# 2. Diagnosis

## 2.1 Clinical Features

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A diagnosis of asthma should be considered when there are characteristic clinical symptoms and signs, such as dyspnoea, coughing, wheezing and tightness of the chest. These symptoms are usually variable, occurring predominantly at night and early in the morning, and are caused by different trigger factors (viral infections, allergens, cigarette smoke, exercise, etc.). Seasonal variations and a family and personal history of atopy are important aspects to be considered [33,34]. However, none of these symptoms and signs are specific for asthma, which is why an objective diagnostic test, usually a respiratory function test, needs to be included. The physical examination may be normal, wheezing being the most characteristic sign, although it is not specific to asthma and may even be absent in severe attacks.

When asthma is suspected, a differential diagnosis that admits the possibility of other obstructive respiratory diseases, including COPD, must be made. Table 2.1 includes some of the most relevant differences between these two diseases.

## 2.2 Pulmonary function

## 2.2.1 Adults

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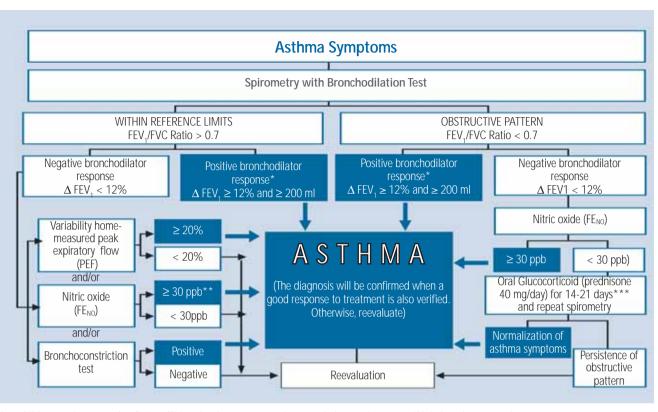
The main functional changes that occur in asthma are airflow obstruction, its reversibility and variability, and bronchial hyperresponsiveness. Spirometry is the diagnostic test of first choice, as the algorithm for the proposed diagnostic process indicates (Figure 2.1). The main parameters to be determined are forced vital capacity (FVC) and forced expiratory volume during the first second (FEV<sub>1</sub>). The reference values must be adjusted to the age and ethnic group/race of each patient. Obstruction is defined as "a FEV<sub>1</sub>/FVC coefficient which falls below the lower cut-off point for the reference values, which are arbitrarily set at 0.7" [35]. However, this criterion may result in the obstruction being overestimated in elderly people [35]. A reduced FEV<sub>1</sub> confirms obstruction, helps to establish its severity and indicates a greater risk of exacerbations [36]. Nevertheless, many asthma patients have a spirometry test result with readings that approximate reference values or that may even show a non-obstructive (restrictive) pattern due to air entrapment.

For the bronchodilation test we recommend administering four successive puffs of 100 µg of salbutamol, or its equivalent, using a pressurized inhaler with a spacing chamber, and then repeating the spirometry test 15 minutes later. A positive response (in other words, significant bronchodilatation) is regarded as an increase in FEV<sub>1</sub> of 12% or more and of 200 ml or more with respect to the baseline value (Table 2.2) [35]. An alternative criterion of bronchodilatation is an increase in peak expiratory flow (PEF) greater than 60 l/minute or 20% [37]. Reversibility can also be identified by an improvement in FEV<sub>1</sub> or PEF after two weeks of systemic glucocorticoid treatment (40 mg/ day of prednisone or its equivalent) or 2-8 weeks of inhaled glucocorticoids (1,500-2,000 mg/day of fluticasone or its equivalent) [38]. Although characteristic of

|   | Asthma      | COPD                       |
|---|-------------|----------------------------|
| Age of onset  | At any age  | After the age of 40        |
| Smoking   | Irrelevant  | Virtually always a feature |
| Presence of rhinitis, conjunctivitis and dermatitis | Frequent    | Infrequent                 |
| Family history                                      | Frequent    | Cannot be evaluated        |
| Variability of symptoms                             | Yes         | No                         |
| Reversibility of obstruction                        | Significant | Usually less significant   |
| Response to glucocorticoids                         | Very good   | Indeterminate or variable  |

Table 2.1. Differential diagnosis between asthma and COPD

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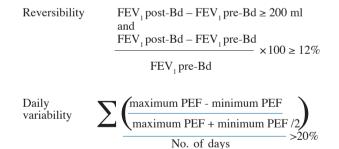


\* In children, an increase of 12% is sufficient for the response to be regarded as positive, even if it is less than 200 ml.

