De la Dyspnée à la Transplantation Pulmonaire

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Definition Dyspnoea

...subjective experience of breathing discomfort, consisting of qualitatively distinct sensations that vary in intensity...

...derives from interactions among multiple physiological, psychological, social, and environmental factors, and may induce secondary physiological and behavioral responses...

ATS Consensus Statement 1999

→ ≠ hypoxia, hypercapnia or respiratory insufficiency

→ may occur without altered blood gases

→ severe hypoxia may be present without dyspnoea
Causes of Dyspnoea

- Chronic > 3 weeks
- and the winner is
  ...pulmonary disorders!
- in 27-33%: multiple causes


Top 4 Causes Chronic Dyspnoea

Pratter MR et al. (Respir Med. 2011 Jul;105(7):1014-21.)
- Asthma 29%
- COPD 14%
- Interstitial Lung Disease 14%
- Cardiomyopathies 9%

De Paso WJ et al. (Chest. 1991 Nov;100(5):1293-9.)
- Hyperventilation-Syndrome 19%
- Unclear 19%
- Asthma 17%
- Heart diseases 14%

Martinez FJ et al. (Chest. 1994 Jan;105(1):168-74.)
- Deconditioning 28%
- Asthma 24%
- Psychogenic 18%
- Heart diseases 14%
### DD Chronic Dyspnoea

#### CARDIAC
- Heart failure
- Coronary heart disease
- Arrhythmia
- Pericardial disease
- Valvular heart disease

#### PULMONARY
- COPD
- Asthma
- Interstitial lung disease
- Pulmonary hypertension
- Pleural effusion
- Neoplasia
- Bronchiectases

#### NON-CARDIAC, NON-PULMONARY CAUSES
- Psychogenic
- Deconditioning
- Obesity
- Anaemia
- Gastro-oesophageal reflux disease
- Metabolic (Acidosis, Uraemia)
- Hepatic cirrhosis
- Thyroid disease
- Neuromuscular (ALS)
- Thoracic deformity (kyphoscoliosis)
- Obstruction upper airways (vocal cord dysfunction, tracheal stenosis)

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### Symptoms & Examination

... yield Diagnosis in ≈ 60%

#### History
- Trigger, worsening / attenuating factors (medications)
- At rest, nocturnal, on exercise
- Acute, chronic, fluctuating, paroxysmal, persistent,
- Positional (orthopnoea, platypnoea)

#### Examination
- Respiratory rate (normal ~12–15/minute)
- Breathing depth (deep – shallow)
- Breathing movements (decreased, symmetric-asymmetric, accessory muscles)
- Breathing pattern (regular – irregular)
- Breathing type (pursed lip breathing, paradox breathing, speech dyspnoea)
- Gasp, Cheyne-Stokes, Kussmaul
- Finger clubbing, anaemia
- Appearance: cachectic, obese, chest deformity
- Emotional status

Pratter MR, Arch Int Med 1989
Gugger M, Schweiz Med Forum 2001
Dyspnoea Scales

Table 1. New York Heart Association Functional Classification of Heart Disease

<table>
<thead>
<tr>
<th>Class</th>
<th>Functional Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Asymptomatic except during severe exertion</td>
</tr>
<tr>
<td>II</td>
<td>Symptomatic with moderate activity</td>
</tr>
<tr>
<td>III</td>
<td>Symptomatic with mild or moderate activity</td>
</tr>
<tr>
<td>IV</td>
<td>Symptomatic with severe activity</td>
</tr>
</tbody>
</table>

The Modified Medical Research Council (MMRC) Dyspnoea Scale

<table>
<thead>
<tr>
<th>Grade of dyspnoea</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not troubled by breathlessness except on strenuous exercise</td>
</tr>
<tr>
<td>1</td>
<td>Shortness of breath when hurrying on the level or walking up a slight hill</td>
</tr>
<tr>
<td>2</td>
<td>Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level</td>
</tr>
<tr>
<td>3</td>
<td>Stops for breath after walking about 100 m or after a few minutes on the level</td>
</tr>
<tr>
<td>4</td>
<td>Too breathless to leave the house or breathless when dressing or undressing</td>
</tr>
</tbody>
</table>

