Acute Respiratory Distress Syndrome
Acute Lung Injury
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Learning Objective
✓ Explain the etiologies, manifestations, diagnostic techniques and current management strategies for acute respiratory distress syndrome and acute lung injury.

Definitions & Etiologies

Acute lung injury/ARDS
✓ ALI/ARDS is a syndrome that is response to injury and not a disease.
✓ There is much variability in pathology and pathophysiology.
✓ Acute Lung Injury (ALI)
  ◆ hypoxemic respiratory failure
  ◆ severe version- Acute Respiratory Distress Syndrome (ARDS).

Characteristics:
✓ Bilateral pulmonary infiltrates on chest x-ray
✓ Pulmonary Capillary Wedge Pressure <18 mm Hg
✓ PaO2/FiO2 <300 = ALI
✓ PaO2/FiO2 <200 = ARDS

Characteristics:
✓ surfactant deficiency
✓ decreased lung compliance
✓ decreased lung volume
**Synonyms (history):**
- Da Nang lung - Viet Nam
- shock lung
- non-cardiogenic pulmonary edema
- leaky capillary syndrome
- acute lung injury
- diffuse alveolar damage

**Etiologic mechanisms**
- direct lung injury (pulmonary)
  - inhalation injury
  - pneumonia
  - aspiration
- indirect lung injury (extrapulmonary)
  - shock
  - sepsis
  - transfusion related injury
  - pancreatitis

**Predisposing Conditions**
- trauma, shock
- aspiration
- oxygen toxicity
- toxic fumes
- sepsis

**Predisposing Conditions**
- narcotic overdose
- pancreatitis
- fat embolism
- near drowning
- transfusion- transfusion-associated lung injury (TRALI)
- eclampsia/pre-eclampsia
- amniotic embolism

**Pathophysiology**

**ARDS Pathophysiology**
- Initial insult
  - directly to lung
  - indirectly, via system
- Pathology stages
  - exudative (4-7D after onset)
  - proliferative (1-3 wks.)
  - recuperative or fibrotic (3-4 wks)

FYI - Link to article on ALI/ARDS
http://www.aafp.org/afp/20030115/315.html
**Exudative Stage**

- Injury to:
  - vascular endothelium or
  - alveolar epithelium

- Leaky capillaries allow influx of proteinaceous fluid (edema)

- Alveolar macrophages release cytokines

- Cytokines attract neutrophils, that release:
  - tumor necrosis factor (TNF-a)
  - free oxygen radicals

- Inflammation

- Cell death - type I pneumocytes

**Proliferative Stage**

- Alveoli filled with:
  - cellular debris
  - oxidants
  - fibrin
**Proliferative Stage**
- Surfactant depleted/inactivated
- Hyaline membrane formation

**Resolution or Fibrosis**
- Phagocytosis of debris or
- Collagen deposition - fibrosis with lung like a liver

Click to see gross pathology of fibrosis following ALI/ARDS
http://library.med.utah.edu/WebPath/LUNGHML/LUNG096.html

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**Manifestations & Complications**

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**Manifestations**

- There is variability in ARDS
  - Pulmonary, vs. extrapulmonary etiology
  - Consolidation vs. edema
  - Post-traumatic vs. non-traumatic

- Variability will affect:
  - Duration of illness
  - Response to ventilation strategies; e.g., PEEP, recruitment maneuvers (RM), pronation
  - Prognosis

- Onset - hours to days after initial insult
- Physical signs
  - Tachypnea
  - Retractions; e.g., supraclavicular
  - Abdominal paradox - diaphragmatic fatigue
  - Crackles, rhonchi, bronchial sounds
- Progressive, refractory hypoxemia
- Decreased lung compliance ($C_L$)
**Manifestations**

- **CXR**
  - Decreased lung volumes
  - Fluffy alveolar infiltrates
  - Air bronchograms
  - Hyaline membrane

