

From wheeze to Asthma and everything in between: PMG lecture

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Conflict of interest

- Past Chairman of



- Extra ordinary Lecturer

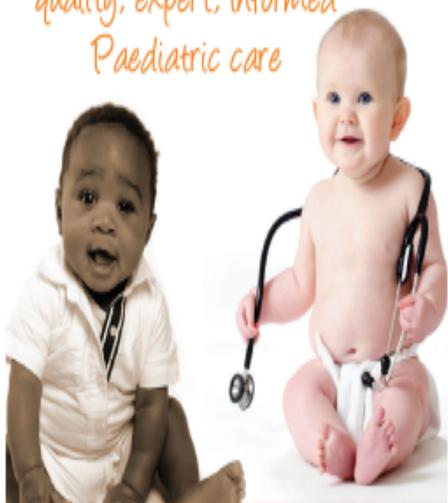


- Chairman -





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Vaccination Schedule 2019

10 YEARS
of excellence

Disease	Vaccine	Birth	6 weeks	10 weeks	14 weeks	6 months	9 months	12 months	15 months	18 months	6 years	9 years	12 years	
TB	BCG	●												
Polio	bOPV	●	●											
Hepatitis B	Heber-Biovac	●												
Diphtheria, Tetanus, Polio, Pertussis, Haemophilus Influenzae, Hepatitis B	Hexaxim OR Infanrix Hexa		●	●	●					●				
			8 weeks ●	12 weeks ●	16 weeks ●									
Pneumococcal	Prevenar 13 OR Synflorix		●	●	●		●	●	Nine and a half months					
Rotavirus	Rotarix OR RotaTeq		●	●	●									
Measles	Measbio OR Priorix					●		●	12 months Measbio not required if giving MMR					
Measles Mumps Rubella	OR MSD OMZYTA							●	MMR at 12 months instead of Measbio		●			
Chickenpox	OR Varilrix ONVARA							●			●			
												Give MMR and Varilrix or Onvara separately at 6 years if not using Priorix Tetra		
Measles Mumps Rubella + Chickenpox	Priorix Tetra	Priorix Tetra can be used at 12 months instead of Measbio, MMR and Varicella. Increased risk of febrile convulsion after the first dose of Priorix Tetra							●			●		
Meningococcal Conjugate	Menactra						●				For individuals 2-55 years administer 1 dose			
Hepatitis A	OR AVAXIM 80 Havrix Junior							●	Hep A with MMR not with Measbio		●			
Tetanus, Diphtheria, Pertussis, Polio	OR TETRAxIM Boostrix Tetra OR ADACEL QUADRA								Tetraxim at 6 years or Boostrix Tetra at 6 years Boostrix Tetra can be given at 12 years if not given at 6 years. Adacel Quadra at 12 years		●		●	
Tetanus, Diphtheria	Td										●		●	
Human Papilloma Virus	OR Cervarix GARDASIL	Cervarix from 9-14 years or Gardasil from 9-13 years as 2 doses 6 months apart State programme: Cervarix to Grade 4 girls in public schools 9-14 years. 2 doses 6 months apart										●		
Influenza	OR INFLUVAC VAXIGRIP	From 6 months, important for children in creche, chronic illness and respiratory problems. Start before the INFLUENZA season in MAY.												
Respiratory Syncytial Virus	SYNAGIS [®] PALVIZUMAB	RSV prophylaxis in high-risk infants-prevention of serious LRTI caused by RSV. Start January and end in May.												
Pneumococcal	PNEUMOVAX [®] 23 <small>(pneumococcal vaccine polyvalent, N/S/D)</small>	Must have at least one dose of Conjugate PCV before Pneumovax 23. Pneumovax only in children older than 2 years with Immune Compromise or high risk of Pneumococcal infection. Two doses with 2nd dose 3-5 years after first.												

● STATE EPI VACCINES These vaccines are available free from Government supplied clinics

● RECOMMENDED OPTIONAL VACCINES Some of the vaccines in this schedule are only available from private clinics

Outline

- Definitions
- What is it about –Asthma and Wheeze
-
- How do we manage them?
-
- What is in between?
- Costs in practice
- Conclusions

