PATIENT-CENTRED ACUTE CARE TRAINING

AN ESICM MULTIDISCIPLINARY DISTANCE LEARNING PROGRAMME FOR INTENSIVE CARE TRAINING

COPD and asthma

Organ specific problems

Update 2012

Module Authors (Update 2012)

Raymond Friolet
Dept of Intensive Care Medicine, University of Bern, Switzerland; Dept of Intensive Care Medicine, Sion Hospital, Centre Hospitalier du Centre du Valais, Wallis, Switzerland

Marco Conti
Service of Intensive Care, Department of Anesthesiology, Pharmacology, and Intensive Care, Geneva University Hospital, University of Geneva, Geneva, Switzerland

Module Authors (first edition)

Raymond Friolet/Roland Dietler
Dept of Intensive Care Medicine, University of Bern, Switzerland

For The Bernese PACT Working Group (in alphabetical order)
Roland Dietler, Raymond Friolet, Roger Lussmann, Hans-Ulrich Rothen, Kay Stricker, Jukka Takala, Eva-Maria Weiss-Guillet, Jeannie Wurz

Module Reviewers Joanna Brown, Fernando Suarez Sipmann, Janice Zimmerman

Section Editor Anders Larsson

EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

COPD and asthma

Update 2012

LEARNING OBJECTIVES

After studying this module on Chronic Obstructive Pulmonary Disease (COPD) and Asthma, you should be able to:

1. Evaluate the severity of respiratory distress and triage patients to the appropriate level of care
2. Understand the pathophysiologic mechanisms that lead to decompensation in COPD and asthma patients
3. Manage ventilatory support of COPD and asthma patients in the ICU
4. Provide non-ventilatory support and manage complications
5. Know how to wean the patient from mechanical ventilation and develop a weaning protocol.

FACULTY DISCLOSURES

The authors of this module have not reported any disclosures.

DURATION

7 hours

Introduction 1
1/ Initial evaluation and triage of patients with respiratory distress 2
Initial assessment and management on ward/in ED 2
Differential diagnosis 3
Severity assessment and risk assessment for respiratory exhaustion 3
2/ Why do COPD and asthma patients decompensate? 9
The chain of events 9
How does expiratory obstruction occur? 10
COPD 10
How does airflow obstruction affect respiratory mechanics? 12
Asthma 15
3/ Managing ventilatory support of COPD and asthma in the ICU 17
Defining a strategy and initial setting of the ventilator 19
Assessment of dynamic hyperinflation 21
When to apply PEEPe 26
How much PEEPe should be applied? 26
Clinical problems in applying PEEPe 27
Cardiopulmonary interactions 27
4/ Providing non-ventilatory support and managing complications 29
Drug treatment 29
Asthma 29
COPD 32
Supportive therapies 35
Correction of fluid imbalance 35
Correction of acidosis 35
Alkalosis 36
Nutritional support 36
Treatment of common complications 36
Fever 36
Atelectasis and sputum retention 37
Tachycardia, tachyarrhythmia 38
5/ Weaning the patient 40
When to start weaning 40
How to wean 42
Weaning failure 46
Role of non-invasive ventilation in weaning 47
Role of tracheostomy 49
Long-term outcome 49
Conclusion 51
6/ Glossary 52
Self-assessment 59
Patient challenges 64

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a worldwide and rapidly growing health problem: it was the sixth leading cause of death worldwide in 1990 and is expected to become the third leading cause by 2020. COPD places a huge economic burden on society.

Transient worsening of the chronically altered lung function (so-called exacerbation of COPD) may lead to life-threatening respiratory insufficiency requiring ventilatory support.

Mortality from asthma is also not negligible: it is estimated at 1.4 per 100,000 annually in the United States. Although most deaths from acute asthma occur outside the hospital, patients who are admitted to the emergency department (ED) or a general ward and fail to improve should be admitted to an ICU or at least to a high-dependency unit (HDU), where ventilatory support and appropriate monitoring is possible.

It is of paramount importance to properly triage patients with COPD and asthma so that those at risk of deterioration or death can benefit from ICU/HDU management.

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011. Available from: http://www.goldcopd.org/

Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2011. Available from: http://www.ginasthma.org/

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Full Report 2007. http://www.nhlbi.nih.gov/guidelines/asthma/index.htm

Hinds CJ, Watson JD. Intensive Care: A Concise Textbook. 3rd edition. Saunders Ltd; 2008. ISBN: 978-0-7020259-6-9.

1/ INITIAL EVALUATION AND TRIAGE OF PATIENTS WITH RESPIRATORY DISTRESS

Initial assessment and management on ward/in ED

The terminal event of respiratory distress in COPD and asthma is respiratory arrest. Regardless of the origin of the distress, any patient, who is not known to be for palliative care, who presents with impending respiratory arrest should immediately receive mechanical ventilatory support, via a tracheal tube or a non-invasive procedure (for details of ventilatory support see Task 3). Warning signs of impending respiratory arrest are lethargy, obtundation, silent chest, cyanosis, bradycardia and hypotension.

There is no universal predictive model for survival or weaning failure in severe exacerbation of COPD. Thus, unless the patient's refusal of intubation has been declared in advance care planning (which should take place for each severe COPD patient during the stable phase), ventilatory support is initiated in patients with severe exacerbation of COPD requiring ventilatory assistance. Indeed, the presence of severe COPD in itself is not enough to withhold ventilatory support. Such a decision has to integrate other prognostic factors such as disease severity, major co-morbidities, age and previous quality of life.

In addition to providing mechanical respiratory support as needed, concurrent immediate treatments include:

	Asthma	COPD
Inhaled β-mimetics	++	++
Inhaled anticholinergics	+	++
Systemic corticosteroids	++	+
Antibiotics	–	+
Oxygen	++	+ (cautious titration)
Non-invasive ventilation	(+)	++
Theophylline	–	–
Mucokinetics	–	–

++ good evidence; + relatively good evidence; – no evidence

For further information, see Task 4.

NOTE Oxygen therapy: If the patient is hypoxaemic, oxygen is applied in acute asthma and also in an exacerbation of COPD.
It is, however, important to know that in COPD, pCO_2 may rise in association with the O_2 therapy. This necessitates iterative blood gas measurement to avoid CO_2 narcosis, and corresponding titration of FiO_2 so that SaO_2 reaches but does not exceed 90%.

Ventilatory support: If reaching this target induces a significant worsening of the respiratory acidosis, there is a clear indication for ventilatory support.

THINK If you are told that the respiratory drive is not dampened by the application of oxygen, what pathophysiological mechanism could explain the increase of pCO_2? The following references can provide information on the mechanism.

Robinson TD, Freiberg DB, Regnis JA, Young IH. The role of hypoventilation and ventilation-perfusion redistribution in oxygen-induced hypercapnia during acute exacerbations of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2000; 161(5): 1524–1529. PMID 10806149

http://ajrccm.atsjournals.org/content/161/5/1524.long

Aubier M, Murciano D, Milic-Emili J, Touaty E, Daghfous J, Pariente R, et al. Effects of the administration of O_2 on ventilation and blood gases in patients with chronic obstructive pulmonary disease during acute respiratory failure. Am Rev Respir Dis 1980; 122(5): 747–754. PMID 6778278

Q. What is the definition of an exacerbation of COPD?

A. There is no universal answer. According to the GOLD update 2011: 'An exacerbation of COPD is defined as an acute event characterised by a worsening of the patient's respiratory symptoms (baseline dyspnoea, cough and/or sputum) that is beyond normal day-to-day variations and leads to a change in medication'.

Differential diagnosis

After initiating the required level of respiratory support (which may include intubation and ventilation), review the possible aetiologies of ventilatory failure e.g. acute pulmonary oedema, pneumothorax, upper airway obstruction. To rule out these pathologies, which can clinically mimic COPD or asthma exacerbation, and to look for the aetiology triggering the exacerbation, the most useful investigation is a baseline chest radiograph. This in turn always has to be evaluated in relation to a patient's symptoms, clinical findings and preferably a previous radiograph.

NOTE Heart failure is often present in decompensated COPD (more often right ventricular than bi- or left ventricular) even in the presence of other possible aetiologies (pulmonary infection, pneumothorax, pulmonary embolism). See the PACT module on Heart failure.

Severity assessment and risk assessment for respiratory exhaustion

It is more difficult to gauge the severity of respiratory distress when respiratory arrest is not impending. It is important to recognise and properly treat patients who are at risk of exhaustion, as exhaustion can rapidly end up in respiratory arrest.

Severity assessment depends on medical history, clinical findings and initial response to therapy.

Medical history (COPD)
(see below for asthma)

Prognosis of COPD exacerbation depends on baseline severity of COPD, on the presence of significant co-morbidities, and the number of previous exacerbations. The severity of the baseline COPD is best evaluated by the GOLD spirometric classification.

Severity	**Post-bronchodilator** FEV1/FVC*	**FEV1** % predicted
Stage 1 – Mild COPD	<0.7	≥80
Stage 2 – Moderate COPD	<0.7	50–80
Stage 3 – Severe COPD	<0.7	30–49
Stage 4 – Very severe COPD	<0.7	<30

* FEV1 = forced expiratory volume in one second; FVC = forced vital capacity

Other clinical features which raise the suspicion of a severe disease:

- Cachexia
- Cough syncope
- Signs of chronic right heart failure

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011. Available from: http://www.goldcopd.org/

Medical history (asthma)

In asthma, the risk factors for near-fatal asthma are a combination of features of severe asthma recognised by one or more of:

- A history of prior mechanical ventilation and intensive care unit admission
- Prescription of oral corticosteroids and theophylline
- Evidence of worsening asthma over a period of 2–7 days with increasing use of short-acting β2-adrenergic receptor agonists
- Poor compliance with inhaled corticosteroid therapy
- Difference in perception of dyspnoea
- Age >40 years
- 'Brittle' asthma

- Type 1: wide peak expiratory flow rate (PEFR) variability (>40% diurnal variation for >50% of the time over a period >150 days) despite intense therapy.
- Type 2: sudden severe attacks on a background of apparently well controlled asthma.

And adverse behavioural or psychosocial issues recognised by one or more of:

- Failure to attend appointments
- Self-discharge from hospital
- Psychosis, depression, other psychiatric illness or deliberate self-harm
- Alcohol or drug abuse
- Obesity
- Employment and income problems
- Social isolation.

Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2011. Available from: http://www.ginasthma.org/

Papiris SA, Manali ED, Kolilekas L, Triantafillidou C, Tsangaris I. Acute severe asthma: new approaches to assessment and treatment. Drugs 2009; 69(17): 2363–2391. PMID 19911854

Jalaludin BB, Smith MA, Chey T, Orr NJ, Smith WT, Leeder SR. Risk factors for asthma deaths: a population-based, case-control study. Aust N Z J Public Health 1999; 23(6): 595–600. PMID 10641349

Rea HH, Scragg R, Jackson R, Beaglehole R, Fenwick J, Sutherland DC. A case-control study of deaths from asthma. Thorax 1986; 41(11): 833–839. PMID 3824270

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC460507/?tool=pubmed

Clinical findings (COPD)

Change in mental status, intercostal retraction, paradoxical thoraco-abdominal movements and use of auxiliary muscles are important clinical findings in assessment of exacerbation severity. Presence of haemodynamic instability and/or right heart failure are also signs of severity as is an inadequate response to initial therapy with persistent or worsening of hypoxaemia and/or of hypercapnia. A good predictor of impending respiratory exhaustion is the occurrence of uncompensated respiratory acidosis (pH <7.35), and in particular its progression over time.

Clinical findings (asthma)

Clinical signs of severe asthma are:

- Inability to complete sentences in one breath
- Utilisation of accessory muscles and suprasternal retractions
- Respiratory rate (RR) >30/min
- Tachycardia >120/min

- PEFR <60% of predicted normal or of best normal if known; or<100 L/min, if not known
- An absence of sustained response to treatment (<2 hrs)
- Hypoxaemia while breathing air (PaO_2 <8 kPa/60 mmHg) and hypercapnia ($PaCO_2$ >6 kPa/45 mmHg)

Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2011. Figure p. 72. Available from: http://www.ginasthma.org/

NOTE Patient deterioration despite optimal treatment with progressive increase of $PaCO_2$ is a sign of impending respiratory exhaustion and a predictor of fatal asthma, even before the occurrence of severe hypercapnia.

Immediately life-threatening clinical features are:

- Silent chest, weak respiratory efforts with paradoxical thoraco-abdominal movement
- Confusion or coma
- Bradycardia and hypotension
- Cyanosis.

Triage

In asthma, the initial response to therapy is an important prognostic finding and will be decisive in triage. If a patient who demonstrates criteria of a severe exacerbation does not improve rapidly, i.e. within 1–2 hours, s/he needs to be admitted to a ward where ventilatory support is possible. Improvement is monitored clinically, physiologically as demonstrated by the blood gases (decreasing pCO_2) and by lung mechanics (i.e. PEFR).

Since in COPD the therapeutic response is usually not as fast, triaging patients does not have the same implications as in asthma. Nevertheless, if the patient responds rapidly to initial treatment, admission to a normal ward may be considered.

NOTE The three tests that are the most useful in evaluating acute respiratory distress are arterial blood gas analysis, PEFR, and baseline radiography of the lungs.

Summary of severity assessment and risk of respiratory failure

	COPD	Asthma
Medical history	Co-morbidities Severity of baseline COPD (spirometry) Number of previous exacerbations	Previous ICU admission Previous mechanical ventilation for asthma Deterioration despite optimal treatment including oral steroids Increasing use of β-mimetics over several days
Clinical signs	Severity of dyspnoea: Resp. Rate Auxiliary muscle use Change in mental status Haemodynamic instability PEFR not useful	Severity of dyspnoea: Resp. Rate Auxiliary muscle use Silent chest Haemodynamic alterations: tachycardia Agitation, anxiety or stupor, coma Failure to improve within 1–2 hours of initial treatment PEFR useful
Blood gases	Hypoxaemia Respiratory acidosis No improvement with treatment	Normocapnic or hypercapnic hypoxaemia No decrease of pCO_2 with treatment No correction of hypoxaemia

The most important question to address in triaging is whether the patient might need ventilatory support. The above-mentioned severity criteria, as well as the initial response to treatment, are the cornerstones for triage: patients with severe COPD exacerbation with respiratory acidosis (pH <7.35), or with severe asthma not clearly improving under initial treatment, should be admitted to a ward with the capability for ventilatory support (non-invasive and/or intubation) such as the ICU or HDU.

Criteria for admission to ICU:

COPD

- Inadequate response to initial therapy (severe dyspnoea, altered mental status)
- Persistent or worsening hypoxaemia (PaO_2 <5.3 kPa/40 mmHg) despite supplemental oxygen and non-invasive ventilation

When in doubt, admit the patient: 'A night in the ICU is better than a life in the grave'

- Persistent or worsening respiratory acidosis (pH <7.25) despite non-invasive ventilation
- Need for invasive mechanical ventilation
- Haemodynamic instability requiring vasopressors.

Asthma

- Poor response to initial 1 to 2 hours of treatment
- Risk factors for near-fatal asthma
- Persistent or worsening of clinical symptoms (respiratory distress, decreased mental status)
- PEFR <30%
- PaO_2 <8 kPa/60 mmHg
- $PaCO_2$ >6 kPa/45 mmHg

Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2011. Table p. 74. Available from: http://www.ginasthma.org/

Papiris SA, Manali ED, Kolilekas L, Triantafillidou C, Tsangaris I. Acute severe asthma: new approaches to assessment and treatment. Drugs 2009; 69(17): 2363–2391. PMID 19911854

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011. p. 43. Available from: http://www.goldcopd.org/

For the next patient you see with asthma, evaluate the severity and the risk of near-fatal asthma and decide where the patient should be treated after initial management in the emergency department. Is there a protocol in your institution? If not, consider approaching your colleagues with suggestions for creating one.

Q. The first blood gases of a patient with acute asthma show hypoxaemic respiratory alkalosis. Thirty minutes after initiation of treatment with inhaled β-mimetics and systemic steroids, the patient tells you that he still feels dyspnoeic. The clinical evaluation is unchanged but the arterial blood gases now show hypoxaemic normocarbia. Can you now transfer the patient to the ward? Give your reasons.

A. No! The fact that the patient is no longer able to hyperventilate in response to the hypoxaemia means that he is beginning to have exhaustion. The initial evolution of this patient (with a rising $PaCO_2$) is worrisome, and he should be kept under intensive surveillance.

NOTE It is of paramount importance to clinically reassess asthma patients frequently during the first few hours, with iterative blood gases and peak flow measurements (initially at least hourly). If there is no clear and sustained improvement, the patient should be admitted to a ward with mechanical ventilation capability – usually the ICU.

