

Asthma

It's Just Asthma.....

The Burden of Asthma

Table 1. Prevalence, Mortality, and Health Care Utilization Among Adults With Asthma in the United States

Measure	Value
Prevalence, %^a	
Overall prevalence	7.4
Sex	
Male	5.1
Female	9.6
Race/ethnicity	
White non-Hispanic	7.6
Black non-Hispanic	8.7
Hispanic	5.8
Others	6.8
Hispanic of Puerto Rican origin	13.3
Hispanic of Mexican origin	4.9
Asthma-Specific Mortality (Deaths per Million per Year)^b	
Overall	14.1
Race/ethnicity	
White non-Hispanic	8.8
Black non-Hispanic	25.4
Hispanic	7.7
Others	9.9
Health Care Utilization	
Inpatient discharges (rate per 10 000 per year)^c	
Overall	13.0
Race	
White	8.7
Black	29.9
Other	12.6
Emergency department visits (in millions per year) ^d	1.8
Physician office visits (in millions per year) ^e	10.5
Hospital outpatient department visits (in millions per year) ^f	1.3

- Described since Hippocrates, affects all ages (peak incidence in childhood).
- Worldwide – estimated 300 million affected
 - Prevalence increasing, especially in children
 - about 180,000 Deaths per year.
- Major cause of school and work absence
- Health care expenditure very high
 - 1 to 2% of total health care expenditures in developed economies.
 - WHO (2004) - total asthma costs probably exceeded those of TB and HIV/AIDS combined
- In US
 - 7.5% of adults in US
 - More common in black (8.7%) and Puerto Rican Hispanic (13.3%) than in white individuals (7.6%)
 - Higher mortality in blacks than in whites (25.4 vs 8.8 per million annually).
 - Predominantly male disease up to puberty; 20-40 years-equal among both genders. After 40-more common in females.
 - 1.8 million hospitalizations and 10.5 million physician office visits per year.
 - 4000 deaths annually.
 - Estimated annual (2011) direct healthcare cost approximately \$50.1 billion

Question 1

The primary pathophysiology of asthma is:

1. Airway Smooth Muscle Dysfunction
2. Chronic Inflammation
3. Autonomic Dysfunction
4. Childhood viral disease

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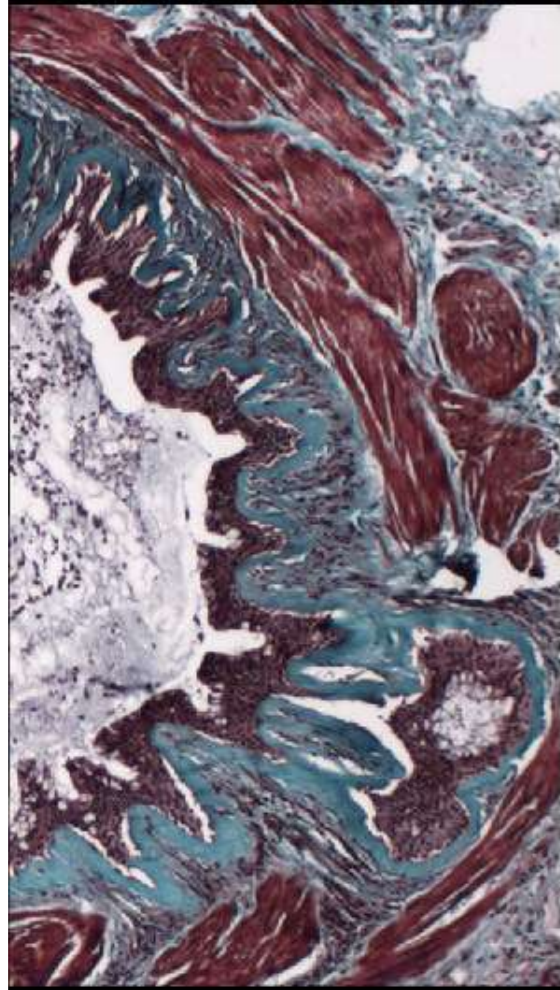
Asthma Pathology

Asthma is a chronic inflammatory disease associated with airway hyperresponsiveness

Short term Consequences

Airway obstruction and symptoms by:

- Bronchoconstriction
- Mucus plugs
- Mucosal edema
- Inflammatory cell infiltration/activation
- Airway hyperresponsiveness



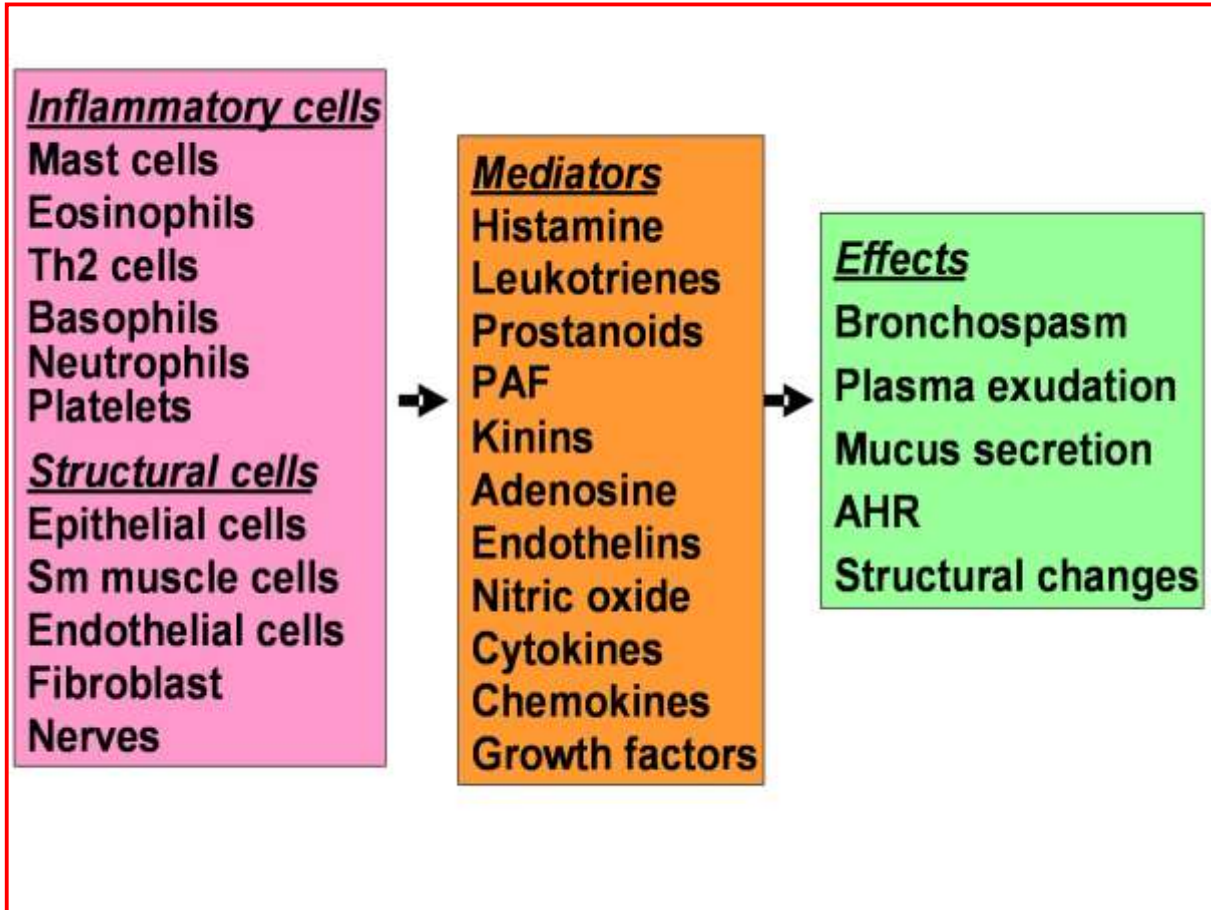
Long Term Consequences

Airway Remodeling

- Increased vascularity
- Epithelial cell disruption
- Increased airway smooth muscle mass (hyperplasia)
- Reticular basement membrane thickening

*No asthma therapy proven to reduce/eliminates airway remodeling

Complex Interactions



- Many different cells and inflammatory mediators responsible
 - Eosinophils, lymphocytes, mast cells, neutrophils
 - IgE occupies a central role in the pathogenesis of allergic asthma;
 - Allergen-dependent release of histamine and other mediators from mast cells and subsequent infiltration of lymphocytes (particularly T-helper type 2 [T_H2]) and granulocytes into the airway.
 - Elevated levels of proinflammatory cytokines IL-4, IL-5, and IL-13 are observed.
- Autonomic nervous system may augment the inflammatory response.

Asthma Initiation

Risk Factors

- Hereditary contribution
 - Familial clustering occurs.
 - Genes regulating:
 - IgE-related mechanisms
 - Glucocorticoid response
 - Airway smooth muscle development (*ADAM33*)
 - Components of the immune system (*HLA-G*)
- Environmental factors
 - Air pollution/Tobacco smoke
 - Cockroach/rodent infestations in the home
- Atopy/Exposure to Allergens
 - **Tree pollen** in early spring
 - **Grass pollen** in late spring/summer
 - **Ragweed in fall** Respiratory infections
- Rhinovirus and RSV, particularly in 1st 3 years of life
- Weight - Over/under
- Socioeconomic factors
 - Income level/access to medical care

Possible Protective Factors

- Hygiene hypothesis
 - Increase exposure to infections in childhood may reduce allergic sensitization and have a protective role.
 - Large family size,
 - Growing up on a farm.
 - Pet ownership
 - Child exposed to older children or a day care.
- Dietary antioxidants/ flavonoids.
- Use of biomass fuels.

Asthma Phenotypes and Endotypes

- **Phenotype:**

- “a single or combination of disease attributes that describe differences between individuals as they relate to clinically meaningful outcomes (symptoms, exacerbations, response to therapy, rate of disease progression, or death)”

- **Endotype:**

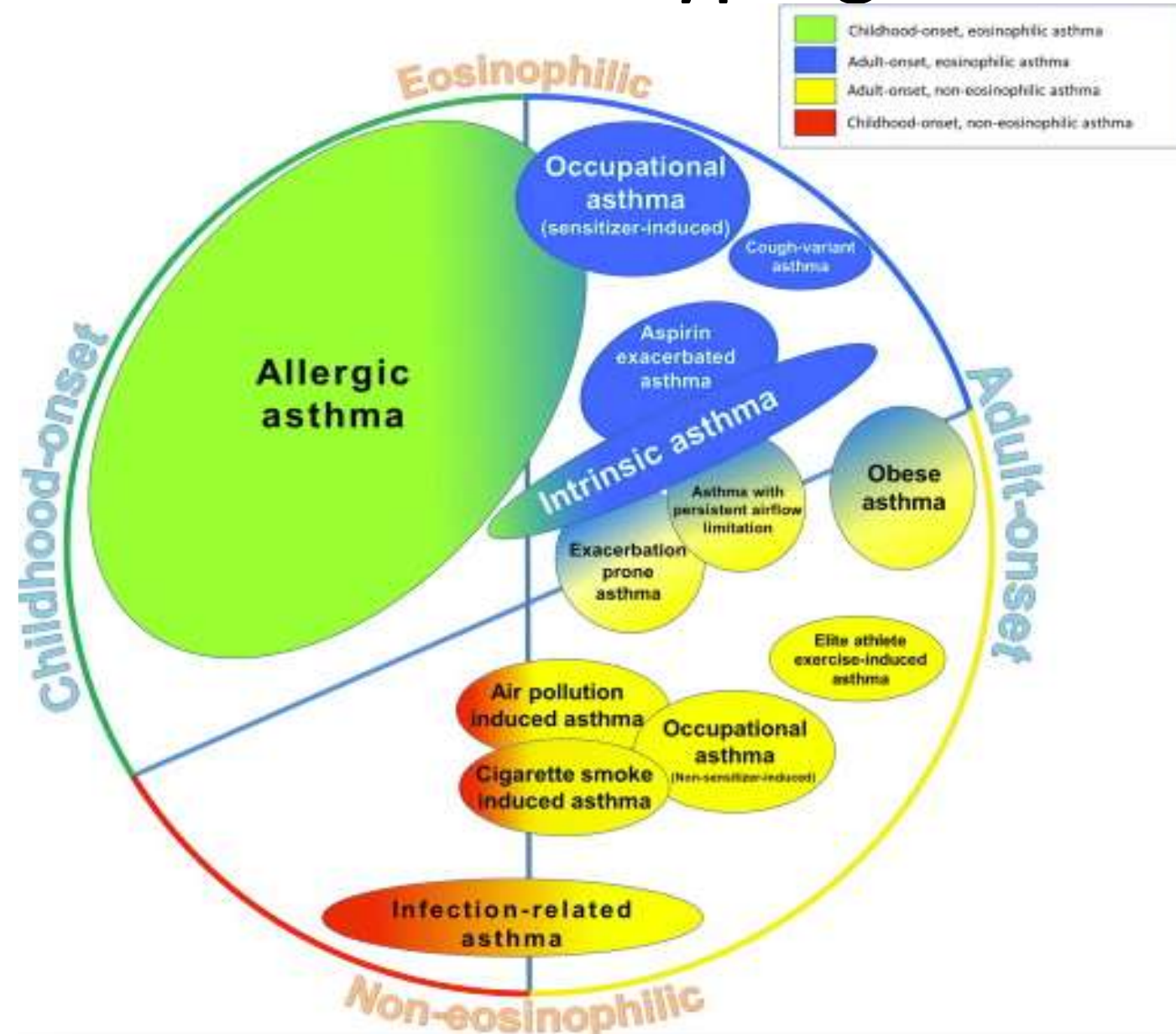
- “a specific biological pathway that explains the observable properties of a phenotype”

Traditional Phenotypes: Atopic Asthma vs Non-Atopic

- Atopic
 - Atopy- genetic susceptibility for developing IgE to epitopes on environmental allergens (Extrinsic asthma).
 - Prevalence increases through childhood (peaks at the second decade of life).
 - Seasonal variation.
 - Aeroallergens often responsible for exacerbations.
 - Frequently associated with allergic rhinitis and conjunctivitis.
 - Food allergies and atopic dermatitis may also be observed.
- Non-Atopic
 - No typical features of atopy (intrinsic asthma).
 - Patients typically older with later onset of symptoms.
 - Possibly unidentified antigens, (viral or “self- antigens.”)

Newer Approaches to Asthma Phenotyping

- Clinical Physiologic
 - Severity Defined
 - Exacerbation Prone
 - Chronic obstruction
 - Response to Treatment/Treatment Resistant
 - Age at onset
- Triggers/Biomarkers
 - ASA/NSAID
 - Environmental
 - Occupational
 - Menses
 - Exercise
- Inflammation Types
 - Eosinophilic (Th2-like inflammation)
 - Neutrophilic (Absence of Th2-like inflammation)
 - Pauci-granulocytic
- **Studies suggest improved outcomes using phenotypes to guide therapy**



Question 2

Asthma:

1. Always begins in childhood
2. Is defined by variable airway obstruction
3. Severity is related to the severity of wheezing
4. Is always associated with allergic triggers.

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Variable Airway Obstruction

- Cardinal feature of asthma
 - Bronchoconstriction in airways containing contractile airway smooth muscle.
 - Variation in airway caliber (minutes to days).
 - Causes: bronchoconstriction, mucosal inflammation, and luminal secretions.
 - Results in increased airflow resistance and work of breathing.
- In severe/longstanding disease, obstruction may be fixed or incompletely reversible with bronchodilator treatment.

