CHAPTER 2

TREATMENT ALGORITHMS FOR RESPIRATORY DISORDERS

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Abstract

The management of respiratory disorders is structured around algorithms that differentiate disease states and guide stepwise therapeutic intervention. Asthma management follows a control-based approach, stratifying patients into steps that dictate the use of inhaled corticosteroids (ICS) and bronchodilators, with a modern emphasis on ICS-formoterol as both a controller and reliever. The algorithm for Chronic Obstructive Pulmonary Disease (COPD) is based on the GOLD classification, using symptom burden and exacerbation history to guide the use of short- and long-acting bronchodilators (LAMA/LABA), with ICS reserved for patients with eosinophilic phenotypes. Pneumonia treatment algorithms are initiated by assessing severity (e.g., CURB-65) to determine the site of care, followed by empiric antibiotic selection based on likely pathogens and patient risk factors, with a mandate for timely de-escalation. The acute algorithm for pulmonary embolism is driven by hemodynamic stability and right ventricular strain, with risk stratification determining the use of anticoagulation, systemic thrombolysis, or embolectomy. Tuberculosis management is distinctly bifurcated into treatment for latent infection, which is a preventive algorithm, and active disease, which requires a prolonged, multi-drug regimen (RIPE) under directly observed therapy to ensure cure and prevent resistance.

Keywords: *Respiratory Algorithms, Asthma, COPD, Pneumonia, Pulmonary Embolism, Tuberculosis*

Learning Objectives

After completion of the chapter, the learners should be able to:

- List the main components of the stepwise management algorithm for persistent asthma based on GINA guidelines.
- Explain the GOLD classification system and its role in guiding the pharmacological treatment algorithm for COPD.
- Formulate an appropriate empiric antibiotic algorithm for a patient with community-acquired pneumonia (CAP) based on their CURB-65 score and comorbidities.
- Differentiate the management algorithms for latent tuberculosis infection (LTBI) versus active multi-drug-resistant tuberculosis (MDR-TB).
- Prioritize the diagnostic and therapeutic steps in the algorithm for a patient with a suspected massive pulmonary embolism.

ASTHMA

Asthma is a heterogeneous chronic inflammatory disorder of the airways characterized by reversible bronchoconstriction and airway hyperresponsiveness. The treatment algorithm is based on a stepwise, control-based approach to mitigate symptoms and reduce the risk of future exacerbations.

Pathophysiology

The pathophysiology is driven primarily by a T-helper 2 (Th2) cell-mediated immune response. In sensitized individuals, exposure to an allergen triggers IgE production, which coats mast cells. Upon re-exposure, these mast cells degranulate, releasing pre-formed mediators like histamine and leukotrienes. This causes the "early-phase" reaction: acute smooth muscle contraction (bronchoconstriction) and vasodilation. This is followed hours later by a "late-phase" reaction, characterized by a massive influx of eosinophils, which release cytotoxic proteins that damage the airway epithelium and perpetuate inflammation. Over years, this chronic inflammation leads to airway remodeling—a structural change involving bronchial smooth muscle hypertrophy, sub-epithelial fibrosis, and mucus gland hyperplasia—which can make the disease less reversible.

Diagnosis and Classification

Diagnosis is established clinically by a history of variable respiratory symptoms (wheeze, cough, dyspnea) and confirmed by objective measures of variable expiratory airflow limitation, most notably via spirometry. A significant reversible response to a bronchodilator (e.g., FEV1 increase > 12% and 200 mL) is a classic diagnostic finding. Classification has moved from traditional "intermittent" and "persistent" categories to a more practical framework based on the level of therapy required to maintain control, as outlined in the Global Initiative for Asthma (GINA) guidelines.

Differential Diagnosis

The differential for asthma-like symptoms is broad. In adults, it critically includes Chronic Obstructive Pulmonary Disease (COPD), which typically demonstrates non-reversible or poorly reversible airflow obstruction. Other considerations include congestive heart failure ("cardiac asthma"), vocal cord dysfunction, gastroesophageal reflux disease (GERD) with cough, and allergic rhinitis with post-nasal drip. In children, viral bronchiolitis and foreign body aspiration must be considered.