\*\* In cases in which the bronchoconstriction test is negative, a diagnosis, of eosinophillic bronchitis should be considered.
\*\*\* As an alternative inhaled glucocorticoids can be used at very high doses (1500-2000 µg of fluticasone) taken three or four times a day over a period of 2-8 weeks.

Figure 2.1. Algorithm for Asthma Diagnosis

Table 2.2. Reversibility and daily variability criteria recommended for asthma diagnosis



FEV<sub>1</sub>: forced expiratory volume during the first second; PEF: peak expiratory flow; Bd: bronchodilation.

C C asthma, reversibility of bronchial obstruction is not found in all patients.

Excessive variability or fluctuation in pulmonary function over time is essential for the diagnosis and control of asthma. The most recommendable daily variability index is the amplitude of PEF with respect to the mean average over a minimum of 1-2 weeks and recorded prior to medication (Table 2.2) [39]. A PEF variability exceeding 20% is indicative of asthma [40].

The identification of an excessive response to a bronchoconstrictor (bronchial hyperresponsiveness) may be useful in patients with normal pulmonary function who are clinically suspected of having asthma. Direct agents, such as methacholine or histamine, or indirect agents, such as adenosine monophosphate, manitol or hypertonic saline solution can be used [41]. The latter show a better correlation with inflammation and greater sensitivity to the effect of glucocorticoids [42]. Furthermore, manitol offers the advantage that it can be administered using a dry powder inhaler [43].

Bronchial hyperresponsiveness is analyzed in terms of sensitivity or threshold values, by determining the dose or concentration that produces a 20% decrease in FEV<sub>1</sub> with respect to its post-dilution value [44]. Bronchial challenge is highly sensitive but exhibits limited specificity [45], so it is more useful for excluding than for confirming a diagnosis of asthma. Bronchial hyperresponsiveness is also present in other diseases, such as allergic rhinitis, COPD, bronchiectasis, cystic fibrosis or cardiac insufficiency.

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Exhaled nitric oxide fraction ( $FE_{NO}$ ) is a non-invasive way of measuring eosinophilic inflammation of the respiratory tract. The procedure for its determination has been standardized [46] and, although there is a certain level of discrepancy amongst different studies, the upper limit for normal values is from 20 to 30 ppb [47]. It is highly sensitive and specific for diagnosing asthma in non-smokers who do not take inhaled glucocorticoids [48], especially if it is associated with a reduced  $\text{FEV}_1$  [49]. However, a normal  $\text{FE}_{NO}$  value does not exclude an asthma diagnosis, especially in non-atopic individuals [47].

## RECOMMENDATIONS

- The diagnosis of asthma must be based on objective measurements of functional impairment. Spirometry is the test of choice.
- An asthma diagnosis should be considered when there is a daily variability of PEF (peak expiratory flow) exceeding 20% or a raised exhaled nitric oxide fraction ( $FE_{NO}$ ) in patients who have not used glucocorticoids, especially if it is associated with a reduced  $FEV_1$ .
- Non-specific bronchoprovocation must be taken into consideration to rule out a diagnosis of asthma.

## 2.2.2 Children

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Respiratory function tests are less useful for classifying asthma severity in children than in adults; most children with asthma, even moderate or severe forms, have a FEV<sub>1</sub> which falls within the range of reference values [50].

## 2.2.2.1 Respiratory Function in Children who Collaborate

The functional diagnosis of asthma in children who cooperate (children over 6 years of age) is similar to that of adults. Forced spirometry combined with a bronchodilator test is the most useful procedure for diagnosing and monitoring asthma. The FEV<sub>1</sub>/FVC ratio correlates better with asthma severity than FEV<sub>1</sub> in children [50].

