DIAGNOSING COMORBIDITIES ASSOCIATED WITH ASTHMA

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PRECISION

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About 54% of adult asthma patients in the United States have been diagnosed with at least 1 chronic nonrespiratory comorbidity, and over 25% of these patients have 2 or more comorbidities.[1] Some of these are comorbid conditions associated with the diagnosis of asthma (eg, nasal polyps), while others may worsen asthma control (eg, gastroesophageal reflux disease) or are important to consider in the differential diagnosis of asthma (eg, vocal cord dysfunction).[2] When chronic comorbidities are managed appropriately, asthma control may improve.[3]

This resource provides information on the clinical features and diagnosis of various comorbidities often associated with asthma. Please note, this resource should not be viewed as a comprehensive list of all available screener or assessment tools for the conditions described here. It is not intended to make any treatment recommendations.

UPPER AIRWAY OR SINUS DISEASE

- Asthma is commonly associated with nasal disease—some studies indicate an overlap in up to 95% of cases[1]
- Chronic rhinosinusitis is often linked to persistent severe asthma[1]
- Treatment of upper airway disease often improves asthma[1]
- Impaired filtering and air conditioning in the nose may lead to mouth breathing that increases exposure of lower airways to allergens or other asthma triggers, potentially leading to inflammatory changes and airway hyperresponsiveness[2]

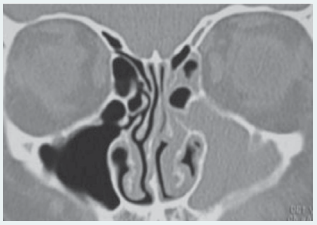
Clinical Features	Diagnosis	Important Considerations
• Frequent cough that may be misattributed to asthma[1] • Sleep disturbance due to nasal obstruction[1] • Mouth breathing[2] • Nasal congestion[3]	• Frequency and severity of nasal symptoms (eg, sneezing, runny nose, postnasal discharge, sleep disturbances, and ear pain or fullness)[4] • For more details refer to SNOT-22 or CSS questionnaire[4] • Clinical evaluation with CT for complications[3] • Peripheral blood eosinophilia[2]	• "United Airway" hypothesis—same inflammatory process causes upper and lower airway diseases[2] • Nasal and bronchial mucosa show similar changes when inflamed, including erosion of epithelium, thickening of basement membrane, and eosinophilic cellular infiltrate[5] • Nasopharyngeal reflux is an etiologic factor for chronic rhinosinusitis after endoscopic sinus surgery[6]

CSS, Chronic Sinusitis Survey; CT, computed tomography; SNOT-22, Sinonasal Outcome Test-22.

Patients with asthma should be evaluated for symptoms of upper airway or sinus disease.[1,5] Ideal asthma management is generally not achieved without control of upper airway disease.[1]

NASAL POLYPS

- Nasal polyps and chronic rhinosinusitis (CRS) are frequently linked to persistent severe asthma and adult-onset asthma[1,2]
- Nasal polyps and comorbid asthma might be an end product of CRS[2]
- About 40% to 67% of patients with nasal polyps have asthma[3]
- About 7% to 25% of patients with asthma have nasal polyps[2]
- Late-onset eosinophilic asthma is a well-defined phenotype often associated with nasal polyps[4]
- The coexistence of asthma, nasal polyps, and aspirin intolerance (ie, Samter's Triad, AERD) is associated with worse asthma severity[5]

Clinical Features	Diagnosis	Important Considerations
• Obstruction and postnasal drainage[6] • Congestion, sneezing rhinorrhea, anosmia, hyposmia, facial pain, and ocular itching[6]	• Frequency and severity of nasal symptoms (eg, runny nose, postnasal discharge, diminished smell sense, and facial pain)[7] • For more details refer to SNOT-22 questionnaire[7] • Physical exam[6] • Sinus endoscopy or CT[7]  CT Image of Nasal Polyps in Sinus Regions[8]	• Polyps may obstruct the airway or promote sinusitis[6] • Polyps may recur if the underlying allergy or infection is uncontrolled[6] • Polyp surgery is indicated for intracranial and intraorbital complications, mucoceles, anatomic variations, allergic fungal disease, massive polyps with bony remodeling, and antrochoanal polyps[9] • Worse surgical outcomes occur in patients who have aspirin-exacerbated respiratory disease, asthma, and frontal sinus disease[9]

AERD, aspirin-exacerbated respiratory disease; CT, computed tomography; SNOT-22, Sinonasal Outcome Test-22.

