



TREATING ASTHMA IN CHILDREN

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I. INTRODUCTION

Asthma is an extremely vexing disease because of both its high incidence and its severely harmful potential (1). It may present as a recurrent bronchitis beginning in the first months of life (2). It represents a precocious pathological phenomenon for the growth of infant lungs (3), and the likelihood of bronchial fibrosis in the young adult secondary to chronic inflammation during asthmatic episodes (4) raises another serious concern with the onset of the disease in infancy. The notion that asthma disappears with puberty has no scientific basis (5-7).

Asthma is a persistent chronic pulmonary inflammation characterized by obstruction or narrowing of the airways and subsides, either totally or in part, spontaneously or with treatment. In addition to inflammation of the airways, different degrees of bronchial hyperresponsiveness (BHR) may be triggered by different stimuli.

BHR (or abnormally exaggerated response of the bronchial wall) may be transitory, as occurs with viral infections, without any clear indication of the individual mechanisms underlying the chronic phase, which is characterized by the inflammation that constitutes asthmatic syndrome (AS).

The principal stimuli of AS are the irritants to the airways, including environmental contamination from automobile exhaust, dust, cigarette smoke, virus, aerosols, and hyperventilation during exercise. In general, the mechanisms are acquired and not genetic, as seen in atopy in families where BHR is brought on by allergens such as mites, animal feces, molds, and pollen.

In atopic patients, children, and certain cases of occupational asthma, AS generally begins with an allergic reaction, such as to a virus, certain foods, mites, and animal nails, followed by

other factors, particularly irritants. The irritant stimuli activate and release a mixture of neural and cellular mechanisms, neurotransmitters, and mediating chemicals that act in combination to constrict and inflame the bronchi, destroy the epithelium, induce spasm in the smooth bronchial muscle, and cause vasoconstriction, exudate, hypersecretion, and edema. The result is a decrease in bronchial lumen and alteration of alveolar ventilation.

At its onset or in milder cases of AS, spasm normally occurs, but as it becomes more chronic or severe, inflammation is more common than spasm. This is why in the beginning the process is reversible either spontaneously or through medication, but may later become irreversible and lead to obstruction, plugging, and/or alveolar distention with alterations in the pulmonary gas exchange and ventilation-perfusion ratio from the mixture of venous blood or as a result of shunting (V_A/Q).

Attacks (or acute episodes) begin with bronchial spasm within about one-half hour of exposure to the stimulus and persist for two to four hours in what is called the precocious phase. Most cases include what is known as the delayed or later phase, in which inflammation and a new bronchial spasm present six to eight hours later and persist for hours, days, or weeks. Other attacks develop into the chronic phase in which inflammation is more common than bronchial spasm.

II. DIAGNOSIS

The diagnosis of AS is based on the clinical findings of both acute episodes and intercritical periods, as well as family and personal history, the evolution of the disease, functional respiratory expiration (FRE), and the patient's response to treatment.

a) Clinical findings

The symptoms depend on the severity of obstruction during and between attacks. In general, the clinical findings for the attacks include recurrent episodes that are reversible either spontaneously or after treatment for cough and wheezing dyspnea. However, when the attacks subside, the only evident symptoms may be cough; or they may become subclinical and observable only through functional respiratory exploration. Small children present recurrent bouts of bronchitis, with or without wheezing, and with chronic cough or forced cough.

Different degrees of AS symptoms are found depending on the degree of obstruction (mild, moderate, or severe; and acute or chronic). Symptoms run the gamut from cough, hypersecretion, and wheezing to dyspnea and cyanosis that lead to respiratory failure in acute episodes and respiratory incapacity in chronic ones.

A light or moderate gradual obstruction presentation, even if it is chronic, may present no symptoms when the patient is at rest, or it may present symptoms as innocuous as a morning cough or a sedentary tendency. Thus, it is important to recall that an apparent absence of symptoms does not necessarily indicate an absence of asthma, obstruction, or air blockage; the severity of bronchial hyperresponsiveness (BHR) and inflammation depends on its long-term clinical response and development, i.e., on the treatment.

b) Aspects of patient history that support diagnosis

- family: asthma, allergic rhinitis, and/or atopic eczema in parents or siblings: 25% probability when one parent is affected, 50% if both are;
- personal: recurrent bouts of bronchitis and/or history of atopic eczema;
- allergic rhinitis;
- episodic clinical manifestations of wheezing dyspnea and/or spasmodic cough;
- dyspnea subsequent to exercise;
- bronchial episodes with or without wheezing, brought on or aggravated by respiratory viral infections, abrupt changes in indoor or outdoor temperature, molds, food, exposure to dust, aerosols, smoke, vapors, gases, odors, or other factors.

c) Functional diagnosis

The functional diagnosis is based on tests of bronchomotor status or bronchial provocation performed between critical periods to trigger, in an experimental fashion, the functional disturbances comparable to those that present during asthma. The purpose of functional diagnosis is to afford an objective appreciation of the alterations in respiratory function and to quantify them. This makes it possible to:

- certify the diagnosis of AS;
- demonstrate the degree and the reversibility of the obstruction in order to adapt treatment;
- control the evolution of AS;
- obtain a prognosis of the long-term severity of the asthma, using the BHR and the variations in peak expiration flow (PEF);
- help to detect precipitating factors.

For diagnosis of AS in a nonobstructed patient, obstruction is provoked using an exercise test or methacholine. The test is positive if:

- wheezing or dyspnea is presented;
- peak expiration flow (PEF) drops by 20% or more;
- forced expiration volume per second (FEV1) drops by 20% or more; or
- forced expiration volume per second over vital capacity (FEV1/VC) falls below 79%.

With the obstructed patient, a bronchodilator is used, generally with an inhaled or vaporized β_2 -agonist stimulant. The test is positive if:

- PEF increases by 20% or more; and if
- FEV1 increases by 20% or more.

The home use of PEF can contribute to management of AS when it is performed 2 or 3 times a day for at least 1 week. Evaluation of the variations between the maximum and minimum values yields:

- in untreated patients: variations > 20% indicate presence of asthma;
- in treated patients: variations > 20% in the morning as compared with the evening, indicating nocturnal asthma. During the day, unstable asthma; that is, the need to correct, increase, or alter drugs, doses, and/or schedules.

