Asthma Management in ICU

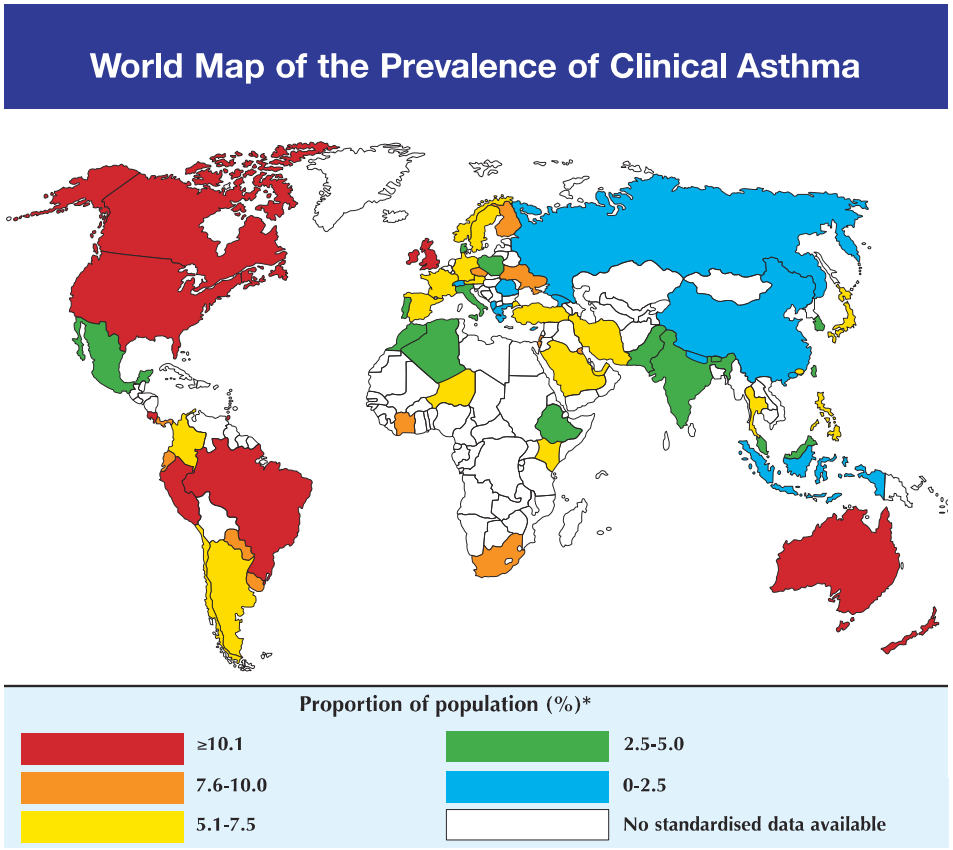
by

Dr Gary Au

From KWH

- Overview of Asthma
- Pathophysiology
- Therapeutic options
  - Medical treatment
  - NPPV
  - Mechanical ventilation
  - Salvage therapy

~ 235 million people worldwide were affected by asthma
~ 250,000 people die per year from asthma
Over all prevalence from 1 – 18%



Statistics showed that Hong Kong had **more than 330,000 people** suffering from asthma.

	Hong Kong population (2011)	Number of asthma patients	% with asthma
Primary students aged 6-7	92,298	7,292	7.9%
Secondary students aged 13-14	147,880	15,084	10.2%
Undergraduates aged 19-21	265,641	19,126	7.2%
Adults aged 22-70	4,983,652	249,183	5%
Elderly aged above 70	662,726	38,438	5.8%

Source《 胸肺疾病手冊》(Thoracic Diseases), Hong Kong Thoracic Society

About 70-90 death per year due to asthma in HK

Asthma Pathophysiology

What is Asthma ?

- a chronic inflammatory disorder of the airway
- airway hyperresponsiveness that leads to recurrent episodes of wheezing and breathlessness
- variable airflow obstruction within the lung that is often reversible either spontaneously or with treatment

