Paediatric Respiratory Updates

References

Supplementary slides

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Cough in healthy children

May have

- On average 11 cough epochs/24 hour
- 50-60 days coughing/year
- 5-8 (URTI)/year

Prospective study of preschool children suggested [1]

- 50% of acute cough recovered by 10 days
- 90% recovered by 3 weeks
- 10% of children still have problems in the third to fourth weeks

Definition of chronic cough in kids [2]

- Acute cough can last up to 3 weeks.
- Chronic cough > 8 weeks.
- 3-8 weeks – prolonged acute cough (slowly resolving post-viral cough).

Paediatric Chronic Cough

Cough Type	Suggested underlying process
Barking or brassy cough	Croup, tracheomalacia, habit cough
Honking	Psychogenic
Paroxysmal (with or without inspiratory “whoop”)	Pertussis and parapertussis
Staccato	Chlamydia in infants
Cough productive of casts	Plastic bronchitis/asthma
Chronic wet cough in mornings only	Suppurative lung disease

Table 2. Questions to Distinguish the Etiology of Wheezing in Children

Question	*Indications*
How old was the patient when the wheezing started?	Distinguishes congenital from noncongenital causes
Did the wheezing start suddenly?	Foreign body aspiration
Is there a pattern to the wheezing?	Episodic: asthma
	Persistent: congenital or genetic cause
Is the wheezing associated with a cough?	GERD, sleep apnea, asthma, allergies
Is the wheezing associated with feeding?	GERD
Is the wheezing associated with multiple respiratory illnesses?	Cystic fibrosis, immunodeficiency
Is the wheezing associated with a specific season?	Allergies: fall and spring
	Croup: fall to winter
	Human bocavirus*
	Human metapneumovirus: December through April
	RSV: fall to spring
Does the wheezing get better or worse when the patient changes position?	Tracheomalacia, anomalies of the great vessels
Is there a family history of wheezing?	Infections, allergic triad

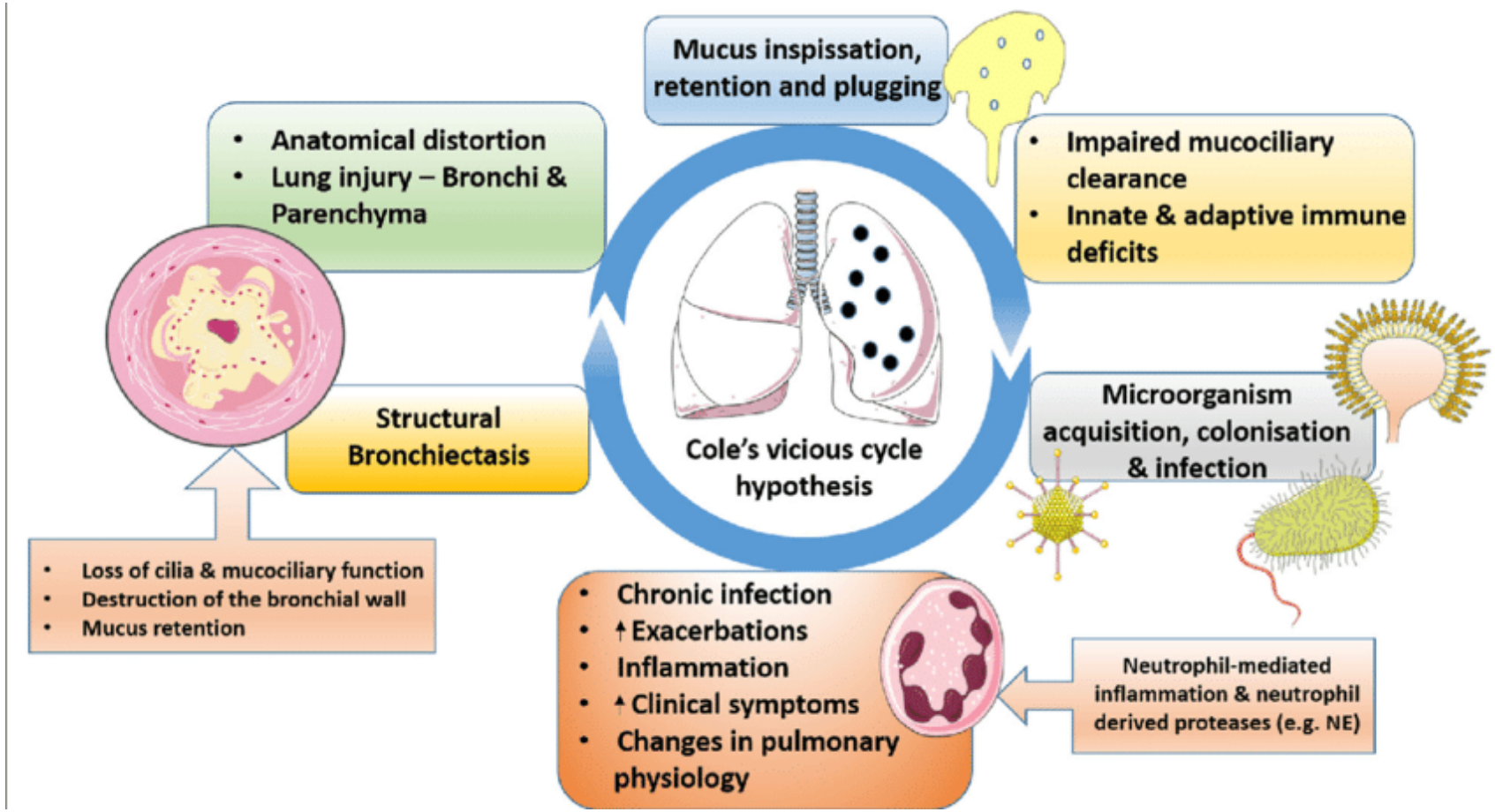
American Family Physician, April 15 2009, Volume 77 Number 8

