

## **EPR3: A Pediatric Asthma Diagnosis and Management Update**

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## **Objectives**

- Define pediatric asthma and describe its personal and public impact.
- Describe the diagnosis of pediatric asthma.
- Understand pediatric asthma management and control.
- Understand effective educational approaches.

## **Definition of Asthma**

**EPR3: Common chronic disorder of the airways that is complex and characterized by variable and recurring symptoms, airflow obstruction and bronchial hyperresponsiveness, and an underlying inflammation. The interaction of these features of asthma determines the clinical manifestations and severity of asthma and the response to treatment.**

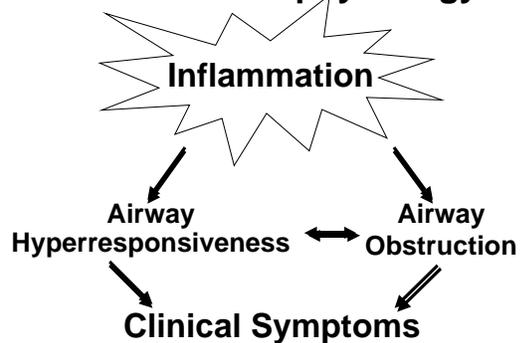
## **Asthma Epidemiology**

- One of the most common chronic diseases of childhood
  - >6 million children, >22 million total
- Increasing prevalence, declining mortality, declining reports of activity limitations
- Atopy, family history strongest predisposing factors

## **Asthma Epidemiology**

- Ongoing disparities: highest morbidity in AA and PR
- >497,000 hospitalizations annually
  - Highest rate in children 0-4 years of age

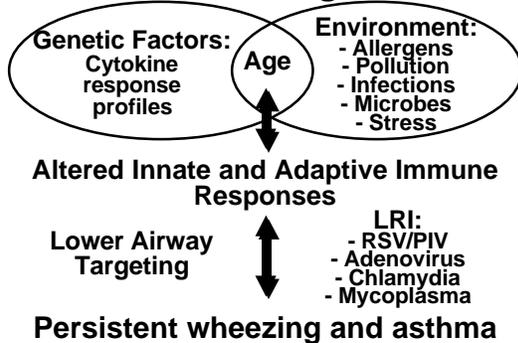
## Asthma Pathophysiology



## Determinants of Airflow Limitation

- Airway hyperresponsiveness
- Bronchoconstriction
- Edema, mucus plugging
- Airway remodeling

## Asthma Pathogenesis



## Asthma: Natural History

- Children: deficits in lung function growth ( $FEV_1$ ) in those with symptoms beginning in first 3 years of life
  - Apparent by age 6, no further loss through adolescence (Tucson and others)
  - Subgroup with progressive loss of lung function ( $\geq 1\%/yr$ ) (CAMP)
  - Reduced  $FEV_1/FVC$  even in mild asthma, that progresses with age (CAMP)

## Asthma: Natural History

- Adults: some studies show progressive decline in  $FEV_1$ , clinical significance uncertain
- No evidence that current treatment alters natural history

## Four Components of Asthma Management

- Assessment and monitoring
- Education for a partnership in care
- Control of environmental factors and comorbid conditions that affect asthma
- Medications

## Assessment and Monitoring

- Closely linked to:
  - Severity: intrinsic intensity, best assessed when not on long-term control Rx
  - Control: degree to which asthma effects are minimized and Rx goals met
  - Responsiveness: ease with which control achieved by Rx

## Assessment and Monitoring

- Severity and control include domains of:
  - Impairment: current/recent sx/impairments
  - Risk: likelihood of flares/decline in lung function/adverse effects from meds

## Assessment and Monitoring: Diagnosis

- Episodic symptoms of airflow obstruction/hyperresponsiveness
- Obstruction at least partially reversible
- Alternative diagnoses excluded

## Assessment and Monitoring: Diagnosis: History: Symptoms

- Cough/worse at night
- Recurrent wheeze
- Recurrent difficulty in breathing
- Recurrent chest tightness

## Assessment and Monitoring: Diagnosis: History: Triggers

- Exercise
- Viral infection
- Furry/feathery animals
- Dust mites
- Mold
- Smoke
- Pollen
- Weather changes
- Emotions (laugh, cry)
- Chemicals/dusts
- Menses

