

# Childhood asthma and pre-school wheeze

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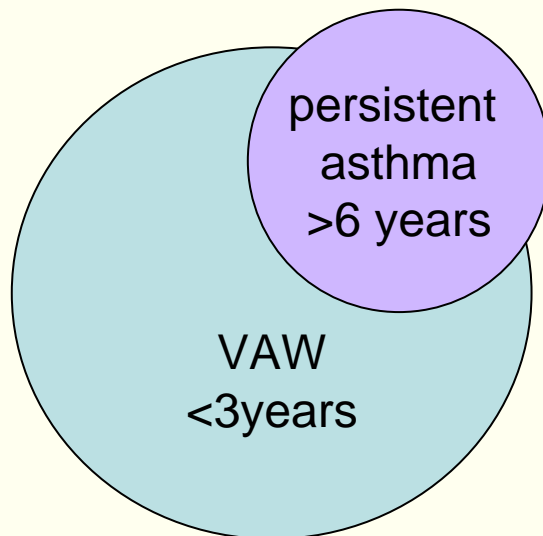
# Definitions

- What is asthma?
- What is viral associated wheeze?
- What is cough-variant asthma?



# Wheeze – is it asthma?

- Episodes of bronchospasm reversed by beta-2 agonist
- >95% of exacerbations of asthma are associated with viral RTI



Doctor diagnosis of asthma can affect employment

- Army
- Police
- Aviation



# Definitions

- The ERS Task Force 2008 proposes to use the terms episodic (viral) wheeze to describe children who wheeze intermittently and are well between episodes, and multiple-trigger wheeze for children who wheeze both during and outside discrete episodes



# Definitions – asthma phenotypes

- Frequency of wheeze
- Severity of wheeze
- Precipitants for wheeze



# Risk factors for persistent wheeze

- Exercise induced wheeze
- Presence of other atopic disorder
- [family history of asthma (esp maternal)]

Frank et al Br Med J 2008



# Diagnosis of pre-school wheeze

- Discrete episodes of wheeze, usually associated with coryza
- Best practice is to see the child during an episode
- Productive sounding coughs without wheeze are not likely to be 'asthma'



# Management of pre-school wheeze

- Options
  - Salbutamol
  - Inhaled steroids
  - Montelukast
  - Oral steroids



# Management of pre-school wheeze

- Options
  - **Salbutamol**
  - Inhaled steroids
  - Montelukast
  - Oral steroids



# Pre-school VAW

- Continuous inhaled corticosteroids do not work
  - Study of 40 children 1-6 years, double blind placebo controlled study of 400mic/day budesonide for 4 months.
    - No difference in symptom score or episode number
  - Study of 60 children 2-5 years, randomized to 6 weeks of fluticasone 200mic/day or placebo.
    - 45 had negative skin prick tests and in this group there was no improvement in airways resistance or BHR
    - 15 had at least one positive SPT, and in this group there was a small beneficial effect of treatment on lung function

Wilson et al Arch Dis Child 1995

Pao et al Am J Respir Crit Care Med 2002



# Preschool VAW

- Intermittent courses of oral prednisolone are not effective
  - 240 pre-school children admitted for VAW. Randomised to pred or placebo 20mg for 5 days for next episode.
  - 65% had a further episode and received treatment
  - No diff in symptom scores
  - No diff in hosp admissions (although there were <5 events).

Oommen et al Lancet 2003



# Pre-school wheeze

- Oral steroids for children admitted to hospital are not effective
  - 700 preschool children admitted for VAW randomised to pred (10 or 20mg for 5 days) or placebo.
  - No difference in length of hosp stay
  - No difference in re-admission rate or length of symptoms.

Panickar et al N Engl J Med 2009



# Pre-school VAW

- Intermittent high dose steroids may be effective
  - 120 pre-school children, 750mcg bd fluticasone at first sign of cold and until clear of symptoms for 48hrs, over 40 weeks.
  - 50% reduction in pred courses (60 to 40% of children) and fewer symptoms
  - no change in acute care visits or hospitalisation.
  - average of 8 courses (ie about 80 days out of 280)
  - **significant negative effect on growth.**

Ducharme et al N Engl J Med 2009



# Pre-school wheeze

- Intermittent montelukast might be helpful
  - 220 children 2-14 years parent initiated montelukast at first sign of URTI and for a minimum of 7 days or until symptoms resolved for 48 hours, over 12 months.
  - 60% reduction in number of acute-care visits and 40% reduction in time of school or child care.

