**ASTHMA**

Asthma is a disease of the human respiratory system in which the airways narrow, often in response to a “trigger” such as exposure to an allergen, cold air, exercise, or emotional stress. This narrowing causes symptoms such as wheezing, shortness of breath, chest tightness, and coughing, which are the hallmarks of asthma. Between episodes, most patients feel fine.

The disorder is a chronic inflammatory condition in which the airways develop increased responsiveness to various stimuli, characterized by bronchial hyper-responsiveness, inflammation, increased mucus production, and intermittent airway obstruction. The symptoms of asthma, which can range from mild to life threatening, can usually be controlled with a combination of drugs and lifestyle changes.

Public attention in the developed world has recently focused on asthma because of its rapidly increasing prevalence, affecting up to one in four urban children. Susceptibility to asthma can be explained in part by genetic factors, but no clear pattern of inheritance has been found. Asthma is a complex disease that is influenced by multiple genetic, developmental, and environmental factors, which interact to produce the overall condition.

**Frequency**

Asthma affects 5-10% of the population or an estimated 14-15 million persons, including 5 million children. The prevalence rate of EIA is 3-10% of the general population if persons who do not have asthma or allergy are excluded, but the rate increases to 12-15% of the general population if patients with asthma are included. The rate of exercise-induced symptoms in persons with asthma has been reported to vary from 40-90%.

Asthma is common in industrialized nations such as Canada, England, Australia, Germany, and New Zealand, where much of the data have been collected. The prevalence rate of severe asthma in industrialized countries ranges from 2-10%. Recent trends suggest an increase in both the prevalence and morbidity of the disease, especially in children younger than 6 years. Factors that have been implicated include urbanization, air pollution, passive smoking, and change in exposure to environmental allergens.

The estimate of lost work and school time is approximately 100 million days of restricted activity. More than 1.8 million emergency department evaluations occur annually. The latest figures from the 1997 National Institutes of Health report indicate an estimated 500,000 hospitalizations and 5000 deaths annually. International asthma mortality is reported as high as 0.86 deaths per 100,000 persons in some countries. Mortality is primarily related to lung function, with an 8-fold increase in patients in the lowest quartile, but has also been linked with management failure, especially in young persons. Other factors that impact mortality include age older than 40 years, cigarette smoking greater than 20-pack years, blood eosinophilia, forced expiratory volume in one second (FEV1) of 40-69% predicted, and greater reversibility.

EIA has not been reported to cause death. Morbidity is associated with exercise limitation. This is observed most dramatically in elite athletes with high levels of exercise who may be limited by airway hyperreactivity.

Asthma predominantly occurs in boys in childhood, with a male-to-female ratio of 2:1 until puberty, when the male-to-female ratio becomes 1:1.

Asthma prevalence is greater in females after puberty, and the majority of adult-onset cases diagnosed in persons older than 40 years occur in females.

Boys are more likely than girls to experience a decrease in symptoms by late adolescence.

Asthma prevalence is increased in very young persons and very old persons because of airway responsiveness and lower levels of lung function. Two thirds of all asthma cases are diagnosed before the patient is aged 18 years. Approximately half of all children diagnosed with asthma have a decrease or disappearance of symptoms by early adulthood.

The diagnosis of EIA is made more often in children and young adults than in older adults and is related to high levels of physical activity. It can be observed in persons of any age based on the level of underlying airway reactivity and the level of physical exertion.

**Classification**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   | Mild Intermittent | Mild Persistent | Mod Persistent | Severe Persistent |
| Symptoms | < 2 / week | > 2 / week | Daily | Continual |
| Night sx | < 2 / month | > 2 / month | > 1 / week | Frequent |
| FEV1 | > 80% predicted | > 80%predicted | 60-80% | < 60% |
| Peak flow Variability | < 20% | 20-30% | > 30 % | > 30% |

**Pathophysiology**

***1. Bronchoconstriction***

During an asthma episode, inflamed airways react to environmental triggers such as smoke, dust, or pollen. The airways narrow and produce excess mucus, making it difficult to breathe.

In essence, asthma is the result of an abnormal immune response in the bronchial airways. The airways of asthmatics are “hypersensitive” to certain triggers, also known as stimuli. In response to exposure to these triggers, the bronchi (large airways) contract into spasm (an “asthma attack”). Inflammation soon follows, leading to a further narrowing of the airways and excessive mucus production, which leads to coughing and other breathing difficulties.

There are seven categories of stimuli:

* allergens, typically inhaled, which include waste from common household insects, such as the house dust mite and cockroach, grass pollen, mould spores and pet epithelial cells;
* medications, including aspirin and β-adrenergic antagonists (beta blockers);
* air pollution, such as ozone, nitrogen dioxide, and sulfur dioxide, which is thought to be one of the major reasons for the high prevalence of asthma in urban areas;
* various industrial compounds and other chemicals, notably sulfites; chlorinated swimming pools generate chloramines - monochloramine (NH2Cl), dichloramine (NHCl2) and trichloramine (NCl3) - in the air around them, which are known to induce asthma;
* early childhood infections, especially viral respiratory infections;
* exercise, the effects of which differ somewhat from those of the other triggers; and
* emotional stress, which is poorly understood as a trigger.

***2. Bronchial inflammation***

The mechanisms behind allergic asthma—i.e., asthma resulting from an immune response to inhaled allergens—are the best understood of the causal factors. In both asthmatics and non-asthmatics, inhaled allergens that find their way to the inner airways are ingested by a type of cell known as antigen presenting cells, or APCs. APCs then “present” pieces of the allergen to other immune system cells. In most people, these other immune cells (TH0 cells) “check” and usually ignore the allergen molecules. In asthmatics, however, these cells transform into a different type of cell (TH2), for reasons that are not well understood. The resultant TH2 cells activate an important arm of the immune system, known as the humoral immune system. The humoral immune system produces antibodies against the inhaled allergen. Later, when an asthmatic inhales the same allergen, these antibodies “recognize” it and activate a humoral response. Inflammation results: chemicals are produced that cause the airways to constrict and release more mucus, and the cell-mediated arm of the immune system is activated. The inflammatory response is responsible for the clinical manifestations of an asthma attack. The following section describes this complex series of events in more detail.

***3. The immune response***

When an inhaled antigen becomes trapped in the airways, it is enzymatically degraded into shorter peptides by APCs such as dendritic cells. APCs express the peptides derived from the antigen on the cell surface, in what is known as the binding groove of the class II major histocompatiblity complex (MHC) molecule. Now located on the cell surface, the antigen-MHC complex is presented to T cells, which express a receptor that is specific to the MHC II peptide.