When home measurement of PEF is feasible and consistent variations under 20% are obtained from the treated patient, the time is right to complete PEF measurements with more specific and sensitive tests such as spirometry, the flow/volume curve, or resistance and conductivity tests, depending on their availability.

In severely affected patients, specific tests should be run at the start to diagnose distention (or trapped air volume) and to determine treatment. Currently, only PEF and occasionally spirometry are employed for diagnosis and follow-up.

Measurements of PEF, FEV₁, CV, and FEV₁/CV provide the most accurate, strictly clinical diagnosis of asthma as well as the most adequate follow-up. Furthermore, a finding during an intercritical period that serum gas is affected by an augmented alveolar-arterial oxygen gradient [D(Aa)O₂], hypoxemia, and/or acidosis should alert one to the patient's poor evolution.

d) Importance and application of PEF measurements in treatment

d.1) PEF in asthmatic children

The correct use of PEF allows asthmatic children to treat themselves at home either by themselves or with their parents. It also affords general control over respiratory function and helps both the patient and physician to make diagnostic and therapeutic decisions.

With a simple lightweight device an outpatient reading of respiratory function can be taken. Rather than explore the entire respiratory function, a reading is taken of the point of maximum flow on the respiratory curve in liters per minute (l/min). The result is compared with the "normal" values for each point of the scale on the device and particularly with the normal values for each patient to determine personal variations.

d.2) Measuring devices

It is important to use the same brand of device with a single flow range, ideally calibrated just as done by the treating physician. Two of the most common devices:

- The miniflowmeter of Wright comes in two models: the high flow for persons over 7 years of age and the low flow for children under 7.

- The Assess® miniflowmeter is as reliable as the Wright (9), but less expensive, and also comes in two models.

d.3) Measuring technique

Because maximum cooperation is required, the technique cannot be conducted with children under 6 or 7 years of age. The steps to follow are the following:

- adjust the funnel or mouthpiece according to the size of the child's mouth;
- verify that the scale is set to zero;
- hold the device in one hand without obstructing the scale;
- the patient should remain standing while placing the funnel in his or her mouth;
- with mouth open, the patient should practice maximum inhalation and close lips over the mouthpiece;
- next, the patient should exhale as strongly and quickly as possible;
- immediately thereafter, a reading should be taken from the scale and recorded with the date and time;
- set the scale to zero once again;
- repeat the maneuver three times and record the best reading;
- compare the result to the theoretical normal reading on the device (or better still, to the highest normal reading or the patient's own best reading). Record the number from the scale on the device. If the scale changes color when the reading is obtained, it can be thought of in terms of a traffic light (14-17) as follows:
 - 0 to 50% of normal value: RED;
 - 50% to 80% of normal value: YELLOW;
 - 80% to 100% of normal value: GREEN.

d.4) Errors in measurement

Errors in PEF measurement occur mainly because:

- mouth is not tightly closed during expiration;
- dental prosthetics present;
- tongue obstructs funnel;
- expiratory effort does not reach peak capacity;
- patient is pursing lips as if whistling when blowing air;
- patient is puffing cheeks when blowing as if through a straw;
- mouthpiece is removed before patient has completed exhalation.

d.5) Practical analysis of results

PEF varies in each person, even in healthy ones. Furthermore, it is proportionate to patient size. The lowest values are found at night between the hours of 2 and 6 a.m.; the highest values are found between 2 and 6 p.m., following the changes in the circadian cycle. The percent change between highest and lowest values is known as the amplitude; it is normally from 10% to 13%, and in asthmatics over 20%. The PEF is first compared with the normal values; after the patient is bronchodilated, the maximum value is also taken for comparison.

The PEF values can be plotted on a graph, with the points representing the values from readings made at 6 a.m., 2 p.m., and 9 or 10 p.m. for at least 7 days. Using the graph to plot the variations, the percentage variations can be grouped in colors as indicated above: between 80% and 100% is considered stable (GREEN), 50% to 80% requires attention (YELLOW), and under 50% is a sign of alarm (RED). If a graph or maximum value for the patient is not available, the PEF reading is simply compared to the expected theoretical value.

Differences in the degree of severity or bronchial hyperresponsiveness and the failure of the PEF to measure the entire obstruction may mean that the asthmatic patient will register, as in low-risk asthma, a normal PEF that dips only during a critical period or fluctuates less than 20%. In more severe asthma, normal values may be obtained even when the airways are obstructed, as in chronic cases. Analysis of variations of at least 20% or higher will help to guide the diagnosis, treatment, and type of medication.

d.6) Indications of use and clinical orientation

Low-risk asthma does not require PEF measurement as does high-risk asthma, which even when it is asymptomatic presents permanent obstruction. PEF measurement makes it possible to:

- recognize unstable asthma with normal values that fluctuate more than 20% in the same day;
- recognize the severity of general asthma and night-time asthma in which the 2-6 a.m. variations exceed 20%;
- specify the exacerbation of functional respiratory status in a chronic patient who may appear clinically "well;" anticipate symptoms, changing treatment as necessary;
- attempt early detection of the first phase of critical obstruction and commence

treatment with timely intervention; anticipate symptoms (PEF values generally fall 48 hours before the onset of symptoms);

- evaluate the response to a specific treatment, objectively justifying any change;
- decide when to consult the physician or hospital emergency service;
- decide on hospitalization as well as appropriate moment to release patient;
- recognize exercise-induced asthma and apply preventive treatment;
- help to specify precipitating factors and take measures to alter the environment; and
- teach the patient to learn his or her own values and variations.

d.7) Limitations and drawbacks of measurement

- The PEF will detect nothing less than a major obstruction, because it measures only the point of maximum expiration. Therefore, it is not the most sensitive technique for studying airway function, much less the respiratory mechanism, which can be measured only in a pulmonary function laboratory with the assistance of a spirometer and arterial gas measurements, among others;
- the devices are extremely fragile and bulky, making them difficult to carry;
- obsessive cleansing may damage them;
- most patients, unless closely supervised, discontinue their monitoring recording after two or three weeks;
- patients grow overconfident and act as if they were “well.” As a result, they fail to go in for check-ups or functional exploration.

Allergy tests cannot diagnose asthma, and can easily be replaced by general air quality and pollen count announcements. Rarely do allergy tests help to isolate an important precipitating factor or to decide on a specific form of treatment.

The following tables provide a summary of the most important parameters for diagnosing the severity of asthma during and between crises, and they compare the risk of asthma development according to different factors (8).