## Assessment and Monitoring: Diagnosis: Physical Examination

- Hyperexpansion of chest
- Wheezing/prolonged exhalation
- Nasal secretion/swelling/polyps
  - If polyp in <10 yo, get sweat test!
- Atopic skin disease
- PE may be normal

### **Assessment and Monitoring: Diagnosis: Spirometry**

- Can't reliably clinically assess degree of obstruction or reversibility
- All MDs who care for asthma should ideally have access to spirometry
- Should be measured before and after bronchodilator
- Effort dependent (can try at age 5-6)
- Dec  $FEV_1$  (12% reversible),  $FEV_1/FVC$
- May take corticosteroid trial to show reversibility

### **Assessment and Monitoring: Diagnosis: Other Tests**

- Lung volumes, inspiratory loops
- Bronchoprovocation
- Chest radiography
- Allergy testing
- Biomarkers of inflammation

### **Assessment and Monitoring: Diagnosis: Differential Diagnosis**

- Extrathoracic airway
  - Rhinitis/sinusitis
- Intrathoracic large airway
  - Foreign body
  - Vocal cord dysfunction
  - Vascular ring/laryngeal web
  - Malacia/stenosis
  - Lymph node/tumor

### **Assessment and Monitoring: Diagnosis: Differential Diagnosis**

- Small airway
  - Viral or obliterative bronchiolitis
  - CF
  - BPD
  - Heart disease/CHF

### **Assessment and Monitoring: Diagnosis: Differential Diagnosis**

- Other
  - Recurrent nonasthmatic cough (habit, drug-induced, etc)
  - Aspiration (GERD or primary)
  - Pulmonary vascular disease (PE, venoocclusive dz, etc)
  - Eosinophilic lung disease

### **Assessment and Monitoring: Diagnosis: Children 0-4 Years**

- Majority who wheeze before age 3 are asymptomatic after age 6 (Tucson)
- Asthma Predictive Index (Tucson)
  - $\geq 4$  episodes wheeze in past year
  - Either one of:
    - Parental asthma hx, MD dx atopic dermatitis, aeroallergen sensitization
  - Or two of:
    - Food sensitization,  $\geq 4\%$  blood eos, wheeze apart from URI
- 76% with asthma after age 6 with + API before 3;  
97% without asthma with – API before 3

## Assessment and Monitoring: Initial Assessment

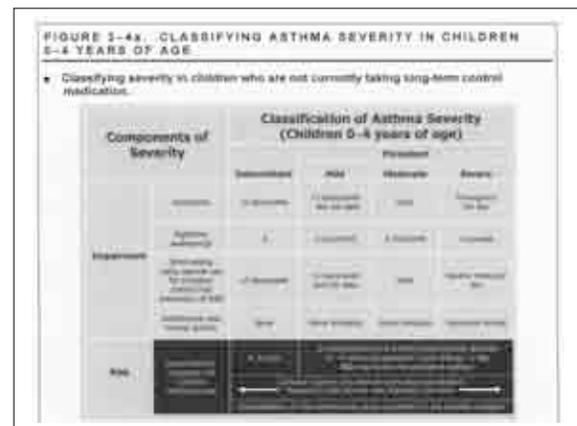
- Precipitating factors
- Comorbid conditions that may aggravate asthma
  - Rhinitis, sinusitis, GERD, OSA, ABPA
- Knowledge and skills for co-management
- Classify severity

## Assessment and Monitoring: Initial Assessment: Classifying Severity

- Impairment
  - Symptoms, QOL
  - Lung function
- Risk
  - Severe exacerbations can occur at any level of severity

## Assessment and Monitoring: Initial Assessment: Classifying Severity

- Predictors:
  - Severe airflow obstruction
  - 2+ ED visits in past year, any intubation/ICU
  - Patients feel in danger/frightened
  - Demographics: female, non-caucasian, non-use of ICS, current smoking
  - Psychosocial: depression, stress, poverty, attitudes/beliefs