Treatment Algorithm

The modern asthma algorithm is designed to ensure that all patients receive an inhaled corticosteroid (ICS) to manage the underlying inflammation, moving away from short-acting beta-agonist (SABA) monotherapy.

Stepwise Controller Therapy (GINA)

The treatment algorithm is organized into five steps.

Step 1

For patients with infrequent symptoms, the preferred algorithm is as-needed low-dose ICS-formoterol (a long-acting beta-agonist, or LABA, with a fast onset). This single inhaler serves as both the controller and reliever

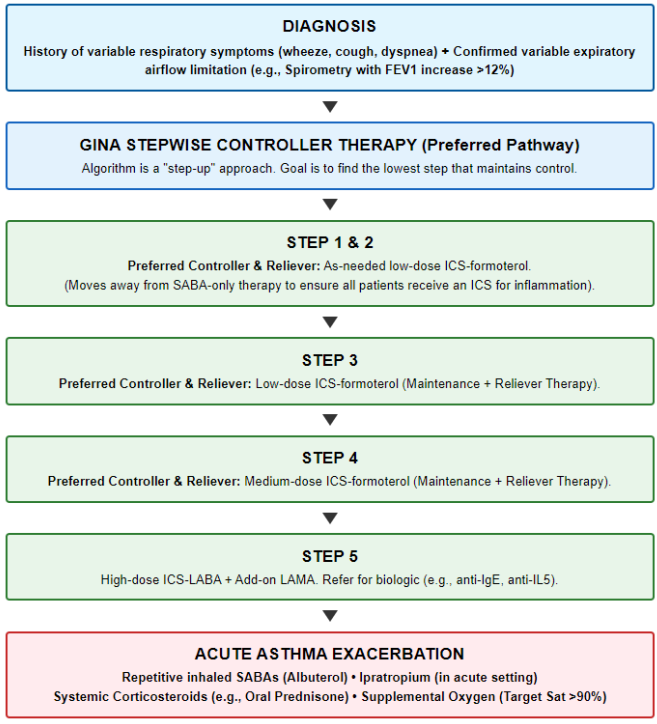

Figure 2.1: Asthma - GINA Stepwise Management

Step 2

For patients with symptoms more frequently, the preferred algorithm is daily low-dose ICS plus as-needed SABA, or the continuation of as-needed low-dose ICS-formoterol.

Step 3

The algorithm advances to a maintenance dose of low-dose ICS-LABA. The ICS-formoterol combination can again be used for both maintenance and relief (known as SMART or MART).

Step 4

This step involves escalating to a medium-dose ICS-LABA combination.

Table 2.1: GINA Stepwise Algorithm for Asthma Management

Step	Preferred Controller	Preferred Reliever
Step 1-2	As-needed low-dose ICS-formoterol*	As-needed low-dose ICS-formoterol*
Step 3	Low-dose ICS-formoterol (Maintenance + Reliever)	As-needed low-dose ICS-formoterol
Step 4	Medium-dose ICS-formoterol (Maintenance + Reliever)	As-needed low-dose ICS-formoterol
Step 5	High-dose ICS-LABA + Add-on LAMA. Refer for biologic.	As-needed low-dose ICS-formoterol

**ICS = Inhaled Corticosteroid. An alternative algorithm using a SABA reliever exists.*

Step 5

For severe asthma, the algorithm proceeds to high-dose ICS-LABA. At this stage, phenotype assessment is required to consider add-on therapies such as a long-acting muscarinic antagonist (LAMA) or biologic agents (e.g., anti-IgE, anti-IL5) for severe eosinophilic or allergic asthma.

Acute Exacerbation Algorithm

The algorithm for an acute asthma exacerbation is time-sensitive. It involves repetitive administration of inhaled SABAs (e.g., albuterol), often with ipratropium bromide in the acute setting, supplemental oxygen to maintain saturation > 90%, and a short course of systemic corticosteroids (e.g., oral prednisone) to control the underlying inflammatory surge.