Table 3. Differential Diagnosis of Wheezing According to Characteristic Signs and Symptoms

Signs and symptoms	*Presumptive diagnosis*	*Further evaluation*
Associated with feeding, cough, and vomiting	Gastroesophageal reflux disease	24-hour pH monitoring Barium swallow
Associated with positional changes	Tracheomalacia; anomalies of the great vessels	Angiography Bronchoscopy Chest radiography CT or MRI Echocardiography
Auscultatory crackles, fever	Pneumonia	Chest radiography
Episodic pattern, cough; patient responds to bronchodilators	Asthma	Allergy testing Pulmonary function testing Trial of albuterol (Proventil)
Exacerbated by neck flexion; relieved by neck hyperextension	Vascular ring	Angiography Barium swallow Bronchoscopy Chest radiography CT or MRI
Heart murmurs or cardiomegaly, cyanosis without respiratory distress	Cardiac disease	Angiography Chest radiography Echocardiography
History of multiple respiratory illnesses; failure to thrive	Cystic fibrosis or immunodeficiency	Ciliary function testing Immunoglobulin levels Sweat chloride testing
Seasonal pattern, nasal flaring, intercostal retractions	Bronchiolitis (RSV), croup, allergies	Chest radiography
Stridor with drooling	Epiglottitis	Neck radiography
Sudden onset of wheezing and choking	Foreign body aspiration	Bronchoscopy