Nasal polyps and CRS can contribute to poor asthma control and lead to upper airway symptoms.[1,2]

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

- Asthma patients are at higher risk of developing GERD because asthma flare-ups can cause the lower esophageal sphincter to relax, allowing stomach contents to reflux into the esophagus[1]
- Acid reflux can make asthma symptoms worse by irritating the airways and lungs, leading to more serious asthma[1]
- Irritation can trigger allergic reactions and make the airways more sensitive to environmental conditions, such as smoke or cold air[1]
- GERD may be present in 60% to 80% of asthma patients[2]

Clinical Features	Diagnosis	Important Considerations
• Heartburn, epigastric or chest pain, or dry cough[3] • Difficulty or pain when swallowing[1] • Sudden excess of saliva[1] • Chronic sore throat, laryngitis, or hoarseness[1] • Inflammation of the gums, cavities, or bad breath[1]	• Frequency and severity of heartburn, regurgitation, upper stomach pain, nausea, and disrupted sleep[4] • For more details refer to GERDQ[4] or FSSG[5] questionnaire • X-ray of the upper digestive system[1] • Endoscopy[1] • Ambulatory acid (pH) test[1] • Esophageal impedance test[1]	• Beta$_2$-agonists relax the lower esophageal sphincter[3] • Systemic corticosteroids may increase gastric acid production and inhaled corticosteroids may cause hoarseness[6] • May be misinterpreted as asthma (especially nocturnal asthma) or rhinitis[6,7] • Aspirated nonacid (silent) and acid reflux may cause frequent asthma exacerbations or pneumonia[8,9] • Asthma may promote esophageal motility abnormalities[10]

FSSG, Frequency Scale for the Symptoms of GERD; GERDQ, Gastroesophageal Reflux Disease Questionnaire.

Persons with asthma are at a higher risk of developing GERD, which can worsen asthma control.[1]

ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS (ABPA) and ALLERGIC BRONCHOPULMONARY MYCOSIS (ABPM)

- ABPA is a hypersensitivity reaction to *Aspergillus* antigens seen in asthma and cystic fibrosis (CF) patients[1]
- ABPM is a rare, but identical syndrome occurring in the absence of underlying asthma or CF, and is caused by other fungi, such as *Penicillium, Candida, Curvularia, Helminthosporium,* and *Drechslera* species[1]
- Complicates up to 6% of all chronic asthma cases[2]
- Genetic predisposition, with familial occurrence[3]
- Occurs in susceptible hosts, unable to efficiently clear respiratory epithelium of inhaled fungal spores, and results from T helper cell 2 (Th2) innate and adaptive immune responses[4]
- Immune responses cause airway obstruction that can lead to bronchiectasis and pulmonary fibrosis if untreated[1]

