Acute Severe Asthma and Status Asthmaticus

When the diagnosis of asthma is confirmed and comorbidities addressed, severe asthma is defined as asthma that requires treatment with high-dose inhaled corticosteroids (ICS) plus a second controller and/or systemic corticosteroids to prevent it from becoming 'uncontrolled', or that remains 'uncontrolled' despite this therapy[1].

Asthma is a common disease and its frequency sometimes detracts from its potential seriousness. In adults with asthma, only 5-10% have severe disease but these individuals carry a substantial proportion of the cost (both in terms of morbidity and economic consideration) and run the highest risk of acute severe exacerbations and death[2].

Status asthmaticus is severe asthma that does not respond well to immediate care and is a life-threatening medical emergency. Ensuing respiratory failure results in hypoxia, carbon dioxide retention and acidosis. The exact mechanism underlying the development of an acute severe asthma attack remains elusive but there appear to be two phenotypes[3, 4]:

- Gradual-onset - in about 80%, severe attacks develop over more than 48 hours. These are associated with eosinophilic infiltration and slow response to therapy.
- Sudden-onset - often in association with significant allergen exposure. Patients tend to be older and to present between midnight and 8 am. This type of attack is associated with neutrophilic inflammation and a swifter response to therapy.

In deaths from asthma there is often a failure to recognise the full severity of the situation. This can be down to the patient, their family/carers or the healthcare team but often a multitude of factors is involved. Patients frequently have adverse psychosocial factors that interact with the ability to judge or manage their disease or have a diminished perception of their dyspnoea that leads to late presentation. Medical care continues to fail sometimes to treat acute severe asthma aggressively enough or to comply with national guidelines[5].

Every emergency consultation for asthma should be regarded as for acute severe asthma* until proven otherwise.
All patients with acute severe asthma* that has not responded to immediate treatment or life-threatening asthma* must be referred to hospital.

*See below for clinical features

Epidemiology[6]

- There were 1,167 deaths from asthma in the UK in 2011.
- An estimated 75% of admissions for asthma are avoidable and as many as 90% of the deaths from asthma are thought to be preventable.

Risk factors
Risk factors for asthma-related death include[5]:

- A background disease pattern of chronic severe asthma:
  - Previous near-fatal asthma.
  - Previous admission for asthma, especially in the preceding year.
  - Three or more classes of asthma medication.
  - Heavy or increasing use of beta2 agonists.
  - Frequent emergency contacts for asthma care, especially in the preceding year.
  - 'Brittle' asthma.

- Inadequately treated disease +/- inadequate medical monitoring.
- Inappropriate beta-blocker prescription or heavy sedation.
- Non-steroidal anti-inflammatory sensitivity.
- Use of a long-acting beta2 agonist (LABA) such as salmeterol, especially if not using a steroid inhaler[7].
- Personal or passive smoking.
- Environmental conditions - air pollution (ozone, sulfur dioxide, nitrogen dioxide and particulates) and pollen levels are thought to influence the rate of hospital admissions.
- Sensitivity to fungi (see 'Severe asthma with fungal sensitisation (SAFS)', below).

Severe asthma:

- Inadequately treated disease +/- inadequate medical monitoring.
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- Personal or passive smoking.
- Environmental conditions - air pollution (ozone, sulfur dioxide, nitrogen dioxide and particulates) and pollen levels are thought to influence the rate of hospital admissions.
- Sensitivity to fungi (see 'Severe asthma with fungal sensitisation (SAFS)', below).
Adverse behavioural/psychosocial factors:
- Non-compliance, frequent failure to attend appointments, self-discharge, denial of illness.
- Psychiatric illness (psychosis, depression, deliberate self-harm), alcohol or street drug use.
- Obesity.
- Learning difficulties.
- Employment problems, income problems, social isolation.
- Childhood abuse.
- Severe domestic, marital or legal stress factors.

Seasonal variation (in the UK, the peak of deaths in those aged under 44 years is in July-August and, in older patients, December-January).
- Pregnancy will exacerbate asthma in about a third of affected women. Treat the asthma - medication should be continued/stepped up where necessary; it is a lesser risk to the fetus than uncontrolled asthma or severe exacerbations.

Severe asthma with fungal sensitisation (SAFS)
Severe asthma may be caused by sensitisation to fungi. See also separate Aspergillosis article for further details regarding allergic bronchopulmonary aspergillosis (ABPA) and SAFS.