III. TREATMENT OF ASTHMA

a) Objective

The major objective of treatment is to prevent and control inflammation in order to preserve or restore maximal possible respiratory function in the patient.

Table 1. Risk parameters in the course of asthma

PARAMETERS	CLASSIFICATION	
	LOW RISK	HIGH RISK
1. FUNCTIONAL EXPLORATION BETWEEN CRITICAL PERIODS		
Bronchial hyperresponsiveness	Positive at high doses of methacholine	Positive at low doses of methacholine
Exercise test	Positive during early stage	Positive during early and late stage
Peak expiratory flow (PEF)	Variation between critical periods $\leq 20\%$	Variation between critical periods $> 20\%$
Functional respiratory expiration (FRE)	Mild obstruction or absent, reversible with a dose of β_2 -agonist; central predominance	Obstruction existing or not reversible; peripheral predominance
Air accumulation	Absent	Present in the majority of cases
Arterial gas	Normal	Normal or with increased $P(Aa)O_2$; hypoxemia and/or respiratory acidosis
2. PHYSICAL EXPLORATION BETWEEN CRITICAL PERIODS		
Respiratory frequency (RF)	Normal	Normal or increased
Anteroposterior diameter of the thorax	Normal	Normal or increased
3. RADIOLOGICAL TESTS BETWEEN CRITICAL PERIODS		
Signs of air accumulation	Absent on X-rays during inspiration or expiration	Present
4. SYMPTOMS		
Periods between attacks	Asymptomatic; normal school and sports activities; dyspnea post-exercise preventable; nocturnal asthma absent	Frequent or continuous symptoms and/or physical limitations; nocturnal asthma; need of permanent medication; incapacitated for exercising.
Crisis	Mild, occasionally	Frequent and/or serious
5. OTHER RISK FACTORS		
Atopic dermatitis	Absent	Present
Age of onset	Pre-school and school child	Infant
Environmental factors	In control or absent	Present
Start of treatment	Early, based on FRE	Late or non FRE based
Treatment	Feasible, controlled	Not feasible (poverty, pollution, others) or difficult

Table 2. Classification of asthma without treatment according to seriousness			
SERIOUSNESS	SYMPTOMS BEFORE ADEQUATE TREATMENT	PULMONARY FUNCTION	MINIMAL TREATMENT FOR MAINTAINING CONTROL
MILD	<ul style="list-style-type: none"> • Brief and intermittent symptoms, less than once or twice per week; • Nocturnal asthma, less than twice a month; • Asymptomatic between critical periods. 	<ul style="list-style-type: none"> • PEF > 80% of normal¹; • Variability of PEF < 20%; • Normal PEF after inhalation of a β_2-agonist. 	<ul style="list-style-type: none"> • Intermittent; • Needs only a short course of inhalation of a β_2-agonist.
MODERATE	<ul style="list-style-type: none"> • More than one or two exacerbations per week; • Nocturnal asthma: more than twice per month; • Symptoms requiring a β_2-agonist almost every day. 	<ul style="list-style-type: none"> • PEF between 60 and 80% of normal¹; • Variability of PEF between 20 and 30%; • Normal PEF after bronchial dilation. 	<ul style="list-style-type: none"> • Inhaled corticoid daily; • Need to add a bronchodilator daily, particularly for preventing the nocturnal symptoms or when these appear.
SEVERE	<ul style="list-style-type: none"> • Frequent exacerbations; • Continuous symptoms; • Frequent symptoms; • Nocturnal asthma; • Physical limitation due to asthma; • History of hospitalization due to asthma; • Previous exacerbations threatening life. 	<ul style="list-style-type: none"> • PEF < 60% of normal¹; • Variability of PEF > 30%; • Abnormal PEF with optimal therapy. 	<ul style="list-style-type: none"> • High doses of inhaled corticoids; • Probably it will be necessary to add a long-acting bronchodilator daily, especially for nocturnal symptoms; • Frequent usage of a systemic corticoid.

¹ Normal PEF from the table or best personal reading during a measurement.

Table 3. Classification of attacks in children by severity

SYMPTOM	CLASSIFICATION			
	MILD	MODERATE	SEVERE	RESPIRATORY FAILURE
Speech	Normal	Sentences	Words	
Consciousness	May be agitated	May be agitated	Agitation	Somnolence or confusion
RF per minute ¹	Increased	Increased	Increased	Normal or diminished
Usage of accessory muscles; retractions	Usually not present	Moderate usage	Intensified usage	Thoracoabdominal imbalance
Wheezings	Moderate	May be heard from a certain distance	Can be heard from a certain distance+++	Totally absent
CF per minute ²	Increased+	Increased++	Increased+++	Bradycardia
Paradoxical pulse ³	Less than 10 mm Hg	Between 10 and 20 mm Hg	Between 20 and 40 mm Hg	Parameter absent, probably due to muscular fatigue
Percentage of PEF established for the patient or of the PEF personal best after two doses of inhaled β_2 -agonist ⁴	70 to 80%	50 to 70%	Less than 50% or no response during the last two hours	
Oxygen saturation	Normal (>95%)	91 to 95%	< 90% (cyanosis possible)	< 90% (cyanosis)
PaCO ₂ ⁵	Less than 40 mm Hg	ca. 40 to 45 mm Hg	> 45 mm Hg	
PaO ₂ ⁵	Normal; it is not necessary to evaluate	ca. 60 mm Hg	< 60 mm Hg	

1 Normal respiratory frequency (per minute) according to age can be < 60 in infants less than 2 months old; < 50 for infants 2 to 12 months; < 40 for 1 to 5 years old; < 30 for 6 to 8 years old; < 20 for older than 8 years.

2 The cardiac frequency (per minute) according to age can be < 160 between 2 and 12 months; < 120 for 1 to 2 years old; < 110 for 2 to 8 years old; and < 100 for older than 8 years.

3 This is not correlated to the breathing phases in small children.

4 PEF for children older than 5 years.

5 At sea level.

Secondary objectives are to:

- decrease the severity and frequency of the attacks or critical bouts;
- prevent attacks for as long as possible and keep patient as asymptomatic as possible by keeping readings from FRE as close to normal as possible;
- enable patient to enjoy a normal social, scholastic, and athletic life (or as close to normal as possible);
- teach patient and patient's family self-treatment of asthma in terms of environment and medication;
- teach how to take proper measures according to clinical symptoms or PEF readings, including boosting drug dose, repeating medication, calling the physician, or going to the hospital;
- keep patient as stable as possible in terms of maximum FRE, with the fewest drugs and smallest doses necessary;
- detect high-risk patients.

