Asthma

Diagnosis/Condition:	Extrinsic asthma Intrinsic asthma Chronic obstructive asthma Other forms Asthma, unspecified
Discipline:	Integrated
ICD-10 Codes:	J44.1, J45.20, J45.21, J45.22
Origination Date:	2006
Review/Revised Date	4/2023
Next Review Date:	4/2025

Asthma is one of the most common chronic diseases, afflicting about 8% of the population of the USA – numbers that have risen in the past decades. The American Lung Association and the Centers for Disease Control (CDC) estimate nearly 25 million Americans have asthma.[1] Studies have estimated that the total costs associated with asthma (direct and indirect) exceed $82 billion annually in the USA.[2] The prevalence and morbidity have increased, especially among children, and are higher in adolescents, women,[3] and those living in poverty. Approximately 75% of persons with asthma are diagnosed before age 7.[4]

While asthma is controllable in most people, it is estimated that 50% of children have uncontrolled asthma.[5] Male children are more likely to have asthma than female children. This trend reverses in adulthood, where female adults are more likely to have asthma than male adults. This is thought to be due to the effects of testosterone, decreasing the swelling of the airways. [6] Obesity associated asthma is increasing and there appears to be a correlation between obesity and more severe asthma.[7]

Asthma can be classified as *allergic* (extrinsic) due to immune system reaction to inhaled allergens and *non-allergic* (intrinsic) which does not involve the immune system but is triggered by other factors such as stress, exercise, cold or dry air, environmental pollutants[8,9] and irritants.[10] Both types are "characterized by variable and recurring symptoms, airflow obstruction, bronchial hyperresponsiveness, and an underlying inflammation".[11,12] Another system recognizes four general types of asthma: *1) Exercise Induced; 2) Nocturnal; 3) Cough-Variant; and 4) Occupational*.[11] Current guidelines also suggest classification based on level of control versus level of severity with tiered broad categories: 1) controlled, 2) partly controlled, or 3) uncontrolled symptoms. Despite advances in understanding this disease, it remains a growing public health issue. Medical treatments are aimed at managing symptoms and reducing long-term risks. Biomarkers in different phenotypes of asthma are increasingly being used to individualize treatments, especially with the onset of biologics.[13] Asthma varies markedly from day to day, seasonally and from year to year, presenting challenges in diagnosis.[14]

Complementary and integrative health (IH) use is highly prevalent among those with asthma, even those using conventional treatments.[15] Thirty to seventy of patients with asthma use Integrative Health (IH) treatments, which is twice the national average for total IH use in adults.[16,17,18]

There are various asthma management guidelines that have been established as this medical condition increases in prevalence. These include the "The National Asthma Education and Prevention Program Expert Panel Report 3, Guidelines for the Diagnosis and Management of Asthma -- Full Report 2007",[19] the Global Initiative for Asthma (GINA) most recently updated in 2022,[20] and the National Heart, Lung, and Blood Institute's National Asthma Education and Prevention Program Expert Panel Report 3 titled "Guidelines for the Diagnosis and Management of Asthma".[21] The National Institute for Health and Care Excellence (NICE) in UK more recently published, "Asthma: diagnosis, monitoring and chronic asthma management" in 2017 and updated it for 2020[22]. They all present similar recommendations for the diagnosis and management of asthma (See Practitioner Resources below). Reviews of clinical practice guidelines for asthma in 2013[23] and 2015[24] concluded that guideline quality has improved over time, however, the quality of published guidelines is still low.

Over the past 2 years, significant progress has been made in the development of new scoring systems and tools to facilitate the diagnosis of asthma and to help providers quantify asthma severity. Biagini Myers et al using the Pediatric Asthma Risk Score developed a quantitative tool to predict asthma development in young children. Overall, the Pediatric Asthma Risk Score performed better than the asthma predictive index in children with mild to moderate asthma.[25]

These management tools have organized recommendations for asthma care around four components considered essential to effective asthma management:

1. Measures of assessment and monitoring of symptoms and lung function, obtained by objective tests, physical examination, patient history, and patient report, to diagnose and assess the characteristics and severity of asthma and to monitor whether asthma control is achieved and maintained.
2. Education for a partnership between patient and clinician in asthma care.
3. Control of environmental factors (triggers) and comorbid conditions that affect asthma.
4. Pharmacologic therapy.

