



The Royal College of **Pathologists**

Pathology: the science behind the cure

## **Guidelines on autopsy practice**

### **Industrial/occupational-related lung disease deaths including asbestos**

**June 2017**

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and Cardiff University  
Dr Allen Gibbs, Cardiff & Vale University Health Board

# Declaration

Dr Richard Attanoos and Dr Allen Gibbs serve as medical experts in asbestos injury claims for claimants, defendants and on joint basis.

## REACTIONS TO OCCUPATIONAL/ENVIRONMENTAL AGENTS

REACTION	AGENT
ASTHMA	ISOCYANATES, METALS
BRONCHIOLITIS	NITROGEN DIOXIDE
NODULAR PNEUMOCONIOSIS	COAL, SILICA, SILICATES
DIFFUSE INTERSTITIAL FIBROSIS	ASBESTOS
GRANULOMATOUS	BERYLLIUM
DIFFUSE ALVEOLAR DAMAGE	TOXIC FUMES
G.I.P.	HARD METAL
ALVEOLAR PROTEINOSIS	SILICA
EMPHYSEMA	COAL, CADMIUM
PLEURAL PLAQUE/FIBROSIS	ASBESTOS
LUNG CANCER	ASBESTOS, NICKEL, ARSENIC, CHROMIUM
MESOTHELIOMA	ASBESTOS

# ASBESTOS

Mineralogy

Spectrum of Disease

Handling of Post Mortem

# ASBESTOS - MINERALOGY

- Natural hydrated fibrous silicates: 2 mineral groups

## COMMERCIAL APPLICATIONS

Amphibole

Serpentine

Crocidolite } 10%

Amosite }

Chrysotile – 90%

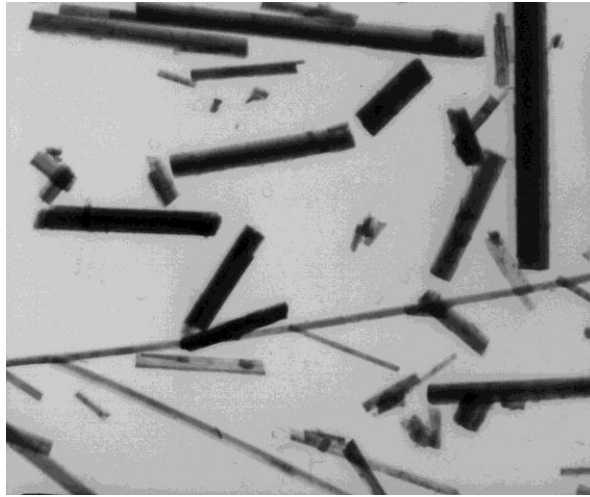
Anthophyllite

Tremolite

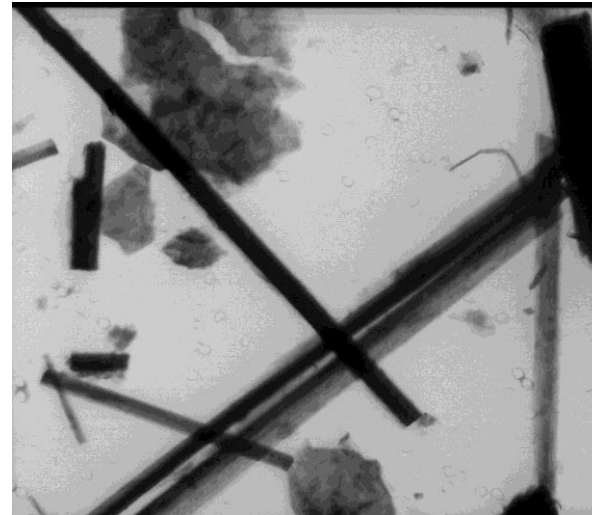
Actinolite

**Physical, Chemical, Biological Differences → Different Toxicity**

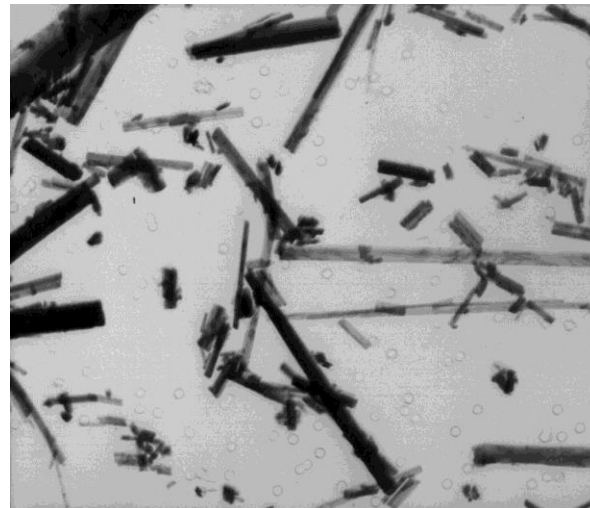
AMPHIBOLES – PHYSICAL TEM Non Fibrillar Types – Straight rigid fibres