Some hypersensitive asthmatics show a propensity toward edema of the bronchial mucosa, which results in prolonged or permanent obstruction. They require prolonged treatment that only very rarely can be discontinued. Other asthmatics are less susceptible or reactive and can be stabilized without special treatment on the basis of the FRE.

In both cases, however, environmental control and personal and family education are essential for successful case management. In a favorable geographical area, the correct measures keep an asthmatic patient free from attacks or subject to only mild attacks that are manageable at home or on an outpatient basis without hospitalization.

The asthmatic syndrome is said to be stable when:

- the patient is asymptomatic or has only minimal symptoms;
- no crises arise or they do so only rarely;
- very little, if any, bronchodilation is required;
- patient has no physical constraints;
- PEF variations are below 20%;
- treatment ensures minimal secondary effects or none at all.

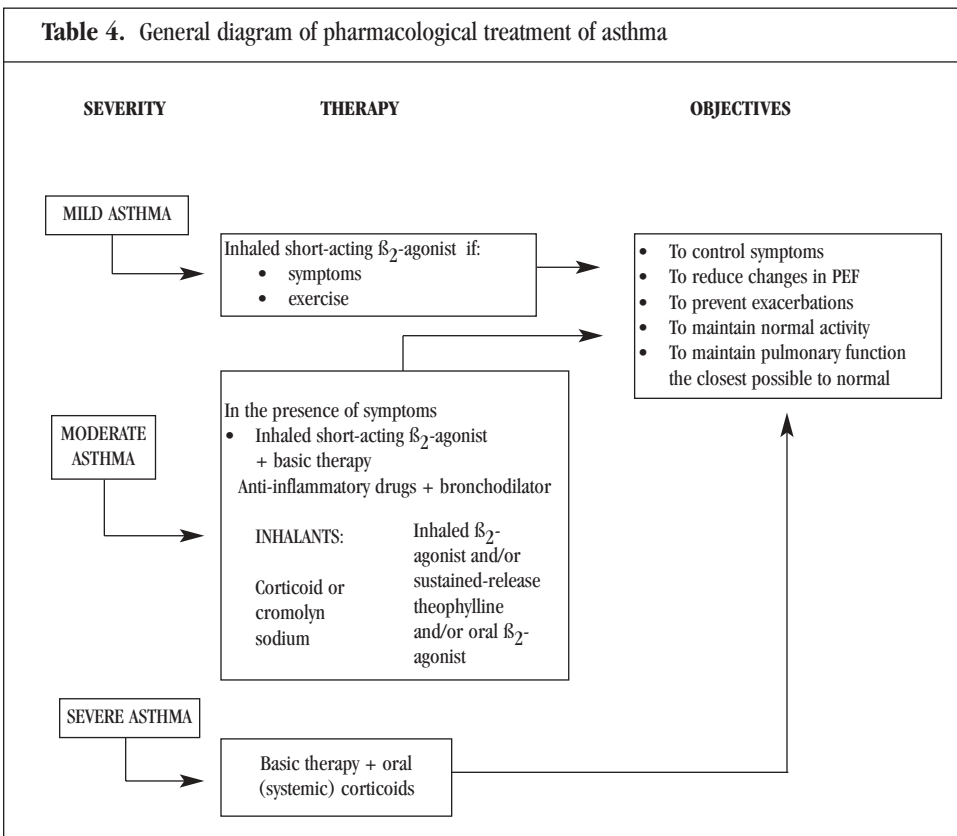
b) General plan of treatment for asthma

Tables 4-8 display a summary of asthma treatment (8) and cover clinical characteristics, pulmonary function assessment (using either PEF or the FEV1), drug therapy, other support measures, and the anticipated outcome. Control of mild asthma, in which FRE and PEF are not used, can be based on clinical control when the patient is at rest and engaged in exercise. Just the same, PEF, FEV1, and other tests may record alterations, and therefore establishing a reading for them is important.

c) Considerations regarding drugs used to treat asthma

c.1) Forms of administration

- Measured-dose aerosol inhalant: Inhaled treatments are preferred because of their fast action and direct effect on the target organ. They make small doses possible, thereby limiting unwanted secondary systemic effects. However, the weak point of the aerosol spray is the need for proper inhalation. Some studies indicate that only 50% of corresponding adults use it correctly, and that even fewer elderly and pediatric patients do so. Use of a spacer or of the drug in dry-powder

