



## REVIEW

# Clinical practice guidelines: Medical follow-up of patients with asthma—Adults and adolescents

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### KEYWORDS

Guideline;  
Asthma;  
Follow-up;  
Control

**Summary** 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 below) 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.

| Criterion                               | Value or frequency*    |
|-----------------------------------------|------------------------|
| Day-time symptoms                       | < 4 days/week          |
| Night-time symptoms                     | < 1 night/week         |
| Physical activity                       | Normal                 |
| Exacerbations                           | Mild, infrequent       |
| Absence from work or school             | None                   |
| Use of short-acting $\beta_2$ -agonists | < 4 doses/week         |
| FEV <sub>1</sub> or PEF                 | > 85% of personal best |
| PEF diurnal variation (optional)        | < 15%                  |

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\*Mean during control assessment period (1 week–3 months).  
FEV: forced expiratory volume; PEF: peak expiratory flow.

→ Follow-up includes monitoring of treatment side effects and adherence.

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

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

| Current therapy                                       | New treatment <sup>a</sup>        |                                                   |
|-------------------------------------------------------|-----------------------------------|---------------------------------------------------|
|                                                       | Option 1                          | Option 2                                          |
| No ICS                                                | Average-dose ICS                  | Average ICS dose+AM <sup>b</sup>                  |
| <i>Patients on ICS only</i>                           |                                   |                                                   |
| Low- or average-dose ICS                              | Add AM                            | Increase ICS dose with or without AM              |
| High-dose ICS                                         | Add AM                            |                                                   |
| <i>Patients on ICS and additional medication (AM)</i> |                                   |                                                   |
| Low dose of ICS (+1 AM)                               | Increase ICS dose                 |                                                   |
| Average dose of ICS (+1 AM)                           | Increase ICS dose                 | Add second AM with or without increasing ICS dose |
| Heavy dose of ICS (+1 AM)                             | Add second AM                     | Oral corticosteroids <sup>c</sup>                 |
| Heavy dose of ICS (+2 AMs)                            | Oral corticosteroids <sup>c</sup> | Add third AM                                      |

<sup>a</sup>The choice between options will depend on symptom frequency and respiratory function (particularly post-bronchodilator FEV<sub>1</sub>).

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

<sup>c</sup>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 (see Table 3 below)

Table 3 Frequency of follow-up visits and LFTs.

| ICS dose       | V (months) | LFT (months) |
|----------------|------------|--------------|
| High           | 3          | 3–6          |
| Low or average | 6          | 6–12         |
| None           | 12         | 12 or +      |

Low, average and high daily dose of ICS ( $\mu\text{g}/\text{day}$ ) in adults.

|                             | Low dose | Average dose | High dose |
|-----------------------------|----------|--------------|-----------|
| Beclomethasone <sup>a</sup> | < 500    | 500–1000     | > 1000    |
| Budesonide                  | < 400    | 400–800      | > 800     |
| Fluticasone                 | < 250    | 250–500      | > 500     |

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

### Synopsis

|                                              |                                                                                                                                                                                                                                                                                                                                                       |
|----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Title                                        | Medical follow-up of patients with asthma—adults and adolescents                                                                                                                                                                                                                                                                                      |
| Publication date                             | September 2004                                                                                                                                                                                                                                                                                                                                        |
| Requested by                                 | French National Health Directorate                                                                                                                                                                                                                                                                                                                    |
| Produced by                                  | Anaes—French National Agency for Accreditation and Evaluation in Healthcare (Guidelines Department)                                                                                                                                                                                                                                                   |
| Intended for                                 | All health professionals who manage patients with asthma                                                                                                                                                                                                                                                                                              |
| Assessment method                            | <ul style="list-style-type: none"> <li>• Systematic review of the literature (with evidence levels)</li> <li>• Discussion among members of an ad hoc working group</li> <li>• External validation by peer reviewers (see Anaes guide “Recommandations pour la pratique clinique—base méthodologique pour leur réalisation en France—1999”)</li> </ul> |
| Objectives                                   | Address the practical aspects of long-term medical follow-up of patients with asthma (adults and adolescents only)                                                                                                                                                                                                                                    |
| Literature search                            | January 1997–December 2003<br>2957 articles identified of which 696 analysed                                                                                                                                                                                                                                                                          |
| Economic study                               | None                                                                                                                                                                                                                                                                                                                                                  |
| Anaes project leader(s)                      | Dr. Philippe Martel (Department head: Dr. Patrice Dosquet)<br>(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<br>Dr. Nicolas Roche, chest physician, Paris                                                                                                                                                                                                                                                                 |
| Collaborations and participants (Appendix A) | <ul style="list-style-type: none"> <li>• Learned societies</li> <li>• Steering committee</li> <li>• Working group (Chair: Professor Philippe Godard, chest physician/allergologist, Montpellier)</li> <li>• Peer reviewers</li> </ul>                                                                                                                 |

## 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)

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## Introduction

### Objective

Asthma is a chronic condition. If follow-up is regular, its management can be tuned to changes in the course of the disease. 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).

### 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 adherence to 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,<sup>\*</sup>
- 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 1 s (FEV<sub>1</sub>), as these tests and devices are still experimental.

## Assessment method

The guidelines were produced using the method described in Appendix B:

- a critical appraisal of the literature published from January 1997 to December 2003,
- discussions within a multidisciplinary working group (three meetings),
- comments by peer reviewers.

They were graded on the basis of the strength of the evidence of the supporting studies (Appendix B). If no grade is given, they are based on agreement among professionals within the working group after taking into account the comments of peer reviewers.

Despite the extensive body of published data on asthma, there are 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. Members of the working group 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.

## 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<sup>†</sup> (Table 1). They are based on agreement among professionals and have not been validated.

- **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.

**Severity** is also used to assess asthma. It refers to the course of the disease over a long period (6–12 months). 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.

<sup>\*</sup>See “Therapeutic education for patients with asthma – adults and adolescents” (Anaes 2001).

<sup>†</sup>Boulet LP, Becker A, Bérubé D, Beveridge R, Ernst P. Canadian asthma consensus report. *Can Med Assoc J* 1999;161(Suppl 11):S1–S61.

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

| Criterion                               | Mean value or frequency during control assessment period (1 week–3 months) |
|-----------------------------------------|----------------------------------------------------------------------------|
| Day-time symptoms                       | <4 days/week                                                               |
| Night-time symptoms                     | <1 night/week                                                              |
| Physical activity                       | Normal                                                                     |
| Exacerbations*                          | Mild <sup>†</sup> , infrequent                                             |
| Absence from work or school             | None                                                                       |
| Use of short-acting $\beta_2$ -agonists | <4 doses/week                                                              |
| FEV <sub>1</sub> or PEF                 | >85% of personal best                                                      |
| PEF diurnal variation (optional)        | <15%                                                                       |

\*See definition in Appendix 3.

<sup>†</sup>Mild exacerbation: exacerbation managed by patient, requiring only a temporary increase (for a few days) in daily use of short-acting  $\beta_2$ -agonists.

## Role of investigations during follow-up

### 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 Appendix C) 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 FEV<sub>1</sub>,
- 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 disease.<sup>‡</sup>

### Lung function tests (LFTs)

LFTs should be carried out during follow-up of patients with asthma (for recommended schedule, see Section “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 FEV<sub>1</sub>, slow vital capacity 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 FEV<sub>1</sub> 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 measuring residual volume, small airway obstruction, and examining the general shape of the forced expiration curve.
- *Bronchial hyperresponsiveness* (BHR) measurement should not be used routinely for adjusting treatment, particularly the dose of inhaled corticosteroids (ICS). Although BHR 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.

### 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).

<sup>‡</sup>“Therapeutic education for patients with asthma – adults and adolescents”, Anaes 2001.

## 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.

## Treatment follow-up

### Follow-up of side effects

- *Long-term  $\beta_2$ -agonists or anticholinergics*  
No specific form of follow-up is recommended within the limits given in the French marketing authorisations of  $\beta_2$ -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 ( $>38^\circ\text{C}$ ) lasting more than 24 h, 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.<sup>§</sup>

<sup>§</sup> *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.

- *Long-term 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.

## Monitoring treatment adherence

Patients should be asked regularly about the medications they are taking, but the risk of overestimating adherence 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 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 adherence may be motivated by scheduling more frequent follow-up sessions. Structured therapeutic education may help.<sup>¶</sup>

## Adjusting treatment during follow-up

These guidelines do not cover the initial management strategy or management of acute events

<sup>¶</sup>See "Therapeutic education for patients with asthma – adults and adolescents", Anaes 2001.

**Table 2** Low, average and high daily dose of ICS ( $\mu\text{g}/\text{d}$ ) in adults.

|                 | Low dose | Average dose | High dose |
|-----------------|----------|--------------|-----------|
| Beclomethasone* | < 500    | 500–1000     | > 1000    |
| Budesonide      | < 400    | 400–800      | > 800     |
| Fluticasone     | < 250    | 250–500      | > 500     |

\*Dose should be halved for QVAR<sup>®</sup> and NEXXAIR<sup>®</sup>.

(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 Definition and Criteria)

Management should be improved in three stages, as follows:

- **Stage 1:** Check that:
  - the disease is actually asthma; this is especially relevant if bronchial obstruction cannot be reversed,
  - adherence to current treatment is satisfactory,
  - the patient is using inhalation devices correctly.
- **Stage 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.
- **Stage 3:** Adjust long-term therapy (see Table 3) to medication taken to date, particularly to current ICS dose (see Table 2).
  - *Patients not taking long-term therapy:* An ICS should be started at the average dose. If symptoms are frequent and  $\text{FEV}_1$  is significantly reduced, give additional medication (AM) (long-acting  $\beta_2$ -agonists, cysteinyl-leukotriene receptor antagonists or theophylline and its derivatives).
  - *Patients on low- or average-dose ICS:* Give AM or increase the dose of ICS. If symptoms are frequent and  $\text{FEV}_1$  is significantly reduced, increase ICS dose and give AM.
  - *Patients on high-dose ICS:* Give AM.

- *Patients on low-dose ICS with AM:* Increase dose of ICS.
- *Patients on average-dose ICS with AM:* Increase dose of ICS or add a second AM. If symptoms are frequent and  $\text{FEV}_1$  is significantly reduced, increase ICS dose and give AM.
- *Patients on high-dose ICS with AM:* Give a second AM. If symptoms are frequent and  $\text{FEV}_1$  is significantly reduced, suggest oral corticosteroids.
- *Patients on high-dose ICS with two AMs:* Start oral corticosteroids, probably as long-term therapy, or add a third AM.

