Cardiopulmonary Failure: Management of the End Stage Patient "Transplant in Waiting"

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Thoracic Organ Transplantation has evolved to become the “standard of care” for patients with end stage cardiopulmonary failure

The major issue affecting these patients include:

• Donor availability

• Distance from the transplanting center

• Deterioration while waiting
• Clinically and physiologically severe disease

• Medical therapy ineffective or unavailable

• Substantial limitations in activities of daily living

• Limited life expectancy

• Adequate cardiac function without significant coronary disease

• Ambulatory, with rehabilitation potential

• Acceptable nutritional status

• Satisfactory psychosocial profile and emotional support system
Common indications include:

- New York Heart Association (NYHA) class III or IV heart failure refractory to maximal medical therapy

- Debilitating ischemia not amenable to interventional or surgical revascularization

- Recurrent, symptomatic ventricular arrhythmias refractory to medical therapy, implantable cardioverter defibrillator (ICD) therapy, and surgical treatment
Chronic Obstructive Pulmonary Disease

• Patients with a BODE index *of 7 to 10 or at least one of the following

* BODE index includes body mass index, degree of airflow obstruction (assessed by percent predicted FEV\textsubscript{1}), degree of dyspnea (assessed by the modified Medical Research Council [MMRC] dyspnea scale), and exercise capacity (assessed by the 6-minute walk distance). The index increases as body mass index, FEV\textsubscript{1}, and distance walked decrease and as the MMRC scale increases.

• History of hospitalization for exacerbation associated with acute hypercapnia (P\textsubscript{\text{CO}}\textsubscript{2} >50 mm Hg)

• Pulmonary hypertension or cor pulmonale, or both, despite oxygen therapy

• FEV\textsubscript{1} < 20% predicted and either DLCO < 20% predicted or homogeneous distribution of emphysema
Cystic Fibrosis and other Causes of Bronchiectasis

- Oxygen-dependent respiratory failure
- Hypercapnia
- Pulmonary hypertension
Idiopathic Pulmonary Fibrosis and NSIP

Histologic or radiographic evidence of usual interstitial pneumonia and any of the following:

- DLCO < 39% predicted
- 10% or greater decrement in FVC during 6 months of follow-up
- A decrease in pulse oximetry below 88% during a 6-MWT
- Honeycombing on high-resolution computed tomography (fibrosis score > 2)

Histologic evidence of NSIP and any of the following:

- DLCO < 35% predicted
- 10% or greater decrement in FVC or 15% decrease in DLCO during 6 months of follow-up
Pulmonary Arterial Hypertension

- Persistent New York Heart Association class III or IV on maximal medical therapy
- Low (< 350 m) or declining 6-MWT
- Failing therapy with intravenous epoprostenol or equivalent
- Cardiac index <2 L/min/m
- Right atrial pressure >15 mm Hg
Acute Cardiac Failure
Contemporary Medical Therapy for Heart Failure Patients with Reduced Ejection Fraction
Robert J. Mentz, Douglas L. Mann and G. Michael Felker
Heart Failure: A Companion to Braunwald's Heart Disease, 34, 535-564
Treatment: Who needs What?

- **WARM AND DRY**
  - Compensated
  - Optimize oral therapy
  - *Outpatient*

- **COLD AND DRY**
  - Low Flow State
  - Inotropes, vasodilators, ?IABP
  - *ICU*

- **WARM AND WET**
  - Congested
  - Diuretics
  - *ED or Inpatient*

- **COLD AND WET**
  - Decompensated
  - Diuretics, vasodilators, inotropes
  - *ICU*

*Adapted from Nohria J Cardiac Failure 2000;6:54*
Anatomic and Physiologic Aspects of the Pulmonary Vasculature
Steven E. Weinberger MD, MACP, FRCP, Barbara A. Cockrill MD and Jess Mandel MD, FACP
Principles of Pulmonary Medicine, 12, 177-183
Indications for Invasive Hemodynamic Monitoring with Pulmonary Artery Catheter

Acute Circulatory Compromise

Diagnostic Uncertainty or Need for Escalating Therapies

a. Whose fluid status, perfusion, or systemic or pulmonary vascular resistances are uncertain *
b. Whose systolic pressure remains low or is associated with symptoms, despite initial therapy
c. Whose renal function is worsening with therapy
d. Who require parenteral vasoactive agents
e. Who may need consideration for mechanical circulatory support or transplantation
Diuretics, intravenous vasodilators, and intravenous inotropic agents are the major medications used during acute management of decompensated heart failure.

