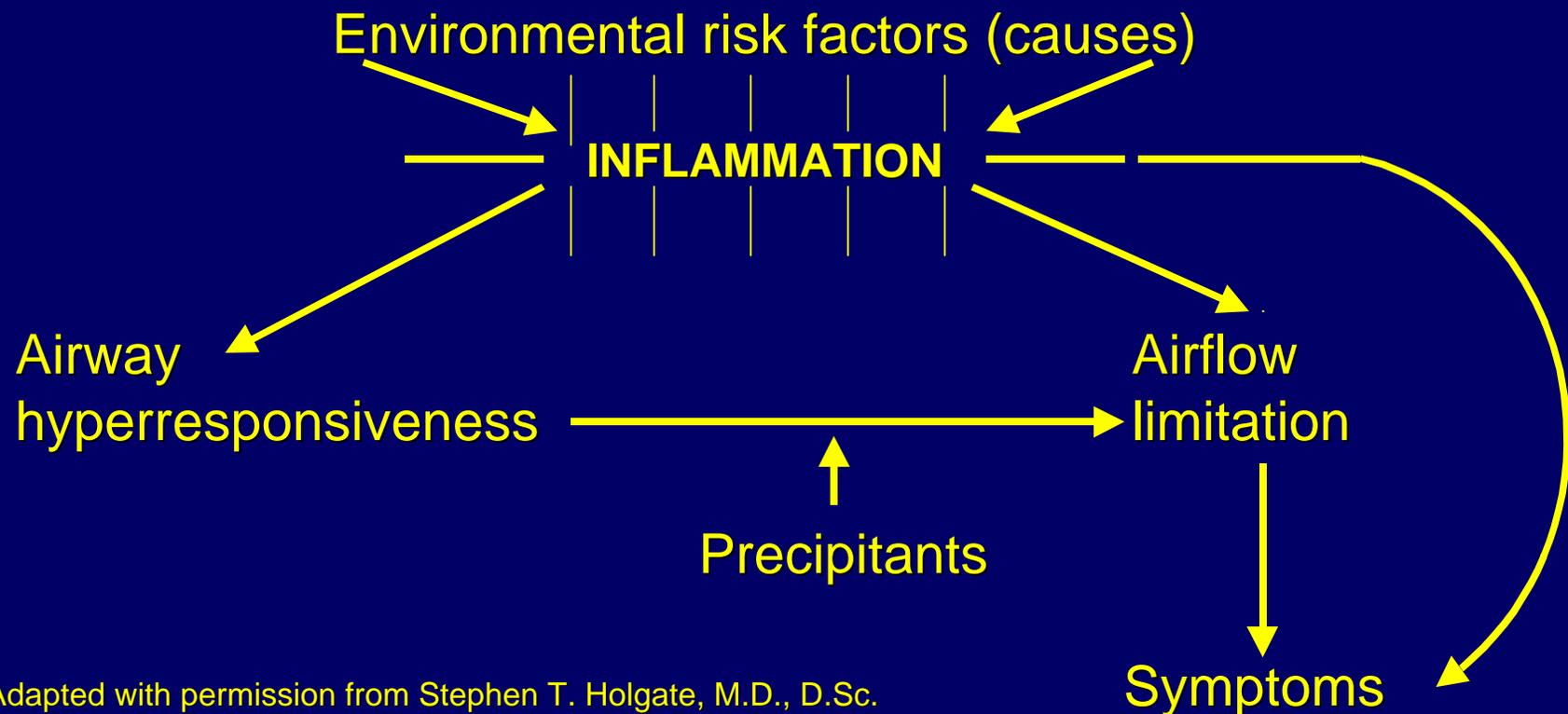


Component 3: Pharmacologic Therapy

- Asthma is a chronic inflammatory disorder of the airways.
- A key principle of therapy is regulation of chronic airway inflammation.



Component 3: Pharmacologic Therapy



Adapted with permission from Stephen T. Holgate, M.D., D.Sc.

- **Asthma is a chronic inflammatory disorder of the airways.**
- **A key principle of therapy is regulation of chronic airway inflammation.**



Inhaled Medication Delivery Devices

- Metered-dose inhaler (MDI)
- Dry powder inhaler (DPI)
- Spacer/holding chamber
- Spacer/holding chamber and face mask
- Nebulizer



Transition to Non-CFC Inhalers

- Most currently available MDIs use chlorofluorocarbons (CFCs) as propellants.
- CFCs are being phased out globally to protect the earth's ozone layer.
- CFC MDIs have a temporary medical exemption to the phaseout.
- Over the next several years, CFC MDIs will be gradually replaced by non-CFC alternatives.
- Non-CFC alternatives will include HFA MDIs, DPIs, and other new devices.



CFC Transition: What Patients and Practitioners Should Know

- Non-CFC products/devices are being developed and introduced into the US market.
- Non-CFC alternatives must be shown to be safe and effective prior to FDA approval.
- FDA will not phase out CFC MDIs until an adequate number of safe, effective, and acceptable non-CFC alternatives are available.
- As non-CFC alternatives become available, patients and practitioners should try them.
- Patients may notice differences in taste and feel of the new products.



