APPROACH TO A PATIENT WITH ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

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Kalurghat (Chittagong) Tragedy

A REPORT ON ACUTE LUNG INJURY CASES IN THE RECENT FIRE VICTIMS OF KALURGHAT, CHITTAGONG.

MMU Hassan[1], AKMS Alam[2], GA Chowdhury[3], MAK Bhuiyan[4]

Kalurghat (Chittagong) Tragedy

- Fire at garments factory
- Smoke inhalation
- 11 victims admitted in ICU (CMCH)
- Received mechanical ventilation and same treatment of Acute Respiratory Distress Syndrome (ARDS) (11 patients)
- 9 died; 2 recovered completely (despite same treatment)

ARDS Objectives

- Epidemiology
- Definition of ARDS
- Etiology/Risk factors
- Briefly review Pathophysiology and Pathogenesis
- Clinical Presentation
- Diagnosis, Differential Diagnosis
- Management

Introduction

- 1st described in 1967
- 28 day mortality 25 – 30%
- Diagnosis clinical

Wheeler, A.P. and Bernard, G.R. 2007,Acute Lung Injury and the Acute Respiratory Distress Syndrome: A Clinical Review. *Lancet*; 369: 1553–65

Epidemiology

- Annual incidence: 60/100,000

- Morbidity / Mortality
  - 26-44%, most (80%) deaths attributed to non-pulmonary organ failure or sepsis
  - Patient with ARDS from direct lung injury has higher incidence of death than those from non-pulmonary injury

Levy BD, & Choi AM, *Harrison's Principles of Internal Medicine*, 2012

The American-European Consensus Conference Definition of Acute Lung Injury and ARDS, AECC

	Timing	Oxygenation (PaO_2/FiO_2)	Chest Radiograph	Pulmonary Artery Wedge pressure
ALI	Acute onset	≤ 300 mmHg (40 kPa) (regardless of PEEP)	Bilateral infiltrates	≤18 mmHg/no evidence of left atrial hypertension
ARDS	Acute onset	≤ 200 mmHg (26 kPa) regardless of PEEP	Bilateral infiltrates	≤ 18 mmHg or no evidence of left atrial hypertension

ARDS

New Definition

Acute Respiratory Distress Syndrome
The Berlin definition

Table 1. The AECC Definition[3]—Limitations and Methods to Address These in the Berlin Definition

	AECC Definition	AECC Limitations	Addressed in Berlin Definition
Timing	Acute onset	No definition of acute[4]	Acute time frame specified
ALI category	All patients with PaO_2/FIO_2 <300 mm Hg	Misinterpreted as PaO_2/FIO_2 = 201-300, leading to confusing ALI/ARDS term	3 Mutually exclusive subgroups of ARDS by severity ALI term removed
Oxygenation	PaO_2/FIO_2 ≤300 mm Hg (regardless of PEEP)	Inconsistency of PaO_2/FIO_2 ratio due to the effect of PEEP and/or FIO_2[5-7]	Minimal PEEP level added across subgroups FIO_2 effect less relevant in severe ARDS group
Chest radiograph	Bilateral infiltrates observed on frontal chest radiograph	Poor interobserver reliability of chest radiograph interpretation[8,9]	Chest radiograph criteria clarified Example radiographs created[a]
PAWP	PAWP ≤18 mm Hg when measured or no clinical evidence of left atrial hypertension	High PAWP and ARDS may coexist[10,11] Poor interobserver reliability of PAWP and clinical assesments of left atrial hypertension[12]	PAWP requirement removed Hydrostatic edema not the primary cause of respiratory failure Clinical vignettes created[a] to help exclude hydrostatic edema
Risk factor	None	Not formally included in definition[4]	Included When none identified, need to objectively rule out hydrostatic edema

JAMA. 2012;307(23):2526-2533. doi:10.1001/jama.2012.5669

ARDS

The Berlin Definition

	Acute Respiratory Distress Syndrome
Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging[a]	Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation[b]	
Mild	200 mm Hg < Pao_2/Fio_2 ≤ 300 mm Hg with PEEP or CPAP ≥5 cm H_2O[c]
Moderate	100 mm Hg < Pao_2/Fio_2 ≤ 200 mm Hg with PEEP ≥5 cm H_2O
Severe	Pao_2/Fio_2 ≤ 100 mm Hg with PEEP ≥5 cm H_2O

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Causes

- Direct Injury
  - Pneumonia
  - Aspiration
  - Drowning
  - Amniotic fluid and fat embolism
  - Alveolar haemorrhage
  - Smoke, toxic gas inhalation
  - Pulmonary contusion
  - Reperfusion (incl rapid drainage pleural effusion)

