

CONTINUING MEDICAL EDUCATION

Bronchial Asthma: Diagnosis and Long-Term Treatment in Adults

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SUMMARY

Introduction: Bronchial asthma is a serious global health problem. 5% to 10% of persons of all ages suffer from this chronic airway disorder. This review article presents important considerations of diagnosis and treatment in view of the current national and international asthma guidelines.

Methods: Selective literature review, with attention to the current national and international guidelines.

Results/Discussion: Bronchial asthma is a chronic inflammatory disease of the airways characterized by bronchial hyperreactivity and a variable degree of airway obstruction. It is diagnosed on the basis of the clinical history, physical examination, and pulmonary function tests, including reversibility testing and measurement of bronchial reactivity. The goal of treatment is to control the symptoms of the disease effectively and in lasting fashion. Long-term treatment with inhaled corticosteroids is the basis of asthma treatment, alongside preventive measures and patient education. Bronchodilators such as beta2 sympathomimetics are used for rapid symptomatic relief of acute attacks.

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Key words: bronchial asthma, bronchial hyperreactivity, lung function, pharmacotherapy, inhaled corticosteroids

Recurrent episodes of acute shortness of breath, typically occurring at night or in the early morning hours, are the cardinal manifestation of bronchial asthma. Further symptoms include cough, wheezing, and a feeling of tightness in the chest. Asthmatic symptoms can often arise after physical exercise.

The following discussion of bronchial asthma is largely based on the German national care guidelines for asthma, on the international recommendations for asthma management of the Global Initiative for Asthma (GINA, www.ginasthma.com), and on the recommendations of the German Airway League (Deutsche Atemwegsliga) (1–3).

The learning objectives of this article are:

- to become acquainted with the various conditions that enter into the differential diagnosis of bronchial asthma, and
- to be able to apply the new types of treatment recommended for adult patients by the current national and international guidelines.

Depending on the severity of bronchial asthma in the individual patient, there may be phases of partial or total freedom from symptoms, alternating with periods of variably severe illness. This fact has been integrated into the definition of bronchial asthma, which is now defined as a chronic inflammatory disease of the airways characterized by bronchial hyperreactivity and a variable degree of airway obstruction (1–3).

Airway obstruction in bronchial asthma is mainly caused by the following four mechanisms (2):

- Contraction of bronchial smooth muscle
- Edema of the airway walls
- Mucous plugging of the bronchioles
- Irreversible changes in the lungs ("remodeling").

Bronchial asthma afflicts about 10% of children and 5% of adults. An atopic diathesis, i.e., a genetic

Manifestations of asthma

The cardinal manifestation of asthma consists of recurrent episodes of shortness of breath of acute onset, typically at night or in the early morning hours.

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BOX 1

Basic diagnostic evaluation of bronchial asthma*1

History

- Sudden onset of symptoms, often at night or in the early morning hours, typically shortness of breath and cough (productive or unproductive), particularly
 - after allergen exposure
 - during (or, more commonly, after) physical exertion or sports (so-called exercise-induced asthma)
 - in the setting of upper respiratory infection
 - on exposure to thermal stimuli, e.g., cold air
 - on exposure to smoke or dust
- Seasonal variation of symptoms (seasonal elevation of pollen count)
- Positive family history (allergy, asthma)
- Precipitants of asthmatic symptoms in the patient's environment at home, at work, and during leisure activities

Symptoms

Intermittent and variable (may also be absent, e.g., during symptom-free intervals or in mild disease)

- Shortness of breath (often in acute episodes)
- Expiratory wheezes
- Chest pressure sensation
- Cough

Findings on physical examination

- Rales, rhonchi, wheezes
- Prolonged expiratory phase
- Tachypnea
- Orthopnea
- Chest constriction

*1 modified from (1), (3).

predisposition toward the production of IgE antibodies in response to (for example) pollen, house dust mites, fungi, or animal-derived proteins, is the most important risk factor for bronchial asthma. In childhood, bronchial asthma is usually due to allergies; on the other hand, in 30% to 50% of adults with asthma, no allergy can be identified, at least not with the standard techniques. Non-allergic asthma in adults can arise, for example, after a viral infection of the lower respiratory tract. Viral infections can, in turn, promote the development of an allergic sensitization. Intrinsic

asthma may reflect the simultaneous presence of sinusitis, nasal polyposis, and an intolerance to acetylsalicylic acid (ASA) or related non-steroidal anti-inflammatory drugs (NSAIDs); this is the so-called Samter's syndrome.