In children, a bronchodilator test is regarded as positive when the increase in  $FEV_1$  with respect to its baseline value is greater than or equivalent to 12%. The requirement to exceed 200 ml cannot be met because the pulmonary volume in children is smaller and depends on their height.

In children with obstruction and no bronchodilator response it may be useful to administer a cycle of oral glucocorticoids at a dosage of 1 mg/kg for two weeks to confirm the reversibility of the obstruction [35].

Only a small percentage of children aged 5 to 19 years are able to use a spirometer in accordance with ERS/ATS regulations when expiration lasts longer than six seconds. Children are able to exhale all the air in 2-3 seconds so an expiration lasting this long can be treated as valid as long as the flow/ volume curve does not tail off abruptly or the volume/ time curve has no plateau, even though it may be short. Less demanding criteria of reproducibility are also acceptable: 100 ml or 10% of FEV<sub>1</sub>[51].

FEF<sub>25-75%</sub> correlates with the degree of non-specific bronchial hyperresponsiveness [51-53]. Its inter-subject

reproducibility over time is much less than for FEV<sub>1</sub>, which reduces its usefulness in clinical practice [54].

If a child undergoes a spirometry test together with a bronchodilator test and the diagnosis of asthma is inconclusive, bronchial challenge tests can be used to demonstrate bronchial hyperresponsiveness. The bronchoprovocation test during exercise is of special interest with children, as it is relatively easy to perform, reproducible and highly specific for diagnosing asthma, although not very sensitive [55].

## 2.2.2.2 Respiratory Function in Pre-school Children

Until recently it was considered impossible to perform forced spirometry in children under the age of 6. However, with the right methodology it is possible to conduct reliable spirometric tests in children as young as three. It is essential to use appropriate reference values and not to extrapolate the values of older children [56,57]. Sometimes the expiration time in these children may be less than a second, so the most useful value will be  $FEV_{0.5}$  and not  $FEV_1$  [58].

Other tests that may be useful in managing pre-school children with asthma include forced impulse oscillometry (IOS), the measurement of occlusion resistances (Rint), flow volume/tidal volume curve analysis or the measurement of resistances by plethysmography, although these procedures are usually used in specialized laboratories. Recently, the ATS/ERS regulations on lung function in pre-school children were published [58]. In infants the most widely used technique is rapid thoracic-abdominal compression. Baseline tests of pulmonary function are not very useful for diagnosing asthma in pre-school children, since it is more helpful to demonstrate a bronchodilator response or to employ a bronchial challenge test using one of the techniques mentioned above. C

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In order to conduct reliable lung function tests in children, especially pre-school children, it is essential to have access to nursing personnel who have been specially trained in pulmonary function techniques designed for children and laboratories adapted for testing children.

The  $FE_{NO}$  measurement is useful for determining levels of eosinophilic bronchial inflammation in children [59]. A  $FE_{NO}$  value above 17 ppb offers a sensitivity of 81% and a specificity of 80% for predicting eosinophilic phenotype asthma [60]. If nitric oxide is measured using electrochemical analyzers,  $FE_{NO}$  values

are slightly higher (range 2030 ppb). Inhaled glucocorticoid treatment reduces  $FE_{NO}$  concentration and its measurement after treatment helps to assess the degree of compliance. A  $FE_{NO}$  value less than 49 ppb four weeks after withdrawal of inhaled glucocorticoids shows a sensitivity of 71% and a specificity of 93% for estimating whether asthma is in remission; a higher value increases the likelihood of relapse [61]. Its usefulness in children who cannot or who fail to cooperate is still under investigation. It is essential to perform measurements following a correctly standardized methodology [46].

#### RECOMMENDATIONS

- Spirometry in conjunction with a bronchodilator test is recommended to confirm a diagnosis of asthma and to assess its severity objectively in all children who are able to collaborate appropriately.
- It is advisable for asthmatic children who require continuous treatment to undergo regular spirometric evaluations, at least once a year.
- The measurement of  $FE_{NO}$  must be considered in the diagnosis and monitorization of asthma in children. A high  $FE_{NO}$  value in a child with symptoms which are suggestive of asthma makes the diagnosis more reliable. A high  $FE_{NO}$  value in a child who is being treated with inhaled glucocorticoids should lead us to suspect non-compliance. In a child a  $FE_{NO}$  value above 49 ppb, when treatment has been withdrawn, should lead us to suspect a possible relapse.

