DIAGNOSIS OF ASTHMA IN INFANTS

"Infantile asthma" Professional Council: Tran Minh Dien, Tran Van Ngoc, Nguyen Thanh Hung, Tran Anh Tuan, Nguyen Tien Dung, Le Thi Minh Huong, Nguyen Thi Dieu Thuy, Bui Binh Bao Son, Phan Huu Nguyet Diem, Pham Van Quang, Le Thi Hong Hanh, Phung Nguyen The Nguyen, Pham Thi Minh Hong, Nguyen Thanh Nam, Nguyen Minh Tien, Tran Quynh Huong, Nguyen Thuy Van Thao, Ho Thien Huong

I. INFANTILE ASTHMA - DIFFICULTIES AND INADEQUACIES IN DIAGNOSIS

The concept of asthma in infants (children under 24 months of age) began to appear in the late 1970s and early 1980s. However, there is currently no worldwide consensus on the definition and diagnostic criteria for asthma in infants.

In fact, the diagnosis of asthma in infants has some major difficulties as follows:

- Spirometry and other alternative respiratory function tests cannot be performed or are not specific enough for diagnosing asthma in infants.

- There are no specific inflammatory markers for asthma in this age group.

- Many children under 2 years of age only wheeze transiently, especially when infected with respiratory viruses, and about 60% are asymptomatic by the age of 6 years.[1],[2]

Due to the above difficulties and the lack of a "gold standard" for diagnosing asthma in this age group, the European Respiratory Society (ERS) has so far recommended avoiding the diagnosis of "asthma" in children under 6 years of age (but only using the term "wheezing").

However, most treatment guidelines in the world believe that there is no lower age limit for diagnosing asthma, even in children under 2-3 years of age ("infants").[3]

II. EPIDEMIOLOGY: INFANTILE ASTHMA - "TO BE OR NOT TO BE?"

One of the important points that many authors consider when talking about infantile asthma is that infants often have wheezing symptoms but the phenotype is different.

2.1. Wheezing phenotypes in children and asthma predictors

A cohort study from the Tucson, Arizona, USA pediatric respiratory study group showed that children have a wide range of wheezing phenotypes [1],[2],[12]:

- Early-onset transient wheezing: starts and ends before age 3 (20%)

- Early-onset, persistent wheezing: starts before age 3, continues until after age 6 (14%)

- Late-onset wheezing/asthma: starts after age 3, continues into adulthood (15%)

- No wheezing (51%)

Thus, 41% of children under 3 years old with wheezing will continue to have persistent symptoms after age 6 and are truly asthmatic according to current diagnostic criteria. [1],[2],[12]

Another cohort study by C. Delacours et al. at Necker Hospital - Paris (France) also showed the results similarly, 60% of children were asymptomatic and only 40% were truly persistent asthmatics at age 5. However, when followed up to age 9, 75% of children who were asymptomatic at age 5 had symptoms again at age 9 and 79% of children who had wheezed at age 5 were still symptomatic at age 9. The authors concluded that infantile asthma is an important risk factor for persistent asthma in children.[13]

From different cohort studies around the world, asthma predictors have been proposed such as API (Asthma Predictive Index), PIAMA (The Prevention and Incidence of Asthma and Mite Allergy), Leicester scale, of which the most popular is the modified Asthma Predictive Index (mAPI)[1],[2]. Many current asthma treatment

guidelines recommend using API to decide on the initiation of asthma prevention treatment for children aged 0-4 years.

2.2. Is infantile asthma really common?

The exact prevalence of infantile asthma is unknown, but according to many studies around the world, the prevalence of asthma in infants ranges from 10%: 7.5% (Herr M, France - 2007), 13.6% (Japan - 2003), 16.9% (Australian Institute of Health and Welfare - 2009), 19.6% (Rothenbacher D, Germany - 2005).[8],[9]

In Vietnam:

- Nguyen Viet Co (2002) when studying asthma in children under 5 years old in Soc Son (Hanoi) and Quang Xuong (Thanh Hoa), recorded 78.9% of children started having symptoms at the age of under 12 months, 14.8% started at the age of 12-24 months.[10]

- At Children's Hospital 1 and Children's Hospital 2 (HCMC), children under 2 years old accounted for 20-30% of children visiting the asthma clinic.

