

Asthma management

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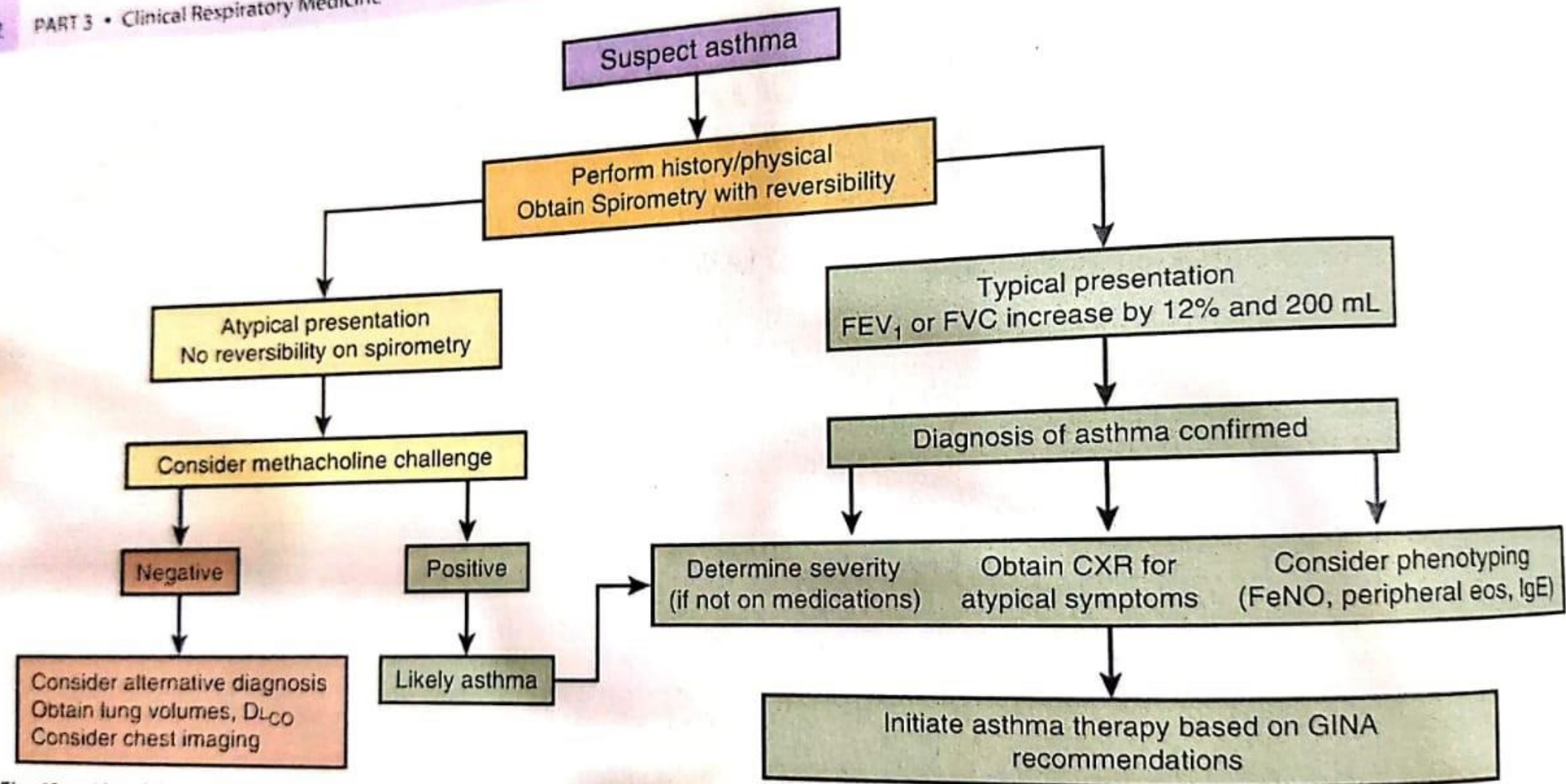