Causes

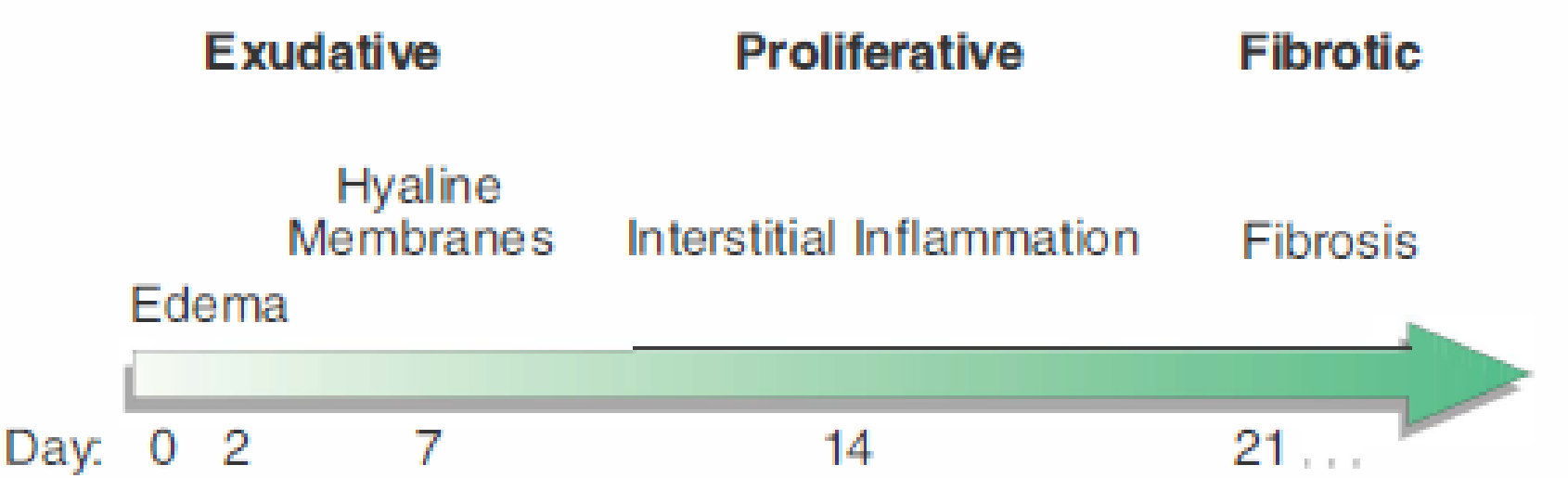
- Indirect Injury
  - Severe Sepsis
  - Massive transfusion
  - Shock
  - Pancreatitis
  - Salicylate/ narcotic overdose
  - Anaphylaxis
  - Cardiopulmonary bypass

PATHOPHYSIOLOGY

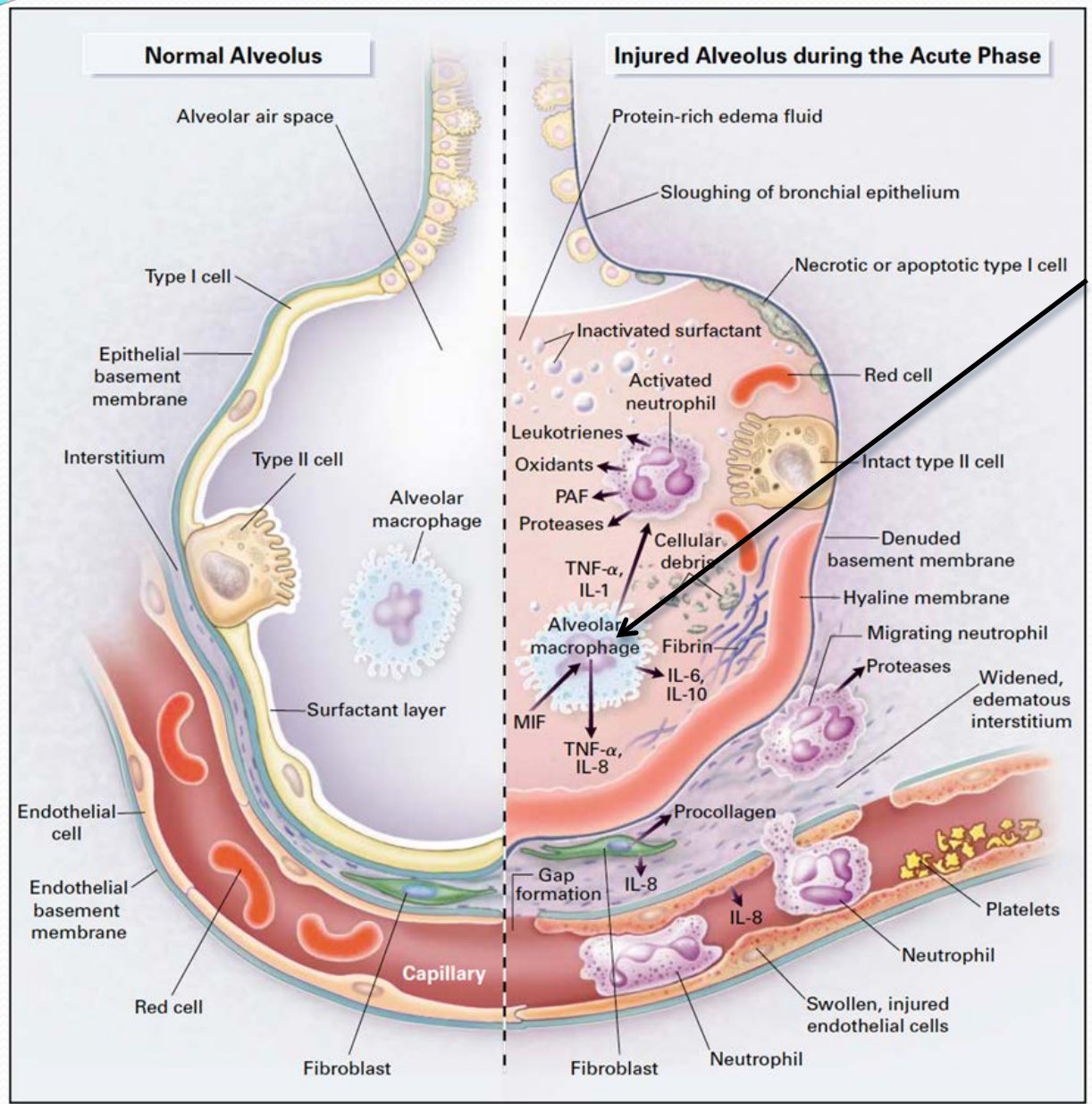
- **The exudative phase** is notable for early alveolar edema and neutrophil-rich leukocytic infiltration of the lungs,with subsequent formation of hyaline membranes from diffuse alveolar damage.

