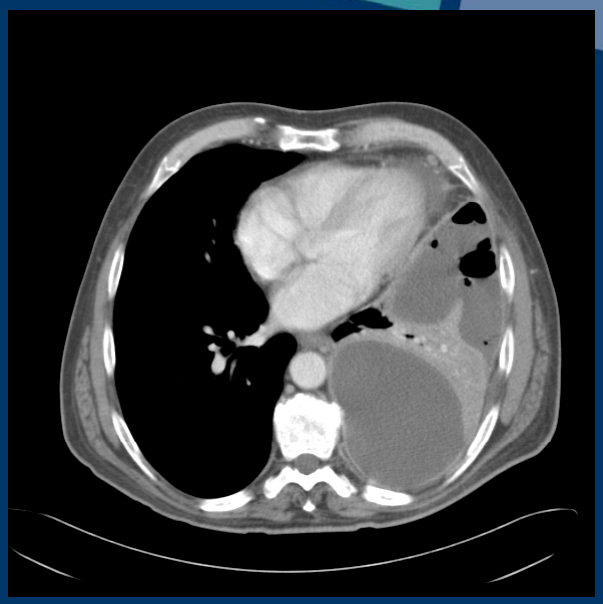
Montefiore
THE UNIVERSITY HOSPITAL

EINSTEIN
Albert Einstein College of Medicine
OF YESHIVA UNIVERSITY

Modern Approaches to Empyema

Amit Bhargava, MD
Attending Thoracic Surgeon
Assistant Professor
Department of Cardiovascular and Thoracic Surgery



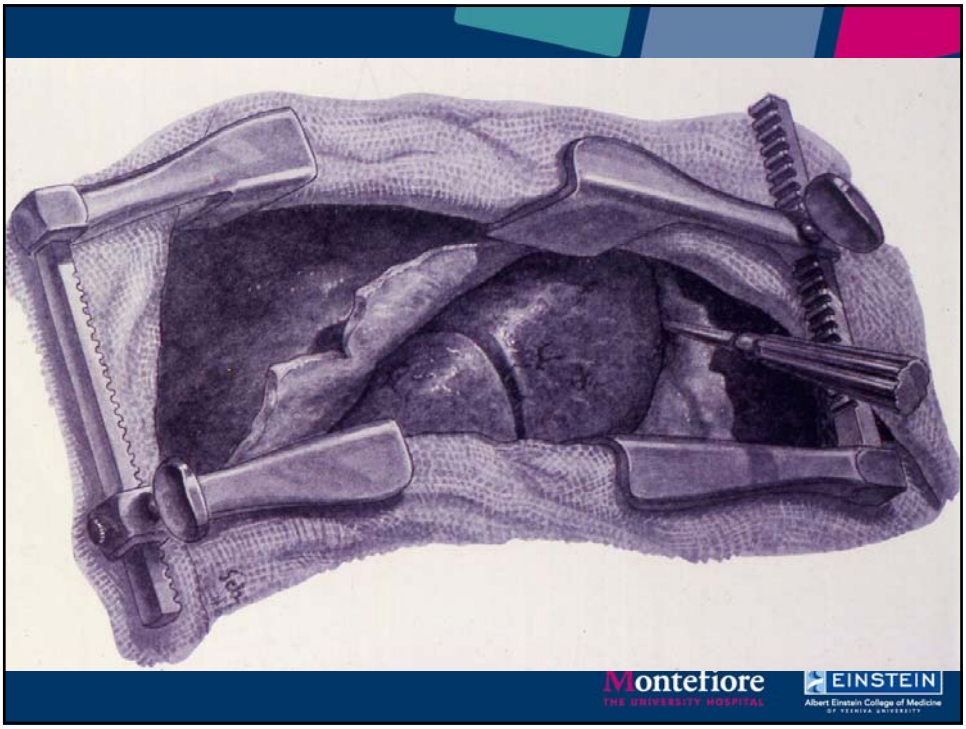
Principles of Treatment

- Adequate drainage
- Sterilization with antimicrobials
- Obliteration of the infected space

Modalities of Treatment

- Thoracotomy, decortication
- Thoracoscopy, decortication
- Chest tube drainage
  - +/- fibrinolytics
- Thoracentesis

Montefiore THE UNIVERSITY HOSPITAL
EINSTEIN Albert Einstein College of Medicine



Montefiore THE UNIVERSITY HOSPITAL
EINSTEIN Albert Einstein College of Medicine

Modalities of Treatment

- Which therapy is appropriate for empyema patients?
  - Does one size fit all?