Fig. 62.1 Algorithm for diagnosing asthma in adults. The diagnosis of asthma is based on a careful personal history, physical examination, and lung function testing. Spirometry should be obtained in every patient in whom asthma is suspected. Other tests are useful when clinical features are atypical, and to determine severity and asthma phenotype. CXR, chest radiograph; DL_{CO} , diffusing capacity for carbon monoxide; eos, eosinophils; FeNO, fraction of exhaled nitric oxide; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; IgE, immunoglobulin E; GINA, Global Initiative for Asthma.

Table 42-1 Classification of Severity of Asthma in Adults and Children Older Than 12 not Currently Taking Long-Term Controllers

Components of Severity	CLASSIFICATION OF ASTHMA SEVERITY (YOUTHS ≥ 12 YR AND ADULTS)			
	Intermittent	Mild	Moderate	Severe
IMPAIRMENT				
Symptoms	≤2 days/wk	>2 days/wk but not daily	Daily	Throughout the day
Nighttime awakenings	<2x/mo	3–4x/mo	>1x/wk but not nightly	Often 7x/wk
Short-acting β ₂ -agonist use for symptom control	≤2 days/wk	>2 days/wk but not daily	Daily	Several times per day
Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Lung function	Normal FEV ₁ between exacerbations ▪ FEV ₁ > 80% predicted ▪ FEV ₁ /FVC normal	▪ FEV ₁ > 80% predicted ▪ FEV ₁ /FVC normal	▪ FEV ₁ > 60% but < 80% predicted ▪ FEV ₁ /FVC reduced 5%	▪ FEV ₁ < 60% predicted ▪ FEV ₁ /FVC reduced > 5%
RISK				
Exacerbations (consider frequency and severity)	0–2/yr Frequency and severity may fluctuate over time Relative annual risk of exacerbations may be related to FEV ₁	>2/yr	>2/yr	>2/yr

FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

National Heart, Lung, and Blood Institute. National Asthma Education and Prevention Program. Full report of the Expert Panel: Guidelines for the diagnosis and management of asthma (EPR-3) DRAFT, page 74, section 3, component 1: Measures of Asthma Assessment and Monitoring.

Symptoms score	25%	20%	15%	10%	5%	Total score
Diurnal symptoms	None	<4 times/w	4-7 times/w	>once /day	Severe	15
Nocturnal symptoms	None	<1 night/w	1-3 nights/ w	4-7 nights/w	Severe	20
β_2 -agonist on demand*	None	<4 doses/w	4-7 times/w	>1 dose/day	>4 doses/day	15
Physical activity	None	Very little limitation	Some limitation	Moderate limitation	Severe limitation	15
Total score						65%

	Total
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Table 42-4 Asthma Therapy Assessment Questionnaire on Asthma Control

1. In the past 4 weeks, did you miss any work, school, or normal daily activities because of your asthma? (1 point for YES)
2. In the past 4 weeks, did you wake up at night because of your asthma? (1 point for YES)
3. Do you believe your asthma was well controlled in the past 4 weeks? (1 point for NO)
4. Do you use an inhaler for quick relief from asthma symptoms? If yes, what is the highest number of puffs in 1 day you took of this inhaler? (1 point for more than 12)

Total points—0–4, with more points indicating more control problems

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Asthma Control Test™

This survey was designed to help you describe your asthma and how your asthma affects how you feel and what you are able to do. To complete it, please mark an X in the one box that best describes your answer.

1. In the **past 4 weeks**, how much of the time did your **asthma** keep you from getting as much done at work, school or at home?

All of the time <input type="checkbox"/> 1	Most of the time <input type="checkbox"/> 2	Some of the time <input type="checkbox"/> 3	A little of the time <input type="checkbox"/> 4	None of the time <input type="checkbox"/> 5
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2. During the **past 4 weeks**, how often have you had shortness of breath?