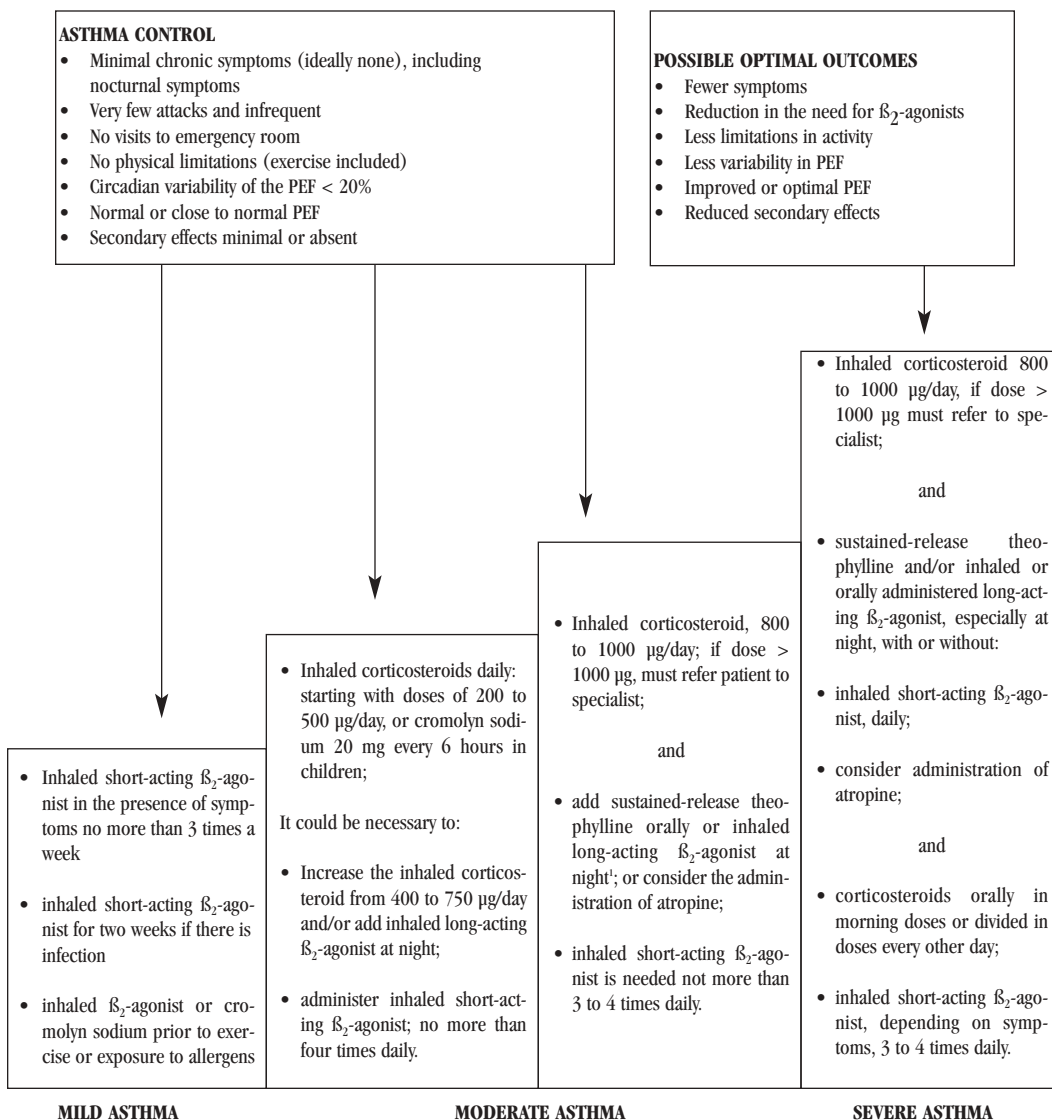


Note: This diagram must be used in conjunction with education and control of the environmental conditions (for detailed therapy see next table).

Table 5. Chronic asthma management: Appropriate levels of therapy

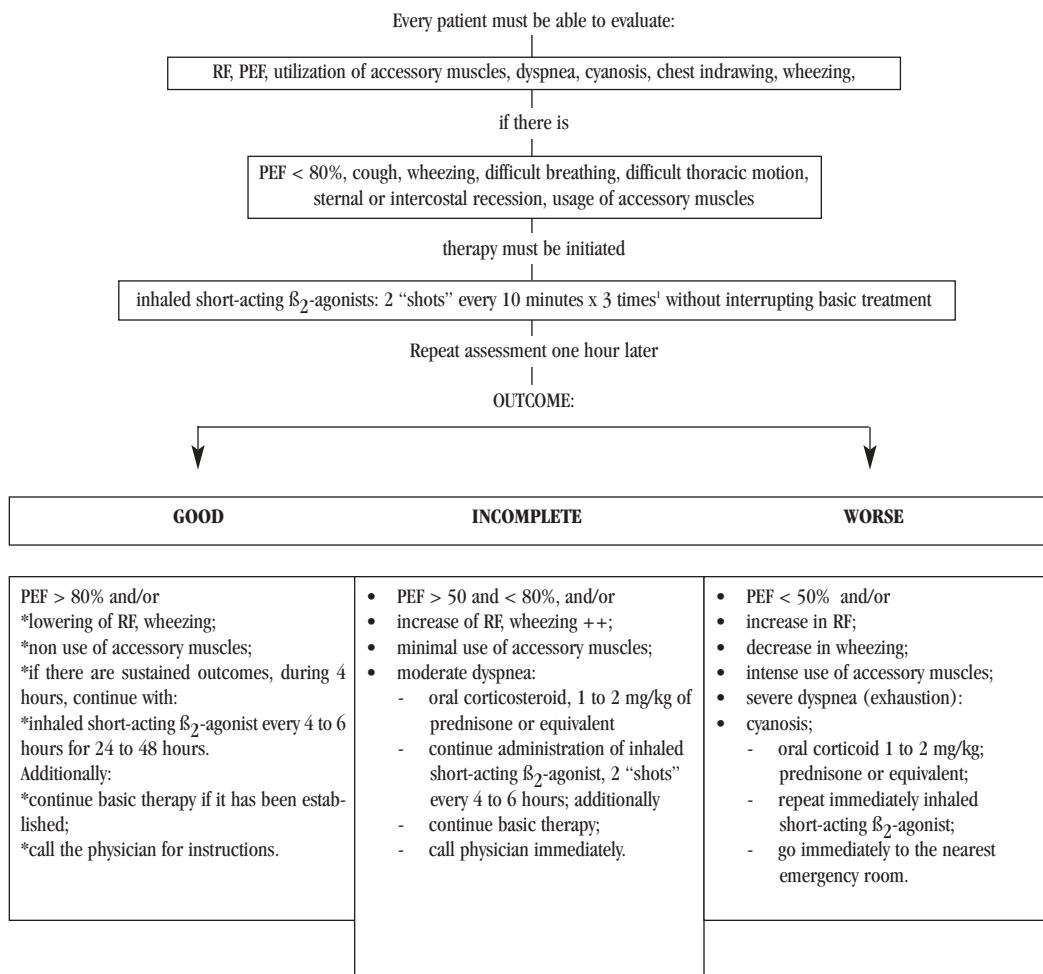
How to follow the diagram:

- When an adequate control level according to severity is not achieved, and having verified that therapy has been properly administered (included education) go to following higher level.
- When control has been sustained for several weeks or months, it is recommended to try to go to the preceding level and then return to the higher one if the patient relapses.



¹ Inhaled long-acting β_2 -agonists are administered to adults; for children under 3 they are administered orally.

- For children younger than 3 years, another diagram follows
- It is necessary to identify the minimal therapy to achieve optimal control
- Administration of β_2 -agonists in infants is always done with a spacer; in children older than 10 years, the use of the spacer may be omitted.

Table 6. Management of attacks at home

¹ The β_2 -agonist must be used always with the spacer.

* The dose of β_2 -agonist referred to as a "shot" is equivalent to 100 mg.

* If the physician has so indicated, call him immediately, as there could be a high risk depending on the clinical background of each patient.

