Approach to the child with recurrent wheeze

Aneesa Vanker
Paediatric Pulmonology
Red Cross War Memorial Children’s Hospital
University of Cape Town
Overview

• Pre-school vs over 5 year-old “wheezer”.
• Is it asthma?
• Alternative causes of wheezing.
• Treatment principles for asthma
• Summarise approach
Burning Question

• Is it Asthma?

• Asthma characterised by airway inflammation and hyperresponsiveness.
• Reversible airflow obstruction.
The Young Child

• “Pre-school” wheezer (under-5 years of age).

• Often wheeze in response to viral infection.

• Categorised as “episodic (viral) wheeze” vs “multi-trigger wheeze”

• **Episodic (viral) wheeze** – wheeze in response to a viral cold - “common”. Well between episodes – absence of wheeze.

• **Multi-trigger wheeze** – wheeze triggered by multiple factors including: viral infections, exercise, allergens. Symptoms maybe present between episodes. *Likely to be asthmatic.*
Duration of Wheeze

<table>
<thead>
<tr>
<th>TRANSIENT WHEEZE</th>
<th>PERSISTENT WHEEZE</th>
<th>LATE-ONSET WHEEZE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms before 3 years of age.</td>
<td>Symptoms continue to &gt;6 years.</td>
<td>Symptoms commence &gt;3 years</td>
</tr>
<tr>
<td>Tend to resolve by 6 years of age.</td>
<td>Maybe “episodic or multi-trigger”</td>
<td>Maybe “episodic or multi-trigger”</td>
</tr>
<tr>
<td>Maybe “episodic or multi-trigger”</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Investigating the cause

History and Physical Examination –
• confirm that the preschool child has a wheezing disorder,
• identify the pattern of symptoms,
• the severity of the condition,
• any possible trigger factors.
• To look for features suggestive of another diagnosis or associated condition.
Investigating the cause

• Diagnosis can usually be made on history and examination alone.
• Adjunctive investigations that may be useful include:
  • Identification of respiratory virus on nasopharyngeal aspirate (PCR or culture)
  • Tests of sensitisation to allergens – Skin prick test (May help identify those at risk for developing asthma).
  • Radiological examinations – no evidence that CXR help in diagnosis or treatment.
Making the diagnosis

- **Asthma Predictive Index** – Clinical index used to predict occurrence of asthma in later childhood. Useful in Europe and America, application more limited in African children → less atopy.

**API**-presence of wheeze before 3 years of age

1 major risk factor
- Parental history of asthma
- Or eczema

2 of 3 minor risk factors
- Eosinophilia
- Wheezing without cold
- Allergic rhinitis
Modified bronchodilator response test

- Child with persistent or recurrent wheezing given a bronchodilator (via nebuliser or MDI) → assess clinical response after 10-15 mins.

- Response usually measured by decrease in wheeze, respiratory rate or improved air entry.
So is it Asthma?

Table III. Features suggestive of asthma in children <5 years

**Evidence A (Based on RCT)**
- Exercise-induced cough or wheeze
- Cough at night
- Symptoms persisting after the age of 3 years

**Evidence B (Observational studies)**
- Absence of seasonal variation
- Symptoms worsening with certain exposures
- Colds repeatedly going to the chest
- Response to a bronchodilator
- Response to a course of steroid
- Concomitant rhinitis, eczema or food allergies
- Family history of allergy or asthma

**Evidence C (Laboratory, animal or case studies)**
- Wheezing more than 1 month

**Evidence D (Expert opinion)**
- Modified bronchodilator response test
Other causes of wheezing in children

Table II. Differential diagnosis of asthma in children 5 years and younger

Infections
Post-viral wheezing
Tuberculosis (e.g. glandular compression of airways)
HIV disease (e.g. lymphocytic interstitial pneumonia)

Congenital/perinatal problems
Tracheomalacia
Cystic fibrosis
Chronic lung disease of the newborn
Congenital malformation causing narrowing of the intrathoracic airways
Primary ciliary dyskinesia syndrome
Immune deficiency
Congenital heart disease (e.g. L-R shunts)

Mechanical problems
Foreign body aspiration
Gastro-oesophageal reflux disease (GORD)
Infections

Post-infectious wheezing

• Disease of bronchioles and alveolar ducts
• Fibrosis and obliteration of small airways
• Aetiology – Adenovirus, invasive serotypes 3, 7 & 21
• Other infective cx’s – Influenza, Parainfluenza, Measles, RSV & Mycoplasma Pneumoniae
• Results in “bronchiolitis obliterans”
Clinical Manifestations

