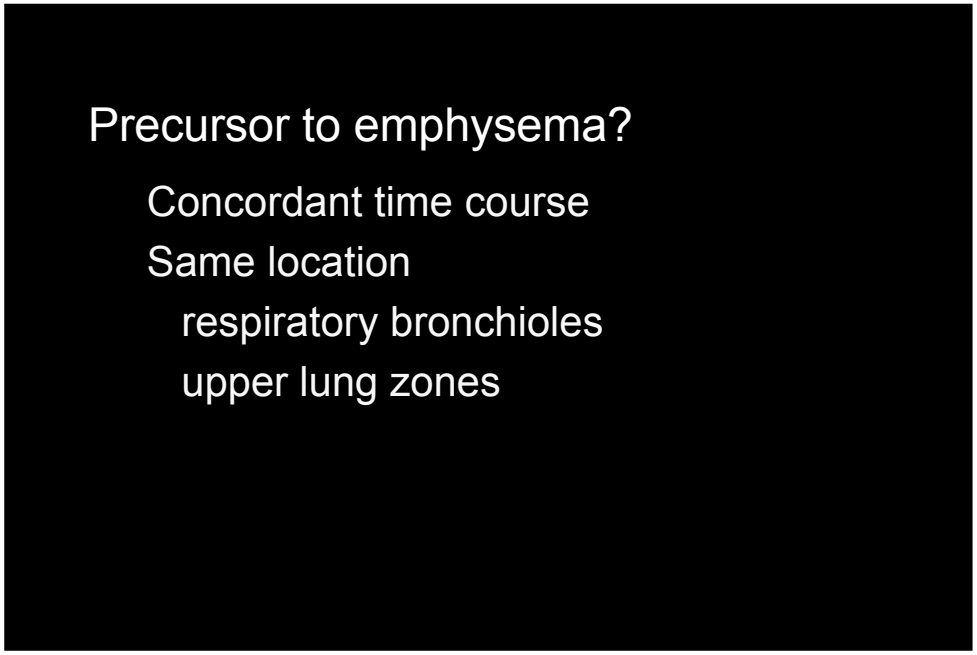
Neutrophils

Proteolytic reaction to activated neutrophils which release elastases and oxygen radicals

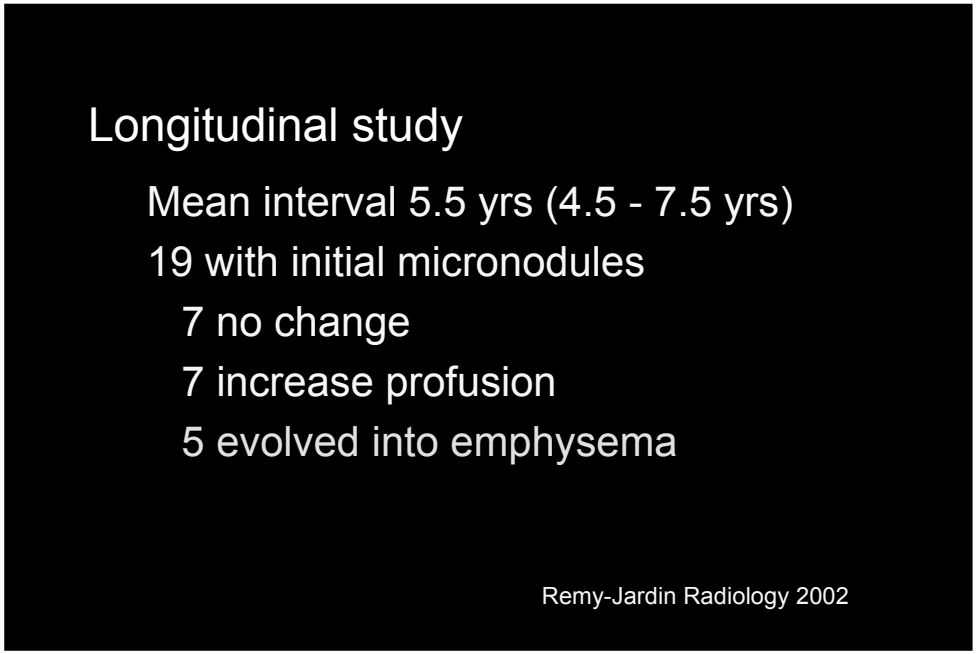
Animal models use trypsin to produce similar lesions. Neutrophils are considered the culprit because these cells are rich in elastases and proteases.