Acute worsening of asthma (an asthma attack or exacerbation) can arise at any time without any prodromal symptoms and independently of the previous severity of the disease. Bronchial obstruction during an acute attack can progress, either slowly or rapidly, to life-threatening severity. The mortality due to asthma in Germany has declined by about one-third in the last decade, yet it nonetheless remains relatively high compared to that in other countries (2141 deaths due to asthma in 2004 according to the German Federal Statistical Office [Statistisches Bundesamt], 2005). The reduction in asthma-related mortality is generally attributed to the introduction of maintenance therapy with inhaled corticosteroids (ICS) (4). Around the world, however, there is little correlation between the lethality of asthma and its prevalence. The World Health Organization (WHO) estimates the number of DALYs ("disability-adjusted life years") lost to asthma at 15 million per year, which corresponds to 1% of the global loss of DALYs due to illness.

Diagnostic assessment

Airway obstruction is measured objectively with pulmonary function tests. The most important such test is spirometry, which measures the forced expiratory volume in one second (FEV₁), the forced vital capacity (FVC), and the Tiffeneau parameters (FEV₁/VC). Normal pulmonary function values do not rule out disease if they have been obtained during a symptom-free interval. Further aspects of the basic diagnostic assessment of bronchial asthma, including history-taking, symptoms, and physical findings, are summarized in *box 1* (1–3).

The practical value of peak expiratory flow (PEF) measurement lies in the determination of circadian variability, which is a suitable parameter for self-monitoring of asthma in outpatient follow-up. "Min % Max" is the minimal value of PEF expressed as a percentage of the maximal value, i.e., the lowest value in the morning prior to the administration of a bronchodilator drug as a percentage of the current best value. A circadian variability greater than 20% is typical of inadequately treated asthma (2, 5).

Standards and individualized norms exist for both PEF measurement and spirometry (2, 3).

Allergy and asthma

About 10% of children suffer from asthma. Childhood asthma is usually due to allergy. In 30% to 50% of asthmatic adults, no allergy is found as the cause of asthma.

History and physical examination

Acute attacks of shortness of breath and cough occurring early in the morning are typical of asthma. Auscultation of the chest reveals rales, rhonchi, and wheezes.

Whole-body plethysmographic pulmonary function analysis provides further information, e.g., for the demonstration of obstruction (airway resistance, Raw) or overdistention (intrathoracic gas volume, ITGV). Objective criteria for the confirmation of the diagnosis of bronchial asthma are given in *box 2*. An algorithm for the diagnostic assessment of asthma is shown in *figure 1*.

Further diagnostic studies include, for example, bronchial provocation testing for the determination of bronchial reactivity; this kind of test is highly sensitive, but not very specific (6). Stepwise allergological testing includes skin-prick testing, the measurement of specific IgE in serum, and an allergen-specific nasal or bronchial provocation test. The use of non-invasive markers of airway inflammation, such as the nitrous oxide (NO) concentration in exhaled air or sputum eosinophilia, has not been prospectively validated for the establishment of the diagnosis of bronchial asthma, but can be helpful in therapeutic follow-up (7, 8). The indications for arterial blood gas analysis, determination of diffusion capacity, and radiological examination of the thoracic organs are determined individually, particularly for the purposes of differential diagnosis.

Differential diagnosis

The following entities should be considered in the differential diagnosis of bronchial asthma because of their frequency and clinical significance (1, 3):

- Chronic obstructive pulmonary disease (COPD)
- Hyperventilation
- Aspiration
- Laryngeal changes/vocal cord dysfunction
- Pneumothorax
- Cystic fibrosis (CF)
- Cardiac diseases, e.g., left heart failure
- Pulmonary embolism
- Gastroesophageal reflux disorder.

In as many as 10% to 20% of cases, a clear-cut distinction between asthma and COPD cannot be drawn.

The definition of controlled asthma

A four-part, multilevel treatment plan was previously recommended for the long-term treatment of bronchial asthma, based on a classification of disease severity by the clinical findings and the results of pulmonary function testing (1, 3). In the current "Global Strategy for Asthma Management and Prevention" issued by the

Diagnostic evaluation

Obstruction of the respiratory tract is objectively demonstrated with pulmonary function testing. Spirometry is the most important testing technique.

BOX 2

Criteria for the diagnosis of asthma*¹

- Demonstration of obstruction ($FEV_1/VC < 70\%$) and FEV_1 increase by $>15\%$ (at least 200 mL) with respect to the initial value, and possibly also decrease of the specific airway resistance by at least $1 \text{ kPa} \times \text{sec}$, measured at least 15 min after the inhalation of four puffs of a short-acting beta2 sympathomimetic agent, e.g., 400 µg of salbutamol
- Or: FEV_1 worsening by $>15\%$ during, or within 30 minutes after, physical exercise (exertional asthma), possibly with an increase of the specific airway resistance by at least 150%
- Or: FEV_1 improvement by $>15\%$ (or by at least 200 mL, if the initial value is below 1300 mL), and possibly also decrease of the specific airway resistance by at least $1 \text{ kPa} \times \text{sec}$, after daily high-dose administration of an inhaled corticosteroid (ICS) for a maximum of four weeks
- Or: in patients with normal pulmonary function despite a typical history for asthma, demonstration of non-specific bronchial hyperreactivity by means of a standardized, multilevel inhalational provocative test and of a more than 20% circadian variation in PEF with measurements taken over 3 to 14 days

*¹ modified from (1), (3).