Stage 3 guidelines are summarised in Table 3.

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  $\text{FEV}_1$  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 stage of treatment 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 AM.

If there are 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

**Table 3** Adjusting long-term therapy (Stage 3).

| Current therapy                                             | New treatment*                    |                                                |
|-------------------------------------------------------------|-----------------------------------|------------------------------------------------|
|                                                             | Option 1                          | Option 2                                       |
| No ICS                                                      | Average-dose ICS                  | Average ICS dose+AM                            |
| Patients on ICS only                                        |                                   |                                                |
| Low or Average-dose ICS                                     | Add AM                            | Increase ICS dose with or without AM           |
| High dose ICS                                               | Add AM                            |                                                |
| Patients on ICS and additional medication (AM) <sup>†</sup> |                                   |                                                |
| Low dose of ICS (+1 AM)                                     | Increase ICS dose                 |                                                |
| Average dose of ICS (+1 AM)                                 | Increase ICS dose                 | Add 2nd AM with or without increasing ICS dose |
| Heavy dose of ICS (+1 AM)                                   | Add second AM                     | Oral corticosteroids <sup>‡</sup>              |
| Heavy dose of ICS (+2 AMs)                                  | Oral corticosteroids <sup>‡</sup> | Add third AM                                   |

\*The choice between options will depend on symptom frequency and function (particularly post-bronchodilator FEV<sub>1</sub>).

<sup>†</sup>Additional medication (AM) covers long-acting  $\beta_2$ -agonists, cysteinyl-leukotriene receptor antagonists, theophylline and its derivatives (bamiphylline).

<sup>‡</sup>Oral corticosteroids are rarely used in adolescents.

**Table 4** Frequency of visits\* and LFT during follow-up depending on ICS dose.

| ICS dose       | Minimum follow-up (months) |         | Optimal follow-up (months) |     |
|----------------|----------------------------|---------|----------------------------|-----|
|                | Visits                     | LFT     | Visit                      | LFT |
| High           | 3 <sup>†</sup>             | 6       | 3                          | 3   |
| Low or average | 6                          | 12      | 6                          | 6   |
| None           | 12                         | 12 or + | 12                         | 12  |

\*Visit with clinical examination including determination of PEF.

<sup>†</sup>An appointment with a specialist should be considered.

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.

## 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.
- 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 1 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 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.

## 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 bronchial 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.

## Acknowledgements

We thank Emmanuelle Blondet for her thorough search of the literature and the members of the working group for their highly professional participation in the production of these guidelines. We also thank Pippa Sandford of the Kiwi Consultants translating group for translating these guidelines.

## Appendix A. 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—Observatoire national des asthmes professionnels*  
*Société française de pharmacie clinique*  
*Société francophone de médecine d'urgence*  
*Société de pneumologie de langue française*

### Steering committee

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 Élisabeth Besnier, senior nursing manager, Soissons

Professor Jean Bousquet, allergologist/chest physician, Montpellier  
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| <b>Peer reviewers</b>                                                                      |                                                                                    | Dr. Josette Dassonville, specialist in lung function tests, Rennes                | Dr. Gilbert Potier, general practitioner, La Possession                                          |
| Joël Barthe, physiotherapist, Paris                                                        | Professor Marc Humbert, chest physician, Clamart                                   | Catherine Delaire, nurse, Montpellier                                             | Dr. Anne Prud'homme, chest physician, Trabes                                                     |
| Professor François Becret, general practitioner, Rouen                                     | Guy Isambart, nurse, Clermont                                                      | Professor Philippe Devillier, pharmacologist, Reims                               | Dr. Pierre Rabany, general practitioner, Nanterre                                                |
| Ayed Benfradj, physiotherapist, Paris                                                      | Dr. Erwan L'Her, medical intensivist, Brest                                        | Professor Alain Didier, chest physician/allergologist, Toulouse                   | Bénédicte Rascol, nurse, Arles                                                                   |
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| Élisabeth Besnier, senior nursing manager, Soissons                                        | Professor Christophe Marguet, chest physician/allergologist, Rouen                 | Henri Foure, physiotherapist, Amiens                                              | Dr. Jacques Robert, paediatrician, allergologist, Vaulx-en-Velin                                 |
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| Dr. Catherine Guelaud,<br>chest physician,<br>Aubergenville                             | Professor André-<br>Bernard Tonnel, chest<br>physician, Lille                                  |
| Dr. Christian Harou,<br>specialist in emergency<br>medicine, Moulins                    | Dr. Marie-Dominique<br>Touze, medical<br>intensivist, Nantes                                   |
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|                                                                                         | Sylvie Yassur, parent of<br>a child with asthma,<br>Paris                                      |

## Appendix B. Assessment method

The Anaes method for producing these clinical practice guidelines\*\* comprised 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 three 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 summarised 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 finalised 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

- 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.

\*\*Full details are given in "Recommandations pour la pratique clinique – base méthodologique pour leur réalisation en France – 1999" (Anaes).

**Table 5** Grading of guidelines.

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

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 5 depending on the level of the evidence of the supporting studies. If no grading is given, they are based on agreement among professionals.

- Specifics 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 6. The search terms were either thesaurus terms (MeSH descriptors for Medline) or terms from titles or abstract (free text).

## Appendix C. Definitions

**Asthma attack:** A paroxysmic episode of symptoms lasting a short time ( $\leq 1$  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  $> 110/\text{min}$ , respiratory rate  $\geq 25/\text{min}$ ,
- inability to finish sentences in a single respiratory cycle,
- $\text{PEF} \leq 50\%$  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 "nearly fatal" asthma or hospitalisation in intensive care with asthma,
  - $\text{FEV}_1 < 40\%$  of theoretical value,
  - $> 50\%$  reversibility on  $\beta_2$ -agonist treatment,

**Table 6** Search strategy.

| Type of study/subject                               | Terms used                                                                                                                                                                                                                                                                        | Search period |
|-----------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| <i>Guidelines</i>                                   |                                                                                                                                                                                                                                                                                   | 1997–2003     |
| Stage 1<br>AND Stage 2                              | Asthma<br>Guideline* OR Practice guideline OR Health<br>planning guideline OR Guideline [title] OR<br>Consensus development conference OR<br>Consensus development conference, NIH<br>OR Consensus conference[title] OR<br>Consensus statement[title]                             |               |
| <i>Meta-analyses, literature reviews</i>            |                                                                                                                                                                                                                                                                                   | 1997–2003     |
| Stage 1<br>AND Stage 3                              | Meta analysis OR Review literature OR<br>Literature review OR Systematic review                                                                                                                                                                                                   |               |
| <i>Management during follow-up</i>                  |                                                                                                                                                                                                                                                                                   | 1997–2003     |
| Stage 1<br>AND Stage 4                              | Management (in title) OR [(Therapy OR<br>Drug therapy OR Rehabilitation) AND Follow<br>up OR Follow-up studies OR Follow*]                                                                                                                                                        |               |
| <i>Care programmes for patients<br/>with asthma</i> |                                                                                                                                                                                                                                                                                   | 1997–2003     |
| Stage 1<br>AND Stage 5                              | Self management program                                                                                                                                                                                                                                                           |               |
| <i>Lung function tests</i>                          |                                                                                                                                                                                                                                                                                   | 1997–2003     |
| Stage 1<br>AND Stage 6                              | (Peak expiratory flow rate OR Expiratory<br>flow rate OR Forced expiratory flow rates<br>OR Forced expiratory volume OR Bronchial<br>hyperreactivity OR Respiratory function<br>tests OR Respiratory sound* OR Spirometry )<br>AND (Follow up OR Follow-up studies OR<br>Follow*) |               |
| <i>Physical examination during<br/>follow-up</i>    |                                                                                                                                                                                                                                                                                   | 1997–2003     |
| Stage 1<br>AND Stage 6                              | (Physical examination OR Clinical<br>examination) AND (Follow up OR Follow-up<br>studies OR Follow*)                                                                                                                                                                              |               |
| <i>Radiography</i>                                  |                                                                                                                                                                                                                                                                                   | 1997–2003     |
| Stage 1<br>AND Stage 7                              | Mass chest X-ray                                                                                                                                                                                                                                                                  |               |
| <i>Patient compliance</i>                           |                                                                                                                                                                                                                                                                                   | 2000–2003     |
| Stage 1<br>AND Stage 8                              | Patient compliance OR Patient acceptance<br>of health care OR Patient education                                                                                                                                                                                                   |               |
| <i>Asthma control during follow-up</i>              |                                                                                                                                                                                                                                                                                   | 1997–2003     |
| Stage 9                                             | Asthma control                                                                                                                                                                                                                                                                    |               |
| <i>Quality of life questionnaires</i>               |                                                                                                                                                                                                                                                                                   | 1997–2003     |
| Stage 1<br>AND Stage 10                             | Quality of life AND Questionnaire<br>OR<br>Juniper E (as author)                                                                                                                                                                                                                  |               |
| <i>Rhinitis</i>                                     |                                                                                                                                                                                                                                                                                   | 1997–2003     |

Table 6 (continued)

| Type of study/subject            | Terms used                                                                      | Search period |
|----------------------------------|---------------------------------------------------------------------------------|---------------|
| Stage 1<br>AND Stage 11          | Rhinitis AND ( <i>Follow up</i> OR <i>Follow-up studies</i> OR <i>Follow*</i> ) |               |
| <i>French literature</i>         |                                                                                 | 1993–2003     |
| Stage 1<br>AND Stage 12          | Asthma*<br>Control* OR <i>Suivi</i> OR <i>Surveillance</i>                      |               |
| Total number of references found |                                                                                 | 2957          |
| Total number of articles studied |                                                                                 | 696           |
| Number of articles cited         |                                                                                 | 296           |

\* Truncature

- frequent visits to accident and emergency or GP or repeated hospital admissions,
- elevated blood eosinophils ( $>1000/\text{mm}^3$ ),
- patients who are “poor perceivers” of their degree of bronchial obstruction,
- smoking  $>20$  packs/year,
- poor adherence and/or denial of disease,
- use of three (or more) asthma medications,
- corticosteroid therapy stopped in last 3 months.