Airway Hyperresponsiveness

- Exaggerated reduction in airway caliber (i.e. airway obstruction) after a stimulus.
- **Not specific**, but virtually **universal** finding in asthma.
- Associated with airway inflammation.
- May be induced by allergens, irritants, pollutants, viral upper respiratory tract infections.
- Both Sympathetic and Cholinergic pathways may contribute to airway hyperresponsiveness
 - Methacholine (a direct cholinergic agonist) used to evoke concentration-dependent airway smooth muscle contraction.

Asthma - Clinical Presentation

- Heterogeneous clinical syndrome affecting the lower respiratory tract.
 - Episodic or persistent symptoms of wheezing, dyspnea, air hunger, and cough.
 - Classic triad - wheezing, breathlessness and cough - Not specific for asthma.
 - Worse in early AM or night.
 - Nocturnal symptoms indicate more severe disease.
 - Often associated with specific precipitating/aggravating factors.
 - Allergens and irritants, viral upper respiratory tract infections, bacterial sinusitis, exercise, and cold air.
 - Symptoms may be immediate after exposure or delayed & occur 6hr or later
 - Periods of prolonged remissions are common.
- Stable asthma – exam findings are nonspecific - can be normal.
 - Poorly controlled asthma may exhibit auscultatory wheezing or rhonchi.
 - Intensity/presence of wheezing a poor indicator of the severity of airflow obstruction or disease pathology.
- Exacerbation
 - Short-lived worsening of symptoms
 - Serious deterioration of lung function of longer duration, associated with increased symptoms

Question 3

The work up and diagnosis of asthma requires

1. A CXR and ABG
2. Spirometry
3. A positive methacholine challenge test
4. Auscultation finding of wheezing

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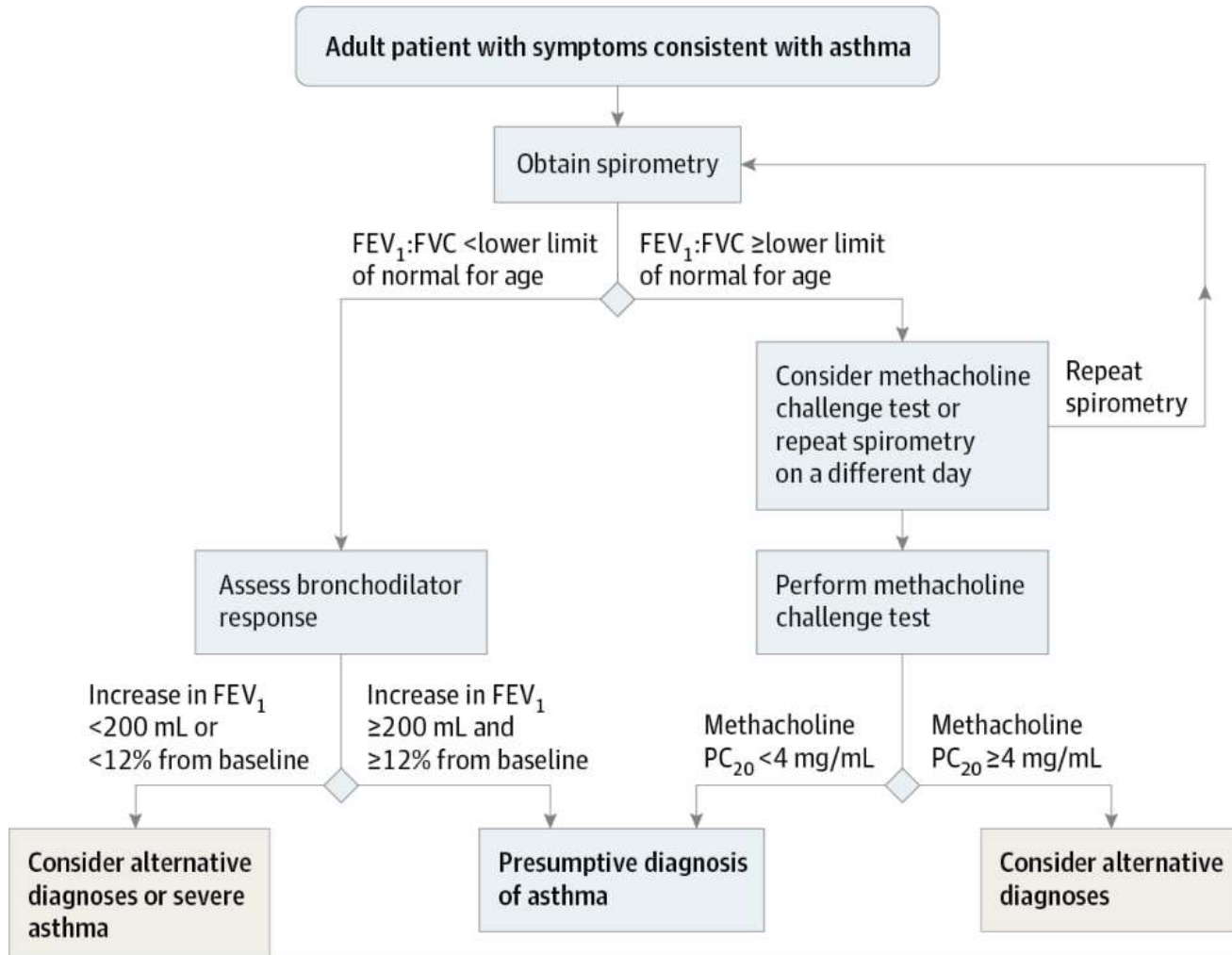
Diagnosis

- History and pattern of symptoms
- Physical examination
- Measurement of lung function
 - Peak expiratory flow (PEF)
 - Forced expiratory volume in 1 second (FEV1)
 - Reversibility test
 - Diurnal variability
- Evaluation of airway responsiveness
 - Exercise challenge
 - Methacholine challenge

Initial Diagnosis/Assessment

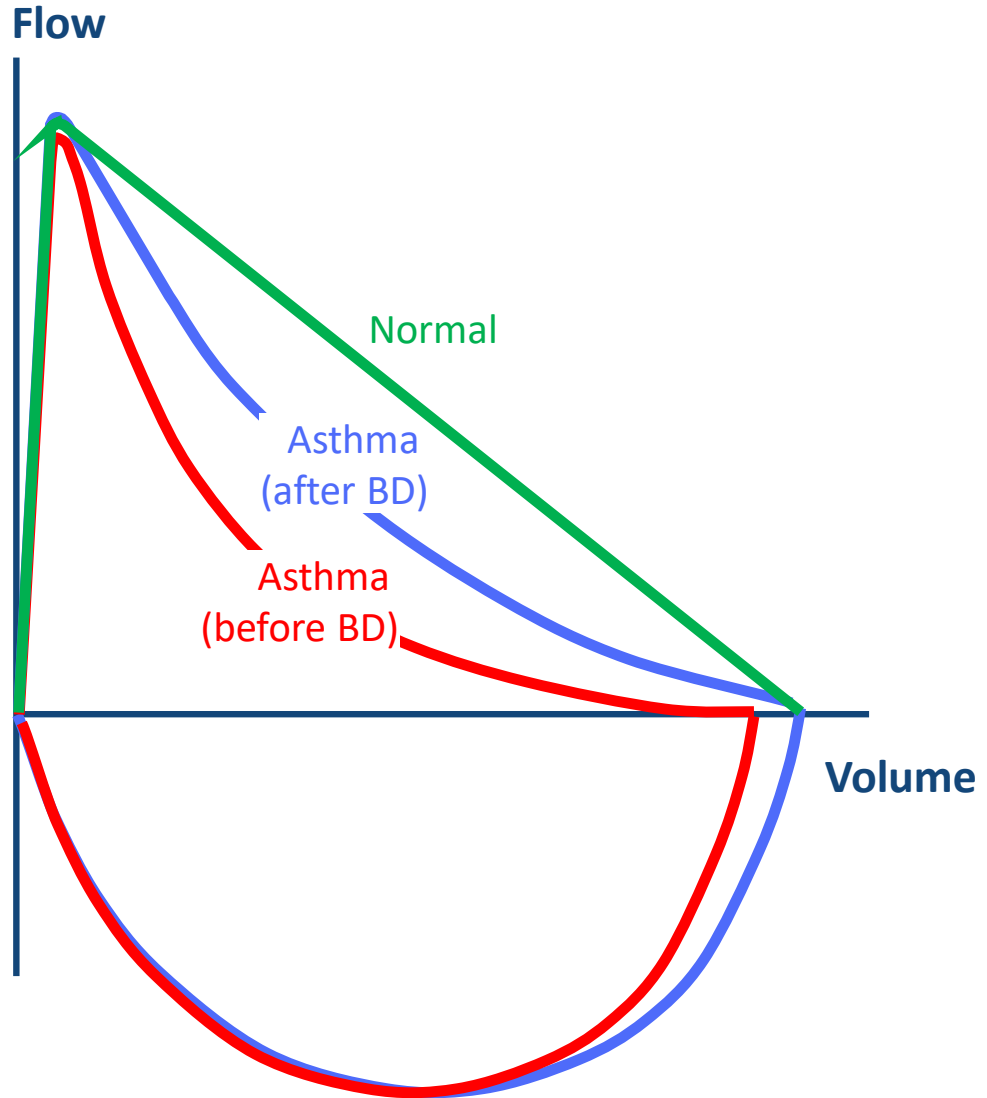
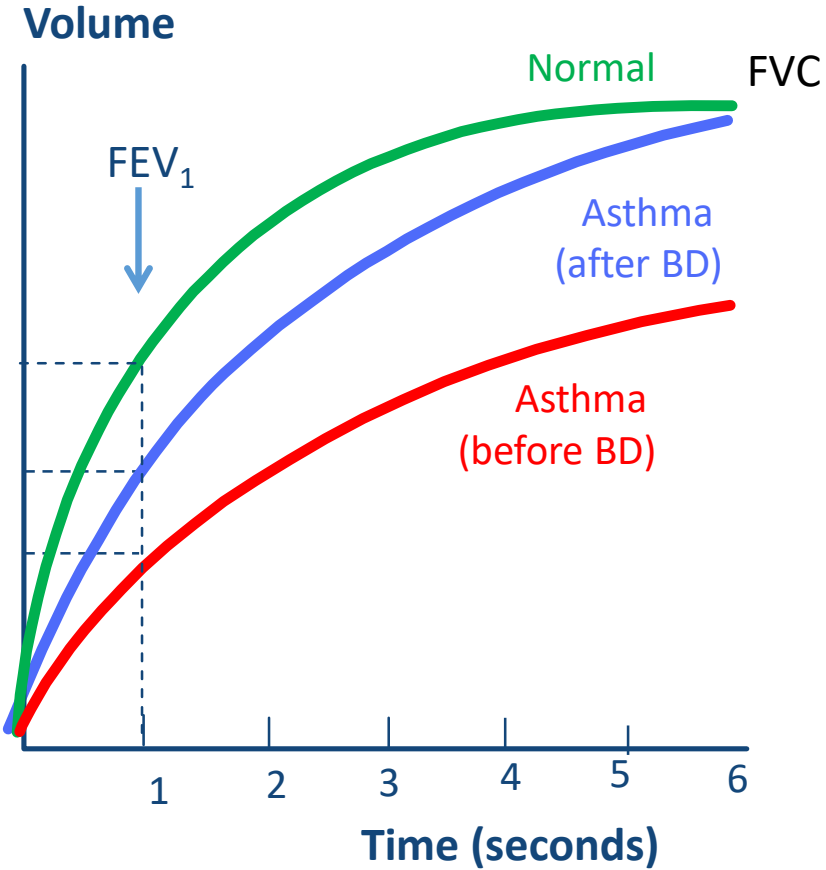
- Combination of asthma-like symptoms and β_2 agonist–reversible bronchial obstruction usually sufficient to establish diagnosis.
- Asthma severity and control based on: **impairment and risk**.
 - Impairment:
 - Measured airway obstruction.
 - Frequency and intensity of daytime and nocturnal symptoms.
 - Frequency of short-acting β_2 agonist use for symptom relief.
 - Interference of daily activities by symptoms.
 - Risk:
 - Assesses the frequency of exacerbations.
- **Spirometry** key for evaluating airway obstruction and reversibility.
- Little benefit of CXR, ABG in routine disease
- Allergy evaluation has become increasingly important to guide therapy and avoid ignitors of disease

Algorithm for Initial Diagnosis of Asthma



- Initial diagnostic test - spirometry,
 - $FEV_1/[FVC] < LLN =$ Obstruction
- If obstruction present check bronchodilator response
 - Short-acting β_2 -agonist
 - FEV1 improves $> 12\%$ and >200 ml.
 - Fixed/partially reversible airway obstruction suggests alternative diagnoses or severe asthma.
- If no airway obstruction but continued suspicion:
 - Bronchoprovacation Study
 - PC_{20} indicates the methacholine concentration required to achieve a 20% decrease in FEV_1 .

Typical Spirometry Tracings

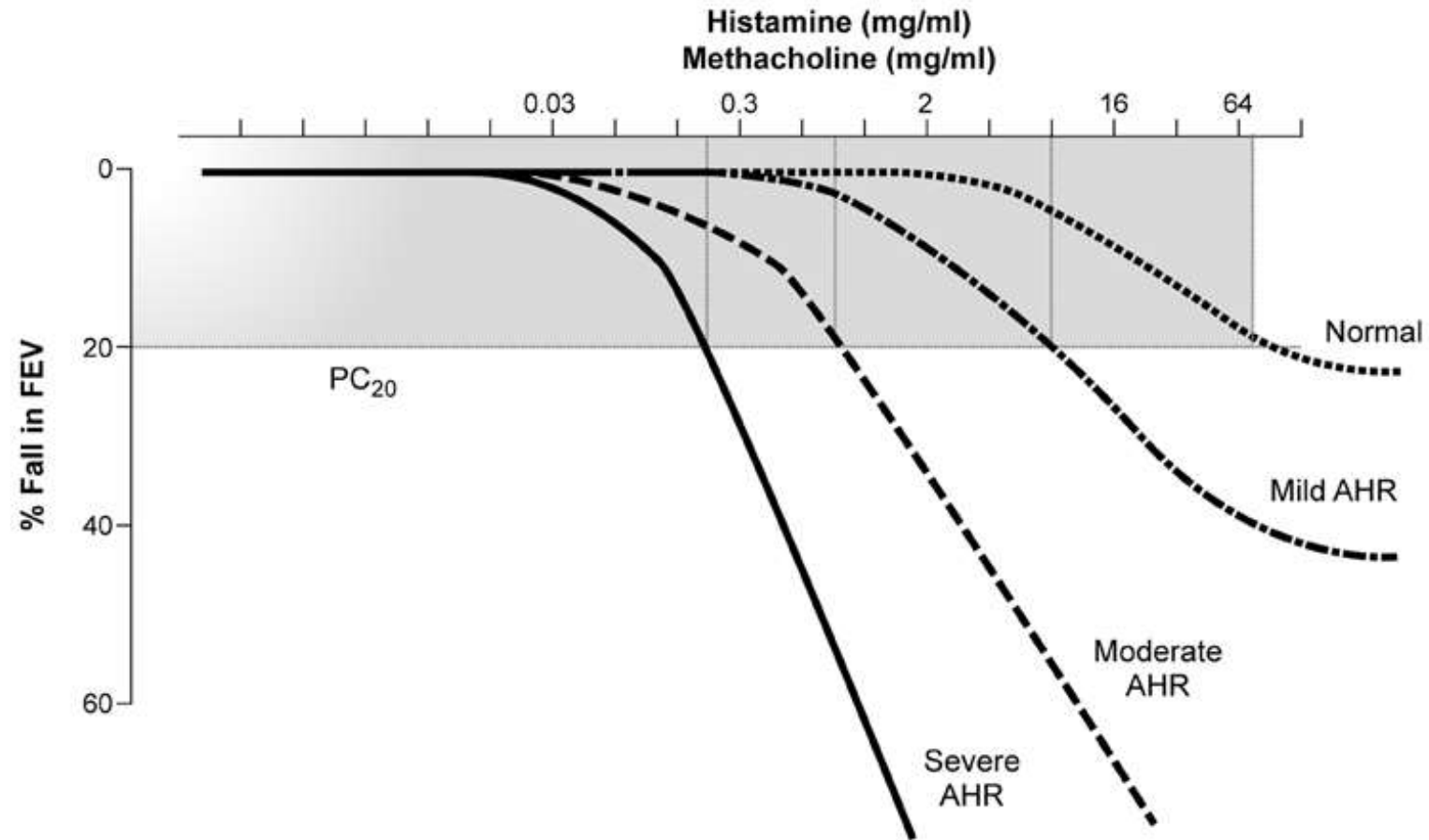


Note: Each FEV₁ represents the highest of three reproducible measurements

Bronchoprovocation Testing

- Testing for Bronchial Hyperreactivity (BHR)
- **Positive test does not equal asthma**
 - COPD, CF, allergic rhinitis, bronchiectasis, sarcoid, post URI, post ARDS, sjogrens, and small amount of normal patients
- **Negative bronchoprovocation test effectively rules out asthma.**
- Several different tests, Methacholine most common
 - **Looking for 20% decrease in FEV₁- aka PC₂₀.**
 - For methacholine: >16 mg/ml- normal and most asthmatics < 8 mg/ml.