- Within 7 days, **a proliferative phase** ensues with prominent interstitial inflammation and early fibrotic changes

- Approximately 3 weeks after the initial pulmonary injury, most patients recover. However, some patients enter the **fibrotic phase**, with substantial fibrosis and bullae formation



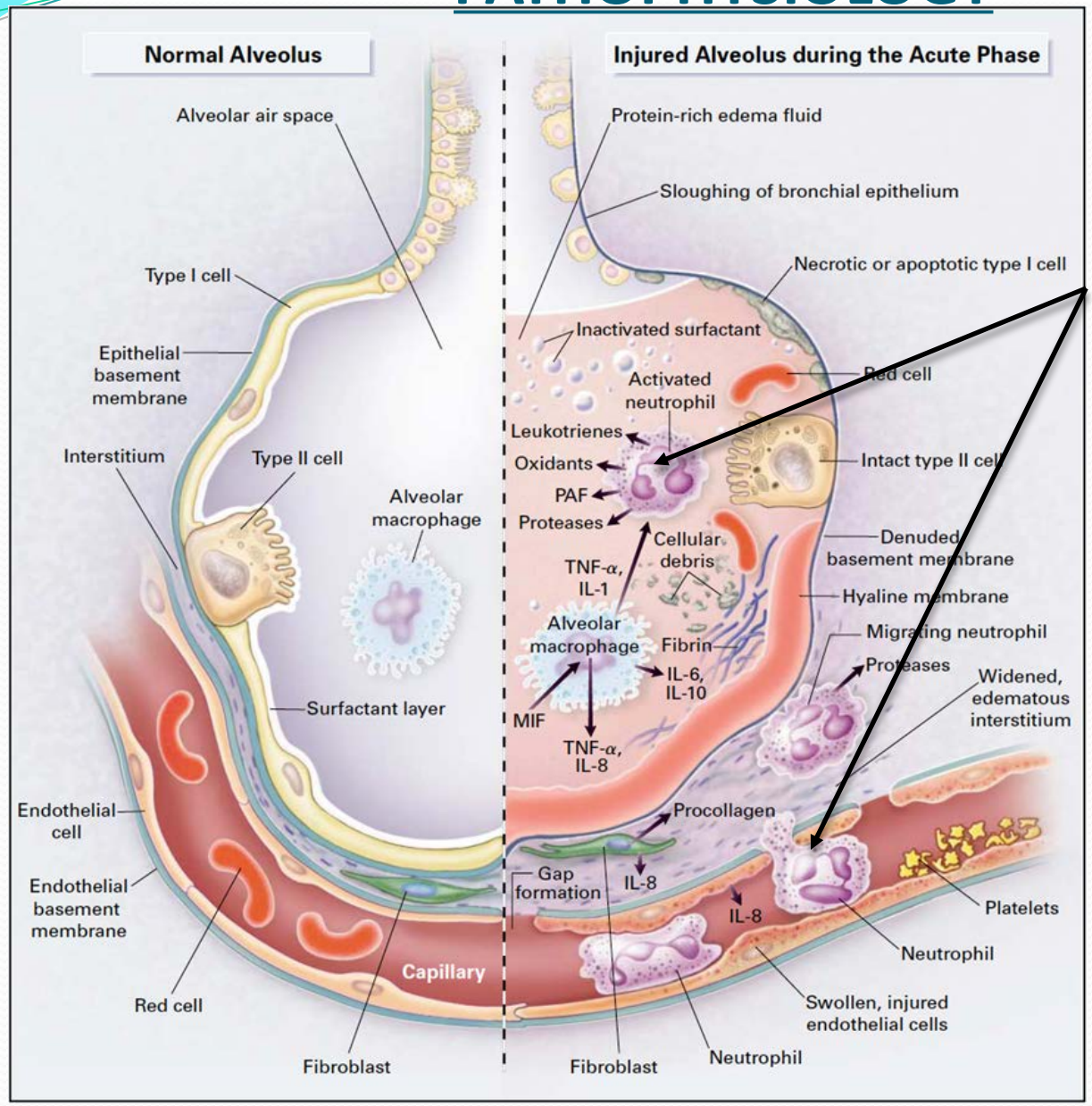
PATHOPHYSIOLOGY



1. Direct or indirect injury to the alveolus causes alveolar macrophages to release pro-inflammatory cytokines