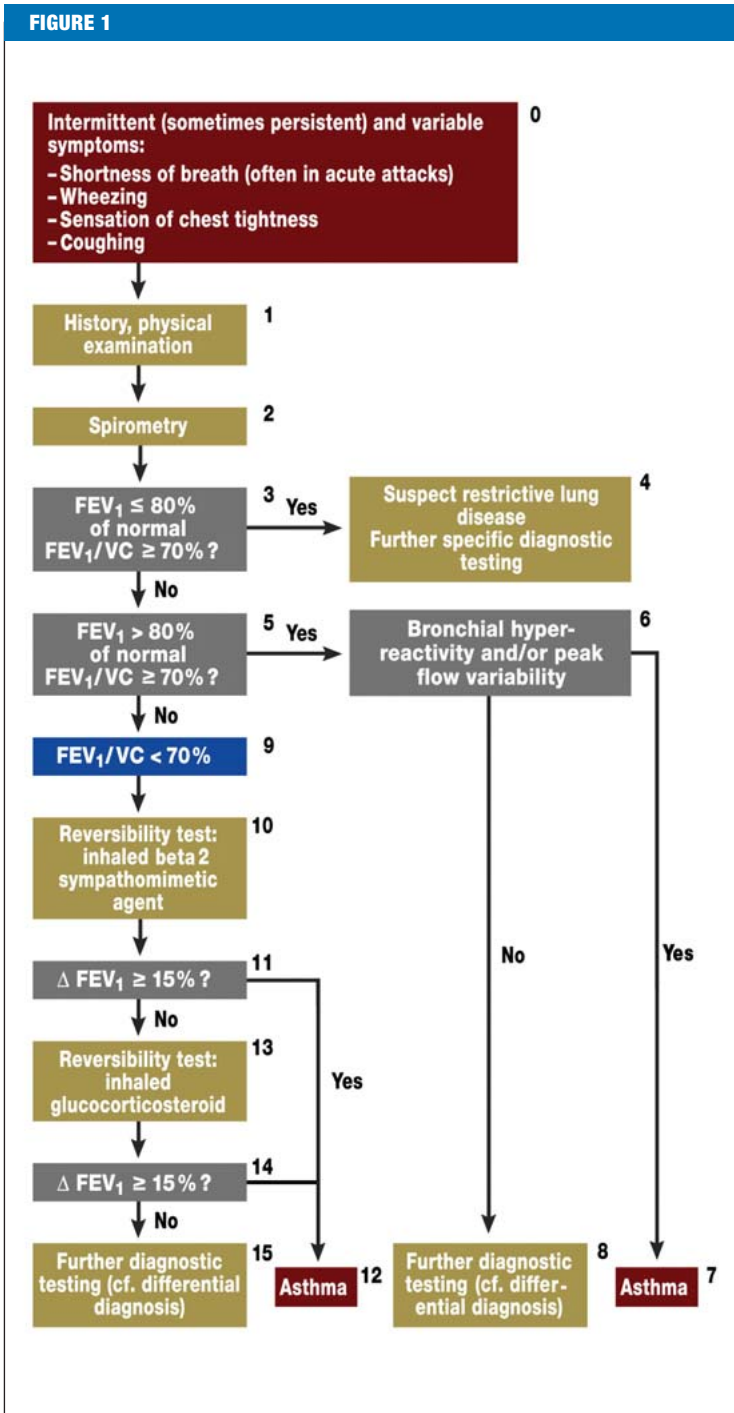
Global Initiative for Asthma (GINA), however, the classification system is based on the degree of clinical control that has been achieved, ranging from "controlled" to "partly controlled" to "uncontrolled" (*table 1*) (2). This new classification is meant to emphasize the point that the severity of asthma depends not just on the severity of the underlying illness itself, but also on its response to treatment. Furthermore, the severity of asthma can fluctuate considerably over a period of months to years.

GINA's Global Strategy defines clinically controlled asthma as follows (2):

- No daytime symptoms at all, or at most two times per week
- No limitation of the activities of everyday living, including physical exercise
- No symptoms at night, or no awakening because of asthma
- No need for rapidly-acting bronchodilators for symptomatic treatment ("relievers"), or at most two times per week
- Normal or nearly normal pulmonary function
- No exacerbations.

Classification

The GINA classification takes account not only of the severity of the underlying illness, but also of its response to treatment.