What is Asthma

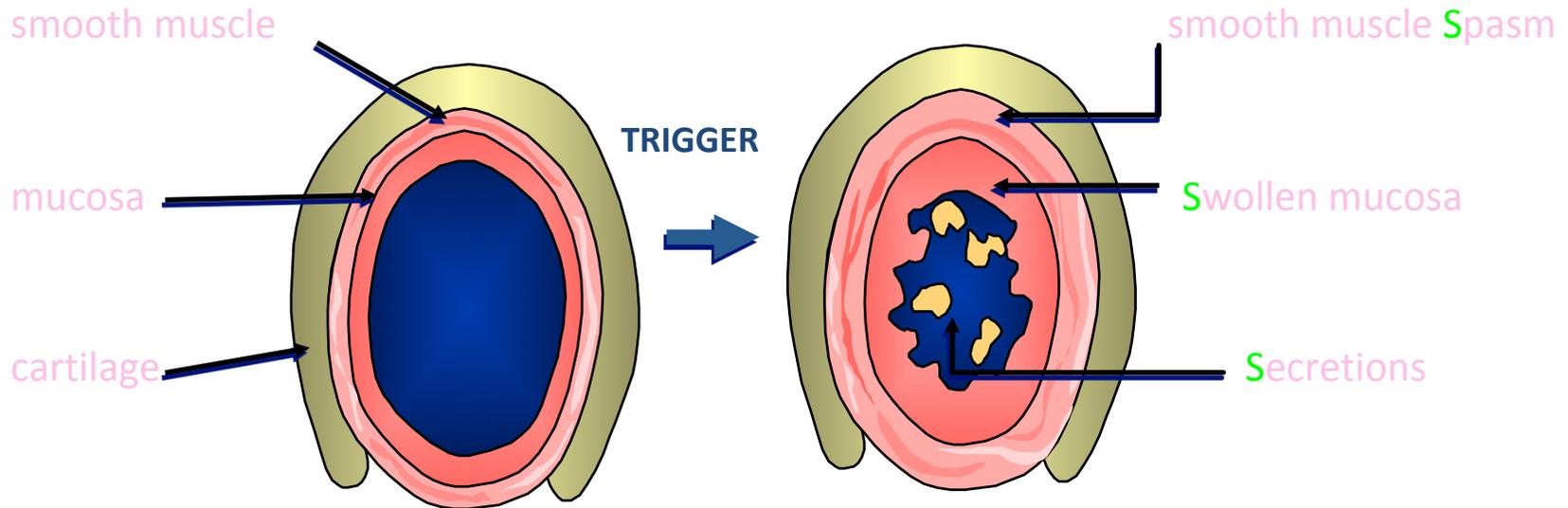
- Asthma as a heterogeneous disease (with different underlying disease processes) characterised by chronic airway inflammation
 - History of respiratory symptoms i.e. cough of variable time and intensity, tightness of the chest, wheeze and shortness of breath. These symptoms are worse at night or with viral infections, and trigger factors include exercise, allergens, emotions and cold air. Physical examination which is often normal but not limited to wheezing, a silent chest and at times signs of respiratory failure.
- Evidence of variable reversible airflow limitation.

