Asthma differential diagnosis

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A comprehensive approach to one of the most common respiratory symptoms in pediatrics

Prevalence of Wheezing

1/3

Children under 3

Experience at least one acute wheezing illness

26%

Ages 2-3

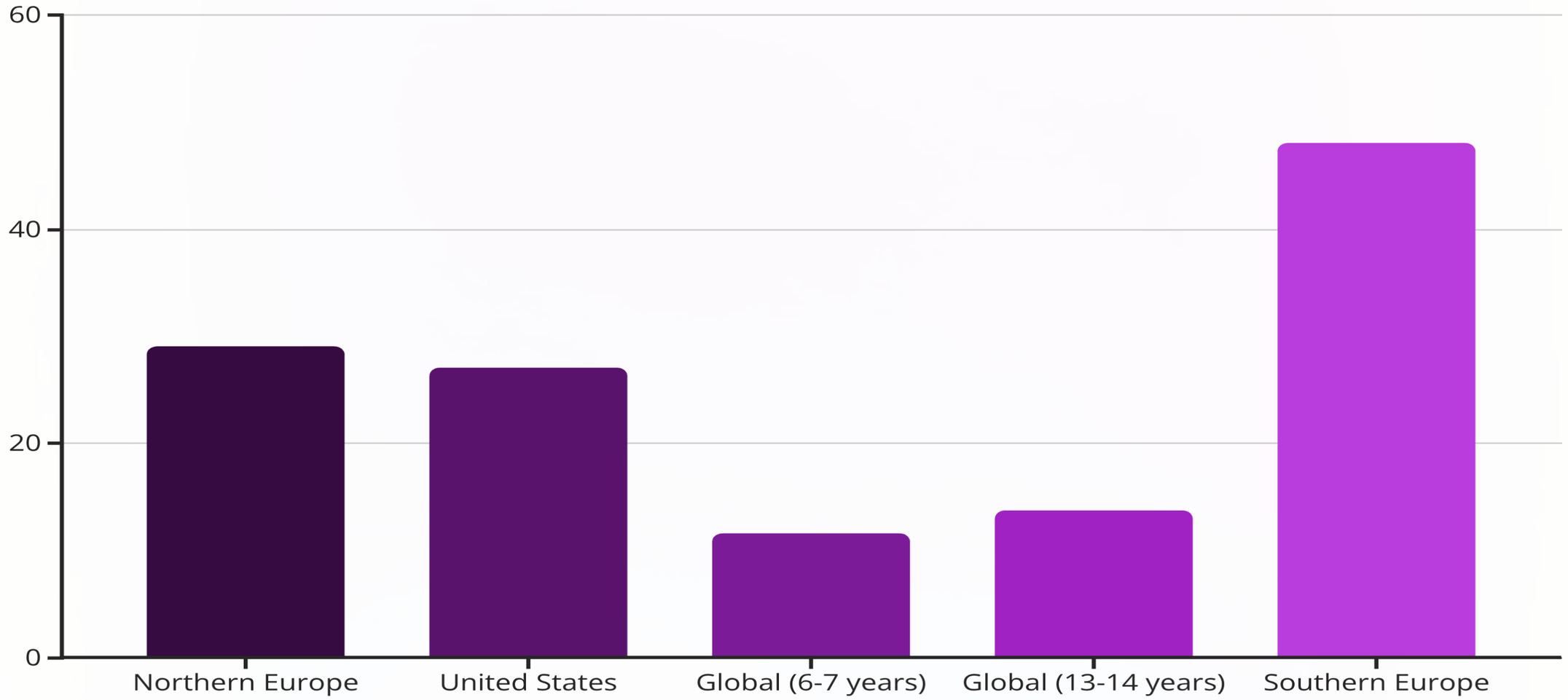
Prevalence in US

13%

Ages 9-11

Prevalence in US

Global Prevalence



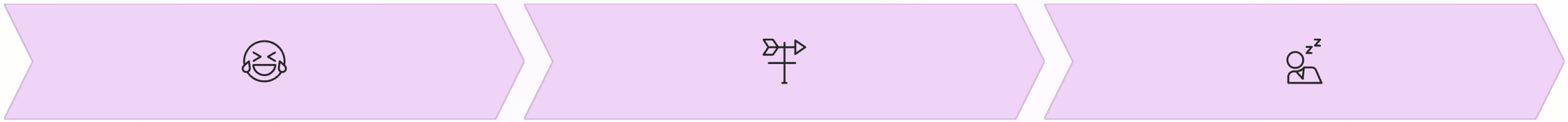
2022 survey showed 32% of children aged 1-5 years had respiratory symptoms in preceding six winter months

What is Wheezing?