Measuring Airway Responsiveness



Differential Diagnosis of Asthma

- Upper respiratory tract
 - Vocal cord dysfunction
 - Congestive rhinopathy
 - OSA
- Lower respiratory tract
 - COPD
 - Occupational bronchitis
 - Cystic fibrosis
 - Bronchiectasis
 - Pneumonia
- Gastrointestinal tract
 - GERD
- Cardiovascular system
 - Congestive heart failure
 - Pulmonary hypertension
 - Chronic thromboembolic pulmonary disease
- Central nervous system
 - Habitual cough

Question 4

All patients with asthma require

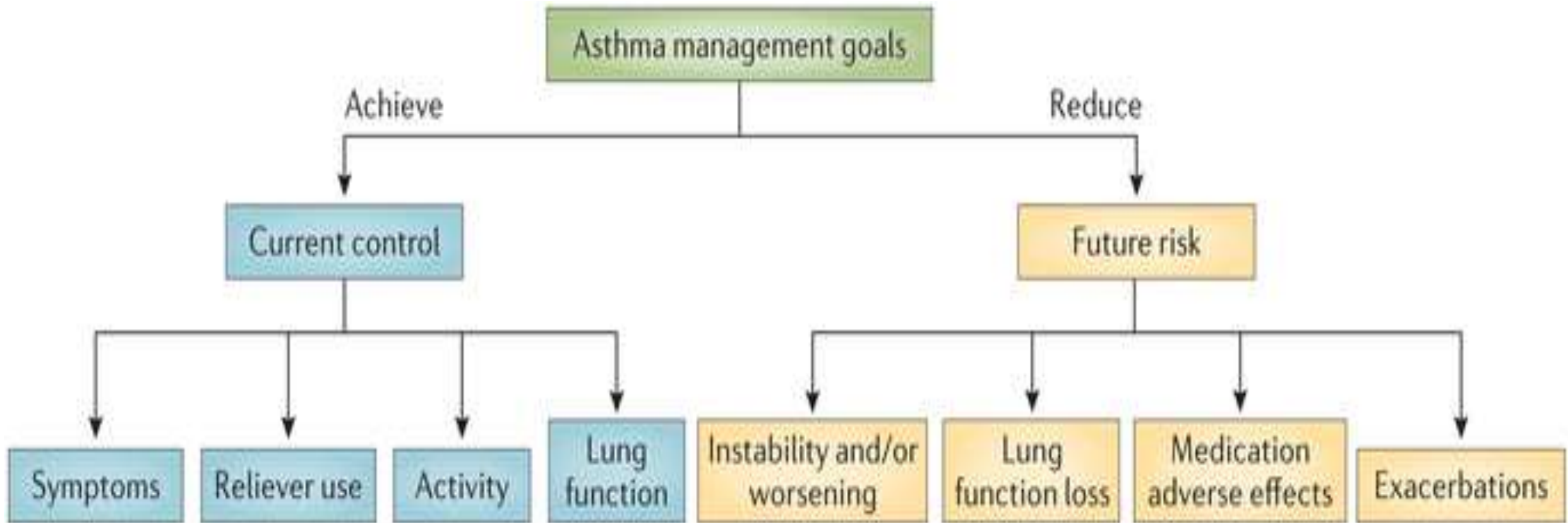
1. Inhaled corticosteroids
2. Allergy shots
3. Scheduled short acting Beta-agonists
4. Staging of asthma severity

Question 4

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4. **Staging of asthma severity**

Goals of Asthma Management



Environmental Control – The First Step

How To Control Things That Make Your Asthma Worse

This guide suggests things you can do to avoid your asthma triggers. Put a check next to the triggers that you know make your asthma worse and ask your doctor to help you find out if you have other triggers as well. Then decide with your doctor what steps you will take.

Allergens

Animal Dander

Some people are allergic to the flakes of skin or dried saliva from animals with fur or feathers.

The best thing to do:

- Keep furred or feathered pets out of your home.

If you can't keep the pet outdoors, then:

- Keep the pet out of your bedroom and other sleeping areas at all times, and keep the door closed.
- Remove carpets and furniture covered with cloth from your home. If that is not possible, keep the pet away from fabric-covered furniture and carpets.

Dust Mites

Many people with asthma are allergic to dust mites. Dust mites are tiny bugs that are found in every home—in mattresses, pillows, carpets, upholstered furniture, bedcovers, clothes, stuffed toys, and fabric or other fabric-covered items.

Things that can help:

- Encase your mattress in a special dust-proof cover.
- Encase your pillow in a special dust-proof cover or wash the pillow each week in hot water. Water must be hotter than 130° F to kill the mites. Cold or warm water used with detergent and bleach can also be effective.
- Wash the sheets and blankets on your bed each week in hot water.
- Reduce indoor humidity to below 60 percent (ideally between 30–50 percent). Dehumidifiers or central air conditioners can do this.
- Try not to sleep or lie on cloth-covered cushions.
- Remove carpets from your bedroom and those laid on concrete, if you can.
- Keep stuffed toys out of the bed or wash the toys weekly in hot water or cooler water with detergent and bleach.

Cockroaches

Many people with asthma are allergic to the dried droppings and remains of cockroaches.

The best thing to do:

- Keep food and garbage in closed containers. Never leave food out.
- Use poison baits, powders, gels, or paste (for example, boric acid). You can also use traps.
- If a spray is used to kill roaches, stay out of the room until the odor goes away.

Indoor Mold

- Fix leaky faucets, pipes, or other sources of water that have mold around them.
- Clean moldy surfaces with a cleaner that has bleach in it.

Pollen and Outdoor Mold

What to do during your allergy season (when pollen or mold spore counts are high):

- Try to keep your windows closed.
- Stay indoors with windows closed from late morning to afternoon, if you can. Pollen and some mold spore counts are highest at that time.
- Ask your doctor whether you need to take or increase anti-inflammatory medicine before your allergy season starts.

Irritants

Tobacco Smoke

- If you smoke, ask your doctor for ways to help you quit. Ask family members to quit smoking, too.
- Do not allow smoking in your home or car.

Smoke, Strong Odors, and Sprays

- If possible, do not use a wood-burning stove, kerosene heater, or fireplace.
- Try to stay away from strong odors and sprays, such as perfume, talcum powder, hair spray, and paints.

Other things that bring on asthma symptoms in some people include:

Vacuum Cleaning

- Try to get someone else to vacuum for you once or twice a week, if you can. Stay out of rooms while they are being vacuumed and for a short while afterward.
- If you vacuum, use a dust mask (from a hardware store), a double-layered or microfilter vacuum cleaner bag, or a vacuum cleaner with a HEPA filter.

Other Things That Can Make Asthma Worse

- Sulfites in foods and beverages: Do not drink beer or wine or eat dried fruit, processed potatoes, or shrimp if they cause asthma symptoms.
- Cold air: Cover your nose and mouth with a scarf on cold or windy days.
- Other medicines: Tell your doctor about all the medicines you take. Include cold medicines, aspirin, vitamins and other supplements, and nonselective beta-blockers (including those in eye drops).

Therapeutics – Next Step

- Pharmacologic options are classified as either:
 - Reliever (short-term benefit)
 - Controller (longer-term benefit)
- Use based on guidelines

Table 2. Major Medical Therapies for Stable Asthma in Adults

Category	Examples	Usual Dosing	Treatment Effect	Adverse Effects	Notes
Standard Therapies					
Relievers					
Short-acting β_2 -agonists (SABAs)	Albuterol Levalbuterol Pirbuterol	2 puffs every 4-6 h	Bronchodilation (7%-15% increase in FEV ₁ , dose dependent)	Nervousness, tremor, bronchospasm, tachycardia, headache, pharyngitis	
Short-acting muscarinic antagonists (SAMAs)	Ipratropium	2-3 puffs every 6 h	Bronchodilation (7%-15% increase in FEV ₁ , dose dependent)	Bronchitis, COPD exacerbation, dyspnea, headache	
Controllers					
Inhaled corticosteroids (ICSs)	Fluticasone	2 puffs twice daily	Decreased daytime and nocturnal symptoms	Upper respiratory tract infection, throat irritation, sinusitis, dysphonia, candidiasis, cough, bronchitis, headache	Comparisons for low, moderate, and high doses of ICSs are detailed elsewhere. ^{12,13}
	Budesonide	2-4 puffs twice daily	Reduced exacerbations and death		
	Mometasone	Varies by device			
	Ciclesonide	160-320 μ g twice daily	Improved FEV ₁ (improvement in symptoms, exacerbations, death, and FEV ₁ are all dose dependent ^{10,19})		
Leukotriene receptor antagonists (LTRAs)	Montelukast	10 mg daily	Decreased daytime and nocturnal symptoms	Headache, fatigue, abdominal pain, dyspepsia, mood changes	
	Zafirlukast	20 mg twice daily	Improved FEV ₁ ²⁰		
Leukotriene synthesis inhibitor	Zileuton	600 mg 4 times daily	Improved FEV ₁ ²¹	Headache, pain, abdominal pain, dyspepsia, nausea, myalgia, increased alanine aminotransferase	Requires monitoring of hepatic enzymes Drug interactions are common
Long-acting β_2 -agonists (LABAs)	Salmeterol	2 puffs twice daily	Improved FEV ₁ ²²	Headache, rhinitis, bronchitis, influenza, dizziness	These agents should not be used without a simultaneous ICS agent
	Formoterol	2 puffs twice daily			
	Vilanterol	NA			
Long-acting muscarinic antagonist (LAMA)	Tiotropium	1 puff daily	Improved FEV ₁ ²³	Dry mouth, upper respiratory tract infection, pharyngitis, sinusitis, chest pain	
Combined ICS/LABAs	Fluticasone/salmeterol inhaler	1 puff twice daily	Benefits of both ICSs and LABAs ²⁴	Nasopharyngitis, URI, headache, sinusitis, influenza, back pain	
	Fluticasone/salmeterol HFA	2 puffs twice daily			
	Budesonide/formoterol	2 puffs twice daily			
	Fluticasone/vilanterol	1 puff daily			
Other Therapies					
Oral corticosteroids	Prednisone	5-20 mg/d		Hypertension, increased appetite, weight gain, insomnia, mood changes, gastritis, skin atrophy, osteoporosis, adrenal suppression, avascular necrosis of bone	Doses listed are for chronic maintenance, not for exacerbations Daily use of oral corticosteroids is not recommended unless other options are ineffective; consult with an asthma specialist
	Methylprednisolone	4-16 mg/d			
Biologics					
Anti-IgE	Omalizumab	Varies by weight	Reduced asthma exacerbations Variable benefit in FEV ₁ ²⁵	Injection site reaction, viral infections, URI, sinusitis, headache, pharyngitis, anaphylaxis	Used primarily by asthma specialists
Anti-IL-5	Mepolizumab	100 mg subcutaneously monthly	Reduced asthma exacerbations	Headache, injection site reaction, back pain, fatigue, oropharyngeal pain	Used primarily by asthma specialists
	Reslizumab	Varies by weight, IV administration	Small improvement in FEV ₁ ²⁶⁻²⁹		
Bronchial thermoplasty		3 Bronchoscopic treatments, once monthly for 3 mo	Reduced asthma exacerbations, emergency department visits through at least 1 y ³⁰	Short-term worsening of asthma symptoms, cough, wheezing, chest pain, URI, infection	Specialty treatment Durability of benefit is controversial

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in first second of expiration; URI, upper respiratory infection.

Medications - Relievers

- Short Acting Beta agonist (SABA):
 - Mainstay of treatment.
 - All asthmatics should have SABA.
 - Adverse Effects: hypokalemia, tremors, and arrhythmias.
- Short Acting Muscarinic Antagonists (SAMA)
 - Anticholinergics
 - Bronchodilator, useful in combination with beta agonist in acute asthma.
 - Ipratropium.
 - Adverse Effects: hoarseness, throat irritation, cough.