AIRWAY INFLAMMATION

Cross-section of Normal Airway

Cross-section of Inflamed Airway

the 3 "S"s:-

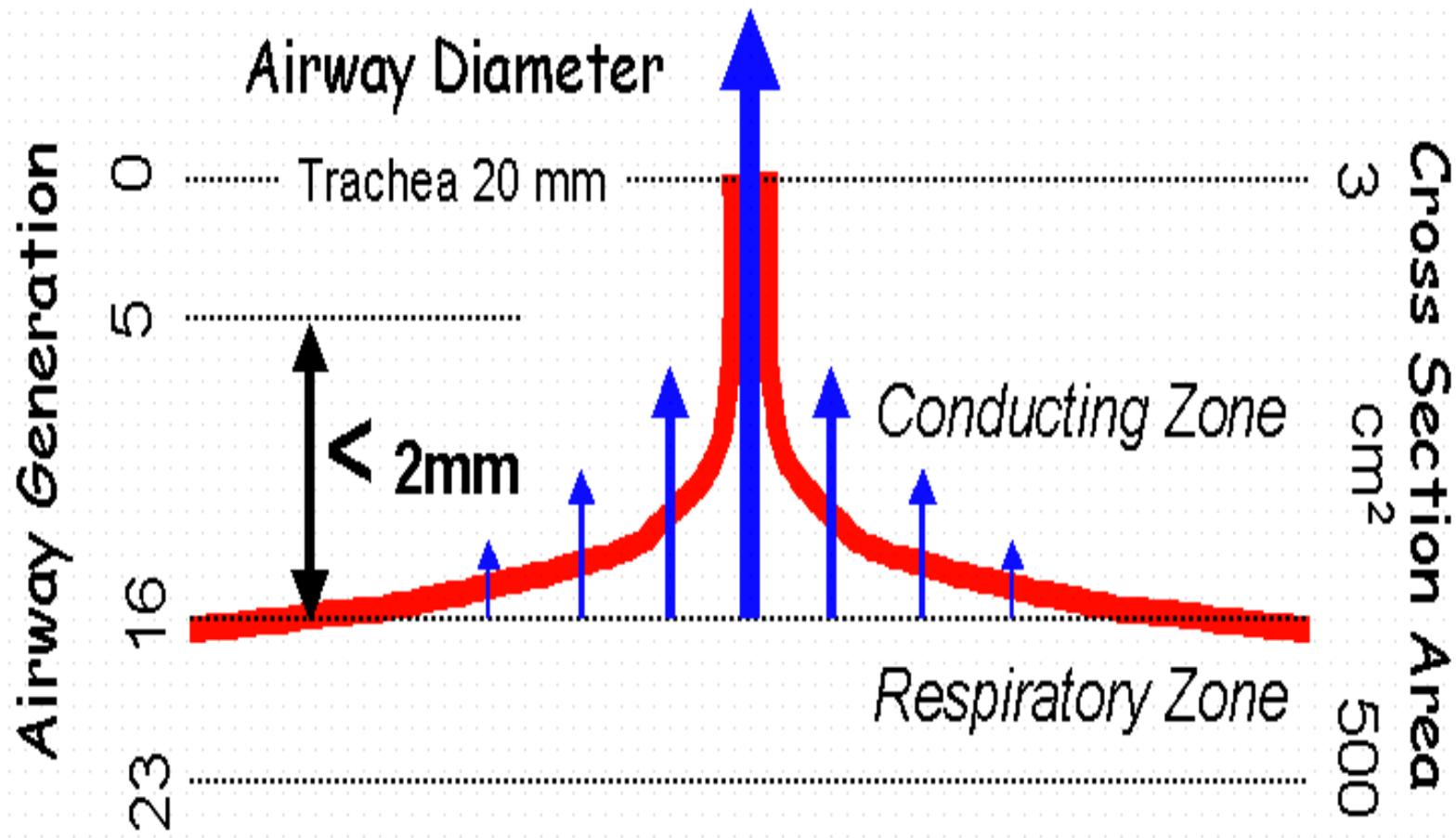


Airways become irritable and narrow

Cause of Wheezing

- Not from obstruction of small airways –
Surface area too large
- From increased intrathoracic pressure +
decreased large airway pressure =
vibration of airway wall in large airways
(Generations 1-5)

	Name	Division	Diameter (mm)	How many?	Cross-sectional area (cm ²)
Conducting system	Trachea	0	15-22	1	2.5
	Primary bronchi	1	10-15	2	↓
	Smaller bronchi	2	1-10	4	
		3			
		4			
		5			
		6-11		1 x 10 ⁴	
Bronchioles	12-23	0.5-1	2 x 10 ⁴	100	
Exchange surface	Alveoli	24	0.3	8 x 10 ⁷	5 x 10 ³
				3-6 x 10 ⁸	>1 x 10 ⁶



Air Trapping

- Hyper-inflated chest
- Barrel shaped
- Loss of cardiac dullness
- Liver pushed down
- Hoover sign

Hoover Sign

- Normal diaphragm movement
- Hyperinflation = diaphragm flattened
- Diaphragm contraction = paradoxical inward movement of lower intercostal area during inspiration

What is the prevalence of wheeze and asthma

- Asthma:
 - 1979- Rural 0.01% vs Urban 3.1%(7-9yrs)
 - 2003-Rural 9% vs Urban 15%
 - Currently worldwide:6-7yrs(11.5%), 13-14yrs(14.1%)
ISAAC III
- Wheeze:
 - 12month prevalence incr 16-20.3%
(CT),Polokoane-18%
 - <5yrs: ¼ persistent symptoms and develop asthma
 - Rhino-conjunctivitis incr wheeze by 107%

What are we doing wrong?

