Clinical practice guidelines

Medical follow-up of patients with asthma - Adults and adolescents -

September 2004
## Synopsis

<table>
<thead>
<tr>
<th>Title</th>
<th>Medical follow-up of patients with asthma – adults and adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Publication date</td>
<td>September 2004</td>
</tr>
<tr>
<td>Requested by</td>
<td>French National Health Directorate</td>
</tr>
<tr>
<td>Produced by</td>
<td>ANAES – French National Agency for Accreditation and Evaluation in Healthcare (Guidelines Department)</td>
</tr>
<tr>
<td>Intended for</td>
<td>All health professionals who manage patients with asthma</td>
</tr>
</tbody>
</table>
| Assessment method | - Systematic review of the literature (with evidence levels)  
- Discussion among members of an *ad hoc* working group  
- External validation by peer reviewers (see ANAES guide “Recommandations pour la pratique clinique – base méthodologique pour leur réalisation en France – 1999”) |
| Objectives | Address the practical aspects of long-term medical follow-up of patients with asthma (adults and adolescents only) |
| Literature search | Jan 1997 – Dec 2003  
696 articles identified of which 296 selected for analysis and cited |
| Economic study | None |
| ANAES project leader(s) | Dr. Philippe Martel (Department head: Dr. Patrice Dosquet)  
(Literature search: Emmanuelle Blondet with the help of Maud Lefèvre  
(Department head: Rabia Bazi); secretarial work: Elodie Sallez) |
| Authors of draft report | Dr Hugues Morel, chest physician, Dinan  
Dr Nicolas Roche, chest physician, Paris |
| Collaborations and participants (annex 1) | - Learned societies  
- Steering committee  
- Working group (Chair: Professor Philippe Godard, chest physician/allergologist, Montpellier)  
- Peer reviewers |
| Internal validation | ANAES Scientific Council (Referees: Professor Bruno Housset, chest physician, Créteil; Michel Paparemborde, Head of physiotherapy training college, Lille)  
Validated on September 2, 2004 |
| Other ANAES publications on the topic | Medical follow-up is complemented by ongoing patient education, which is dealt with in the guidelines “Therapeutic education for patients with asthma – adults and adolescents” (ANAES 2001). |
I. Introduction

I.1 Objective

Asthma is a chronic condition. With regular follow-up, management of the disease can be tuned to changes in its course. The aim of follow-up is to improve the patient’s quality of life and prognosis. The aim of these guidelines is to address the long-term medical follow-up of patients with asthma (adults and adolescents only).

I.2 Scope of the guidelines

These guidelines
- define follow-up criteria for patients with asthma
- assess the role of investigations during follow-up: peak expiratory flow rate (PEF), lung function tests (LFTs) including arterial blood gas, chest radiograph, laboratory tests (blood eosinophils and eosinophils in induced sputum)
- define patients at risk of severe acute asthma and death from asthma
- propose methods for monitoring side-effects and compliance with treatment
- propose ways of adjusting long-term therapy
- propose a schedule for medical follow-up
- describe specific aspects of follow-up in occupational asthma.

The guidelines do not cover:
- initial diagnosis of asthma
- management of acute episodes (attacks, exacerbations and severe acute asthma)
- allergy-related aspects of management, notably elimination of allergens and hyposensitisation
- education for patients with asthma
- efficacy of asthma treatments
- the role of nitric oxide measurement in exhaled air, examination of exhaled breath condensates, or devices for ambulatory monitoring of forced expiratory volume in one second (FEV₁), as these tests and devices are still experimental.

II. Assessment method

The guidelines were produced using the method described in Annex 2:
- a critical appraisal of the literature published from Jan 1997 to Dec 2003
- discussions within a multidisciplinary working group (3 meetings)
- comments by peer reviewers.

They were graded on the basis of the strength of the evidence of the supporting studies (Annex 2). If no grade is given, they are based on agreement among

---

1 See “Therapeutic education for patients with asthma – adults and adolescents” (ANAES 2001)
professionals within the working group after taking into account the comments of peer reviewers.

Despite the extensive body of published data on asthma, there is insufficient long-term data to produce guidelines on follow-up criteria and schedules that are supported by strong evidence. Some of the classifications proposed here were therefore determined on the basis of agreement among professionals. Peer reviewers were especially keen to provide healthcare professionals with a practical decision-making tool suited to most clinical situations, while emphasising that recommendations can be adapted for specific circumstances.

### III. Asthma control: Definition and criteria

Asthma control should be assessed over at least 1 week up to 3 months on the basis of clinical and functional respiratory events, and their effects on daily life. According to the working group and peer reviewers,
- follow-up of asthma patients should focus on asthma control
- asthma control should be assessed at each follow-up visit.

Control is graded in three levels: unacceptable, acceptable and optimal. The criteria used to define acceptable control are adapted from the Canadian asthma consensus report\(^2\) (Table 1). They are based on agreement among professionals and have not been validated.