A musical sound heard during chest auscultation that:

- *Lasts longer than 100 msec*
- *Has sound energy 100-1000 Hz*
- *Produced by oscillation of narrowed airway walls*
- *Can be high or low pitched*
- *Can occur during inspiration, expiration, or both*

Wheezing Physiology



Airway Narrowing

Airways narrowed almost to point of closure

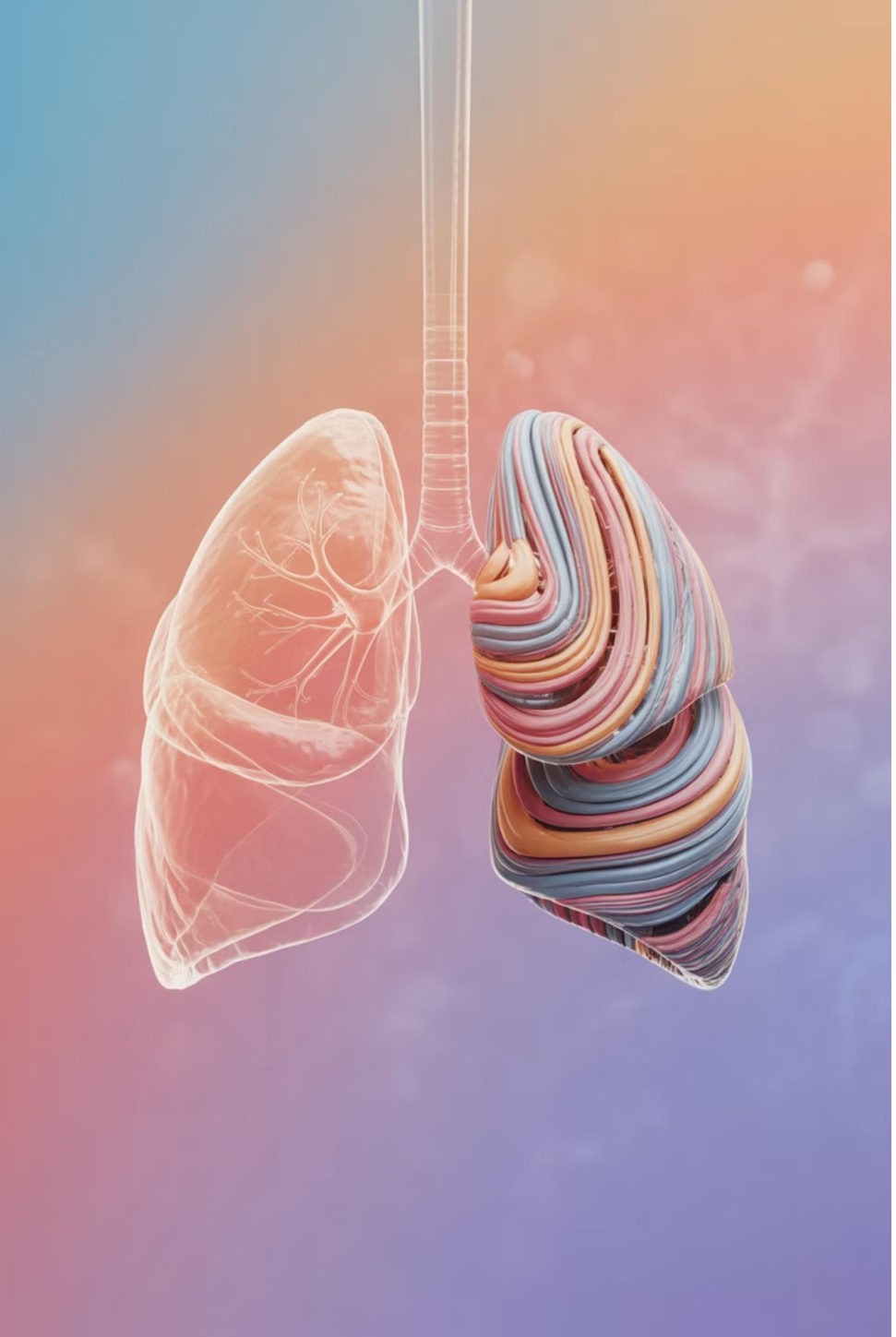
Sufficient Airflow

Required to generate oscillation

Sound Production

Oscillation creates musical sound

Absence of wheezing in acute asthma may indicate impending respiratory failure



Types of Wheezing

Homophonous Wheezing

- *Fixed large/central airway obstruction*
- *Low pitch*
- *Constant acoustic character throughout lung*
- *Varies in loudness by distance from obstruction*

Heterophonous Wheezing

- *Small airway obstruction*
- *Varying degree of narrowing throughout lung*
- *Sounds vary in quality and acoustic character*
- *Common in asthma*

Wheezing vs. Stridor

Wheezing

- *Heard throughout lungs*
- *Often expiratory*
- *Multiple pitches possible*
- *Often from small airways*

Stridor

- *Monophonic sound*
- *Loudest over anterior neck*
- *Can be inspiratory, expiratory, or biphasic*
- *Indicates airway obstruction*

Inspiratory stridor: extrathoracic obstructionExpiratory stridor: intrathoracic obstructionBiphasic stridor: severe fixed obstruction

Wheezing Phenotypes: Historical View

First described in the Tucson childhood respiratory study by Martinez et al.