Overview of Asthma Medications

- Daily: Long-Term Control
 - Corticosteroids (inhaled and systemic)
 - Cromolyn/nedocromil
 - Long-acting beta₂-agonists
 - Methylxanthines
 - Leukotriene modifiers



Overview of Asthma Medications (continued)

- As-needed: Quick Relief
 - Short-acting beta₂-agonists
 - Anticholinergics
 - Systemic corticosteroids



Inhaled Corticosteroids

- Most effective long-term-control therapy for persistent asthma
- Small risk for adverse events at recommended dosage
- Reduce potential for adverse events by:
 - Using spacer and rinsing mouth
 - Using lowest dose possible
 - Using in combination with long-acting beta₂-agonists
 - Monitoring growth in children



Inhaled Corticosteroids

(continued)

- Benefit of daily use:
 - Fewer symptoms
 - Fewer severe exacerbations
 - Reduced use of quick-relief medicine
 - Improved lung function
 - Reduced airway inflammation



Inhaled Corticosteroids and Linear Growth in Children

- Potential risks are well balanced by benefits.
- Growth rates in children are highly variable. Short-term evaluations may not be predictive of attaining final adult height.
- Poorly controlled asthma may delay growth.
- Children with asthma tend to have longer periods of reduced growth rates prior to puberty (males > females).



Inhaled Corticosteroids and Possible Effect on Linear Growth

- Most studies show no effect with low-to-medium doses, but some short-term studies show growth delay.
- Potential risk appears to be dose dependent:
 - Medium doses may be associated with possible, but not predictable, effect on linear growth. The clinical significance has not yet been determined.
 - High doses have greater potential for growth delay or suppression.
- For severe persistent asthma, high doses of inhaled corticosteroids have less risk than oral corticosteroids.



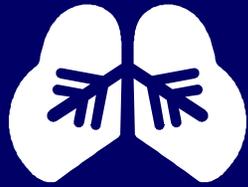
Inhaled Corticosteroids and Possible Effect on Linear Growth (continued)

- Some caution is suggested while studies continue:
 - Monitor growth
 - Use the lowest dose necessary to maintain control (step down therapy when possible)
 - Administer with spacers/holding chambers
 - Advise patients to “rinse and spit” following inhalation
 - Consider adding a long-acting inhaled beta₂-agonist to a low-to-medium dose of inhaled corticosteroids (vs. using a higher dose of the corticosteroid)



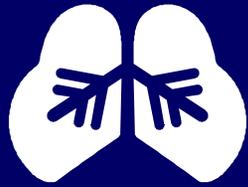
Estimated Comparative Dosages of Inhaled Corticosteroids

- Preparations are not equivalent per puff or per microgram.
- Comparative doses are *estimated*.
 - Few data directly compare preparations.
- Most important determinant of dosing is clinician judgment.
 - Monitor patient's clinical response to therapy.
 - Adjust dose accordingly.



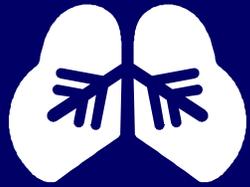
Estimated Comparative Daily Dosages of Inhaled Corticosteroids for Adults

Drug	Low Dose	Medium Dose	High Dose
Beclomethasone	168 - 504 mcg	504 - 840 mcg	> 840 mcg
Budesonide DPI	200 - 400 mcg	400 - 600 mcg	> 600 mcg
Flunisolide	500 - 1,000 mcg	1,000 - 2,000 mcg	>2,000 mcg
Fluticasone	88 - 264 mcg	264 - 660 mcg	> 660 mcg
Triamcinolone	400 - 1,000 mcg	1,000 - 2,000 mcg	>2,000 mcg



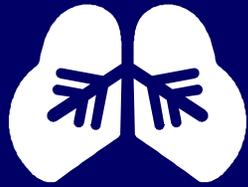
Estimated Comparative Daily Dosages of Inhaled Corticosteroids for Children ≤ 12 Years

Drug	Low Dose	Medium Dose	High Dose
Beclomethasone	84 - 336 mcg	336 - 672 mcg	> 672 mcg
Budesonide DPI	100 - 200 mcg	200 - 400 mcg	> 400 mcg
Flunisolide	500 - 750 mcg	1,000 - 1,250 mcg	>1,250 mcg
Fluticasone	88 - 176 mcg	176 - 440 mcg	> 440 mcg
Triamcinolone	400 - 800 mcg	800 - 1,200 mcg	>1,200 mcg



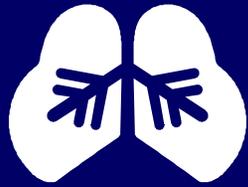
Long-Acting Beta₂-Agonists

- Not a substitute for anti-inflammatory therapy
- Not appropriate for monotherapy
- Beneficial when added to inhaled corticosteroids
- Not for acute symptoms or exacerbations



Short-Acting Beta₂-Agonists

- Most effective medication for relief of acute bronchospasm
- More than one canister per month suggests inadequate asthma control
- Regularly scheduled use is not generally recommended
 - May lower effectiveness
 - May increase airway hyperresponsiveness



