

# WHEEZING IN INFANCY: IS IT ASTHMA?

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Wheezing is common symptoms throughout infancy and childhood except the neonatal period. Up to 25%-30% of infants have at least one episode of wheeze, half of whom have recurrent wheeze. Two-thirds of preschool wheezers stop wheezing by the age of six years. Although asthma is the common cause of recurrent wheezing in childhood, the younger the child the greater the chance that it is caused by other alternative diagnosis, for example, anatomical defect or other systemic conditions (Table 1).

## Diagnostic approach to infant wheezing

Essential steps in diagnosing wheezing infants should include history taking, physical examination and laboratory investigation. One should bear in mind that history is the most important part while

physical examination may be normal, and that laboratory test is often difficult to perform in young children. Any atypical features or presentations should be sought in detail in order to do not miss the unusual causes of wheezing.

### 1. History taking

Careful history taking could provide information to suggest cause of wheezing.

1.1 History favoring non-asthma: Onset of wheeze since birth or neonatal respiratory problems; History of choking associated with shortness of breath and cough; Very sudden onset of symptoms; Symptoms that change with position; Poor weight gain and recurrent infections; History of progressive dyspnea, exercise intolerance; Poor response to bronchodilators.

1.2 History favoring asthma: Onset after

Table 1  
Causes of recurrent wheezing in childhood.

Category	Diseases
Anatomical	Extrinsic compression <i>eg</i> , vascular ring, lymphadenopathy Intrinsic compression <i>eg</i> , foreign body, airways anomalies, bronchopulmonary dysplasia
Inflammation	Asthma, cow's milk protein allergy, chronic aspiration, gastroesophageal reflux
Infection	Bronchiolitis, respiratory syncytial virus ( RSV) infection, influenza, mycoplasma
Systemic diseases	Cystic fibrosis, immotile cilia syndrome, immune deficiency

one year of age, with intermittent or episodic pattern of wheezing; Wheezing triggers by multiple factors (eg, viral infection, exercise, smoking); History of clinical atopy or family history of asthma or atopy; History of nocturnal cough or diurnal variation of symptoms (that is, worse at night and early morning); and History of treatment response to bronchodilator.

## 2. Physical examination

Most children with asthma have no abnormal physical signs. The key features that help suggest non-asthmatic wheezing are clubbing of fingers, failure to thrive, adenoid hypertrophy, severe chest deformity, fixed monophonic or asymmetric wheezing, and clinical signs of cardiac or systemic diseases.

## 3. Investigations

Chest x-rays are not recommended to perform routinely on wheezy children. The indications to perform chest x-ray AP and lateral are severe persistent wheeze not responding to treatment, cyanotic or choking episodes, chronic wet cough, and those with poor weight gain. If a mass, vascular anomaly, or bronchiectasis is suspected, then a chest CT may be helpful. A barium swallow is recommended to confirm the presence of gastroesophageal reflux, swallowing dysfunction, or tracheoesophageal fistula.

### Wheezing phenotypes

Wheezing phenotypes in children may be classified into epidemiological or

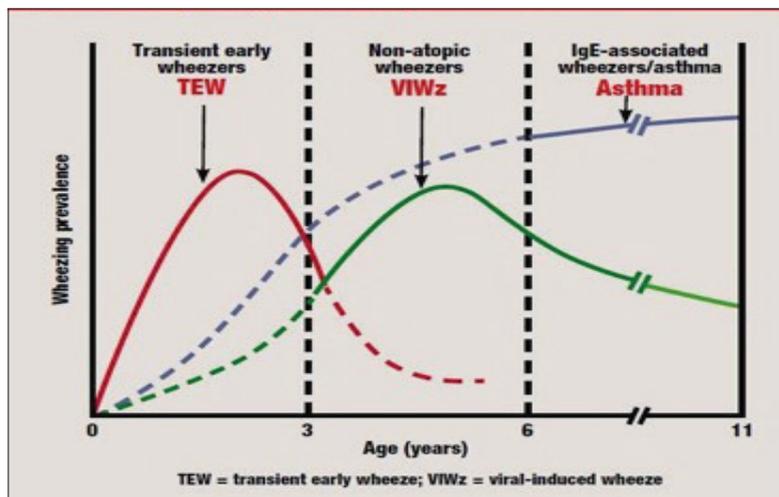


Fig 1–Wheezing phenotypes.