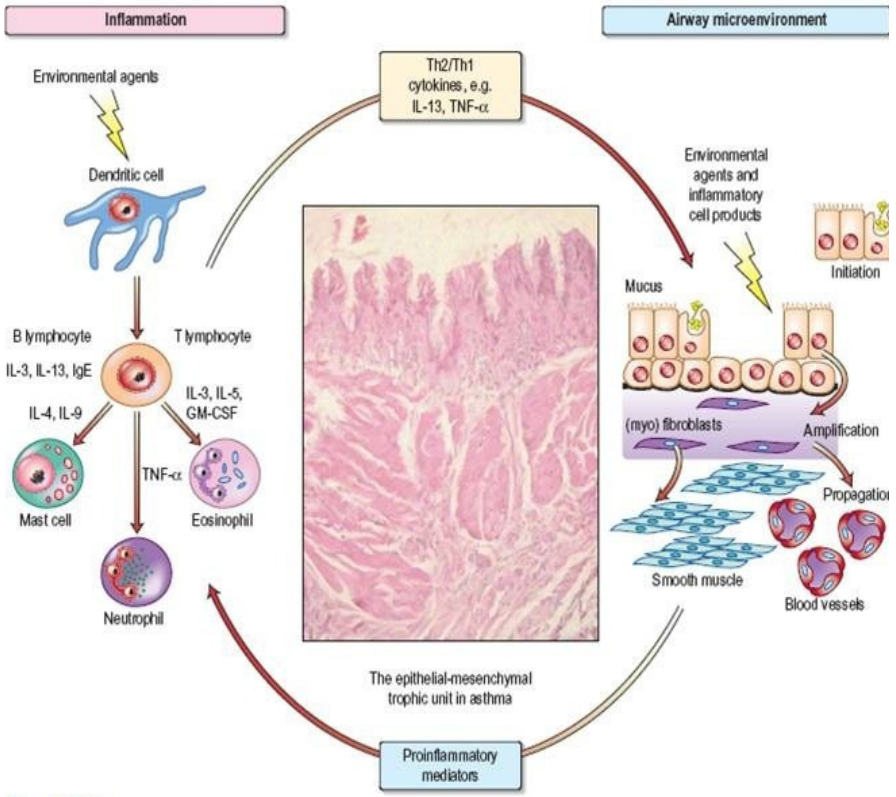
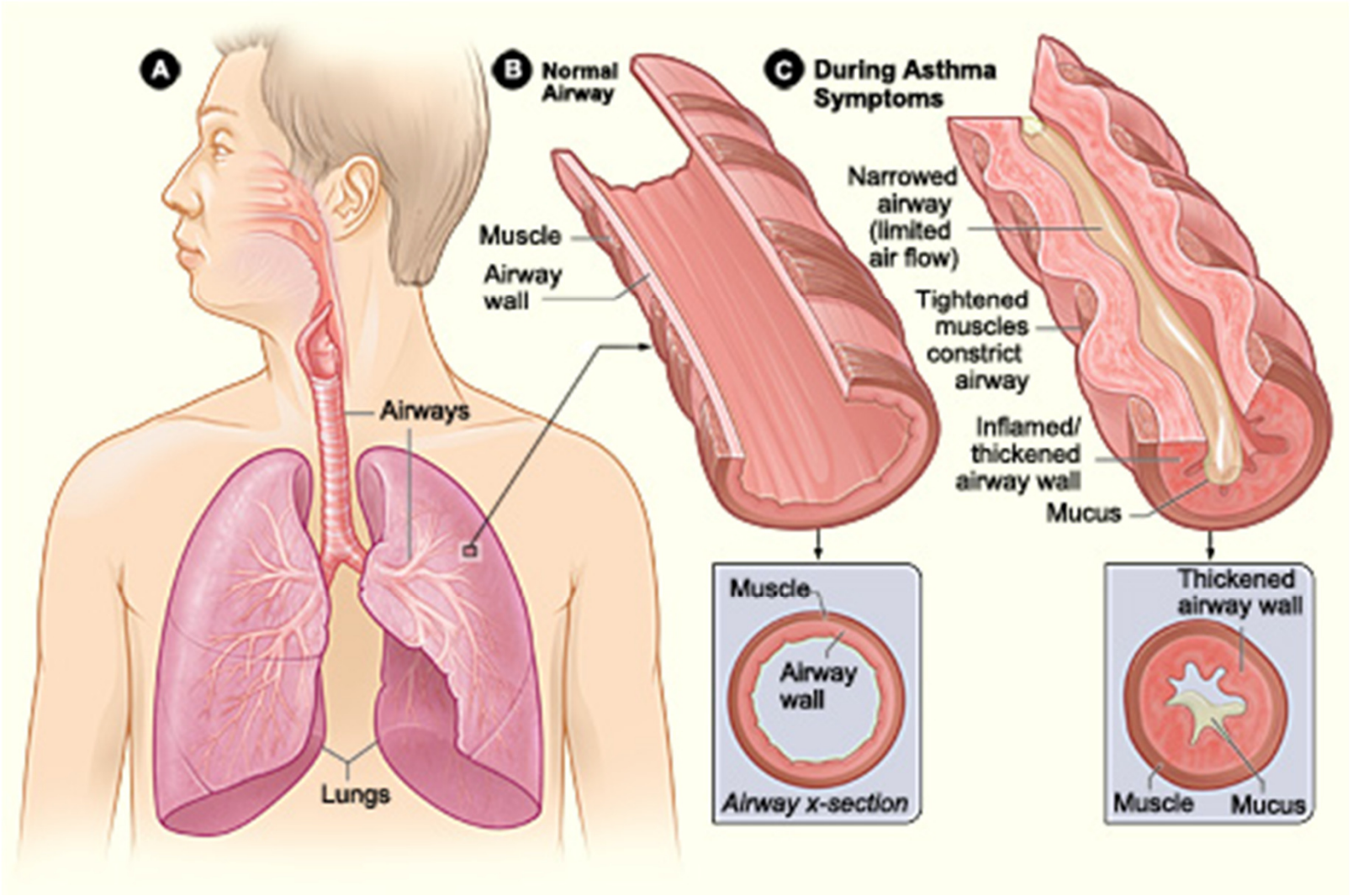


Fig. 14.34 **Inflammatory and remodelling responses in asthma with activation of the epithelial mesenchymal trophic unit.** Epithelial damage alters the set point for communication between bronchial epithelium and underlying mesenchymal cells, leading to myofibroblast activation, an increase in mesenchymal volume, and induction of structural changes throughout airway wall. Adapted from Holgate ST, Polosa R. The mechanisms, diagnosis, and management of severe asthma in adults. *Lancet* 2006; 368: 780–793 with permission from Elsevier.