More than once a day <input type="checkbox"/> 1	Once a day <input type="checkbox"/> 2	3 to 6 times a week <input type="checkbox"/> 3	Once or twice a week <input type="checkbox"/> 4	Not at all <input type="checkbox"/> 5
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3. During the **past 4 weeks**, how often did your **asthma** symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

4 or more nights a week <input type="checkbox"/> 1	2 to 3 nights a week <input type="checkbox"/> 2	Once a week <input type="checkbox"/> 3	Once or Twice <input type="checkbox"/> 4	Not at all <input type="checkbox"/> 5
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4. During the **past 4 weeks**, how often have you used your rescue inhaler or nebulizer medication (such as Albuterol, Ventolin®, Proventil®, or Maxair®)?

3 or more times per day <input type="checkbox"/> 1	1 or 2 times per day <input type="checkbox"/> 2	2 or 3 times per week <input type="checkbox"/> 3	Once a week or less <input type="checkbox"/> 4	Not at all <input type="checkbox"/> 5
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5. How would you rate your **asthma** control during the **past 4 weeks**?

Not Controlled at all <input type="checkbox"/> 1	Poorly Controlled <input type="checkbox"/> 2	Somewhat Controlled <input type="checkbox"/> 3	Well Controlled <input type="checkbox"/> 4	Completely Controlled <input type="checkbox"/> 5
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Figure 42-3 The Asthma Control Test is a validated questionnaire that assesses the presence of asthma symptoms and use of asthma medications over the prior 4-week period. (Copyright 2002, 2004 by QualityMetric Incorporated. All rights reserved. Asthma Control Test™ [ACT] is copyrighted by QualityMetric Incorporated. No part of the Asthma Control Test™ may be reproduced or transmitted in any form or by any means electronic, mechanical, including photocopy, recording, or any information storage or retrieval system—without permission of the copyright holder. It should be used only as text. Licensing & Registration. For permission to reproduce the survey and/or any associated intellectual property [e.g., trademarks, scoring algorithms, interpretation guidelines, and normative data] for any purpose, registration must be made and license obtained at www.qualitymetric.com.)