Clinical Features	Diagnosis	Important Considerations
• Productive cough with dirty-green or brown plugs[1] • Fever and anorexia[1] • Frequent exacerbations for unclear reasons[1] • Migratory or unresolving infiltrates on chest X-ray[1] • Recurrent airway infections and otitis media[2]	• Predisposing condition of asthma or CF[4] • Total baseline serum IgE >1000 ng/mL or >417 IU/mL[1] • Positive immediate hypersensitivity skin test or elevated *in vitro* specific IgE to *A fumigatus*[4] • Supportive criteria (≥2 present)[4] o Eosinophilia >500 cells per microliter o Serum precipitating or IgG Ab to *A fumigatus* o Consistent pulmonary radiographic opacities, including transient (consolidation, nodules, tram-track, or finger-in-glove) or permanent (bronchiectasis or fibrosis)	• Distinguish from invasive aspergillosis (immune-compromised patients) or *Aspergillus* pneumonia (low-dose prednisone-dependent patients)[1] o Evaluate for *A flavus, A niger,* or *A terreus*[5] • No uniform diagnostic criterion or standardized test[2] • Other fungi that cause endemic mycoses include, *Coccidioides* spp, *Histoplasma* spp, *Blastomyces dermatitidis,* and *Paracoccidioides brasiliensis*[6]

Ab, anti-body; Ig, immunoglobulin.

ABPA should be suspected in patients who have asthma and have the presence or a history of pulmonary infiltrates, specifically in patients who have evidence of IgE sensitization to *Aspergillus* and in corticosteroid-dependent patients who have asthma.[7]

COMMON VARIABLE IMMUNODEFICIENCY (CVID)

- CVID is when the body is deficient in antibodies and as a result the immune system is unable to defend against bacteria and viruses[1]
- The most common types of recurrent infections involve the ears, sinuses, nose, bronchi and lungs. These include[1]:
  - Pneumonia
  - Sinusitis
  - Ear infections
  - Gastrointestinal infections
- Can lead to bronchiectasis[1]

Clinical Features	Diagnosis	Important Considerations
• Recurrent sinopulmonary infections[2]	• Frequency and severity of quality of life changes including mood, diet, independence, and fear of health changes, including cough, pain, and diarrhea[3] • Measurement of serum Ig and Ab titers[2] • Flow cytometry for T and B cell subsets[2] • Serum protein electrophoresis[2] • Recurrent sinopulmonary infections and all of these criteria[2]: o Low levels of IgG (≥2 SD below the mean) and either a low level of IgA or IgM, or both o Impaired response to polysaccharide and protein vaccine immunizations o Exclusion of other immunodeficiency disorders	• Consider when immunodeficiency is suspected[2] • Poor response to vaccination[2] • Differentiate between secondary immunodeficiency from medications, such as prednisone or methylprednisone and primary immunodeficiency from CVID[4]

Ab, anti-body; Ig, immunoglobulin.

Consider CVID in those with frequent asthma-like symptoms and recurrent infections of the ears, sinuses, and respiratory tract (sinopulmonary infections).[1]

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

- Asthma and COPD each include several different clinical phenotypes, and are likely to have several different underlying mechanisms, some of which may be common to both asthma and COPD[1]
- Distinguishing asthma from COPD can be difficult, particularly in smokers and older adults, and some patients may have features of both asthma and COPD[1]
- COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, a history of recurrent lower respiratory tract infections, and/or a history of exposure to risk factors for the disease[2]
- COPD is associated with later onset compared with asthma, and is typically seen after the age of 40[1]
- The characterization of asthma (ie, variable expiratory airflow limitation) and COPD (ie, persistent airflow limitation) are not mutually exclusive[1]:
  - In adults with a history of long-standing asthma, persistent airflow limitation may be found
  - Patients with COPD may show evidence of response to a rapid-acting bronchodilator, but will not be reversed to normal spirometry

Clinical Features	Diagnosis	Important Considerations
• Dyspnea[2] • Cough[2] • Sputum production[2]	• Spirometry is required to make the diagnosis; a post-bronchodilator FEV_1/FVC <0.70 confirms the presence of persistent airflow limitation[2]	• Risk factors include: host factors, tobacco smoke, indoor/outdoor pollution and occupational irritants[2] • Asthma and COPD may share some common traits and clinical features (eg, eosinophilia, some degree of reversibility)[2]

FEV_1, forced expiratory volume in one second; FVC, forced vital capacity.