Chest x-rays are insensitive for emphysema. HRCT is the most sensitive radiographic exam. Note the holes have no discernable walls.



Respiratory bronchiolitis and centriacinar emphysema were juxtaposed for this reason. Are they related? One occurs early and the other late in the natural history of smoking. The location and distribution of pathology are identical in each. Respiratory bronchiolitis is composed of inflammatory cells. Confirmation of this hypotheses would require a longitudinal study of smokers with HRCT.

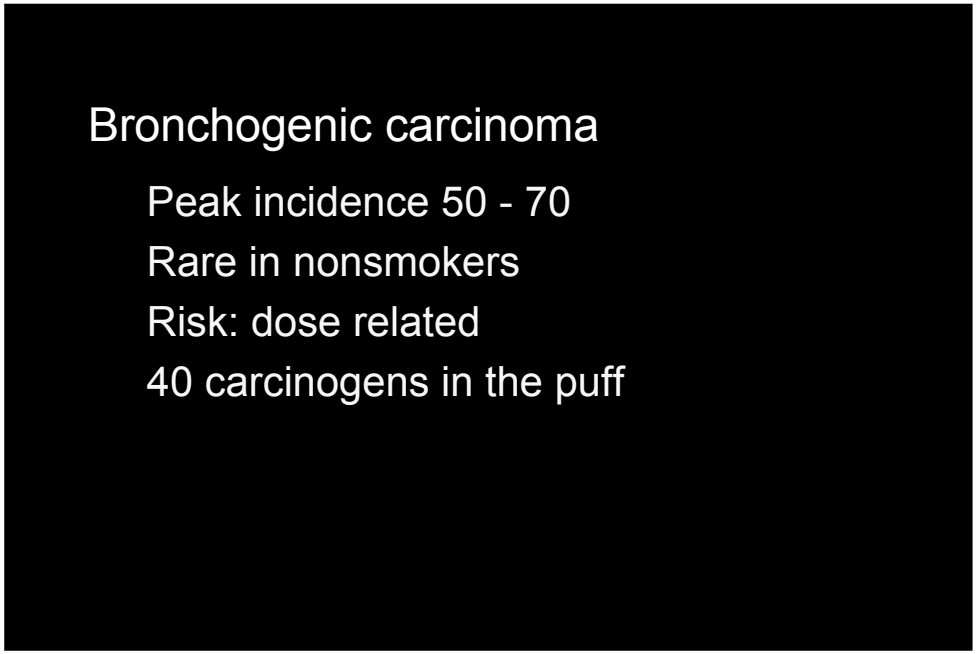


There is now good evidence that indeed respiratory bronchiolitis is the precursor of emphysema. In a longitudinal study of smokers, micronodules (in the upper lung zones) evolved into emphysema.

Smoking related diseases

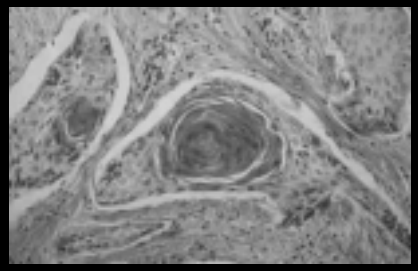
- Respiratory bronchiolitis
- Centriacinar emphysema
- Bronchogenic carcinoma
- Eosinophilic granuloma

Bronchogenic carcinoma is the leading cause of cancer death in both men and women. 90% are related to smoking.



