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Asthma Therapy Guidelines

Asthma is a chronic inflammatory disease of the lungs characterized by reversible airway obstruction. This obstruction is caused by a reduction in size of the bronchi and bronchioles. Asthma symptoms include dyspnea, wheezing, and cough. Acute asthma attacks can be induced by allergens, exercise, respiratory infection, stress, or other factors. It is estimated that nearly 18 million Americans have been diagnosed with asthma in their lifetime. Asthma accounts for nearly 2 million emergency room visits each year. Each day, 14 Americans die of asthma. [1]

The goals of asthma therapy include: [2]

1) Prevent chronic and troublesome symptoms.
2) Maintain a near normal pulmonary function.
3) Maintain normal activity levels.
4) Prevent recurrent exacerbations of asthma and minimize need for hospitalization and emergency room visits.
5) Provide optimal therapy with minimal or no adverse effects.
6) Meet the patients' and families' expectations and satisfaction with asthma care.

A stepwise approach to asthma therapy is recommended by most treatment guidelines. In this step-wise approach, the dose, frequency, and administration of medications are increased based on the severity of the patient's asthma. A patient is initially assigned to the most severe step at which any of the defining symptoms occur.

Asthma Treatment Steps [2]

Step 1 patients would be classified as having ***mild intermittent asthma***. Mild intermittent asthma means that the patient has symptoms less than twice a week, and suffers nighttime symptoms less than twice a month. The step 1 patient suffers only brief exacerbations of asthma. Step 1 patients have a FEV_1 and PEF of greater than 80 percent of predicted values with less than 20 percent variation in these values. Treatment of mild intermittent asthma includes the use of short-acting $beta_2$-agonists for relief of symptoms on an as-needed basis.

Step 2 patients would be classified as having ***mild persistent asthma***. These patients have symptoms greater than twice a week, but do not have daily symptoms. These patients may also have nighttime symptoms more than twice a month. Exacerbations of symptoms may affect patient activity. These patients FEV_1 and PEF are still greater than 80 percent of predicted values, but can vary 20 to 30 percent. Patients with mild persistent asthma should be treated with daily anti-inflammatory medication. Low dose inhaled corticosteroids are the drug of choice; however, cromolyn or nedocromil can be considered. Leukotriene modifiers may be another option, but they have not been shown to be as effective as corticosteroids in reducing inflammatory symptoms.[3,4] Sustained release theophylline can also be utilized but is not preferred due to potential toxicities and the need for close monitoring. All patients with mild persistent asthma should also have access to an inhaled $beta_2$-agonist for quick relief of symptoms not otherwise controlled.

Step 3 patients would be classified as having ***moderate persistent asthma***. Step 3 patients have daily symptoms if not treated. These patients have exacerbations of symptoms at least twice weekly and these exacerbations may affect daily activities. These patients often have nighttime symptoms more than once a week. Step 3 patients= FEV_1 or PEF range between 80 percent and 60 percent of expected values. Moderate persistent asthma should be treated with a daily-inhaled corticosteroid at a low to medium dose. These patients also require other daily medications in a step-up therapy approach. The daily-inhaled corticosteroid dose can be increased or a long-acting $beta_2$-agonist can be added to treat symptoms. Leukotriene modifiers or theophylline can also be considered as additive therapy options. Step 3 patients also require access to a short-acting $beta_2$-agonist for quick-relief/rescue from symptoms.

Step 4 patients are defined as having ***severe persistent asthma***. Patients with severe asthma have continual symptoms, which limit physical activity, and have frequent exacerbations and nighttime symptoms. A decrease in FEV_1 or PEF of greater than 60 percent occurs in severe asthma. Severe asthma must be treated with daily oral inhaled corticosteroids, the addition of long-acting $beta_2$-agonists, and/or the addition of theophylline or leukotriene modulators. Patients with severe asthma still require a short-acting $beta_2$-agonist for rescue medication. Severe asthma patients may also require oral steroids on a long-term basis if needed to control symptoms.

In each step of treatment, **patient education** is critical. How to use MDIs is an important component of patient education. Patients should be advised to avoid

allergens, irritants, or factors that exacerbate their asthma. Proper use of medications should be assessed frequently. Patient quality of life, ability to perform daily tasks, and use of rescue medication should also be assessed at each visit. Daily use of a peak flow meter can be useful to asthma patients to assist with monitoring for signs of asthma exacerbation. Peak flow monitoring provides a simple, quantitative, reproducible measure of airway obstruction for patients and doctors to help assess asthma. Peak flow monitoring is recommended in all patients with moderate to severe asthma.[2]

Stepwise Approach to Managing Asthma in Patients Older than 5 Years of Age [2,5,6]