## References analysed for guideline production

1. Guidelines for the evaluation of impairment/disability in patients with asthma. American Thoracic Society. Medical Section of the American Lung Association. *Am Rev Respir Dis* 1993;147(4):1056–61.
2. The impact of allergic rhinitis on quality of life and other airway diseases. Summary of a European conference. *Allergy* 1998;53(41, Suppl):1–31.
3. Proceedings of the ATS workshop on refractory asthma: current understanding, recommendations, and unanswered questions. American Thoracic Society. *Am J Respir Crit Care Med* 2000;162(6):2341–51.
4. Abdulwadud O, Abramson M, Forbes A, James A, Light L, Thien F, et al. , Attendance at an asthma educational intervention: characteristics of participants and non-participants. *Respir Med* 1997;91(9):524–9.
5. Adams RJ, Boath K, Homan S, Campbell DA, Ruffin RE. A randomized trial of peak-flow and symptom-based action plans in adults with moderate-to-severe asthma. *Respirology* 2001;6(4):297–304.
6. Agence Nationale d'Accréditation et d'Evaluation en Santé. Education thérapeutique du patient asthmatique adulte et adolescent. *Rev Pneumol Clin* 2001;58(3):169–84.
7. Agence Nationale pour le Développement de l'Evaluation Médicale. Indications des E.F.R. (Epreuves Fonctionnelles Respiratoires): place des E.F.R. et des gaz du sang dans la surveillance de l'asthme et des bronchopneumopathies chroniques obstructives. *Rev Mal Respir Suppl* 1995;12(3):R115–31.
8. Agency for Healthcare Research and Quality. *Management of chronic asthma. Evidence Report/Technology assessment no. 44*. Rockville (MD), AHRQ, 2001.
9. Allen DB, Bielory L, Derendorf H, Dluhy R, Colice GL, Szefer SJ. Inhaled corticosteroids: past lessons and future issues. *J Allergy Clin Immunol* 2003;112(3, Suppl):S1–S40.
10. Ameille J, Choudat D, Dewitte JD, Faucon D, Letourneux M, Pairon J, et al. Reconnaissance et réparation des asthmes professionnels. *Arch mal prof méd trav* 2000;61(8):568–73.
11. Ameille J, Pairon JC, Bayeux MC, Brochard P, Choudat D, Conso F, et al. , Consequences of occupational asthma on employment and financial status: a follow-up study. *Eur Respir J* 1997;10(1):55–8.
12. Ameille J, Pauli G, Calastreng-Crinquand A, Vervloët D, Iwatsubo Y, Popin E, et al. Reported incidence of occupational asthma in France, 1996–99: the ONAP programme. *Occup Environ Med* 2003;60(2):136–41.
13. American Thoracic Society. Standardization of spirometry, 1994 update. *Am J Respir Crit Care Med* 1995;152(3):1107–36.
14. Anthonisen NR. Prognosis in chronic obstructive pulmonary disease: results from multicenter clinical trials. *Am Rev Respir Dis* 1989;140(3 Pt 2):S95–9.
15. Apter AJ, Boston RC, George M, Norfleet AL, Tenhave T, Coyne JC, et al. Modifiable barriers to adherence to inhaled steroids among adults with asthma: it's not just black and white. *J Allergy Clin Immunol* 2003;111(6):1219–26.
16. Apter AJ, Reisine ST, Affleck G, Barrows E, ZuWallack RL. Adherence with twice-daily dosing of inhaled steroids. Socioeconomic and health-belief differences. *Am J Respir Crit Care Med* 1998;157(6 Pt 1):1810–7.
17. Apter AJ, ZuWallack RL, Clive J. Common measures of asthma severity lack association for describing its clinical course. *J Allergy Clin Immunol* 1994;94(4):732–7.
18. Ayres JG, Campbell LM. A controlled assessment of an asthma self-management plan involving a budesonide dose regimen. *Eur Respir J* 1996;9:886–92.
19. Aziz I, Tan KS, Hall IP, Devlin MM, Lipworth BJ. Subsensitivity to bronchoprotection against adenosine monophosphate challenge following regular once-daily formoterol. *Eur Respir J* 1998;12(3):580–4.
20. Badgett RG, Tanaka DJ, Hunt DK, Jelley MJ, Feinberg LE, Steiner JF, et al. , The clinical evaluation for diagnosing obstructive airways disease in high-risk patients. *Chest* 1994;106(5):1427–31.

21. Bailey WC, Higgins DM, Richards BM, Richards Jr. JM. Asthma severity: a factor analytic investigation. *Am J Med* 1992;**93**(3):263-9.
22. Balland S, Deprez P, Freslon L, Schmit B, Charlon R. La maladie asthmatique de l'adulte. Etat clinique, facteurs de risques et suivi médical des patients en régions Centre. *Rev Med Ass Mal* 2002;**33**(2):89-97.
23. Barbier R. *Pourquoi, quand, comment prescrire des EFR?*. Paris: Laboratoire Boehringer Ingelheim; 1998.
24. Baren JM, Shofer FS, Ivey B, Reinhard S, DeGeus J, Stahmer SA, et al. A randomized, controlled trial of a simple emergency department intervention to improve the rate of primary care follow-up for patients with acute asthma exacerbations. *Ann Emerg Med* 2001;**38**(2):115-22.
25. Barker RD, Harris JM, Welch JA, Venables KM, Newman Taylor AJ. Occupational asthma caused by tetrachlorophthalic anhydride: a 12-year follow-up. *J Allergy Clin Immunol* 1998;**101**(6 Pt 1):717-9.
26. Barr RG, Somers SC, Speizer FE, Camargo CA. Patient factors and medication guideline adherence among older women with asthma. *Arch Intern Med* 2002;**162**(15):1761-8.
27. Bateman ED, Bousquet J, Braunstein GL. Is overall asthma control being achieved? A hypothesis-generating study. *Eur Respir J* 2001;**17**(4):589-95.
28. Baur X, Degens P, Weber K. Occupational obstructive airway diseases in Germany. *Am J Ind Med* 1998;**33**:454-62.
29. Bender B, Milgrom H, Rand C. Nonadherence in asthmatic patients: is there a solution to the problem? *Ann Allergy Asthma Immunol* 1997;**79**(3):177-86.
30. Bhagat R, Kalra S, Swystun VA, Cockcroft DW. Rapid onset of tolerance to the bronchoprotective effect of salmeterol. *Chest* 1995;**108**(5):1235-9.
31. Bhagat R, Swystun VA, Cockcroft DW. Salbutamol-induced increased airway responsiveness to allergen and reduced protection versus methacholine: dose response. *J Allergy Clin Immunol* 1996;**97**(1 Pt 1):47-52.
32. Blanc PD, Jones M, Besson C, Katz P, Yelin E. Work disability among adults with asthma. *Chest* 1993;**104**(5):1371-7.
33. Blanc PD, Toren K. How much adult asthma can be attributed to occupational factors? *Am J Med* 1999;**107**(6):580-7.
34. Boniface S, Donati Y, Romanet-Manent S, Lorec AM, Dupuy P, Mamessier E, et al. L'analyse de l'expectoration induite dans l'asthme permet une nouvelle approche de l'inflammation. *Rev Mal Respir* 2002;**19**(6):747-59.
35. Bosley CM, Fosbury JA, Cochrane GM. The psychological factors associated with poor compliance with treatment in asthma. *Eur Respir J* 1995;**8**(6):899-904.
36. Boulet L, Phillips R, O'Byrne P, Becker A. Evaluation of asthma control by physicians and patients: comparison with current guidelines. *Can Respir J* 2002;**9**(6):417-23.
37. Boulet LP, Becker A, Bérubé D, Beveridge R, Ernst P. Canadian asthma consensus report. *Can Med Assoc J* 1999;**161**(11, Suppl):S1-S61.
38. Boulet LP, Boulet V, Milot J. How should we quantify asthma control? A proposal. *Chest* 2002;**122**(6):2217-23.
39. Boulet LP, Cartier A, Milot J, Côté J, Malo JL, Laviolette M. Tolerance to the protective effects of salmeterol on methacholine-induced bronchoconstriction: influence of inhaled corticosteroids. *Eur Respir J* 1998;**11**(5):1091-7.
40. Boulet LP, Milot J, Turcotte H. Relationship between changes in diurnal variation of expiratory flows, lung volumes and respiratory symptoms after acute asthma. *Respir Med* 1991;**85**(6):487-93.
41. Boulet LP, Turcotte H, Brochu A. Persistence of airway obstruction and hyperresponsiveness in subjects with asthma remission. *Chest* 1994;**105**(4):1024-31.
42. Bousquet J, Jeffery P, Busse W, Johnson M, Vignola A. Asthma from bronchoconstriction to airways inflammation and remodeling. *Am J Respir Crit Care Med* 2000;**161**:1720-45.
43. British Thoracic Association. Death from asthma in two regions of England. *BMJ* 1982;**285**(6350):1251-5.
44. British Thoracic Society. British guideline on the management of Asthma. *Thorax* 2003;**58**(Suppl 1).
45. Brocklebank D, Wright J, Cates C. Systematic review of clinical effectiveness of pressurised metered dose inhalers versus other hand held inhaler devices for delivering corticosteroids in asthma. *BMJ* 2001;**323**(7318):896-900.
46. Bronnimann S, Burrows B. A prospective study of the natural history of asthma. Remission and relapse rates. *Chest* 1986;**90**(4):480-4.
47. Bukstein DA, Henk HJ, Luskin AT. A comparison of asthma-related expenditures for patients started on montelukast versus fluticasone propionate as monotherapy. *Clin Ther* 2001;**23**(9):1589-600.
48. Burrows B. Course and prognosis of patients with chronic airways obstruction. *Chest* 1980;**77**(2, Suppl):250-1.
49. Carswell F, Heck G, Robinson E, Hallows D, Peters T, Stanton T. Family stress and childhood asthma. *Nurs Pract* 1990;**3**(3):10-5.
50. Caughey GH. Chairman's summary. Mechanisms of airway remodeling. *Am J Respir Crit Care Med* 2001;**164**(10 Pt 2):S26-7.
51. Cerveri I, Locatelli F, Zoia MC, Corsico A, Accordini S, de Marco R. International variations in asthma treatment compliance: the results of the European Community Respiratory Health Survey (ECRHS). *Eur Respir J* 1999;**14**(2):288-94.
52. Chambers CV, Markson L, Diamond JJ, Lasch L, Berger M. Health beliefs and compliance with inhaled corticosteroids by asthmatic patients in primary care practices. *Respir Med* 1999;**93**(2):88-94.
53. Chan-Yeung M, Chang JH, Manfreda J, Ferguson A, Becker A. Changes in peak flow, symptom score, and the use of medications during acute exacerbations of asthma. *Am J Respir Crit Care Med* 1996;**154**(4 Pt 1):889-93.
54. Chan-Yeung M, Malo JL. Occupational asthma. *N Engl J Med* 1995;**333**(2):107-12.
55. Chan-Yeung M, Malo J. Natural History of occupational asthma. In: Bernstein I, Chan-Yeung M, Malo J, Bernstein D, editors. *Asthma in the workplace*. New York: Marcel Dekker; 1999. p. 129-44.
56. Charlton I, Charlton G, Broomfield J, Mullee MA. Evaluation of peak flow and symptoms only self management plans for control of asthma in general practice. *BMJ* 1990;**301**:1355-9.
57. Cheung D, Timmers MC, Zwinderman AH, Bel EH, Dijkman JH, Sterk PJ. Long-term effects of a long-acting  $\beta_2$ -adrenoceptor agonist, salmeterol, on airway hyperresponsiveness in patients with mild asthma. *N Engl J Med* 1992;**327**(17):1198-203.
58. Cheung D, Wever AM, de Goeij JA, de GRAAFF CS, Steen H, Sterk PJ. Effects of theophylline on tolerance to the bronchoprotective actions of salmeterol in asthmatics in vivo. *Am J Respir Crit Care Med* 1998;**158**(3):792-6.
59. Cochrane MG, Bala MV, Downs KE, Mauskopf J, Ben Joseph RH. Inhaled corticosteroids for asthma therapy: patient compliance, devices, and inhalation technique. *Chest* 2000;**117**(2):542-50.

