Developments in the diagnosis and management of asthma

Neil C Thomson MD, FRCP

Despite receiving asthma therapy, many patients have poorly controlled symptoms and experience frequent exacerbations. Our Drug review focusses on key points and recent advances in the diagnosis and management of asthma, followed by a review of the prescription data and sources of further information.

Asthma is a chronic inflammatory disease of the airways that affects 300 million people worldwide and 5.4 million children and adults in the UK. Despite advances in the diagnosis and management of asthma in the last 20 years, surveys indicate that many patients have poorly controlled symptoms and experience frequent exacerbations. The financial impact of asthma is considerable, in large part due to the cost of asthma medications, hospital admissions and time lost from work. Improving the morbidity from asthma is an important objective for healthcare professionals.

Evaluation and diagnosis
A systematic approach to the evaluation of patients suspected or known to have asthma is helpful and should include assessment of the diagnosis, identification of the cause(s) of persistent symptoms and development of a patient-specific management plan.

An algorithm based on an assessment of the probability of asthma and a measure of airflow obstruction is recommended by the British Thoracic Society (BTS)/Scottish Intercollegiate Guidelines Network (SIGN) guideline in order to diagnose asthma and to direct further investigations and treatment (see Figure 1 and Table 1). Spirometry is the preferred lung function test to demonstrate the presence and severity of airflow obstruction, because the results are less dependent on effort and more specific for airway obstruction than peak expiratory flow (PEF).

Common conditions to be considered in the differential diagnosis in adults include COPD, bronchiectasis, heart failure and pulmonary thromboembolism, as well as vocal cord dysfunction and psychogenic breathlessness. Measurements of airway hyper-reactivity and biomarkers of airway inflammation, such as exhaled nitric oxide, can be used to help support or rule out a diagnosis of asthma or to predict steroid responsiveness, particularly in symptomatic patients with normal spirometry.
Vocal cord dysfunction and dysfunctional breathing can be difficult to diagnose and manage, particularly in patients who also have asthma.

**Trigger factors and co-morbidities**

Several nonpharmaceutical management approaches targeting triggers of asthma and co-morbidities are likely to be effective in improving asthma control and quality of life, although an evidence base from clinical trials supporting the efficacy of a number of these interventions is generally weak. Avoidance of trigger factors such as allergens, NSAIDs or occupational agents in sensitive individuals, as well as exposure to environmental irritants such as second-hand smoke, is likely to prevent exacerbations.

Targeting smokers with asthma to quit smoking or patients with a high body mass index (BMI) to lose weight may result in improvements in asthma control. Treating co-existing GORD does not improve asthma symptoms.

**Importance of adherence, inhaler technique and action plans**

Nonadherence with treatment is one of the most important factors in poor asthma control. Around a quarter of exacerbations are thought to be due to nonadherence with inhaled corticosteroids (ICS). An indication of possible nonadherence can be assessed by reviewing prescription refill frequency, including looking for overuse of short-acting bronchodilators as the ability to detect poor adherence based on history alone is poor, though the patient may be collecting their ICS along with their bronchodilator but not using it. Improving adherence can be difficult and effective interventions are often complex.

Strategies that may help include adequate explanation of the indications for treatment, discussion of real and perceived concerns of adverse effects of treatment (particularly ICS), simplifying drug treatment regimens, reminders and reinforcement.

Around half of all patients have poor inhaler technique irrespective of the device used. Assessing inhaler technique needs to be part of routine clinical review. The choice of device is based on the drug to be administered and patient preference, as well as demonstration by the patient that they are able to use an inhaler correctly. Patients should be asked to bring their inhalers with them to each consultation.

Written action plans are a component of asthma self-management and, when combined with regular review, improve asthma control including reduced hospital admissions and attendance at A&E for exacerbations.
Current symptom control and risk of future exacerbations

Assessing asthma control should incorporate the dual components of current clinical control (eg symptoms, reliever use and lung function) and the future risk of exacerbations and decline in lung function.8

Current clinical control can be determined by history taking and/or by the use of specific asthma control questionnaires, eg the Royal College of Physicians (RCP) three questions (see Table 2), asthma control questionnaire (ACQ) score or the asthma control test (ACT).