Monitoring and Follow-Up

The goal of monitoring is to assess asthma control and adjust therapy in a stepwise fashion (e.g., per GINA guidelines). Control is assessed by two domains: symptom control (daytime symptoms, nighttime awakenings, rescue inhaler use, activity limitation) and future risk (exacerbations, lung function decline). Clinically, the "Rule of Twos" is a useful heuristic: if a patient uses their rescue SABA >2 times per week, wakes at night

>2 times per month, or refills their SABA >2 times per year, their asthma is uncontrolled. Objective monitoring involves spirometry (FEV1 and FEV1/FVC ratio) at diagnosis and periodically (e.g., annually) to assess long-term lung function. Peak Expiratory Flow (PEF) monitoring at home can be useful for patients with poor symptom perception or those in the "yellow zone" of their action plan. Follow-up visits should be scheduled every 1-3 months for uncontrolled asthma and every 6-12 months for well-controlled asthma.

Long-Term Management / Secondary Prevention

Long-term management is focused on preventing exacerbations and minimizing symptom burden. The cornerstone of prevention is controlling the underlying inflammation with an inhaled corticosteroid (ICS). The paradigm has shifted away from SABA-only treatment; all patients, even with mild asthma, should receive an ICS, either as a daily controller or as-needed in combination with their rescue bronchodilator. For persistent symptoms, the next step is adding a long-acting beta-agonist (LABA) in a combination inhaler with the ICS. It is critical to note that LABAs should never be used as monotherapy for asthma. Other long-term strategies include trigger avoidance (e.g., dust mite covers, HEPA filters, pet dander control) and the creation of a personalized "Asthma Action Plan." This plan empowers the patient to recognize worsening symptoms (the "yellow zone") and initiate pre-prescribed therapy (e.g., increasing ICS dose or adding oral steroids) to prevent a severe exacerbation.

Patient Counseling Points

- Inhaler Technique: This is the most common cause of treatment failure. The clinician must demonstrate and have the patient demonstrate back the use of their specific device (e.g., MDI with a spacer, or a DPI) and re-check technique at every visit.
- Controller vs. Rescuer: The most important concept to teach is the difference between the "rescuer" (SABA, e.g., albuterol) which opens the tubes immediately, and the "controller" (ICS, e.g., fluticasone) which reduces the

inflammation and prevents attacks. Over-reliance on the rescuer is a red flag for poor control.

- Asthma Action Plan: The patient must understand their "Green," "Yellow," and "Red" zones. They must know what to do when they enter the "Yellow zone" (e.g., "I will add my 'yellow zone' inhaler and call the office") and "Red zone" ("I will use my rescue inhaler, take my oral steroid, and go to the emergency room").
- Trigger Avoidance: Counsel on identifying and mitigating personal triggers, such as dust, pollen, cold air, or exercise-induced bronchospasm.

Common Pitfalls in Management

The most significant pitfall is the historical over-reliance on SABA monotherapy, which manages symptoms but not inflammation, thereby increasing exacerbation risk. Other common errors include poor inhaler technique, failure to identify and mitigate environmental triggers (e.g., allergens, smoke), and misdiagnosing COPD as asthma (or vice-versa), leading to inappropriate therapy.

Case Study

A 22-year-old college student (Ms. Lee) presents with a cough and wheeze. She reports "getting colds" 3-4 times per month that "go to her chest." She has to use her albuterol (SABA) rescue inhaler 4-5 days a week and wakes up with a cough about twice a week. She has no daily controller medication.

Discussion

Ms. Lee's symptoms (rescue inhaler use >2x/week, nighttime awakenings) indicate her asthma is **uncontrolled**. The GINA algorithm has a major paradigm shift: SABA-only therapy is no longer recommended, as it does not treat the underlying inflammation. She is at high risk for an exacerbation. The algorithm dictates she should be on, at minimum, a daily controller or a combination ICS-formoterol reliever.

Treatment Algorithm

- **Classification:** Uncontrolled asthma, consistent with GINA Step 2/3.
- **Algorithm Step-Up:** The patient is currently on SABA-only (an outdated Step 1). She needs to be moved to a therapy that includes an Inhaled Corticosteroid (ICS).
- **Therapeutic Choice:** You select the **GINA "Preferred Pathway"**
- **Option (GINA Step 3):** Low-dose ICS-Formoterol (e.g., budesonide-formoterol) to be used for *both* daily maintenance and as-needed relief (this is the "MART" or "SMART" algorithm).
- **Counseling:** You explain that her new single inhaler is now her "controller" and "reliever" in one. You also provide an "Asthma Action Plan" to help her manage symptoms.
- **Outcome:** Ms. Lee is prescribed a budesonide-formoterol inhaler to use twice daily and as needed for symptoms. You schedule a follow-up in 4 weeks to assess her control, checking her reliever use and nighttime symptoms

CHRONIC OBSTRUCTIVE PULMONARY DISORDER (COPD)

COPD is a common, preventable, and treatable disease characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities, usually caused by significant exposure to noxious particles or gases.