Table 42-3 Sample Question from The Asthma Control Questionnaire*

Table 42-4 Asthma Therapy Assessment Questionnaire on Asthma Control

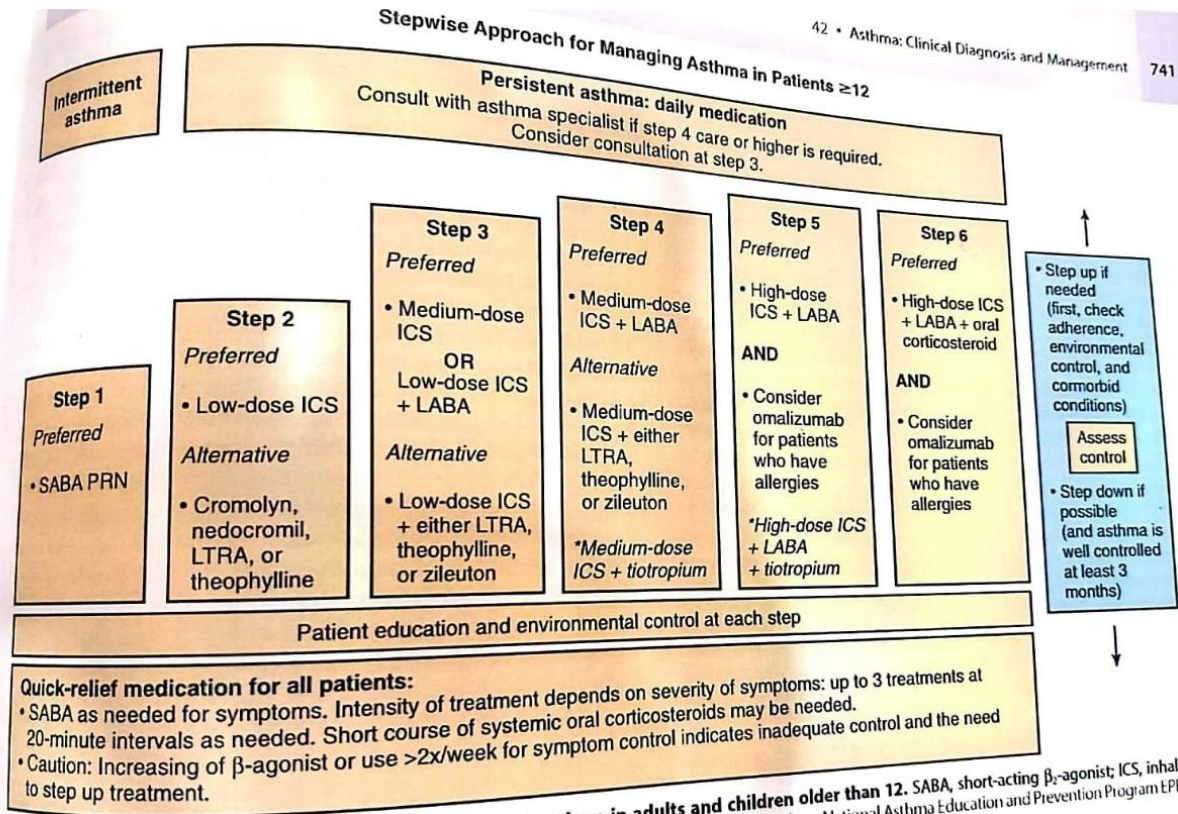


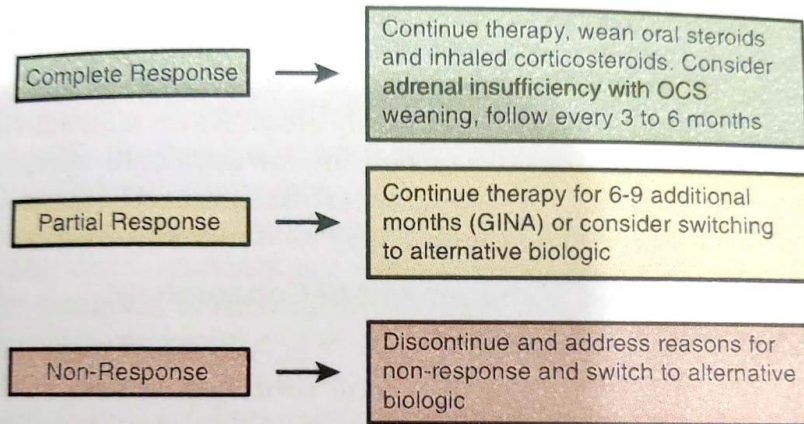
Figure 42-5 Medication recommendations for control of asthma in adults and children older than 12. SABA, short-acting β_2 -agonist; ICS, inhaled corticosteroid; LTRA, leukotriene receptor antagonist; LABA, long-acting β_2 -agonist. (Adapted from National Asthma Education and Prevention Program EPR guidelines from the National Heart, Lung, and Blood Institute 2007.)

... and uncoupling of receptors from downstream response appears to be se

	Step 1	Step 2	Step 3	Step 4	Step 5
Preferred Controller <i>To prevent exacerbations and control symptoms</i>	As-needed low-dose ICS-formoterol*	Low-dose ICS, or as-needed ICS-formoterol*	Low-dose ICS-LABA	Medium-dose ICS-LABA	High-dose ICS-LABA Refer for phenotypic assessment ± add-on therapy (e.g., tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R)
<i>Other controller options</i>	Low-dose ICS taken whenever SABA is taken†	LTRA or low-dose ICS taken whenever SABA is taken†	Medium-dose ICS, or low-dose ICS+LTRA‡	High-dose ICS, add-on tiotropium, or add-on LTRA‡	Add low-dose oral corticosteroids, but consider side effects
Preferred Reliever	As-needed low-dose ICS-formoterol*				
<i>Other reliever option</i>	As-needed SABA				
At all levels:	Assess	Adjust		Review Response	
	Confirmation of diagnosis Symptom control & modifiable risk factors (including lung function) Comorbidities Inhaler technique & adherence Patient goals	Treatment of modifiable risk factors & comorbidities Non-pharmacological strategies Education & skills training Asthma medications		Symptoms Exacerbations Side effects Lung function Patient satisfaction	