A
B Normal Airway
C During Asthma Symptoms
Muscle
Airway wall
Airways
Lungs
Narrowed airway (limited air flow)
Tightened muscles constrict airway
Inflamed/ thickened airway wall
Mucus
Muscle
Airway wall
Airway x-section
Thickened airway wall
Muscle
Mucus

Dynamic hyperinflation

- Air-trapping, failure of the lung to return to its relaxed volume or FRC at end-exhalation
- Increase work of breathing
- Leading to refractory hypercapnia
- Hypotension
- Barotrauma

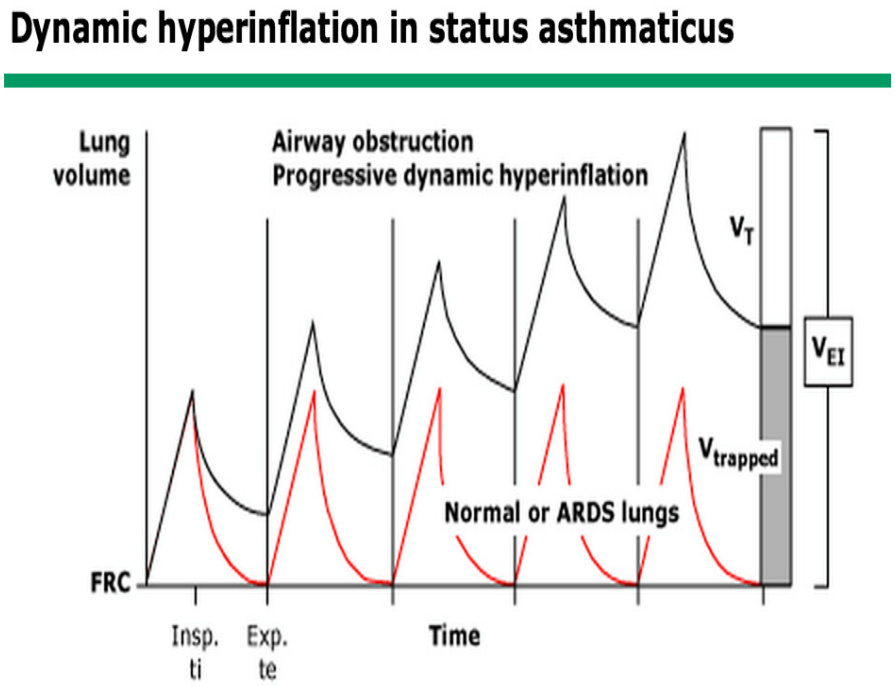


Table 1: Two characteristic presentations of acute severe asthma

Type 1: Slow progression	Type 2: Sudden progression
Slow-onset acute asthma	Sudden-onset, asphyxic, brittle, hyperacute asthma
Progressive deterioration: more than 6 h (usually days or weeks)	Rapid deterioration
80–90% Patients who present to ED	10–20% Patients who present to ED
Female predominance	Male predominance
More likely to be triggered by URI	More likely to be triggered by respiratory allergens, exercise, and psychological stress
Less severe obstruction at presentation	More severe obstruction at presentation
Slow response to treatment and higher hospital admissions	Rapid response to treatment and lower hospital admissions
Airflow inflammation mechanism	Bronchospastic mechanism
Predominance of eosinophils	Predominance of neutrophils

Table 3: Classification of severity of asthma exacerbation

Symptoms	**Mild**	**Moderate**	**Severe**	**Respiratory arrest imminent**
Breathlessness	While walking	While talking	While at rest	
Can lie down	Prefers sitting	Sits upright		
Talks in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
Signs				
Respiratory rate	Increased	Increased	Often (>30/min)	
Use of accessory muscles; thoracoabdominal suprasternal retractions	Usually not	Commonly	Usually	Paradoxical movement
Wheeze	Moderate, often only end-expiratory	Loud, throughout exhalation	Usually loud, throughout inhalation and exhalation	Absence of wheeze
Pulse/min	<100	100–120	>120	Bradycardia
Pulsus paradoxus (mm Hg)	<10 (absent)	10–25 (may be present)	>25 (often present)	Absence suggests respiratory muscle fatigue
Functional assessment				
PEF (% predicted or personal best)	>80	Approximately 50–80 or response response last <2h	<50	
PaO_2 (mm Hg)	Normal	>60	<60; possible cyanosis	
$PaCO_2$ (mm Hg)	<42	<42	≥42; possible respiratory failure	
SaO_2 (%; on air)	>95	91–95	<91	