60. Collard P, Njinou B, Nejadnik B, Keyeux A, Frans A. Single breath diffusing capacity for carbon in stable asthma. *Chest* 1994;**105**:1426–9.
61. Combesure C, Chanez P, Saint-Pierre P, Daurès JP, Proudhon H, Godard P. Assessment of variations in control of asthma over time. *Eur Respir J* 2003;**22**(2):298–304.
62. Connolly CK, Alcock SM, Prescott RJ. Mortality in asthmatics over 15 yrs: a dynamic cohort study from 1983–1998. *Eur Respir J* 2002;**19**(4):593–8.
63. Connolly CK, Mamun M, Alcock SM, Prescott RJ. The Dartington and Northallerton prospective asthma study: best function predicts mortality during the first 10 years. *Respir Med* 1998;**92**(11):1274–80.
64. Cote J, Kennedy S, Chan-Yeung M. Outcome of patients with cedar asthma with continuous exposure. *Am Rev Respir Dis* 1990;**141**(2):373–6.
65. Coutts JAP, Gibson NA, Paton JY. Measuring compliance with inhaled medication in asthma. *Arch Dis Child* 1992;**67**(3):332–3.
66. Couturaud F, Proust A, Frachon I, Dewitte JD, Oger E, Quiot JJ, et al. Education and self-management: a one-year randomized trial in stable adult asthmatic patients. *J Asthma* 2002;**39**(6):493–500.
67. Cowie RL, Revitt SG, Underwood MF, Field SK. The effect of a peak flow-based action plan in the prevention of exacerbations of asthma. *Chest* 1997;**112**(6):1534–8.
68. Côté J, Cartier A, Malo JL, Rouleau M, Boulet LP. Compliance with peak expiratory flow monitoring in home management of asthma. *Chest* 1998;**113**(4):968–72.
69. Côté J, Cartier A, Robichaud P, Boutin H, Malo JL, Rouleau M, et al. Influence on asthma morbidity of asthma education programs based on self-management plans following treatment optimization. *Am J Respir Crit Care Med* 1997;**155**(5):1509–14.
70. Crane J, Pearce N, Burgess C, Woodman K, Robson B, Beasley R. Markers of risk of asthma death or readmission in the 12 months following a hospital admission for asthma. *Int J Epidemiol* 1992;**21**(4):737–44.
71. Cumming RG, Mitchell P, Leeder SR. Use of inhaled corticosteroids and the risk of cataracts. *N Engl J Med* 1997;**337**(1):8–14.
72. Currie GP, Lee DKC, Lipworth BJ. Asthma exacerbations and sputum eosinophil counts. *Lancet* 2003;**361**(9365):1302–3.
73. Dahl R, Bjerner L. Nordic consensus report on asthma management. *Respir Med* 2000;**94**(4):299–327.
74. D'Alonzo G, Steijnmans V, Keller A. Measurements of morning and evening airflow grossly underestimate the circadian variability of FEV<sub>1</sub> and peak expiratory flow rate in asthma. *Am J Respir Crit Care Med* 1995;**152**(3):1097–9.
75. Davis BE, Reid JK, Cockcroft DW. Formoterol thrice weekly does not result in the development of tolerance to bronchoprotection. *Can Respir J* 2003;**10**(1):23–6.
76. Devine EC. Meta-analysis of the effects of psychoeducational care in adults with asthma. *Res Nurs Health* 1996;**19**(5):367–76.
77. Dickinson J, Hutton S, Atkin A. Implementing the British Thoracic Society's guidelines: the effect of a nurse-run asthma clinic on prescribed treatment in an English general practice. *Respir Med* 1998;**92**(2):264–7.
78. Diette GB, Wu AW, Skinner EA, Markson L, Clark RD, McDonald RC, et al. Treatment patterns among adult patients with asthma: factors associated with overuse of inhaled  $\beta$ -agonists and underuse of inhaled corticosteroids. *Arch Intern Med* 1999;**159**(22):2697–704.
79. Donovan JL, Blake DR. Patient non-compliance: deviance or reasoned decision-making? *Soc Sci Med* 1992;**34**(5):507–13.
80. Drexler H, Schaller KH, Nielsen J, Weber A, Weihrauch M, Welinder H, et al. Efficacy of measures of hygiene in workers sensitised to acid anhydrides and the influence of selection bias on the results. *Occup Environ Med* 1999;**56**(3):202–5.
81. Drummond N, Abdalla M, Beattie J, Buckingham J, Lindsay T, Osman L, et al. Effectiveness of routine self monitoring of peak flow in patients with asthma. *BMJ* 1994;**308**:564–7.
82. Eason J, Markowe HLJ. Controlled investigation of deaths from asthma in hospitals in the North East Thames region. *Br Med J (Clin Res Ed)* 1987;**294**(6582):1255–8.
83. Enright PL, Lebowitz MD, Cockcroft DW. Physiologic measures: pulmonary function tests. Asthma outcome. *Am J Respir Crit Care Med* 1994;**149**(2 Pt 2):S9–S18.
84. Erickson SR, Coombs JH, Kirking DM, Azimi AR. Compliance from self-reported versus pharmacy claims data with metered-dose inhalers. *Ann Pharmacother* 2001;**35**(9):997–1003.
85. FitzGerald JM, Ernst P, Boulet LP, O'Byrne P. *Evidence-based asthma management*. Hamilton (Canada): BC Decker; 2001.
86. Foo AL, Sly PD. Pulmonary function in a hospital population of asthmatic children. *J Asthma* 1991;**28**(4):273–80.
87. Fourgaut G, Popin E, Kopferschmitt MC, Newinger G, Pauli G. L'asthme à la farine: étude clinique de 27 cas (nécessite d'un algorithme décisionnel). *Rev Fr Allergol Immunol Clin* 2002;**42**(7):633–9.
88. Fukuda T, Dunnette SL, Reed CE, Ackerman SJ, Peters MS, Gleich GJ. Increased numbers of hypodense eosinophils in the blood of patients with bronchial asthma. *Am Rev Respir Dis* 1985;**132**(5):981–5.
89. Gallefoss F, Bakke PS. How does patient education and self-management among asthmatics and patients with chronic obstructive pulmonary disease affect medication? *Am J Respir Crit Care Med* 1999;**160**(6):2000–5.
90. Gannon PFG, Weir DC, Robertson AS, Burge PS. Health, employment, and financial outcomes in workers with occupational asthma. *Br J Ind Med* 1993;**50**(6):491–6.
91. Gannon P, Burge PS. The SHIELD scheme in the West Midlands Region, United Kingdom. *Br J Ind Med* 1993;**50**:791–6.
92. Garbe E, LeLorier J, Boivin J, Suissa S. Inhaled and nasal glucocorticoids and the risks of ocular hypertension or open-angle glaucoma. *JAMA* 1997;**277**(9):722–7.
93. Garcia-Marcos L, Schuster A, Pérez-Yarza E. Benefit-risk assessment of antileukotrienes in the management of asthma. *Drug Safety* 2003;**26**(7):483–518.
94. Garcia R, Guerra P, Feo F, Galindo PA, Gomez E, Borja J, et al. Tachyphylaxis following regular use of formoterol in exercise-induced bronchospasm. *J Invest Allergol Clin Immunol* 2001;**11**(3):176–82.
95. Gassert TH, Hu H, Kelsey KT, Christiani DC. Long-term health and employment outcomes of occupational asthma and their determinants. *J Occup Environ Med* 1998;**40**(5):481–91.
96. Gavin LA, Wamboldt MZ, Sorokin N, Levy SY, Wamboldt FS. Treatment alliance and its association with family functioning, adherence, and medical outcome in adolescents with severe, chronic asthma. *J Pediatr Psychol* 1999;**24**(4):355–65.
97. Gelb AF, Licuanan J, Shinar C, Zamel N. Unsuspected loss of lung elastic recoil in chronic persistent asthma. *Chest* 2002;**121**(3):715–21.
98. Gelb A, Zamel N. Unsuspected pseudophysiologic emphysema in chronic persistent asthma. *Am J Respir Crit Care Med* 2000;**162**:1778–82.