Presented with the antigen-MHC II complex, T helper 0 (TH0) cells become activated and start to differentiate into either T helper type 1 (TH1) or type 2 (TH2) cells. The selective differentiation of TH0 cells has profound consequences for the immune system: TH1 cell production leads to cell-mediated immunity, while the production of predominantly TH2 cells provides humoral immunity. The resulting balance of TH1 or TH2 cells is a crucial variable in the development of asthma; the dominance of the TH2 cell type appears to be necessary for the development of asthma. In one study, mice that lacked the ability to create TH1 cells displayed an asthma-like phenotype. The variables that decide the fate of TH1 vs. TH2 cells are not well understood, but depend on many factors, including childhood exposure to infectious agents and the cytokines elicited by those agents.

One cytokine secreted by TH2 cells—IL-4—combined with the action of other cytokines induces synthesis by antigen-stimulated B cells of IgE, an allergen-specific antibody. IgE binds allergens and then receptors on mast cells, basophils, and eosinophils in the airway epithelium. Subsequent exposure of the same antigen to these cells in the airway epithelium initiates the acute-phase reaction of asthma. Stimulated mast cells in the airway release preformed granules of mediators such as histamine, eicosanoids, and cytokines. These molecules are responsible for the symptoms of asthma. They affect the mucosa of the airways, increasing mucosal edema, and mucus production, smooth muscle constriction, and recruit other immune cells, thereby exacerbating the reaction.

The late phase of an asthmatic reaction is characterized by an influx of inflammatory and immune cells during the first several hours after antigen exposure. These cells—particularly eosinophils—secrete a series of cytokines, leukotrienes, and polypeptides, which contribute to hyperresponsiveness, mucus secretion, bronchoconstriction, and sustained inflammation.

* **Pathogenesis**

The fundamental problem in asthma appears to be immunological: young children in the early stages of asthma show signs of excessive inflammation in their airways. Epidemiological findings give clues as to the pathogenesis: the incidence of asthma seems to be increasing worldwide, and asthma is now very much more common in affluent countries.

One theory of pathogenesis is that asthma is a disease of hygiene. In nature, babies are exposed to bacteria and other antigens soon after birth, “switching on” the TH1 lymphocyte cells of the immune system that deal with bacterial infection. If this stimulus is insufficient—as it may be in modern, clean environments—then TH2 cells predominate, and asthma and other allergic diseases may develop. This “hygiene hypothesis” may explain the increase in asthma in affluent populations. The TH2 lymphocytes and eosinophil cells that protect us against parasites and other infectious agents are the same cells responsible for the allergic reaction. In the developed world, these parasites are now rarely encountered, but the immune response remains and is wrongly triggered in some individuals by certain allergens.

Another theory is based on the correlation of air pollution and the incidence of asthma. Although it is well known that substantial exposures to certain industrial chemicals can cause acute asthmatic episodes, it has not been proved that air pollution is responsible for the development of asthma. In Western Europe, most atmospheric pollutants have fallen significantly over the last 40 years, while the prevalence of asthma has risen.

**Physical**

* General

Evidence of respiratory distress manifests as increased respiratory and cardiac rates, diaphoresis, and use of accessory muscles of respiration.

Marked weight loss or severe wasting may indicate severe emphysema.

Pulsus paradoxus: This is an exaggerated fall in systolic blood pressure during inspiration and may occur during an acute asthma exacerbation.

Depressed sensorium: This finding suggests a more severe asthma exacerbation with impending respiratory failure.

* Chest examination

End-expiratory wheezing or a prolonged expiratory phase is found most commonly, although inspiratory wheezing can be heard.

Diminished breath sounds and chest hyperinflation may be observed during acute exacerbations.

The presence of inspiratory wheezing or stridor may prompt an evaluation for an upper airway obstruction such as vocal cord dysfunction, vocal cord paralysis, thyroid enlargement, or a soft tissue mass (eg, malignant tumor).

Upper airway

Look for evidence of erythematous or boggy turbinates or the presence of polyps from sinusitis, allergic rhinitis, or upper respiratory infection.

Any type of nasal obstruction may result in worsening of asthma or symptoms of EIA.

* Skin

Observe for the presence of atopic dermatitis, eczema, or other manifestations of allergic skin conditions.

 **CLINICAL**

**History**

A detailed medical history should address

1) whether symptoms are attributable to asthma,

2) whether findings support the likelihood of asthma (eg, family history),

3) asthma severity,

4) the identification of possible precipitating factors.

Symptoms may include the following:

* Cough
* Wheezing
* Shortness of breath
* Chest tightness
* Sputum production

Symptom patterns can vary as follows:

* Perennial versus seasonal
* Continual versus episodic
* Duration, severity, and frequency
* Diurnal variations (nocturnal and early-morning awakenings)

Precipitating or aggravating factors, also discussed in Causes, may include the following:

* Allergens
* Occupation
* Medications
* Exercise

Disease development variables include the following:

* Age at onset
* History of injury early in life due to infection or passive smoke exposure
* Progress of disease
* Current response to management
* Comorbid conditions

Family history may reveal the following conditions:

* Asthma
* Allergy
* Sinusitis
* Rhinitis

Social history may reveal the following conditions:

* Home characteristics
* Smoking
* Workplace or school characteristics
* Educational level
* Employment
* Social support
* Determine the profile of a typical exacerbation.

The impact on the patient and family may have involved the following:

* Emergency department visits, hospitalizations, intensive care unit (ICU) admissions, intubations
* Missed days from work or school or activity limitation
* Assess the patient's disease perception based on the following elements:
* Knowledge of asthma and treatment
* Use of medications
* Coping mechanisms
* Family support

**Lab Studies:**

Laboratory studies are not routinely indicated for asthma but may be used to exclude other diagnoses.

Eosinophilia greater than 4% or 300-400/mL supports the diagnosis of asthma, but an absence of this finding is not exclusionary. Eosinophil counts greater than 8% may be observed in patients with concomitant atopic dermatitis, but this finding should prompt an evaluation for allergic bronchopulmonary aspergillosis, Churg-Strauss syndrome, or eosinophilic pneumonia.

Total serum immunoglobulin E levels greater than 100 IU are frequently observed in patients experiencing allergic reactions, but this finding is not specific for asthma and may be observed in patients with other conditions (eg, allergic bronchopulmonary aspergillosis, Churg-Strauss syndrome). A normal total serum immunoglobulin E level does not exclude the diagnosis of asthma.

**Imaging Studies:**

In most patients, chest radiography findings are normal or indicate hyperinflation. Findings may help rule out other pulmonary diseases such as allergic bronchopulmonary aspergillosis or sarcoidosis, which can manifest with symptoms of reactive airway disease.

Sinus CT scan may be useful to help exclude acute or chronic sinusitis as a contributing factor. In patients with chronic sinus symptoms, a CT scan of the sinuses can also help rule out chronic sinus disease.

**Other Tests:**

Allergy skin testing is a useful adjunct in individuals with atopy. Results help guide indoor allergen mitigation or help diagnose allergic rhinitis symptoms.

