What’s new in Asthma?

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Asthma is an inflammatory disease

In the asthmatic airway, the wall is inflamed and thickened

During an asthma attack, tightened smooth muscles constrict the airway

Asthma is an inflammatory disease.
Asthma: The scale of the problem

5.4 million
People living with asthma in the UK

Every 10 seconds
someone is having a potentially life-threatening asthma attack in the UK

Every day, the lives of three families are devastated by the death of a loved one to an asthma attack...

...yet two-thirds of these deaths are preventable

The NRAD report highlighted failings in medical care and prescribing

The National Review of Asthma Deaths (NRAD) was the first national investigation of asthma deaths in the UK. It aimed to understand the circumstances surrounding asthma deaths to identify avoidable factors and make recommendations to improve care and reduce the number of deaths. The report, published by the Royal College of Physicians in May 2014, highlighted issues with the quality of asthma care.

Of 195 asthma deaths occurring between February 2012 and January 2013:

- The majority of people (58%) who died were thought to have mild or moderate asthma
- PAAPs were provided in only 44 (23%) individuals who died from asthma
- For 84 (43%) of those who died, there was no evidence of an asthma review in the previous year
- Exacerbating factors, or triggers (e.g., drugs, allergic reactions, and viral infections), were documented in only half of those who died (95 patients)

NRAD=National Review of Asthma Deaths; PAAP=personalised asthma action plans
NRAD report: Excessive prescribing of SABAs and under-prescribing of preventer medication

Evidence of excessive prescribing of reliever medication

- 39% of patients who were on short-acting relievers at the time of death had been prescribed more than 12 short-acting reliever inhalers in the year before they died.
- 4% had been prescribed more than 50 reliever inhalers.

Evidence of under-prescribing of preventer medication

- To comply with recommendations, most patients would usually need at least 12 preventer prescriptions per year.
- 38% of patients on preventer inhalers* received fewer than 4 inhalers in the year leading up to their death...
- 80% received fewer than 12 preventer inhalers.

*Of those patients for which the number of prescriptions was known. Among 189 patients who were on short-acting relievers at the time of death, the number of prescriptions was known for 165. Among 168 patients on preventer inhalers at the time of death, either as stand-alone or in combination, the number of prescriptions was known for 128.

NRAD=National Review of Asthma Deaths; SABA=short-acting β-agonist
Guidelines
BTS/SIGN 2016 guidelines: What has changed?

Updated national guidance has been launched to help reduce asthma attacks and save lives.1,2

A revision of the section on diagnosis1
No single test can definitively diagnose asthma
HCPs should undertake a structured clinical assessment to assess the initial probability of asthma

A revision of pharmacological management1,2
SABAs are no longer the first-line treatment for asthma1
Instead, SABAs are the key ‘rescue therapy’ from symptoms or asthma attacks and can form part of all treatment plans. They should rarely be used on their own2

A key emphasis on medication to prevent future asthma attacks; ICSs remain the most effective ‘preventer’ drug2

An emphasis on supported self-management1
Each patient should have an agreed written PAAP, as it is key to the effective management of their asthma

BTS=British Thoracic Society; ICS=inhaled corticosteroid; PAAP=personalised asthma action plans; SABA=short-acting β-agonist; SIGN=Scottish Intercollegiate Guidelines Network

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Presentation with respiratory symptoms

Structured clinical assessment

High probability of asthma
- Code as suspected asthma
- Initiation of treatment
- Assess response objectively
  - Good response
  - Poor response
    - Asthma
      - Adjust maintenance dose. Provide self-management advice. Arrange ongoing review
    - Other diagnosis likely
    - Investigate/treat for other more likely diagnosis

Intermediate probability of asthma
- SPIROMETRY
  - Options for investigations are:
    - Test for variability
    - Test for eosinophilic inflammation or atopy
  - Suspected asthma
    - Watchful waiting (if asymptomatic) or commence treatment and assess response objectively
    - Good response
    - Poor response
  - Other diagnosis likely
  - Investigate/treat for other more likely diagnosis

Low probability of asthma
- Investigate/treat for other more likely diagnosis
- Other diagnosis confirmed

FEV=forced expiratory volume; FVC=forced vital capacity; PEF=peak expiratory flow