Algorithm for the diagnosis of bronchial asthma. The numbers attached to each panel indicate the hierarchical level (modified from 1,3)

The treatment of bronchial asthma

The definitive endpoint of asthma management is the achievement of the best possible quality of life. This includes, for example (1, 3) (evidence level D):

- No limitation of physical, emotional, or intellectual development in childhood and adolescence
- No symptoms and no asthma attacks
- Normal, or the best possible, physical and social activities in everyday life
- The best possible pulmonary function.

Non-pharmacological treatments are listed in Text box 3 (1, 3).

The goals of pharmacotherapy are the suppression of the inflammation of asthma and the reduction of bronchial hyperreactivity and airway obstruction. The medications used for these purposes belong to two groups:

- Relievers (medications taken for symptomatic relief as necessary) include mainly the inhaled, rapidly-acting beta2 sympathomimetic agents, e.g. the short-acting drugs salbutamol, fenoterol, and terbutaline and the long-acting drug formoterol. Inhaled anticholinergic drugs and rapidly-acting theophylline (solution or drops) play a secondary role as relievers.
- Controllers (medications used for preventive, maintenance therapy) include the inhaled corticosteroids (ICS), inhaled long-acting beta2 agonists (LABA) such as formoterol or salmeterol, montelukast, and delayed-release theophylline preparations.

Formoterol can be used as a reliever because of its rapid onset of action or as a controller in combination with corticosteroids.

The undesired adverse effects that these medications can produce are listed in the *e-box*.

The anti-asthmatic drugs have been re-evaluated in the new GINA recommendations (2), as follows:

- Inhaled long-acting beta2 sympathomimetic agents (LABA), such as formoterol and salmeterol, should not be used for asthma monotherapy, but must always be given in combination with adequate doses of ICS. The reason for this is the possible association of LABA use with asthma-related death (9, 10).
- Leukotriene antagonists (in Germany, montelukast) are now more highly valued than before as asthma controllers, especially for patients who cannot or do not want to inhale corticosteroids, who experience intolerable ICS side effects such as persistent hoarseness, or who simultaneously suffer from allergic rhinitis.

The goal of treatment
is the best possible quality of life for the patient.

Pharmacotherapy
is given to suppress asthma-related inflammation and to lesson bronchial hyperreactivity and airway obstruction.

TABLE 1

Levels of control of bronchial asthma*1

Characteristic	Controlled (all of the following)	Partly controlled (any measure present in any week)	Uncontrolled
Daytime symptoms	None (twice or less/week)	More than twice/week	Three or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms/awakening	None	Any	
Need for reliever/rescue treatment	None (twice or less/week)	More than twice/week	
Lung function (PEF or FEV ₁)	Normal	<80% predicted or personal best (if known)	
Exacerbations**2	None	One or more/year	One in any week

*1 modified from (2); **2 any exacerbation in one week fulfills the definition of uncontrolled asthma

- Cromones, such as cromoglicic acid (DNCG) or nedocromil, are not a valid alternative to monotherapy with ICS for adult asthmatics.

The current GINA recommendations propose five steps of treatment (figure 2) (2). Often, the treatment of a previously untreated asthmatic is begun at step 2. For patients with "uncontrolled" asthma, as defined by the GINA classification, it is recommended that treatment should be begun at step 3.

At every step of treatment, a reliever (rapidly-acting bronchodilator) is used if necessary, e.g., a short-acting beta2 sympathomimetic agent or formoterol. The need to use a reliever is a sensitive indicator of the quality of asthma control; the reduction or elimination of this need is a good indicator of successful treatment (2). The symptomatic use of a rapidly acting bronchodilator characterizes step 1 (evidence level A).

In step 2, the preferred type of controller medication consists of inhaled corticosteroids (ICS) in a low dose (e.g., fluticasone, 100 to 250 µg/day, or budesonide, 200 to 400 µg/day [table 2]) (evidence level A). Alternatively, montelukast can be used as a controller (evidence level A).

In step 3, a combination of an inhaled corticosteroid (ICS) at a low dose and a LABA is the recommended treatment option, either as a fixed combination or as

separate components (evidence level A). No advantage of fixed ICS/LABA combinations over a free combination of these two types of medication has yet been demonstrated.

Further options in step 3 – albeit with lesser clinical effectiveness – include intermediate- to high-dose ICS monotherapy (evidence level A) and a combination of low-dose ICS with montelukast (evidence level A).

In step 4, high-dose ICS is generally used in combination with LABA and montelukast, and possibly also with theophylline (evidence level B). In step 5, anti-IgE treatment is an option if the patient suffers from allergic asthma with multiple, severe exacerbations despite daily treatment with high-dose ICS and a LABA (evidence level B) (11). Patients with persistent, severe asthma may additionally need to take oral glucocorticosteroids either intermittently or as a maintenance medication, preferably as a single dose in the morning to minimize systemic side effects (evidence level D) (1–3).