#### Table 1. Criteria defining acceptable asthma control

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Mean value or frequency during control assessment period (1 wk to 3 mths)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime symptoms</td>
<td>&lt; 4 days/wk</td>
</tr>
<tr>
<td>Night-time symptoms</td>
<td>&lt; 1 night/wk</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Normal</td>
</tr>
<tr>
<td>Exacerbations(^a)</td>
<td>Mild(^b), infrequent</td>
</tr>
<tr>
<td>Absence from work or school</td>
<td>None</td>
</tr>
<tr>
<td>Use of short-acting β(_2)-agonists</td>
<td>&lt; 4 doses /wk</td>
</tr>
<tr>
<td>FEV(_1) or PEF</td>
<td>&gt; 85% of personal best</td>
</tr>
<tr>
<td>PEF diurnal variation (optional)</td>
<td>&lt; 15%</td>
</tr>
</tbody>
</table>

\(^a\) See definition in Annex 3; \(^b\) Mild exacerbation: exacerbation managed by patient, requiring only a temporary increase (for a few days) in daily use of short-acting β\(_2\)-agonists

- **Unacceptable control**: One or more of the criteria in Table 1 are not met. A change in disease management is required.
- **Acceptable control**: All the criteria are met. This is the minimum target level for all patients.
- **Optimal control** (i.e. best possible control):

all the control criteria are either absent or normal
- or, in a patient with acceptable control, the best compromise has been achieved between degree of control, acceptance of treatment and possible side-effects.

**Disease severity** over a long period (6 to 12 months) is also used to assess asthma. The severity criteria defined in the guideline on therapeutic education for patients with asthma are not given here, as follow-up should focus on criteria for asthma control. Severity may be defined simply as the minimum level of treatment required for lasting disease control.

### IV. Role of investigations during follow-up

#### IV.1 Ambulatory peak expiratory flow (PEF) measurement

PEF should be measured at follow-up visits. Results should be expressed as a percentage of the patient’s best value.

PEF monitoring at home using an ambulatory device may be proposed:
- for patients at risk of severe acute asthma (see definition in Annex 3) or death from asthma
- to “poor perceiver” patients, i.e. when the patient’s symptoms are not proportional to the degree of bronchial obstruction measured by PEF or FEV₁
- when a high-risk period is anticipated (notably the pollen season)
- during periods of unacceptable asthma control
- when treatment is being changed.

However, it has not been demonstrated that routine follow-up of all patients with home measurement of PEF improves disease control.

PEF is a tool that can be used as part of the patient’s therapeutic education to help them assess their asthma and understand their disease³.

#### IV.2 Lung function tests (LFTs)

LFTs should be carried out during follow-up of patients with asthma (for recommended schedule, see Section VI “Follow-up schedule”). Long-term therapy should not be interrupted before the LFTs in order to be able to assess the bronchial obstruction that persists despite therapy.

- **Spirometry** and in particular measurement of FEV₁, slow vital capacity (SVC) and forced vital capacity (FVC) are sufficient in most cases for assessing the functional impact of asthma. These variables should be measured before and after administration of fast-acting, short-duration bronchodilators. Bronchial obstruction is given by relating FEV₁ after use of bronchodilator to the theoretical value. In asthma that is difficult to control, particularly in smokers, and while treatment is being reduced, specialists may choose to assess bronchial obstruction by

³ “Therapeutic education for patients with asthma – adults and adolescents” - ANAES 2001

---

**Medical follow-up of patients with asthma – adults and adolescents**

- ANAES – AFSSAPS / ANAES Guidelines Department / September 2004
- 5 -
measuring residual volume, small airway obstruction, and examining the general shape of the forced expiration curve.

- **Airway hyperresponsiveness (AHR)** measurement should not be used routinely for adjusting treatment, particularly the dose of inhaled corticosteroids. Although AHR may be useful in dose adjustment (one level 2 study), follow-up values cannot be measured routinely outside specialist centres.

- **Arterial blood gas measurement** is indicated in severe acute asthma. It is not indicated during follow-up except in chronic respiratory failure.

**IV.3 Chest radiography**

Chest radiography is used at initial diagnosis but should not be a routine part of follow-up in patients with asthma. It is indicated in severe exacerbations, if there are problems with long-term disease control or if complications are suspected (pneumothorax, pneumonia).

**IV.4 Laboratory tests**

The course of asthma should not be monitored:
- by eosinophil counts or activation
- by measuring eosinophils in induced sputum. Although this may be useful in adjusting long-term therapy (one level 2 study), it cannot be monitored outside specialist centres.

**V. Treatment follow-up**

**V.1 Follow-up of side-effects**

- **Long-term β₂-agonists or anticholinergics**
  No specific form of follow-up is recommended within the limits given in the French marketing authorisations of β₂-agonists or anticholinergics.

- **Theophylline**
  Patients should be monitored at each visit, especially clinically, as theophylline has a narrow therapeutic margin, and drug interactions and side-effects are common. If side-effects occur or the drug is felt to be clinically ineffective, blood theophylline concentration should be measured. Measurements after treatment has started may be routine and should be so if there are risk factors for side-effects, e.g.:
  - young children
  - the elderly
  - acute heart failure (reduce the dose because of risk of overdose)
  - coronary insufficiency
  - obesity (adjust the dose in relation to ideal weight)
  - hyperthyroidism
- impaired liver function
- history of seizures
- prolonged fever (> 38°C) lasting more than 24 hours, particularly in young children (halve the dose because of risk of overdose)
- concomitant therapy likely to increase blood theophylline concentration, or discontinuation of drugs likely to reduce it.

