Asthma - the basics and beyond

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AUSTRALIA'S NATIONAL GUIDELINES FOR ASTHMA MANAGEMENT

The Australian Asthma Handbook provides best-practice, evidence-based guidance translated into practical advice for primary care health professionals. The Handbook is proudly published by Australia’s lead asthma authority, the National Asthma Council Australia.

Enter the handbook ➤
Asthma diagnosis and initial management
Ms A

50 y.o.
- Dry cough, intermittent chest tightness and mild wheeze for 2 months
- Variable exertional breathlessness
- No specific triggers

Rhinosinusitis
Hiatus hernia
Current smoker - 15-50 years old, 10 per day, ~17 pack years
O/E chest clear

Spirometry
Pre-bronchodilator
- FEV\textsubscript{1} 2.07 81% predicted
- VC 3.63 99% predicted
Post-bronchodilator
- FEV\textsubscript{1} 2.40 16% increase
- VC 3.66

Diagnosis?
Initial management?
A working definition of asthma

Asthma is a chronic lung disease, which can be controlled but not cured. In clinical practice, asthma is defined by the presence of both the following:

• excessive variation in lung function (‘variable airflow limitation’, i.e. variation in expiratory airflow that is greater than that seen in healthy people)

• respiratory symptoms (e.g. wheeze, shortness of breath, cough, chest tightness) that vary over time and may be present or absent at any point in time.

Untreated asthma is usually characterised by chronic inflammation involving many cells and cellular elements, airway hyperresponsiveness, and intermittent airway narrowing (due to bronchoconstriction, congestion or oedema of bronchial mucosa, mucus, or a combination of these).
There is no single reliable test ('gold standard') and there are no standardised diagnostic criteria for asthma.

The diagnosis of asthma is based on:
- history
- physical examination
- considering other diagnoses
- documenting variable airflow limitation.
Pathogenesis of asthma

Figure 2: Mechanisms and characteristic pathological features of asthma immunopathology

Features are divided into eosinophilic (allergic and non-allergic), non-eosinophilic (neutrophilic type 1 and type 17 and paucigranulocytic), and mixed granulocytic inflammation. Reproduced from Russell and Brightling. By permission of Portland Press. IL=Interleukin, T=helper. PDGF=prostaglandin D2, TSLP=thymic stromal lymphopoietin. ILC2=type 2 innate lymphoid cells.

CCL8=C-C motif chemokine ligand 8. ILC2-type 2 innate lymphoid cells.
Asthma management in adults is based on:

- confirming the diagnosis
- assessing asthma control (recent asthma symptom control and risk factors)
- identifying management goals in collaboration with the patient
- choosing initial treatment appropriate to recent asthma symptom control, risk factors and patient preference
- reviewing and adjusting drug treatment periodically
- providing information, skills and tools for self-management, including:
  - training in correct inhaler technique
  - information and support to maximise adherence
  - a written asthma action plan
  - information about avoiding triggers, where appropriate
- managing flare-ups when they occur
- managing comorbid conditions that affect asthma or contribute to respiratory symptoms
- providing advice about smoking, healthy eating, physical activity, healthy weight and immunisation
STEPWISE MANAGEMENT OF STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

HOLD

Typical symptoms
- Few symptoms or moderate exertion
- Occasional chest infections
- Little or no effect on daily activities

Moderate

Typical symptoms
- Breathlessness on mild exertion
- Increasing limitation of daily activities
- Arousal and appetite reduced
- Exacerbations requiring oral corticosteroids and/or antibiotics

Severe

Typical symptoms
- Breathlessness on minimal exertion
- Daily activities severely curtailed
- Experiencing regular hospitalisation
- Chronic cough
- Significant loss of increasing frequency and severity

Non-pharmacological interventions

RISE REDUCTION
- Check smoking status, smoking cessation, recommend annual influenza vaccine and pneumococcal vaccine according to NNTT guidelines

OPTIMISE FUNCTION
- Encourage regular exercise and physical activity, weight management, provide education, development of management plans and written COPD action plans

CONSIDER CO-MORBIDITIES
- Especially cardiovascular disease, arthritis, depression, lung cancer and osteoporosis

REFILL symptomatic patients to pulmonary rehabilitation

Consider oxygen therapy for hypoxemia, surgery, bronchoscopic interventions, patient care services and advanced care planning

Steps-wise pharmacological interventions

START with short-acting relievers (as needed)

LAMA
- Inducing short-acting, against
SABA, SAMA (bronchial mucosa, bronchodilator)

ADD long-acting bronchodilators

LABA (long-acting bronchodilator monotherapy), OR LAMA (long-acting beta-agonist, agonist)
- Slightly lower cost therapy. LAMA/LABA may be suitable

CONTINUE adding SABA

Access and optimise inhaler device technique at each visit

REVIEW PATIENTS TO LUNG FOUNDATION AUSTRALIA FOR INFORMATION AND SUPPORT - FREECALL 1800 654 301
Lung Foundation Australia has a range of resources to promote understanding of COPD and assist with management.

