

## Mesothelioma

### Clinical Background

Mesothelioma is a rare malignancy involving the serous lining of body cavities (pleura, peritoneum, pericardium or tunica vaginalis testis).

#### Epidemiology

- Incidence – 1/100,000
- Age – peaks in 40s-50s
- Sex – M>F
- Occurrence – rising in males  $\geq 75$  years; however, it is not increasing in males and females  $< 75$  years (coincides with OSHA restrictions of permissible limits of asbestos exposure)
  - Maximum lifetime risk for the development of mesothelioma falls in the 1925-1929 birth cohort

#### Risk factors

- Asbestos exposure (amphiboles more carcinogenic than chrysotile fibers)
  - 80% of mesothelioma cases occur in patients with history of asbestos exposure
  - At-risk occupations include shipbuilding, construction, fireproofing, automobile brakes and clutches, ceiling tiles and boilers (especially in construction prior to 1970)
- Genetics
  - Chromosome deletions (1p, 3p, 9p, 6q)

#### Pathophysiology

- 3 types of malignant pleural mesothelioma
  - Epithelial – 50%
  - Sarcomatous – 15%
  - Biphasic (or mixed) – 25%
- May be mistaken for adenocarcinoma; histologically heterogeneous tumors
  - Histology affects survival
- Long latency period ( $> 20$  years) between asbestos exposure and development of mesothelioma
- Asbestos fibers are mutagenic and carcinogenic to several cells
  - Commonly found in excised tumors
- Peritoneal mesothelioma
  - Cystic – no association with asbestos
  - Well-differentiated papillary
  - Malignant – no association with asbestos

#### Clinical Presentation

- Pleural
  - Dyspnea, nonpleuritic chest pain, pleural effusion, cough, fatigue
- Peritoneal
  - Abdominal pain, ascites, anorexia, bloating
- Pericardial
  - Chest pain, constrictive pericarditis
- Disease process is usually advanced at time of presentation

## Diagnosis

- Indications for testing – high suspicion including abnormal chest x-ray (pleural effusion, pleural plaques) and history of asbestos exposure
- Laboratory testing
  - Histology – special stains for tissue specimens
    - Body cavity fluid cytology – may be negative
      - Not all patients with mesothelioma develop effusions
    - Pleural biopsy – CT guided or thorascopic biopsy
    - Open thoracotomy – last resort
  - Serum testing is not useful in diagnosis
  - Immunohistochemistry
    - Pancytokeratin (AE1/AE3), CK-7, CK-20
      - Typically positive for pancytokeratin and CK-7; may or may not be positive for CK-20 in epithelioid mesothelioma
    - Mesothelial markers – CK5/6, WT-1, calretinin, mesothelin, HBME-1, thrombomodulin, D2-40
      - Tendency to stain higher in epithelioid tumors
    - Sarcomatoid mesothelioma
      - Main differential is adenocarcinoma
      - 2/3 positive for calretinin; usually positive for keratin
    - Typically negative stains include CEA, BG8, moc-31 (ERA), E-Cadherin, Ber-Ep4, TTF-1, CD15
- Imaging studies
  - CT/MRI for initial evaluation of abnormal chest x-ray

## Differential Diagnosis

- Pleural
  - Tuberculosis
  - Adenocarcinoma
  - Metastatic malignancy
  - Other malignancy – lymphoma, sarcoma
  - Pneumonia
  - Solitary fibrous tumor
- Peritoneal
  - Ovarian cancer with metastatic disease
  - Tuberculosis
  - Lymphomatosis
  - Peritoneal carcinomatosis
  - Endometriosis

## Monitoring

- Soluble mesothelial-related peptides (Mesomark)
  - Useful for monitoring epithelial or biphasic mesothelioma
  - Requires serial measurement
  - Not useful as a diagnostic test

## Lab Tests

### Indications for Laboratory Testing

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at [www.aruplab.com](http://www.aruplab.com).

Test Name and Number	Recommended Use	Limitations	Follow Up
Cytology, Body Cavity Fluid <b>8209701</b> Method: Routine Cytopathologic Evaluation	Aid in the diagnosis of mesothelioma		
Cytology, Pulmonary <b>8209702</b> Method: Routine Cytopathologic Evaluation	Aid in the diagnosis of mesothelioma		
Immunohistochemistry Stain Offering <b>arup005</b> Method: Immunohistochemistry	For fixed tissue samples, consultative services as well as immunohistochemical staining for AE1/AE3 (pan cytokeratin), Ber-Ep4, calretinin, CEA, CK 5/6, CK-7, CK-20, E-cadherin, EMA, ERA (moc-31), keratin 903 (HMW), WT-1 (monoclonal), calretinin, TTF-1, leu M1 (CD15), D2-40 are available		
Soluble Mesothelin Related Peptides (MESOMARK®) <b>0081284</b> Method: Enzyme-Linked Immunosorbent Assay	Monitor mesothelioma	Not a diagnostic test Humanitarian use device which requires IRB approval for use	Requires serial measurements

### Additional Information

Interpretation of most stains is only available in conjunction with a consultation. Stains can be performed and returned for client pathologists to interpret unless otherwise noted.

### Guidelines

BTS statement on malignant mesothelioma in the UK, 2007. *Thorax*. 2007; 62 Suppl 2 :ii1-ii19.

### General References

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