Ware et al. NEJM 2000; 342:1334

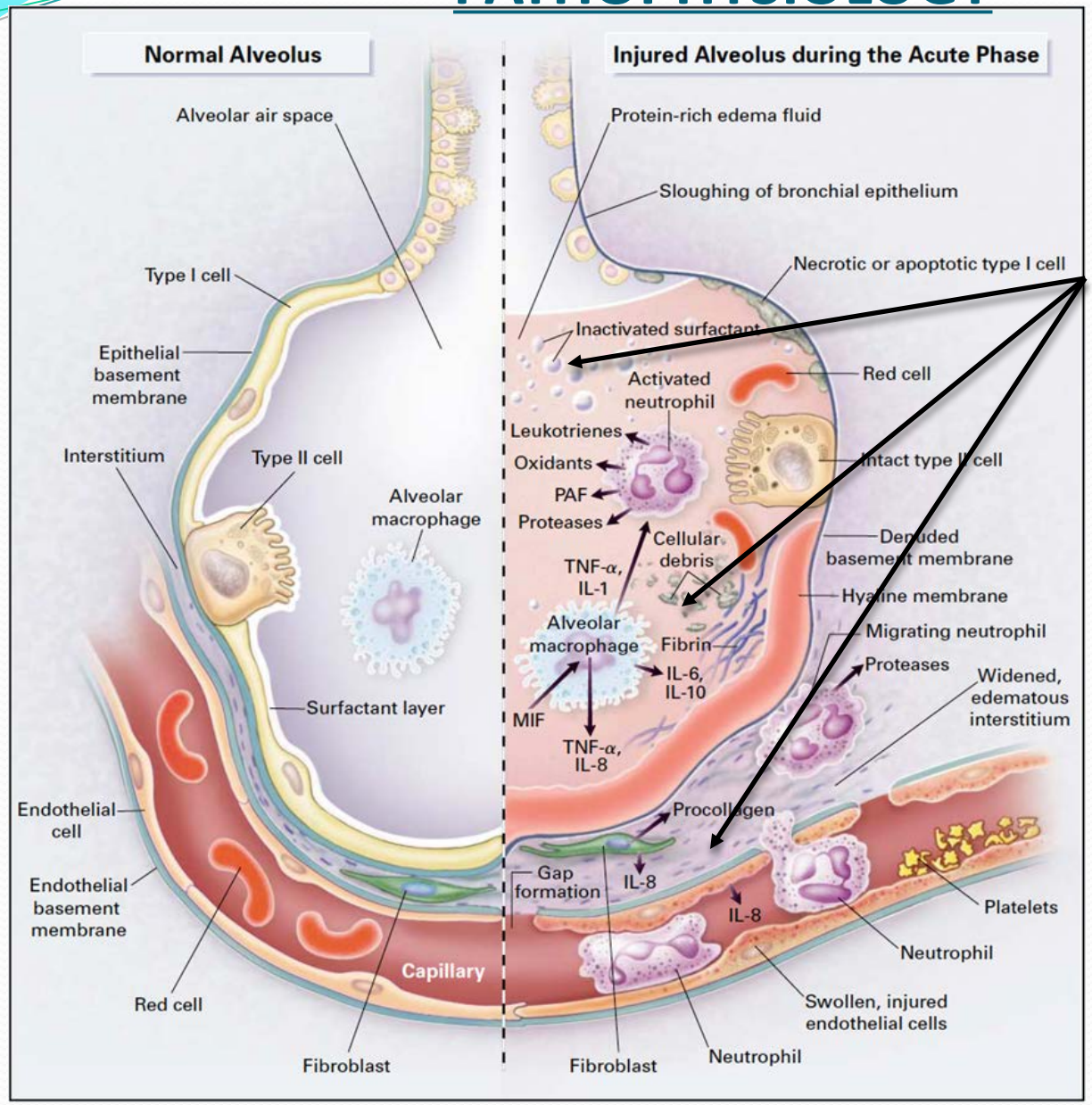
PATHOPHYSIOLOGY



2. Cytokines attract neutrophils into the alveolus and interstitum, where they damage the alveolar-capillary membrane (ACM).

Ware et al. NEJM 2000; 342:1334

PATHOPHYSIOLOGY



3. ACM integrity is lost, interstitial and alveolus fills with proteinaceous fluid, surfactant can no longer support alveolus

