



Worsening asthma in adults

Part 2: Assessment and management of asthma exacerbations

Key points

- Undertake triage and risk-stratification of patients presenting in primary care with an asthma exacerbation to determine therapeutic management.
- Identify patients who are high risk or have acute severe asthma early and transfer to hospital.
- Inhaled bronchodilators and corticosteroids are the cornerstone of therapy.
- Assess patient response to therapy regularly and frequently (e.g. monitor every 15 minutes for the first hour and re-evaluate after one hour).
- Transfer patients to hospital if there is no response to treatment or deterioration despite treatment.
- Before discharging patients home after management in general practice, ensure they have a written asthma action plan, good inhaler technique and a review appointment organised.

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This second part of a two-part article discusses the assessment and management of patients who present to their GP with an asthma exacerbation. Moderate exacerbations can be managed in the community but urgent hospital transfer is required if the exacerbation is severe or the patient has high-risk features or deteriorates despite treatment.

The first part of this two-part article, in the December 2013 issue of *Medicine Today*, discussed early identification of worsening asthma and implementation of appropriate therapy by patients through self-monitoring and use of an asthma action plan.¹ In this second part of the article, we discuss assessment, risk stratification and management of patients who present with an asthma exacerbation in primary care.

A patient-centric approach, tailoring

therapy to match the severity of the current exacerbation and the patient's past history, should be the focus for all clinicians. A major decision is whether to treat in general practice or to transfer urgently to hospital. For those treated in general practice, frequent reassessment is required to monitor response to therapy. Management of children follows similar principles to that of adults but is sufficiently different that this article will focus only on management of acute asthma in adults.

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ASSESSMENT

Patients may present to their primary care physician during an episode of worsening asthma, either spontaneously or prompted by their asthma action plan. The spectrum of clinical features may range from very mild wheezing through to life-threatening asthma.

Early identification of patients requiring urgent transfer

On presentation, there should be an immediate assessment of 'A-B-C' (Airways, Breathing, Circulation) and of the need for emergency resuscitation, intubation or referral to the nearest hospital. Urgent transfer by ambulance is required not only for patients in cardiac or respiratory arrest but also for those with indicators of imminent arrest, including bradypnoea, physical exhaustion, altered consciousness (lethargy) or an apparently 'silent' chest.² For patients with severe or life-threatening asthma, treatment with bronchodilators and oxygen should be commenced immediately (as described below) while urgent transfer is being arranged. 'A' for airway should also include assessment of the possibility of anaphylaxis and the need for immediate administration of adrenaline.

Assessment of patient risk and exacerbation severity

Patients who are not in, or at imminent risk of, cardiac or respiratory arrest should be assessed rapidly to identify those with high-risk features (see the Box) and to stratify the exacerbation as mild, moderate or severe (see Table 1).³⁻⁹ Assessment should be carried out concurrently with prompt initiation of treatment. Risk assessment and severity stratification assist in the choice of therapy and the most suitable location to deliver that therapy (home, GP office or emergency department). In hospital and emergency settings, the more severe end of the spectrum is often referred to as 'acute severe asthma'.

After initial treatment has been commenced (as described below), it is important also to assess:

- the time course of the exacerbation (sudden onset or gradual worsening over days or weeks)
- the presence of any identifiable trigger for the exacerbation
- any management initiated before presentation

FEATURES ASSOCIATED WITH A HIGHER RISK OF DEATH FROM ASTHMA³⁻⁹

- Any previous near-fatal asthma episode requiring intubation
- Two or more asthma-related hospitalisations within the previous 12 months
- Three or more emergency department visits for asthma in the previous 12 months
- Requirement for three or more classes of asthma medications for control
- Frequent β_2 -agonist use (e.g. more than two 200-dose canisters of salbutamol 100 μg per month), particularly in the absence of regular inhaled corticosteroids
- Recent use of oral corticosteroids (a marker of severity of the episode)
- Ethnic and socioeconomic factors
- Previously documented reduced lung function
- Use of a major tranquilliser
- Food allergy

Care should also be taken with patients who have any of the following features.

- No current preventer medication or no action plan, or poor adherence to these
- Current smoking
- Current or past psychological illness
- Low socioeconomic background

- the frequency of recent bronchodilator use
- effectiveness of inhaler technique.

