



Diagnosis and treatment

Allergic asthma[☆]

Asma alérgica

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Introduction

Asthma is one of the most important allergic diseases in our country due to its high prevalence, chronic nature, its influence in patients' quality of life and its economic repercussions. In the Alergológica 2005 study, asthma occupies the second place in frequency for consultation in the Allergy services, after allergic rhinitis, and in up to 80% of the cases, the allergic asthma diagnosis was confirmed.¹

At the moment, one of the most accepted definitions of asthma is the concept of chronic inflammatory disease of the respiratory tract, whose pathogenesis involves various types of cells and inflammation mediators. It is a process partly determined by genetic factors and is characterised by bronchial hyperresponsiveness (BHR) and varying degrees of airflow obstruction, which is total or partially reversible, either as a result of pharmacological action, or spontaneous event.²

Importance of asthma and a good control

Asthma is a global health problem that affects 300 million people worldwide. In Spain, asthma prevalence in the paediatric population oscillates around 10%, whereas in adult population it is around 5%, and the last data indicate that the asthma prevalence increases in both children and adults. At present, it is known that asthma is, after the chronic obstructive pulmonary disease, the cause of greater number of absenteeism from work due to respiratory

diseases. The World Health Organisation estimates 15 million years of life are lost annually adjusted for impairment due to the asthma.³

According to the AsmaCost study of 2007, the economic cost of the asthmatic adult patient in Spain ascends to 1726 and 1533€ from the perspective of the society and the National Health System, respectively. The cost is higher in severe asthmatics (2635€) and in patients older than 65 years of age (2069€).⁴ In children, the average annual cost in Spain in 2008 was of 1490€, and of 5380€ in the severe asthma cases.⁵ In addition, it is known that around 70% of the total cost of the disease is determined by the poor control of the disease. The cost of hospitalisation, emergency department visits or death are major causes of the consumption of economic resources due to asthma.^{6,7}

According to the Asthma Control in Spain study, more than two thirds of the studied patients had a poorly controlled asthma.⁸ A recent study, conducted in our country in 1363 patients with asthma, shows that only 12% of the patients are well controlled based on the criteria of the *Global Initiative for Asthma* (GINA), although 60% of the patients consider their asthma is well controlled, and 50% of the doctors assume asthma can be controlled.^{9,10}

Asthma diagnosed as a syndrome

The diagnostic process is based on the definition of the disease, which includes, on the one hand, the symptoms and the variable obstruction of the airflow, and on the other hand, the underlying inflammation and the BHR.

The medical history of the patient and the symptoms are essential to establish the diagnosis. The relevant data we must gather in the medical history are summarised in [Table 1](#).¹¹ In the allergic patient, it is important to assess extra-pulmonary manifestations of atopy such as atopic eczema, allergy to foods or the nasal inflammation in the allergic rhinitis that frequently accompanies the asthma.

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Table 1
Relevant clinical aspects for the diagnosis and follow-up of the bronchial asthma.

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| <p>Symptoms and signs that should lead to a suspicion of possible asthma</p> <p>Expiratory wheezes, especially in the children (although an examination of normal thorax does not exclude asthma)</p> <p>History of any of the following symptoms: recurrent nocturnal coughing, recurrent wheezing, recurrent dyspnoea, recurrent tightness of the chest</p> <p>The symptoms appear or get worse at night, waking up the patient</p> <p>The symptoms appear or get worse following a seasonal pattern</p> <p>The patient also has eczema or a family history of asthma or atopic diseases</p> <p>Symptoms appear or get worse in the presence of:</p> <ul style="list-style-type: none"> Animals with hair Chemical agents Changes of temperature House dust mite Medications (acetylsalicylic acid, beta-blockers) Exercise Pollen Respiratory infections (viral) Smoke of the tobacco Emotional stress <p>Symptoms respond to anti-asthma treatment</p> <p>The patient with flu feels “his chest falls” or takes more than 10 days to recover</p> <p>Essential data on medical history</p> <p>Characteristic clinical symptoms of the disease (dyspnoea, coughing, wheezing, tightness of the chest)</p> <p>Other symptoms to exclude other diseases or comorbidities (posterior rhinorrhoea, heartburn, reduction of the urine output or emotional situation)</p> <p>Family history</p> <p>Smoking</p> <p>Exposure to allergens at home, school or work</p> <p>Medication used for the asthma (always asking about the technique, the tolerance and the compliance)</p> <p>Risk factors of asthma exacerbations</p> <p><i>Potentially modifiable</i></p> <ul style="list-style-type: none"> Exposure to tobacco smoke Exposure to aeroallergens Exposure to occupational allergens Obesity Gastroesophageal reflux Sinusitis Acetylsalicylic acid and other drugs Psychological factors <p><i>Non-modifiable</i></p> <ul style="list-style-type: none"> Viral infections Race/ethnic group Pre-menstrual asthma Genetic factors |
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It is also relevant to look into possible intolerance to acetylsalicylic acid or to non-steroidal anti-inflammatory drugs (NSAIDs).

