

ASTHMA

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PATHOGENESIS

- Inflammation in asthmatic airways: Inflammatory cells (mast cells, eosinophils, T lymphocytes, neutrophils), chemical mediators (histamine, leukotrienes, platelet-activating factor, bradykinin), and chemotactic factors (cytokines, eotaxin)
- Inflammation ➤ airway hyperresponsiveness
- Bronchoconstriction, ↑mucus production in the lungs, influx of inflammatory cells into the airway tissue, and epithelial cell denudation.
- Chronic inflammation ➤ to airway remodeling :proliferation of extracellular matrix proteins +vascular hyperplasia ➤ progressive loss of pulmonary function

Epidemiology

- Asthma is the most common chronic disease of childhood
- affecting nearly 7 million children younger than 18 years of age in US
- In adults, females are more likely than males to have asthma, but in children the reverse is true.
- Among children less than 18 years of age, asthma prevalence increased by 1.4% per year.
- For children, the death rate is 2.5 per million.

CLINICAL SYMPTOMS

- In Children : coughing, wheezing, shortness of breath, exercise intolerance, or chest tightness.
- The history should elicit :the frequency, severity, and precipitating factors as well as a family history of asthma and allergy
- Common exacerbating factors include viral infections, exposure to allergens and irritants (e.g., smoke, air pollution, strong odors, fumes), exercise, emotions, and change in weather/humidity.
- Nocturnal symptoms are common.
- Rhinosinusitis, gastroesophageal reflux, and aspirin can aggravate asthma. Treatment of these conditions may lessen the frequency and severity of asthma.

ACUTE ASTHMA SYMPTOMS

- tachypnea, tachycardia, cough, wheezing, and a prolonged expiratory phase may be present.
- Physical findings may be subtle,
- As the attack progresses, cyanosis, diminished air movement, here is poor aeration from airway
- retractions, agitation, inability to speak, tripod sitting position, diaphoresis, and pulsus paradoxus (decrease in blood pressure of >15 mm Hg with inspiration)
- Physical examination may show evidence of other atopic diseases such as eczema or allergic rhinitis.

Laboratory and Imaging Studies

- no single test or study can confirm the diagnosis of asthma
- Many elements contribute to establishing the diagnosis the most important is clinical history
- pulmonary function (spirometry) aid in the diagnosis and direct the treatment of asthma.
- Children older than 5 years of age can usually perform spirometry maneuvers
- For younger children peak flow or, a therapeutic trial of controller medications aids in the diagnosis of asthma

Laboratory and Imaging Studies

- Allergy skin testing should be included in the evaluation of all children with
- persistent asthma but not during an exacerbation of symptoms. Positive skin test
- results, identifying sensitization to aeroallergens (e.g., pollens, mold, dust mite,
- pet dander), correlate strongly with bronchial allergen provocative challenges. In
- vitro serum tests, such as enzyme-linked immunosorbent assay (ELISA), are
- generally less sensitive in defining clinically pertinent allergens, are more
- expensive, and require several days for results, compared to several minutes for
- skin testing

Laboratory and Imaging Studies

- An x-ray should be performed with the first episode of asthma or with recurrent episodes of undiagnosed cough or wheeze to exclude anatomic abnormalities.
- Repeat chest x-rays are not needed with new episodes unless there is fever (suggesting pneumonia) or localized findings on physical examination.
- exhaled nitric oxide
- analysis and quantitative analysis of expectorated sputum for eosinophilia.

Differential Diagnosis of Cough and Wheeze in Infants and Children

UPPER AIRWAY DISEASES	OBSTRUCTION INVOLVING LARGE AIRWAYS	OBSTRUCTION INVOLVING SMALL AIRWAYS	OTHER
Allergic rhinitis Sinusitis	Tracheal or bronchial foreign body Paradoxical vocal fold motion Vascular rings or laryngeal webs Enlarged lymph nodes or tumor	Viral bronchiolitis or obliterative bronchiolitis Cystic fibrosis Bronchopulmonary dysplasia (chronic lung disease of prematurity)	Recurrent cough not caused by asthma (infection, habit cough, postnasal drip) Aspiration from swallowing mechanism dysfunction or gastroesophageal reflux disease