Asthma may be a risk factor for the development of chronic airflow limitation and COPD.[2]

BRONCHIECTASIS

- Considered a common sequela of various disorders predisposing to chronic airway inflammation[1]
- May be risk factor for asthma exacerbations[2]
- Annual incidence of asthma exacerbations, with associated steroid use and emergency room visits, is higher in patients with asthma and bronchiectasis than in patients with asthma alone[2]
- Higher prevalence in patients with severe asthma, compared to milder cases[3]
- Common causes are recurrent infections, allergic bronchopulmonary aspergillosis (ABPA), immune defects, and cystic fibrosis (CF); some cases may be idiopathic[1]
- Typical patient has predisposition to chronic infection and inflammation due to impaired airway clearance, damaged cilia, and impaired host defenses[1]

Clinical Features	Diagnosis	Important Considerations
• Chronic cough with thick purulent sputum expectorations and frequent acute exacerbations[1] • Dyspnea and wheezing[1] • Pleuritic chest pain[1] • Low-grade fever, fatigue, or malaise[1]	• Frequency and severity of cough, wheezing, dyspnea, expectoration, previous pneumonia, and FeNO ≤20.5 ppb[3] • Clinical history[1] • Chest X-ray[1] • High-resolution chest CT imaging[1] • Pulmonary function testing[1] • Staining and culture for bacteria *(H influenzae, P aeruginosa, M catarrhalis, S aureus,* and *S pneumoniae)*, mycobacteria *(M avium* and *M tuberculosis)*, and fungi *(Aspergillus* spp)[1]	• Clinical symptoms overlap significantly with asthma[2] • May manifest as diffuse bronchiectasis in patients with genetic, immunologic, or anatomic airway defects (eg, CF, CVID, primary ciliary dyskinesia, rheumatoid arthritis, or ABPA)[1] • May manifest as focal bronchiectasis from untreated pneumonia or obstruction (eg, foreign body, lymphadenopathy, tumor, or postsurgical changes)[1] • May be caused by tuberculous or nontuberculous mycobacteria[1]

CT, computed tomography; FeNO, fractional exhaled nitric oxide; ppb, parts per billion.

Patients with uncontrolled moderate-to-severe asthma can have a high prevalence of bronchiectasis.[3]

NONTUBERCULOUS MYCOBACTERIAL (NTM) INFECTION

- Common in patients with chronic lung diseases, including asthma, COPD, alpha-1 anti-trypsin deficiency, pneumoconiosis, cystic fibrosis (CF), non-CF bronchiectasis, primary ciliary dyskinesia, and ABPA, because chronic epithelial cell inflammation and structural lung changes that result in impaired mucociliary clearance predisposes to NTM infection[1,2]
- Comorbidities, including GERD, rheumatoid arthritis, low vitamin D, low BMI, and malnutrition may potentially contribute to NTM acquisition, as well as immunodeficiency, immunosuppression, or gastric aspiration with proton pump inhibitor use[1]
- Not clear whether *M avium* complex (MAC) leads to bronchiectasis or bronchiectasis leads to MAC[3]
- Association between biomarkers of dysregulated Th2-type (T helper lymphocyte type 2) immune responses and *Mycobacterium avium-intracellulare* (MAI) complex NTM infection[4]
- Associated with difficult-to-treat asthma, especially in older individuals, late onset asthma, those with frequent exacerbations or hospitalizations, severe airflow obstruction, or substantial exposure to inhaled or systemic corticosteroids[5]

