Childhood asthma: A best-practice strategy for diagnosis and assessment of control in South Africa

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The South African (SA) Childhood Asthma Working Group of the Allergy Society of SA (ALLSA) advises on best-practice strategy for childhood asthma management. The strategy is in accordance with current evidence and consensus. The aim of this review is to inform on a best-practice strategy for asthma diagnosis and the assessment of asthma control in SA children who attend public and private healthcare services. The diagnosis of asthma is more difficult in preschool-aged than school-aged children. This review proposes a four-step diagnostic approach in both groups, with an added obligation to objectively measure variable expiratory airflow limitation in school-aged children. Asthma control refers to the degree to which the effects of asthma can be seen in patients, or to which these have been reduced by treatment. After initiation of treatment, it is essential to assess asthma control at regular follow-up visits, and to adjust treatment accordingly. Patient education is key to attaining control.

S Afr Med J 2021;111(8):705-709. https://doi.org/10.7196/SAMJ.2021.v111i5.15851

Asthma should be diagnosed in children who present with episodes of variable expiratory airflow limitation. An accurate diagnosis relies on the clinical skills of the clinician. The clinical diagnosis should be supported by objective measurements, such as lung function testing, in school-aged children.

The symptoms of asthma may include episodic wheeze (owing to bronchoconstriction), shortness of breath, difficult or laboured breathing, chest tightness and reduced activity with or without cough. The intensity varies over time, and symptoms improve after a correctly administered rapid-acting inhaled bronchodilator.[1] More than one symptom is usually present. An isolated cough is seldom due to asthma. The variation in symptoms may be triggered by factors such as viral airway infections, allergens, irritants, cold air, exercise and sudden emotional changes (e.g. crying or laughing).

The symptoms are not specific to asthma, and other conditions may mimic the disease. Chronic airway inflammation with variable expiratory airflow limitation defines asthma. It is unfortunately difficult to directly measure airway inflammation and variable expiratory airflow inflammation in young children. Every opportunity should be exploited to define and demonstrate these two key features. The child should show clinical improvement after a correctly administered inhaled bronchodilator, or during a 2 - 3-month pragmatic trial of correctly administered inhaled controller treatment, with worsening of symptoms after treatment cessation, before asthma can be diagnosed. A four-step diagnostic approach is supported.

The four-step diagnostic approach in preschool-aged children

One in three children will wheeze before their third birthday. Young children are prone to recurring viral airway infections, with which wheeze can be associated. Deciding when this is an initial manifestation of asthma can be difficult. There are many other reasons for wheezing in preschool-aged children. Asthma must therefore be distinguished from these other causes. A practical approach is to follow four basic steps to distinguish asthmatic children from children who wheeze because of an alternative cause. These steps include: detailed history-taking; a clinical examination to exclude an alternative reason for wheezing; assessing inflammation; and seeking objective evidence of variable airflow limitation.

Step 1: Detailed history-taking

The history is often the most helpful instrument in diagnosing preschool-aged asthma. It should focus on two important aspects: a background history to signal the risk for the inception of asthma; and the history related to the wheeze episodes or 'chest events' themselves (Table 1).[2]

The inception of asthma is associated with a number of risk factors. The influence of the genome (e.g. parental asthma or asthma in first-degree relatives), epigenetic expression (e.g. caesarean section birth or maternal smoking during pregnancy), dysbiosis (e.g. with formula feeding and early antibiotic use), the early development of allergic sensitisation[3] and recurrence of wheeze associated with viral (or bacterial) airway infections are associated with an increased risk for the inception of asthma.[4] Early airway colonisation with encapsulated pathogens[5] and a past personal history of other allergic disease (such as atopic dermatitis or allergic rhinitis) also indicate an increased risk for the inception of asthma.