- Excellent: EML



World ranking

Prevalence -25th

Mortality- 4th

Case fatality-5th (18.5 per 100 000asthmatics)

Asthma is a chronic inflammatory disorder

Airway inflammation leads to

✓ **Hyper responsiveness** - responses to triggers



✓ **Obstruction** - usually fully reversible



✓ **Symptoms** – cough, wheeze, dyspnoea

✓ While symptoms are easily appreciated, symptoms are not the fundamental aspect of asthma

National Asthma Education and Prevention Program. Highlights of the *Expert panel Report 2*

Guidelines for the diagnosis and management of asthma. Bethesda, MD., Feb 2002 NIH
Publication No 02-3659

Risk factors

- Eczema
 - 30-50% of children develop asthma
 - SA-39%-Symptoms ISAAC questionnaire
 - 29% diagnosed by Dr
- Air pollution
 - KZN- 32% symptoms
 - 13-16.5%-Dr diagnosed
 - 21% Marked BHR on methacholine
- ETS

Diagnosis

- Asthma-clinical diagnosis
- Modified bronchodilator test
- Exercise challenge test
- Allergy testing



Asthma Diary

NAME

MEDICATION / DOSE

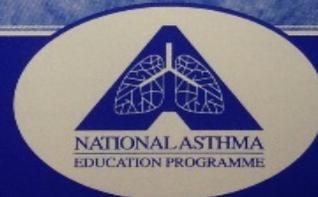
CONTROLLER / PREVENTER

RELIEVER / EMERGENCY PUMP

OTHER



SOUTH
AFRICAN
THORACIC
SOCIETY



NATIONAL ASTHMA
EDUCATION PROGRAMME



Initiate treatment

- Severity-RR incr req O2
- Freq -3 wheezes/yr symptoms>10days
- Association with allergens, worsening of symptoms @night
- Reversibility- Level D
- Positive fam history –atopy level B