Clinical Features	Diagnosis	Important Considerations
• Chronic cough[3] • Expectoration and intermittent acute exacerbations[3] • Low-grade fever, fatigue, or weight loss[3] • Female patients may have comorbid bronchiectasis, scoliosis, pectus excavatum, or mitral valve prolapse[3] • Male patients may have comorbid chronic bronchitis, emphysema, healed tuberculosis (TB), bronchiectasis, or silicosis[3]	• Sputum samples for acid-fast bacilli (AFB) smear and culture[1] • Pulmonary symptoms, nodular, or cavity opacities on chest X-ray or high-resolution CT that show multifocal bronchiectasis with multiple small nodes and exclusion of other diagnoses[1] • Positive culture results from at least 2 separate expectorated sputum samples; or at least 1 bronchial wash or lavage; or transbronchial or other lung biopsy with mycobacterial histological features and positive culture for NTM (or from sputum or bronchial washing)[1]	• Most cases of pulmonary *Mycobacterium avium-intracellulare* (MAI) infection involve MAC, but may also be due to *M kansasii, M xenopi*, or *M abscessus*[3] • *M pneumoniae* infection may induce asthma onset through Th-2 type inflammation of the airways[6] • Sputum examination and culture used to diagnosis and distinguish MAC infection from TB[3]

ABPA, allergic bronchopulmonary aspergillosis; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CT, computed tomography; GERD, gastroesophageal reflux disease.

NTM infection is more common in persons with asthma and should be considered in difficult-to-treat disease, especially in older individuals, late-onset asthma, and poorly controlled disease.[1,5]

ECZEMA (ATOPIC DERMATITIS [AD])

- Many patients, as well as their family members who have AD, may also have asthma or allergic rhinitis[1]
- About 70% of patients with severe AD may develop asthma[2]
- Genetic factors, epidermal barrier dysfunctions, immunological mechanisms, and environmental triggers contribute to development of AD[1]

Clinical Features	Diagnosis	Important Considerations
• Intense pruritus[1] • Acute phase lesions are red, edematous, scaly patches, or weepy plaques[1] • Chronic phase lesions are dry and lichenified[1]	• Clinical evaluation, and personal or family history of atopic disease[1] • Assess for allergic triggers with skin prick, patch, or intracutaneous testing[1] • Allergen-specific IgE levels[1]	• It is hypothesized that there may be an optimal window of opportunity early in life when targeting the skin barrier with therapeutic interventions may prevent subsequent chronic atopic disorders, such as asthma[2]

Ig, immunoglobulin.

Respiratory symptoms are often more likely to be due to asthma in persons with a history of eczema. Therefore, it is important to evaluate any respiratory symptoms in patients with eczema for the possibility of asthma.[3]

OBESITY

- Asthma may be difficult to control in obese patients due to an inflammation-modified inflammatory response, comorbidities, such as obstructive sleep apnea (OSA) and GERD, mechanical factors affecting the lungs, or undefined factors[1]
- Lack of fitness (deconditioning) and reduction in lung volume from abdominal fat may contribute to dyspnea[1]
- Asthma obesity phenotype is associated with low lung volume breathing, less eosinophilic inflammation, and a reduced response to asthma medicine[2]

Clinical Features	Diagnosis	Important Considerations
• Body mass index (BMI)[3] ≥30 kg/m^2	• BMI calculator[3] • Confirm asthma diagnosis with objective measurement of variable airflow limitation and bronchoprovocation testing[1] • Patients with a BMI ≥35 kg/m^2 and 1 or more severe obesity-related complications may be considered for bariatric surgery[4]	• Reduced response to ICS in obese patients[1] • A 5% to 10% weight loss may lead to improved asthma control, lung function, and reduced medication needs[1]

GERD, gastroesophageal reflux disease; ICS, inhaled corticosteroid.

- **There is an increased risk of comorbid obesity in patients with asthma who have more severe disease and are treated with higher cumulative systemic corticosteroid doses[5]**
- **Asthma is more common and difficult to control in persons classified as obese[1]**
- **Respiratory symptoms associated with obesity can mimic asthma, therefore, an asthma diagnosis should be confirmed with objective measurement of variable expiratory airflow limitation[1]**

DECONDITIONING

- Declining skeletal, muscular, circulatory, and respiratory systems following periods of inactivity, bed rest, sedentary lifestyle, and aging[1]
- Cardiopulmonary deconditioning can lead to dyspnea[2]