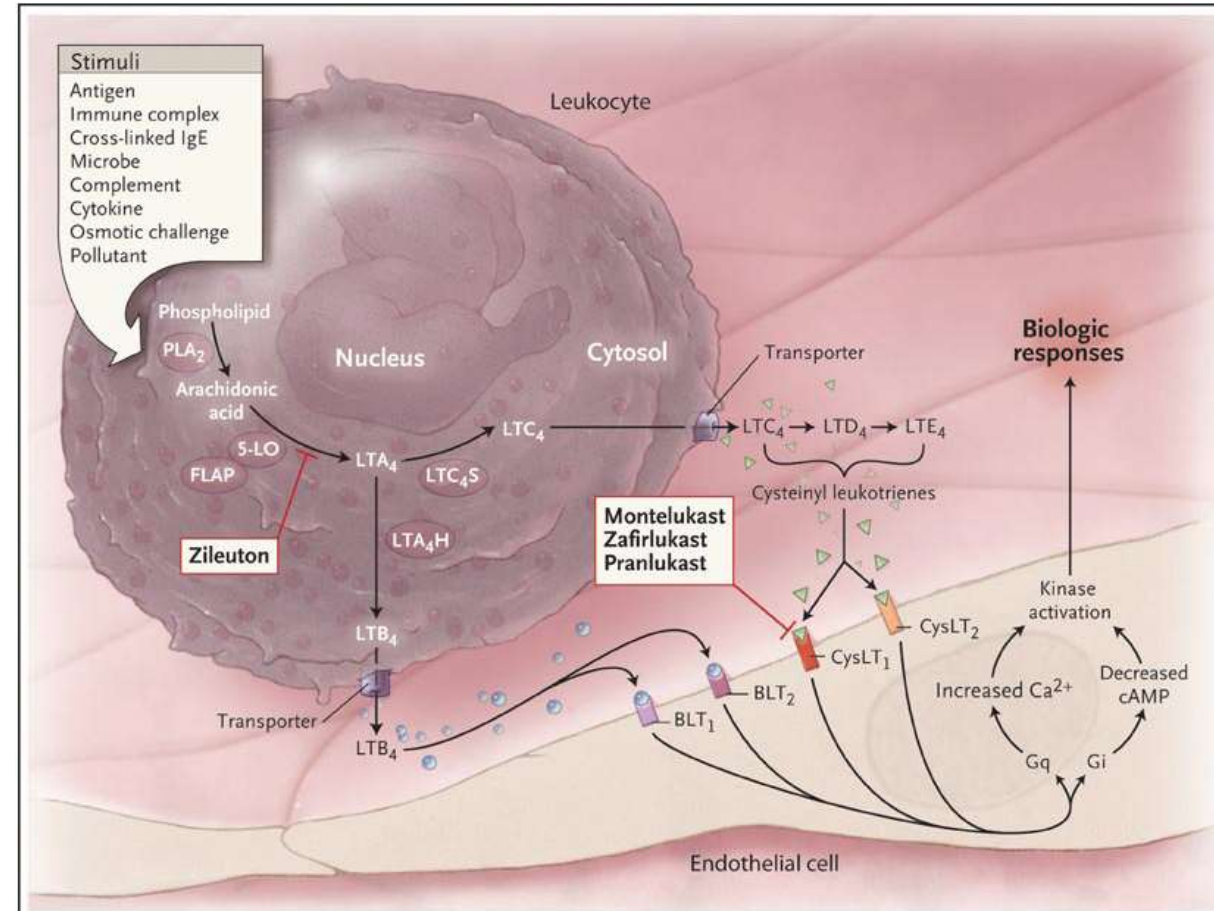
Medications - Controllers

- Inhaled Corticosteroids (ICS)
 - Mainstay for persistent asthma.
 - Decreases the number of mast cells, eosinophils, and lymphocytes.
 - Upregulates Beta receptors.
 - Regular usage improves lung function, decreases airway hyperresponsiveness.
 - Reduces exacerbations/mortality.
 - Example: fluticasone, budesonide.
 - Adverse Effects: Thrush, cough, dysphonia, can have systemic effects with high dose.
- Long Acting Beta Agonists (LABA):
 - Adjunct therapy, not a monotherapy- used concomitantly with inhaled corticosteroid.
 - Black box warning - increased risk of death and serious adverse events (large observational study with limitations)
 - Use with ICS not associated with increased serious adverse events.
 - Improved FEV1
 - Formoterol, Salmeterol.
 - Should never be used without an accompanying inhaled corticosteroid.
- LAMA
 - Effects of both ICS and LABA
 - Tiotropium

Medications – Controllers

Leukotriene Modifiers

- Effects:
 - Improve lung function
 - Decreased symptoms
 - Improved quality of life
 - Decreased albuterol use
 - Prevent exercise induced bronchospasm
 - Modest anti-inflammatory
- Montelukast, zafirlukast, and zileuton.
- Adverse Effects: Agitation, depression, suicide, associated with Churg-Strauss



Medications - Other

- Cromolyn/nedocromil
 - Anti inflammatory, inhibits mast cell degranulation, reduces leukotriene release.
 - Good for prophylactic treatment.
 - Adverse Effects: bronchospasm, cough, throat irritation.
- Theophylline
 - Mild bronchodilator, limited anti-inflammatory.
 - Improves respiratory muscle and ciliary function.
 - Adverse Effects: Tremor, palpitations, headache, nausea/ vomiting, arrhythmia, seizures.
- Oral steroids
 - Effective option for uncontrolled disease and for asthma exacerbations
 - Significant adverse effects: glucose intolerance, weight gain, and salt and water retention, infection.

Asthma Guidelines

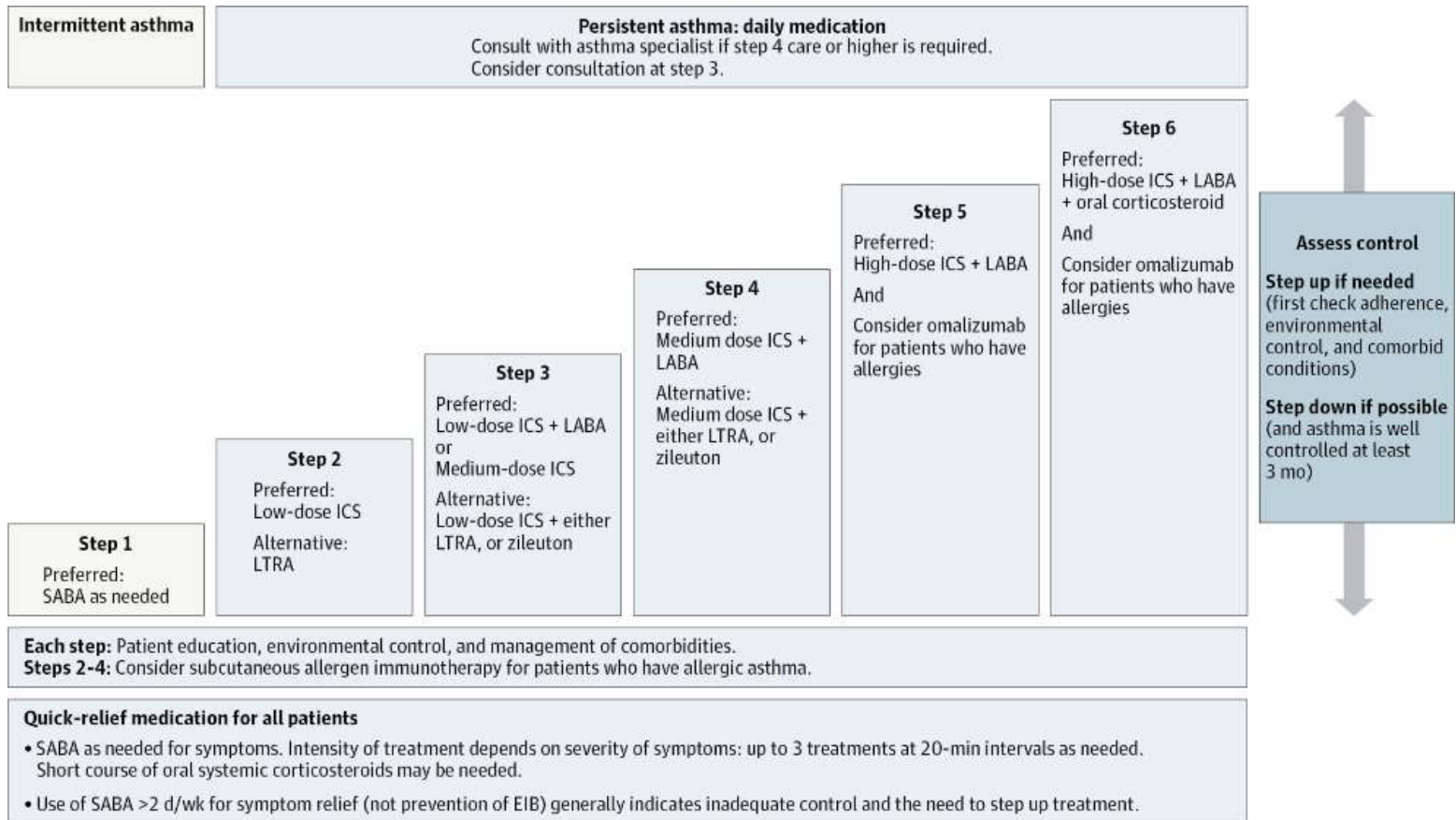
- Asthma is heterogeneous in nature with limited predictors for treatment success.
- Must approach patients with a guideline-based plan.
 - Severity and treatment classification system
 - Based on historical features and spirometric measurements.
- Two major guidelines
 - The US National Asthma Education and Prevention Program (NAEPP) – 6 steps
 - Global Initiative for Asthma (GINA) – 5 steps

NAEPP Initial Approach to Classification of Asthma Severity

Components of severity		Classification of asthma severity (age ≥12 y)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment	Symptoms	≤2 d/wk	>2 d/wk but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2× mo	3-4× mo	>1× wk but not nightly	Often 7× wk
	Short-acting β ₂ -agonist use for symptom control (not prevention of EIB)	≤2 d/wk	>2 d/wk but not daily, and not more than 1× on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function Normal FEV ₁ : FVC ratio 20-39 y 80% 40-59 y 75% 60-80 y 70%	• 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 normal	• FEV ₁ , <60% predicted • FEV ₁ :FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/y	≥2/y	≥2/y	≥2/y
		Consider severity and interval since last exacerbation Frequency and severity may fluctuate over time for patients in any severity category Relative annual risk of exacerbation may be related to FEV ₁			
Recommended step for initiating treatment (see Figure 3 for treatment steps)		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	Step 4 or 5
		In 2-6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly			

- Initial severity estimate on basis of:
 - Daytime and nocturnal symptoms,
 - Frequency of SABA use
 - Degree to which asthma interferes with normal activity,
 - Degree of airway obstruction (spirometry)
 - History of asthma exacerbations.
- Asthma categorized as:
 - Intermittent,
 - Persistent
 - Mild
 - Moderate
 - Severe
- Informs initial therapeutic approach.

NAEPP Recommendations for Asthma Therapy



- **All** patients should have a rescue inhaler.
- Preferred initial therapy outlined by step.
- Periodic reevaluation of asthma symptoms, lung function, and exacerbations is necessary to guide adjustments in treatment.

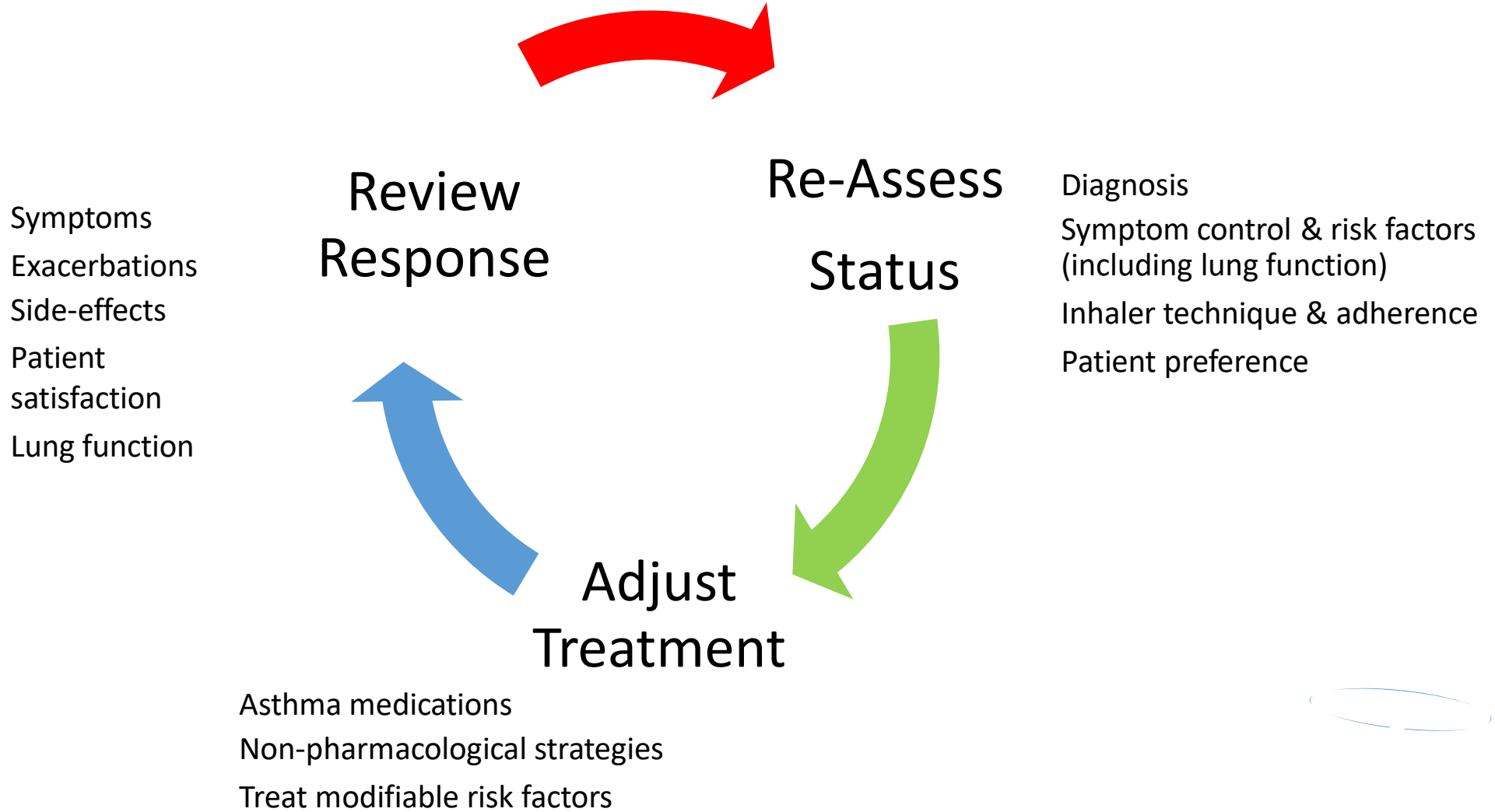
Treatment Caveats

- If suboptimal control:
 - Incorrect inhaler technique
 - Poor adherence
 - Exposure to allergens/irritants/tobacco smoke
 - Management of comorbid conditions (allergic rhinitis, sinusitis, GERD, OSA) improves asthma control
 - Exercise in overweight patients appears to improve asthma control
 - Wrong Disease
 - Asthma syndromes
- If control not optimal, intensification indicated.
 - Precise timing of follow-up visits is a matter of clinical judgment
- Once well controlled for 2 to 3 months, treatment may be stepped down to the lowest dose of medication that adequately controls symptoms and lung function.
 - Guidelines for deintensification of asthma therapy are not as well established as those for intensification.

Asthma Syndromes

- Occupational- Improvement on vacations/ weekends (not always).
- Reactive Airway Dysfunction Syndrome (RADS) - usually after large exposure of irritant.
- Cough Variant Asthma- predominant/ only symptom cough.
- Allergic Broncho-Pulmonary Mycoses, (Allergic Bronchopulmonary Aspergillosis – ABPA)
 - Difficult to control asthma, recurrent infiltrates, eosinophilia, central bronchiectasis, elevated IgE (total and to *A. fumigatus*,) + skin test to *A. fumigatus*
 - Prevalence may be as high as 25% among people with asthma.
- Exercise Induced Asthma (EIA)
 - 5 to 10 minutes after intense exercise,
 - Usually preventable with appropriate prophylactic measures or premedication.
- Aspirin Sensitive Asthma
 - Bronchoconstriction after treatment with NSAID's or ASA,
 - Treatment is avoidance, Leukotriene modifiers, or desensitization.

After Initial Treatment



Monitoring

- Symptoms and pulmonary function may not correlate well - measurement of both can inform adjustments to therapy.
- Asthma symptom control
 - Validated patient questionnaires (Asthma Control Test [ACT], Asthma Quality of Life Questionnaire [AQLQ], or Asthma Control Questionnaire [ACQ]) at each visit.
 - Spirometry should be repeated every 1 to 2 years or with clinically significant change.
- Peak flow monitoring.
 - Useful in some patients.
 - Personal best - highest value with 2 weeks of stable asthma.
- Exhaled Nitric Oxide (NO)
 - Marker of eosinophilic inflammation
 - Correlates with sputum eosinophils, BHR, IgE levels, and lung function.
 - No correlation with disease severity.
 - Low levels not inconsistent with asthma
 - May predict response to inhaled corticosteroids, anti-IgE, Anti-IL5 and anti IL-13.
 - Levels drop with treatment with ICS, anti-IL-13 but not with anti-IL-5
 - Utility of eNO has not been definitively established.