## Classifying Asthma Severity in Older Patients

- Grouped in ages 5-11 and  $\geq 12$  years
- Allowance for more nocturnal awakenings
  - INT  $< 2$ /mo; MIP 3-4/mo; MOP  $> 1$ /wk, not nightly; SP often nightly
- Lung function criteria
  - INT and MIP: nl FEV<sub>1</sub> and FEV<sub>1</sub>/FVC ( $> 80\%$  except in 5-11 should be  $> 85\%$  in INT)
  - MOP: FEV<sub>1</sub> 60%-80% pred; FEV<sub>1</sub>/FVC 75%-80% in 5-11, reduced 5% in  $\geq 12$
  - SP: FEV<sub>1</sub>  $< 60\%$  pred; FEV<sub>1</sub>/FVC  $< 75\%$  in 5-11, reduced  $> 5\%$  in  $\geq 12$

## Assessment and Monitoring: Monitoring Control to Meet Therapeutic Goals

- Reduce impairment
  - Prevent chronic/troublesome sx
  - Infrequent need for rescue SABA ( $\leq 2x/wk$ )
  - Maintain (near) “normal” pulmonary function
  - Maintain normal activity levels
  - Meet expectations of pt and family

### Assessment and Monitoring: Monitoring Control to Meet Therapeutic Goals

- Reduce risk
  - Prevent exacerbations/need for ED
  - Prevent reduced lung growth
  - Optimize pharmacotherapy and minimize side effects

### Assessment and Monitoring: Measures of Asthma Control

- Signs and symptoms
  - 2-4 week recall
- Pulmonary function
- Quality of life
- History of exacerbations

### Assessment and Monitoring: Measures of Asthma Control

- Pharmacotherapy adherence/side effects
  - Don't forget inhaler technique!
- Communication/satisfaction
- Biomarkers/genetics (investigational)

### Assessment and Monitoring: What About Peak Flow?

- Symptom monitoring alone may be as effective
- Yardstick: personal best
- Consider for:
  - Moderate/severe persistent asthma
  - History of severe exacerbations
  - Poor perceivers

### Assessment and Monitoring: What About Peak Flow?

- May be helpful to:
  - Detect early changes in disease status
  - Assess responses to changes in therapy
  - Quantify impairment
  - Determine severity of exacerbation

**FIGURE 3-54. ASSESSING ASTHMA CONTROL IN CHILDREN 0-4 YEARS OF AGE**

Components of Control		Classification of Asthma Control (Children 0-4 years of age)		
		Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	≤ 2 days/week	> 2 days/week	Throughout the day
	nighttime awakenings	0/month	1-4/month	> 4/month
	Interference with normal activity	None	Some limitation	Extremely limited
Risk	Exacerbations requiring oral corticosteroids or ED	≤ 2/year	> 2 days/week	Severe exacerbations
	Exacerbations requiring all-oral corticosteroids	0/year	1-2/year	> 2/year

Exacerbations may be defined as any increase in symptoms from usual or very mild/moderate and persistent. The level of severity should correspond to specific levels of control but should be considered in the overall assessment of risk.

## Assessing Asthma Control in Older Patients

- Nocturnal awakenings
  - In 5-11, NWC  $\geq 2$ /mo, VPC  $\geq 2$ /wk
  - In  $\geq 12$ , NWC 1-3/wk, VPC  $\geq 4$ /wk
- Lung function
  - FEV<sub>1</sub> or PEF: WC >80%, NWC 60-80%, VPC <60%; FEV<sub>1</sub>/FVC criteria in 5-11
- Exacerbations needing systemic steroids
  - WC 0-1/yr, NWC/VPC  $\geq 2$ /yr, consider severity
- ACT: WC  $\geq 20$ , NWC 16-19, VPC  $\leq 15$

The image shows a portion of the Asthma Control Test (ACT) form. It includes a title 'Asthma Control Test (ACT)' and a brief introduction. The main part of the form is a grid of 25 questions, each with five response options (A, B, C, D, E) corresponding to different levels of control. The questions cover various aspects of asthma control, such as waking up at night, using rescue inhalers, and needing oral steroids. The form is designed to be filled out by a patient or a caregiver.

## Education for Partnership in Care

- Repetition, reinforcement, all team members, all care points
- Open communication, preferences, barriers (affordability!), shared decision making

## Education for Partnership in Care

- Topics
  - Basic facts, role of meds, inhaler technique, monitoring, adherence, trigger avoidance
  - Patient's control vs. optimal control
  - Management of flare-ups
- Written action plan
  - New JCAHO requirement for hospital d/c

The image shows a 'My Asthma Action Plan' form. It includes a title 'My Asthma Action Plan' and a diagram of a person using an inhaler. The form is designed to be filled out by a patient or a caregiver. It includes sections for 'Green Zone', 'Yellow Zone', and 'Red Zone', each with specific instructions on what to do when symptoms worsen. The form also includes a section for 'Allergies' and 'Triggers'.