Clinical Features	Diagnosis	Important Considerations
• Dyspnea or complaint of breathlessness[3]	• Full lung examination[3] • Pulse oximetry and chest X-ray[3] • CT, pulmonary function tests (PFTs), or echocardiogram[3] • Cardiopulmonary exercise testing (CPET) to evaluate dyspnea of uncertain cause[4]	• May occur more frequently in obese patients[2] • CPET suggests deconditioning, obesity, and cardiac or pulmonary limitations[4] • Acute respiratory steroid myopathy can be caused by long-term use of high-dose systemic corticosteroid therapy[5]

CT, computed tomography.

Persons with asthma may have reduced functional capacity, which can contribute to worsening asthma symptoms (eg, dyspnea with lower levels of physical activity).[2,5]

Consider alternative causes for exercise intolerance as part of the differential diagnosis for asthma, especially in patients with poor response to appropriate treatment for exercise-induced bronchospasm.[6]

OBSTRUCTIVE SLEEP APNEA (OSA)

- High prevalence in patients with uncontrolled asthma[1]
- OSA is 7 times more common in people who are obese (BMI >30 kg/m^2)[2]
- Obesity and OSA tend to aggravate existing asthma and make symptom control more difficult[3]

Clinical Features	Diagnosis	Important Considerations
• Unrefreshing sleep, restlessness, snoring, recurrent awakening with breath holding, gasping, choking, and excessive daytime sleepiness[2] • Sore throat, dry mouth, or morning headache[2] • Congestion of nasopharynx, with mouth breathing[1] • Hypoxemia leading to increased bronchial reactivity[1]	• BMI calculator[4] • Frequency and severity of symptoms including: loud snoring, daytime sleepiness, choking, gasping, or stopped breathing during sleep, and high blood pressure[5] • For more details refer to STOP-Bang (SBQ)[5] or Berlin questionnaire[6] • Sleep history[2] • Polysomnography[2]	• OSA may be mistaken for nocturnal asthma because of similar presentation[1] • Risk factors include a neck circumference >17 inches in males and >16 inches in females, thick lateral pharyngeal walls, and lateral parapharyngeal fat pads[2]

BMI, body mass index.

Patients who have nocturnal asthma symptoms, particularly those who are overweight or obese, should be evaluated for symptoms that suggest OSA.[1]

UNRECOGNIZED CARDIOVASCULAR CONDITIONS AND UNCOMMON PULMONARY DISEASES

- Chronic heart disease is more prevalent in those with asthma than without (4.5% vs 3.6%, respectively)[1]
- Active, adult-onset asthma is an unrecognized risk factor for myocardial infarction[2]

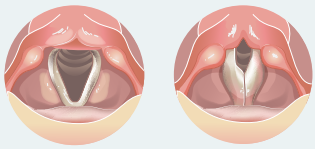
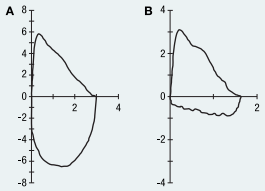
Clinical Features	Diagnosis	Important Considerations
• Dyspnea, cough,[3] wheezing,[1] or chest tightness[2]	• Chest CT, EKG, and echocardiogram[4] • Bronchoscopy and cardiopulmonary exercise testing[5,6] • Consider bronchial airway or pulmonary parenchymal diseases in a differential diagnosis for asthma[3]	• Asthma patients may be at increased risk for these CV conditions: hypertension, cardiac ischemia, arrhythmia, congestive heart failure, and cerebrovascular disease/atherosclerosis[7] • In patients with both asthma and COPD, use of beta$_2$-agonist medicines may be associated with new heart failure and hospitalizations[8] • Diseases or conditions associated with dyspnea or cough include: anemia, deconditioning, pulmonary embolus, pulmonary hypertension, thyroid compression of trachea, vascular ring, or vasculitis[3] • If asthma is difficult to control, other etiologies, including mitral valve disease should be taken into consideration[9] • Diseases or conditions associated with differential diagnosis include: bronchiolitis, diffuse idiopathic pulmonary neuroendocrine cell hyperplasia, foreign body aspiration (eg, food or drink), hypersensitivity pneumonitis, interstitial pulmonary fibrosis, pulmonary lymphoma, tracheoesophageal fistula, or tracheomalacia/laryngomalacia[3]

COPD, chronic obstructive pulmonary disease; CT, computed tomography; CV, cardiovascular; EKG, electrocardiogram.