Fig. 62.3 Medication recommendations for control of asthma in adults and children older than 12 years. Controller medications should be initiated and subsequently adjusted up or down in a stepwise approach with a goal of achieving good control of symptoms and minimizing future risk of exacerbations, air flow obstruction, and adverse effects from medications. At onset of treatment and every 2 to 3 months thereafter, assess clinical factors, adjust medications, and review response. *Off-label; data only available for budesonide-formoterol. †Off-label; separate or combination ICS and SABA inhalers. ‡Consider adding house dust mite sublingual immunotherapy for sensitized patients with allergic rhinitis and FEV₁ >70% predicted. ICS, inhaled corticosteroid; Ig, immunoglobulin; ginasthma.org).

Management Based on Response



Consistently assess and document response markers: Asthma control, medication use, exacerbations, and biomarkers in all patients.

Fig. 62.6 Assessing response to biologic therapy. Before initiating biologic therapy, choose markers of response that will be monitored (e.g., exacerbations, oral corticosteroid use, asthma control, lung function, rescue bronchodilator use, patient comfort, and satisfaction). Most patients will experience at least a partial response to biologic therapy, 10–15% will have no response, and a small proportion will have a complete response. Assess response continuously and adjust asthma medications and/or biologics based on response. GINA, Global Initiative for Asthma; OCS, oral corticosteroids.