Asthma Control Test

IF YOUR SCORE IS **19 OR LESS**, Your asthma symptoms may not be as well controlled as they could be. No matter what the score, bring this test to your healthcare provider to talk about the results. NOTE: If your score is **15 or less**, your asthma may be very poorly controlled. Please contact your healthcare provider right away. There may be more you and your healthcare provider could do to help control your asthma symptoms.

					SCORE
1. In the <u>past 4 weeks</u> , how much of the time did your <u>asthma</u> keep you from getting as much done at work, school or at home?					
All of the time [1]	Most of the time [2]	Some of the time [3]	A little of the time [4]	None of the time [5]
2. During the <u>past 4 weeks</u> , how often have you had shortness of breath?					
More than Once a day [1]	Once a day [2]	3 to 6 times a week [3]	Once or twice a week [4]	Not at all [5]
3. During the <u>past 4 weeks</u> , 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 [1]	2 to 3 nights a week [2]	Once a week [3]	Once or twice [4]	Not at all [5]
4. During the <u>past 4 weeks</u> , how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?					
3 or more times per day [1]	1 to 2 times per day [2]	2 or 3 times per week [3]	Once a week or less [4]	Not at all [5]
5. How would you rate your asthma control during the past 4 weeks?					
Not Controlled at All [1]	Poorly Controlled [2]	Somewhat Controlled [3]	Well Controlled [4]	Completely Controlled [5]

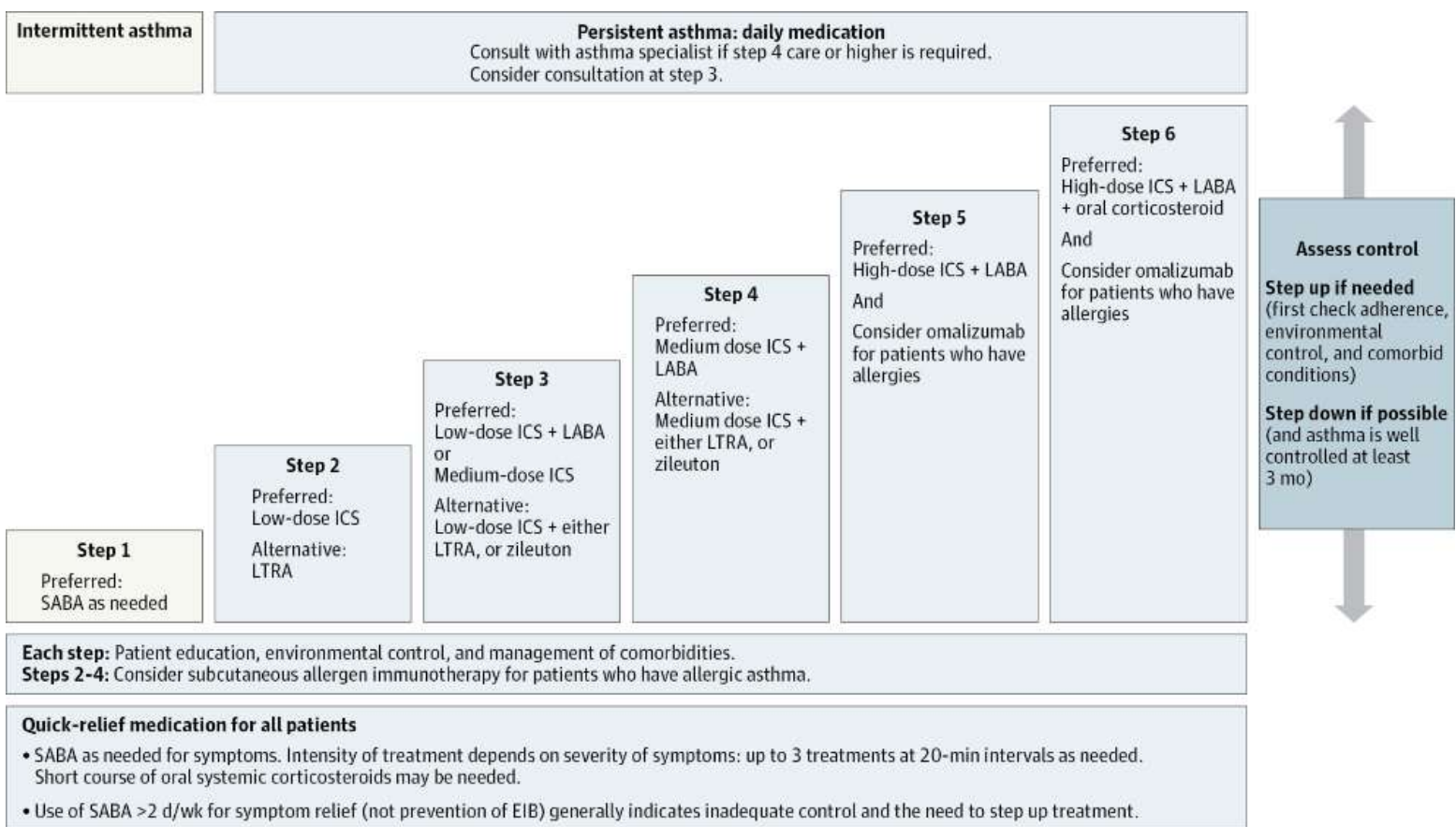
Assessing Asthma Control in Patients >12 Years

Components of Severity		Classification of Asthma Control (Youths ≥ 12 years of age & adults)		
		Well-Controlled	Not Well-Controlled	Very Poorly Controlled
Impairment	Symptoms	≤ 2 days/week	> 2 days/week	Throughout the day
	Nighttime awakenings	≤ 2 /month	1-3/month	≥ 4 /week
	Short-acting β_2 -agonist use for symptom control	≤ 2 days/week	> 2 days/week	Several times per day
	Interference with normal activity	None	Some limitation	Extremely limited
	FEV ₁ or peak flow	$> 80\%$ pred/personal best	60-80% pred/personal best	$< 60\%$ pred/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 per year	2-3 per year	> 3 per year
	Reduction in lung growth	Evaluation requires long-term follow-up care.		
	Treatment-related adverse effects	Medication side effects vary in intensity from none to very troublesome. Level of intensity does not correlate to specific levels of control but should be considered in overall assessment of risk.		

Recommended Actions

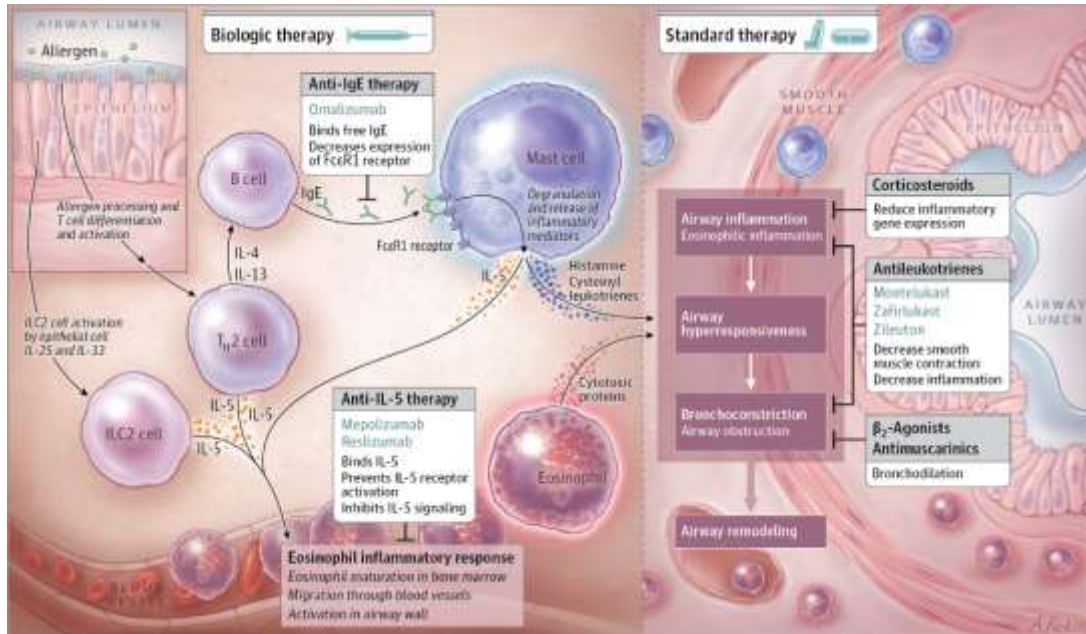
- Well-Controlled
 - Maintain current step.
 - Regular follow-up (q1–6 mo).
 - Consider step down if well controlled for at least 3 months.
- Not Well Controlled
 - Step Up 1 step
 - Reevaluate in 2–6 weeks.
- Very Poorly Controlled
 - Consider short course of oral systemic corticosteroids.
 - Step up 1–2 steps.
 - Reevaluate in 2 weeks

NAEPP Recommendations for Asthma Therapy



- Step up or down from current step as indicated by reassessment.

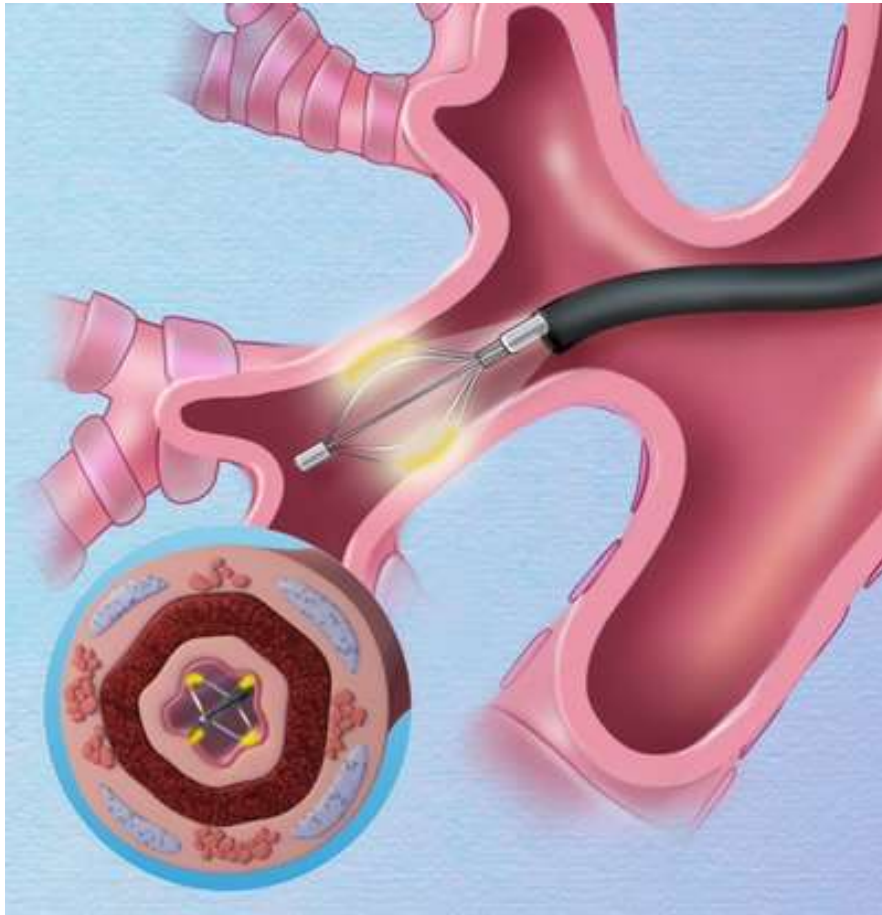
Standard vs Biologic Therapies



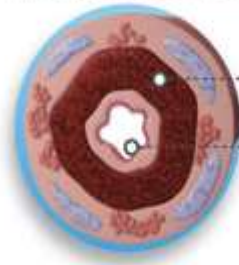
- Standard therapy effects limited to the airway.
- Biologic therapy (uncontrolled asthma despite standard therapies) act upstream of the inflammatory process in the airway.

- IgE an attractive target for allergic asthma therapy.
 - Omalizumab (Anti-IgE monoclonal antibody) for allergic asthma with moderately elevated IgE and sensitization to perennial aeroallergens.
 - Reduces mast cell activation and release of mediators of bronchoconstriction
 - Reduces exacerbations/need for oral steroids, little improvement in PFTs.
- IL 5
 - Involved in the synthesis, maturation, homing, and activation of eosinophils,
 - Anti-IL-5 monoclonal antibodies reduce activity of IL-5 and reduce eosinophilic inflammatory in severe asthma with peripheral eosinophilia.
 - Mepolizumab
 - Reduces the rate of exacerbations and the need for oral corticosteroids by about 50%, little effect on lung function.
 - Reslizumab
 - Reslizumab reduces the rate of exacerbations by about 50%, reduces symptoms, and improves FEV₁ by 110 mL.
- Use is generally limited to asthma specialists.
 - Parenteral administration
 - expensive (\$15 000-\$30 000 annually).
 - Omalizumab and reslizumab carry black box warnings for anaphylaxis

Bronchial Thermoplasty



Airway of Person with Severe Asthma



More airway muscle causes airway to narrow
This is the area where Alair applies heat to the airway wall during BT treatment

Airway of Person with Severe Asthma after Treatment



Reduced airway muscle after BT treatment
After BT, the inside airway wall and other tissue heals, but airway muscle is reduced

- Delivers radiofrequency energy to airway.
- Mechanism unclear:
 - Changes in adaptive immunity
 - Airway smooth muscle
- Outcomes (1 Year)
 - Reduced exacerbations (50%)
 - Reduced ED visits (85%)
- Evidence for long-term benefit limited.
- GINA (not NAEPP) specifies a role.
- ATS and ERS Guidelines
 - Use within a clinical trial or registry.

Other

- Consultation with an asthma specialist is warranted for patients who:
 - Step 4 or higher in the US guideline
 - Have a life-threatening exacerbation
 - Poor responsiveness to prescribed treatment
 - Occupational triggers
 - Atypical presentation
 - Need for more than 2 bursts of oral corticosteroids
- Exercise Induced Asthma - symptoms generally within a few minutes of cessation of exercise
 - Pretreatment with albuterol 15 minutes prior to anticipated exercise can minimize or eliminate these symptoms.
- Asthma-COPD Overlap (ACO)
 - Many patients with symptoms of chronic airways disease have features of both asthma and COPD (15–55%)
 - Likely a range of different underlying mechanisms and origins
 - Worse outcomes than those with asthma or COPD alone
 - Frequent exacerbations
 - Poor quality of life
 - More rapid decline in lung function
 - Higher mortality
 - Greater health care utilization
 - Start treatment as for asthma

Question 5

The diagnosis and management of an acute asthma exacerbation:

1. Requires hospitalization
2. Requires wheezing on physical exam
3. Should be treated with SABA (2 puffs or 1 nebulized treatment) with reassessment in 2-4 hours.
4. Should be treated with systemic corticosteroids

Question 5

The diagnosis and management of an acute asthma exacerbation:

1. Requires hospitalization
2. Requires wheezing on physical exam
3. Should be treated with SABA (2 puffs or 1 nebulized treatment) with reassessment in 2-4 hours.
4. **Should be treated with systemic corticosteroids**

Asthma Exacerbation

Acute or sub-acute worsening of symptoms and lung function

Fatal/Near Fatal Asthma risk factors

- Three or more medication usage
- Marked variation in AM and evening peak flows
- History of near-fatal asthma requiring intubation/ventilation
- Asthma hospitalization/emergency care in last 12 months
- Not currently using/poor adherence with ICS
- Currently using or recently stopped using OCS
- Over-use of SABAs - more than 1 canister/month
- Lack of a written asthma action plan
- History of psychiatric disease or psychosocial problems
- Confirmed food allergy in a patient with asthma.