 Spirometry

Volume – Time Curve

Flow - Volume Curve

Healthy

COPD

FEV₁

FEV₁

1 Second

Time

Expiration

Inspiration

FVC

FVC
**Spirometry: Quality-Check**

- Minimum 3 acceptable curves
- Maximum 8 tries (! exhaustion)
- Steep start of curve
- Expiration over at least 6 seconds
- No coughing
- 2 max. FVC-values <0,15 l deviation
- 2 max. FEV1-values <0,15 l deviation
- Good cooperation?

**Obstructive Ventilatory Disorder**

**GOLD**

- FEV1/FVC < 70%
- post-bronchodilation

**ATS/ERS 2005:**

- FEV1/FVC < LLN
- (5th percentile)

<table>
<thead>
<tr>
<th>Severity</th>
<th>%FEV1</th>
</tr>
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<tbody>
<tr>
<td>mild</td>
<td>&gt;80%</td>
</tr>
<tr>
<td>moderate</td>
<td>50-80%</td>
</tr>
<tr>
<td>severe</td>
<td>30-50%</td>
</tr>
<tr>
<td>very severe</td>
<td>&lt;30%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severity</th>
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</thead>
<tbody>
<tr>
<td>mild</td>
<td>&gt;70%</td>
</tr>
<tr>
<td>moderately severe</td>
<td>60-70%</td>
</tr>
<tr>
<td>mod. severe - severe</td>
<td>50-60%</td>
</tr>
<tr>
<td>severe</td>
<td>30-50%</td>
</tr>
<tr>
<td>very severe</td>
<td>&lt;30 %</td>
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</table>
Age-Dependent Normal Values

Prevalence of COPD per 1000 population

- Fixed ratio
- LLN
- Doctor diagnosis

1° INVESTIGATIONS
- History & Examination
- Oxygen saturation
Lab:
- Full blood count, chemistry (pro) BNP, TSH
- Chest XRay
- ECG
- Pulmonary function tests: Spirometry
- Arterial blood gases
- Plethysmography
- CO diffusion capacity
- Bronchial provocation test

2° INVESTIGATIONS
- Spiroergometry

3° INVESTIGATIONS
- Angio-Chest CT
- VQ Scintigraphy
- Sinus CT
- Bronchoscopy
- Lung biopsy
- Echocardiography
- Holter Monitor
- Cardiac catheter
- pH-manometry
- Respiratory polygraphy

DIAGNOSIS
Consider:
Psychogenic
Specialist Consult

Possible diagnoses:
Valvular, coronary HD
Arrhythmia
Pericardial disease
GERD
Pulmonary hypertension

Spiro-Ergometry
(cardio-pulmonary exercise testing)

- Symptom-limited, progressive exercise test
- Measurements
  - Watts
  - Ventilation: VO₂, VCO₂, VE, VD/VT, SaO₂
  - Anaerobic threshold
  - Heart: HR, BP, ECG, O₂-Pulse
  - aBG: PaO₂, PaCO₂, pH, base excess
  - Spirometry and flow-volume curves
Indications CPET

1. Investigation of dyspnoea
   - Differentiate causes
   - Objective limitation of exercise capacity

2. Pre-operative risk assessment
   - Thoracic surgery (respiratory reserves)
   - Other surgical interventions

3. Functional assessment
   - Standardised follow-up of chronic disorders
     (function, response to therapy and/or rehabilitation)
   - Sports medicine (planning of training)

4. Evaluation (insurance medicine)

Lung Transplant Adults

J Heart Lung Transplant 2007;26: 782-795
General Criteria for Lung Transplantation

- Life expectancy <24-36 months (maximal medical therapy)
- Class III - IV New York Heart Association (NYHA) dyspnea
- Stable nutritional status
- Motivated for rehabilitation
- Intact psychological support system
Optimal Timing of Lung Transplantation