2.3. Delay in diagnosing infantile asthma and its consequences

The lack of a unified diagnostic standard has made late diagnosis common in infantile asthma. According to Levy N (1984), 86.5% of asthma in children started before 24 months of age, but only 36% of these children were diagnosed with asthma.6 Hessel PA (1996) recorded that 20.2% of asthma in children in Alberta - Canada started before 12 months of age.7 At Children's Hospital 1 (HCMC) (2005), 28.4% of hospitalized infants with asthma were diagnosed late [14].

The lack of diagnosis of asthma in practice leads to the use of many unclear, inappropriate or ambiguous diagnostic terms ("viral wheezing", "wheezing bronchitis", "recurrent bronchiolitis", "spastic bronchitis", "allergic bronchitis", "asthmatic bronchitis", etc.). The inevitable consequence is that many children with true asthma do not receive early, appropriate treatment, increasing the burden of disease.

Indeed, infants are at the highest risk of emergency room visits, hospitalizations, and death from asthma compared to other age groups.

- In France (2004-2006), the number of days hospitalized for asthma in children under 36 months of age accounted for about a quarter of the number of days hospitalized for asthma in all ages.[11]

- At Children's Hospital 1 (2017), the rate of hospitalization for asthma in children under 2 years of age was three times higher than the rate of hospitalization for asthma in children over 2 years of age (9.5% compared to 3.3%).

In addition, wheezing in early life adversely affects the development of the lungs and respiratory function of children later in life. This is an early indicator of respiratory dysfunction at age 6, which often persists into adulthood, as well as airway remodeling, and is even associated with chronic obstructive pulmonary disease in adults later in life.[4],[5]

III. HOW IS INFANTILE ASTHMA DEFINED?

According to Tabachnik E and Levison H (1981): it is considered infantile asthma when a child has episodes of difficulty breathing with wheezing occurring at least 3 times in the first 2 years of life, regardless of the age of onset, the presence or absence of triggers, or the presence or absence of personal and family allergic background.[16]

However, currently, there is no worldwide consensus on the definition and diagnostic criteria for asthma in infants.

With GINA, so far, it has only mentioned the possibility of diagnosing asthma in children under 5 years old depending on the number of episodes and duration of symptoms (cough, wheezing, difficulty breathing) during upper respiratory infections, as well as the child's condition between episodes, taking into account the child's and family's allergic background.

Table 1. Definition of infantile asthma according to international recommendations

Author	Definition
Tabachnik E, Levison H (1981)[16]	Dyspnea + wheezing ≥ 3 times/ < 2 years Regardless of: age of onset, atopy, triggers
PRACTALL (2008)[17]	Consider diagnosis of asthma if there is evidence of > 3 episodes of reversible bronchial obstruction in the previous 6 months
French Society of Pediatric Allergy and Respiratory Sciences (SP2A) (2009)[11]	Diagnosis according to the definition of Tabachnik and Levison
NAEPPEPR3 (USA) (2013)[5]	No clear definition. But it is recommended that children aged 0-4 years with 4 episodes of wheezing/year (each lasting more than 24 hours) should be treated to control asthma.
Canadian Thoracic Society and Canadian Pediatric Society (2015-202) [4],[18]	Diagnosis criteria for asthma in children aged 1-5 years: • Evidence of airway obstruction: wheezing confirmed by a doctor or trained health care professional • Evidence of reversible airway obstruction: ▪ Improvement in signs of obstruction with SABA ± OCS ▪ Response after 3 months of trial treatment with medium dose ICS (± SABA as needed) • No clinical evidence of other diagnosis

Therefore, in 2023, the Vietnam Pediatric Association in collaboration with the Ho Chi Minh City Respiratory Association organized an Expert Council to compile "Guidelines for diagnosis and treatment of infantile asthma" with the following main contents

IV. DIAGNOSIS OF INFANTILE ASTHMA

4.1. Diagnosis of infantile asthma [4],[11],[17],[18],[20]

Diagnosis is mainly clinical, suggested by medical history.

There is no specialized routine diagnostic test.