The criteria include  $\geq 3$  wheezing episodes per year

PLUS

1 major criteria

- Parental asthma
- Atopic dermatitis
- Inhalant allergen sensitization

OR

2 minor criteria

- Allergic rhinitis
- Wheezing apart from cold
- Eosinophilia  $\geq 4\%$
- Food allergen sensitization

Fig 2–The asthma predictive index.

symptom-based types. The Tucson Children's Respiratory Study (TCRS) on over 1,200 children found four groups based on epidemiological phenotype: never wheezing (51%), transient early wheezing (20%), late onset wheezing (15%) and persistent wheezing (14%). If we approach by the age of onset, it could be categorized into 3 groups as shown in Fig 1.

The transient early wheezer has its onset during the first two to three years of life and resolve by pre-school age. It is not associated with atopy or asthma but is linked to reduced lung function at birth, maternal smoking during pregnancy and daycare attendance.

A non-atopic wheezer or virus-induced wheezer usually develops symptoms in infancy, often with viral infection, and resolves by mid-childhood. It is not associated with allergy.

An IgE-associated wheezer, or asthma, peaks from six years onwards. Some children develop symptoms in early childhood. The patients who develop early onset usually have worse outcomes. There is an association with personal and family history of allergy.

### **Symptom-based phenotypes**

These are divided into two subgroups: episodic wheeze and multiple-trigger wheeze.

The episodic wheeze is usually triggered by viral infection. The child is well between episodes, and the conditions ceases by adolescent.

The multiple-trigger wheeze is usually triggered by many factors, such as virus, cigarette smoke, crying, laughing, or allergens. A child has wheezing during exacerbation and also between episodes. It is usually associated with an allergy.

### **Diagnosis of asthma**

The diagnosis of asthma in the long term largely depends on the degree of persistency. It is helpful to document reversible airflow obstruction in lung function, allergen sensitization, increased IgE, or blood eosinophil. Asthma predictive index

(API) is commonly used for the diagnosis of asthma (Figs 2,3). Children with a positive API are eight-times more likely to have asthma at 7 years of age than those with a negative index.

### **Case demonstration 1**

A one-month-old infant presented with noisy breathing and persistent wheezing 3 weeks earlier. The child was diagnosed as having cow's milk protein allergy and was advised to change formula to Nutramigen® by the general practitioner. Three days before admission, the child presented with coughing and fast breathing. Examination showed the body temperature to be 37°C, respiratory rate 52 per minute, and oxygen saturation of 97%. On auscultation of the chest, there were crepitations and wheezing bilaterally. The diagnosis of pneumonia was given and ceftriaxone, oseltamivir, oxygen headbox, nebulized adrenaline and ventolin started. The clinical condition worsened and required ventilator support. Chest x-ray is shown in Fig 4. The trachea and carina could not be identified. Subsequent bronchoscopy revealed a non-circular, narrow trachea suggesting that there was an external pressure effect. Computed tomography angiography (CTA) showed double aortic arch. Surgical procedure then followed.