- **CXR - ALI/ARDS**
  - Click to see images of ARDS following pulmonary contusion
    http://www.trauma.org/archive/thoracic/CHESTcontusion.html
  - Click to see images of transfusion associated lung injury
    http://www.cmaj.ca/cgi/content/figsonly/177/2/149
  - Click to see images of acute lung injury with air bronchograms
    http://www.ccmtutorials.com/rs/ali/01_ali.htm

**Complications**

- Ventilator-induced lung injury
  - ALI/ARDS is non-uniform
  - Posterior lungs edematous, collapsed
  - Normal lung units are subject to:
    - Overdistension
    - Loss of perfusion

- Ventilator-associated pneumonia - prolonged intubation
- Multiple organ system failure - release of mediators from lung
- Hemodynamic compromise (shock)
- Sepsis
- Pulmonary fibrosis

**Prognosis**

- Mortality - about 40%
- Prognosis better for trauma victims
  - Younger
  - Less comorbidity
- Severity correlates with duration of precipitating injury, not type of injury

- 66% survivors have lung dysfunction
- Psychiatric illness - depression
- Cognitive impairment
Diagnosis

Differential diagnosis
- cardiogenic pulmonary edema
- inhalation injury
- aspiration
- pneumonia (many types)
- hypersensitivity pneumonitis
- drug toxicity; e.g., amiodarone
- alveolar hemorrhage
- severe acute respiratory distress syndrome (SARS) - coronavirus

ARDS vs. cardiogenic pulmonary edema
- ARDS - PAOP (PCWP) < 18 mm Hg
- ARDS - alveolar exudate (proteins)
- Cardiogenic - cardiomegaly
- Brain natriuretic peptide (BNP) does not accurately differentiate

FYI - Link to study on BNP for differentiation of ARDS from cardiogenic pulmonary edema
http://ccforum.com/content/12/1/R3

Diagnostic Studies
- CT scan
  - determine anteroposterior distribution of consolidation
  - may predict effectiveness of pronation

FYI - Link to article on CT scanning and ARDS
http://ajrccm.atsjournals.org/cgi/content/full/164/9/1701

Diagnostic Studies
- Bronchoalveolar lavage
  - distinguish between transudate and exudate
  - identify or R/O infection
  - identify inflammatory cells
  - identify inflammatory mediators
Diagnostic Studies

- Open lung biopsy
  - identify pathologic process
  - identify etiology

FYI - Link to article on open lung biopsy in ARDS

Management

General strategies

- Treat underlying cause, if possible
- Conservative fluid management improves outcomes
- Pulmonary artery catheter monitoring
  - no improvement in outcomes
  - more complications

FYI - Link to study FACTT study synopsis (Requires free Medscape registration)

Ventilation Strategies

- Lung protective strategies
  - open lung technique
    - pressure control with volume guarantee (my recommendation)
    - optimal PEEP
    - TV < 7mL/kg IBW
    - recruitment maneuvers (RM)

FYI - Link to predicted body weight chart
http://www.ardsnet.org/system/files/pbwtables_2005-02-02_0.pdf

Ventilation Strategies

- effectiveness of PEEP and RM
  - contingent upon potentially recruitable alveoli
  - fluid-filled alveoli are not recruitable

Ventilation Strategies

- Pressure-controlled inverse ratio ventilation
  - effective
  - pressure control with volume guarantee and inverse ratio ventilation may be effective
### Ventilation Strategies

- **Airway pressure release ventilation**
  - effective in selected patients
  - less likely to impair hemodynamics

FYI - Link to article on APRV and cardiac performance
http://ccforum.com/content/5/4/221

- **Permissive hypercapnea**
  - allows non-advancement of settings
  - may reduce inflammation
  - may reduce mortality
  - acidemia can be managed with Tromethamine (THAM)

### Ventilation Strategies

- **Pronation**
  - transient improvements in oxygenation
  - many studies found no changes in mortality
  - Mancebo et al- reduced mortality, if applied for 17H/d
  - CT may determine those who will benefit