The best predictors of future exacerbations are a history of an exacerbation in the previous year and reduced forced expiratory volume in one second (FEV1). A proportion of patients with asthma develop persistent airflow obstruction, although whether treatment prevents this is uncertain.9 For most patients symptom-based monitoring is adequate. Serial measurements of PEF are often unreliable, but can be helpful in selected patients with poor perception of asthma symptoms or with severe disease. In primary care, monitoring of asthma is best undertaken by a routine review at least yearly. See Table 3 for Quality and Outcomes Framework (QOF) indicators in asthma.

Role of inflammatory biomarkers

There is considerable interest in the use of inflammatory biomarkers to predict and monitor response to therapy. Total circulating immunoglobulin E (IgE) concentration is used as a criterion for the selection of patients with severe allergic asthma suitable for anti-IgE treatment, ie omalizumab (Xolair). Induced sputum eosinophil count can guide ICS treatment and reduces exacerbations in severe asthma,10 although the procedure is unsuitable for use in primary care and is unavailable in most centres in secondary care.

Monitoring exhaled nitric oxide does not improve asthma control in mild to moderate asthma compared to a symptom-based approach,10,11 although when used in combination with an assessment of current symptom control it may be of value in selected asthmatic populations, such as in pregnancy.12

In general, identifying a patient’s inflammatory phenotype by the use of inflammatory biomarkers is at a developmental stage; however, this approach is likely to be increasingly used to stratify patients for specific treatments for asthma in the future, particularly in those with severe disease.

Step-wise approach as part of an integrated management plan

The step-wise approach to treatment should be integrated into a management plan that includes nonpharmacological management approaches where appropriate, as well as regular assessment of current symptom control, risk of future exacerbations and adherence as well as inhaler technique (see Figure 2).1 These assessments should be undertaken prior to a step-up or step-down in treatment.

Several issues concerning the efficacy and safety of commonly used drugs for asthma within the context of this approach are discussed briefly below.

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### Increased probability of asthma

- Symptoms worse at night and in the morning
- Symptoms associated with triggers such as exercise, allergen exposure, cold air
- Symptoms after taking aspirin or beta-blockers
- History of atopic disorder
- Family history of asthma/atopic disorder
- Widespread wheeze on examination
- Unexplained low lung function or blood eosinophilia

### Decreased probability of asthma

- Prominent dizziness, light-headedness
- Chronic productive cough in the absence of wheeze or breathlessness
- Repeatedly normal physical examination of chest when symptomatic
- Voice disturbance
- Symptoms with colds only
- Cardiac disease
- Significant smoking history (ie >20 pack-years)
- Normal lung function when symptomatic

### Spirometry

Normal spirometry (or PEF) does not exclude the diagnosis of asthma in a patient who is asymptomatic

### Smokers with asthma

The prevalence of smoking in asthma is similar to the general population; asthma can occur in patients with a significant smoking history

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**Table 1.** Notes on the diagnosis of asthma

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**Safety of long-acting beta₂-agonists**

The safety of long-acting beta₂-agonists (LABAs) has been questioned, particularly by the Food and Drug Administration (FDA) in the USA, due to possible increased mortality rates. In the UK the Medicines and Healthcare products Regulatory Agency (MHRA) concluded that the benefits when used in conjunction with ICS outweigh any possible risk.13 The asthma guideline recommends that LABAs should be prescribed in fixed-dose combination with an ICS to aid adherence and reduce the likelihood of LABA monotherapy.1

**Combination maintenance and reliever therapy**

Clinical trials of the Single inhaler Maintenance And Reliever Therapy (SMART) regimen, using both budesonide and formoterol (Symbicort SMART) for maintenance treatment of asthma and relief of symptoms, have reported reductions in the frequency of severe exacerbations but no improvement in current symptom control compared to a fixed-dose combination plus a short-acting beta₂-agonist (SABA) as a reliever.14 The design of these studies may not be optimal due in part to possible undertreatment of the fixed-dose treatment groups and thus not a true comparison with current ‘best practice’.

The combination of inhaled extra-fine particle size beclomethasone and formoterol as Maintenance And Reliever Therapy (Fostair MART) is recently also licensed for use in the UK.
Overall, studies indicate that the single combination inhaler approach and the fixed-dose combination strategy are both effective options for patients at Step 3 who are poorly controlled. A decision on which strategy to use is likely to be influenced by patient preference and the ability of the patient to understand the correct use of the single combination inhaler regimen.1

Real-life studies
There is a concern that guideline recommendations are based on clinical trials that recruit a highly selective group of participants and that the findings may not be applicable to ‘real-life’ patients.