## 2.3 Diagnosis of Allergies

The aim of an allergy test is to determine the allergens that influence the development of asthma or its exacerbations, and it should be performed on every asthma patient with persistent symptoms. On the basis of clinical records, exposure to aeroallergens, the seasonal variation of symptoms and when and where they appear (at home, at work/school, in the patient's free time) are assessed, together with the patient's personal history (especially rhinitis) or a family history of atopy (asthma, rhinitis, eczema, food allergies). The selection of suspected aeroallergens (pollen, mites, fungi, animal epithelia or occupational allergens) varies, depending on the patient's clinical history and the geographical region in question [62] (Table 2.3).

Prick tests are the diagnostic method of choice (Table 2.4) [63], even in small children [63]. They have a high predictive value and show good correlation with other in vitro or bronchoprovocation diagnostic tests. For their correct interpretation it is necessary to know the variables that affect both their results (drugs, age, seasonal variations, dermographism, etc.) and their assessment (crossreactivity between allergens, panallergens, etc [64].

The measurement of serum IgE specific to individual allergens has the same clinical significance as the prick test, but is less sensitive and more specific [65]. Although its

#### Table 2.3. Standard Aeroallergen Battery\* used for prick tests

| Mites       | Dermatophagoides pteronyssinus<br>Dermatophagoides farinae<br>Lepidoglyphus destructor          |
|-------------|---|
| Epithelia   | Cat, dog  |
| Cockroaches | Blatella orientalis<br>Blatella germanica   |
| Pollen      | Cypress, plane trees, olive,<br>grass mixtures, <i>Artemisia, Parietaria,</i><br><i>Salsola</i> |
| Fungi       | Altenaria, Cladosporium, Aspergillus,<br>Penicillium  |

\* Other allergens that are suspicious because of clinical history or geographical prevalence can be added (modified by Heinzerling) [62].

titration does not correlate with severity, it is more likely that symptoms will be persistent when specific IgE levels are raised for prolonged periods [66]. Although its predictive value is good, the determination of IgE to different allergens in the same assay is only justified when screening for allergic disease, given its cost-effectiveness profile [67]. tests

| Advantages of the Prick Test       | Advantages of the Specific<br>IgE Assay                   |
|------------------------------------|---|
| More sensitive                     | More specific   |
| Cheaper                            | Knowledge of the tecnique is not required                 |
| Immediate assessment               | Allergenic extracts are not required                      |
| Results are visible to the patient | No risk of systemic reactions                             |
| Safe and minimally invasive        | Does not interfere with taking medication                 |
| Extensive battery of allergens     | Can be performed in patients with eczema or dermographism |

Table 2.4. Comparison of in vivo (prick) and in vitro (specific IgE) diagnosis

The results of prick tests or the measurement of specific circulating IgE determine the sensitization to allergens, but they do not predict their clinical transcendence, just as in some asymptomatic patients positive results can be obtained. This is why, in the end, it is necessary to evaluate the clinical relevance of the sensitizations to allergens identified. Similarly, a specific bronchial challenge tests can be performed when there is a discrepancy between the clinical history and the sensitization results obtained, and in the case of occupational asthma [68].

## RECOMMENDATIONS

 In persistent asthma it is advisable to assess the potential role of aeroallergens by clinical evaluation and prick or IgE tests. It is important to base the diagnosis on the concordance between the clinical history and diagnostic tests.

### **R2**

## 2.4 Classification of Adult Asthma

## 2.4.1 Asthma Severity

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Asthma has generally been classified in accordance with its severity [69-71], although it is difficult to assess, especially when the patient is already receiving anti-inflammatory treatment. Its severity is an intrinsic aspect of the disease and it reflects the intensity of any physiopathological abnormalities [72]. It is important to remember that the severity of the disease includes both the intensity of the process and its response to treatment [73]. Traditionally, the disease has been divided into four categories: intermittent, mild persistent, moderate persistent and severe persistent asthma [71].