Leukotriene Modifiers

■ Mechanisms

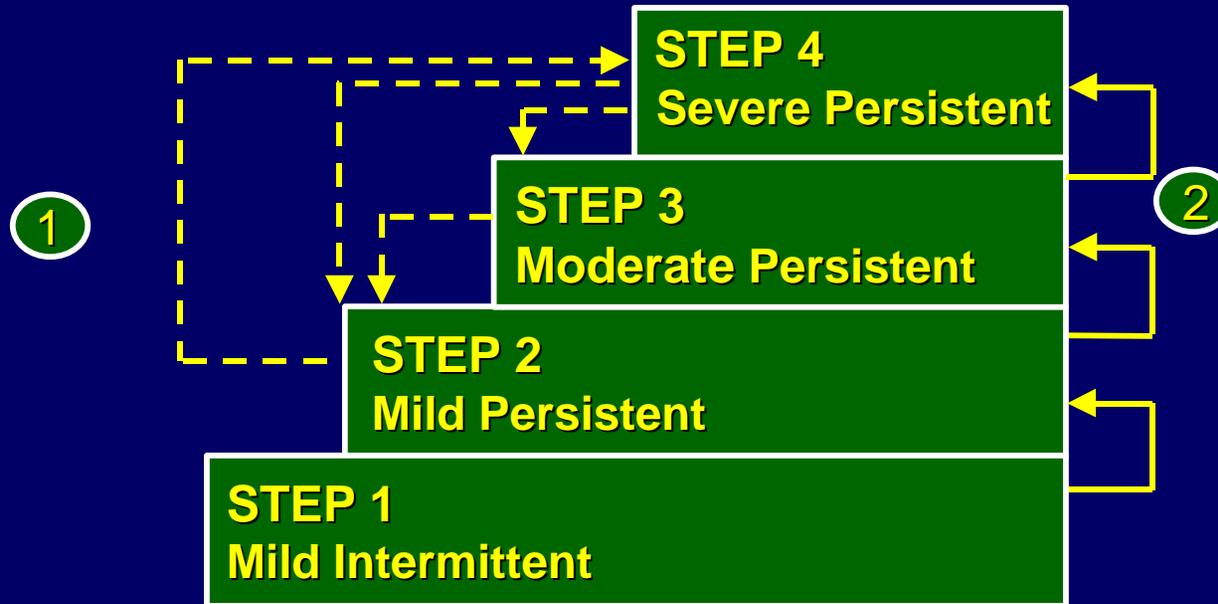
- 5-LO inhibitors
- Cysteinyl leukotriene receptor antagonists

■ Indications

- Long-term-control therapy in mild persistent asthma
 - Improve lung function
 - Prevent need for short-acting beta₂-agonists
 - Prevent exacerbations
- Further experience and research needed



Stepwise Approach to Therapy: Gaining Control



1. Start high and step down.
2. Start at initial level of severity; gradually step up.



Stepwise Approach to Therapy for Adults and Children >Age 5: Maintaining Control

STEP 4
Multiple long-term-control medications, include oral corticosteroids

STEP 3
≥ 1 Long-term-control medications

STEP 2
1 Long-term-control medication: anti-inflammatory

STEP 1
Quick-relief medication: PRN

- ↓ Step down if possible
- ↑ Step up if necessary
- Patient education and environmental control at every step
- Recommend referral to specialist at Step 4; consider referral at Step 3



Indicators of Poor Asthma Control

- Step up therapy if patient:
 - Awakens at night with symptoms
 - Has an urgent care visit
 - Has increased need for short-acting inhaled beta₂-agonists
 - Uses more than one canister of short-acting beta₂-agonist in 1 month



Indicators of Poor Asthma Control (continued)

- Before increasing medications, check:
 - Inhaler technique
 - Adherence to prescribed regimen
 - Environmental changes
 - Also consider alternative diagnoses



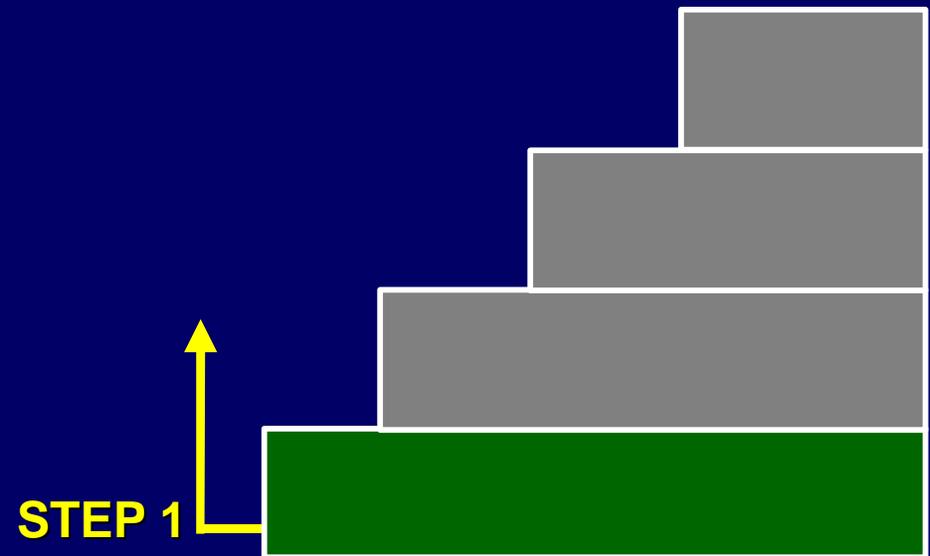
Step 1 Treatment for Adults and Children >5: Mild Intermittent

Daily Long-Term Control

- Not needed

Quick Relief

- Short-acting inhaled beta₂-agonist PRN
- Increasing use, or use more than 2x/week, may indicate need for ↑ long-term-control therapy
- Intensity of treatment depends on severity of exacerbation