- **Long-term inhaled corticosteroids (ICS)**

  During follow-up:
  - look for local side-effects (candidiasis of the mouth, dysphonia) and skin fragility
  - monitor growth in adolescents
  - refer patients with a history or risk of cataracts or glaucoma to an ophthalmologist.

  Extended prescription or sudden withdrawal of high doses of ICS should be avoided if possible.

  No specific monitoring of bone effects from ICS is recommended when doses are low or average or when treatment lasts < 5 years (Grade A). However, the safety of high ICS doses for periods > 5 years and in patients with other risk factors for osteopenia has not been assessed.

  Unexplained asthenia in patients taking long-term, high-dose ICS should prompt investigation for adrenal insufficiency or Cushing’s syndrome; rare cases of acute adrenal insufficiency have been described, mainly in children.

- **Long-term oral corticosteroids**

  Patients should be monitored as recommended in the French marketing authorisations of the drugs concerned.

- **Leukotriene receptor antagonists**

  No specific form of follow-up is recommended within the limits given in the French marketing authorisation of the drugs concerned.

## V.2 Monitoring treatment compliance

Patients should be asked regularly about the medications they are taking, but the risk of overestimating compliance persists. This risk can be reduced by telling patients that it is in their interest to report as accurately as possible what medication they have taken so that treatment can be adjusted to their real needs (Grade C). They can be

---

4 - **Drugs that increase blood theophylline concentration** are allopurinol, cimetidine, fluconazole, ciprofloxacin, norfloxacin, pefloxacin, fluvoxamine, clarithromycin, erythromycin, josamycin, roxithromycin, mexiletine, pentoxifylline, stiripentol.

- **Drugs that reduce blood theophylline concentration** (i.e. discontinuation is likely to increase blood theophylline concentration) are enzyme inducers such as carbamazepine, phenobarbital, phenytoin, primidone, rifampicin, rifabutin, griseofulvin, ritonavir, lopinavir, nelfinavir.

- The range of active ingredients likely to interfere with theophylline metabolism will vary as new drugs are licensed.
asked to keep a diary during the week or weeks preceding each visit (including a record of medication and asthma control criteria).

Patients with known or suspected lack of compliance may be motivated by scheduling more frequent follow-up sessions. Structured therapeutic education may help\(^5\).

**V.3 Adjusting treatment during follow-up**

These guidelines do not cover the initial management strategy or management of acute events (attacks, exacerbations, severe acute asthma). Treatment should be adjusted to:
- degree of asthma control
- current long-term therapy.

- **If asthma control is unacceptable** (see Section II.1)
  Management should be improved in 3 steps, as follows:

  - **Step 1:** Check that:
    - the disease is actually asthma; this is especially relevant if bronchial obstruction cannot be reversed
    - compliance with current treatment is satisfactory
    - the patient is using inhalation devices correctly.

  - **Step 2:** Look for and treat:
    - aggravating factors such as exposure to allergens, rhinitis, active or passive smoking, medication (e.g. \(\beta\)-blockers), exposure to air pollution, ENT infection, gastro-oesophageal reflux
    - concomitant disease such as COPD or heart failure
    - rare specific clinical forms such as allergic bronchopulmonary aspergillosis, Churg-Strauss vasculitis.

  - **Step 3:** Adjust long-term therapy (see Table 3) to medication taken to date, particularly to current ICS dose.
    - *Patients not taking long-term therapy:* An ICS should be started at the average dose. If symptoms are frequent and FEV\(_1\) is significantly reduced, give additional medication (long-acting \(\beta_2\)-agonists, cysteinyl-leukotriene receptor antagonists or theophylline and its derivatives).
    - *Patients on low- or average-dose ICS:* Give additional medication or increase the dose of ICS. If symptoms are frequent and FEV\(_1\) is significantly reduced, increase ICS dose and give additional medication.
    - *Patients on high-dose ICS:* Give additional medication.
    - *Patients on low-dose ICS with additional medication:* Increase dose of ICS.
    - *Patients on average-dose ICS with additional medication:* Increase dose of ICS or add a second additional medication. If symptoms are frequent and FEV\(_1\) is significantly reduced, increase ICS dose and give additional medication.

---

\(^5\) See “Therapeutic education for patients with asthma – adults and adolescents”, ANAES 2001
Patients on high-dose ICS with additional medication: Give a second additional medication. If symptoms are frequent and FEV₁ is significantly reduced, suggest oral corticosteroids.

Patients on high-dose ICS with two additional medications: Start oral corticosteroids, probably as long-term therapy, or add a third additional medication.

Table 2. Low, average and high daily dose of ICS (µg/d) in adults

<table>
<thead>
<tr>
<th>Low dose</th>
<th>Average dose</th>
<th>High dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt; 500</td>
<td>500-1 000</td>
</tr>
<tr>
<td>Budesonide</td>
<td>&lt; 400</td>
<td>400-800</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>&lt; 250</td>
<td>250-500</td>
</tr>
</tbody>
</table>

<sup>a</sup> Dose should be halved for QVAR® and NEXXAIR®

Step 3 guidelines are summarized in Table 3.

