## Severe Asthma

- Over 2.2 million Australians have currently diagnosed asthma
- 406 deaths attributed to asthma in 2006
- Highest risk of dying from asthma is in the elderly over 70
- The emergency clinician's goal in treating acute severe asthma is preventing intubation
- Severe/Critical asthma is a life threatening condition

**Near fatal asthma**

- Near-fatal asthma (NFA) is described as acute asthma associated with a respiratory arrest or arterial carbon dioxide tension greater than 50 mmHg, with or without altered consciousness.
- In a study of asthma patients admitted with a near-fatal episode, two-thirds of subsequent severe attacks or deaths occurred within 1 year of the previous life-threatening admission.
- Two distinctive phenotypes of NFA have been identified:
- Most common, responsible for 80-85% of all fatal events is characterised by eosinophilic inflammation associated with gradual deterioration over days-weeks occurring in patients with severe or poorly controlled asthma, and is slow to respond to therapy.
- The second phenotype, with neutrophilic inflammation, has both rapid onset and response to therapy.

**Assessment of the asthmatic patient**

- The immediate assessment of patients with asthma should include the degree of respiratory distress (ability to speak, respiratory rate, use of accessory muscles, air entry), degree of hypoxia (cyanosis, pulse oximetry, level of consciousness) and cardiovascular stability (arrhythmias, blood pressure).
- Accessory muscle use, wheeze and tachypnoea might diminish as the patient tires.
- Asthmatics with poor perception of the severity of their asthma appear deceptively well, despite severe decrements in lung function.
- Although the assessment relies on clinical signs, additional information might be obtained from chest radiography or blood gas analysis.
- No investigation should delay the initiation of appropriate therapy

**Pathophysiology of severe asthma**

- Physiologically, there is abnormal distribution of ventilation, perfusion and altered gas exchange.
- Expiratory flow limitation with incomplete expiration leads to hyperinflation of the lungs, adding to the elastic burden of the thorax.
- Passive elastic recoil is no longer sufficient to achieve effective expiration, and expiratory muscles are then actively involved in expiration.
- Progression of dynamic hyperinflation is associated with a higher intrathoracic pressure at the end of expiration (intrinsic Positive End Expiratory Pressure – iPEEP or auto-PEEP).

- Hyperinflation and higher intra-thoracic pressures mean the respiratory muscles start at greater stretch (hence less efficient, more fatigable), and greater inspiratory effort is needed to commence flow into the lungs, which also increases work of breathing.
- Barotrauma, which refers to the adverse effects of this increased intra-lung pressure on both the lung structure as well as that transmitted to the vascular structures, can result in bullae rupture, pneumothorax and reduced venous return with hypotension.
- Blood gas analyses might reveal respiratory alkalosis, hypoxaemia and hypocarbia.
- Generally, asthma attacks are not characterized by marked arterial desaturations until very late in life-threatening episodes.
- Hypercarbia occurs in 10% of cases presenting to the ED. These patients have greater airway obstruction and respiratory rate than non-hypercapnic patients.
- A quiet chest on auscultation, inability to talk and cyanosis suggest the presence of hypercarbia.
- The finding of normocarbia in acute asthma should also be viewed as a sign of impending respiratory failure that requires aggressive treatment.
- Patients who fail to respond to therapy (PEFR improved by less than 10–20%) or with persistent hypercapnia, tachypnoea (respiratory rate > 30), altered mental status, arrhythmias or significant comorbidities should be referred to the ICU.

**Oxygen for severe asthma**

- Hypoxaemia in asthma results from ventilation/perfusion mismatching and is thus usually easily corrected with modest increases in the fraction of inspired oxygen (e.g. 1–3 L/min via a nasal cannula or mask).
- Treatment should be based on achieving target arterial oxygen tension and oxygen saturations (most guidelines suggest 92%) rather than giving predetermined concentrations or flow rates of inspired oxygen.
- The inspired oxygen must be humidified to prevent the broncho-constrictive effect of dry gas.