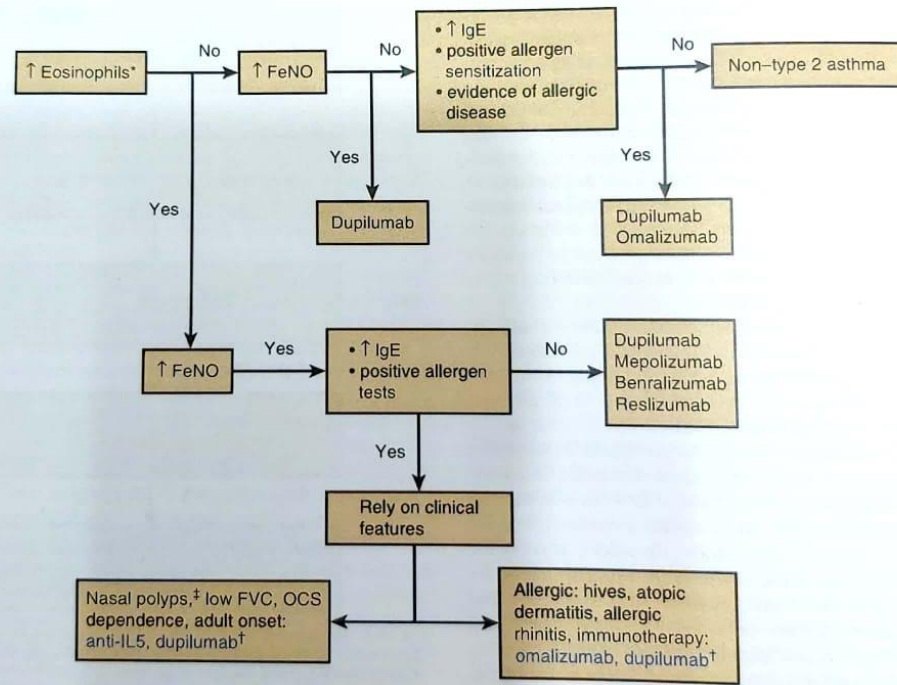


Fig. 62.5 Decision tree for selecting initial biologic therapy for severe asthma in patients with type 2 features. This algorithm is guided by high-quality evidence from clinical trials and supporting data. Medications are listed alphabetically, not in order of preference. Patients should have regular assessment of clinical benefit, and treatment should be adjusted until asthma control is achieved. *Increased eosinophils is defined by blood eosinophil counts >150–300/ μ L. Dupilumab should not be used for patients with >1500 eosinophils/ μ L. †At the time of publication, dupilumab is also FDA approved for use in nasal polyps and atopic dermatitis. Omalizumab is also FDA approved for use in chronic urticaria. ‡Nasal polyps predict an enhanced response to these T2 biologics when targeting asthma. The efficacy of each biologic for nasal polyps may differ. FDA, U.S. Food and Drug Administration; FeNO, fraction of exhaled nitric oxide; FVC, forced vital capacity; IgE, immunoglobulin E; OCS, oral corticosteroid.

Table 42-5 Asthma Biomarkers and Associated Phenotypes as Predictors of Response to Specific Therapies

Biomarker	Asthma Phenotype	Predicts
Periostin	Th2 high	Response to anti-IL-13 and IL-4 therapy ^{112,116}
Elevated exhaled nitric oxide (>50 ppb in adults, >35 ppb in children)	Th2 high	Response to inhaled steroids ^{65,110}
Sputum eosinophils >3%	Th2 high	Response to inhaled steroids ^{103-107,109,207}
Peripheral eosinophils ($>0.3 \times 10^9/L$ or $300/\mu L$)	Th2 high	Response to anti-IL-5 therapy ^{99,100,292}
Elevated total IgE > 30 IU	Allergic	Response to omalizumab ^{111,202}
Allergy skin tests and elevated specific IgE	Allergic asthma with atopy	Response to immunotherapy, omalizumab
Lack of elevated peripheral and sputum eosinophils and low FeNO	Th2 low	Response to tiotropium and macrolides (likely to be poor responders to steroids) ^{215,216}

Table 62.1 Classification of Asthma Control in Adults and Adolescents >11 Years per GINA Guidelines

Asthma Symptom Control	Yes	No
<p>In the past 4 weeks, has the patient had:</p> <ul style="list-style-type: none"> ■ Daytime asthma symptoms more than twice per week? ■ Any night waking due to asthma? ■ Reliever needed for symptoms more than twice per week? ■ Any activity limitation due to asthma? 		
<p>Total:</p> <p>Level of asthma symptom control is based on total number of “yes” responses:</p> <ul style="list-style-type: none"> ■ If 0, asthma is well controlled ■ If 1–2 of these, asthma is partly controlled ■ If 3–4 of these, asthma is uncontrolled 		
<p>Risk factors for poor asthma outcomes:</p> <ul style="list-style-type: none"> ■ Uncontrolled symptoms ■ Medication challenges (frequent short-acting bronchodilator use, poor adherence, incorrect technique, not on inhaled corticosteroid) ■ Comorbidities (obesity, chronic rhinosinusitis, GERD, pregnancy) ■ Exposures (smoking, allergens, air pollution) ■ Low lung function (FEV_1 <60% predicted) or highly reversible bronchoconstriction ■ Psychological or socioeconomic factors ■ History of severe exacerbation 	<p>Any of these risk factors increases the patient’s risk of exacerbations even if they have few asthma symptoms</p>	

Table 62.2 Classification of Asthma Severity (GINA 2019)

ASSESS SYMPTOM CONTROL WHEN PATIENT HAS BEEN ON REGULAR CONTROLLER TREATMENT FOR SEVERAL MONTHS

Mild asthma	Well controlled with step 1 or step 2
Moderate asthma	Well controlled with step 3
Severe asthma	Requires step 4 or step 5 to prevent it from being uncontrolled, or is still uncontrolled despite this therapy

Steps are levels of treatment, as defined in Fig. 62.3.