Robertson et al Am J Respir Crit Care Med 2007



# Preschool VAW

- Intermittent montelukast might be helpful
  - 238 pre-school children with VAW randomised to montelukast, neb budesonide (1mg bd) or placebo at first sign of URTI for 7 days, over 12 months.
  - No difference in episode free days or oral corticosteroid use.
  - During RTIs budesonide and montelukast both reduced symptoms (difficulty breathing and effects on activity levels) by 40% c/w placebo

Bacharier et al J Allergy Clin Immunol 2008



# Conclusions?

- Evidence base for any intervention is weak
- Need to carry out n=1 trials of treatment
- Avoid over-treating
- Accept that some children will have symptoms we can't easily control



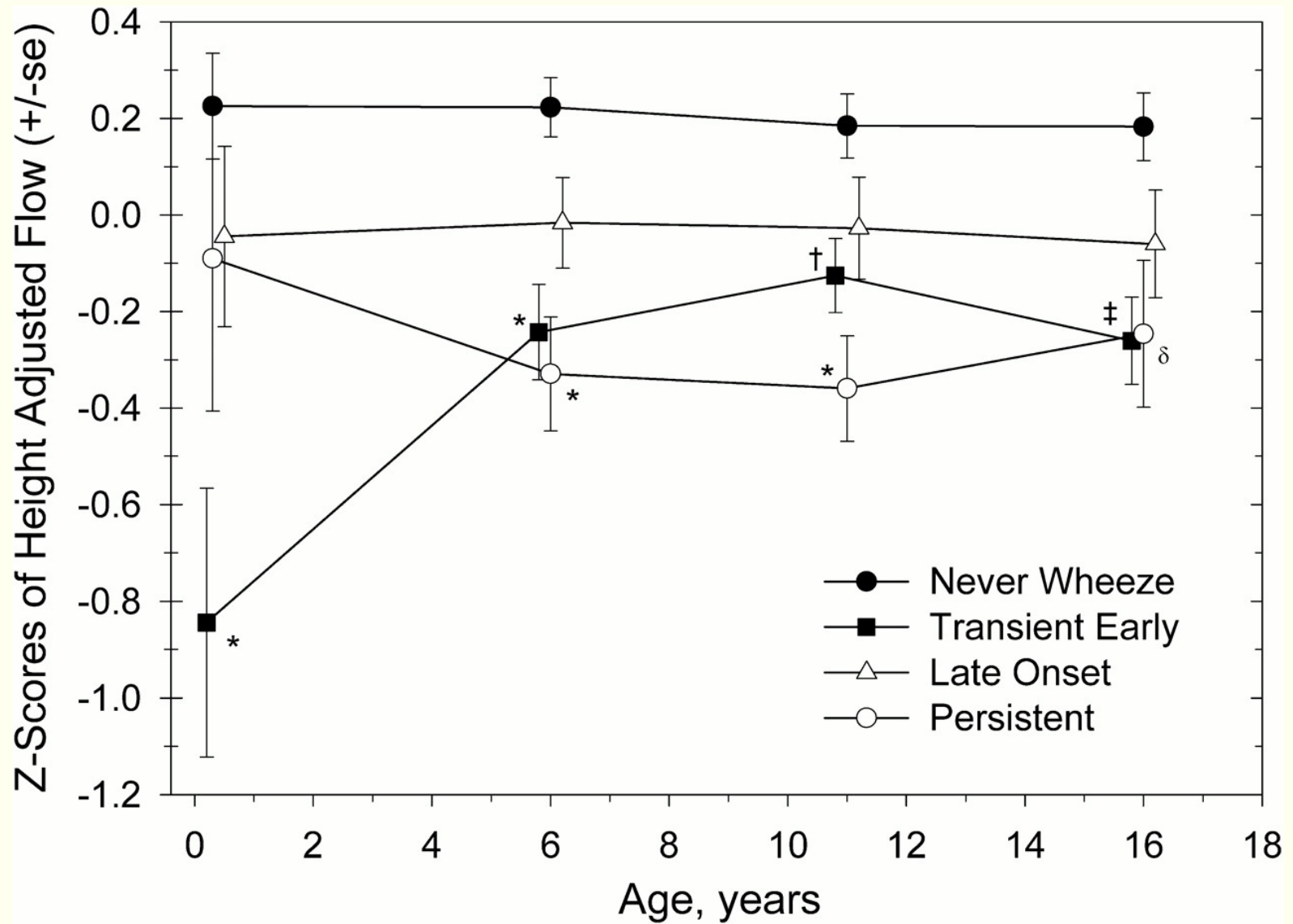
# Management is symptomatic

- No disease modifying effect of maintenance inhaled steroids (but no such studies on montelukast)
  - 2-3 year olds at high risk for asthma randomised to FP 88bd or placebo for 2 years. Improved control for the 2 years, but no difference in a 3<sup>rd</sup> treatment free year on symptoms or lung function
  - 200 children randomised to FP 100mcg bd or placebo after 2 episodes of wheeze or one prolonged episode (>4 weeks) for 5 years. Open label FP given if poor control. At 5 years no effect of FP on current wheeze, use of medication, lung function or BHR
  - 294 infants of asthmatic mothers randomised to budesonide or placebo given via MDI and spacer for 2 weeks for each episode of wheeze. Evaluated after 3 years. No difference in those with current wheeze or number of symptom free days

Guilbert et al NEJM 2006, Murray et al Lancet 2006  
Bisgaard et al NEJM 2008

Oxford Children's Hospital





# Pattern of wheeze - phenotypes

- Possible evidence that persistent wheeze does affect airways in a permanent way
- Possible that an intervention may prevent this, but this intervention is probably not steroids



# Childhood asthma



# Childhood asthma

- Symptoms usually intermittent
- Diagnosis is largely based on history
- Trial of treatment or return when symptomatic
- Examination – presence of wheeze, hyperinflation, other chest signs not c/w asthma (clubbing, crackles), growth, eczema
- Lung function tests
- Bronchial challenge tests
  - Direct (eg histamine, methacholine)
  - Indirect (eg exercise, adenosine)



# Childhood asthma

- Control:
  - Night time symptoms
  - Day time symptoms – cough, wheeze, breathlessness
  - Exercise limitation
  - School attendance
- Precipitants
  - Animals
  - Cigarette smoke exposure
  - Grass/pollen/seasonality
  - Bedroom environment
  - Association with other atopic disorder
  - Association with other allergy
- Medication
  - What, how often, how much, how delivered, compliance



# Childhood asthma

- Poor control suggests
  - Wrong diagnosis
  - Not adherent to prescribed therapy
  - Poor inhaler technique
  - Continued allergen exposure
  - Severe disease (probably least likely)



# Childhood asthma

- Written asthma management plans
- Peak flow monitoring



# Children age 5-12 yrs

Patients should start treatment at the step most appropriate to the initial severity of their asthma. Check concordance and reconsider diagnosis if response to treatment is unexpectedly poor.

MOVE DOWN TO FIND AND MAINTAIN LOWEST CONTROLLING STEP

MOVE UP TO IMPROVE CONTROL AS NEEDED

Inhaled short-acting  $\beta_2$  agonist as required

## STEP 1

Mild intermittent asthma

Add inhaled steroid 200-400 mcg/day\* (other preventer drug if inhaled steroid cannot be used) 200 mcg is an appropriate starting dose for many patients

Start at dose of inhaled steroid appropriate to severity of disease.

## STEP 2

Regular preventer therapy

1. Add inhaled long-acting  $\beta_2$  agonist (LABA)
2. Assess control of asthma:
  - good response to LABA  
- continue LABA
  - benefit from LABA but control still inadequate  
- continue LABA and increase inhaled steroid dose to 400 mcg/day\* (if not already on this dose)
  - no response to LABA  
- stop LABA and increase inhaled steroid to 400 mcg/day.\*If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline

## STEP 3

Initial add-on therapy

Increase inhaled steroid up to 800 mcg/day\*

## STEP 4

Persistent poor control

Use daily steroid tablet in lowest dose providing adequate control

Maintain high dose inhaled steroid at 800 mcg/day\*

Refer to respiratory paediatrician

## STEP 5

Continuous or frequent use of oral steroids

\* BDP or equivalent

SYMPTOMS

vs

TREATMENT

# Children Less than 5 yrs

Patients should start treatment at the step most appropriate to the initial severity of their asthma. Check concordance and reconsider diagnosis if response to treatment is unexpectedly poor.