Table 3. Adjusting long-term therapy (Step 3)

<table>
<thead>
<tr>
<th>Current therapy</th>
<th>New treatment&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Option 1</th>
<th>Option 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ICS</td>
<td>Average dose ICS</td>
<td>Average ICS dose + AM</td>
<td></td>
</tr>
<tr>
<td>Patients on ICS only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low or average dose ICS</td>
<td>Add AM</td>
<td>Increase ICS dose with or without AM</td>
<td></td>
</tr>
<tr>
<td>High dose ICS</td>
<td>Add AM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients on ICS and additional medication (AM)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low dose of ICS (+ 1 AM)</td>
<td>Increase ICS dose</td>
<td>Add 2&lt;sup&gt;nd&lt;/sup&gt; AM with or without increasing ICS dose</td>
<td></td>
</tr>
<tr>
<td>Average dose of ICS (+ 1 AM)</td>
<td>Increase ICS dose</td>
<td>Oral corticosteroids&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Heavy dose of ICS (+ 1 AM)</td>
<td>Add 2&lt;sup&gt;nd&lt;/sup&gt; AM</td>
<td>Add 3&lt;sup&gt;rd&lt;/sup&gt; AM</td>
<td></td>
</tr>
<tr>
<td>Heavy dose of ICS (+ 2 AMs)</td>
<td>Oral corticosteroids&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> The choice between options will depend on symptom frequency and function (particularly post-bronchodilator FEV₁).

<sup>b</sup> Additional medication (AM) covers long-acting β<sub>2</sub>-agonists, cysteinyl-leukotriene receptor antagonists, theophylline and its derivatives (bamiphylline).

<sup>c</sup> Oral corticosteroids are rarely used in adolescents

Oral corticosteroids should be avoided if possible, particularly in adolescents. If it is difficult to decide on the best treatment, consult a specialist.

If symptoms are frequent and/or FEV₁ is considerably reduced, an increase in long-term therapy may be combined initially with short-term oral corticosteroids (<15 days at a dose of 0.5-1 mg/kg/d) to achieve faster control.

Each treatment step lasts from 1 to 3 months depending on clinical and functional response. If acceptable control is not achieved despite maximal therapy, patients should be referred to a specialist.
• **If asthma control is acceptable or optimal**

Once control has been achieved, the minimum effective therapy to maintain acceptable - and ideally optimal - control should be found. In adolescents, the younger the patient, the more desirable it is to achieve optimal control.

Generally, long-term therapy should be reduced in 3-month steps but no studies have compared different step durations. ICS can be reduced in 25-50% steps. There are no data to support a specific program for discontinuing additional medication.

If there any side-effects with long-term therapy or if the patient is at risk of side-effects, reassess benefit/risk ratio more often.

In patients who receive long-term oral corticosteroids from the start, the dose should be reduced very gradually, and concomitant high-dose ICS and long-acting $\beta_2$-agonists should be given. Each step may last about 3 months, and complete withdrawal may take several years.

### VI. Follow-up schedule

The proposed follow-up schedule should be adjusted to each individual patient. For example, it does not take account of therapeutic education sessions, visits because of an intercurrent event or possible increased frequency of visits during initial management or changes in therapy.

• **When control is acceptable or optimal**

The minimum and optimum frequency of visits when control is acceptable or optimal is given in Table 4.

<table>
<thead>
<tr>
<th>ICS dose</th>
<th>Minimum follow-up (mths)</th>
<th>Optimal follow-up (mths)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Visits</td>
<td>LFT</td>
</tr>
<tr>
<td>High</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Low or average</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>None</td>
<td>12</td>
<td>12 or +</td>
</tr>
</tbody>
</table>

*a Visit with clinical examination including determination of PEF
*b An appointment with a specialist should be considered

• **When control is unacceptable**

- **Patient on short-term oral corticosteroids.** Visit with at least a clinical examination including determination of PEF, and ideally LFT, during the week following withdrawal of oral corticosteroids and one month later. An appointment with a specialist should be considered.
- **Patient not taking short-term oral corticosteroids.** Visit with at least a clinical examination including determination of PEF, and ideally LFT, 1-3 months after change in therapy.

• **In the presence of risk factors**
Follow-up frequency should be increased in patients at risk of severe acute asthma or death from asthma and in patients experiencing frequent exacerbations, i.e. asthma that is difficult to control. These patients may benefit from:
- scheduled visits to the surgery after they leave hospital
- structured therapeutic education
- a rigorous search for and elimination of trigger factors (allergens, tobacco, domestic and industrial toxins)
- possibly a home visit from a domestic environment adviser.

VII. The case of occupational asthma

Follow-up of occupational asthma involves both medical and socioprofessional aspects, which are complementary and inseparable.

Patients who are no longer exposed to the risk should be followed-up medically for a long time, as symptoms and non-specific airway hyperresponsiveness persist in > 50% of cases (Grade C).