The 2017 NICE guidelines

• Take a history but do not use symptoms alone without an objective test to diagnose asthma
  • Wheeze, cough or SOB particularly if diurnal or seasonal variation
  • Ask about triggers
  • Personal or family history of atopy

• Examination
  • Listen for a polyphonic wheeze – normal examination common in asthma

• Diagnosis of asthma must be made using **objective tests**
The 2017 NICE guidelines

- **Spirometry**
  - Offer if the diagnosis is being considered
  - Remember that in between asthma exacerbations, many asthmatics have unobstructed spirometry

- **Exhaled Nitric Oxide (FeNO)**
  - Offer a FeNO to patients over 17 in whom a diagnosis of asthma is being considered
  - Positive test is FeNO ≥ 40 ppb
  - Smoking can lower FeNO both acutely and cumulatively
  - Inhaled ICS can also lower FeNO
Updated national guidance has been launched to help reduce asthma attacks and save lives.\(^1,2\)

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**An emphasis on supported self-management\(^1\)**

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The BTS/SIGN 2016 guidelines include a revision of pharmacological management.

**Adult asthma: suspected**

- **Diagnosis and assessment**
  - Consider monitored initiation of treatment with low-dose ICS

**Adult asthma: diagnosed**

- **Evaluation**: • assess symptoms, measure lung function, check inhaler technique and adherence
  • adjust dose • update self-management plan • move up and down as appropriate

- **Regular preventer**
  - Low-dose ICS

- **Initial add-on therapy**
  - Add inhaled LABA to low-dose ICS (normally as a combination inhaler)

- **Additional add-on therapies**
  - No response to LABA – stop LABA and consider increased dose of ICS
  - If benefit from LABA but control still inadequate – continue LABA and increase ICS to medium dose
  - If benefit from LABA but control still inadequate – continue LABA and ICS and consider trial of other therapy - LTRA, SR theophylline, beta agonist tablet, LAMA

- **High-dose therapies**
  - Consider trials of:
    - Increasing ICS up to high dose
    - Addition of a fourth drug, eg LTRA, SR theophylline, beta agonist tablet, LAMA
    - Refer patient to specialist care

- **Continuous or frequent use of oral steroids**
  - Use daily steroid tablet in the lowest dose providing adequate control
  - Maintain high-dose ICS
  - Consider other treatments to minimise use of steroid tablets
  - Refer patient to specialist care

**Summary of management in adults**

- Short-acting β₂ agonists as required – consider moving up if using three doses a week or more

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BTS=British Thoracic society; ICS=inhaled corticosteroid; LABA=long-acting β-agonist; LAMA=long-acting muscarinic antagonist; LTRA=leukotriene receptor antagonists; SABA=short-acting β-agonist; SR=sustained release

Treatment

- Infrequent wheeze with normal lung function
  
  **Short acting Beta$_2$ agonist – Salbutamol**

- If more symptomatic (eg nocturnal waking or symptoms 3x week)
  
  **Low dose inhaled corticosteroid - Beclomethasone (Clenil) or Fluticasone (Flixotide)**

- If still uncontrolled
  
  **Add ICS/LABA combination or Montelukast**

- Still symptomatic **SEEK HELP!**
  
  **High dose LABA/ICS combination – initially low dose ICS via MART and then consider fixed dose LABA/ICS**

  **Consider LAMA or theophylline. SEEK HELP!**

NICE 2017
What can specialist care offer?

- Difficult asthma is defined as persistent symptoms and/or frequent asthma attacks despite treatment with high-dose therapies or continuous/frequent use of oral steroids
- Patients with difficult asthma should be systematically evaluated, including:
  - confirmation of the diagnosis of asthma, and
  - identification of the mechanism of persisting symptoms and assessment of adherence to therapy
- This assessment should be facilitated through a dedicated multidisciplinary difficult asthma service
- Patients in specialist care may benefit from the other medications, including:
  - omalizumab (anti-IgE monoclonal antibody)
  - mepolizumab, reslizumab (anti-IL-5 monoclonal antibody)
  - immunosuppressants (eg methotrexate)

IL-5=interleukin 5
Development of targeted therapies based on asthma phenotype

- AMG317
- dupilimab
- pitrakinra
- AMG157
- GSK679586
- IMA-638
- lebrikizumab
- tralokinumab
- SB-240563
- mepolizumab
- reslizumab
- benralizumab
- rhuMab-E25
- omalizumab