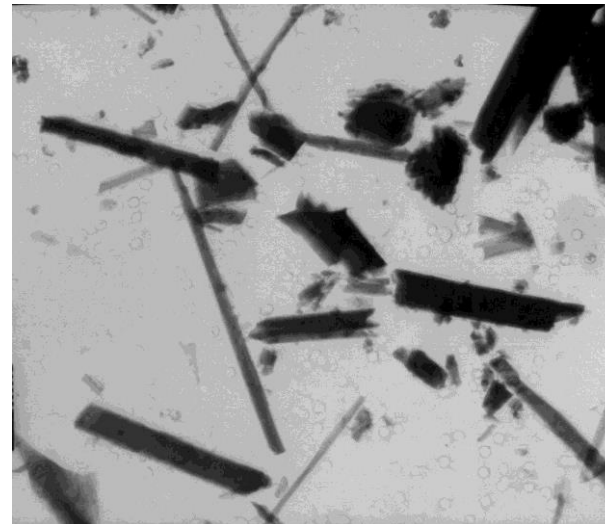
AMOSITE



ANTHOPHYLLITE

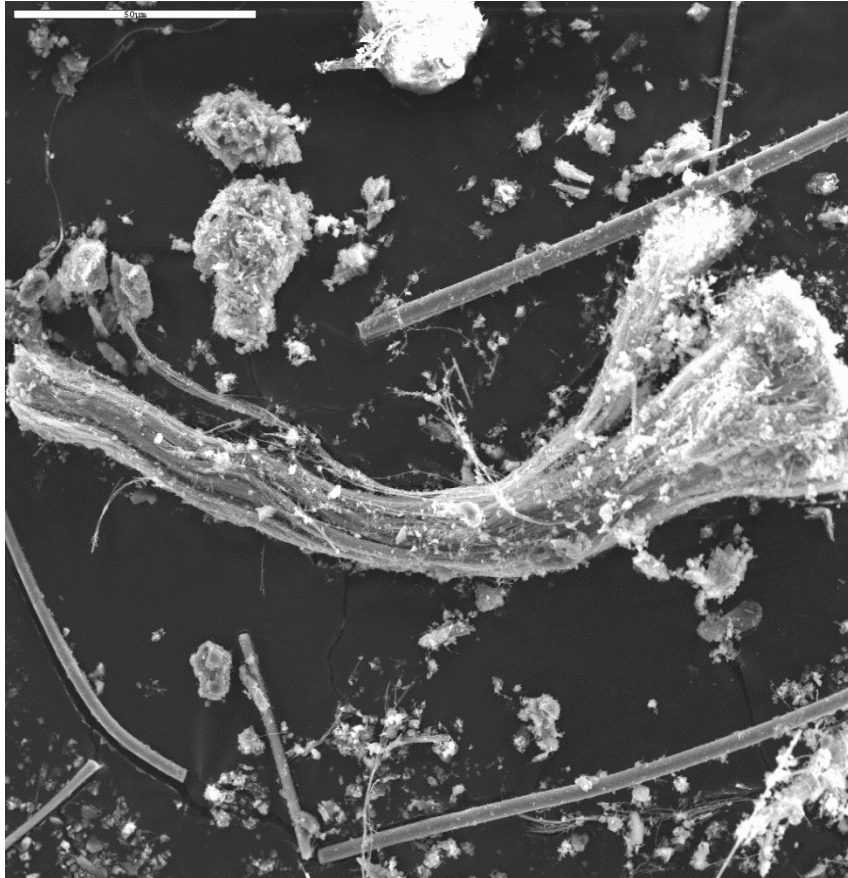


CROCIDOLITE

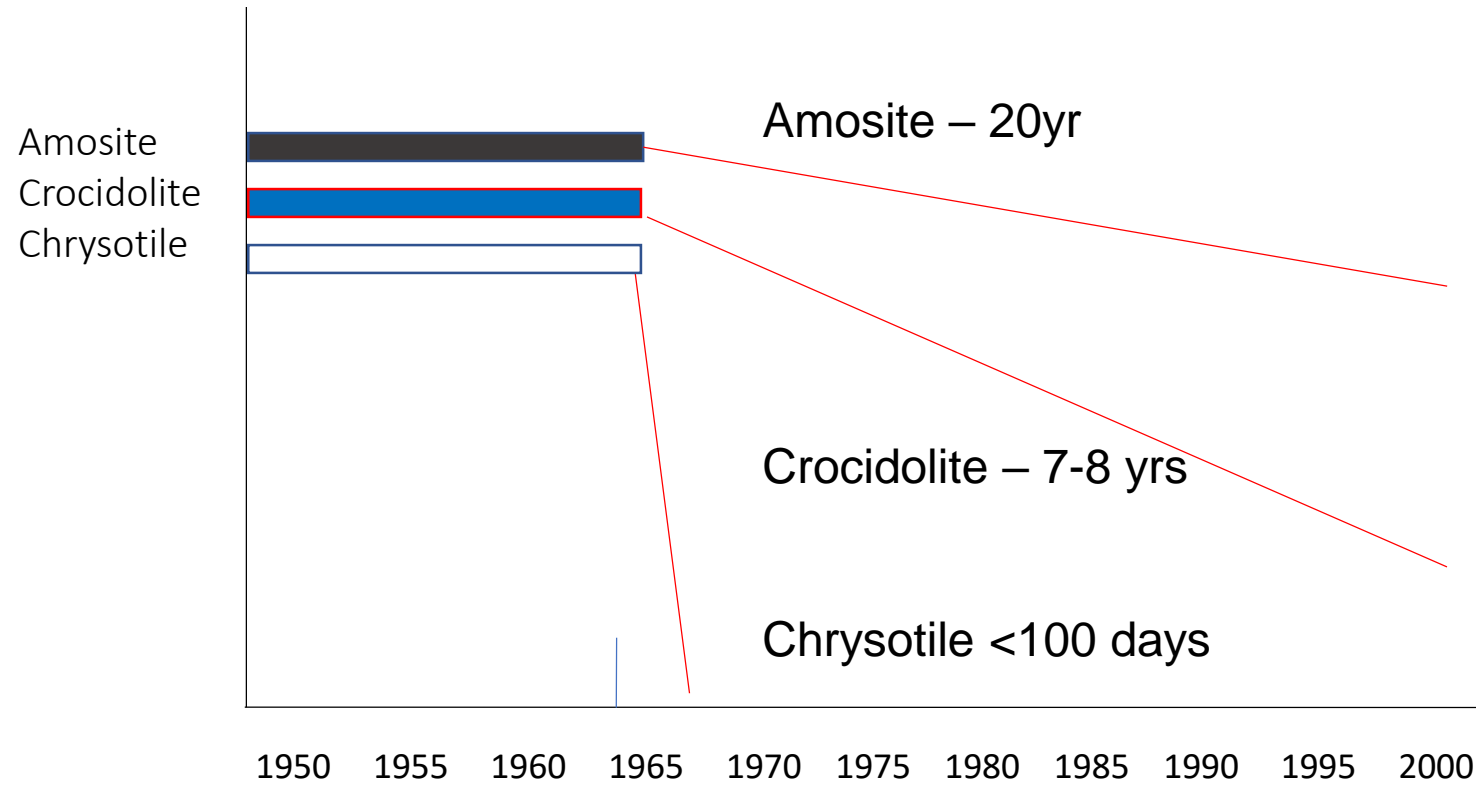


TREMOLITE

SERPENTINE – PHYSICAL TEM Chrysotile – curled flexible fibres



# FIBRE CLEARANCE





# Fibre Potency (HSE,2000)

- For Mesothelioma

500: 100: 1

Crocidolite: amosite: Chrysotile

- For Lung cancer

50-10: 1

Amphiboles: Chrysotile

# Role of the Autopsy

- To describe and diagnose all occupational/industrial disease manifestations
- To determine the aetiology
- To determine the extent and severity of any other disease present (that would affect life expectancy or quality). This is evaluated in assessing compensation.

# Consider Exposure How & When?

1. Occupational Direct
2. Occupational Indirect – Bystander
3. Para-occupational Exposure
4. Environmental



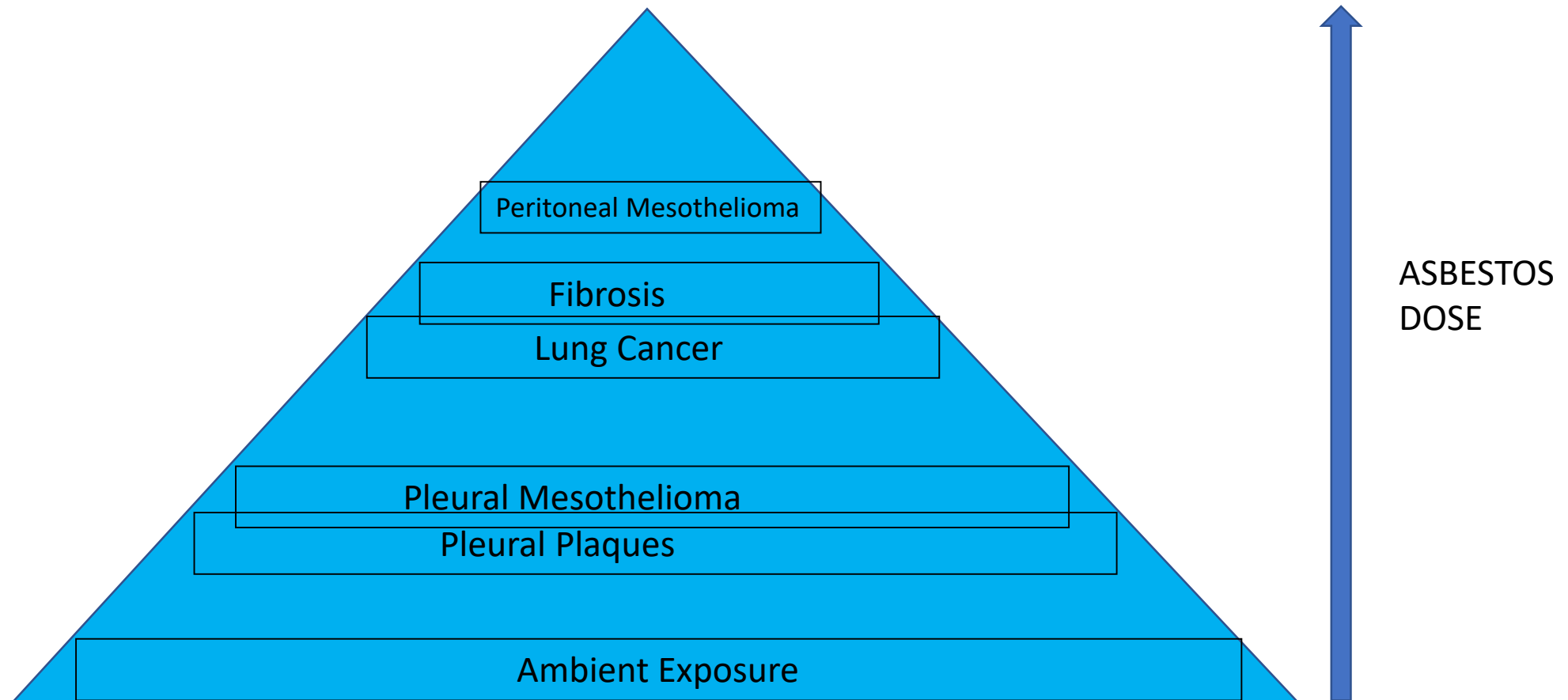
Potential pathways for environmental exposure to asbestos.