In patients with reflux symptoms and asthma, 24-hour pH monitoring can help determine if gastroesophageal reflux disease is a contributing factor.

**Procedures:**

* Pulmonary function testing (spirometry)

Perform spirometry measurements before and after inhalation of a short-acting bronchodilator in all patients in whom the diagnosis of asthma is considered. Spirometry measures the forced vital capacity, the maximal amount of air expired from the point of maximal inhalation, and the FEV1. A reduced ratio of FEV1 to forced vital capacity, when compared with predicted values, demonstrates the presence of airway obstruction. Reversibility is demonstrated by an increase of 12% or 200 mL after administration of a short-acting bronchodilator.

The diagnosis of asthma cannot be based on spirometry findings alone because many other diseases are associated with obstructive spirometry indices.

As a preliminary evaluation for EIA, perform spirometry in all patients with exercise symptoms to determine if any baseline abnormalities (ie, the presence of obstructive or restrictive indices) are present.

* Methacholine- or histamine-challenge testing

Bronchoprovocation testing with either methacholine or histamine is useful when spirometry findings are normal or near normal, especially in patients with intermittent or exercise-induced symptoms. Bronchoprovocation testing helps determine if hyperreactive airways are present, and a negative test result usually excludes the diagnosis of asthma.

Trained individuals should perform this testing in an appropriate facility and in accordance with the guidelines of the American Thoracic Society published in 1999. Methacholine is administered in incremental doses up to a maximum dose of 16 mg/mL, and a 20% decrease in FEV1 is considered a positive test result for the presence of bronchial hyperresponsiveness. The presence of airflow obstruction with an FEV1 less than 65-70% at baseline is generally an indication to not perform the test.

* Exercise testing

Exercise spirometry is the standard method for evaluating patients with EIA. Testing involves 6-10 minutes of strenuous exertion at 85-90% of predicted maximal heart rate and measurement of postexercise spirometry for 15-30 minutes. The defined cutoff for a positive test result is a 15% decrease in FEV1 after exercise.

Exercise testing may be accomplished in 3 different ways, using cycle ergometry, a standard treadmill test, or free running exercise. This method of testing is limited because laboratory conditions may not subject the patient to the usual conditions that trigger EIA symptoms, and results have a lower sensitivity compared with other methods.

* Eucapnic hyperventilation

Eucapnic hyperventilation with either cold or dry air is an alternate method of bronchoprovocation testing.

It has been used to evaluate patients for EIA and has been shown to produce results similar to those of methacholine-challenge testing.

* Peak-flow monitoring

Peak-flow monitoring is designed for ongoing monitoring of patients with asthma because the test is simple to perform and the results are a quantitative and reproducible measure of airflow obstruction.

It can be used for short-term monitoring, exacerbation management, and daily long-term monitoring.

Results can be used to determine the severity of an exacerbation and to help guide therapeutic decisions.

* Guidelines for the use of peak-flow meters are as follows:

1. Advise the patient to use the peak-flow meter upon awakening in the morning before using a bronchodilator.

2. Instruct the patient on how to establish a personal best peak expiratory flow (PEF) rate.

3. Inform the patient that a peak flow of less than 80% of the patient's personal best indicates a need for additional medication and a peak flow below 50% indicates severe exacerbation.

4. Advise the patient to use the same peak-flow meter over time.

**Diagnosis and natural history**

The diagnosis of asthma is a clinical one; there is no confirmatory diagnostic blood test, radiographic or histopathological investigation. In some people, the diagnosis can be corroborated by suggestive changes in lung function tests.

The International Consensus Report describes asthma as *.a chronic inflammatory disorder of the airways .. in susceptible individuals, inflammatory symptoms are usually associated with widespread but variable airflow obstruction and an increase in airway response to a variety of stimuli. Obstruction is often reversible, either spontaneously or with treatment.*.

**Diagnosis of asthma in adults**

Some of the symptoms of asthma are shared with diseases of other systems. Even when the symptom of breathlessness is thought to be due to lung disease, there are numerous relatively common lung diseases and differentiation of an airway disorder needs to be made from both infections, and pulmonary thromboembolic disease and restrictive lung disorders. Features of an airway disorder such as cough, wheeze and breathlessness should be corroborated where possible by measurement of airflow limitation. They may be due either to a localised airway obstruction (e.g. tumour, foreign body, vocal cord dysfunction or post tracheostomy stenosis), or to a generalised problem (such as asthma, chronic obstructive airways disease (COPD), bronchiectasis, cystic fibrosis or obliterative bronchiolitis).

**TREATMENT**

The goals for successful management of asthma the following:

Achieve and maintain control of symptoms. Prevent asthma exacerbations. Maintain pulmonary function as close to normal levels as possible. Maintain normal activity levels, including exercise. Avoid adverse effects from asthma medications. Prevent the development of irreversible airflow limitation. Prevent asthma mortality.

**MEDICATION**

**Bronchodilators**

Provide symptomatic relief of bronchospasm due to acute asthma exacerbation (short-acting agents) or long-term control of symptoms (long-acting agents). Also used as the primary medication for prophylaxis of EIA. A metered-dose inhaler (MDI) can be used for administration.

Albuterol (Ventolin, Proventil) -- Beta-agonist for bronchospasm. Relaxes bronchial smooth muscle by action on beta-2 receptors, with little effect on cardiac muscle contractility.

Adult Dose PO: 2-4 mg/dose divided tid/qid; not to exceed 32 mg/dMDI: 1-2 puffs q4-6h; not to exceed 12 puffs/d; may use 2-4 puffs q20min for 3 doses to treat an acute exacerbation; a tube spacer is recommended unless the patient can demonstrate excellent technique without itNebulizer: Dilute 0.5 mL (2.5 mg) 0.5% inhalation solution in 1-2.5 mL of NS; administer 2.5-5 mg q4-6h, diluted in 2-5 mL sterile saline or water

Metaproterenol (Alupent, Metaprel) -- Beta-2 adrenergic agonist that relaxes bronchial smooth muscle with little effect on heart rate.

Adult Dose MDI: 2 puffs q4-6h prnNebulizer: 0.3 mL 5% solution diluted in 2.5 mL 0.45% or 0.9% NS, nebulized over 5-15 min q4h

Salmeterol (Serevent) -- Can relieve bronchospasms by relaxing the smooth muscles of the bronchioles in conditions associated with bronchitis, emphysema, asthma, or bronchiectasis. Effect also may facilitate expectoration.Adverse effects are more likely when administered at high doses or more frequent doses than recommended; prevalence of adverse effects is higher. Regular use in patients with EIA associated with smaller decrease in FEV1 during exercise.