Over 40 carcinogens are identified in the puff. The latent period between the onset of smoking and the development of lung cancer is generally 30 - 50 years.

Pathology

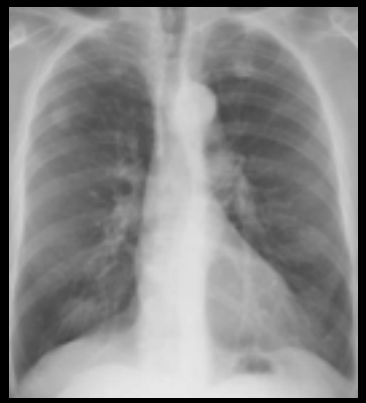


Squamous cell: central airways,

Adenocarcinoma peripheral lung

Thgough the 1980's, squamous cell carcinoma was the most common histologic type. Primarily involving the central lobar and segmental airways. Since then, adenocarcinoma, usually a peripheral SPN has become the most common subtype. Why the change, In response to the health effects of smoking, tobacco companies introduced the filtered ('safer') cigarette in the early 1950's. By the mid 50's, the filtered cigarette had become the most popular form of tobacco consumption. The filter only removed the largest particles, those that because of their size impacted on the central airways, leaving the small particles to be deposited in the smaller airways in the lung periphery.

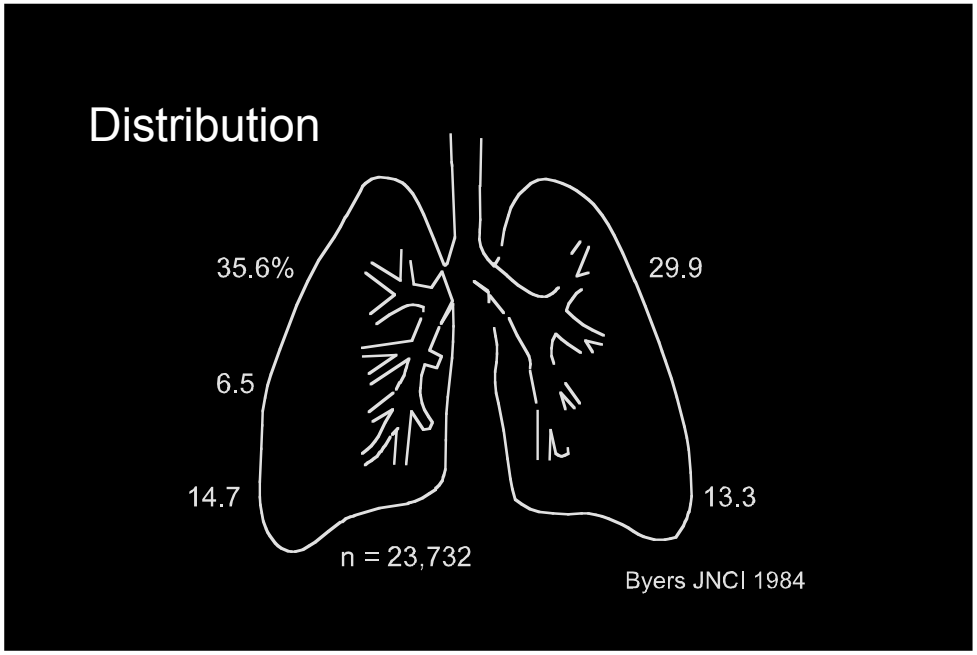
Radiology



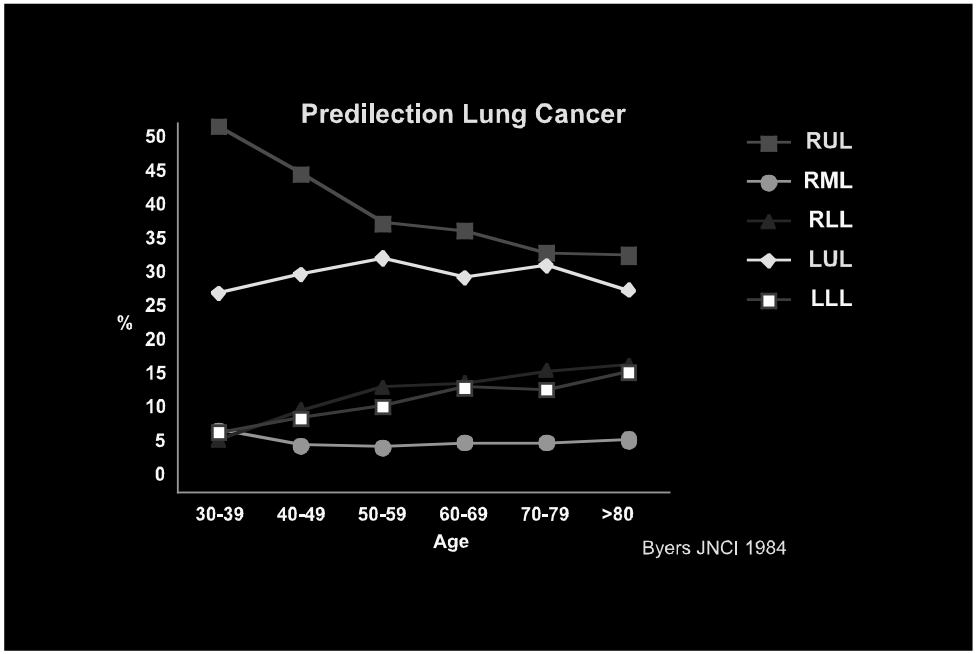
Peripheral: SPN

Central: airway obstruction

The radiographic manifestations are many. In general, they can be divided into peripheral tumors which present as SPN's or central tumors which obstruct the airways.



Similar to the other smoking related diseases. The distribution primarily affects the upper lobes, particularly the right.

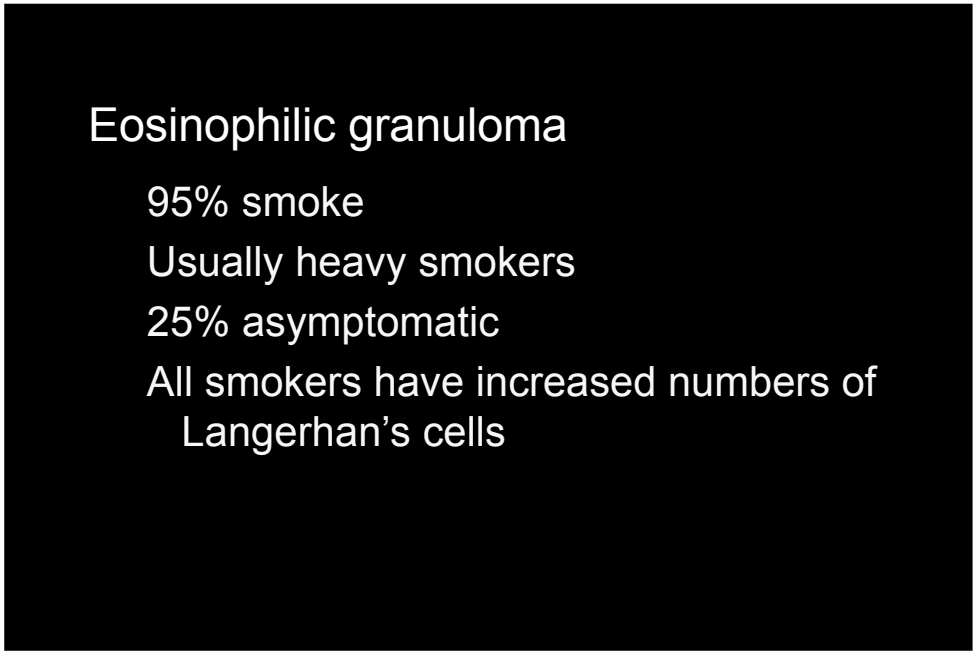


The predilection for the upper lobes, especially the right upper lobe is most pronounced in the young individual. Note that the gap between the upper and lower lobes gradually narrows with age.