American Family Physician, April 15 2009, Volume 77 Number 8

Pathophysiology of chronic wet cough



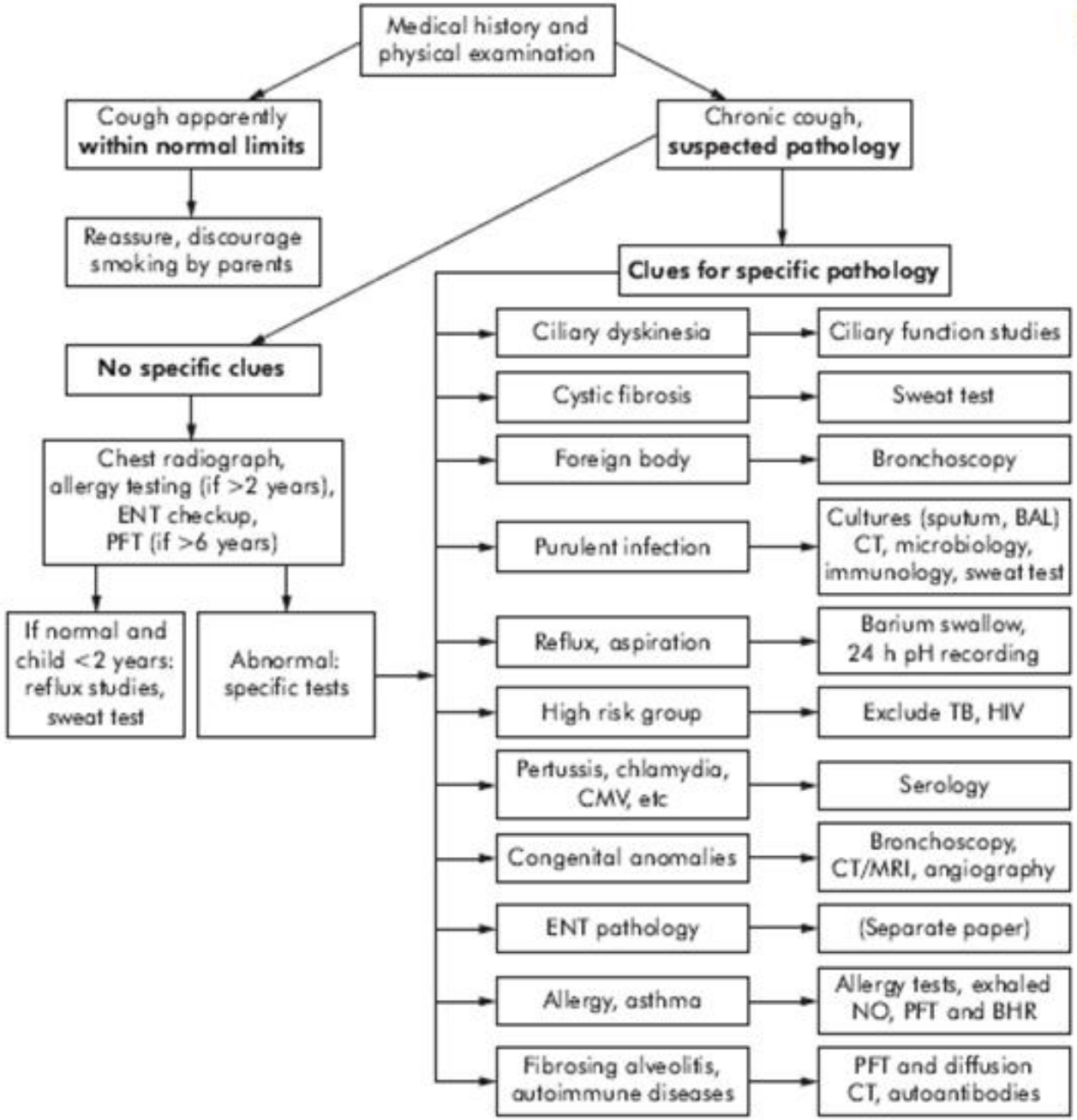
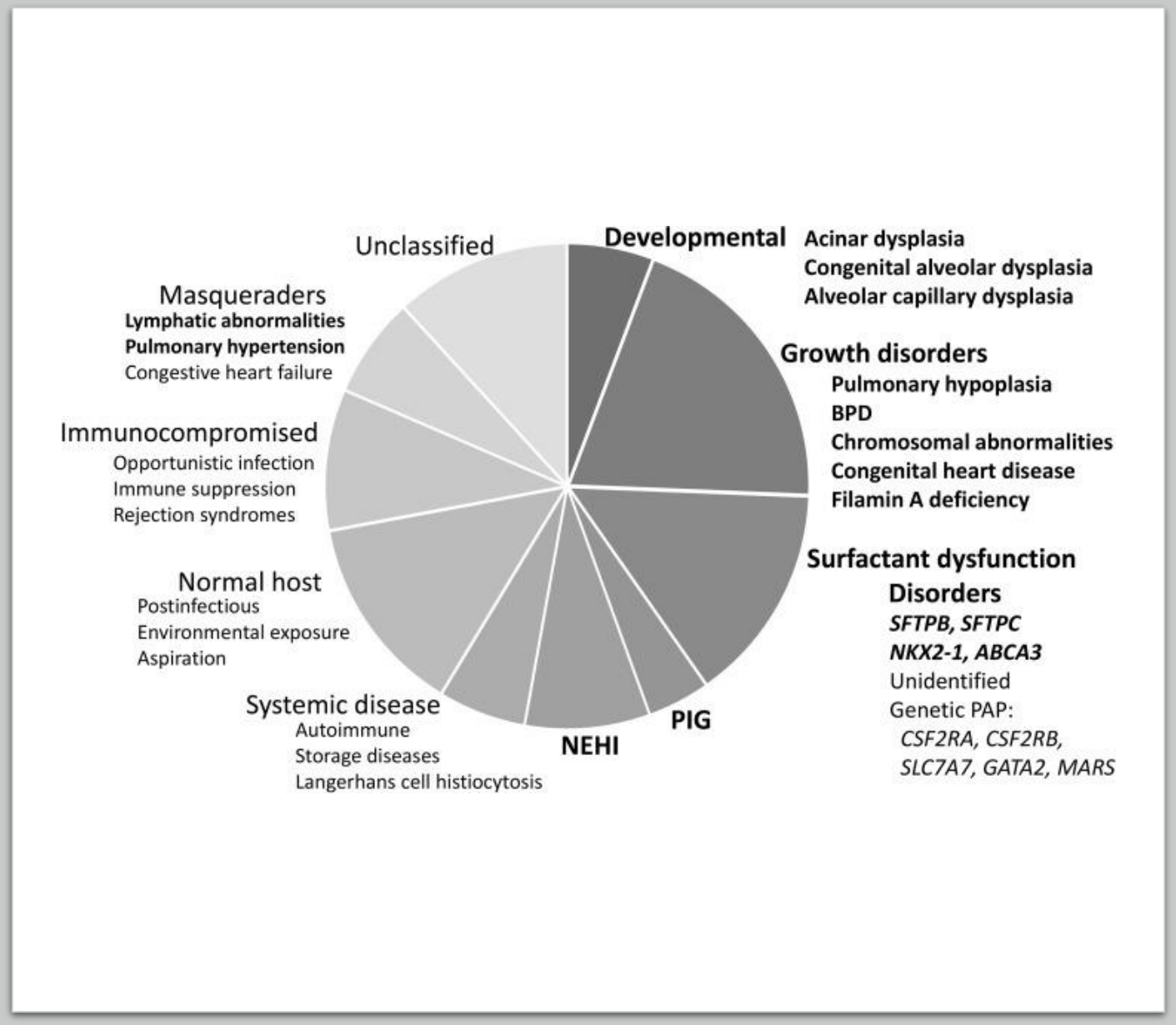