FYI - click for abstract of study of prolonged pronation (2013)

- **High frequency oscillatory ventilation**
  - as good as conventional ventilation
  - no improvement in mortality

### Non-ventilatory therapeutics

- **Surfactant instillation (children)**
  - decreased mortality
  - decreased duration of ventilation

- **Surfactant instillation (adults)**
  - no effects on mortality
  - quantity of surfactant for adults- expensive

- **Surfactant aerosol- Aerosurf™ under study**
Non-ventilatory therapeutics

Nitric oxide
- dilates vessels in ventilated alveoli
- short-term improvement in oxygenation
- no effects on mortality
- very expensive
- off-label use - no payment

Aerosolized prostacyclin (Flolan)
- same effects as NO
- less costly than NO

Partial liquid ventilation

Lungs filled to FRC with perflubron (LiquiVent), with these properties:
- high density - flows to dependent areas of lung
- low surface tension - increases compliance
- high solubility for O2 and CO2 - transports gases
- high volatility - quickly excreted

Aerosolized prostacyclin (Flolan)
- same effects as NO
- less costly than NO

Partial liquid ventilation

Physiologic effects:
- increased lung compliance, due to:
  - decreased surface tension
  - alveolar recruitment
- decreased VILI due to increased compliance
- decreased shunt due to alveolar recruitment & diffusion across perflubron

Partial liquid ventilation

Potential applications:
- RDS - neonates
- meconium aspiration - not effective for adults
- alveolar proteinosis (1 case)
- ALI/ARDS

Partial liquid ventilation

Procedure
- perflubron instilled to FRC
- re-instillation required, due to evaporation

Partial liquid ventilation

Research findings
- neonates - non-responders to surfactant survived (n = 10)
- adults - most recent trial (2006) found negative for PLV
- earlier trials did not compare PLV with lung protective ventilation

FYI - Click to download article on PLV for neonates with RDS
http://content.nejm.org/cgi/content/full/335/11/761
FYI - Click to download article on PLV for adults with ARDS
http://ajrccm.atsjournals.org/cgi/reprint/173/8/882
### Partial liquid ventilation

- **Barriers to adoption**
  - expense
  - perfluorobron
  - time - dosing, re-dosing
  - lack of positive research findings
- **Opinion** - PLV will not become a widely-used technique, at least for adults

### Non-ventilatory therapeutics

- **Corticosteroids**
  - many investigations (since 1970s)
  - no benefits
  - if started late, may increase mortality

- **Enteral EPA + GLA + antioxidants**
  - increased lung compliance
  - decreased duration of ventilation
  - no effects on mortality

- **n-acetylcysteine (Mucomyst)**
  - intravenous infusion
  - antioxidant properties
  - more research needed

- **Albuterol aerosol**
  - increases $C_{DYN}$ ==> decreased ventilation pressure
  - decreases lung edema
  - anti-inflammatory action - decrease TNF-$\alpha$
  - randomized trial (2011) found no benefit
  - multi-center trial (2012) found that IV albuterol increased mortality

### Summary & Review

- **Definitions - ALI/ARDS**
- **Etiologies**
- **Characteristics**
  - infiltrates
  - stiff lungs
  - refractory hypoxemia
  - PCWP <18 mm Hg
### Summary & Review

#### Pathophysiology
- insult
- capillary permeability - edema
- inflammation
- alveolar injury
- surfactant depletion
- fibrosis/resolution

#### Manifestations
- refractory hypoxemia
- increased WOB
- CXR - consolidation, air bronchograms

#### Complications
- sepsis
- ventilator-induced lung injury
- ventilator-associated pneumonia

#### Diagnosis
- differential diagnosis - many conditions
- chest radiograph
- bronchoscopy
- open lung biopsy

#### Management
- treat underlying cause
- supportive measures
- lung protective strategies
- non-ventilatory measures

#### References
References


References