- SAFS refers to patients with severe asthma (despite standard treatment) with evidence of fungal sensitisation who do not meet the criteria for ABPA\[^8\]. The total IgE is usually lower than for patients with ABPA (total IgE <1000 IU/mL).
- Most affected patients only react to one of two fungi, most often Aspergillus fumigatus or Candida albicans.
- Patients with SAFS usually have chronic severe asthma symptoms despite maximal treatment, including steroids.
- Treatment of SAFS should initially be similar to that of severe asthma\[^9\].
- Antifungal therapy with itraconazole is beneficial (fluconazole may be beneficial in those sensitised to Trichophyton spp.). The duration of antifungal therapy required is not yet fully established\[^10\].

Presentation

Symptoms
- Shortness of breath may develop over hours or days but is usually progressive rather than sudden.
- A history of poor control is common.
- Often there has been a recent increase in use of reliever inhalers, with decreasing response.
- Possible respiratory tract infection or exposure to an allergen or trigger.

Signs
- The patient will usually appear pink. Cyanosis is a serious sign.
- Their respiratory rate is raised.
- Tachycardia is usual and may be increased by use of beta\(_2\) agonists.
- Accessory muscles of respiration are employed (best assessed by palpation of the neck muscles) and the chest appears hyper-inflated.
- In normal breathing, the ratio of the duration of inspiration to expiration is about 1:2 but, as asthma becomes more severe, the expiratory phase becomes relatively more prolonged.
- Wheeze is usually expiratory but may also be inspiratory in more severe asthma.

Pitfalls
- A very tight chest may not wheeze at all due to poor air entry. Beware the silent chest.
- Patients with severe or life-threatening asthma may not appear distressed.
- The presence of any relevant abnormality should alert the doctor.
- Where signs/symptoms cross categories of severity, always assign the most severe category.

- Pulsus paradoxus is no longer recommended as a reliable indicator of the severity of an asthma attack.

Differential diagnosis
Status asthmaticus must be distinguished from other causes of acute breathlessness, including:

- Wheezing in children, which can be caused by a variety of infective conditions - eg, respiratory syncytial virus - causing bronchiolitis.
- Foreign body inhalation and other causes of stridor (eg, epiglottitis, croup, tracheitis, vascular ring, tracheomalacia, etc).
- Allergic reaction, anaphylaxis.
- Primary pulmonary hypertension.
- Pneumothorax with or without asthma.
- Inhalation injury.
- Acute exacerbations of chronic obstructive pulmonary disease (COPD).
- Bronchiectasis.
- Lung cancer.
Cardiac failure ('cardiac asthma').

Assessment[5]
The following summary applies to adults. See separate Management of Childhood Asthma article.

Many deaths from asthma are preventable. Delay can be fatal. Factors leading to poor outcome include:

- Clinical staff failing to assess severity by objective measurement.
- Patients or relatives failing to appreciate severity.
- Under-use of corticosteroids.

Regard each emergency asthma consultation as for acute severe asthma until shown otherwise. Assess and record:

- Peak expiratory flow rate (PEFR).
- Heart and respiratory rates.
- Oxygen saturation (by pulse oximetry).

Patients with severe or life-threatening attacks may not be distressed and may not have all the abnormalities listed below. The presence of any should alert the doctor.

Assessment of severity[5]
If a patient has signs and symptoms across categories, always treat according to their most severe features.

- Moderate asthma exacerbation:
  - PEFR >50-75% best or predicted.
  - Oxygen saturations (SpO₂) ≥92%.
  - Speech normal.
  - Respiration <25 breaths per minute.
  - Pulse <110 beats per minute.

- Acute severe asthma - any one of:
  - PEFR 33-50% best or predicted.
  - Oxygen saturations (SpO₂) ≥92%.
  - Can't complete sentences.
  - Respiratory rate ≥25 breaths per minute.
  - Pulse ≥110 beats per minute.

- Life-threatening asthma - any one of the following in a patient with severe asthma:
  - PEFR <33 best or predicted.
  - Oxygen saturations (SpO₂) <92%.
  - Silent chest, cyanosis or poor respiratory effort.
  - Arrhythmia or hypotension.
  - Exhaustion, altered consciousness.

Management

Moderate asthma
Treat at home or in the surgery and assess response to treatment.

- If PEFR >50-75% predicted/best:
  - Beta₂ bronchodilator. Depending on the equipment available, use either:
    - Beta₂ bronchodilator via spacer (give four puffs initially and give a further two puffs every two minutes according to response up to maximum of 10 puffs); or
    - Nebuliser (preferably oxygen-driven) with salbutamol 5 mg.
  - Give prednisolone 40-50 mg.
  - Continue or increase usual treatment.

- If good response to first treatment (symptoms improved, respiration and pulse settling and PEFR >50%), continue or increase usual treatment and continue prednisolone.
  - Admit to hospital if there are any of the following:
    - Life-threatening features.
    - Features of acute severe asthma present after initial treatment.
    - Previous near-fatal asthma.