The classification of asthma in accordance with its severity is useful in the initial assessment of an asthma patient because D

## Table 2.5. Classification of asthma severity in adults

|   | Intermittent                   | Mild Persistent                                  | Moderate Persister          | nt Severe Persistent                                 |
|---|--------------------------------|--|-----------------------------|--|
| Daily symptoms  | No (2 days or less<br>a week)  | More than 2 days<br>a week                       | Daily symptoms              | Continuous symptoms a week)<br>(several times a day) |
| Relief medication<br>(short-acting $\beta_2$<br>adrenergic agonist) | No (2 days or less/<br>a week) | More than 2 days<br>a week, but not<br>every day | Every day                   | Several times a day                                  |
| Nocturnal symptoms  | No more than twice<br>a month  | More than twice<br>a month                       | Quite often                 | Often  |
| Limitations on activity   | None                           | Some limitation                                  | A fair degree of limitation | Considerable   |
| Pulmonary function (FEV <sub>1</sub> o P theoretical percentage     | EF) > 80%                      | > 80%  | > 60% - < 80%               | ≤ 60%  |
| Exacerbations   | None                           | One or none per year                             | Two or more a yea           | r Two or more a year                                 |

Abbreviations: FEV, forced expiratory volume in the first second; PEF, peak expiratory flow.

the choice of treatment, dosage and treatment regimen depend on the severity of the disease [69-71].

Severity is a feature of asthma that is not necessarily constant, but can vary over time (months or years), so it is necessary to reevaluate it regularly. Severity is easier to establish in a patient who is not receiving maintenance treatment or treatment to control asthma. Nevertheless, severity can also be determined in a patient whose asthma is controlled, depending on the therapeutic stage to which he has been assigned, in other words on the basis of the amount of medication which is required to keep the disease under control [74,75]. Asthma severity is determined by the most affected parameter. Table 2.5 shows the different levels of adult asthma.

#### 2.4.2 Control

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Asthma control is the extent to which the manifestations of asthma are absent or reduced by therapeutic interventions and to which treatment targets are met [74,75]. To a large extent, control reflects the suitability of asthma treatment [76] (Figure 2.2). However, there is another factor that differs from one patient to another that must be taken into account. This factor is the response to treatment or the ease and speed with which control is achieved [73]. Although the term "control" is broad in meaning and can include all clinical and physiopathological aspects of asthma, for practical purposes it includes the clinical features of the disease (symptoms and exacerbations) and lung function tests.

Depending on its level of control, asthma has been arbitrarily

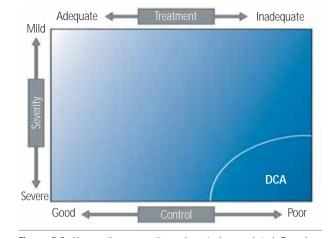


Figure 2.2. How asthma severity and control are related. To a large extent the level of control reflects the suitability of treatment. Some patients have severe asthma that is difficult to control (DCA). (Modified by Osborne) [76].

classified into: well controlled, partially controlled and poorly controlled asthma, in accordance with the criteria in Table 2.6 [2]. However, this classification has not been validated from a clinical point of view. Some asthma patients can achieve good control of symptoms and pulmonary function and at the same time experience frequent exacerbations, while other

|  | WELL controlled (all of the following)               | PARTIALLY controlled (any measure in any week)       | POORLY controlled                 |  |
|--|--|--|-----------------------------------|--|
| Daytime symptoms   | None or ≤ 2 days<br>a week                           | > 2 days a week                                      |                                   |  |
| Limitation on activities   | None   | Any activity   | If $\geq 3$ asthma                |  |
| Symptoms at night or on waking   | None   | Any  | features are partially controlled |  |
| Need for relief (rescue) medication (short-acting) ( $\beta_2$ adrenergic agonist) | None or<br>≤ 2 days a week                           | > 2 days per week                                    |                                   |  |
| Pulmonary function<br>– FEV <sub>1</sub><br>– PEF                                  | > 80% theoretical value<br>> 80% best personal value | < 80% theoretical value<br>< 80% best personal value |                                   |  |
| Validated symptom questionnaires   |  |  |                                   |  |
| -ACT   | ≥ 20   | 16-19  | ≤ 15                              |  |
| – ACQ  | ≤ 0.75   | ≥ 1.5  | not applicable                    |  |
| Exacerbations  | None   | ≥ 1/year   | $\geq 1$ in any week              |  |

Abbreviations: FEV<sub>1</sub>, forced expiratory volume in the first second; PEF, peak expiratory flow; ACT: asthma control test; ACQ: asthma control questionnaire.