In the acutely ischemic ventricle, compliance is decreased with little change in volume, and the curve is shifted to the right.

In the chronically dilated ventricle, the “Starling curve” is actually reversed in that reduction of markedly elevated filling pressures leads to higher stroke volume.

Management of Acute Decompensated Heart Failure
Lynne Warner Stevenson
Heart Failure: A Companion to Braunwald's Heart Disease, 33, 514-534
Intravenous Vasodilators

<table>
<thead>
<tr>
<th>AGENT</th>
<th>INITIAL DOSE</th>
<th>EFFECTIVE DOSE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitroglycerine</td>
<td>20 µg/min</td>
<td>40-400 µg/min</td>
</tr>
<tr>
<td>Nitroprusside</td>
<td>10 µg/min</td>
<td>30-350 µg/min * Usually &lt;4 µg/kg/min</td>
</tr>
<tr>
<td></td>
<td>With or without 1-2-µg/kg bolus</td>
<td>0.005-0.03 µg/kg/min</td>
</tr>
</tbody>
</table>
### Intravenous Inotropic Agents

<table>
<thead>
<tr>
<th>AGENT</th>
<th>INITIAL DOSE</th>
<th>EFFECTIVE DOSE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dobutamine</td>
<td>1-2 µg/kg/min</td>
<td>2-10 µg/kg/min for inotropy and vasodilation</td>
</tr>
<tr>
<td>Dopamine (augment Diuresis)</td>
<td>2µg/kg/min</td>
<td>2-4 µg/kg/min for inotropy and vasodilation</td>
</tr>
<tr>
<td>Dopamine (treat hypotension)</td>
<td>4 -5 µg/kg/min</td>
<td>5 -15µg/kg/min for inotropy and vasoconstriction</td>
</tr>
<tr>
<td>Milrinone</td>
<td>50 to 75 µg/kg bolus over 10 minutes</td>
<td>0.10-.075µg/kg/min for inotropy and vasodilation</td>
</tr>
</tbody>
</table>
Acute Pulmonary Failure
(COPD) refers to chronic disorders that disturb airflow, whether the most prominent process is within the airways or within the lung parenchyma

- **Emphysema** is a diagnosis made on the basis of destruction of lung parenchyma and enlargement of air spaces distal to the terminal bronchiole

- **Chronic bronchitis** is a diagnosis made on the basis of chronic cough and sputum production
Schematic diagram of the effect of smoking on airway inflammation and structural components of alveolar walls—the latter by altering the relationship between elastase and $\alpha_1$-antitrypsin (also called $\alpha_1$-protease inhibitor).

Chronic Obstructive Pulmonary Disease  Steven E. Weinberger MD, MACP, FRCP, Barbara A. Cockrill MD and Jess Mandel MD, FACP
Principles of Pulmonary Medicine, 6, 93-112
Fletcher C, Peto R: The natural history of chronic air flow obstruction.
An acute exacerbation of chronic obstructive pulmonary disease (AECOPD)

- A clinical diagnosis made when a patient with COPD experiences a sustained (e.g., 24–48 h) increase in cough, sputum production, and/or dyspnea

- The average experiences two episodes per year, and 10% of these episodes require hospitalization

- Data from the National Emphysema Treatment Trial show that patients with severe emphysema and who are eligible for lung volume reduction surgery have 6.1 days/year of hospitalization if they remain on medical therapy but only 3.2 days/year if given lung volume reduction surgery (P = 0.005)
ETIOLOGY AND CONFOUNDING FACTORS

