Encouraging physical activity in adults and children with asthma, and identifying and managing exercise-induced bronchoconstriction in people with asthma, including elite athletes

ABOUT

This PDF is a print-friendly reproduction of the content included in the Clinical issues – Exercise section of the Australian Asthma Handbook at asthmahandbook.org.au/clinical-issues/exercise

Please note the content of this PDF reflects the Australian Asthma Handbook at publication of Version 1.2 (October 2016). For the most up-to-date content, please visit asthmahandbook.org.au

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ABBREVIATIONS

CFC      chlorofluorocarbon
COPD     chronic obstructive pulmonary disease
COX      cyclo-oxygenase
ED       emergency department
EIB      exercise-induced bronchoconstriction
FEV1     forced expiratory volume over one second
FVC      forced vital capacity
FSANZ    Food Standards Australia and New Zealand
GORD     gastro-oesophageal reflux disease
HFA      formulated with hydrofluoralkane propellant
ICS      inhaled corticosteroid
ICU      intensive care unit
IgE      Immunoglobulin E
IV       intravenous
LABA     long-acting beta2-adrenergic receptor agonist
LAMA     long-acting muscarinic antagonist
LTRA     leukotriene receptor antagonist
MBS      Medical Benefits Scheme
NIPPV    non-invasive positive pressure ventilation
NSAIDs   nonsteroidal anti-inflammatory drugs
OCS      oral corticosteroids
OSA      obstructive sleep apnoea
PaCO     carbon dioxide partial pressure on blood gas analysis
PaO      oxygen partial pressure on blood gas analysis
PBS      Pharmaceutical Benefits Scheme
PEF      peak expiratory flow
pMDI     pressurised metered-dose inhaler or ‘puffer’
SABA     short-acting beta2-adrenergic receptor agonist
LABA     long-acting beta2-adrenergic receptor agonist
TGA      Therapeutic Goods Administration

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ENDORSEMENT

The Australian Asthma Handbook has been officially endorsed by:
- The Royal Australian College of General Practitioners (RACGP)
- The Australian Primary Health Care Nurses Association (APNA)
- The Thoracic Society of Australia and New Zealand (TSANZ)

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Exercise and asthma

Overview

People with asthma can and should participate in physical activity. For adults or children involved in competitive sport, prescribers need to check which asthma medicines are permitted in the sport.

Exercise-induced bronchoconstriction can develop in people who do not have a history of known asthma, and can be the only or predominant symptom of asthma.

The diagnosis of exercise-induced bronchoconstriction is based on spirometric demonstration of abnormal reduction in lung function after exercise or a surrogate for exercise (defined as a fall in FEV₁ of at least 10% in adults or at least 13% in children).

Exercise-induced bronchoconstriction can be managed effectively with relievers and preventers (or both) and should not stop people with asthma participating in physical activity, including competitive sport.

In elite athletes, the regulations of sporting governing bodies must be considered when investigating suspected asthma or prescribing asthma medicines.

Table. Managing persistent exercise-induced respiratory symptoms in adults and adolescents
Please view and print this figure separately: https://www.asthmahandbook.org.au/table/show/85

Table. Managing persistent exercise-induced respiratory symptoms in children
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Physical activity and asthma
Physical activity, sport and asthma

Exercise-induced bronchoconstriction
Investigation and management of exercise-induced bronchoconstriction


eib

Elite athletes
Exercise-induced bronchoconstriction and asthma in elite athletes
### Table. Managing persistent exercise-induced respiratory symptoms in adults and adolescents

<table>
<thead>
<tr>
<th>Clinical scenario</th>
<th>Action</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Prior confirmed asthma diagnosis and recent asthma symptom control is assessed as partial or poor*</td>
<td>Start low-dose ICS (if not already using a preventer) or step up preventer regimen#</td>
<td>Review in 4–12 weeks†</td>
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<tr>
<td>Prior confirmed asthma diagnosis, recent asthma symptom control is assessed as partial or good,* and symptoms only occur with exercise</td>
<td>Exercise symptoms on most or all days</td>
<td>Consider alternative causes (e.g. poor cardiopulmonary fitness, upper airway dysfunction) EIB can occur despite otherwise well-controlled asthma</td>
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<td>Start low-dose ICS (if not already using a preventer) or step up preventer regimen# and review in 4–12 weeks†</td>
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<td></td>
<td>Salbutamol 15 minutes before exercise§</td>
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<td></td>
<td>Continue preventer if used</td>
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<tr>
<td>No previous diagnosis of asthma</td>
<td>Investigate as for asthma (history, physical examination and spirometry before and after bronchodilator)**</td>
<td>For adolescents, consider early referral to an accredited respiratory function laboratory for indirect challenge testing or respiratory physician for investigation to rule out other common causes of exercise-related respiratory symptoms</td>
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<td>If asthma confirmed, follow management recommendations</td>
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<td>If asthma not confirmed by spirometry, consider:</td>
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<td>• a trial of salbutamol 15 minutes before exercise§</td>
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<td></td>
<td>• whether regular preventer treatment is indicated</td>
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<td></td>
<td>• indirect challenge testing</td>
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<td></td>
<td>Review in 4–12 weeks†</td>
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<tr>
<td>Competing athletes</td>
<td>Consider indirect challenge testing. (Check which tests are</td>
<td>Advise warm-up before planned exercise</td>
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<td>required)</td>
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<td>Clinical scenario</td>
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<tr>
<td>required to demonstrate airway hyperresponsiveness) Check which medicines are permitted in the particular sport by consulting ASADA (<a href="http://www.asada.gov.au">www.asada.gov.au</a>) before prescribing any medicine</td>
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* See [Table. Definition of levels of recent asthma symptom control in adults and adolescents (regardless of current treatment regimen)](#)

# Before stepping up, check that inhaler technique is correct and adherence is adequate. See [Figure. Stepped approach to adjusting asthma medication in adults](#)

† If exercise-induced symptoms do not resolve after adjusting medicines, and checking adherence and inhaler technique, consider alternative diagnoses, referral to an accredited respiratory function laboratory for indirect challenge testing, or referral to a respiratory physician for assessment.

§ Reliever should also be taken at other times as needed to manage symptoms

** See [Figure. Steps in the diagnosis of asthma in adults](#)

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## Table. Managing persistent exercise-induced respiratory symptoms in children

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</thead>
<tbody>
<tr>
<td>Prior confirmed asthma diagnosis and recent asthma symptom control is assessed as partial or poor*</td>
<td>Consider preventer treatment based on age and pattern of symptoms§</td>
<td>Consider alternative causes (e.g. poor cardiopulmonary fitness, upper airway dysfunction)</td>
</tr>
<tr>
<td>Prior confirmed asthma diagnosis, recent asthma symptom control is assessed as partial or good,* and symptoms only occur with exercise</td>
<td>If child 2–14, consider regular montelukast (as sole preventer or added to ICS)# Review in 4–12 weeks†</td>
<td>If symptoms do not respond to montelukast alone, consider low-dose ICS#</td>
</tr>
<tr>
<td>Exercise symptoms most or all days</td>
<td>If child 6 years and over, salbutamol 15 minutes before exercise##</td>
<td>If child currently taking ICS/LABA combination, consider a treatment trial of ICS alone (and salbutamol taken before exercise) or ICS plus montelukast.</td>
</tr>
<tr>
<td>Exercise symptoms some days but not every day</td>
<td>If child 2–5 years, consider regular montelukast</td>
<td>Poor cardiopulmonary fitness is a common reason for exercise-related respiratory symptoms</td>
</tr>
<tr>
<td>No previous history of asthma</td>
<td>Investigate as for asthma (history, physical examination and spirometry before and after bronchodilator if child can do test)** If asthma confirmed, manage as for asthma If asthma not confirmed by spirometry (in children able to perform the test), consider: a trial of salbutamol 15 minutes before exercise</td>
<td>Some children with asthma avoid exercise</td>
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<tr>
<td>Clinical scenario</td>
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| • whether regular preventer treatment is indicated  
  • exercise testing for cardiopulmonary function to rule out exercise-related dyspnoea due to poor cardiopulmonary fitness  
  • indirect challenge testing | Review in 4–12 weeks† | |
| **Competing athletes** | Consider indirect challenge testing. (Check which tests are required to demonstrate airway hyperresponsiveness)  
  Check which medicines are permitted in the particular sport by consulting ASADA (www.asada.gov.au) before prescribing any medicine | Advise warm-up before planned exercise |

* Advise parents about potential adverse psychiatric effects of montelukast

† If exercise-induced symptoms do not resolve after adjusting medicines, and checking adherence and inhaler technique, consider alternative diagnoses, referral to an accredited respiratory function laboratory for indirect challenge testing, or referral to a respiratory physician for assessment.

§ See Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

See Table. Initial preventer treatment for children aged 0–5 years and Table. Initial preventer treatment for children aged 6 years and over

Before stepping up, check that inhaler technique is correct and adherence is adequate. See Figure. Stepped approach to adjusting asthma medication in children

** See Figure. Steps in the diagnosis of asthma in children

## Reliever should also be taken at other times as needed to manage symptoms

Notes

For some children with asthma, exercise-related symptoms are their only asthma symptoms.

PBS status of montelukast as at October 2016: Montelukast is not subsidised for children aged 2–5 years when used in addition to another preventer, or for children of any age when used addition to a long-acting beta-agonist.
Physical activity, sport and asthma

Recommendations

Recommend physical training to adults and children with asthma, as part of overall asthma management, for its beneficial effect on quality of life.

How this recommendation was developed

Evidence-based recommendation (Grade A)

Based on systematic literature review

Clinical question for literature search:

Does planned physical activity (e.g. structured physical activity programs, exercise training/intervention such as swimming, running, cycling) improve asthma outcomes (e.g. lung function, asthma control, quality of life, effect on exercise-induced bronchoconstriction), compared with no planned physical activity (e.g. usual clinical care, treatment regimens that do not included planned physical activity) in children and adults with asthma?

Key evidence considered:

- Arandelovic et al. 2007
- Basaran et al. 2006
- Chandratilleke et al. 2012
- Onur et al. 2011
- Shaw and Shaw, 2011
- Shaw and Shaw, 2011
- Singh et al. 2012
- Turner et al. 2011

See: Systematic review of physical activity and asthma outcomes

Advise patients that having asthma does not prevent them doing physical activity, including exercise training.

How this recommendation was developed

Evidence-based recommendation (Grade A)

Based on systematic literature review.

Clinical question for literature search:

Does planned physical activity (e.g. structured physical activity programs, exercise training/intervention such as swimming, running, cycling) improve asthma outcomes (e.g. lung function, asthma control, quality of life, effect on exercise-induced bronchoconstriction), compared with no planned physical activity (e.g. usual clinical care, treatment regimens that do not included planned physical activity) in children and adults with asthma?