2/ WHY DO COPD AND ASTHMA PATIENTS DECOMPENSATE?

The chain of events

The hallmark of COPD is a mainly irreversible, expiratory airflow limitation caused by either an increase in the resistance of the small conduction airways, or an increase in lung compliance due to emphysematous lung destruction, or both. The product of resistance and compliance (the 'time constant', reflecting the time necessary for lung emptying) is always increased in COPD patients, and is best reflected by measurements of the FEV1 (the maximal volume that can be expired in one second) and its ratio to the forced vital capacity (FEV1/FVC).

There are two pathophysiological mechanisms leading to hyperinflation:

- Increased airway resistance, which impedes airflow and can lead to so-called dynamic hyperinflation if expiratory time is too short to exhale the whole tidal volume (predominant in asthma). We will refer to this as 'without expiratory flow limitation' or 'without EFL' during normal, quiet tidal volume expiration.
- Airway collapse, leading to the stopping of airflow in the airway and loss of communication with the airway opening; this leads to air trapping distal to the point(s) where airflow has stopped and is predominant in COPD. We will refer to this as 'with expiratory flow limitation' or 'with EFL' during normal, quiet tidal volume expiration.

These two pathophysiological pathways are important to keep in mind when you are applying external PEEP (PEEPe) to COPD and asthma patients:

- In situations where there is **no EFL**, serial resistances are additive, and therefore PEEPe should not be used because it may increase the dynamic hyperinflation.
- Serial resistances in situations **with EFL** are not additive: the airways are collapsing (COPD) or are plugged (asthma), and there is no more airflow downstream from the obstruction during expiration. Thus any further resistance has no effect on airflow or on resistance upstream. In this case the Starling resistor (waterfall principle) applies (see Figure 4-9 and 7-18 in JB West chapters 4 and 7) and there is no hazard in using PEEPe, as long as PEEPe < PEEPi.
  See the references below and also Task 3, 'How much PEEPe to apply'.

Not infrequently of course, a certain degree of both phenomena co-exist in the same patient.

Techniques for bedside detection of EFL are based on the lack of an increase in expiratory flow in response to an increase in the driving pressure (Alveolar Pressure – Mouth Pressure). This should help to determine which patient might benefit from PEEPe (see 'When to apply PEEPe' section).

West JB. Respiratory Physiology – The Essentials. Philadelphia 7th ed. Lippincott Williams & Wilkins; 2005. ISBN 0-7817-5152-7

Koulouris NG, Hardavella G. Physiological techniques for detecting expiratory flow limitation during tidal breathing. Eur Respir Rev 2011; 20(121): 147–155. PMID 21881143

Ninane V, Leduc D, Kafi SA, Nasser M, Houa M, Sergysels R. Detection of expiratory flow limitation by manual compression of the abdominal wall. Am J Respir Crit Care Med 2001; 163(6): 1326–1330. PMID 11371396

http://ajrccm.atsjournals.org/content/163/6/1326.long

See the PACT module on Respiratory assessment and monitoring

How does expiratory obstruction occur?

COPD

Exposure to inhaled noxious particles and gases (such as cigarette smoke or environmental pollution) causes an inflammatory response of the lungs. In at least 15% to 20% of smokers, this leads to the classical pathological findings of COPD – narrowing of the airways by excessive mucus secretion, inflammatory mucosal oedema and increased fluid and cell exudation in the airways. These phenomena are reversible and are the target of our therapy.

Even more important, however, is the structural remodelling of the airway wall caused by the repeated injury and repair process, which leads to irreversible airway obstruction (decreased diameter caused by increased fibrous wall thickness).

NOTE Only a minor portion of airway obstruction is reversible in COPD.

The impact of these alterations on total airway resistance is most important in the peripheral airways (<2 mm diameter), which are the major site(s) of airway obstruction in COPD.

Q. Given that most of the airway resistance in healthy lungs is located in the intermediate sized bronchi (about the 4th to 5th bronchus generation), why is the major airway resistance located in the small airways in COPD patients?

A. The alterations of the airway wall occur throughout the bronchial tree, but since the resistance to laminar flow (Poiseuille's law) is inversely proportional to the 4th power of the radius, the relative narrowing of the airways due to the wall thickening is greatest in the small airways.

Hogg JC, Chu F, Utokaparch S, Woods R, Elliot WM, Buzatu L, et al. The nature of small-airway obstruction in chronic obstructive pulmonary disease. N Engl J Med 2004; 350(26): 2645–2653. PMID 15215480

http://www.nejm.org/doi/full/10.1056/NEJMoa032158

Hogg JC. Pathophysiology of airflow limitation in chronic obstructive pulmonary disease. Lancet 2004; 364(9435): 709–721. Review. PMID 15325838

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2010. Chapter 4. Available from: http://www.goldcopd.org

The other pathological finding contributing (although to a lesser extent) to expiratory airflow impediment is destruction of the parenchyma (emphysema). This destruction is believed to originate from an imbalance of proteinases and antiproteinases (as in α1-antitrypsin deficiency) and/or an imbalance of oxidative stress and anti-oxidants – as in smoking.

The destruction of the lung parenchyma has two deleterious effects on expiratory airflow:

- The ability of the small airways to maintain patency is impaired by the loss of surrounding lung parenchyma. This leads to airway collapse, to so-called 'air trapping', and to an increase in residual volume (functional residual capacity, FRC), and so to hyperinflation.
- The pathological decrease in lung elastic recoil forces. These recoil forces are responsible for the negative pleural pressure and their compromise results in a less negative pleural pressure.

The difference between the alveolar pressure and the pleural pressure (i.e. transpulmonary pressure) is the maximal effective driving force in expiration, and thus the limiting factor for airflow in forced expiration. If recoil forces are diminished and this driving force becomes very small, as in severe emphysema, expiration can become flow-limited even during normal tidal breathing (as mentioned above: **EFL**).

The extent of the expiratory flow limitation is of course compounded by increased airway resistance. This increases the pressure reduction along the airways so that the point of collapse (the 'equal pressure point' – see below) is reached faster.

West JB. Respiratory Physiology – The Essentials. Philadelphia 7th ed. Lippincott Williams & Wilkins; 2005. Chapter 7. ISBN 0-7817-5152-7

Q. Bronchi act as 'starling resistors' i.e. they collapse and no longer allow any flow as soon as the pressure around the airway exceeds that inside (collapsible tube in a pressure chamber). What are the two determinants of airway collapse during expiration?

A. The first determinant of airway collapse during expiration is the transalveolar pressure, which is the gradient between the pressure in the adjacent interstitial space and the alveolar pressure. The other is the pressure drop along the airway which is related to airway resistance.

Q. Explain the 'equal pressure point', the point at which airway collapse occurs?

A. This is the point where the pressure within the airway has fallen to a level which is equalled (or overcome) by the transalveolar/'intrathoracic' pressure.

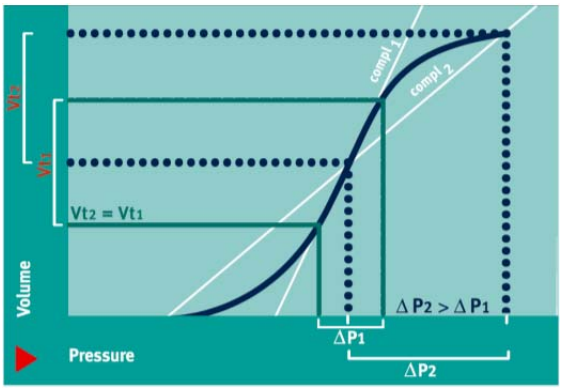
Note that in terms of therapeutic options we have capacity to influence the airway resistance but given that transalveolar pressure is dependent on passive factors, we do not have pharmacologic options to influence it.

How does airflow obstruction affect respiratory mechanics?

Airflow impediment increases the work of breathing (WOB), and alters the effectiveness of respiratory muscles in several ways:

- It increases the change in pressure necessary to overcome airway resistance for a given airflow (ΔP = Airway resistance × Airflow).
- It creates hyperinflation, which partly counteracts increased resistance by increasing airway diameter, but also decreases compliance of the respiratory system if tidal volume is shifted to the very right of the lung pressure–volume curve (see figure below).

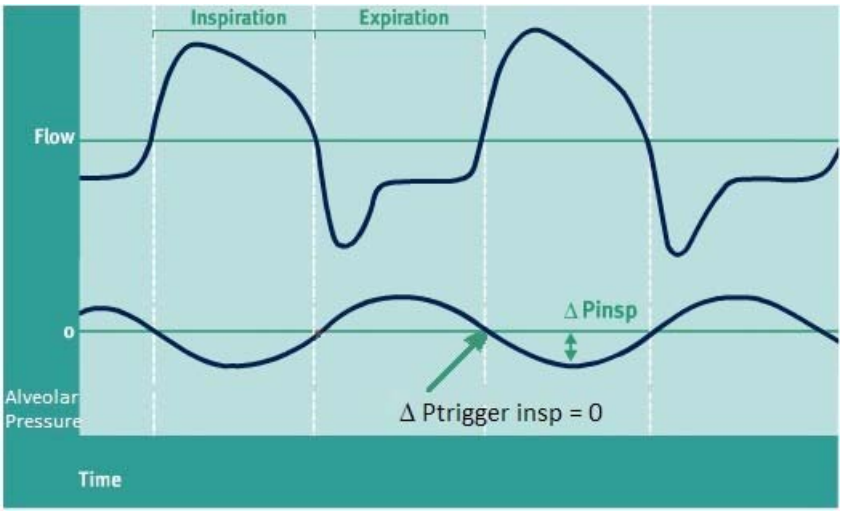
Pressure–volume curve showing the increased pressure (ΔP2) required to achieve the same Vt, when tidal ventilation is 'shifted to the right' on the curve.



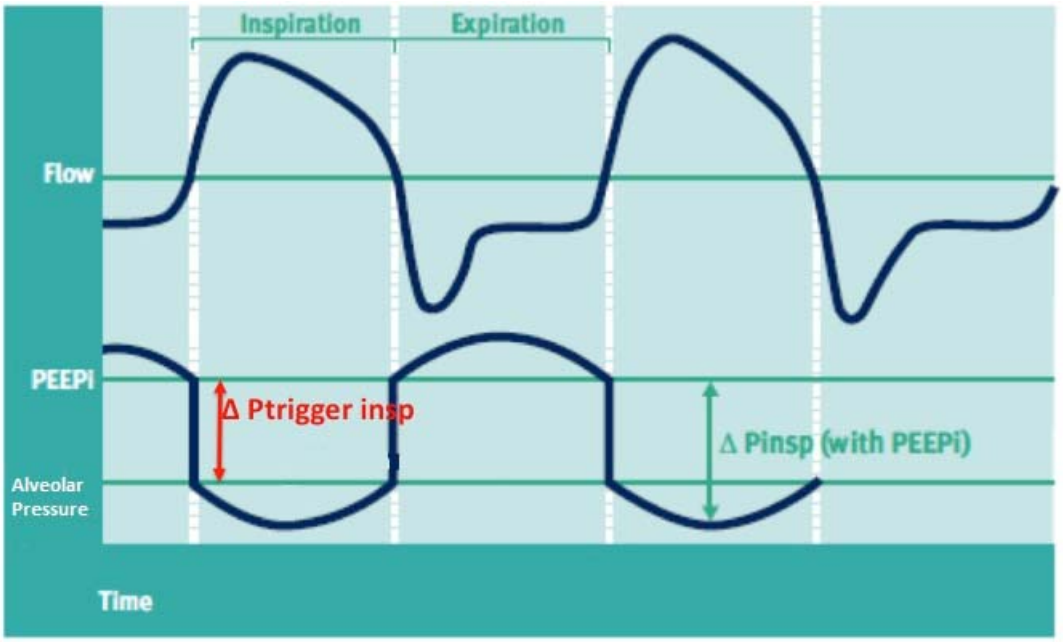
- Hyperinflation (and destruction of lung parenchyma) increases dead space ventilation and so the total minute ventilation required to maintain normal alveolar ventilation

- Auto-PEEP (intrinsic PEEP or PEEPi)) greatly increases the inspiratory trigger workload. At the beginning of each inspiration, auto-PEEP must first be 'overcome' before air can flow in, either during spontaneous breathing or in order to trigger the ventilator during assisted mechanical ventilation (trigger work). See diagrams below.

Alveolar pressure and flow curves during spontaneous breathing in the **absence** of auto-PEEP (PEEPi) demonstrating the minimal inspiratory pressure change required ('trigger' work) to initiate inspiration.



Alveolar pressure and flow curves during spontaneous breathing in the **presence** of auto-PEEP (PEEPi) where the pressure change required to initiate inspiration ('trigger' work) is evidently increased.



At the same time, the ability of the muscles to deal with this increased WOB is impaired in several ways:

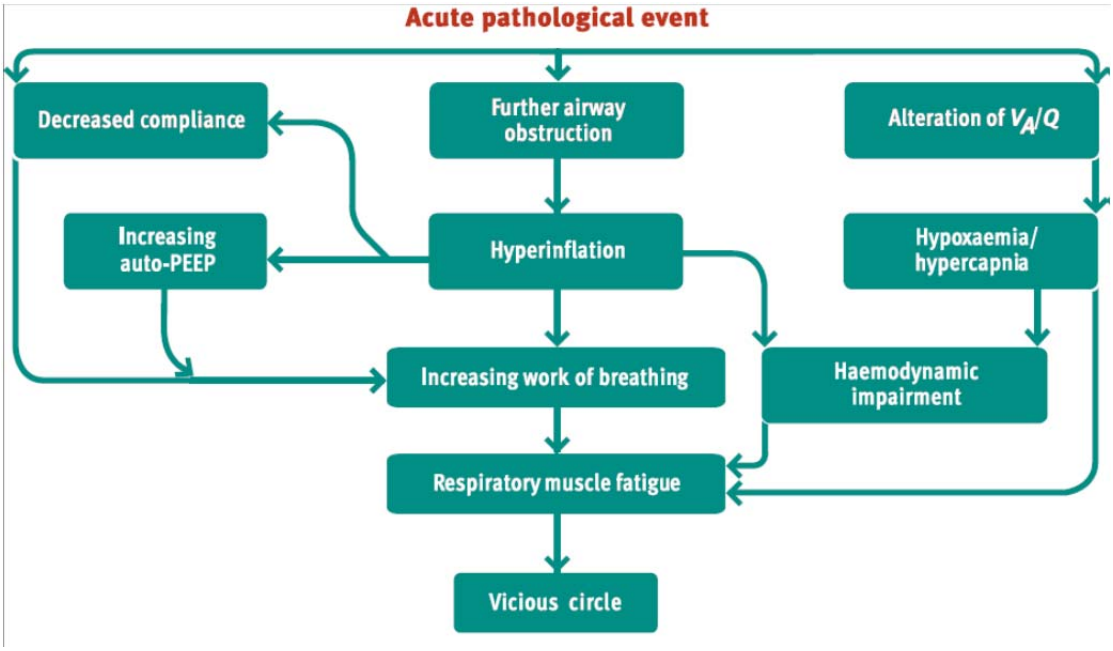
- The altered geometry of chest wall and diaphragm (flattened diaphragm, shortened diaphragm and intercostal muscles) due to hyperinflation leads to a large decrease in muscle efficiency.
- Hypoxaemia and respiratory acidosis disturb the energy metabolism of the muscles.
- Respiratory cachexia, as seen in severe COPD, also impairs muscle strength.

In severe COPD, the balance between respiratory workload and respiratory working capacity is difficult to maintain. Even a small disturbance can precipitate a vicious circle ending up in respiratory failure:

Increased hyperinflation → decreased compliance → increased minute ventilation and tachypnoea → increased auto-PEEP → increased hyperinflation.

All of this increases the work of breathing and leads to increased muscle fatigue due to decreased muscle perfusion/oxygenation and to respiratory acidosis – see figure (Pathophysiological mechanisms) below.

Pathophysiological mechanisms leading to acute decompensation of COPD



Based on what you have learned about the pathophysiology of COPD and COPD exacerbation, you will of course specifically treat triggering factors such as infection. How do you consider these further possible therapies:

Q. How useful is bronchodilator therapy?

A. The reversible components of bronchial obstruction are smooth muscle contraction and inflammatory oedema of the bronchial epithelium, for which bronchodilating therapy (β2-agonists) and anti-inflammatory drugs (steroids) are given. We have to be aware, though, that the reversible part is minor.

Airflow limitation, which is substantially dependent on the destroyed lung parenchyma and the decreased recoil forces, is further limited by dynamic airway collapse.

