MESOTHELIOMA

Not Just a Late Night Commercial

Graciela Hoal, RN, MSN, ACNP-BC
Saturday Session
Thoracic Surgery Nurse Practitioner
Greater Los Angeles Veteran Affairs
Objectives

Course Objectives:
• Discuss risk factors for malignant pleural mesothelioma
• Discuss clinical and radiologic findings in mesothelioma
• Discuss current treatment/disease management options

At the end of the presentation, participant will be able to:
• State at least 3 mesothelioma risk factors
• Identify at least 3 clinical and radiologic finding in patients with mesothelioma
• Describe current lung-sparing treatment modalities for mesothelioma
Mesothelioma

- Tumor arising from the mesothelium
  - Pleural
  - Pericardium
  - Peritoneum

- 80% are Pleural Mesotheliomas (MPM)
  - 60% right-sided

- Usually spreads locally along ipsilateral pleura

- Linked to asbestos exposure in 1960

---

MPM Epidemiology

Incidence

• US 2000-3000/yr²
  • Overall: 1.2/100,000
  • High risk males: 63.6/100,000
  • High risk females: 9.6/100,000

• Global³
  • Overall mortality 1994 – 2008: 4.9/million
MPM Epidemiology

• Latency period of 20-40+ years
• Median age = 60 yrs (5th-7th decades)
• Age range 28-90+
• Male:female = 3:1
• Etiology: Asbestos
Asbestos
Asbestos

- Group of hydrated magnesium silicate fibrous minerals
- 2 Major types
  - Serpentine
  - Amphibole
- Resistant to heat and combustion
- Used in production of
  - Cement
  - Ceiling
  - Tiles
  - Brake linings
  - Ship buildings

Asbestos

Fiber Types

• Serpentine (large curly pliable fibers)
  • Chrysotile

• Amphibole (long narrow rod-like fibers)
  • Crocidolite
  • Amosite
  • Tremolite
  • Anthophyllite
  • Actinolite

• Silicates (contaminated with tremolite)
  • Zeolite (Turkey)
  • Vermiculite (Libby, Montana)
Asbestos Geological Hot Spots

California
Asbestos Regulation

OSHA Regulation

- 1970: 5 fibres/ml$^3$ of air
- Now: 0.2 fibres/ml$^3$ of air

How small is asbestos?

www.AsbestosDiseaseAwarenessOrganization.org
Asbestos

911
9/11 AIR TOXINS RELATED TO CANCER
10 YEARS LATER
presented by Asbestos.com

The four terrorist attacks on Sept. 11, 2001, two of them on the Twin Towers at the World Trade Center in New York City, changed America forever. In the decade since, researchers and doctors have discovered just how toxic dust can be. One recent study found that every first responder to the fallen Twin Towers has suffered some degree of lung impairment.

410,000 PEOPLE EXPOSED
Nearly half a million people were impacted by contaminated air in the wake of the Twin Towers' collapse, including first responders, nearby residents and workers charged with cleaning up the massive amounts of debris at the site and nearby dust.

204 THE NUMBER OF FIRST RESPONDERS THAT HAVE DIED AFTER 9/11
55 THE NUMBER OF PEOPLE THAT HAVE DIED FROM LUNG OR OTHER CANCERS RELATED

112,000x The magnitude of the asbestos level above the legal limit of a building next to Ground Zero. Tests showed the building essentially had become toxic.

$2.775 BILLION
The amount of money in a 9/11 compensation fund now able to be accessed by families of victims and survivors. The fund was reopened in July 2011 as part of James Zadroga 9/11 Health and Compensation Act. The law was universally hailed until cancer victims learned they are not covered. However, the law ensures that some 25,000 survivors and 25,000 responders have access to specialized medical services and promotes and provides funding for medical research.