Smoking related diseases

- Respiratory bronchiolitis
- Centriacinar emphysema
- Bronchogenic carcinoma
- Eosinophilic granuloma

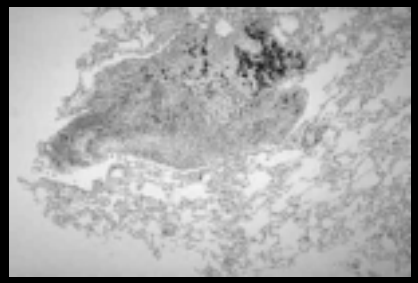
Eosinophilic granuloma is an interesting disorder now thought to be related to smoking related.



Over 95% of patients with EG smoke. This disease usually occurs in the younger - heavier smokers. Curiously 25% of cases are asymptomatic, discovered on chest radiographs obtained for other reasons. This high percentage suggests that the disease is more common than appreciated. All smokers have increased numbers of Langerhan's cells in the lung even though they don't have EG.

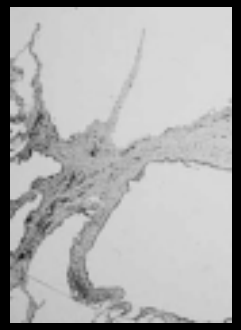
Pathology

Granuloma contains Langerhan's cell.



The Langerhans cell normally resides in the lung, skin, and reticuloendothelial system. It is an antigen processing cell. In this granuloma the Langerhans cell stains black with S-100 protein.

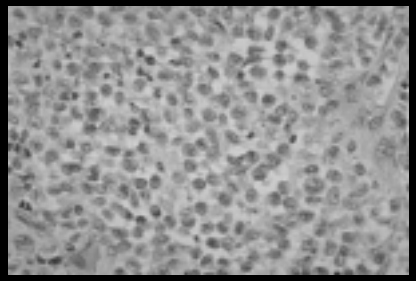
Pathology



“discrete, roughly symmetric stellate lesions with central scarring and cellular peripheral tentacles”

The granulomas of EG have tentacles, similar to a starfish.

Allergic reaction?



Langerhan cell is an antigen processing cell, granulomatous reaction similar to other allergic patterns.

EG may be an allergic reaction to some constituent of the puff. Evidence includes, the role of the Langerhans cell in processing antigen and the granulomatous response similar to other allergic pathologies.

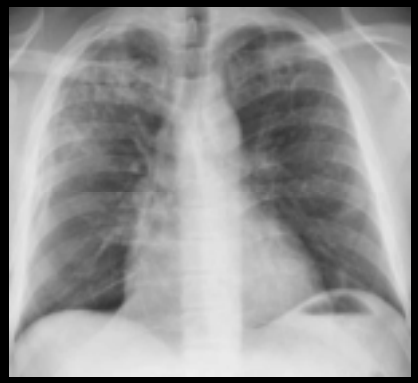
Allergen

TGA known potent allergen

Birbeck granules - Soil?

The allergen is unknown. One pathology report links the Birbeck granule, shown here, with a component of the soil that the tobacco plant grows in.