Q. Are there pharmacological options in this area?

A. No. These parenchymal parameters are fixed and not responsive to any pharmacologic treatment.

Q. You may wish to increase maximal expiratory airflow by increasing the lung volume at end inspiration. Is there a hazard to this approach?

A. Yes. In EFL patients with an exacerbation of COPD, lungs are already overinflated and further increase in lung volume could be deleterious (high Pplat, worsening heart – lung interactions).

THINK Try to imagine how external PEEP could help a patient with decompensated COPD.

NOTE The most common acute event resulting in severe COPD exacerbation and thus leading to respiratory failure is airway infection.

Inflammatory oedema of the airway mucosa, mucus hypersecretion, and bronchoconstriction result in increased airway resistance and contribute to worsening of the VA/Q relationship; these may trigger the vicious circle mentioned above.

Q. Other than pneumonia, name some other causes/disease processes that could disturb the fragile balance between respiratory workload and respiratory working capacity?

A. There are numerous events that can disturb the balance, either by increasing workload or decreasing the work capacity. These include cardiac failure, inhalation of noxious gases, pneumothorax (rupture of bullae), pulmonary embolism, strenuous physical activity, decreased inspired partial oxygen pressure as in high altitude, air travelling.

Asthma

Although inflammation is important in both COPD and asthma, the inflammatory response is quite different in the two diseases. In asthma, a chronic inflammatory disorder of the airways, many cells (mast cells, eosinophils, ...) and cellular elements (cytokines, histamine, ...) play a central role (see figure 1-4 to 1-

6 pp. 7 and 8, GINA 2011). Hypertrophy and hyperplasia of smooth muscle or goblet cells and submucosal glands for instance (see figure 1-7 p. 8 GINA 2011) are the structural changes in airways resulting from this chronic inflammatory disease.

Acute exacerbation may occur as a result of exposure to risk factors for asthma symptoms (see figure 1-2 p. 4 GINA 2011), or triggers such as exercise, air pollutants or allergens, for instance. Occasionally infections can trigger acute exacerbation (mostly viral).

The chronic inflammation is associated with airway hyperresponsiveness (see figure 1-9 p. 9 GINA 2011) that leads to recurrent episodes of obstructive symptoms (wheezing, breathlessness, chest tightness) or coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible (in contrast to COPD).

The final pathophysiological mechanisms leading to airway narrowing (see figure 1-8 p. 8 GINA 2011) in asthma exacerbation are:

- Exaggerated and abnormal contraction of airway smooth muscle cells (predominant and reversible mechanism)
- Airway oedema (important component during exacerbation)
- Mucus hypersecretion (airway plugging)
- Airway thickening (due to structural changes, not fully reversible).

Thus, even if in obstructive patients, EFL or no EFL often co-exist, in asthma patients, no EFL is predominant. However, as for COPD patients (mostly EFL), hyperinflation is the main mechanism leading to respiratory muscle fatigue.

Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2011. Available from: http://www.ginasthma.org/

3/ MANAGING VENTILATORY SUPPORT OF COPD AND ASTHMA IN THE ICU

Once the ventilatory muscles can no longer match the ventilatory demand, patients become progressively exhausted. At this point ventilatory support is needed to interrupt the above vicious circle. The aim of ventilatory support is to give the respiratory muscles the opportunity to rest until the cause of exacerbation is treated and the bronchial obstruction and inflammation has been reversed.

In severe COPD exacerbation with respiratory acidosis, ventilatory support should first be applied non-invasively (if not contraindicated), since the intubation rate, the length of stay in the ICU and even mortality, have been shown to be reduced.

In asthmatic patients, non-invasive ventilation could have potential benefits such as off-setting the PEEPi, re-expanding collapsed lung and reducing the work of breathing. An early non-invasive mechanical ventilation trial may be individually assessed but only in an ICU environment. These benefits have not been established for severe asthma.

The indications for ventilatory support include:

- Signs of respiratory distress (dyspnoea, with use of accessory muscles and paradoxical abdominal motion, tachypnoea)
- Hypercapnic acidosis (pH <7.35).

See the following references:

Brochard L, Mancebo J, Wysocki M, Lofaso F, Conti G, Rauss A, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. N Engl J Med 1995; 333(13): 817–822. PMID 7651472

http://www.nejm.org/doi/full/10.1056/NEJM199509283331301

Evans TW. International Consensus Conferences in Intensive Care Medicine: non-invasive positive pressure ventilation in acute respiratory failure. Intensive Care Med 2001; 27(1): 166–178. Review. PMID 11280630

Soroksky A, Stav D, Shpirer I. A pilot prospective, randomized, placebo-controlled trial of bilevel positive airway pressure in acute asthmatic attack. Chest 2003; 123(4): 1018–1025. PMID 12684289

http://chestjournal.chestpubs.org/content/123/4/1018.long

Keenan SP, Sinuff T, Cook DJ, Hill NS. Which patients with acute exacerbation of chronic obstructive pulmonary disease benefit from noninvasive positive-pressure ventilation? A systematic review of the literature. Ann Intern Med 2003; 138(11): 861–870. PMID 12779296

Non-invasive ventilatory support

The most commonly used ventilatory mode is pressure support with PEEP or bilevel positive-pressure ventilation with a minimal mandatory frequency in case of insufficient respiratory drive.

Practical aspects:

- Patient must be seated and reassured
- Choose a facial mask for the interface
- Start with pressure support mode
- Initial settings:
  - Inspiratory pressure 6–8 cmH_2O
  - PEEP 3–5 cmH_2O, FiO_2 to ensure SaO_2 ≥88%
  - Inspiratory trigger set at 0.5 to 1 L/min
  - Expiratory trigger set in the upper range (40–70% of maximal inspiratory flow)
  - Pressurisation time set at shorter range (0.1 to 0.2 sec)
- Titrate PEEP by steps of 1–2 cmH_2O according to patient's comfort (observe and assess ineffective triggering attempts)
- Titrate pressure support level by steps of 2 cmH_2O to patient's comfort, respiratory rate (≤25/min) and tidal volume (6–8 mL/kg), avoid total airway pressure above 20 cmH_2O.

NOTE As titration of settings is guided by patient comfort, communication is paramount.

Failure criteria (see also below):

- Absence of improvement (or a deterioration) within first two hours using clinical and $PaCO_2/PaO_2$ criteria
- pH <7.25, respiratory rate >35/min, GCS <11 after the first two hours of NIV.

NOTE Don't delay intubation if patient worsens during NIV trial.

Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. Lancet 2009; 374(9685): 250–259. PMID 19616722

Confalonieri M, Garuti G, Cattaruzza MS, Osborn JF, Antonelli M, Conti G, et al.; Italian noninvasive positive pressure ventilation (NPPV) study group. A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation. Eur Respir J 2005; 25(2): 348–355. PMID 15684302

http://erj.ersjournals.com/content/25/2/348.long

Invasive ventilatory support

There are no clearly defined criteria for the initiation of invasive mechanical ventilation in COPD or asthma.

In COPD, the current approach is to intubate the patient if non-invasive ventilation fails, i.e. if blood gases and clinical status do not improve within the first two hours of initiation of non-invasive mechanical ventilation (see Figures 5.4–9, pp. 42–44 GOLD update 2011).

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011. Available from: http://www.goldcopd.org/

In asthma, the primary goal of intubation and mechanical ventilation is to maintain oxygenation and prevent respiratory arrest; thus intubation should not be deferred too long, but should rely on worsening of clinical signs (changes in alertness, speech and posture as well as respiratory rate decrease, for instance). Once a decision to intubate has been made, the goal is to gain rapid and complete control of the patient's cardiorespiratory status. The most experienced physician available should handle the intubation.

Whenever possible, use a large diameter tracheal tube to decrease total airway resistance and facilitate clearance of secretions.

In obstructive lung disease, it is the avoidance of further overinflation and the threat of volu-/barotrauma what should guide the ventilator settings. Thus, in patients ventilated for severe asthma, for instance, the therapeutic targets are limited to obtain an adequate oxygenation and minimise overinflation and its consequences, using the minimum minute ventilation required to avoid severe respiratory acidosis.

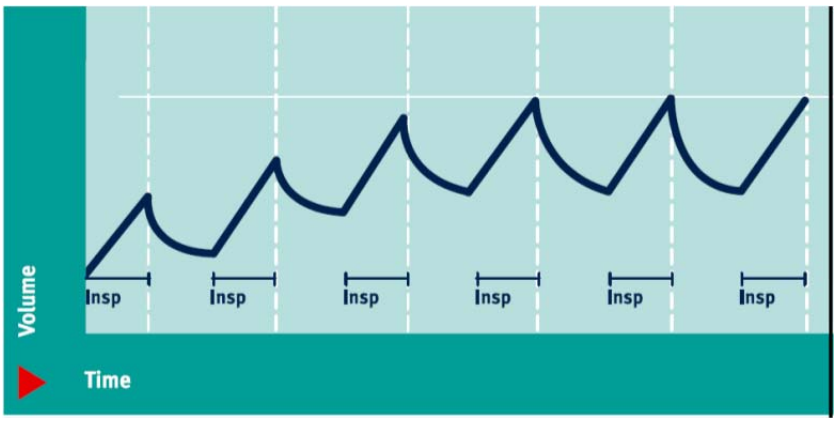
NOTE In very severe cases of bronchial obstruction, neuromuscular paralysis might be necessary to ventilate the patient. We should, however, be aware of the high risk of myopathy in these patients, who are often treated with corticosteroids, and thus balance the risk against the benefits. Heavy sedation might obviate the necessity for neuromuscular paralysis.

For information on myopathy see the PACT module on Neuromuscular conditions. See Task 5, for information on weaning difficulties.

Defining a strategy and initial setting of the ventilator

The main problem in ventilating a patient with bronchial obstruction is hyperinflation and its associated complications: volutrauma, barotrauma and haemodynamic compromise.

Hyperinflation arises when the inspired air cannot be totally expired (so-called dynamic hyperinflation).



The main determinants for the occurrence of dynamic hyperinflation are:

- The expiratory time
- The volume of air that has to be expired (tidal volume: Vt).

In the initial phase, we choose a controlled mode and set the parameters so that expiration is as long as possible (low RR and low **I:E** ratio) and tidal volume is kept low. The general strategy also called controlled hypoventilation or permissive hypercapnia, combines a relatively low expired minute volume (Ve = RR × Vt) with a high inspiratory flow (to ensure a short Ti and thus a low I:E ratio).

NOTE Regarding respiratory terminology – see combined glossary of respiratory terms:
RR for 'respiratory rate' is synonymous with the term Fr (frequency).
I:E ratio, the ratio of time in inspiration to time in expiration, is sometimes written as Ti:Te ratio.

There is consensus on how to start mechanical ventilation in severe bronchial obstruction:

- Minute ventilation <115 mL/kg
- Tidal volume <8 mL/kg
- Respiratory rate 10 to 14 per minute
- Inspiratory flow 80 to 100 L/min

There is no consensus as to which ventilator mode should be initially set.

Be careful to avoid overventilating patients with chronic compensated respiratory acidosis as this may lead to dangerous metabolic/respiratory alkalosis. Aim at normal pH rather than normal $PaCO_2$.

Williams TJ, Tuxen DV, Scheinkestel CD, Czarny D, Bowes G. Risk factors for morbidity in mechanically ventilated patients with acute severe asthma. Am Rev Respir Dis 1992; 146(3): 607–615. PMID 1519836

Assessment of dynamic hyperinflation

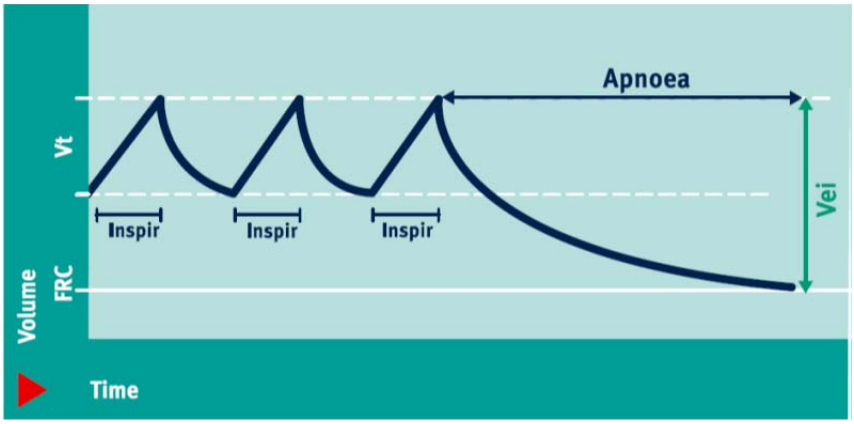
See Glossary.

You can suspect hyperinflation, when inspiration starts before expiratory flow returns to zero in the monitored flow time curve.

The only measure that has been shown to predict complications of hyperinflation (hypotension and barotrauma) is the end-inspiratory volume (Vei) above functional respiratory capacity (FRC). It is measured by collecting total exhaled volume in a paralysed patient over 60 seconds of apnoea.

Tuxen DV, Williams TJ, Scheinkestel CD, Czarny D, Bowes G. Use of a measurement of pulmonary hyperinflation to control the level of mechanical ventilation in patients with acute severe asthma. Am Rev Respir Dis 1992; 146(5 Pt 1): 1136–1142. PMID 1443862

Vei: the end-inspiratory volume above functional residual capacity (FRC)



Vei >20 mL/kg is predictive of complications such as hypotension and barotrauma.

Since Vei is difficult to determine in clinical practice, surrogate measures are used to reflect hyperinflation:

- Intrinsic PEEP
- Pplateau (also called Pplat or Ppause)

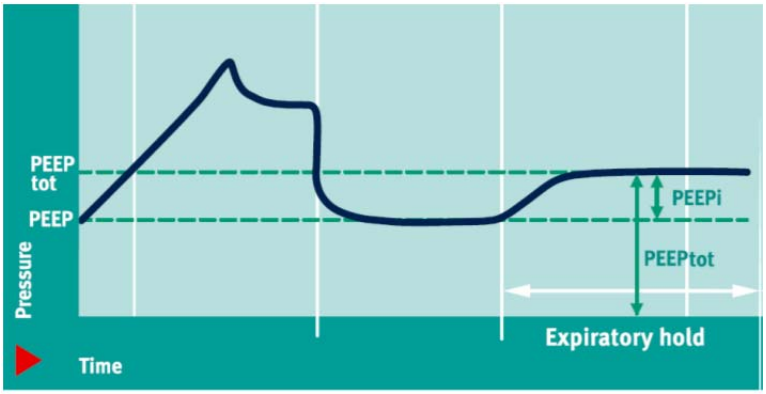
Ppeak (peak or maximal inspiratory airway pressure) also increases proportionally to Pplat and PEEPi with hyperinflation, but it has no pathological implication in the clinical setting, since Ppeak is not transmitted to alveoli.

See PACT module on Acute respiratory failure.

NOTE COPD and asthma patients always have high Ppeak because of increased airway resistance and of the high inspiratory flow rate often required to shorten the inspiratory time (Ti), thus ensuring a longer expiratory time(Te).

PEEPi is measured at end-expiration and is the lowest average alveolar pressure achieved during the respiratory cycle, and is best measured during an end-expiratory hold manoeuvre on the ventilator in a relaxed, but not necessarily (pharmacologically) paralysed, patient. See the following figure and the PACT module on Mechanical ventilation.

How to measure PEEPi by expiratory breath-hold

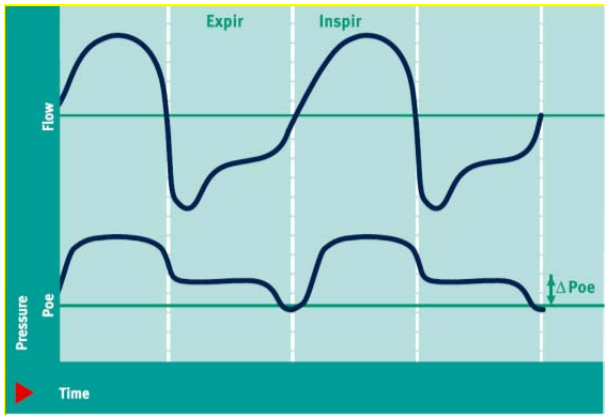


During this manoeuvre there is no airflow, and pressures equilibrate within the respiratory system and so reflect the mean end-expiratory alveolar pressure.

Measuring PEEPi (also called auto-PEEP) in a spontaneously breathing patient is more difficult. If you measure oesophageal pressure (Poe, also called P_{es}) in your unit, you might approximate PEEPi in spontaneous, assisted ventilation, by the negative inflexion of Poe at the beginning of a triggered inspiration, until inspiratory flow starts (see figure below).