Mnemonic of Causes of Cough in the First Months of Life

- C—Cystic fibrosis
- R—Respiratory tract infections
- A—Aspiration (swallowing dysfunction, gastroesophageal reflux, tracheoesophageal fistula, foreign body)
- D—Dyskinetic cilia
- L—Lung and airway malformations (laryngeal webs, laryngotracheomalacia, tracheal stenosis, vascular rings and slings)
- E—Edema (heart failure, congenital heart disease)

- Allergic bronchopulmonary aspergillosis is a hypersensitivity reaction to
- antigens of the mold *Aspergillus fumigatus*. It occurs primarily in patients with
- steroid-dependent asthma and in patients with cystic fibrosis.

Controlling Factors Contributing to Asthma Severity

MAJOR INDOOR TRIGGERS FOR ASTHMA	SUGGESTIONS FOR REDUCING EXPOSURE
Viral upper respiratory tract (RSV, influenza virus)	Limit exposure to viral infections (day care with fewer children)
	Annual influenza immunization for children with persistent asthma
Tobacco smoke, wood smoke	No smoking around the child or in child's home
	Help parents and caregivers quit smoking
	Eliminate use of wood stoves and fireplaces
Dust mites	ESSENTIAL ACTIONS
	Encase pillow, mattress, and box spring in allergen-impermeable encasements
	Wash bedding in hot water weekly

	DESIRABLE ACTIONS
	Avoid sleeping or lying on upholstered furniture
	Minimize number of stuffed toys in child's bedroom
	Reduce indoor humidity to <50%
	If possible, remove carpets from bedroom and play areas; if not possible, vacuum weekly
Animal dander	Remove the pet from the home or keep outdoors (if removal is not acceptable)
	Keep pet out of bedroom/no sleeping with pet
	Use a filter on air ducts in child's room
	Wash pet weekly (the evidence to support this has not been firmly established)
Cockroach allergens	Do not leave food or garbage exposed
	Pesticides
	Sealing cracks and holes
Indoor mold	Avoid vaporizers
	Reduce indoor humidity to <50%
	Use of mold inhibiting cleaner
	Use of dehumidifier
	Fix leaky faucets, pipes

Treatment

- includes several key components:
- environmental control,
- pharmacologic therapy,
- and patient education, including attainment of self-management skills.
- Because many children with asthma have coexisting allergies, steps to minimize allergen exposure should be taken
- For all children with asthma,
- exposures to tobacco and wood smoke and to should be minimized
- Influenza immunization is indicated.
- Asthma medications can be divided into long-term control medications and quick-relief medications.

Long-Term Control Medications

- Inhaled corticosteroids are the most effective anti inflammatory medications for the treatment of chronic, persistent asthma and are the preferred therapy when initiating long-term control therapy
- :Low-to-medium dose inhaled corticosteroids may decrease growth velocity, although these effects are small (approximately 1 cm in the first year of treatment), Height measurements should be monitored.
- Inhaled corticosteroids do not have clinically significant adverse effects on hypothalamic-pituitary-adrenal axis function, glucose metabolism, subcapsular cataracts, or glaucoma when used at low-to-medium doses in children.
- Rinsing the mouth after inhalation and using large volume spacers help lessen the local adverse effects of dysphonia and candidiasis and decrease systemic absorption from the gastrointestinal tract.
- Inhaled corticosteroids should be titrated to the lowest dose needed to maintain control of a child's asthma.
- For children with severe asthma, high dose inhaled corticosteroids may be needed to minimize oral corticosteroid use, but other “add-on” therapy should be considered

Long-Term Control Medications

- Leukotriene Modifiers are potent mediators of inflammation and smooth muscle bronchoconstriction.
- Two classes of leukotriene modifiers include cysteinyl leukotriene receptor antagonists (zafirlukast and montelukast) and leukotriene synthesis inhibitors (zileuton).
- Long-Acting β 2-Agonists: formoterol and salmeterol, have twice-daily dosing and relax airway smooth muscle for 12 hours but do not have any significant antiinflammatory effects.
- Adding a long-acting bronchodilator to inhaled corticosteroid therapy is more beneficial than doubling the dose of inhaled