Not all that wheezes is asthma

Care should be taken to exclude important differential diagnoses for the presentation of shortness of breath with wheeze. Acute pulmonary oedema, or 'cardiac wheeze', is still commonly mistreated as asthma. Large airway tumours causing monophonic wheeze are similarly misdiagnosed. Vocal cord dysfunction is also a common mimic of acute severe asthma. Anaphylaxis is a medical emergency that may present with wheeze; however, its rapid onset and other clinical features, such as itching, urticaria, oedema of the tongue or lips and hypotension, help to differentiate it from asthma.

EXAMINATION

Significant examination findings that are useful to stratify severity of the exacerbation and to direct appropriate treatment are listed in Table 1. The 'end of the bed' test (assessing the patient's general condition and level of distress) is still particularly useful, and clinical judgement needs to be applied rather than just an algorithm. During auscultation, care should be taken with the apparently 'silent' chest, which is often mistaken by junior doctors as a clear chest but instead is a sign of very severe airflow limitation. Frequent

TABLE 1. CLINICAL ASSESSMENT OF ASTHMA EXACERBATIONS

Feature	Mild exacerbation	Moderate exacerbation	Acute severe asthma
Clinical features (the most severe feature determines the severity category)			
Breathlessness	When walking	With movement in bed	At rest
Talks in	Sentences	Phrases	Words, or cannot talk
Pulse rate (beats per minute)	<100	100 to 120	>120
FEV ₁ or PEF (% of predicted or % of personal best)	>75%	50 to 75%	PEF<50% or FEV ₁ <1 litre or unable to perform
O ₂ saturation by oximetry	>95%	90 to 95%	<90%
pCO ₂ on ABG measurement	ABG generally not needed	≤40 mmHg	>40 mmHg
Examination features that may be suggestive			
Respiratory rate	Normal or increased	Increased	>30 breaths per minute
Wheeze	Moderate, end-expiratory	Loud, pan-expiratory	Usually loud, but chest may be silent
Use of accessory muscles and suprasternal recession	Usually not	Increased	Increased; may have paradoxical thoracoabdominal movement
ABBREVIATIONS: ABG = arterial blood gases; FEV ₁ = forced expiratory volume in 1 second; PEF = peak expiratory flow.			

monitoring of vital signs, including respiratory rate, heart rate and peripheral oxygen saturation by pulse oximetry, is essential. Management of acute asthma is not a situation in which an algorithm can be applied and then left as ‘set and forget’.

INVESTIGATIONS

In primary care, measurement of respiratory rate, peak expiratory flow or forced expiratory volume in one second by spirometry, and oxygen saturation by pulse oximetry are important in the initial assessment of a patient with worsening asthma (Table 1). Where possible, oxygen saturation should be measured before supplemental oxygen is commenced. An oxygen saturation level below 90% when breathing room air or when oxygen is decreased or removed indicates clinical urgency. A peak expiratory flow below 50% of predicted or personal best indicates a severe exacerbation and that the patient is likely to need transfer.

Chest radiography is not routinely required in adults with an asthma exacerbation but is recommended if a

pneumothorax, pneumomediastinum or consolidation is suspected. In primary care, if a patient is so unwell that an x-ray is indicated then referral to an emergency department is probably appropriate.

In the hospital setting, arterial blood gases may be measured for more severe presentations or when the patient has low peripheral oxygen saturation (e.g. 92% or less on room air), to assess for evidence of hypercapnia (a marker of respiratory failure). In primary care, hypercapnia should be suspected if the patient becomes fatigued or somnolent, and urgent transfer to hospital should be arranged.

TO TREAT OR TRANSFER?

The first question the primary care physician needs to answer is ‘Does this patient require transfer to hospital?’ If the patient displays any features of acute severe asthma or life-threatening asthma (see Table 1), treatment should be started immediately and the patient should be transferred by ambulance to the nearest emergency department.

For moderate exacerbations, the primary care physician can initiate therapy as described below. However, assessment of the early response to therapy is a guide to the potential success of outpatient therapy. Frequent assessment is recommended while treatment continues. This may mean the patient is kept on site with frequent monitoring (e.g. every 15 minutes for the first hour), and re-evaluated by the physician one to two hours after initial treatment. Failure to respond to treatment should be taken seriously, and the patient referred to hospital. Patients who report on presentation in primary care that they have deteriorated despite adhering to their asthma action plan, including commencing oral corticosteroids, should also be considered for early transfer to hospital.