To confirm the bronchial obstruction, its reversibility and/or the BHR, there should be conducted a lung basal function test, bronchodilator test, monitoring of the peak expiratory flow (PEF) and/or bronchoconstriction tests. The obstruction is defined as the ratio between the *forced expiratory volume* (FEV)₁ in one second and the *forced vital capacity* (FVC), (FEV₁/FVC) in the basal forced spirometry below the inferior limit of the reference values, which is arbitrarily established in 0.7. The reversibility of this obstruction is observed through the bronchodilator test, generally, with inhaled salbutamol and repeating the spirometry 15 min later. The Spanish Guideline on the Management of Asthma (Guía Española para el Manejo del Asma, GEMA)² considers the test is positive if FEV₁ or FVC increases by 12% and to more than 200 ml compared to the previous (Fig. 1). In children, the bronchodilator test is positive when FEV₁ increase on the baseline value is greater or equal to 12%. The BHR to different stimuli is quantified by means of the exposure to bronchoconstrictor agents, classified according to their mechanism of action (Table 2).

The variability of the pulmonary function can be determined by means of portable devices to measure the PEF. The index of

Table 2
Bronchoconstrictor agents used in bronchial hyperresponsiveness tests.

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| <p><i>Direct bronchoconstrictors</i></p> <ul style="list-style-type: none"> Cholinergic agonist: methacholine^a, carbachol, acetylcholine Histamine^a Prostaglandin D₂ Cysteinyl leukotriene (LTC 4, LTD₄, LTE₄) <p><i>Indirect bronchoconstrictors</i></p> <ul style="list-style-type: none"> Osmotic stimuli: physical exercise^a, mannitol^a, hyperventilation with cold air, non-isotonic aerosols (distilled water, saline hypotonic, saline hypertonic) Pharmacological stimuli: adenosine (AMP)^a, taquines, bradykinin, metabisulphite, propranolol, acetaldehyde Endotoxins Platelet-activating factor Ozone Others: allergens, non-steroidal anti-inflammatory drugs |
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^a Bronchoconstrictor agents more frequently used in provocation tests.

variability of PEF equal or higher than 20% is a criterion to asthma diagnosis.^{2,11,12}

Unfortunately, all these lung function tests are not applicable to infants or to pre-school children with asthma. This is why GEMA and the *American Thoracic Society/European Respiratory Society*^{2,12} recommend alternative tests such as the forced impulse oscillometry (IOS), the measurement of occlusion resistances, flow volume/tidal volume curve analysis or the measurement of resistances by plethysmography. Fig. 2 shows the recommended diagnostic procedures to control severe asthma.

Diagnosis of allergic sensitisation

The allergy test has to be conducted in all patients diagnosed with asthma, due to the high prevalence of sensitisation to inhaled allergens and the comorbidity with other allergic manifestations. It is known that sensitisation to aeroallergens mediated by IgE antibodies constitutes a very significant risk factor to develop asthma.^{13,14} It has been confirmed that exposure to high concentrations of allergens increases the severity of the asthma, and that there exists a synergy between the allergic sensitisation and viral infections.¹⁵

The skin test (*prick-tests*) is the diagnostic method of choice to detect sensitisation to allergens mediated by IgE, due to its high sensitivity and specificity. It is a safe, simple, fast and painless method. Generally, it is conducted with a series of allergens that are present in the geographic area where the patient lives. However, it is recommended to use a standard allergen battery to test all the European patients diagnosed with asthma (Table 3).¹⁶ A positive skin test will only indicate sensitisation, which will be assessed according to the relation between allergen exposure and the symptoms of patient. The aeroallergens most frequently associated with allergic asthma in Spain are pollen (44%), the house dust mites (41%), the animal epithelia (20%) and fungi (8%) (Table 3).¹

The determination of IgE specific to whole allergen extracts or the IgE to individual recombinant or purified natural allergen molecules leads to a more accurate diagnosis of sensitisation. They are more specific than skin tests and will be useful in cases of dermatographic urticaria, extensive dermatitis and if the patient receives pharmacological treatments that inhibit the skin tests, besides confirming them.^{17,18} Moreover, it is important to distinguish, in patients that present sensitisation to multiple allergens, those patients who are genuinely sensitised to several allergenic sources from crossed-sensitised patients, since it will be relevant to establish strategies of avoidance and/or allergen immunotherapy.¹⁹

In order to establish a relationship between the allergic sensitisation and the symptoms of the patient and, therefore, to establish

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