$\Delta Poe \cong Ptrigger + PEEPi$ and thus
$PEEPi \cong \Delta Poe - Ptrigger$ where Ptrigger is the set trigger on the ventilator.

Oesophageal pressure trace during triggered assisted positive pressure ventilation.



The value determined this way (so-called $PEEPi_{dyn}$ as opposed to PEEPi static) is usually lower than with the expiratory hold method, since inspiratory flow starts to the region with the lowest PEEPi (non-homogeneity of time constant) as soon as auto-PEEP is balanced. Thus this method gives the value of the lowest auto-PEEP in the lungs, whereas the expiratory hold method gives the mean value.

Appendini L. About the relevance of dynamic intrinsic PEEP (PEEPi, dyn) measurement. Intensive Care Med 1999; 25(3): 252–254. PMID 10229157

There is no value for auto-PEEP (PEEPi) that is predictive of barotrauma, but successive measurements give an indication of the evolution of hyperinflation: increasing auto-PEEP (PEEPi) reflects increasing hyperinflation. There is general agreement that to minimise the risk of volutrauma and barotrauma of the lungs, Pplateau (Ppause) should be kept below 30 cmH_2O.

Slutsky AS. Consensus conference on mechanical ventilation--January 28–30, 1993 at Northbrook, Illinois, USA. Part I. European Society of Intensive Care Medicine, the ACCP and the SCCM. Intensive Care Med 1994; 20(1): 64–79. PMID 8163765

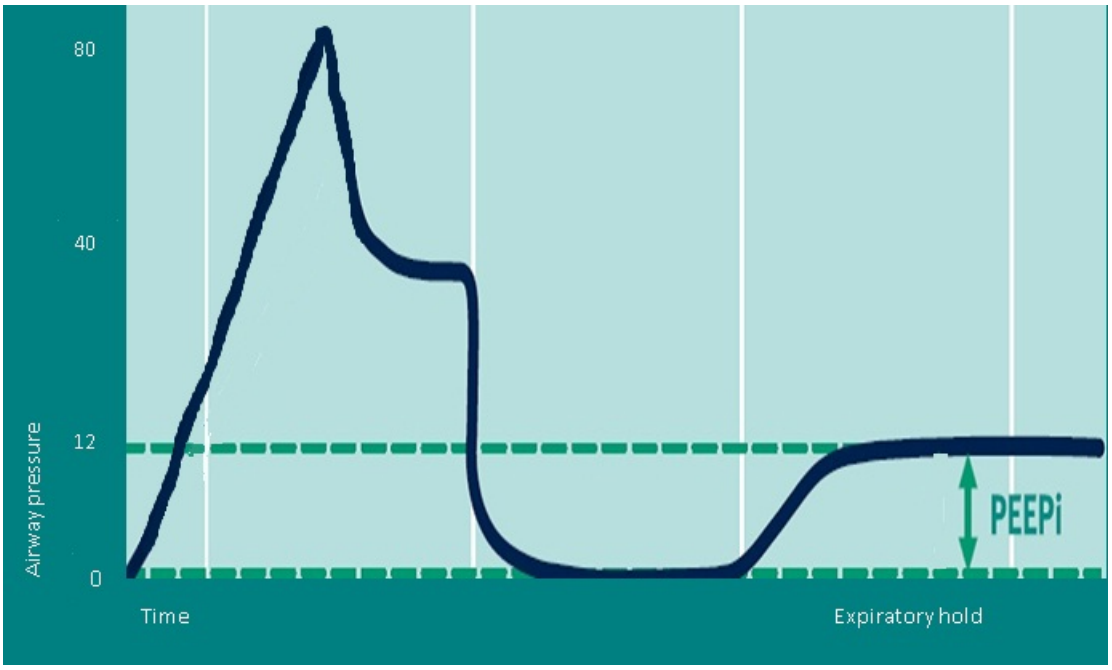
Slutsky AS. Consensus conference on mechanical ventilation--January 28–30, 1993 at Northbrook, Illinois, USA. Part 2. Intensive Care Med 1994; 20(2): 150–162. PMID 8201097

Don't keep Ppeak below an arbitrary limit; you may increase hyperinflation by decreasing inspiratory air flow. Pplateau (Ppause) is the parameter to watch for.


Evaluate one of your intubated patients with regard to whether hyperinflation could be present. Measure auto-PEEP (PEEPi).

Q. In a severe asthma patient, you set the initial settings in Volume-controlled ventilation: Minute ventilation (Vm) <115 mL/kg, Tidal volume(Vt) <8 mL/kg, Respiratory rate(Fr) 10 to 14 per minute, Inspiratory flow 80 to 100 L/min to ensure a short Ti and thus a low Ti:Te (I:E) ratio and you measure the following values: Ppeak of 80 cmH_2O, Pplateau of 40 cmH_2O, as measured by an end-inspiratory occlusion manoeuvre, auto-PEEP of 12, and respiratory acidosis of pH 7.30 with good oxygenation. What is your assessment, particularly of the Ppause?

A. The Pplateau (Ppause) is definitely above the safe range and is indicative of hyperinflation.



Q. What is your priority in terms of minimising the risk of barotrauma? What do you do?

A. Even if there is already respiratory acidosis, the priority is to decrease Ppause (Pplateau) and the likely related hyperinflation. This may be achieved by reducing Vm by decreasing Vt. Vm may also be decreased by reducing RR, thereby prolonging expiration and also allowing a reduction in hyperinflation.

Q. Is the elevated Ppeak a concern?

A. The high Ppeak is not bothersome, since it arises from the increased airway resistance and the high inspiratory flow rate and is mainly dissipated in the airways and so does not reach the alveoli.

If it is not possible to reach normoventilation within the safe parameters as mentioned above, it is recommended to use so-called **permissive hypercapnia** to avoid mechanical lung damage. Hypercapnic acidosis is usually well tolerated.


Permissive hypercapnia is contraindicated in the presence of intracerebral hypertension because of the cerebral vasodilation that it induces.

Q. You decide to reduce the respiratory rate alone from 12 to 8 breaths/min and you achieve the following findings:
Ppeak 70 cmH_2O,
Pplateau 30 cmH_2O,
PEEPi of 4 cmH_2O,
pH and pCO_2 unaltered (slight hypercapnic acidosis) and good oxygenation.

Are you satisfied that safety criteria have been achieved?

A. Yes, the safety criteria are now satisfied.

The presumed mechanism is that there has been a significant reduction in hyperinflation.

Q. Since the Vm has been reduced, how can we explain the unchanged pCO_2?

A. We can assume that the hyperinflation was associated with an increase in dead space. So despite a decrease in Vm, alveolar ventilation **(V'A)** may have remained unchanged due to the decrease in dead space ventilation.

Q. And how do you interpret the fact that the change in Pplateau (ΔPpause) is greater than the change in intrinsic PEEP (ΔPEEPi)?

A. Hyperinflation shifted the ventilation toward the right and upper part of lung pressure–volume curve, where the compliance was lower. So by changing the setting we reached the steeper (more compliant) part of the lung pressure-volume curve.


For the next intubated patient who is ventilated in volume-controlled mode, calculate expiratory time (Te) with the actual setting. Then, increase Te by decreasing RR, and calculate the new Te. Afterwards, increase Te by shortening Ti e.g. by increasing inspiratory flow.

Decreasing RR is the most effective manoeuvre to increase Te and thus decrease hyperinflation. As in ARDS, the solution to prevent volutrauma and barotrauma in obstructive lung disease may be permissive hypercapnia (see above).

When to apply PEEPe

Anytime that auto-PEEP (PEEPi) is present, external PEEP (PEEPe) can and should be applied to decrease inspiratory trigger efforts.


Attempts to overcome PEEPi are thought to be one of the major causes of respiratory failure in acute exacerbations of COPD, as well as a major cause of weaning failure in mechanically ventilated patients with airway obstruction. External PEEP may be of use in counterbalancing PEEPi thus diminishing work of breathing but does not minimise hyperinflation (see the references below and the PACT module on Mechanical ventilation).

NOTE In obstructive patients, be careful in applying PEEPe during fully controlled mode since you might worsen hyperinflation without any proven benefit on lung mechanics. The main indication for applying PEEPe in this context is to improve oxygenation; start applying PEEPe as soon as the patient is on assisted mode since it reduces inspiratory trigger work.

Brochard L. Intrinsic (or auto-) PEEP during controlled mechanical ventilation. Intensive Care Med 2002; 28(10): 1376–1378. PMID 12373460

Ward NS, Dushay KM. Clinical concise review: Mechanical ventilation of patients with chronic obstructive pulmonary disease. Crit Care Med 2008; 36(5): 1614–1619. PMID 18434881

How much PEEPe should be applied?

Defining an adequate amount of external PEEP is difficult. Thinking of the waterfall principle (situation with airflow limitation), setting **PEEPe = PEEPi** would bring the greatest relief to inspiratory efforts, without carrying the risk of increasing hyperinflation.

There are two reasons, however, why PEEPe should be set lower than measured PEEPi.

- There might be a mixed picture of airflow limitation and no-airflow limitation.
- The PEEPi distribution within a COPD or an asthma lung is uneven (because of an inhomogeneous time constant distribution) and thus, in some areas, the effective PEEPi might be lower than the measured static PEEPi (see above figures on PEEPi measurement).

Both of these reasons might lead to an increased total PEEP (PEEPtot), if PEEPe were equal to PEEPi.

NOTE The current consensus is that external PEEP (PEEPe) should be set at about 80% of PEEPi, in order to give a substantial relief on inspiratory workload without risk of increasing hyperinflation.

Brochard L. Intrinsic (or auto-) positive end-expiratory pressure during spontaneous or assisted ventilation. Intensive Care Med 2002; 28(11): 1552–1554. PMID 12583374


In a controlled mechanically ventilated COPD patient, determine auto-PEEP (PEEPi) and then apply different levels of PEEPe (≤ to PEEPi). Observe the absence of change in total PEEP as long as PEEPe is below 80% of PEEPi.

Clinical problems in applying PEEPe

In clinical practice, there is another everyday difficulty: PEEPi changes in relation to the respiratory parameters (RR, Vm), body position, and variability of changes in respiratory mechanics related to disease course and response to treatment. Thus the measured values of PEEPi under controlled ventilation in a relaxed patient might be quite different from the actual PEEPi in spontaneous ventilation, the situation in which we want to apply external PEEP.

Measuring PEEPi in a spontaneously ventilating patient is rather difficult (see figures on how to measure PEEPi). In clinical practice it is therefore helpful to ask the patient about his comfort and his dyspnoea, while increasing external PEEP (PEEPe) very gradually. He will notice the relief of workload due to counterbalancing of PEEPi until hyperinflation is increasing. Dyspnoea is proportional to Vei and thus the patient can notice increasing hyperinflation.

Cardiopulmonary interactions

Since the lung, heart, and pulmonary circulation are within the same 'box', i.e. the thoracic cage, intra-pleural pressure variations might greatly influence cardiac function.

Positive intrathoracic pressure:

- Decreases venous return and thus the preload of both ventricles
- Increases pulmonary vascular resistance, and thus the afterload of the right ventricle.

Hyperinflation further increases intrathoracic pressure and thus accentuates these haemodynamic effects.

Hypotension is the more common effect of the decreased preload, and is accentuated by hypovolaemia.

 Always consider hyperinflation in the mechanically ventilated patient with hypotension, especially if bronchial obstructive lung disease is present.

NOTE If you suspect hyperinflation in a mechanically ventilated patient, briefly disconnect the ventilator and hypotension will rapidly improve.

Due to the increasing afterload of the right ventricle, hyperinflation could induce **acute right ventricular failure** with ensuing RV dilation, septal shift and LV filling deficiency due to ventricular interdependency.

Intrathoracic pressure is partially transmitted to the circulation and thus influences the measured values of central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP). This has to be taken into account when haemodynamic measurements are assessed. The extent of alveolar pressure transmission is proportional to the compliance of the lungs and is thus minimised in the presence of severe ARDS. However, it is inversely proportional to the compliance of the chest wall.

Feihl F, Broccard AF. Interactions between respiration and systemic hemodynamics. Part I: basic concepts. Intensive Care Med 2009; 35(1): 45–54. PMID 18825367

Feihl F, Broccard AF. Interactions between respiration and systemic hemodynamics. Part II: practical implications in critical care. Intensive Care Med 2009; 35(2): 198–205. PMID 18825366

Jardin F. Ventricular interdependence: how does it impact on hemodynamic evaluation in clinical practice? Intensive Care Med 2003; 29(3): 361–363. PMID 12577152

Jardin F, Genevray B, Brun-Ney D, Bourdarias JP. Influence of lung and chest wall compliances on transmission of airway pressure to the pleural space in critically ill patients. Chest 1985; 88(5): 653–658. PMID 3902386

http://chestjournal.chestpubs.org/content/88/5/653.long

4/ PROVIDING NON-VENTILATORY SUPPORT AND MANAGING COMPLICATIONS

The basic ICU management of an acute exacerbation of COPD or asthma is supportive, (euvolaemia, correction of acid-base balance and electrolytes, adequate nutrition, and the treatment of common complications) and specific, particularly the drug treatment.

Drug treatment

The drugs and their importance partly differ in the treatment of patients with acute exacerbations of asthma or COPD.

Asthma

THINK about a patient with status asthmaticus. If an airway obstruction is responsible for the exacerbation, does it make sense to perform intubation as early as possible?

Beta-sympathomimetic agents

β2-adrenergic agonists are the most effective bronchodilating agents, and are the first-line treatment for smooth-muscle-mediated bronchoconstriction. Nebulised therapy has a rapid onset of action and is as effective as intravenous therapy, but is less likely to cause cardiac arrhythmias, hypokalaemia, tremor, and lactic acidosis.

Epinephrine isn't a more potent bronchodilator than β2-mimetics. It should be avoided (either nebulised or systemically) because of its numerous side effects

Oxygen-driven nebulised therapy should be given until an adequate clinical response is achieved or until adverse side effects limit further administration. Intubated patients need higher drug doses to accomplish adequate delivery of drugs to the lung. If the response is poor or the patient is moribund, use the intravenous form (e.g. albuterol 200 µg over 10 min, then 3–20 µg/min). (Note: in the USA, albuterol has not been approved for intravenous use).

Corticosteroids

Airway-wall inflammation is central to the pathogenesis of asthma, and thus systemic corticosteroid therapy is an essential part of the first-line treatments for status asthmaticus. Hydrocortisone and methylprednisolone have both been demonstrated to be very effective.

No definitive consensus exists in the dose and molecule to use. There is no efficacy difference between oral and parenteral administration. The British Thoracic Society guidelines recommend parenteral hydrocortisone 400 mg daily (100 mg six-hourly) or oral prednisolone 40–50 mg daily. There is no evidence that higher doses of steroids are more effective. Lower doses are probably as effective but there are no sufficient data to support this. Duration of systemic corticosteroid therapy should be 5 to 10 days.

Inhaled corticosteroids can be continued or added to the systemic therapy when possible in order to prepare for the chronic asthma management plan.

NOTE The peak response for steroid action does not occur until four to six hours after administration, therefore start early with the steroid treatment.

Manser R, Reid D, Abramson M. Corticosteroids for acute severe asthma in hospitalised patients. Cochrane Database Syst Rev 2001; (1): CD001740. PMID 11279726

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001740/full

Papiris SA, Manali ED, Kolilekas L, Triantafillidou C, Tsangaris I. Acute severe asthma: new approaches to assessment and treatment. Drugs 2009; 69(17): 2363–2391. PMID 19911854

Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2011. Available from: http://www.ginasthma.org/

British Guideline on the Management of Asthma (2011 revision). http://www.brit-thoracic.org.uk/guidelines.aspx

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Full Report 2007. http://www.nhlbi.nih.gov/

Additional bronchodilators

Anticholinergics such as ipatroprium bromide inhibit the vagal tone with medium-potency bronchodilation. In combination with inhaled β2-adrenergic agonists, the effect of bronchodilation will be increased and it has been shown that it can lead to a faster recovery and reduce hospitalisation rates. Anticholinergic treatment is not necessary and may not be beneficial in milder exacerbations of asthma or after stabilisation.

Add nebulised ipratropium bromide (0.5 mg 4–6 hourly) to β2 agonist treatment for patients with acute severe or life-threatening asthma or those with a poor initial response to β2 agonist therapy.

Leukotriene receptor antagonists

Leukotrienes are derived from arachidonic acid metabolism through the 5-lipoxygenase pathway. They are potent mediators of inflammation implicated in asthma. Leukotriene receptor antagonists have bronchodilator and anti-inflammatory effects and are clinically active following a single dose. There is only sparse literature, however, suggesting that montelukast is effective in the treatment of acute asthma as an adjunct therapy to avoid intubation.