Based on the COPD-X Plan, Australian and New Zealand Guidelines for the Management of COPD and COPD Care Guide for Primary Care

REFER TO PBS Online: www.pbs.gov.au
Register at www.copdx.org.au to receive an alert when the COPD-X Guidelines are updated.
Underdiagnosis and Overdiagnosis of Asthma

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**Underdiagnosis**
- Under-reporting of symptoms
- Poor socioeconomic status

**Overdiagnosis**
- Lack of variable airflow obstruction
- Unrecognised sustained clinical remission of symptoms
  - Canadian study: 613 patients – 30% had no features of current asthma on extensive workup and could discontinue asthma inhalers

Aaron et al. JAMA 2017;317:269-279

Aaron et al. Am J Respir Crit Care Med 2018;198:1012-1020
Box 3-5A

**Adults & adolescents 12+ years**

**Personalized asthma management:**
Assess, Adjust, Review response

**Asthma medication options:** Adjust treatment up and down for individual patient needs

**PREFERRED CONTROLLER**
to prevent exacerbations and control symptoms

**PREFERRED RELIEVER**
Other reliever option

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**STEP 1**
As-needed low dose ICS-formoterol *

**STEP 2**
Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *

**STEP 3**
Low dose ICS-LABA

**STEP 4**
Medium dose ICS-LABA

**STEP 5**
High dose ICS-LABA

Refer for phenotypic assessment ± add-on therapy, e.g. tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R

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Confirmation of diagnosis if necessary Symptom control & modifiable risk factors (including lung function) Comorbidities Inhaler technique & adherence Patient goals

Treatment of modifiable risk factors & comorbidities Non-pharmacological strategies Education & skills training Asthma medications

Symptoms Exacerbations Side-effects Lung function Patient satisfaction

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As-needed low dose ICS-formoterol ‡

As-needed low dose ICS-formoterol ✱

As-needed low dose ICS-formoterol †

As-needed low dose ICS-formoterol ‡ low-dose ICS-form is the reliever for patients prescribed bud-form or BDP-form maintenance and reliever therapy

# Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV1 >70% predicted

Note: At June 2019 – as needed ICS/LABA alone is not available on PBS for asthma
Inhaled Combined Budesonide–Formoterol as Needed in Mild Asthma

Paul M. O’Byrne, M.B., B. J. Mark FitzGerald, M.D., Eric D. Bateman, M.D., Peter J. Barnes, M.D., Nanshan Zhong, Ph.D., Christina Keen, M.D., Carin Jorup, M.D., Rosa Lamarca, Ph.D., Stefan Ivanov, M.D., Ph.D., and Helen K. Reddel, M.B., B.S., Ph.D.

RESULTS
A total of 3849 patients underwent randomization, and 3836 (1277 in the terbutaline group, 1277 in the budesonide–formoterol group, and 1282 in the budesonide maintenance group) were included in the full analysis and safety data sets. With respect to the mean percentage of weeks with well-controlled asthma per patient, budesonide–formoterol was superior to terbutaline (34.4% vs. 31.1% of weeks; odds ratio, 1.14; 95% confidence interval [CI], 1.00 to 1.30; P=0.046) but inferior to budesonide maintenance therapy (34.4% and 44.4%, respectively; odds ratio, 0.64; 95% CI, 0.57 to 0.73). The annual rate of severe exacerbations was 0.20 with terbutaline, 0.07 with budesonide–formoterol, and 0.09 with budesonide maintenance therapy; the rate ratio was 0.36 (95% CI, 0.27 to 0.49) for budesonide–formoterol versus terbutaline and 0.83 (95% CI, 0.59 to 1.16) for budesonide–formoterol versus budesonide maintenance therapy. The rate of adherence in the budesonide maintenance group was 78.9%. The median metered daily dose of inhaled glucocorticoid in the budesonide–formoterol group (57 μg) was 17% of the dose in the budesonide maintenance group (340 μg).

CONCLUSIONS
In patients with mild asthma, as-needed budesonide–formoterol provided superior asthma-symptom control to as-needed terbutaline, assessed according to electronically recorded weeks with well-controlled asthma, but was inferior to budesonide maintenance therapy. Exacerbation rates with the two budesonide-containing regimens were similar and were lower than the rate with terbutaline. Budesonide–formoterol used as needed resulted in substantially lower glucocorticoid exposure than budesonide maintenance therapy. (Funded by AstraZeneca; SIGMA 1 ClinicalTrials.gov number, NCT02149199.)

Note: At June 2019 – as needed ICS/LABA alone is not available on PBS for asthma
Asthma/COPD overlap
Mr B

72 y.o.
• Exertional breathlessness up hills
• Cough and dark green sputum
• No wheeze, occasional left chest pain
• No recent chest infections
• Triggers: pollen

Rhinosinusitis. Childhood asthma.
IHD - STEMI, PCI
Former smoker - 15-68 years old, 
15 per day, ~30 pack years

O/E chest - reduced breath sounds

Fractional exhaled nitric oxide (FeNO): elevated at 35 parts per billion (RR<25)

Spirometry
Pre-bronchodilator
  FEV₁ 1.40 43% predicted
  VC 3.89 100% predicted
Post-bronchodilator
  FEV₁ 1.56 18% increase
  VC 4.36

CXR - mild hyperinflation
CT chest - moderate emphysema
FBC - eosinophils: normal
IgE – 300: elevated
Alpha1-antitrypsin level 1.70: normal.

Diagnosis? Initial management?
Asthma-COPD overlap

Position paper:
National Asthma Council and Lung Foundation Australia

Diagnosis and initial treatment of asthma, COPD and asthma-COPD overlap (ACO)

A joint project of GINA and GOLD

GINA Global Strategy for Asthma Management and Prevention

GOLD Global Strategy for Diagnosis, Management and Prevention of COPD

© Global Initiative for Asthma3.
## Definitions

### Asthma

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation. [GINA 2017]

### COPD

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. [GOLD 2017]

### Asthma-COPD overlap [not a definition, but a description for clinical use]

Asthma-COPD overlap (ACO) is characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD. Asthma-COPD overlap is therefore identified in clinical practice by the features that it shares with both asthma and COPD.

This is not a definition, but a description for clinical use, as asthma-COPD overlap includes several different clinical phenotypes and there are likely to be several different underlying mechanisms.
Stepwise approach to diagnosis and initial treatment

For an adult who presents with respiratory symptoms:

1. Does the patient have chronic airways disease?
2. Syndromic diagnosis of asthma, COPD and overlap
3. Spirometry
4. Commence initial therapy
5. Referral for specialized investigations (if necessary)
Step 1 – Does the patient have chronic airways disease?

