Asthma and Wheeze

FRACP Residential Course
December 2015
Innes Asher

What is the Māori term for asthma?
What is one of the Aboriginal terms for asthma?

The Māori term for asthma is
He mate huango

www.globalasthmanetwork.org
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True or false?

Australia and New Zealand have THE highest rate of symptoms of asthma (wheeze in the last 12 months) of any country in the world (in which it has been measured)

Sources:
ISAAC http://isaac.auckland.ac.nz/
The International Study of Asthma and Allergies in Childhood

 Almost true!

Australia and New Zealand have among the highest rates of symptoms of asthma in children (wheeze in the last 12 months) of any country in the world (in which it has been measured)

Ahead of them by a whisker are Isle of Man & El Salvador

FOUR of the following countries have the highest asthma death rate for 5-34 years (2001-2010). Which ONE of the following countries has a much lower rate (less than half rate of each of the highest 4?)

a) Australia
b) Canada
c) USA
d) UK
e) New Zealand

FOUR of the following countries have the highest asthma death rate for 5-34 years (2001-2010). Which ONE of the following countries has a much lower rate (less than half rate of each of the highest 4?)

a) Australia  

b) **Canada** (WHO detailed mortality database 2014)  
c) USA  
d) UK  
e) New Zealand

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**Scenario 1 - Asthma**

A seven year old girl presents with recurrent **breathlessness** on exertion, which started 6 months ago. She is well in herself now, and in the past, is free of symptoms between episodes, and has never been diagnosed with asthma.

What symptoms with the breathlessness would make exercise induced asthma (EIA) likely?
Wheeze or Cough

What type of exercise is the most potent stimulus to EIA?

Running, also cycling

Why are running or cycling more likely to result in EIA than walking or swimming?

Discuss with your buddy

EIA is precipitated by

vigorous exercise

high minute ventilation

with HR nearly maximal

with drier rather than moister air

Pathophysiology of EIA

The mechanism of EIA is still not certain.

Airway dehydration as a result of increased ventilation is likely to play a key role, resulting in augmented osmolarity of the airway-lining fluid.

This is thought to trigger the release of mediators — such as histamine, cysteinyl leukotrienes, and prostaglandins — from airway inflammatory cells, which leads to airway smooth-muscle contraction and airway edema.
After vigorous exercise **starts**, when does the peak of EIA bronchoconstriction occur?

A) 1 minute  
B) 2 minutes  
C) 5 minutes  
D) 10 minutes  
E) 20 minutes

Choose one

**Answer:** d) 10 minutes

Standard exercise provocation test:  
6-8 minutes of exercise  
HR 85% max  

Within 3 mins of stopping,  
FEV1 falls >10-15%, resolves within 60 mins

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How do you prevent EIA?  
What are the two first line management strategies?

Discuss with your buddy

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Warm up  
Inhaled $\beta_2$ agonist 10 minutes before exercise.

These strategies are tried in this 7 year old girl with breathlessness on exertion and do not work. What do you do now?

Discuss with your buddy
Asthma may be more poorly controlled than you thought.

Reassess diagnosis.

What are the alternative diagnoses?

Can you think of 4?

- Ordinary exercise breathlessness
- Hyperventilation
- Vocal cord dysfunction – vocal cords paradoxically narrow on inspiration
- Major airway narrowing e.g. tracheomalacia
- Other lung disease such as lobar collapse, interstitial lung disease
- Cardiac defect e.g. aortic stenosis, arrhythmia

How effective are these drugs in preventing EIA?

- Salbutamol
- Salmeterol
- Eformoterol
- Inhaled corticosteroid (ICS)
- Theophylline
- Montelukast

Discuss with your buddy
How effective are they at preventing it?
How fast is the onset of action?

How effective are these drugs in preventing EIA?

- Short acting Beta-agonists (SABA) are best. Onset 1-3 minutes
- Salmeterol – prevents EIA. Slow onset of action 15-20 minutes
- Eformoterol – prevents EIA. Rapid onset of action 1-3 minutes
- ICS –Over weeks or months reduce the size of bronchoconstriction
- Theophylline – slight prevention or no effect.
- Montelukast – prevention of EIA two hours after the dose, and accelerates recovery.
What are the serious adverse events with long acting β2 agonists (LABAs)?

Discuss with your buddy

What are the serious adverse events with LABAs?

- poorer control
- near-fatal asthma attack
- asthma death

Thus
Don’t use LABA alone
Use a combination product (LABA and ICS)

Pathophysiology of LABAs

Long acting beta agonists are not recommended for isolated use in children. The reason for this is

a. Depletion of secondary messengers
b. Increasing binding affinity to β2 receptors
c. Internalisation of beta receptors
d. Reduction of β2 density
e. Upregulation of β2 receptors

Pathophysiology of LABAs

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Th1 Th2 dichotomy and asthma

Possible markers for eosinophilic inflammation include all of the following EXCEPT

- a) serum peristin
- b) numbers of blood eosinophils
- c) eosinophilic cationic protein
- d) calcitonin
- e) eosinophil-derived neurotoxin

Scenario 2 – The wheezy preschool child

A two year old boy has recurrent episodes of wheezing, and has been hospitalised twice for these. Between the episodes he is free of symptoms.

He was born at term and had no neonatal complications.
Do YOU ever diagnose asthma in children under 5 years?