Papiris SA, Manali ED, Kolilekas L, Triantafillidou C, Tsangaris I. Acute severe asthma: new approaches to assessment and treatment. Drugs 2009; 69(17): 2363–2391. PMID 19911854

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Full Report 2007. http://www.nhlbi.nih.gov/

Magnesium sulfate

There are randomised controlled trials suggesting that a single intravenous dose of 2 gm of magnesium sulfate can have an additional bronchodilatory benefit in patients with severe acute asthma, even with normal serum magnesium levels. It may be that magnesium inhibits calcium channels.

Rowe BH, Camargo CA Jr. The role of magnesium sulfate in the acute and chronic management of asthma. Curr Opin Pulm Med 2008; 14(1): 70–76. PMID 18043278

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Full Report 2007. http://www.nhlbi.nih.gov/

Methylxanthines (aminophylline, theophylline)

Aminophylline is an inhibitor of phosphodiesterase. It causes weak bronchodilation, dilation of the pulmonary vessels, and has a positive inotropic effect, especially for the right heart. The use of methylxanthines in acute asthma is not routinely recommended (no additional benefit, increased frequency of side effects).

However, some patients with near-fatal asthma or life-threatening asthma with a poor response to initial therapy may gain additional benefit from IV aminophylline, (5 mg/kg loading dose over 20 minutes (unless on maintenance oral therapy) and then by infusion (0.5–0.7 mg/kg/hr). Such patients are likely to be rare and could not be identified in a meta-analysis of trials.

Toxicity should be monitored and levels checked regularly in patients on aminophylline infusions.

Parameswaran K, Belda J, Rowe BH. Addition of intravenous aminophylline to beta2-agonists in adults with acute asthma. Cochrane Database Syst Rev 2000; (4): CD002742. PMID 11034753

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002742/full

Papiris SA, Manali ED, Kolilekas L, Triantafillidou C, Tsangaris I. Acute severe asthma: new approaches to assessment and treatment. Drugs 2009; 69(17): 2363–2391. PMID 19911854

British Guideline on the Management of Asthma (2011 revision). http://www.brit-thoracic.org.uk/home.aspx

Heliox

Heliox is a mixture of 60–80% helium and 20–40% oxygen, and has a lower gas density. It decreases respiratory work by reducing airflow resistance, but requires substantial technical adaptation of the respirator and thus is limited to experienced centres. It has no effect on bronchospasm although it could improve the spirometric effect of albuterol, if used to nebulise it instead of oxygen. It might, however, be a bridge to resolution of bronchospasm thus avoiding intubation in patients not responding to standard therapy. There is no proven benefit on relevant outcomes. Heliox cannot be used in patients who require a high FiO_2 (the benefit of low density is lost with FiO_2 above 0.4).

Rodrigo G, Pollack C, Rodrigo C, Rowe BH. Heliox for nonintubated acute asthma patients. Cochrane Database Syst Rev 2006 Oct 18; (4): CD002884. PMID 17054154

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002884.pub2/full

Kress JP, Noth I, Gehlbach BK, Barman N, Pohlman AS, Miller A, et al. The utility of albuterol nebulized with heliox during acute asthma exacerbations. Am J Respir Crit Care Med 2002; 165(9): 1317–1321. PMID 11991886

http://ajrccm.atsjournals.org/content/165/9/1317.long

Anti-infective therapy

Most exacerbations of asthma are due to non-infective factors or to viral infections. Anti-infection therapy should only be given for asthma if there is very good evidence of bacterial infection.

NOTE Acute asthma often shows discoloured or purulent sputum (due to eosinophils) even in the absence of infection.

COPD

Beta-sympathomimetic agents and other bronchodilators

Patients with COPD have a limited degree of reversible airflow obstruction compared to patients with asthma. Nevertheless, the role of bronchodilators remains prominent in the management of exacerbated COPD.

Inhalation of short-acting β2-adrenergic agonists is recommended and combine them with anticholinergics if a prompt response does not occur. Both nebulisers

and hand-held inhalers can be used to administer inhaled therapy during exacerbations of COPD, depending on the severity of the exacerbation. If a patient is hypercapnic or acidotic, it is advised that the nebuliser should be driven by compressed air rather than oxygen (to avoid worsening hypercapnia). If oxygen therapy is needed, administer it simultaneously by nasal cannulae.

Intravenous β2-adrenergic agonists are not indicated.

The addition of theophylline adds minimal, if any, efficacy and should only be considered if there is an inadequate response to nebulised bronchodilators. Theophylline levels are monitored daily in the acute setting.

Corticosteroids

The efficacy of systemic corticosteroids has been demonstrated for patients with severe exacerbations of COPD.

Systemic corticosteroids are indicated only for patients with severe exacerbation or lack of response to other therapy. There is no consensus about the exact dose or the route of administration (oral or intravenous). Guidelines suggest 30–40 mg of prednisolone (or equivalent) per day for no longer than 7–10 days.

Duration of mechanical ventilation (invasive or not) is shortened with systemic corticosteroids therapy as is the rate of NIV failure.

Walters JAE, Gibson PG, Wood-Baker R, Hannay M, Walters EH. Systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2009 Jan 21; (1):CD001288. PMID 19160195

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001288.pub3/full

Walters JAE, Wang W, Morley C, Soltani A, Wood-Baker R. Different durations of corticosteroid therapy for exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2011 Oct 5; (10): CD006897. PMID 21975757

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006897.pub2/full

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011. Available from: http://www.goldcopd.org/

Alía I, de la Cal MA, Esteban A, Abella A, Ferrer R, Molina FJ, et al. Efficacy of corticosteroid therapy in patients with an acute exacerbation of chronic obstructive pulmonary disease receiving ventilatory support. Arch Intern Med 2011; 171(21): 1939–1946. PMID 22123804

http://archinte.jamanetwork.com/article.aspx?doi=10.1001/archinternmed.2011.530

Anti-infective therapy

Bronchial infections are the most common precipitating factor for an acute exacerbation of COPD. Viral infections are an important trigger, and a majority of these are due to rhinovirus.

Between 25% and 50% of patients with COPD have lower airway colonisation by bacteria. This colonisation is variable over time, and is associated with greater airway inflammation.

If the patient's initial symptoms are increased dyspnoea, sputum volume and purulence, treat with an antibiotic that is effective against *Haemophilus influenzae, Streptococcus pneumoniae,* and *Moraxella catharalis*. If available, previous bacterial airway samples are used to target initial antibiotic therapy especially if the patient is known to be colonised with Gram negative bacteria such as *Pseudomonas aeruginosa*.

NOTE Check the immunisation status of your COPD patients. If they have not received a seasonal influenza vaccination and a pneumococcal vaccination, it should be administered after recovery from the acute illness.

Rothberg MB, Pekow PS, Lahti M, Brody O, Skiest DJ, Lindenauer PK. Antibiotic therapy and treatment failure in patients hospitalized for acute exacerbations of chronic obstructive pulmonary disease. JAMA 2010; 303(20): 2035–2042. PMID 20501925

http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2010.672

NOTE Mucolytic agents such as *N*-acetylcysteine have no place in the treatment of acute exacerbation of asthma and COPD.

Be aware of using sedatives in COPD patients because it decreases the ventilatory drive.

ANECDOTE A patient with exacerbated COPD and severe shortness of breath became increasingly agitated and frightened while using his auxiliary breathing muscles. He was therefore put on non-invasive ventilatory support. Afterwards the patient was absolutely calm without any sedation. The relief of his exhausted breathing muscles with good ventilatory support was the best anxiolytic for this patient.

Supportive therapies

Correction of fluid imbalance

The chronic inflammation seen in patients with COPD and asthma leads to lung remodelling and in the end stages to emphysema. The capacity of pulmonary lymphatic drainage is decreased and there is a greater chance of developing lung oedema thus causing more respiratory problems, even at moderate levels of fluid replacement.

COPD patients are frequently elderly with chronic heart disease. In the context of an acute exacerbation, congestive heart failure can be superimposed. Measurement of plasma B-type natriuretic peptide level can be useful to guide diagnosis and treatment, especially the fluid balance.

 Chest radiographs are often unremarkable in spite of too much water in the lungs.

Mueller C, Laule-Kilian K, Frana B, Rodriguez D, Scholer A, Schindler C, et al. Use of B-type natriuretic peptide in the management of acute dyspnea in patients with pulmonary disease. Am Heart J 2006; 151(2): 471–477. PMID 16442916

Correction of acidosis

There are several reasons why acidosis develops in critically ill patients with exacerbated COPD and asthma. Although metabolic acidosis (e.g. lactic acidosis) may (co-)exist, most of the patients with severe exacerbations of COPD and asthma have respiratory acidosis (hypercapnia).

Increased PCO_2 may lead to:

- Increased cerebral blood flow and intracranial pressure
- Increased pulmonary artery pressure and overloading of the right heart
- Decreased peripheral vascular tone/resistance
- Increased levels of epinephrine and norepinephrine
- Increased cardiac output
- Inadequate oxygenation due to hypercapnia by reducing FAO_2
  $FAO_2 = FiO_2 - FACO_2$ where
  FAO_2 = alveolar fraction of O_2, FiO_2 = inspired fraction of O_2 and
  $FACO_2$ = alveolar fraction of CO_2

Identify the causes of acidosis and correct the factors which may be reversible.

- Increase FiO_2 in case of hypoxaemia and respiratory acidosis
- Optimise the mechanical ventilation
- Optimise the circulatory situation.

THINK Metabolic acidosis increases the work of breathing; where possible, correct it appropriately e.g. extra-renal replacement, correction of haemodynamics.

Alkalosis

Alkalosis may become symptomatic when pH exceeds 7.55. Above pH 7.6, seizures, coma, arrhythmias and cardiac arrest are possible.

Iatrogenic respiratory alkalosis due to excessive minute ventilation in patients requiring ventilatory support can aggravate pre-existing compensatory metabolic alkalosis in chronically hypercapnic COPD patients. See section: 'Defining a strategy and initial setting of the ventilator'.

Nutritional support

Patients with asthma normally have no nutritional deficit, whereas patients with severe COPD have an imbalance between energy intake and energy consumption. The chronic inflammation and increased effort needed to breathe lead to higher energy consumption. COPD patients are characterised by loss of weight, loss of muscle mass and intrinsic changes in the muscles, so-called pulmonary cachexia.

Early nutritional support, preferably delivered enterally, should aim to meet the increased metabolic needs of the COPD patient. Care should be given to avoid overfeeding because it can lead to increased CO_2 production and O_2 consumption. Measuring the energy requirements with a calorimeter may be considered.

 For the next two intubated COPD patients, make a nutritional plan after calculating the caloric requirements.

THINK Does additional administration of vitamins have a place in the feeding plan of a patient with exacerbated COPD?

For more information see the PACT module on Nutrition.

Treatment of common complications

Fever

Fever is a common symptom during the ICU stay. Both asthma and COPD exacerbations are inflammatory syndromes with increased numbers of infiltrating cells, alterations of epithelial cells and the non-cellular components of the airway wall accompanied by increased levels of pro-inflammatory cytokines. Infections and superinfections play a major role during exacerbations. A large number of COPD patients have bacterial colonisation of lower airways, and deterioration of asthma is often triggered by chronic sinusitis or gastro-oesophageal reflux disease with micro-aspiration.

If fever appears or persists, look for a pulmonary superinfection and exclude sinusitis. Of course, all other possible causes of fever during an ICU stay should be excluded as well.
See the PACT modules on Pyrexia and Severe infection.

Atelectasis and sputum retention

Often the clinical course of patients with COPD and asthma is negatively affected by atelectasis and sputum retention. Atelectasis is a collapse of alveoli with reduction of intrapulmonary air and an abnormal ventilation-to-perfusion ratio. This causes an intrapulmonary shunt, with passage of venous blood into the arterial system without oxygenation, leading to hypoxaemia. Atelectasis is one major risk factor for developing a pulmonary infection.

Mechanisms of atelectasis

- Chronic hyperinflation leads to an increase in lung volume.
  The diaphragm stays deeper and is flatter, so the potential for sufficient diaphragmatic contractility is reduced
- If high concentrations of oxygen have to be inspired, with high differences of the partial gas pressures between alveoli and venous (pulmonary arterial) blood, the oxygen diffuses rapidly from the poorly-ventilated alveoli into the venous blood, leading to volume loss and subsequent collapse of these alveoli – known as 'absorption atelectasis'
- Extrapulmonary compression (pneumothorax, pulmonary contusion) results in passive atelectasis
- Accumulation of bronchial secretions can lead to airway obstruction

NOTE Development of atelectasis in COPD patients is most commonly caused by the stagnation of bronchial secretions in conjunction with increased sputum volume, sometimes called sputum retention.

Mechanisms underlying the stagnation of bronchial secretions

- **Mucociliary clearance**
  - Chronic inflammation destroys the normal airway wall, and particularly interferes with the normal function of the cilia
  - Drugs such as opioids and anticholinergics depress the mucociliary clearance
  - Mechanisms associated with mechanical ventilation (high oxygen concentration, high inspiration pressure) reduce mucociliary clearance
- **Cough**
  - Reduced ability to cough due to absent occlusion of the glottis during tracheal intubation. Drug-induced suppression (opioids, anaesthetics)
  - Diaphragmatic weakness (anatomical configuration, critical illness polyneuromyopathy)
  - Depression of consciousness.

The successful treatment of atelectasis and sputum retention is important in the prevention of infective and other complications and in shortening the ICU stay.

- Wean as early as possible from mechanical ventilation
- Perform endotracheal aspiration if abundant tracheal secretions are present
- Suction in accordance with a standard safe procedure
  - Hand hygiene and sterile catheters
  - Be careful not to injure the tracheobronchial mucosa
  - Use pre- and post-oxygenation with 100% oxygen to avoid severe hypoxia
  - Do not suction too often (loss of surfactant) or for too long (risk of aspiration atelectasis)
- Fibre-optic bronchoscopy only performed when indicated e.g. for lobar/lung collapse. Aspiration can be harmful; suctioning can induce bronchial collapse or injure the mucosa

 For the next five long-term intubated patients, work with the physiotherapist to make a plan for preventing or treating atelectasis and sputum retention.

Q. An intubated patient with an exacerbation of COPD also has a hypertensive crisis. You treat the hypertension with an infusion of the vasodilator, sodium nitroprusside. Afterwards, a higher FiO_2 is required. Why?

A. Sodium nitroprusside causes vasodilation of the pulmonary vessels also. In a patient with atelectasis, the hypoxic vasoconstriction in these badly ventilated areas may be compromised resulting in these areas being supplied with more blood. The consequence may therefore be an increase in right–left shunting, thereby delivering more poorly oxygenated blood to the left heart.

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) update 2010. http://www.goldcopd.org/.

PACT module on Hypertension

Tachycardia, tachyarrhythmia

Patients with an exacerbation of COPD or asthma have several reasons for developing a sinus tachycardia or tachyarrhythmia.

Pathogenic mechanisms

- Tachycardia can result from hypoxia, stress, and high work of breathing.

- If severe hyperinflation exists, decreased systemic venous return and heart-lung interaction affect steady-state cardiac output, with resulting decreased cardiac output, hypotension and shock.
- Cardiomyopathy can occur with pulmonary hypertension, right heart insufficiency (and sometimes coronary vascular disease) in association with COPD.
- Tachycardia and tachyarrhythmia can result from aggressive therapy with β-sympathomimetics and/or aminophylline.

Management

- If clinically relevant tachycardia or tachyarrhythmia persists, reduction or discontinuation of β-sympathomimetics and aminophylline should be considered.
- Reduce stress and work of breathing with sedation and controlled ventilation.
- Exclude the possibility of myocardial ischaemia.
- Optimise the mechanical ventilation to reduce hyperinflation and intrathoracic pressure.

5/ WEANING THE PATIENT

Mechanical ventilation, especially in COPD patients, is associated with many life-threatening complications and it should be discontinued as early as possible. Weaning patients from a ventilator is one of the everyday and sometimes most challenging problems for an ICU physician. Using an empirical approach alone to manage the weaning process can prolong the duration of mechanical ventilation. Indeed, using only intuitive 'clinical assessments' of the status of the patient's respiratory failure is not enough to make decisions on the discontinuation of ventilator support. The sensitivity of clinical judgment is only 35%; the specificity is 79%. Prospective studies have shown that the application of weaning protocols leads to a more rapid weaning process without increasing weaning failure. No specific weaning strategy for obstructive patients has been proven superior to others.

Aggressive weaning and extubation criteria maximise the withdrawal from ventilatory support, with fewer complications (such as nosocomial infections) and shorter ICU stays.

For more information, see the PACT modules on Mechanical ventilation and Respiratory assessment and monitoring.