Figure 1 Diagnostic algorithm for use in children with chronic cough.

CHILDHOOD ILD

Childhood ILD describes a diverse group of rare diseases in which there is remodelling of the interstitium and distal airspaces, resulting in abnormal gas exchange and diffuse radiographic infiltrates.54 55

- Repeated occurrences of pneumonia, bronchiolitis, and/or cough
- Tachypnoea, shortness of breath, respiratory distress
- Failure to thrive despite adequate feeding
- Crackles, wheezing, or other abnormal sounds in lungs
- CXR may show hyperinflation, increased pulmonary markings



Post-infectious bronchiolitis obliterans

- Bronchiolitis obliterans is a small airway injury-related chronic inflammation airflow obstruction syndrome.
- Post-infectious bronchiolitis obliterans (PIBO) occurs in children mainly following Adenovirus, Rhinovirus, RSV and Mycoplasma infection[16].
- Patients at risk include:
  - LRTI during the first 2 years of life and need hospitalization and requiring O2 and additional supportive care.
- Azithromycin, Montelukast and inhaled corticosteroids are found to be beneficial in these cases [16].

Intermittent Montelukast for Preschool Wheeze

- Wheeze And Intermittent Treatment (WAIT) trial (1358 preschool children) with a history of previous wheezing episodes [28].
  - no significant difference in the primary outcome of unscheduled medical attendances for wheezing episodes.

- A systematic review and meta-analysis including two RCTs on the use of intermittent or continuous montelukast in children with episodic viral wheeze and no interval symptoms showed
  - no statistically significant difference between the treatment with montelukast and placebo in the number of exacerbations requiring OCS [29]

Regular ICS in Preschool Wheeze

TABLE 1 | Inhaled corticosteroid by recommended dose.

Inhaled corticosteroid	Very low dose	Low dose	Medium dose
Fluticasone propionate HFA	50 mcg one puff twice a day	50 mcg two puffs twice a day	125 mcg two puffs twice a day
Beclomethasone dipropionate HFA	50 mcg two puffs twice a day	100 mcg two puffs twice a day	200 mcg two puffs twice a day
Budesonide nebulized	250 mcg/day	500 mcg/day	>500–1,000 mcg/day

Fluticasone and beclomethasone are considered as pressurized metered dose inhalers (pMDI) with spacer. Adapted from BTS guidelines and GINA recommendations (55, 59). HFA, Hydrofluoroalkane propellant.

Thorax 2008;**63**:974–980. doi:10.1136/thx.2007.093187

APRIL Trial (NHLBI AsthmaNet)

- 607 children (ages 1-5 years)
- Episodic wheeze events, but minimal day-to-day symptoms
- Multicenter, blinded, randomized, placebo controlled

- Azithromycin vs. Placebo
  - Parent-initiated at the start of an upper respiratory tract infection
  - 5 day course with each infection (12 mg/kg/day)
  - Children were not on any controller therapies

Bacharier LB, JAMA, 2015

Macrolides as a treatment for asthma

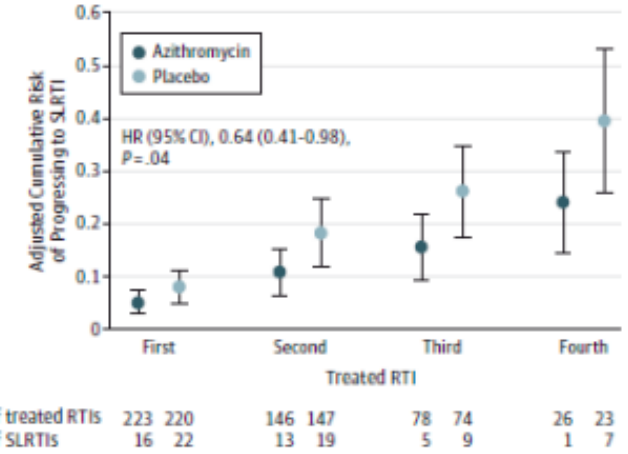
- Macrolides have been shown to have beneficial anti-inflammatory effects in other inflammatory chronic lung disease.

- Macrolides reduce neutrophilic inflammation which is prominent during respiratory infections.

- Macrolides may have a beneficial effect on the airway microbiome.