Key evidence considered:

- Chandratilleke et al. 2012
- Turner et al. 2011

See: Systematic review of physical activity and asthma outcomes
Reassure patients that exercise-induced bronchoconstriction can be managed effectively and should not be a reason to avoid physical activity.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

For adults or children involved in competitive sport, check which asthma medicines are permitted in the sport before prescribing.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

More information

Benefits of physical activity (exercise) among people with asthma

Regular, moderately intense physical activity improves cardiopulmonary fitness and quality of life in people with asthma, and is well tolerated, but has no effect on lung function or asthma symptoms.\(^3\)

These conclusions are based on a meta-analysis\(^3\) of randomised controlled trials clinical trials that involved 'physical training', defined as any type of whole-body aerobic exercise lasting at least 20 minutes and undertaken twice a week for a minimum duration of 4 weeks, which included running, cycling, treadmill, swimming, circuit training, pool exercises and step-ups. Various aerobic training programs involved multiple types of activity in a structured program (e.g. supervised warm-up, stretching, aerobic exercise and endurance exercises, followed by cooling down). Some studies involved both supervised and home-based exercises.\(^3\)

Evidence for specific types of physical activity

There is not enough evidence to recommend one form of physical activity over another in people with asthma. Current evidence does not support the historical belief that swimming is the preferred form of physical training for people with asthma, but few studies have compared effects of swimming with those of other activities:

- Swimming appears to improve lung function in children\(^9,10\) and is well tolerated.\(^9\)
- Overall, swimming does not appear to improve lung function in adults with asthma;\(^11\) but some studies have reported that swimming in non-chlorinated pools improved lung function in adults.\(^3\)
- Humid air above the surface of swimming pools might be less likely to trigger asthma than dry air environments.
  However, repeated chlorine exposure over time is associated with chronic airway injury.\(^10\)

There is not enough evidence to determine the benefits of other types of exercises, such as tai chi and chi kung (qi gong), in people with asthma.

Safety considerations for physical activity

Airway injury due to cold air, dry air, or air pollutants (including chlorine in indoor pools) is associated with development of exercise-induced bronchoconstriction in elite athletes.\(^12\) Cold air, dry air or air pollutants may also trigger asthma symptoms,\(^13,14\) particularly in athletes.\(^13\)

Anti-doping agencies

Australian Sports Anti-Doping Authority
The Australian Sports Anti-Doping Authority (ASADA) is the Australian federal government statutory authority with a mission to protect Australia’s sporting integrity through the elimination of doping.

Go to: ASADA or call 13 000 ASADA (13 000 27232)
Go to: ASADA’s Check your substances webpage

World Anti-Doping Agency
The World Anti-Doping Agency (WADA) is the international independent anti-doping agency composed of representatives from the Olympic movement and public authorities from around the world. Its mission is to lead a collaborative worldwide campaign for doping-free sport.

References

Investigation and management of exercise-induced bronchoconstriction

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Investigating exercise-induced bronchoconstriction

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Investigating exercise-induced bronchoconstriction in adults and children with asthma

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**Without known asthma**
Investigating exercise-induced respiratory symptoms in people without a diagnosis of asthma

eib/investigation/without-known-asthma
Investigating exercise-induced bronchoconstriction in people with asthma

Recommendations

Before altering treatment to manage exercise-related symptoms, review asthma and rule out other causes.

How this recommendation was developed
Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

For an adult or child with asthma who has new-onset or worsening symptoms that suggest exercise-induced bronchoconstriction, ask about:

- the type of physical activity and environment that provokes symptoms
- timing of symptom onset (symptoms of exercise-induced bronchoconstriction are typically worst 5–10 minutes after stopping exercise, not during exercise)
- exposure to allergens or other triggers.

How this recommendation was developed
Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

If the patient is already using a preventer medicine, check adherence and inhaler technique.

How this recommendation was developed
Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

For adults and for children able to do the spirometry test reliably, perform or arrange spirometry before and after bronchodilator.

Notes
If reliable equipment and appropriately trained staff are available, spirometry can be performed in primary care. If not, refer to an appropriate provider such as an accredited respiratory function laboratory.

Most children aged 6 years and older are able to perform spirometry reliably.

How this recommendation was developed
Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

Consider the possibility of an alternative cause for new-onset exercise-related symptoms, including:

- poor cardiopulmonary fitness
- upper airway dysfunction (relatively common in young women)
- hyperventilation
- psychological conditions (e.g. anxiety)
• obesity
• cardiac abnormalities
• other lung conditions (including COPD, infection).

Consider further investigations for cardiopulmonary function to rule out exercise-related dyspnoea due to poor cardiopulmonary fitness or left ventricular dysfunction.

More information

Exercise-induced bronchoconstriction and asthma
Exercise-induced bronchoconstriction is a manifestation of airway hyperresponsiveness. Exercise-induced bronchoconstriction is one of the first symptoms to appear when asthma control is suboptimal, and one of the last symptoms to resolve with treatment.

Asthma control measured by the Asthma Score does not correlate with the finding of exercise-induced bronchoconstriction. Exercise-induced bronchoconstriction can occur despite well-controlled asthma.

Symptoms and signs of exercise-induced bronchoconstriction
Symptoms of exercise-induced bronchoconstriction include cough, wheeze, a feeling of tightness in the chest, breathlessness, excessive mucus production. Some children experience chest pain with exercise-induced bronchoconstriction. Young children recover from exercise-induced bronchoconstriction faster than older children and adults.

Symptoms typically peak at 5–10 mins after exercise unlike physiological exercise-induced dyspnoea, which resolves rapidly when the person stops the strenuous activity. (Physiological exercise-induced dyspnoea is a normal response and does not require treatment.) Because exercise-induced bronchoconstriction usually occurs after exercise, it may not affect exercise performance.

After an episode of exercise-induced bronchoconstriction, approximately 50% of people with this condition experience a refractory period of 2–3 hours, during which they do not develop bronchoconstriction even if they exercise. Some athletes make use of this phenomenon to their advantage.

Exercise-related wheezing and breathlessness are poor predictors of exercise-induced bronchoconstriction, particularly in elite athletes and adolescents. Other diagnoses associated with consistent exercise-induced symptoms in adolescents include normal physiological exercise limitation, with and without poor cardiopulmonary fitness, upper airway dysfunction and hyperventilation.
**Definition and prevalence of exercise-induced bronchoconstriction**

Exercise-induced bronchoconstriction is transient narrowing of the lower airways, occurring after vigorous exercise.\(^1\) It may occur in people with asthma or in people who do not have a history of known asthma.\(^1\) It is defined as a reduction in FEV\(_1\) from the value measured before exercise of 10% or more in adults\(^1\) and 13% or more in children. In people with asthma who experience exercise-induced bronchoconstriction, exercise does not cause asthma but is an asthma trigger.\(^1\) Recovery from exercise-induced bronchoconstriction is usually spontaneous. FEV\(_1\) usually returns to 95% baseline value within 30–90 minutes.\(^12\) Up to 90% of people with asthma and 50% of competitive athletes may experience exercise-induced bronchoconstriction.\(^1\) An estimated 18–26% of school children experience exercise-induced bronchoconstriction.\(^13\)

**Note:** The term ‘exercise-induced asthma’ is no longer used.\(^1\)

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**Correct use of inhaler devices**

The majority of patients do not use inhaler devices correctly. Australian research studies have reported that only approximately 10% of patients use correct technique.\(^14, 15\)

High rates of incorrect inhaler use among children with asthma and adults with asthma or COPD have been reported,\(^16, 17, 18, 19, 20\) even among regular users.\(^21\) Regardless of the type of inhaler device prescribed, patients are unlikely to use inhalers correctly unless they receive clear instruction, including a physical demonstration, and have their inhaler technique checked regularly.\(^22\)

Poor inhaler technique has been associated with worse outcomes in asthma and COPD. It can lead to poor asthma symptom control and overuse of relievers and preventers.\(^16, 22, 23, 24, 25\) In patients with asthma or COPD, incorrect technique is associated with a 50% increased risk of hospitalisation, increased emergency department visits and increased use of oral corticosteroids due to flare-ups.\(^21\)

Correcting patients’ inhaler technique has been shown to improve asthma control, asthma-related quality of life and lung function.\(^26, 27\)

**Common errors and problems with inhaler technique**

Common errors with manually actuated pressurised metered dose inhalers include:\(^22\)

- failing to shake the inhaler before actuating
- holding the inhaler in wrong position
- failing to exhale fully before actuating the inhaler
- actuating the inhaler too early or during exhalation (the medicine may be seen escaping from the top of the inhaler)
- actuating the inhaler too late while inhaling
- actuating more than once while inhaling
- inhaling too rapidly (this can be especially difficult for children to overcome)
- multiple actuations without shaking between doses.

Common errors for dry powder inhalers include:\(^22\)

- not keeping the device in the correct position while loading the dose (horizontal for Accuhaler and vertical for Turbuhaler)
- failing to exhale fully before inhaling
- failing to inhale completely
- inhaling too slowly and weakly
- exhaling into the device mouthpiece before or after inhaling
- failing to close the inhaler after use
- using past the expiry date or when empty.

Other common problems include:

- difficulty manipulating device due to problems with dexterity (e.g. osteoarthritis, stroke, muscle weakness)
- inability to seal the lips firmly around the mouthpiece of an inhaler or spacer
- inability to generate adequate inspiratory flow for the inhaler type
• failure to use a spacer when appropriate
• use of incorrect size mask
• inappropriate use of a mask with a spacer in older children.

How to improve patients’ inhaler technique

Patients’ inhaler technique can be improved by brief education, including a physical demonstration, from a health professional or other person trained in correct technique. The best way to train patients to use their inhalers correctly is one-to-one training by a healthcare professional (e.g. nurse, pharmacist, GP, specialist), that involves both verbal instruction and physical demonstration. Patients do not learn to use their inhalers properly just by reading the manufacturer’s leaflet. An effective method is to assess the individual’s technique by comparing with a checklist specific to the type of inhaler, and then, after training in correct technique, to provide written instructions about errors (e.g. a sticker attached to the device). The National Asthma Council information paper on inhaler technique includes checklists for correct technique with all common inhaler types used in asthma or COPD.

Inhaler technique must be rechecked and training must be repeated regularly to help children and adults maintain correct technique.

Spirometry in diagnosis and monitoring

Spirometry is the best lung function test for diagnosing asthma and for measuring lung function when assessing asthma control. Spirometry can:

• detect airflow limitation
• measure the degree of airflow limitation compared with predicted normal airflow (or with personal best)
• demonstrate whether airflow limitation is reversible.

It should be performed by well-trained operators with well-maintained and calibrated equipment. Before performing spirometry, check if the person has any contraindications (e.g. myocardial infarction, angina, aneurysm, recent surgery, suspected pulmonary embolism, suspected pneumothorax, fractured ribs). Advise them to stop if they become dizzy.