* Using this diagram, included appropriate basic therapy, education of the patient and/or his family and control of the environmental conditions, most of the attacks can be overcome.

Table 7. Management of attacks in the emergency room

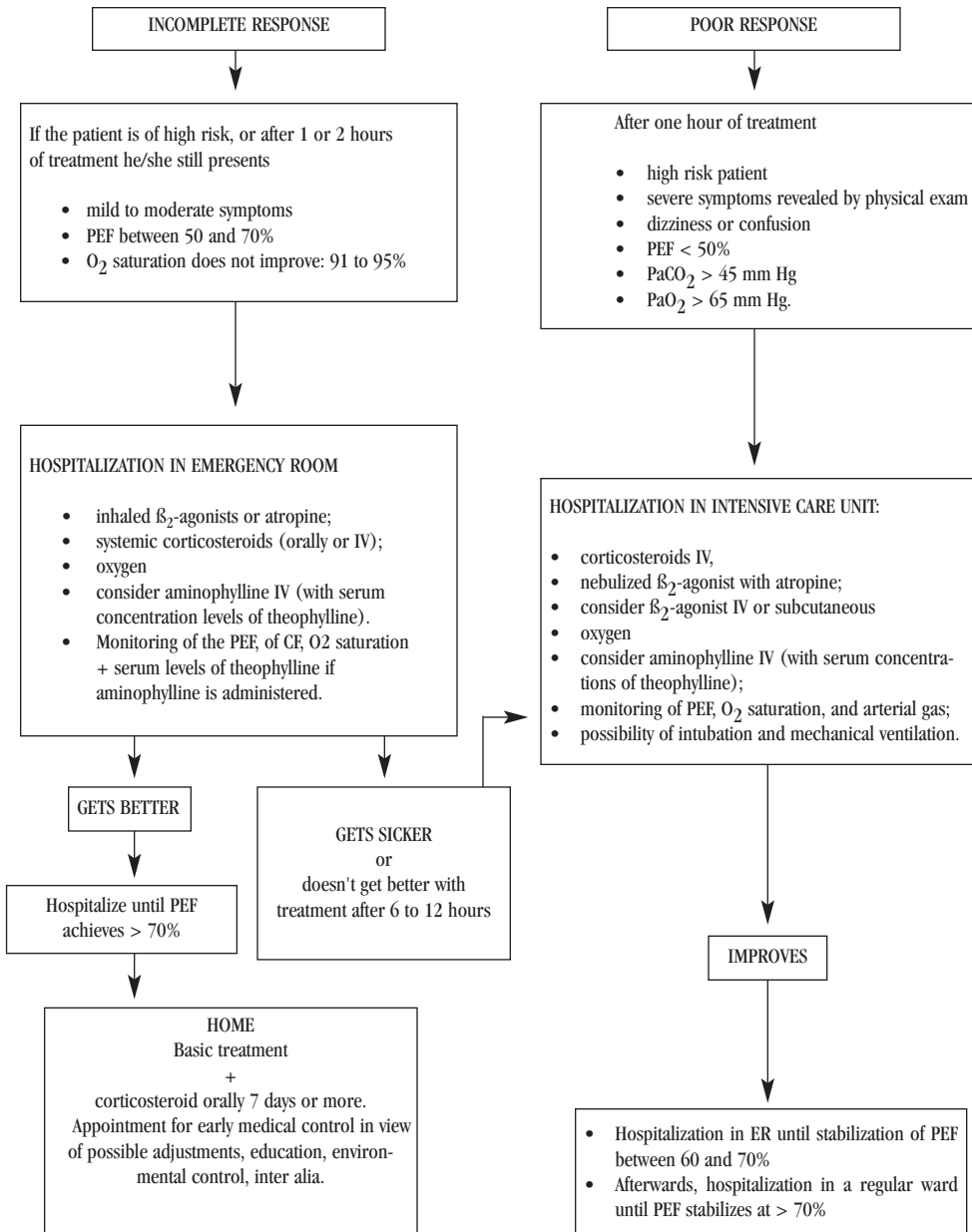


Table 8. Management of asthma in children under 3 years of age

MILD	➔	MODERATE	➔	SEVERE
<p>β_2-agonist orally or inhaled every 6 hours or long-acting every 8-12 hours (orally)</p> <ul style="list-style-type: none"> • If symptoms are under control: stop medication • If there is a crisis <ul style="list-style-type: none"> - oral corticosteroid during 3 to 5 days - β_2-agonist and/or inhaled atropine • If chronic symptoms are still present <ul style="list-style-type: none"> - Add an inhaled corticosteroid at 400 to 500 mg daily: 8 a.m. and 3 p.m. • If there is improvement: <ul style="list-style-type: none"> - Stop the β_2-agonists and/or the atropine as soon as possible and then the corticosteroid. • If there is no improvement: _____ 		<ul style="list-style-type: none"> • Add: Nebulized cromolyn sodium, 20 mg every 6 hours • or: Ketotifen, 1 mg every 12 hours • After 3 months of control: <ul style="list-style-type: none"> - Stop the β_2-agonists and/or atropine and administer them only if symptoms are observed then <ul style="list-style-type: none"> - stop the corticosteroid and afterwards the cromolyn sodium and/or ketotifen. • If a crisis occurs <ul style="list-style-type: none"> - Oral corticosteroid during 5 more days - inhaled β_2-agonist and/or atropine. • If there is no improvement: _____ 		<ul style="list-style-type: none"> • Switch to: <ul style="list-style-type: none"> - inhaled corticosteroid at 800 mg/day, distributed in 2 or 3 doses; More: <ul style="list-style-type: none"> - inhaled β_2-agonist and/or atropine. • In children older than one year try: <ul style="list-style-type: none"> - sustained-release theophylline (in granules) every 12 hours • If there is improvement: <ul style="list-style-type: none"> - Stop the β_2-agonists and/or the atropine, then the theophylline and later the corticosteroid. • If there is no improvement: <ul style="list-style-type: none"> - short course therapy with oral corticosteroid¹, reducing the weekly dose by 25%.

1 This can be prednisone of 1 to 2 mg/kg/day or its equivalent, in a morning dose, during 5 to 7 days, then decrease the dose 25% weekly.

- For each patient the minimal dose maintaining an optimal control must be established.
- Inhaled medications (drugs) must be administered with a spacer using a mask.
- If the scheme is properly utilized it is infrequent to go from the first column to the second. Nevertheless, good education and environmental control are needed.

form can correct the problem.