TREATMENT IN PRIMARY CARE

A guide to initial treatment of acute asthma exacerbations in primary care is outlined in Table 2 and the flowchart on page 23. The general principles behind treatment include the use of systemic corticosteroids

TABLE 2. INITIAL TREATMENT OF ASTHMA EXACERBATIONS^{2,10}

Management	Mild exacerbation	Moderate exacerbation	Acute severe asthma
Location of care	<ul style="list-style-type: none"> Can be managed in primary care if adequate monitoring available 	<ul style="list-style-type: none"> Can be initially managed in primary care if adequate monitoring available Transfer to acute care facility if not responding after 1 hour or deteriorating before then 	<ul style="list-style-type: none"> Commence bronchodilator therapy and oxygen as below, and Arrange immediate ambulance transfer to acute care facility
Controlled oxygen therapy (if available)	<ul style="list-style-type: none"> Usually not necessary 	<ul style="list-style-type: none"> If hypoxaemic; titrate to maintain SpO₂ between 93 and 95% (94 to 98% for pregnant women) 	<ul style="list-style-type: none"> If hypoxaemic; titrate to maintain SpO₂ between 93 and 95% (94 to 98% for pregnant women)
Short-acting β ₂ -agonists*	<ul style="list-style-type: none"> Salbutamol 100 µg via pMDI plus large volume spacer,* 4 to 10 inhalations (1 at a time), 3- to 4-hourly, or Terbutaline 500 µg dry powder inhaler, 2 to 4 inhalations (12 inhalations/day maximum), 3- to 4-hourly, or Salbutamol 2.5 to 5 mg via nebuliser, 3- to 4-hourly 	<ul style="list-style-type: none"> Salbutamol 100 µg via pMDI plus large volume spacer,* 4 to 10 inhalations, or Salbutamol 2.5 to 5 mg via nebuliser Administer initially every 20 minutes for three doses, then 1- to 4-hourly 	<ul style="list-style-type: none"> Salbutamol 5 mg via nebuliser If no response to the initial dose, repeat immediately and then every 15 to 30 minutes or give continuously If nebuliser and oxygen are not readily available, administer by pMDI as outlined for a moderate exacerbation
Ipratropium bromide	–	–	<ul style="list-style-type: none"> Ipratropium bromide 0.5 mg via nebuliser every 20 minutes for three doses, then 2- to 4-hourly
Corticosteroids*	<ul style="list-style-type: none"> Start regular daily ICS or ICS/LABA or increase the current maintenance preventer dose for at least 2 weeks[†] 	<ul style="list-style-type: none"> Prednisolone 25 to 50 mg orally, daily, usually for 5 to 10 days; taper dose if given for more than 2 weeks and Start regular daily ICS or ICS/LABA or increase current maintenance preventer dose for at least 2 weeks[†] Ensure inhaler technique is correct and adherence is optimised 	<ul style="list-style-type: none"> Prednisolone 50 mg orally, daily, usually for 5 to 10 days; taper dose if given for more than 2 weeks, or Hydrocortisone 100 mg IV, 6-hourly (or equivalent dose of alternative corticosteroid), then review and convert to oral therapy as soon as possible When able, start regular daily ICS or ICS/LABA or increase current maintenance preventer dose for at least 2 weeks[†] Ensure inhaler technique is correct and adherence is optimised
Adrenaline (for anaphylaxis only)	–	–	<ul style="list-style-type: none"> Adrenaline 0.5 mg (0.5 mL of 1:1000 ampoule) IM, or Adrenaline 0.3 mg IM via autoinjector

ABBREVIATIONS: ICS = inhaled corticosteroid; IM = intramuscular; IV = intravenous; LABA = long-acting β₂-agonist; pMDI = pressurised metered dose inhaler.

* Where the table refers to use of multiple puffs from a metered dose inhaler, they should be delivered one at a time, and by large volume spacer:

- For patients with mild to moderate exacerbations, the patient should take a single slow inhalation from the spacer after each actuation and hold the breath for a few seconds.
- For patients with more severe exacerbations, the tidal breathing method should be used. For each puff, actuate the inhaler immediately after each inhalation.
- Spacers should on purchase be pre-treated to reduce static charge by washing with detergent (without rinsing) and air-drying, so they are ready for immediate use in an emergency; if a pre-treated spacer is not available, the spacer should be primed with at least 20 puffs from a pressurised metered-dose inhaler.

