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DIAGNOSIS AND MANAGEMENT OF ASTHMA IN PRESCHOOLERS: A CANADIAN THORACIC SOCIETY AND CANADIAN PAEDIATRIC SOCIETY POSITION PAPER

Developed by Dr. Dayae Jeong and Dr. Francine Ducharme for PedsCases.com.
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Introduction:

Hi everyone, my name is Dayae Jeong and I am a pediatrics resident at the University of Toronto. Today, we will be covering the Canadian Paediatric Society Position Statement titled “Diagnosis and management of asthma in preschoolers”.

This podcast was developed together with Dr Francine M. Ducharme, pediatrician, past co-chair of the Asthma Assembly of the Canadian Thoracic Society, and the first author on this statement.

After completing this podcast, the learner should be able to:

- 1) Define asthma and explain the importance of early diagnosis
- 2) Master the diagnostic criteria of asthma in a preschooler in the setting of either an acute exacerbation or a non-acute care visit.
- 3) Recommend appropriate asthma treatment strategies in preschool children
- 4) Understand when to consider a trial of cessation of asthma controller in preschool children

We will not be going into the detailed management of an acute asthma exacerbation. For this, please refer to the podcast titled “Acute Asthma Exacerbations”.

Asthma, and the challenge in preschoolers:

To start off, let’s clarify what asthma is, and why it is a challenging diagnosis in preschoolers.

Asthma is an inflammatory disorder of the airways characterized by episodic or persistent symptoms, such as dyspnea, chest tightness, wheezing, sputum production and cough. These symptoms are associated with airway hyper-responsiveness to endogenous and exogenous stimuli (such as allergens), and lead to variable degrees of airflow obstruction.

Diagnoses of asthma are typically made with pulmonary function tests. Unfortunately, these tests are difficult to complete in children less than 6 years old. This is an issue as most children with asthma will experience symptom onset during their preschool years. While up to 60% of children may outgrow their symptoms at school age, wheezing in these early years has been associated with airway remodeling and reduced lung function by 6 years of age. Moreover,

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preschool wheeze is still often associated with persistence or recurrence of symptoms into adulthood. Importantly, preschoolers have the highest rate of emergency room visits and hospital admissions from their asthma symptoms. So, it's clear that an early diagnosis is beneficial in this age group as it could avoid delays in treatment, reducing morbidity and maximizing lung function.

Historically, preschoolers have been diagnosed with asthma if they have suggestive symptoms or symptoms that predict asthma at 6 years of age (when they can perform spirometry), or by excluding alternate diagnoses. However, these approaches have suboptimal predictive values and are difficult to implement. As a consequence, several inappropriate labels such as “reactive airway disease”, “wheezy bronchitis” and “recurrent bronchiolitis” are often used, leading to a delay in or inappropriate treatment. These terms are unclear, sometimes incorrect, and should not be used.

So how do you diagnose asthma in preschoolers? We'll go over that next!

CPS Criteria for Asthma Diagnoses in Preschoolers:

The CPS diagnostic criteria for asthma in preschoolers can be broken down into:

- 1) Presence of airflow obstruction
- 2) Reversibility of airflow obstruction
- 3) Recurrent episodes (2 or more) of asthma-like symptoms
- 4) No other probable diagnosis

A personal or family history of atopy can heighten the suspicion for asthma, but is not necessary for the diagnosis.

Let's go through a few cases to work through the criteria.

CASE 1: Diagnosis in a child presenting with signs of airflow obstruction

You're working in the urgent care clinic and see Taylor, an 18-month-old girl coming in with “noisy breathing” according to her mother. She came in today because her mother felt that she was also breathing more quickly than usual. She has also had some nasal congestion for the past 3 days and a fever for one day.