COVID-19 and Asthma

Based on studies worldwide in 2020, people with controlled asthma do not appear to be a group at increased risk for severe infection or death from COVID-19. Social distancing and other infection mitigation procedures throughout 2020 have probably ensured that asthmatics are experiencing fewer respiratory infections and other triggers to their asthma, resulting in fewer exacerbations of asthma worldwide. However, recent use of oral corticosteroids due to asthma exacerbations may increase risk for various infections, including COVID-19. Hence. monitoring symptoms is considered essential.[26,27,28,29]

Subjective Findings and History

- Key criteria in making diagnosis of asthma: 1) variable respiratory patterns 2) variable expiratory airflow limitation.
- History of episodic symptoms of shortness of breath (SOB), dyspnea on exertion (DOE), sensation of "tightness" when breathing, and cough (dry or productive of mucoid or pale-yellow sputum). May be complicated with acute exacerbations of severe breathlessness, chest tightness, and fatigue.
- "Classic triad of symptoms" is dyspnea, cough (often worse at night), and wheezing (high-pitched whistling sound, usually upon exhalation). Patient may report expirations more difficult than inspirations.
- Patients with respiratory disorders including asthma may be more likely to suffer from mid- and low back pain.[30]
- Characteristic triggers maybe an exposure to environmental allergens or aggravated by stress, exercise, or an upper respiratory infection (URI). A large percentage of people experience asthma due to work-related conditions.
- Possible history of prolonged URI and /or history of smoking in the adult or exposure to second-hand smoke (especially in children).
- May have a personal or family history of asthma, allergic rhinitis,[31] or other atopic disease.
- May be seen in young children as frequent URI with cough and wheezing.
- Infants may have trouble feeding and may grunt during suckling.
- Complications may include severe dyspnea, cyanosis, repeated respiratory infections, and death.
- Diagnoses in special populations should be considered: pregnancy, smokers and former smokers, children, occupational asthma, and the elderly.

Objective Findings

- Audible (high-pitched) wheezing, cyanosis, difficult breathing, use of accessory muscles with respiration, increased pulse rate, cough, and anxiety.
- Tachypnea, tachycardia, and prolonged expiratory phase of respiration (decreased I:E Inspiration/Expiration ratio).
- Signs of an asthma exacerbation - diaphoresis, the "tripod position" (a seated position with use of extended arms to support the upper chest), use of the accessory muscles of breathing (e.g., sternocleidomastoid) during inspiration, and a pulsus paradoxus (greater than 12 mmHg fall in systolic blood pressure during inspiration).
- Pulmonary function testing (spirometry) may detect a decrease (obstruction) in peak expiratory flow rate (PEFR) or forced expiratory volume. Patient self-monitoring with a portable peak flow meter (available OTC) may aid early recognition of declining lung function.
- The presence of altered postural patterns may indicate chronic low-grade symptoms.[32]
- The patient can perform some form of physical activity to increase the breathing rate and be checked for changes in lung capacity. In addition, a bronchodilator (such as Albuterol) response test can be used for supporting diagnosis of asthma.

- Chronic asthma may show any of the previous findings with large amounts of thick mucus, barrel chest, chest x-ray (CXR) with signs of emphysema and/or hyperinflation.
- Physical findings may include nasal polyps, pale swollen nasal cavities, and concomitant atopic dermatitis, indicating a general atopic condition.
- Exhaled nitrous oxide testing (FENO) can indicate eosinophilic airway inflammation is useful in tailoring treatment.[33]

Differential Diagnoses (DDX)

Bronchitis, allergic rhinitis, bronchiolitis, bronchiectasis, foreign body aspiration, vocal cord dysfunction, pulmonary embolism, gastroesophageal reflux disease (GERD), panic disorder, sarcoidosis, chronic obstructive pulmonary disease (COPD), and left-ventricular heart failure.