[†] For patients not taking regular preventer medication, an exacerbation requiring treatment by a health professional usually indicates that ongoing daily ICS or ICS/LABA therapy is needed. In the context of an exacerbation, treatment should be started with high-dose ICS (high-level evidence) or with moderate dose ICS/LABA (consensus), and reduced to standard maintenance doses after 2 to 4 weeks. Ensure the patient is trained to use the inhaler correctly.

For patients already taking preventer medication, the ICS dose should be increased according to the current regimen:¹⁰

- For maintenance ICS or fixed-dose ICS/eformoterol, quadruple or double patient's usual dose.
- For budesonide/eformoterol for maintenance and relief, increase as-needed use according to the SMART action plan (maximum dose of eformoterol, 72 µg/day).
- For fixed dose fluticasone/salmeterol, add high-dose ICS inhaler to quadruple or double the patient's usual ICS dose.
- Doubling is more appropriate than quadrupling if the patient is already taking a high ICS dose.
- Continue the high preventer dose for at least 2 weeks, then reduce to a maintenance dose.
- Ensure inhaler technique is correct and adherence is optimised.

to decrease airway inflammation and β_2 -agonists to reverse bronchoconstriction. A general guide is to treat early and aggressively with regular bronchodilators, supplemental oxygen if required and oral or systemic corticosteroids. Regular and frequent reassessment is required to monitor response to therapy.

Resources for managing acute asthma exacerbations in primary care

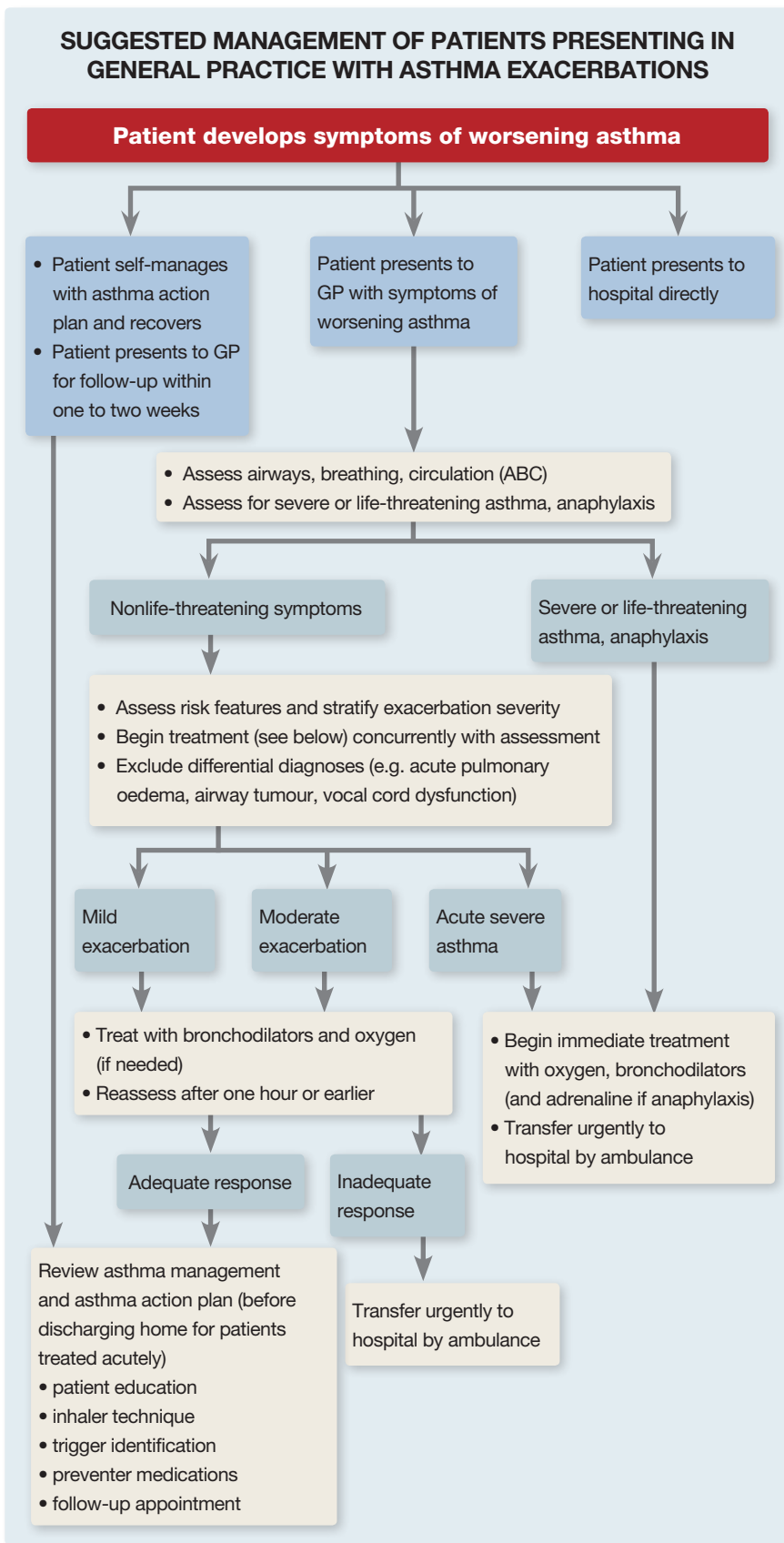
As part of their accreditation, primary care practices in Australia are required to have access to resuscitation equipment, materials for intravenous access, oxygen, a peak flow meter and a pulse oximeter.¹¹ Emergency medical supplies for the ‘doctor’s bag’ are available through the Pharmaceutical Benefits Scheme, including salbutamol pressurised metered-dose inhaler or nebuliser solution, hydrocortisone and adrenaline.¹² Although a spacer is not mandatory for accreditation at present, it is essential for adequate delivery of salbutamol by pressurised metered-dose inhaler. A portable spirometer is also helpful for managing asthma exacerbations.