**B2-agonists**

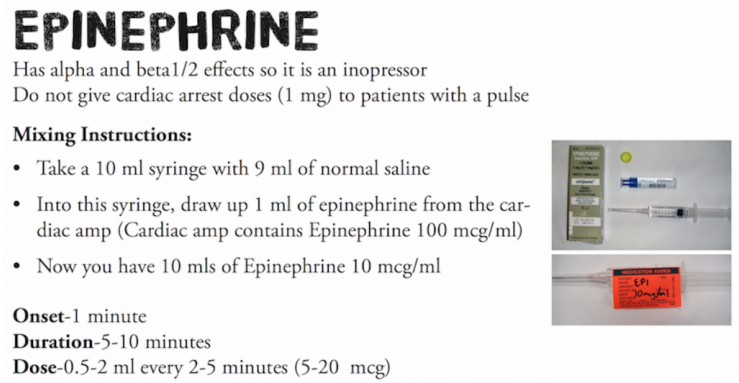
- Short-acting, inhaled b2 -agonists are the drugs of choice for treating acute asthma. Their onset of action is rapid and their side-effects are well tolerated.
- Salbutamol, the most frequently used b2 -agonist in ED around the world, has an onset of action of 5 min and a duration of action of 6 h.
- In acute severe asthma, salbutamol might be administered either by wet nebulization or repeated activations of a metered dosed inhaler via a large volume spacer.
- Continuous nebuliser therapy appears to be more effective than intermittent nebulisers for delivering beta-agonist drugs to relieve airway spasm in acute severe asthma. (Cochrane Review, 2009)
- I.V. b2 -agonists have been described as rescue therapy for use in patients unresponsive to inhaled bronchodilator and systemic corticosteroid therapy, or when the inhaled route is not practical.

**Ipatropium bromide**

- Ipratropium bromide has a mild additional bronchodilating effect when added to b -agonists that might only be significant in severe asthma.
- The safety profile and the fact that individual patients might obtain benefit have resulted in aerosolized ipratropium being recommended for the treatment of acute severe asthma.
- No unfavourable interactions between these two classes of agents have been reported.
- Because anticholinergic agents and b2 -agonists exert effects by different mechanisms, affect different-sized airways and have different pharmacodynamic and pharmacokinetic properties, the combined use of them is rational and is likely to result in improved bronchodilation
- There is an increasing body of evidence that more frequent dosing of ipratropium bromide (20 m g every 20 min) at initial presentation might be beneficial.

**IV Adrenaline**

- At the current time no recommendations regarding adrenaline infusions can be made, except that it's use would be reasonable as a rescue therapy in severe asthma complicated by hypotension that is not secondary to dynamic hyperinflation.




**Corticosteroids**

- Corticosteroids have been shown to improve asthma symptoms by reducing airway inflammation, airway reactivity and decrease airway secretions.
- In addition to their anti-inflammatory effect, steroids increase the number and sensitivity of b -receptors on the bronchial smooth muscle.
- In contrast to chronic asthma, research on the use and mechanisms of action of corticosteroids during an acute exacerbation of asthma has been limited.
- Objective improvements in airflow obstruction have usually not been demonstrated during the first 6–12 h of treatment with corticosteroids in acute asthma.
- Corticosteroids are recommended for most patients in the ED, particularly in those who do not respond completely to initial b2 -agonist therapy.
- Corticosteroid administration reduces admission rates, decreases relapse rates and might also reduce the number of cases of fatal asthma.
- Because benefits from corticosteroid treatment are not usually seen for 6–24 h after administration, therapy should be instituted early.

- Low dose corticosteroids ( 80 mg/day of methylprednisolone or 400 mg/day of hydrocortisone) appear to be adequate in the initial management of adult patients.
- Higher steroid doses do not appear to offer a therapeutic advantage, and because the risk of myopathy is significant, especially in the mechanically ventilated patients, the concomitant use of systemic corticosteroids and paralytic agents should be avoided if at all possible.
- Importantly oral and i.v. routes of corticosteroid administration are equally efficacious with respect to rate of resolution of airflow limitation. The parenteral route is required in patients unable to take oral medication (intubated) or if absorption might be compromised (e.g. vomiting).

**Magnesium Sulphate**

- The role of magnesium as an antiinflammatory agent has been identified in adults with asthma.
- Magnesium is safe (no life-threatening side-effects noted in any of the trials), inexpensive, and familiar to most physicians.
- A single dose of i.v. $MgSO_4$ administered to patients with severe acute asthma has been shown to be effective.
- A multicentre trial demonstrated that 2 g of i.v. magnesium sulphate administered as an adjunct to standard therapy improved pulmonary function in patients presenting to the ED with severe asthma.
- Several systematic reviews conclude that this agent is most effective in patients with severe asthmatic exacerbations (defined as severe airflow limitation, a relative failure to respond to inhaled bronchodilators and high risk of admission).

**Antibiotics**

- There is no benefit to the routine use of antibiotics in the management of an acute asthma episode. Antibiotics should only be used when findings are consistent with pneumonia or other clinical bacterial infections in which case therapy is then directed to the most likely pathogen.

**Aminophyline**

- Aminophyline use for severe asthma has been associated with a relatively high incidence of significant adverse events.
- At the current time routine use of aminophylline in severe asthma cannot be recommended.

**NIV for severe asthma**

- A Cochrane review performed in 2005 concluded there are promising results in favour of the use of NPPV in severe acute asthma; however, the regular use of NPPV in status asthmaticus still remains controversial.
- Until large randomized controlled trials are completed, this therapy should be restricted, and routine clinical use cannot be recommended.

**Intubation of the severe asthma patient**

- Deteriorating consciousness, severe exhaustion and cardiopulmonary arrest are absolute indications for intubation and mechanical ventilation.