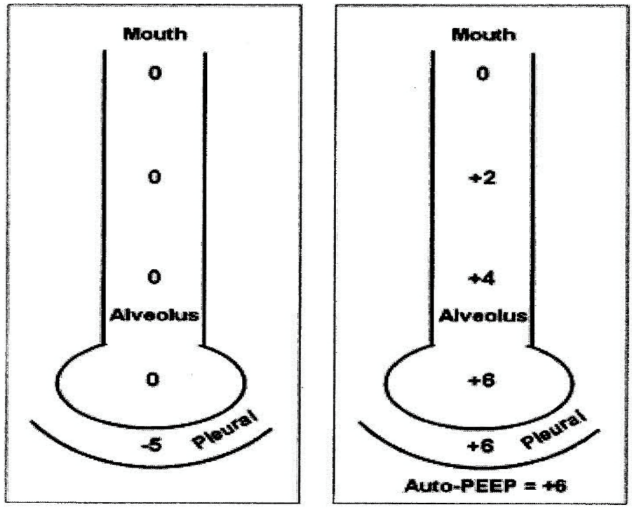
Adapted from Ref. 11. The presence of several parameters, but not necessarily all, indicates the general classification of the exacerbation. Many of these parameters have not been systematically studied, so they serve only as general guides.

Asthmatic patient in ICU

- Treatment Aim
  - optimize oxygenation
  - reduce airway obstruction
  - avoid complications
- Medical therapy
  - Bronchodilators (both beta2 agonist and anti-cholinergic agent)
  - Systemic Steroid
- NPPV
- Mechanical ventilation
- Salvage therapy

NPPV

- Is NPPV useful for severe asthma ?
  - Dynamic hyperinflation leading to high intrinsic-PEEP / Auto-PEEP
    - Additional negative intrathoracic pressure is required to overcome auto PEEP in order to achieve airflow during inspiration
    - Increase work of breathing
    - Increase muscle fatigue



NPPV

TABLE 1 Previous reports of noninvasive positive pressure ventilation (NPPV) in asthmatic patients

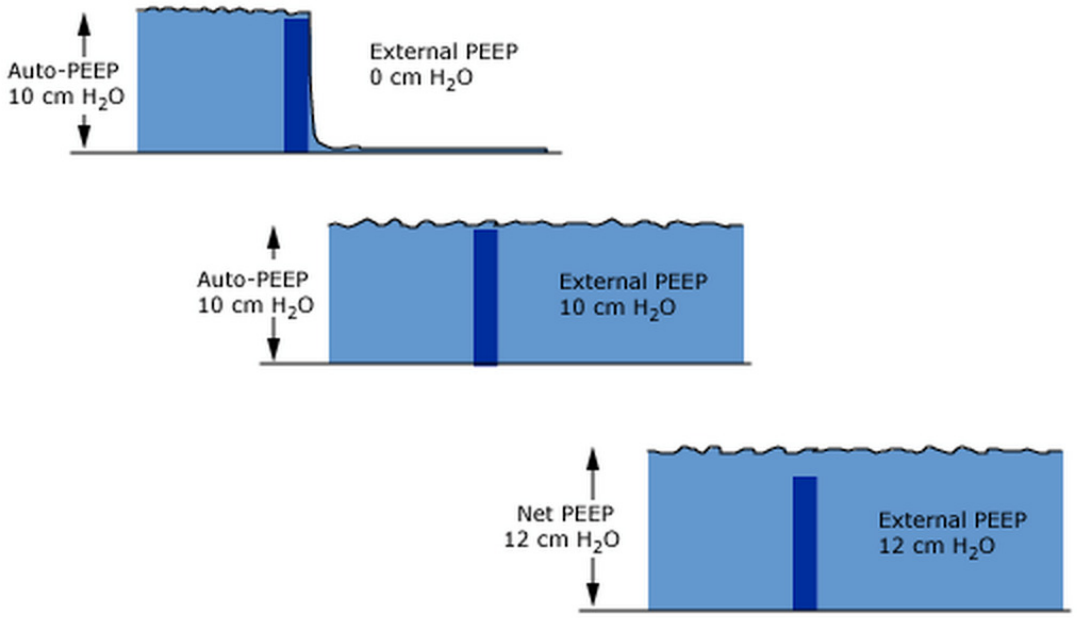
First author [Ref.]	Type of study	Patients n	Study design	Mode of ventilatory support/duration of application	Outcome
MEDURI [44]	Prospective observational	17	A report of 17 episodes of status asthmaticus treated with NPPV over 3 yrs	CPAP mask with pressure support using commercial ventilator for 16 h	NPPV improved gas exchange in status asthmaticus
FERNANDEZ [45]	Retrospective observational	33	Retrospecrive comparison of 22 patients treated with NPPV *versus* 11 patients treated with invasive mechanical ventilation	CPAP with or without pressure support, using commercial ventilators for 12 h	Improved gas exchange in both groups, with the possibility of prevented endotracheal intubation in NPPV group
SOROKSKY [46]	Prospective, randomised, sham controlled	30	15 patients on BiPAP compared with sham BiPAP with standard treatment	BiPAP circuit for 3 h	Improved FEV_1 and decreased hospitalisation rate in NPPV group
SOMA [47]	Prospective randomised	44	Prospective comparison of low- and high-pressure groups to standard medical group	BiPAP circuit for 1 h	Improved FEV_1 with increasing pressure support

BiPAP: bilevel positive airway pressure; CPAP: continuous positive airway pressure; FEV_1: forced expiratory volume in 1 s.

