# 2. Diagnosis

## 2.1 Clinical features

C A diagnosis of asthma should be considered in the presence of suggestive clinical symptoms and signs, such as wheezing (the most characteristic)[1], dyspnea or breathing difficulty, cough, and chest tightness (key symptoms)[2,3]. These clinical manifestations are usually variable, occur mainly at night or at early morning and are caused by different triggers (viral infections, allergens, tobacco smoke, exercise, emotions, etc.). Seasonal variations and family and personal history of atopy are important aspects to be considered[4-7].

C Usually, several signs or symptoms appear at the same time; isolated clinical manifestations are poorly predictive of asthma[4,8,9]. None of these symptoms and signs are specific of asthma[10], hence the need to include some objective diagnostic test, usually respiratory function tests.

C The patient's clinical history should also include other aspects, such as the onset of symptoms, the presence of allergic rhinitis or eczema, and a family history of asthma or atopy[5], all of which increases the probability to establish a diagnosis of asthma. Table 2.1 shows the key questions for the identification of patients with suspected asthma[2,3].

C On physical examination, wheezing on auscultation is the most characteristic, and in some occasions, nasal obstruction on anterior rhinoscopy, and dermatitis or eczema. However, a normal unrevealing physical examination does not exclude the diagnosis of asthma.

C In the presence of acute symptoms at the onset of the disease, a short anamnesis and physical examination will be performed, and treatment will be started. Objective diagnostic tests will be performed once symptoms have been controlled[8].

C If asthma is suspected, a differential diagnosis with other diseases, particularly chronic obstructive pulmonary disease (COPD) should be established as shown in Table 2.2.

## 2.2 Pulmonary function in adults

### *2.2.1 Adults*

D The diagnosis of asthma is established when in a patient with suspected symptoms of disease, a pulmonary function test (preferably spirometry) objectively demonstrates an alteration compatible with asthma.

Table 2.1. Key questions for the diagnostic suspicion of asthma

| |
|---|
| • Have you ever had "whistling" in the chest? |
| • Have you ever had cough especially at night? |
| • Have you had cough, wheezing, breathing difficulty in certain periods of the year or when in contact with animals, plants, tobacco or at the workplace? |
| • Have you had a cough, "whistling", breathing difficulty after a moderate or intense physical exercise? |
| • Have you had colds lasting more than 10 days or "going down into the chest"? |
| • Have you used inhaled medications that relieve your symptoms? |
| • Do you have any kind of allergy? Do you have any relatives with asthma or allergy? |

Modified from García Polo 2012 and Martín Olmedo 2001[2,3].

Table 2.2. Differential diagnosis of asthma in adults

| | ASTHMA | COPD |
|---|---|---|
| Age at onset | Any age | After 40 years of age |
| Smoking | Irrelevant | Practically always present |
| Atopy | Common | Uncommon |
| Family history | Common | Not assessable |
| Symptom variability | Yes | No |
| Reversibility of bronchial obstruction | Significant | Usually less significant |
| Response to glucocorticoids | Very good, almost always | Indeterminate or variable |
| | **Other possible conditions** | **Characteristic symptoms** |
| Age between 15 and 40 years | • Inducible laryngeal obstruction | • Dyspnea, inspiratory stridor |
| | • Hyperventlation | • Fainting, paresthesia |
| | • Inhaled foreign body | • Sudden onset of symptoms |
| | • Cystic fibrosis | • Excessive cough and mucus |
| | • Bronchiectasis | • Recurrent infections |
| | • Congenital heart disease | • Heart murmurs |
| | • Pulmonary thromboembolism | • Sudden onset of dyspnea, tachypnea, chest pain |
| Age older than 40 years | • Inducible laryngeal obstruction | • Dyspnea, inspiratory stridor |
| | • Hyperventilation | • Fainting, paresthesia |
| | • Bronchiectasis | • Recurrent infections |
| | • Parenchymal lung disease | • Exertional dyspnea, non-productive cough |
| | • Heart failure | • Exertional dyspnea, nighttime symptoms |
| | • Pulmonary thromboembolism | • Sudden onset dyspnea, tachypnea |

Modified from GINA 2019 and Plaza 2019[6,10].