- Persistent wheezing, cough, tachypnoea, dyspnoea
- Severe irreversible airway obstruction – minimal response to bronchodilators.
- Hypoxic, respiratory distress, crackles & wheezes on auscultation.
- Digital clubbing
- Bronchiectasis
Diagnosing Bronchiolitis Obliterans

Typical clinical history

- Identifying previous lung insult
- CXR & CT findings
- History:
  unresolving wheezing or cough after pneumonia
  prolonged localised crepitations or wheezing after after severe acute respiratory failure
  prolonged exercise intolerance
  respiratory symptoms which are severe in disproportion to chest xray findings
  severe lung disease with over inflation often localized with difficulty in ventilation.
- Exclude other causes of persistent wheezing
Infections

*Tuberculosis – Lymphobronchial TB*

- Children under 5 years of age, TB lymph gland disease affecting the airways is common,
- Most cases of airway obstruction present early in the course of disease.
- Often present with an audible wheeze – sometimes mistaken for stridor.
- Airway compression of large airways.
Lymph node obstructing left main bronchus
Congenital malformations

**Vascular compression of the large airways**

*Vascular Rings causing Airway Compression*

- Term given to a combination of vascular and ligamentous structures that encircle the trachea and oesophagus.

- Clinical manifestations – spectrum from no symptoms to feeding difficulties, repeated infections and life-threatening respiratory compromise.

- Large airway obstruction clinically manifests as a “monophonic wheeze” often mistaken for “stridor”.

- Compression maybe severe and life-threatening.
Chest X-ray: Proximal part of trachea is visible (orange arrow) but distal part not visible (red arrow)
Contrast study: Oesophageal compression from posterior due to the posterior part of the double aortic arch
Mechanical problems

*Foreign body aspiration*

- More common in children between 1 – 4 years of age.
- Most commonly foodstuff – PEANUTS
- Often lodge in right main bronchus (anatomical location).
- May give a history of choking – often don’t!
- Present with large airway obstruction or localised wheezing.
- Sudden onset with no preceding illness.
- Don’t respond to bronchodilators.
- Retained FB → localised bronchiectasis.
• Hyperlucent left lung – “ball-valve” effect, obstruction of left main bronchus.
- Foreign body removal from bronchus
Aspiration Syndromes

- Children may present with recurrent wheezing from aspiration of milk, food or even saliva.
- Aspiration can occur from “over the top”, “through the middle”, “from below”.
  - *Over the top* – refers to aspiration occurring during the swallowing process.
  - *Through the middle* – occurs with tracheo-oesophageal fistulas
  - *From below* – gastro-oesophageal reflux disease.
<table>
<thead>
<tr>
<th>Aspiration over the top</th>
<th>Aspiration through the middle</th>
<th>Aspiration from below</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structurally normal</td>
<td>Congenital</td>
<td>Gastroesophageal reflux</td>
</tr>
<tr>
<td>Prematurity</td>
<td>Tracheoesophageal fistula (TEF)</td>
<td>Primary GER</td>
</tr>
<tr>
<td>Fatigue aspiration</td>
<td>Bronchopulmonary foregut malformations</td>
<td>Idiopathic</td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td>Bronchopulmonary fistula</td>
<td>Hiatus hernia</td>
</tr>
<tr>
<td>Bronchopulmonary dysplasia</td>
<td></td>
<td>Secondary GER</td>
</tr>
<tr>
<td>Idiopathic oropharyngeal incompetence</td>
<td></td>
<td>Obesity</td>
</tr>
<tr>
<td>Accidental foreign body aspiration</td>
<td></td>
<td>Neurological disorders</td>
</tr>
<tr>
<td></td>
<td>Acquired</td>
<td>Caffeine</td>
</tr>
<tr>
<td></td>
<td>Crohn's disease</td>
<td>Theophylline</td>
</tr>
<tr>
<td>Structurally abnormal</td>
<td>Post tracheostomy</td>
<td></td>
</tr>
<tr>
<td>Congenital</td>
<td>Abrasive foodstuffs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Caustic ingestants</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Poststent erosion</td>
<td></td>
</tr>
<tr>
<td>Cleft palate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laryngeal cleft</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laryngomalacia/tracheomalacia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choanal anomalies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micrognathia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pierre Robin sequence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macroglossia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharyngeal pouch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular rings and slings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cysts or tumors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquired</td>
<td>Tracheostomy</td>
<td>Esophageal dysmotility</td>
</tr>
<tr>
<td></td>
<td>Prolonged endotracheal intubation</td>
<td>Primary</td>
</tr>
<tr>
<td></td>
<td>Vocal cord paralysis (also congenital)</td>
<td>Achalasia</td>
</tr>
<tr>
<td>Functionally abnormal</td>
<td></td>
<td>Diffuse esophageal spasm</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td></td>
<td>Idiopathic</td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td></td>
<td>Secondary</td>
</tr>
<tr>
<td>Moebius syndrome</td>
<td></td>
<td>Cerebral palsy</td>
</tr>
<tr>
<td>Worster-Drought syndrome</td>
<td></td>
<td>Myasthenia gravis</td>
</tr>
<tr>
<td>Myopathy</td>
<td></td>
<td>Myotonic dystrophy</td>
</tr>
<tr>
<td>Myotonic dystrophy</td>
<td>Hypotonia for example, Trisomy 21</td>
<td>SMA Type 1</td>
</tr>
<tr>
<td>Hypotonia</td>
<td>Spinal muscular atrophy</td>
<td>Familial dysautonomia</td>
</tr>
<tr>
<td>Spinal muscular atrophy</td>
<td>Familial Dysautonomia</td>
<td>Hirschsprung's disease</td>
</tr>
</tbody>
</table>