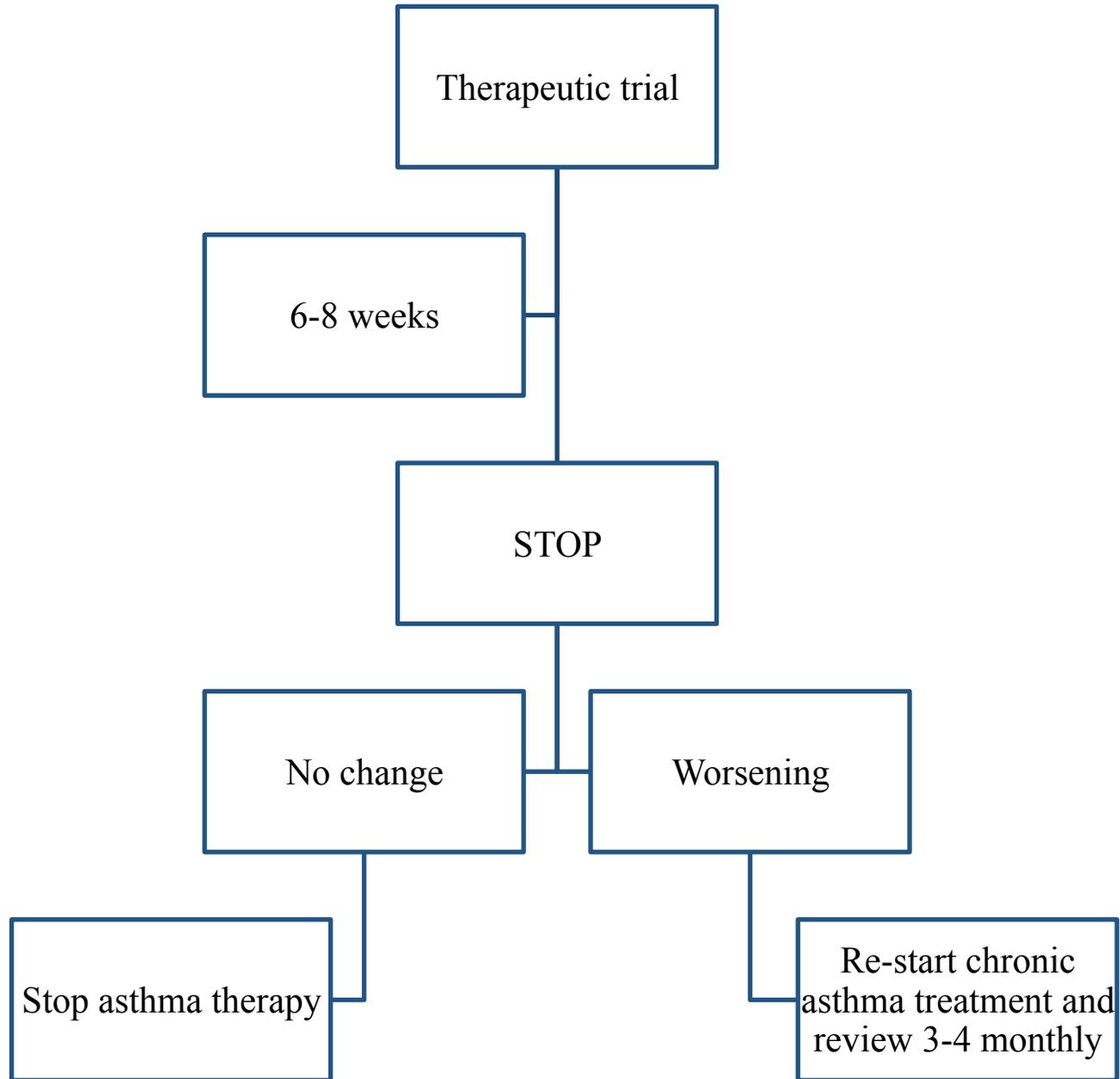


Table 2. Diagnostic characteristics of asthma in children <5 years of age and grade of recommendation*

Characteristics	Grade
Exercise-/activity-induced symptoms	A
Nocturnal coughing (problematic, with awakening)	
Symptoms persisting in children >3 years old	
Response to a bronchodilator (short-acting beta-agonist)	B
No seasonal variation in symptoms	
Viral colds with accompanying chest involvement	
Symptoms with specific trigger exposure, including emotional upsets (e.g. crying and laughing)	
Response to a short course of oral corticosteroids during acute exacerbation of symptoms	
Comorbid allergic rhinitis, proven food allergy and atopic dermatitis	
Absence of seasonal variation	
Wheezing lasting >1 month	C
A positive modified bronchodilator test	D

*Adapted from Global Initiative for Asthma.²⁴

Table 5. Asthma treatment options for children 2 - 5 years of age

Step 1	
Intermittent reliever therapy	SABA as needed
Step 2	
Low-dose controller and as-needed reliever medication	Low-dose ICS Intermittent ICS (second choice if seasonal symptoms) LTRA
Step 3	
Additional controller and as-needed reliever medication	Medium-dose ICS Low-dose ICS and LTRA
Step 4	
Refer to specialist (paediatrician, paediatric allergologist or paediatric pulmonologist)	

SABA = short-acting beta₂-agonist; ICS = inhaled corticosteroid; LTRA = leukotriene receptor antagonist.

Table 6. Asthma treatment options for children ≥6 years old

Step 1	
Intermittent reliever therapy	SABA as needed
Step 2	
Low-dose controller and as-needed reliever medication	Low-dose ICS
Step 3	
Additional controller and as-needed reliever medication	Low-dose ICS/LABA combination therapy (first choice) Medium-dose ICS (second choice)
Step 4	
≥2 controllers and as-needed reliever medication	Low-dose ICS/LABA and LTRA Medium-dose ICS and LABA Tiotropium (>12 years of age) – add to step 3 drugs Theophylline (>12 years of age)
Step 5	
Refer to specialist (paediatrician, paediatric allergologist or paediatric pulmonologist)	

SABA = short-acting beta₂-agonist; ICS = inhaled corticosteroid; LABA = long-acting beta₂-agonist; LTRA = leukotriene receptor antagonist.

Stepping down treatment once Asthma is controlled

Current step	Current medication and dose	Options for stepping down	Evidence
Step 5	High dose ICS/LABA plus oral corticosteroids (OCS)	<ul style="list-style-type: none"> • Continue high dose ICS/LABA and reduce OCS dose • Use sputum-guided approach to reducing OCS • Alternate-day OCS treatment • Replace OCS with high dose OCS 	D B D D
	High dose ICS/LABA plus other add-on agents	<ul style="list-style-type: none"> • Refer for expert advice 	D
Step 4	Moderate to high dose ICS/LABA maintenance treatment	<ul style="list-style-type: none"> • Continue combination ICS/LABA with 50% reduction in ICS components , by using available formulas • Discontinuing LABA is more likely to lead to deterioration 	B A
	Medium dose ICS /formoterol* as maintenance and reliever	<ul style="list-style-type: none"> • Reduce maintenance ICS/formoterol* to low dose, and continue as needed low dose ICS/ formoterol* reliever 	D
	High dose ICS plus second controller	<ul style="list-style-type: none"> • Reduce ICS dose by 50% and continue second controller 	B
Step 3	Low dose ICS/LABA maintenance	<ul style="list-style-type: none"> • Reduce ICS/LABA to once a daily • Discontinuing LABA is more likely to lead to deterioration 	D A
	Low dose ICS/formoterol* as maintenance and reliever	<ul style="list-style-type: none"> • Reduce maintenance ICS/formoterol* dose to once daily and continue as-needed low dose ICS/formoterol* relieve 	C
	Moderate-or high -dose ICS	<ul style="list-style-type: none"> • Reduce ICS dose by 50% 	A
Step 2	Low dose ICS	<ul style="list-style-type: none"> • Once -daily dosing (budesonide, ciclesonide, mometasone) 	A
	Low dose ICS or LTRA	<ul style="list-style-type: none"> • Consider stopping controller treatment only if there have been no symptoms for 6-12 months, and patient has no risk factors (Box 2-2, p17). Provide a written asthma action plan, and monitor closely. 	D
		<ul style="list-style-type: none"> • Complete cessation of ICS in adults is not advised as the risk of exacerbations is increased. 	A