For example, in a pragmatic ‘real-life’ trial in primary care in the UK a leukotriene receptor antagonist (LTRA) was as effective as an ICS at Step 2 and the addition of a LABA at Step 3 at two months. These findings are contrary to guideline recommendations,15 possibly due to the recruitment of patients such as the elderly, the obese or cigarette smokers3 who are often excluded from clinical trials.

Although further studies are required to confirm these findings, they highlight the importance of recruiting ‘real-life’ participants to clinical trials in asthma.

Antimuscarinic bronchodilators
Recent clinical trials have demonstrated the efficacy of the long-acting antimuscarinic bronchodilator tiotropium in asthma (unlicensed indication; currently ipratropium bromide is the only antimuscarinic bronchodilator licensed for the treatment of asthma). In patients with poorly controlled asthma who have reduced lung function despite the use of combination therapy (ICS + LABA), the addition of tiotropium administered via a fine-mist Respimat device increased the time to the first severe exacerbation and provided modest sustained bronchodilatation.16 It should be noted that concern has been raised about the safety of tiotropium in patients with pre-existing cardiovascular disease when administered via a Respimat device, although not via the HandiHaler device that delivers a lower dose of tiotropium to the airways.17

Ultra LABAs and once-daily ICS
Several once-daily ICS used alone or in combination with inhaled ultra LABAs are under development, but are not yet licensed for use in the UK. Adherence may be improved by once-daily administration of these products.

Severe asthma
For the 5–10 per cent of patients with severe asthma, there are limited treatment options (Steps 4 and 5, see Figure 2).18 These patients often have poorly controlled asthma despite treatment with high-dose ICS and LABAs plus other add-on therapies and, at Step 5, oral corticosteroids.

### Table 2. The RCP ‘three questions’ for determining asthma control

<table>
<thead>
<tr>
<th>Question</th>
<th>Response Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>in the last month/week have you had difficulty sleeping due to your asthma (including cough symptoms)?</td>
<td>‘Yes’ indicates mild morbidity and 2 or 3 ‘yes’ answers indicate high morbidity</td>
</tr>
<tr>
<td>have you had your usual asthma symptoms (eg cough, wheeze, chest tightness, shortness of breath) during the day?</td>
<td>‘Yes’ indicates mild morbidity and 2 or 3 ‘yes’ answers indicate high morbidity</td>
</tr>
<tr>
<td>has your asthma interfered with your usual daily activities (eg school, work, housework)?</td>
<td>‘Yes’ indicates mild morbidity and 2 or 3 ‘yes’ answers indicate high morbidity</td>
</tr>
</tbody>
</table>

Table 3. 2013–2014 QOF indicators for asthma

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Points</th>
<th>Achievement thresholds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Records</td>
<td>4</td>
<td>45–80%</td>
</tr>
<tr>
<td>AST001. The contractor establishes and maintains a register of patients with asthma, excluding patients with asthma who have been prescribed no asthma-related drugs in the preceding 12 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial diagnosis</td>
<td>15</td>
<td>45–70%</td>
</tr>
<tr>
<td>AST002. The percentage of patients aged 8 or over with asthma (diagnosed on or after 1 April 2006), on the register, with measures of variability or reversability recorded between 3 months before or anytime after diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ongoing treatment</td>
<td>20</td>
<td>45–70%</td>
</tr>
<tr>
<td>AST003. The percentage of patients with asthma, on the register, who have had asthma review in the preceding 12 months that includes an assessment of asthma control using the 3 RCP questions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST004. The percentage of patients with asthma aged 14 or over and who have not attained the age of 20, on the register, in whom there is a record of smoking status in the preceding 12 months</td>
<td>6</td>
<td>45–80%</td>
</tr>
</tbody>
</table>

Table 3. 2013–2014 QOF indicators for asthma
Table: Step-wise approach to the pharmacological management of asthma in adults