It should be pointed out, as a critical observation, that neither the national nor the international treatment guidelines provide any information about the absolute risk reduction or NNT (number needed to treat) associated with the treatment modalities that they recommend (1–3).

Steps of treatment according to GINA

The treatment of previously untreated asthma is often begun at step 2. If the patient's symptoms meet the criteria for "uncontrolled asthma," it is recommended that treatment should be begun at step 3.

Relievers (symptomatic medication)

The reduction or elimination of the need for relief medication is an important indicator of the successful treatment of asthma.

BOX 3

Non-pharmacological treatment*1

- Removal of allergens (especially pets with feathers or fur) (evidence level A)
- Structured patient education: improved self-management leading to better symptomatic control, reduction of the number of asthma attacks and emergency situations, improved quality of life, and improvement in various other parameters of disease course including days taken off from school or work and days spent in hospital (evidence level A)
- Physical training (reduction of asthma symptoms, improved exercise tolerance, improved quality of life, reduced morbidity) (evidence level C)
- Respiratory therapy and physiotherapy (e.g., breathing techniques, pursed-lip breathing) (evidence level C)
- Smoking cessation (with medical and non-medical aids, if necessary) (evidence level B)
- Psychosocial treatment approaches (family therapy) (evidence level C)
- For obese patients, weight loss (evidence level B)

*1 modified from (1).

New therapeutic concepts

As fixed combinations of ICS with LABA have become available over the last few years, new concepts for the treatment of asthma have been developed and clinically tested, with the goal of better control of bronchial asthma. These concepts take the varying pharmacological properties of the LABA into account (e.g., the rapid onset of activity of formoterol and the delayed onset of activity of salmeterol [12]).

The so-called GOAL concept ("gaining optimal asthma control") involves treatment with relatively high doses of fluticasone and salmeterol (e.g., twice-daily inhalation of 500 µg of fluticasone and 50 µg of salmeterol) in an attempt to achieve the best possible control (evidence level A) (13). If the patient becomes entirely asymptomatic, the treatment can be de-escalated in steps.

The SMART concept ("symbiocort maintenance and reliever therapy"), on the other hand, involves the use of a fixed combination of budesonide and formoterol not just as a low-dosed maintenance therapy but also for the treatment of acute symptoms (asthma treatment with an inhaler) (evidence level A) (14, 15). This therapeutic modality can be helpful, for example, to patients whose asthma is poorly controlled with inhaled corticosteroids and acute bronchodilators.

Non-pharmacological treatment

The removal of allergens, especially of pets with feathers or fur, is an important element of non-pharmacological treatment (evidence level A).

Moreover, for patients with mild, persistent bronchial asthma, the use of a fixed combination of an inhaled corticosteroid and a short-acting beta2 sympathomimetic agent for symptomatic relief has been shown to be just as effective as maintenance therapy with an inhaled corticosteroid (evidence level B) (16).

These studies, taken together, imply a future shift in asthma therapy away from the treatment of acute symptoms with a bronchodilator alone and toward their treatment with a combination of an anti-inflammatory drug (i.e., an ICS) and a bronchodilator. This, in turn, implies a reduction in the need for maintenance therapy with controllers and an intensification of acute interventions. The long-term effects of this strategy, e.g., with respect to remodeling changes in the lungs, are as yet unknown.

Inadequate treatment benefit

If the initial treatment fails to achieve adequate control of the patient's bronchial asthma after it has been given for a certain period of time, e.g., one month, various further aspects should be considered:

- Checking the patient's adherence to treatment (drug-taking compliance)
- Checking the patient's inhalation technique through direct observation by the physician
- Re-evaluating the diagnosis: other differential diagnoses that may have to be considered include, for example, chronic obstructive pulmonary disease (COPD), airway narrowing by a tumor, vasculitis, and pulmonary embolism
- Persistent exposure to toxic substances and allergens
- Aggravating factors such as gastroesophageal reflux and chronic sinusitis.

Various treatment measures whose effectiveness has been demonstrated inadequately, or not at all, are listed in box 4.