Clearly explain and physically demonstrate correct spirometry technique:

• Sit upright with legs uncrossed and feet flat on the floor and do not lean forward.
• Breathe in rapidly until lungs feel absolutely full. (Coaching is essential to do this properly.)
• Do not pause for more than 1 second.
• Place mouthpiece in mouth and close lips to form a tight seal.
• Blast air out as hard and fast as possible and for as long as possible, until the lungs are completely empty or you are unable to blow out any longer.
• Remove mouthpiece.

Repeat the test until you obtain three acceptable tests and these meet repeatability criteria.

Acceptability of test

A test is acceptable if all the following apply:

• forced expiration started immediately after full inspiration
• expiration started rapidly
• maximal expiratory effort was maintained throughout the test, with no stops
• the patient did not cough during the test
• the patient did not stop early (before 6 seconds for adults and children over 10 years, or before 3 seconds for children under 10 years).

Record the highest FEV₁ and FVC result from the three acceptable tests, even if they come from separate blows.
Repeatability criteria

Repeatability criteria for a set of acceptable tests are met if both of the following apply:  
- the difference between the highest and second-highest values for FEV$_1$ is less than 150 mL  
- the difference between the highest and second-highest values for FVC is less than 150 mL.

For most people, it is not practical to make more than eight attempts to meet acceptability and repeatability criteria.

Testing bronchodilator response (reversibility of airflow limitation)

Repeat spirometry 10-15 minutes after giving 4 separate puffs of salbutamol (100 mcg/actuation) via a pressurised metered-dose inhaler and spacer.  
(For patients who have reported unacceptable side-effects with 400 mcg, 2 puffs can be used.)

For adults and adolescents, record a clinically important bronchodilator response if FEV$_1$ increases by $\geq$ 200 mL and $\geq$ 12%.

For children, record a clinically important bronchodilator response if FEV$_1$ increases by $\geq$ 12%.

Upper airway dysfunction

Upper airway dysfunction is intermittent, abnormal adduction of the vocal cords during respiration, resulting in variable upper airway obstruction. It often mimics asthma and is commonly misdiagnosed as asthma. It can cause severe acute episodes of dyspnoea that occur either unpredictably or due to exercise. Inspiratory stridor associated with vocal cord dysfunction is often described as 'wheezing', but symptoms do not respond to asthma treatment. Upper airway dysfunction can coexist with asthma. People with asthma who also have upper airway dysfunction experience more symptoms than those with asthma alone and this can result in over-treatment if vocal cord dysfunction is not identified and managed appropriately.

Upper airway dysfunction probably has multiple causes. In some people it is probably due to hyperresponsiveness of the larynx in response to intrinsic and extrinsic triggers. Triggers can include exercise, psychological conditions, airborne irritants, rhinosinusitis, gastro-esophageal reflux disease, and medicines.

Upper airway dysfunction should be considered when spirometry shows normal FEV$_1$/FVC ratio in a patient with suspected asthma or symptoms do not respond to short-acting beta$_2$ agonist reliever. The shape of the maximal respiratory flow loop obtained by spirometry may suggest the diagnosis. Direct observation of the vocal cords is the best method to confirm the diagnosis of upper airway dysfunction.

References


Investigating exercise-induced respiratory symptoms in people without a diagnosis of asthma

Recommendations

For adults or children with exercise-related respiratory symptoms who do not have a previous asthma diagnosis, investigate as for patients with suspected asthma: take a history, perform a physical examination and perform or arrange spirometry (before and after bronchodilator).

See: Diagnosing asthma in adults
See: Diagnosing asthma in children

Notes

If reliable equipment and appropriately trained staff are available, spirometry can be performed in primary care. If not, refer to an appropriate provider such as an accredited respiratory function laboratory.

Most children aged 6 years and older are able to perform spirometry reliably.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

Do not rely on peak expiratory flow meters to investigate exercise-induced bronchoconstriction.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Weiler et al. 2010

In younger children unable to perform spirometry, investigate as for child with suspected asthma.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

Consider the possibility of an alternative cause for exercise-related symptoms, including:

- poor cardiopulmonary fitness
- upper airway dysfunction
- exercise-induced dyspnoea
- hyperventilation
- psychological conditions (e.g. anxiety)
- obesity
- cardiac abnormalities
- other lung conditions (including COPD, bronchiolitis, infection).
Consider exercise testing for cardiopulmonary function to rule out exercise-related dyspnoea due to poor cardiopulmonary fitness.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

In patients with exercise-related respiratory symptoms but without a clear diagnosis of asthma, do not initiate inhaled corticosteroid treatment before ruling out alternative diagnoses (e.g. upper airway dysfunction), because it is much more difficult to confirm the diagnosis after the person has begun inhaled corticosteroid treatment.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

In children, if symptoms only occur during exercise, consider specialist referral for investigation (e.g. paediatric respiratory physician).

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

For adolescents, consider objective testing (e.g. referral to an accredited respiratory function laboratory for indirect challenge testing) or referral to a paediatric respiratory physician for assessment.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Tilles, 2010
- Towns and van Asperen, 2009
- Weinberger and Abu-Hasan, 2007

If the post-bronchodilator spirometry reading demonstrates acute reversibility of airflow limitation, and other diagnoses have been excluded, make the diagnosis of asthma and manage according to the individual's age, pattern of symptoms and risk factors.
If history is consistent with exercise-induced bronchoconstriction but other investigations do not demonstrate variable airflow limitation (e.g. spirometry before and 10–15 minutes after bronchodilator shows no or little response), consider referral to a respiratory physician for investigation or referral to an accredited respiratory function laboratory for indirect challenge testing.

If the history is consistent with exercise-induced bronchoconstriction and indirect challenge test is positive, this confirms the diagnosis of asthma.

If initial indirect challenge test is negative, consider referring patient for a sports-specific field challenge test or refer to a respiratory physician.

Challenge tests should be performed only in accredited respiratory function laboratories.

If the person is involved in competitive sport, check whether specific tests are required to confirm the presence of exercise-induced bronchoconstriction before medicines are permitted.

Note: Testing rules differ between competitive sports – check with ASADA.

More information
Symptoms of exercise-induced bronchoconstriction

Symptoms of exercise-induced bronchoconstriction include cough, wheeze, a feeling of tightness in the chest, breathlessness, excessive mucus production. Some children experience chest pain with exercise-induced bronchoconstriction. Young children recover from exercise-induced bronchoconstriction faster than older children and adults.

Symptoms typically peak at 5–10 mins after exercise – unlike physiological exercise-induced dyspnoea, which resolves rapidly when the person stops the strenuous activity. (Physiological exercise-induced dyspnoea is a normal response and does not require treatment.) Because exercise-induced bronchoconstriction usually occurs after exercise, it may not affect exercise performance.

After an episode of exercise-induced bronchoconstriction, approximately 50% of people with this condition experience a refractory period of 2–3 hours, during which they do not develop bronchoconstriction even if they exercise. (Some athletes make use of this phenomenon to their advantage.)

Exercise-related wheezing and breathlessness are poor predictors of exercise-induced bronchoconstriction, particularly in elite athletes and adolescents. Other diagnoses associated with consistent exercise-induced symptoms in adolescents include normal physiological exercise limitation, with and without poor cardiopulmonary fitness, upper airway dysfunction and hyperventilation.

Definition and prevalence of exercise-induced bronchoconstriction

Exercise-induced bronchoconstriction is transient narrowing of the lower airways, occurring after vigorous exercise. It may occur in people with asthma or in people who do not have a history of known asthma.

It is defined as a reduction in FEV₁ from the value measured before exercise of 10% or more in adults and 13% or more in children.

In people with asthma who experience exercise-induced bronchoconstriction, exercise does not cause asthma but is an asthma trigger. Recovery from exercise-induced bronchoconstriction is usually spontaneous. FEV₁ usually returns to 95% baseline value within 30–90 minutes.

Up to 90% of people with asthma and 50% of competitive athletes may experience exercise-induced bronchoconstriction.

An estimated 18–26% of school children experience exercise-induced bronchoconstriction.

Note: The term ‘exercise-induced asthma’ is no longer used.

Aetiology of exercise-induced bronchoconstriction

Both genetics and environment may contribute to exercise-induced bronchoconstriction.

Exercise-induced bronchoconstriction occurs when a person’s ventilatory rate is high and their airways must heat and humidify a large volume of air in a short time. Dehydration of the airway leads to release of inflammatory mediators within the airway and contraction of airway smooth muscle. Dry air is one risk factor.

Exercise-induced bronchoconstriction in athletes who do not have chronic asthma may have different pathogenesis and presentation than exercise-induced bronchoconstriction in people with asthma. Elite athletes often report onset of exercise-induced bronchoconstriction after age 20 years and after many years of high-level training.

In elite athletes, exercise-induced bronchoconstriction is probably due to chronic injury to airway epithelium associated with long-term frequent prolonged high ventilation rates in the presence of environmental exposure to cold air, dry air, and airborne pollutants such as ozone, particulate matter:

- The high prevalence of exercise-induced bronchoconstriction in ice-rink athletes has been linked to inhalation of cold dry air in combination with airborne pollutants from fossil-fuelled ice resurfacing machines
- Exercise-induced bronchoconstriction in skiers and other winter athletes has been linked to injury of airway epithelium due to conditioning large volumes of cold dry air
- The high prevalence of asthma and exercise-induced bronchoconstriction reported among competitive swimmers has been associated with exposure to chlorine in indoor swimming pools
- The increased prevalence of exercise-induced bronchoconstriction among distance runners, compared with the general population, has been attributed to exposure to high levels of airborne allergens and ozone
• Certain airborne viruses inhaled during exercise may also contribute to exercise-induced bronchoconstriction.¹

**Exercise-induced bronchoconstriction in people without a previous asthma diagnosis**

Exercise-induced bronchoconstriction in people without a previous diagnosis of asthma can be associated with airway inflammation, but is not always. Laboratory studies show that exercise-induced bronchoconstriction is likely to respond to inhaled corticosteroids if it is associated with airway inflammation and the presence of eosinophils.¹ However, sputum testing is not necessary to make the diagnosis.