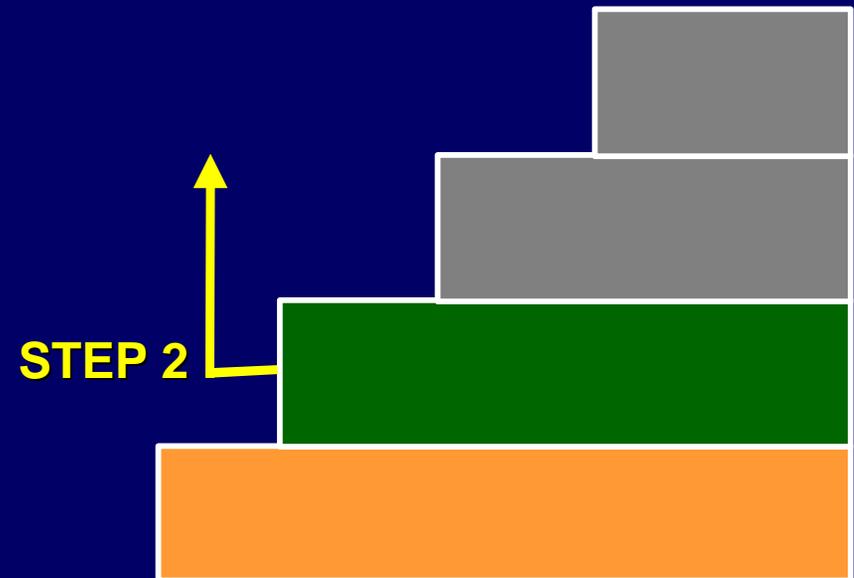
Step 2 Treatment for Adults and Children >5: Mild Persistent

Daily Long-Term Control

- Anti-inflammatory
 - Inhaled corticosteroid (low dose) or
 - Cromolyn or nedocromil

OR

- Sustained-release theophylline (to serum concentration 5-15 mcg/mL) is an alternative but not preferred
- Leukotriene modifier may be considered

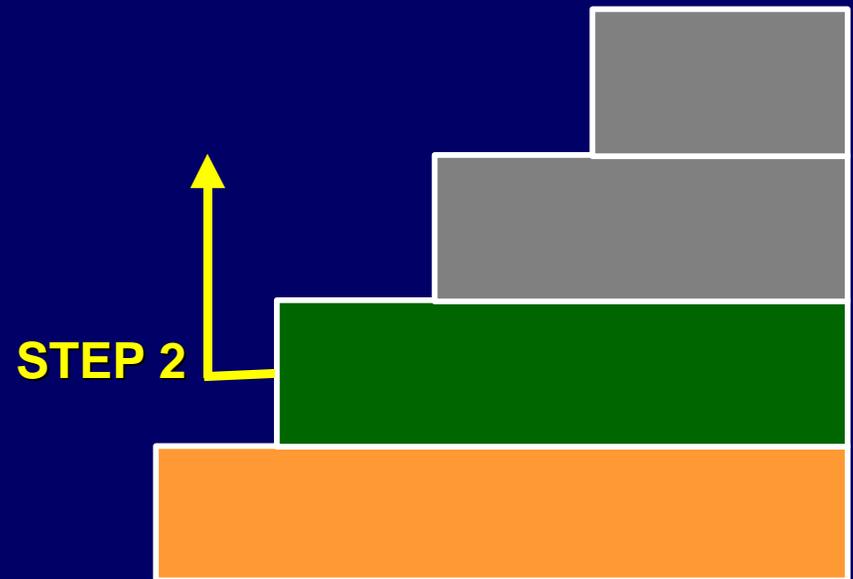




Step 2 Treatment for Adults and Children >5: Mild Persistent (continued)

Quick Relief

- Short-acting inhaled beta₂-agonist PRN
- Daily or increasing use indicates need for ↑ long-term-control therapy
- Intensity of treatment depends on severity of exacerbation





Step 3 Treatment for Adults and Children >5: Moderate Persistent

Daily Long-Term Control

- Inhaled corticosteroid (medium dose)

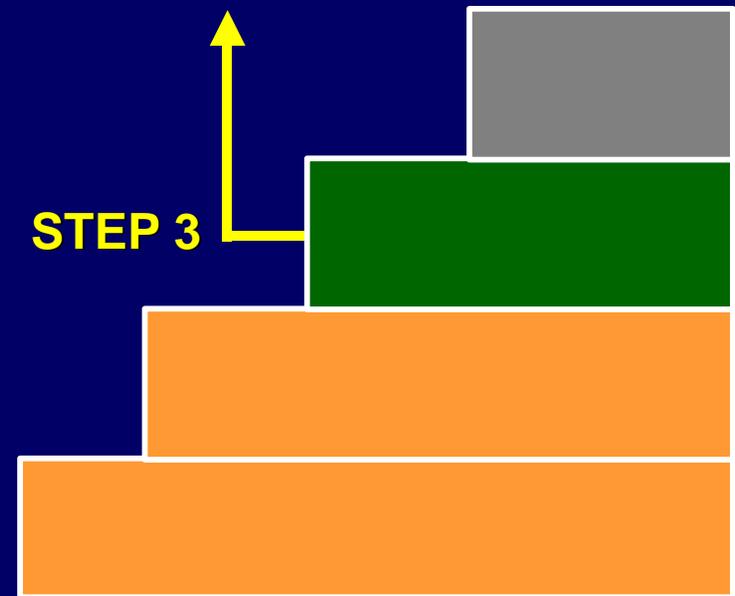
OR

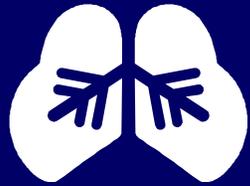
- Inhaled corticosteroid (low-to-medium dose) **AND**
- Long-acting bronchodilator (long-acting beta₂-agonist or sustained-release theophylline)

IF NEEDED, increase to:

- Inhaled corticosteroid (medium-to-high dose) and long-acting bronchodilator

Consider referral to a specialist

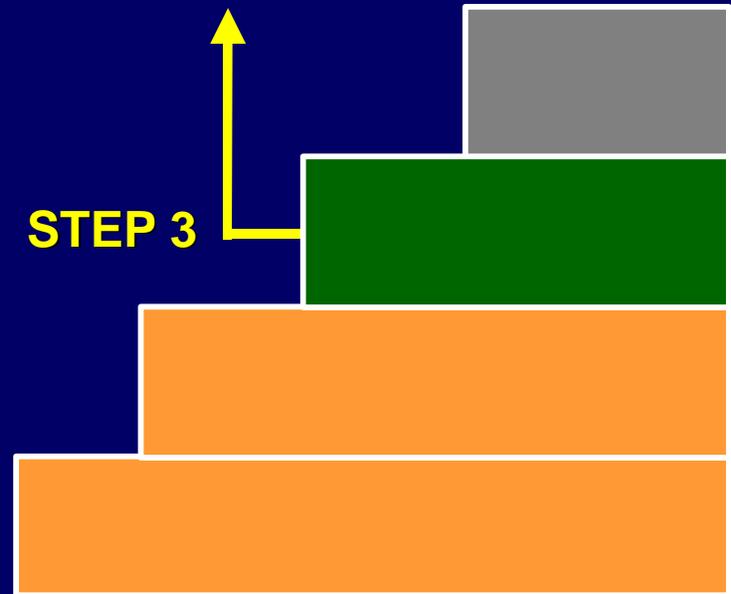


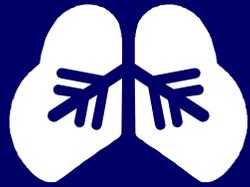


Step 3 Treatment for Adults and Children >5: Moderate Persistent (continued)

Quick Relief

- Short-acting inhaled beta₂-agonist PRN
- Daily or increasing use indicates ↑ need for long-term-control therapy
- Intensity of treatment depends on
- severity of exacerbation



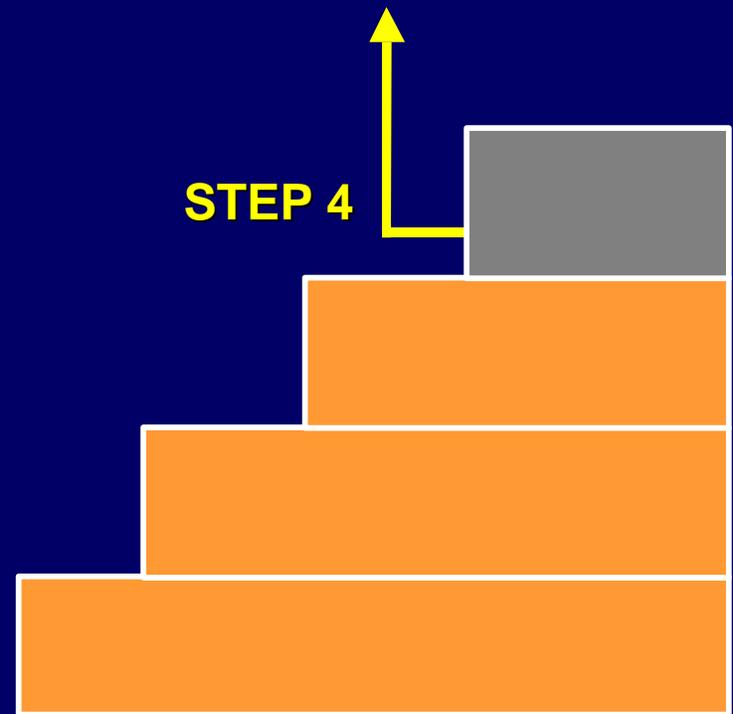


Step 4 Treatment for Adults and Children >5: Severe Persistent

Daily Long-Term Control

- Inhaled corticosteroid (high dose) **AND**
- Long-acting bronchodilator
 - Long-acting inhaled beta₂-agonist **OR**
 - Sustained-release theophylline **OR**
 - Long-acting beta₂-agonist tablets **AND**
- Oral corticosteroid, long term

Recommend referral to a specialist



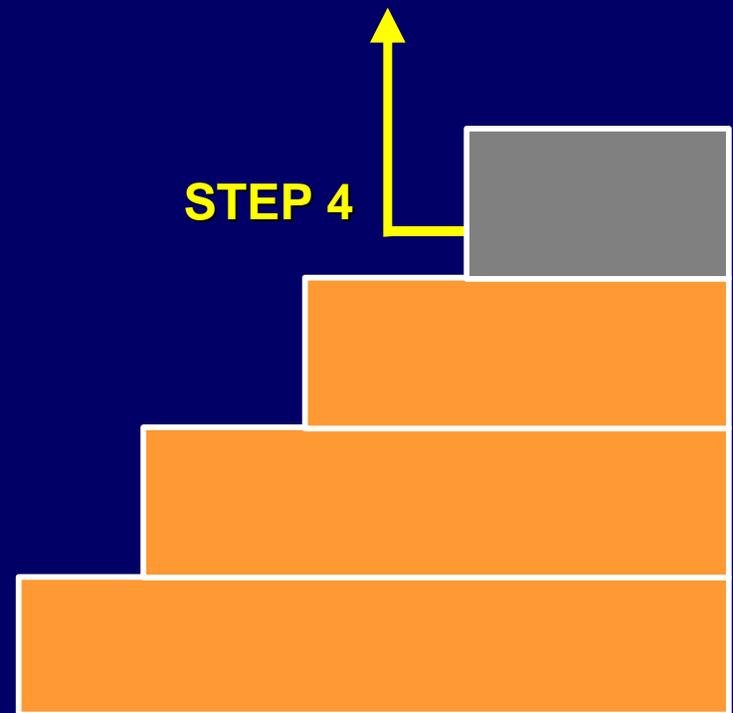


Step 4 Treatment for Adults and Children >5: Severe Persistent

(continued)