## Control of Environmental Factors

- Allergy testing/avoidance of allergen exposure
- Avoid irritants (smoke, strong smells, air pollution)
- Avoid nonselective beta blockers, sulfites
- Inactivated flu vaccine, hygiene
- ASA/NSAID
- Consider immunotherapy by allergist

### **Medications: Long-Term Control**

- Inhaled corticosteroids
  - Systemic corticosteroids in severe persistent disease
- Cromolyn/nedocromil
- Immunomodulators (omalizumab)
- Leukotriene modifiers
- LABAs (long-acting  $\beta$  agonists)
- Methylxanthines

### **Medications: Quick Relief**

- Anticholinergics
- SABAs (short-acting  $\beta$  agonists)
- Systemic corticosteroids

### **Medications: Inhaled Corticosteroids**

- Most potent and consistently effective long-term control medication for asthma
- Anti-inflammatory: suppress cytokine generation, eosinophil recruitment and release of inflammatory mediators

### **Medications: Inhaled Corticosteroids**

- Clinical effects:
  - Fewer symptoms, better asthma control/QOL
  - Better PEF/spirometry, less hyperresponsiveness
  - Less use of PO steroids
  - Fewer flares/ED/hospitalizations/deaths

### **Medications: Inhaled Steroids**

- Low dose generally effective in mild-moderate persistent disease, severe patients need higher doses, responsiveness less in smokers
- Dose may be adjusted over time as disease control varies
  - Severity may be inferred by lowest dose it takes to maintain control

### **Medications: Inhaled Steroids: Safety**

- Generally well tolerated, safe, small risk balanced by huge benefit
- Local effects:
  - Thrush, dysphonia, reflex cough/wheeze
- Systemic effects (low risk, generally high dose):
  - Linear growth, osteopenia, dermal thinning, cataracts, glaucoma (if fam hx), HPA axis dysfct, insulin resistance

### **Medications: Inhaled Steroids: Safety**

- Monitor growth velocity, DEXA (adults), eye evaluation
- Spacers, rinsing, lowest effective dose, avoid triggers, adherence/technique, adjunctive Rx

### **Medications: Oral Steroids**

- Used for flares; as long-term med reserved for most severe cases
- Adverse effects:
  - Adrenal suppression
  - Growth suppression
  - Dermal thinning
  - Hypertension

### **Medications: Oral Steroids**

- Adverse effects:
  - Cushing's syndrome
  - Cataracts
  - Muscle weakness
  - Diabetes
  - Immune suppression (reactivated TB, disseminated varicella, other infection)

### **Medications: Cromolyn/Nedocromil**

- Chloride channel blockade, inhibit mast cell mediator release and eosinophil recruitment
- Alternative, not preferred, controller for mild persistent asthma, also preventive Rx pre-exercise and pre-allergen exposure

### **Medications: Cromolyn/Nedocromil**

- QID administration (nedocromil can be done BID)
- CAMP: nedocromil less effective than budesonide in improving outcomes measures

### **Medications: Immunomodulators: Omalizumab**

- Anti-IgE; prevents binding of IgE to high affinity receptor on mast cells and basophils (FcεRI)
- Decreased allergic inflammation
- Small improvement in lung function, decreased flares/ED, modest steroid sparing, improved QOL

### **Medications: Immunomodulators: Omalizumab**

- Expensive, anaphylaxis risk. Approved in age 12+
  - Epi-pen
- Other immunomodulators (IVIg, MTX, etc) of unproven efficacy

### **Medications: Leukotriene Modifiers**

- LTs released from mast cells, eos and basophils, contract smooth muscle, increase vascular permeability, mucus secretagogue, inflammatory cell chemotaxis
- Zileuton: 5-lipoxygenase inhibitor
- Montelukast, zafirlukast: block effects of CYSLT1 receptor, approved in children

### **Medications: Leukotriene Modifiers**

- Modest improvement in lung function, other asthma control outcomes, attenuate EIB, may be helpful in those with ICS insensitivity, role in rhinitis
- Alternate, less preferred controller for mild persistent asthma; alternate, less preferred adjunctive therapy