**Upper airway dysfunction**

Upper airway dysfunction is intermittent, abnormal adduction of the vocal cords during respiration, resulting in variable upper airway obstruction. It often mimics asthma²,⁴ and is commonly misdiagnosed as asthma.⁸,²³ It can cause severe acute episodes of dyspnoea that occur either unpredictably or due to exercise.⁸ Inspiratory stridor associated with vocal cord dysfunction is often described as ‘wheezing’,⁸ but symptoms do not respond to asthma treatment.⁴,⁵

Upper airway dysfunction can coexist with asthma.² People with asthma who also have upper airway dysfunction experience more symptoms than those with asthma alone and this can result in over-treatment if vocal cord dysfunction is not identified and managed appropriately.²

Upper airway dysfunction probably has multiple causes.² In some people it is probably due to hyperresponsiveness of the larynx in response to intrinsic and extrinsic triggers.²,²⁴ Triggers can include exercise, psychological conditions, airborne irritants, rhinosinusitis, gastro-esophageal reflux disease, and medicines.⁴,²³

Upper airway dysfunction should be considered when spirometry shows normal FEV₁/FVC ratio in a patient with suspected asthma²³ or symptoms do not respond to short-acting beta₂ agonist reliever. The shape of the maximal respiratory flow loop obtained by spirometry may suggest the diagnosis.⁸ Direct observation of the vocal cords is the best method to confirm the diagnosis of upper airway dysfunction.²

**Exercise-related symptoms in adolescents**

In adolescents, exercise-related wheezing and breathlessness are poor predictors of exercise-induced bronchoconstriction. Only a minority of adolescents referred for assessment of exercise-induced respiratory symptoms show objective evidence of exercise-induced bronchoconstriction.³

For adolescents with exercise-related symptoms, common conditions that should be considered in the differential diagnosis include poor cardiopulmonary fitness, exercise-induced upper airway dysfunction and exercise-induced hyperventilation.⁷,⁶

In addition to spirometry, other objective tests (e.g. cardiopulmonary fitness testing, bronchial provocation tests) may be helpful to clarify the diagnosis and inform management.

▶️ See: [Investigation and management of exercise-induced bronchoconstriction](#)

**Challenge tests for exercise-induced bronchoconstriction**

**Role of challenge tests**

Self-reported symptoms are not sensitive enough to detect exercise-induced bronchoconstriction reliably or specific enough to rule out other conditions, particularly in elite athletes.¹,²⁵,¹⁴ Single office FEV₁ readings or peak expiratory flow measurement are not adequate to demonstrate exercise-induced bronchoconstriction.⁹

Standardised, objective bronchial provocation (challenge) tests using spirometry are necessary for the investigation of suspected exercise-induced bronchoconstriction in elite athletes. These tests involve serial spirometry measurements after challenge with exercise (or exercise surrogates e.g. dry powder mannitol, eucapnic voluntary hyperpnoea or hyperventilation, or hyperosmolar aerosols such as 4.5% saline).¹,⁹,¹⁸,²⁶ Severity of exercise-induced bronchoconstriction is assessed by percentage fall in FEV₁ after challenge.⁹

Challenge testing is mandated by sports governing bodies before the athlete is given permission to use some asthma medicines, and the required testing protocol varies between specific sports. The latest information is available from the Australian Sports Anti-Doping Authority (ASADA) and the World Anti-Doping Agency (WADA).
Challenge tests are also used in the investigation of exercise-related symptoms in recreational and non-athletes, when objective demonstration of exercise-induced bronchoconstriction is needed to guide management decisions.

Choice of challenge test

There is no single challenge test that will identify all individuals with exercise-induced bronchoconstriction. The most appropriate test or tests for an individual depend on clinical and individual factors:

- The eucapnic voluntary hyperpnoea test can provoke a severe response. For safety reasons, the eucapnic voluntary hyperpnoea test should only be used in adults who regularly exercise at high intensity (e.g. elite athletes). It should not be used in children.
- When an exercise challenge test is used, inhalation of dry air is recommended to diagnose or exclude exercise-induced bronchoconstriction because it increases the sensitivity of the test.
- Mannitol challenge can be used as an alternative to exercise provocation testing to investigate suspected exercise-induced bronchoconstriction, including in children.
- For safety reasons, exercise challenge in dry air should be avoided in patients with FEV$_1$ <70% predicted.

Referral

If challenge testing is needed, consider referring to a respiratory physician for investigation, or discussing with a respiratory physician before selecting which test to order. Do not test during a respiratory infection, or initiate inhaled corticosteroid treatment in the few weeks before challenge testing, because these could invalidate the result.

A list of accredited respiratory function laboratories is available from the Australian and New Zealand Society of Respiratory Science.

Anti-doping agencies

Australian Sports Anti-Doping Authority

The Australian Sports Anti-Doping Authority (ASADA) is the Australian federal government statutory authority with a mission to protect Australia’s sporting integrity through the elimination of doping.

Go to: ASADA or call 13 000 ASADA (13 000 27232)

Go to: ASADA’s Check your substances webpage

World Anti-Doping Agency

The World Anti-Doping Agency (WADA) is the international independent anti-doping agency composed of representatives from the Olympic movement and public authorities from around the world. Its mission is to lead a collaborative worldwide campaign for doping-free sport.

Go to: WADA

References


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Managing exercise-induced bronchoconstriction

In this section

**Adults**
Managing exercise-induced bronchoconstriction in adults

eib/management/adults

**Children**
Managing exercise-induced bronchoconstriction in children

eib/management/children
Managing exercise-induced bronchoconstriction in adults

Recommendations

If the person is involved in competitive sport (including recreational sport), check which medicines are permitted in the particular sport by consulting the Australian Sports Anti-Doping Authority (ASADA) before prescribing any medicine.

Go to: ASADA or call 13 000 ASADA (1300 027 232)
Go to: ASADA’s Drugs, medications, substances and methods in sport index web page
Go to: ASADA’s Check your substances web page

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

For an adult with asthma who does not need maintenance inhaled corticosteroid treatment (e.g. mild exercise-induced bronchoconstriction with no symptoms at other times), recommend salbutamol to be taken 15 minutes before exercise. The usual dose range is salbutamol 1–4 puffs via pMDI (100 mcg/actuation). Advise the person to take their reliever as needed to relieve asthma symptoms at other times.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons et al. 2013
- Weiler et al. 2010

For an adult who experiences exercise-related symptoms on most days and is not already using a preventer, consider daily treatment with an inhaled corticosteroid starting at a low dose. Advise the person to use salbutamol 15 minutes before exercise until the full effect of inhaled corticosteroid has been achieved (usually 2–4 weeks, but can be up to 12 weeks).

Table. Definitions of ICS dose levels in adults

<table>
<thead>
<tr>
<th>Inhaled corticosteroid</th>
<th>Low (mcg)</th>
<th>Medium (mcg)</th>
<th>High (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclometasone dipropionate †</td>
<td>100–200</td>
<td>250–400</td>
<td>&gt;400</td>
</tr>
<tr>
<td>Budesonide</td>
<td>200–400</td>
<td>500–800</td>
<td>&gt;800</td>
</tr>
<tr>
<td>Ciclesonide</td>
<td>80–160</td>
<td>240–320</td>
<td>&gt;320</td>
</tr>
<tr>
<td>Fluticasone furoate*</td>
<td>—</td>
<td>100</td>
<td>200</td>
</tr>
</tbody>
</table>

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons et al. 2013
- Weiler et al. 2010

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons et al. 2013
- Weiler et al. 2010

For an adult who experiences exercise-related symptoms on most days and is not already using a preventer, consider daily treatment with an inhaled corticosteroid starting at a low dose. Advise the person to use salbutamol 15 minutes before exercise until the full effect of inhaled corticosteroid has been achieved (usually 2–4 weeks, but can be up to 12 weeks).

Table. Definitions of ICS dose levels in adults

<table>
<thead>
<tr>
<th>Inhaled corticosteroid</th>
<th>Daily dose (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>Beclometasone dipropionate †</td>
<td>100–200</td>
</tr>
<tr>
<td>Budesonide</td>
<td>200–400</td>
</tr>
<tr>
<td>Ciclesonide</td>
<td>80–160</td>
</tr>
<tr>
<td>Fluticasone furoate*</td>
<td>—</td>
</tr>
<tr>
<td>Inhaled corticosteroid</td>
<td>Daily dose (mcg)</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td></td>
<td>Low</td>
</tr>
<tr>
<td><strong>Fluticasone propionate</strong></td>
<td>100–200</td>
</tr>
</tbody>
</table>

† Dose equivalents for Qvar (TGA-registered CFC-free formulation of beclometasone dipropionate).

*Fluticasone furoate is not available as a low dose. TGA-registered formulations of fluticasone furoate contain a medium or high dose of fluticasone furoate and should only be prescribed as one inhalation once daily.

Note: The potency of generic formulations may differ from that of original formulations. Check TGA-approved product information for details.

**Sources**


Asset ID: 22

**Table. Initial treatment choices (adults and adolescents not already using a preventer)**

<table>
<thead>
<tr>
<th>Clinical situation</th>
<th>Suggested starting regimen †</th>
<th>Alternative options and notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms less than twice per month and no flare-up that required oral corticosteroids within previous 12 months</td>
<td>SABA as needed</td>
<td></td>
</tr>
</tbody>
</table>
| Symptoms twice per month or more                                    | Regular ICS starting at a low dose (plus SABA as needed) | Montelukast†  
Cromones§                                                                 |
| Waking due to asthma symptoms at least once during the past month   | Regular ICS starting at a low dose (plus SABA as needed) | If patient also has frequent daytime symptoms consider either of:  
• medium- to high-dose ICS (plus SABA as needed)  
• (private prescription) combination low-dose ICS/LABA§                                                             |
| Oral corticosteroids required for an asthma flare-up within the last 12 months (even if symptoms infrequent, e.g. less than twice per month on average) | Regular ICS starting at a low dose (plus SABA as needed) |                                                                                                 |
### Clinical situation

<table>
<thead>
<tr>
<th>History of artificial ventilation or admission to an intensive care unit due to acute asthma (even if symptoms infrequent, e.g. less than twice per month on average)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular ICS starting at a low dose (plus SABA as needed)</td>
</tr>
<tr>
<td>• Monitor frequently</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient not currently taking a preventer whose symptoms are severely uncontrolled or very troublesome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular ICS (plus SABA as needed)</td>
</tr>
<tr>
<td>For very uncontrolled asthma at presentation (e.g. frequent night waking, low lung function), consider (either of):</td>
</tr>
<tr>
<td>• high-dose ICS (then down-titrate when symptoms improve)</td>
</tr>
<tr>
<td>• a short course of oral corticosteroids in addition to ICS</td>
</tr>
</tbody>
</table>

### Alternative options and notes

| Consider (private prescription) combination ICS/LABA |

‡ When prescribing inhaled asthma medicines, take into account the person’s preferences, ability to use the device, and cost issues.

§ Requires multiple daily doses and daily maintenance of inhaler.

‡ PBS status as at October 2016: Montelukast treatment is not subsidised by the PBS for people aged 15 years or over. Special Authority is available for Department of Veteran’s Affairs gold card holders or white card holders with approval for asthma treatments.

# PBS status as at October 2016: ICS/LABA combination therapy as first-line preventer treatment is not subsidised by the PBS, except for patients with frequent symptoms while taking oral corticosteroids.

Asset ID: 32

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**How this recommendation was developed**

**Consensus**

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons *et al.* 2013
- Weiler *et al.* 2010

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For patients starting inhaled corticosteroid treatment, review efficacy after 4–12 weeks’ treatment. If exercise-induced bronchoconstriction has resolved, advise patient to try omitting pre-exercise salbutamol to test whether it is no longer needed.