- Severe hypercapnia, acidosis and fatigue might not warrant immediate intubation, but rather aggressive and continuous bronchodilator therapy.
- Intubation and mechanical ventilation in the asthmatic should not be embarked upon lightly.
- 1-3% of acute severe asthma requires intubation.
- Prevention of intubation and mechanical ventilation are the goals of managing acute severe asthma, this can be achieved by maximising pre-intubation therapy, however you don't want to wait too long or let the severe asthmatic tire before trying to intubate them.
- Once an asthmatic is intubated and ventilated their morbidity and mortality increasing dramatically, and it can be difficult to wean from the ventilator.

**RSI for severe asthma**

- Once it is apparent that invasive ventilation is required experienced help should be sought.
- The optimal means of intubation is usually direct laryngoscopy, following rapid sequence induction.
- The best agents to use are those most familiar to the operator.
- Induction might effectively be achieved with propofol or thiopentone; however, careful dosage adjustment is required for potential haemodynamic compromise.
- The asthmatic patient is often volume-depleted, with induction resulting in both loss of sympathomimetic tone and drug-induced vasodilation.
- The development of intrinsic PEEP with an inappropriate ventilation strategy might rapidly result in catastrophic circulatory collapse.
- Ketamine with its sympathomimetic and bronchodilating properties has been advocated by many as the induction agent of choice.
- The usual dose of ketamine for intubation is 1–2 mg/kg given intravenously over 2 min.
- Suxamethonium might be used safely to achieve rapid paralysis for intubation, but the known complications need to be considered.
- Following induction, maintenance with fentanyl and midazolam is appropriate.
- Fentanyl is the opiate of choice because it inhibits airway reflexes, causes less histamine release than morphine, but on rare occasions can induce chest wall rigidity with rapid bolus dosing.

**Post-intubation paralysis**

- Ongoing paralysis might initially be required to facilitate ventilation; however, because of the significant risk of critical illness polyneuromyopathy (especially given the combination with steroids), neuromuscular blockade should be withdrawn as soon as possible
- The incidence of myopathy in asthmatics on long-term non-depolarizing neuromuscular blocking agents has been reported as high as 30%.

**Ventilation strategy**

- The mode of ventilation might be a crucial factor for a successful outcome of NFA.

- Mechanical ventilation is often difficult because the obstructive defect might result in dynamic hyperinflation. This might then lead to barotrauma, volutrauma or catastrophic haemodynamic compromise secondary to impairment of venous return.
- Initial BVM ventilation allows for an assessment of severity of bronchospasm and avoids dynamic hyperinflation by using a slow breath rate of 4–5 breaths/min. Once the situation is considered stable an attempt to mechanically ventilate the patient is made.
- Regardless of the mode of ventilation selected, the goals of mechanical ventilation are to maintain adequate oxygenation, minimize dynamic hyperinflation, avoid barotrauma and accept some degree of hypercapnia until bronchodilators and steroids improve airflow.
- Outcome is improved in mechanically ventilated asthmatics by limiting airway pressure using a low respiratory rate and tidal volume whereas permitting a moderate degree of hypercarbia and respiratory acidosis.
- Hypercarbia has not been found to be detrimental except in patients with severe myocardial depression.
- Moderate degrees of hypercarbia with an associated acidosis (pH 7.15–7.2) are generally well tolerated.
- To prolong the expiratory time and allow adequate time for expiration, the breath rate can be reduced, or inspiratory time decreased thereby extending the inspiratory to expiratory (I : E) ratio to much greater than 1:2.
- Expiration should ideally be observed both clinically and on the ventilator graphics to be complete before the next breath is delivered.
- Pressure control ventilation might not be an ideal mode of ventilation for patients with NFA as frequent fluctuations in airway resistance lead to variable tidal volumes and a risk of significant hypoventilation.
- The use of extrinsic PEEP remains controversial, in mechanically ventilated paralysed patients. Extrinsic PEEP might prevent airway collapse by splinting the airways open; however, as a general rule, extrinsic PEEP should not exceed intrinsic PEEP and ongoing clinical assessment for the presence of gas trapping and magnitude of FRC are mandatory.
- Ensuring adequate humidification of inspired gas is particularly important in the ventilated asthmatic to prevent further thickening of secretions and drying of airway mucosa that might stimulate further bronchospasm.

**Initial ventilation strategy for NFA**

1. FiO2 1.0, then titrate to keep SpO2 >94%
2. Tidal volume 5–6 mL/kg
3. Ventilator rate 6–8 breaths/min
4. Long expiratory time (I: E ratio >1:2)
5. Minimal PEEP 5 cmH2O
6. Limit peak inspiratory pressure to <40 cmH2O
7. Target plateau pressure <20 cmH2O
8. Ensure effective humidification