2,000 TONS The amount of asbestos fibers that were released into the air by the towers' collapse. That is the equivalent of 182 SCHOOL BUSES

1,506,124 The tons of debris that was removed from Ground Zero.
Risk Factors

• ASBESTOS EXPOSURE\(^4\)
  • Lifetime risk 8 – 13%
  • Latency period 30 – 40 yrs from exposure

• Ship yard workers/ship builders
• Electricians
• Plumbers
• Carpenters
• Insulation installers
• Construction Workers
• Auto mechanics (brake removal and installation)
Clinical Presentation

Subjective

• Cough*
• Shortness of breath*
• Chest pain/discomfort*

• History of asbestos exposure

*(>90% of patients present with combinations of these symptoms)*
Clinical Presentation

Objective

- Unilateral dullness to percussion
- Unilateral distant breath sounds
- Scoliosis towards side of malignancy
- Abnormal x-ray
  - Unilateral pleural thickening
  - Unilateral pleural effusion
MPM Presentation
MPM Presentation (6/2013)
MPM (8/4/13)
Patient J.G.
Patient J.G.  2/2014
CT scan shows right sided nodular circumferential pleural thickening exceeding 1 cm in thickness, typical of a malignant process (arrows). No clear cut invasion of the chest wall is present. A slightly enlarged pretracheal lymph node proved to be reactive in nature.
MPM Diagnosis

- Often misdiagnosed
- Thoracentesis or closed pleural biopsy
  - Cytology of effusion can be diagnostic of MPM, but negative results DOES NOT exclude the possibility of mesothelioma
  - Sample errors

- Thoracoscopic or open pleural biopsy
  - Gold standard
  - Highest diagnostic value

**mesothelioma will seed biopsy site(s)**
MPM Diagnosis

Two Diseases

Epithelioid MPM

Sarcomatoid MPM

Biphasic MPM

Predominant cell type?
MPM Diagnosis

Histology

Epithelioid

Biphasic

Sarcomatoid

Undifferentiated
MPM Diagnosis

Epithelioid

• Better prognosis
• 50 – 60% of cases
• Less invasive
• Fewer distant metastases
• Requires local control more than systemic control

Sarcomatoid

• Worse prognosis
• 10 – 15% of cases
• More invasive
• More likely to metastasis
• Requires more systemic control than local control
# IMIG TNM Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>T1a N0 M0</td>
<td>Primary tumour limited to ipsilateral parietal pleura</td>
</tr>
<tr>
<td>Ib</td>
<td>T1b N0 M0</td>
<td>As stage Ia plus focal involvement of visceral pleura</td>
</tr>
<tr>
<td>II</td>
<td>T2 N0 M0</td>
<td>As stage Ia or Ib plus confluent involvement of diaphragm or visceral pleura or involvement of the lung</td>
</tr>
<tr>
<td>III</td>
<td>Any T3 M0</td>
<td>Locally advanced tumour</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ipsilateral, bronchopulmonary or hilar lymph node involvement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subcarinal or ipsilateral mediastinal lymph node involvement</td>
</tr>
<tr>
<td>IV</td>
<td>Any T4</td>
<td>Locally advanced technically unresectable tumour</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contralateral mediastinal, internal mammary, and ipsilateral or contralateral supraclavicular lymph node involvement</td>
</tr>
<tr>
<td></td>
<td>Any N1 M0</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>
Stage Ia
Stage Ib
Stage II
Stage III
Stage III
Stage IV
Stage IV
"The only realistic treatment goal in advanced MPM is control of disease progression." 

MPM Treatment Options

• Median survival is ~9 – 12 months\textsuperscript{6}
• No known curative treatment\textsuperscript{6}
• Chemotherapy
• Radiation Therapy
• Surgery
  • Radical Extrapleural pneumonectomy (EPP)
  • Radical pleurectomy/decortication (P/D)
  • Pleurodesis

MPM Treatment Options

Chemotherapy

- Cisplatin and pemetrexed
- ~ 3-month survival benefit

MPM Treatment Options

FDA Pemetrexed Approval

On February 4, 2004, the FDA approved pemetrexed disodium for injection (Alimta®, made by Eli Lilly and Company) in combination with cisplatin for the treatment of patients with malignant pleural mesothelioma whose disease is either unresectable or who are not otherwise candidates for curative surgery.
MMPM Treatment: Surgery

**EPP**

En bloc resection of lung, pleura, pericardium, and diaphragm

**P/D**

Resection of the parietal and visceral pleurae, pericardium, and diaphragm when necessary, but sparing lung

--

Keep existing tissue planes intact (pericardium, diaphragm, etc.) to prevent seeding of additional areas