Ware et al. NEJM 2000; 342:1334

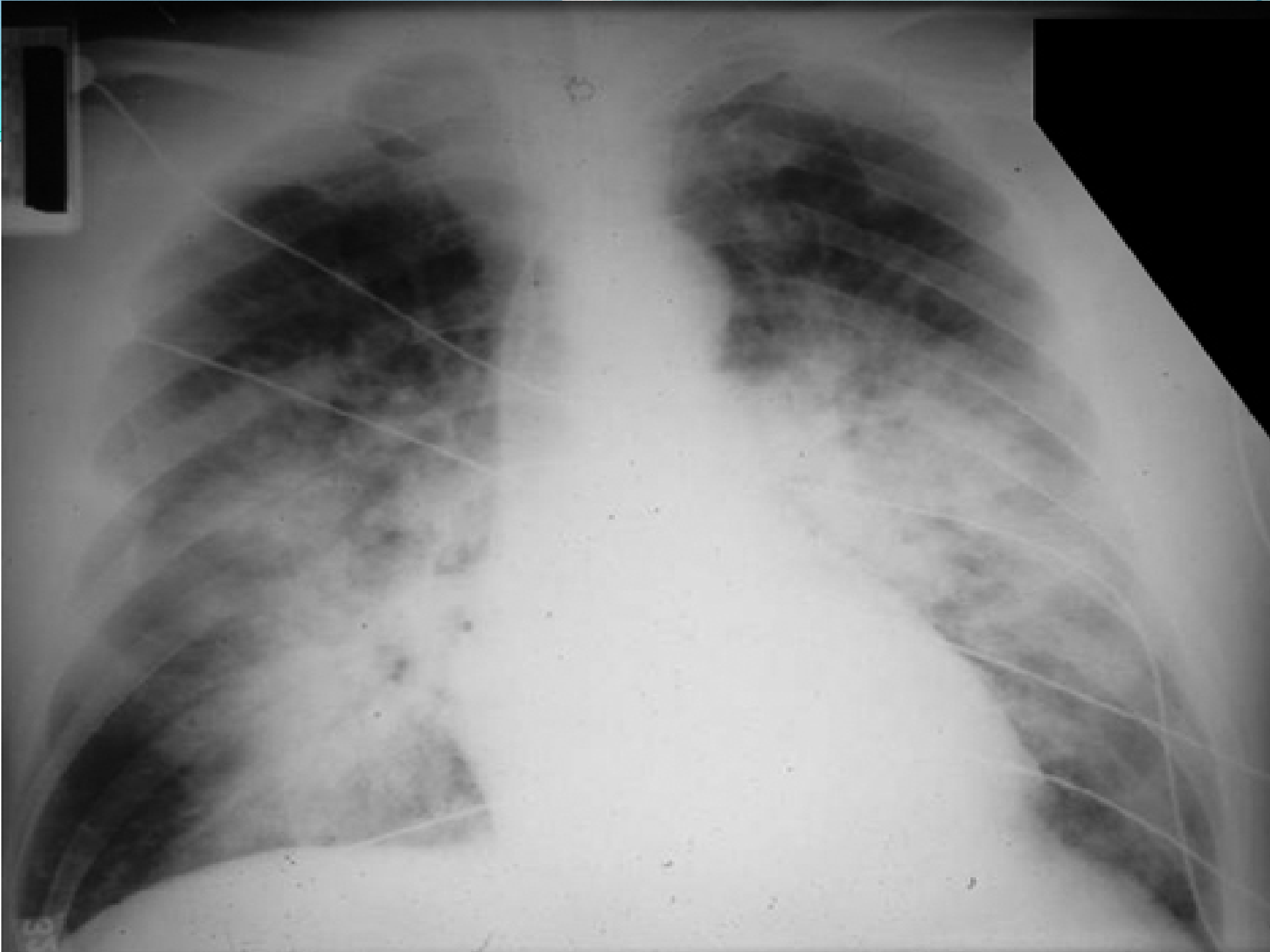
Clinical Stages

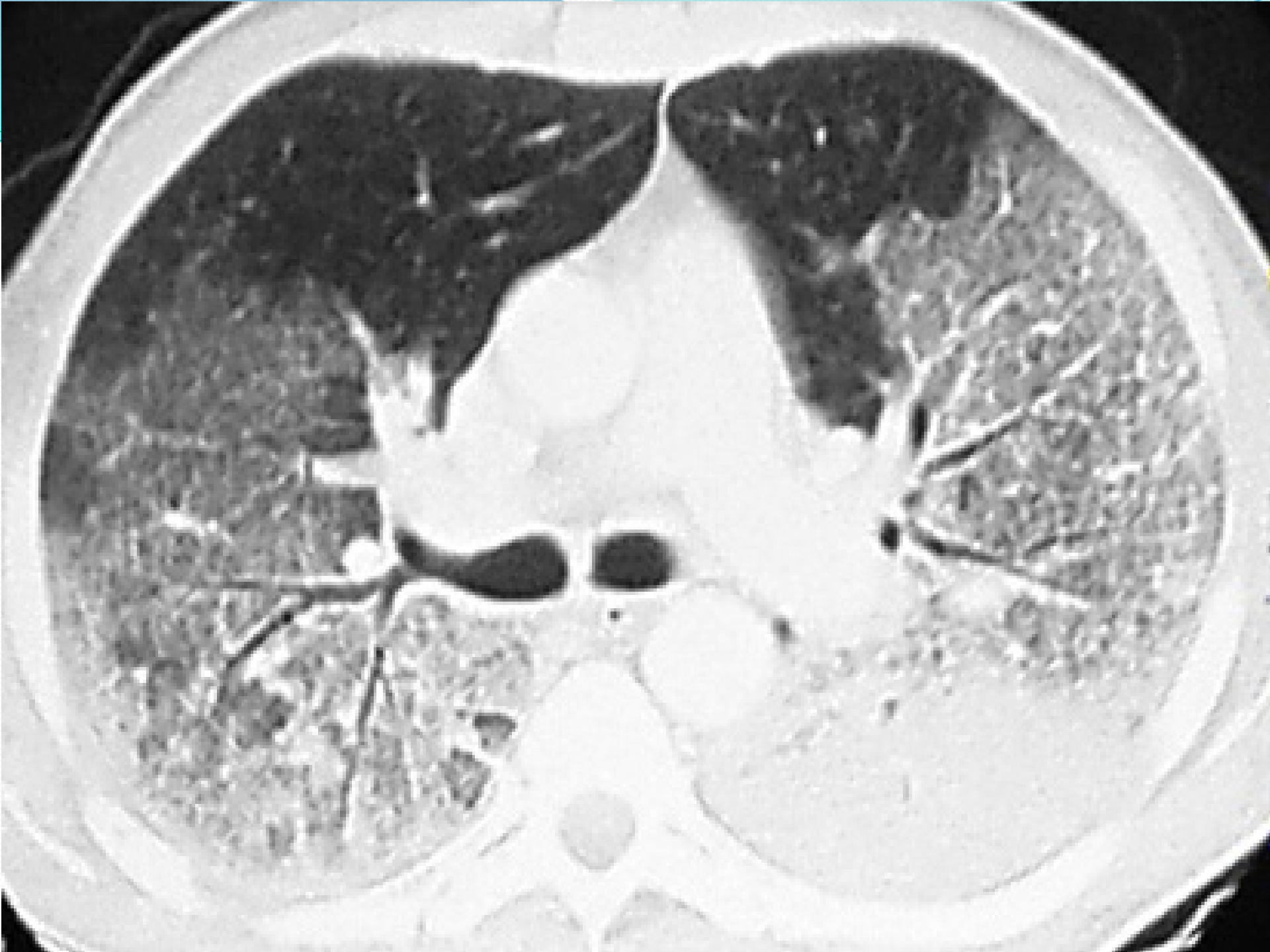
A. Initial Course (exudative phase):