<table>
<thead>
<tr>
<th>Step 1:</th>
<th>Mild intermittent asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and children &gt;12 years</td>
<td>Inhaled SABA as required</td>
</tr>
<tr>
<td>Children 5–12 years</td>
<td>Add inhaled steroid 200–800µg per day*</td>
</tr>
<tr>
<td>Children &lt;5 years</td>
<td>Add inhaled SABA as required</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 2:</th>
<th>Regular preventer therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and children &gt;12 years</td>
<td>Add inhaled steroid 200–800µg per day*</td>
</tr>
<tr>
<td>Children 5–12 years</td>
<td>Add inhaled steroid 200–400µg per day*</td>
</tr>
<tr>
<td>Children &lt;5 years</td>
<td>Add inhaled steroid 200–400µg per day*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 3:</th>
<th>Initial add-on therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and children &gt;12 years</td>
<td>Add inhaled LABA:</td>
</tr>
<tr>
<td>• if good response, continue</td>
<td></td>
</tr>
<tr>
<td>• if benefit but control still inadequate, continue LABA and increase inhaled steroid to 800µg (children &lt;12 400µg) per day*</td>
<td></td>
</tr>
<tr>
<td>• if no response to LABA, stop and increase inhaled steroid to 800µg (children &lt;12 400µg) per day*</td>
<td></td>
</tr>
<tr>
<td>• if control still inadequate, trial other therapies such as LTRA, SR theophylline</td>
<td></td>
</tr>
<tr>
<td>Children 5–12 years</td>
<td>In children taking inhaled steroid 200–400µg per day*, consider adding LTRA</td>
</tr>
<tr>
<td>Children &lt;5 years</td>
<td>In children taking LTRA alone, reconsider adding inhaled steroid 200–400µg per day*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 4:</th>
<th>Persistent poor control</th>
</tr>
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<tbody>
<tr>
<td>Adults and children &gt;12 years</td>
<td>Trials of</td>
</tr>
<tr>
<td>• increase inhaled steroid up to 2000µg per day*</td>
<td></td>
</tr>
<tr>
<td>• adding in further drugs such as LTRA, SR theophylline, beta2-agonist tablet</td>
<td></td>
</tr>
<tr>
<td>Children 5–12 years</td>
<td>Trial of increasing inhaled steroid up to 800µg per day*</td>
</tr>
<tr>
<td>Children &lt;5 years</td>
<td>Daily steroid tablets</td>
</tr>
<tr>
<td>Maintain high-dose inhaled steroid (2000µg* adults, 800µg* children &lt;12)</td>
<td></td>
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<tr>
<td>Consider other treatments such as immunosuppressives, omalizumab</td>
<td></td>
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<tr>
<td>Refer to respiratory physician</td>
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<table>
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<tr>
<th>Step 5:</th>
<th>Continuous or frequent oral steroid</th>
</tr>
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<tbody>
<tr>
<td>Adults and children &gt;12 years</td>
<td>Daily steroid tablets</td>
</tr>
<tr>
<td>Maintain high-dose inhaled steroid (2000µg* adults, 800µg* children &lt;12)</td>
<td></td>
</tr>
<tr>
<td>Consider other treatments such as immunosuppressives, omalizumab</td>
<td></td>
</tr>
<tr>
<td>Refer to respiratory physician</td>
<td></td>
</tr>
<tr>
<td>Children 5–12 years</td>
<td>Refer to respiratory physician</td>
</tr>
<tr>
<td>Children &lt;5 years</td>
<td>At each step check:</td>
</tr>
<tr>
<td>• current symptoms</td>
<td></td>
</tr>
<tr>
<td>• risk of exacerbation</td>
<td></td>
</tr>
<tr>
<td>• adherence</td>
<td></td>
</tr>
<tr>
<td>• inhaler technique</td>
<td></td>
</tr>
<tr>
<td>• triggers</td>
<td></td>
</tr>
<tr>
<td>• co-morbidities</td>
<td></td>
</tr>
<tr>
<td>• consider nonpharmacological approach</td>
<td></td>
</tr>
<tr>
<td>• action plan</td>
<td></td>
</tr>
<tr>
<td>• need for specialist referral (particularly at steps 4 and 5)</td>
<td></td>
</tr>
</tbody>
</table>

SABA: short-acting beta2-agonist; LABA: long-acting beta2-agonist; LTRA: leukotriene receptor antagonist; SR: slow release
*refers to beclometasone or budesonide; equivalent dosages for fluticasone and mometasone should be halved; ciclesonide is also more potent although its precise equivalence to beclometasone is unclear

Figure 2. Step-wise approach to the pharmacological management of asthma in adults
Omalizumab is recommended as an option for treating severe persistent confirmed allergic IgE-mediated asthma as an add-on to optimised standard therapy in people aged 6 years and older who need continuous or frequent treatment with oral corticosteroids (defined as 4 or more courses in the previous year).

Optimised standard therapy is defined as a full trial of and, if tolerated, documented compliance with inhaled high-dose corticosteroids, LABAs, LTRAs, theophyllines, oral corticosteroids and smoking cessation if clinically appropriate.