---

# MPM Treatment: Surgery

<table>
<thead>
<tr>
<th>EPP</th>
<th>P/D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radical surgery</td>
<td>Radical surgery</td>
</tr>
<tr>
<td>Allows higher radiation doses</td>
<td>Lower radiation doses &amp; more specialized technique</td>
</tr>
<tr>
<td>Longer disease free period</td>
<td>Disease free period shorter</td>
</tr>
<tr>
<td>Less local recurrence</td>
<td>Local recurrence</td>
</tr>
<tr>
<td>Higher mortality and morbidity</td>
<td>Lower mortality and morbidity</td>
</tr>
<tr>
<td>Patient selection: less comorbidities</td>
<td>Patient selection: more comorbidities</td>
</tr>
<tr>
<td>At best: R1 resection</td>
<td>At best: R1 resection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Site of Recurrence</th>
<th>EPP (n = 219) n (%)</th>
<th>P/D (n = 133) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local recurrences</td>
<td>73 (33%)</td>
<td>86 (65%)</td>
</tr>
<tr>
<td>Ipsilateral chest</td>
<td>68 (31%)</td>
<td>84 (63%)</td>
</tr>
<tr>
<td>Pericardium</td>
<td>5 (2%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Distant recurrences</td>
<td>146 (66%)</td>
<td>47 (35%)</td>
</tr>
<tr>
<td>Contralateral lung/pleura</td>
<td>49 (22%)</td>
<td>14 (11%)</td>
</tr>
<tr>
<td>Peritoneum</td>
<td>57 (26%)</td>
<td>24 (18%)</td>
</tr>
<tr>
<td>Peritoneum + chest</td>
<td>17 (8%)</td>
<td>1</td>
</tr>
<tr>
<td>Abdominal viscera</td>
<td>12 (5%)</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Bone</td>
<td>7 (3%)</td>
<td>–</td>
</tr>
<tr>
<td>Brain</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cutaneous (distant)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>2 (2%)</td>
</tr>
</tbody>
</table>

*EPP, Extrapleural pneumonectomy; P/D, pleurectomy/decortication.*
Figure 3  Overall survival of EPP versus P/D, by univariate analysis.  EPP, Extrapleural pneumonectomy;  P/D, pleurectomy/decortication.

Raja M. Flores , Harvey I. Pass , Venkatraman E. Seshan , Joseph Dycoco , Maureen Zakowski , Michele Carbone , Man...

**Extrapleural pneumonectomy versus pleurectomy/decortication in the surgical management of malignant pleural mesothelioma: Results in 663 patients**

Figure 4  Overall survival of EPP versus P/D for patients with stage I.  EPP, Extrapleural pneumonectomy;  P/D, pleurectomy/decortication.

Raja M. Flores , Harvey I. Pass , Venkatraman E. Seshan , Joseph Dycoco , Maureen Zakowski , Michele Carbone , Man...

Extrapleural pneumonectomy versus pleurectomy/decortication in the surgical management of malignant pleural mesothelioma: Results in 663 patients

Mesothelioma: The Problem

**Pleural Mesothelioma**

<table>
<thead>
<tr>
<th>Healthy Lung</th>
<th>Diseased Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>visceral pleura</td>
<td>visceral pleura</td>
</tr>
<tr>
<td>parietal pleura</td>
<td>parietal pleura</td>
</tr>
<tr>
<td>pleural space</td>
<td>pleural space</td>
</tr>
<tr>
<td>cancer</td>
<td>cancer</td>
</tr>
<tr>
<td>diaphragm</td>
<td>diaphragm</td>
</tr>
</tbody>
</table>

**Mesothelioma**

- compressed lung
- chest wall
- mesothelioma
MPM Treatment: Surgery

Classification of Surgical Oncology Resections

- R0: Radical resection (amputation, muscle groups, wide local resection with 2-3 cm margins)
- R1: Marginal resection (within tumor “capsule”)
- R2: Incomplete resection of gross tumor
Mesothelioma: The Problem

- Radical Resection
- Marginal Resection

- Tumor
- Lung
- Septa
MPM Treatment: The Problem

“You are only as good as your \textbf{CLOSEST} surgical margin”
# Mesothelioma: EPP versus P/D