Quick Relief

- Short-acting inhaled beta₂-agonist PRN
- Daily or increasing use indicates need for ↑ long-term control therapy
- Intensity of treatment depends on severity of exacerbation





Stepwise Approach to Therapy for Infants and Young Children

STEP 4

Multiple long-term-control medications; include oral corticosteroids

STEP 3

≥ 1 Long-term-control medications

STEP 2

1 Long-term-control medication:
anti-inflammatory

STEP 1

Quick-relief medication: PRN

- ↓ Step down if possible
- ↑ Step up if necessary
- Patient education and environmental control at every step
- Recommend referral to specialist at Steps 3 and 4; consider referral at Step 2.



Step 1 Treatment for Infants and Young Children ≤ 5 : Mild Intermittent

■ Daily Long-Term Control

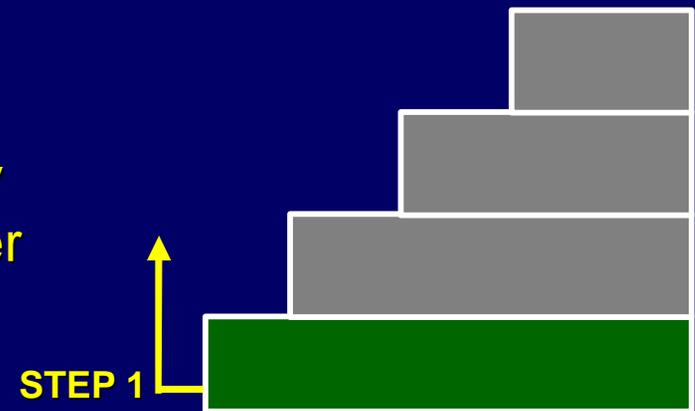
- Not needed

■ Quick Relief

- Bronchodilator PRN. Either:
 - Inhaled short-acting beta₂-agonist by nebulizer or by face mask and spacer

OR

- Oral beta₂-agonist
 - Use more than 2x/week or increasing use may indicate need for ↑ long-term control therapy
 - Intensity of treatment depends on severity of exacerbation





Treatment for Infants and Young Children With Viral Respiratory Infection

- Short-acting inhaled beta₂-agonist q 4 to 6 hours up to 24 hours (longer with physician consult)
- Consider step up if repeated more than once every 6 weeks
- Consider systemic corticosteroid if:
 - Current exacerbation is severe
 - OR**
 - Patient has history of previous severe exacerbations



Step 2 Treatment for Infants and Young Children ≤ 5 : Mild Persistent

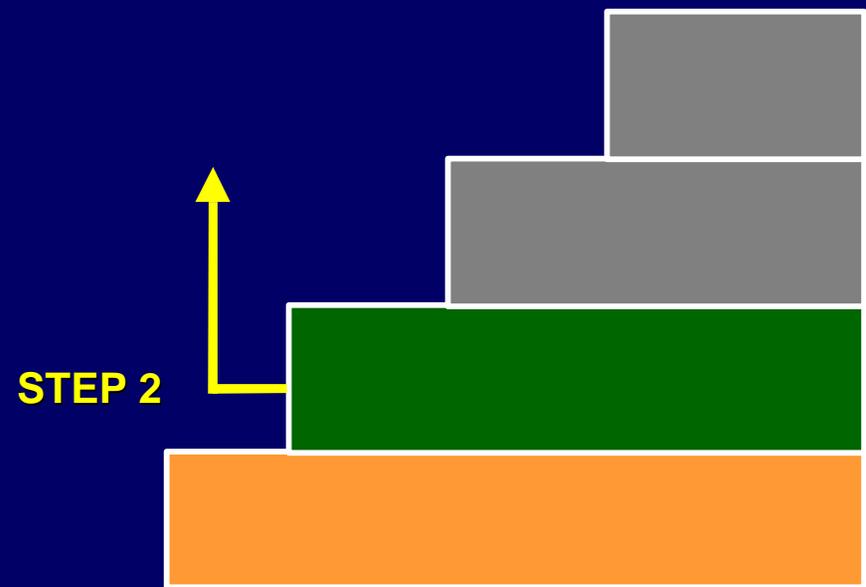
Daily Long-Term Control

- Anti-inflammatory
 - Cromolyn (nebulizer preferred) or nedocromil

OR

- Low-dose inhaled corticosteroid (spacer/face mask)

Consider referral to specialist

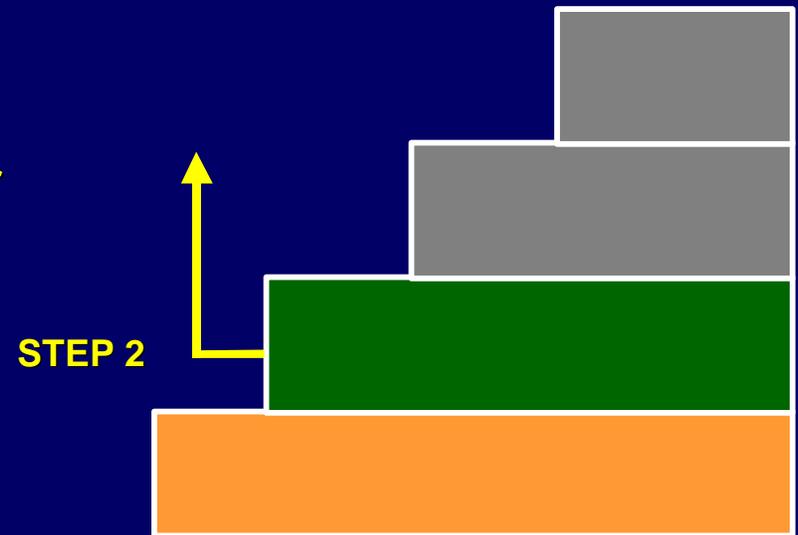




Step 2 Treatment for Infants and Young Children ≤ 5 : Mild Persistent (continued)