Chinese Medicine - there are four syndromes for asthma:

Shi Type:	Wind-cold – cough with thin sputum, shortness of breath with accompanying symptoms of fever, chills, sweating. Tongue: white coating	Pulse: superficial
	Phlegm-heat – Rapid and coarse breathing, stifling sensation in the chest, thick purulent sputum. Tongue: thick yellowish coating	Pulse: Rapid, rolling, and forceful
Xu Type:	Xu of the Lung – short and quick breathing, weak and low voice	Pulse: weak
	Xu of the Kidney – dyspnea upon exertion, chills with cold extremities	Pulse: deep, thready, and feeble

Labs/Tests/Imaging

Consider:

- CBC with differential (to rule out infection, e.g., pneumonia, anemia, and eosinophilia).
- CXR if persistent or suggestive of infection.
- Arterial blood gases to assess PO2 and PCO2.
- Exhaled nitric oxide (NO) testing.
- Spirometry – Forced Expiratory Volume at 1 second (FEV1) and Forced Vital Capacity (FVC).
- Bronchoprovocation testing and bronchodilator response.
- Allergy tests (to help to confirm sensitivity to suspected respiratory allergic triggers).
- Serum alpha-1 antitrypsin level.
- Sputum smear may reveal Curschmann's spirals, eosinophils, or Charcot-Leyden crystals.
- Consider serum vitamin D testing.[34]

Assessment

- Full history and physical examination to assess degree of respiratory distress.
- Detect the presence of other comorbid or contributing conditions, e.g., allergic rhinitis, interstitial lung disease, cystic fibrosis, nasal polyps, COPD, and atopic dermatitis.
- In Chinese Medicine, clinical impressions should be correlated to history, complaints, and objective findings to differentiate syndromes according to TCM.

Asthma severity should be assessed using the following three factors and to determine appropriate treatment options:

1. Reported symptoms over the previous two to four weeks.
2. Current level of lung function (FEV_1 and FEV_1/FVC values).
3. Number of exacerbations requiring oral glucocorticoids per year.

Severity can be broken down in a stepwise manner into intermittent vs. persistent asthma and this can be further classified into mild, moderate, and severe. As severity increases, so does risk. In general, more frequent, and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate greater disease severity. For treatment purposes, patients who have intermittent asthma who have had ≥2 exacerbations requiring oral systemic glucocorticoids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

Components of severity, risk guidelines, and recommendations for pharmacological treatment are included here: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf

Treatment

- The goals of treatment are two-fold: 1) reduction in impairment (intensity, frequency, and degree of symptoms) and 2) reduction in medical risk of asthma exacerbations, suboptimal lung development (in children), loss of lung function over time (in adults), and adverse effects from asthma medications.
- Acute attacks must be managed safely. For chronic asthma, a treatment plan to minimize attacks, reduce bronchial inflammation, and limit long-term bronchial hypertrophy and medical risks must be implemented.
- Monitoring and avoiding known triggers, such as dust mites, molds, furry animals, cockroaches, pollens,[35] medications (NSAIDs or aspirin) or dietary sulfites.
- Bronchial overgrowth, especially when inhaled steroids are being used must be assessed and treated.
- Educate patient in rinsing out mouth after inhaled steroid use.
- Personalized treatment is needed, based on asthma phenotypes and gender differences.[36]
- Monitor Improvements in Asthma Quality of Life Questionnaire (AQLQ).[33.34.35.36]