So, what is the next step? First, you want to look for objective signs of airflow obstruction – wheezing is the most specific sign; other signs include decreased air entry to the lungs, tachypnea, prolonged expiration, accessory muscle use, hypoxemia, cough, and if very severe, an altered level of consciousness. If any of these are present, make sure to document them clearly in the medical chart: it will be useful for you and any physician to ascertain the diagnosis.

Getting back to Taylor, you find that she her oxygen saturation is 94% on room air. She is tachypneic with a respiratory rate of 35/min and has tracheal tug, otherwise known as suprasternal indrawing. On auscultation, she has expiratory wheeze diffusely with decreased air entry at the bases. It's clear that she has several signs of airway obstruction. You calculate Taylor's PRAM score, and get a total of 5 points, which corresponds to a moderate asthma exacerbation. The PRAM score components can be found in Appendix 1.

The next step is to assess whether the airflow obstruction is reversible with a short-acting-beta-agonist, with or without systemic steroids. SABAs like Ventolin have their peak

effect at 20 minutes, and you should expect to see a response after 1 dose in mild exacerbations and after 2-3 doses in moderate to severe exacerbations, provided the majority of the obstruction is secondary to bronchospasm. If there is a substantial contribution of airway inflammation and/or bronchial secretions, there may be a suboptimal response, as the SABA only acts on bronchospasm, not inflammation or secretions. In that case, you might see more improvement once the steroids start to take effect, usually within 3 to 4 hours. It is helpful to document improvement in symptoms with objective measures of airflow obstruction, such as the PRAM score or oxygen saturation. If using the PRAM score, a change of 3 points or more is clinically significant.

Because Taylor is older than 12 months, this episode of airflow obstruction could very well be an asthma exacerbation. But you need to first document reversibility with a therapeutic trial. Because her PRAM is 5, indicating moderate obstruction, you give her 4 puffs of Ventolin every 20 minutes for an hour and immediately start oral corticosteroids. When you assess her 60 minutes later, her PRAM is 4. You continue Ventolin and re-assess her 4 hours after the oral corticosteroids. By that time, she looks much more comfortable and her oxygen saturation is 96%. She is breathing at a rate of 22/min. She no longer has suprasternal retractions. She has occasional expiratory wheeze but good air entry. You recalculate her PRAM score and get 1. You document both her initial symptoms of airway obstruction and their reversibility in her chart.

It is important to verify that the medical history and physical exam do not point towards other diagnoses. For example, babies under 2 years of age with bronchiolitis can present with similar symptoms of fever, upper respiratory tract symptoms and wheeze or crackles. Importantly, a bronchiolitis wheeze does not respond to SABAs as there is no component of bronchoconstriction. If there was an acute onset of cough and wheeze with choking, you would need to rule out a foreign body aspiration. If there was stridor rather than wheeze, rule out an upper airway obstruction such as croup. Table 2 (Appendix 2) details more possible alternate diagnoses. However, keep in mind that, in the absence of suspicion for other diagnoses, you don't need to conduct investigations to rule them out.

In Taylor's episode, there are no indications that you need to consider these alternate diagnoses. The fact that her airway obstruction was responsive to a SABA and oral steroids is not consistent with bronchiolitis. The history of congestion and fever do point towards a viral respiratory infection being the trigger for this episode but whatever the trigger may be (whether it's viral, allergic, an irritant or temperature), a reversible obstruction suggests asthma.

You remember that a diagnosis of asthma requires at least 2 documented or convincingly reported episodes of both airflow obstruction and reversibility. In reviewing Taylor's chart and upon further questioning, this seems to be the first episode.

Your diagnosis for Taylor is 'suspected asthma'. You ask her to follow-up with her primary care physician who can monitor symptoms and pursue the diagnosis if necessary. If she develops a second episode of asthma-like symptoms that respond to SABA (or oral corticosteroids if it is a moderate or severe exacerbation), her physician will be able to confirm the diagnosis of asthma. If Taylor had had a previous episode with documented airflow obstruction or an episode with convincing parental report of symptoms of airflow obstruction, particularly with reversibility, you could have made the diagnosis of asthma on the spot today.