Quick Relief

- Brochodilator PRN. Either:
 - Inhaled short-acting beta₂-agonist by nebulizer or face mask and spacer
- OR**
- Oral beta₂-agonist
- Increasing use, daily use, or use >3 or $4x/day$ indicate need for \uparrow long-term-control therapy
- Intensity of treatment depends on severity of exacerbation



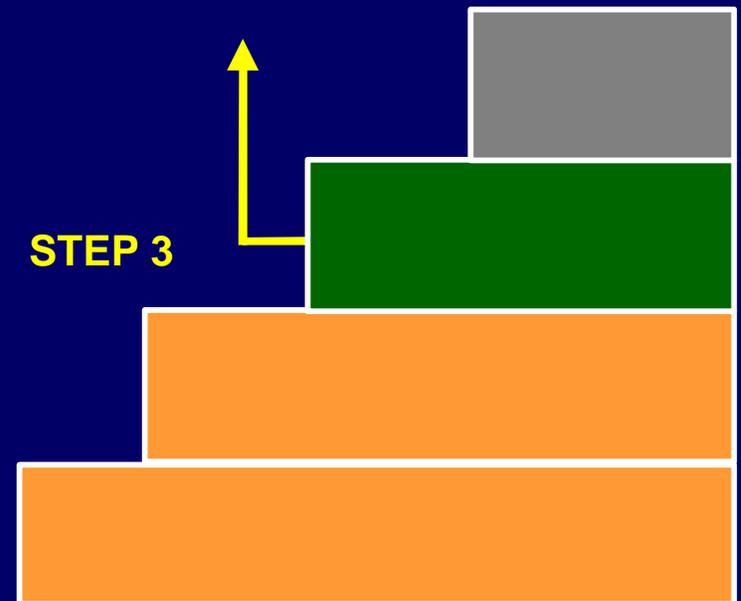


Step 3 Treatment for Infants and Young Children ≤ 5 : Moderate Persistent

Daily Long-Term Control

- Anti-inflammatory
 - Medium-dose inhaled corticosteroid (spacer/face mask)
- Or, once control is established
 - Lower medium-dose inhaled corticosteroid **AND** nedocromil or theophylline

Recommend referral to specialist

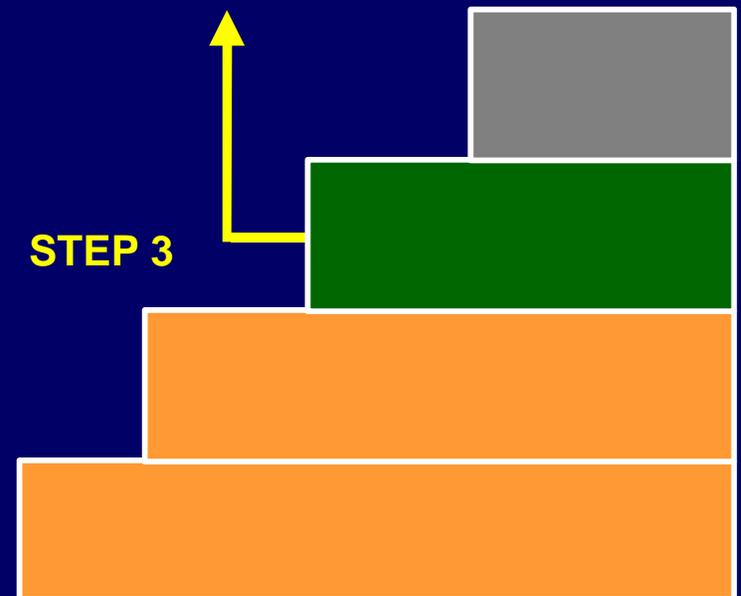




Step 3 Treatment for Infants and Young Children ≤ 5 : Moderate Persistent (continued)

Quick Relief

- Brochodilator PRN. Either:
 - Inhaled short-acting beta₂-agonist by nebulizer or face mask and spacer**OR**
 - Oral beta₂-agonist
- Increasing use, daily use, or use >3 or $4x/day$ indicate need for  long-term-control therapy
- Intensity of treatment depends on severity of exacerbation