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**D** patients have daily symptoms and very few exacerbations. When severity or control is assessed, these factors must be taken into account.

> Therefore, when we try to minimize the clinical expression of asthma, we need to bear in mind two key aspects [3]: on the one hand, the manifestations of the disease which are present on a day-to-day basis (current control) and, on the other, its future consequences (future risk), as indicated in Figure 2.3.

When we use the term "current control", control is defined as the ability to prevent the presence of symptoms during the day or at night and the frequent use of rescue medication to relieve these

persistent asthma (Table 2.7).

symptoms, the maintenance of lung function within or close to normal limits, the absence of limitations on daily life, including family, social, occupational or school activities and physical exercise and finally the satisfaction of the expectations of the patient and his family with regard to the care he receives.

With respect to the term "future risk", control includes the absence of severe exacerbations, the avoidance of visits to emergency departments and hospitalizations, the prevention of a progressive loss of lung function or, in the case of children, abnormal lung development and finally the prescription of optimal pharmacotherapy with minimal or no side effects.

The concepts of severity and control are used as follows in the treatment of asthma:

When the disease is first assessed, if the patient is not receiving

maintenance treatment its severity must be evaluated (see

previous classification) and used for guidance purposes in

choosing the pharmacological treatment and making other

therapeutic decisions. Once the patient is being treated, the

severity of the disease is determined in accordance with the

minimal medication requirements needed to maintain control

[75]. Thus, controlled patients in therapeutic stage 1 will have

intermittent asthma, in stage 2 mild persistent asthma, in stages

3 and 4 moderate persistent asthma and in stages 5 and 6 severe

- Evaluation of control in order to adjust treatment. Once

- Determination of severity before initiating treatment.

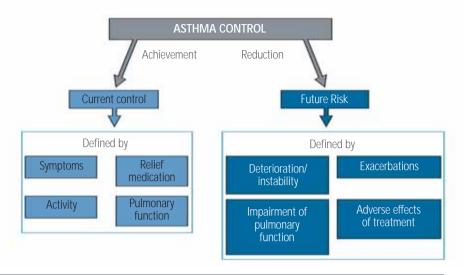


Figure 2.3. Terms that define and determine level of control

asthma treatment has begun, the clinical and therapeutic management of the disease must aim to achieve and maintain control. As such, the level of control will determine decisions about maintenance treatment and dose adjustment, in accordance with the therapeutic steps or stages shown in the corresponding section.

## 2.4.3 Methods for Measuring Control

According to our definition of control, a combination of tests need to be used for its evaluation [77]. The basic tool for assessing the control of the process is the ongoing medical follow-up visit. At these visits the presence of symptoms is evaluated, as well as the signs of disease activity, the presence of exacerbations and visits to ED departments, the influence of the disease on the patient's daily life and activity, the presence of possible side effects and, finally, and of crucial importance, therapeutic adherence, which includes reminding the patient about his self-care plan and the steps to be taken when there is decompensation, always trying to reinforce the relationship between medical personnel and the patient at each visit.

In order to facilitate and standardize the evaluation of control there are various questionnaires that are simple and

Table 2.7. Classification of Asthma Severity when it is Well Controlled by Treatment (Distributed into Stages).

| Sourceitu   | Intermittent | Persistent |                       |                    |
|---|--------------|------------|-----------------------|--------------------|
| Severity  | Internittent | Mild       | Moderate              | Severe             |
| Minimum treatment<br>requirements to<br>achieve control | Stage 1      | Stage 2    | Stage 3 or<br>stage 4 | Stage 5 or stage 6 |

easy for the patient to complete. The Asthma Control Test (ACT) [78,79] and the Asthma Control Questionnaire (ACQ) [80,81] have been validated and culturally adapted for use in Spain. The ACT has a more detailed validation so it can be used in daily clinical practice, given that it has well defined cut-off points. A score equivalent to or higher than 19 is very consistent with well controlled asthma, scores from 19 to 16 with asthma that is partially or not well controlled and scores lower than 15 with poorly controlled asthma [78,79].