Long-Term Control Medications

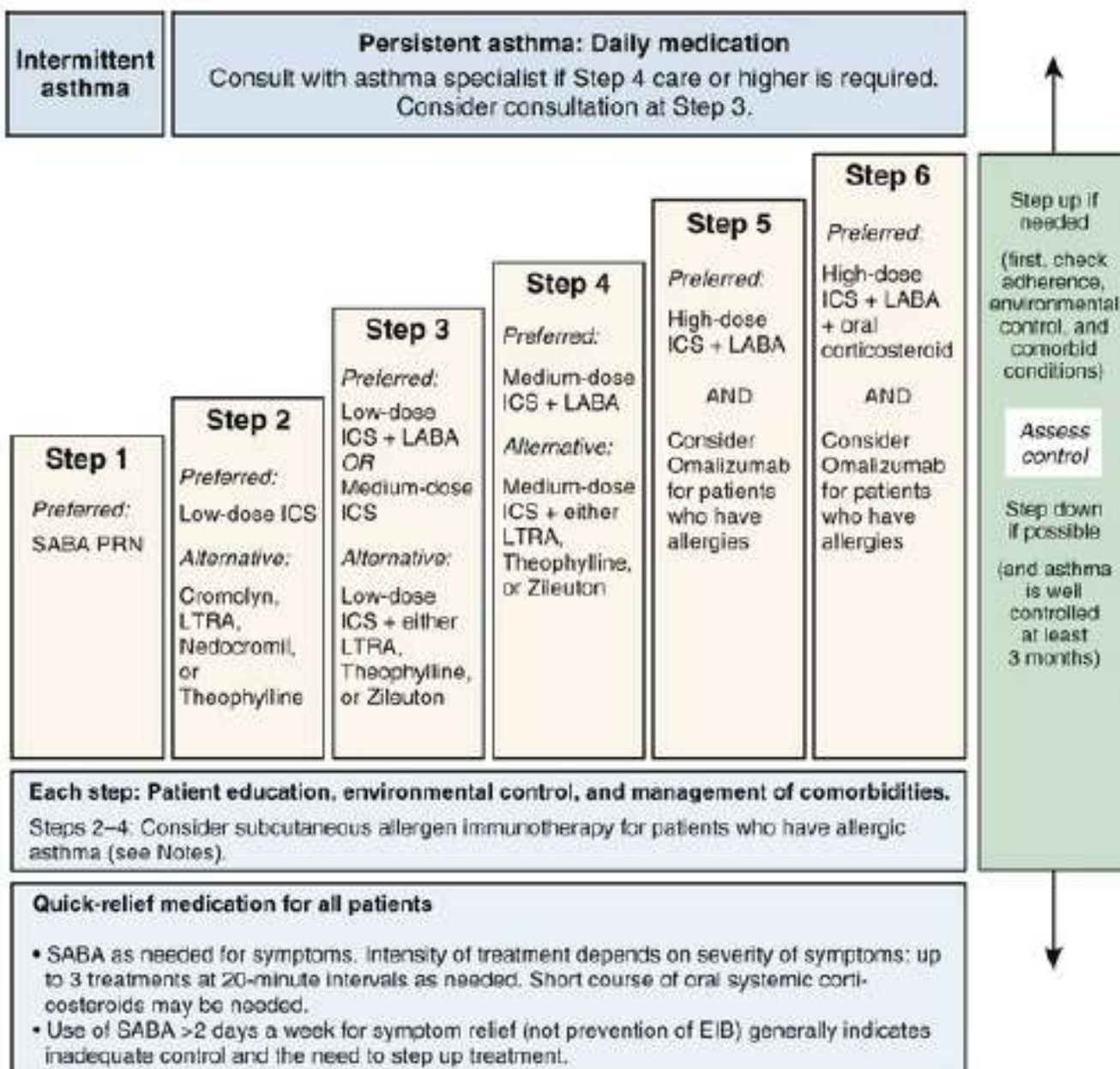
- Theophylline (usage declined)
- It is mildly to moderately effective as a bronchodilator and is considered an alternative, add-on treatment to low- and medium-dose inhaled corticosteroids
- Quick-Relief Medications
- Short-Acting β 2-Agonists: albuterol and levalbuterol are effective :relaxing bronchial smooth muscle within 5-10 minutes of administration.,
- a short-acting β 2-agonist is prescribed for acute symptoms and as prophylaxis before allergen exposure and exercise.
- Anticholinergic Agents Ipratropium bromide is a short-acting anticholinergic bronchodilator that relieves bronchoconstriction, decreases mucus hypersecretion, and counteracts cough receptor (additive effect with β 2-agonists) in asthma attack