Omalizumab for asthma

Atopic asthma – perennial allergen

IgE 30-700* (approx)

4 courses of corticosteroids / year or maintenance dose

16 week trial

* dosing table according to kg weight!
### Xolair dosing table

#### Subcutaneous XOLAIR Doses Every 2 Weeks for Patients 12 Years of Age and Older With Asthma

<table>
<thead>
<tr>
<th>Pretreatment serum IgE (IU/mL)</th>
<th>Body weight</th>
<th>Body weight</th>
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<tr>
<td></td>
<td>Pounds</td>
<td>Kilograms</td>
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<tr>
<td>&gt;230-100</td>
<td>66-132 lbs</td>
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<td>&gt;132-154 lbs</td>
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</tbody>
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**Dose (mg)**

- See table on the right.
- 225
- 225
- 300
- 300
- 300
- 375
- 375
- DO NOT DOSE

#### Subcutaneous XOLAIR Doses Every 4 Weeks for Patients 12 Years of Age and Older With Asthma

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**Dose (mg)**

- 150
- 150
- 150
- 300
- 300
- 300
- 300
- 300
- See table on the left.
**Targeting IL-5 or IL-5Rα**

**Benralizumab**: A humanised monoclonal antibody that depletes blood eosinophils in a rapid manner by specifically targeting the IL-5α receptor on eosinophils and then recruits effector cells through ADCC.

**Mepolizumab**: A humanised monoclonal anti-IL-5 antibody, specifically targeting the α chain of IL-5 and preventing interaction of IL-5α with its receptor.

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ADCC, antibody-dependent cell-mediated cytotoxicity; IL, interleukin
**Mepolizumab / Reslizumab**

**Mepolizumab:**
Severe asthma with
blood eosinophil count $\geq 0.3 \times 10^9$/L
4 or more courses of OCS / maintenance OCS

**Reslizumab:**
Severe asthma with
blood eosinophil count $\geq 0.4 \times 10^9$/L
3 or more courses of OCS / maintenance OCS
Management of acute asthma
Assessment of acute asthma

Moderate acute asthma

- PEF >50–75% best or predicted
- No features of acute severe asthma

Acute severe asthma

Any one of:
- PEF 33–50% best or predicted
- Respiratory rate ≥25/min
- Heart rate ≥110/min
- Inability to complete sentences in one breath

Near-fatal asthma

- Defined as raised PaCO$_2$ and/or requiring mechanical ventilation with raised inflation pressures

Life-threatening asthma

- SpO$_2$ <92%
- PaO$_2$ <8 kPa
- Normal PaCO$_2$ (4.6–6.0 kPa)

Clinical signs

- Silent chest
- Cyanosis
- Poor respiratory effort
- Arrhythmia
- Exhaustion
- Altered conscious level
- Hypotension

Hospital admission
NICE quality statement 7: People with asthma who present with an exacerbation of their symptoms receive an *objective measurement of severity* at the time of presentation.

NICE quality statement 8: People aged 5 years or older presenting to a healthcare professional with a severe or life-threatening acute exacerbation of asthma receive oral or intravenous steroids *within one hour* of presentation.

NICE quality statement 10: People who received treatment in hospital or through out-of-hours services for an acute exacerbation of asthma are followed up by their own GP practice within *two working days* of treatment.
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PAAPs are an essential component of supported self-management

All patients (and/or their family or carers) should receive self-management education, including a written PAAP

**PAAPs should:**
- Be easy to understand
- Be linked to the patient’s individual treatment goals
- Include information on trigger avoidance and the importance of a smoke-free environment
- Be supported by regular professional review

**Other considerations for self-management**
- For adults, written PAAPs are based on symptoms and/or peak flow values
- All patients admitted into hospital should undergo a review of their self-management skills, and HCPs should ensure a PAAP is in place. A follow-up consultation should be considered
- During consultations for URTIs or other known triggers, ensure the patient knows what to do in the event of their asthma deteriorating

PAAP=personalised asthma action plan; URTI=upper respiratory tract infection

There are resources to help patients assess their risk of having an asthma attack

Example questions

1. In the last month, have you had difficulty sleeping due to your asthma (including cough symptoms)?
2. Has your asthma interfered with your usual daily activities (such as with your work, housework or exercise)?
3. Have you had an asthma review with your GP or asthma nurse in the last 12 months?

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