Adult Dose MDI: 2 puffs (42 mcg) bidDiskus: 1 puff (50 mcg) bid

Ipratropium (Atrovent) -- Decreases vagal tone in the airways through antagonism of muscarinic receptors and inhibition of vagally mediated reflexes. Chemically related to atropine. Has antisecretory properties and, when applied locally, inhibits secretions from serous and seromucous glands lining the nasal mucosa. Only 50% of patients who are asthmatic bronchodilate with ipratropium and, to a lesser degree, with beta-adrenergic agonists. Used primarily in conjunction with beta-agonists for severe exacerbations. No additive or synergistic effects observed with long-term treatment of asthma.

Adult Dose Nebulizer: 1-dose vial (500 mcg) q2h for acute exacerbationsMDI: 2 puffs qid; not to exceed 12 puffs/d

Theophylline (Slo-bid, Theo-Dur, Uniphyl) -- Mild-to-moderate bronchodilator used as an adjuvant in the treatment of stable asthma and prevention of nocturnal asthma symptoms. Potentiates exogenous catecholamines and stimulates endogenous catecholamine release and diaphragmatic muscular relaxation, which, in turn, stimulates bronchodilation.

Adult Dose 5-8 mg/kg/d initially to maintain concentration in the range of 5-15 mcg/mL; 5.6 mg/kg loading dose (based on aminophylline) IV over 20 min, followed by maintenance infusion of 0.1-1.1 mg/kg/h

**Corticosteroids**

Highly potent agents that are the primary DOC for treatment of chronic asthma and prevention of acute asthma exacerbations. Numerous inhaled corticosteroids are used for asthma and include beclomethasone (Beclovent, Vanceril), budesonide (Pulmicort Turbuhaler), flunisolide (AeroBid), fluticasone (Flovent), and triamcinolone (Azmacort).

Fluticasone (Flovent) -- Alters level of inflammation in airways by inhibiting multiple types of inflammatory cells and decreasing production of cytokines and other mediators involved in the asthmatic response.

Triamcinolone (Azmacort) -- Alters level of inflammation in airways by inhibiting multiple types of inflammatory cells and decreasing production of cytokines and other mediators involved in the asthmatic response.

Adult Dose 2 puffs tid/qid or 4 puffs bid; not to exceed 4 puffs qid for mild persistent or easily controlled moderately severe asthma

Beclomethasone (Vanceril, Beclovent, QVAR) -- Alters level of inflammation in airways by inhibiting multiple types of inflammatory cells and decreasing production of cytokines and other mediators involved in the asthmatic response.

Adult Dose 2 puffs (84 mcg) tid/qid; alternatively, 4 puffs (168 mcg) bidSevere asthma: 12-16 puffs (504-672 mcg)/d; adjust dose downward to response; not to exceed 20 puffs (840 mcg)/dQVAR: 80 and 160 mcg/puff

Prednisone (Deltasone, Orasone, Meticorten) -- Systemic steroidal anti-inflammatory medication. Used primarily for moderate-to-severe asthma exacerbations to speed recovery and prevent late-phase response. May be used long-term to control severe asthma.

Adult Dose 5-60 mg/d PO qd or divided bid/qid; taper over 2 wk as symptoms resolve

Budesonide (Pulmicort Turbuhaler, Rhinocort) -- Inhibits bronchoconstriction mechanisms, produces direct smooth muscle relaxation, and may decrease number and activity of inflammatory cells, which, in turn, decreases airway hyperresponsiveness.

Adult Dose 200-400 mcg via PO inhalation twice initially; may increase to 800 mcg bid

**Mast cell stabilizers**

Prevent the release of mediators from mast cells that cause airway inflammation and bronchospasm. Indicated for maintenance therapy of mild-to-moderate asthma or prophylaxis for EIA.

Cromolyn (Intal) -- Inhibits degranulation of sensitized mast cells following exposure to specific antigens. Attenuates bronchospasm caused by exercise, cold air, aspirin, and environmental pollutants.

Adult Dose Chronic asthma: 2 puffs qidEIA: 2 puffs 15-60 min prior to exercise or exposure

Nedocromil (Tilade) -- Inhibits activation and release of mediators of variety of inflammatory cell types associated with asthma, to include eosinophils, mast cells, neutrophils, and others.

Adult Dose 2 puffs qid (14 mg/d)

The long-term outpatient management of asthma should follow the stepwise therapy model based on the Global Initiative for Asthma guidelines (BTC, 2005).

The pharmacologic treatment of asthma is based on stepwise therapy.

Medications should be added or deleted as the frequency and severity of the patient's symptoms change.

**Step 1:** Intermittent asthma is present.

A controller medication is not needed.

The reliever medication is a short-acting beta-agonist as needed for symptoms.

**Step 2:** Mild persistent asthma is present.

The controller medication is an inhaled corticosteroid (200-500 mcg), cromolyn, nedocromil, or a leukotriene antagonist. If needed, increase the dose of corticosteroid and add a long-acting beta-agonist or sustained-release theophylline, especially for nocturnal symptoms.

The reliever medication is a short-acting beta-agonist as needed for symptoms.

**Step 3:** Moderate persistent asthma is present.

The controller medication is an inhaled corticosteroid (800-2000 mcg) and a long-acting bronchodilator (either beta-agonist or sustained-release theophylline).

The reliever medication is a short-acting beta-agonist as needed for symptoms.

**Step 4:** Severe persistent asthma is present.

The controller medication is an inhaled corticosteroid (800-2000 mcg), a long-acting bronchodilator (beta-agonist and/or theophylline), and long-term oral corticosteroid therapy.

**Management of acute asthma**

Prediction and prevention of a severe asthma attack

Most (88-92%) attacks of asthma severe enough to require hospital admission develop relatively slowly over a period of six hours or more. In one study, over 80% of attacks developed over more than 48 hours.227-232 There should therefore be time for effective action and the potential to reduce the number of attacks requiring hospitalisation. There are many similarities between patients who die from asthma, patients with near fatal asthma and asthmatic controls who are admitted to hospital.

A respiratory specialist should follow up patients admitted with severe asthma for at least one year after the admission.

*Levels of severity of acute asthma exacerbations*



**1. Give high flow oxygen to all patients with acute severe asthma.**

Patients with acute severe asthma are hypoxaemic. This should be corrected urgently using high concentrations of inspired oxygen (usually 40-60%) and a high flow mask such as a Hudson mask. Unlike patients with COPD there is little danger of precipitating hypercapnea with high flow oxygen. Hypercapnea indicates the development of near fatal asthma and the need for emergency specialist/anaesthetic intervention. Oxygen saturations of at least 92% must be achieved.

In view of the theoretical risk of oxygen desaturation while using air driven compressors to nebulise β2-agonist bronchodilators, oxygen-driven nebulisers are the preferred method of delivery in hospitals, ambulances and primary care.

The absence of supplemental oxygen should not prevent nebulised therapy from being administered where appropriate.