- (A) Para-occupational exposure. (A1) or through contact with worker clothes or other dust deposits in the home (A2).
- (B) Environmental exposure from industrial operations. mining operations (B1) or asbestos industry (B2).
- (C) Exposure to commercial asbestos-containing products during home maintenance or renovation projects (C2).
- (D) Naturally occurring asbestos (NOA)

# ASBESTOS RELATED CONDITIONS

- Pleural effusion
- Pleural plaque
- Diffuse pleural fibrosis/ thickening
- Asbestosis
- Malignant mesothelioma – Pleura & Peritoneum
- Lung cancer

# Asbestos Exposure, Disease



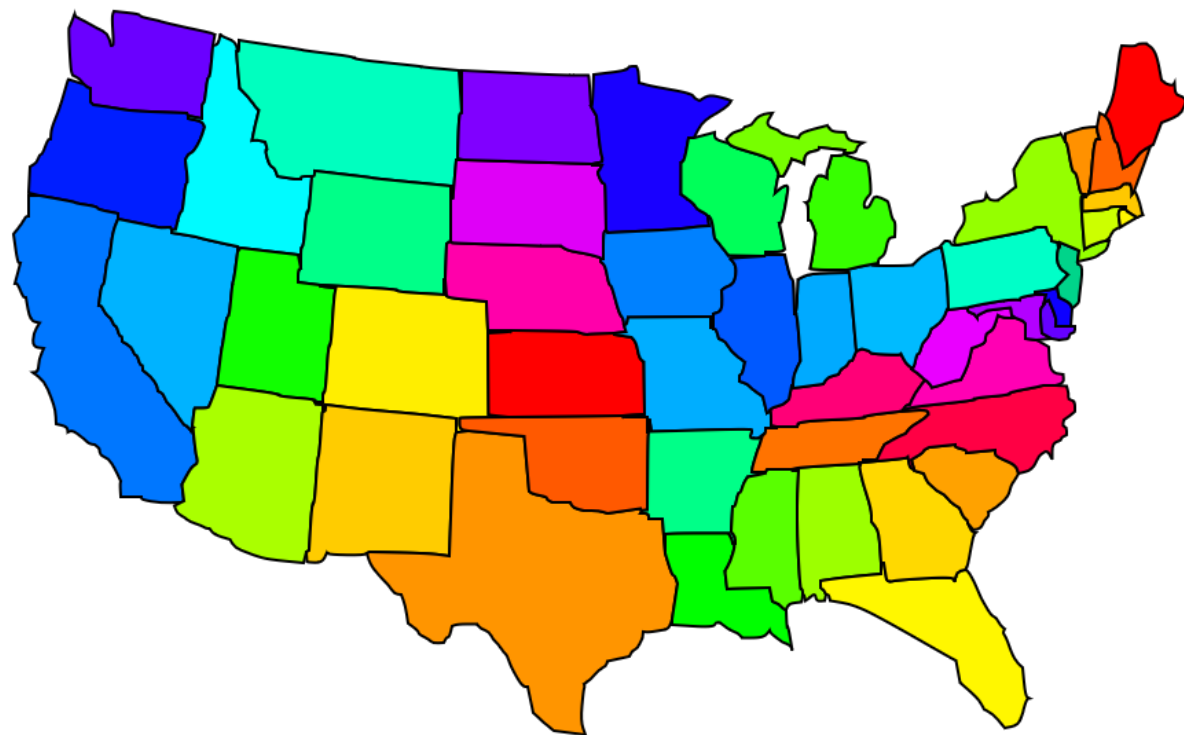
# Mesothelioma

# Mesothelioma Incidence

3000 /year & ↓

Population: 330 million

2500/year & ↗  
60 million



Median Age – 70 years  
Male: Female; 5:1

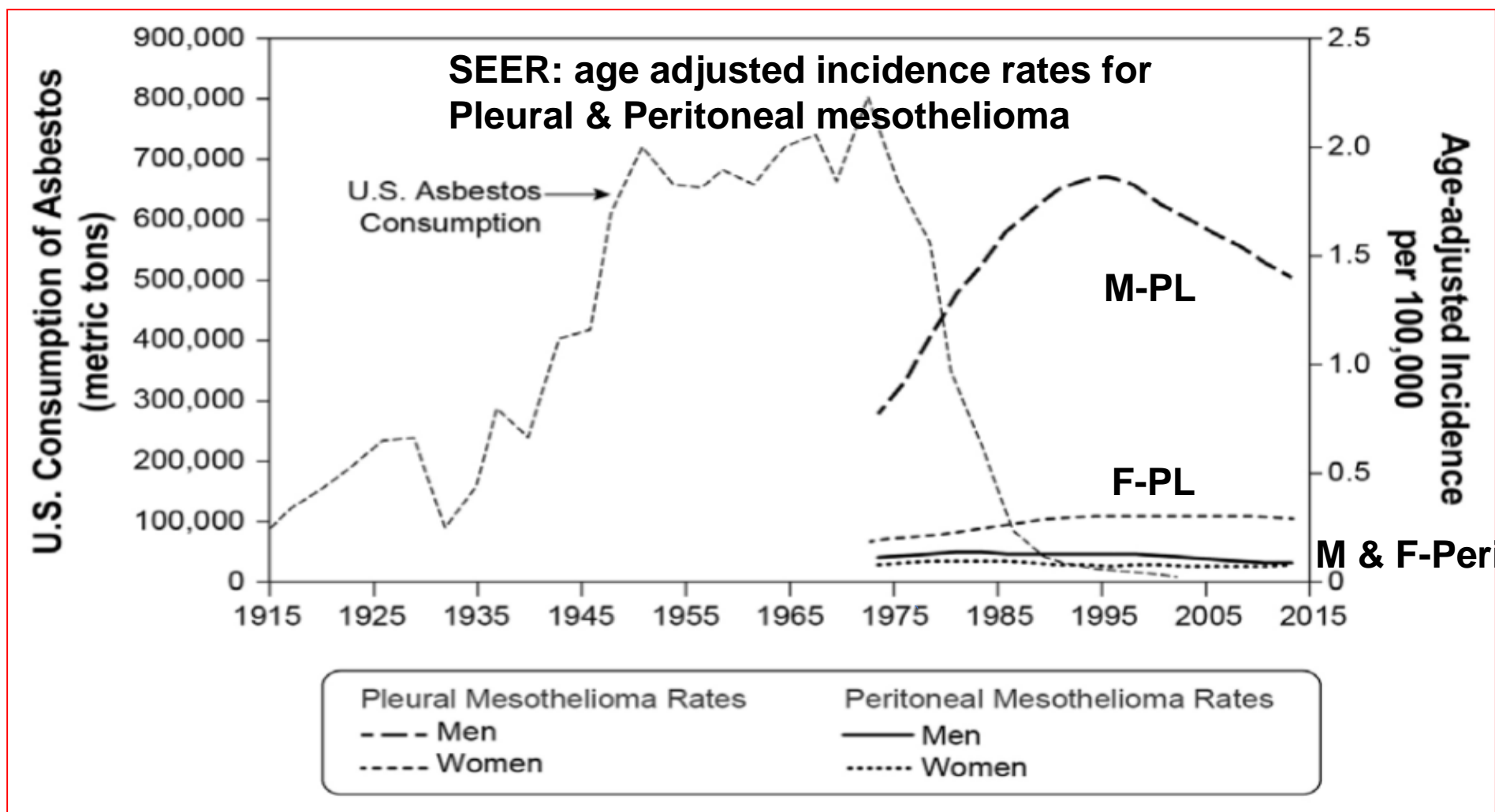


Median Age – 70 years  
Male: Female; 7:1

# CAUSES OF MESOTHELIOMA

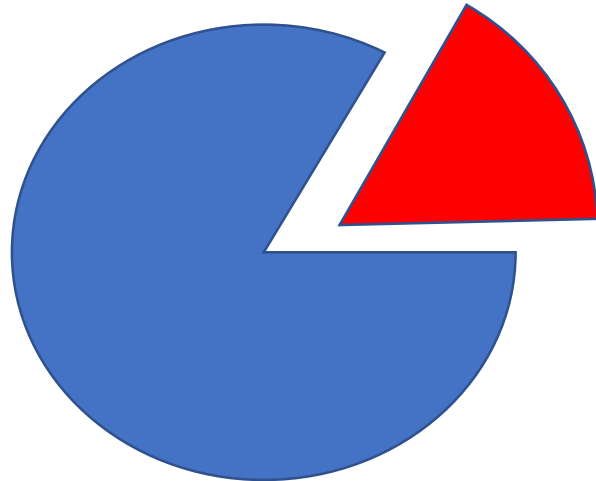
- (1) **Asbestos** – Gender & Site Variation
- (2) Erionite
- (3) Fluoroedenite
- (4) Radiation
- (5) Chronic inflammation
- (6) Genetic
- (7) **Spontaneous/idiopathic**