The history related to the wheeze episodes (or 'chest events') themselves provides helpful information with regard an asthma diagnosis. The decision to consider an asthma diagnosis, and to start controller therapy, is often primarily determined by:

- A history of variability of airflow limitation: Clinicians must make efforts, at every opportunity, to document the response to

Table 1. Features in history to support an asthma diagnosis, especially in preschool-aged children[2]

Feature	Characteristic suggesting asthma
Past or family history	Other allergic disease (atopic dermatitis or allergic rhinitis); asthma in first-degree relatives
Cough	Recurrent or persistent non-productive cough that may be worse at night or accompanied by some wheezing and breathing difficulties; cough occurring with exercise, laughing, crying or exposure to tobacco smoke in the absence of an apparent respiratory infection
Wheeze	Recurrent wheezing, including during sleep or with triggers such as activity, laughing, crying or exposure to tobacco smoke or air pollution
Difficult or heavy breathing, or shortness of breath	Occurring with exercise, laughing, or crying
Reduced activity	Not running, playing or laughing at the same intensity as other children; tires earlier during walks (wants to be carried)

Table 2. Alternative reasons for wheezing in children

Infective	Structural	Functional
Bronchiolitis	Tracheo- and bronchomalacia	Wheezy phenotypes
Atypical infection	Tracheal webs; tracheal and bronchial stenosis	Primary ciliary dyskinesia
Bacterial airway infection	Lymphadenopathy; tumours	Cystic fibrosis
Laryngotracheobronchitis	Vascular compression: • double aortic arch • innominate artery compression • left pulmonary artery sling • patent ductus arteriosus ligament • cardiac chamber or pulmonary artery enlargement	Gastro-oesophageal reflux disease
Protracted bacterial bronchitis	Cystic lesions and masses	Retained foreign body
	H-type tracheo-oesophageal fistula	Pulmonary oedema/cardiac disease
	Laryngeal clefts	Interstitial lung disease
		Bronchiolitis obliterans
		Bronchopulmonary dysplasia
		Bronchiectasis
		Immunodeficiency
		Perceived tight chest

a correctly administered rapid acting bronchodilator. A history of (preferably doctor-confirmed) bronchodilator responsiveness will support an asthma diagnosis.

- Severity of 'chest events': A history of more severe wheeze (e.g. with respiratory distress or a need for oxygen supplementation) will favour an asthma diagnosis but not exclude alternative diagnoses.
- Frequency and duration of episodes: Events that occur more frequently (>3 episodes per year) and that last longer (>10 days at a time) may indicate an asthma diagnosis, but will not exclude an alternative diagnosis.
- Temporal pattern of symptoms: 'Chest events' that do not only occur during airway infections, but also in response to other triggers in between infections, will support an asthma diagnosis. Events that persist >3 years of age, night-time worsening, an association with exercise or environmental change (e.g. cold air exposure) will further support an asthma diagnosis.

Step 2: Exclude an alternative reason for wheezing

The next step is to consider an alternative diagnosis for wheezing. This step is especially important at a younger age. The aim of the clinical examination is often not to find signs of asthma, but rather to document the presence or absence of atopic disease (atopic dermatitis, allergic rhinitis, etc.) and to seek clinical findings that would indicate an alternative diagnosis (e.g. digital clubbing, growth faltering, asymmetric wheeze, etc.) (Table 2).

Appropriate special investigations (chest X-ray, sweat chloride and contrast studies) may be needed to exclude an alternative diagnosis. A poor response to controller therapy will warrant referral to a specialist for specialised investigations such as bronchoscopy.

Step 3: Assessing inflammation

Asthma is characterised by chronic airway inflammation. Direct assessment of airway inflammation may not be practical, but indirect cues can inform an opinion on the nature of underlying airway inflammation. Biomarkers that predict asthma, and likely improvement on corticosteroid treatment, include markers of type 2 inflammation such as serum eosinophilia and aeroallergen sensitisation determined through antigen-specific IgE skin-prick testing or ImmunoCAP. Clinical findings of other atopic disease (e.g. atopic dermatitis and allergic rhinitis) may support an asthma diagnosis.

A pragmatic therapeutic trial will confirm the presence of corticosteroid-responsive inflammation. A step-wise trial of correctly administered low-dose inhaled corticosteroid (ICS) should be carried out when starting treatment in any child with a wheezing disorder. Any treatment given should be viewed as a therapeutic trial, and the initial treatment response must be evaluated in 6 - 8 weeks.[2,4,6,7] If there is no clinical response to correctly administered ICS therapy, this should be discontinued, and the child investigated further. Symptoms that resolve during ICS therapy may be due to the natural history of a preschool wheezing disorder or to an effect of treatment. This must

be distinguished by withdrawing treatment again. Treatment should only be restarted if symptoms recur. An ongoing benefit of ICS treatment should be reviewed every 3 months, and the ICS kept at the lowest possible dose for symptom control.[6-9]

Step 4: Seek objective evidence of variable expiratory airflow limitation

It is seldom possible to perform objective measurements on variable expiratory airflow limitation in young children. A clinical assessment of the response to correctly administered rapid-acting inhaled bronchodilator can be helpful. The clinician should pursue every opportunity to document improvement in wheeze and hyperinflation after the administration of a rapid-acting inhaled bronchodilator. The more it is confirmed clinically, the more likely that the correct diagnosis is asthma; and conversely the more it cannot be confirmed clinically, the more unlikely an asthma diagnosis will be.