### **Case demonstration 2**

A two-year-old boy presented with recurrent lower respiratory tract infections with wheezing. The first episode occurred at the age of 8 months and the second episode at 14 months, which responded to a bronchodilator. He had a past history of seborrheic dermatitis, atopy, and food allergies to eggs and possibly cow's milk. His mother has asthma and allergic

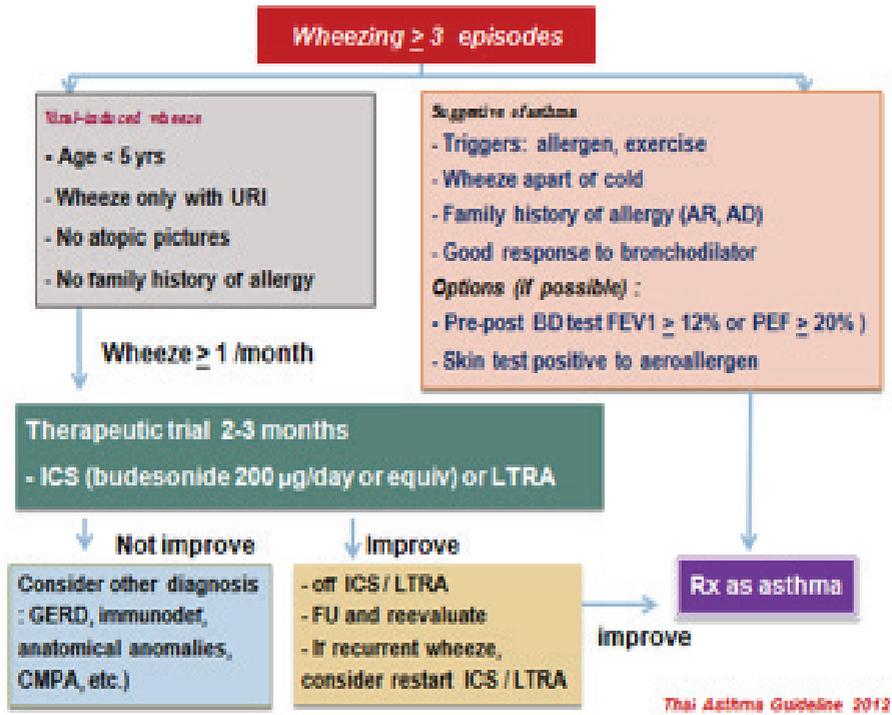


Fig 3–The Thai Asthma Guideline 2012. ISC, Inhaled corticosteroid; LTRA, Leukotrieme receptor antagonist.



A



B

Fig 4–One-month-old infant presented with persistent wheezing;(A) Chest x-ray: the trachea and carina could not be identified; (B) Computed tomography angiography (CTA) showed double aortic arch.

rhinitis. A working diagnosis of cow's milk protein allergy and asthma were given. The child was taken off cow's milk and started on budesonide MDI via spacer. Despite regular use of preventative medication, the child continued to have upper respiratory tract infections with wheezing, culminating in two hospitalizations.

On examination, he was active with weight and height being on the 25<sup>th</sup> and 60<sup>th</sup> percentile, respectively. Of note, there were mild chest retraction, minimal crepitations, rhonchi, and occasional wheeze bilaterally. Investigation revealed eosinophil of 6% and serial chest x-rays at 8 months, 14 months, 22 months; and 2 weeks prior to admission showed hyperinflation and perihilar infiltration. The important differential diagnosis was gastroesophageal reflux. A gastroesophageal reflux (GER) scan was done. The GER scan showed radiotracer accumulation in both bronchi. The diagnosis in this child was multiple high-grade GER with chronic aspiration. Treatment for GER including lansoprazole (Prevacid<sup>®</sup>) and domperidone (Motilium<sup>®</sup>) were prescribed. He subsequently could reduce the use of budesonide controller and also had no new episode of hospitalization.

In summary, wheezing in infancy can be a sign of various conditions. The diagnosis of asthma in infancy relies on detailed history and physical examination, which give clues to rule out other causes of wheezing and also identify risk factors for asthma. Episodic wheezing and multi-trigger wheezing are two major phenotypes of wheezing in young children, which have different prognoses. Therapeutic trial of asthma treatment is indicated in children with recurrent wheezing. A three-step

protocol is mandatory, stopping therapy if there appears to be a response and only restarting if symptom recurs.

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