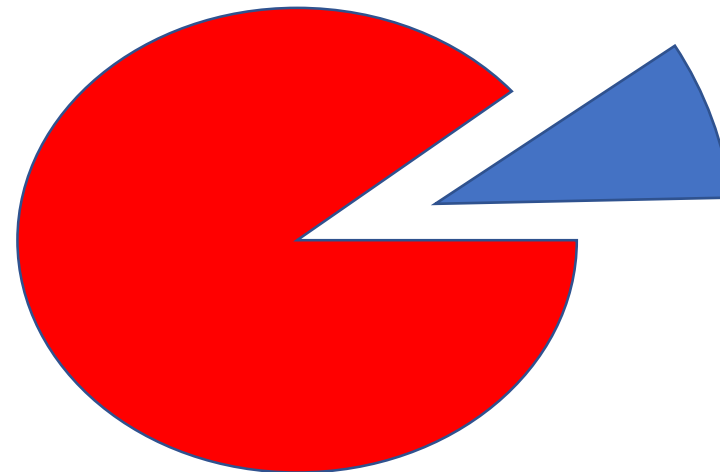


# PERITONEAL MESOTHELIOMA IS NOT A SIGNAL TUMOUR FOR ASBESTOS

- Pleural Mesothelioma
- Peritoneal Mesothelioma



20-30% **NOT** RELATED TO ASBESTOS



70-85% **NOT** RELATED TO ASBESTOS

# MESOTHELIOMA: APPROACH

- ALWAYS CONSIDER ALL INFORMATION
  - Clinical
  - Radiological
  - Pathological
  
- Exposure data – Not a diagnostic criterion

SPECIFICITY INCREASE



# Guidelines for Pathologic Diagnosis of Malignant Mesothelioma

## 2017 Update of the Consensus Statement From the International Mesothelioma Interest Group

*Aliya Noor Husain, MD; Thomas V. Colby, MD; Nelson G. Ordóñez, MD; Timothy Craig Allen, MD, JD;  
Richard Luther Attanoos, MBBS, MD, FRCPath; Mary Beth Beasley, MD; Kelly Jo Butnor, MD; Lucian R. Chirieac, MD;  
Andrew M. Churg, MD; Sanja Dacic, MD, PhD; Françoise Galateau-Sallé, MD; Allen Gibbs, MD; Allen M. Gown, MD;  
Thomas Krausz, MD; Leslie Anne Litzky, MD; Alberto Marchevsky, MD; Andrew G. Nicholson, DM; Victor Louis Roggli, MD;  
Anupama K. Sharma, MD; William D. Travis, MD; Ann E. Walts, MD; Mark R. Wick, MD*

# Guidelines for Pathologic Diagnosis of Malignant Mesothelioma

## 2012 Update of the Consensus Statement from the International Mesothelioma Interest Group

*Aliya N. Husain, MD; Thomas Colby, MD; Nelson Ordonez, MD; Thomas Krausz, MD; Richard Attanoos, MB, BS;  
Mary Beth Beasley, MD; Alain C. Borczuk, MD; Kelly Butnor, MD; Philip T. Cagle, MD; Lucian R. Chirieac, MD;  
Andrew Churg, MD; Sanja Dacic, MD, PhD; Armando Fraire, MD; Francoise Galateau-Salle, MD; Allen Gibbs, MD;  
Allen Gown, MD; Samuel Hammar, MD; Leslie Litzky, MD; Alberto M. Marchevsky, MD; Andrew G. Nicholson, DM;  
Victor Roggli, MD; William D. Travis, MD; Mark Wick, MD*

### Epithelioid mesothelioma

Tubulopapillary

Micropapillary

Trabecular

Acinar

Adenomatoid

Solid

Clear cell

Deciduoid

Adenoid cystic

Signet ring cell

Small cell

Rhabdoid

Pleomorphic

### Sarcomatoid mesothelioma

Conventional, spindle cell

Desmoplastic

Heterologous differentiation (osteosarcomatous,  
chondrosarcomatous, etc)

Lymphohistiocytoid (may also be classified as epithelioid)

Biphasic/mixed



# IMMUNOHISTOCHEMISTRY

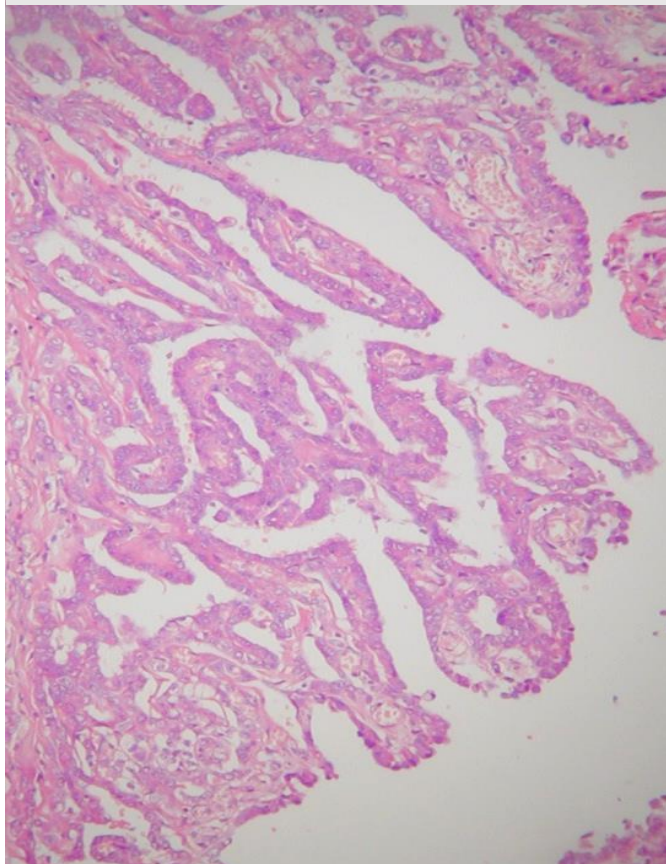
MESOTHELIAL MARKERS	EPITHELIAL / CARCINOMA MARKERS
Calretinin	CEA
CK 5/6	CD 15
WT 1	AUA – 1
D2 – 40	Ber – EP4
Thrombomodulin	MOC – 31
Mesothelin	TTF - 1

No marker is wholly specific or sensitive for any given tumour

International Mesothelioma Panel /W.H.O. Recommendations:

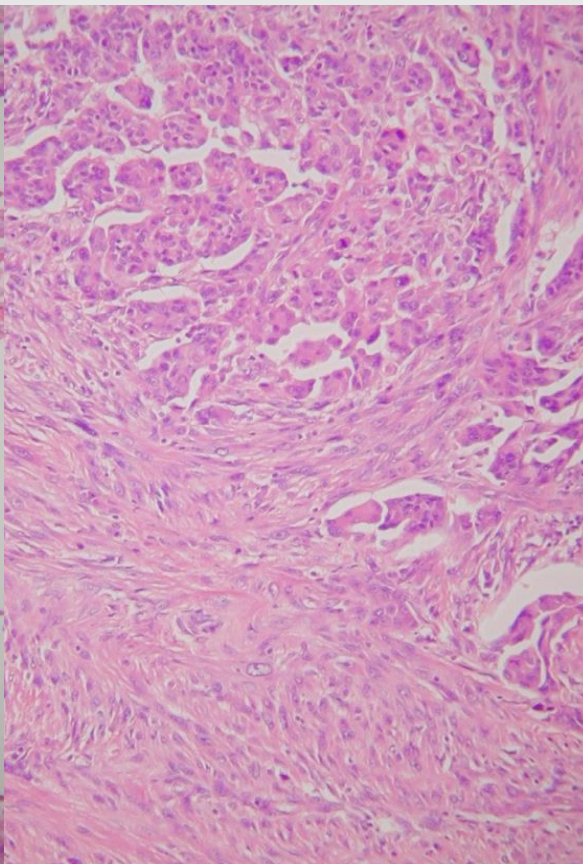
Pan-Keratin plus 2 mesothelial & 2 epithelial markers