99. George M, Freedman TG, Norfleet AL, Feldman HI, Apter AJ. Qualitative research-enhanced understanding of patients' beliefs: results of focus groups with low-income, urban, African American adults with asthma. *J Allergy Clin Immunol* 2003;**111**(5):967-73.
100. Giannini D, Bacci E, Dente FL, Di Franco A, Vagaggini B, Testi R, et al. Inhaled beclomethasone dipropionate reverts tolerance to the protective effect of salmeterol on allergen challenge. *Chest* 1999;**115**(3):629-34.
101. Giannini D, Carletti A, Dente FL, Bacci E, Di Franco A, Vagaggini B, et al. Tolerance to the protective effect of salmeterol on allergen challenge. *Chest* 1996;**110**(6):1452-7.
102. Giannini D, Di Franco A, Bacci E, Dente FL, Bartoli ML, Vagaggini B, et al. Tolerance to the protective effect of salmeterol on allergen challenge can be partially restored by the withdrawal of salmeterol regular treatment. *Chest* 2001;**119**(6):1671-5.
103. Gibson PG, Powell H, Coughlan J, Wilson A, Abramson M, Haywood P, et al. Self-management education and regular practitioner review for adults with asthma (Cochrane Review). In: *The cochrane library*, Issue 2. Oxford: Update Software; 2003.
104. Gibson PG, Wong BJO, Hepperle MJE, Kline PA, Girgis-Gabardo A, Guyatt G, et al. A research method to induce and examine a mild exacerbation of asthma by withdrawal of inhaled corticosteroid. *Clin Exp Allergy* 1992;**22**(5):525-32.
105. Global initiative for asthma. Global strategy for asthma management and prevention. Available from <http://www.ginasthma.com2002> [consulté le 02/02/2004].
106. Global initiative for asthma. Global strategy for asthma management and prevention (updated 2003). Available from <http://www.ginasthma.com2003> [consulté le 01/09/2003].
107. Godard P. Contrôle de l'asthme: quels objectifs pour le patient, le médecin, le payeur? *Rev Pneumol Clin* 2002;**58**(3 Part 2):157-1511.
108. Godard P, Chanez P, Bousquet J, Demoly P, Pujol JL, Michel FB. *Asthmologie*. Paris: Masson; 2000.
109. Górski P, Kolacinska B, Wittczak T. Analysis of the clinical state of patients with occupational asthma following cessation of exposure to allergens. *Occup Med* 1999;**49**(5):285-9.
110. Green RH, Brightling CE, McKenna S, Hargadon B, Parker D, Bradding P, et al. Asthma exacerbations and sputum eosinophil counts: a randomised controlled trial. *Lancet* 2002;**360**(9347):1715-21.
111. Greening AP, Ind PW, Northfield M, Shaw G. Added salmeterol versus higher-dose corticosteroid in asthma patients with symptoms on existing inhaled corticosteroid. *Lancet* 1994;**344**(8917):219-24.
112. Grenier P, Beigelman-Aubry C, Fétita C, Prêteux F, Brauner M, Lenoir S. New frontiers in CT imaging of airway disease. *Eur Radiol* 2002;**12**:1022-44.
113. Grol MH, Gerritsen J, Vonk JM, Schouten JP, Koëter GH, Rijcken B, et al. Risk factors for growth and decline of lung function in asthmatic individuals up to age 42 years. A 30-year follow-up study. *Am J Respir Crit Care Med* 1999;**160**(6):1830-7.
114. Grove A, Lipworth BJ. Bronchodilator subsensitivity to salbutamol after twice daily salmeterol in asthmatic patients. *Lancet* 1995;**346**(8969):201-6.
115. Halpern M, Schmier J, van Kerkhove M, Watkins M, Kalberg C. Impact of long-term inhaled corticosteroid therapy on bone mineral density: results of a meta-analysis. *Ann Allergy Asthma Immunol* 2004;**92**(2):201-7.
116. Hancox RJ, Aldridge RE, Cowan JO, Flannery EM, Herbison GP, McLachlan CR, et al. Tolerance to beta-agonists during acute bronchoconstriction. *Eur Respir J* 1999;**14**(2):283-7.
117. Hancox RJ, Cowan JO, Flannery EM, Herbison GP, McLachlan CR, Wong CS, et al. Randomised trial of an inhaled  $\beta_2$  agonist, inhaled corticosteroid and their combination in the treatment of asthma. *Thorax* 1999;**54**(6):482-7.
118. Hancox RJ, Subbarao P, Kamada D, Watson RM, Hargreave FE, Inman MD.  $\beta_2$  agonist tolerance and exercise-induced bronchospasm. *Am J Respir Crit Care Med* 2002;**165**(8):1068-70.
119. Hansen E, Vestbo J, Phanareth K, Kok-Jensen A, Dirksen A. Peak flow as predictor of overall mortality in asthma and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001;**163**:690-3.
120. Hewson PH, Tippet EA, Jones DM, Madden JP, Higgs P. Routine pulmonary function tests in young adolescents with asthma in general practice. *Med J Aust* 1996;**165**(9):469-72.
121. Holleman Jr. DR, Simel DL. Does the clinical examination predict airflow limitation? *JAMA* 1995;**273**(4):313-9.
122. Horn BR, Robin ED, Theodore J, Van Kessel A. Total eosinophil counts in the management of bronchial asthma. *N Engl J Med* 1975;**292**(22):1152-5.
123. Ignacio-Garcia J, Gonzales-Santos P. Asthma self-management education program by home monitoring of peak flow expiratory flow. *Am J Respir Crit Care Med* 1995;**151**:353-9.
124. Innocenti A. Occupational asthma: considerations on epidemiology and criteria of damage evaluation. *Med Lav* 1997;**88**:3-12.
125. Institute for Clinical Systems Improvement. Health care guideline: diagnosis and management of asthma. <http://www.csi.org/knowledge/2003> [consulté le 04/08/03].
126. int Veen J, Beekman AJ, Bel EH, Sterk PJ. Recurrent exacerbations in severe asthma are associated with enhanced airway closure during stable episodes. *Am J Respir Crit Care Med* 2000;**161**(6):1902-6.
127. int Veen J, Smits H, Hiemstra P, Zwinderman AE, Sterk P, Bel E. Lung function and sputum characteristics of patients with severe asthma during an induced exacerbation by double-blind steroid withdrawal. *Am J Respir Crit Care Med* 1999;**160**:93-9.
128. Jaakkola JJK, Piipari R, Jaakkola MS. Occupation and asthma: a population-based incident case-control study. *Am J Epidemiol* 2003;**158**(10):981-7.
129. Jalaludin BB, Smith MA, Chey T, Orr NJ, Smith WT, Leeder SR. Risk factors for asthma deaths: a population-based, case-control study. *Aust N Z J Public Health* 1999;**23**(6):595-600.
130. James PNE, Anderson JB, Prior JG, White JP, Henry JA, Cochrane GM. Patterns of drug taking in patients with chronic airflow obstruction. *Postgrad Med J* 1985;**61**(711):7-10.
131. Japanese Society of Allergology. Guidelines for the diagnosis and management of bronchial asthma. Committee on the definition, treatment, and management of bronchial asthma. *Allergy* 1995;**50**(27, Suppl):1-42.
132. Jatakanon A, Lim S, Barnes PJ. Changes in sputum eosinophils predict loss of asthma control. *Am J Respir Crit Care Med* 2000;**161**(1):64-72.
133. Jayaram L, Parameswaran K, Sears MR, Hargreave FE. Induced sputum cell counts: their usefulness in clinical practice. *Eur Respir J* 2000;**16**(1):150-8.
134. Johnson AR, Dimich-Ward HD, Manfreda J, Becklake MR, Ernst P, Sears MR, et al. Occupational asthma in adults in