- Bacterial infections are implicated in the majority of AECOPD episodes
- Rhinovirus and respiratory syncytial virus have been implicated as causes for AECOPD in several studies
- Air pollution
- Acute left heart dysfunction was present in 25–30% of patients with AECOPD
- Pulmonary embolism
- About 30% of cases of AECOPD, no specific etiology could be identified
Clinical manifestations of AECOPD using the THE WINNIPEG CRITERIA

Type of Exacerbations

• Type 1       All three of the following symptoms: increase in sputum volume, increase in sputum purulence, increase in shortness of breath

• Type 2       Any two of the following symptoms: increase in sputum volume, increase in sputum purulence, increase in shortness of breath

• Type 3       Any one of the following symptoms: increase in sputum volume, increase in sputum purulence, increase in shortness of breath, plus at least one of the following: upper respiratory tract infection lasting 5 d, fever; increase in wheezes, increase in cough, increase in heart rate $\geq 20\%$
• Older age
• Severe underlying chronic obstructive pulmonary disease/already receiving long-term oxygen therapy
• Marked increase in breathlessness
• Poor or deteriorating general condition with little activity
• Cyanosis or worsening peripheral edema
• Impaired level of consciousness or confusion
• Difficulty in coping at home
• Significant comorbidities (particularly arrhythmias, heart failure, and insulin-dependent diabetes)
• Failure to respond to initial medical treatment
• Oxygen saturation < 90%
COPD/Heart Failure: Hormuth

Acute hypervolaemia
Myocardial wall stress (↑ BNP)
Myocardial damage (↑ hs troponin)

Sympathetic overdrive
Activation of RAAS system
Increase in LV filling pressure
Increase in pulmonary vascular resistance

Precipitating bacterial and viral infections
Activation in inflammatory state (↑ CRP)

Increased airflow obstruction
Increased hyperinflation
Severe hypercapnia

Increased intrathoracic pressure

Pulmonary oedema
Impaired lung diffusion
Worsening hypoxaemia

Increased congestion
Increased RV afterload
Reduced stroke volume
Decreased LV filling
Decrease in cardiac output
Challenges of Treating Acute Heart Failure in Patients with Chronic Obstructive Pulmonary Disease

Card Fail Rev. 2017 Apr; 3(1): 56–61

Jelena Čelutkienė, Mindaugas Balčiūnas, Denis Kablučko, Liucija Vaitkevičiūtė, Jelena Blaščiuk, and Edvardas Danilacorresponding author
Modalities available for treatment of COPD are:

1. Bronchodilators
2. Antibiotics
3. Corticosteroids
4. Phosphodiesterase-4 inhibitors
5. Supplemental oxygen
6. Exercise rehabilitation
7. Chest physiotherapy
8. Surgery (selected cases)
Idiopathic pulmonary fibrosis (IPF) is a progressive, life-threatening, interstitial lung disease of unknown etiology.

- IPF is the most common of the idiopathic interstitial pneumonias and carries the worst prognosis, with median survival ranging from 2.5 to 3.5 years.

- Rate of decline and progression to death in patients with IPF may take several clinical forms:
  - slow physiologic deterioration with worsening severity of dyspnea
  - rapid deterioration and progression to death
  - periods of relative stability interposed with periods of acute respiratory decline sometimes manifested by hospitalizations for respiratory failure
Acute Exacerbations of IPF (Acute exacerbation of IPF is defined by the onset of rapid deterioration (within days to a few weeks) in symptoms, lung function, and radiographic appearance (bilateral ground-glass opacities and consolidation superimposed on a reticular pattern on HRCT) in the absence of infection, heart failure, pulmonary embolism, or other identifiable cause)
Acute IPF exacerbations (within 4 wk., all of the following):

- Decline of ≥5% in resting room air SpO2 from last recorded level OR decline of ≥8 mm Hg in resting room air PaO2 from last recorded level
- Clinically significant worsening of dyspnea or cough within 30 d, triggering unscheduled medical care (e.g. clinic, study visit, hospitalization)
- New, superimposed ground-glass opacities or consolidation on CT scan or new alveolar opacities on chest radiograph
- No clinical (i.e., absence of grossly purulent sputum, fever > 39°C orally) or microbiologic evidence for infection
- Other causes excluded (e.g., pneumothorax, cardiac events, infections, and thromboembolism)
Progression of IPF