Initial treatment

Short-acting bronchodilators – all patients

Short-acting β_2 -agonists can be delivered by metered-dose inhaler via a large volume spacer, or by nebuliser. The former is recommended as the most cost-effective and efficient therapy in most situations, but it may be inappropriate for very severe exacerbations associated with rapid respiratory rate and poor oxygen saturation.¹³ Short-acting β_2 -agonist therapy may be started during a consultation as soon as an asthma exacerbation is diagnosed and then continued in a treatment room where the patient can be observed.

Plastic spacers should be pre-treated on purchase to reduce static charge by washing with detergent (without rinsing) and air-drying, so they are ready for immediate use in an emergency; if a pre-treated spacer is not available, the spacer should be primed



with at least 20 puffs of a pressurised metered-dose inhaler.¹⁴

Delivery of a β_2 -agonist by spacer depends on good patient technique and should be supervised by trained staff, using either the tidal breathing method or a single slow breath and breath hold per puff, depending on the patient's condition.

If a nebuliser is required (e.g. in patients with acute severe asthma while awaiting transfer to hospital), salbutamol solution can be nebulised using air or, if oxygen is needed, with 6 to 8 L/minute of oxygen via mask (see below for titration of oxygen therapy). If nebulisers are used, precautions should be taken to avoid transmission of infection to staff and other patients.¹⁵

Initial treatment with four to 10 puffs of salbutamol (delivered one puff at a time), or 2.5 to 5 mg of nebulised salbutamol solution, should be administered every 20 to 30 minutes, for a total of three doses. Readministration at a frequency tailored to the patient should be based on clinical response.

Inhaled short-acting anticholinergics (ipratropium) can augment β_2 -agonist therapy in acute severe asthma.¹⁶

Corticosteroids – almost all patients

Oral prednisolone (or, in some cases intravenous hydrocortisone) should be used for all patients with moderate to severe exacerbations and those who do not respond to initial β_2 -agonist therapy. This therapy should be started as soon as practicable, and if prednisolone (or prednisone) is available in the primary care practice, it should be initiated immediately if indicated. We use parenteral corticosteroids in patients whose symptoms have progressed despite the use of oral corticosteroids, patients with features of life-threatening asthma and those who are vomiting. Oral corticosteroids should usually be continued for five to 10 days.