- six Canadian communities. *Am J Respir Crit Care Med* 2000;**162**(6):2058–62.
135. Johnson PH, Wilkinson I, Sutherland AM, Johnston IDA, Hall IP. Improving communication between hospital and primary care increases follow-up rates for asthmatic patients following casualty attendance. *Respir Med* 1998;**92**(2):289–91.
136. Joly N, Ameille J. Maladie professionnelle: comment préserver l'emploi. *Rev Prat Med Gen* 2002;**16**(578):934–7.
137. Jones C, Santanello NC, Boccuzzi SJ, Wogen J, Strub P, Nelsen LM. Adherence to prescribed treatment for asthma: evidence from pharmacy benefits data. *J Asthma* 2003;**40**(1):93–101.
138. Jones KP, Mullee MA, Middleton M, Chapman E, Holgate S. British Thoracic Society Research Committee. Peak flow based asthma self-management: a randomised controlled study in general practice. *Thorax* 1995;**50**:851–7.
139. Jorgensen I, Jensen V, Bulow S, Dahm T, Prahl P, Juel K. Asthma mortality in the Danish child population: risk factors and causes of asthma death. *Pediatr Pulmonol* 2003;**36**(2):142–7.
140. Jónasson G, Carlsen KH, Mowinckel P. Asthma drug adherence in a long term clinical trial. *Arch Dis Childhood* 2000;**83**(4):330–3.
141. Juniper EF, O'Byrne PM, Ferrie PJ, King DR, Roberts JN. Measuring asthma control. Clinic questionnaire or daily diary? *Am J Respir Crit Care Med* 2000;**162**(4 Pt 1):1330–4.
142. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999;**14**(4):902–7.
143. Juniper EF, O'Byrne PM, Roberts JN. Measuring asthma control in group studies: do we need airway calibre and rescue  $\beta_2$ -agonist use? *Respir Med* 2001;**95**(5):319–23.
144. Kalra S, Swystun VA, Bhagat R, Cockcroft DW. Inhaled corticosteroids do not prevent the development of tolerance to the bronchoprotective effect of salmeterol. *Chest* 1996;**109**(4):953–6.
145. Karjalainen A, Kurppa K, Martikainen R, Klaukka T, Karjalainen J. Work is related to a substantial portion of adult-onset asthma incidence in the Finnish population. *Am J Respir Crit Care Med* 2001;**164**(4):565–8.
146. Katz PP, Yelin EH, Smith S, Blanc PD. Perceived control of asthma: development and validation of a questionnaire. *Am J Respir Crit Care Med* 1997;**155**(2):577–82.
147. Katz PP, Yelin EH, Eisner MD, Blanc PD. Perceived control of asthma and quality of life among adults with asthma. *Ann Allergy Asthma Immunol* 2002;**89**(3):251–8.
148. Kelloway JS, Wyatt RA, Adlis SA. Comparison of patients' compliance with prescribed oral and inhaled asthma medications. *Arch Intern Med* 1994;**154**:1349–53.
149. Kennedy WA, Laurier C, Gautrin D, Ghezze H, Paré M, Malo JL, et al. Occurrence and risk factors of oral candidiasis treated with oral antifungals in seniors using inhaled steroids. *J Clin Epidemiol* 2000;**53**(7):696–701.
150. Kikuchi Y, Okabe S, Tamura G, Hida W, Homma M, Shirato K, et al. Chemosensitivity and perception of dyspnea in patients with a history of near-fatal asthma. *N Engl J Med* 1994;**330**(19):1329–34.
151. Kolbe J, Vámos M, Fergusson W, Elkind G. Determinants of management errors in acute severe asthma. *Thorax* 1998;**53**(1):14–20.
152. Koshak EA, Alamoudi OS. Do eosinophil counts correlate differently with asthma severity by symptoms versus peak flow rate? *Ann Allergy Asthma Immunol* 1999;**83**(6 Pt 1):567–71.
153. Kruse W, Rampmaier J, Ullrich G, Weber E. Patterns of drug compliance with medications to be taken once and twice daily assessed by continuous electronic monitoring in primary care. *Int J Clin Pharmacol Ther* 1994;**32**(9):452–7.
154. Kuwano K, Bosken C, Paré P, Bai T, Wiggs B, Hogg JC. Small airways dimensions in asthma and in chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1993;**148**(5):1220–5.
155. Kyngäs H, Rissanen M. Support as a crucial predictor of good compliance of adolescents with a chronic disease. *J Clin Nurs* 2001;**10**(6):767–74.
156. Labbé A, Dutau G. *Pneumologie de l'enfant*. Rueil-Malmaison: Arnette Groupe Liaisons; 2003.
157. Lacoste J, Bousquet J, Chanez P, Van Vyve T, Simony-Lafontaine J, Lequeu N, et al. Eosinophilic and neutrophilic inflammation in asthma, chronic bronchitis, and chronic obstructive pulmonary disease. *J Allergy Clin Immunol* 1993;**92**:537–48.
158. Laennec T. *Traité de l'auscultation médiate et des maladies des poumons et du coeur*. Paris: J-S Chaudé; 1831.
159. Lange P, Parner J, Vestbo J, Schnohr P, Jensen G. A 15-year follow-up study of ventilatory function in adults with asthma. *N Engl J Med* 1998;**339**(17):1194–200.
160. Laprise C, Boulet LP. Asymptomatic airway hyperresponsiveness: a three-year follow-up. *Am J Respir Crit Care Med* 1997;**156**(2 Pt 1):403–9.
161. Lee T, Weiss K. Fracture risk associated with inhaled corticosteroid use in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004;**169**(855):9.
162. Lemièrre C, Cartier A, Malo JL, Lehrer SB. Persistent specific bronchial reactivity to occupational agents in workers with normal nonspecific bronchial reactivity. *Am J Respir Crit Care Med* 2000;**162**(3 Pt 1):976–80.
163. Leuppi JD, Salome CM, Jenkins CR, Anderson SD, Xuan W, Marks GB, et al. Predictive markers of asthma exacerbation during stepwise dose reduction of inhaled corticosteroids. *Am J Respir Crit Care Med* 2001;**163**(2):406–12.
164. Li JTC, Sheeler RD. Getting the most out of a 15-min asthma visit. *J Respir Dis* 1997;**18**(2):135–41.
165. Lin F, Dimich-Ward H, Chan-Yeung M. Longitudinal decline in lung function in patients with occupational asthma due to western red cedar. *Occup Environ Med* 1996;**53**:753–6.
166. Linna O. Spirometry, bronchodilator test or symptom scoring for the assessment of childhood asthma. *Acta Paediatr* 1996;**85**(5):564–9.
167. Lipworth BJ. Systemic adverse effects of inhaled corticosteroid therapy: A systematic review and meta-analysis. *Arch Intern Med* 1999;**159**(9):941–55.
168. López-Viña A, del Castillo-Arévalo E. Influence of peak expiratory flow monitoring on an asthma self-management education programme. *Respir Med* 2000;**94**(8):760–6.
169. Magadle R, Berar-Yanay N, Weiner P. The risk of hospitalization and near-fatal and fatal asthma in relation to the perception of dyspnea. *Chest* 2002;**121**(2):329–33.
170. Malo JL, Cartier A, Ghezze H, Lafrance M, McCants M, Lehrer SB. Patterns of improvement in spirometry, bronchial hyperresponsiveness, and specific IgE antibody levels after cessation of exposure in occupational asthma caused by snow-crab processing. *Am Rev Respir Dis* 1988;**138**(4):807–12.
171. Malo JL, Dewitte JD, Cartier A, Ghezze H, L'Archevêque J, Boulet LP, et al. Le système d'indemnisation pour asthme professionnel. Description, efficacité et coûts. *Rev Mal Respir* 1993;**10**(4):313–23.
172. Mann M, Eliasson O, Patel K, ZuWallack R. A comparison of the effects of *bid* and *qid* dosing on compliance with inhaled fluticasone. *Chest* 1992;**101**(2):496–9.

173. Manning P, Murphy E, Clancy L, Callaghan B. Asthma mortality in the Republic of Ireland 1970–84 and an analysis of hospital deaths in a single year. *Ir Med J* 1987;**80**(12): 406–9.
174. Marquette C, Saulnier F, Leroy O, Wallaert B, Chopin C, Demarcq J, et al. Long-term prognosis of near-fatal asthma. A 6-year follow-up study of 145 asthmatic patients who underwent mechanical ventilation for a near-fatal attack of asthma. *Am Rev Respir Dis* 1992;**146**(1):76–81.
175. Martinat Y, Rogeaux Y, Giraud V, Mezzi K. Maîtrise de l'asthme et atteinte des petites voies aériennes: enquête transversale Jacinthe (Juniper Asthma Control in a National Transversal Evaluation) en Pneumologie libérale. *Rev Fr Allergol Immunol Clin* 2002;**42**(4):358–66.
176. McCarthy D, Sigurdson M. Lung elastic recoil and reduced airflow in clinically stable asthma. *Thorax* 1980;**35**: 298–302.
177. McFadden Jr. ER. Observations on asthma mortality. *Ann Intern Med* 1997;**127**(2):142–7.
178. McFadden Jr. ER. Acute severe asthma. *Am J Respir Crit Care Med* 2003;**168**(7):740–59.
179. Meng YY, Leung KM, Berkgigler D, Halbert RJ, Legorreta AP. Compliance with US asthma management guidelines and specialty care: a regional variation or national concern? *J Eval Clin Pract* 1999;**5**(2):213–21.
180. Meredith S, Nordman H. Occupational asthma: measures of frequency from four countries. *Thorax* 1996;**51**: 435–40.
181. Merget R, Schulte A, Gebler A, Breitstadt R, Kulzer R, Berndt ED, et al. Outcome of occupational asthma due to platinum salts after transferral to low-exposure areas. *Int Arch Occup Environ Health* 1999;**72**(1):33–9.
182. Meyer JD, Holt DL, Cherry NM, McDonald JC. SWORD '98: surveillance of work-related and occupational respiratory disease in the UK. *Occup Med* 1999;**49**(8):485–9.
183. Ministry of Health, National Medical Research Council. *Management of asthma: clinical practice guidelines*. Singapore: MOH; 2002.
184. Molema J, van Herwaarden CLA, Folgering HTM. Effects of inhaled budesonide on the relationships between symptoms, lung function indices and airway hyperresponsiveness in patients with allergic asthma. *Pulm Pharmacol* 1989;**1**(4):179–85.
185. Molino NA, Nannini LJ, Rebuck AS, Slutsky AS. The fatality-prone asthmatic patient. Follow-up study after near-fatal attacks. *Chest* 1992;**101**(3):621–3.
186. Morris NV, Abramson MJ, Rosier MJ, Strasser RP. Assessment of the severity of asthma in a family practice. *J Asthma* 1996;**33**(6):425–39.
187. Moscato G, Dellabianca A, Perfetti L, Bramè B, Galdi E, Niniano R, et al. Occupational asthma: a longitudinal study on the clinical and socioeconomic outcome after diagnosis. *Chest* 1999;**115**(1):249–56.
188. Muñoz X, Cruz MJ, Orriols R, Bravo C, Espuga M, Morell F. Occupational asthma due to persulfate salts: diagnosis and follow-up. *Chest* 2003;**123**(6):2124–9.
189. National Asthma Council Australia. Asthma management handbook 2002. <http://www.nationalasthmaorgau/2002> [consulté le 30/07/03].
190. Newnham DM, Grove A, McDevitt DG, Lipworth BJ. Subsensitization of bronchodilator and systemic  $\beta_2$  adrenoceptor responses after regular twice daily treatment with eformoterol dry powder in asthmatic patients. *Thorax* 1995;**50**(5):497–504.
191. Nowak RM, Tomlanovich MC, Sarkar DD, Kvale PA, Anderson JA. Arterial blood gases and pulmonary function testing in acute bronchial asthma. Predicting patient outcomes. *JAMA* 1983;**249**(15):2043–6.
192. Nunn A, Gregg I. New regression equations for predicting peak expiratory flow in adults. *BMJ* 1989;**298**:1068–70.
193. OByrne PM, Imman MD. Airway hyperresponsiveness. *Chest* 2003;**123**:411S–6S.
194. O'Connor BJ, Aikman SL, Barnes PJ. Tolerance to the nonbronchodilator effects of inhaled  $\beta_2$ -agonists in asthma. *N Engl J Med* 1992;**327**(17):1204–8.
195. Ohnishi A, Kato M, Kojima J, Ushiyama H, Yoneko M, Kawai H. Differential pharmacokinetics of theophylline in elderly patients. *Drugs Aging* 2003;**20**(1):71–84.
196. Onyirimba F, Apter A, Reisine S, Litt M, McCusker C, Connors M, et al. Direct clinician-to-patient feedback discussion of inhaled steroid use: its effect on adherence. *Ann Allergy Asthma Immunol* 2003;**90**(4):411–5.
197. Padoan M, Pozzato V, Simoni M, Zedda L, Milan G, Bononi I, et al. Long-term follow-up of toluene diisocyanate-induced asthma. *Eur Respir J* 2003;**21**(4):637–40.
198. Paggiaro PL, Vagaggini B, Bacci E, Bancalari L, Carrara M, Di Franco A, et al. Prognosis of occupational asthma. *Eur Respir J* 1994;**7**(4):761–7.
199. Pal TM, De Monchy JGR, Groothoff JW, Post D. Follow up investigation of workers in synthetic fibre plants with humidifier disease and work related asthma. *Occup Environ Med* 1999;**56**(6):403–10.
200. Panhuysen CIM, Vonk JM, Koëter GH, Schouten JP, van Altena R, Bleecker ER, et al. Adult patients may outgrow their asthma: a 25-year follow-up study. *Am J Respir Crit Care Med* 1997;**155**(4):1267–72.
201. Park HS, Lee SK, Kim HY, Nahm DH, Kim SS. Specific immunoglobulin E and immunoglobulin G antibodies to toluene diisocyanate-human serum albumin conjugate: useful markers for predicting long-term prognosis in toluene diisocyanate-induced asthma. *Clin Exp Allergy* 2002;**32**(4):551–5.
202. Park JW, Whang YW, Kim CW, Park YB, Hong CS. Eosinophil count and eosinophil cationic protein concentration of induced sputum in the diagnosis and assessment of airway inflammation in bronchial asthma. *Allergy Asthma Proc* 1998;**19**(2):61–7.
203. Pauli G, Kopferschmitt-Kubler M. Pronostic Medical. In: *L'asthme professionnel*. Paris: Margaux Orange; 1999. p. 523–36.
204. Pauwels R, Löfdahl C, Postma D, Tattersfield AE, O'Byrne P, Barnes P, et al. Effect of inhaled formoterol and budesonide on exacerbations of asthma. *N Engl J Med* 1997;**337**(20):1405–11.
205. Peat J, Woolcock A, Cullen K. Rate of decline of lung function in subjects with asthma. *Eur J Respir Dis* 1987;**70**(3):171–9.
206. Pedersen S. Do inhaled corticosteroids inhibit growth in children? *Am J Respir Crit Care Med* 2001;**164**(4): 521–35.
207. Peiffer C, Toumi M, Razzouk H, Marsac J, Lockhart A. Relationship between spontaneous dyspnoea and lability of airway obstruction in asthma. *Clin Sci* 1992;**82**:717–24.
208. Perfetti L, Cartier A, Ghezzi H, Gautrin D, Malo JL. Follow-up of occupational asthma after removal from or diminution of exposure to the responsible agent: relevance of the length of the interval from cessation of exposure. *Chest* 1998;**114**(2):398–403.
209. Peroni DG, Piacentini GL, Costella S, Pietrobello A, Bodini A, Loiacono A, et al. Mite avoidance can reduce air trapping and airway inflammation in allergic asthmatic children. *Clin Exp Allergy* 2002;**32**(6):850–5.