Because Taylor's symptoms were moderate (PRAM 5), you discharge her home with daily inhaled corticosteroids, ventolin as-needed for relief, good anticipatory guidance, and instructions to follow up with her family doctor in the next few weeks.

Of note, if Taylor had presented with a PRAM of less than 4, correlating with a mild exacerbation, you would have given a dose of SABA as a therapeutic trial in the ED and re-assessed her 20 to 30 minutes later to confirm reversibility. You would have discharged her with an as-needed SABA but no inhaled corticosteroid. A pathway detailing these steps can be found in Figure 1 in the CPS statement and in Appendix 4.

CASE 2: Diagnosis in children presenting without signs of airflow obstruction

Applying the diagnostic criteria can be a little less straightforward when you are seeing a child without an acute airflow obstruction. Let's move on to the next case.

After a busy night in the urgent care clinic, you're back at your pediatrics practice. Your next patient is Robbie, a 4 year-old who is here for a well-child visit. He's doing pretty well, but his dad mentions that he coughs a lot, enough to wake him up for at least 2 nights during colds during which he has also been making some wheezing noises. You verify what the father means by 'wheezing' and he describes a whistling sound, mostly on expiration. The night cough may drag for 1 to 2 additional weeks and the colds seem to occur every 4 to 6 weeks with the same pattern. Robbie went to the emergency room for his symptoms a few months ago at another institution, but you have no access to the medical chart. The father reports that the diagnosis was "wheezy bronchitis" and he was given a course of antibiotic and advice to go back to see you, your regular physician. When questioned about the response, the father admits that it took about 10 days for the symptoms to resolve, suggesting that the symptoms were unlikely to have been due to a bacterial infection.

On further questioning, Robbie has been coughing a bit when he runs or laughs a lot, which happens at least twice a week, even when he does not have a cold.

Like Robbie, many children who present in the non-acute ambulatory setting are not acutely ill. In this case, you can also suspect a diagnosis of asthma if:

- a) There have been 2 or more convincingly reported episodes with asthma-like symptoms, even if these were not documented by a health care professional
- b) The history and physical examination are not consistent with other diagnoses

In Robbie's case, you have a convincing report of wheezing with colds on more than 2 occasions, confirming airflow obstruction. Because he did not receive any asthma medication, you don't have documentation of reversibility. You have no suspicion of another diagnosis. You must document reversibility to confirm the diagnosis of asthma with a therapeutic trial of asthma medication over the next 3 months.

What agent to use for the therapeutic trial depends on the frequency and severity of symptoms. Recommended inhaled corticosteroids and their dosing for this age group are displayed in Table 5 of the position statement, also found in Appendix 3. Symptoms are deemed frequent, if they occur 8 days or more in a month or 2 days or more in a week, including during colds. Symptoms are considered moderate or severe if requiring systemic steroids or hospital admission.

Together with the symptoms during colds, Robbie has asthma symptoms at least 13-14 days per month which qualifies as “frequent”. Thus, he deserves a 3-month therapeutic trial with a medium dose of inhaled corticosteroid along with an as-needed SABA. The same trial would be applicable if he had visited the ED for a prior episode during which he received SABA and oral corticosteroids, indicating at least a moderate exacerbation.

Inhaled corticosteroids take 1-4 weeks to start working with a maximal effect after 3 to 6 months of continuous use. To be informative, the therapeutic trial should therefore be at least 3 months long, with good adherence and inhalation technique. Make sure you go over the proper inhaler technique and ask the parent or guardian to keep a diary of symptom frequency, rescue SABA use, functional limitations, acute care medical visits and hospitalizations, and steroid use for asthma to document response. As parents tends to stop medication when the child is better, often before the end of the 3-month trial, it is a good idea to see or call them at 6 weeks.