MOVE UP TO IMPROVE CONTROL AS NEEDED

MOVE DOWN TO FIND AND MAINTAIN LOWEST CONTROLLING STEP

Inhaled short-acting  $\beta_2$  agonist as required

**STEP 1**

Mild intermittent asthma

Add inhaled steroid 200-400 mcg/day\*† or leukotriene receptor antagonist if inhaled steroid cannot be used.

Start at dose of inhaled steroid appropriate to severity of disease.

**STEP 2**

Regular preventer therapy

In those children taking inhaled steroids 200-400 mcg/day consider addition of leukotriene receptor antagonist.

In those children taking a leukotriene receptor antagonist alone reconsider addition of an inhaled steroid 200-400 mcg/day.

In children under 2 years consider proceeding to step 4.

**STEP 3**

Initial add-on therapy

Refer to respiratory paediatrician.

**STEP 4**

Persistent poor control

\* BDP or equivalent

† Higher nominal doses may be required if drug delivery is difficult

SYMPTOMS

vs

TREATMENT

# Childhood asthma

- Start with beta agonist
- If intermittent viral wheeze only, try montelukast
- If frequent symptoms used inhaled steroid
- If poor control despite inhaled steroid, check technique, and consider increasing dose, or adding LABA or montelukast
- Troublesome nights – LABA may help, as may theophylline



# Cough-variant asthma



# Cough variant asthma

- “The recognised under-diagnosis of asthma led to the importance of cough as a symptom being stressed. However, there is increasing evidence that children are inappropriately treated for asthma based on cough as the sole symptom”
- BTS guideline March 2008



# Cough variant asthma

- BUT.....
  - However, as it can be difficult to rule out asthma as a cause of coughing in young children, a trial of anti-asthma therapy (typically inhaled corticosteroids) may be used. In such a trial the treatment should be effectively delivered in adequate doses with clearcut outcomes recorded.
  - A definite period of time should be set (eg, 8–12 weeks), after which the trial of anti-asthma medication should be stopped. If the child has responded to anti-asthma therapy and the treatment has subsequently been stopped, cough variant asthma is suggested by an early relapse that again responds to treatment. If there is no response, the treatment should be stopped as asthma is unlikely and the cough is unresponsive to asthma medication. This is important so that children with simple recurrent viral bronchitis or postviral cough do not end up on long-term high doses of inhaled corticosteroid.
- BTS guideline March 2008



# Inhalers

- CFC-free inhalers
  - Inhaled steroids
    - QVAR (double potency of becotide)
    - Clenil Modulite (equivalent to becotide)
    - Flixotide (double potency of becotide)
    - Ciclesonide (Alvesco) (>12 year olds – double potency of becotide, fewer SE than flixotide)
  - Salmeterol is CFC-free
  - Salbutamol non proprietary is CFC-free



# Wheeze - devices

- Spacers – mask or mouthpiece
- Dry powder inhalers



# Treatment tips

- Do check inhaler technique
- Do ask about compliance in a non-confrontational way
- Do think about precipitants and allergen avoidance
- Do not use LABAs without inhaled steroid
- Montelukast can be used as primary prevention; especially helpful for viral-associated wheeze, exercise induced wheeze and wheeze with associated allergic rhinitis



# Who to refer

- Troublesome symptoms poorly responsive to treatment
- Need for high dose ( $\geq 800$  mcg/day) steroids (with continuing symptoms)
- Atypical symptoms – poor growth, productive cough



# What else can be tried?

- **SMART**— symbicort maintenance and reliever therapy. In children 4-11 years SMART treatment decreased time to first exacerbation, reduced rates of exacerbation and reduced symptoms compared to fixed dose combination or high dose ICS alone (400 bd). Bisgaard et al Chest 2006
- **Xolair**— omalizumab. MAb anti IgE. For severe steroid dependant asthmatics. Licence is for children over 12 years, positive SPT, high dose (>1000ug/day) plus LABA or oral steroids and 2 admissions to hospital (or 1 admission and 2 attendances) in last 12 months, IgE<700