Nutritional(s):	Emerging evidence indicates that diet plays an important role in the development and management of asthma.[37] Assess food allergies, sensitivities and reactions.[38,39,40,41] Reduce mucus-forming foods.[42,43] Consider anti-inflammatory, antihistamine, and mast-cell stabilizing therapies:[44] Quercetin, hesperidin, Vitamin C,[45,46] carotenoids,[47] Vitamin B12 (topical),[48] magnesium (inhaled or IV to reduce bronchospasm),[49,50,51,52] choline,[53] Vitamin D,[54,55,56,57,58,59,60,61] antioxidants,[62] fish oils,[63] omega 3 fatty acids,[64,65,66,67] minerals,[68] and natural dietary immunomodulators. Probiotics early in life seems to have an important preventative role to play.[69] Dietary changes and improvement in digestive function.[70] The use of fermented foods can be beneficial.[71] The Mediterranean diet has been well studied as protective in asthma.[72,73,74] Improved diet quality has been associated with decreased inflammatory markers in patients with poor asthma control.[75]
Botanicals/Nutraceuticals:	To tonify the lungs, bronchodilators, thin mucus secretions, nervines for sleep and muscle relaxation, reduce allergic response.[76] Curcumin is well tolerated and effective.[77] Some mixed evidence exists for *Tylophora indica, Boswellia serrata, Coleus forskolli, Petasites hybrids,*[78] *and Pinus pinaster* pine bark (Pycnogenol).[79,80] Preliminary research has been done on propolis, but is not widely used due to frequent allergic reactions to the product. Eucalyptol, *Rosemarinus officinalis* and Lyprinol function as anti-inflammatories.[81,82,83] Caffeine and other tannin containing herbs as an adjunct bronchodilator.[84,84,85] Several botanicals have been placed in a nanoparticle delivery system due to their poor solubility, and results are promising.[86,87] Phytosterols have been shown to have similar pharmacokinetic properties compared to dexamethasone and can be effective in asthma management.[88]
Traditional East Asian Medicine (TEAM) Herbs:	Prescribe herbal treatment according to syndrome differentiation. These patients can be very sensitive to herbs, foods, or other medications so it may be prudent to prescribe herbal formulas conservatively until it is known how the patient is going to react.[89] Specific Chinese herbal formulas have been researched and one review suggest overall positive results.[90,91]

Homeopathy: Individualized prescribing. A staged approach, based on severity and acuteness of symptoms. Acute remedy including concomitant symptoms, chronic constitutional remedy, anti-miasmatic nosode, and antigenic isotherapy. Attention to complementary remedies may improve outcome. Repeated-dose schedules may be preferred for acute cases, chronic patients on inhaled or systemic steroids, and to avoid homeopathic aggravation in stable chronic asthma.

Acupuncture: Approximately 20 RCTs have been conducted to assess the effects of acupuncture on asthma, dating back to 1982.[92] Since then, approximately ten reviews have been conducted.[93,94,95,96,97,98,99,100,101,102] The most recent comprehensive systematic review is dated, (2004)[114] and since then, eight RCTs (7 newly published and 1 overlooked) have been published. Based on the literature the following conclusions can be drawn:

The evidence is promising to suggest benefits from acupuncture for the treatment of asthma related symptoms; more research is required to draw definitive conclusions.

- The largest RCT to date (2017) (n=357) suggests acupuncture adds benefit when provided adjunctively to usual medical care.[103]
    - A sub-analysis (n=306) suggests acupuncture adjunctive to usual care is a cost-effective treatment in patients with allergic bronchial asthma.[104]
- Three additional RCTs (not included in the SRs) suggest benefit of acupuncture adjunctive to usual medical care for the treatment of asthma-related symptoms, e.g., QOL scales.[105,106,107]
- The most recent (2004) comprehensive systematic review[114] concluded:
    - Heterogeneity precluded pooling of data for meta-analysis.
    - "...not enough evidence to make recommendations about the value of acupuncture in asthma treatment."

Spinal Manipulation:	Three randomized controlled studies showed benefit in subjective measures, such as quality of life, symptoms, and decreased bronchodilator use; however, the differences were not statistically significant between controls and treated groups.[108,109,110,111] A recent "preliminary study" reported a trial in a small group of stroke patients (n=36) and found improved forced vital capacity and residual volume, suggesting that mechanical factors may have led to improved function.[112] It is likely that physical medicine and manipulation all reduce the side effects of atypical postures and muscle tension resulting from prolonged difficult breathing.
Massage Therapy:	Massage therapy is contraindicated for acute bronchial asthma but may prove to be an effective treatment for allergic and infectious bronchial asthma that is not acute. Massage to the shoulders, chest and upper back may reduce muscle spasms and improve discomfort and breathing patterns. Vibrations and tapotement over the lungs and upper back may help loosen phlegm to relieve symptoms. Reflexology and foot massage has been used to control asthma.[113]
Functional, Relaxation and Physical Modalities:	Exercise as tolerated.[114] Yoga (mixed reviews, but increases QOL scores).[115,116,117] Cognitive behavior therapy.[118] Pranayama (derived from yoga), the Buteyko breathing technique and the Papworth method,[119,120] inspiratory muscle training (IM), mindfulness training,[121] and muscular relaxation all have promising research.[122,123,124,125] Modified breathing programs show statistically significant improvement in asthma control test (ACT), increase in quality of life, and reduced medication usage.[126,127] A 2020 Cochrane meta-analysis supports breathing exercises and techniques as referenced above to have positive effects on quality of life, hyperventilation symptoms, and lung function.[128]
Hydrotherapy:	Steam inhalation when acute. Hot fomentation to chest, steam bath in chronic presentations. Avoid cold applications.
Salt Chamber Treatment:	Used as an adjunct to conventional care.[129]