Adapted from Pocket guide for asthma management and prevention for adults and children older than 5years (updated 2016). GINA guidelines.

Education

- Programmes-improve control, QOL, PFT, decr hosp:Level A
- Influence effective mod severe> mild mod asthma: Level A
- Written plans more effective than oral plans-Level A
- Follow up> Emergency-Level A
- Asthma action plan- no effect on PFT BUT: fewer night symptoms, ER visits, less rescue meds, less loss of time from work/school, better QOL: Level A

SA Certificate in Asthma Care

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March 2019

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A meta-analysis of montelukast for recurrent wheeze in preschool children

[Eur J Pediatr.](#) 2017 Jul;176(7):963-969

- Primary endpoint **examined was frequency of wheezing episodes**
- Five trials containing 3960 patients with a preschool wheezing disorder were analysed. Meta-analyses of studies of intermittent montelukast showed no benefit in preventing episodes of wheeze
- **CONCLUSIONS:**

This review highlights that the **currently available evidence does not support the use of montelukast in preschool children with recurrent wheeze**. It does not help preventing wheezing episodes or reducing unscheduled medical attendances

A specific montelukast responder phenotype may exist, but such patients should be sought in larger multicentre RCTs.

Stories doing rounds in practice

- Probiotics

Probiotic supplementation during pregnancy or infancy for the prevention of asthma and wheeze: systematic review and meta-analysis. [BMJ](#). 2013 Dec 4

OBJECTIVE:To evaluate the association of probiotic supplementation during pregnancy or infancy with childhood asthma and wheeze

CONCLUSIONS:

We found **no evidence to support a protective association between perinatal use of probiotics and doctor diagnosed asthma or childhood wheeze.**

Association between probiotic supplementation and asthma incidence in infants: a meta-analysis of randomized controlled trials. [J Asthma](#). 2019 Jan 18:1-12

OBJECTIVE:We performed a meta-analysis of RCTs to investigate whether probiotics are associated with a lower asthma incidence in infants.

CONCLUSIONS:

The use of probiotic supplementation compared with placebo **was not associated with a lower risk of asthma in infants.** These findings do not support recommendation to use probiotics in the prevention of asthma in infants.

- Vit D

Vitamin D for the management of asthma. [Cochrane Database Syst Rev.](#) 2016 Sep

OBJECTIVES: To evaluate the efficacy of administration of vitamin D and its hydroxylated metabolites in **reducing the risk of severe asthma exacerbations** (defined as those requiring treatment with systemic corticosteroids) and improving asthma symptom control.

AUTHORS' CONCLUSIONS:

Meta-analysis of a modest number of trials in people with **predominantly mild to moderate asthma suggests that vitamin D is likely to reduce both the risk of severe asthma exacerbation and healthcare use.** It is as yet unclear whether these effects are confined to people with lower baseline vitamin D status; further research, including individual patient data meta-analysis of existing datasets, is needed to clarify this issue. Children and people with frequent **severe asthma exacerbations were under-represented**; additional primary trials are needed to establish whether vitamin D can reduce the risk of severe asthma exacerbation in these groups.

- **Early life vitamin D status and asthma and wheeze: a systematic review and meta-analysis.**
[BMC Pulm Med.](#) 2018 Jul 20;18(1)

BACKGROUND:

Vitamin D deficiency has been linked to an increased risk of asthma. This study aimed to **quantify the effect of early life vitamin D status on asthma and wheeze later in life.**

CONCLUSIONS:

The pooled estimates from cohort studies show **no association between antenatal blood vitamin D level and asthma/wheeze in later life. Further trials with enough power and longer follow-up time should be conducted to confirm the results.**

- **Vitamin D and childhood asthma: causation and contribution to disease activity.**
[Curr Opin Allergy Clin Immunol.](#) 2019 Jan 2

To review the literature of the past 18 months (April 2017 through September, 2018) relating to vitamin D and childhood asthma.