Table 4. NICE guidance on the use of omalizumab in severe persistent allergic asthma (TA278)

Omalizumab, a humanised monoclonal antibody that binds circulating IgE antibody, is indicated for patients with severe allergic asthma (see Table 4). Its use is associated with improvements in quality of life and a reduction in exacerbations, although the yearly cost per patient is considerable.19

Bronchial thermoplasty, which involves the delivery of radio frequency energy to the airways to reduce airway smooth muscle mass has been shown to improve quality of life and reduce exacerbation in severe asthma.20 The procedure is available for treating patients with moderate to severe asthma in several specialist centres in the UK, although a recommendation on its place in management is not yet included in the asthma guideline.

Biological agents targeting proinflammatory cytokines such as interleukin-5 and interleukin-13 are under development for severe asthma.18

Conclusion
The diagnosis of asthma is based on an assessment of the probability of asthma and evidence of variable airflow obstruction.

The step-wise approach to drug treatment should be integrated into a patient-centered management plan that includes nonpharmacological management approaches and regular assessment of current symptom control, risk of future exacerbations and adherence, as well as inhaler technique. Better therapies are required for the 5–10 per cent of cases with severe asthma.

References

Declaration of interests
Professor Thomson has participated in advisory boards and/or received consultancy fees from Asmacure, Boston Scientific, Chiesi, Respivert. He has received lecture fees from AstraZeneca, Chiesi, GlaxoSmithKline, Novartis; industry-sponsored grant funding to the University of Glasgow from Aerovance, Asthmatix, AstraZeneca, Centocor, Genentech, GlaxoSmithKline, MedImmune, Novartis, and Synairgen for participating in clinical trials.

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KEY POINTS
- Evaluation should include assessment of the diagnosis, identification of the cause(s) of persistent symptoms and development of a management plan
- Avoidance of trigger factors in sensitive individuals is likely to prevent exacerbations
- Nonadherence with treatment is one of the most important factors in poor asthma control
- Assessing inhaler technique needs to be part of routine clinical review
- The best predictors of future exacerbations are history (previous year) and reduced FEV1
- The step-wise approach to treatment should be integrated into a management plan that includes nonpharmacological approaches where appropriate and routine clinical review
- LABAs should be prescribed in fixed-dose combination with an ICS to aid adherence
- Omalizumab is indicated in severe allergic asthma
Prescription review

GPs in England wrote over 18 million prescriptions for ICS in 2012 at a total cost of £661 million. Of these, 60 per cent (accounting for 84 per cent of spending) were for combined inhalers with a LABA, though some of these prescriptions would be for the treatment of COPD.

As monotherapy, beclometasone continues to be the most frequently prescribed ICS, with 86 per cent of scripts and 75 per cent of costs. Most of the remaining scripts are for budesonide and fluticasone, with the latter costing about 50 per cent more.

The highest cost per item for monotherapy with budesonide or fluticasone is a result of formulations for nebulisers, whereas for beclometasone it is due to Becodisks 400µg plus Diskhaler (discontinued in 2012). The newer ICS ciclesonide (Alvesco) and mometasone furoate (Asmanex Twifhaler) are otherwise generally more expensive than the older alternatives.

Almost two-thirds of the 11 million scripts for combined inhalers are for fluticasone/salmeterol (Seretide) and 29 per cent are for budesonide/formoterol (Symbicort). These statistics do not accurately reflect the level of prescribing of fluticasone/formoterol (Flutiform), which was introduced in the autumn of 2012.

<table>
<thead>
<tr>
<th></th>
<th>No. scripts (000s)</th>
<th>Cost (£000s)</th>
<th>Mean cost per scrip (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>beclometasone dipropionate</td>
<td>6 344</td>
<td>78 198</td>
<td>12.33</td>
</tr>
<tr>
<td>budesonide</td>
<td>436</td>
<td>9 575</td>
<td>21.96</td>
</tr>
<tr>
<td>ciclesonide</td>
<td>38</td>
<td>1 117</td>
<td>29.39</td>
</tr>
<tr>
<td>fluticasone propionate</td>
<td>542</td>
<td>15 503</td>
<td>28.60</td>
</tr>
<tr>
<td>mometasone furoate</td>
<td>8</td>
<td>234</td>
<td>29.25</td>
</tr>
<tr>
<td>ICS/bronchodilator</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>beclometasone/formoterol (Fostair)</td>
<td>565</td>
<td>19 364</td>
<td>34.27</td>
</tr>
<tr>
<td>budesonide/formoterol (Symbicort)</td>
<td>3 220</td>
<td>159 567</td>
<td>49.55</td>
</tr>
<tr>
<td>fluticasone/formoterol (Flutiform)</td>
<td>2</td>
<td>69</td>
<td>34.50</td>
</tr>
<tr>
<td>fluticasone/salmeterol (Seretide)</td>
<td>7 282</td>
<td>377 378</td>
<td>51.82</td>
</tr>
</tbody>
</table>