C

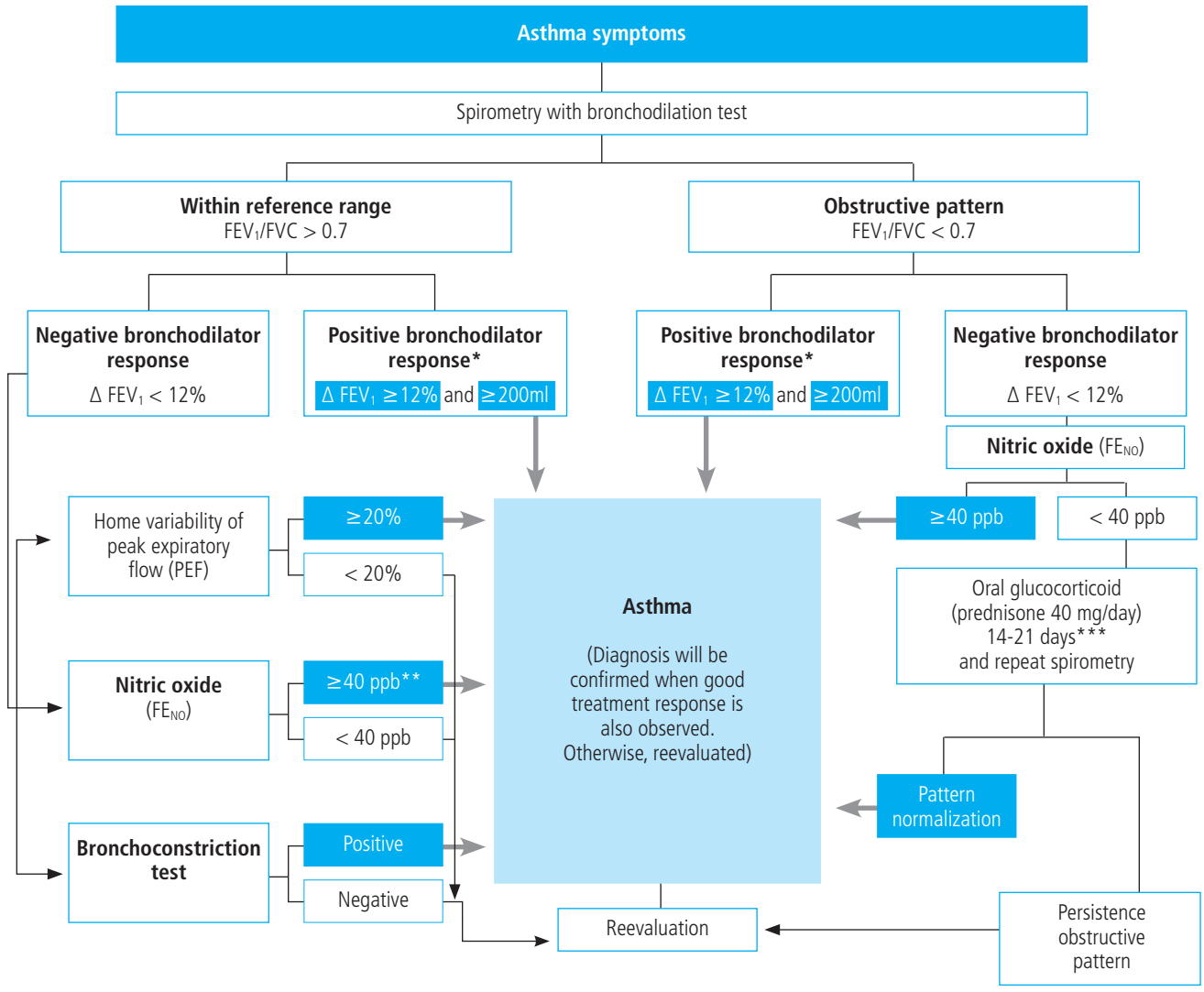
The main functional alterations in asthma are airflow obstruction, reversibility, variability, and bronchial hyperresponsiveness.

C

**Spirometry** is the first-choice diagnostic test, as shown in the algorithm of the diagnostic process (Figure 2.1). The main parameters to be determined are forced expiratory volume in one second ($FEV_1$) and forced vital capacity (FVC); their reference values should be adjusted to the age and ethnic group/race of each patient. Airway obstruction is defined as $FEV_1$/FVC ratio below the lower limit of reference values, which has been arbitrarily set at 0.77[12]. This criterion, however, may lead to an overestimation of airway obstruction in patients of advanced age[12]. For this reason, it is recommended to use international reference values, adequate for all ages, which allow to express results as deviations of the mean (z-score), with a lower limit or normal (LLN) of -1.64[13]. A reduced $FEV_1$ value confirms the obstruction, helps to establish its severity and indicates a greater risk of exacerbations[14]. On the other hand, many patients with asthma may show spirometric values close to the reference range or even a non-obstructive (restrictive) pattern due to air trapping.

C

For the **bronchodilation test**, the administration of 4 successive/puffs of 100 µg *salbutamol*, or its equivalent, using a pressurized inhaler with a spacer chamber and repeating the spirometry after 15 minutes is recommended. A response is considered to be positive (or significant bronchodilatation) when there is a ≥ 12% and a ≥ 200 ml increase in $FEV_1$ from baseline (Table 2.3)[12]. An alternative criterion for bronchodilatation is a > 60 l/min or > 20% rise in the peak expiratory flow (PEF)[15]. Reversibility can also be identified as an improvement in $FEV_1$ or PEF after 2 weeks of treatment with systemic glucocorticoids (prednisone 40 mg/day or equivalent) or 2-8 weeks of inhaled glucocorticoids (1500-2000 mg/day of fluticasone propionate or equivalent)[16]. Although reversibility of bronchial obstruction is a typical characteristic of asthma, it is not present in all patients.




*In children, a 12% increase is sufficient to consider this test as positive, even if < 200 ml. **In cases of a negative broncoconstriction test, a diagnosis of eosinophilic bronchitis should be considered. ***Alternatively, inhaled glucocorticoids at very high doses, 1500-2000 µg of fluticasone, 3 or 4 times a day for 2-8 weeks may be used.

**Figure 2.1.** Diagnostic algorithm.

**Table 2.3.** Reversibility and daily variability criteria recommended for the diagnosis of asthma

| | |
|---|---|
| **Reversibility** | Post-Bd $FEV_1$ – pre-Bd $FEV_1 \geq 200$ ml and $\frac{\text{Post-Bd } FEV_1 - \text{pre-Bd } FEV_1}{\text{pre-Bd } FEV_1} \times 100 \geq 12\ \%$ |
| **Daily variability** | $\frac{\text{Maximum PEF} - \text{minimum PEF}}{\text{Maximum PEF}} \times 100$ Variability ≥ 20 % during ≥ 3 days per week, in a 2-week recording |

$FEV_1$: forced expiratory volume in one second; PEF: peak expiratory flow; Bd: broncodilatation.