Note: All patients with asthma should carry a reliever at all times, for use as needed in response to symptoms.
For patients who are taking regular combination inhaled corticosteroid/long-acting beta₂ agonist treatment and have significant exercise-induced symptoms despite correct inhaler technique and good adherence, consider replacing with inhaled corticosteroid alone as regular maintenance treatment (with as-needed short-acting beta-agonist).

A higher dose of inhaled corticosteroid may be needed to maintain good control.

Regular montelukast can be used in addition to inhaled corticosteroid.

- Stopping a long-acting beta₂-agonist may cause flare-ups or loss of asthma control.
- Do not prescribe long-acting beta₂-agonists as monotherapy, either intermittently or regularly.

Note: PBS status as at October 2016: Montelukast treatment is not subsidised by the PBS for people aged 15 years or over (Special Authority is available for DVA gold card holders, or white card holders with approval for asthma treatments), or for people of any age when used in addition to a long-acting beta-agonist.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons et al. 2013
- Weiler et al. 2010

If exercise-induced symptoms do not resolve after adjusting medicines, and checking adherence and inhaler technique, consider:

- alternative diagnoses
- referral to an accredited respiratory function laboratory for indirect challenge testing
- referral to a respiratory physician for assessment.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

Advise warm-up before planned exercise.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons et al. 2013
- Weiler et al. 2010

More information

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**Challenge tests for exercise-induced bronchoconstriction**

**Role of challenge tests**
Self-reported symptoms are not sensitive enough to detect exercise-induced bronchoconstriction reliably or specific enough to rule out other conditions, particularly in elite athletes. Single office FEV₁ readings or peak expiratory flow measurement are not adequate to demonstrate exercise-induced bronchoconstriction.

Standardised, objective bronchial provocation (challenge) tests using spirometry are necessary for the investigation of suspected exercise-induced bronchoconstriction in elite athletes. These tests involve serial spirometry measurements after challenge with exercise (or exercise surrogates e.g. dry powder mannitol, eucapnic voluntary hyperpnoea or...
hyperventilation, or hyperosmolar aerosols such as 4.5% saline). Severity of exercise-induced bronchoconstriction is assessed by percentage fall in FEV\(_1\) after challenge. Challenge testing is mandated by sports governing bodies before the athlete is given permission to use some asthma medicines, and the required testing protocol varies between specific sports. The latest information is available from the Australian Sports Anti-Doping Authority (ASADA) and the World Anti-Doping Agency (WADA). Challenge tests are also used in the investigation of exercise-related symptoms in recreational and non-athletes, when objective demonstration of exercise-induced bronchoconstriction is needed to guide management decisions.

**Choice of challenge test**

There is no single challenge test that will identify all individuals with exercise-induced bronchoconstriction. The most appropriate test or tests for an individual depend on clinical and individual factors:

- The eucapnic voluntary hyperpnoea test can provoke a severe response. For safety reasons, the eucapnic voluntary hyperpnoea test should only be used in adults who regularly exercise at high intensity (e.g. elite athletes). It should not be used in children.
- When an exercise challenge test is used, inhalation of dry air is recommended to diagnose or exclude exercise-induced bronchoconstriction because it increases the sensitivity of the test.
- Mannitol challenge can be used as an alternative to exercise provocation testing to investigate suspected exercise-induced bronchoconstriction, including in children.
- For safety reasons, exercise challenge in dry air should be avoided in patients with FEV\(_1\) <70% predicted

**Referral**

If challenge testing is needed, consider referring to a respiratory physician for investigation, or discussing with a respiratory physician before selecting which test to order. Do not test during a respiratory infection, or initiate inhaled corticosteroid treatment in the few weeks before challenge testing, because these could invalidate the result.

A list of accredited respiratory function laboratories is available from the Australian and New Zealand Society of Respiratory Science.

**Medical treatment for exercise-induced bronchoconstriction**

The effectiveness of medicines for exercise-induced bronchoconstriction varies between individuals. An individual may experience different effects over time due to various factors including changes in asthma, environmental conditions, the intensity of the exercise stimulus, or down-regulation of beta\(_2\) receptors. The management of exercise-induced bronchoconstriction in elite athletes who do not have asthma is an emerging area of research and is not yet well understood.

**Beta-2 agonists for exercise-induced bronchoconstriction**

Inhaled beta\(_2\) adrenergic receptor agonists are the most effective medicines for short-term protection against exercise-induced bronchoconstriction and for accelerating recovery of lung function after exercise. However, short-acting beta\(_2\) agonists should only be taken intermittently (i.e. less than daily), as necessary for preventing exercise-induced bronchoconstriction or relieving exercise-induced bronchoconstriction. Daily use of short-acting beta\(_2\) agonists may actually increase the severity of exercise-induced bronchoconstriction.

**Beta-2 agonists for exercise-induced bronchoconstriction: doses**

Intermittent short-acting beta\(_2\) agonists administered by inhalation 5 to 20 minutes before exercise are effective in protecting against exercise-induced bronchoconstriction for 2–4 hours. Salbutamol and terbutaline are equally effective. Recommended doses are as follows:
• salbutamol 100–400 micrograms by inhalation, 15 minutes before exercise
• terbutaline 500–1000 micrograms by inhalation, 15 minutes before exercise.

The World Anti-Doping Agency (WADA) no longer requires a Therapeutic Use Exemption application for an athlete to use salbutamol (maximum 1600 mcg per day) or to declare use during drug testing.

• Terbutaline is prohibited by WADA. Exemption may be given in certain circumstances. WADA guidelines prohibit all beta_2 agonists except salbutamol (maximum 1600 micrograms over 24 hours), formoterol (maximum 36 micrograms over 24 hours) and salmeterol when taken by inhalation in accordance with the manufacturers’ recommended therapeutic regime.
• When prescribing for competitive athletes, check which substances are permitted. Refer to ASADA or WADA for a current list of prohibited substances.

➤ Go to: Australian Sports Anti-Doping Authority
Go to: World Anti-Doping Agency

**Over-use of short-acting beta-2 agonists**

High use of short-acting beta_2 agonists may, itself, increase the risk of asthma flare-ups:11,12

• Data from population and case-control studies has led to concerns that the frequent use of short-acting beta_2 agonists, including salbutamol, is associated with increased risk of asthma deaths.13 The risk of asthma deaths was greatest for fenoterol, which has since been withdrawn from use.11 For salbutamol, the risk is greatest for doses above 1000 mcg/day (10 puffs).
• Regular use of salbutamol 16 puffs/day (rather than as-needed use during symptoms) was associated with increased risk of asthma flare-ups requiring oral corticosteroids in a placebo-controlled clinical trial.14 Subsequent statistical modelling showed that the risk was associated with increased fluctuation in lung function.15
• Regular use of short-acting beta_2 agonists leads to receptor tolerance (down-regulation) to their bronchoprotective and bronchodilator effects. Tolerance becomes more apparent with worsening bronchoconstriction. In severe asthma, this could result in a poor response to emergency treatment.16

When high doses of short-acting beta_2 agonist are needed (e.g. dose repeated at intervals of less than 4 hours in a person with acute severe asthma), the patient should be under medical supervision and should usually also be receiving systemic corticosteroids.

➤ See: Managing acute asthma in clinical settings

**Beta-2 agonists for exercise-induced bronchoconstriction: receptor tolerance**

Regular daily use of short-acting beta_2 agonists and long-acting beta_2 agonists results in loss of efficacy due to receptor tolerance (tachyphylaxis), regardless of whether these medicines are used in combination with an inhaled corticosteroid.2 Laboratory studies suggest that receptor tolerance may result in:

• a reduction in the degree of protection against exercise-induced bronchoconstriction when a short-acting beta_2 agonist or long-acting beta_2 agonist is taken before exercise5
• a reduction in the duration of protection against exercise-induced bronchoconstriction when a short-acting beta_2 agonist or long-acting beta_2 agonist is taken before exercise5
• a reduction in the effectiveness of short-acting beta_2 agonist taken as reliever after exercise if the person experiences exercise-induced bronchoconstriction, seen as an increase in the time to recovery from the episode of bronchoconstriction.2

Receptor tolerance may resolve within 72 hours of discontinuing a short-acting beta_2 agonist or long-acting beta_2 agonist.2

**Implications for use of short-acting beta_2 agonists**

International consensus recommends against the over-use of short-acting beta_2 agonists.17

**Implications for use of long-acting beta_2 agonists**

Go to: Australian Sports Anti-Doping Authority
Go to: World Anti-Doping Agency

See: Managing acute asthma in clinical settings
The evidence for adverse effects due to beta_2 receptor down-regulation in patients with asthma is unclear and the implications of current evidence are controversial.\textsuperscript{18,19,20} Most of the available evidence is from laboratory studies.

In adults, clinical trials and meta-analyses assessing regular use of long-acting beta_2 agonists in combination with inhaled corticosteroids indicate that the benefits outweigh the risks,\textsuperscript{21} but extremely large studies would be necessary to define the risk of very rare events.\textsuperscript{21}

There is evidence that the risk of adverse events associated with long-acting beta_2 agonist use (severe asthma episodes, hospitalisation, loss of effectiveness of short acting beta_2 agonists, and loss of protection against exercise-induced bronchoconstriction) may be higher in children than adults.\textsuperscript{18,20} A beta_2 receptor genotype (Arg16 polymorphism in the beta_2 receptor gene) pre-disposes children with asthma to down-regulation of the beta_2 receptor and increased susceptibility to flare-ups during regular treatment with long-acting beta_2 agonists.\textsuperscript{22} A recent study in children with this genotype, and with asthma not adequately controlled despite inhaled corticosteroid treatment, demonstrated that the addition of montelukast was more effective than the addition of salmeterol.\textsuperscript{22} However, routine genetic testing to tailor asthma therapy is not yet available in clinical practice.

\textbf{Inhaled corticosteroids for exercise-induced bronchoconstriction}

Inhaled corticosteroids taken regularly long term (4 weeks or more\textsuperscript{23}) are effective in reducing the frequency and severity of exercise-induced bronchoconstriction in 30–60% of people with asthma.\textsuperscript{2} The degree of protection experienced by individuals ranges from complete to minimal.\textsuperscript{2}

Patients may need to take inhaled corticosteroid for 12 weeks to experience maximal therapeutic effect.\textsuperscript{2} If exercise-induced symptoms have resolved, the person may no longer need to take a beta_2 agonist before exercise.\textsuperscript{2} However, some patients taking regular inhaled corticosteroids may still need to take short-acting beta_2 agonists before exercise.\textsuperscript{2}

Few comparative studies have compared the effectiveness of inhaled corticosteroid with that of other classes of medicines.\textsuperscript{23}

\textbf{Inhaled corticosteroid/long-acting beta-2 agonist combinations for exercise-induced bronchoconstriction}

- To avoid the possibility of patients taking a long-acting beta_2 agonist without an inhaled corticosteroid, long-acting beta_2 agonists should (whenever possible) be prescribed as inhaled corticosteroid/long-acting beta_2 agonist combination in a single inhaler, rather than in separate inhalers. If no combination product is available for the desired medications, carefully explain to the patient that it is very important that they continue taking the inhaled corticosteroid.