When to start weaning

To identify the right moment to start the process of weaning from the ventilator, a persistent search for and assessment of possible underlying causes of continuing ventilator dependency is important.

NOTE Optimally, weaning begins with the onset of mechanical ventilation. A protocol implemented by intensivists, nurses (and respiratory therapists where applicable) begins testing for the opportunity to reduce support very soon after intubation and at every further opportunity.

Causes of ventilator dependency/weaning problems

Gas-exchange factors	Ventilation–perfusion imbalance Shunts (e.g. atelectasis, pulmonary embolism)
Ventilatory muscle factors	Muscle fatigue Atrophy and remodelling Disadvantageous muscle position Hyperinflation High resistance with elevated ventilatory muscle work
Ventilator factors	High resistance to gas flow by tracheal tube, ventilator hoses, humidifiers, demand valves
Metabolic factors	Overfeeding with excess CO_2 production Malnutrition with protein

	catabolism Electrolyte abnormalities (phosphate/magnesium deficiency)
Cardiovascular factors	Left heart failure with pulmonary oedema Pulmonary arterial hypertension with right heart failure Changes of preload and afterload
Neurological factors	Cortical feedback failure from chemo- and mechanoreceptors by sedation, narcotics and metabolic disturbances Critical illness polyneuromyopathy Severe agitation and delirium

NOTE Critical illness neuromyopathy is a common cause of weaning failure in COPD/asthma, since the combined treatment with corticosteroids and neuromuscular blockade is not rare

See the PACT module on Neuromuscular conditions.

Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, et al. Weaning from mechanical ventilation. Eur Respir J 2007; 29(5): 1033–1056. PMID 17470624

http://erj.ersjournals.com/content/29/5/1033.long

MacIntyre N. Discontinuing mechanical ventilatory support. Chest 2007; 132(3): 1049–1056. PMID 17873200

http://chestjournal.chestpubs.org/content/132/3/1049.long

Prognostic factors for successful weaning

Reversal of underlying cause for respiratory failure	
Pulmonary criteria	PaO_2/FiO_2 ratio >19.9–26.6 kPa/150–200 mmHg Positive end-expiratory pressure (PEEP) ≤ 8 cmH_2O pH >7.3 Rapid shallow breathing index <105 (breathing frequency/tidal volume in litres) Less important factor: Maximum inspiratory pressure >minus 20–30 cmH_2O

Haemodynamic stability	Absence of: Low cardiac output Pulmonary oedema Myocardial ischaemia Important arrhythmias
Adequate respiratory forces and coordination	No thoracic instability Normal intra-abdominal pressure Capacity for inspiratory effort (i.e. enough force to breathe) No need for respiratory accessory muscles No paradoxical breathing No relevant hyperinflation/intrinsic PEEP

See also the PACT modules on Respiratory assessment and monitoring and Mechanical ventilation.

NOTE Some patients with unresolved respiratory failure who required high levels of ventilatory support and who did not meet these criteria have nonetheless been shown to be capable of successful weaning from the ventilator.

How to wean

The two most widely used methods are pressure support ventilation (PSV) with stepwise reductions of support and daily T-piece trial.

Pressure support ventilation (PSV)

The level of pressure support is set to avoid Vt over 8 mL/kg of ideal body weight (IBW) and is reduced accordingly during weaning. The inspiratory fraction of oxygen (FiO_2), the positive end-expiratory pressure (PEEP), and the level of pressure support can be reduced in steps. The criteria for the speed of the different reductions are, as above, the Vt, respiratory pattern, adequacy of gas exchange, haemodynamic stability and subjective patient comfort.

 In a mechanically ventilated patient with broncho-obstruction who has already begun the weaning process, talk with the patient to try to determine optimal PEEP (consider different levels of pressure support at different times of the day).

It is important to consider inefficient triggering attempts because they increase substantially the work of breathing. Spontaneous ventilation in pressure support depends on four distinct phases: inspiratory trigger, flow rate, amount of pressure support, and expiratory trigger. Inefficient triggering and patient–ventilator interactions can originate from any of these phases. To improve patient comfort and reduce work of breathing, the inspiratory trigger must be set at the more sensitive value possible while avoiding auto-triggering phenomena.

To favour expiration and avoid dynamic hyperinflation, a high flow rate is used with a pressurisation time between 0.1 and 0.2 sec. If available, the expiratory trigger has to be set to a highest value (40 to 70% of the maximal inspiratory flow).

Interestingly, the number of unsuccessful triggering attempts may increase with the level of ventilator assistance. These triggering failures seem to be due to an increased level of hyperinflation and might thus be reduced by reducing the level of pressure support and/or applying higher PEEPe.

In clinical practice, the occurrence of inefficient triggering attempts means that it:

- Should not necessarily impede the weaning process
- Warrants a trial of increasing PEEPe, decreasing pressure support, and checking the trigger level (inspiratory and expiratory).

Jolliet P, Tassaux D. Clinical review: patient-ventilator interaction in chronic obstructive pulmonary disease. Crit Care 2006; 10(6): 236. PMID 17096868

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1794446/?tool=pubmed

Leung P, Jubran A, Tobin MJ. Comparison of assisted ventilator modes on triggering, patient effort, and dyspnea. Am J Respir Crit Care Med 1997; 155(6): 1940–1948. PMID 9196100

http://ajrccm.atsjournals.org/content/155/6/1940.long

Nava S, Bruschi C, Rubini F, Palo A, Iotti G, Braschi A. Respiratory response and inspiratory effort during pressure support ventilation in COPD patients. Intensive Care Med 1995; 21(11): 871–879. PMID 8636518

Vitacca M, Bianchi L, Zanotti E, Vianello A, Barbano L, Porta R, et al. Assessment of physiologic variables and subjective comfort under different levels of pressure support ventilation. Chest 2004; 126(3): 851–859. PMID 15364766

http://chestjournal.chestpubs.org/content/126/3/851.long

Daily T-piece trial

In a spontaneous breathing trial (SBT), warm and moistened air is brought to the patient via a T-piece, in a flow high enough to avoid CO_2 rebreathing. The T-piece is placed on top of the intratracheal tube and the patient breathes spontaneously, without ventilator support. Research has shown successful discontinuation from the ventilator 77% of the time after a tolerance of 30 minutes of SBT. Because a tracheal tube increases resistance and breathing work, the duration of SBT should not be longer than 120 minutes to avoid breathing muscle fatigue. The criteria mentioned earlier are used to assess weaning success.

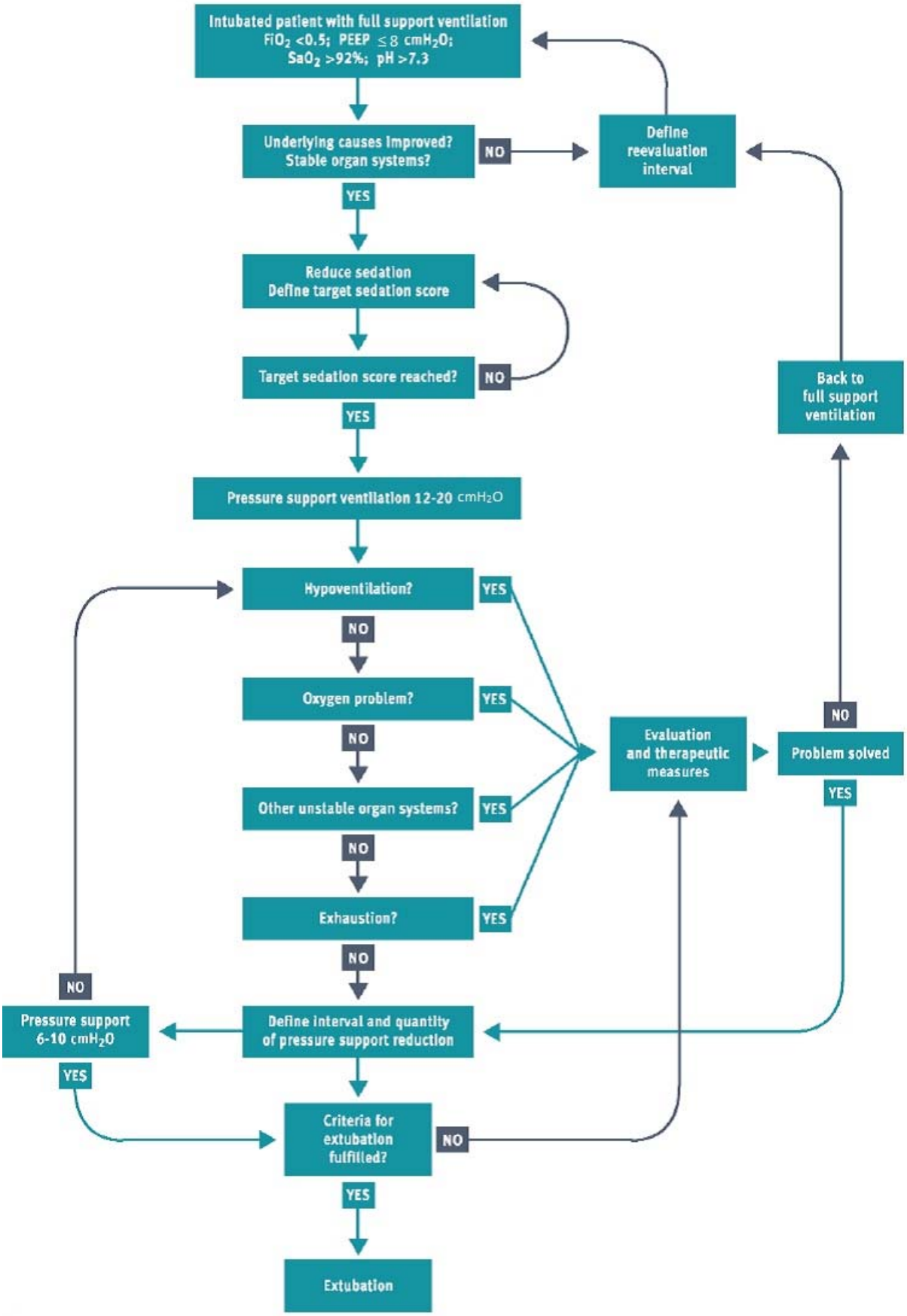
NOTE Neither of these two weaning methods has been proven superior. Whichever mode is chosen, a weaning protocol is generally recommended – see example below. Synchronised intermittent mandatory ventilation (SIMV) is no longer recommended since it has been proven less efficient for weaning.

Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, et al. Weaning from mechanical ventilation. Eur Respir J 2007; 29(5): 1033–1056. PMID 17470624

http://erj.ersjournals.com/content/29/5/1033.long

Kollef MH, Shapiro SD, Silver P, St John RE, Prentice D, Sauer S, et al. A randomized, controlled trial of protocol-directed versus physician-directed weaning from mechanical ventilation. Crit Care Med 1997; 25(4): 567–574. PMID 9142019

Example of a protocol for difficult to wean patients



 Check whether your ICU has a weaning protocol. If it does, do the staff use the protocol? In the next five patients, strictly adhere to the protocol. Evaluate how weaning differs with and without the protocol.

In asthma patients, if the mucous membrane hyperactivity/airway obstruction is resolved, early extubation is generally possible.

COPD patients, on the other hand, not only have airway obstruction with hyperinflation but also several other organ problems e.g. muscle fatigue, cardiocirculatory problems, infections, metabolic and nutrition problems. If these patients are alert, cooperative, and ready to breathe without an artificial airway, there may nevertheless be a benefit to early extubation, with the institution of non-invasive positive-pressure ventilation (NPPV) after the extubation. See below for the 'Role of non-invasive ventilation in weaning'.

Nava S, Ambrosino N, Clini E, Prato M, Orlando G, Vitacca M, et al. Noninvasive mechanical ventilation in the weaning of patients with respiratory failure due to chronic obstructive pulmonary disease. A randomized, controlled trial. Ann Intern Med 1998; 128(9): 721–728. PMID 9556465

Q. Weaning is proceeding successfully for a patient with an exacerbation of COPD, but the patient has persistently high PCO_2 levels. What do you do?

A. Normally, patients with advanced COPD have chronically higher levels of PCO_2 thus aim at pH rather than PCO_2. You should look at the values before exacerbation and the corresponding pH. If these values correspond to the typical pre-exacerbation levels, and the patient is otherwise ready for extubation, extubate the patient and then consider following with non-invasive ventilation.

Weaning failure

If patients receiving mechanical ventilation fail the weaning procedure, immediate evaluation of the cause is necessary (see Causes of ventilator dependency/weaning problems, above), along with specific therapeutic measures.

NOTE Except in patients recovering from sedatives, muscle relaxants, pneumothorax and atelectasis, respiratory system abnormalities are rarely resolved over a short period (a few hours).

NOTE Patients who fail a weaning trial should have a stable, non-fatiguing, and comfortable form of ventilatory support for at least 24 hours. Which ventilatory form to use is patient-dependent. Controlled ventilation is often necessary to enable the patient to relax, but whenever possible, assisted modes of ventilation with levels of pressure support high enough to ensure comfortable breathing (with Vt not exceeding 8 mL/kg of IBW) should be used as this should allow better patient–ventilator synchrony and prevent muscle atrophy. After a rest of at least 24 hours, a new protocol-driven weaning trial should be started.

New ventilatory modes such as proportional assist ventilation, adaptive support ventilation, knowledge-based expert system, or neurally adjusted ventilatory assist could be useful for difficult to wean patients. You will find further information in the PACT module on Mechanical ventilation.

Q. Is it helpful to use the carbo-anhydrase inhibitor acetazolamide in treating a patient who has COPD, hypercapnia and a pH of 7.34?

A. No.

Q. Give reasons for not using acetazolamide?

A. A patient with severe COPD has a decreased ability to eliminate the CO_2; hypercapnia allows the patient to keep the alveolar ventilation and thus respiratory workload low. Chronic hypercapnia leads to a compensatory increase in serum bicarbonate and thus to normalisation of pH.

Once the patient is compensated again and the blood gases show metabolic alkalosis, there is some controversy as to whether acetazolamide should be given. It can accelerate the return to steady state values of bicarbonate and induce helpful diuresis (decreasing water load, leading to better respiratory system compliance). Trying to normalise bicarbonate levels, however, might lead to weaning failure by mandating increasing ventilatory workload.

There are some data showing that if normalisation of bicarbonate is possible, the interval to the next exacerbation might be prolonged.

Role of non-invasive ventilation in weaning

There are three different situations when NIV can be considered.

Shortening of invasive ventilation:
It has been demonstrated that application of NIV in case of failed spontaneous breathing test shortens invasive mechanical ventilation duration, length of ICU stay and lowers nosocomial pneumonia incidence.

Nava S, Ambrosino N, Clini E, Prato M, Orlando G, Vitacca M, et al. Noninvasive mechanical ventilation in the weaning of patients with respiratory failure due to chronic obstructive pulmonary disease. A randomized, controlled trial. Ann Intern Med 1998; 128(9): 721–728. PMID 9556465

Burns KE, Adhikari NK, Keenan SP, Meade MO. Noninvasive positive pressure ventilation as a weaning strategy for intubated adults with respiratory failure. Cochrane Database Syst Rev 2010 Aug 4; (8): CD004127. PMID 20687075

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004127.pub2/full

Prevention of post-extubation respiratory failure:
Early NIV application after extubation prevents post-extubation respiratory failure, decreases re-intubation rate and ICU mortality.

Nava S, Gregoretti C, Fanfulla F, Squadrone E, Grassi M, Carlucci A, et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. Crit Care Med 2005; 33(11): 2465–2470. PMID 16276167

Ferrer M, Valencia M, Nicolas JM, Bernadich O, Badia JR, Torres A. Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. Am J Respir Crit Care Med 2006; 173(2): 164–170. PMID 16224108

http://ajrccm.atsjournals.org/content/173/2/164.long

Treatment of post-extubation respiratory failure:
No study has proven any benefit of NIV in post-extubation respiratory failure and there is even an increased ICU mortality. Nevertheless, in very selected, mainly COPD patients, a trial of NIV could be considered as long as it does not delay re-intubation in the case of failure.

Esteban A, Frutos-Vivar F, Ferguson ND, Arabi Y, Apezteguía C, González M, et al. Noninvasive positive-pressure ventilation for respiratory failure after extubation. N Engl J Med 2004; 350(24): 2452–2460. PMID 15190137

http://www.nejm.org/doi/full/10.1056/NEJMoa032736

Keenan SP, Powers C, McCormack DG, Block G. Noninvasive positive-pressure ventilation for postextubation respiratory distress: a randomized controlled trial. JAMA 2002; 287(24): 3238–3244. PMID 12076220

http://jama.jamanetwork.com/article.aspx?volume=287&page=3238

Role of tracheostomy

When it becomes apparent that a patient will require prolonged ventilator assistance, a tracheostomy should be considered. The right timing and the impact on the duration of mechanical ventilation have not been clearly answered by literature.