**Variability, or excessive fluctuation of pulmonary function** over time, is essential for the diagnosis and control of asthma. The most widely recommended daily variability index is the PEF amplitude in relation to the averaged mean over at least 1-2 weeks and recorded before the administration of medication (Table 2.3)[17]. A PEF variability ≥ 20 % is diagnostic for asthma[18]. C

**Bronchial hyperresponsiveness** is the term that defines an excessive narrowing of the bronchial lumen in the presence of physical or chemical stimuli that usually only provokes little or no reduction of airway caliber[19]. The identification of this excessive response to a bronchoconstrictor by means of a **non-specific bronchoprovocation (challenge) test** may be useful in patients with clinical suspicion of asthma and normal C

C pulmonary function. Either direct agents, such as methacholine or histamine, or indirect agents, such as monophosphate adenosine, mannitol or hypertonic saline can be used[20]. These latter agents show a better relationship with inflammation and a higher sensitivity to the effect of glucorticoids[21]. Furthermore, mannitol offers the advantage of being administered via a dry powder inhaler[22].

C The analysis of bronchial hyperresponsiveness is carried out in terms of sensitivity or threshold, by determining the dose or concentration leading to a 20% decrease in $FEV_1$ as compared to the post-diluent value[19,23]. In the case of methacholine, it has been recently recommended to use the cumulative dose associated with a 20% reduction of $FEV_1$ (PD20) in respect to the value obtained after administration of the diluent[24]. This type of bronchial challenge test has a high sensitivity but a limited specificity[25], thereby being more useful for excluding than for confirming the diagnosis of asthma. Bronchial hyperresponsiveness is also present in other diseases, such as allergic rhinitis, COPD, bronchiectasis, cystic fibrosis or heart failure

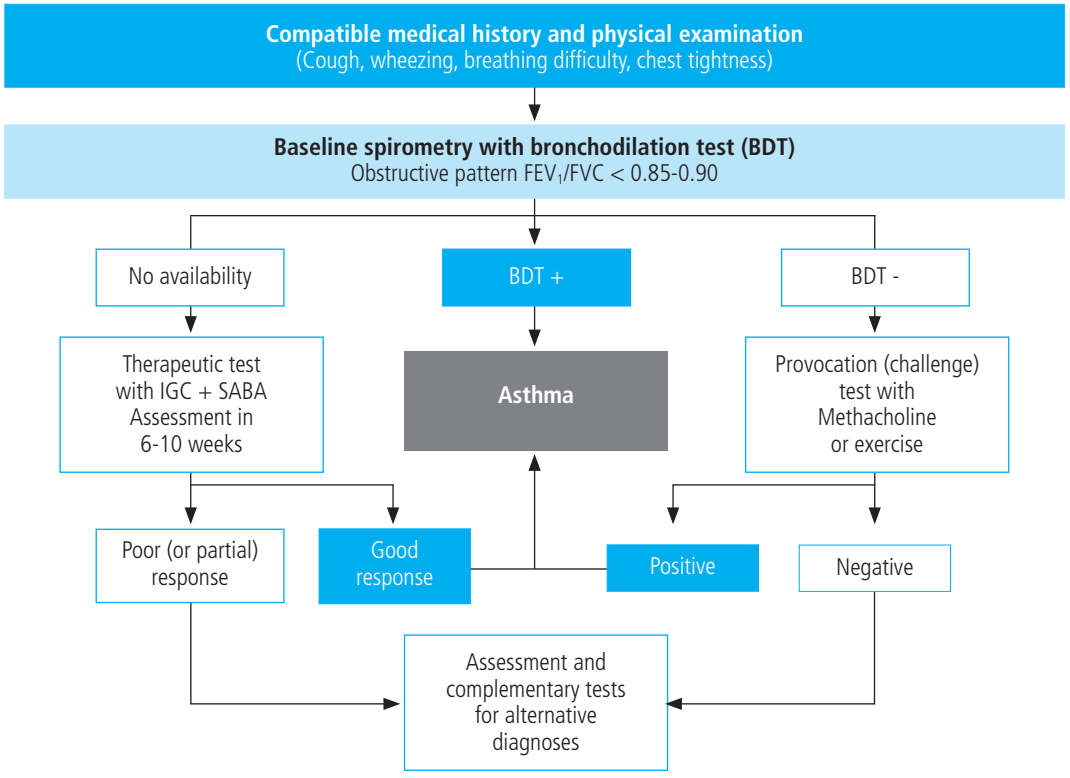
C The mannitol test is considered to be positive when a 15% fall in $FEV_1$ from baseline (PD15) occurs or when there is an incremental decrease of $FEV_1$ of ≥ 10% between two consecutive doses[19]. This test is more useful to confirm the diagnosis of asthma (particularly in cases of exercise-induced bronchoconstriction) because its specificity is > 95%, although its sensitivity is of 60%.

B The **fractional exhaled nitric oxide ($FE_{NO}$)** is a non-invasive measurement of bronchial inflammation of allergic-T2 phenotype (see section 7.3) and related in part with eosinophilic inflammation. Although both $FE_{NO}$ and eosinophils are involved in the T2 inflammatory cascade, the two biomarkers are regulated by different inflammatory pathways. The measurement procedure has been standardized[26] and the recently recommended cut-off point has been established at < 40 ppb in adults not being treated with glucocorticoids[8,27]. $FE_{NO}$ has a high sensitivity and specificity for the diagnosis of asthma in non-smoking patients not receiving inhaled glucocorticoids[28], particularly in association with reduced $FEV_1$[29]. However, a normal $FE_{NO}$ value does not exclude the diagnosis of asthma especially in non-atopic subjects[30].