Montefiore THE UNIVERSITY HOSPITAL | EINSTEIN Albert Einstein College of Medicine

Stages of Empyema
Stage I - Exudative

- Uncomplicated Parapneumonic effusion
  - Non-purulent culture-negative effusion associated with pneumonia
- Fibrin deposition
- Lung is compliant, can reexpand with evacuation of fluid

Montefiore THE UNIVERSITY HOSPITAL | EINSTEIN Albert Einstein College of Medicine

Stage I
Parapneumonic Effusion

- Treatment options:
  - Spontaneous resolution with antibiotic therapy
  - Thoracentesis
  - Chest tube drainage

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Stages of Empyema
Stage II - Fibrinopurulent

- Heavy fibrin deposits over parietal and visceral pleura
  - Loculations/adhesion
- Pleural fluid
  - Characteristics:
    - Ph <7
    - Glucose < 50
    - LDH > 1000
- Lung less mobile but still expandable

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Stages of Empyema
Stage II - Fibrinopurulent

- Treatment options:
  - Chest tube with fibrinolytics
  - Thoracotomy Decortication
  - VATS Decortication

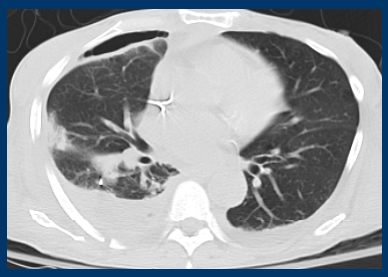
Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Stages of Empyema
Stage III – Fibrotic (Chronic)

- In-growth of fibroblasts and formation of collagen fibers over both parietal and visceral surfaces
  - Inelastic pleural peel, trapping lung
- Frank pus

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Stages of Empyema
Stage III – Fibrotic (Chronic)



- Treatment options:
  - Chest tube with fibrinolytics
  - Thoracotomy Decortication
  - VATS Decortication

Montefiore THE UNIVERSITY HOSPITAL | EINSTEIN Albert Einstein College of Medicine

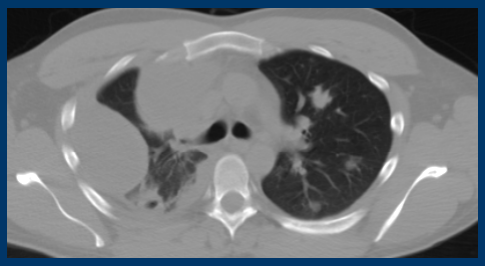
Imaging- CXR

- Pleural effusion +/- underlying lung pathology
- Usually posterior and lateral extending to diaphragm on lateral view
- Decubitus views help delineate loculations

Montefiore THE UNIVERSITY HOSPITAL | EINSTEIN Albert Einstein College of Medicine

Imaging – CT Scan

- Differentiate between abscess, consolidation and empyema
- Determines loculations and stage of empyema
- Evaluate pleura
- Signs:
  - thickened and separated pleural surfaces
  - compression of parenchyma
  - pleural enhancement



- Assess possible intervention

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Can Empyema be treated nonsurgically?

- Thoracentesis or chest tube drainage for stage I, uncomplicated parapneumonic effusion is uncontroversial
- Debate over whether chest tube drainage with fibrinolytic therapy can be a definitive treatment for stages II and III

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Fibrinolytic Therapy

- First described in 1950's with streptokinase
  - Initial literature was retrospective case series
  - Few randomized controlled trials
    - Compared to placebo
    - Increased chest tube drainage
    - Reduced referral for surgery
    - Decrease in treatment length, mortality
- Small studies, not confirmed in larger ones

Davies et al, Thorax 1997; Chin et al, Chest 1997; Diacon et al, J Resp Crit Care Med 2004; Misthos et al EJCTS 2005

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Fibrinolytic Therapy

- Streptokinase compared to VATS
  - 20 patients per arm
  - Loculated effusion or ph < 7.2
  - VATS with shorter hospital stay (8.7 v 12.8) and higher success rate (91 v 44%)

Wait et al, Chest 1997

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Fibrinolytic Therapy – MIST-1

- 454 patients, randomized, double-blind
- Streptokinase BID for 3 days v placebo
- Primary endpoints:
  - Death
  - Surgery requirement
- Efficacy determined by reduction in pleural opacity on CXR
- No difference noted in any parameters

Maskell et al, NEJM 2005

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Fibrinolytic Therapy – Is it enough?