Work-related (determination of ability to work) and medical/legal aspects (compensation) are further reasons for objective assessment of the disease by spirometry and methacholine challenge testing.

Elimination or reduction of exposure to risk, continued employment and/or maintenance of income requires a support network around the patient – doctors, social workers, and advisers from work reclassification services. The main tools that can be used are notification of occupational disease, a request for classification as a handicapped worker and visiting the occupational physician before going back to work.

VIII. Summary of guidelines

A brief summary of these guidelines is given in Annex 4.
Annex 1 – Participants

Learned societies consulted

Association asthme et allergies
Association pour les études en pneumologie libérale
Association française de recherche et d’évaluation en kinésithérapie
Association nationale des kinésithérapeutes salariés
Association pédagogique nationale pour l’enseignement de la thérapeutique
Association pour la promotion de l’expertise et de la recherche en soins infirmiers
Association de recherche en soins infirmiers
Collège national des généralistes enseignants
Fédération française de santé au travail
Fédération nationale des infirmiers
Ministère de l’éducation nationale – Inspection académique des Pyrénées-atlantique
Société française d’allergologie et d’immunologie clinique
Société française de kinésithérapie
Société française de médecine générale
Société française de médecine du travail – Observation national des asthmes professionnels
Société française de pharmacie clinique
Société francophone de médecine d’urgence
Société de pneumologie de langue française

Steering committee

Professor Jacques Ameille, chest physician/occupational physician, Garches
Ayed Benfradj, physiotherapist, Paris
Élisabeth Besnier, senior nursing manager, Soissons
Professor Jean Bousquet, allergologist/chest physician, Montpellier
Professor Nathalie Brion, pharmacist, Le Chesnay
Dr Gilles Capochichi, chest physician/allergologist, Paris

Professor Philippe Godard, chest physician/allergologist, Montpellier
Guy Isambart, nurse, Clermont
Dr Philippe Martel, ANAES
Dr Hugues Morel, chest physician, Dinan
Dr Jean-Marc Philippe, specialist in emergency medicine, Aurillac
Gérard Pierron, physiotherapist, Lamorlaye
Dr Yves Rogeaux, chest physician, Villeneuve d’Ascq
Christine Rolland, asthma association director, Paris

Working group

Professor Philippe Godard, chest physician, allergologist, Montpellier, chair
Dr Hugues Morel, chest physician, Dinan, draft report author
Dr Nicolas Roche, chest physician, Paris, draft report author
Dr Philippe Martel, ANAES, project manager

Professor Jacques Ameille, chest physician, Garches
Dr Guy Amelineau, general practitioner, Le Fenouiller
Dr Agnès Bellocq, specialist in respiratory physiology, Paris
Dr Jean-Christophe Branchet-Allinieu, specialist in emergency medicine, Nantes

Professor Frédéric De Blay, allergologist/physician, Strasbourg
Michèle Gerbe, respiratory nurse, Soissons
Pascal Gouilly, physiotherapist, Metz
Professor Dominique Huas, general practitioner, Nanterre
Marie-Dominique Le Borgne, asthma and allergy association representative, Tours
Medical follow-up of patients with asthma – adults and adolescents

Dr Catherine Le Gall, specialist in emergency medicine, Argenteuil
Dr Thierry Mathevon, specialist in emergency medicine/internal medicine, Clermont-Ferrand
Sandrine Naze, French Health Products Safety Agency (AFSSAPS), Saint-Denis

Dr Luc Refabert, chest physician/paediatrician, Paris
Dr Martine Reidboym, French Health Products Safety Agency (AFSSAPS), Saint-Denis
Dr Sergio Salmeron, chest physician, Paris
Dr Bruno Stach, chest physician, Anzin

Peer reviewers

Joël Barthe, physiotherapist, Paris
Professor François Becret, general practitioner, Rouen
Ayed Benfradji, physiotherapist, Paris
Dr Jean-Louis Bensoussan, general practitioner, Castelmourot
Élisabeth Besnier, senior nursing manager, Soissons
Dr Christian Blontz, general practitioner, Nantes
Dr Louis-Philippe Boulet, chest physician, Sainte-Foy
Dr Marie-Françoise Bourrillon, occupational physician, Paris La Défense
Professor Jean Bousquet, allergologist/asthma specialist, Montpellier
François Bridon, physiotherapist, Vichy
Professor Nathalie Brion, pharmacist, Le Chesnay
Dr Dominique Brun-Ney, specialist in emergency medicine, Boulogne
Dr Didier Cadinot, general practitioner, Broglie
Dr Gilles Capochichi, chest physician/allergologist, Paris
Dr Josette Dassonville, specialist in lung function tests, Rennes
Catherine Delaire, nurse, Montpellier
Professor Philippe Devillier, pharmacologist, Reims
Professor Alain Didier, chest physician/allergologist, Lille
Dr Nathalie Dumarcet, French Health Products Safety Agency (Afssaps), Saint-Denis
Henri Foure, physiotherapist, Amiens
Professor Jean-Louis Fumery, regional inspector, occupational medicine, Paris
Dr Gilles Garcia, chest physician, Clamart
Dr José Gomes, general practitioner, Mornac
Dr Dominique Gras, general practitioner, Strasbourg
Dr Jean-Pierre Grignet, chest physician, Denain