## 2.3 Pulmonary function in children

C The usefulness of pulmonary function tesrs in children for the diagnosis of asthma is lower than in adults, since most children (including moderate and severe forms) showed $FEV_1$ values within the reference range[31,32]. Pulmonary function tests may contribute to the diagnosis, but normal results do not exclude the diagnosis. These tests do not sufficiently discriminate the level of severity[33].

C With an appropriate method, it is possible to obtain reliable forced spirometries in children since the age of 3 years. From 5




Positive bronchodilation test (BDT): increase of $FEV_1$ >12 % as compared with baseline.

**Figure 2.2.** Asthma diagnostic algorithm in children.

C to 6 years onwards, functional diagnosis of asthma is similar to that made in adults. In children, $FEV_1$/FVC is bettter correlated with severity of asthma than $FEV_1$[21,34]. In children, obstruction is defined by $FEV_1$/FVC ratio < 85-90 % (Figure 2.2).

C A bronchodilaton test is considered positive when the increase of $FEV_1$ from baseline is equal or greater than 12%, although it is possible that an 8% increase from baseline or a 9% increase in relation to the predicted value may define better the bronchodilator response in children[35,36].

C As children can exhale all the air in 2-3 seconds, an expiration lasting this amount of time may be considered valid provided its validity can be confirmed by visual inspection of the correctness of the maneuver by an expert[37]. Less strict reproducibility criteria are also acceptable: 100 ml or 10% of $FEV_1$[38].

C $FEF_{25-75\%}$ values do not provide relevant additional information and, therefore, do no contribute to clinical decision-making[39]. At present, international reference values, *all ages equations*, which are suitable for all ages, are available[13], allowing to express the results as deviations of the mean (z-score), with a lower limit or normal (LLN) of -1.64.

C If diagnosis is uncertain, methacholine and exercise challenge tests may be of special interest in children, since exercise challenge test is relatively easy to perform, reproducible and has a high specificity for the diagnosis of asthma, although its sensitivity is low[40].

D Between 3 and 5 years of age, it is indispensable tu use adequate methodology and appropriate reference values and do not extrapolate values of older children[41-43]. Since these children may occasionally have expiration times lower than 1 second, the most useful value would be $FEV_{0.5}$ or $FEV_{0.75}$ rather than $FEV_1$[44]. In this age segment, the normal $FEV_1$/FVC value would be greater than 90%.

D As for the use of the bronchodilation test at this age, the cut-off point for both $FEV_1$ and $FEV_{0.5}$ or $FEV_{0.75}$ remains to be determined[45,46]. Other tests that may be useful in the management of preschool children with asthma include forced impulse oscillometry (FIO)[47-49], the measurement of airway resistance using the interrupter technique (Rint), the tidal flow-volume curve analysis or measurement of airway resistance by plethysmography. Any of these techniques must be adapted to ATS/ERS guidelines on pulmonary function in preschool children[44]. For children under 2 years of age, the rapid thoracoabdominal compression is the most widely used technique.

D To perform reliable pulmonary function tests in children, particularly in those younger than 5-6 years of age, it is essential to have nursing staff specifically trained in these techniques as well as laboratories adapted for children.

D Measurement of $FE_{NO}$ allows assessing the degre of bronchial inflammation also in children[50]. The assessment of $FE_{NO}$ in young children is not relevant for predicting a diagnosis of asthma at school age[51]. The diagnostic reliability of $FE_{NO}$ for asthma is compromised by the wide confidence intervals and the overlapping of values between children without asthma and those with atopic dermatitis. Population-based studies[52] have established cut-off values quite similar to those proposed by the ATS[53], with positivity in children above 35 ppb.

C Regarding the usefulness of $FE_{NO}$ in the follow-up and treatment adjustment, it has not been possible to consistently demonstrate its benefits. It is necessary, a better knowledge of the personal value and to make therapeutic decisions based on changes in relation to this optimal value[54]. Treatment with inhaled glucocorticoids reduces $FE_{NO}$ concentration, so that measurement of $FE_{NO}$ may be a predictor of response[55]. In some cases (especially in the most severe), increasing trends as compared to the optimal value may be useful to estimate the future risk of relapse[56].

C Although potentially useful as guidance, the available evidence does not confirm the reliability of $FE_{NO}$ to evaluate adherence to IGC treatment.

C $FE_{NO}$ can be determined in young children using the multiple breath-exhalation technique, with reference values having being established for the age between 1 and 5 years[57]. In this age group, although some study has shown an association between high levels of $FE_{NO}$ and the risk of asthma[58], this correlation remains to be established.

C Overall, there is no consistent evidence to recommend the routine use of $FE_{NO}$ in the follow-up of children with asthma, and its use should be limited to specialized consultation settings[59].

## 2.4 Allergy evaluation

C The aim of allergy testing is to determine the presence of a potential sensitization to aeroallergens that may influence the development of the allergic asthma phenotype or to trigger exacerbations. These tests can be performed in all patients with asthma regardless of their age. The anamnesis helps to evaluate personal and family history of atopy (rhinoconjunctivitis, eczema, food allergy) and the relationship between symptoms and allergen exposure. To make a diagnosis of allergic asthma,