Diagnosing asthma in school-aged children

For children >6 years of age, the same diagnostic steps should be followed. A proper history, exclusion of an alternative reason for wheezing and an assessment for inflammation should still be undertaken. Objective evidence of variable expiratory airflow limitation can now be demonstrated, and should ideally be investigated before commencement of controller therapy. Peak expiratory flow (PEF) measurements or preferably spirometry can be used (Table 3).[10] Normal tests do not exclude the diagnosis of asthma.[11] In the case that the history is suggestive of asthma, and the spirometry does not support the diagnosis, other specialised tests such as exercise bronchoprovocation or methacholine challenge may be done by a pulmonologist to confirm the diagnosis.

Assessment of asthma control and future risk

Asthma control means the extent to which the effects of asthma can be seen in the patient, or to which they have been reduced or removed by treatment.[2] Evaluation of asthma control includes two broad concepts, namely symptom control and future risk of adverse outcomes. Symptom control is assessed by frequency of symptoms, reliever medication use and activity limitation over the last week and month. Formal tools that provide scores to distinguish levels of symptom control (e.g. the Childhood Asthma Control Test (c-ACT) and Asthma Control Questionnaire (ACQ)) can offer insight into asthma control.[12] Future risk refers to the possibility of exacerbations, medication side-effects (oral symptoms and growth in children) or loss of lung function. No test is a gold standard, and all tests must be used in conjunction with a good history and clinical examination to assess control.[13,14] After initiation of treatment, it is essential to assess asthma control at every follow-up visit, no less than 6-monthly, and to adjust treatment accordingly.

Asthma control is significantly more likely in patients who are educated (know their disease), are regularly taught to use the inhaler device, are encouraged to use controller medication regularly and have a written action plan and educational material (www.allergyfoundation.co.za). It is important in patients with problematic severe asthma to distinguish between 'difficult asthma' due to poor adherence and/or incorrect inhaler technique and/or environmental or social factors, 'asthma plus' due to associated comorbidities, and true 'severe therapy-resistant asthma'.[15] If control is sub-optimal, check for all reasons, and educate the patient. A small number of patients need treatment adjustment (Tables 4 and 5).

Goals of asthma treatment

The long-term goals of asthma management include the following:

- to achieve good symptom control
- to maintain normal activity levels
- to minimise future risk of asthma-related mortality
- to reduce exacerbations
- to maintain lung function and normal lung development
- to minimise side-effects of treatment
- to provide a written action plan
- to consider the patient's own goals with regard to treatment

Table 3. Confirmation of variable airflow limitation with PEF or spirometry (adapted from Masekela *et al.*[10])

For PEF measurements
PEF variability with an average daily diurnal variability >13% when documented twice daily for 2 weeks
Positive exercise challenge test with decrease in PEF >15% after reaching target heart rate of 0.8 × 220 minus age in years
Excessive variation of PEF >15% between outpatient visits (using same equipment) with or without airway infections
For spirometry measurements
Decreased FEV_1/FVC ratio due to decreased FEV_1 (normal ratio >0.9)
Positive bronchodilator reversibility with increase in FEV_1 >12%
Positive exercise challenge test with decrease in FEV_1 >12% after reaching target heart rate of 0.8 × 220 minus age in years
Excessive variation of FEV_1 >12% between outpatient visits (using same equipment) with or without airway infections

PEF = peak expiratory flow; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity.

Table 4. GINA assessment of asthma symptom control in children aged 6 - 11 years, adolescents and adults

Symptom control	Well controlled	Partly controlled	Uncontrolled
In the past 4 weeks, has the patient had: • daytime asthma symptoms (wheeze, chest tightness, shortness of breath, cough) more than twice per week? • any night-time awakening due to asthma? • reliever (SABA) use more than twice per week? • limitation of activity – sport and school?	None of these	1 - 2 of these	3 - 4 of these

GINA = Global Initiative for Asthma; SABA = short-acting beta-2 agonist.