Dr Yves Grillet, chest physician, Valence
Dr Catherine Guélaud, chest physician, Aubergenville
Dr Christian Harou, specialist in emergency medicine, Moulins
Dr Salah Hassoun, allergologist, Challans
Professor Bruno Houssuet, chest physician, Créteil, ANAES Scientific Council
Professor Marc Humbert, chest physician, Clamart
Guy Isambart, nurse, Clermont
Dr Erwan L'Herm, medical intensivist, Brest
Sophie Loiseau, nurse/child carer, La Roche sur Yon
Professor Christophe Marguet, chest physician/allergologist, Rouen
Dr Dominique Martinez, general practitioner, Lattes
Professor Mathieu Molimard, chest physician/pharmacologist, Bordeaux
Dr Franck Monchard, specialist in emergency medicine, Aurillac
Michel Paparemborde, director of physiotherapy training college, Lille, ANAES Scientific Council
Dr Hervé Peglasco, chest physician/allergologist, Marseille
Dr Thierry Piegeanne, chest physician, Les Sables d'Orléans
Dr Jean-Marc Philippe, specialist in emergency medicine, Aurillac
Gérard Pierron, physiotherapist, Lamorlaye
Dr Louis-Marie Pommier, general practitioner, Esves-sous-Indre
Dr Gilbert Potier, general practitioner, La Possession
Dr Anne Prud'homme, chest physician, Trabes
Dr Pierre Rabany, general practitioner, Nanterre
Bénédicte Rascol, nurse, Arles
Marie-Pierre Rinn, president of the Asthma and Allergy association, Ballan Mire

Dr Jacques Robert, paediatrician, allergologist, Vaulx-en-Velin
Dr Yves Rogeaux, chest physician, Villeneuve d'Ascq
Christine Rolland, Director of the association "Asthme et Allergies", Paris
Dr Lisa Rosencher, chest physician, Paris
Professor Pierre Scheinmann, chest physician/allergologist, Paris
Charline Simon, nurse, Soissons
Janine Sorgniard, member of the association "Asthme et Allergies", Ballan Mire

Professor André-Bernard Tonnel, chest physician, Lille
Dr Marie-Dominique Touze, medical intensivist, Nantes
Dr Florence Trebuchon, allergologist, Monferrier-sur-Lez
Dr Albert Trinh-Duc, specialist in emergency medicine, Agen
Sylvie Yassur, parent of a child with asthma, Paris
Annex 2 – Assessment method

The ANAES method for producing these clinical practice guidelines\textsuperscript{6} consisted of the following steps:

**Defining the scope of the guidelines (Steering committee).** ANAES invited representatives from learned societies concerned by the topic to take part in a steering committee whose job was to define the scope of the guidelines, to review previous work on the subject and to nominate professionals to take part in a working group or act as peer reviewers.

**Literature search (Documentation Department of ANAES):** See below

**Drafting the guidelines (Working group).** The ANAES project manager formed a working group of 19 professionals from a number of disciplines, working in public or private practice, from all over the country. The chair of the working group coordinated the production of the guidelines with the help of the project manager whose job was to ensure conformity with the methodological principles of guideline production. Two members of the working group identified, selected, and analysed relevant studies (from a literature search performed by the ANAES Documentation Department) and wrote a draft report. This draft report was discussed by the working group over 3 meetings and amended in the light of comments from other members of the working group and from peer reviewers. Proposals for future studies and action were made.

**External validation (Peer reviewers).** Peer reviewers were appointed according to the same criteria as working group members. They were consulted by post after the second working group meeting, primarily with regard to the readability and applicability of the guidelines (scores from 1 to 9). The ANAES project manager summarized their comments and submitted them to the working group prior to the third meeting. Peer reviewers were asked to undersign the final document.

**Internal validation (Evaluation Section of the ANAES Scientific Council).** Two members of the Council acted as referees reporting to the Council, together with the ANAES report manager. The working group finalized the guidelines with due regard to the Council’s suggestions.

- **Literature search and analysis (general procedure)**

  The scope of the literature search was defined by the steering committee and the project manager. The search was carried out by the ANAES Documentation Department and focused on searching:

\textsuperscript{6} Full details are given in “Recommandations pour la pratique clinique – base méthodologique pour leur réalisation en France – 1999” (ANAES)
- medical and scientific databases over an appropriate period, with special emphasis on retrieving clinical practice guidelines, consensus conferences, articles on medical decision-making, systematic reviews, meta-analyses and other assessments already published nationally or internationally (articles in French or English)
- specific and/or financial/economic databases, if necessary
- all relevant websites (government agencies, professional societies, etc.)
- the grey literature (documents not identified through the usual information distribution circuits)
- legislative and regulatory texts

Further references were obtained from citations in the articles retrieved above and from working group members’ and peer reviewers’ own reference sources. The search was updated until the project was completed.