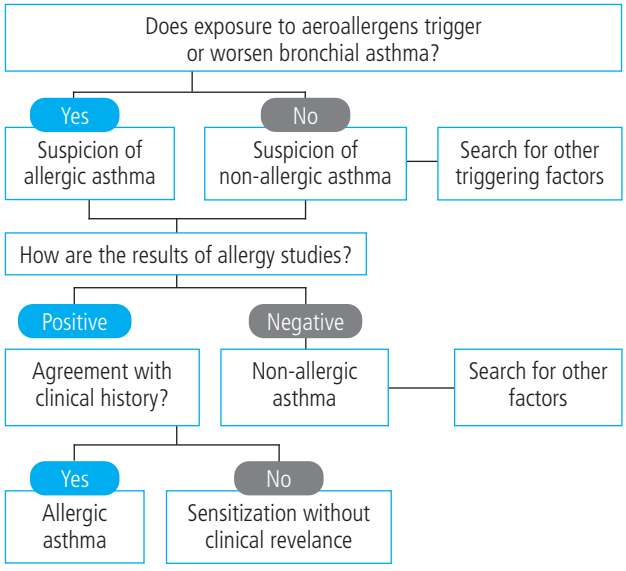



**Figure 2.3.** Allergy study: to establish the diagnosis of allergic asthma, there should be agreement between the medical history and the result of the allergic study.

C in addition to sensitization to inhaled allergens, it is important to assess the clinical relevance of the results obtained[60] (Figure 2.3).

B C The **intradermal puncture testing or *prick* test** with standardized extracts[61] (Table 2.4) is the first-choice method because of its high sensitivity, low cost and immediate availability of results. It is necessary to be aware of the variables that may affect the results (drugs, dermographism, etc.), and to have experience for a correct interpretation of results (false positives due to cross-reactivity)[62].

B Measurement of **specific serum IgE against complete aeroallergens**, although having the same significance as the *prick* test, is less sensitive and more expensive[63]. Specific serum IgE to allergenic components allows to differentiate primary sensitization from cross-reactivity[64], and in polysensitized patients improves the selection of the composition of specific immunotherapy with allergens[65].

C The **specific bronchial challenge test** may be useful when there is a discrepancy between clinical history and the results of sensitization tests, although it is not routinely recommended and should be performed by expert professionals

## 2.5 Classification of severity in adults

D Asthma has usually been classified according to its severity, although the definition and assessment of these characteristics has changed over time[6,11,66]. Severity of asthma is an intrinsic property of the disease that reflects the intensity of its pathophysiological abnormalities[67].

D Traditionally, the classification of asthma based on clinical and functional parameters includes 4 categories: intermittent, mild persistent, moderate persistent, and severe persistent[6,11,66].

Table 2.4. Standard battery of aeroallergens used in intraepidermal puncture skin tests or prick*

| | |
|---|---|
| Mites | *Dermatophagoides pteronyssinus/farinae*<br>*Lepidoglyphus destructor, Blomia tropicalis* |
| Dander | Cat, dog |
| Pollens | Grasses, *Olea europaea, Cupressus* spp,<br>*Platanus* spp,<br>*Salsola kali, Parietaria judaica,*<br>*Artemisia vulgaris* |
| Molds | *Alternaria alternata, Aspergillus fumigatus* |

*Extracts of other allergens according to environmental exposure (such as professional allergens) or geographical prevalence can be added.

D It should be remember that asthma severity involves both the intensity of the process and its response to treatment[68,69]. Severity is usually evaluated while the patient is being treated and is classified according to the need for maintenance therapy to achieve control of symptoms and exacerbations[68,69] (Table 2.5).

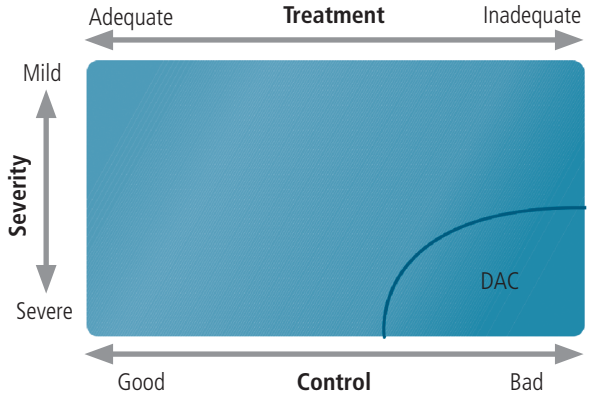
D Severity is not necessarily a constant characteristic of asthma and needs to be periodically reassessed since may vary with time (months or years).

A Most asthma populations suffer from intermittent or mild persistent asthma[70,71]. The inflammatory features of these apparently non-severe foms of the disease should not be underestimated[72,73]. Despite the absence of symptoms in mild and intermittent asthma, a correct clinical and functional evaluation of the patient is needed for proper classification and adjustment of treatment.

## 2.6 Control and measuring methods

D Asthma control is the extent to which manifestations of the disease can be either absent or maximally reduced by therapeutic interventions, and treatment goals are fulfiled[67,69], largely reflecting the adequacy of asthma treatment (Figure 2.4).

D Asthma has been arbitrarily classified according to the degree of disease control in: well-controlled asthma, partially controlled asthma and poorly controlled asthma, based on the criteria shown in Table 2.6[6]. Some asthma patients may show a good control of both symptoms and pulmonary function, while simultaneously experiencing exacerbations, whereas other patients may have daily symptoms and very few exacerbations.




Modified from Osborne, et al.[74]

Figure 2.4. Relationship between severity and control of asthma. The degree of control largely reflects the adequacy of treatment. Some paients have a difficult asthma control (DAC).