Radiology

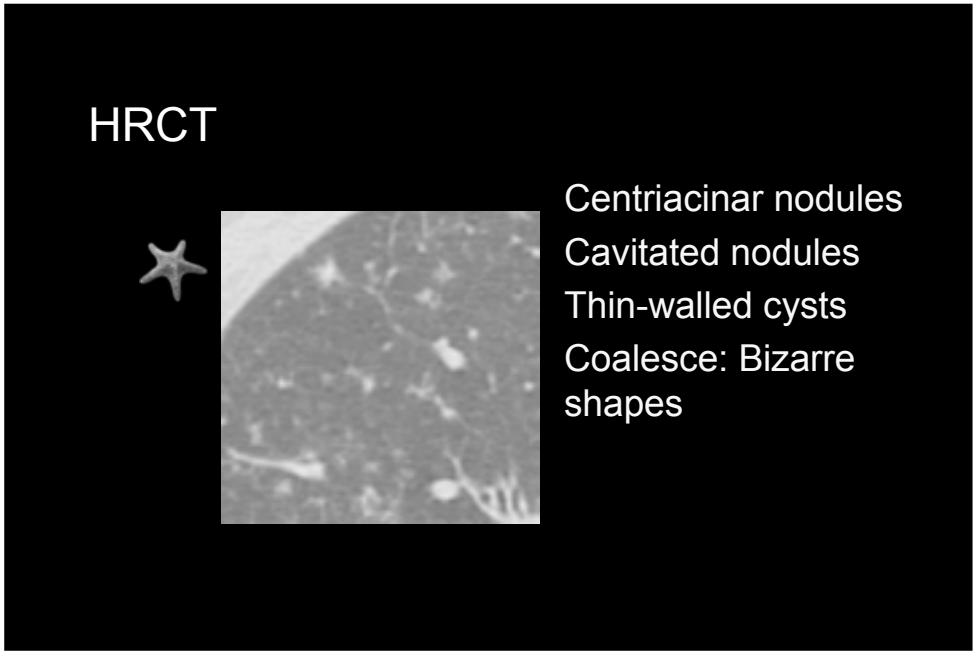


Lung volumes normal or increased

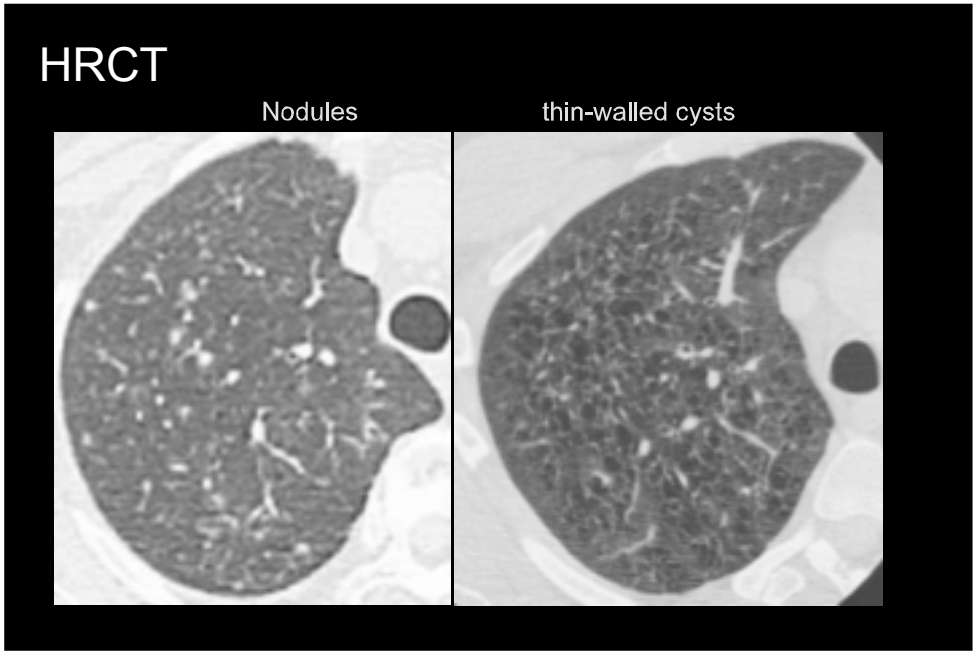
Prefers mid-upper lung

Pattern: nodules or honeycombing

The disease primarily involves the mid and upper lung zones. The pattern is that of nodules or honeycombing. In contrast to other interstitial lung diseases, the lung volumes are normal or increased. Many patients present with spontaneous pneumothorax, as did this patient.