The articles selected were analysed according to the principles of a critical appraisal of the literature, using a checklist, to allocate a level of scientific evidence to each study. Whenever possible, the working group based their guidelines on this review of the literature. Guidelines were graded from A to C as shown in Table 1 depending on the level of the evidence of the supporting studies. If no grading is given, they are based on agreement among professionals.

Table 1. Grading of guidelines

<table>
<thead>
<tr>
<th>Level of published scientific evidence</th>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>A</td>
<td>Established scientific evidence</td>
</tr>
<tr>
<td>Randomised controlled trials of high power</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meta-analyses of randomised controlled trials</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decision analyses based on properly conducted studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 2</td>
<td>B</td>
<td>Presumption of scientific foundation</td>
</tr>
<tr>
<td>Randomised controlled trials of low power</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Properly conducted non-randomised controlled trials</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cohort studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 3</td>
<td>C</td>
<td>Low level of evidence</td>
</tr>
<tr>
<td>Case-control studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comparative studies with major bias</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case series</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Specifcics of the literature search for this study

The following databases were searched:

- Medline (National Library of Medicine, United States)
- Embase (Elsevier, Netherlands)
- Pascal (CNRS-INIST, France)
- Cochrane Library (Great Britain)
- National Guideline Clearinghouse (United States)
- HTA Database (International network of agencies for health technology assessment - INAHTA)
- BDSP (Public health database, Rennes)
The strategy for searching the Medline, Embase and Pascal databases is given in Table 2. The search terms were either thesaurus terms (MeSH descriptors for Medline) or terms from titles or abstract (free text).

Table 2. Search strategy

<table>
<thead>
<tr>
<th>Type of study/Subject</th>
<th>Terms used</th>
<th>Search period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-analyses, Literature reviews</td>
<td>Stage 1 Meta analysis OR Review literature OR Literature review OR Systematic review</td>
<td>1997-2003</td>
</tr>
<tr>
<td>Management during follow-up</td>
<td>Stage 1 Management (in title) OR [(Therapy OR Drug therapy OR Rehabilitation) AND Follow up OR Follow-up studies OR Follow*)]</td>
<td>1997-2003</td>
</tr>
<tr>
<td>Care programmes for patients with asthma</td>
<td>Stage 1 Self management program</td>
<td>1997-2003</td>
</tr>
<tr>
<td>Lung function tests</td>
<td>Stage 1 (Peak expiratory flow rate OR Expiratory flow rate OR Forced expiratory flow rates OR Forced expiratory volume OR Bronchial hyperreactivity OR Respiratory function tests OR Respiratory sound* OR Spirometry ) AND (Follow up OR Follow-up studies OR Follow*)</td>
<td>1997-2003</td>
</tr>
<tr>
<td>Physical examination during follow-up</td>
<td>Stage 1 (Physical examination OR Clinical examination) AND (Follow up OR Follow-up studies OR Follow*)</td>
<td>1997-2003</td>
</tr>
<tr>
<td>Radiography</td>
<td>Stage 1 Mass Chest X-ray</td>
<td>1997-2003</td>
</tr>
<tr>
<td>Patient compliance</td>
<td>Stage 1 Patient compliance OR Patient acceptance of health care OR Patient education</td>
<td>2000-2003</td>
</tr>
<tr>
<td>Asthma control during follow-up</td>
<td>Stage 9 Asthma control</td>
<td>1997-2003</td>
</tr>
<tr>
<td>Quality of life questionnaires</td>
<td>Stage 1 Quality of life AND Questionnaire OR Juniper E (as author)</td>
<td>1997-2003</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>Stage 1 Rhinitis AND (Follow up OR Follow-up studies OR Follow*)</td>
<td>1997-2003</td>
</tr>
<tr>
<td>French literature</td>
<td>Stage 1 Asthma* OR Control* OR Suivi OR Surveillance</td>
<td>1993-2003</td>
</tr>
<tr>
<td>Total number of references found</td>
<td>2 957</td>
<td></td>
</tr>
<tr>
<td>Total number of articles studied</td>
<td>696</td>
<td></td>
</tr>
<tr>
<td>Number of articles cited</td>
<td>296</td>
<td></td>
</tr>
</tbody>
</table>
Annex 3 – Definitions

Asthma attack: A paroxystic episode of symptoms lasting a short time (≤1 day).

Exacerbation: An episode of gradual deterioration, over several days, in one or more clinical signs, and functional parameters of bronchial obstruction. It is classed as severe if oral corticosteroids are needed or if PEF falls by more than 30% below baseline values for 2 consecutive days.