You give Robbie a prescription for Flovent 125 mcg twice a day (which is medium dose) and instruct his father to give it daily for 3 months. You also give him a prescription for Ventolin to take as needed. You insist on the importance of not stopping the orange puffer until the next appointment, even if the child is better or the appointment is delayed. You ask Robbie’s dad to keep a diary of symptoms and any hospital visits. You also make sure to go over the spacer technique.

A positive therapeutic trial is associated with a clear and consistent improvement in the frequency and severity of symptoms to confirm reversibility. Based on randomized controlled trials, the frequency and severity of symptoms usually improve by 40% within 3 months. If the improvement is unclear, despite good adherence and inhalation technique, and the child only displays mild and infrequent symptoms, one option is to stop the therapy and monitor for the possible recurrence of symptoms in the next 3 to 6 months. A recurrence of symptoms is diagnostic of asthma. If the trial is satisfactory but the outcome is still inconclusive, consider comorbidities and other diagnoses.

At the 3-month follow up visit, Robbie’s dad states that there has been a tremendous improvement with the daily Flovent that he has continued. His cough with effort and laughing now only occurs 2-3 times a month and with longer, more strenuous effort or laugh than before. Wheezing has disappeared and his cough responds very well to Ventolin, both at nighttime and with colds. He did not need any emergency room visits. You can confidently confirm the diagnosis of asthma in Robbie as you have a convincing report of recurrent episodes of airflow obstruction, convincing report of reversibility with asthma medication and no suspicion of another diagnosis.

Management:

Once a diagnosis of asthma is confirmed, there are both non-pharmacologic and pharmacologic strategies that can be implemented.

In terms of non-pharmacologic approaches, it is important to ensure an appropriate inhaler and spacer technique. If the child is 1-3 years old, he/she should use a spacer with a face mask, but once the child reaches approximately 4 years old, many can transition to a spacer with a mouthpiece. You should also counsel to avoid any possible irritants, such as cigarette smoke, wood heating, etc. and assess for possible environmental allergens.

In terms of pharmacological options, you want to identify the minimal effective dose of daily inhaled corticosteroids needed to maintain control of symptoms. Control is defined based on the Canadian Thoracic and Pediatric Society consensus statement, and more stringent criteria are used in preschoolers – as less than 8 days of symptoms per month (equating to <2 per week) instead of <4 days per week.

If a child has started a daily ICS as a therapeutic trial, it is important not to stop this after the trial period of 3 months if child's symptoms are controlled. As long as the child has asthma symptoms with their usual triggers that respond to a SABA, even if they are milder, they still have asthma.

Figure 2 in the CPS statement, found in Appendix 5, applies to a child with a diagnosis of asthma who is not yet on daily ICS. For example, after seeing a child in the ED with a PRAM of 3 (mild symptoms) with infrequent symptoms (<8 days/ week) who responded to a SABA alone, you can start therapy with just a SABA as needed and monitor the child. If the child has persistent symptoms, meaning that they occur 8 or more days a month, or on average 2 or more days a week, or has had a moderate to severe asthma-like episode needing steroids or hospital admission, they should be started on a daily inhaled corticosteroid. In that case, you can start with a low dose and increase the dose if the response is insufficient. In practice, we tend to start with a medium dose and step down because parents are usually poorly adherent (often taking half the prescribed doses) and actually give the equivalent of a low dose. Common inhaled corticosteroids and their doses can be found in Table 5 of the CPS statement, or Appendix 3.

The CPS/CTS statement does not recommend starting leukotriene receptor agonists in the context of a therapeutic trial because they are less effective than ICS and thus would increase the risk of not clearly documenting reversibility (leading to a false negative therapeutic trial). For the same reason, it should remain a second-line option for therapy. Also not recommended are increasing the doses of daily ICS at the onset of respiratory infection (an untested approach in preschoolers) or intermittent use of regular dose of ICS at the onset of a cold (not convincingly shown to reduce the severity of asthma exacerbations). In contrast, use of pre-emptive high-dose ICS at the onset of a cold is effective, but should be considered only if daily ICS fails, under the supervision of an asthma specialist.