Long-Term Control Medications

- Oral Corticosteroids :Short bursts of oral corticosteroids (3-10 days) are administered to children with acute exacerbations. The usual dose is 1-2 mg/kg/day of prednisone for 5 days.
- Administration of two doses of dexamethasone for the treatment of acute asthma exacerbations has been used
- This oral corticosteroid has properties that may increase compliance with therapy

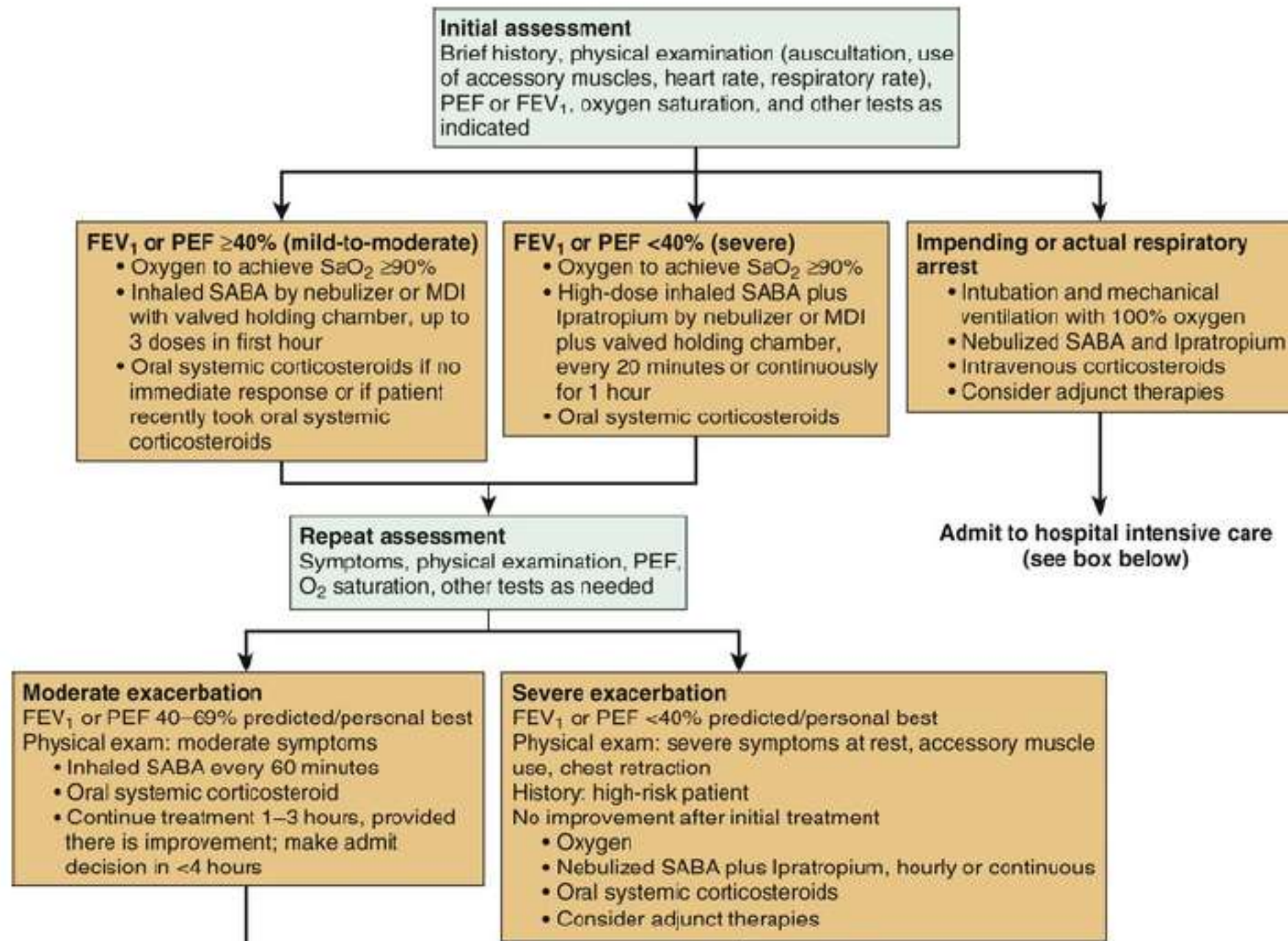
Stepwise Approach to Therapy

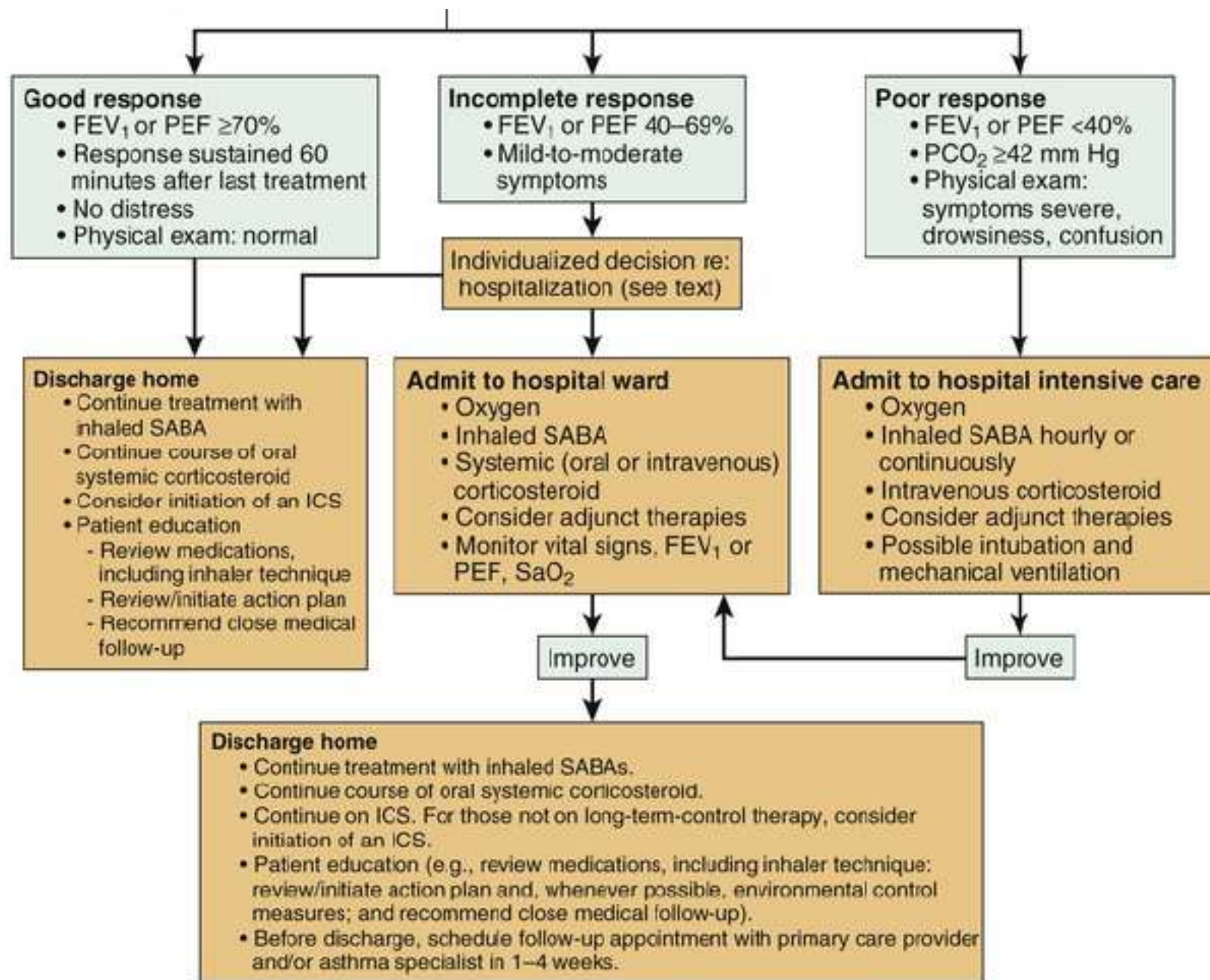
- in 3 level of age :children 0-4 years of age, children 5-11 years of age and youths 12 years or older, and adults
- Medication type, dose, and dosing intervals are determined by the level of asthma severity or asthma control.
- Therapy is then increased (stepped up) as necessary and decreased (stepped down) when possible.
- using the Rules of Two is helpful: daytime symptoms occurring two or more times per week or nocturnal awakenings two or more times per month implies a need for daily anti inflammatory medication.