4.2. Criteria for diagnosing infantile asthma [4],[17],[18],[20]

1. Evidence of airway obstruction: wheezing 3 or more times. Wheezing must be confirmed by a doctor, preferably by stethoscope (wheezing, snoring)

2. Response to asthma treatment

3. No evidence suggesting other diagnoses

Note that wheezing symptoms must be evidenced and confirmed by a doctor (abnormal breathing sounds with a low pitch, best heard at the end of expiration if listening with the bare ear, or wheezing - snoring if listening with a stethoscope).

Subclinical tests: not performed routinely and the indications must be appropriate to the condition of each child and the capabilities and conditions of the medical facility. In which, a straight chest X-ray is recommended for all children to rule out other diagnoses.

Always consider other differential diagnoses.

Monitoring and evaluating response to treatment: will strengthen the diagnosis of asthma.

- Bronchodilator test: perform when the child shows signs of airway obstruction (wheezing, difficulty breathing) to assess the reversibility of this airway obstruction. Correct procedures must be followed for accurate assessment [19,20]:

• Bronchodilator dose:

o Salbutamol nebulization: 2.5 mg/time, or

o Salbutamol MDI with spacer and mask: 4 puffs (100 mcg/puff)

• It can be repeated a second time after 20 minutes.

• The child needs to be assessed by the same person at the following times: before, during and after nebulization

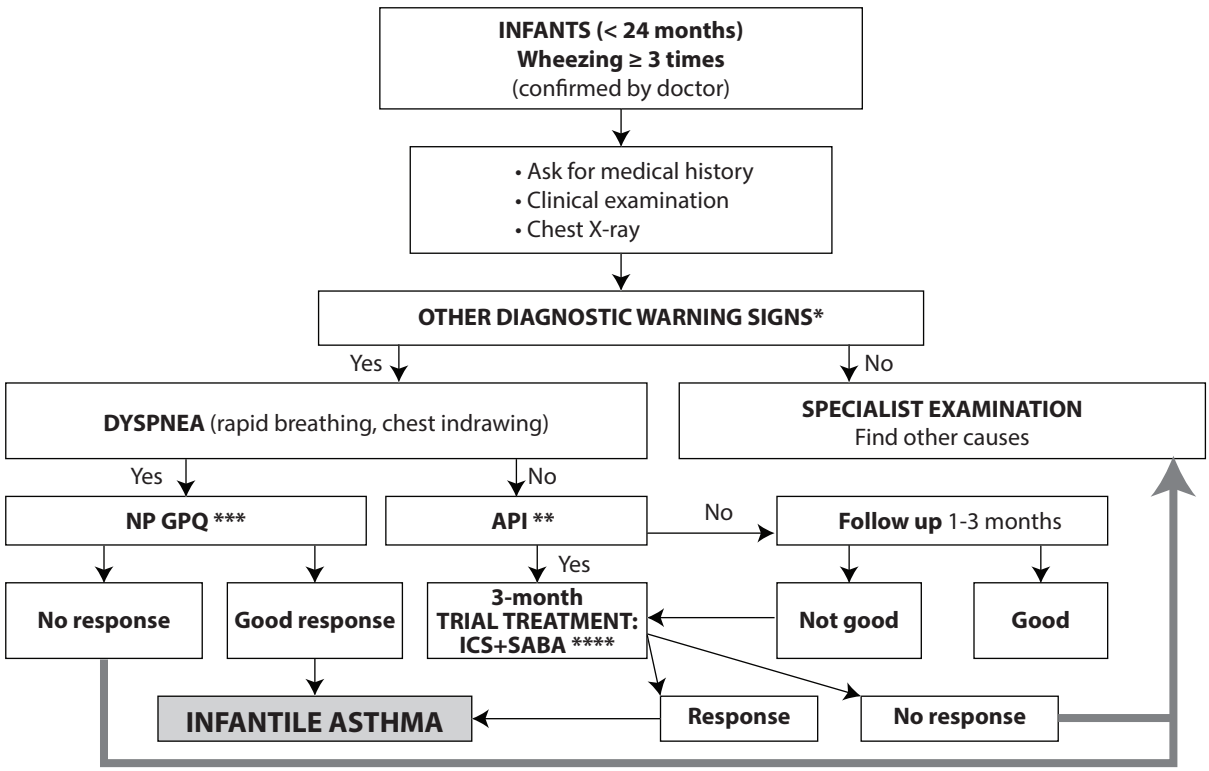
• Assess the child's response at 30 minutes, 60 minutes: need to be comprehensively assessed:

It is best to rely on respiratory scores: for example, PRAM (Preschool Respiratory Assessment Measure) score, there is a response when the score decreases ≥3[19]

In practice, rely on: perception, vital signs (pulse, breathing rate), accessory respiratory muscle contraction, ventilation (alveolar murmur), pulmonary rales, wheezing, SpO_2.

- Response to trial treatment with medium dose ICS for 3 months (± SABA when needed): when the child has no clinical signs of airway obstruction, especially when mAPI is positive [4],[18],[20].

4.3. Flow chart for diagnosing infantile asthma



*** OTHER DIAGNOSTIC WARNING SIGNS**

Early onset wheezing (especially in newborns)
Biphasic wheezing/stridor
Continuous wheezing
Wheezing with vomiting or related to meals
Special conditions: severe malnutrition, chromosomal abnormalities, congenital heart disease, neuromuscular disease, congenital esophageal atresia, thoracic malformations

**** ASTHMA PREDICTIVE INDEX (API)**

1 MAIN CRITERIA
- Parents with asthma
- Eczema (diagnosed by a doctor)
- Sensitivity/allergy to inhaled allergens

or

2 SECONDARY CRITERIA
- Sensitivity/allergy to milk, eggs, peanuts
- Eosinophil/blood ≥ 4%
- Wheezing not related to cold

***** BRONCHODILATOR TEST**

Salbutamol:
- Nebulization: 2.5 mg/time or
- MDI+ spacer +mask: 4 puffs (100 mcg/puff)

It can be repeated a second time after 20 minutes. Assess response after 30-60 minutes. It must be assessed by 1 person: before - during - after test

ASSESSMENT OF RESPONSE (after 30 min, 60 min)

Improved general condition
Improved vital signs (pulse, respiratory rate)
Reduced use of accessory respiratory muscles
Improved alveolar murmurs
Reduced wheezing
Improved SpO_2

****** TRIAL TREATMENT WITH ICS**

Dose: medium dose.
Evaluate technical factors to choose: (MDI + mask + spacer) (preferred) or nebulization
Evaluate response: after 3 months

4.4. Differential diagnosis of infantile asthma

Not all wheezing children have asthma. It is important to note the warning signs that are not consistent with asthma and some important differential diagnoses below.[4],[15],[20],[21]

- Wheezing appears immediately after birth
- Children vomit excessively
- Children do not grow, are slow to grow or are malnourished
- Examination: there are rales or decreased breath sounds in a localized area or only one lung; there is accompanying wheezing, difficulty swallowing, heart murmur, clubbing of fingers.

When children have any other warning signs of diagnosis, they need to be examined by a specialist for in-depth examination, testing, and exploration to rule out other diagnoses.

Table 1.2. Diseases that need to be differentiated from asthma

Acute	Respiratory infections: bronchiolitis, pneumonia Airway foreign bodies
Chronic	
- Structural abnormalities	Tracheobronchial abnormalities: tracheobronchial chondromalacia Cardiovascular system abnormalities: - Congenital heart disease with pulmonary hypertension - Pulmonary artery rings or slings Mediastinal tumors: bronchial cysts, thymoma, lymphadenopathy
- Functional abnormalities	Aspiration syndrome: forgotten airway foreign body, gastroesophageal reflux, swallowing disorders, tracheoesophageal fistula Abnormalities of the body's resistance: primary immunodeficiency (IgG, IgA deficiency), primary ciliary dysfunction Cystic fibrosis Bronchopulmonary dysplasia Interstitial lung disease Post-infectious bronchiolitis obliterans Prolonged bacterial bronchitis

V. CONCLUSION

Of course, like any other clinical approach, there is a possibility of overdiagnosis of asthma in infants. But considering the negative short-term and long-term effects of asthma when not properly diagnosed and treated, a clinical approach to diagnosing infantile asthma still has many advantages, both short-term and long-term.

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