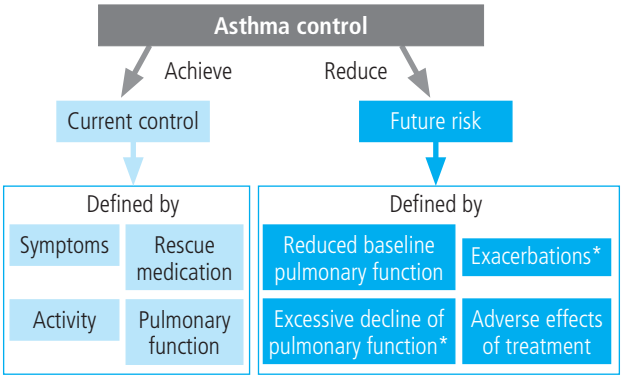
Table 2.5. Classification of asthma severity when it is well-controlled with treatment (stratified by steps

| **Severity** | **Intermittent** | **Persistent** | | |
|---|---|---|---|---|
| | | **Mild** | **Moderate** | **Severe** |
| Minimal treatment requirements to maintain control | Step 1 | Step 2 | Step 3 or Step 4 | Step 5 or Step 6 |

Table 2.6. Classification of asthma control in adults

| | Well-controlled (all of the following) | Partially controlled (any measure in a week) | Poorly controlled |
|---|---|---|---|
| Daytime symptoms | None or ≤ 2 days a month | > 2 days a week | If ≥ 3 characteristics of partially controlled asthma |
| Limitation of activities | None | Any | |
| Nighttime symptoms/ awakenings | None | Any | |
| Neeed for reliever medication (rescue) (short-acting ß$_2$-adrenergic agonist) | None or ≤ 2 days a month | > 2 days a week | |
| Pulmonary function<br>FEV$_1$<br><br>PEF | <br>> 80 % predicted value or z-score (-1.64)<br>> 80 % better personal value | <br>< 80 % predicted value or z-score (-1.64)<br>< 80 % better personal value | |
| Exacerbations | None | ≥ 1/year | ≥ 1 in any week |

FEV$_1$: forced expiratory volumen in one second; PEF: peak expiratory flow.




*Evaluate risk factors.

Figure 2.5. Domains and risk factors that determine the degree of asthma control.

D Thus, when trying to minimize the clinical expression of asthma two major domains should be take into account[69]: on the one hand, the day-to-day disease manifestations (current control), and on the other hand, its possible consequences (future risk), as shown in Figure 2.5.

D Regarding the current control domain, control would be defined by the ability to prevent the presence of daytime and nighttime symptoms; the frequent use of rescue medication for the relieve of these symptoms; maintenance of pulmonary function within or close to normal limits; the absence of limitations of daily living activities, including family, social, work or school activities, and physical exercise; and finally, the fulfillment of expectations of both patients and their families regarding the quality of care received.

D As for the future risk domain, control includes: the absence of exacerbations; the absence of the need of using systemic glucocorticoids, visits to emergency departments and hospitalizations; the prevention of an excessive loss of pulmonary function and the development of a fixed airway obstruction or, in the case of children, an anomalous lung development; and finally, the prescription of an optimal treatment with minimum or no adverse effects.

D As defined in the control of asthma, a number of procedures should be used for its evaluation[75]. The essential tool for assessing asthma control is **the continued follow-up medical visit**. In this visit, the domains of current control and future risk of exacerbationes should be evaluated, together with possible presence of fixed airflow obstruction and treatment-associated adverse effects, and finally and most importantly, the adherence to treatment, including a reminder of the self-management plan and actions to be taken in case of disease decompensation, and trying to reinforce the patient-healthcare professional relationship at each visit.

C In order to facilitate and standardize the evaluation of the domain of current control of asthma, different simple questionnaires and easy to be completed by the patient have been developed. The Asthma Control Test (ACT)[76,77] and the Asthma Control Questionnaire (ACQ)[78,79] have been validated and culturally adapted for use in Spain. Validation of the ACT questionnaire is more detailed for its use in clinical practice with well-defined cut-off points, so that a score equal to or greater than 20 is highly consistent with well-controlled asthma, between 19 and 16 with partially controlled/not well-controlled asthma, and equal to or lower than 15 with poorly controlled asthma[76,77]. The minimum clinically relevant difference is 3 points[80]. Also, the Spanish version of the ACQ questionnaire has been validated, with cut-off values based on actual clinical practice[81,82] with < 0.5 for well-controlled asthma, between 0.5 and 0.99 for partially controlled asthma, and ≥ 1 for poorly controlled asthma. Nevertheless, the reliability of both questionnaires to detect poorly controlled asthma is low[83], and for this reason they should never be used as single tools to evaluate asthma control.

C Factors assocated with the risk of exacerbations include the presence of uncontrolled asthma symptoms and history

Table 2.7. Main risk factors for exacerbations

- Poor current control: ACT < 20 or ACQ > 1.5.
- History of exacerbations: ≥ 1 severe exacerbation in the previous year or history of almost life-threatening asthma
- Undertreatment with inhaled steroids: not prescribed, por adherence or critical errors with the use of inhalers.
- Excessive use of rescue medication: ≥ 3 inhalers per year (≥ 2 puffs/day).
- Type 2 inflammation: increased peripheral blood/sputum eosinophils, increased $FE_{NO}$.
- Pulmonary function: low baseline $FEV_1$, reversibility with the bronchodilator.
- Psychosocial problems, low socioenconomic level.
- Exposures: tobacco smoke, allergens, pollution.
- Comorbidities: obesity, sleep apnea-hypopnea síndrome, chronic rinosinusitis, gastroesophageal reflux, food allergy, pregnancy.

Adapted from GINA 2019[6].

C of severe exacerbations. Other factors that may increase the risk of exacerbations in the absence of uncontrolled asthma or previous severe exacerbations are shown in Table 2.7.

C Assessment of biomarkers of type 2 inflammation may contribute to stratify the paient's risk, and taking into account that peripheral blood eosinophilia[84-86] or sputum eosinophilia[87] as well as increased $FE_{NO}$ in a patient treated with inhaled glucocorticoids[88] are additional factors that increase the risk of exacerbations.