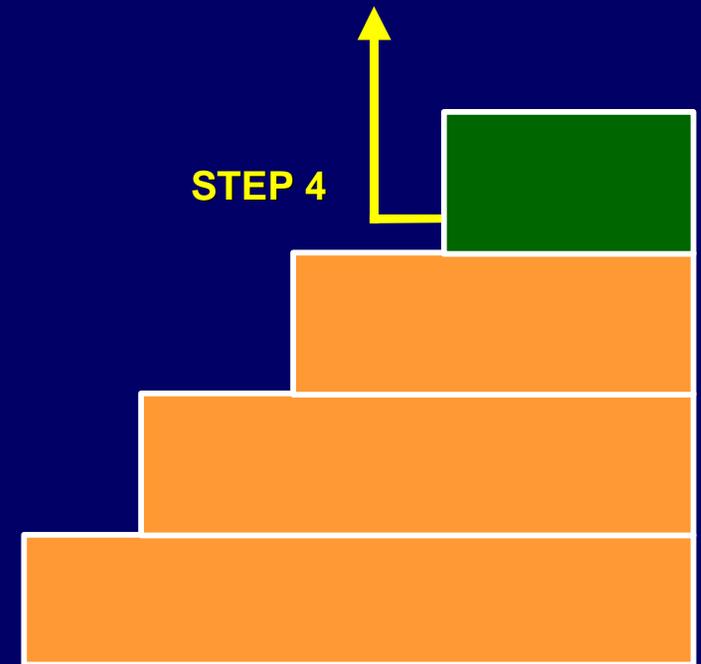




Step 4 Treatment for Infants and Young Children ≤ 5 : Severe Persistent

Daily Long-Term Control

- High-dose inhaled corticosteroid (spacer/face mask)
- If needed, add oral corticosteroid and reduce to lowest daily or alternate-day dose that stabilizes symptoms



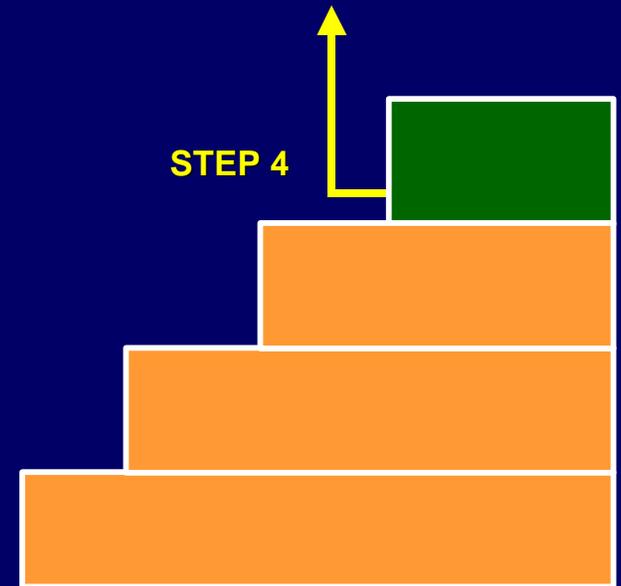


Step 4 Treatment for Infants and Young Children ≤ 5 :

Severe Persistent (continued)

Quick Relief

- Brochodilator PRN. Either:
 - Inhaled short-acting beta₂-agonist by nebulizer or face mask and spacer
- OR**
- Oral beta₂-agonist
- Increasing use, daily use, or use >3 or 4x/day indicate need for \uparrow long-term-control therapy
- Intensity of treatment depends on severity of exacerbation





School-Age Children: Special Considerations

- In addition to following adult management principles:
 - Give special consideration to school and developmental issues
 - Monitor growth in children receiving corticosteroids
 - Consider use of cromolyn or nedocromil first for Step 2 care
 - Encourage active participation in physical activity
 - Provide written asthma management plan for home and school
 - Involve children in developing plan



Older Adults: Special Considerations

- High prevalence of coexisting obstructive lung disease
 - Determine the extent of reversible airflow obstruction
 - Use 2- to 3-week trial of systemic corticosteroids
- Essential to review patient technique in using medications and devices



Older Adults: Special Considerations (continued)

- Asthma medications may have increased adverse effects
 - Bronchodilators
 - Airway response to bronchodilators may change with age
 - Patients with pre-existing ischemic heart disease may experience tremor and tachycardia
 - Concomitant use of anticholinergics and beta₂-agonists may be beneficial



Older Adults: Special Considerations (continued)

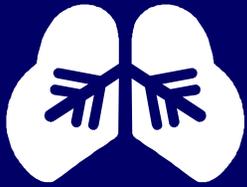
– Theophylline

- Theophylline clearance is reduced, causing increased blood levels
- Age is independent factor for developing life-threatening events from iatrogenic chronic theophylline overdose
- Potential for drug interactions (e.g., with epinephrine, antibiotics, H₂-histamine antagonists)



Older Adults: Special Considerations (continued)

- Systemic corticosteroids can provoke confusion, agitation, changes in glucose metabolism
- Inhaled corticosteroids
 - May be associated with dose-dependent reduction in bone mineral content
 - Treat concurrently with:
 - Calcium supplements and
 - Vitamin D and, when appropriate,
 - Estrogen replacement



Older Adults: Special Considerations (continued)

- Medications for other diseases may exacerbate asthma
 - NSAIDs
 - Nonselective beta-blockers
 - Beta-blockers found in some eye drops



Managing Exercise-Induced Bronchospasm (EIB)

- Anticipate EIB in all patients
- Teachers and coaches need to be notified
- Diagnosis
 - History of cough, shortness of breath, chest pain or tightness, wheezing, or endurance problems during exercise
 - Conduct exercise challenge **OR** have patient undertake task that provoked the symptoms
 - 15% decrease in PEF or FEV₁ is compatible with EIB



Managing Exercise-Induced Bronchospasm (EIB) (continued)

■ Management Strategies

- Short-acting inhaled beta₂-agonists used shortly before exercise last 2 to 3 hours
- Salmeterol may prevent EIB for 10 to 12 hours
- Cromolyn and nedcromil are also acceptable
- A lengthy warmup period before exercise may preclude medications for patients who can tolerate it
- Long-term-control therapy, if appropriate



Managing Seasonal Asthma Symptoms

- Medical history is usually sufficient to determine sensitivity to seasonal allergens.
- Just before allergy season:
 - Start daily anti-inflammatory therapy
- During allergy season:
 - Continue anti-inflammatory therapy
 - Use stepwise approach to control symptoms