Drug	Low Daily Dose			Medium Daily Dose			High Daily Dose		
	Child 0–4 Years of Age	Child 5–11 Years of Age	≥12 Years of Age and Adults	Child 0–4 Years of Age	Child 5–11 Years of Age	≥12 Years of Age and Adults	Child 0–4 Years of Age	Child 5–11 Years of Age	≥12 Years of Age and Adults
Beclomethasone HFA 40 or 80 µg/puff	NA	80–160 µg	80–240 µg	NA	>160–320 µg	>240–480 µg	NA	>320 µg	>480 µg
Budesonide DPI 90, 180, or 200 µg/inhalation	NA	180–400 µg	180–600 µg	NA	>400–800 µg	>600–1,200 µg	NA	>800 µg	>1,200 µg
Budesonide Inhaled Inhalation suspension for nebulization	0.25–0.5 mg	0.5 mg	NA	>0.5–1.0 mg	1.0 mg	NA	>1.0 mg	2.0 mg	NA
Flunisolide 250 µg/puff	NA	500–750 µg	500–1,000 µg	NA	1,000–1,250 µg	>1,000–2,000 µg	NA	>1,250 µg	>2,000 µg
Flunisolide HFA 80 µg/puff	NA	160 µg	320 µg	NA	320 µg	>320–640 µg	NA	>640 µg	>640 µg
Fluticasone HFA/MDI: 44, 110, or 220 µg/puff DPI: 50, 100, or 250 µg/inhalation	176 µg	88–176 µg	88–264 µg	>176–352 µg	>176–352 µg	>264–440 µg	>352 µg	>352 µg	>440 µg
	NA	100–200 µg	100–300 µg	NA	>200–400 µg	>300–500 µg	NA	>400 µg	>500 µg
Mometasone DPI 200 µg/inhalation	NA	NA	200 µg	NA	NA	400 µg	NA	NA	>400 µg
Triamcinolone acetonide 75 µg/puff	NA	300–600 µg	300–750 µg	NA	>600–900 µg	>750–1,500 µg	NA	>900 µg	>1,500 µg

- Inhaled corticosteroids are the preferred initial long-term control therapy for children of all ages
- Daily long-term control therapy is recommended for infants and young children 0-4 years of age who had four or more episodes of wheezing in the previous year that lasted more than 1 day, affected sleep, and who have a positive asthma predictive index
- For children over 5 years of age :with moderate persistent asthma, combining long-acting bronchodilators with low-to-medium doses of inhaled corticosteroids improves lung function and reduces rescue medication use.
- For children with severe persistent asthma, a high-dose inhaled corticosteroid combined with a long-acting bronchodilator is the preferred therapy.
- Reevaluation within 4-6 weeks when the asthma is well controlled for at least 3 months ➤ stepping down