Durbin CG Jr. Tracheostomy: why, when, and how? Respir Care 2010; 55(8): 1056–1068. PMID 20667153

http://www.rcjournal.com/contents/08.10/08.10.1056.pdf

Diehl JL, El Atrous S, Touchard D, Lemaire F, Brochard L. Changes in the work of breathing induced by tracheotomy in ventilator-dependent patients. Am J Respir Crit Care Med 1999; 159(2): 383–388. PMID 9927347

http://ajrccm.atsjournals.org/content/159/2/383.long

Link to the PACT module on Airway management

Long-term outcome

A precise prediction of outcome for individual patients with acute respiratory failure and COPD or asthma is not realistic, and each case must be considered individually.

The majority of patients with asthma have a good long-term prognosis, depending on the longitudinal changes in lung function triggered by airway inflammation. A patient with status asthmaticus and the need for intubation and ventilation does not make the long-term outcome worse per se.

The outcome of patients with COPD and acute exacerbation depends on their clinical situation before exacerbation. Factors predicting a poor long-term outcome are:

- Dyspnoea at rest with hypoxaemia and hypercapnia
- Pulmonary hypertension and cor pulmonale
- Irreversible airway obstruction despite treatment with β-sympathomimetics
- Pulmonary cachexia with weight loss
- Several acute exacerbations in the history
- Other organ diseases, such as cardiomyopathy or nephropathy.

Studies of mortality associated with exacerbated COPD have had varying results, but mortality is generally extremely high. The hospital mortality is around 10%, at one year it is approaching 40% and is even higher for elderly patients.

NOTE For each patient with end-stage COPD and acute respiratory failure, we have to consider an ICU stay with the possibility of prolonged intubation and ventilation. If possible, the patient and family should be consulted in advance regarding their preferences for the use of mechanical ventilation and prolongation of life under these circumstances.

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011. Available from: http://www.goldcopd.org/

Seneff MG, Wagner DP, Wagner RP, Zimmerman JE, Knaus WA. Hospital and 1-year survival of patients admitted to intensive care units with acute exacerbation of chronic obstructive pulmonary disease. JAMA 1995; 274(23): 1852–1857. PMID 7500534

Weiss SM, Hudson LD. Outcome from respiratory failure. Crit Care Clin 1994; 10(1): 197–215. PMID 8118729

CONCLUSION

Proper triage of patients with exacerbated COPD or severe asthma is very important: the aim of the assessment is to identify patients who might need ventilatory support and hospitalise them on a ward with ventilatory assistance capability such as the ICU.

If ventilatory assistance is necessary for COPD patients, a non-invasive route is tried first.

If a COPD patient in respiratory distress has not refused mechanical ventilation in advance care planning, do not hesitate to intubate, since there are no criteria that predict weaning failure.

In a ventilated patient with bronchial obstruction, be aware of hyperinflation to avoid its haemodynamic and pulmonary complications.

The long-term prognosis of asthma is quite good; thus asthma patients should always be admitted to the ICU if required. The long-term prognosis for patients with severe COPD is worse, and patients and their relatives should be encouraged to consider (and write down) their preferences concerning the intensity of intervention in advance, in case of a later worsening of the patient's status. This is best done while the patient is in a stable situation.

6 / GLOSSARY

Combined glossary of terms for the modules Mechanical Ventilation, Respiratory Assessment and Monitoring and COPD and asthma with acknowledgement to Dr Ed Carton for finalising its composition.

Airway pressure — Pressure at a specified point in the patient's airway.

ALI — A descriptor of an Acute Lung Injury process; since a recent consensus conference, no longer recommended as a categorisation of the severity of ARDS. Recommended categorisation of ARDS now changed to Mild, Moderate and Severe.

AP_L — (Transpulmonary pressure). This is the pressure distending the respiratory system (and the functional residual capacity of the lung) and is the airway pressure minus the pleural pressure. (**AP_L** =Ppause – Poes). However, Poes (equivalent to pleural pressure) and FRC measurement at the bedside are not common in clinical practice.

ARDS — Acute Respiratory Distress Syndrome.

Atelectrauma — Lung injury caused by the cyclic collapse and reopening of unstable small airways and alveoli resulting in 'shear injury'.

Auto-triggering — The inadvertent triggering of inspiratory ventilatory support when a patient is not breathing.

Barotrauma — Lung injury due to high airway (distending) pressure.

Biotrauma — A diffuse lung injury and possible injury to other organs due to the release of inflammatory mediators.

CaO_2 — Content of oxygen in arterial blood. CaO_2 is calculated as $1.34 \times Hb \times SaO_2$; the normal value is 16 to 20 mL O_2/100 mL blood.

Compliance

- **C_{rs}** — Compliance of the respiratory system. It is defined as the lung volume change per unit airway pressure change or the slope of the pressure–volume curve. In positive pressure ventilation, it is measured by dividing the Vt by the inflation pressure. See below for dynamic (**C_{dyn}**)and static (**C_{stat}**) compliance.
- **C_{cw}** — Compliance of the chest wall.
- **C_{dyn}** — Dynamic compliance. It is calculated as $\frac{Vt}{Peak\ Paw - PEEP}$
- **C_L** — Lung compliance.
- **C_{qs}** — Compliance–quasi-static. Compliance derived from measurements made during a 'relaxed' double prolonged

	occlusion manoeuvre i.e. during a four second pause at end-inspiration and at end-expiration. It mimics true static compliance and is termed quasi-static compliance. True static compliance is utilised mainly in research and is performed using pressure measurements after serial volume increments with a 'super syringe'.
C_{stat}	Static compliance (see above).It is calculated as $\frac{Vt}{Ppause - PEEP}$
CO	Cardiac output.
COHb	Carboxyhaemoglobin.
CPAP	Continuous positive airway pressure. Refers, by convention, to the end-expiratory airway pressure in a spontaneous breathing respiratory system.
$C\bar{v}O_2$	Mixed venous oxygen content. It is measured as 1.34 × Hb × Sv̄O2 (mixed venous oxygen saturation).
ΔPCO_2	Difference between arterial to end-tidal PCO_2.
De-escalation	A continuous effort to reduce the mechanical ventilatory support as soon and as much as possible.
DO_2	Oxygen delivery – measured as CO × CaO_2.
$EtCO_2$	End-tidal CO_2– see also $PetCO_2$.
EVLW	Extravascular lung water.
EWS	Expert weaning system.
FRC	Functional residual capacity. The volume of gas in the patient's respiratory system at end-expiration. Its capacity is a key determinant of oxygenation.
Fr	Frequency.The number of ventilatory or patient breaths per minute; also termed the ventilatory (or respiratory) rate.
Hb	Haemoglobin content of blood. Usually expressed as in g% or as g/100mLs (normal value varies between males and females but is approx. 15 g/dL).
Hypercapnia	More than the normal level of carbon dioxide in the blood.
Hypocapnia	Less than the normal level of carbon dioxide in the blood.
Hypoxaemia	An abnormally low PO_2 in arterial blood.
I:E ratio	The ratio between the time (duration) of inspiration relative to duration of expiration. It is normally 1:1.5 to 1:2.

Impedance	The combined effects of airway resistance, respiratory system (including chest wall) compliance and intrinsic PEEP (PEEPi – see below) in opposing the flow and volume change produced by the ventilator.
k	Constant that represents the alveolar end-expiratory pressure (in the 'driving pressure' equation).
LSF	Least square fitting.
MetHb	Methaemoglobin.
MIP	Maximal inspiratory pressure, see also PI_{max}.
MVV	Maximum voluntary ventilation.
NI(M)V	Non-invasive (mechanical) ventilation.
NIF	Negative inspired force.
Normoxaemia	Normal blood levels of oxygen.
$PaCO_2$	Partial pressure of arterial carbon dioxide – normal range 4.7–6 kPa (35–45 mmHg).
P_{alv}	Alveolar pressure.
P_{AO}	Pressure at airway opening.
PaO_2	Partial pressure of arterial oxygen – normal range 10–13.3 kPa (75–100 mmHg).
P_{atm}	Atmospheric pressure.
P_{aw}	Airway pressure.
PCV	Pressure-controlled ventilation.
Peak airway pressure	The peak (or highest) pressure measured by the ventilator; the pressure at the level of the major airways.
$PECO_2$	Partial pressure of CO_2 in mixed expired gas – usually collected/measured in a Douglas bag but not a standard clinical measurement.
PEEP	Positive end-expiratory pressure. Defined as an elevation of airway pressure at the end of expiration. End-expiratory pressure is normally zero (atmospheric) during spontaneous breathing but is often set at a positive level (measured in cms H_2O) during mechanical ventilation.
PEEPe	PEEPexternal. The PEEP effected by the ventilator and set by the operator.
PEEPi	PEEPintrinsic. Elevated positive end-expiratory pressure which is 'intrinsic to the patient'. It is associated with certain lung pathologies particularly where there is

	destructive lung disease, dynamic collapse of airways and active expiration and may be present during normal spontaneous breathing or while on a ventilator. It is sometimes termed **auto-PEEP**. Its main reversible cause is a limitation to expiratory flow and it is exacerbated by insufficient expiratory time (Te) and dynamic pulmonary hyperinflation may result. It is usually measured during a prolonged, 'relaxed' expiratory ventilatory pause.
PEEPtot	Total PEEP. This is the combination of the above two pressures (PEEPi and PEEPe). However, in certain circumstances the effect of external PEEP may be to reduce the level of PEEPi.
P_{es}	Oesophageal pressure. Is the pressure in the lower one third of the oesophagus when the patient is upright. It equates to pleural/extra-alveolar pressure. It is also called **Poe.**
$PetCO_2$	End-tidal CO_2. The highest value of CO_2 partial pressure during the alveolar plateau of the capnography curve.
PI_{max}	Maximal inspiratory pressure.
PIP	Peak inspiratory pressure.
Pmax	The sum of the pressures produced by the ventilator to overcome the elastic and resistive forces (airways and endotracheal tube) of the respiratory system.
Pmus	Pressure generated by muscle contraction.
Ppause	The airway pressure observed during prolonged (4-second), 'relaxed' end-inspiratory pause/hold. Also termed **Plateau**(Pplat) or **End-inspiratory hold pressure,** it is used in the determination of static compliance. In the absence of airflow (no resistance), it represents the pressure applied to the small airways and alveoli during peak inspiration. It depends on a number of factors including the Vt, PEEP, intrinsic PEEP and compliance.
PPV	Positive pressure ventilation. Process of exerting a pressure, which is positive relative to atmospheric pressure, to achieve entry of air or respiratory gases into the lungs. Term IPPV used for Intermittent Positive Pressure Ventilation.
P_{pl}	Pleura pressure.
P_{rs}	Respiratory system pressure.
PSG	Polysomnography.
PSV	Pressure support ventilation.

R	Resistance. Respiratory system resistance (**R_{rs}**)– refers to airway resistance and comprises the inflating pressure divided by the (gas) flow.
Recruitment manoeuvre	Manually or ventilator-assisted lung inflation to achieve an increase in FRC (by 'alveolar recruitment') and thereby an improved oxygenation.
RCe	Respiratory system expiratory time constant. The product of resistance and compliance and quantifies the speed of exhalation. It may vary between different lung units in pathological circumstances.
Rmax	Total resistance.
SaO_2	Oxygen saturation percentage of the available haemoglobin (normal value is 98%).
Shunt	Is due to perfusion of non-ventilated lung regions and is the commonest cause of clinical hypoxaemia. Extrapulmonary causes are those (right to left shunts) that may occur in the presence, for example, of an atrial septal defect (ASD).
Te	(Expiratory time). The time from the start of expiratory flow to the start of inspiratory flow.
Ti	Inspiratory time.
Transthoracic pressure	The pressure in the pleural space measured relative to the pressure of the ambient atmosphere outside the chest.
Trigger	Usually relates to inspiratory rather than expiratory triggering (see below) and as such, it refers to the process of initiating the inspiratory breath of the ventilator. Inspiratory triggering is usually effected by a pressure change or flow change in the breathing system generated by patient effort.
Triggering	The mechanism of initiating the inspiratory (and expiratory) phase(s) of the ventilator function.
T_{TOT}	is the respiratory duty cycle
V	Volume.
$\dot{V}$	Flow (Volume per unit of time).
VALI (or **VILI)**	Ventilator-associated lung injury or Ventilator-induced lung injury.
VAP	Ventilator-associated pneumonia.
VCV	Volume-controlled ventilation.

VA	Alveolar volume. The proportion of Vt that is useful in gas exchange.
V'A	Alveolar ventilation. The proportion of Vm that is useful in gas exchange. It is comprised of Alveolar volume (VA) multiplied by respiratory rate (Fr) i.e. V'A = VA × Fr. V'A is directly proportional to CO_2 elimination.
Vd	Dead space. The volume of inspired gas that does not take part in gas exchange.
Vd_{phys}	Physiologic dead space. This is comprised of the anatomic dead space (**Vd_{anat}**) and the alveolar dead space (**Vd_{alv}**). It has also been termed total dead space (Vdtot)
Vd_{alv}	Alveolar dead space (where alveoli are ventilated but are receiving minimal or no blood flow).
Vd_{anat}	Anatomic dead space (upper and lower airways to the tips of the terminal bronchioles).
Vd_{ins}	Instrumental dead space i.e. the dead space resulting from parts of the breathing system, ventilator equipment, endotracheal tubes, humidification devices and connectors. It is considered part of the anatomic dead space.
V,ee	End-expiratory lung volume. The volume of gas in the patient's respiratory system at end-expiration. Though, it is often used interchangeably with FRC (see above), this acronym should be used only for patients mechanically ventilated and receiving PEEP.
Vei	End-inspiratory volume above FRC
Ventilation mode	Represents a specific operating logic (or software program) for the mechanical ventilator, based on one or more approaches to respiratory cycle management. The specific mode is chosen by the operator.
Vm	Minute Volume. The volume of gas ventilating the respiratory system per minute. It is comprised of Tidal volume multiplied by the Respiratory rate (Vt× Fr).
Ve	Expired minute volume.
Vi	Inspired minute volume.
VO_2	Oxygen consumption by the tissues.
Volutrauma	Lung injury due to alveolar overexpansion secondary to high lung volume (with or without high pressure).
Vt	Tidal volume. The volume of gas intermittently inhaled or exhaled, by the patient or ventilator, with each breath 'on

	top of' the volume of the functional residual capacity (FRC).
Weaning	Is the final step in de-escalation, involving the patient's complete and continuing freedom from mechanical support and removal of the artificial airway.
W_{exp}	Work of breathing performed during the expiratory phase.
W_{insp}	Work of breathing performed during the inspiratory phase of the cycle.
WOB	Work of breathing. The work required to accelerate gas in the airways, to overcome airway resistance and to expand the elastic lung tissue so that air can be brought into the lungs and then exhaled.
W_{pat}	Work of breathing performed by the patient.
W_{vent}	Work of breathing performed by the ventilator.

SELF-ASSESSMENT

EDIC-style Type K

Q1. In a patient with an exacerbation of COPD or asthma, warning signs of impending respiratory arrest include:

A. SpO_2 <80%
B. Lethargy
C. Silent chest
D. Tachycardia (110/min)

Q2. Clinical signs of severe asthma include:

A. Tachycardia >120/min
B. Peak expiratory flow rate (PEFR) <200 L/min
C. Hypoxaemia (PaO_2 <8kPa) while breathing air
D. Respiratory rate >30/min

Q3. Hyperinflation of the lung is a central phenomenon in both COPD and asthma. The pathophysiology underlying hyperinflation includes:

A. Increased airway resistance resulting in dynamic hyperinflation during expiration
B. Hypoxic hyperventilation with increased functional residual capacity (FRC)
C. Destruction of lung parenchyma resulting in a decrease in pulmonary elastic recoil forces
D. Airway collapse with trapping of air distal to the point of airflow cessation (equal pressure point) in the airway

Q4. The work of breathing (WOB) is often found to be increased in COPD patients. Reasons for such increased WOB are:

A. Increased Δ pressure necessary to overcome increased airway resistance
B. Altered geometry of diaphragm (flattened and shortened)
C. Disturbed energy metabolism in the respiratory muscles as a consequence of hypoxaemia and acidosis
D. Increased muscle mass as a consequence of increased breathing efforts

Q5. The end inspiratory volume above FRC (Vei) has been shown to be predictive of the complications of hyperinflation (hypotension and barotrauma). Hyperinflation may be measured directly or by surrogate measures (indirectly) in the clinical setting by the following methods:

A. Total exhaled volume (over 60 secs of apnoea)
B. Peak inspiratory pressure
C. Plateau pressure
D. Intrinsic PEEP

Q6. Intrinsic PEEP (PEEPi) is:

A. Measured by subtraction of set PEEP from the plateau (Pplat) or pause pressure (Ppause)
B. The lowest average alveolar pressure during respiratory cycle
C. Measured during an end-expiratory hold manoeuvre
D. Normally 5–10 cmH_2O

Q7. When you know (have measured) the PEEPi, your applied (external) PEEP (PEEPe) in a patient with acute exacerbation of COPD should be:

A. Equal to PEEPi
B. 20% above PEEPi
C. 20% less than PEEPi
D. Zero

Q8. Regarding different methods for weaning a patient from the ventilator:

A. Pressure support ventilation is superior to other methods
B. Pressure support and daily spontaneous breathing trials on a T-piece are equally effective
C. SIMV is particularly effective in COPD weaning
D. Weaning protocols have a definite role in promoting successful weaning.