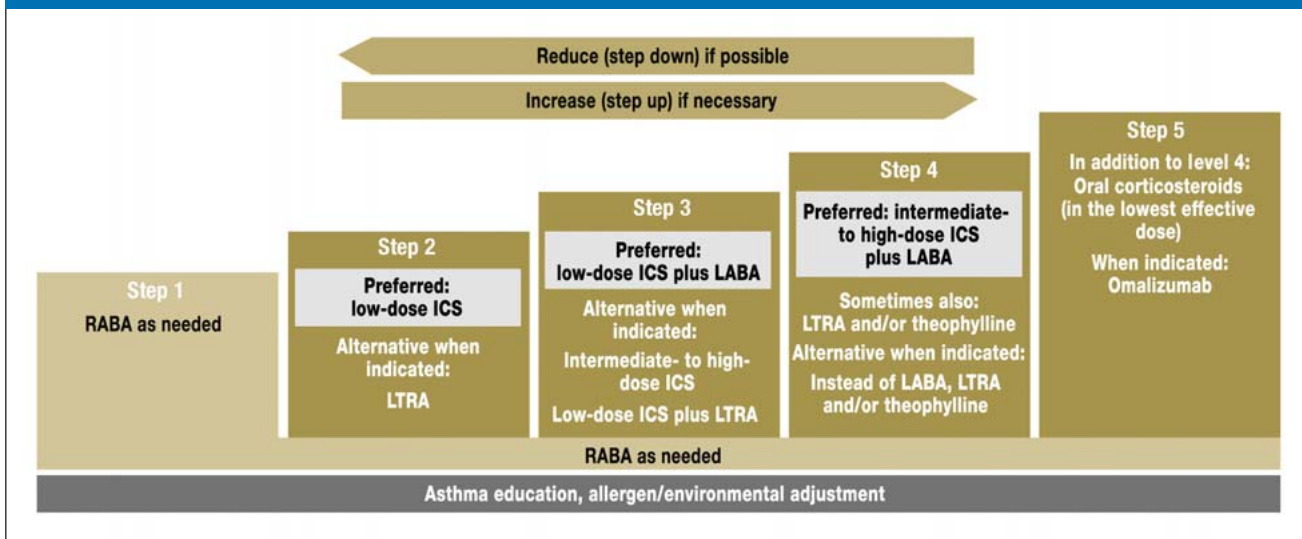
Allergen-specific subcutaneous immunotherapy

Allergen-specific subcutaneous immunotherapy (SCIT), also called "desensitization," has been shown to reduce medication use and bronchial hyperreactivity, as compared with placebo, in mild to moderately severe asthma, although it does not improve pulmonary function values (evidence level A) (3, 17). This statement applies mainly to younger patients. SCIT has a markedly lower chance of success in older patients who have had asthma

New treatment concepts

Fixed combinations of ICS and LABA have been developed in recent years with the goal of improved treatment of asthma and have been tested in clinical trials.

FIGURE 2



The long-term pharmacotherapy of asthma in adults. ICS, inhaled corticosteroid; LABA, long-acting beta2 agonist; LTRA, leukotriene receptor antagonist; RABA, rapid-acting beta2 agonist. Source: Ukena and Fishman 2008, with kind permission of the ÄZQ.

for a long time, whose symptoms arise independently of allergen exposure, and for whom anti-inflammatory pharmacotherapy has been less effective. SCIT is contraindicated in patients whose pulmonary function is persistently impaired with FEV₁ values below 70%. Specific immunotherapy should be performed only by a physician with experience in allergology. It does not replace effective anti-asthmatic pharmacotherapy, but should rather be seen as a complementary element of asthma management. There is accumulating evidence

that SCIT can help prevent the progression of allergic rhino-conjunctivitis to allergic asthma in children and adolescents (evidence level B).

No definitive recommendation can be given as yet with regard to sublingual immunotherapy (SLIT) because of a lack of pertinent data from clinical trials.

Rehabilitation measures (evidence level B)

In- or outpatient pneumological rehabilitation should be considered particularly in the following situations (1, 3):

TABLE 2

Daily doses of inhaled corticosteroids (ICS)*1

Medication	Low dose	Intermediate dose	High dose
Beclomethasone	200–500 µg	> 500–1000 µg	> 1000–2000 µg
Budesonid	200–400 µg	> 400–800 µg	> 800–1600 µg
Ciclesonide	80 µg	160 µg	> 160 µg
Fluticasone	100–250 µg	> 250–500 µg	> 500–1000 µg
Mometasone	200–400 µg	> 400–800 µg	> 800–1200 µg

*1 modified from (2)

If the treatment is unsuccessful

review treatment compliance, inhalation technique, diagnosis, and exacerbating factors.

Desensitization (SCIT)

The persistent impairment of pulmonary function to FEV₁ values below 70% is a contraindication to allergen-specific subcutaneous immunotherapy (SCIT).

BOX 4

Treatments whose effectiveness has been inadequately demonstrated, or not at all*¹

- Acupuncture
- "Alexander technique" training of breathing
- Air moisture control
- Breathing exercises
- Buteyko breathing technique
- Chiropractic manipulation
- Dietary measures: fish oil, fatty acids, mineral supplementation or restriction, vitamin C
- Homeopathy
- Hypnosis
- Ionizers (room-air purifiers)
- Plant extracts (phytotherapeutic agents)
- Relaxation therapy, including progressive relaxation as described by Jacobson, hypnotherapy, autogenic training, biofeedback training, transcendental meditation
- Speleotherapy (living in underground caves and mines)
- Traditional Chinese medicine

*¹ modified from (1), (3).