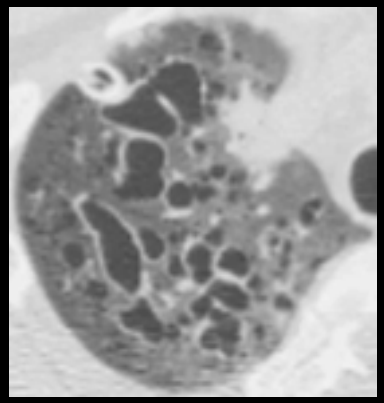


The nodules in EG are centriacinar in distribution. As they get larger they may have tentacles.



Centriacinar nodules are thought to evolve into thin-walled cysts. These examples are from different patients.

HRCT



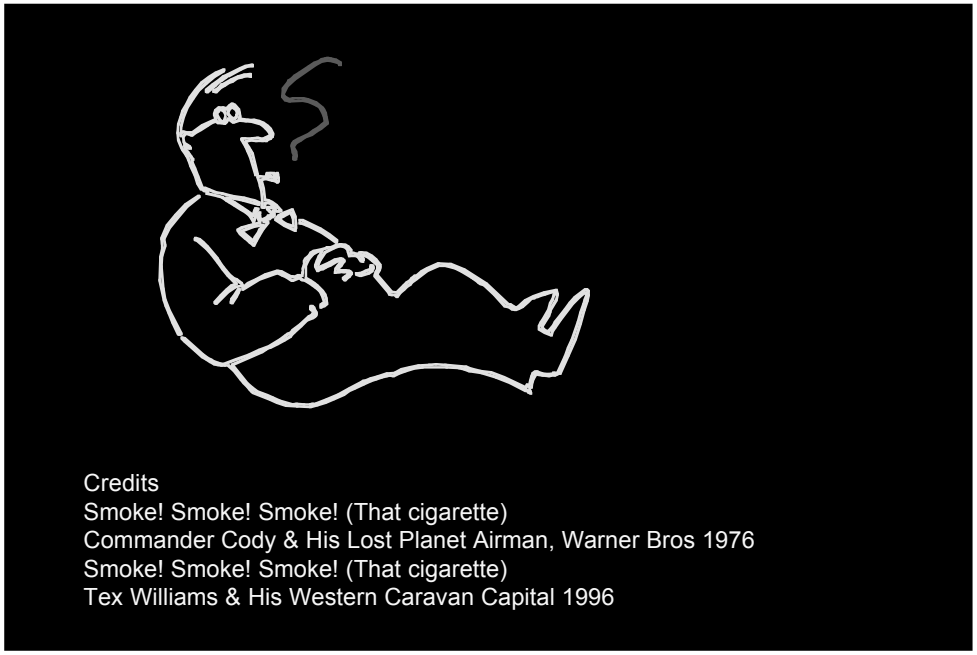
Bizarre shapes

Cysts may aggregate and form shapes which are bizarre, this is nearly pathognomonic of EG. Note the chest tube anteriorly.

Smoking related disease

	Respiratory Bronchiolitis	Centriacinar Emphysema	Bronchogenic Carcinoma	Eosinophilic Granuloma
Age	25	60	50 - 70	32
Prev %	100	100	10	<1
Pathology	Pigmented Macrophage	Neutrophil	Malignant cell	Langerhan cell
Distribution	Upper Lung	Upper Lung	Upper Lung	Upper Lung

The puff produces a wide variety of responses in the lung. The distribution is similar and reflects how the lung handles gas and particulate material.



Thanks for stopping by.