The use of high-dose inhaled corticosteroids, if instituted early in the treatment of acute asthma exacerbations, may help relieve symptoms and reduce hospital admissions, with few side effects.¹⁷ The early up-titration of inhaled corticosteroids

and the use of written asthma action plans were discussed in detail in Part 1 of this article.¹ During an exacerbation of asthma, the inhaled corticosteroid dose should be increased for most patients (see Table 2), but there is insufficient evidence that inhaled corticosteroids can substitute for systemic corticosteroids in patients with moderate to severe exacerbations.

Most patients with an exacerbation severe enough to require acute care should be prescribed regular inhaled corticosteroid treatment on an ongoing basis, to reduce the risk of future exacerbations; this can most appropriately be started during discharge planning (as described below). When initiating inhaled corticosteroid treatment in the context of an exacerbation, available evidence supports the use of a high-dose inhaled corticosteroid, but by consensus, combination therapy with a moderate-dose inhaled corticosteroid and long-acting β_2 -agonist may be considered as an alternative.

Oxygen – controlled therapy in patients with hypoxaemia

Oxygen supplementation is used in patients with hypoxaemia to maintain peripheral oxygen saturation between 93 and 95% in adults (94 to 98% in pregnant women). However, the need for supplemental oxygen is a poor prognostic sign, and these patients will generally need referral to an emergency department for admission. Low-flow oxygen is sufficient in most patients, and titrating oxygen therapy against oxygen saturation level reduces the risk of increasing $p\text{CO}_2$, which sometimes occurs with the administration of high-flow oxygen during severe exacerbations.^{18,19} However, oxygen should not be withheld if oximetry is not available.

Adrenaline – essential first-line treatment for anaphylaxis but not recommended otherwise

Intramuscular or intravenous adrenaline is essential first-line treatment for bronchoconstriction caused by anaphylaxis. However, in the general management of acute

asthma, there seems to be no advantage in using adrenaline (a nonselective adrenergic agonist) rather than selective β_2 -agonists, and its risk profile is higher. Adrenaline is not currently recommended by guidelines for the management of acute asthma, except in the context of anaphylaxis.

Review of response to treatment after one hour or earlier

Once therapy has begun, it is important to assess response and to escalate therapy if there is deterioration despite treatment. Review of the severity of the exacerbation (as described in Table 1) one hour after therapy begins or earlier if the patient is deteriorating allows the clinician to determine whether there has been a response to, or a progression despite, treatment. This may help to identify patients who are suitable for community-based management versus those who will need ongoing observation and management in hospital.²⁰ Frequency of review depends on the severity of the exacerbation, the response to initial bronchodilator therapy and the general trend of improvement. For both community-based and inpatient management, patient measurements of peak flow can give an early indication of deterioration or improvement but should not be used in isolation to assess the safety of discharging the patient home.²¹ Hand-held spirometry performed by trained staff can provide a more formal assessment to supplement clinical observation. Decreasing frequency of the need for β_2 -agonist or oxygen therapy, and improved exercise tolerance are all markers of clinical improvement.

Escalation of therapy

Other therapies listed below may be available to primary care physicians (e.g. in the doctor's bag) but are not recommended for use outside a hospital setting. These therapies are best administered in a controlled and monitored environment, such as in the resuscitation bay of an emergency department or in an intensive care setting.

Magnesium – may be useful in acute severe asthma

Evidence on the use of intravenous or nebulised magnesium in acute exacerbations is mixed. In adults, magnesium may be beneficial in acute severe asthma or life-threatening asthma, but it has no significant benefits above standard care in the management of moderately severe exacerbations, and there is a small increase in risk of adverse outcomes.^{22,23} This is in contrast to data suggesting a benefit in children and adolescents with severe asthma exacerbations.²⁴

Intravenous β_2 -agonist – only in life-threatening asthma, and only with close monitoring in an intensive care unit

An intravenous β_2 -agonist probably confers no benefit over nebulised salbutamol and has greater toxicity. It should not be used in primary care.

Aminophylline – not recommended

Aminophylline was previously widely used in the treatment of moderate to severe exacerbations but is no longer recommended. It has been shown to have no additional benefit compared with standard care.²⁵ It has a very narrow therapeutic window and a significantly increased risk of adverse effects, including vomiting and arrhythmias. Its use is probably limited to patients with life-threatening asthma in an intensive care unit who have failed all other therapies.