- Usually symptoms predominated by cause of ARDs (eg abd pain from pancreatitis, fever and shock from sepsis)
- Pulmonary dysfunction develops within 24-48 hrs of inciting event.
- Worsening tachypnea, dyspnea, hypoxemia and diffuse crackles on exam.

Clinical Stages

- A. Initial Course (exudative phase) (contd):
- Labs non-specific. May show inc WBC, DIC and lactic acidosis.
- ABG= acute resp alkalosis, inc $DAaO_2$, severe hypoxemia
- CXR= Bilateral patchy infiltrates, does not need to be widespread or severe opacification.
- CT= generally demonstrates patchy abn with increased density in dependent lung zones.





Clinical Stages

B. Proliferative stage:

- Oxygenation tends to improve somewhat over first few days as edema resolves, most patients remain ventilator-dependent due to:

1) Continued hypoxemia

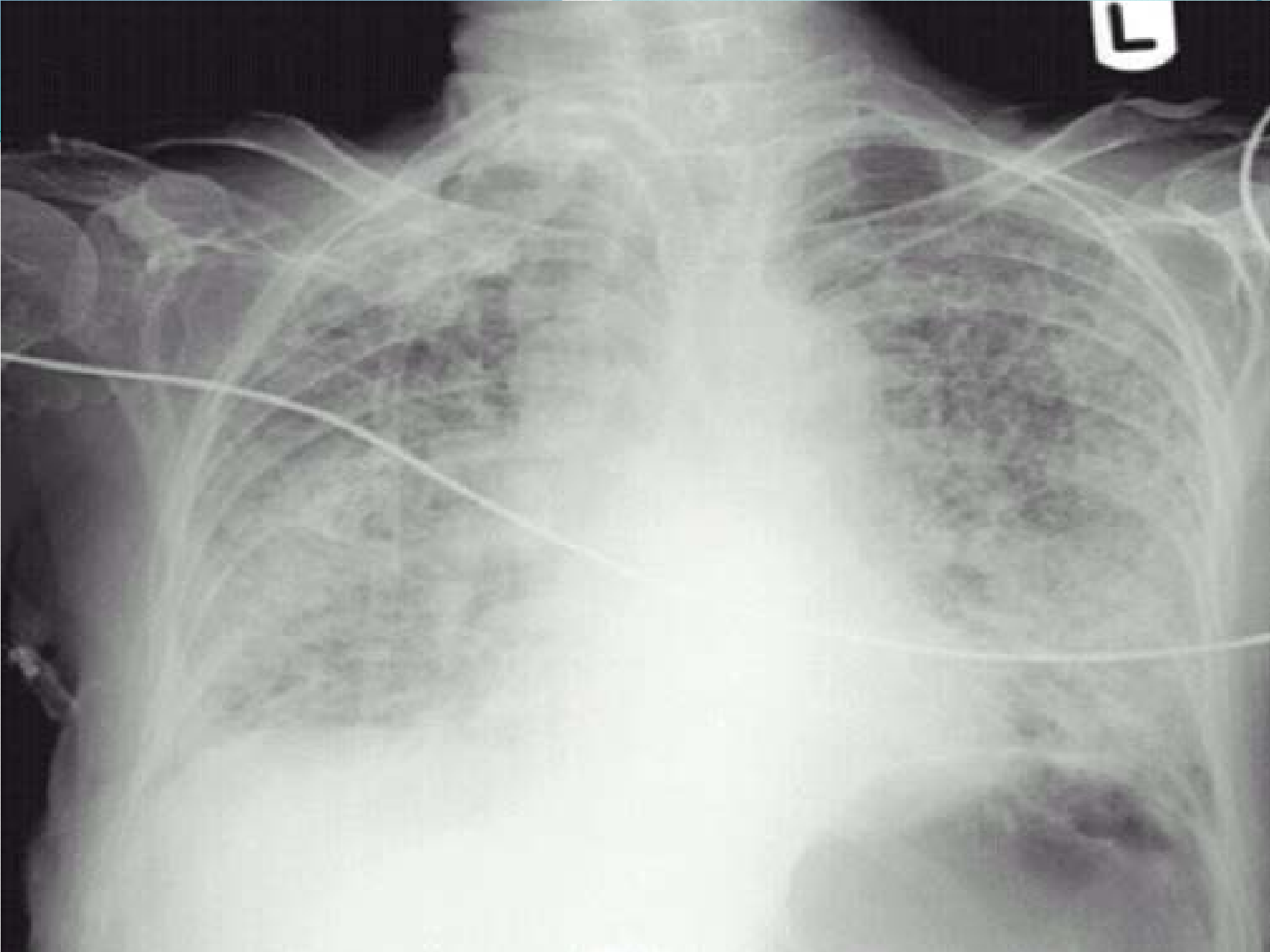
2) High minute vent requirements (Classically the Dead Space may begin to increase at this stage and ventilation may become more of an issue)