Epithelioid



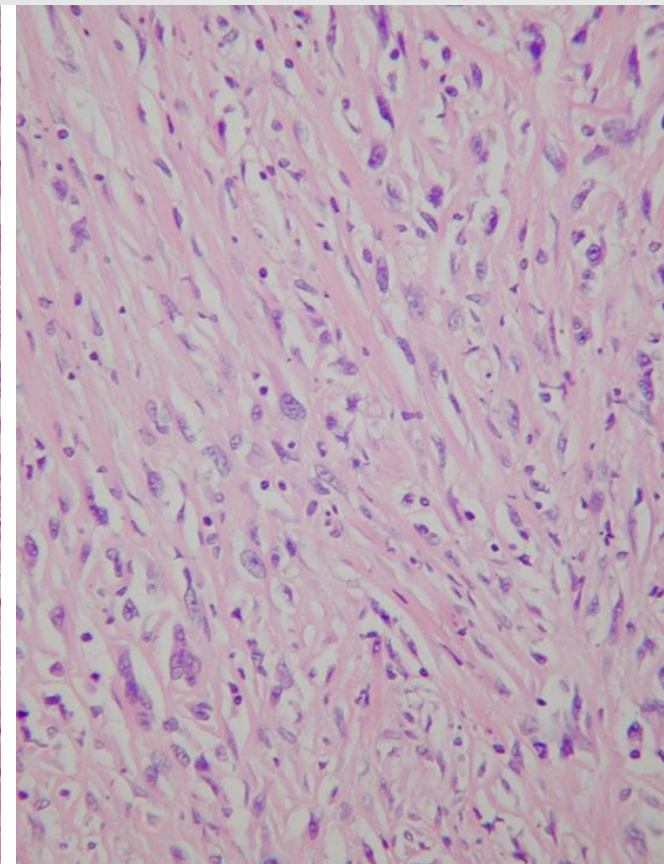
AE1+  
Calretinin, CK5/6, WT-1+

Biphasic

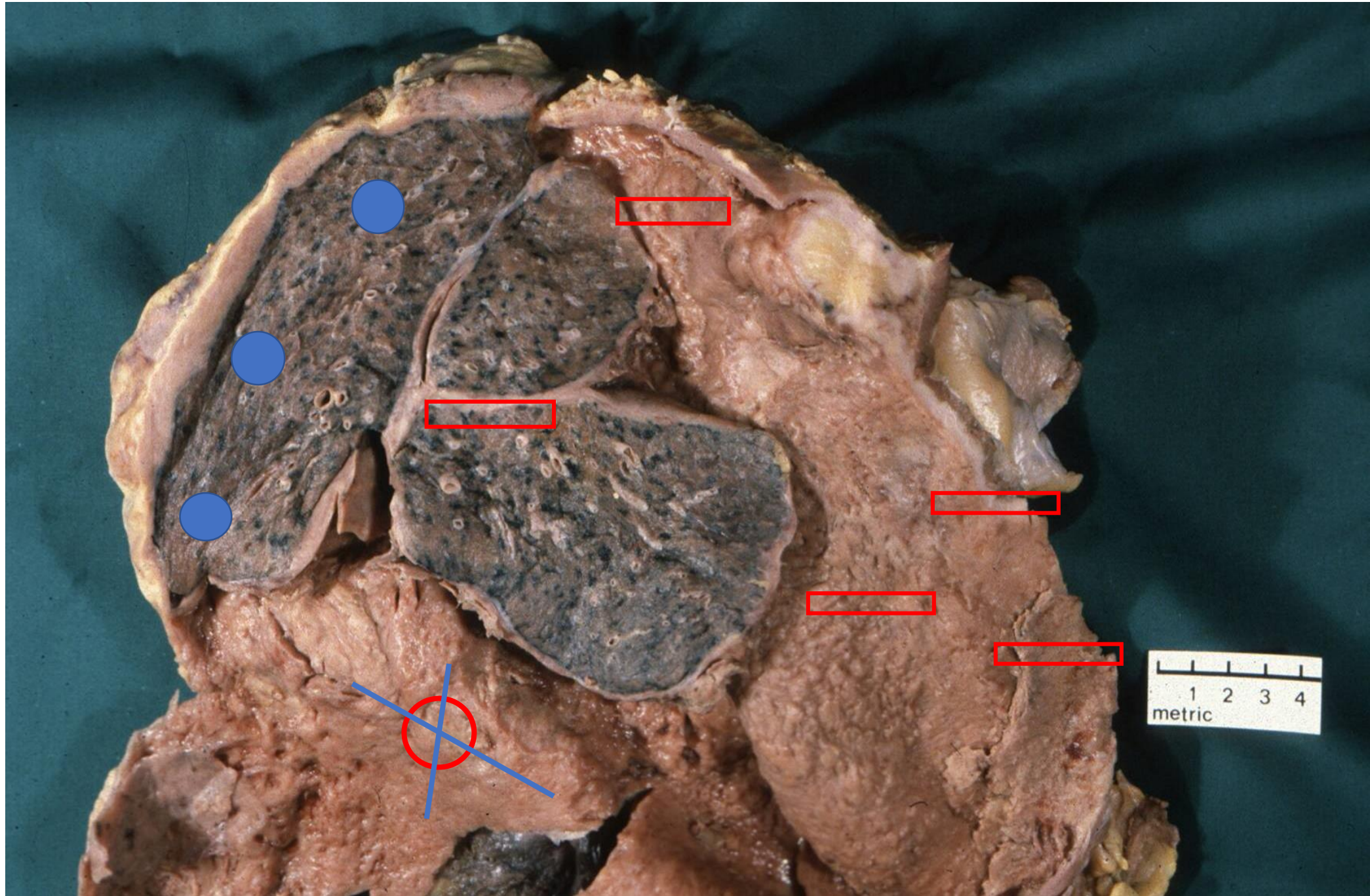


AE1+  
Calretinin, CK5/6, WT-1+

Sarcomatoid

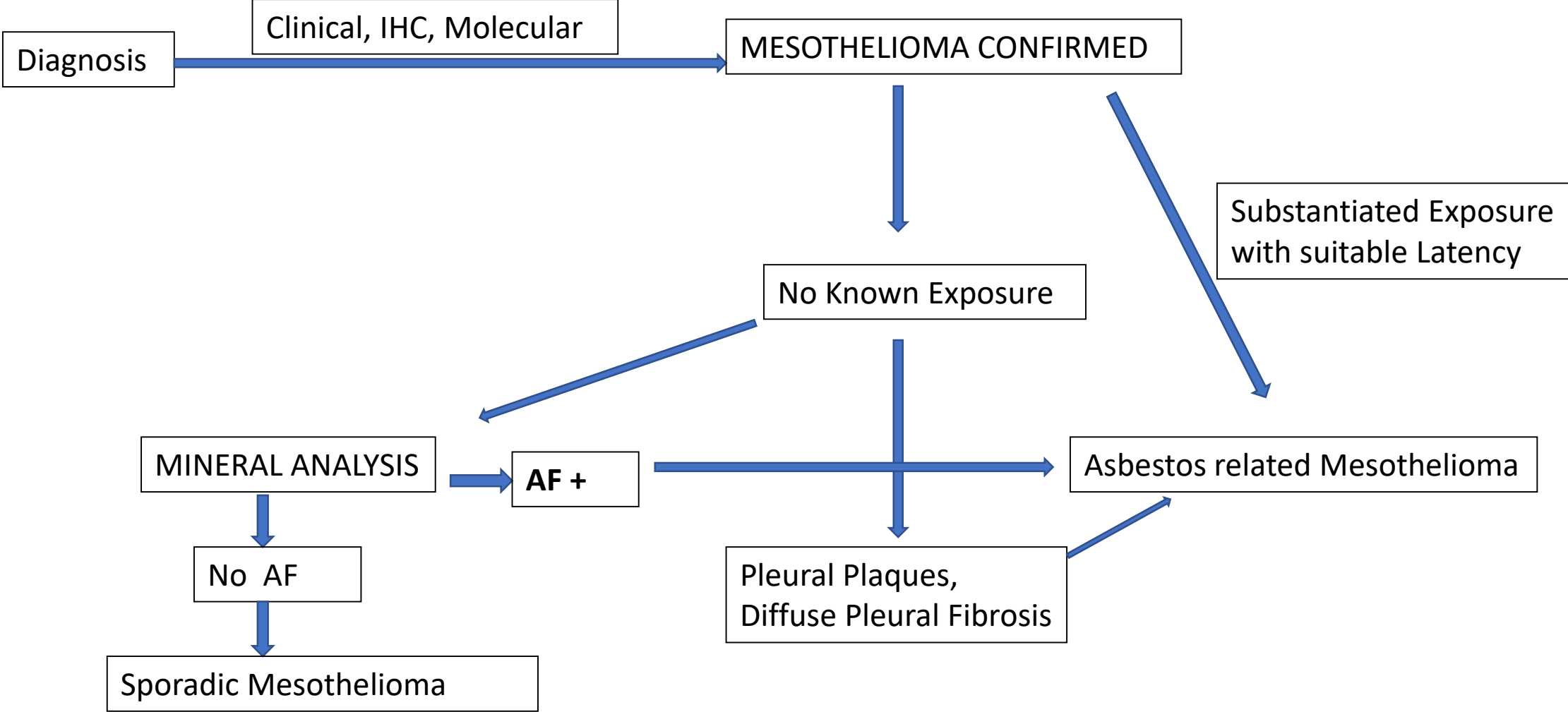


AE1+  
Calretinin, CK5/6, WT-1 - -





# Mesothelioma Summary



# Pathology of Asbestosis—An Update of the Diagnostic Criteria

Report of the Asbestosis Committee of the College of American Pathologists and Pulmonary Pathology Society

*Victor L. Roggli, MD; Allen R. Gibbs, MD; Richard Attanoos, MD; Andrew Churg, MD; Helmut Popper, MD; Philip Cagle, MD; Bryan Corrin, MD; Teri J. Franks, MD; Françoise Galateau-Salle, MD; Jeff Galvin, MD; Philip S. Hasleton, MD; Douglas W. Henderson, MD; Koichi Honma, MD*