- Lower threshold for admission if afternoon or evening attack, recent nocturnal symptoms or hospital admission, previous severe attacks, patient unable to assess own condition, or concern over social circumstances.
Acute severe asthma
Consider admission.

- Oxygen to maintain SpO\textsubscript{2} 94-98\% if available.
- β\textsubscript{2} bronchodilator: nebuliser (preferably oxygen-driven) with salbutamol 5 mg, or via spacer (give four puffs initially and give a further two puffs every two minutes according to response up to maximum of 10 puffs).
- Prednisolone 40-50 mg or intravenous (IV) hydrocortisone 100 mg.
- If there is no response in acute severe asthma: ADMIT. If admitting the patient to hospital:
  - Stay with patient until the ambulance arrives.
  - Send written assessment and referral details to the hospital.
  - β\textsubscript{2} bronchodilator via oxygen-driven nebuliser in the ambulance.
Life-threatening asthma

Arrange immediate admission.

- Oxygen to maintain \( \text{SpO}_2 \) 94-98%.
- Beta\(_2\) bronchodilator and ipratropium: nebuliser (preferably oxygen-driven) with salbutamol 5 mg and ipratropium 0.5 mg; or via spacer (give four puffs initially and give a further two puffs every two minutes according to response up to maximum of 10 puffs).
- Prednisolone 40-50 mg or IV hydrocortisone 100 mg immediately.

GP review within two working days of discharge from hospital

- Monitor symptoms and PEFR.
- Check inhaler technique.
- Written asthma action plan.
- Modify treatment according to guidelines for chronic persistent asthma.
- Address potentially preventable contributors to admission.

Referral

In addition to the indications for admission outlined above, the following factors should lower the threshold for admission:\[11\]:

- People under 18 years.
- Poor concordance.
- Person lives alone.
- Psychological problems such as depression, and alcohol or drug misuse.
- Physical or learning disability.
- Previous near-fatal attack or brittle asthma.
- Persistent exacerbation despite an adequate dose of oral corticosteroids before presentation.
- Presentation at night or in the afternoon.
- Pregnancy.

Further hospital-based management\[5\]

Following initial assessments and initial treatment with oxygen, salbutamol and prednisolone or hydrocortisone, further management will depend on the severity of asthma and response to treatment. Further treatments may include intravenous magnesium and correction of fluid/electrolyte disturbances. The patient may need to be treated in the Intensive Care Unit (ICU).

Not all patients admitted to the ICU need ventilation, but those with worsening hypoxia or hypercapnia, drowsiness or unconsciousness and those who have had a respiratory arrest require intermittent positive pressure ventilation. Intubation in such patients is very difficult and should be performed by an anaesthetist or ICU consultant.

Evidence on the efficacy of bronchial thermoplasty for severe asthma shows some improvement in symptoms and quality of life, and reduced exacerbations and admission to hospital\[12\].

Complications

Complications of status asthmaticus include:

- Aspiration pneumonia.
- Pneumomediastinum.
- Pneumothorax.
- Rhabdomyolysis.
- Respiratory failure and arrest.
- Cardiac arrest.
- Hypoxic-ischaemic brain injury.

The risk of death is increased where there is delay in getting treatment, particularly time to starting steroids, comorbidities such as congestive heart failure or COPD and in smokers. Mortality is highest in the very young and the very old.

Prevention\[5\]

- All patients with asthma - but especially those with poorly controlled disease - should have access to education about their condition and to regular review, and should have an asthma action plan.
- In addition to an asthma register, an 'at-risk' asthma register may help. If 'at-risk' patients fail to attend for appointments this should be actively followed up.
- Those who are difficult to control need referral to specialist services.
- Be especially vigilant about those with psychosocial adverse factors too.
- Beta\(_2\)-agonist therapy used in isolation is only appropriate for those with the mildest variant of asthma.
- Receptionists, ambulance control workers and those who are first point of contact by patients must appreciate that a patient with asthma having difficulty breathing needs to be seen as an emergency.
Hospital admission should be an opportunity to review the patient's care plan.
Anyone who has required admission should be followed up by a respiratory physician for at least a year.
Patients who have had near-fatal asthma or brittle asthma should remain under specialist care indefinitely.

Further reading & references

- Global Initiative for Asthma (GINA)
- Why asthma still kills; Royal College of Physicians, August 2015
- International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma; European Respiratory Society (2014)
- British Guideline on the management of asthma; Scottish Intercollegiate Guidelines Network - SIGN (2016)
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