EDIC-style Type A

Q9. Which of the following initial treatments of an exacerbation of asthma is NOT a standard therapy:

A. Inhaled β-mimetic
B. Systemic corticosteroids
C. Antibiotics
D. Oxygen
E. Inhaled anticholinergic

Q10. The GOLD classification of COPD baseline severity is based on:

A. Clinical development
B. $PaCO_2$
C. % of predicted Forced Expiratory Volume 1 (FEV1)
D. PaO_2
E. % of predicted peak inspiratory flow (PIF)

Q11. In making the triage decision as to whether a patient needs to have ventilatory support initiated quickly, important signs include the following EXCEPT:

A. Inadequate response to initial therapy
B. Worsening of hypoxaemia (PaO_2 <5.3 kPa
C. $PaCO_2$ >10 kPa
D. Haemodynamic instability
E. Worsening of respiratory acidosis (pH <7.25)

Q12. Several benefits have been shown from the use of non-invasive ventilation in the treatment of severe exacerbations of COPD. The single most compelling reason for this choice is to:

A. Reduce the need for additive sedation in the patient
B. Reduce ICU length of stay
C. Avoid ventilator-associated pneumonia
D. Decrease hospital mortality
E. Avoid iatrogenic pneumothorax

Q13. The initial settings of non-invasive pressure support in a patient with COPD include all of the following EXCEPT:

A. Inspiratory pressure 15–20 cmH_2O regardless of tidal volume (Vt) achieved
B. PEEP 3–5 cmH_2O
C. Lowest possible FiO_2 to ensure SaO_2 >88%
D. Inspiratory trigger 0.5 to 1 L/min
E. Inspiratory pressure time set at shorter range (0.1 to 0.2 sec)

Q14. A 32-year-old male with a severe asthmatic attack is admitted to the ED at 20.00 hrs. He is given steroids, inhalation with beta-adrenergic drugs and inhaled anticholinergic. After two hours of observation and treatment his vital signs and arterial blood gases (ABGs) have not improved. On 10-litre oxygen on open mask, they now are:

- BP 140/70
- Pulse rate 130
- Respiratory rate 28
- Still has audible wheezing
- Unable to speak full sentences
- pH 7.23
- PaO_2 10 kPa
- $PaCO_2$ 7.9 kPa
- HCO_3 23 mmol/L
- BE -2 mmol/L

What is your preferred option?

A. Transfer to an intermediate unit for further medical treatment
B. Transfer to an ICU for further observation
C. Transfer to an ICU for immediate intubation and IPPV
D. Keep the patient in the ED for another 2–3 hours
E. Transfer to the ICU for non-invasive ventilation

Q15. If you intubate and ventilate an acute asthmatic patient with pressure support ventilation, what might the main adverse patient consequence be compared with the choice of volume control ventilation:

A. Unacceptably high Peak inspiratory airway pressure (Pmax) and Pplat (Ppause)
B. Air trapping
C. High PEEPi
D. A resultant high or low tidal volume (Vt) depending on the evolution of the disease process
E. Increased airway resistance

Explanation: If the increased airway resistance suddenly improves or decreases (because of therapy or spontaneously), there is a risk to the patient. For example, if improvement occurs, there is a risk of hyperinflation of the lungs due to a large (Vt) if the level of pressure support is not reduced immediately. Volume control ventilation will not have this danger.

Q16. Factors which predict successful weaning include all of the following EXCEPT:

A. PaO_2/FiO_2 ratio >26.6 kPa (200 mmHg)
B. PEEP = 10 cmH_2O
C. Rapid shallow breathing index <105
D. Inspiratory pressure < 20–30 cmH_2O
E. Cardiac index > 3 L/min

Answers

1. FTTF
2. TFTT
3. TFTT
4. TTTF
5. TFTT
6. FTTF
7. FFTF
8. FTFT
9. Correct: C
10. Correct: C
11. Correct: D
12. Correct: D
13. Correct: A
14. Correct: C
15. Correct: D
16. Correct: B

PATIENT CHALLENGES

A 63-year-old man is brought by his daughter to the emergency department of your hospital because of progressive difficulty in breathing. On arrival, the patient is non-responsive and has a dark purple colour, without perceptible breathing movements or any perceptible pulse.

Q. What are your immediate actions?

A. Start evaluation and treatment concurrently according to guidelines: address ABC (**A**irway **B**reathing and **C**irculation) and start CPR if breathing and a pulse is absent.

NOTE Given that the current ACLS therapeutic sequence for CPR, after breathlessness (or gasping) and pulselessness is confirmed, starts with compressions (>100/min), the ACLS therapeutic acronym is now CAB (circulation, airway, breathing).

Travers AH, Rea TD, Bobrow BJ, Edelson DP, Berg RA, Sayre MR, et al. Part 4: CPR overview: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010; 122(18 Suppl 3): S676–S684. PMID 20956220

http://circ.ahajournals.org/content/122/18_suppl_3/S676.long

Berg RA, Hemphill R, Abella BS, Aufderheide TP, Cave DM, Hazinski MF, et al. Part 5: adult basic life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010; 122(18 Suppl 3): S685–S705. PMID 20956221

http://circ.ahajournals.org/content/122/18_suppl_3/S685.long

http://www.acls.net

Link to PACT module on Airway management

You intubate the patient, without the need for sedative or neuromuscular blocking drugs, and ventilate him by resuscitation bag device. After one dose of epinephrine 1 mg intravenously, you have a good carotid pulse, the purple colour is disappearing and pulmonary auscultation and percussion is symmetrical. You transfer the patient to the ICU.

LEARNING ISSUES

Initial evaluation and triage of patients with respiratory distress

The patient's daughter tells you that her father is a heavy smoker, that he doesn't like going to the doctor and that he doesn't take any medicine. She says his condition has worsened over the past ten days. As well as having increasing difficulty with breathing,

in the last two days he could no longer walk and he was coughing up a lot of brownish sputum.

> **NOTE** Often at the beginning of an emergency procedure you have only limited historical information, if it is not possible to speak with the patient. Acute resuscitative management is more important initially than a refined differential diagnosis.

Q. What is the most common cardiorespiratory sequence in an adult with cardiorespiratory arrest?

A. The most frequent pattern is a cardiac arrest either as pulseless ventricular tachycardia, ventricular fibrillation, asystole or other cause of pulseless electrical activity (PEA). The respiratory arrest is therefore normally secondary in nature.

The initial electrocardiogram (ECG) showed regular QRS complexes despite an absent pulse i.e. pulseless electrical activity (PEA). There was a rapid return of spontaneous circulatory activity after intubation and oxygenation.

Q. Given the clinical picture (history and clinical events), what is the likely sequence of cardiorespiratory arrest in this patient?

A. This picture is suggestive of hypoxia (+/- respiratory acidosis) as the cause of the PEA.

Q. Evaluation, using the ABC approach, confirms that airway obstruction has been excluded by inspection. What B (breathing) causes might be considered?

A. A tension pneumothorax has a low probability because of a symmetrical auscultation and percussion. Consider, and seek clinical supportive evidence for, 'breathing' impairment due to central nervous system pathology, CNS intoxication or neuromuscular disease.

Q. What do you suspect as the cause of the hypoxia/respiratory arrest? Why?

A. The history of a progressive dyspnoea over days in a heavy smoking, COPD patient makes respiratory exhaustion the most likely diagnosis; the most frequent cause of exhaustion/decompensation is an infection.

> **NOTE** Together with a short clinical examination, a concise and targeted medical history is the cornerstone of the diagnostic process.

As you re-examine the patient you hear hardly any breath sounds in both lungs and high airway pressures are required to achieve even a small tidal volume (Vt). The palpable carotid pulse is disappearing again.

Q. In this patient with severe hypotension after intubation (which required no facilitating drug therapy), what complications must be considered?

A. First exclude a misplacement of the tracheal tube then consider a pneumothorax after auscultation and percussion of the lungs.

Q. How would you confirm or exclude tracheal tube misplacement?

A. Measure the expired CO_2; consider a check laryngoscopy.

Q. If clinical exam suggests pneumothorax and auscultation findings are asymmetric, what would you do?

A. Immediately perform a needle decompression on the side on which the pneumothorax is suspected, followed by a chest tube placement. Then perform a chest X-ray without delay.

The lung percussion is symmetrical and normal and the breath sounds are also symmetrical, so pneumothorax is unlikely.

Q. Given the onset of hypotension after initiation of positive pressure ventilation, what is the diagnosis to consider now, particularly in a COPD patient?

A. Elevated intrathoracic pressure which may be exacerbated by dynamic hyperinflation – an entity which is common in bronchial obstruction.

Q. A high intrathoracic pressure decreases venous return and thus cardiac output. What common circulatory state might exacerbate this?

A. This phenomenon is exacerbated by hypovolaemia.

LEARNING ISSUES

Cardiopulmonary interactions

NOTE Always consider pneumothorax and auto-PEEP in a ventilated patient who rapidly becomes hypotensive.

You manage this presumed diagnosis by disconnecting the resuscitation bag from the tracheal tube for a while and the carotid pulse becomes palpable again. You then re-connect the patient to the ventilator.

LEARNING ISSUES

Assessment of dynamic hyperinflation
Disconnection of manual or mechanical ventilation to treat air trapping
Ventilator adjustment

Link to PACT module on Mechanical ventilation

Q. To minimise the adverse effect of severe air trapping, which two ventilator settings do you modify?

A. To prolong the expiration time, set a low respiratory rate and keep a low I:E ratio. To shorten the time needed to exhale inspired gas, give a smaller tidal volume.

Ventilating the patient eight times/min with 500 mL (the patient weighs 70 kg), zero PEEP, and FiO_2 of 1.0, you measure a PaO_2 of 26.6 kPa/200 mmHg, a $PaCO_2$ of 8.0 kPa/60 mmHg, and a pH of 7.3. The peak airway pressure is 60 cmH_2O and the plateau pressure is 35 cmH_2O.

Q. What could explain the high peak and plateau pressures and the substantial difference between them?

A. The peak pressure reflects dynamic compliance. The dynamic measurement (peak pressure) is related to static compliance and to airway resistance but the plateau pressure only to static compliance. Hence the majority of the pressure difference between peak and plateau pressure reflects the elevated airway resistance related to the obstructive lung disease.

Regarding the high plateau pressure, it could reflect progressive dynamic hyperinflation.

Q. How can you verify the presence of dynamic hyperinflation?

A. The easiest way to assess dynamic hyperinflation is by assessing and measuring auto-PEEP, either by measuring pressure at the end of an end-expiratory hold or by checking (on the ventilator flow-time curve) if there is still an expiratory flow when the next inspiration cycle starts.

LEARNING ISSUES

How to measure auto-PEEP
See the PACT module on Respiratory assessment and monitoring (Task 3 – monitoring ventilator waveforms)

In the deeply sedated and 'relaxed' patient, you measure a total PEEP of 18 cmH_2O.

Q. How could you modify the pertinent ventilatory settings?

A. You could further reduce the respiratory rate and the tidal volume.

NOTE Sometimes you need very low (RR 4–5/min and Vt 5–6 mL/kg of IBW) ventilatory minute volume (Vm) to avoid air trapping.

Following tidal volume and respiratory rate reduction, the plateau pressure drops to 30 cmH_2O and the pH to 7.2 – as a result of hypercarbia.

LEARNING ISSUES

Principles that guide mechanical ventilation, ventilator adjustments
Permissive hypercarbia

Link to PACT module on Mechanical ventilation

Q. Which medical treatments do you start to try to further improve the lung mechanics?

A. Try to reduce the bronchospasm with inhaled β-mimetics and anticholinergics, as well as intravenous steroids. Treat the probable infective cause of the decompensation with antibiotics after bacteriologic sampling. Use of sedatives and muscle 'relaxants' may reduce O_2 demand and CO_2 production.

LEARNING ISSUES

Non-ventilatory support

NOTE Always monitor sedation, analgesia and neuro-blockade on a proper scale e.g. a sedation scale. Neuromuscular blockade, if required, is monitored using a nerve stimulator.

After a few days of full mechanical respiratory support and of the above-mentioned medication, the patient has been stabilised and you decide to start to wean the patient from the ventilator.

LEARNING ISSUES

Link to PACT module on Sedation and analgesia

Q. How do you proceed?

A. You stop neuromuscular blockade if still in place, reduce/stop sedation and switch the ventilator from a controlled (or assist-controlled) mode to an assist mode such as PSV.

LEARNING ISSUES

Weaning the patient

Link to the PACT module on Mechanical ventilation

Q. Do you apply PEEP?

A. In spontaneous ventilation, the patient might profit from a certain level of PEEP, assuming he still has some auto-PEEP. The set PEEP should never exceed auto-PEEP.

LEARNING ISSUES

External PEEP: when to apply it
External PEEP: how much

PACT module on Mechanical ventilation

NOTE Remember that decompensation in COPD patients e.g. during weaning reflects respiratory muscle exhaustion resulting from a mismatch between the required workload of breathing and the workload the patient is able to provide.

Two days later, the patient becomes febrile and hypotensive. You put him on controlled mechanical support again, after excluding mechanical complications (pneumothorax and increasing auto-PEEP).

Q. Which complication should you consider?

A. Always consider a nosocomial infection in a febrile intubated patient who remains a long time in the ICU.

The new infiltrates on the chest X-ray and the copious and purulent bronchial secretions cause you to suspect a nosocomial pneumonia. After taking blood cultures and sputum samples, you change antibiotics to a broader spectrum regimen that covers nosocomial organisms. Two days later, the bacteriological results confirm a nosocomial pneumonia and you adapt the antibiotics to the antibiogram. Over the next few days, the patient's progress is favourable, so that you again start to wean the patient from the ventilator. Every time you try to decrease the pressure support below 20 cmH_2O, however, the patient's breathing becomes rapid and shallow.

LEARNING ISSUES

Diagnosis of nosocomial/ventilator-associated pneumonia
Treatment of ventilator-associated pneumonia (VAP)
See the PACT module on Severe infection

Q. Although the facial expressions are intact, the patient appears to be weak. You have excluded a mechanical problem with the tube and ventilator. What would you do to determine the cause of the weaning failure?

A. You examine the patient for other recognised causes of weaning failure particularly a critical illness polyneuromyopathy.

You determine that the patient cannot lift his arms and legs from the bed and his deep tendon reflexes have disappeared. Since the weaning is now likely to be prolonged, it is decided to carry out a tracheostomy.

Finally, after two months of ICU stay, the patient is weaned from the ventilator and leaves the ICU for rehabilitation in a specialised clinic. He is expected to return home approximately two months later.

LEARNING ISSUES

Causes of failure to wean from mechanical ventilation
Tracheostomy
Long-term outcome

See the PACT modules on Airway management, Mechanical ventilation, Respiratory assessment and monitoring and Neuromuscular conditions.

On reflection, this module reflects the severity of acute illness which can occur in COPD and asthma patients, often against a background of quite varying comorbidity. The critical care treatments and support in severe acute disease are generally life-saving and, when successful, may allow the rapid return, particularly of a young asthmatic patient, to a normal life-style in the community. Achieving this will have required a high level of expertise and critical care input, including a comprehensive and consistent capacity to provide advanced, individualised ventilatory management. This will have obvious benefit to the patient and, in terms of healthcare economic analysis, is also evidently beneficial. However, similar expertise may entail a prolonged ICU and hospital stay including a higher level of intervention and likely patient morbidity but with a less evidently favourable outcome for the patient. In times when healthcare costs and life expectancy are increasing, and the mortality from COPD is expected, by 2020, to have doubled (relative to 1990), do you think guidelines for rationing the distribution of medical resources are needed? If so, how and by whom should these guidelines be created?

See the PACT module on Quality Assurance and cost-effectiveness