SUMMARY:

Evidence continues to accumulate that **vitamin D supplementation helps to prevent the development of asthma and recurrent wheeze in early life**, and may also help in the management of asthma. The **level(s) of circulating vitamin D that maximizes these effects remains to be identified.**

- **Impact of two oral doses of 100,000 IU of vitamin D₃ in preschoolers with viral-induced asthma: a pilot randomised controlled trial.**

[Trials.](#) 2019 Feb 18;20(1):138

The objective was to ascertain the **efficacy of high-dose vitamin D₃** in increasing serum vitamin D in preschoolers with asthma and provide preliminary data on **safety and efficacy outcomes.**

Two oral boluses of 100,000 IU vitamin D₃, once in the fall and once in the winter, **rapidly, safely, and significantly raises overall serum vitamin D metabolites.** However, it is sufficient to maintain 25OHD \geq 75 nmol/L throughout 7 months in only slightly more than half of participants.

Asthma Treatment



CONTROLLERS

CONTROLLERS should be used every day - even if you are well and don't have any symptoms.

When used daily, controllers will control the inflammation in your lungs. By controlling the inflammation in your lungs, your symptoms (for example coughing, wheezing, a tight chest or waking at night) will become less and can even disappear.



ANTI-INFLAMMATORIES

Inhaled corticosteroids are the most effective controller treatment for asthma. Leukotriene receptor antagonists may be used as monotherapy in mild-moderate asthma and as add-on therapy (particularly for children under the age of 5 years).



LONG-ACTING BRONCHODILATORS

Long acting bronchodilators are never used on their own as monotherapy. They may be considered for step-up therapy for children older than 5 years, or adults where asthma is uncontrolled with corticosteroids.



COMBINATION MEDICATIONS

Combination products may be considered for step-up therapy for children older than 5 years, or adults where asthma is uncontrolled with inhaled corticosteroids.



RELIEVERS are only used when you have symptoms (as an emergency measure to open up a tight chest). If the inflammation in your lungs is not well controlled, your symptoms will increase. The number of times you need to use your reliever is, therefore, an indication of whether or not your chest inflammation is under control.

If you need to use a reliever more than twice a week, your asthma is not well controlled. Consult with your doctor about your medication and technique, to check if you are getting enough controller medication. If you are getting enough controller, your symptoms (for example coughing, wheezing, a tight chest or waking at night) will become less and can even disappear.

RELIEVERS



Our thanks to MSD for sponsoring artwork of this poster

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Website: www.asthmasa.org



Table 1. Differential diagnosis of wheeze in children <5 years of age*

Category	Disease entity
Congenital upper airway	Complete tracheal rings
	Tracheomalacia
	Laryngomalacia
	Vocal cord palsy/paresis
	Subglottic stenosis/post-intubation/ congenital
Congenital lower airway	Vascular rings/slings
	Bronchomalacia
Aspiration	Gastroesophageal reflux disease
	Swallowing inco-ordination
	Laryngeal cleft
	Tracheo-oesophageal fistula
Bronchiectasis	Cystic fibrosis
	Primary ciliary dyskinesia
	Persistent bacterial bronchitis
	Primary immunodeficiency
	HIV
Endobronchial lesions	Foreign body
	Tuberculosis granuloma
	Malignancies
Cardiac	Enlarged heart
	Congenital heart disease (left-to-right shunts)