Preschool Wheeze Types


Episodic (viral) wheeze – Wheezing during discrete time periods, often in association with clinical evidence of a viral cold, with absence of wheeze between episodes.
- The most common type
- Mostly disappears by 6 yrs

Multiple-trigger wheeze – Wheezing that shows discrete exacerbations, but also symptoms between episodes.
- The less common type
- Mostly persists after 6 yrs

Preschool Wheeze – asthma more likely

(www.sign.ac.uk/guidelines)

- More than one of the following symptoms: wheeze, cough, difficulty breathing, chest tightness, especially
  - frequent and recurrent
  - worse at night and in the early morning
  - in response to, or are worse after, exercise, pets, cold or damp air, with emotions or laughter
  - occur apart from colds
- Personal or family history of atopic disorder
- Widespread wheeze heard on auscultation
- Improvement in symptoms or lung function with adequate therapy

Scenario 2 –
The wheezy preschool child

A two year old boy has recurrent episodes of wheezing, and has been hospitalised twice for these. Between the episodes he is free of symptoms.

He was born at term and had no neonatal complications.

What is your differential diagnosis?

Can you think of 5 diagnoses?

1. Asthma or “viral–induced wheeze”
2. Bronchiolitis
3. Cystic Fibrosis
4. Bronchiectasis
5. Tracheomalacia
6. Aspiration pneumonitis
7. Inhaled foreign body
8. TB
9. Immunodeficiency
10. Aspiration
11. Gastroesophageal reflux
12. Lobar atelectasis
13. Developmental anomaly
14. Bronchiolitis obliterans
15. Central airway or laryngeal disorder
16. Ciliary dyskinesia

Question 2.3:
If this is “asthma”, what would be the criteria which would make you prescribe an asthma preventer?

Discuss with your buddy
He meets criteria for a preventer. What asthma **preventer** would you prescribe and in what **dose** and **delivery system** and **duration**?

Can you come up with the prescription? Discuss with your buddy

**a) Drug choices and daily starting doses**

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<tr>
<td>Beclomethasone (HFA)</td>
<td>200 mcg</td>
</tr>
<tr>
<td>Extra fine</td>
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HFA= hydrofluoralkane (has replaced CFC= chlorofluorocarbon)

**b) Delivery system** spacer and mask (tight fit).

Do not use inhaled powder device as children under 5yr cannot inspire fast enough to empty the device.

Mask causes some nasal deposition, so stop mask as soon as the child is capable of using mouthpiece.
(The nose is a wonderful filter of particles and also warms and humidifies air).
c) **Duration**-stop after 3 months if no improvement

- natural history is to improve, so if improves, consider trial of withdrawal of treatment after 3 months or so.

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**Inhaled Corticosteroids (ICS)**

In a 2 year old boy, long-term ICS are used for asthma prevention from 2 to 5 years of age, then stopped.

**Question:**

What effects do ICS thus used have at 6 years of age on his lung function, symptom-free days and number of exacerbations?

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**NO lasting effect of ICS**

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**Montelukast (Singulair)**

*(Anti-leukotriene agent)*

Montelukast blocks leukotriene receptors in the lungs and, as a result, blocks the actions of the leukotrienes.

This prevents the excess mucus production, inflammation and narrowing of the airways and so prevents asthma attacks.

It is also useful for preventing asthma triggered by exercise.

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### Montelukast in preschool children

- Don’t use under 2 yrs (chewable tablet)
- Daily Montelukast may reduce frequency of interval symptoms and wheezing episodes.
- Intermittent Montelukast may reduce frequency of symptoms but not hospitalisations.
- **NZ** (Special authority): Can be used as a preventer or intermittently for children under 5 years with frequent viral induced exacerbations.
- **Australia**: No prescription restrictions, but not registered for intermittent use.

### Montelukast in older children

- For those with mild to moderate asthma (children and adolescents) - Adding montelukast to ICS does not reduce the need for rescue oral corticosteroids or hospital admission (Cochrane Jan 2013)

### NZ (Special authority)

- Add montelukast for exercise induced asthma if EIA on ICS, and did not improve with LABA.

### Omalizumab (Xolair)

- Omalizumab is a humanized, monoclonal anti-IgE antibody that binds specifically to circulating IgE molecules, thus interrupting the allergic cascade.
- Consider > 12 years for severe allergic asthma when all other avenues exhausted.
- Given by a subcut injection – may get site reactions
- Well tolerated, but occasional anaphylaxis (medical supervision needed)
- Costly. NZ$500 per 150mg vial, 1-2 every 2-4 weeks (specific doses)

### Omalizumab

- Effective in reducing asthma exacerbations and hospitalisations as an adjunctive therapy to inhaled steroids, and may help reduce inhaled steroids.
- Not clear whether there is a threshold level of baseline serum IgE for optimum efficacy of omalizumab. (Cochrane June 2013)
**Omalizumab – PHARMAC criteria**

- Over 6 yrs
- Severe life-threatening asthma
- Atopic
- Serum IgE 76 -1300 IU/ml
- Compliant with high dose ICS + LABA
- >28 days oral steroid in last year
- 4 hospital admissions in last 2 years
- ACQ-5 at least 3 (symptoms, night time awakening, interference with normal activity, SABA use, FEV1)

**Which viruses are associated with increased risk of wheezing persisting at age 6 years?**

Think of 2 viruses

- RSV – but risk gone by 11 years
- Rhinovirus – don’t know how long the increased risk persists for.

**The End**

Good Luck in your exam preparation! You are well on the way to being paediatricians!