Intermittent long-acting beta_2 agonists administered by inhalation before exercise are effective in protecting against exercise-induced bronchoconstriction:\textsuperscript{2}

- for formoterol, onset of bronchodilation and bronchoprotective action is 1-3 minutes after administration\textsuperscript{24}
- for salmeterol, onset of bronchodilation and bronchoprotective action is 10 - 30 minutes after administration\textsuperscript{25}

The duration of effect of both formoterol and salmeterol is up to 12 hours for patients who have not taken a short-acting beta_2 agonist or long-acting beta_2 agonist within the previous 72 hours. However, the duration of bronchoprotection is reduced for subsequent doses due to receptor tolerance.\textsuperscript{2}

\textbf{Montelukast for exercise-induced bronchoconstriction}

Montelukast is less effective against exercise-induced bronchoconstriction than short-acting beta_2 agonists, but regular use is not associated with receptor tolerance.\textsuperscript{2}

Montelukast taken either intermittently before exercise or daily is at least partially effective in protecting against exercise-induced bronchoconstriction in some, but not all patients.\textsuperscript{2} Some experience strong protection against exercise-induced bronchoconstriction while others experience only partial protection or no effect.\textsuperscript{2} Very few patients experience complete protection against exercise-induced bronchoconstriction.\textsuperscript{2}
In children, regular montelukast, either as the child’s only preventer or in combination with an inhaled corticosteroid, is more effective than long-acting beta2 agonists in protecting against exercise-induced bronchoconstriction, and is associated with a greater bronchodilator response to short-acting beta2 agonist after exercise.

The onset of protection occurs within 2 hours of dosing. The duration of protective effect is 12–24 hours. Recommended doses are as follows:

- children aged 2–5 years 4 mg daily, or 1–2 hours before exercise
- children aged 6–14 years 5 mg daily, or 1–2 hours before exercise
- adults 10 mg daily, or 1–2 hours before exercise.

Notes

PBS status as at October 2016: Montelukast treatment is not subsidised by the PBS for:

- people aged 15 years or over (Special Authority is available for DVA gold card holders, or white card holders with approval for asthma treatments.)
- children aged 2 to 5 years in combination with any other preventer
- children aged 6 to 14 years with moderate to severe asthma, when used use as a single second-line preventer as an alternative to corticosteroids
- people of any age, when used in addition to a long-acting beta-agonist.

Cromones for exercise-induced bronchoconstriction

Cromolyn sodium and nedocromil sodium administered by inhalation as single doses before exercise partially protect against exercise-induced bronchoconstriction in approximately half of patients. The onset of action is rapid. The duration of action is up to 2 hours. Recommended doses are as follows:

- nedocromil sodium 4–8 mg by inhalation, 5–10 minutes before exercise
- sodium cromoglycate 10–20 mg by inhalation, 5–10 minutes before exercise.

Cromolyn sodium and nedocromil sodium are less effective than short-acting beta2 agonists in protecting against exercise-induced bronchoconstriction. However, they have a good safety profile and tolerance does not occur when either of these medicines is taken regularly.

Sodium cromoglycate and nedocromil sodium inhalers must be washed daily to prevent blockage.

Adjunctive strategies for managing exercise-induced bronchoconstriction

The following strategies may help people with exercise-induced bronchoconstriction manage their symptoms:

- warming up before exercise (may enable the athlete to achieve a refractory period)
- being as fit as possible – increasing fitness raises the threshold for exercise-induced bronchoconstriction, so that moderately strenuous exercise will not cause an attack
- exercising in a warm humid environment
- avoiding environments with high levels of allergens, irritant gases or airborne particles
- breathing through nose
- after strenuous exercise doing cooling down exercise, breathing through the nose and covering the mouth in cold, dry weather
- reducing sodium intake
  - Some small clinical trials have suggested that a low-sodium diet might improve lung function after exercise in people with exercise-induced bronchoconstriction, but the clinical importance of this is unknown
- fish oil supplementation
  - Some very small, short-term clinical trials reported that fish oil reduced the severity of exercise-induced bronchoconstriction in elite athletes or improve lung function in people with exercise-induced bronchoconstriction, but overall evidence does not support the use of fish oil in asthma.
- ascorbic acid supplementation
A very small, short-term clinical trial reported that ascorbic acid supplementation improved exercise symptoms and asthma control in people with exercise-induced bronchoconstriction, but the clinical importance of this is unknown.

Use of medicines in sport

Many sporting bodies require athletes to provide objective evidence of exercise-induced bronchoconstriction before they are permitted to use asthma medicines during competition.

The Australian Sports Anti-Doping Authority provides information about Therapeutic Use Exemptions for athletes who require treatment with prohibited substances.

Go to: Australian Sports Anti-Doping Authority
Go to: World Anti-Doping Agency

References


Managing exercise-induced bronchoconstriction in children

Recommendations

If the child is involved in competitive sport, check which medicines are permitted in the particular sport by consulting ASADA before prescribing any medicine.

How this recommendation was developed
Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

For a child aged 6 years or older who does not need treatment every day, consider salbutamol taken 15 minutes before exercise. Advise that the child should take reliever as needed to relieve asthma symptoms at other times.

How this recommendation was developed
Consensus
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons et al. 2013
- Weiler et al. 2010

For a child aged 2–14 years with symptoms on most days who is not already using a regular preventer medicine, consider regular montelukast.

Alternatively, montelukast can be given intermittently before exercise. It should be taken at least 2 hours before exercise or on the night before morning exercise.

- Advise parents about potential adverse psychiatric effects of montelukast

How this recommendation was developed
Consensus
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons et al. 2013
- Weiler et al. 2010

If symptoms do not respond to montelukast, consider a low dose of inhaled corticosteroid.

Table. Definitions of ICS dose levels in children

<table>
<thead>
<tr>
<th>Inhaled corticosteroid</th>
<th>Daily dose (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>Beclometasone dipropionate †</td>
<td>100–200</td>
</tr>
</tbody>
</table>

1. Parsons et al. 2013
2. Weiler et al. 2010
### Inhaled corticosteroid Daily dose (mcg)

<table>
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<tr>
<th>Inhaled corticosteroid</th>
<th>Low</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Budesonide</strong></td>
<td>200–400</td>
<td>&gt;400 (up to 800)</td>
</tr>
<tr>
<td><strong>Ciclesonide</strong> ‡</td>
<td>80–160</td>
<td>&gt;160 (up to 320)</td>
</tr>
<tr>
<td><strong>Fluticasone propionate</strong></td>
<td>100–200</td>
<td>&gt;200 (up to 500)</td>
</tr>
</tbody>
</table>

† Dose equivalents for Qvar (TGA-registered CFC-free formulation of beclometasone dipropionate)
‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

**Source**

**How this recommendation was developed**

**Consensus**
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons et al. 2013
- Weiler et al. 2010

For a child aged 6–14 years who is already taking an inhaled corticosteroid, consider adding regular montelukast and continuing low-dose inhaled corticosteroids.

- Advise parents about potential adverse psychiatric effects of montelukast

**Table. Definitions of ICS dose levels in children**

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<tr>
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<td>80–160</td>
</tr>
<tr>
<td><strong>Fluticasone propionate</strong></td>
<td>100–200</td>
</tr>
</tbody>
</table>

† Dose equivalents for Qvar (TGA-registered CFC-free formulation of beclometasone dipropionate)
‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

**Source**
For an adolescent aged 15 years or over who is not already taking a preventer, consider either of the following options:

- montelukast
- regular inhaled corticosteroid, starting at a low dose. Advise the young person to keep taking salbutamol before exercise until full the effect of inhaled corticosteroid has been achieved (up to 12 weeks).

- Advise parents about potential adverse psychiatric effects of montelukast

Note: PBS status as at October 2016: Montelukast treatment is not subsidised by the PBS for people aged 15 years or over.

**Table. Definitions of ICS dose levels in adults**

<table>
<thead>
<tr>
<th>Inhaled corticosteroid</th>
<th>Daily dose (mcg)</th>
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<td>Low</td>
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<tr>
<td><strong>Beclometasone dipropionate †</strong></td>
<td>100–200</td>
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<tr>
<td><strong>Budesonide</strong></td>
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<td><strong>Ciclesonide</strong></td>
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<td><strong>Fluticasone furoate</strong></td>
<td>—</td>
</tr>
<tr>
<td><strong>Fluticasone propionate</strong></td>
<td>100–200</td>
</tr>
</tbody>
</table>

† Dose equivalents for Qvar (TGA-registered CFC-free formulation of beclometasone dipropionate).

*Fluticasone furoate is not available as a low dose. TGA-registered formulations of fluticasone furoate contain a medium or high dose of fluticasone furoate and should only be prescribed as one inhalation once daily.

Note: The potency of generic formulations may differ from that of original formulations. Check TGA-approved product information for details.

**Sources**


For children who are taking regular combination inhaled corticosteroid/long-acting beta\(_2\) agonist treatment and have significant exercise-induced symptoms despite good inhaler technique and adequate adherence, consider replacing with inhaled corticosteroid alone as regular maintenance treatment. Regular montelukast can be used in addition to inhaled corticosteroid.

- Stopping a long-acting beta\(_2\) agonist may cause flare-ups or loss of asthma control, so the patient should be monitored closely.
- Do not prescribe long-acting beta\(_2\) agonists as monotherapy, either intermittently or regularly.
- Advise parents about potential adverse psychiatric effects of montelukast.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons et al. 2013\(^1\)
- Weiler et al. 2010\(^2\)
- van Asperen et al. 2010\(^3\)

For patients starting inhaled corticosteroid treatment, review efficacy after 4–12 weeks’ treatment. If exercise-induced bronchoconstriction has resolved, advise patient to try omitting pre-exercise salbutamol to test whether it is no longer needed.

Note: All patients should carry a reliever at all times, for use as needed in response to symptoms.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

If exercise-induced symptoms do not resolve after adjusting medicines, and checking adherence and inhaler technique, consider:

- alternative diagnoses
- referral to an accredited respiratory function laboratory for indirect challenge testing
- referral to a respiratory physician for assessment.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

More information

Anti-doping agencies

Australian Sports Anti-Doping Authority

The Australian Sports Anti-Doping Authority (ASADA) is the Australian federal government statutory authority with a mission to protect Australia’s sporting integrity through the elimination of doping.

Go to: ASADA or call 13 000 ASADA (13 000 27232)

Go to: ASADA’s Check your substances webpage
The World Anti-Doping Agency (WADA) is the international independent anti-doping agency composed of representatives from the Olympic movement and public authorities from around the world. Its mission is to lead a collaborative worldwide campaign for doping-free sport.