- ≥10% decrease in % predicted FVC or ≥15% decrease in % predicted DlCO/TlCO
- Confirmation of worsening must be documented with repeat assessments at least 4 wk apart
Pathogenesis of AE-IPF

• It is not clear whether AE-IPF is secondary to acceleration of the primary disease process or represents a clinically silent trigger such as a viral infection or silent aspiration

• Presently AE-IPF lacks an effective treatment

Figure 2. Schematic Drawing of the Potential Clinical Course of Patients with Idiopathic Pulmonary Fibrosis\(^2,10\)

As disease progresses, there is a subclinical period in which only radiographic findings of disease may be present, followed by a symptomatic period consisting of both pre-diagnosis and post-diagnosis clinical phases. The rate of decline and progression to death may be rapid (line A), slow (lines C and D), or mixed (curve B), with periods of relative stability interspersed with periods of acute decline (star).

The Clinical Time Frame
• Complex genetic disease affecting many organs, although 85% of the mortality is a result of lung disease

• Begins early in life with inflammation and impaired mucociliary clearance and consequent chronic infection of the airways

• There is progressive decline of lung function with episodes of acute worsening of respiratory

• Symptoms, often referred to as “pulmonary exacerbations.”
Clinical features of an exacerbation may include:

- increased cough
- Increased sputum production
- shortness of breath
- chest pain
- loss of appetite
- loss of weight
- lung function decline
Pulmonary exacerbations have an adverse impact on patients’ quality of life and a major impact on the overall cost of care.

Identifying optimal treatment methods for these events could produce significant improvements in quality and length of life for patients with CF.
Cystic Fibrosis: Hormuth

American Journal of Respiratory and Critical Care Medicine
Volume 168, Issue 8 | October 15 2003
Pathophysiology and Management of Pulmonary Infections in Cystic Fibrosis
Acute Pulmonary Failure
Classification and Pathophysiologic Aspects of Respiratory Failure
Steven E. Weinberger MD, MACP, FRCP, Barbara A. Cockrill MD and Jess Mandel MD, FACP
Principles of Pulmonary Medicine, 27, 350-356
Definition of Respiratory Failure

Inability of the respiratory system to maintain adequate gas exchange

For patients with normal baseline arterial blood gas measurements, criteria for respiratory failure are $P_{O_2} < 60$ mm Hg or $P_{CO_2} > 50$ mm Hg

Categories of acute respiratory failure are:

1. Hypoxemic (with normal or low $P_{CO_2}$)
2. Hypercapnic/hypoxemic

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Steven E. Weinberger MD, MACP, FRCP, Barbara A. Cockrill MD and Jess Mandel MD, FACP
Principles of Pulmonary Medicine, 27, 350-356
Pulmonary Vascular Response to Hypoxia

- Alveoli in an area of lung contain gas with a low $P_{O_2}$, generally less than 60 to 70 mm Hg, the vessels supplying that region of lung undergo vasoconstriction
- Protective mechanism for decreasing perfusion to poorly ventilated alveoli.
- Hypoxia may alter the release of vasoactive mediators, either increasing the release of vasoconstrictors or decreasing the release of vasodilators
- Nitric oxide, is produced by vascular endothelial cells, acts via increasing cyclic guanosine monophosphate to produce vascular smooth muscle relaxation
Clinical and Therapeutic Aspects of Hypercapnia/Hypoxemic Respiratory Failure

Frequent precipitants of acute-on-chronic respiratory failure are:

1. Respiratory infection
2. Drugs (e.g., sedatives, narcotics)
3. Heart failure
4. Less common: pulmonary emboli, exposure to environmental pollutant

Classification and Pathophysiologic Aspects of Respiratory Failure
Steven E. Weinberger MD, MACP, FRCP, Barbara A. Cockrill MD and Jess Mandel MD, FACP
Principles of Pulmonary Medicine, 27, 350-356
Therapeutic approach to these patients has three main components:

(1) support of gas exchange

(2) treatment of the acute precipitating event

(3) treatment of the underlying pulmonary disease

Classification and Pathophysiologic Aspects of Respiratory Failure
Steven E. Weinberger MD, MACP, FRCP, Barbara A. Cockrill MD and
Jess Mandel MD, FACP
Principles of Pulmonary Medicine, 27, 350-356
Ventilation and hypercapnic respiratory failure
Judd W. Landsberg MD
Clinical Practice Manual for Pulmonary and Critical Care Medicine,
Chapter 2, 11-21
Management strategies for patients with ARDS

- Identify and treat underlying/predisposing cause of ARDS
- Ventilatory support
- Lung protective ventilatory support strategy
- Application of PEEP (per ARDSnet protocol)
- Restore and maintain hemodynamic function
- Conservative fluid replacement strategy using goal-oriented approach
- Vasopressor and inotropic support as needed to meet goal
Management strategies for patients with ARDS

- Prevent complications of critical illness
- Stress ulcer (stress-related mucosal disease) prophylaxis
- Strategies for PE and DVT
- Prevent ventilator-associated pneumonia (VAP)
- Control glucose and metabolic function
- Prevent development of multiple organ dysfunction/failure
- Adequate nutrition
- Avoid over sedation and medication errors
- Use of weaning protocol with spontaneous breathing trials when ready to wean
- Cautious use of steroids for fibroproliferative phase (avoid if patient has received neuromuscular blocking drugs)

Acute Respiratory Failure
David P. Gurka and Robert A. Balk
Critical Care Medicine: Principles of Diagnosis and Management in the Adult, 37, 629-644.e6
Acute hypoxemic respiratory failure

An acute drop in $\text{PaO}_2 < 60 \text{ mm Hg}$
The Goal of Invasive Mechanical Ventilation

- Provide adequate respiratory support
- Avoid causing ventilator-associated lung injury
- Lung-protective ventilation strategy: low lung volumes (6–8 mg/kg)
- Prioritizes low lung volumes over normal pH and pCO₂ [increasing the minute ventilation is done by increasing the rate, not the TV]
Mild chronic hypoxemic respiratory failure where PaO2 falls gradually over time (typical PaO2 values in the 55-59 range)

- Caused by heterogeneous lung destruction, most commonly seen in chronic obstructive pulmonary disease (COPD)

- Hypoxemia occurs from VQ mismatch (pink puffers) or hypoventilation (blue bloaters)

- Causes mild symptoms of cognitive impairment (not exercise limitation), and increases the risk of heart failure

- In COPD Exercise is limited by ventilation

- Treat to prevent heart failure, arrhythmia, and risk of sudden death (not to improve exercise tolerance)
Chronic severe hypoxemic respiratory failure, Pa \( \text{O}_2 < 55 \) mm Hg

- Commonly seen in pulmonary fibrosis
- Fibrotic thickening of the pulmonary interstitium leads to diffusion limitation
- Less commonly caused by small vessel pulmonary vascular disease (eg, idiopathic pulmonary arterial hypertension [IPAH])
- Loss of vascular cross-sectional area from obliteration of small to medium pulmonary arteriole
Acute on Chronic Hypercapnic Respiratory Failure and Mixed Acute Hypercapnic Failure

**Acute on chronic hypercapnic respiratory failure**

- Patients with chronic hypercapnic respiratory failure are extremely vulnerable to superimposed acute hypercapnic respiratory failure because they have no reserve (already have a baseline increase in their WOB or P co 2 )

- An individual with COPD who develops a renal tubular acidosis (RTA), may experience respiratory failure from the increased MV demand

- An individual without lung disease, renal failure may only complain of fatigue and a decreased exercise tolerance when faced with a RTA

**Mixed acute hypercapnic failure**

- Any combination of impaired pulmonary mechanics, metabolic acidosis, and blunted respiratory drive may (and commonly do) occur
Mechanical Ventilation: Hormuth