- Clinical history: consider chronic airways disease if
  - Chronic or recurrent cough, sputum, dyspnea or wheezing, or repeated acute lower respiratory tract infections
  - Previous doctor diagnosis of asthma and/or COPD
  - Previous treatment with inhaled medications
  - History of smoking tobacco and/or other substances
  - Exposure to environmental hazards, e.g. airborne pollutants

- Physical examination
  - May be normal
  - Evidence of hyperinflation or respiratory insufficiency
  - Wheeze and/or crackles
Step 1 – Does the patient have chronic airways disease?

- Radiology (CXR or CT scan performed for other reasons)
  - May be normal, especially in early stages
  - Hyperinflation, airway wall thickening, hyperlucency, bullae
  - May identify or suggest an alternative or additional diagnosis, e.g. bronchiectasis, tuberculosis, interstitial lung disease, cardiac failure

- Screening questionnaires
  - Designed to assist in identification of patients at risk of chronic airways disease
  - May not be generalizable to all countries, practice settings or patients
  - See GINA and GOLD reports for examples
Step 2 – Syndromic diagnosis of asthma, COPD and asthma-COPD overlap

- Assemble the features that, **when present**, most favor a diagnosis of typical asthma or typical COPD
- Compare the number of features on each side
  - If the patient has ≥3 features of either asthma or COPD, there is a strong likelihood that this is the correct diagnosis
- Consider the level of certainty around the diagnosis
  - Diagnoses are made on the weight of evidence
  - The absence of any of these features does not rule out either diagnosis, e.g. absence of atopy does not rule out asthma
  - When a patient has a similar number of features of both asthma and COPD, consider the diagnosis of asthma-COPD overlap
### Step 2: Syndromic Diagnosis in Adults

(i) Assemble the features for asthma and for COPD that best describe the patient.
(ii) Compare number of features in favour of each diagnosis and select a diagnosis.

<table>
<thead>
<tr>
<th>Features: if present suggest -</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age of onset</strong></td>
<td>Before age 20 years</td>
<td>After age 40 years</td>
</tr>
<tr>
<td><strong>Pattern of symptoms</strong></td>
<td>Variation over minutes, hours or days</td>
<td>Persistent despite treatment</td>
</tr>
<tr>
<td></td>
<td>Worse during the night or early morning</td>
<td>Good and bad days but always daily symptoms and exertional dyspnea</td>
</tr>
<tr>
<td></td>
<td>Triggered by exercise, emotions including laughter, dust or exposure to allergens</td>
<td>Chronic cough &amp; sputum preceded onset of dyspnea, unrelated to triggers</td>
</tr>
<tr>
<td><strong>Lung function</strong></td>
<td>Record of variable airflow limitation (spirometry or peak flow)</td>
<td>Record of persistent airflow limitation (FEV₁/FVC &lt; 0.7 post-BD)</td>
</tr>
<tr>
<td><strong>Lung function between symptoms</strong></td>
<td>Normal</td>
<td>Abnormal</td>
</tr>
<tr>
<td><strong>Past history or family history</strong></td>
<td>Previous doctor diagnosis of asthma</td>
<td>Previous doctor diagnosis of COPD, chronic bronchitis or emphysema</td>
</tr>
<tr>
<td></td>
<td>Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)</td>
<td>Heavy exposure to risk factor: tobacco smoke, biomass fuels</td>
</tr>
<tr>
<td><strong>Time course</strong></td>
<td>No worsening of symptoms over time. Variation in symptoms either seasonally, or from year to year</td>
<td>Symptoms slowly worsening over time (progressive course over years)</td>
</tr>
<tr>
<td></td>
<td>May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks</td>
<td>Rapid-acting bronchodilator treatment provides only limited relief</td>
</tr>
<tr>
<td><strong>Chest X-ray</strong></td>
<td>Normal</td>
<td>Severe hyperinflation</td>
</tr>
</tbody>
</table>

**Diagnosis Confidence**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Asthma</th>
<th>Some features of asthma</th>
<th>Features of both</th>
<th>Some features of COPD</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Confidence in Diagnosis</strong></td>
<td>Asthma</td>
<td>Asthma</td>
<td>Could be ACO</td>
<td>Possibly COPD</td>
<td>COPD</td>
</tr>
</tbody>
</table>

**Note:** • These features best distinguish between asthma and COPD. • Several positive features (3 or more) for either asthma or COPD suggest that diagnosis. • If there are a similar number for both asthma and COPD, consider diagnosis of ACO.
Step 3 - Spirometry

- Essential if chronic airways disease is suspected
  - Confirms chronic airflow limitation
  - More limited value in distinguishing between asthma with fixed airflow limitation, COPD and asthma-COPD overlap

- Measure at the initial visit or subsequent visit
  - If possible measure before and after a trial of treatment
  - Medications taken before testing may influence results

- Peak expiratory flow (PEF)
  - Not a substitute for spirometry
  - Normal PEF does not rule out asthma or COPD
  - Repeated measurement may confirm excessive variability, found in asthma or in some patients with asthma-COPD overlap
### Step 3 - Spirometry