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There are specific tools validated and adapted to provide Spanish versions for measuring the quality of life of adults [82] and children with asthma [83]. However, currently their use is considered more appropriate for research purposes than for clinical practice. Moreover, their application is usually quite time-consuming, despite the availability of abbreviated versions [84]. For both reasons their use is not recommended in daily clinical practice [3]. The second tool for controlling the disease is forced spirometry.  $FEV_1$  measurements are capable of adjusting what we have defined as current control more accurately [78,79] and also provides data for estimating the future risk of exacerbations [85]. It is a good way of quantifying the progressive and irreversible loss of pulmonary function.

The usefulness of so-called non-invasive markers of inflammatory activity for measuring asthma control continues to be a matter of debate and the subject of intense research, especially the determination of  $FE_{NO}$ . Recent studies, including a meta-analysis, have demonstrated that their measurement does not add any benefits to traditional monitoring defined by guidelines [86,87]. Nevertheless, these markers are useful in certain groups of patients. The cytological analysis of sputum samples may have a role to play in assessing the control of adult patients with severe asthma characterized by multiple exacerbations, thus significantly reducing the incidence of exacerbations [88].

## RECOMMENDATIONS

Asthma severity must be established at the onset, when the patient is not receiving treatment. If the patient is already being treated, severity must be determined in accordance with the minimum maintenance treatment requirements needed to achieve control.
 Control must be evaluated regularly and treatment must be adjusted to achieve and maintain control. Control has two basic components: current control and future risk.
 It is advisable to determine the level of asthma control by means of regular medical follow-up visits, which consist of taking well structured and extensive medical notes, a detailed physical examination and a forced spirometry test.
 The level of control can be assessed objectively by means of validated symptom questionnaires (ACT and ACQ) and, in individualized cases, by measuring inflammatory biomarkers.

## 2.5 Classification of Childhood Asthma

## 2.5.1 Asthma Severity

Traditional classifications based on adult asthma are difficult to apply to children, especially when they are very small. Childhood asthma is essentially episodic, sometimes involving serious attacks, but with few symptoms in the interludes between exacerbations. The level of severity depends on the symptoms (number of attacks and the situation between attacks: basically, tolerance of exercise and nocturnal symptoms), the need for a rescue bronchodilator and respiratory function test values. In young children, in whom it is not possible to perform a pulmonary function test, severity is classified exclusively in accordance with symptomatology.

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Two major patterns have been defined in children: episodic and persistent asthma. Episodic asthma may be occasional or frequent, depending on the number of attacks. Persistent childhood asthma cannot be treated as if it were a mild disease, but rather as at least moderate or severe [29] (Table 2.8).

Childhood asthma is a disease that is highly variable over time. It can even vary throughout the year, which makes classification difficult. Most young children only have asthma during viral infections and, consequently, they may have moderate or severe asthma in the winter and have no symptoms in the spring and summer.

Other patients, for example children who are allergic to pollen, will only have asthma in the spring (this occurs most often in regions with a continental climate). To classify a case correctly, it is necessary to specify asthma trigger factors in a particular patient and its level of control, as well as its severity.