Go to: WADA

**Challenge tests for exercise-induced bronchoconstriction**

**Role of challenge tests**

Self-reported symptoms are not sensitive enough to detect exercise-induced bronchoconstriction reliably or specific enough to rule out other conditions, particularly in elite athletes. 2, 4, 5 Single office FEV1 readings or peak expiratory flow measurement are not adequate to demonstrate exercise-induced bronchoconstriction. 1

Standardised, objective bronchial provocation (challenge) tests using spirometry are necessary for the investigation of suspected exercise-induced bronchoconstriction in elite athletes. These tests involve serial spirometry measurements after challenge with exercise (or exercise surrogates e.g. dry powder mannitol, eucapnic voluntary hyperpnoea or hyperventilation, or hyperosmolar aerosols such as 4.5% saline). 2, 1, 6, 7 Severity of exercise-induced bronchoconstriction is assessed by percentage fall in FEV1 after challenge. 1

Challenge testing is mandated by sports governing bodies before the athlete is given permission to use some asthma medicines, and the required testing protocol varies between specific sports. The latest information is available from the Australian Sports Anti-Doping Authority (ASADA) and the World Anti-Doping Agency (WADA).

Challenge tests are also used in the investigation of exercise-related symptoms in recreational and non-athletes, when objective demonstration of exercise-induced bronchoconstriction is needed to guide management decisions.

Go to: Australian Sports Anti-Doping Authority
Go to: World Anti-Doping Agency

**Choice of challenge test**

There is no single challenge test that will identify all individuals with exercise-induced bronchoconstriction. 2 The most appropriate test or tests for an individual depend on clinical and individual factors:

- The eucapnic voluntary hyperpnoea test can provoke a severe response. 2 For safety reasons, the eucapnic voluntary hyperpnoea test should only be used in adults who regularly exercise at high intensity (e.g. elite athletes). 2 It should not be used in children.
- When an exercise challenge test is used, inhalation of dry air is recommended to diagnose or exclude exercise-induced bronchoconstriction because it increases the sensitivity of the test. 2
- Mannitol challenge can be used as an alternative to exercise provocation testing to investigate suspected exercise-induced bronchoconstriction, 2, 8, 9 including in children. 10, 11
- For safety reasons, exercise challenge in dry air should be avoided in patients with FEV1 <70% predicted 2

**Referral**

If challenge testing is needed, consider referring to a respiratory physician for investigation, or discussing with a respiratory physician before selecting which test to order. Do not test during a respiratory infection, or initiate inhaled corticosteroid treatment in the few weeks before challenge testing, because these could invalidate the result.

A list of accredited respiratory function laboratories is available from the Australian and New Zealand Society of Respiratory Science.

Go to: Australian and New Zealand Society of Respiratory Science

**Medical treatment for exercise-induced bronchoconstriction**

The effectiveness of medicines for exercise-induced bronchoconstriction varies between individuals. 2 An individual may experience different effects over time due to various factors including changes in asthma, environmental conditions, the intensity of the exercise stimulus, or down-regulation of beta2 receptors. 2

The management of exercise-induced bronchoconstriction in elite athletes who do not have asthma is an emerging area of research and is not yet well understood. 2
**Beta-2 agonists for exercise-induced bronchoconstriction**

Inhaled beta-2-adrenergic receptor agonists are the most effective medicines for short-term protection against exercise-induced bronchoconstriction and for accelerating recovery of lung function after exercise. However, short-acting beta_2_ agonists should only be taken intermittently (i.e. less than daily), as necessary for preventing exercise-induced bronchoconstriction or relieving exercise-induced bronchoconstriction. Daily use of short-acting beta_2_ agonists may actually increase the severity of exercise-induced bronchoconstriction.

**Beta-2 agonists for exercise-induced bronchoconstriction: doses**

Intermittent short-acting beta_2_ agonists administered by inhalation 5 to 20 minutes before exercise are effective in protecting against exercise-induced bronchoconstriction for 2–4 hours. Salbutamol and terbutaline are equally effective. Recommended doses are as follows:

- salbutamol 100–400 micrograms by inhalation, 15 minutes before exercise
- terbutaline 500–1000 micrograms by inhalation, 15 minutes before exercise.

The World Anti-Doping Agency (WADA) no longer requires a Therapeutic Use Exemption application for an athlete to use salbutamol (maximum 1600 mcg per day) or to declare use during drug testing.

- Terbutaline is prohibited by WADA. Exemption may be given in certain circumstances. WADA guidelines prohibit all beta_2_ agonists except salbutamol (maximum 1600 micrograms over 24 hours), formoterol (maximum 36 micrograms over 24 hours) and salmeterol when taken by inhalation in accordance with the manufacturers’ recommended therapeutic regime.
- When prescribing for competitive athletes, check which substances are permitted. Refer to ASADA or WADA for a current list of prohibited substances.

**Beta-2 agonists for exercise-induced bronchoconstriction: receptor tolerance**

Regular daily use of short-acting beta_2_ agonists and long-acting beta_2_ agonists results in loss of efficacy due to receptor tolerance (tachyphylaxis), regardless of whether these medicines are used in combination with an inhaled corticosteroid.

Laboratory studies suggest that receptor tolerance may result in:

- a reduction in the degree of protection against exercise-induced bronchoconstriction when a short-acting beta_2_ agonist or long-acting beta_2_ agonist is taken before exercise
- a reduction in the duration of protection against exercise-induced bronchoconstriction when a short-acting beta_2_ agonist or long-acting beta_2_ agonist is taken before exercise
- a reduction in the effectiveness of short-acting beta_2_ agonist taken as reliever after exercise if the person experiences exercise-induced bronchoconstriction, seen as an increase in the time to recovery from the episode of bronchoconstriction.

Receptor tolerance may resolve within 72 hours of discontinuing a short-acting beta_2_ agonist or long-acting beta_2_ agonist.

**Implications for use of short-acting beta_2_ agonists**

International consensus recommends against the over-use of short-acting beta_2_ agonists.

**Implications for use of long-acting beta_2_ agonists**

The evidence for adverse effects due to beta_2_ receptor down-regulation in patients with asthma is unclear and the implications of current evidence are controversial. Most of the available evidence is from laboratory studies.
In adults, clinical trials and meta-analyses assessing regular use of long-acting beta_2 agonists in combination with inhaled corticosteroids indicate that the benefits outweigh the risks, but extremely large studies would be necessary to define the risk of very rare events.

There is evidence that the risk of adverse events associated with long-acting beta_2 agonist use (severe asthma episodes, hospitalisation, loss of effectiveness of short acting beta_2 agonists, and loss of protection against exercise-induced bronchoconstriction) may be higher in children than adults. A beta_2 receptor genotype (Arg16 polymorphism in the beta_2 receptor gene) pre-disposes children with asthma to down-regulation of the beta_2 receptor and increased susceptibility to flare-ups during regular treatment with long-acting beta_2 agonists. A recent study in children with this genotype, and with asthma not adequately controlled despite inhaled corticosteroid treatment, demonstrated that the addition of montelukast was more effective than the addition of salmeterol. However, routine genetic testing to tailor asthma therapy is not yet available in clinical practice.

**Over-use of short-acting beta-2 agonists**

High use of short-acting beta_2 agonists may, itself, increase the risk of asthma flare-ups:

- Data from population and case-control studies has led to concerns that the frequent use of short-acting beta_2 agonists, including salbutamol, is associated with increased risk of asthma deaths. The risk of asthma deaths was greatest for fenoterol, which has since been withdrawn from use. For salbutamol, the risk is greatest for doses above 1000 mcg/day (10 puffs).
- Regular use of salbutamol 16 puffs/day (rather than as-needed use during symptoms) was associated with increased risk of asthma flare-ups requiring oral corticosteroids in a placebo-controlled clinical trial. Subsequent statistical modelling showed that the risk was associated with increased fluctuation in lung function.
- Regular use of short-acting beta_2 agonists leads to receptor tolerance (down-regulation) to their bronchoprotective and bronchodilator effects. Tolerance becomes more apparent with worsening bronchoconstriction. In severe asthma, this could result in a poor response to emergency treatment.

When high doses of short-acting beta_2 agonist are needed (e.g. dose repeated at intervals of less than 4 hours in a person with acute severe asthma), the patient should be under medical supervision and should usually also be receiving systemic corticosteroids.

► See: Managing acute asthma in clinical settings

**Inhaled corticosteroids for exercise-induced bronchoconstriction**

Inhaled corticosteroids taken regularly long term (4 weeks or more) are effective in reducing the frequency and severity of exercise-induced bronchoconstriction in 30–60% of people with asthma. The degree of protection experienced by individuals ranges from complete to minimal.

Patients may need to take inhaled corticosteroid for 12 weeks to experience maximal therapeutic effect. If exercise-induced symptoms have resolved, the person may no longer need to take a beta_2 agonist before exercise. However, some patients taking regular inhaled corticosteroids may still need to take short-acting beta_2 agonists before exercise.

Few comparative studies have compared the effectiveness of inhaled corticosteroid with that of other classes of medicines.

**Inhaled corticosteroid/long-acting beta-2 agonist combinations for exercise-induced bronchoconstriction**

- To avoid the possibility of patients taking a long-acting beta_2 agonist without an inhaled corticosteroid, long-acting beta_2 agonists should (whenever possible) be prescribed as inhaled corticosteroid/long-acting beta_2 agonist combination in a single inhaler, rather than in separate inhalers. If no combination product is available for the desired medications, carefully explain to the patient that it is very important that they continue taking the inhaled corticosteroid.

Intermittent long-acting beta_2 agonists administered by inhalation before exercise are effective in protecting against exercise-induced bronchoconstriction.
• for formoterol, onset of bronchodilation and bronchoprotective action is 1-3 minutes after administration

• for salmeterol, onset of bronchodilation and bronchoprotective action is 10 - 30 minutes after administration

The duration of effect of both formoterol and salmeterol is up to 12 hours for patients who have not taken a short-acting beta\textsubscript{2} agonist or long-acting beta\textsubscript{2} agonist within the previous 72 hours. However, the duration of bronchoprotection is reduced for subsequent doses due to receptor tolerance.

**Montelukast for exercise-induced bronchoconstriction**

Montelukast is less effective against exercise-induced bronchoconstriction than short-acting beta\textsubscript{2} agonists, but regular use is not associated with receptor tolerance.

Montelukast taken either intermittently before exercise or daily is at least partially effective in protecting against exercise-induced bronchoconstriction in some, but not all patients. Some experience strong protection against exercise-induced bronchoconstriction while others experience only partial protection or no effect. Very few patients experience complete protection against exercise-induced bronchoconstriction.

In children, regular montelukast, either as the child’s only preventer or in combination with an inhaled corticosteroid, is more effective than long-acting beta\textsubscript{2} agonists in protecting against exercise-induced bronchoconstriction, and is associated with a greater bronchodilator response to short-acting beta\textsubscript{2} agonist after exercise.