<table>
<thead>
<tr>
<th>Spirometric variable</th>
<th>Asthma</th>
<th>COPD</th>
<th>Overlap</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal FEV₁/FVC pre- or post-BD</td>
<td>Compatible with asthma</td>
<td>Not compatible with diagnosis (GOLD)</td>
<td>Not compatible unless other evidence of chronic airflow limitation</td>
</tr>
<tr>
<td>Post-BD FEV₁/FVC &lt;0.7</td>
<td>Indicates airflow limitation; may improve</td>
<td>Required for diagnosis by GOLD criteria</td>
<td>Usual in asthma-COPD overlap (ACO)</td>
</tr>
<tr>
<td>FEV₁ ≥80% predicted</td>
<td>Compatible with asthma (good control, or interval between symptoms)</td>
<td>Compatible with GOLD category A or B if post-BD FEV₁/FVC &lt;0.7</td>
<td>Compatible with mild ACO</td>
</tr>
<tr>
<td>FEV₁ &lt;80% predicted</td>
<td>Compatible with asthma. A risk factor for exacerbations</td>
<td>Indicates severity of airflow limitation and risk of exacerbations and mortality</td>
<td>Indicates severity of airflow limitation and risk of exacerbations and mortality</td>
</tr>
<tr>
<td>Post-BD increase in FEV₁ &gt;12% and 200mL from baseline (reversible airflow limitation)</td>
<td>Usual at some time in course of asthma; not always present</td>
<td>Common in COPD and more likely when FEV₁ is low</td>
<td>Common in ACO, and more likely when FEV₁ is low</td>
</tr>
<tr>
<td>Post-BD increase in FEV₁ &gt;12% and 400mL from baseline</td>
<td>High probability of asthma</td>
<td>Unusual in COPD. Consider ACO</td>
<td>Compatible with diagnosis of ACO</td>
</tr>
</tbody>
</table>

GINA 2017, Box 5-3
Step 4 – Commence initial therapy

- Initial pharmacotherapy choices are based on both efficacy and safety
- If syndromic assessment suggests asthma as single diagnosis
  - Start with low-dose ICS
  - Add LABA and/or LAMA if needed for poor control despite good adherence and correct technique
  - Do not give LABA alone without ICS
- If syndromic assessment suggests COPD as single diagnosis
  - Start with bronchodilators or combination therapy
  - Do not give ICS alone without LABA and/or LAMA
- If differential diagnosis is equally balanced between asthma and COPD, i.e. asthma-COPD overlap
  - Start treatment as for asthma, pending further investigations
  - Start with ICS at low or moderate dose
  - Usually also add LABA and/or LAMA, or continue if already prescribed
Step 4 – Commence initial therapy

- For all patients with chronic airflow limitation:
  - Treat modifiable risk factors including advice about smoking cessation
  - Treat comorbidities
  - Advise about non-pharmacological strategies including physical activity, and, for COPD or asthma-COPD overlap, pulmonary rehabilitation and vaccinations
  - Provide appropriate self-management strategies
  - Arrange regular follow-up

- See GINA and GOLD reports for details
Step 5 – Refer for specialized investigations if needed

- Refer for expert advice and extra investigations if patient has:
  - Persistent symptoms and/or exacerbations despite treatment
  - Diagnostic uncertainty, especially if alternative diagnosis (e.g. TB, cardiovascular disease) needs to be excluded
  - Suspected airways disease with atypical or additional symptoms or signs (e.g. hemoptysis, weight loss, night sweats, fever, chronic purulent sputum). Do not wait for a treatment trial before referring
  - Suspected chronic airways disease but few features of asthma, COPD or asthma-COPD overlap
  - Comorbidities that may interfere with their management
  - Issues arising during on-going management of asthma, COPD or asthma-COPD overlap
### Step 5 – Refer for specialized investigations if needed

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLCO</td>
<td>Normal or slightly elevated</td>
<td>Often reduced</td>
</tr>
<tr>
<td>Arterial blood gases</td>
<td>Normal between exacerbations</td>
<td>In severe COPD, may be abnormal between exacerbations</td>
</tr>
<tr>
<td>Airway hyperresponsiveness</td>
<td>Not useful on its own in distinguishing asthma and COPD. Higher levels favor asthma</td>
<td></td>
</tr>
<tr>
<td>High resolution CT scan</td>
<td>Usually normal; may show air trapping and increased airway wall thickness</td>
<td>Air trapping or emphysema; may show bronchial wall thickening and features of pulmonary hypertension</td>
</tr>
<tr>
<td>Tests for atopy (sIgE and/or skin prick tests)</td>
<td>Not essential for diagnosis; increases probability of asthma</td>
<td>Conforms to background prevalence; does not rule out COPD</td>
</tr>
<tr>
<td>FENO</td>
<td>If high (&gt;50ppb) supports eosinophilic inflammation</td>
<td>Usually normal. Low in current smokers</td>
</tr>
<tr>
<td>Blood eosinophilia</td>
<td>Supports asthma diagnosis</td>
<td>May be found during exacerbations</td>
</tr>
<tr>
<td>Sputum inflammatory cell analysis</td>
<td>Role in differential diagnosis not established in large populations</td>
<td></td>
</tr>
</tbody>
</table>

**GINA 2017, Box 5-5**
Asthma exacerbations
**Ms C - acute presentation**

**TRIAGE NURSE SUMMARY:**
1/7 INCREASED SOB

HAS TAKEN OWN VENTOLIN NEBS AND PUFFER WITH MINIMAL RELIEF
PMHX ASTHMA - HOSPITAL ADM. NIL ICU ADM.

**A:** Patent.  **B:** Spont, speaking in full sentences, SaO2 97% RA, RR 24.  **C:** warm, pink, dry, reg radial pulse, HR 125.  **D:** alert, denies pain.  **Wheezing+++**

**What management should be initiated?**

A. Discharge home immediately, as anxiety is the main cause
B. Diuretics to treat heart failure
C. Intubation and mechanical ventilation in the Intensive Care Unit
D. Primary assessment of asthma severity, with early use of bronchodilators
E. Spirometry before any treatment starts, since baseline lung function needs to be known in the Emergency Department
‘Asthma attack’

Asthma Attack: Trapped Air

- inspired air
- expired air
- larynx (voice box)
- trachea (windpipe)
- right lung
- left lung
- bronchi
- bronchioles
- bronchial tube
- alveoli (air pockets)
- blood vessels
- lumen
- mucus lining
- normal airway
- obstructed airway
- contracted smooth muscle
- decreased lumen diameter
- inflammation and swelling
- excess mucus
- surrounded by immune cells

Encyclopedia Britannica
**Figure. Managing acute asthma in adults**

**IMMEDIATELY**

**ASSESS SEVERITY AND START BRONchodilATOR**

- **Mild/Moderate**
  - Can walk and speak whole sentences in one breath
  - Use an inhaled bronchodilator (e.g., salbutamol or ipratropium)