<table>
<thead>
<tr>
<th></th>
<th>EPP</th>
<th>P/D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Margins</td>
<td>Minimal</td>
<td>Minimal</td>
</tr>
<tr>
<td>$\Delta$ PFT’s</td>
<td>---</td>
<td>+/-</td>
</tr>
<tr>
<td>Mortality</td>
<td>3-6%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Operative time</td>
<td>Intermediate</td>
<td>Long</td>
</tr>
<tr>
<td>Surgeon’s Fee</td>
<td>$1348.46-$2676.83</td>
<td>$1249.68-$2444.26</td>
</tr>
<tr>
<td>Ages</td>
<td>Younger</td>
<td>Almost any</td>
</tr>
<tr>
<td>Lung Status</td>
<td>Good PFT’s</td>
<td>Almost any</td>
</tr>
<tr>
<td>Radiation</td>
<td>Easy</td>
<td>Hard</td>
</tr>
<tr>
<td>Recurrence</td>
<td>Hard to detect</td>
<td>Easy to detect</td>
</tr>
</tbody>
</table>
Mesothelioma: “Rational” Therapy

• Surgery may provide benefit from “debulking” tumor mass (ovarian cancer as prototype)

• Radical procedures do not provide safer “margin” than more conservative procedures

• Radiation may provide benefit with microscopic disease

• Chemotherapy provides minimal benefit
Mesothelioma: GLA VA Approach

- Radical parietal pleurectomy
- Complete pulmonary decortication (radical visceral pleurectomy)
- Removal of all pleural tumor off diaphragm, pericardium, mediastinum, and hilum
- Lymph node dissection
- Preservation of all tissue planes possible
- Postoperative radiation therapy
- Novel biologic therapies when available
Mesothelioma: GLA VA Surgical Goals

- Remove/destroy all tumor (gross)
- Preserve tissue boundaries
- Preserve vital organ function
- Use effective adjuvant therapies
- Use maintenance therapies
- Develop screening/detection tests
- Develop prevention stratagies
Mesothelioma: GLA VA P/D

The Incision
Mesothelioma: GLA VA P/D
Initial View
Mesothelioma: The UCLA P/D

Chest Wall Retractor

Diaphragm

Tumor
Mesothelioma: GLA VA P/D

Diaphragm
Mesothelioma:GLA VA  P/D

Diaphragm Repair
Mesothelioma: GLA VA  P/D

Visceral Pleurectomy

Lung

Tumor
Mesothelioma: GLA VA P/D

Decortication

Tumor

Lung
Mesothelioma: GLA VA P/D

Tumor in the Fissure
Mesothelioma: GLA VA P/D

Tumor in the Fissure
Mesothelioma: GLA VA P/D

Pericardium

Diaphragm
Mesothelioma: GLA VA P/D

Complete Decortication

Fissure
Mesothelioma: GLA VA P/D

Final Appearance
Mesothelioma: GLA VA P/D

Pathology Specimen
P/D Post-op Management

- ICU care (at UCLA: PCU care)
- Average LOS 10 days
- Extubate in OR
- CT x4 to -20 cm H20 continuous wall suction
- Begin ambulation POD1
- Epidural x 7-8 days

- Replace pleural fluid drainage
- DC f/c POD2
MPM: GLA VA Protocol

Epithelioid Histology
↓
P/D
↓
IMRT
↓
+/− chemotherapy
↓
Immunotherapy
↓
Survivellance PET q3m

Sarcomatoid Histology
↓
Neoadjuvant Chemo
↓
+/− P/D
↓
IMRT
↓
Immunotherapy vs chemo
↓
Survivellance PET q3m
Neoadjuvant IMRT

Goal is to radiate edges and surgical incision while sparing the lung
Mesothelioma: IMRT

Coronal Image 270

Sagittal Image 319

Axial Image 121

Color codes:
- Yellow: 60.0% (39.0 Gy)
- Yellow: 70.0% (45.4 Gy)
- Orange: 80.0% (51.9 Gy)
- Red: 90.0% (58.4 Gy)
- Purple: 83.0% (53.9 Gy)
Mr. S Before and After
Mr. S Before and After
Cryoablation
References


2 American Cancer Society