- High (>50%) mortality risk within 2 years
- High (>80%) likelihood 90 days survival post lung-transplantation
- High (>80%) likelihood of 5-year post-transplant survival without graft dysfunction

COPD

- Chronic cough ± sputum
- Progressive dyspnoea
- Exacerbations
- Co-morbidities
  - Coronary heart disease
  - Peripheral vascular disease
  - Diabetes type 2
  - Lung cancer
  - Depression
- Loss of weight
BMI, Airflow Obstruction, Dyspnoea, & Exercise Capacity (BODE) Index

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (%SW)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distance metres (6MWT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRC</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
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</tbody>
</table>

↑ Point BODE Score =

Probability of Survival

Hazard ratio mortality:
- generally 1.34 (95% CI 1.26-1.42)
- respiratory cause 1.62 (1.48-1.77)

Celli BR NEJM 2004;350:1005
Endobronchial Valve

Hypothesis Mechanism of Action

Hyper-inflated lung → Volume reduction & Airflow re-distribution

Target Lobe Volume Reduction
Improved Respiratory Mechanics
Improved Exercise & QOL
COPD: Timing of Referral

- Progressive disease despite optimal treatment (medication, pulmonary rehabilitation, oxygen therapy)
- No candidate for endoscopic or surgical lung volume reduction (LVR); simultaneous referral for both lung transplant and LVR evaluation appropriate
- BODE index >5
- \( \text{PaCO}_2 >50 \text{ mmHg} \) and/or \( \text{PaO}_2 <60 \text{ mm Hg} \)
- \( \text{FEV1} <25\% \) predicted


Interstitial lung disease

- Occupational / environmental exposure
- Autoimmune (rheumatologic) disorders
- Hypersensitivity pneumonia
- Drugs
- Radiation
- Eosinophil lung disease
- Sarcoidosis
- Infectious
- Idiopathic
- Vasculitis
- LAM, LC Histiocytosis, alv. proteinosis
Clinical Presentation ILD

History & examination non-specific!
- insidious start of symptoms
- progressive dyspnoea on exercise
- dry cough
- crackles
- finger clubbing
- Erythema nodosum
- Arthritis
- Muscle weakness and/or myalgia
- Uveitis/conjunctivitis
- Lymphadenopathies, hepato-splenomegaly
- Neurologic signs
- Enlargement lacrymal / saliva-/ parotis glands

Interstitial Pulmonary Fibrosis (IPF)
**Prognosis Interstitial Pulmonary Fibrosis**

- IPF median lifespan: 2-6 years after diagnosis
- IPF 5-year survival rate: 20-40%

![Graph showing survival rates and causes of death in IPF](image)

**Progression Interstitial Pulmonary Fibrosis**

- Slowly progressive
- Rapidly progressive
- Frequent exacerbations
- Acute exacerbation

![Diagram showing lung function and time](image)

**ILD: Timing of Referral**

- Usual interstitial pneumonitis (UIP) or fibrosing nonspecific interstitial pneumonitis (NSIP), regardless of lung function
- Forced vital capacity (FVC) <80% predicted or carbon monoxide diffusing capacity (DLCO) <40% predicted
- Dyspnea or functional limitation attributable to lung disease
- Oxygen requirement, even if only during exertion
- Failure to improve dyspnea, oxygen requirement, and/or lung function after a clinically indicated trial of medical therapy


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**Bronchiectases**

Dilatation of airways
- genetic (cystic fibrosis), acquired (immune deficiency, post-infectious)
Cystic Fibrosis: Survival Predictors

- FEV1
- Age
- Gender
- Weight-for-age z-score
- Pancreatic insufficiency
- Diabetes mellitus
- Infection with Staphylococcus aureus
- Infection with Burkholderia cepacia
- Annual number of acute pulmonary exacerbations