210. Picado C, Montserrat JM, de Pablo J, Plaza V, Agusti-Vidal A. Predisposing factors to death after recovery from a life-threatening asthmatic attack. *J Asthma* 1989;**26**(4): 231–6.
211. Pin I, Gibson PG, Kolendowicz R, Girgis-Gabardo A, Denburg JA, Hargreave FE, et al. Use of induced sputum cell counts to investigate airway inflammation in asthma. *Thorax* 1992;**47**(1):25–9.
212. Pinto Pereira LM, Clement Y, Da Silva CK, McIntosh D, Simeon DT. Understanding and use of inhaler medication by asthmatics in specialty care in Trinidad: a study following development of Caribbean guidelines for asthma management and prevention. *Chest* 2002;**121**(6):1833–40.
213. Pisati G, Baruffini A, Zedda S. Toluene diisocyanate induced asthma: outcome according to persistence or cessation of exposure. *Br J Ind Med* 1993;**50**(1):60–4.
214. Pizzichini E, Pizzichini MMM, Efthimiadis A, Dolovich J, Hargreave FE. Measuring airway inflammation in asthma: eosinophils and eosinophilic cationic protein in induced sputum compared with peripheral blood. *J Allergy Clin Immunol* 1997;**99**(4):539–44.
215. Pizzichini MMM, Pizzichini E, Clelland L, Efthimiadis A, Mahony J, Dolovich J, et al. Sputum in severe exacerbations of asthma: kinetics of inflammatory indices after prednisone treatment. *Am J Respir Crit Care Med* 1997;**155**(5):1501–8.
216. Pizzichini MMM, Pizzichini E, Clelland L, Efthimiadis A, Pavord I, Dolovich J, et al. Prednisone-dependent asthma: inflammatory indices in induced sputum. *Eur Respir J* 1999;**13**(1):15–21.
217. Powell H, Gibson PG. Options for self-management education for adults with asthma (Cochrane Review). In: *The cochrane library*. Oxford: Update Software; 2003.
218. Price J, Kemp J. The problems of treating adolescent asthma: what are the alternatives to inhaled therapy? *Respir Med* 1999;**93**(10):677–84.
219. Quanjer PH, Lebowitz MD, Gregg I, Miller MR, Pedersen OF. Peak expiratory flow: conclusions and recommendations of a working party of the European Respiratory Society. *Eur Respir J* 1997;**10**(24, Suppl):25–85.
220. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Volumes pulmonaires et débits ventilatoires forcés. Groupe de travail sur la standardisation des épreuves fonctionnelles respiratoires. Communauté européenne du charbon et de l'acier. Position Officielle de l'European Respiratory Society. *Eur Respir J* 1994;**6**(Suppl 16):5–40.
221. Quirk F, Jones P. Patient's perception of distress due to symptoms and effects of asthma on daily living and an investigation of possible influence factors. *Clin Sci* 1990;**79**(1):17–21.
222. Ramage L, Lipworth BJ, Ingram CG, Cree IA, Dhillon DP. Reduced protection against exercise induced bronchoconstriction after chronic dosing with salmeterol. *Respir Med* 1994;**88**(5):363–8.
223. Rasmussen F, Taylor DR, Flannery EM, Cowan JO, Greene JM, Herbison GP, et al. Risk factors for airway remodeling in asthma manifested by a low postbronchodilator FEV<sub>1</sub>/vital capacity ratio: a longitudinal population study from childhood to adulthood. *Am J Respir Crit Care Med* 2002;**165**(11):1480–8.
224. Rea HH, Scragg R, Jackson R, Beaglehole R, Fenwick J, Sutherland DC. A case-control study of deaths from asthma. *Thorax* 1986;**41**(11):833–9.
225. Reddel H, Jenkins C, Woolcock A. Diurnal variability—time to change asthma guidelines? *BMJ* 1999;**319**(7201):45–7.
226. Reddel HK, Salome CM, Peat JK, Woolcock AJ. Which index of peak expiratory flow is most useful in the management of stable asthma? *Am J Respir Crit Care Med* 1995;**151**(5): 1320–5.
227. Robertson CF, Rubinfeld AR, Bowes G. Deaths from asthma in Victoria: a 12-month survey. *Med J Aust* 1990;**152**(10): 511–7.
228. Roisman GL, Peiffer C, Lacronique JG, Le Cae A, Dusser DJ. Perception of bronchial obstruction in asthmatic patients. Relationship with bronchial eosinophilic inflammation and epithelial damage and effect of corticosteroid treatment. *J Clin Invest* 1995;**96**(1):12–21.
229. Rosenman K, Reilly M, Kalinowski D. A state-based surveillance system for work-related asthma. *J Occup Environ Med* 1997;**39**(5):415–25.
230. Ross DJ, McDonald JC. Health and employment after a diagnosis of occupational asthma: a descriptive study. *Occup Med* 1998;**48**(4):219–25.
231. Rossi OVJ, Lähde S, Laitinen J, Huhti E. Contribution of chest and paranasal sinus radiographs to the management of acute asthma. *Int Arch Allergy Immunol* 1994;**105**(1): 96–100.
232. Rubinfeld AR, Pain MCF. Perception of asthma. *Lancet* 1976;**1**(7965):882–4.
233. Salmeron S, Liard R, Elkharrat D, Muir JF, Neukirch F, Ellrodt A. Asthma severity and adequacy of management in accident and emergency departments in France: a prospective study. *Lancet* 2001;**358**(9282):629–35.
234. Santanello NC, Barber BL, Reiss TF, Friedman BS, Juniper EF, Zhang J. Measurement characteristics of two asthma symptom diary scales for use in clinical trials. *Eur Respir J* 1997;**10**(3):646–51.
235. Sawyer G, Miles J, Lewis S, Fitzharris P, Pearce N, Beasley R. Classification of asthma severity: should the international guidelines be changed? *Clin Exp Allergy* 1998;**28**:1565–70.
236. Saydain G, Beck K, Decker P, Cowl C, Scanlon P. Clinical significance of elevated diffusing capacity. *Chest* 2004;**125**:446–52.
237. Schatz M, Rodriguez E, Falkoff R, Zeiger RS. The relationship of frequency of follow-up visits to asthma outcomes in patients with moderate persistent asthma. *J Asthma* 2003;**40**(1):49–53.
238. Scherer YK, Bruce S. Knowledge, attitudes, and self-efficacy and compliance with medical regimen, number of emergency department visits, and hospitalizations in adults with asthma. *Heart Lung* 2001;**30**(4):250–7.
239. Schmalzing KB, Afari N, Blume AW. Predictors of treatment adherence among asthma patients in the emergency department. *J Asthma* 1998;**35**(8):631–6.
240. Sears MR, Greene JM, Willan AR, Wiecek EM, Taylor DR, Flannery EM, et al. A longitudinal, population-based, cohort study of childhood asthma followed to adulthood. *N Engl J Med* 2003;**349**:1414–22.
241. Sharma PK, Malhotra S, Pandhi P, Kumar N. Effect of inhaled steroids on bone mineral density: a meta-analysis. *J Clin Pharmacol* 2003;**43**(2):193–7.
242. Sidebotham H, Roche W. Asthma deaths; persistent and preventable mortality. *Histopathology* 2003;**43**(2):105–17.
243. Simons FER, Gerstner TV, Cheang MS. Tolerance to the bronchoprotective effect of salmeterol in adolescents with exercise-induced asthma using concurrent inhaled glucocorticoid treatment. *Pediatrics* 1997;**99**(5):655–9.
244. Sin DD, Bell NR, Svenson LW, Man SF. The impact of follow-up physician visits on emergency readmissions for patients