Normal to Moderately Impaired Resistance or Compliance:
Initial Ventilator Settings, Preferred Mode = Volume Control

- Normal pulmonary mechanics
  - TV 8mg/KG
  - Rate 15
  - FiO2 ≥50%
  - PEEP 5 cm H2O

- Increased airways resistance
  - TV 8mg/KG
  - Rate 8–15
  - FiO2 ≥100%
  - PEEP 5 cm H2O

- Decreased lung compliance
  - TV 6mg/KG
  - Rate 20–25
  - FiO2 100%
  - PEEP 5–10 cm H2O

Obtain:
- Peak inspiratory pressure (PIP)
- Plateau pressure (Pplat)
- Arterial blood gas (ABG)

- PIP >35 cm H2O
  - pH <7.35*
  - OR
  - Pplat >30 cm H2O
  - pH >7.44

  - ↑ Rate
    - (to maximum† before ↑ Tidal volume)
  - ↓ Tidal volume

  - ↓ Tidal volume
    - (6 mg/kg before ↓ Rate)
  - (by 2–5 cm H2O)

  - ↑ FiO2 to 100%
    - and
    - ↑ PEEP
      - (by 2–5 cm H2O)

  - ↓ FiO2 to ≤60%
    - before ↓ PEEP
      - (by 2–5 cm H2O)*

 Avoid acidosis to avoid dyspnea, patient discomfort, and increased sedation needs
Maximum rate = as fast as possible without breath stacking (typically 12–15 b/m for obstructive disease, 25–35 b/m for ARDS)
In ARDS wean PEEP slowly (ie, decrease by 2–5 cm H2O q 12–24 hrs) to avoid derecruitment. In cardiogenic edema PEEP may be weaned more quickly

Invasive mechanical ventilation
Judd W. Landsberg MD
Clinical Practice Manual for Pulmonary and Critical Care Medicine, Chapter 19, 270-28
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Cardiopulmonary Failure: Management of the End Stage Patient "Transplant in Waiting"

SUMMARY
• Optimize volume status (decongest, reduce pulmonary capillary wedge pressure)

• Optimize hemodynamics (improve low output state, increase cardiac index)

• Identify etiology

• Cause of heart failure (HF)

• Cause of acute decompensated heart failure (ADHF)

• Optimize long-term oral therapy

• Minimize therapeutic side effects and adverse treatment effects

• Identify indications for revascularization
• Identify indications for cardiac resynchronization therapy or implantable cardioverter-defibrillator or both

• Identify thromboembolism risk and need for anticoagulation

• Educate patient, family members, and caregivers about self-management

• Consider using disease management programs

• Consider referral for hospice
Management of Acute Decompensated Heart Failure
Lynne Warner Stevenson
Heart Failure: A Companion to Braunwald's Heart Disease, 33, 514-534

**TWO-MINUTE ASSESSMENT OF HEMODYNAMIC PROFILE**

<table>
<thead>
<tr>
<th>Congestion at rest?</th>
<th>Evidence for congestion</th>
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<tbody>
<tr>
<td>NO</td>
<td>Orthopnea</td>
</tr>
<tr>
<td></td>
<td>Elevated jugular venous pressure</td>
</tr>
<tr>
<td></td>
<td>Bendopnea</td>
</tr>
<tr>
<td>YES</td>
<td>Rales (rarely)</td>
</tr>
<tr>
<td></td>
<td>New S3</td>
</tr>
<tr>
<td></td>
<td>Hepatomegaly</td>
</tr>
<tr>
<td></td>
<td>Ascites</td>
</tr>
<tr>
<td></td>
<td>Edema (more common in older patients)</td>
</tr>
<tr>
<td></td>
<td>Valsalva square wave</td>
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</table>

<table>
<thead>
<tr>
<th>Low perfusion at rest?</th>
<th>Evidence for low perfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>Narrow auscultated pulse pressure</td>
</tr>
<tr>
<td></td>
<td>Cool extremities</td>
</tr>
<tr>
<td></td>
<td>May be sleepy, obtund</td>
</tr>
<tr>
<td>YES</td>
<td>Suspect from ACEI/ARB hypotension</td>
</tr>
<tr>
<td></td>
<td>Progressive oliguria</td>
</tr>
</tbody>
</table>
Diuretics, intravenous vasodilators, and intravenous inotropic agents are the major medications used during acute management of decompensated heart failure.
An exacerbation - acute event characterized by worsening of symptoms that requires a change in medication.