Once the diagnosis is made, it is important to follow up and reassess asthma control frequently, every 3 to 4 months. If there is adequate control over 3 months despite exposure to a child's usual unavoidable triggers (such as respiratory tract infections or cold air), you could consider stepping down the dose of the ICS to the minimal effective dose and observe. A deterioration despite good adherence and technique, in the absence of a co-morbidity mimicking asthma symptoms and no suspected environmental triggers would call for stepping back up to a medium dose and perhaps investigation for the possibility of unidentified allergies.

There is a high rate of symptom resolution in preschoolers, with 50%-60% of children outgrowing their symptoms by age 6-8 years. So, if a child's symptoms have disappeared while on a minimal dose of ICS during the season when they are usually most symptomatic, this may mean that either the child is still asthmatic but perfectly controlled on a low dose of ICS or that he/she no longer has asthma. To distinguish one from the other, one should consider a therapeutic trial of cessation of ICS during the season when the child is usually most symptomatic, with a diary of symptoms and instructions to restart daily ICS if chronic or acute asthma symptoms recur (sometimes up to 12 months after cessation).

Since Robbie's asthma symptoms seem well controlled after the 3-month therapeutic trial, you step down his Flovent dosing to the "low dose" of 50 micrograms twice a day or 125 mcg 1 puff once a day. He gets through the next winter with no asthma exacerbations and well controlled symptoms, but you will maintain him on ICS until he has no more asthma symptoms and no need for rescue salbutamol during and between colds (typically this takes about 1-2 years). Only then, should you consider a trial of ICS cessation, perhaps next fall or winter.

Lastly, there are times when a patient should be referred to an asthma specialist for consultation or co-management. These include:

- 1) Diagnostic uncertainty or suspicion of comorbidity
- 2) Repeated (at least 2) exacerbations requiring rescue oral steroids or hospitalization, or frequent symptoms (at least 8 days a month) despite moderate daily doses of ICS
- 3) Life threatening events such as an ICU admission
- 4) Need for allergy testing to determine a role of environmental allergies
- 5) Other considerations like parental anxiety or need for further education

Summary:

And that's it for our podcast on diagnosing and managing asthma in preschoolers. To recap, here are some take home points:

- 1) It is important to diagnose preschool asthma as it can be associated with significant morbidity and impact on long-term lung function
- 2) Asthma can be diagnosed in preschoolers if there are recurrent (>2) episodes of airflow obstruction, with reversibility of the obstruction, and no clinical suspicion for an alternative diagnosis. This can be done if:
 - a. There are at least 2 episodes where both obstruction and reversibility have been documented by healthcare providers or convincingly reported by the parents
 - b. There are only one documented or convincingly reported episode of obstruction, with a convincingly reported response to a therapeutic trial of a medium dose of daily inhaled corticosteroid or to as-needed SABA for at least 3 months.
- 3) For the therapeutic trial, the choice of treatment depends on both the frequency and severity of symptoms:
 - a. If the symptoms are mild and infrequent, the trial could be started with an as-needed SABA only
 - b. If the symptoms are moderate to severe or frequent, the trial should be started with a daily ICS at the medium dose, as well as an as needed SABA
 - c. Emphasizing the importance of adherence to daily ICS (without stopping until the trial is completed), good inhalation technique and close monitoring of symptoms are keys to adequately interpreting a therapeutic trial.
- 4) After a diagnosis of asthma is confirmed, the choice of treatment to start depends on both the frequency and severity of symptoms while the patient was not on daily ICS:
 - a. If the symptoms are mild and infrequent, treatment can be started with an as-needed SABA only
 - b. If the symptoms are moderate to severe or frequent, treatment with a daily ICS is recommended, with as needed SABA. If satisfactory control has been achieved, a decrease to a low dose of ICS should be considered, aiming for the minimal effective dose. In case of suboptimal control after the dose reduction (assuming good adherence and inhalation technique, no co-morbidity mimicking asthma symptoms and no suspected environmental trigger), increasing to a medium ICS dose should be considered.