Arch. Pathol. Lab. Med. 2010; 134: 462 - 480



# ASBESTOSIS

- Diffuse interstitial fibrosis caused by asbestos

- **Assess Fibrosis**

- *Fibrosis of Appropriate pattern*

PLUS

- **Assess Asbestos bodies**

- *Average rate of 2 per cm<sup>2</sup>*

- *Iron sections*

OR

- **Assess Mineral Fibre analyses**

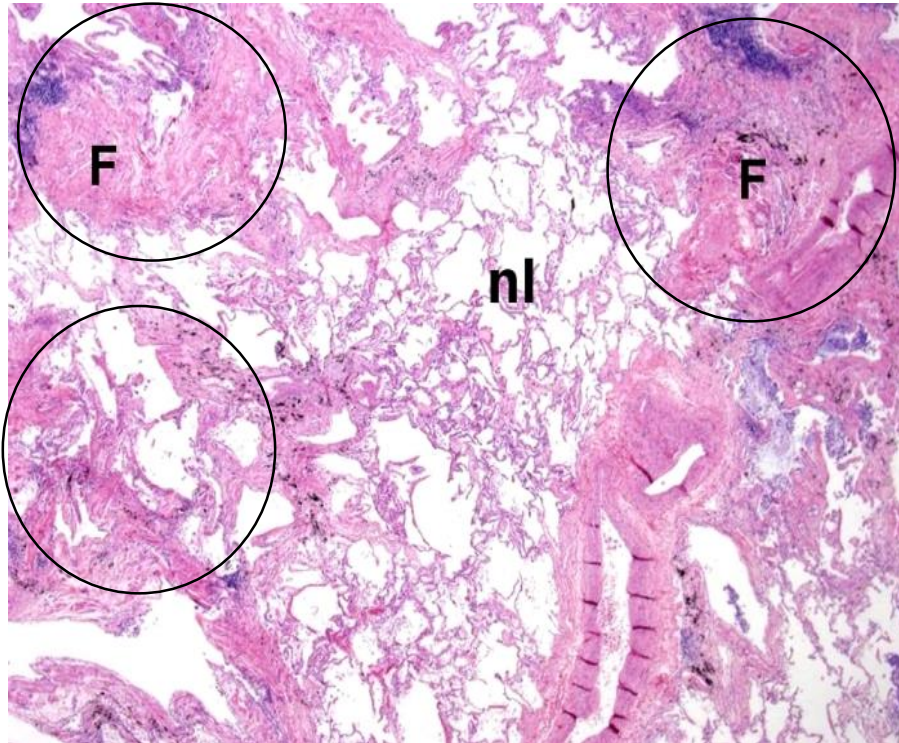
- *Asbestosis range*

## ASBESTOSIS

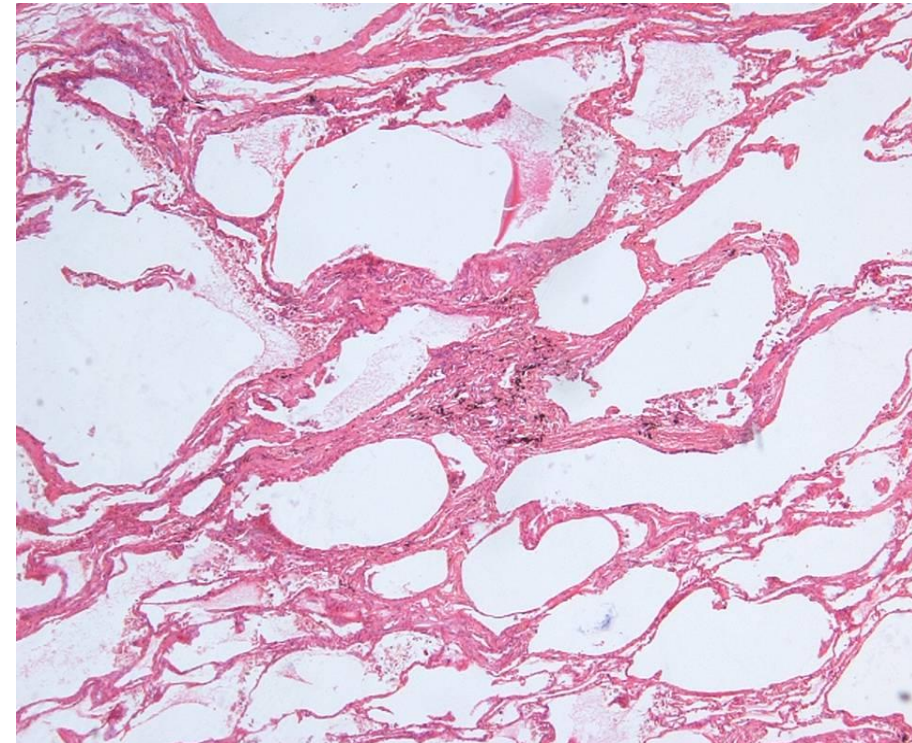
'Fibrosis of Appropriate pattern' (CAP-PPS 2010)

Always acellular and collagenous rather than fibroblastic and inflammatory'