NPPV

– However, NPPV may worsen lung hyperinflation

- Bronchospasm leading to one way valve airway



NPPV

TABLE 4 Criteria for use of noninvasive positive pressure ventilation (NPPV)

Criteria for selecting severe asthmatic patients for NPPV trial[#]
Tachypnea with respiratory rate >25 breaths·min^{-1}
Tachycardia with *f*C >110 breaths·min^{-1}
Use of accessory muscles of respiration
Hypoxia with a $P_{a,O_2}/F_{I,O_2}$ ratio >200 mmHg
Hypercapnia with P_{a,CO_2} <60 mmHg
FEV1 <50% pred[¶]

*f*C: cardiac frequency; P_{a,O_2}: arterial oxygen tension; F_{I,O_2}: inspiratory oxygen fraction; P_{a,CO_2}: arterial carbon dioxide tension; FEV1: forced expiratory volume in 1 s; % pred: % predicted. [#]: in the absence of absolute contraindication the presence of at least one criterion would suffice for an NPPV trial; [¶]: FEV1 <50% pred after at least two consecutive nebulisations with salbutamol 2.5 mg and ipratropium 0.25 mg.

TABLE 3 Absolute and relative contraindications for noninvasive positive pressure ventilation (NPPV) trial

Contraindications for NPPV trial
Absolute contraindications
Need for immediate endotracheal intubation
Decreased level of consciousness
Excess respiratory secretions and risk of aspiration
Past facial surgery precluding mask fitting
Relative contraindications
Haemodynamic instability
Severe hypoxia and/or hypercapnia, $P_{a,O_2}/F_{I,O_2}$ ratio of <200 mmHg, P_{a,CO_2} >60 mmHg
Poor patient cooperation
Severe agitation
Lack of trained or experienced staff

P_{a,O_2}: arterial oxygen tension; P_{a,CO_2}: arterial carbon dioxide tension; F_{I,O_2}: inspiratory oxygen fraction.

NPPV

- Conclusion
  - It is reasonable to give asthmatic patients a trial of NPPV over 1-2 hours in HDU or ICU if no contraindications
  - Start with low NPPV support
  - Use EPAP to against Auto PEEP
    - Limited by 5cm H2O at most to avoid dynamic hyperinflation