In hospital, ambulance and primary care, nebulised β2 agonist bronchodilators should be driven by oxygen.

Outside hospital, high dose β2agonist bronchodilators may be delivered via large volume spacers or nebulisers.

The use of heliox (helium/oxygen mixture in a ratio of 80:20 or 70:30) in acute adult asthma cannot be recommended on the basis of present evidence.

**2. β2 agonist bronchodilators**

In acute asthma without life threatening features, β2agonists can be administered by repeated activations of a pMDI via an appropriate large volume spacer (four to six puffs given one at a time and separately inhaled at intervals of 10-20 minutes) or by wet nebulisation driven by oxygen, if available. Inhaled β2agonists are at least as efficacious and preferable to intravenous β2agonists (meta-analysis has excluded subcutaneous trials) in adult acute asthma in the majority of cases.A

Use high dose inhaled β2agonists as first line agents in acute asthma and administer as early as possible. Intravenous β2agonists should be reserved for those patients in whom inhaled therapy cannot be used reliably. In acute asthma with life threatening features the nebulised route (oxygen-driven) is recommended.

Parenteral β2agonists, in addition to inhaled β2agonists, may have a role in ventilated patients or those patients *in extremis* in whom nebulised therapy may fail; however there is limited evidence to support this.

Continuous nebulisation of β2agonists is at least as efficacious as bolus nebulisation in relieving acute asthma. It is more effective in airflow obstruction that is severe or unresponsive to initial treatment. However, most cases of acute asthma will respond adequately to bolus nebulisation of β2agonists.

In severe asthma (PEF or FEV1<50% best or predicted) and asthma that is poorly responsive β2 to an initial bolus dose of β2agonist, consider continuous nebulisation, using an appropriate nebuliser system.

Continuous nebulisation cannot be achieved with all nebuliser systems, and is not equivalent to continuously repeating conventional nebuliser doses.

Repeated doses of β2agonists should be given at 15-30 minute intervals or continuous nebulisation of salbutamol at 5-10 mg/hour (requires appropriate nebuliser) used if there is an inadequate response to initial treatment. Higher bolus doses, e.g. 10 mg of salbutamol, are unlikely to be more effective.

**3. Steroid therapy**

Steroid tablets reduce mortality, relapses, subsequent hospital admission and requirement for β2agonist therapy. The earlier they are given in the acute attack the better the outcome.

**A** Give steroid tablets in adequate doses in all cases of acute asthma.Steroid tablets are as effective as injected steroids, provided tablets can be swallowed and retained. Doses of prednisolone of 40-50 mg daily or parenteral hydrocortisone 400 mg daily (100 mg six-hourly) are as effective as higher doses.260 For convenience, steroid tablets may be given as 2 x 25 mg tablets daily rather than 8-12 x 5 mg tablets.

Continue prednisolone 40-50 mg daily for at least five days or until recovery.

Following recovery from the acute exacerbation steroid tablets can be stopped abruptly and doses do not need tapering provided the patient receives inhaled steroids (apart from patients on maintenance steroid treatment or rare instances where steroids are required for three or more weeks).

There is no evidence to suggest that inhaled steroids should be substituted for steroid tablets in treating patients with acute severe, or life threatening asthma. Further randomised controlled trials to determine the role of inhaled steroids in these patients are required. Inhaled steroids do not provide benefit in addition to the initial treatment, but should be continued (or started as soon as possible) to form the start of the chronic asthma management plan.

Combining nebulised ipratropium bromide with a nebulised β2agonist has been shown to produce significantly greater bronchodilation than a β2 agonist alone, leading to a faster recovery and shorter duration of admission. Anticholinergic treatment is not necessary and may not be beneficial in milder exacerbations of asthma or after stabilisation.

Nebulised ipratropium bromide (0.5 mg 4-6 hourly) should be added to β2 agonist treatment for patients with acute severe or life threatening asthma or those with a poor initial response to β2agonist therapy.

**4. Intravenous aminophylline**

In acute asthma, the use of IV aminophylline is not likely to result in any additional bronchodilation compared to standard care with inhaled bronchodilators and steroid tablets. Side-effects such as palpitations, arrhythmias and vomiting are increased if IV aminophylline is used.

Some individual patients with near fatal asthma or life threatening asthma with a poor response to initial therapy may gain additional benefit from IV aminophylline (5 mg/kg loading dose over 20 minutes unless on maintenance oral therapy, then infusion of 0.5-0.7 mg/kg/hr).

**5. Intravenous fluids**

There are no controlled trials or even observational or cohort studies of differing fluid regimes in acute asthma. Some patients with acute asthma require rehydration and correction of electrolyte imbalance. Hypokalaemia can be caused or exacerbated by β2agonist and/or steroid treatment and must be corrected.

**Complications**

The most common complications of asthma include pneumonia, pneumothorax or pneumomediastinum, and respiratory failure requiring intubation in severe exacerbations.

Risk factors for death from asthma include the following:

* Past history of sudden severe exacerbations, history of prior intubation, or ICU admission
* Two or more hospitalizations or 3 or more emergency department visits in the past year; hospitalization or emergency department visit in the past month
* Use of more than 2 beta-agonist canisters per month
* Current use of systemic corticosteroids or recent taper
* Comorbidity from cardiovascular disease
* Psychosocial, psychiatric, or illicit drug use problems
* Low socioeconomic status or urban residence

Complications associated with most medications used for asthma are relatively rare. However, in those patients requiring long-term corticosteroid use, complications may include osteoporosis, immunosuppression, cataracts, myopathy, weight gain, addisonian crisis, thinning of skin, easy bruising, avascular necrosis, diabetes, and psychiatric disorders.

The most important factor in the diagnosis of asthma is to recognize exacerbating factors or other diagnoses that may affect the treatment of the disease.

**Aspirin-induced asthma**

The triad of asthma, aspirin sensitivity, and nasal polyps affects 5-10% of patients with asthma. Most patients experience symptoms during the third to fourth decade. A single dose can provoke an acute asthma exacerbation, accompanied by rhinorrhea, conjunctival irritation, and flushing of the head and neck. It can also occur with other nonsteroidal anti-inflammatory drugs and is caused by an increase in eosinophils and cysteinyl leukotrienes after exposure. Primary treatment is avoidance of these medications, but leukotriene antagonists have shown promise in treatment, allowing these patients to take daily aspirin for cardiac or rheumatic disease.

**Special Concerns**

**Nocturnal asthma**

A large percentage of patients with asthma experience nocturnal symptoms once or twice a month. Some patients only experience symptoms at night and have normal pulmonary function in the daytime. This is due, in part, to the exaggerated response to the normal circadian variation in airflow.

Bronchoconstriction is highest between the hours of 4:00 am and 6:00 pm (the highest morbidity and mortality from asthma is observed during this time). These patients may have a more significant decrease in cortisol levels or increased vagal tone at night. Studies also show an increase in inflammation compared with controls and with patients with daytime asthma.