- with asthma and chronic obstructive pulmonary disease: a population-based study. *Am J Med* 2002;112(2):120–5.
245. Sin D, Man J, Man SFP. The risk of osteoporosis in Caucasian men and women with obstructive airways disease. *Am J Med* 2003;114(1):10–4.
  246. Société de Pneumologie de Langue Française. Recommandations pour la prise en charge des bronchopneumopathies chroniques obstructives. *Rev Mal Respir* 1997;14(Suppl 2):251–2592.
  247. Sont JK, Willems LNA, Bel EH, van Krieken JHM, Vandenbroucke JP, Sterk PJ. Clinical control and histopathologic outcome of asthma when using airway hyperresponsiveness as an additional guide to long-term treatment. *Am J Respir Crit Care Med* 1999;159(4 Pt 1):1043–51.
  248. Sorgdrager B, De Looft A, Pal T, Van Dijk F, De Monchy J. Factors affecting FEV1 in workers with potroom asthma after their removal from exposure. *Int Arch Occup Environ Health* 2001;74(1):55–8.
  249. Spanevello A, Confalonieri M, Sulotto F, Romano F, Balzano G, Migliori GB, et al. Induced sputum cellularity. Reference values and distribution in normal volunteers. *Am J Respir Crit Care Med* 2000;162(3 Pt 1):1172–4.
  250. Spector S. Noncompliance with asthma therapy—are there solutions? *J Asthma* 2000;37(5):381–8.
  251. Stanescu D. Small airways obstruction syndrome. *Chest* 1999;116(1):231–3.
  252. Ståhl E. Correlation between objective measures of airway calibre and clinical symptoms in asthma: a systematic review of clinical studies. *Respir Med* 2000;94(8):735–41.
  253. Sturdy PM, Victor CR, Anderson HR, Bland JM, Butland BK, Harrison BDW, et al. Psychological, social and health behaviour risk factors for deaths certified as asthma: a national case-control study. *Thorax* 2002;57(12):1034–9.
  254. Suissa S, Ernst P, Benayoun S, Baltzan M, Cai B. Low-dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med* 2000;343:332–6.
  255. Tan KS, Grove A, McLean A, Gnosspelius Y, Hall IP, Lipworth BJ. Systemic corticosteroid rapidly reverses bronchodilator subsensitivity induced by formoterol in asthmatic patients. *Am J Respir Crit Care Med* 1997;156(1):28–35.
  256. Tashkin DP. Multiple dose regimens: impact on compliance. *Chest* 1995;107(5, Suppl):176S–82S.
  257. Teeter JG, Bleeker ER. Relationship between airway obstruction and respiratory symptoms in adult asthmatics. *Chest* 1998;113(2):272–7.
  258. Todd G, Acerini C, Ross-Russell R, Zahra S, Warner J, McCance D. Survey of adrenal crisis associated with inhaled corticosteroids in the United Kingdom. *Arch Dis Child* 2002;87:457–61.
  259. Toelle BG, Ram FSF. Written individualised management plans for asthma in children and adults (Cochrane Review). In: *The cochrane library*. Oxford: Update Software; 2003.
  260. Torén K. Self reported rate of occupational asthma in Sweden 1990–2. *Occup Environ Med* 1996;53:757–61.
  261. Tsai TW, Gallagher EJ, Lombardi G, Gennis P, Carter W. Guidelines for the selective ordering of admission chest radiography in adult obstructive airway disease. *Ann Emerg Med* 1993;22(12):1854–8.
  262. Turner MO, Noertjojo K, Vedal S, Bai T, Crump S, FitzGerald JM. Risk factors for near-fatal asthma: a case-control study in hospitalized patients with asthma. *Am J Respir Crit Care Med* 1998;157(6 Pt 1):1804–9.
  263. Turner MO, Taylor D, Bennett R, FitzGerald JM. A randomized trial comparing peak expiratory flow and symptom self-management plans for patients with asthma attending a primary care clinic. *Am J Respir Crit Care Med* 1998;157(2):540–6.
  264. US Food and Drug Administration. Serevent® (salmeterol xinafoate inhalation aerosol. Bronchodilator aerosol for oral inhalation only. Product information, [http://www.fda.gov/medwatch/SAFETY/2003/03AUG\\_PI/Servent\\_Inhalation\\_Aerosol\\_IP.pdf](http://www.fda.gov/medwatch/SAFETY/2003/03AUG_PI/Servent_Inhalation_Aerosol_IP.pdf)2003 [consulté le 20/02/2004].
  265. Ullman A, Hedner J, Svedmyr N. Inhaled salmeterol and salbutamol in asthmatic patients: an evaluation of asthma symptoms and the possible development of tachyphylaxis. *Am Rev Respir Dis* 1990;142(3):571–5.
  266. Ulrik CS, Backer V, Dirksen A. A 10 year follow up of 180 adults with bronchial asthma: factors important for the decline in lung function. *Thorax* 1992;47(1):14–8.
  267. Ulrik CS, Lange P. Decline of lung function in adults with bronchial asthma. *Am J Respir Crit Care Med* 1994;150(3):629–34.
  268. Ulrik C, Frederiksen J. Mortality and markers of risk of asthma death among 1075 outpatients with asthma. *Chest* 1995;108:10–5.
  269. Uwytyk K, Springer C, Avital A, Bar-Yishay E, Godfrey S. Home recording of PEF in young asthmatics: does it contribute to management? *Eur Respir J* 1996;9(5):872–9.
  270. van der Palen J, Klein JJ, Rovers MM. Compliance with inhaled medication and self-treatment guidelines following a self-management programme in adult asthmatics. *Eur Respir J* 1997;10(3):652–7.
  271. van der Woude HJ, Aalbers R. Compliance with inhaled glucocorticoids and concomitant use of long-acting  $\beta_2$ -agonists. *Respir Med* 2001;95(5):404–7.
  272. van der Woude HJ, Winter TH, Aalbers R. Decreased bronchodilating effect of salbutamol in relieving methacholine induced moderate to severe bronchoconstriction during high dose treatment with long acting  $\beta_2$  agonists. *Thorax* 2001;56(7):529–35.
  273. van Es S, Nagelkerke A, Collard V, Scholten R, Bouter LM. An intervention programme using the ASE-model aimed at enhancing adherence in adolescents with asthma. *Patient Educ Couns* 2001;44(3):193–203.
  274. van Ganse E, Hubloue I, Vincken W, Leufkens HGM, Gregoire J, Ernst P. Actual use of inhaled corticosteroids and risk of hospitalisation: a case-control study. *Eur J Clin Pharmacol* 1997;51(6):449–54.
  275. van Grunsven PM, van Schayck CP, van Deuveren M, van Herwaarden CL, Akkermans RP, van Weel C. Compliance during long-term treatment with fluticasone propionate in subjects with early signs of asthma or chronic obstructive pulmonary disease (COPD): results of the detection, intervention, and monitoring program of COPD and asthma (DIMCA) Study. *J Asthma* 2000;37(3):225–34.
  276. van Grunsven PM, van Schayck CP, van Kollenburg HJM, van Bosheide K, van den Hoogen HJM, Molema J, et al. The role of “fear of corticosteroids” in nonparticipation in early intervention with inhaled corticosteroids in asthma and COPD in general practice. *Eur Respir J* 1998;11(5):1178–81.
  277. van Schayck CP, Bijl-Hofland ID, Folgering H, Cloosterman SG, Akkermans R, van den Elshout F, et al. Influence of two different inhalation devices on therapy compliance in asthmatic patients. *Scand J Prim Health Care* 2002;20(2):126–8.
  278. Van Vyve T, Chanez P, Bousquet J, Lacoste JY, Michel F, Godard P. Safety of bronchoalveolar lavage and bronchial biopsies in patients with asthma of variable severity. *Am Rev Respir Dis* 1992;146:116–21.

279. Vandeplass O, Jamart J, Delwiche J, Evrard G, Larbanois A. Occupational asthma caused by natural rubber latex: outcome according to cessation or reduction of exposure. *J Allergy Clin Immunol* 2002;**109**(1):125–30.
280. Vandentorren S, Baldi I, Annesi Maesano I, Charpin D, Neukirch F, Filleul L, et al. Long-term mortality among adults with or without asthma in the PAARC study. *Eur Respir J* 2003;**21**(3):462–7.
281. Venables KM, Chan-Yeung M. Occupational asthma. *Lancet* 1997;**349**(9063):1465–9.
282. Veterans Health Administration. *Clinical practice guideline for the management of persons with COPD or Asthma*. Washington, DC: Veterans Health Administration; 1997.
283. Vlachos-Mayer H, Leigh R, Sharon RF, Hussack P, Hargreave FE. Success and safety of sputum induction in the clinical setting. *Eur Respir J* 2000;**16**(5):997–1000.
284. Vollmer WM, Markson LE, O'Connor E, Sanocki LL, Fitterman L, Berger M, et al. Association of asthma control with health care utilization and quality of life. *Am J Respir Crit Care Med* 1999;**160**(5 Pt 1):1647–52.
285. Weitzenblum E. *L'exploration fonctionnelle respiratoire en pneumologie*. Paris: Margaux Orange; 2004.
286. Weitzman R, Wilson A. Diffusing capacity and over-all ventilation: perfusion in asthma. *Am J Med* 1974;**57**:767–74.
287. West J, trad Seigneur F. *Physiopathologie respiratoire*. Paris: Ed Pradel; 1989.
288. Williams SG, Schmidt DK, Redd SC, Storms W. Key clinical activities for quality asthma care. Recommendations of the national asthma education and prevention program. *MMWR Recomm Rep* 2003;**52**(RR-6):1–8.
289. Williamson J, Chopin J. Adverse reactions to prescribed drugs in the elderly: a multicentre investigation. *Age Ageing* 1980;**9**(2):73–80.
290. Windsor RA, Bailey WC, Richards J, Manzella B, Soong S, Brooks M. Evaluation of the efficacy and cost effectiveness of health education methods to increase medication adherence among adults with asthma. *Am J Public Health* 1990;**80**(12):1519–21.
291. Woolcock AJ, Rebuck AS, Cade JF, Read J. Lung volume changes in asthma measured concurrently by two methods. *Am Rev Respir Dis* 1971;**104**(5):703–9.
292. World Health Organization. *Allergic rhinitis its impact on asthma ARIA*. Geneva: WHO; 2001.
293. Wraight JM, Cowan JO, Flannery EM, Town GI, Taylor DR. Adherence to asthma self-management plans with inhaled corticosteroid and oral prednisone: a descriptive analysis. *Respirology* 2002;**7**(2):133–9.
294. Wraight JM, Hancox RJ, Herbison GP, Cowan JO, Flannery EM, Taylor DR. Bronchodilator tolerance: the impact of increasing bronchoconstriction. *Eur Respir J* 2003;**21**(5):810–5.
295. Yates DH, Kharitonov SA, Barnes PJ. An inhaled glucocorticoid does not prevent tolerance to the bronchoprotective effect of a long-acting inhaled  $\beta_2$ -agonist. *Am J Respir Crit Care Med* 1996;**154**(6 Pt 1):1603–7.