GER, gastroesophageal reflux; SMA, spinal muscular atrophy.
<table>
<thead>
<tr>
<th>Table 2. Clinical Features of Aspiration on Presentation—in Rough Order of Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic cough</td>
</tr>
<tr>
<td>Gagging, choking with feeds</td>
</tr>
<tr>
<td>Increased respiratory mucous and congestion/pooling of oral secretions</td>
</tr>
<tr>
<td>Unexplained oxygen dependency</td>
</tr>
<tr>
<td>Refusal to feed (may be associated with GER)</td>
</tr>
<tr>
<td>Stridor or hoarseness</td>
</tr>
<tr>
<td><strong>Recurrent wheezing, asthma</strong></td>
</tr>
<tr>
<td>Prolonged feeding, abnormal tearing</td>
</tr>
<tr>
<td>Failure to thrive</td>
</tr>
<tr>
<td>Apnea or acute life-threatening event/foreign-body aspiration</td>
</tr>
<tr>
<td>Recurrent pneumonia/chronic endobronchitis</td>
</tr>
<tr>
<td>Bronchiectasis with clubbing</td>
</tr>
<tr>
<td>Unexplained chest X-ray changes which may include areas of atelectasis or hyperinflation</td>
</tr>
</tbody>
</table>
Over 5-year-old “wheezer”

- “Is it asthma?”
- Recurrent wheeze with or without cough triggered by multiple factors such as viral infections, allergens, irritants or exercise ➔ response to bronchodilators.
- History and physical examination – suggestive of Asthma.
- Objective evidence of airway obstruction reversibility with a short-acting B2-agonist:
  FEV1 >12% - Spirometry
  PEF > 15% - Peak flow meter
**Table I. Differential diagnosis of asthma in children older than 5 years**

- Hyperventilation syndrome and panic attacks
- Vocal cord dysfunction
- Upper airway obstruction and inhaled foreign bodies
- Other forms of obstructive lung disease (e.g. cystic fibrosis)
- Non-respiratory causes of symptoms (e.g. left ventricular failure)
Goals of Management for Asthma

Achieve a “normal” life

- Free of symptoms – cough, wheeze, breathlessness
- Attend school and participate in sport
- Sleep restfully – without cough or wheeze
- Grow and develop normally
- Minimise acute attacks and hospitalisations
- Minimise medication side effect
Principles of management

• Early diagnosis and assessment of severity.
• Avoidance of irritants and allergens.
  Tobacco smoke, pollutants
  Specific allergens (e.g., house dust mite, cockroaches, mould) – can be identified with skin prick testing or specific IgE.
• Pharmacotherapy – appropriate medication with limited side-effects and costs and appropriate delivery systems.
• Patient and care-giver education – encourage adherence.
Principles of Medical Therapy

- Anti-inflammatory therapy for persistent asthma.
- Inhaled route preferable.
- *Relievers* – Short acting bronchodilators → acute relief
- *Controllers* – Anti-inflammatory or sustained bronchodilator response.

- Mode of administration –
  - <4 years – Pressurised metered dose inhaler (MDI) + spacer + face mask
  - 4-6 years – Pressurised MDI + spacer with mouthpiece
  - >6 years – Pressurised MDI + spacer with mouthpiece, OR dry powder inhaler or breath-actuated MDI
- MDI + spacer as effective or even more effective than a nebuliser. Home nebulisers should be discouraged.
Relievers

- *Short acting B2-agonists (SABA)* – used on prn basis – acute relief, use can be minimised with effective anti-inflammatory therapy.