Certain cardiovascular or pulmonary diseases may cause dyspnea or cough that can be misdiagnosed as asthma; consider differential diagnosis.[3]

VOCAL CORD DYSFUNCTION (VCD)

- Causes upper airway obstruction and mimics symptoms of severe asthma[1]
- Occurs in response to irritation of the larynx or hypopharynx, as well as secondary to anxiety, or emotional or physical stress[2]
- Flow-volume inspiratory loop may help identify VCD as it exhibits flattened flow rate with variability[2]
- Up to 50% of patients have VCD concomitant with asthma[3]

Clinical Features	Diagnosis	Important Considerations
• Inspiratory stridor and some expiratory wheezing[1] • Hoarseness, throat tightness, choking sensation, and cough[1] • Symptoms are periodic and can range from no symptoms to mild dyspnea to acute-onset respiratory distress that mimics an asthma attack[3] • Episodic symptoms may be provoked by respiratory or laryngeal irritants, such as strong odors or dust[2]	• Frequency and severity of throat restriction, inspiratory stridor, shortness of breath on inhale, loss of voice during attack, sensation of light pressure on neck, previous intubation for asthma attack, history of anxiety, or hyperventilation symptoms[3] • For more details refer to VCD[3] or VCD questionnaire[4] • Laryngoscope to distinguish asthma from VCD[2]  Normal Vocal Cord — Dysfunctional Vocal Cord • Flow-volume loop[3]  Normal — VCD	• Frequent use of metered-dose or dry-powder inhaler therapy can trigger or exacerbate symptoms, while nebulizer medication can provide relief[3] • Exercise can be a common trigger of VCD, which is often misdiagnosed as exercise-induced bronchospasm[2] • Confirmation is obtained by direct visualization of inspiratory adduction of vocal folds by laryngoscopy during symptoms (acute attack), and ideally after a bronchoprovocation challenge; however, a normal exam does not rule out VCD[3] • Larynx inflammation may also be associated with GERD or laryngopharyngeal reflux[2] • Severe symptoms and impressions of respiratory failure can lead to intubation[3]

GERD, gastroesophageal reflux disease.

VCD should be considered in the differential of difficult-to-treat, atypical asthma patients; however, VCD may coexist with asthma and complicate asthma management.[5]

ANXIETY AND DEPRESSION

- More prevalent in people with asthma[1]
- Associated with worse asthma symptom control, adherence to medicine, and asthma-related quality of life[1]
- Symptoms associated with increased asthma-related exacerbations and emergency room visits[1]
- Can be found in 25% to 49% of adults with severe asthma[2]

Clinical Features	Diagnosis	Important Considerations
• Depressive symptoms[3] • Behavioral problems[3] • Emotional problems[3] • Disregard of perceived asthma symptoms[3]	• Frequency and severity of depression symptoms, including loss of interest, feeling hopeless, sleep or appetite issues, and lacking energy[4] or anxiety symptoms, including nervousness, excess worrying, trouble relaxing, or restlessness[5] • For more details refer to PHQ-9 depression[4] or GAD-7 anxiety questionnaire[5]	• Panic attack may be misdiagnosed as asthma[1] • Most anxiety or depression screening surveys have not been validated in asthma populations[1] • Consider educating patient on coping-skill strategies[3]

GAD-7, Generalized Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9.

Anxiety and depression are more prevalent among persons with asthma and can be difficult to distinguish from symptoms of asthma.[1]

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