- c. Non-pharmacological strategies such as education on proper spacer technique, maintaining good adherence, and avoidance of environmental triggers is also important
- 5) Frequent follow up is important. 60% of preschoolers outgrow their symptoms by age 6-8 years, so the need for maintenance ICS dosing should be reassessed when symptoms seem to have disappeared particularly despite exposure to a child's usual unavoidable triggers.

Appendix 1

Signs	0	1	2	3
Suprasternal retractions	Absent		Present	
Scalene muscle constriction	Absent		Present	
Air entry*	Normal	Decreased at bases	Widespread decrease	Absent/minimal
Wheezing*	Absent	Expiratory only	Inspiratory and expiratory	Audible without stethoscope/silent chest with minimal air entry
O ₂ saturation	≥95%	92%-94%	<92%	

*If asymmetric findings between the right and left lungs, the most severe side is rated.

Figure from Chalut, D. S., Ducharme, F. M. & Davis, G. M. *The Preschool Respiratory Assessment Measure (PRAM): A responsive index of acute asthma severity. The Journal of Pediatrics* 137,762–768 (2000).

Appendix 2

Signs/symptoms* (red flags) suggesting an alternative diagnosis to asthma	Alternative diagnoses
Signs and/or symptoms	Alternative diagnoses
Persistent nasal discharge	Infectious/allergic rhinosinusitis [†]
Stridor; noisy breathing worse when crying, eating, supine or with respiratory infection	Upper airway narrowing: (200) Infection: croup, tracheitis (ii) Intrinsic: laryngomalacia, tracheal stenosis (iii) Extrinsic: vascular ring, tumour
Acute onset of cough, wheeze or stridor during eating or playing; history of choking, recurrent pneumonia in same location	Foreign-body inhalation Aspiration of food/gastric contents
First episode wheeze in child <1 year	Bronchiolitis [†]
Sick contacts, focal signs on chest radiograph	Pneumonia [†] , atelectasis [†] , tuberculosis, pertussis
Severe, paroxysms of cough, possibly initially associated with a 'whoop',	Pertussis
Premature birth, needed prolonged supplemental oxygen ± mechanical ventilation	Bronchopulmonary dysplasia
Symptoms since infancy, recurrent pneumonia, focal signs on chest radiograph	Congenital pulmonary airway malformation