- **Severe**
  - Any of the following within 6 hours:
    - Increased work of breathing
    - Oxygen saturation ≤ 92%

**Life-threatening**

- Any of the following:
  - Cyanosis
  - Paradoxical abdominal distension
  - Inability to talk
  - Reduced level of consciousness
  - Oxygen saturation < 89%

**ARRANGE IMMEDIATE TRANSFER TO HIGHER-LEVEL CARE**

- Notify emergency medical services
- Ventilation if needed
- Oxygen if needed

**ARRANGE IMMEDIATE TRANSFER TO HIGHER-LEVEL CARE**

- Notify emergency medical services
- Ventilation if needed
- Oxygen if needed

**WITHIN MINUTES**

**REASSESS SEVERITY**

- Table: Severe asthma: rapid assessment of acute asthma in adults and children aged 6 years and over
- Arranx immediate transfer if no improvement

**CONTINUE BRONchodilATOR**

- Use an inhaled bronchodilator every 6–12 hours
- If there is no improvement, consider an oral corticosteroid

**IF POOR RESPONSE, ADD IV MAGNESIUM SULFATE**

- If intravenous (IV) magnesium sulfate is used as an add-on treatment

**CONSIDER OTHER ADD-ON TREATMENT OPTIONS**

- Inhaled corticosteroid

**WITHIN FIRST HOUR**

**START SYSTEMIC CORTICOSTEROIDS**

- Prednisolone 40–60 mg (or equivalent) orally or IV
- Prednisolone 1 mg/kg (or equivalent) orally or IV

**REASSESS RESPONSE TO TREATMENT (1 HOUR AFTER STARTING BRONchodilATOR)**

- Dyspnoea resolved
  - Symptoms and signs unresolved
  - Persisting severe or life-threatening acute asthma

**AFTER 1-HOUR CHECK**

- **OBSERVE**
  - No more than 1 hour after diagnosis
- **POST–ACUTE CARE**
  - Provide ongoing support to the patient and manage underlying triggers
  - Prophylactic antibiotics for > 55 years
  - Prognostic and preventative measures

**CONTINUE BRONchodilATOR AND ADD-ON TREATMENT**

- Table: Add-on treatment options for acute asthma

**TRANSFER TO HIGHER-LEVEL CARE OR DISCUSS TRANSFER OR RETRIEVAL WITH SENIORITY MEDICAL STAFF**

For more details on the initial management of life-threatening acute asthma, see Initial management of life-threatening acute asthma in adults and children.
Primary assessment

Complete a rapid primary assessment and start initial treatment

- Make a rapid clinical assessment with the person in a sitting position
- Measure pulse oximetry while the person is breathing air (unless life-threatening)
- Start bronchodilator immediately, according to severity and age

Australian Asthma Handbook v2.0, 2019
**ASSESS SEVERITY AND START BRONCHODILATOR**

- Immediately
  - Consider anaphylaxis and manage if suspected
  - Table. Rapid primary assessment of acute asthma in adults and children

**Mild/Moderate**
- Can walk and speak whole sentences in one breath
- Give 4–12 puffs salbutamol (100 microg per actuation) via pMDI plus spacer

**Severe**
- Any of: unable to speak in sentences, visibly breathless, increased work of breathing, oxygen saturation 90–94%
- Salbutamol 12 puffs (100 mcg per actuation) via pMDI plus spacer
  - Ipratropium 8 puffs (21 microg/actuation) via pMDI plus spacer
  - OR
    - Use intermittent nebulisation if patient cannot breathe through spacer.
    - Give 5 mg nebul salbutamol. Add 500 microg ipratropium to nebulised solution.
    - Drive nebuliser with air unless oxygen needed
- Start oxygen
- Titrate to target oxygen saturation 93–95%

**Life-threatening**
- Any of: drowsy, collapsed, exhausted, cyanotic, poor respiratory effort, oxygen saturation less than 90%
- Salbutamol 2 x 5 mg nebules via continuous nebulisation.
  - Ipratropium 500 microg added to nebulised solution.
- Start oxygen
- Titrate to target oxygen saturation of 93–95%

**ARRANGE IMMEDIATE TRANSFER TO HIGHER-LEVEL CARE**

- Notify senior staff
- Ventilate if required (NPPV or intubate and ventilate)

*Figure. Initial management of life-threatening acute asthma in adults and children*
ED RMO assessment (11pm)

16yo F
Presented with 1/7 of increased dyspnoea and wheeze. B/g of asthma
Reports using salbutamol, 3 puffs every 5 minutes today since waking up to minimal relief
2/7 history of "hayfever' - runny nose, dry cough, sneezing
Has an asthma action plan, however it is with the GP. No copy at home

PMHx:
Asthma
- rare asthmatic attacks. Nil hospital admissions although has had previous ED presentations
Eczema

Med:
Salbutamol PRN
Should be on Seretide 2puff BD, however has been non-compliant

NKDA
Social hx:
Lives w family
Studying at school
Non-smoker

O/E:
HR 125, BP 141/115, 96% RA, RR 24, GCS 15
Increased BMI
Speaking in normal sentences
Nil obvious accessory muscle use
Chest - generalised insp and exp wheeze bilaterally
Pulses regular, warm peripherally bilat

Imp: Exacerbation of asthma
Secondary assessment

**Complete a brief history**, including:

- reliever taken for this episode (dose, number of doses, time of last dose)
- current asthma medicines (regular and as-needed, including type of devices used)
- assessment of adherence to preventer (if prescribed)
- what triggered this episode, if known (e.g. allergies, immediate hypersensitivity, medicines, respiratory infections)
- coexisting heart or lung disease, including chronic obstructive pulmonary disease
- assess smoking status and exposure to second-hand smoke
Corticosteroids