Manage exacerbations as a continuum

- Self-management with a written asthma action plan
- Management in primary care
- Management in the emergency department and hospital
- Follow-up after any exacerbation

Written Asthma Action Plans

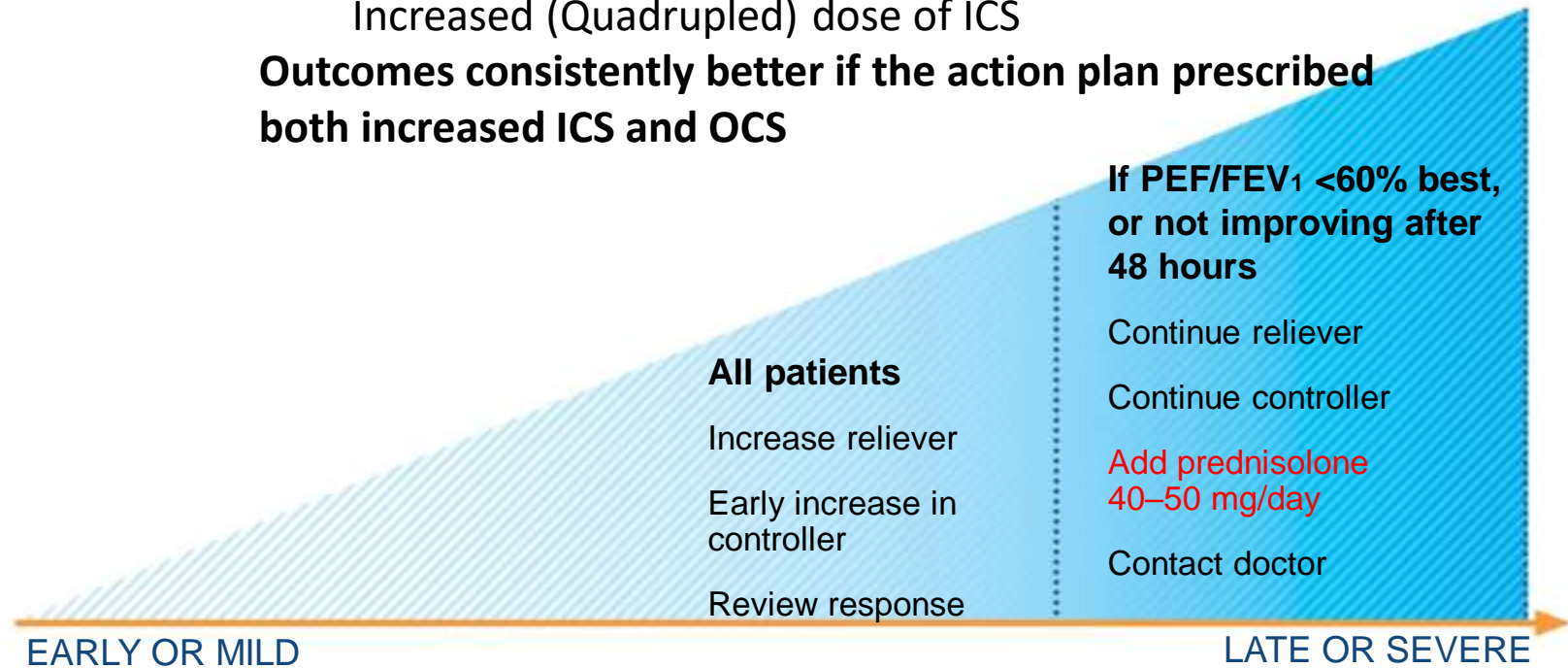
All Patients Should Have One

- Help patients recognize and respond to worsening asthma.
- Individualized
- Based on symptoms and/or PEF (children: only symptoms)
- Include:
 - Usual asthma medications
 - When/how to increase reliever and controller or start OCS
 - How to access medical care if symptoms fail to respond
- When combined with self-monitoring and regular medical review, action plans are **highly effective in reducing asthma mortality and morbidity**

Traditionally exacerbations treated worsening asthma with SABA alone until OCS were needed, but ...

Exacerbations characterised by increased inflammation
Exacerbations are reduced by short-term treatment with
Increased (Quadrupled) dose of ICS

Outcomes consistently better if the action plan prescribed both increased ICS and OCS



Asthma Action Plan

Asthma Action Plan

For: _____ Doctor: _____ Date: _____
 Doctor's Phone Number _____ Hospital/Emergency Department Phone Number _____

GREEN ZONE

Doing Well

- No cough, wheeze, chest tightness, or shortness of breath during the day or night
- Can do usual activities

And, if a peak flow meter is used,

Peak flow: more than _____
 (80 percent or more of my best peak flow)

My best peak flow is: _____

Before exercise 2 or 4 puffs _____ 5 minutes before exercise

Take these long-term control medicines each day (include an anti-inflammatory).

Medicine	How much to take	When to take it
_____	_____	_____
_____	_____	_____
_____	_____	_____

YELLOW ZONE

Asthma Is Getting Worse

- Cough, wheeze, chest tightness, or shortness of breath, or
- Waking at night due to asthma, or
- Can do some, but not all, usual activities

-Or-

Peak flow: _____ to _____
 (50 to 79 percent of my best peak flow)

First Add: quick-relief medicine—and keep taking your GREEN ZONE medicine.

_____ 2 or 4 puffs, every 20 minutes for up to 1 hour
 (short-acting beta₂-agonist) Nebulizer, once

Second If your symptoms (and peak flow, if used) return to GREEN ZONE after 1 hour of above treatment:
 Continue monitoring to be sure you stay in the green zone.

-Or- If your symptoms (and peak flow, if used) do not return to GREEN ZONE after 1 hour of above treatment:

Take: _____ 2 or 4 puffs or Nebulizer
 (short-acting beta₂-agonist)
 Add: _____ mg per day For _____ (3–10) days
 (oral steroid)
 Call the doctor before/ within _____ hours after taking the oral steroid.

RED ZONE

Medical Alert!

- Very short of breath, or
- Quick-relief medicines have not helped, or
- Cannot do usual activities, or
- Symptoms are same or get worse after 24 hours in Yellow Zone

-Or-

Peak flow: less than _____
 (50 percent of my best peak flow)

Take this medicine:

_____ 4 or 6 puffs or Nebulizer
 (short-acting beta₂-agonist)
 _____ mg
 (oral steroid)

Then call your doctor NOW. Go to the hospital or call an ambulance if:

- You are still in the red zone after 15 minutes AND
- You have not reached your doctor.

DANGER SIGNS ■ Trouble walking and talking due to shortness of breath ■ Take 4 or 6 puffs of your quick-relief medicine AND
 ■ Lips or fingernails are blue ■ Go to the hospital or call for an ambulance _____ NOW!
 (phone)

See the reverse side for things you can do to avoid your asthma triggers.

How To Control Things That Make Your Asthma Worse

This guide suggests things you can do to avoid your asthma triggers. Put a check next to the triggers that you know make your asthma worse and ask your doctor to help you find out if you have other triggers as well. Then decide with your doctor what steps you will take.

Allergens

Animal Dander

Some people are allergic to the flakes of skin or dried saliva from animals with fur or feathers.

The best thing to do:

- Keep furred or feathered pets out of your home.

If you can't keep the pet outdoors, then:

- Keep the pet out of your bedroom and other sleeping areas at all times, and keep the door closed.
- Remove carpets and furniture covered with cloth from your home. If that is not possible, keep the pet away from fabric-covered furniture and carpets.

Dust Mites

Many people with asthma are allergic to dust mites. Dust mites are tiny bugs that are found in every home—in mattresses, pillows, carpets, upholstered furniture, bedcovers, clothes, stuffed toys, and fabric or other fabric-covered items.

Things that can help:

- Encase your mattress in a special dust-proof cover.
- Encase your pillow in a special dust-proof cover or wash the pillow each week in hot water. Water must be hotter than 130° F to kill the mites. Cold or warm water used with detergent and bleach can also be effective.
- Wash the sheets and blankets on your bed each week in hot water.
- Reduce indoor humidity to below 60 percent (ideally between 30–50 percent). Dehumidifiers or central air conditioners can do this.
- Try not to sleep or lie on cloth-covered cushions.
- Remove carpets from your bedroom and those laid on concrete, if you can.
- Keep stuffed toys out of the bed or wash the toys weekly in hot water or cooler water with detergent and bleach.

Cockroaches

Many people with asthma are allergic to the dried droppings and remains of cockroaches.

The best thing to do:

- Keep food and garbage in closed containers. Never leave food out.
- Use poison baits, powders, gels, or paste (for example, boric acid). You can also use traps.
- If a spray is used to kill roaches, stay out of the room until the odor goes away.

Indoor Mold

- Fix leaky faucets, pipes, or other sources of water that have mold around them.
- Clean moldy surfaces with a cleaner that has bleach in it.

Pollen and Outdoor Mold

What to do during your allergy season (when pollen or mold spore counts are high):

- Try to keep your windows closed.
- Stay indoors with windows closed from late morning to afternoon, if you can. Pollen and some mold spore counts are highest at that time.
- Ask your doctor whether you need to take or increase anti-inflammatory medicine before your allergy season starts.

Irritants

Tobacco Smoke

- If you smoke, ask your doctor for ways to help you quit. Ask family members to quit smoking, too.
- Do not allow smoking in your home or car.

Smoke, Strong Odors, and Sprays

- If possible, do not use a wood-burning stove, kerosene heater, or fireplace.
- Try to stay away from strong odors and sprays, such as perfume, talcum powder, hair spray, and paints.

Other things that bring on asthma symptoms in some people include:

Vacuum Cleaning

- Try to get someone else to vacuum for you once or twice a week, if you can. Stay out of rooms while they are being vacuumed and for a short while afterward.
- If you vacuum, use a dust mask (from a hardware store), a double-layered or microfilter vacuum cleaner bag, or a vacuum cleaner with a HEPA filter.

Other Things That Can Make Asthma Worse

- Sulfites in foods and beverages: Do not drink beer or wine or eat dried fruit, processed potatoes, or shrimp if they cause asthma symptoms.
- Cold air: Cover your nose and mouth with a scarf on cold or windy days.
- Other medicines: Tell your doctor about all the medicines you take. Include cold medicines, aspirin, vitamins and other supplements, and nonselective beta-blockers (including those in eye drops).



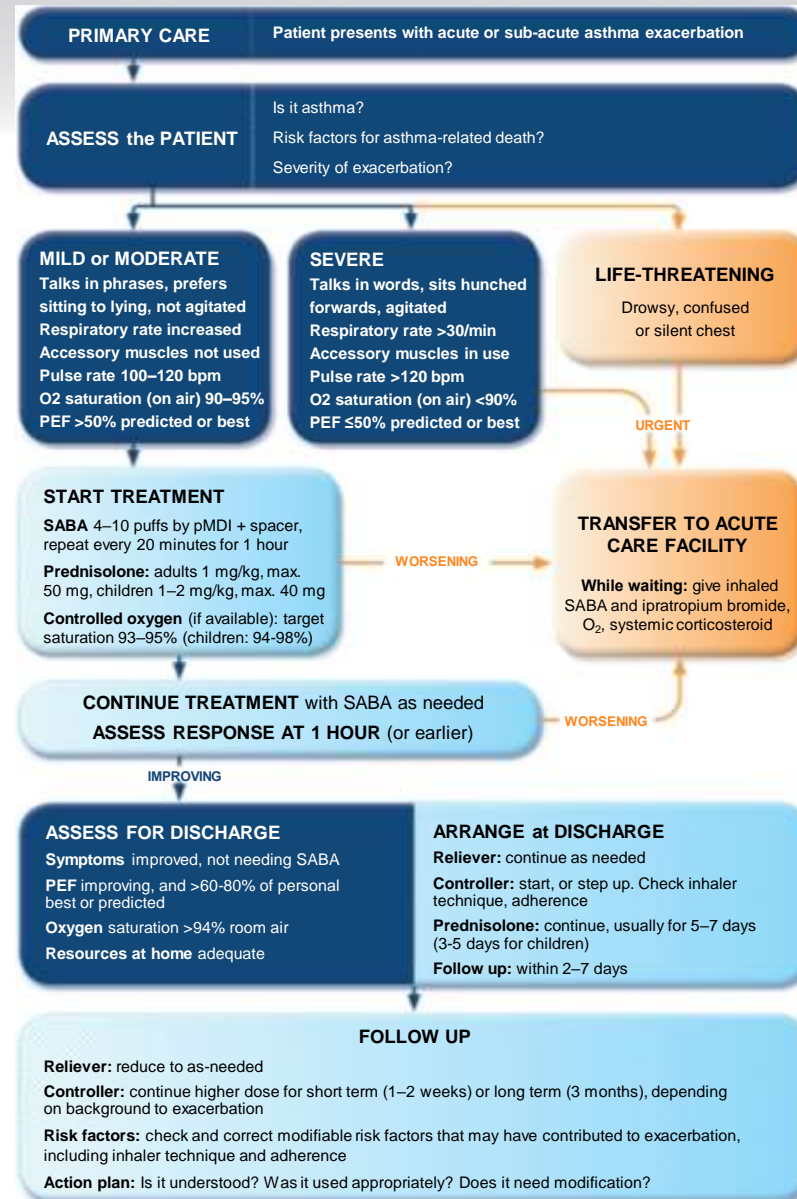
U.S. Department of Health and Human Services
 National Institutes of Health