### **Medications: LABAs**

- Stimulation of  $\beta_2$  receptors, relaxation of smooth muscle
- Duration of 12 hr
  - EIB effect attenuates over time
- Preferred adjunctive in  $\geq 12$  years of age
- Salmeterol, formoterol
- Not anti-inflammatory, not for monotherapy

### **Medications: LABAs**

- Not for quick relief in exacerbations
  - Studies underway with formoterol
- Black box warning: increased asthma deaths in salmeterol (1/1000 vs 1/4400), severe exacerbations in formoterol
  - Give equal weight to option to increase ICS dose

### **Medications: Methylxanthines**

- Theophylline: phosphodiesterase inhibitor, possibly mildly anti-inflammatory
- Adjunctive therapy to ICS, (alternative step 2 controller in age 5+) not preferred
- Narrow therapeutic/toxic ratio (HA, tachycardia, N/V, seizures)
- Monitor levels



### Medications: Quick Relief

- Anticholinergics
  - Ipratropium in ED management of flares
- SABA
  - Albuterol, levalbuterol, pirbuterol
  - Before exercise and PRN, drug of choice for quick relief
  - Daily scheduled use not recommended
    - Risk of worse asthma with drug use and Arg/Arg 16 β receptor?
- Systemic steroids
  - >3 courses per year should prompt reevaluation of asthma management plan

### Medications: Administration of Inhaled Medicines

- Non-CFC propellants
- Breath actuated vs. pressurized MDI
- Dry powder vs. aerosol droplet
- Valved holding chambers/spacers
  - Use with pressurized MDIs
  - VHC prevent exhalation into device
  - Expensive, insurance may limit or just not pay!

### Long-term Management: General Considerations

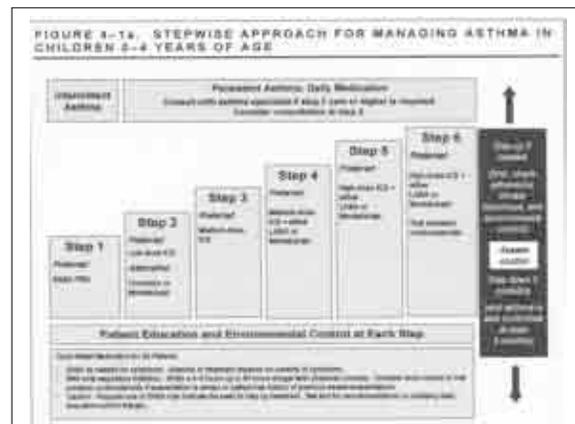
- Maintain focus on meeting goals for asthma control
- Stepwise approach to gain and maintain control
  - Type, amount and frequency determined by severity (initiation) and control (adjustment)
  - Step-down therapy to identify minimum necessary Rx to maintain control

### Long-Term Management: General Considerations

- Monitoring and follow-up are essential
  - Initially every 2-6 weeks
  - Then at 1-6 month intervals, depending on level of control

### Long-Term Management: General Considerations

- Most effective Rx is daily anti-inflammatory medication
- Partnership, education
- Avoidance of allergens, irritants, comorbid conditions
- Written action plans for home and school



## Stepwise Approach for Managing Asthma in Older Patients

- Step 2: 5-11 and  $\geq 12$ , alternatives include cromolyn, LTRA, nedocromil, theophylline
- Step 3:
  - Preferred: low-dose ICS plus LABA, LTRA or theophylline; or medium-dose ICS (in  $\geq 12$ , combo of low-dose ICS plus LTRA, theo or zileuton is less preferred alternative)
- Step 4:
  - Preferred: med-dose ICS plus LABA
  - Alternative: med-dose ICS plus LTRA or theo (or zileuton in  $\geq 12$ )

## Stepwise Approach for Managing Asthma in Older Patients

- Step 5:
  - Preferred: high-dose ICS plus LABA; consider omalizumab in allergic pts  $\geq 12$
  - Alternative: high-dose ICS plus LTRA or theo (alternatives listed for 5-11 only)
- Step 6:
  - Preferred: high-dose ICS plus LABA plus oral steroid; consider omalizumab in  $\geq 12$
  - Alternative: high dose ICS plus oral steroid plus LTRA or theo (listed for 5-11 only)