- in severe asthma with major sequelae despite adequate medical treatment,
- when the patient's working ability and earning capacity are endangered,
- when the need for nursing care and help with the activities of everyday life appears imminent,
- or when medically indicated non-pharmacological treatment measures such as patient education or training therapy cannot be carried out on an ambulatory basis.

Coordination of care

The long-term care of the patient, in the framework of a structured treatment program, is the responsibility of the primary care physician (1). Additional treatment by a physician specialized in respiratory medicine may be medically necessary as well, for any of the following reasons:

- Recurrent, severe exacerbations
- Complicating accompanying illnesses such as COPD or gastroesophageal reflux disorder
- Inadequate therapeutic benefit despite maximal treatment
- Maintenance therapy with oral corticosteroids
- Possible occupationally induced asthma
- Worsening control of asthma during pregnancy.

Conflict of interest statement

Professor Dr. med. Dieter Ukena has received lecture fees from Altana, AstraZeneca, GlaxoSmithKline, and Boehringer Ingelheim. Ms. Liat Fishman and Prof. Dr. med. Wilhelm-Bernhard Niebeling declare no conflict of interest as defined by the guidelines of the International Committee of Medical Journal Editors.

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Sublingual immunotherapy (SLIT)

No definitive recommendation is possible at present because relevant trial data are lacking.

Coordination of care

The primary care physician treats the patient over the long term in the setting of a structured treatment program.

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A case report is available at:
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The solutions to the following questions will be published in volume 28–29/2008. The CME unit "Epilepsy in Childhood and Adolescence" (volume 17/2008) can be accessed until 6 June 2008.

For volume 25/2008 we plan to offer the topic "Urticaria: Its History-Based Diagnosis and Etiologically Oriented Treatment."

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 Kujath P, Michelsen A: Wounds: From Physiology to Wound Dressing:
 1/a, 2/c, 3/b, 4/c, 5/c, 6/c, 7/e, 8/d, 9/c, 10/a

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Question 1

Which of the following symptoms is typical of bronchial asthma?

- a) Early-morning shortness of breath
- b) Spontaneous hemoptysis
- c) Expectoration of putrid sputum
- d) Tearing chest pain
- e) Chronic pain in the extremities

Question 2

Which of the following mechanisms contributes to airway obstruction in bronchial asthma?

- a) Bilateral vocal cord paresis due to recurrent tonsillitis
- b) Bronchoconstriction and the filling of small bronchi with highly viscous secretions
- c) The parasympatholytic effect of atropine combined with an antihistamine drug
- d) Unilateral phrenic nerve palsy caused by a vertical infraclavicular plexus block
- e) Depletion of dopamine beta-hydroxylase in the adrenal medulla

Question 3

What percentage of children suffer from allergic asthma?

- a) Less than 5%
- b) About 10%
- c) About 30%
- d) About 40%
- e) About 50%

Question 4

Which of the following physical findings is characteristic of bronchial asthma?

- a) Wheezing
- b) Galloping rhythm
- c) Clubbing
- d) Hepatojugular reflux
- e) Hourglass nails

Question 5

Which of the following diagnostic tests is useful for the primary diagnosis of bronchial asthma?

- a) Arterial blood gas measurement during exercise
- b) Bronchoscopy with transbronchial lung biopsy
- c) Measurement of the number of activated neutrophils in the blood
- d) Measurement of the circadian peak flow variability
- e) High-resolution computerized tomography (HR-CT)

Question 6

Which of the following is a diagnostic criterion for bronchial asthma?

- a) Normal bronchial reactivity in a standardized provocative test
- b) FEV₁ decrease >15% during, or within 30 minutes after, physical exercise

- c) Spirometric demonstration of FEV₁/VC >75%
- d) The distance the patient can walk in 6 minutes is 20% shorter in the morning than in the evening
- e) FEV₁ increase <5–7% of initial value after inhalation of a short-acting bronchodilator

Question 7

Which of the following diseases is only of secondary importance in the differential diagnosis of bronchial asthma?

- a) Gastroesophageal reflux disorder
- b) Foreign-body aspiration
- c) Pulmonary embolism
- d) Pertussis
- e) Left heart failure

Question 8

Which of the following is a reasonable medical treatment of bronchial asthma?

- a) Administration of a short-acting beta₂ sympathomimetic agent in a standard dose of two inhalations q.i.d.
- b) Administration of theophylline in combination with inhaled corticosteroids, which is roughly as effective as giving a long-acting beta₂ sympathomimetic agent
- c) Inhalation of formoterol, which leads to a rapidly occurring and long-lasting dilatation of the bronchi and bronchioles
- d) Long-term treatment with systemic glucocorticoids, because their risk/benefit ratio is similar to that of inhaled corticosteroids (ICS)
- e) Long-term treatment with montelukast, which is an antihistamine drug that is highly effective locally

Question 9

Which of the following medications or classes of medications is the most important one in the long-term treatment of bronchial asthma?