For adults with acute asthma:

**Start systemic corticosteroids within 1 hour of presentation** (unless contraindicated), regardless of severity at initial assessment

- Give starting dose of oral **prednisolone** 37.5–50 mg, then repeat each morning on second and subsequent days (total 5–10 days)
- It is usually not necessary to taper the dose unless the duration of treatment exceeds 2 weeks

If corticosteroids cannot be given orally, give **IV hydrocortisone** 4 mg/kg (maximum 100 mg) every 6 hours for 24 hours then reduce over next 24 hours or switch to oral prednisolone
Ms C – investigations and treatment

salbutamol MDI 100 microg, 9 puffs via spacer
ipratropium MDI 21 microg, 8 puffs via spacer
prednisolone PO 50 mg

20 min later:
salbutamol MDI 100 microg, 12 puffs via spacer

20 min later:
salbutamol MDI 100 microg, 12 puffs via spacer
ipratropium MDI 21 microg, 8 puffs via spacer

2 hr later:
salbutamol neb 5mg
salbutamol neb 5mg (20 min later)
salbutamol neb 5mg (20 min later)
iprotrpinium neb 250 mcg
**Mild/Moderate**

**REASSESS RESPONSE TO TREATMENT (1 HOUR AFTER STARTING BRONCHODILATOR)**
- Perform spirometry (if patient capable)
- Repeat pulse oximetry
- Check for dyspnoea while supine

---

**Severe**

- Dyspnoea resolved
- Symptoms and signs unresolved
  - Any of: any persisting dyspnoea, inability to lie flat without dyspnoea, FEV₁ <60% predicted,

---

**Life-threatening**

- Persisting severe or life-threatening acute asthma

---

**1 HOUR**

**AFTER 1-HOUR CHECK**

**OBSERVE**
- for more than 1 hour after dyspnoea resolves

---

**POST-ACUTE CARE**
- Ensure person (or carer) is able to monitor and manage asthma at home
- Provide oral prednisolone for 5–10 days
- Ensure person has regular inhaled corticosteroid
- Check and coach in correct inhaler technique
- Provide spacer if needed
- Provide interim asthma action plan
- Advise/arrange follow-up review

---

**ARRANGE HOSPITAL ADMISSION**

**CONTINUE BRONCHODILATOR AND ADD-ON TREATMENT**

**TRANSFER TO HIGHER-LEVEL CARE OR DISCUSS TRANSFER OR RETRIEVAL WITH SENIOR MEDICAL STAFF**

---

*Australian Asthma Handbook v2.0, 2019*
Add-on treatment for life-threatening asthma

- Inhaled ipratropium bromide - MDI, or nebulised (500 mcg)
- IV magnesium sulfate - 10 mmol infusion over 20 min
- IV salbutamol (in ED or ICU) - 200 microg over 1 min, then 5 microg/min (and increasing)
- IV aminophylline
- IM or IV adrenaline - 0.3 to 0.5 mg IM, or 50 mcg IV slow injection, or infusion

- Non-invasive positive pressure ventilation
- Intubation and mechanical ventilation
Ms C - progress

Issues:
1. Asthma - since primary school years
2. Suboptimal adherence - intermittent use of ICS/LABA (salmeterol/fluticasone = Seretide)
3. Obesity - BMI 40

Progress:
- Admitted to Short Stay ED unit; brought back to Acute ED
- Admitted to Thoracic Ward - bronchodilators; 5 days of oral steroids
- Recommenced on regular ICS/LABA
- Reviewed by asthma nurse educator, dietitian, physiotherapist, pharmacist, thoracic medical team
- Discharged home after 3 day admission; GP review arranged
Management of mild-moderate exacerbations

Self-management - based on patient's written asthma action plan

Increase **reliever** use to control symptoms

Keep taking regular **preventer** during a flare-up (even if needing oral corticosteroids)

Prescribe an increase in **preventer** and/or a course of **oral corticosteroids** (37.5–50 mg for 5–10 days) for patients with (any of):

- acute asthma symptoms that recur within 3 hours of taking a rapid-onset beta₂ agonist reliever
- increasing difficulty breathing over one or more days
- night-time asthma symptoms that interfere with sleep over more than one night in a row
- peak flow below a pre-defined level (for those monitoring peak flow each day; level determined based on individual’s personal best and history of peak flow levels before and during flare-ups)
SUMMARY of acute asthma management

• Emergency assessment
• If asthma, start bronchodilators
• Assess severity, trigger factors, differential diagnoses
• Use oral or IV steroids early
• Monitor response
• Escalate treatment if needed
• Decide on admission or discharge
• Plan for longer term asthma management

Check Australian Asthma Handbook for more details, assessment tools and evidence
Severe asthma and biologic therapy
Ms D

72 y.o.

- Asthma since childhood
- Worsening cough and exertional breathlessness
- 5 courses of prednisolone in 12 mth
- No specific triggers

Rhininositis. GORD. Never smoker

Seretide MDI 250 mcg 2 bd via spacer
Alvesco MDI 160 mcg 2 mane via spacer

Tried Spiriva, montelukast, Tilade

O/E chest - expiratory wheezes

**Spirometry**

<table>
<thead>
<tr>
<th>Pre-bronchodilator</th>
<th>Post-bronchodilator</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁</td>
<td>1.45</td>
</tr>
<tr>
<td>VC</td>
<td>2.57</td>
</tr>
<tr>
<td>FEV₁</td>
<td>1.81</td>
</tr>
<tr>
<td>VC</td>
<td>2.55</td>
</tr>
</tbody>
</table>

FBC - eosinophils 1.10: elevated
IgE - 20: normal

**Diagnosis?**

**Management?**
Severe asthma is defined as:

- asthma that remains **uncontrolled** despite regular treatment with high-dose inhaled corticosteroids plus long-acting beta$_2$ agonist, or with maintenance oral corticosteroids, or

- asthma that requires this level of treatment (Step 4) to prevent it becoming uncontrolled.