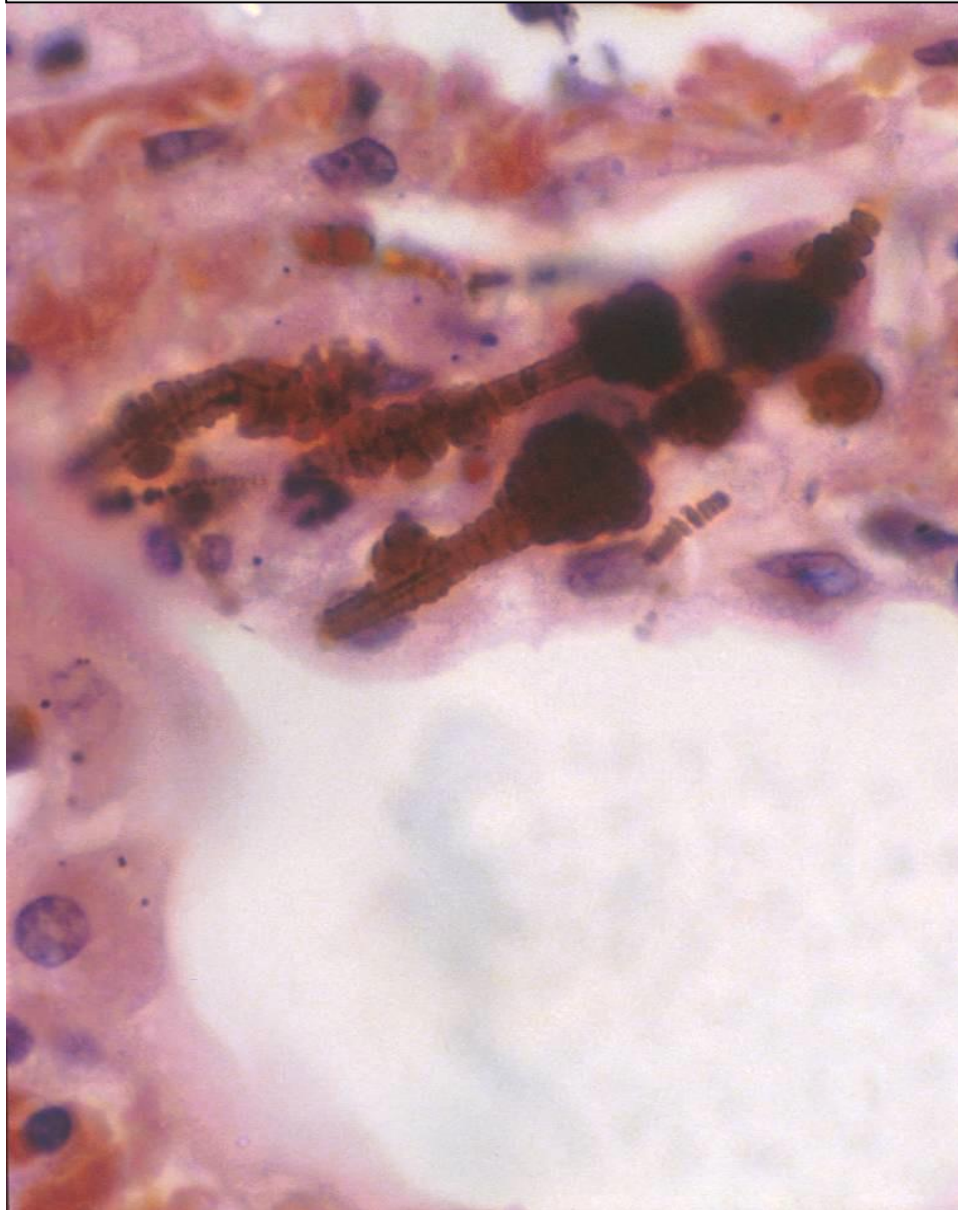
### IPF - UIP



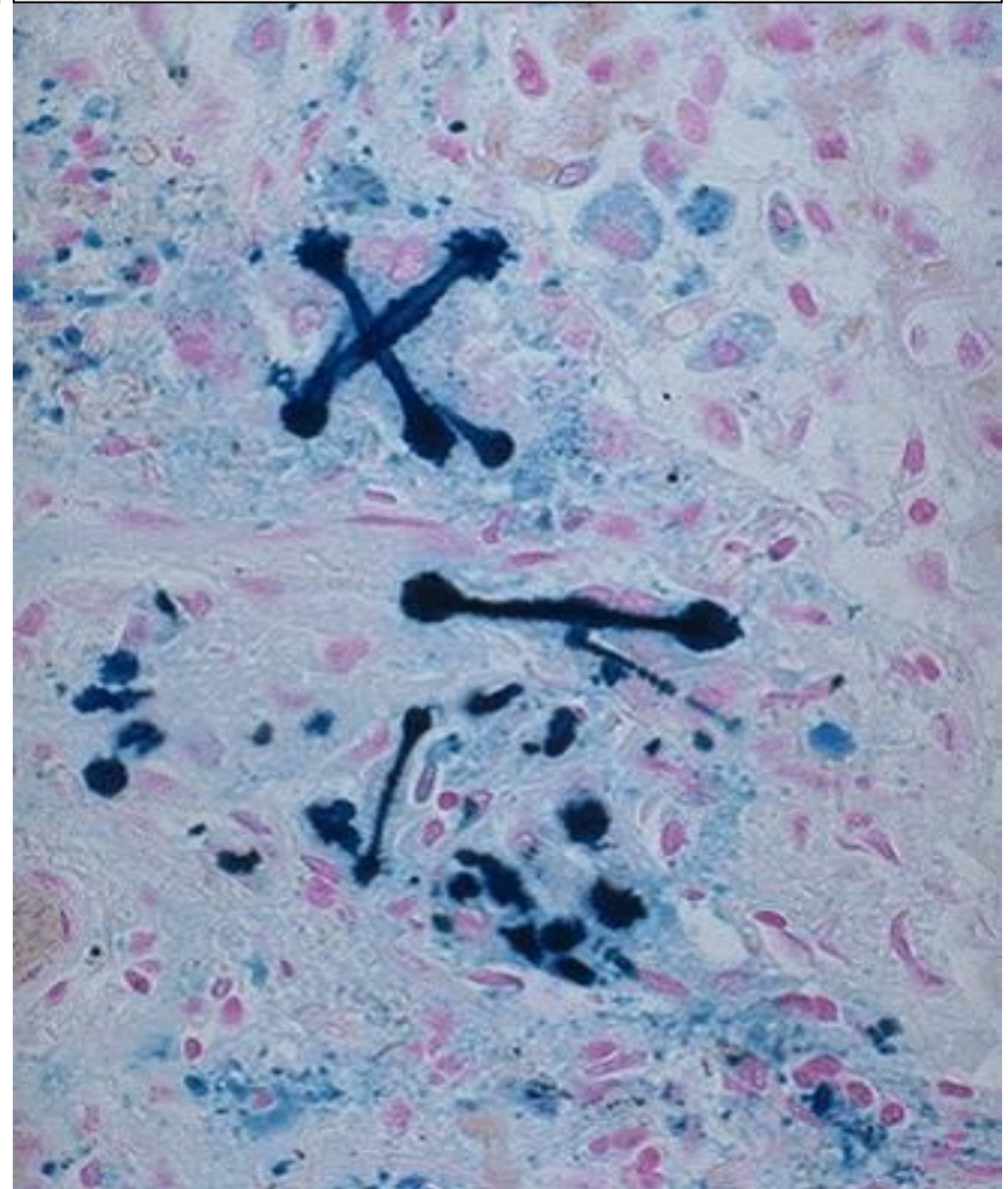
### ASBESTOSIS- Fibrotic NSIP



NO RELIANCE ON THICK UNSTAINED SECTIONS  
NO RELIANCE ON 'SQUEEZE' SAMPLES



PERLS IRON STAINS ESSENTIAL  
An average rate of at least 2 per 1cm<sup>2</sup>



# Asbestosis range

## CAP-PPS Asbestosis Committee

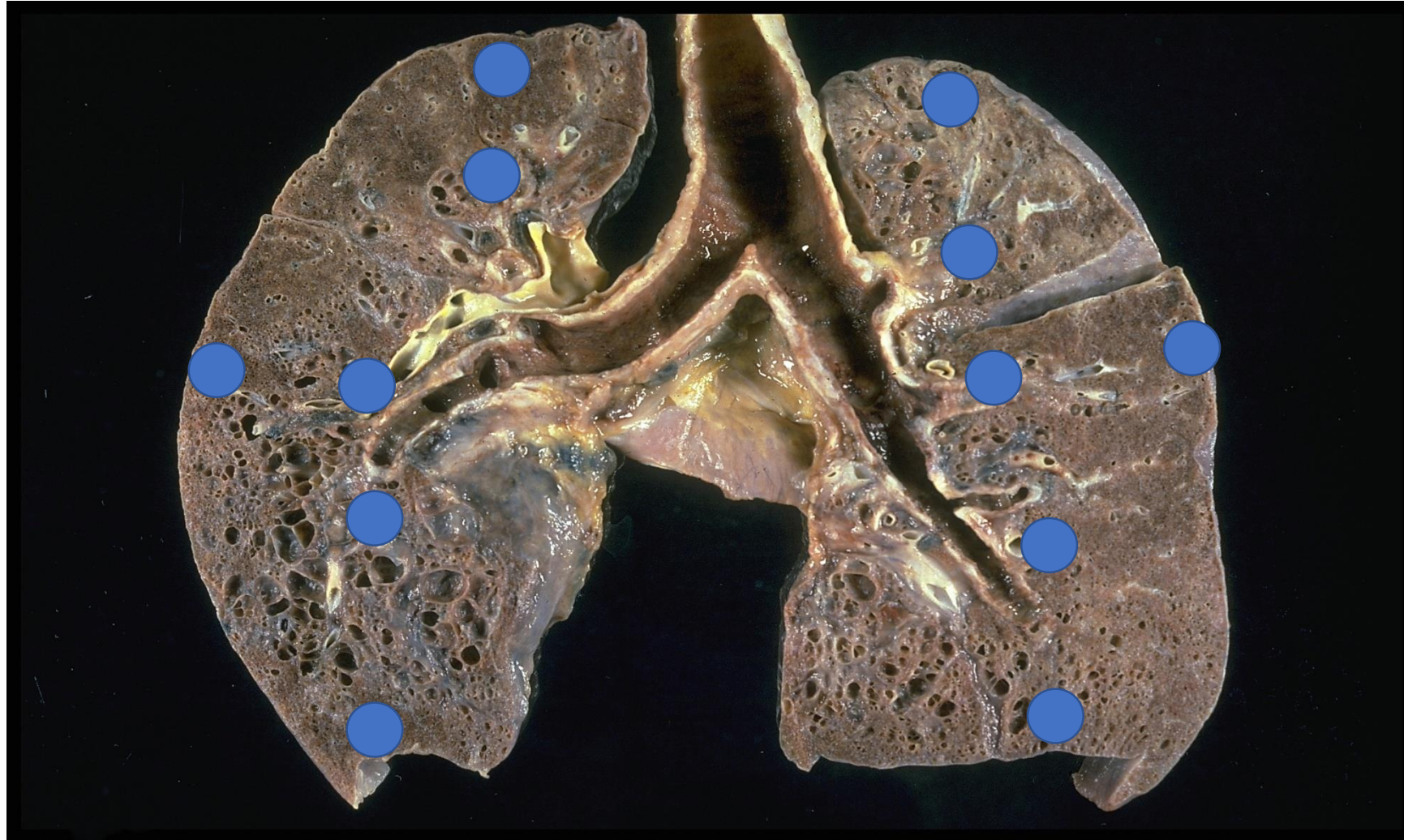
- Total retained amphibole asbestos fibre count in cases of asbestosis
  - Lower range value is 5<sup>th</sup> percentile
    - Chrysotile count excluded

# Potential Asbestosis – Red Flags?

- Rapid clinical progression 3-5 yrs → IPF
  - Subjects with Collagen disease
- UIP-like pathology (grade 4) → IPF
  - No / low asbestos bodies
  - No / low asbestos fibres

# Tissue Sampling for Interstitial lung disease/Asbestosis

Upper, mid-, lower lobes – central & peripheral = 10 blocks: 2x2x2cm





# Asbestos Assessment: Pathology

AIM: Determine Inhaled, retained asbestos

- Light microscopy
  - Asbestos body counts
  - Mineral analysis
- Electron microscopy
  - Scanning (SEM)
  - Transmission (TEM)