Complications

- Most asthma exacerbations can be successfully managed at home.
- Status asthmaticus is an acute exacerbation of asthma that does not respond adequately to therapeutic measures and may require hospitalization.
- Exacerbations may progress over several days or occur suddenly and can range in severity from mild to life threatening.
- Significant respiratory distress, dyspnea, wheezing, cough, and a decrease in spirometry or peak expiratory flow rate (PEFR) characterize deterioration in asthma control.
- During a severe episode pulse oximetry is helpful in monitoring oxygenation. In status asthmaticus, arterial blood gases may be necessary for measurement of ventilation.
- As airway obstruction worsens and chest compliance decreases, carbon dioxide retention can occur.
- In tachypnea, a normal PCO₂ (35-45 mm Hg) indicates impending respiratory arrest

management of asthma exacerbations

- First-line includes supplemental oxygen
- if needed and repetitive or continuous administration of short-acting bronchodilators.
- Early administration of oral or intravenous corticosteroids is important in treating the underlying inflammation.
- Administration of anticholinergic agents (ipratropium) with bronchodilators decreases rates of hospitalization and duration of time in the emergency department.
- Intravenous magnesium sulfate is administered in the emergency department if there is clinical deterioration despite treatment with β_2 -agonists, ipratropium, and systemic corticosteroids.
- The typical dose of magnesium sulfate is 25-75 mg/kg (maximum 2.0 g) intravenously administered over 20 minutes.
- Intramuscular epinephrine or subcutaneous terbutaline are rarely used except when severe asthma is associated with anaphylaxis or unresponsive to continuous administration of short-acting bronchodilators.

Prognosis

- For some children, symptoms of wheezing with respiratory infections subside in the preschool years, whereas others have more persistent asthma symptoms.
- Prognostic indicators for children younger than 3 years of age who are at risk for persistent asthma are known as the Modified Asthma Predictive Index for children
- Atopy is the strongest predictor for wheezing continuing into persistent asthma

Modified Asthma Predictive Index for Children

At least four wheezing episodes <i>plus</i> :	
1 Major criteria	Or 2 Minor criteria
Parental asthma	Allergic rhinitis
Eczema	Wheezing apart from colds
Inhalant allergen sensitization	Eosinophils $\geq 4\%$
	Food allergen sensitization

Risk Factors for Persistent Asthma

Allergy	Atopic dermatitis
	Allergic rhinitis
	Elevated total serum IgE levels (first year of life)
	Peripheral blood eosinophilia >4% (2-3 yr of age)
	Inhalant and food allergen sensitization
Gender	Males
	<ul style="list-style-type: none"> • Transient wheezing
	<ul style="list-style-type: none"> • Persistent allergy-associated asthma
	Females
	<ul style="list-style-type: none"> • Asthma associated with obesity and early-onset puberty
	<ul style="list-style-type: none"> • “Triad” asthma (adulthood)
Parental asthma	
Lower respiratory tract infections	Rhinovirus, respiratory syncytial virus
	Severe bronchiolitis (i.e., requiring hospitalization)
	Pneumonia
Environmental tobacco smoke exposure (including prenatal)	

Prevention

- Education plays an important role in helping patients and their families adhere to therapy
- Successful education :
 - teaching basic asthma facts,
 - explaining the role of medications,
 - teaching environmental control measures,
 - and improving patient skills in the use of spacer devices for metered dose inhalers and peak flow monitoring.
- Families should have an asthma management plan for daily care and for exacerbations.

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: _____

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

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

Identify and avoid and control the things that make your asthma worse, like (list here):

Before exercise, if prescribed, take: ☐ 2 or ☐ 4 puffs _____ 5 to 60 minutes before exercise

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)



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

If applicable, remove yourself from the thing that made your asthma worse.

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 corticosteroid)

☐ Call the doctor _____ ☐ before/ ☐ within _____ hours after taking the oral corticosteroid.
(phone)

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 corticosteroid)

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

■ Lips or fingernails are blue



■ Take ☐ 4 or ☐ 6 puffs of your quick-relief medicine AND

■ Go to the hospital or call for an ambulance _____ NOW!

(phone)