**FIGURE 4-2a. CLASSIFYING ASTHMA SEVERITY AND INITIATING TREATMENT IN CHILDREN 5-4 YEARS OF AGE**

Assessing severity and initiating therapy in children who are not currently using long-term control medications

Components of Severity	Classification of Asthma Severity (0-4 years of age)			
	Intermittent	Mild	Moderate	Severe
Frequency	≤ 2 episodes	3-4 episodes	≥ 4 episodes	≥ 6 episodes
Daytime symptoms	≤ 2 days	3-4 days	≥ 4 days	≥ 6 days
Nighttime symptoms	≤ 2 nights	3-4 nights	≥ 4 nights	≥ 6 nights
Exacerbations	≤ 2 episodes	3-4 episodes	≥ 4 episodes	≥ 6 episodes
Exacerbation severity	None	Mild	Moderate	Severe
Peak	≤ 200	200-300	300-500	≥ 500

**Recommended Stepwise Initiating Therapy**

Step 1: Intermittent therapy (SABA as needed)

Step 2: Low-dose ICS (or cromolyn, LTRA, nedocromil, or theophylline)

Step 3: Low-dose ICS plus LABA, LTRA, or theophylline; or medium-dose ICS (in  $\geq 12$ , combination of low-dose ICS plus LTRA, theo, or zileuton)

Step 4: Medium-dose ICS plus LABA

Step 5: High-dose ICS plus LABA; consider omalizumab in allergic pts  $\geq 12$

Step 6: High-dose ICS plus LABA plus oral steroid; consider omalizumab in  $\geq 12$

Class Source: G. L. et al. *Medical Management of Asthma*, 2011

## Initiating Treatment in Older Children

- 5-11:
  - MOP: step 3, medium dose ICS option, consider short course OCS
  - SP: step 3, medium dose ICS option or step 4, consider short course OCS
- $\geq 12$ :
  - MOP: step 3, consider short course OCS
  - SP: step 4 or 5, consider short course OCS

**FIGURE 4-2b. ASSESSING ASTHMA CONTROL AND ADJUSTING THERAPY IN CHILDREN 5-4 YEARS OF AGE**

Components of Control	Classification of Asthma Control (0-4 years of age)		
	Well Controlled	Not Well Controlled	Very Poorly Controlled
Frequency	≤ 2 episodes	3-4 episodes	≥ 6 episodes
Daytime symptoms	≤ 2 days	3-4 days	≥ 6 days
Nighttime symptoms	≤ 2 nights	3-4 nights	≥ 6 nights
Exacerbations	≤ 2 episodes	3-4 episodes	≥ 6 episodes
Exacerbation severity	None	Mild	Severe
Peak	≤ 200	200-300	≥ 500

**Recommended Action for Treatment**

Well Controlled: Continue current therapy

Not Well Controlled: Step up therapy (e.g., increase ICS dose, add LABA, LTRA, or theophylline)

Very Poorly Controlled: Step up therapy (e.g., increase ICS dose, add LABA, LTRA, or theophylline, consider oral steroid)

Class Source: G. L. et al. *Medical Management of Asthma*, 2011

## Long-Term Management: Special Situations: EIB

- Exercise is only trigger for some, but need to be sure there are no sx or reductions in lung function apart from exercise
- Cough, SOB, chest pain/tightness, wheeze, endurance problems during exercise
- Long-term control Rx reduces EIB

### **Long-Term Management: Special Situations: EIB**

- Pre Rx with SABA, LABA (LABA may mask poorly controlled persistent asthma)
- LTRA effective in up to 50%
- Cromones less effective than SABA
- Warm up period before exercise may attenuate EIB
- Mask/scarf over mouth (rapid cooling occurs)

### **Referral to Specialist**

- History of life-threatening exacerbation
- Unresponsive to therapy, not meeting goals
- Atypical signs/symptoms, diagnostic uncertainty
- Complicating conditions (ex: ABPA, VCD, etc.)
- Additional testing needed

### **Referral to Specialist**

- Additional education/guidance needed
- Immunotherapy
- Requires step 4 or higher (step 3 in age 0-4 years)
  - Consider if requires step 3 care (step 2 in age 0-4 years)
- 2+ steroid bursts or one hospitalization in a year