## **Fibre analysis is applicable in cases of potential/claimed:**

- **Asbestosis**- This applies if light microscopic asbestos body counts are low or absent i.e. an average rate of  $>2$  asbestos bodies per  $1 \text{ cm}^2$  lung section area determined by routine thickness Perls stained section at 400x magnification.
- **Lung cancer ex asbestosis**
- **Pleural malignant mesothelioma with no exposure history**
- **Extrapleural mesotheliomas and mesotheliomas in women.**

# Mineral Analysis

## Light microscopy

Quick, cheap

400 X mag.

Low resolution  
( $>0.3$  micron)

No fibre type data

## Electron microscopy

High resolution ( $<0.01$  micron)

Fibre typing possible

Detect low fibre concentrations

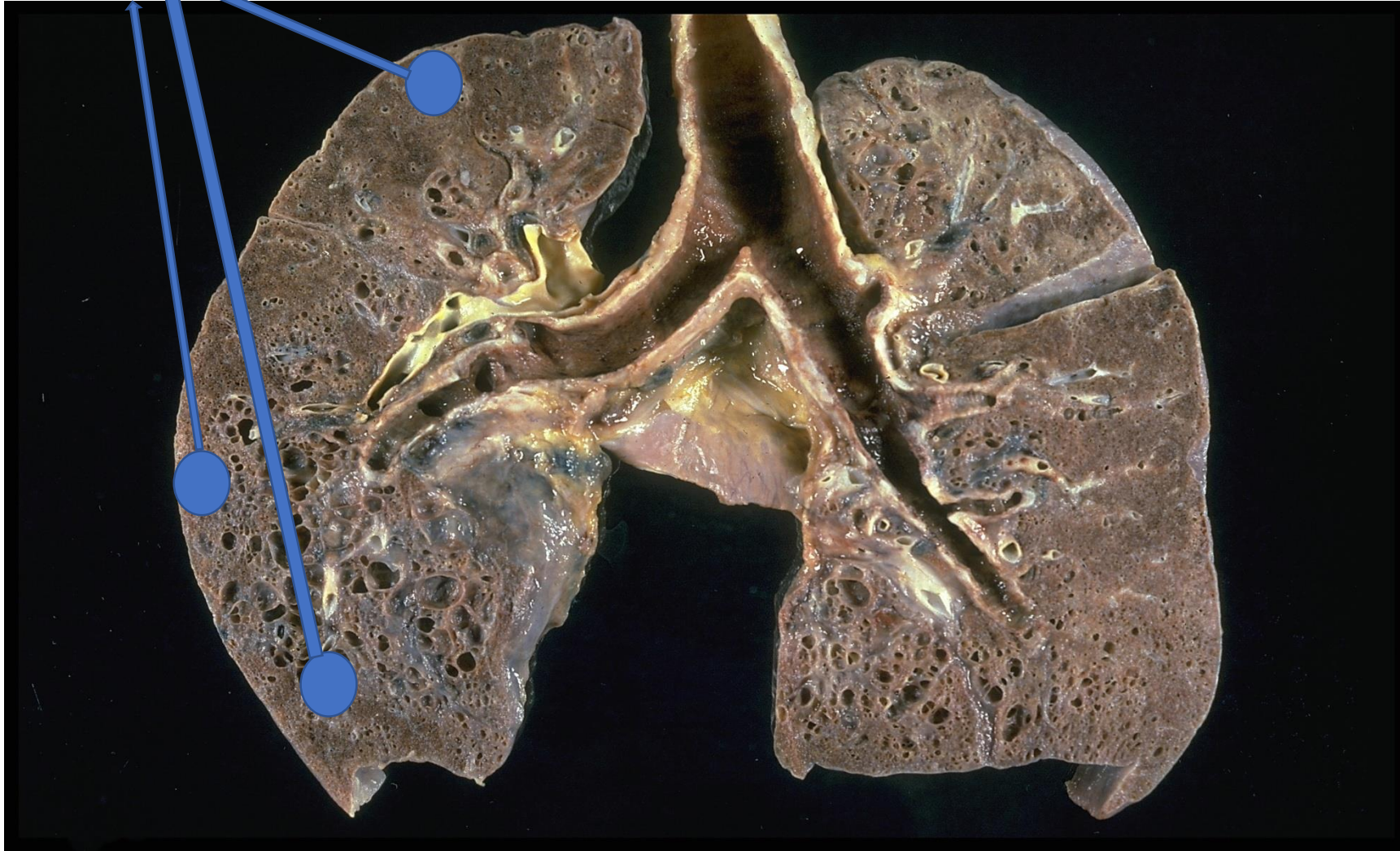
20,000 X mag.

Expensive, time factors

# Tissue sampling for Mineral Fibre Analysis

**POOLED ANALYSIS**

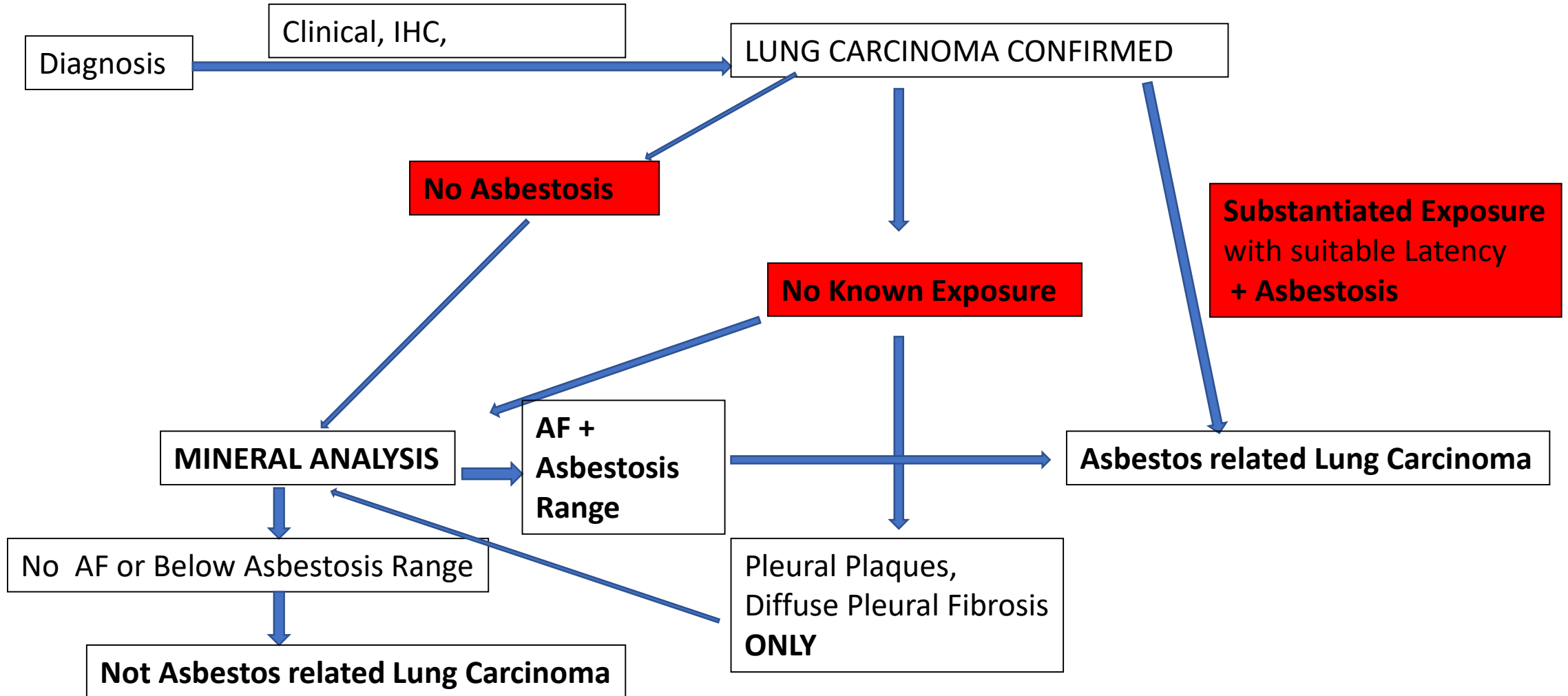
Three 2 x 2 x 2 cm samples



# Asbestos related lung cancer - attribution

- Heavy direct exposure
- Amphiboles more potent than chrysotile
- All major histological types
- Latency
- Asbestosis present or ~ Dose of asbestosis ie Asbestosis range
- Plaques are not a good indicator of sufficient dose for asbestos related lung cancer

# Lung Cancer - Summary



# Clinicopathological Summary

- Document Macroscopic & Microscopic Findings
- Correlate Exposure History from Medical records, Witness statements, Pathology - Mineral counts
- Determine significance of Fibre Count
- Document Concurrent Pathology
- Determine Cause of Death