Intermittent azithromycin reduced the risk of progression to severe wheezing exacerbations

Figure 2. Cumulative Risk of Experiencing an Episode of Severe LRTI Across Treated RTIs for Preschool Children With a History of Severe LRTI



No. of treated RTIs	223	220	146	147	78	74	26	23
No. of SLRTIs	16	22	13	19	5	9	1	7

Bacharier LB, JAMA, 2015

Summary of the APRIL Trial

- Intermittent early initiation of azithromycin was able to reduce the risk of an upper RTI progressing to a severe wheezing episode by 36% (similar to ICS effect) when compared to placebo.
- Additionally, the azithromycin group had significantly decreased illness severity during episodes that progressed to an exacerbation.
- There was no difference in the treatment effects between children with and without a positive mAPI (modified Asthma Predictive Index)
  - Suggesting that azithromycin may be a good option for children with a negative mAPI (often under-represented in asthma studies)

Bacharier LB, JAMA, 2015

Macrolides as treatment for asthma

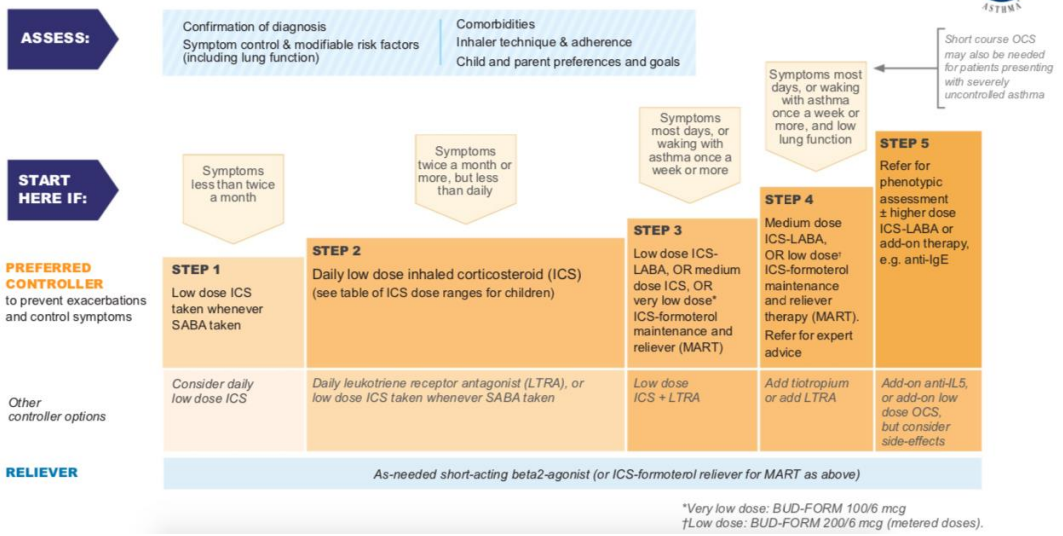
- After the APRIL trial, similar beneficial results were reported from children aged 1-3 years in the Copenhagen Prospective Studies on Asthma in Childhood (COPSAC)

- These studies indicate that intermittent azithromycin therapy may be a therapeutic approach for young children with recurrent and severe episodic wheeze.
  - Including those children with a negative mAPI

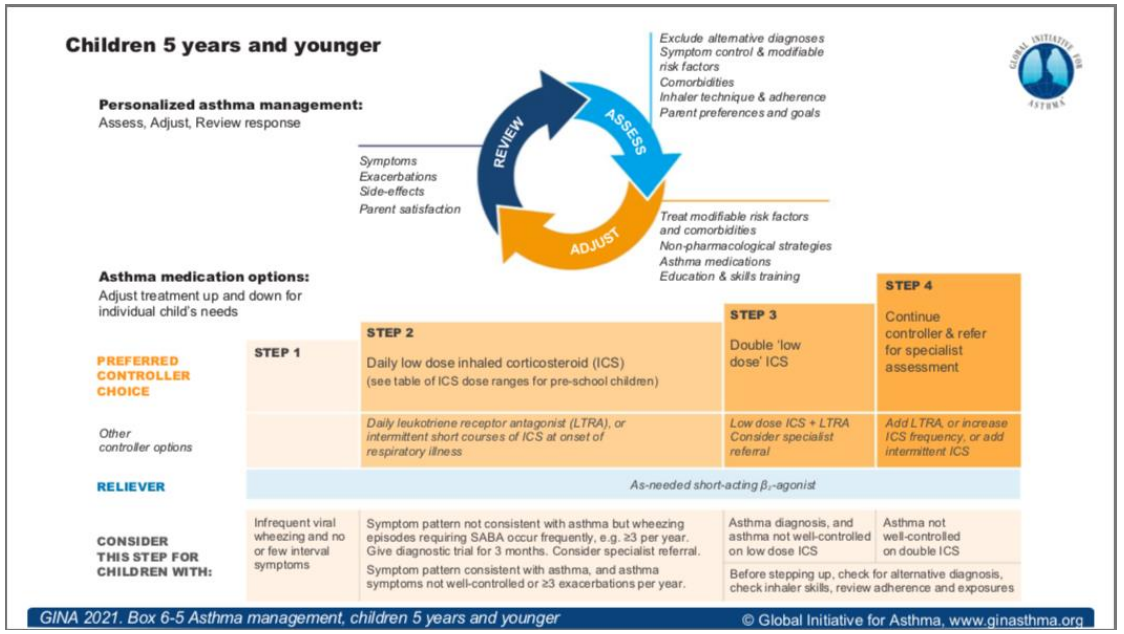
Bacharier LB, JAMA, 2015
Stockholm J, Lancet Respir Med, 2016