If a patient continues to experience **poor control of asthma**, frequent flare-ups, or poor quality of life due to asthma, despite regular treatment with a high dose of an inhaled corticosteroid plus a long-acting beta$_2$ agonist, make a full assessment to **rule out common problems** (including poor inhaler technique and suboptimal adherence) before applying the label of severe asthma.

Australian Asthma Handbook v2.0, 2019
Severe asthma model of care

Primary Care

<table>
<thead>
<tr>
<th>Poorly Controlled Asthma</th>
<th>Well Controlled Asthma</th>
</tr>
</thead>
</table>

- Monitoring and administration of biological therapy

General Respiratory Review
- Confirmation of diagnosis
- Standard care (disease and inhaler education, action plan)

Diagnostic uncertainty
- High symptom burden
- Poor lung function
- Frequent exacerbations

Stabilised patients
- Ongoing monitoring

Severe Asthma Service
- Multi-disciplinary assessment and management for asthma, comorbidities and risk factors
- Phenotypic selection of patients most likely to respond to different biologics

### The role of primary care in the multidimensional model of care for asthma

#### Assessment of airway pathology

<table>
<thead>
<tr>
<th>Question</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Is it asthma?</strong></td>
<td>• Confirm history is compatible</td>
</tr>
<tr>
<td></td>
<td>• Obtain spirometry for evidence of variable airflow limitation:</td>
</tr>
<tr>
<td></td>
<td>‣ training available through asthma foundations, NAC Australia, ALF; online</td>
</tr>
<tr>
<td></td>
<td>resources also available*</td>
</tr>
<tr>
<td></td>
<td>‣ consider external referral for spirometry</td>
</tr>
<tr>
<td><strong>Is it severe asthma?</strong></td>
<td>• Definition:</td>
</tr>
<tr>
<td></td>
<td>‣ high dose ICS plus one other maintenance therapy, or oral corticosteroid for</td>
</tr>
<tr>
<td></td>
<td>&gt; 50% of the previous year required to keep asthma under control; or</td>
</tr>
<tr>
<td></td>
<td>‣ uncontrolled asthma despite such therapies</td>
</tr>
<tr>
<td><strong>Is the asthma controlled?</strong></td>
<td>• Definition:</td>
</tr>
<tr>
<td></td>
<td>‣ no nocturnal or early morning symptoms</td>
</tr>
<tr>
<td></td>
<td>‣ no limitation of activities</td>
</tr>
<tr>
<td></td>
<td>‣ daytime symptoms ≤ 2 days per week</td>
</tr>
<tr>
<td></td>
<td>‣ need for reliever ≤ 2 days per week</td>
</tr>
<tr>
<td></td>
<td>• More than two exacerbations per year</td>
</tr>
<tr>
<td></td>
<td>• Assess at every opportunity with specific questioning</td>
</tr>
<tr>
<td></td>
<td>• Consider use of validated questionnaires (eg, ACQ or ACT)¹</td>
</tr>
<tr>
<td></td>
<td>• If not controlled, review and escalate therapy, as below, followed by referral to respiratory physician</td>
</tr>
</tbody>
</table>

Chung *et al.* MJA 2018;209(2 Suppl): S34-S40
## Severe asthma in primary care (2)

### Management

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
</table>
| Is inhaler therapy optimised? | • Escalate maintenance therapy as required in stepwise manner according to guideline recommendation.³  
  ‣ low dose ICS  
  ‣ low dose ICS/LABA  
  ‣ medium/high dose ICS/LABA  
  • Assess adherence and inhaler technique, and address as required. Ask:  
  ‣ how often the patient is actually taking their maintenance therapy  
  ‣ what makes it difficult to take  
  ‣ what makes it easier to take  
  • Consider use of trained practice nurse, pharmacists, asthma educator from asthma foundations, online resource such as videos and patient resource from NAC Australia |

### Asthma action plan³

• Should explain:  
  ‣ what patient should do when well  
  ‣ how to recognise worsening symptoms  
  ‣ what patient should do when symptoms worsen

### Smoking cessation advice

• Provide advice and support for smoking cessation (eg, through motivational interviewing, opportunistic counselling, pharmacotherapy, QUIT line)
### Ongoing coordinated care

**Comorbidities**
- Review and manage common contributory comorbidities (e.g., GORD, obesity, anxiety and depression, allergic rhinitis)
- Consider specialist referral and coordinate care for assessment and management of complex comorbidities (e.g., vocal cord dysfunction, dysfunctional breathing, OSA and bronchiectasis)
- Coordinate community allied health professional involvement as required (e.g., dietitian, clinical psychologist)

**Targeted therapies**
- Assist with ongoing administration of biological therapies once patient is stabilised by respiratory physician
  - appropriate GP training and support can be provided by treating respiratory physician or Centre of Excellence in Severe Asthma

**Collaboration between primary and specialist care**
- Refer back to treating respiratory physician in event of:
  - deterioration in asthma symptom control after a period of stability
  - frequent exacerbations
  - deteriorating lung function
  - intolerance or adverse effects to therapies
- Respiratory physician may support GPs by providing streamlined re-referral pathways
- Communication between primary and specialist care may be improved by increased use of eHealth records

---

Add-on therapies for severe asthma

1. Stepwise treatment of asthma, showing possible add-on therapies for particular asthma phenotypes

**Possible add-on therapies**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAMA (eg, tiotropium mist inhaler)</td>
<td>Exacerbation despite optimised ICS/LABA</td>
</tr>
<tr>
<td>Leukotriene antagonist (eg, montelukast)</td>
<td>Asthma with aspirin sensitivity</td>
</tr>
<tr>
<td>Antifungal*</td>
<td>ABPA or fungal sensitivity</td>
</tr>
<tr>
<td>Macrolides*</td>
<td>Uncontrolled asthma despite optimised ICS/LABA</td>
</tr>
<tr>
<td>Biologicals Anti-IgE (omalizumab) Anti-IL-5 (mepolizumab, benralizumab, reslizumab+)</td>
<td>Severe atopic asthma Severe eosinophilic asthma</td>
</tr>
<tr>
<td>Bronchial thermoplasty</td>
<td>Unknown</td>
</tr>
<tr>
<td>Continuous oral corticosteroid</td>
<td>Uncontrolled asthma</td>
</tr>
</tbody>
</table>