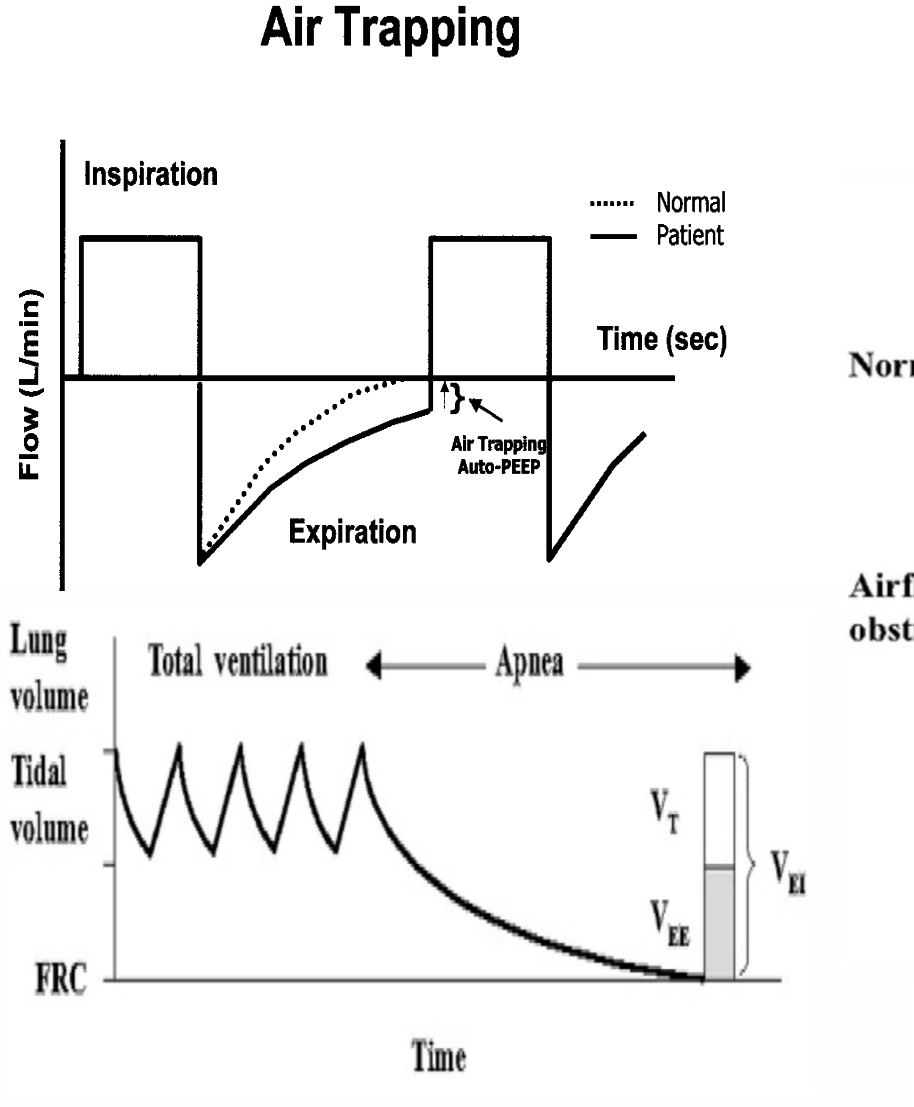
Intubation for mechanical ventilation

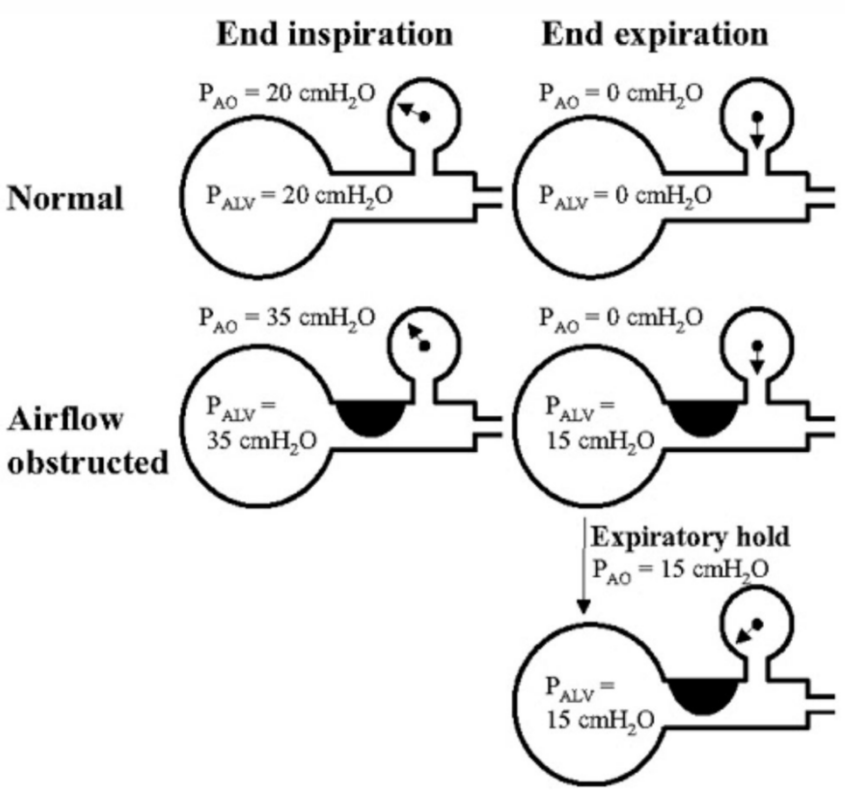
- Watch out for catastrophic hypotension
  - Dehydration
  - Auto PEEP
  - Loss of endogenous catecholamines
  - Vasodilating properties of anaesthetic agents
- Ketamine
  - Sympathomimetic and bronchodilator properties
  - 1-2mg/kg for intubation
- Avoid drugs causing histamine release
  - Morphine, atracurium
- Use large bore endotracheal tube to reduce resistance

Mechanical ventilation

- Around 2% of severe asthma requiring mechanical ventilation.
- Death is usually as a result of
  - Severe gas-trapping, barotrauma, hypotension, refractory respiratory acidosis, cardiac arrhythmia
- Ventilation Strategy
  - Maintain Oxygenation
  - Permissive hypercapnia
  - Avoid dynamic hyperinflation
  - Adequate PEEP
  - Keep patient ventilator synchronization

Measuring Air Trapping





Clinicians should question about low Auto-PEEP measurements

Ventilation Strategy

Limiting air-trapping

Controlled hypoventilation

Box 3 Initial ventilator settings in paralysed patients (adapted from Finfer and Garrard[109])

- FiO_2 = 1.0 (initially)
- Long expiratory time (I:E ratio >1:2)
- Low tidal volume 5–7 ml/kg
- Low ventilator rate (8–10 breaths/min)
- Set inspiratory pressure 30–35 cm H_2O on pressure control ventilation or limit peak inspiratory pressure to <40 cm H_2O
- Minimal PEEP <5 cm H_2O