- In vitro studies showed that free DNA cleavage reduces fluid viscosity which allows for pleural clearance by the fibrinolytic agents
- This is distinct from pediatric empyemas
  - Predominant organism *s. pneumo*
  - Clearance with streptokinase works
  - Adults have polymicrobial or nosocomial infections

Corcoran and Rahman , Chest 2014

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Fibrinolytic Therapy – MIST-2

- Prospective randomized, double blinded, multi-institutional trial
- 4 arms:
  - Double placebo (n=55)
  - tPA/placebo (n=52)
  - DNase/placebo (n=51)
  - tPA 10 mg/DNase 5 mg (n=52)
- BID administration for 3 days
  - Tube clamped for 1 hour

Rahman et al, NEJM 2011

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Fibrinolytic Therapy – MIST-2

- Eligibility:
  - Clinical evidence infection
    - Fever
    - Elevated WBC, CRP
  - Purulent pleural fluid
    - Positive culture or Gram's stain
    - Ph< 7.2

Rahman et al, NEJM 2011

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Fibrinolytic Therapy – MIST-2

- Primary endpoint – change in pleural opacity on chest x-ray from day 1 to day 7
- Secondary endpoints
  - Referral for surgery (by 3 mos. and 12 mos.)
    - If sx/signs present >48 hours after completion of treatment
    - Poor CXR response with improved sx not reason
  - Hospital LOS
  - Adverse events
- 97% followup at 12 months

Rahman et al, NEJM 2011

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Fibrinolytic Therapy – MIST-2

- tPA/DNase group had increased change in opacity compared to placebo
  - tPA alone and DNase alone no diff. compared to placebo
- tPA/DNase group with decreased surgical referral at 3 months compared to placebo
  - tPA alone more referrals compared to placebo
  - DNase alone with non-significant reduction

Rahman et al, NEJM 2011

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Fibrinolytic Therapy – MIST-2

- tPA/DNase with shorter hospital stay (6.7 days shorter, but still 11.8 day mean)
- No change in mortality at both time points
- Inflammatory measures not significantly different

Rahman et al, NEJM 2011

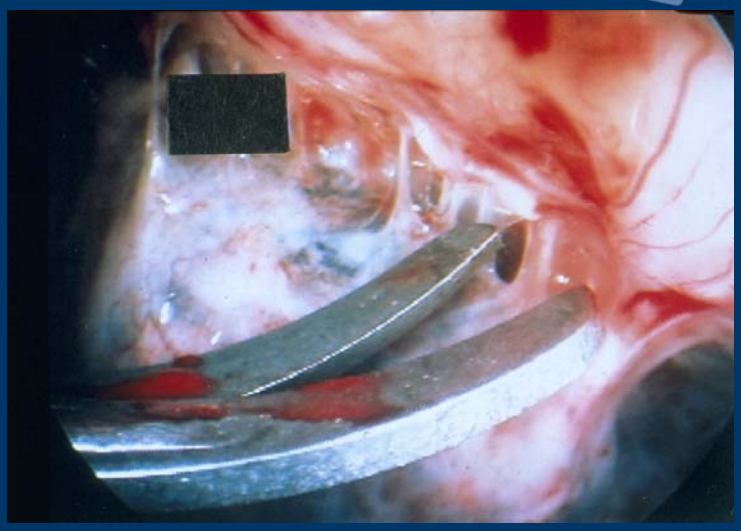
Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Fibrinolytic therapy – MIST-2

- 91% pts with loculated effusion
  - 70% in MIST1
- Only used CXR for analysis, not CT
- Meta-analysis in Chest 2012 shows potential benefit in patients with loculated effusions

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Montefiore
THE UNIVERSITY HOSPITAL
EINSTEIN
Albert Einstein College of Medicine



Montefiore
THE UNIVERSITY HOSPITAL
EINSTEIN
Albert Einstein College of Medicine

Surgical treatment of empyema

- British Thoracic Society:
  - Referral 5-8 days if initial therapy fails
- ACCP:
  - Surgery acceptable for advanced-stage empyema

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Surgical treatment of empyema

- Retrospective series show surgery compared to simple drainage has:
  - Increased likelihood of success
  - Fewer deaths
- No randomized trials comparing VATS to open

Wozniak et al, Ann Thor Surg, 2009
Shin et al JTCVS 2013

Montefiore THE UNIVERSITY HOSPITAL EINSTEIN Albert Einstein College of Medicine

Surgical treatment of empyema

- Stage 2 outcomes similar for VATS and thoracotomy approach
- Stage 3 outcomes
  - VATS equivalent in one study with Stage 2 and 3 patients
  - Stage 3 conversion rates up to 59%
    - Delay from onset of symptoms to OR
    - Fever
    - Pleural thickening on scan

Muhammad, Asian CV Thor Ann 2012
Angelillo et al Ann Thor Surg 1996

Montefiore THE UNIVERSITY HOSPITAL
EINSTEIN Albert Einstein College of Medicine

Conclusions

- Chest tube drainage with fibrinolytic therapy is a reasonable approach in selected patients with loculated pleural effusions
- VATS appropriate for stage II
- VATS reasonable initial approach for stage III with low threshold for conversion

Montefiore THE UNIVERSITY HOSPITAL
EINSTEIN Albert Einstein College of Medicine