The onset of protection occurs within 2 hours of dosing. The duration of protective effect is 12–24 hours. Recommended doses are as follows:

- children aged 2–5 years 4 mg daily, or 1–2 hours before exercise
- children aged 6–14 years 5 mg daily, or 1–2 hours before exercise
- adults 10 mg daily, or 1–2 hours before exercise.

**Notes**

PBS status as at October 2016: Montelukast treatment is not subsidised by the PBS for:

- people aged 15 years or over (Special Authority is available for DVA gold card holders, or white card holders with approval for asthma treatments.)
- children aged 2 to 5 years in combination with any other preventer
- children aged 6 to 14 years with moderate to severe asthma, when used use as a single second-line preventer as an alternative to corticosteroids
- people of any age, when used in addition to a long-acting beta-agonist.

Montelukast for children: warning parents about potential psychiatric adverse effects

Montelukast is generally very well tolerated. However, post-marketing surveillance reports suggested a slight increase in the rate of psychiatric disorders that was possibly associated with use of leukotriene receptor antagonists in children; this association may have been confounded by asthma severity and concomitant medication. Montelukast use has also been associated with suicidal ideation, but a recent nested case-control study concluded that children with asthma aged 5 –18 years taking leukotriene receptor antagonists were not at increased risk of suicide attempts. Behavioural and psychiatric adverse effects were rare in clinical trials.

The Thoracic Society of Australia and New Zealand advises that it is prudent to mention to parents the potential association of montelukast with behaviour-related adverse events when commencing treatment, and to cease therapy if such adverse events are suspected.

Cromones for exercise-induced bronchoconstriction

Cromolyn sodium and nedocromil sodium administered by inhalation as single doses before exercise partially protect against exercise-induced bronchoconstriction in approximately half of patients.

The onset of action is rapid. The duration of action is up to 2 hours.
Recommended doses are as follows:\(^\text{27}\)

- nedocromil sodium 4–8 mg by inhalation, 5–10 minutes before exercise
- sodium cromoglycate 10–20 mg by inhalation, 5–10 minutes before exercise.

Cromolyn sodium and nedocromil sodium are less effective than short-acting beta\(_2\) agonists in protecting against exercise-induced bronchoconstriction.\(^\text{32}\) However, they have a good safety profile and tolerance does not occur when either of these medicines is taken regularly.\(^\text{2}\)

Sodium cromoglycate and nedocromil sodium inhalers must be washed daily to prevent blockage.

**Adjunctive strategies for managing exercise-induced bronchoconstriction**

The following strategies may help people with exercise-induced bronchoconstriction manage their symptoms:

- warming up before exercise\(^\text{2}\) (may enable the athlete to achieve a refractory period)
- being as fit as possible – increasing fitness raises the threshold for exercise-induced bronchoconstriction, so that moderately strenuous exercise will not cause an attack\(^\text{33}\)
- exercising in a warm humid environment
- avoiding environments with high levels of allergens, irritant gases or airborne particles\(^\text{6}\)
- breathing through nose
- after strenuous exercise doing cooling down exercise, breathing through the nose and covering the mouth in cold, dry weather
- reducing sodium intake\(^\text{2, 1}\)
  - Some small clinical trials have suggested that a low-sodium diet might improve lung function after exercise in people with exercise-induced bronchoconstriction, but the clinical importance of this is unknown\(^\text{34}\)
- fish oil supplementation\(^\text{2, 1}\)
  - Some very small, short-term clinical trials reported that fish oil reduced the severity of exercise-induced bronchoconstriction in elite athletes or improve lung function in people with exercise-induced bronchoconstriction,\(^\text{35, 36}\) but overall evidence does not support the use of fish oil in asthma.\(^\text{37}\)
- ascorbic acid supplementation.\(^\text{2}\)
  - A very small, short-term clinical trial reported that ascorbic acid supplementation improved exercise symptoms and asthma control in people with exercise-induced bronchoconstriction, but the clinical importance of this is unknown.\(^\text{38}\)

**Use of medicines in sport**

Many sporting bodies require athletes to provide objective evidence of exercise-induced bronchoconstriction before they are permitted to use asthma medicines during competition.

The Australian Sports Anti-Doping Authority provides information about Therapeutic Use Exemptions for athletes who require treatment with prohibited substances.

► Go to: Australian Sports Anti-Doping Authority

Go to: World Anti-Doping Agency

**References**


Asthma and exercise-induced bronchoconstriction in elite athletes

Recommendations

If possible, refer elite athletes to a sports medicine expert or specialist with expertise in the investigation and management of exercise-induced bronchoconstriction in competitive athletes, to ensure that all investigations and treatments comply with requirements of sports governing bodies.

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

Do not rely on history alone to diagnose or exclude exercise-induced bronchoconstriction.

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons et al. 2013
- Weiler et al. 2010

Advise athletes that some sports stipulate a specific testing protocol to demonstrate asthma and allow the person to use medicines (refer to sports governing bodies).

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

If baseline (pre-bronchodilator) FEV₁ is ≥ 70% predicted, consider indirect challenge testing such as exercise challenge with dry air, or mannitol challenge test. Refer or discuss with a respiratory physician before ordering these tests.

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Parsons et al. 2013
- Weiler et al. 2010

For elite athletes who also have chronic asthma, manage exercise-induced bronchoconstriction as for other patients with asthma.

Consensus
Before prescribing any medicine for an elite athlete, check whether it is permitted in sport via the Australian Sports Anti-Doping Authority or the World Anti-Doping Agency.

How this recommendation was developed

Consensus
Based on clinical experience and expert opinion (informed by evidence, where available).

More information

Aetiology of exercise-induced bronchoconstriction

Both genetics and environment may contribute to exercise-induced bronchoconstriction. Exercise-induced bronchoconstriction occurs when a person’s ventilatory rate is high and their airways must heat and humidify a large volume of air in a short time. Dehydration of the airway leads to release of inflammatory mediators within the airway and contraction of airway smooth muscle. Dry air is one risk factor.

Exercise-induced bronchoconstriction in athletes who do not have chronic asthma may have different pathogenesis and presentation than exercise-induced bronchoconstriction in people with asthma. Elite athletes often report onset of exercise-induced bronchoconstriction after age 20 years and after many years of high-level training.

In elite athletes, exercise-induced bronchoconstriction is probably due to chronic injury to airway epithelium associated with long-term frequent prolonged high ventilation rates in the presence of environmental exposure to cold air, dry air, and airborne pollutants such as ozone, particulate matter:

- The high prevalence of exercise-induced bronchoconstriction in ice-rink athletes has been linked to inhalation of cold dry air in combination with airborne pollutants from fossil-fuelled ice resurfacing machines
- Exercise-induced bronchoconstriction in skiers and other winter athletes has been linked to injury of airway epithelium due to conditioning large volumes of cold dry air
- The high prevalence of asthma and exercise-induced bronchoconstriction reported among competitive swimmers has been associated with exposure to chlorine in indoor swimming pools
- The increased prevalence of exercise-induced bronchoconstriction among distance runners, compared with the general population, has been attributed to exposure to high levels of airborne allergens and ozone
- Certain airborne viruses inhaled during exercise may also contribute to exercise-induced bronchoconstriction.

Challenge tests for exercise-induced bronchoconstriction

Role of challenge tests

Self-reported symptoms are not sensitive enough to detect exercise-induced bronchoconstriction reliably or specific enough to rule out other conditions, particularly in elite athletes. Single office FEV₁ readings or peak expiratory flow measurement are not adequate to demonstrate exercise-induced bronchoconstriction.

Standardised, objective bronchial provocation (challenge) tests using spirometry are necessary for the investigation of suspected exercise-induced bronchoconstriction in elite athletes. These tests involve serial spirometry measurements after challenge with exercise (or exercise surrogates e.g. dry powder mannitol, eucapnic voluntary hyperventilation, or hyperosmolar aerosols such as 4.5% saline). Severity of exercise-induced bronchoconstriction is assessed by percentage fall in FEV₁ after challenge.

Challenge testing is mandated by sports governing bodies before the athlete is given permission to use some asthma medicines, and the required testing protocol varies between specific sports. The latest information is available from the Australian Sports Anti-Doping Authority (ASADA) and the World Anti-Doping Agency (WADA).

Challenge tests are also used in the investigation of exercise-related symptoms in recreational and non-athletes, when objective demonstration of exercise-induced bronchoconstriction is needed to guide management decisions.

Go to: Australian Sports Anti-Doping Authority
Go to: World Anti-Doping Agency
Choice of challenge test

There is no single challenge test that will identify all individuals with exercise-induced bronchoconstriction. The most appropriate test or tests for an individual depend on clinical and individual factors:

- The eucapnic voluntary hyperpnoea test can provoke a severe response. For safety reasons, the eucapnic voluntary hyperpnoea test should only be used in adults who regularly exercise at high intensity (e.g. elite athletes). It should not be used in children.
- When an exercise challenge test is used, inhalation of dry air is recommended to diagnose or exclude exercise-induced bronchoconstriction because it increases the sensitivity of the test.
- Mannitol challenge can be used as an alternative to exercise provocation testing to investigate suspected exercise-induced bronchoconstriction, including in children.
- For safety reasons, exercise challenge in dry air should be avoided in patients with FEV$_1$ <70% predicted.

Referral

If challenge testing is needed, consider referring to a respiratory physician for investigation, or discussing with a respiratory physician before selecting which test to order. Do not test during a respiratory infection, or initiate inhaled corticosteroid treatment in the few weeks before challenge testing, because these could invalidate the result.

A list of accredited respiratory function laboratories is available from the Australian and New Zealand Society of Respiratory Science.

Exercise-induced bronchoconstriction in people without a previous asthma diagnosis

Exercise-induced bronchoconstriction in people without a previous diagnosis of asthma can be associated with airway inflammation, but is not always. Laboratory studies show that exercise-induced bronchoconstriction is likely to respond to inhaled corticosteroids if it is associated with airway inflammation and the presence of eosinophils. However, sputum testing is not necessary to make the diagnosis.

Use of medicines in sport

Many sporting bodies require athletes to provide objective evidence of exercise-induced bronchoconstriction before they are permitted to use asthma medicines during competition.

The Australian Sports Anti-Doping Authority provides information about Therapeutic Use Exemptions for athletes who require treatment with prohibited substances.

Anti-doping agencies

Australian Sports Anti-Doping Authority

The Australian Sports Anti-Doping Authority (ASADA) is the Australian federal government statutory authority with a mission to protect Australia’s sporting integrity through the elimination of doping.

Go to: ASADA or call 13 000 ASADA (13 000 27232)
Go to: ASADA’s Check your substances webpage

World Anti-Doping Agency

The World Anti-Doping Agency (WADA) is the international independent anti-doping agency composed of representatives from the Olympic movement and public authorities from around the world. Its mission is to lead a collaborative worldwide campaign for doping-free sport.

Go to: WADA
References