- a) Inhaled corticosteroids
- b) Oral theophylline
- c) Oral glucocorticosteroids
- d) Inhaled anticholinergic agents
- e) Inhaled cromones

Question 10

Which of the following is an indispensable initial measure in the treatment of chronic asthma?

- a) Intermittent allergen provocation
- b) Long-term oxygen therapy
- c) Patient education
- d) Vaccination against pneumococci
- e) Avoiding excessive physical exercise

CONTINUING MEDICAL EDUCATION

Bronchial Asthma: Diagnosis and Long-Term Treatment in Adults

Dieter Ukena, Liat Fishman, Wilhelm-Bernhard Niebling

E-BOX

The main adverse effects of anti-asthmatic medication

- **Inhaled short-acting beta2 sympathomimetic agents**
Fine tremor of voluntary muscle; agitation; tachycardia; palpitations
- **Inhaled long-acting beta2 sympathomimetic agents (LABA)**
Same adverse effects as short-acting agents; also: tolerance of bronchoprotective effect in the presence of bronchoconstricting stimuli (while the bronchodilating effect of the drug is maintained); to be used over the long term only in combination with glucocorticoids (usually ICS)
- **Inhaled corticosteroids (ICS)**
Local: oropharyngeal candidiasis (thrush); hoarseness
Systemic: depending on the dose and the duration of administration, osteoporosis; cataracts; glaucoma; delayed growth in childhood; suppression of adrenocortical function
- **Systemic corticosteroids**
Cushing syndrome; osteoporosis; myopathy; glaucoma; cataracts; endocrine psychosyndrome; worsening of diabetes mellitus; sodium retention; hypertension; adrenocortical atrophy; elevated susceptibility to infection
- **Montelukast**
Abdominal symptoms; headache; unclear association with Churg-Strauss syndrome, thus the dose of simultaneously administered systemic glucocorticoids should be lowered cautiously
- **Theophyllin**
Depending on the serum concentration: gastrointestinal disturbances; gastroesophageal reflux disorder; tachycardia; diuresis; agitation; insomnia
When the serum concentration exceeds 25 mg/L: epileptic seizures; gastrointestinal bleeding; ventricular arrhythmia; hypotension
- **Omalizumab**
Local reactions at the subcutaneous injection site; headache

CONTINUING MEDICAL EDUCATION

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Case Report

Bronchial Asthma: Diagnosis and Long-Term Treatment in Adults
Three clinical vignettes

Case No. 1

A 23-year-old woman with known bronchial asthma presents with acute dyspnea. She is already taking maintenance therapy with an inhaled corticosteroid twice daily and, when needed, an inhaled short-acting beta2 sympathomimetic agent.

The clinical and laboratory findings are as follows:

- Shortness of breath while speaking and at rest
- Respiratory rate 32/min
- Orthopnea
- Expiratory wheezes
- Prolonged expiratory phase
- FEV₁ = 2.2 L (61% of normal)
- FEV₁/IVC = 53%
- Arterial blood gases: pO₂ = 65 mmHg, pCO₂ = 25 mmHg, pH = 7.49

A severe asthma attack is diagnosed.

Treatment is provided, consisting of the administration of prednisolone 50 mg b.i.d. along with continued inhalational therapy.

Three days later, the FEV₁ is 3.52 L, corresponding to 96% of the normal value. The FEV₁/IVC ratio is 79%. Systemic glucocorticoid therapy is stopped after one week.

Case No. 2

A 17-year-old girl presents to medical attention one night with acute shortness of breath after a visit to a discotheque. She is not known to be asthmatic.

Physical examination reveals a respiratory rate of 30/min and, on auscultation, vesicular breathing sounds without any additional auxiliary sounds. An arterial blood gas analysis yields the following findings: pO₂ = 95 mmHg, pCO₂ = 25 mmHg, pH = 7.51.

Hyperventilation syndrome is considered to be the most likely diagnosis, with the underlying cause being a crisis in the patient's relationship with her boyfriend (they had just had an argument).

Pharmacotherapy is not necessary in this case; all that is needed is reassurance.

Case No. 3

A 53-year-old man complains of a dry cough of six weeks' duration. He had a lower respiratory infection about two months ago. He is not known to have bronchial asthma. The physical examination is unremarkable. Pulmonary function tests reveal an FEV₁ that is 75% of the normal value and an FEV₁/IVC ratio of 70%. Peak flow measurements yield values of 480/min in the morning and 600/min in the evening.

A diagnosis of bronchial asthma of post-infectious onset is given. The patient is treated with inhaled corticosteroids b.i.d. combined with a beta2 sympathomimetic agent as needed. Two weeks later, the patient is free of symptoms and his pulmonary function is normal.

FEV₁: forced expiratory volume in one second; IVC: inspiratory vital capacity