Inhaled corticosteroids and long-acting theophyllines have demonstrated the most benefit. Long-acting beta-agonists and leukotriene antagonists have also been shown to improve symptoms.

**Pregnancy**

The most important issue in the treatment of asthma during pregnancy is to maintain sufficient lung function and an adequate oxygen supply to the fetus. Approximately one third of women will have worse asthma, one third will have less severe disease, and one-third will have no change.

With the exception of alpha-adrenergic compounds other than pseudoephedrine and some antihistamines, most drugs used to treat asthma and allergic rhinitis have not been shown to increase any risk to the mother or fetus. The National Institutes of Health stated that albuterol, cromolyn, beclomethasone, budesonide, prednisone, and theophylline, when clinically indicated, are considered appropriate for the treatment of asthma in pregnancy.

Poorly controlled asthma can result in low birth weight, increased prematurity, and increased perinatal mortality.

**STATUS ASTHMATICUS**

Status asthmaticus is a medical emergency in which asthma symptoms are refractory to initial bronchodilator therapy in the emergency department. Patients report chest tightness, rapidly progressive shortness of breath, dry cough, and wheezing. Typically, patients present a few days after the onset of a viral respiratory illness, following exposure to a potent allergen or irritant, or after exercise in a cold environment. Frequently, patients have underused or have been underprescribed anti-inflammatory therapy. Illicit drug use may play a role in poor adherence to anti-inflammatory therapy. Patients may have increased their beta-agonist intake (either inhaled or nebulized) to as often as every few minutes.

**Frequency**

The prevalence and severity of asthma cases are on the rise. Also increasing are the occurrences of asthma hospitalization and mortality resulting from status asthmaticus. Status asthmaticus is usually more common among persons in low socioeconomic groups, regardless of race, and particularly in people who live alone.

Patients who delay medical treatment, particularly treatment with systemic steroids, have a greater chance of dying.

Patients with other preexisting conditions (eg, restrictive lung disease, congestive heart failure, chest deformities) are at particular risk of death from status asthmaticus.

Patients who smoke regularly have chronic inflammation of the small airways and are at particular risk of death from status asthmaticus.

Status asthmaticus is slightly more common in males than in females.

Status asthmaticus can occur in persons of any age group, including infants and geriatric patients. Mortality rates are higher in very young children and elderly adults.

**Causes**

In persons with acute asthma, bronchospasms occur as a result of one or more inciting factors that may include, but are not limited to, a viral upper or lower respiratory tract infection, significant allergic response to an allergen (eg, pollen, mold, animal dander, house dust mites), exposure to an irritant, or vigorous exercise in a cold environment.

Precipitating factors can include infection, allergen or irritant exposure, poor adherence to the medical regimen, strenuous exercise, and a rapid decrease in long-term oral steroid therapy.

Inflammation can be the result of infection; lymphocyte, mast cell, eosinophilic, and neutrophilic responses; and airway epithelial damage.

**Pathophysiology**

Inflammation in asthma is characterized by an influx of eosinophils during the early-phase reaction and a mixed cellular infiltrate composed of eosinophils, mast cells, lymphocytes, and neutrophils during the late-phase (or chronic) reaction. The simple explanation for allergic inflammation in asthma begins with the development of a predominantly helper T2 lymphocyte–driven, as opposed to helper T1 lymphocyte–driven, immune milieu, perhaps caused by certain types of immune stimulation early in life. This is followed by allergen exposure in a genetically susceptible individual. Specific allergen exposure (eg, dust mites) under the influence of helper T2 lymphocytes leads to B-lymphocyte elaboration of immunoglobulin E (IgE) antibodies specific to that allergen. The IgE antibody attaches to surface receptors on airway mucosal mast cells. One important question is whether atopic individuals with asthma, in contrast to atopic persons without asthma, have a defect in mucosal integrity that makes them susceptible to penetration of allergens into the mucosa.

Subsequent specific allergen exposure leads to cross-bridging of IgE molecules and activation of mast cells, with elaboration and release of a vast array of mediators. These mediators include histamine; leukotrienes C4, D4, and E4; and a host of cytokines. Together, these mediators cause bronchial smooth muscle constriction, vascular leakage, inflammatory cell recruitment (with further mediator release), and mucous gland secretion. These processes lead to airway obstruction by constriction of the smooth muscles, edema of the airways, influx of inflammatory cells, and formation of intraluminal mucus. In addition, ongoing airway inflammation is thought to cause the airway hyperreactivity characteristic of asthma. The more severe the airway obstruction, the more likely ventilation-perfusion mismatching will result in impaired gas exchange and hypoxemia.

**Histologic Findings**

Autopsy results from patients who died from status asthmaticus of brief duration (ie, developed within hours) show neutrophilic infiltration of the airways.

In contrast, results from patients who developed status asthmaticus over days show eosinophilic infiltration. Autopsy results also show extensive mucus production and severe bronchial smooth muscle hypertrophy. However, the predominant response, based on results from bronchoalveolar lavage studies, is eosinophilic in nature. The eosinophil itself can lead to epithelial destruction through its own degrading products (eg, cationic proteins). This destruction can result in inflammation and, later, a neutrophilic response.

**CLINICAL**

**History**

Patients with status asthmaticus have severe dyspnea that has developed over hours to days.

Frequently, patients have a prior history of endotracheal intubation and mechanical ventilation, frequent emergency department visits, and previous use of systemic corticosteroids.

Patients usually present with audible wheezing.

**Physical**

Patients are usually tachypneic upon examination and, in early stages of status asthmaticus, may have significant wheezing. Initially, wheezing is heard only during expiration, but, later, wheezing occurs during both expiration and inspiration.

The chest is hyperexpanded, and accessory muscles, particularly the sternocleidomastoid, scalene, and intercostal muscles, are used. Later, as bronchoconstriction worsens, patients' wheezing may disappear, which may indicate severe airflow obstruction.

Normally, the pulsus paradoxus (ie, the difference in systolic blood pressure between inspiration and expiration) does not exceed 15 mm Hg. In patients with severe asthma, a pulsus paradoxus of greater than 25 mm Hg usually indicates severe airway obstruction.

**Lab Studies**

Obtain a CBC count and differential to evaluate for infectious causes (eg, pneumonia, viral infections such as croup), allergic bronchopulmonary aspergillosis, and Churg-Strauss vasculitis.