A In the patient with severe asthma, adjustment of treatment with inhaled glucocorticoids has been recommended, taking into account results of sputum eosinophils or $FE_{NO}$, since this strategy is associated with a lower risk of exacerbations, although it has no effect on symptoms or pulmonary function[89].

C Forced spirometry is another tool that can help in the assessment of future asthma control, since a low baseline $FEV_1$ value, in particular < 60%90, and the presence of reversibility have been reported as factors that increase the risk of exacerbations.

D Asthma control should be evaluated at each medical visit. Once asthma treatment is started, clinical and therapeutic management of the disease should be directed toward achieving and maintaining control (including symptoms, exacerbations, and lung function). Therefore, the degree of control will determine the decisions on maintenance treatment and dose adjustment, according to the therapeutic steps shown in the corresponding section.

## 2.7 Control and classification of severity in children

### *2.7.1 Clinical severity*

D The classification of severity is different according to the moment at which asthma is evaluated: at the onset, at the time of diagnosis or thereafter once control of the disease has been achived. In the first case, the level of severiry depends on the frequency and intensity of symptoms (number of attacks and between-attack status: mainly exercise tolerance and nighttime symptoms), the need for a rescue bronchodilator and the values of respiratory function tests. In small children in whom lung function testing is not feasible, severity is only classified according to symptomatology.

D Some children with asthma present symptoms intermittently, episodically, more or less frequently, while others suffer from more persistent symptoms. The character of moderate or severe asthma is determined by the frequency and intensity of the symptoms. In any case, the classification of severity i s established once treatment is started, based on the medication necessary to keep the child well controlled.

C In this way, the patient who requires step 5 or 6 treatment will have severe asthma, the one who needs step 3 or 4, a moderate asthma, the one who requires step 1 or 2, a mild asthma.

D

Childhood asthma varies substantially over time, even during a single year, which makes its classification difficult. Most young children experience asthma symptoms during viral infections only; they may experience, therefore, moderate or severe asthma in the winter and remain asymptomatic in spring and summer seasons. In order to typify correctly a case of asthma in children, it is necessary to specify, in addition to severity, the triggering factors in the individual patient and the degree of control of asthma.

### 2.7.2 Control

C

Asthma control is defined by the extent to which clinical manifestations have declined or disappeared with the treatment prescribed[92]. It includes the two components: current symptom control and future risk (future consequences of such control)[6].

C

The **current control of symptoms** is evaluated by the presence and frequency of symptoms, both at daytime and nighttime, the need of rescue medication and the presence of some limitation for daily life activities. The criteria established to define the degree of control vary from one guideline to another, but generally it is classified as good or poorly controlled asthma, although some guidelines also introduce the concept of partially controlled[6].

C

To facilitate symptom control evaluation, there are available specific Spanish validated questionnaires. One of these questionnaires is the CAN questionnaire (Control de Asma en Niños, Asthma Control Questionnaire in Children) with a version for 9-14 year-old children and another version for parents (2-8 year-old children). This instrument evaluates nine questions about clinical manifestations within the last 4 weeks and is scored between 0 (good control) and 36 (poor control). A patient is considered to be poorly controlled when scores are equal to or higher than 8[95] (Table 2.8). Also available is the Childhood Asthma Control Test (c-ACT), validated in Spanish[95,96] for 4-11 year-old children, which includes 7 questions (4 for the child and 3 for the parents/caregivers). A patient is considered to be poorly controlled when the score is lower than 20 (Table 2.9).

C

The **future risk** assesses the presence of risk factors for exacerbations (Table 2.10), to develop a fixed airflow limitation (undertreatment with IGC, prematurity[97], environmental exposure to tobacco smoke, low $FEV_1$, severe asthma, previous hospitalizations) and for suffering treatment-related side effects (frequent courses of oral glucocorticoids, high doses of IGC)[98].

C

In addition to the control of clinical symptoms and pulmonary function, measurement of $FE_{NO}$ has been advocated as an approach to assess the control of inflammation. Although potentially useful in some patients, this procedure does not seem to add any relevant benefits to the aforementioned follow-up and treatment strategies[99].

Table 2.8. Asthma Control Questionnaire in Children (CAN)[93]

| **1. In the last 4 weeks, how often have you coughed during the day without having a cold?** | **4. In the last 4 weeks, how often have you had wheezing at night?** | **7. When the child exercises (plays, runs, etc.) or bursts out laughing, does he/she coughs or wheezes?** |
|---|---|---|
| 4. More than once a day | 4. More than once a night | 4. Always |
| 3. Once a day | 3. Once a night | 3. Almost always |
| 2. 3 to 6 times a week | 2. 3 to 6 times a week | 2. Sometimes |
| 1. Once or twice a week | 1. Once or twice a week | 1. Almost never |
| 0. Never | 0. Never | 0. Never |
| **2. In the last 4 weeks, how often have you coughed at night without having a cold?** | **5. In the last 4 weeks, how often have you had breathing difficulty during the day?** | **8. In the last 4 weeks, how many times has he/she had to visit the emergency department because of his/her asthma?** |
| 4. More than once a night | 4. More than once a day | 4. More than 3 times |
| 3. Once a night | 3. Once a day | 3. 3 times |
| 2. 3 to 6 times a week | 2. 3 to 6 times a week | 2. Twice |
| 1. Once or twice a week | 1. Once or twice a week | 1. Once |
| 0. Never | 0. Never | 0. Never |
| **3. In the last 4 weeks, how often have had wheezing/whistling sounds in your chest during the day?** | **6. In the last 4 weeks, how often have you had breathing difficulty during the night?** | **9. In the last 4 weeks, how many times has the child been admitted to hospital because of her/his asthma?** |
| 4. More than once a day | 4. More than once a night | 4. More than 3 times |
| 3. Once a day | 3. Once a night | 3. 3 times |
| 2. 3 to 6 times a week | 2. 3 to 6 times a week | 2. Twice |
| 1. Once or twice a week | 1. Once or twice a week | 1. Once |
| 0. Never | 0. Never | 0. Never |