Pathophysiology

Chronic Obstructive Pulmonary Disease (COPD is caused by an abnormal inflammatory response to noxious particles, primarily cigarette smoke. The pathophysiology encompasses two overlapping phenotypes:

Emphysema

This is a disease of the acinus (the gas-exchanging units).

Oxidative stress from smoke leads to an imbalance between proteases (like neutrophil elastase) and anti-proteases (like alpha-1-antitrypsin). This protease activity destroys alveolar walls, creating large, non-functional air sacs (bullae). This reduces the surface area for gas exchange and causes loss of elastic recoil, leading to "air trapping" and lung hyperinflation.

Chronic Bronchitis

This is a disease of the conducting airways. It is defined clinically by a productive cough for ≥3 months in ≥2 consecutive years. Pathologically, it involves neutrophilic inflammation (distinct from the eosinophilic inflammation of asthma), smooth muscle hypertrophy, and profound goblet cell and mucus gland hyperplasia, leading to chronic airway obstruction and a productive cough.

Diagnosis and Classification

Diagnosis is confirmed by spirometry in a patient with appropriate symptoms (dyspnea, chronic cough) and risk factors (e.g., tobacco smoke). A post-bronchodilator FEV1/FVC ratio < 0.70 confirms the presence of persistent airflow limitation. The GOLD (Global Initiative for Chronic Obstructive Lung Disease) classification system is the cornerstone of the management algorithm. It classifies patients into groups (A, B, E) based on symptom burden (using mMRC or CAT scores) and exacerbation history, which guides initial therapy.

Differential Diagnosis

The primary differential diagnosis for COPD is asthma. The main distinguishing features include age of onset (COPD typically > 40), smoking history, and the significant reversibility of airflow limitation seen in asthma. Other differentials include heart failure, bronchiectasis, and, in younger patients or non-smokers, alpha-1 antitrypsin deficiency, which must be screened for.

Treatment Algorithm

The COPD algorithm focuses on symptom reduction, risk reduction (exacerbations), and slowing disease progression.

Stable COPD Algorithm

The algorithm begins universally with smoking cessation and pulmonary rehabilitation.

- **Group A:** Patients with low symptoms and low exacerbation risk. The algorithm starts with a short- or long-acting bronchodilator (SABA or LABA/LAMA).
- **Group B:** Patients with high symptoms but low exacerbation risk. The algorithm dictates initial therapy with a long-acting bronchodilator. Dual therapy with a LAMA + LABA is often used if symptoms are severe.
- **Group E:** Patients with high exacerbation risk (e.g., ≥ 2 moderate exacerbations or ≥ 1 hospitalization in the past year). The algorithm mandates initial therapy with a LAMA + LABA combination. If the patient has a high blood eosinophil count (≥ 300 cells/μL), indicating an "asthma-like" inflammatory component, the algorithm supports the addition of an ICS (triple therapy: LAMA+LABA+ICS).

Table 2.2: Pharmacological Algorithm for Stable COPD (GOLD Groups)

Patient Group	Symptoms	Exacerbation Risk	Initial Pharmacotherapy
Group A	Low (mMRC 0-1)	Low (0-1)	A Bronchodilator (SABA or SAMA)
Group B	High (mMRC ≥ 2)	Low (0-1)	A Long-Acting Bronchodilator (LABA or LAMA)
Group C	Low (mMRC 0-1)	High (≥ 2 or ≥ 1 hosp.)	LAMA (Long-Acting Muscarinic Antagonist)
Group D	High (mMRC ≥ 2)	High (≥ 2 or ≥ 1 hosp.)	LAMA or LAMA + LABA (or LABA + ICS if eos ≥ 300)

Acute Exacerbation Algorithm

Management of an acute exacerbation of COPD (AECOPD)