The precipitating factor is often a respiratory tract infection of either viral or bacterial origin.

A variety of bacteria are often chronically present in the tracheobronchial tree of patients with COPD, and an acute exacerbation can sometimes be due to the acquisition of a new strain of the colonizing bacteria.

Other factors that cause acute deterioration in patients include exposure to air pollutants, bronchospasm (particularly if patients have a superimposed asthmatic component to their disease), and heart failure.

However, in up to one-third of cases, the cause of an exacerbation cannot be identified. When exacerbations are severe, patients may go into frank respiratory failure.
Figure 2. Schematic Drawing of the Potential Clinical Course of Patients with Idiopathic Pulmonary Fibrosis

As disease progresses, there is a subclinical period in which only radiographic findings of disease may be present, followed by a symptomatic period consisting of both pre-diagnosis and post-diagnosis clinical phases. The rate of decline and progression to death may be rapid (line A), slow (lines C and D), or mixed (curve B), with periods of relative stability interposed with periods of acute decline (star).


The Clinical Time Frame
Schematic diagram illustrates interrelationships between various pathologic and physiologic features of diffuse parenchymal lung disease.
Thank You
Chronic Obstructive Pulmonary Disease  Steven E. Weinberger MD, MACP, FRCP, Barbara A. Cockrill MD and Jess Mandel MD, FACP
Principles of Pulmonary Medicine, 6, 93-112

The mounted section of the whole lung shows diffuse involvement seen with panacinar emphysema.
(From Thurlbeck WM. Chronic Airflow Obstruction in Lung Disease . Philadelphia, PA: WB Saunders; 1976.)
• A large group of disorders affects the alveolar wall in a fashion that ultimately may lead to diffuse scarring or fibrosis

• more than 150 diffuse parenchymal lung disease

• the diffuse parenchymal lung diseases, regardless of cause, have two major pathologic components: an inflammatory process in the alveolar wall and alveolar spaces (sometimes called an alveolitis) and a scarring or fibrotic process
Photomicrograph of diffuse parenchymal lung disease shows markedly thickened alveolar walls. Cellular inflammatory process and fibrosis are present.
Overview of Diffuse Parenchymal Lung Diseases  Steven E. Weinberger MD, MACP, FRCP, Barbara A. Cockrill MD and Jess Mandel MD, FACP
Principles of Pulmonary Medicine, 9, 132-144

Low-power photomicrograph of usual interstitial pneumonia shows prominent fibrosis accompanied by honeycombing
• End-Stage Diffuse Parenchymal Lung Disease

• result of the inflammation and fibrosis affecting the alveolar walls (1) decreased compliance (increased stiffness) of the lung, (2) generalized decrease in lung volumes, (3) loss of alveolar-capillary surface area resulting in impaired diffusing capacity, (4) abnormalities in small airway function without generalized airflow obstruction, (5) disturbances in gas exchange, usually consisting of hypoxemia without CO 2 retention, and (6) in some cases, pulmonary hypertension.
Schematic diagram illustrates interrelationships between various pathologic and physiologic features of diffuse parenchymal lung disease.
Criterion for ECMO fulfilled

(Primary requirement)