Maintain Oxygenation

Allow time to for expiration

Adequate sedation for patient-ventilator synchronization

How about CO2 level

Permissive hypercapnia

- allow raised CO2 level
- adjust RR to keep pH > 7.2

Unless contraindicated

- raised ICP
- renal failure
- seizure disorder

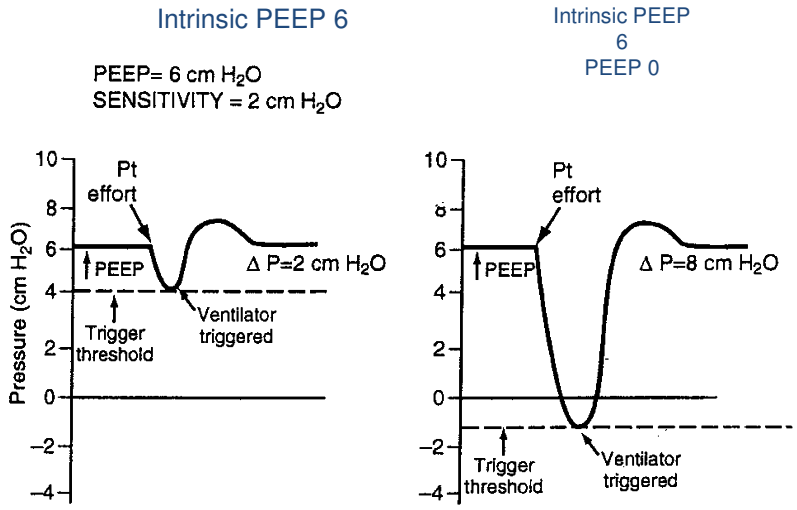
Ventilation Strategy - PEEP

Zero PEEP

- Totally controlled ventilation of patients under deep sedation or being paralysed
- Prevent air-trapping and worsening of Auto-PEEP

Low PEEP

- Reduce the work of breathing by enhancing ventilator triggering
- Maintain FRC



Ventilation strategy - Mode

Volume control

- Secure minute ventilation even though airway resistance may be variable during asthmatic attack
- Limited by high inspiratory pressure
  - Insp pressure not reflecting the truth alveolar/ plateau pressure
  - Need to adjust airway pressure limit

Pressure Control

- Better patient-ventilator synchronization
- Variable minute ventilation according to the change of airway resistance.
  - Leads to profound hypercapnia during bronchospasm attack

Ventilation Strategy – Muscle relaxant

- For refractory asthma and failure conventional ventilation strategy with heavy sedation
- To optimize patient ventilator synchronization
  - Allow controlled ventilation
- Side effect
  - Myopathy, particular with the use of corticosteroid
- Avoid or to be kept as minimum dose required

Ventilation Strategy - Others

- Bronchodilators delivery

Metered dose inhaler (MDI) system

- Spacer or holding chamber
- Location in inspiratory limb rather than Y piece
- No humidification (briefly discontinue)
- Actuate during lung inflation
- Large endotracheal tube internal diameter
- Prolonged inspiratory time

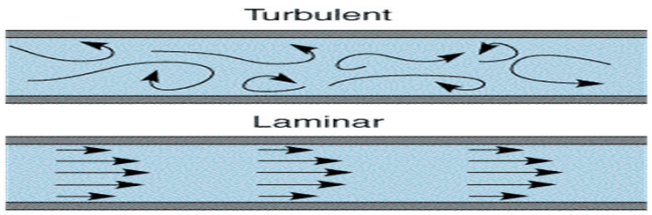
- Humidification
  - Adequate humdification of inspired gas is particular important in asthmatic patient to prevent thickening of secretions and dying of airway mucosa
  - Mucus flow is markedly reduced when RH at 37C falls below 75% (AH of 32g/m3)
  - Mucus flow ceases when RH falls to 50% (AH of 22g/m3)

Salvage Therapy

- Heliox
- General anaesthesia
- ECMO
- $MgSO_4$
- Ketamine

Heliox

- Helium (an inert low density gas) mix with Oxygen in the usual ratio 7:3
- Reduce resistance to airflow



- Helium also enhance CO2 diffusion up to 4-5 times
- However, Helium can interfere with the ventilator volume measurements.
  - Required further calibration

Anaesthetic Agent

- Inhalational anaesthetic agents, such as halothane, isoflurane and sevoflurane, are potent bronchodilators for asthma patients
- Effective scavenging systems are required
- Only few ICU ventilators can be fitted for vaporising anaesthetic agent
  - Seimens Servo 900 series
- Side effect includes hypotension and myocardial irritability

ECMO

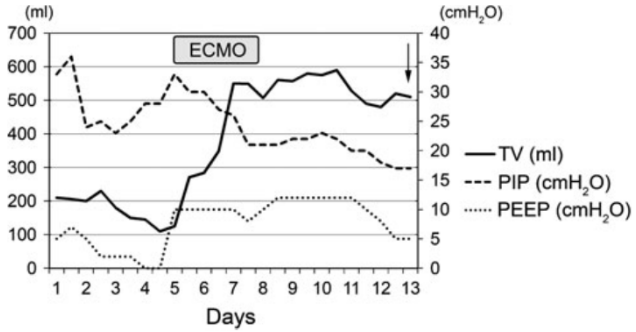
- For reversible respiratory failure diseases
- Any evidence for status asthmaticus ?