3) Poor compliance

Clinical Stages

B. Proliferative stage (contd):

- CXR= Densities become less dense as edema resolves, interstitial infiltrates remain.
- May start to develop interstitial emphysema and lung cysts.
- At this point may become dominated by complications such as barotrauma, nosocomial infection or dev of MODS.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Clinical Stages

C. Fibrotic Stage:

Will see

- progressive increasing airway pressures,
- progressive pulmonary HTN and a
- honeycomb appearance on CXR

Differentials

- **Common**

  - Cardiogenic plumonary edema
  - Diffuse pneumonia
  - Alveolar hemorrhage

- **Less Common**

  - Acute ILD (acute interstitial pneumonia)
  - Acute immunological injury (hypersensitivity pneumonitis)
  - Toxin injury (radiation pneumonitis)
  - Neurogenic pulmonary edema

Differential diagnosis

Condition	Differentiating signs/symptoms	Differentiating investigations
Acute exacerbation of CHF	A history of cardiac disease, acute myocardial ischaemia or infarction, or a know low ejection fraction suggests cardiogenic pulmonary oedema, as do an S3 and elevated neck veins on physical examination.	• CXR: heart failure is suggested by an enlarged cardiac silhouette, a vascular pedicle width >70 mm, central infiltrates, and Kerley B lines. •Brain natriuretic peptide (BNP) levels >500 nanograms/L (>500 picograms/mL) also suggest cardiogenic oedema. •Echocardiography and measurement of the pulmonary artery occlusion pressure (PAOP) may be needed if the history and physical and laboratory tests do not rule out cardiogenic pulmonary oedema

Differential diagnosis contd..

Condition	Differentiating signs/symptoms	Differentiating investigations
Bilateral pneumonia	•A history of fever and cough with or without sputum production. •Patients may have pleuritic chest discomfort.	•CXR. Severe pneumonia with bilateral infiltrates meets the radiographic criteria for ARDS. •PaO_2. If patients do not have severe hypoxaemia with their pneumonia ($PaO_2/FiO_2 \leq 300$ or $SpO_2/FiO_2 \leq 315$), they do not have ARDS.
Acute interstinal pneumonia	•Onset is usually subacute, over days to weeks. •Patients are previously healthy, with the lung disease not related to a systemic illness. •Some authors have termed this disease idppathic ARDS.	•Meets all the clinical criteria for ARDS. •Best differentiated by history

Differential diagnosis contd..

Condition	Differentiating signs/symptoms	Differentiating investigations
Diffuse alveolar haemorrhage	•Associated with bleeding from the small vessels of the airways (capillaritis) and seen in many conditions, ranging from autoimmune to mitral valve diseases. •Almost alwyal a reversible from of respiratory failure, once the underlying cause is known	•A syndrome of hypoxia with infiltrates on CXR. •The hallmark is finding sequentially bloodier aliquots of fluid during serial bronchoalveolar lavage. •Serological tests to look for autoimmune disease may help to differentiate from ARDS.

Differential diagnosis contd..

Condition	Differentiating signs/symptoms	Differentiating investigations
Acute eosinophilic pneumonia	•Presents as mild to severe pneumonia in previously healthy people. •Patients have an excellent response it IV corticosteroids.	•The hallmark of this disease is increased numbers of eosinophils (upwards of 50%) on bronchoalveolar lavage.
Hypersensitivity pneumonia	•A pneumonitis after inhalation of an orange antigen. •Patients presents with infiltrates and a pneumonia syndrome that is clinically indistinguishable from ARDS if severe. •Differentiated from ARDS by clinical history of an inhalational allergen, usually of avian origin. •Corticosteroids may be beneficial	•No differentiating investigations.

Differential diagnosis contd..

Condition	Differentiating signs/symptoms	Differentiating investigations
Post-obstructive pulmonary oedema	•Acute pulmonary oedema after removal of an upper airway obstruction, most commonly caused by laryngospasm. •Causes an acute respiratory failure often requiring mechanical ventilation with varying levels of PEEP. •The keys to differentiation are the history of upper airway obstruction, post-surgical development, and the rapid resolution of symptoms.	•No differentiating investigations.