*Adapted from White et al.¹²

Differential Diagnosis of asthma in children 6-11 years of age

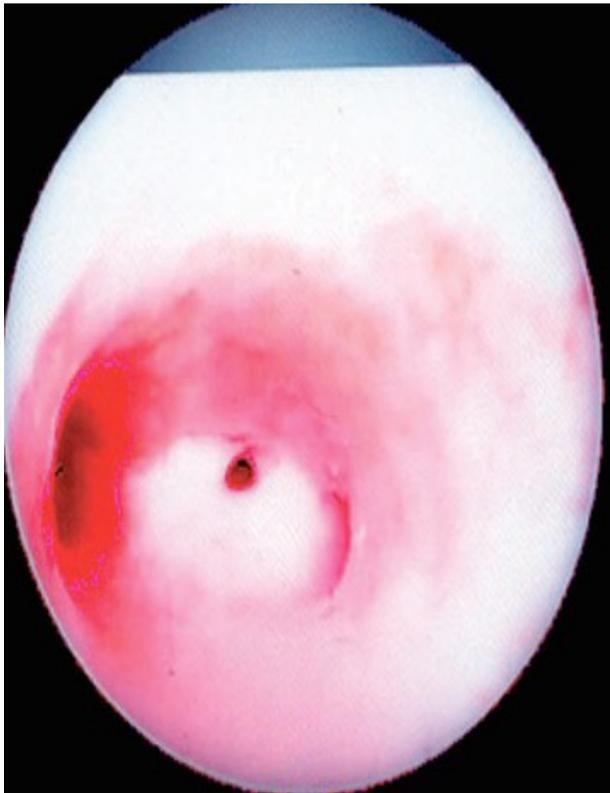
Condition	Symptoms
1. Chronic upper airway cough syndrome	Sneezing, itching, blocked nose, throat-clearing
1. Inhaled foreign body	Sudden onset of symptoms, unilateral wheeze
1. Bronchiectasis	Recurrent infections, productive cough
1. Primary ciliary dyskinesia	Recurrent infections, productive cough, sinusitis
1. Congenital heart disease	Cardiac murmurs
1. Bronchopulmonary dysplasia	Pre-term delivery, symptoms since birth
1. Cystic fibrosis	Excessive cough and mucus production, gastrointestinal symptoms

Adapted from Pocket guide for asthma management and prevention for adults and children older than 5years (updated 2016). GINA guidelines.

What is in between?

Bronchial Anomalies in VACTERL Association.

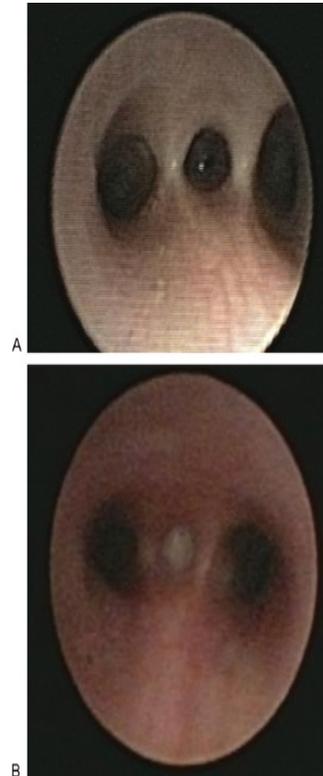
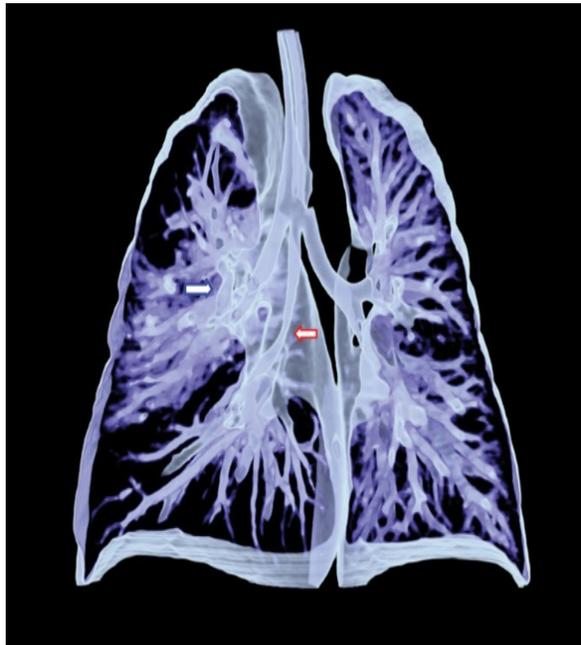
Adaobi Kanu, MD, David Tegay, DO, and Richard Scriven, MD. Pediatric Pulmonology
43:930–932 (2008)



Congenital trifurcation of the trachea.

[European J Pediatr Surg Rep.](#) 2014 Jun;2(1):35-7. doi: 10.1055/s-0033-1353367. Epub 2013 Sep 9

[Kiarash Taghavi](#) ET AL.



Costs

	LAB A	LAB B	LAB C
Multiplex PCR	R 2665.60	R 2180.00	R 3858.80
FBC	R 226.80	R 231.00	R 328.20
UE	R 346.00	R 355.00	R 500.60
CRP	R 192.50	R 196.00	R 278.60

Nebis in casualty- 7am-5pm R550
-5pm to 7am R950

CXR- 8am to 6pm R650
-6pm to 8am R 800



Conclusions

- Oral steroids: 0.5-1mg/kg for 3/7
- Start Rx and stop if no response
- Use age appropriate therapy
- All that wheeze is not asthma
- Think about costs
- Education, education, education
- Join NAEP and ask your patient to join