Intubation

Ideally, patients should be referred to the emergency department before their asthma worsens to a point requiring intubation. Infrequently, primary care physicians may need to perform emergency endotracheal intubation for worsening asthma. The following factors suggest the potential need for intubation:

- decreasing level of consciousness
- slowing respiratory rate or apnoea in association with hypoxia
- persistently elevated or rising pCO_2 ,³

MANAGEMENT AT HOME AND ONGOING REVIEW

Inhaled β_2 -agonists, as well as oral and inhaled corticosteroids, should be continued and weaned as tolerated by the patient. If oxygen is used then oxygen saturation should be checked during and after its withdrawal.

It can be considered safe to send patients home if:

- they do not require oxygen supplementation
- the frequency of β_2 -agonist requirements has decreased to a level that the patient can manage without significant impairment of daily activities (e.g. every two to four hours)

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- ideally, symptoms do not impact on activities of daily living
- ideally, lung function has improved and is at least 50% of predicted or personal best.

If a patient is to be sent home after management of an exacerbation in primary care, the clinician should be confident that the patient:

- has access to and can use all prescribed inhaled medications correctly
- is able and confident to monitor any improvement or deterioration in symptoms
- has a plan in place to present to a hospital if there is a deterioration
- is followed up in the practice in a timely manner, for example, within two to seven days, to ensure adequate resolution of the exacerbation.

Before leaving the practice, patients should be provided with the prescriptions, medications and training needed to continue managing the exacerbation at home. Patients should also be provided with:

- a five to ten day supply of oral corticosteroids for moderate to severe exacerbations (prednisolone 1 mg/kg/day, maximum 50 mg, taken in the morning – see Part 1 of this article)^{1,26}
- a prescription for regular preventer therapy and confirmation that they are able to obtain this medication
- an action plan and education as to when and how to implement the plan. This should include instructions for tapering β_2 -agonists as symptoms improve, and when and where to seek help if symptoms deteriorate
- training in how to take their medications (β_2 -agonist and preventer) and good inhaler technique observed on checking.

A follow-up appointment should be made within seven days, and preferably within two to three days depending on the severity of the asthma exacerbation. A telephone consultation may be useful to assess symptomatic improvement and also increases adherence to asthma action plans and follow up.²⁷ During the follow-up

appointment, the primary care physician should ensure the patient continues to take adequate preventer medications, which are titrated according to the patient's level of asthma control, and also review the asthma action plan and reinforce the education previously provided.

Particular care should be taken in reinforcing the need for ongoing asthma treatment, as adherence with inhaled corticosteroids has been found to drop by 50% within a week of discharge from the emergency department.²⁸

WHEN TO REFER TO A RESPIRATORY PHYSICIAN

After recovery from an exacerbation requiring treatment in primary care, referral to a respiratory physician is indicated if the patient:

- has severe persistent asthma
- has had more than one asthma exacerbation within a year requiring oral corticosteroids
- requires three or more classes of asthma medications for control
- has frequent β_2 -agonist use (e.g. more than one canister of short-acting β_2 -agonist per month), despite the use of regular inhaled corticosteroids.²⁷

CONCLUSION

The management of asthma exacerbations should be a continuum, starting with the patient's perception of worsening symptoms, the triggering of an individualised asthma action plan and the initiation of appropriate therapy suitable for the severity of the exacerbation. If needed, the patient should progress to assessment and risk stratification by the primary care physician, with frequent reassessment to monitor response to therapy. The target is to improve symptoms and assess safety to discharge the patient home or, if treatment fails, transfer them to a hospital setting.

Finally, for all patients, regardless of where they are managed, the occurrence of any exacerbation should prompt review of their asthma management and action

plan, in combination with patient education, with the aims of better control of asthma symptoms and prevention of future exacerbations. A patient-centric approach, tailoring therapy to match the severity of the current exacerbation and the patient's past history, should be the focus for all clinicians. **MT**

REFERENCES

A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

COMPETING INTERESTS: Dr Yan has received honoraria for giving lectures from AstraZeneca, GlaxoSmithKline, Novartis and Takeda (Nycomed). Associate Professor Reddel has participated in advisory boards for AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline and Novartis; has received consultancy fees from GlaxoSmithKline and research funding from AstraZeneca and GlaxoSmithKline; has provided independent continuing medical education for AstraZeneca, GlaxoSmithKline and Novartis; and is participating in a data safety monitoring committee for AstraZeneca, GlaxoSmithKline, Merck and Novartis. Dr Hamor: None.

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