Obtain an arterial blood gas (ABG) value to assess the severity of the asthma attack and to substantiate the need for more intensive care. ABG determinations are indicated when the peak expiratory flow (PEF) rate or forced expiratory volume in one second (FEV1) is less than or equal to 30% of the predicted value or when the patient shows evidence of fatigue or progressive airway obstruction despite treatment. ABG values are important to help determine the severity of the asthma attack. The 4 stages of blood gas progression in persons with status asthmaticus are as follows:

* The first stage is characterized by hyperventilation with a normal partial pressure of oxygen (PO2).
* The second stage is characterized by hyperventilation accompanied by hypoxemia (ie, a low partial pressure of carbon dioxide [PCO2] and low PO2).
* The third stage is characterized by the presence of a false-normal PCO2; ventilation has decreased from the hyperventilation present in the second stage. This is an extremely serious sign of respiratory muscle fatigue that signals the need for more intensive medical care, such as admission to the ICU and, probably, intubation with mechanical ventilation.
* The last stage is characterized by a low PO2 and a high PCO2, which occurs with respiratory muscle insufficiency. This is an even more serious sign that mandates intubation and ventilatory support.

**Imaging Studies**

Obtain a chest radiograph to evaluate for pneumonia, pneumothorax, congestive heart failure, and signs of chronic obstructive pulmonary disease, which would complicate the patient's response to treatment or reduce the patient's baseline spirometry values.

**Other Tests**

The most important and readily available test to evaluate the severity of an asthma attack is the measurement of PEF. PEF monitors are commonly available to patients for use at home, and they provide patients with asthma with a guideline for changes in lung function as they relate to changes in symptoms. In most patients with asthma, a decrease in peak flow as a percent of predicted value correlates with changes in spirometry values.

According to the guidelines of the National Heart, Lung, and Blood Institute/National Asthma Education and Prevention Program, severe asthma exacerbation is usually associated with a PEF rate or FEV1 of less than 50% of the predicted value. Also, hospitalization is generally indicated when the PEF or FEV1 after treatment is greater than 50% of the predicted value but less than 70% of the predicted value. Hospitalization in the ICU is indicated when the PEF value or FEV1 is less than 50% of predicted.

A drop in the FEV1 to less than 25% of the predicted value indicates a severe airway obstruction.

A patient with an FEV1 of greater than 60% of the predicted value may be treated in an outpatient setting, depending on the clinical situation. However, if the patient's FEV1 or PEF rate drops to less than 50% of predicted, admission to the hospital is recommended.

Pulse oximetry and spirometry values should be used to monitor the progression of asthma. As the results indicate improvement, treatment may be adjusted accordingly.

If a portable spirometry unit is not available, a PEF rate of 20% or less of the predicted value (ie, usually <100 L/min) suggests severe airflow obstruction and impending respiratory failure.

**Procedures**

With forced oscillation testing using the impulse oscillometry system (IOS), patients are tested for 30-40 seconds during quiet breathing, without forced respiratory efforts. A small loudspeaker pushes “burps” of air into patients and pulls them back from the mouthpiece 5 times each second.

The measurement of airflow resistance during normal breathing requires no maximal forced expiratory efforts and does not subject patients to bronchoprovocation from forced expiration. Resistance is distributed between large airways and smaller more peripheral airways, with distinct patterns attributable to each.

Bronchospasms and increased large airway resistance appear as increases in resistance at higher (25-35 cycles/s) components of oscillation frequency. Additionally, a pattern of increased resistance with increasing airflow is typical of a large airway bronchospasm. In such patients, resistance at the beginning and end of both inspiration and expiration is at its minimum, with increased levels during mid inspiration and mid expiration. In such patients, a deep inspiration is often followed by reflex bronchoconstriction and increased resistance for 30 seconds or more, signaling increased airway reactivity.

Peripheral airway inflammation and obstruction are signaled by increased resistance at low (5 cycles/s) oscillation frequencies that are decreased at higher oscillation frequencies (15 or 20 cycles/s). In association with the fall in resistance from 5 to 15 cycles per second, the magnitude of respiratory reactance in peripheral airway inflammation and obstruction increases.

Careful attention must be paid to whether patients have their lips fully closed around the mouthpiece. Patients with acute dyspnea may feel constrained breathing through a mouthpiece and may reflexively open their mouths to increase airflow during late inspiration. This is analogous to flaring alae nasi with dyspnea and results in characteristic airflow leak patterns. This causes underestimation of true airflow resistance. IOS tests with such airflow leak patterns must be repeated after reassuring the patient and ensuring closure of the lips around the mouthpiece.

**Staging**

The 4 stages of status asthmaticus are based on ABG progressions in status asthma.

Patients in stage 1 or 2 may be admitted to the hospital, depending on the severity of their dyspnea, their ability to use accessory muscles, and their PEF values or FEV1 after treatment (>50% but <70% of predicted values).

Patients with ABG determinations characteristic of stages 3 and 4 require admission to the ICU. The PEF value or FEV1 is less than 50% of the predicted value after treatment.

* **Stage 1**

Patients are not hypoxemic, but they are hyperventilating and have a normal PO2.

Recent data suggest that to possibly facilitate hospital discharge, these patients may benefit from ipratropium treatment via a handheld nebulizer in the emergency setting as an adjunct to beta-agonists.

* **Stage 2**

This stage is similar to stage 1, but patients are hyperventilating and hypoxemic.

Such patients may still be discharged from the emergency department, depending on their response to bronchodilator treatment, but will require systemic corticosteroids.

* **Stage 3**

These patients are generally ill and have a normal PCO2 due to respiratory muscle fatigue. Their PCO2 is considered a false-normal value and is a very serious sign of fatigue that signals a need for expanded care. This is generally an indication for elective intubation and mechanical ventilation, and these patients require admission to the ICU.

Parenteral corticosteroids are indicated, as is continued aggressive use of an inhaled beta2-adrenergic bronchodilator.

These patients may benefit from theophylline.

* **Stage 4**

This is a very serious stage in which the PO2 is low and the PCO2 is high, signifying respiratory failure.

These patients have less than 20% lung function or FEV1 and require intubation and mechanical ventilation.

Patients in stage 4 should be admitted to the ICU. Switching from inhaled beta-2 agonists and anticholinergics to metered-dose inhalers (MDIs) via mechanical ventilator tubing is indicated.

Parenteral steroids are essential, and theophylline may be added, as with patients in stage 3.

**TREATMENT**

After confirming the diagnosis and assessing the severity of the asthma attack, direct treatment toward controlling bronchoconstriction and inflammation.

**Oxygen monitoring**

Monitoring the patient's oxygen saturation is essential during the initial treatment.

ABG values are usually used to assess hypercapnia during the patient's initial assessment.

Oxygen saturation is then monitored via pulse oximetry throughout the treatment protocol.

1. **Oxygen therapy**

Oxygen therapy is essential. It can be administered via a nasal canula or mask, although patients with dyspnea often do not like masks.

With the advent of pulse oximetry, oxygen therapy can be easily titrated to maintain the patient’s oxygen saturation above 92% (>95% in pregnant patients or those with cardiac disease).

* Mechanical ventilation

Consider mechanical ventilation as a last resort in patients with status asthmaticus.