- Nebulization: When a major obstruction or severe crisis occurs, large doses are necessary, requiring expensive devices, including a gas impeller and a micronebulizer. Medication is inhaled through a mask or mouth funnel. It is used in a severe crisis.
- Subcutaneous or intravenous route: This method is required in a severe crisis when the nebulizations are repeated often. The intravenous route requires a monitor.
- Oral route: The oral route is used in children whose night-time asthma is treated by long-acting drugs.

c.2) Sustained-release theophyllines

- These drugs inhibit phosphodiesterase. In addition to bronchodilation, they increase mucociliary motility and contraction of the striated muscle. Their bronchodilation is not as great as that of the β_2 -agonists. Strict dosage per kg of current weight according to age is required to avoid important side effects such as nausea, vomiting, headaches, tachycardia, and convulsions. Theophylline is not used as a monotherapy to treat asthma.
- When administered as prophylaxis it prevents the early stage. Once this stage has begun, the drug will alleviate.
- It also alleviates the later stage and chronic stage of asthma.
- It can be used on a long-term basis in severe chronic asthma as well as during an attack.
- Although controversial, a serum concentration between 10 and 20 $\mu\text{g/ml}$ at night is considered effective.
- It is essential to increase dosage slightly to obtain greater effectiveness and increase tolerance. In obese patients the dose should be calculated according to ideal weight.
- The dose should be administered every 12 hours, beginning at 8 mg/kg without exceeding 200 mg per dose. After 3 days, up to 10 mg/kg in children 6-9 years old; 8 mg/kg in children 9-12 years; and 6 mg/kg in children 12-16 years, without exceeding 300 mg per dose. Three days later, the dose can be increased by 2 mg/kg without exceeding 400 mg.
- In children 1-6 years of age, a dose of 12 mg/kg every 12 hours may be given.
- Therapeutic levels in blood can be measured after the fifth day of treatment, 4-6 hours after the morning dose. If the concentration is under 10 $\mu\text{g/ml}$, the dose may be increased by 25%. This allows 80% of patients to reach adequate thera-

peutic levels, even though only 20% actually require measurement of blood levels, particularly in the absence of a good therapeutic response.

- The dose should also be adjusted according to an increase in weight in a patient passing through a growth spurt.
- Unwanted effects with the described dosage levels are exceptional and tend to occur when dosage is not progressively increased. Digestive intolerance, and, to a lesser degree, irritability, insomnia, and headaches are all known to occur. With serum levels above 20 µg/ml, irritability, possible difficulty on the spatial-visual plane, inability to concentrate during psychomotor tests, and slight trembling may present.

c.3) β_2 -Adrenergic stimulants or β_2 -agonists

- These are the most potent and effective bronchodilators used to treat asthma. The most commonly used are salbutamol (albuterol), terbutaline, clenbuterol, and fenoterol; formeterol and salmeterol are among the long-acting drugs.
- Their action is focused in the small airways.
- They are first line medications during an attack.
- They lose effectiveness with prolonged use.
- They act immediately when inhaled or within 15 to 30 minutes when taken orally.
- Their effect lasts for 3-6 hours.
- Long-lasting β_2 -agonists are still not used in children.
- They will inhibit the early stage if administered beforehand and reverse it if administered after onset. They also will prevent exercise-induced asthma.
- In the late phase, they are used if the patient is obstructed, according to PEF or symptoms.
- They are effective when inhaled at low doses and have virtually no negative secondary effects as compared to IV administration. However, they are often improperly inhaled, resulting in low dosages or overdoses during severe attacks.
- Oral administration affords less bronchodilation and more systemic effect, even though it reaches the small airways better than with inhalation. Therefore, oral administration is advantageous against severe asthma, particularly nocturnal obstruction.
- The most common types taken orally are salbutamol, terbutaline, and clenbuterol in small children. Clenbuterol, for example, is administered every 12 hours.
- Among the most frequently observed undesirable effects is trembling hands—particularly at the beginning of treatment—and tachycardia.
- The use of β_2 -agonists in conjunction with theophylline is indicated to reduce oral corticosteroids in unstable severe asthma, nocturnal asthma, or in the event that normal doses of corticosteroids cannot be used.

- In order to use β_2 -agonists in aerosol form, such as salbutamol, terbutaline, or fenoterol, a spacer with a unidirectional valve is indicated, although a plastic bottle without a valve may also be used, 1 liter in size for children or 2 liters for adults.
- The Rotohaler or Tubohaler systems use dry powder in a “jar-capsule” whose proper use requires less hand-lung coordination. The patient should inhale deeply and completely, using his or her entire lung capacity. But these systems should not be used if dyspnea is present.
- Aerosol β_2 -agonists are the preferred drugs in treating moderate and severe attacks, the most common being salbutamol (albuterol), terbutaline, and isoetharine. These should be used with oxygen to avoid a drop in PaO_2 .
- The child’s cooperation is not necessary during the breathing cycle; however, an air or oxygen impeller with a supply capacity of 6-8 liters per minute, a mask, and micronebulizer are all required. The dose should be diluted in 3 cc of physiological saline and nebulized, ideally, in an uninterrupted flow for 4 or 5 minutes.
- During nebulization, the walls of the device need to be tapped in order to loosen drops that cling to the interior casing.
- At present, the nebulizer is used at home only in exceptional or particularly severe cases.

c.4) Corticoids

- Corticoids perform several actions in asthma treatment, including potent anti-inflammatory action that controls the hyperpermeability, hypersecretion, and inflammation of different cells, and it decreases bronchial hyperresponsiveness. The secondary actions and effects depend on the dose administered. They act on obstruction within 30 minutes and last a maximum of 4 to 8 hours.
- They do not act in the early stage. When used for prophylaxis, they inhibit the later stage. They correct or diminish the bronchial inflammation and hyperresponsiveness of the chronic stage.
- Inhaled drugs are most effective in preventing asthma. For the oral route, they are used in cases of severe chronic asthma and as a complement in the treatment of acute bouts. Intravenous administration is indicated in moderate or severe bouts, until it is replaced by short oral cycles (morning doses) for periods of 5 to 7 days.
- In long-term treatment, small doses of 440 $\mu\text{g}/\text{day}$ are inhaled in the morning. In severe cases, the dose may be increased to 800-1,200 $\mu\text{g}/\text{day}$ and even 1,500 $\mu\text{g}/\text{day}$, preferably in divided doses, the last of which is administered before 3:00 p.m. with a spacer or inhalant bottle.
- Secondary effects from the inhaled route concerning the hypothalamus hypophysis axis are most frequently found with doses greater than 800 to 1,000 $\mu\text{g}/\text{day}$.