Uncontrolled asthma is defined by the International European Respiratory Society/American Thoracic Society Guidelines for Severe Asthma as described later.

FEV₁, forced expiratory volume in 1 second; GINA, Global Initiative for Asthma. Courtesy GINA, www.ginasthma.org.

Table 62.5 Factors That Contribute to Worsening Asthma Control and Coexisting Conditions

Contributing Factor	Proposed Intervention
Tobacco use	Encourage tobacco cessation and assist with both nonpharmacologic and pharmacologic methods to help patients quit smoking; discuss avoidance of secondhand smoke
GERD	Consider empiric therapy for symptomatic GERD Barium swallow or pH probe study to diagnose GERD Impedance study if nonacid reflux is suspected Referral to gastroenterology for evaluation and treatment Consider surgical management for refractory cases
Atopy and allergic rhinitis	Consider empiric therapy with nasal steroids, nasal and oral antihistamines, leukotriene antagonists Consider skin prick testing or specific IgE testing to guide allergen identification and avoidance Referral to allergist or otolaryngologist for evaluation Consider allergen immunotherapy
Nasal polyps and chronic sinusitis	Refer to otolaryngologist for evaluation and treatment Possible surgical intervention for refractory cases Consider aspirin desensitization for patients with nasal polyps and aspirin sensitivity
Vocal cord dysfunction*	Laryngoscopy to diagnose vocal cord dysfunction Referral to speech pathologist for evaluation and treatment
Obesity*	Encourage weight loss Consider bariatric surgery
Obstructive sleep apnea*	Referral for sleep study and initiate therapy for sleep apnea Referral to sleep specialist for complex cases
Psychological factors*	Evaluate for anxiety and depression

*May coexist with asthma with overlapping symptoms (see also Chapter 61).
GERD, gastroesophageal reflux disease; Ig, immunoglobulin.

Table 42-2 Classification of Asthma Control in Adults and Children Older Than 12

Components of Control	CLASSIFICATION OF ASTHMA CONTROL (YOUTHS ≥ 12 YR AND ADULTS)		
	Well Controlled	Not Well Controlled	Very Poorly Controlled
IMPAIRMENT			
Symptoms	≤2 days/wk	>2 days/wk	Throughout the day
Nighttime awakening	≤2 times/mo	1–3 times/wk	≥4 times/wk
Interference with normal activity	None	Some limitation	Extremely limited
Short-acting β ₂ -agonist use for symptom control (not prevention of EIB)	≤2 days/wk	>2 days/wk	Several times/day
FEV ₁ or peak flow	>80% predicted/personal best	60%–80% predicted/personal best	<60% predicted/personal best
Validated questionnaires			
ATAQ	0	1–2	3–4
ACQ	≤0.75*	≥1.5	N/A
ACT	≥20	16–19	≤15
RISK			
Exacerbations	0–1/yr	≥2/yr [†]	
Progressive loss of lung function	Consider severity and interval since last exacerbation		
Treatment-related adverse effects	Evaluation requires long-term follow-up care Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk		

*ACQ values of 0.76–1.4 are indeterminate regarding well-controlled asthma.

[†](1) The level of control is based on the most severe impairment or risk category. Assess impairment domain by patient's recall of previous 2–1 wk and by spirometry or peak flow measures. Symptom assessment for longer periods should reflect a global assessment, such as inquiring whether the patient's asthma is better or worse since the last visit. (2) At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma control. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or intensive care unit admission) indicate poorer disease control. For treatment purposes, patients who had two or more exacerbations requiring oral systemic corticosteroid: the past year may be considered the same as patients who have not-well-controlled asthma, even in the absence of impairment levels consistent with not-well-controlled asthma.

ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; ATAQ, Asthma Therapy Assessment Questionnaire; EIB, exercise-induced bronchospasm; FEV₁, forced expiratory volume in 1 second; N/A, not applicable.

Adapted from National Heart, Lung, and Blood Institute as a part of the National Institutes of Health and the U.S. Department of Health and Human Services, 2007.

Asthma Drugs

- Beta Agonists
- ICS
- LTM_s
- Phosphodiesterase Inhibitor
- Anticholinergic agents
- Macrolides
- Targeted Biologic Agents
- Nonpharmacologic treatments

Management of acute Asthma

eTable 62.1 Inhaled Steroid Preparations and Dosages

Inhaler	Dosage Forms	Age (yr)	DAILY DOSE		
			Low	Medium	High
Beclomethasone (QVAR)	Redihaler MDI: 40 or 80 µg/puff	5-11	80-160	>160-320	>320
		≥12	80-240	>240-480	>480
Budesonide (Pulmicort, Symbicort [with formoterol])	Respules for nebulization: 0.25, 0.5, 1.0 mg/neb Flexhaler DPI: 90 or 180 µg/inh HFA MDI: 110 or 220 µg/puff Symbicort HFA MDI: 80/4.5 or 160/4.5 µg/puff	0-4	0.25-0.5	>0.5-1.0	>1.0
		5-11	0.5	1.0	2.0
		5-11	180-400	>400-800	>800
		≥12	180-600	>600-1200	>1200
Ciclesonide (Alvesco)	HFA MDI: 80 or 160 µg/puff	5-11*	80-160	>160-320	>320
		≥12	160-320	>320-640	>640 (mfr highest recommended dose)
Fluticasone propionate (Flovent, Advair [with salmeterol])	HFA MDI: 44, 110, or 220 µg/puff Flovent Diskus DPI: 50, 100, or 250 µg/inh Advair HFA MDI: 45/21, 115/21, or 230/21 µg/puff Advair Diskus DPI: 100/50, 250/50, or 500/50 µg/inh	0-11	88-176	>176-352	>352
		≥12	88-264	>264-440	>440
		5-11	100-200	>200-400	>400
		≥12	100-300	>300-500	>500
		4-11	180 (45/21 2 puffs bid)		460-920 (115-230/21 2 puffs bid)
		≥12	180 (45/21 2 puffs bid)	460 (115/21 2 puff bid)	920 (230/21 2 puffs bid)
Fluticasone furoate (Arnuity, Breo [with vilanterol], Trelegy [with vilanterol and umeclidinium])	Arnuity Ellipta DPI: 50, 100 or 200 µg/inh Breo Ellipta: 100/25 or 200/25 µg/inh Trelegy Ellipta: 100/62.5/25 µg/inh, 200/62.5/25 µg/inh	4-11	200 (100/50 1 inh bid)	500 (250/50 1 inh bid)	1000 (500/50 1 inh bid)
		5-11		50, 1 inh daily	200, 1 inh daily
		≥12		100, 1 inh daily	200/25, 1 inh daily
		≥12		100/25, 1 inh daily	200/25, 1 inh daily
Mometasone (Asmanex, Dulera [with formoterol])	Asmanex Twisthaler DPI: 110 or 220 µg/inh Dulera HFA MDI: 100/5 or 200/5 µg/puff	4-11	110 (mfr highest recommended dose)	220-440	>440
		≥12	220	440	>440 (mfr highest recommended dose 800 µg/day)
		≥12		400 (100/5 2 puffs bid)	800 (200/5 2 puffs bid)

*Not Food and Drug Administration approved for children <12 years.
DPI, dry powder inhaler; HFA, hydrofluoroalkane, a safe propellant; MDI, metered-dose inhaler; mfr, manufacturer.

ارزیابی و درمان تشخیصی‌های همراه

1 Vocal cord dysfunctionss

- Psychogenic vcd
- Irritant associated vcd
- Exercise induced vcd

2 allergic bronchopulmonary aspergilosis