Lifestyle and Psycho-emotional Counseling:	Emotional counseling, stress management, self-monitoring of lung function and avoidance of triggers.
Pharmaceuticals:	Ephedrine or albuterol with careful monitoring. Inhaled corticosteroids treatment to reduce bronchial inflammation. Long-acting beta-agonists. Low, medium, and high dose inhaled glucocorticoids. Epinephrine (Epi-pen) available for severe acute attack. Theophylline (methylxanthine), leukotriene inhibitors, immunomodulators, mast-cell stabilizers, beta-2-selective adrenergic agonists, oral systemic glucocorticoids, and short-term beta-agonists should be considered for use. Biologics are being used more commonly for severe cases and are targeted at specific types of asthma.[130] There is current trend towards not using a short-acting beta agonist alone and using single maintenance and reliever therapy (MART) based on clinical presentations and endotypes of asthma.[131]

Length of Treatment

- Depends on the response to treatment.
- Acute therapies should have results within several minutes or referral to emergency department may be warranted to avoid patient experiencing respiratory distress.
- Patients generally require regular follow up until symptoms are resolved, and this may mean lifetime review.

Referral Criteria

An integrated multi-disciplinary approach to these patients is often used as a primary treatment plan as the combination of therapies enhances the efficacy of all treatment modalities.

Patients with chronic asthma with frequent acute attacks should be evaluated with regular pulmonary function tests and CXRs to determine the degree of hyperinflation and evaluated for ongoing inflammatory processes. Patients who continue to use short acting beta agonists more than a few times a week or who are hospitalized for asthma symptoms are well-controlled and should be referred for assessment.

Referral to a specialist (pulmonologist/allergist) is appropriate if the patient's condition does not get better, if they have frequent exacerbations, or if their condition worsens with treatment. Peak flow rate less than 80% of "personal best" indicates that current treatment is inadequate and less than 50% indicates need for immediate intervention to prevent complications.

Treatment plans will differ when treating acute cases verses chronic cases. It is essential to differentiate the degree of severity of symptomatology and the type of asthma (acute/chronic) before proceeding with treatment (See Precautions and Contraindications). Patient condition should be monitored and if improvements are not seen, a step-wise treatment should be

followed. (See Guidelines for the Diagnosis and Management of Asthma (EPR-3). (http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines).[132] IH treatments should be discussed openly between patients and medical providers as to not compromise quality of care.[133]

Precautions and Contraindications

A patient with acute respiratory distress that does not resolve immediately with treatment should be referred to an ED.

Resources for Clinicians

Clinical Practice Guideline. National Heart, Lung, and Blood Institute National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. 2007. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf

Centers for Disease Control and Prevention (CDC) - http://www.cdc.gov/asthma/most-recent-data.htm

Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2021; http://www.ginasthma.org

See new 2018 Pocket Guide for Asthma Management and Prevention. https://ginasthma.org/2018-pocket-guide-for-asthma-management-and-prevention/

Silvers WS, Bailey HK. Integrative approach to allergy and asthma using complementary and alternative medicine. *Ann Allergy Asthma Immunol.* 2014;112(4):280-5.

Society for Acupuncture Research. Acupuncture for the Treatment of Asthma: An Evidence-Based Assessment. Revised March 2019. www.AcupunctureResearch.org.

Resources for Patients

The National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health provides leadership for a national program in diseases of the heart, blood vessels, lung, and blood; blood resources; and sleep disorders.
http://www.nhlbi.nih.gov/health/dci/Diseases/Asthma/Asthma_WhatIs.html

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