- Dysphonia from pharyngeal candidiasis decreases significantly when the spacer or inhalant bottle is used and with gargling after the dosage is taken.
- If bronchodilators are used in conjunction with inhaling, then inhaling should follow bronchodilation.
- Because of multiple secondary effects, oral therapy is recommended only for severe chronic patients and ideally under expert supervision.
- Inhaled corticosteroids are generally indicated for prophylaxis in severe and moderate chronic asthma; IV and oral corticosteroids are indicated in asthma attacks and the later phase and oral corticosteroids for severe uncontrolled chronic asthma. Short cycles are recommended during attacks.
- The most common corticosteroids used in the IV route are methylprednisolone and hydrocortisone; in the oral route, prednisone and prednisolone; when inhaled such as with the Rotahaler system, beclomethasone, budesonide, and flunisolone are indicated.

c.5) Sodium cromoglycate

- Cromoglycate is non-bronchodilator with prophylactic action that inhibits the precocious and later stages.
- It prevents exercise-induced asthma.
- It prevents bronchial hyperresponsiveness at the basal level.
- Therefore, it is indicated for treating chronic asthma in children, specifically to prevent attacks and not to treat symptoms.
- It is available in aerosol or capsules for nebulization.
- Its action is evident after 8-12 weeks of continuous use.
- It should be used in aerosol with the spacer or plastic bottle. With children under 3, a nebulizer is used.
- Its use should not be suspended if attacks occur.
- Some unusual secondary effects include painful skin in 2% of the cases, pharyngeal irritation and cough in 10 to 20%, bronchoconstriction in very rare cases, as well as urticaria, dermatitis, myositis, Löffler's syndrome, and anaphylaxis.

c.6) Ketotifen

- This is a prophylactic drug for oral administration that inhibits eosinophil flow and degranulation in the lungs, in particular, and possibly the activation of other cells.
- Its use is indicated in small children with chronic moderate asthma. In pollen-induced rhinitis, it should be introduced 2-3 months before the pollen season and suspended after the season has passed.

- Its action takes effect after 4-12 weeks of use.
- It tends to be used to modify the physiopathology in the chronic phase rather than to treat symptoms.
- It is more effective in children than in adults.
- Its use should not be suspended if attacks occur.
- The secondary effects are mild and few.
- It should not be used in conjunction with antihistamines or sedatives.
- Drowsiness is common but tends to subside after the first few weeks of use.
- It may lead to weight gains in the first 3 months of treatment.

c.7) Atropines

- Atropines are anticholinergics that compete with acetylcholine and act against bronchospasm in the broad-gauge bronchi of the central passages.
- The most common is ipratropium bromide in aerosol or nebulizer.
- It is indicated in asthma with obstruction of the central airways, especially in children under 6 years. In combination with β_2 -agonists, it boosts central and peripheral bronchodilation.
- It is most useful for chronic asthma and severe attacks.

d) Educating the patient and family

d.1) Objectives

Every asthmatic patient needs to know the following information:

- Asthma is a chronic disease with asymptomatic periods that may present undetected obstruction and inflammation which gradually worsens.
- The disease should be treated and controlled regularly.
- The patient's environment should be free from animals, gases, vapors, combustion, aerosols, smoke (from cigarettes and car exhaust), humidity, feathers (in pillows, mattresses, comforters, or blankets), paints, factory smoke, and humidifiers.
- Efforts should be made to eliminate house dust and, as much as possible, to keep the home clean and free from objects that accumulate dust. The room should be kept as bare as possible. Ideally, a mattress should not be used. Instead, a cot is recommended with a sleeping bag, which should be washed along with the blankets every 15 days at 55° C. Alternatively, the mattress should be hermetically sealed in plastic or with a plastic sheet.
- Abrupt changes in temperature or humidity should be avoided. Rainy and cloudy weather should be avoided, or if it is unavoidable the mouth and nose should be

covered with a handkerchief or scarf.

- Processed food and non-prescribed drugs should be avoided.
- The decision to suspend or continue treatment should be based on whether the disease has progressed successfully and should be made only by the treating physician, not by the family.
- Dosage levels, schedules, the route of administration, and the secondary effects involved should be well understood and strictly observed.
- When viral infections that precipitate asthma are present, physician's instructions should be followed immediately.
- Complete vaccinations should be received as appropriate for the patient's age.
- Efforts should be made to avoid exposure to factors precipitating symptoms, or when exposure is inevitable (stress, surgery, contact with animals), to take prior preventive action.
- Exercise and sports are necessary for good development and should therefore not be discontinued. The physician should recommend how to prevent symptoms and improve the condition.
- If a device to measure PEF is available, the patient should learn to use it and base decisions on the readings.

d.2) Respiratory reeducation

An asthmatic child should be taught to:

- decrease nasal obstruction;
- control cough;
- improve spasm with prolonged expirations and inspirations;
- use the breathing technique required for the aerosols and the technique for performing PEF;
- expectorate without spasmodic coughing through accelerated exhaling with the mouth remaining open;
- perform exercises that help to improve breathing or prevent thoracic dysfunction, including abdominal breathing to improve diaphragm movement, and those that correct or improve kyphosis.

d.3) Aerosol inhalation techniques

- Have child expectorate prior to inhalation.
- Shake container and remove cover.
- Insert the aerosol inhaler through a hole previously made in the bottom of the spacer or bottle.

- Place the top of the spacer or bottle in the patient's mouth and press the button on the aerosol inhalant.
- Have child breathe as slowly as possible for 5 or 6 cycles. The child should take a long deep breath and hold it for 10 seconds before exhaling.
- The procedure should be repeated the number of times indicated by the physician. In children under 3 years of age, a plastic face mask can be placed over the bottle and the child can be allowed to take 5 or 6 normal breaths at his or her normal pace. The same type of mask used with nebulizers is required but with the holes sealed.
- The same technique can be used with aerosol inhalers of β_2 -agonists, corticosteroids, and sodium cromoglycate.

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