Step	Medications
Step 1- Mild Intermittent Asymptoms # 2 times per week \night-time symptoms # 2 times per month Abrief exacerbations \$FEV$_1$ or PEF $ 80% of predicted with a variation of # 20 %	***Daily Medications*** Ano long-term control medications needed Ause quick-relief medicationsCshort-acting beta2-agonists (preferred)
Step 2- Mild Persistent \symptoms $ 2 times a week but # 1 time a day \night-time symptoms $ 2 times a month Aexacerbations may affect activities \$FEV$_1$ or PEF $ 80% but with a variation in PEF of 20-30 %	***Daily Medications*** Alow dose inhaled corticosteroids (preferred) \leukotriene modifiers, theophylline, nedocromil or cromolyn may also be considered + Aquick-relief medication as needed
Step 3- Moderate Persistent Adaily symptoms \night-time symptoms $ 1 time a week Aexacerbation affects activity \ FEV$_1$ or PEF $ 60- # 80% predicted with variation of $ 30% in PEF	***Daily Medications*** \ inhaled corticosteroids (low to medium dose) PLUS inhaled long-acting beta2-agonist \leukotriene modifiers or theophylline may also be considered in place of or along with long-acting beta2-agonist + Aquick-relief medication as needed
Step 4- Severe Persistent Acontinual symptoms Alimitations to activity \frequent exacerbations and night-time symptoms \$FEV$_1$or PEF # 60% with PEF variation of $ 30%	***Daily Medications*** \inhaled corticosteroids (medium to high dose) PLUS inhaled long-acting beta2-agonist \leukotriene modifiers or theophylline again may be considered + \oral systemic corticosteroids as needed for exacerbations and quick-relief medication as needed
All asthma patients should have quick-relief medications available for symptoms not otherwise controlled. Short-acting beta2-agonists preferred. Use of short-acting inhaled medications on a daily base or with increased frequency may indicate the need for a step-up in treatment.	
If control of symptoms is not maintained.	Consider if patient has been controlled long term at one level.

*Devices can be used to aide in delivery of medication, such as spacers and nebulizers.

Short-acting beta$_2$-agonists are used as needed to treat symptoms of mild intermittent asthma or for quick-relief/rescue as needed. Daily use of these agents is not generally recommended. Beta$_2$-agonists work as bronchodilators. If beta$_2$-agonists are being utilized daily or more than one inhaler is being used per month a step-up in therapy may be indicated. Beta$_2$-agonists are the drug of choice for acute bronchospasm. Beta$_2$-agonists include albuterol (Proventil[7], Ventolin[7]), bitolterol (Tornalate[7]_, pirbuterol (MaxairJ), levalbuterol (Xopenex[7]) and terbutaline (Brethaire[7]), and metaproterenol (Alupent[7]).

Anticholinergics are indicated for use in the relief of acute bronchospasm. Ipratropium bromide (Atrovent[7]) can be used along with beta$_2$-agonists and may have additive effects, however; use in long-term management of asthma has not been demonstrated.[2] Ipratopium can also be considered in patients who cannot tolerate beta$_2$-agonists. Prescribers should remember that ipratropium does have a slower onset of action than short-acting beta$_2$-agonists.

Corticosteroids are used to treat asthma for their anti-inflammatory properties. Oral systemic corticosteroids should only be used in moderate to severe asthma to control exacerbations. Inhaled corticosteroids are the most effective long-term-control medication for asthma. Long-term use of corticosteroids has been shown to reduce symptoms and improve pulmonary function in patients with asthma.[3] Currently there are several oral inhaled corticosteroid products available; they include beclomethasone (Beclovent[7], Vanceril[7]), budesonide (Pulmicort[7]), fluticasone (Flovent[7]), triamcinolone acetonide (Azmacort[7]), and flunisolide (Aerobid[7]).

Cromolyn and nedocromil are indicated for the treatment of mild or moderate asthma. These are often used as an alternative for corticosteroids especially in children, because of their adverse effect profile. These drugs inhibit the asthmatic response to allergens and exercise-induced bronchospasm. Cromolyn is currently available as Intal[7] pulmonary aerosol or over-the-counter Nasalcrom[7] nasal spray. Nedocromil is available as Tilade[7] oral inhalation aerosol.

Long-acting beta$_2$-agonists are used as an adjunct to anti-inflammatory therapy in the long-term treatment of asthma symptoms. They are especially beneficial in preventing nocturnal bronchospasm. Long-acting beta$_2$-agonists should NOT be used to treat acute asthma symptoms, exacerbations, or to replace anti-inflammatory treatment. These agents have an onset of 15 to 30 minutes and duration of action of greater than 12 hours.[2] Agents currently available in this class include: salmeterol (Serevent[7]), formoterol (Foradil[7]), and sustained-release albuterol tablets.