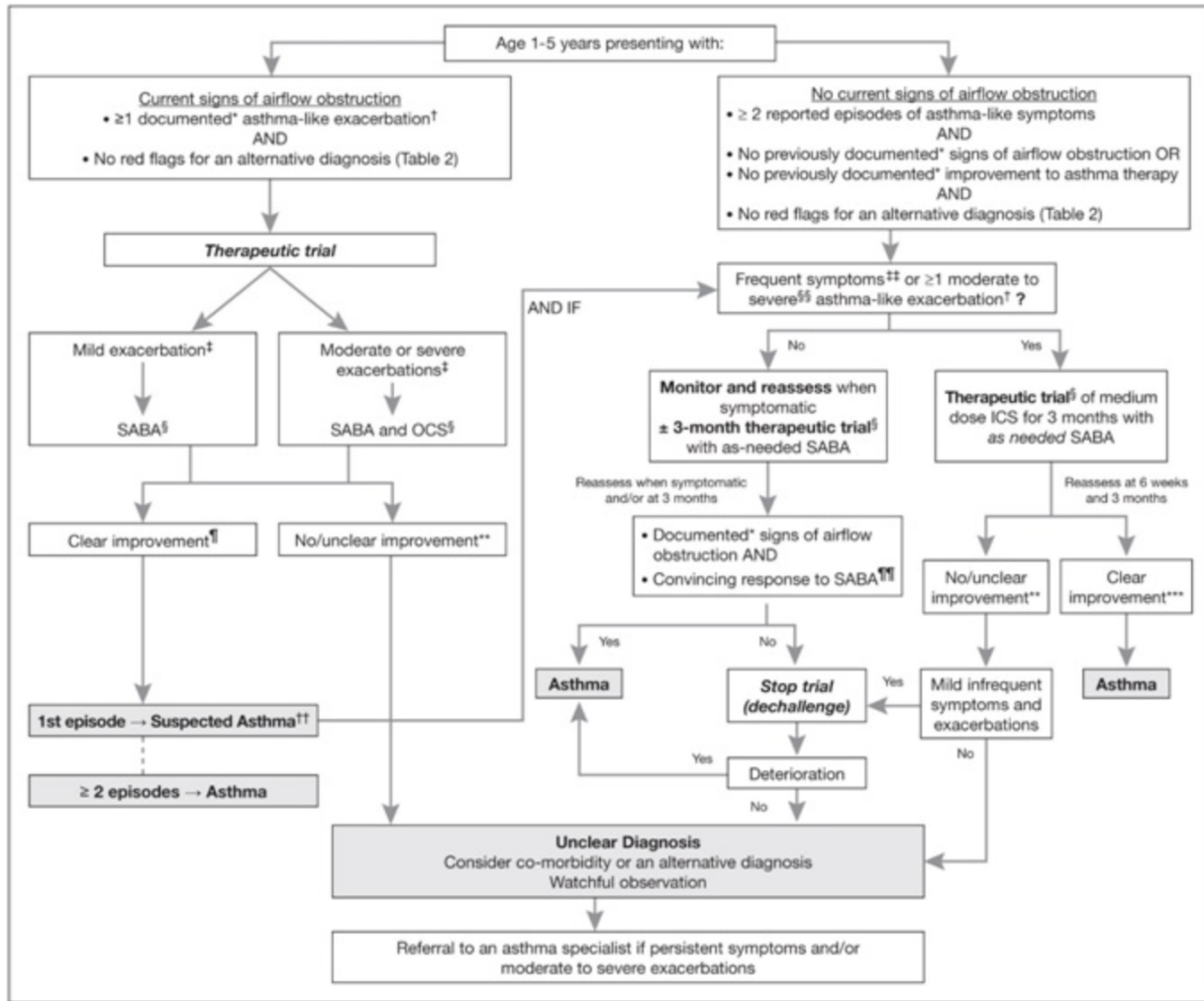
Chronic wet cough, clubbing, failure to thrive, recurrent pneumonia, onset in infancy, ± steatorrhea	Bronchiectasis, cystic fibrosis
Neonatal respiratory distress, early onset year-round daily cough and nasal congestion ± situs inversus	Primary ciliary dyskinesia
Cough when supine, when feeding; vomiting after feeding, abdominal discomfort	Gastroesophageal reflux disease [†]
Dysphagia, cough triggered by eating/drinking	Eosinophilic esophagitis
Feeding intolerance, wet cough or noisy breathing after eating	Swallowing problem ± aspiration
Recurrent, persistent, severe or unusual infections	Immune dysfunction
Cardiac murmur, cardiac failure, cyanosis when eating, failure to thrive, tachypnea, hepatomegaly	Pulmonary edema due to: (200) Acute myocarditis/pericarditis (ii) Congenital heart disease
<i>Nonexhaustive list of signs and symptoms suggestive of possible alternative diagnoses, prompting additional investigations and/or a different management in the preschool child. Symptoms and signs listed may overlap among different diseases; [†]Indicates the most frequent alternative diagnoses to, or comorbidities associated with, asthma</i>	