STARTING TREATMENT

Children 6–11 years with a diagnosis of asthma

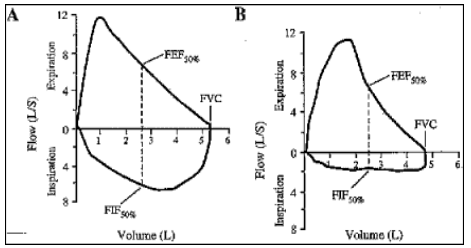


Children 5 years and younger



GINA 2021. Box 6-5 Asthma management, children 5 years and younger

Vocal Cord Dysfunction



- Full or partial closure occurring mainly on inhalation resulting in airflow obstruction
- Presents as dyspnoea, wheezing, coughing, tightness in throat, stridor
- Primary cause : GORD, exposure to aeroallergens, PND, anxiety or stress
- Mimics asthma, anaphylaxis, collapsed lungs, PE
- Among children and teenage patients – associated with high participation in competitive sports and family orientation towards high achievement
- Ix of choice - nasolaryngoscopy

E-cigarettes

- Tobacco uses causes over 7 million deaths globally per year
- Secondhand smoke causes another 1.2 million deaths including 65000 children.
- 1 in 2 smokers will be killed by smoking and the ratio is up to two-thirds if smoking started young.
- E-cigarettes and heated tobacco products are rapidly emerging and propaganda as less harmful products.
- United States National Youth Tobacco Survey 2019 (NYTS 2019)

  → Higher prevalence of current e-cigarette use (27.5%) than cigarette use (5.8%) among high school (27.5% vs 5.8%) and middle school (10.5% vs 2.3%) students.

  → Nearly one-third of adolescent e-cigarette users in NYTS 2016 have used e-liquid containing cannabis.

E-cigarettes – are they safer?

- E-cigarettes contain chemical substances that can be toxic, carcinogenic and can cause significant impact on the cardiorespiratory system.
- Nicotine is highly addictive and may have permanent effects on the brain and behaviours resulting in long-term difficulties with behavioural regulation, attention, memory, and motivation, especially affecting the developing adolescent brain.
- E-cigarettes have also been reported to explode and resulted in burn injuries and even deaths.
- Heavy use was associated with seizures in adolescents.
- E-cigarette, or vaping, product use-associated lung injury (EVALI) have resulted in 2,668 hospitalised cases in the US including 60 deaths as of 14 January 2020, mostly associated with cannabis-containing e-cigarettes

E-cigarettes – are they safer?

- Multiple studies have shown e-cigarette use may act as a gateway to conventional cigarette use.
  - A recent randomised controlled trial in the UK has found e-cigarettes more effective than nicotine replacement therapy in quitting cigarette smoking. However, 80% of subjects in the e-cigarette arm were stilling using e-cigarettes at 52-week follow-up and hence remained addicted to nicotine.