Table 2.9. Childhood Asthma Control Test (ACT) validated in Spanish[95,96]

**Have your child complete these questions**

| **1. How is your asthma today?** | | | |
|---|---|---|---|
|  0 Very bad |  1 Bad |  2 Good |  3 Very good |
| **2. How much of a problema is your asthma when you run, exercise or play sports?** | | | |
|  0 It's a big problem, I can't do what I want to do |  1 It's a problem and I don't like it |  2 It's a little problem but it's okay |  3 It's not a problem |
| **3. Do you cough because of your asthma?** | | | |
|  0 Yes, all of the time |  1 Yes, most of the time |  2 Yes, some of the time |  3 No, none of the time |
| **4. Do you wake up during the night because of your asthma?** | | | |
|  0 Yes, all of the time |  1 Yes, most of the time |  2 Yes, some of the time |  3 No, none of the time |

**Please complete the folowing questions on your own**

| **5. During the last 4 weeks, how many days did your child have any daytime asthma symptoms?** | | | | | |
|---|---|---|---|---|---|
| 5 Not, at all | 4 1-3 days | 3 4-10 days | 2 11-18 days | 1 19-24 days | 0 Everyday |
| **6. During the last 4 weeks, how many days did your child wheeze during the day because of asthma?** | | | | | |
| 5 Not, at all | 4 1-3 days | 3 4-10 days | 2 11-18 days | 1 19-24 days | 0 Everyday |
| **7. During the last 4 weeks, how many days did your child wake up during the night because of the asthma?** | | | | | |
| 5 Not, at all | 4 1-3 days | 3 4-10 days | 2 11-18 days | 1 19-24 days | 0 Everyday |

Table 2.10. Risf factors for asthma exacerbations in children[98,99]

- At least one exacerbation in the previous year.
- Previous care in the ICU or need of intubation.
- Excessive use of SABA.
- Persistent and/or uncontrolled symptoms.
- Lack of adherence to treatment*, inadequate inhalation technique.
- Low $FEV_1$. Positive bronchodilation test.
- Exposure to allergens in case of allergy/atopy.
- Exposure to tobacco smoke.
- Comorbilidities: obesity, allergic rhinitis, food allergy.
- Important psychological or socioenconomic problems.
- Other: peripheral blood or sputum eosinophilia; increase of $FE_{NO}$ in routine control visits.

*The ratio between the number of control medications administered and control medications prescribed is < 0.5.

## RECOMMENDATIONS

| | | |
|---|---|---|
| 2.1. | Asthma should be suspected in a patient with wheezing, dyspnea (or breathing difficulty), cough and chest tightness of variable intensity and frequency. | R2 |
| 2.2. | In case of suspected asthma, seasonal variations and personal or family history of asthma or atopy are important aspects to be considered, although none of these or none of the signs or symptoms, especially isolated, are specific of asthma. | R2 |
| 2.3. | **The diagnosis** of asthma should be based on objective measures of functional involvement. Spirometry with a bronchodilation test is the diagnostic study of choice. | R2 |
| 2.4. | The diagnosis of asthma should be considered in the presence of daily **variability** of peak expiratory flow (PEF) > 20 %, or an **increased fractional exhaled nitric oxide ($FE_{NO}$)** > 40 ppb in patients wo have not been treated with glucocorticoids, particularly in association with reduced $FEV_1$. | R2 |
| 2.5. | **Non-specific bronchial challenge** test should be considered to exclude the diagnosis of asthma. | R2 |
| 2.6. | Periodic spirometry tests (at least once a year) are recommended for children with asthma requiring continuous treatment. | R2 |
| 2.7. | In children, except for specialized consultation, it is not necessary to measure $FE_{NO}$ routinely. | R2 |
| 2.8. | Allergy studies are especially indicated when aeroallergens are suspected to be involved in the development of asthma or its exacerbations, or when other associated atopic diseases are present. | R2 |
| 2.9. | The diagnosis of allergic asthma will be based on the agreement between the patient's clinical history and the results of diagnostic studies. | R2 |
| 2.10. | The severity of asthma (in adults and children) will be established according to the mínimum maintenance treatment needed to achieve control. In untreated patients, the severity of asthma should be establish at the beginning of treatment, with further re-evaluations once control is attained. | R2 |
| 2.11. | The severity of asthma (in adults and children) is not necessarily a constant feature that can change over time (months or years), so that periodic re-evaluation is required. | R2 |
| 2.12. | Control of asthma (in adults and children) should be evaluated at each consultation, and treatment should be adjusted to achieve and maintain control. Control has two main components that should be identified: current control and future risk. | R2 |
| 2.13. | In the objective assessment of the degree of current control of asthma (in adults and children), it is recommended using validated questionnaires for symptoms (preferably ACT in adults, and cACT and CAN in children). In the assessment of future risk of exacerbations, recommendations include questioning on previous events, spirometry, use of inhaled glucocorticoids and reliever/rescue medication, comorbidities and, in selected cases, inflammatory biomarkers (peripheral blood or sputum eosinophils and $FE_{NO}$). | R2 |

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