Appendix 3:

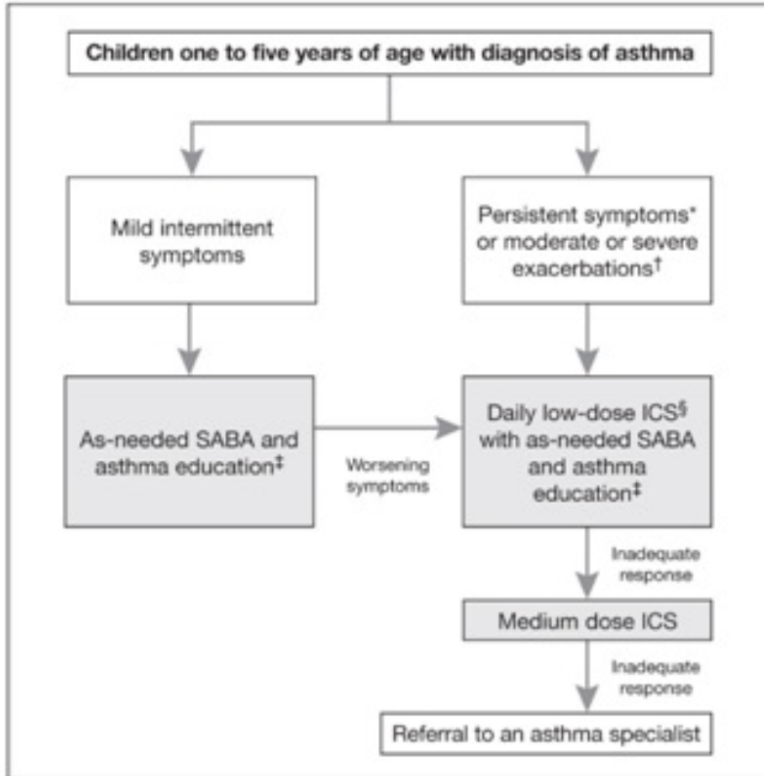
TABLE 5		
Inhaled corticosteroid (ICS) dosing categories* in children one to five years of age		
Corticosteroid (trade name)	Daily ICS dose, micrograms (mcg) [†]	
	Low	Medium
Beclomethasone (QVAR [®])	100	200
Ciclesonide [‡] (Alvesco [®])	100	200
Fluticasone (Flovent [®])	100-125 [§]	200-250

**Proposed dosing categories are based on a combination of approximate dose equivalency as well as safety and efficacy data rather than the available product formulations. Shaded area indicates that these medications are not approved for use in this age group by Health Canada with the exception of Beclomethasone (QVAR), which is approved for use in children ≥5 years of age. Because delivery by metered-dose inhaler is preferred, budesonide is not included in this table because it is only available for use by nebulization in Canada in children <6 years of age. High doses of ICS are not recommended in this age group and referral to an asthma specialist is suggested if asthma is not controlled on a medium dose of ICS; [†]The ICS doses are reported ex-valve as the total daily dose; they should be divided in half for twice-daily administration, except where indicated otherwise. ICS are to be administered by metered-dose inhaler with an age-appropriate valved spacer; [‡]Licensed for once daily dosing in Canada; [§]Fluticasone is not licensed for once-daily dosing in Canada but 125 µg once daily is sometimes used to improve adherence over twice-daily use of 50 µg*

Appendix 4:



Appendix 5:



References:

Ducharme, F. M. *et al.* Diagnosis and management of asthma in preschoolers: A Canadian Thoracic Society and Canadian Paediatric Society position paper. *Paediatrics & Child Health* **20**,353–361 (2015).

Chalut, D. S., Ducharme, F. M. & Davis, G. M. The Preschool Respiratory Assessment Measure (PRAM): A responsive index of acute asthma severity. *The Journal of Pediatrics* **137**,762–768 (2000).