Mechanical ventilation in patients with asthma requires careful monitoring because these patients have high end-expiratory pressure and, therefore, are at very high risk for pneumothorax.

Mechanical ventilation, when used in patients with asthma, is usually required for less than 72 hours; however, in occasional patients with severe bronchospasm, mechanical ventilation can be prolonged. In these situations, consultation with a pulmonologist or another expert in mechanical ventilatory techniques is likely useful.

**2. Glucocorticosteroids**

Steroids are the most important treatment for status asthmaticus.

The usual dose is oral prednisone at 1-2 mg/kg/d.

In the authors' experience, methylprednisolone provides excellent efficacy when given intravenously at 1 mg/kg/dose every 6 hours.

Some authorities report that pulse therapy with steroids at a high dose (eg, 10-30 mg/kg/d as a single dose) is associated with a more rapid response and shorter hospitalization and has similar adverse effects; however, this is not standard therapy. Adverse effects of pulse therapy, in the authors' experiences, are minimal and comparable to the traditional doses of intravenous steroids. The adverse effects may include hyperglycemia, which is usually reversible once steroid therapy is stopped; increased blood pressure; weight gain; increased striae formation; and hypokalemia. Long-term adverse effects depend on the duration of steroid therapy after the patient leaves the hospital.

Steroid treatment for acute asthma is necessary but has potential adverse effects. The serum glucose value must be monitored, and insulin can be administered on a sliding scale if needed. Monitoring a patient's electrolyte levels, especially potassium, is essential. Hypokalemia can cause muscle weakness, which may worsen respiratory distress and cause cardiac arrhythmias.

* Nebulized steroids

The use of nebulized steroids for treating status asthmaticus is controversial. Recent data comparing nebulized budesonide with prednisone in children suggest that the latter therapy is more effective for treating status asthmaticus.

**3. Bronchodilator treatment with beta-2 agonists**

The first line of therapy is bronchodilator treatment with a beta-2 agonist, typically albuterol.

Handheld nebulizer treatments may be administered either continuously (10-15 mg/h) or by frequent timing (eg, q5-20min), depending on the severity of the bronchospasm.

The dose of albuterol for intermittent dosing is 0.3-0.5 mL of a 0.5% formulation mixed with 2.5 mL of normal saline. Many of these preparations are available in a premixed form with a concentration of 0.083%.

Studies have also shown an excellent response to well-supervised use of albuterol via an MDI with a chamber. The dose is 4 puffs, repeated at 15- to 30-minute intervals as needed. Most patients respond within 1 hour of treatment.

These drugs, especially albuterol, are safe to use during pregnancy.

* Nonselective beta-2 agonists

Patients whose bronchoconstriction is resistant to continuous handheld nebulizer treatments with traditional beta-2 agonists may be candidates for nonselective beta-2 agonists (eg, epinephrine [0.3-0.5 mg] or terbutaline [0.25 mg]) administered subcutaneously. However, systemic therapy has no proven advantage over aerosol therapy with selective beta-2 agents.

Exercise caution in patients with other complicating factors (eg, congestive heart failure, history of cardiac arrhythmia).

Intravenous isoproterenol is not recommended for the treatment of asthma because of the risk of myocardial toxicity.

* Ipratropium treatment

Ipratropium, which comes in premixed vials at 0.2%, can be synergistic with albuterol or other beta-2 agonists. Ipratropium is administered every 4-6 hours.

**4. Aminophylline**

Starting intravenous aminophylline may be reasonable in patients who do not respond to medical treatment with bronchodilators, oxygen, corticosteroids, and intravenous fluids within 24 hours.

Recent data suggest that aminophylline may have an anti-inflammatory effect in addition to its bronchodilator properties.

The loading dose is usually 5-6 mg/kg, followed by a continuous infusion of 0.5-0.9 mg/kg/h.

Adverse effects can include tachyarrhythmia, nausea, seizures, and anxiety.

**5. Fluid replacement**: Intravenous fluids are administered to restore euvolemia.

**6. Antibiotics**

**7. Sedatives**

Patients may benefit from sedatives in very small doses and under controlled, monitored settings. Sedatives should be used judiciously, if at all. For example, lorazepam (0.5 or 1 mg intravenously) could be used for patients who are very anxious and are undergoing appropriate and aggressive bronchodilator therapy.

More powerful agents (eg, oxybutynin) can be administered to intubated patients to achieve sedative, amnestic, and anxiolytic effects.

* **Further Outpatient Care**

Instruct patients to use of inhalers appropriately, to be compliant with therapy, and to practice stress-avoidance measures. Stress factors (ie, triggers of asthma attacks) include pet dander, house dust, and mold. Strongly discourage patients from smoking; this practice should be avoided at all costs. Finally, appropriate follow-up is important, as is checking the patient's peak flow meter and FEV1 at home or in the office, respectively.

* **Prevention**

Status asthmaticus can be prevented if patients are compliant with their medications and they avoid stress factors; however, it can occur even when patients are compliant and doing well as outpatients. In such situations, search for an occult infection (eg, RSV in children but rarely in adults; occult sinus infection).

Prevention of status asthmaticus may be aided by monitoring forced oscillation test results rather than spirometry findings. This is particularly true for children younger than 12 years; however, adults with reactive airways may be undertreated if the criterion for stability and normality is a spirometric FEV1 greater than 80% of the predicted value.

* **Complications**

Pneumothorax may complicate acute asthma, either because of increased airway pressure or as a result of mechanical ventilation. Superimposed infection can also occur in intubated patients. Patients may require a chest tube for pneumothorax or aggressive antibiotic therapy for a superimposed infection.

* **Prognosis**

In general, unless a complicating illness such as congestive heart failure or chronic obstructive pulmonary disease is present, with appropriate therapy status asthmaticus has a good prognosis. A delay in initiating treatment is probably the worst prognostic factor. Delays can result from poor access to health care on the part of the patient or even delays in using steroids. Patients with acute asthma should use steroids early and aggressively.

* **Patient Education**

One important aspect of patient education is that asthma is a disease of airway inflammation; it is not simply bronchospasms. Airway inflammation is a continuing process that renders patients with asthma vulnerable to acute bronchospasms. Symptoms are more dependent on bronchospasms than on inflammation; thus, symptoms may become minimal in the presence of continued peripheral airway inflammation. Because patients often wish to discontinue inhaled corticosteroids when they are free of acute bouts of wheezing, educating them regarding the need for controller medications to minimize peripheral airway inflammation is important.

Patients can be shown the results of forced oscillation testing that occur with peripheral airway inflammation and obstruction. Review the test results with patients and show them the improvement with inhaled corticosteroids and the deterioration when they are not compliant with anti-inflammatory medications. This information may materially enhance patients' awareness of the need for continuing treatment, despite an absence of wheezing.