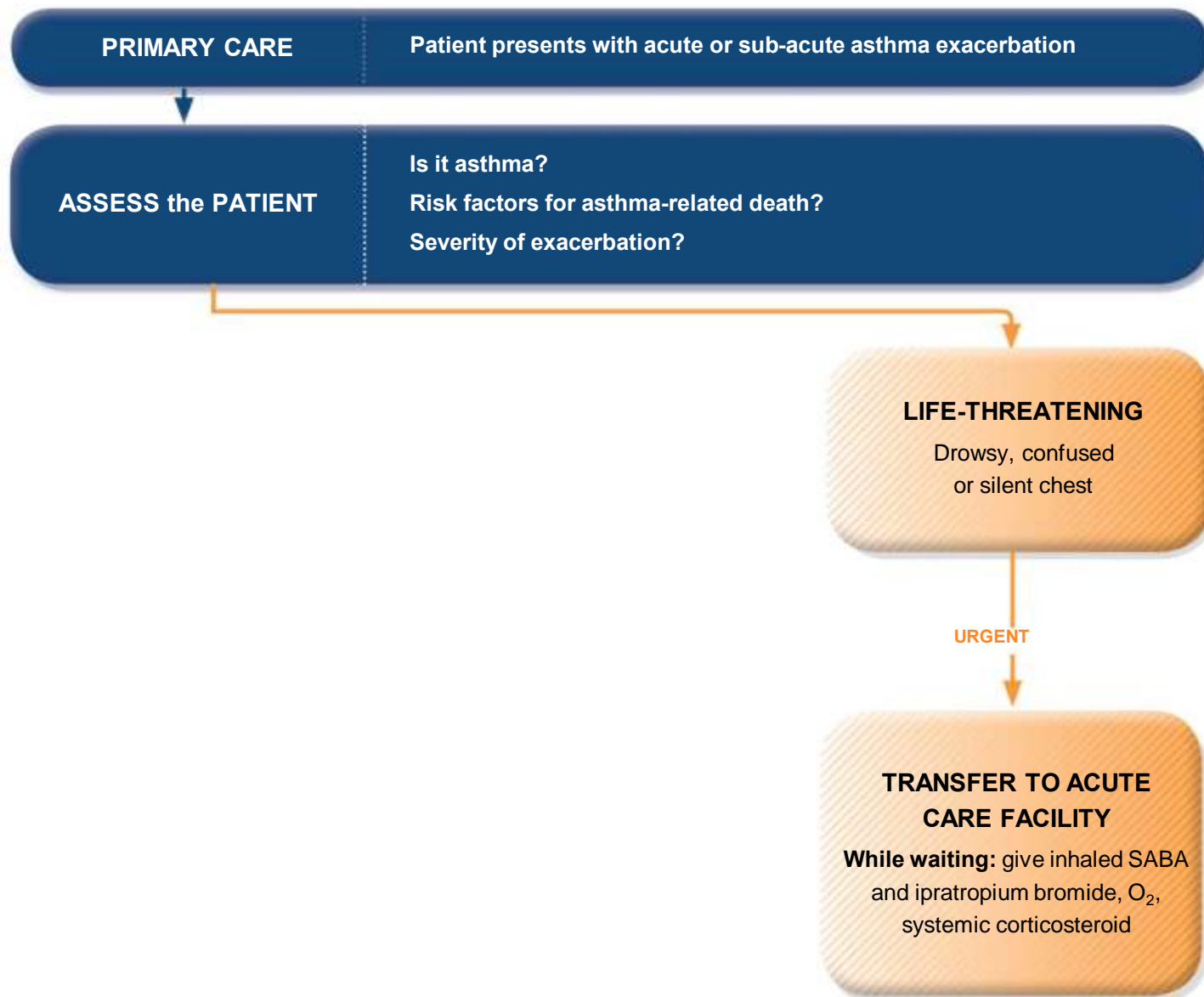


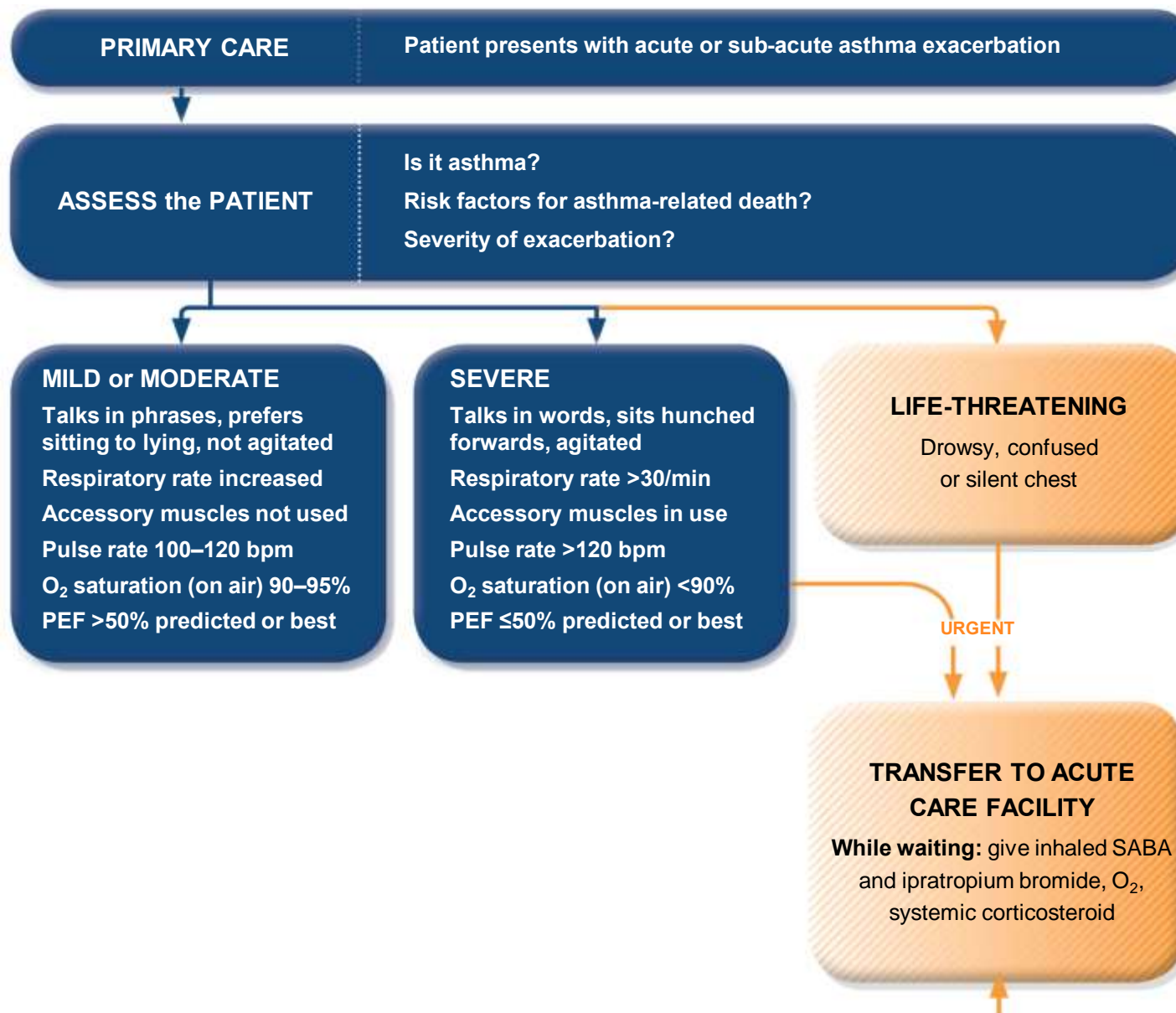
For More Information, go to: www.nhlbi.nih.gov

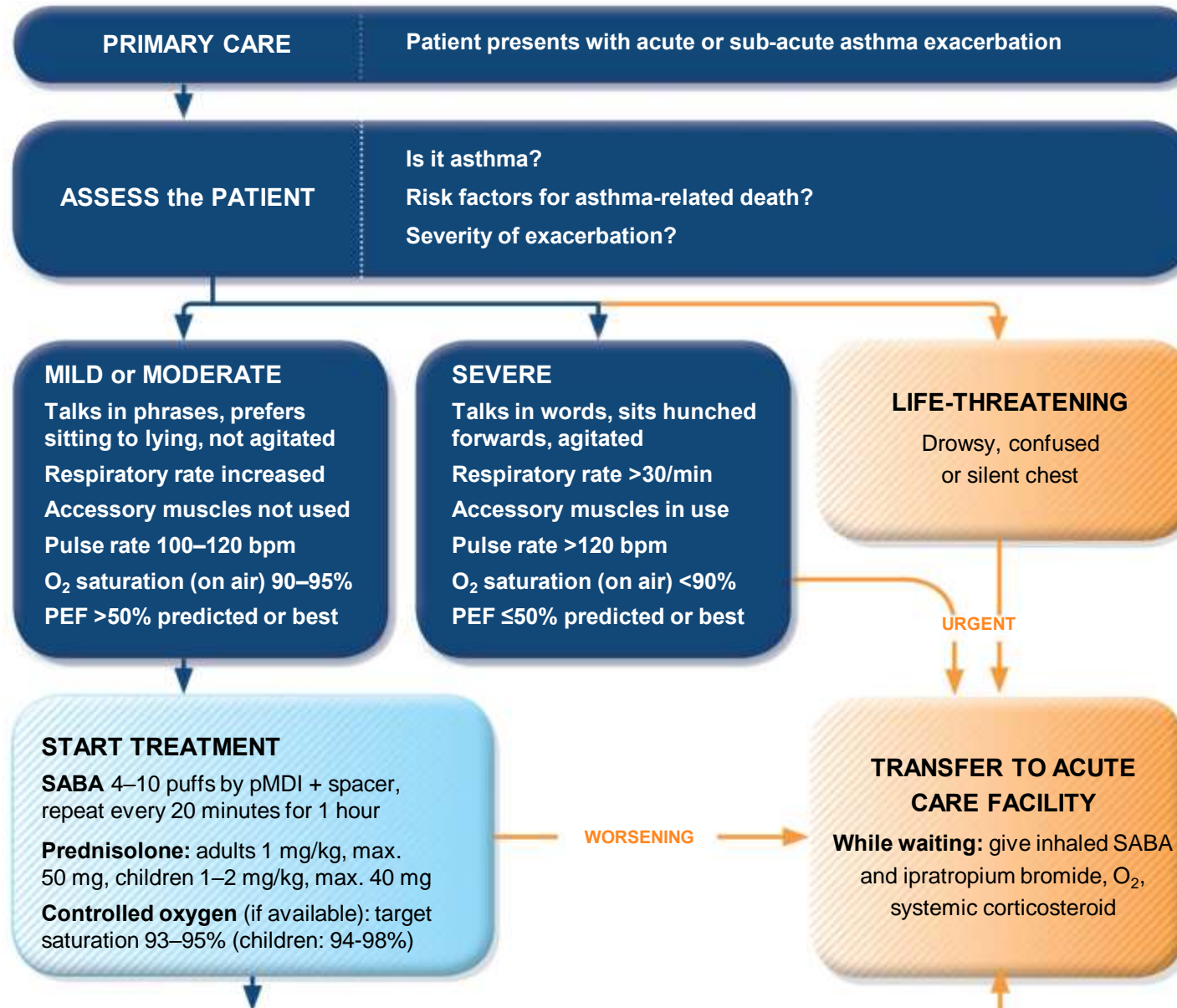
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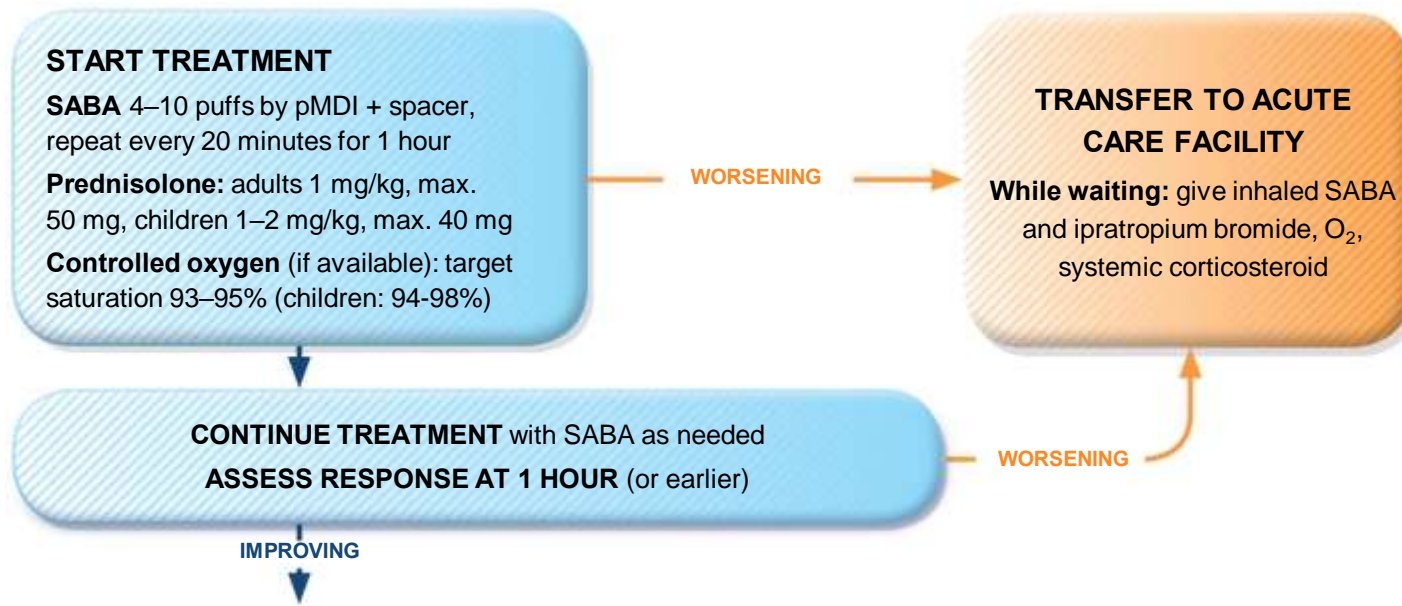
Managing Exacerbations in Primary Care