*non-TGA approved in Australia  +non-PBS funded in Australia

**Legend**
- **GINA STEP 2**: Low dose ICS
- **GINA STEP 3**: Medium/high dose ICS/LABA
- **GINA STEP 4**: Respiratory specialist referral for add-on therapy
- **GINA STEP 5**: Stepwise treatment of asthma, showing possible add-on therapies for particular asthma phenotypes

**ABPA = allergic bronchopulmonary aspergillosis. GINA = Global Initiative for Asthma. IL-5 = interleukin-5. ICS = inhaled corticosteroids. LABA = long-acting β2-agonists. LAMA = long-acting anti-muscarinic antagonists. PBS = Pharmaceutical Benefits Scheme. TGA = Therapeutic Goods Administration.**

Upham et al. MJA 2018;209 (2 Suppl):S22-S27
Biologic therapy - mechanisms

Allergens, viruses, and irritants → Dendritic cell → Th2 cell differentiation → IL-4

Approved drug target
Investigational drug target

IL-4

Eosinophil activation in bone marrow → Inflammatory cell trafficking to the tissue → IgE

M2 macrophage polarization → Epithelial damage/shedding

Fibrosis

Bronchial enlargement → Basement membrane thickening → Goblet cell hyperplasia/mucus production → SM contractility

Tight junction → Goblet cell → Airway epithelium

IL-5

IL-13

IL-33 IL-25 IL-12 CRTh2 ILC2 cell

Biologic therapy for severe asthma

**Anti-IgE**
omalizumab (Xolair)
SC every 2-4 wk

**Anti-interleukin-5 (IL-5)**
(anti-eosinophilic)
mepolizumab (Nucala)
SC every 4 wk
benralizumab (Fasenra)
SC every 4 wk then 8 wk

~50% reduction in exacerbation rates
Normansell et al. Cochrane Database Syst Rev 2014;CD003559
Biologic therapy for severe asthma

**Anti-IgE**
omalizumab (Xolair)
   SC every 2-4 wk

**Anti-interleukin-5 (IL-5)**
(anti-eosinophilic)
mepolizumab (Nucala)
   SC every 4 wk
benralizumab (Fasenra)
   SC every 4 wk then 8 wk

~53% reduction in exacerbation rates
~50% reduction in oral steroids

Biologic therapy for severe asthma

**Anti-IgE**
omalizumab (Xolair)
   SC every 2-4 wk

**Anti-interleukin-5 (IL-5)**
   (anti-eosinophilic)
mepolizumab (Nucala)
   SC every 4 wk
benralizumab (Fasenra)
   SC every 4 wk then 8 wk

~75% reduction in oral steroid dose
~55% reduction in exacerbation rates

Nair et al. New Engl J Med 2017;376:2448-2458
Practice tips

• Add-on treatment for uncontrolled severe eosinophilic asthma or severe allergic asthma

• Hospital authority script prescribed by specialist
  - initiation (6 months) then continuation (6 months) – required to meet PBS criteria

• First 3 doses in hospital, then primary care/community

• Rare incidence of anaphylaxis
  - resuscitation facilities
  - recommend Epipen
  - observe after subcutaneous injection for specified time
    1 to 2 hr initially, 30 min subsequently

• Continue inhaled preventer medications
Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): a randomised, double-blind, placebo-controlled trial

Peter G Gibson, Ian A Yang, John W Upham, Paul N Reynolds, Sandra Hodge, Alan L James, Christine Jenkins, Matthew J Peters, Guy B Marks, Melissa Baraket, Heather Powell, Steven L Taylor, Lex E X Leong, Geraint B Rogers, Jodie L Simpson

Lancet 2017; 390: 659–68

Findings Between June 12, 2009, and Jan 31, 2015, 420 patients were randomly assigned (213 in the azithromycin group and 207 in the placebo group). Azithromycin reduced asthma exacerbations (1.07 per patient-year [95% CI 0.85–1.29]) compared with placebo (1.86 per patient-year [1.54–2.18]; incidence rate ratio [IRR] 0.59 [95% CI 0.47–0.74]; p<0.0001). The proportion of patients experiencing at least one asthma exacerbation was reduced by azithromycin treatment (127 [61%] patients in the placebo group vs 94 [44%] patients in the azithromycin group, p<0.0001). Azithromycin significantly improved asthma-related quality of life (adjusted mean difference, 0.36 [95% CI 0.21–0.52]; p=0.001). Diarrhoea was more common in azithromycin-treated patients (72 [34%] vs 39 [19%]; p=0.001).

Interpretation Adults with persistent symptomatic asthma experience fewer asthma exacerbations and improved quality of life when treated with oral azithromycin for 48 weeks. Azithromycin might be a useful add-on therapy in persistent asthma.

Note: Maintenance therapy in asthma is not an approved indication for azithromycin
Diagnosis and treatment
- Variable symptoms
- Variable airflow obstruction
- Inhaled steroids, bronchodilators
- Trigger avoidance, action plan

Asthma and COPD
- Overlapping features of both asthma and COPD on history and spirometry
- Inhaled steroids, long-acting bronchodilators

Exacerbations
- Assess acute severity and start bronchodilators
- Early use of systemic steroids for exacerbations and acute asthma

Severe asthma
- Check diagnosis, optimise management, treat comorbidities
- Consider add-on therapy including tiotropium, montelukast, biologic therapy (anti-IgE, anti-IL5)