CF: Timing of Referral

- FEV1 ≤ 30% or advanced disease with rapidly falling FEV1
- 6-minute walk distance < 400 m
- Pulmonary hypertension (Normoxia)
- Clinical decline - increasing frequency of exacerbations with:
  - Episode of acute respiratory failure requiring non-invasive ventilation
  - Increasing antibiotic resistance
  - Poor clinical recovery from exacerbations
  - Worsening nutritional status despite supplementation
  - Pneumothorax
  - Life-threatening hemoptysis despite bronchial embolization

**TRIAD:**

1. Dyspnoea
2. ‘normal’ chest XRay
3. normal lung function

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**Remember pulmonary Hypertension!**

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<table>
<thead>
<tr>
<th>Group 1</th>
<th>Pulmonary arterial hypertension (PAH)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Idiopathic (IPAH)</td>
</tr>
<tr>
<td></td>
<td>Heritable (HPAH)</td>
</tr>
<tr>
<td></td>
<td>Drug- and toxin-induced</td>
</tr>
<tr>
<td></td>
<td>Associated with (APAH):</td>
</tr>
<tr>
<td></td>
<td>Connective tissue diseases</td>
</tr>
<tr>
<td></td>
<td>Human immunodeficiency virus (HIV)</td>
</tr>
<tr>
<td></td>
<td>infection</td>
</tr>
<tr>
<td></td>
<td>Portal hypertension</td>
</tr>
<tr>
<td></td>
<td>Congenital heart disease (CHD)</td>
</tr>
<tr>
<td></td>
<td>Schistosomiasis</td>
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<tr>
<td></td>
<td>Chronic haemolytic anaemia</td>
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<td></td>
<td>Persistent pulmonary hypertension of the newborn (PPHN)</td>
</tr>
</tbody>
</table>

| Group 1’ | Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary haemangiomatosis (PCH) |

<table>
<thead>
<tr>
<th>Group 2</th>
<th>Pulmonary hypertension due to left heart diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic dysfunction, Diastolic dysfunction, Valvular disease</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Group 3</th>
<th>Pulmonary hypertension due to lung diseases and/or hypoxemia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chronic obstructive pulmonary disease (COPD)</td>
</tr>
<tr>
<td></td>
<td>Interstitial lung disease (ILD)</td>
</tr>
<tr>
<td></td>
<td>Other pulmonary diseases with mixed restrictive and obstructive pattern</td>
</tr>
<tr>
<td></td>
<td>Sleep-disordered breathing</td>
</tr>
<tr>
<td></td>
<td>Alveolar hypoventilation disorders</td>
</tr>
<tr>
<td></td>
<td>Chronic exposure to high altitude</td>
</tr>
<tr>
<td></td>
<td>Developmental abnormalities</td>
</tr>
</tbody>
</table>

| Group 4 | Chronic thromboembolic pulmonary hypertension (CTEPH) |

<table>
<thead>
<tr>
<th>Group 5</th>
<th>PH with unclear multifactorial mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Haematological disorders: myeloproliferative disorders, splenectomy</td>
</tr>
<tr>
<td></td>
<td>Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis, lymphangioliomyomatosis, neurofibromatosis, vasculitis</td>
</tr>
<tr>
<td></td>
<td>Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders</td>
</tr>
<tr>
<td></td>
<td>Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis</td>
</tr>
</tbody>
</table>
PAH: Timing of Referral

- NYHA functional class III or IV despite intensified therapy
- Rapidly progressive disease
- Parenteral targeted pulmonary arterial hypertension (PAH) therapy regardless of symptoms or NYHA Functional Class
- Known or suspected pulmonary veno-occlusive disease or pulmonary capillary hemangiomatosis
**Dyspnea – take home message**

- Chronic dyspnea frequent symptom
- Step-wise pragmatic work-up
- Majority of diagnoses possible in GP practice (e.g. anemia, COPD, Asthma, heart failure)
- Specialist consult required with specific investigations

**To Transplant, or not…**

Red flags ➔ Specialist consult advisable for assessment:

- COPD ≥ 3, frequent exacerbator, rapid decline
- α1-anti-trypsin deficiency
- Interstitial lung disease, regardless of type and stage
- Bronchiectatic lung disease, especially in young patients
- Pulmonary hypertension