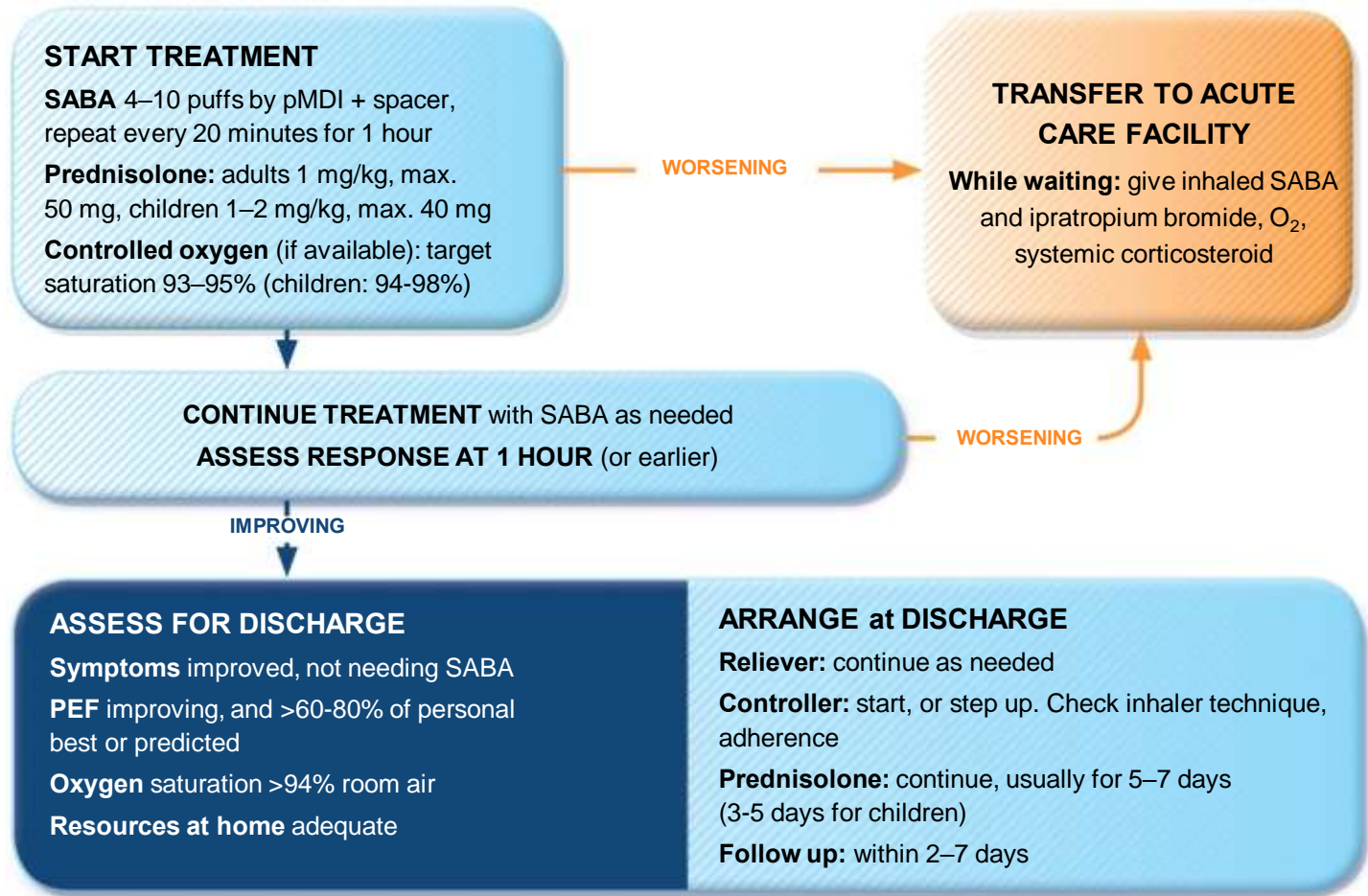


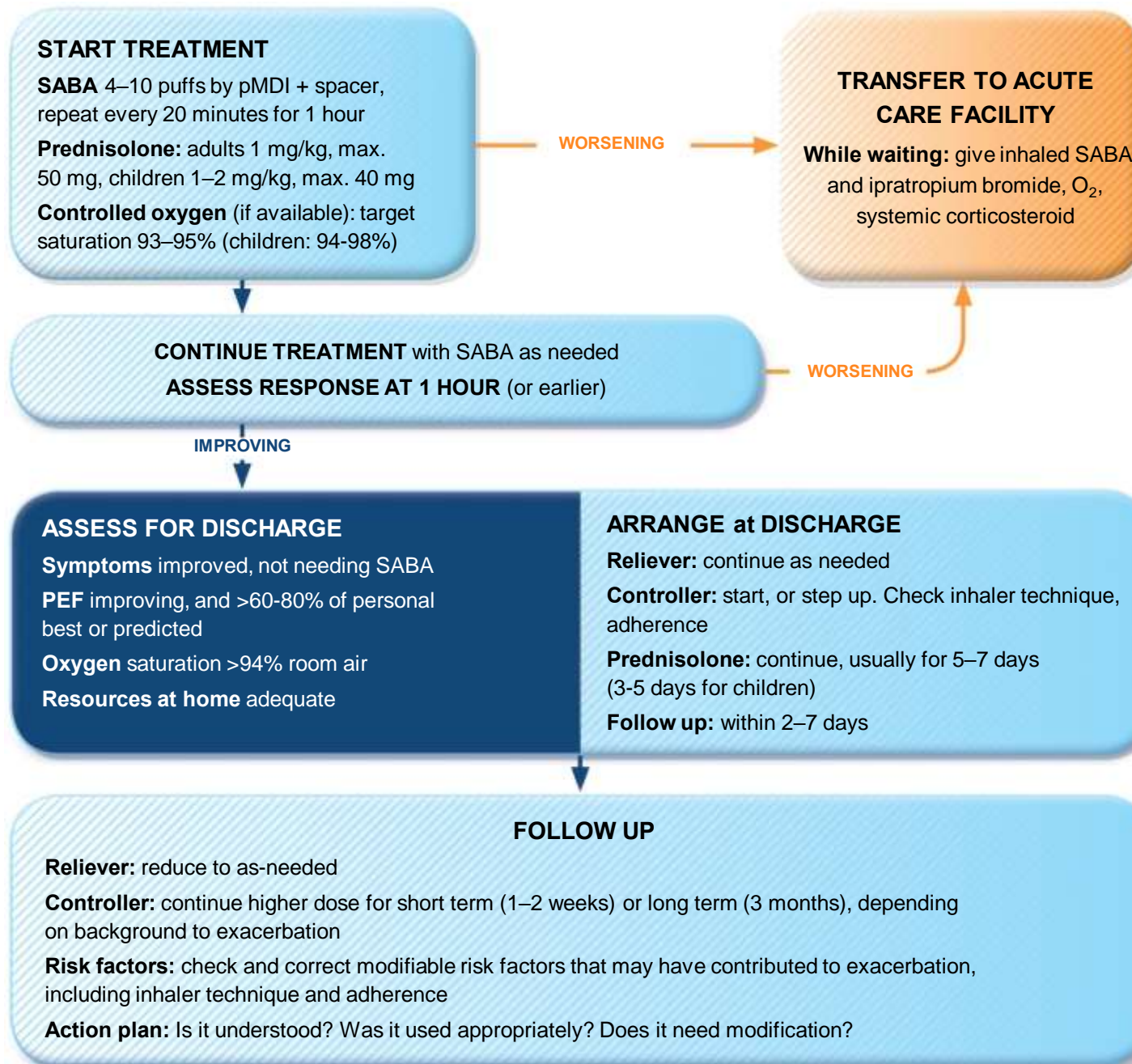




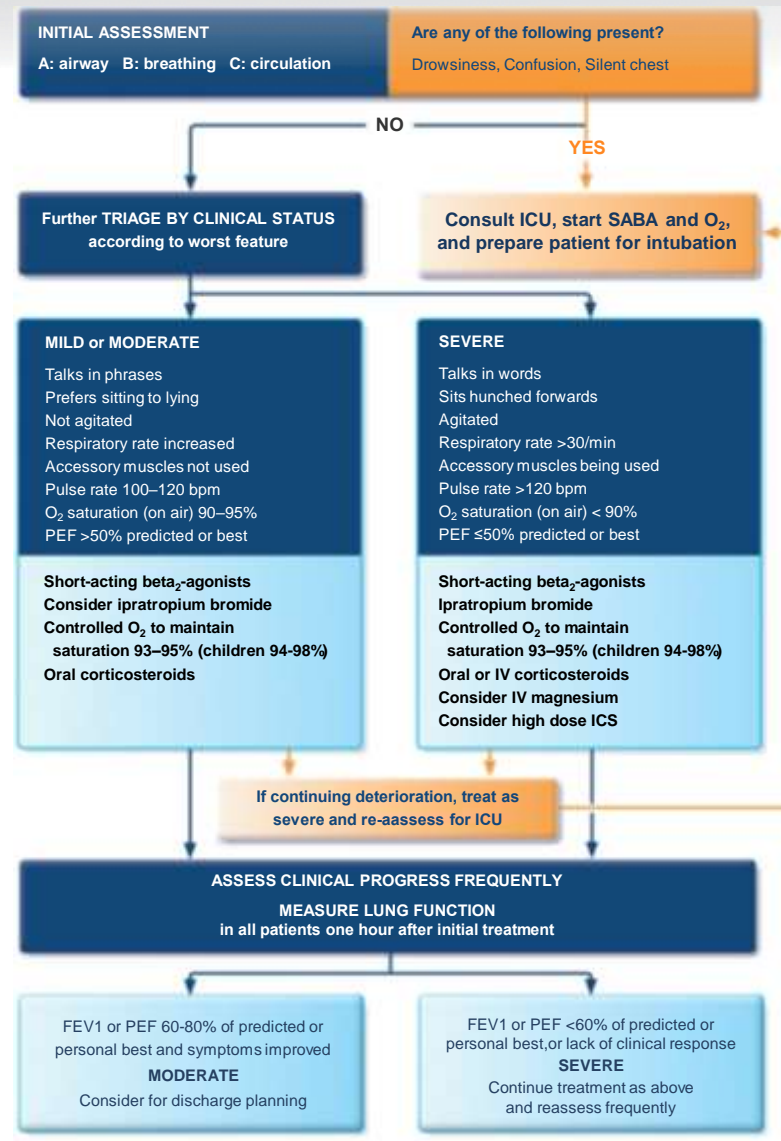


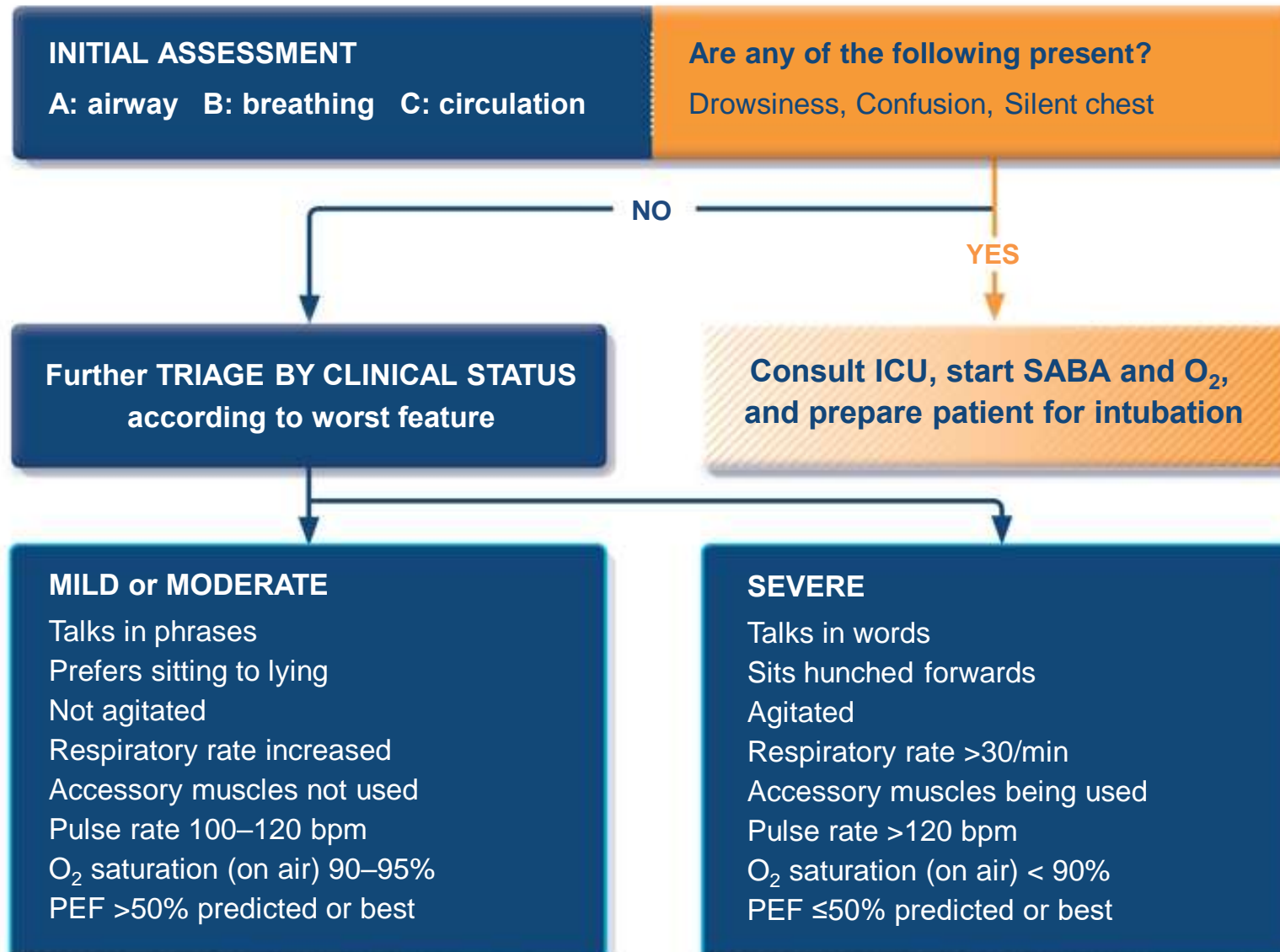






Managing Exacerbations in Acute Care Settings





MILD or MODERATE

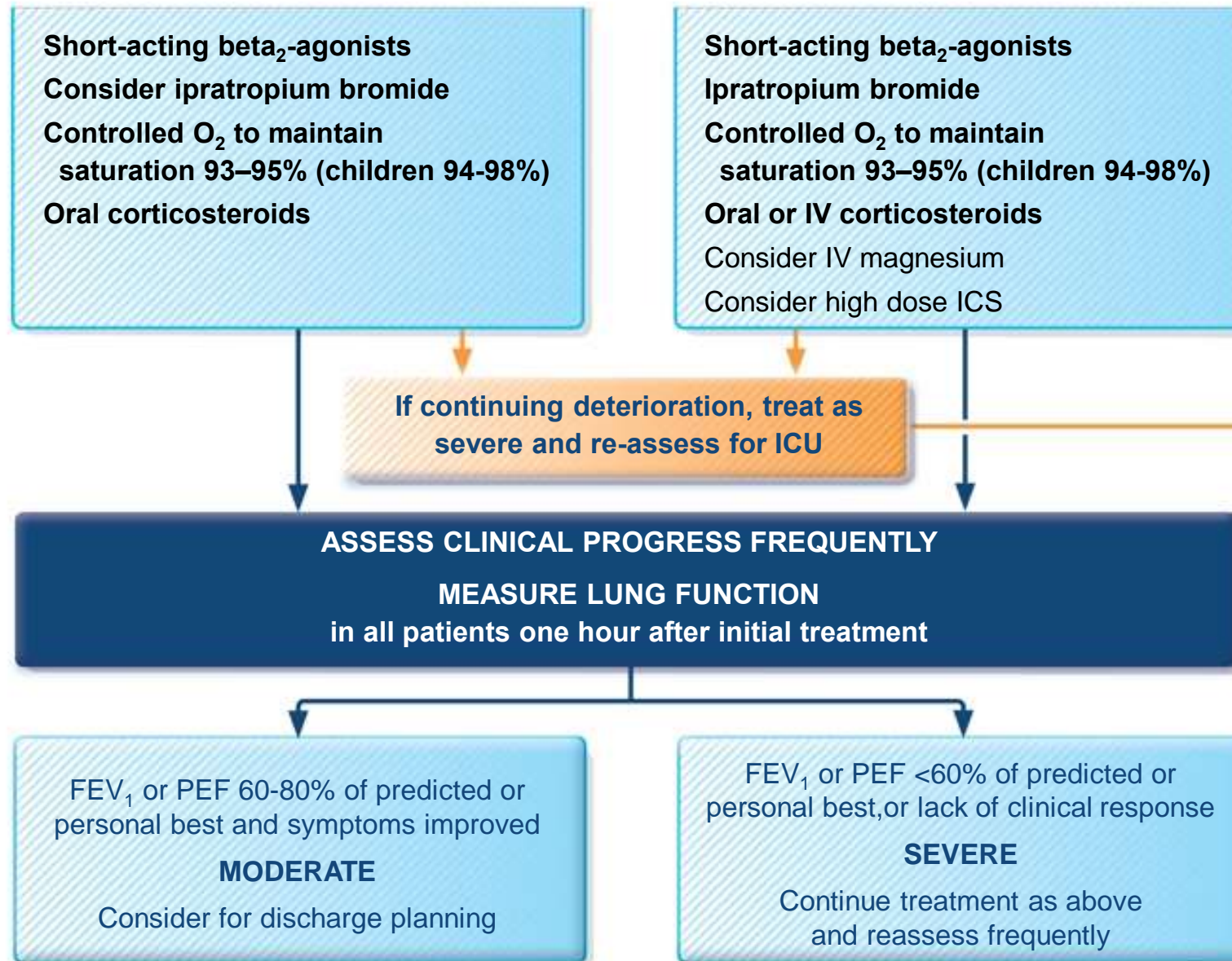
Talks in phrases
Prefers sitting to lying
Not agitated
Respiratory rate increased
Accessory muscles not used
Pulse rate 100–120 bpm
O₂ saturation (on air) 90–95%
PEF >50% predicted or best

Short-acting beta₂-agonists
Consider ipratropium bromide
Controlled O₂ to maintain
saturation 93–95% (children 94-98%)
Oral corticosteroids

SEVERE

Talks in words
Sits hunched forwards
Agitated
Respiratory rate >30/min
Accessory muscles being used
Pulse rate >120 bpm
O₂ saturation (on air) < 90%
PEF ≤50% predicted or best

Short-acting beta₂-agonists
Ipratropium bromide
Controlled O₂ to maintain
saturation 93–95% (children 94-98%)
Oral or IV corticosteroids
Consider IV magnesium
Consider high dose ICS



Follow Up

- Follow up all patients regularly after an exacerbation, until symptoms and lung function return to normal
 - Patients are at increased risk during recovery from an exacerbation
- The opportunity
 - Exacerbations often represent failures in chronic asthma care, and they provide opportunities to review the patient's asthma management
- At follow-up check:
 - The patient's understanding of the cause of the flare-up
 - Modifiable risk factors, e.g. smoking
 - Adherence with medications, and understanding of their purpose
 - Inhaler technique skills
 - Written asthma action plan