Respiratory Failure

Cardiac Failure
(Biventricular failure/left ventricular
Failure)
Severe PAH

Yes

No

Cardiac & pulmonary Support

Venous - Venous Support

Venous - Venous ECMO

Venous-Arterial/ Venous/Arterial - Venous ECMO

Pulmonary Support

Yes

easy

easy
TWO-MINUTE ASSESSMENT OF HEMODYNAMIC PROFILE

- **Congestion at rest?**
  - **NO**
    - Warm & dry
    - Cold & dry
    - A
    - Evidence for low perfusion
      - Narrow auscultated pulse pressure
      - Cool extremities
      - May be sleepy, obtunded
      - Suspect from ACEI/ARB hypotension
      - Progressive oliguria
  - **YES**
    - Warm & wet
    - Cold & wet
    - B
    - C
    - Evidence for congestion
      - Orthopnea
      - Elevated jugular venous pressure
      - Bendopnea
      - Rales (rarely)
      - New S3
      - Hepatomegaly
      - Ascites
      - Edema (more common in older patients)
      - Valsalva square wave

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Acute Pulmonary Failure
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<tbody>
<tr>
<td>Progression of underlying heart disease</td>
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<tr>
<td>Cardiac arrhythmias</td>
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<tr>
<td>New ventricular dyssynergy</td>
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<td>Poorly controlled or uncontrolled hypertension</td>
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<td>Myocardial ischemia or infarction</td>
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<td>Progression of valvular heart disease</td>
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<table>
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<td>Anemia</td>
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<td>Thyroid disorders</td>
</tr>
<tr>
<td>Adverse effects of medications</td>
</tr>
<tr>
<td>Steroids</td>
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<tr>
<td>Nonsteroidal anti-inflammatory drugs</td>
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<tr>
<td>Cyclooxygenase-2 inhibitors</td>
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<tr>
<td>Thiazolidinediones</td>
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<tr>
<td>Pregabalin</td>
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<tr>
<td>Anthracyclines</td>
</tr>
<tr>
<td>“Targeted” chemotherapy agents</td>
</tr>
</tbody>
</table>
Chronic Obstructive Pulmonary Disease  Steven E. Weinberger MD, MACP, FRCP, Barbara A. Cockrill MD and Jess Mandel MD, FACP Principles of Pulmonary Medicine, 6, 93-112

The mounted section of the whole lung shows diffuse involvement seen with panacinar emphysema. (From Thurlbeck WM. Chronic Airflow Obstruction in Lung Disease. Philadelphia, PA: WB Saunders; 1976.)
<table>
<thead>
<tr>
<th>Subcategory</th>
<th>Clinical Diagnosis</th>
<th>Pathologic Pattern</th>
<th>Common Radiographic Description</th>
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</thead>
<tbody>
<tr>
<td>Chronic fibrosing interstitial pneumonias</td>
<td>Idiopathic pulmonary fibrosis (IPF)</td>
<td>Usual interstitial pneumonia (UIP)</td>
<td>Reticular (fibrosis), honeycombing</td>
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<tr>
<td></td>
<td>Idiopathic nonspecific interstitial pneumonia</td>
<td>Nonspecific interstitial pneumonia (NSIP)</td>
<td>Ground glass</td>
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<tr>
<td>Smoking-related interstitial pneumonias</td>
<td>Respiratory bronchiolitis–interstitial lung disease (RB-ILD)</td>
<td>Respiratory bronchiolitis</td>
<td>Bronchial wall thickening, centrilobular nodules, ground glass</td>
</tr>
<tr>
<td></td>
<td>Desquamative interstitial pneumonia (DIP)</td>
<td>Desquamative interstitial pneumonia (DIP)</td>
<td>Ground glass</td>
</tr>
<tr>
<td>Acute/subacute interstitial pneumonias</td>
<td>Cryptogenic organizing pneumonia (COP)</td>
<td>Organizing pneumonia (formerly bronchiolitis obliterans with organizing pneumonia, BOOP)</td>
<td>Patchy consolidation, often peripheral (subpleural)</td>
</tr>
<tr>
<td></td>
<td>Acute interstitial pneumonia (AIP)</td>
<td>Diffuse alveolar damage (DAD)</td>
<td>Diffuse alveolar filling</td>
</tr>
</tbody>
</table>
Overview of Diffuse Parenchymal Lung Diseases  Steven E. Weinberger MD, MACP, FRCP, Barbara A. Cockrill MD and Jess Mandel MD, FACP
Principles of Pulmonary Medicine, 9, 132-144
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