Table 5. GINA assessment of future risk of asthma in children aged 6 - 11 years, adolescents and adults

Measures of asthma control		Risk factors for poor asthma outcomes	
History	Uncontrolled symptoms (as in Table 4) (plus or minus symptom control scores e.g c-ACT, ACQ	-	Risk of exacerbations
	Exacerbations	≥1 severe exacerbation in last 12 months ICU (plus or minus intubation)	Risk of exacerbations
	Birth history	Preterm birth Low birth-weight Greater infant weight gain	Risk factors for development of persistent airflow limitation
	Past medical history	Bronchiolitis	Risk factor for development of persistent airflow limitation
	Medications	High SABA use	Risk of exacerbations
		Incorrect inhaler technique	Risk of exacerbations and persistent airflow limitation
		Poor adherence Inadequate ICS No ICS	Risk factors for local and systemic medication side-effects
		Frequent OCS Long-term, high-dose ICS	Poorly controlled asthma can affect growth (check child's height at least yearly) Growth velocity may be lower in the first 1 - 2 years of ICS treatment Local side-effect includes oral thrush
	Comorbidities	Obesity Chronic rhinosinusitis GORD Confirmed food allergy Obstructive sleep apnoea Pregnancy	Risk factors for poor asthma control Confirmed food allergy is a risk factor for asthma-related death
	Exposures	Tobacco smoke Allergen exposure if sensitised (e.g. house dust mite, cockroach, pets, mould) Indoor or outdoor air pollution	Risk of exacerbations
	Psychosocial	Psychological – depression, anxiety Socioeconomic – poor access to care, lack of education	Risk of exacerbations
Lung function tests	FEV_1 Measure at start of treatment, after 3 - 6 months of controller treatment, periodically thereafter	Low FEV_1	Risk of exacerbations and lung function decline
	FEV_1/FVC	FEV_1/FVC <0.90	Risk of exacerbations
	Persistent bronchodilator reversibility	Increase of FEV_1 >12% predicted	Suggests uncontrolled asthma Risk factor for adverse outcome
	PEFR	Short-term twice daily readings Average daily diurnal PEF variability >13% (day's highest – day's lowest)/mean of day's highest and lowest, averaged over 1 week	Suggests uncontrolled asthma and increases risk of exacerbations
	Additional tests although not routine		Risk of exacerbations
	FeNO	Elevated ≥35 ppb	
	Exercise challenge	Assess airway hyper-responsiveness and fitness Fall in FEV_1 >12%, PEF >15%	
Blood	Eosinophilia	-	Risk factor for persistent airflow limitation
Sputum	Eosinophilia	-	Risk factor for persistent airflow limitation

GINA = Global Initiative for Asthma; ICU = intensive care unit; c-ACT = childhood asthma control test; ACT = asthma control questionnaire; SABA = short-acting beta-2 agonist; ICS = inhaled corticosteroid; OCS = oral corticosteroids; GORD = gastroesophageal reflux disease; FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity; PEFR = peak expiratory flow rate; PEF = peak expiratory flow; FeNO = fractional exhaled nitric oxide.

The goals of asthma management can only be achieved through a good understanding between the patient/parent/caregiver and the medical team. A cycle of *assess* (diagnosis, symptom control, risk factor assessment, medication technique and adherence), *adjust treatment* (medications, non-pharmacological strategies, treatment of modifiable risk factors) and *review response* (medication effects and side-effects), in combination with education of both the parent/caregiver and the child with regard to effective inhaler use, adherence, symptom monitoring and a written personalised action plan, should be carried out at every visit. Medication should be adjusted up or down depending on the level of asthma control, and the lowest effective dose of ICS should always be sought.

Conclusion

The diagnosis of asthma in a child, especially at preschool age, can be complex, and should be considered in any child with recurrent episodes of wheeze and tight chest with or without cough that vary over time and improve after a correctly administered rapid-acting inhaled bronchodilator. Assessment of airway inflammation and objective evidence of variable expiratory limitation should be sought at every opportunity. Asthma control refers to the degree to which the manifestations and risk of asthma have been reduced by effective management, and should be assessed at every visit. Measuring control helps to determine whether treatment should be adjusted up or down or maintained. Patient education is key to attaining the goals of asthma management.

Declaration. None.

Acknowledgements. None.

Author contributions. Equal contributions.

Funding. None.

Conflict of interest. None.

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Accepted 2 June 2021.