J Anesth (2012) 26:265–268
DOI 10.1007/s00540-011-1288-z

CLINICAL REPORT

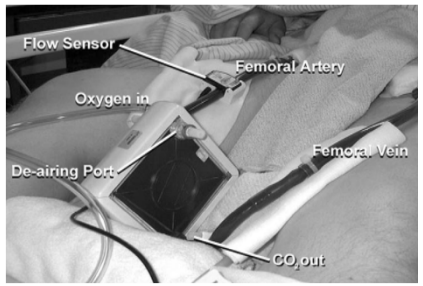
Successful treatment of severe asthma-associated plastic bronchitis with extracorporeal membrane oxygenation

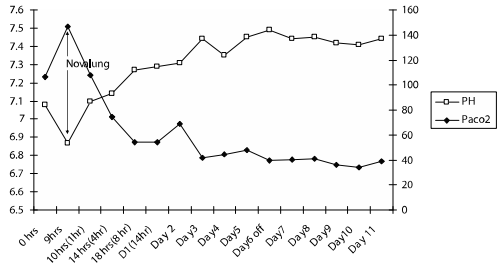
Momoka Tonan · Soshi Hashimoto · Akio Kimura · Hiroki Matsuyama · Hiromi Kinose · Maiko Sawada · Nobuaki Shime · Natsuko Tokuhira · Yuko Kato · Masayuki Sasaki · Kunihiko Tsuchiya · Satoshi Higaki · Tadaki Oomae · Satoru Hashimoto



Pumpless extracorporeal carbon dioxide removal for life-threatening asthma

Stuart C. Elliot, BHSc; Kumar Paramasivam, MD, MRCP; John Oram, MB ChB, FRCA; Andrew R. Bodenham, FRCA; Simon J. Howell, MD, FRCA; Abhiram Mallick, MD, FRCA





Magnesium Sulphate

- MgSO4 has bronchodilator activity due to inhibition of calcium influx into airway smooth muscle cells
- Single dose 2g infused over 20mins
- Excellent safety profile, only contraindicated in the presence of renal failure

Table 3.
Interventions and outcomes in 7 randomized trials of intravenous magnesium sulfate for acute asthma.

Study	Start of Magnesium Sulfate*	Magnesium Sulfate Regimen	Control Regimen	Corticosteroid Regimen	Reported Outcomes	Authors' Overall Conclusion	Jadad Quality Score
Skobeloff et al[38]	90 min	1.2-g loading dose over 20 min	50 mL saline solution	125 mg IV MP	Admissions, PFTs	Effective	5
Green & Rothrock[39]	60 min	2-g loading dose over 20 min	No placebo	125 mg IV MP	Admissions, PFTs	No effect	1
Tiffany et al[41]	90 min	2-g loading dose ± 2-g/h infusion	Saline solution loading dose and infusion	125 mg IV MP	Admissions, PFTs	No effect	4
Bloch et al[40]	30 min	2-g loading dose over 20 min	50 mL saline solution	125 mg IV MP if initial FEV_1 ≤40% or oral CS in the last 6 mo	Admissions, Borg Index	Overall: no effect; Severe group: effective	5
Silverman et al[42]	30 min	2-g loading dose over 20 min	50 mL saline solution	125 mg IV MP	Admissions, Borg Index, PFTs	Effective	4†
Devi et al[36]	60 min	100 mg/kg loading dose over 35 min; maximum 2 g	30 mL saline solution	IV or PO cortico-steroids (no dose provided)	Admissions, Pulmonary Index score, PFTs	Effective	4
Ciarallo et al[37]	After 3 ED β-antagonist treatments	25-mg/kg loading dose over 20 min; no maximum	"equi-volume" saline solution	2 mg/kg IV MP (75% of patients in study)	Admissions, PFTs	Effective	4

MP, Methylprednisolone; **PFTs**, pulmonary function test results reported; **CS**, corticosteroids.
*In minutes from time of arrival to ED.
†Jadad score results based on unpublished data.

Ketamine

- It has bronchodilator effect
  - Prevent reuptake of circulating catecholamines
  - Blocking calcium influx
  - Relaxing smooth muscle by reducing vagally mediated bronchoconstriction
- Evidence of efficacy mainly on pediatric group
- Side effect
  - Lower seizure threshold, hypertension, tachycardia, alter mood, delirium

Take Home Message

- In severe asthma, bronchospasm leading to dynamic hyperinflation, which causes complication, such as air-trapping, barotrauma, respiratory muscle fatigue, cardiovascular collapse
- Apart from bronchodilators and steroid, mechanical ventilation strategy is essential to improve patient prognosis.
- Consider Salvage therapy for refractory case.