Table 5. Number and cost of prescriptions for ICS and ICS/bronchodilator combinations in England, 2012

Resources

Guidelines


Further reading


Information

Asthma management plans and a wealth of other material are available from the Asthma UK website: www.asthma.org.uk.

The ADMIT group is a group of European physicians interested in promoting the correct use of inhalers for asthma and COPD control. The website – www.admit-online.info – contains comprehensive, user-friendly information for patients and health professionals on how to use each and every inhaler device properly.

The Primary Care Respiratory Society UK (PCRS-UK) – www.pcrs-uk.org/index.php – is an independent charity representing primary-care health professionals interested in delivering the best standards of respiratory care.

The Asthma Control Test can be accessed on the Asthma UK website: www.asthma.org.uk/applications/control_test.

Groups and organisations

British Lung Foundation. Tel: 020 7688 5555; e-mail: enquiries@blf.org.uk; web: www.blf.org.uk.

British Thoracic Society. Tel: 020 7831 8778; e-mail: bts@brit-thoracic.org.uk; web: www.brit-thoracic.org.uk.

European Federation of Asthma and Allergy Association (EFA). Tel: +32 (0) 2 218 3141 e-mail: info@efanet.org; web: www.efanet.org.
CPD: Management of asthma

Answer these questions online at Prescriber.co.uk and receive a certificate of completion for your CPD portfolio. Utilise the Learning into Practice form to record how your learning has contributed to your professional development.

For each section, one of the statements is false – which is it?

1a. Spirometry is the preferred lung function test to demonstrate the presence and severity of airflow obstruction.
1b. Common conditions to be considered in the differential diagnosis in adults include COPD, bronchiectasis and heart failure.
1c. The results of spirometry are more specific for airway obstruction than PEF.
1d. Monitoring exhaled nitric oxide improves asthma control in mild to moderate asthma compared to a symptom-based approach.

2a. Assessment of current symptom control, risk of future exacerbations and adherence as well as inhaler technique should be undertaken prior to a step up or step down in treatment.
2b. A long-acting inhaled bronchodilator should be tried as monotherapy before taking a fixed-dose combination with an inhaled steroid.
2c. The management plan includes nonpharmacological approaches where appropriate.
2d. Total circulating immunoglobulin E (IgE) concentration is used to select patients suitable for anti-IgE treatment with omalizumab.

3a. A clinical trial of the SMART regimen shows that it improves current symptom control compared to a fixed-dose combination plus a SABA as a reliever.
3b. A clinical trial of the SMART regimen shows that it reduces the frequency of exacerbations.
3c. The single combination inhaler approach and the fixed-dose combination strategy are both effective options for patients at Step 3 whose asthma is poorly controlled.
3d. Fostair MART is indicated for use as maintenance and relief therapy.

4a. Avoidance of trigger factors does not prevent exacerbations.
4b. Written action plans, when combined with regular review, reduce hospital admissions and attendance at emergency rooms for exacerbations.
4c. Around a quarter of exacerbations are thought to be due to nonadherence with ICS.
4d. The best predictors of future exacerbations are a history of an exacerbation in the previous year and reduced FEV1.

5a. There is concern that guideline recommendations based on clinical trials may not be applicable to ‘real-life’ patients.
5b. In patients with poor asthma control despite using an ICS and a LABA, tiotropium administered via Respimat provides modest sustained bronchodilatation.
5c. Serial measurements of PEF are unreliable for monitoring patients with severe disease.
5d. Around a half of patients have poor inhaler technique irrespective of the device used.

6a. Omalizumab is associated with a reduction in exacerbations in patients with severe allergic asthma.
6b. Patient preference is the sole determinant of the choice of inhaler.
6c. Targeting patients with a high body mass index to lose weight may improve asthma control.
6d. It is uncertain whether treatment prevents the development of persistent airflow obstruction in people with asthma.

Letters

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