- *Anti-cholinergics (Ipratropium bromide)* – inhibit vagally mediated bronchoconstriction. Slower onset of action (30-60mins) than SABA and less potent. Adjunctive Rx in acute asthma.
Controllers

- **Inhaled corticosteroids (ICS)** – cornerstone of asthma management. Dose should be titrated according to patients response to Rx.
- Most children controlled on daily doses of 200ug – 400ug of budesonide or equivalent.
- Can also be used in the under 5 year-old “multitrigger wheezer” however, use in “viral induced” wheezing remains controversial.
- Children <2 years – little data on safety and efficacy of ICS use. Should only be used if symptoms severe and clear benefit demonstrated.

<table>
<thead>
<tr>
<th>Table VIII. Estimated equipotent daily dosage of ICS for children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Beclomethasone</td>
</tr>
<tr>
<td>dipropionate</td>
</tr>
<tr>
<td>Budesonide*</td>
</tr>
<tr>
<td>Ciclesonide *</td>
</tr>
<tr>
<td>Fluticasone</td>
</tr>
</tbody>
</table>

*Approved for once-daily dosing in patients with mild asthma.
As CFC preparations are taken off the market, medication inserts for HFA preparations should be carefully reviewed for the equivalent correct dosage.
Controllers

*Long-acting inhaled B2 agonists (LABA)*

- Used in combination with ICS.
- Adjunctive therapy to improve control.
- Combination inhalers – ICS + LABA → preferable to improve adherence.
- No studies to recommend use of LABA’s in children <4 years of age.
Controllers

*Leukotriene receptor antagonists (Monteleukast)* –

- Accepted form of treatment for childhood asthma
- Oral preparation → useful in children who have difficulty in using inhalational Rx, with poor compliance or have predominantly exercise-induced symptoms.
- Children > 5 years – used as add on therapy to ICS.
- Children < 5 years – safe to use from 6 months of age.
- Has beneficial effects on the treatment of allergic rhinitis that may be associated with asthma.
Controllers

*Oral corticosteroids* –

- Used for acute exacerbations of asthma.
- Dose 1-2mg/kg for 5-7 days.
- Risk of systemic side-effects – growth suppression, obesity and adrenal suppression therefore use with caution.
**Level of control** | **Treatment action**
---|---
Controlled | Maintain and find lowest controlling step
Partly controlled or uncontrolled | Step up until controlled

**Before stepping up treatment:**
- Check adherence
- Check inhaler technique
- Assess for co-morbid conditions
- Review diagnosis

**Controller treatment (Level 1)**
- Low-dose inhaled corticosteroid (ICS) – any age
  Alternative: Leukotriene receptor antagonist (LTRA)

**Controller treatment (Level 2)**
- ≤5 years: Medium-dose ICS
  Alternative: Low-dose ICS plus LTRA
  - >5 years: Medium-dose ICS or low-dose ICS plus long-acting β₂-agonist (LABA)*
  Alternative: Low-dose ICS plus LTRA

**Controller treatment (Level 3) – Specialist care**
- ≤5 years: Medium-dose ICS plus LTRA
- >5 years: Medium-high dose ICS plus LABA*
  Alternative: Medium-high dose ICS plus LTRA
  Consider adding oral steroids (alternate-day regimen) if asthma is poorly controlled on medium-high dose ICS plus another controller

**All patients**
- Asthma education
- Environmental control
- As-needed reliever

Preferred controller options are shown in grey-shaded areas.
*LABA approved in children ≥4 years old, but must only be used in combination with ICS.
Sustained-release (SR) theophylline may be used as alternative adjunctive therapy with ICS in children ≥5 years old if other controllers unavailable.

Fig. 1. Adjusting treatment of asthma based on control.
Summary approach to recurrent wheezing

- Age of the child.
- History of symptoms, associations and any preceding events. Duration of symptoms and any exacerbating factors.
- Features in keeping with “asthma”?
- If not – consider alternate diagnosis.
- Refer for further investigation.
Take home message

• Maybe difficult to diagnose “asthma” in pre-school children.
• Viral infections are common and often present with wheezing in young children.
• “Not all that wheezes is asthma”.
• Careful history and clinical examination can be the key to diagnosis.
References


• Wallis C, Assessing the role of aspiration in pediatric lung disease; Paediatric Allergy, Immunology and Pulmonology; Vol 25, Number 3, 2012