The disease must be classified when the patient is not receiving any treatment. Once asthma is controlled, the

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|   | Occasional Episodic   | Frequent Episodic  | Moderate persistent          | Severe persistent      |
|---|---|--|------------------------------|------------------------|
| Episodes  | <ul> <li>Lasting a few<br/>hours or days;</li> <li>one every<br/>10-12/weeks</li> <li>Maximum 4-5 attacks/year</li> </ul> | <ul> <li>- &lt; one every</li> <li>5-6 weeks</li> <li>- Maximum 6-8<br/>crises/year</li> </ul> | > one every<br>4-5 weeks     | Frequent               |
| Inter-crisis symptoms   | No symptoms with good tolerance of exercise   | No symptoms  | Mild                         | Frequent               |
| Wheezing  | -   | With intense<br>effort   | With moderate effort         | With minimum<br>effort |
| Nocturnal symptoms  | -   | _  | ≤ 2 nights a<br>week         | > 2 nights a<br>week   |
| Relief medication (short-acting $\beta_2$ adrenergic agonist) | -   | -  | ≤ 3 days a<br>week           | > 3 days a<br>week     |
| Pulmonary Function<br>– FEV <sub>1</sub><br>– PEF Variability | > 80%<br>< 20%  | < 80%<br>< 20%   | > 70% - < 80%<br>> 20% - 30% | < 70%<br>> 30%         |

#### Table 2.8. Classification of the severity of asthma in children

Abbreviations: FEV,: forced expiratory volume in the first second; PEF: peak expiratory flow.

#### Table 2.9. Childhood Asthma Control Questionnaire (CAN) [89]

1. During the last four weeks, how often have you coughed during the day without having a cold?

- 4. More than once a day
- 3. Once a day
- 2. 3 to 6 times a week
- 1. Once or twice a week
- 0. Not at all

2. During the last four weeks, how often have you coughed at night without having a cold?

- 4. More than once a night
- 3. Once a night
- 2. 3 to 6 times a week
- 1. Once or twice a week
- 0. Not at all

3. During the last four weeks, how often have you had whistling sounds in your chest or wheezing symptoms during the daytime?

- 4. More than once a night
- 3. Once a night
- 2. 3 to 6 times a week
- 1. Once or twice a week
- 0. Not at all

4. During the last four weeks, how often have you had whistling sounds in your chest or wheezing symptoms at night?

- 4. More than once a night
- 3. Once a night
- 2. 3 to 6 times a week
- 1. Once or twice a week
- 0. Not at all

5. During the last four weeks, how often has it been difficult for you to breathe during the daytime?

- 4. More than once a day
  - 3. Once a day
  - 2. 3 to 6 times a week
  - 1. Once or twice a week
- 0. Not at all

6. During the last four weeks, how often has it been difficult for you to breathe at night?

- 4. More than once a night
- 3. Once a night
- 2. 3 to 6 times a week
- 1. Once or twice a week
- 0. Not at all

7. When the child does exercise (plays, runs, etc.) or laughs a lot, does he/she have a cough or whistling sounds in his/her chest/wheezing symptoms?

- 4. Always
- 3. Nearly always
- 2. Sometimes
- 1. Very seldom
- 0. Never

8. During the last four weeks, how many times has he/she had to go to the ED department because of his/her asthma?

- 4. More than 3 times
- 3. Three times
- 2. Twice
- 1. Once
- 0. Not at all

9. During the last four weeks, how many times has the child been admitted to hospital because of his/her asthma?

- 4. More than 3 times
- 3. Three times
- 2. Twice
- 1. Once
- 0. Not at all

medication required to ensure a child is symptom-free will be a better indication than his/her symptoms of how severe the condition is.

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## 2.5.2 Control

There are various questionnaires that estimate the extent to which asthma is controlled in children, but the only one that has been validated in Spanish is the CAN (Childhood Asthma Control) questionnaire (Table 2.9). There is a version for children from 9 to 14 years of age and another for parents (children from 2 to 8 years), which evaluates nine questions about clinical symptoms in the preceding four weeks and scores the results from 0 (good control) to 36 (poor control). A patient's asthma is regarded as poorly controlled when his score is 8 or higher [89]. In addition to clinical control, which is evaluated by means of the CAN questionnaire, it is important to assess lung function by spirometry and probably to control inflammation by measuring  $FE_{NO}$ .

| RECOMMENDATIONS   |           |
|---|-----------|
| - Childhood asthma should be classified when the child is receiving no treatment  | <b>R2</b> |
| - With the aim of classifying asthma correctly, as well as its severity, in children it is important to identify its<br>trigger factors and to establish the level of control | <b>R2</b> |