Leukotriene modifiers are indicated for the long-term control and prevention of symptoms of asthma. These drugs also demonstrate anti-inflammatory effects. They have not been shown to be as effective as inhaled corticosteroids in reducing symptoms and exacerbations of asthma and should not be considered as a replacement for inhaled corticosteroids.[3,4] Currently there are three leukotriene modifying agents available: montelukast (Singulair[7]), zafirlukast (Accolate[7]), and zileuton (Zyflo[7].)

Theophylline is used to control and prevent symptoms of asthma. Theophylline is a bronchodilator. Theophylline use should be coupled with close monitoring because of toxicities. Signs of toxicity include nausea, vomiting, anxiety, headache and abdominal discomfort. Theophylline concentrations should be maintained in the range of 5-15 mg/L. Theophylline also has numerous side effects and drug interactions that must be recognized.

Systemic corticosteroids are indicated for short-term (3-10 day) burst therapy to control exacerbations of asthma not otherwise controlled or for long-term control of symptoms after all other treatments fail. Systemic corticosteroids (prednisone, prednisolone, and methylprednisolone) should be used at the lowest effective dose and for a limited time. Patients with severe asthma may require long-term use of oral systemic corticosteroids to control symptoms and prevent exacerbations.

In general **antibiotics** are not recommended for the treatment of acute asthma unless indicated for other comorbid conditions i.e. pneumonia, bacterial sinusitis, or otitis media.[6]

As in any therapy, treatment should be on an individual patient basis. Control of symptoms should be attempted as quickly as possible; then, treatment should be decreased to the minimum medication necessary to maintain control. Gaining control may be accomplished by either starting treatment at the step most appropriate to the initial severity of their condition, or by starting at a higher level of therapy (a course of systemic corticosteroids or higher dose of inhaled corticosteroids). A rescue course of systemic corticosteroid may be necessary at any time and step to control asthma symptoms and/or exacerbations. In general, use of short-acting beta2-agonist on a daily basis indicates the need for additional long-term-control therapy. Healthcare providers should also remember that patient education is critical at every step of treatment to gain effective asthma control.

Please send comments and suggestions regarding this newsletter to Jayne Zemmer,DUR Coordinator, Division of Medical Services, P.O. Box 6500 Jefferson City, MO 65102-6500

Resources

1. Asthma and AllergiesCAsthma Facts. Asthma and Allergy Foundation of America. Available from: URL: http://www.aafa.org/templ/display.cfm\ Accessed on June 10, 2002.
2. National Asthma Education and Prevention Program Expert Panel Report II, Guidelines for the Diagnosis and Management of Asthma. National Institutes of Health. Available from: URL: http://www.nhlbi.nih.gov Accessed on June 10, 2002.

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4. Meltzer EO, Lockey RF, Friedman BF, et al. Efficacy and Safety of Low-Dose Fluticasone Propionate Compared With Montelukast for Maintenance Treatment for Persistent Asthma. Mayo Clinic Proceedings. 2002;77(5):437-445.
5. Health Care Guideline. Diagnosis and Management of Asthma. Institute for Clinical Systems Improvement. Available from: URL : http://www.nhlbi.nih.gov/guideline/asthma Accessed on June 10, 2002.
6. Executive Summary of the NAEPP Expert Panel Report. Guidelines for the Diagnosis and Management of Asthma-Update on Selected Topics 2002. National Institutes of Health. Available from URL: http://www.nhlbi.nih.gov Accessed on June 13, 2002.

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Top Ten Products Ranked by Amount Paid
06/2001 to 05/2002

DRUG CLASS/DRUG	PAID
OLANZAPINE	$48,454,257
RISPERIDONE	$26,158,457
CELECOXIB	$16,489,686
ATORAVASTATIN	$13,306,290
GABAPENTIN	$13,136,997
QUETIAPINE	$13,076,204
DIVALPROATE	$13,060,558
SERTRALINE	$13,016,014
PAROXETINE	$12,644,908
OXYCODONE	$12, 387,305
TOTALS	$181,730,675

TOP TEN PRODUCTS RANKED BY NUMBER OF PRESCRIPTIONS
06/2001 TO 05/2002

DRUG CLASS/DRUG	NUMBER OF PRESCRIPTIONS
FUROSEMIDE	317,535
HYDROCODONE/APAP	296,315
AMOXICILLIN	282, 766
POTASSIUM SUPPLEMENTS	258,007
LEVOTHYROXINE	246,350

RANITIDINE	**231,967**
ALBUTEROL: METERED DOSE	**207,607**
AZITHROMYCIN	**199,760**
PROPOXYPHENE/APAP	**197,249**
SERTRALINE	**184,967**
TOTALS	**2,422,523**