Severe acute asthma: defined in adults by one of the following signs:
- pulse > 110/min, respiratory rate = 25/min
- inability to finish sentences in a single respiratory cycle
- PEF ≤ 50% of theoretical value or patient’s best known value
- bradycardia
- hypotension
- no sounds audible on auscultation
- cyanosis
- confusion or coma
- exhaustion

Risk factors for severe acute asthma and death by asthma (level of evidence 3):
- poor socioeconomic circumstances
- adolescent or elderly subjects
- history of “near fatal” asthma or hospitalisation in intensive care with asthma
- FEV₁ < 40% of theoretical value
- > 50% reversibility on β₂-agonist treatment
- frequent visits to Accident and Emergency or GP or repeated hospital admissions
- elevated blood eosinophils (> 1 000/mm³); patients who are “poor perceivers” of their degree of bronchial obstruction
- smoking > 20 packs/year
- poor compliance and/or denial of disease
- use of 3 (or more) asthma medications
- corticosteroid therapy stopped in last 3 months
Annex 4 – Brief summary of guidelines

The follow-up of patients with asthma should focus on asthma control (disease course over a number of weeks)

There are 3 levels of asthma control

- **Acceptable**: all control criteria (Table 1) are met
- **Unacceptable**: one or more criteria are not met
- **Optimal**: all control criteria are normal or, in a patient with acceptable control, the best compromise has been achieved between degree of control, acceptance of treatment and possible side-effects.

**Table 1. Criteria defining acceptable asthma control**

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Value or frequency*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime symptoms</td>
<td>&lt; 4 days/wk</td>
</tr>
<tr>
<td>Night-time symptoms</td>
<td>&lt; 1 night/wk</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Normal</td>
</tr>
<tr>
<td>Exacerbations</td>
<td>Mild, infrequent</td>
</tr>
<tr>
<td>Absence from work or school</td>
<td>None</td>
</tr>
<tr>
<td>Use of short-acting $\beta_2$-agonists</td>
<td>&lt; 4 doses/wk</td>
</tr>
<tr>
<td>FEV$_1$ or PEF</td>
<td>&gt; 85% of personal best</td>
</tr>
<tr>
<td>PEF diurnal variation (optional)</td>
<td>&lt; 15%</td>
</tr>
</tbody>
</table>

* Mean during control assessment period (1 wk to 3 mos)

FEV: forced expiratory volume; PEF: peak expiratory flow

Follow-up includes monitoring of treatment side-effects and compliance.

Treatment should be adjusted to level of control and current long-term therapy.

- **If control is unacceptable**
  - Check: that the disease is asthma, compliance, correct use of inhalation devices.
  - Look for and treat: aggravating factors, concomitant disease, specific clinical forms.
  - Adjust long-term therapy (see Table 2) in steps of 1 to 3 months.

- **If control is acceptable or optimal**
  - Find the minimum effective treatment to maintain at least acceptable and ideally optimal control. Each step should last 3 months.
Table 2. Adjusting long-term therapy if control is unacceptable

<table>
<thead>
<tr>
<th>Current therapy</th>
<th>New treatment (^a)</th>
<th>Option 1</th>
<th>Option 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ICS</td>
<td>Average dose ICS</td>
<td></td>
<td>Average ICS dose + AM</td>
</tr>
<tr>
<td><strong>Patients on ICS only</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low or average dose ICS</td>
<td>Add AM</td>
<td></td>
<td>Increase ICS dose with or without AM</td>
</tr>
<tr>
<td>High dose ICS</td>
<td>Add AM</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patients on ICS and additional medication (AM) (^b)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low dose of ICS (+ 1 AM)</td>
<td>Increase ICS dose</td>
<td></td>
<td>Add 2(^{nd}) AM with or without increasing ICS dose</td>
</tr>
<tr>
<td>Average dose of ICS (+ 1 AM)</td>
<td>Increase ICS dose</td>
<td></td>
<td>Oral corticosteroids (^c)</td>
</tr>
<tr>
<td>Heavy dose of ICS (+ 1 AM)</td>
<td>Add 2(^{nd}) AM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heavy dose of ICS (+ 2 AMs)</td>
<td>Oral corticosteroids (^c)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) The choice between options will depend on symptom frequency and respiratory function (particularly post-bronchodilator FEV\(_1\)).

\(^b\) Additional medication (AM) covers long-acting \(\beta_2\)-agonists, cysteinyl-leukotriene receptor antagonists, theophylline and its derivatives (bamiphylline).

\(^c\) Oral corticosteroids are rarely used in adolescents.

---

**Frequency of follow-up visits (V) and lung function tests (LFTs) according to the dose of inhaled corticosteroids (ICS) needed for acceptable control**

Table 3. Frequency of follow-up visits and LFTs

<table>
<thead>
<tr>
<th>ICS dose</th>
<th>Follow-up visits (mths)</th>
<th>LFT (mths)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>3</td>
<td>3 - 6</td>
</tr>
<tr>
<td>Low or average</td>
<td>6</td>
<td>6 - 12</td>
</tr>
<tr>
<td>None</td>
<td>12</td>
<td>12 or +</td>
</tr>
</tbody>
</table>

Low, average and high daily dose of ICS (µg/day) in adults

<table>
<thead>
<tr>
<th></th>
<th>Low dose</th>
<th>Average dose</th>
<th>High dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone(^a)</td>
<td>&lt; 500</td>
<td>500-1 000</td>
<td>&gt; 1 000</td>
</tr>
<tr>
<td>Budesonide</td>
<td>&lt; 400</td>
<td>400-800</td>
<td>&gt; 800</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>&lt; 250</td>
<td>250-500</td>
<td>&gt; 500</td>
</tr>
</tbody>
</table>

\(^a\) Dose should be halved for QVAR\(^\oplus\) and NEXXAIR\(^\oplus\)