Management Strategies for ARDS

A. General

1. Recognition and treatment of underlying medical and surgical disorders

2. Minimizing procedures and complications of a critically ill patient

3. Prophylaxis against venous thrombo-emobolism, gastrointestinal bleeding, aspiration, excessive sedation, and central venous catheter infections

4. Prompt recognition of nosocomial infections

5. Provision of adequate nutrition and fluid electrolytes

Management Strategies for ARDS (contd)

B. Specific

1. Restore and maintain hemodynamic function
   - Conservative fluid replacement strategy
   - Vasopressors and inotropics support

2. Ventilatory support
   - Lung protective ventilatory support strategy
   - Application of PEEP

3. use of steroids

4. Nutrition in ARDS patients

Management Strategies for ARDS (contd)

B. Specific (contd)

5. Other Modalities of treatment-some value

- Prone Position
- Inhaled NO
- Early Neuromuscular blockade
- Extracorporeal Membrane Oxygenation (ECMO)

Evidence Base Recommendations

Treatment	Recommendation
• Mechanical ventilation	
Low tidal volume	A
Minimized left atrial filling pressures	B
High-PEEP or *open lung*	C
Prone position	C
Recruitment maneuvers	C
High-frequency ventilation	D
• ECMO	C
• Early neuromuscular blockade	A
• Glucocorticoid treatment	D
• Surfactant replacement, inhaled NO, inhaled epoprostenol, and other anti-inflammarory therapy (e.g., ketoconazole, PGE1, NSAIDs)	D

Evidence Base Recommendations

- A- recommended therapy based on strong clinical evidence from RCTs
- B- recommended therapy based on supportive but limited clinical data
- C- recommended only as alternative therapy on the basis of indeterminate evidence
- D- not recommended therapy on the basis of clinical evidence against efficacy of therapy

Fluid Management

1. The Use of Conservative fluid management strategy was associated with
   - Significant improvement in oxygenation index
   - Significant improvement in Lung Injury score
   - increase in the number of ventilator- free days

Mechanical Ventilation

- A protective ventilation strategy using low tidal volumes and limited plateau pressures improves survival when compared with conventional tidal volumes and pressures.

Steroids

Recent RCTs of steroids for ARDS have answered some, but not all, questions regarding efficacy for prevention and treatment.

I. First, there is no evidence that corticosteroids prevent the development of ARDS among patients at risk.

II. Second, high dose and short course treatment with steroids does not improve the outcomes of patients with ARDS.

- Hough CL. Clin Chest Med. 2014 Dec; 35(4): 781–795.

Steroids

III. And third, while there is compelling data that low dose and prolonged treatment with steroids improves pulmonary physiology in patients with ARDS, additional studies are needed to recommend treatment with steroids for ARDS.

Hough CL. Clin Chest Med. 2014 Dec; 35(4): 781–795.

Nutrition

High-Fat, Low-Carbohydrate Enteral Formula

- Improves outcome in ARDS

Prone positioning

- Prone positioning has been used for many years to improve oxygenation in patients who require mechanical ventilatory support for management of the acute respiratory distress syndrome (ARDS).

- Randomized, controlled trials have confirmed that oxygenation is significantly better when patients are in the prone position than when they are in the supine position.

- However, meta-analyses have suggested that survival is significantly improved with prone positioning as compared with supine positioning among patients with severely hypoxemic ARDS at the time of randomization.

Inhaled Nitric Oxide

- Improves Ventilation –Perfusion ratio
- Reduction in Pulmonary Artery Pressure and pulmonary Vascular Resistance
- Trials have failed to demonstrate an improvement in the survival ie., no effect on mortality and also on the duration of mechanical ventilation
- However, there was improvement in the oxygenation/gas exchange
- There may be a role for NO in some ALI/ARDS patients with severe refractory hypoxemia and pulmonary arterial hypertension

Early neuromuscular blockade

- Patients with severe ARDS receiving mechanical ventilation responded more favorably to early administration of a neuromuscular blocking agent (ie, cisatracurium) than to placebo.

- Compared with the placebo group, the cisatracurium group showed improvement in 90-day survival and increased time off the ventilator.

Extracorporeal Membrane Oxygenation

- ECMO is still used as a rescue therapy in selected cases.

- During the H1N1 epidemic in 2009, ECMO appeared to improve survival in patients with H1N1-associated ARDS who could not be oxygenated with conventional mechanical ventilation

FUTURE DIRECTION

1. Various modalities of mechanical ventilation, eg. High-jet, Partial liquid ventilation

1. Promising Drugs
   a. Surfactant
   b. Aerosolised Prostacyclin (PGI2)
   c. Antioxidants

Summary

- Common causes are pneumonia, sepsis, aspiration, and severe trauma.
- Most common symptoms and signs are dyspnoea and hypoxaemia, which progress to acute respiratory failure.
- Diagnostic criteria are acute onset (<1 week), bilateral opacities on CXR, hypoxaemia with PaO2/inspired oxygen ratio < 300 on PEEP pr CPAP ≥5 cm H2O. In patients with no risk factor for ARDS, heart failure should be ruled out.
- Mortality is between 30% and 50%
- Low tidal volume, plateau-pressure-limited mechanical ventilation is the only therapy that has been shown to reduce mortality.
- Complications include pneumothorax, ventilator-associated pneumonia, multiple organ failure, and pulmonary fibrosis with respiratory failure.

THANK YOU