Never Wheezing

Early Transient Wheezing

Persistent Wheezing

Late-onset Wheezing

Further Classification

Nonatopic Persistent Wheezing

Not associated with allergies

Atopic/IgE-associated Wheezing

Associated with allergic sensitization

Later research identified up to 5-6 different subtypes through longitudinal studies

Simplified Classification by Pattern

Episodic Wheeze

Wheezing within discrete periods, often with viral colds

No wheezing between episodes

Multitrigger Wheeze

Wheezing with and apart from acute viral episodes

Multiple factors can trigger symptoms

Causes of Wheezing

Most likely diagnosis: Asthma

Regardless of age of onset, evidence of atopic disease, precipitating causes, or frequency

Differential Diagnosis

1 Acute Wheezing (Hours to Days)

- *Asthma exacerbation*
- *Viral bronchiolitis (RSV, rhinovirus)*
- *Foreign body aspiration*
- *Laryngotracheobronchitis*

2 Chronic/Recurrent Wheezing

- *Asthma*
- *Structural abnormalities*
- *Aspiration syndromes*
- *Bronchopulmonary dysplasia*

Acute Wheezing: Infections

Viral Bronchiolitis

Most common cause in infants under 2 years

- *RSV most common*
- *Rhinovirus*
- *Parainfluenza*
- *Metapneumovirus*

Clinical Presentation

- *Rhinorrhea prodrome*
- *Cough*
- *Intermittent fever*
- *Wheezing and tachypnea*
- *Nasal congestion*
- *Increased work of breathing*

Acute Wheezing: Foreign Body

When to Suspect

- *Sudden onset of wheezing*
- *Unilateral wheeze*
- *Unequal breath sounds*

Important Note

History of choking may be absent

Can lodge in any bronchus in children

Esophageal Foreign Body

Can present with wheezing due to airway compression

Structural Causes of Chronic Wheezing

Tracheomalacia/Bronchomalacia

Congenital weakness of airway walls; presents early in life with noisy breathing

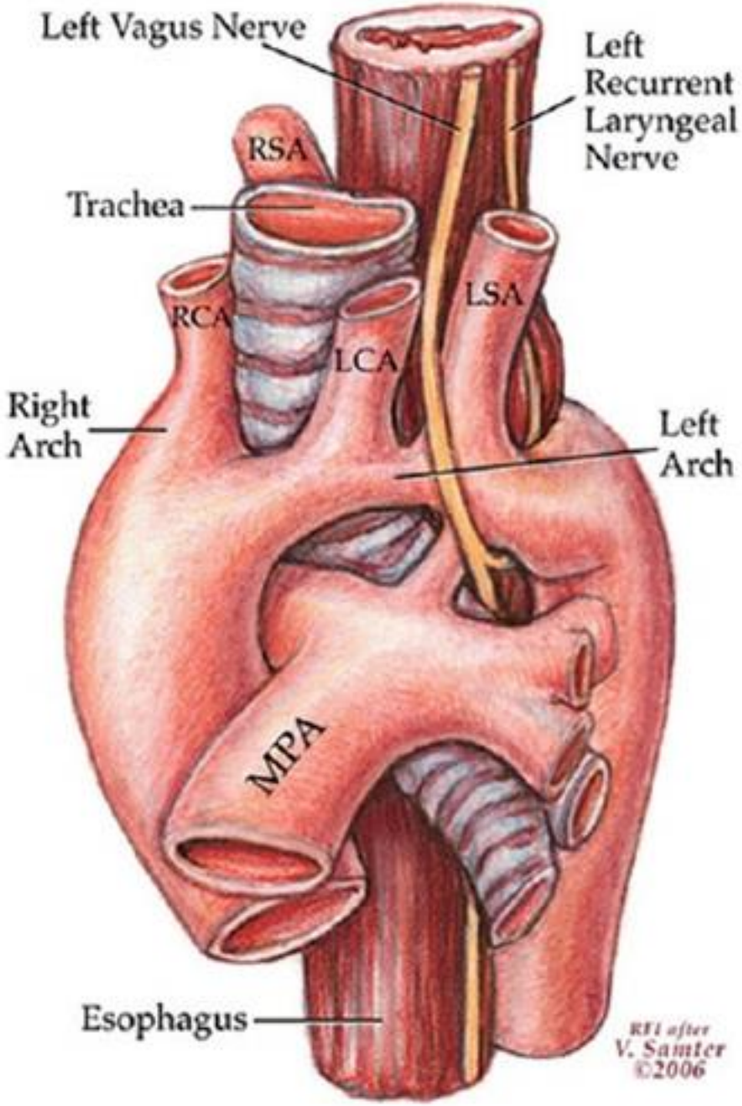
Vascular Rings/Slings

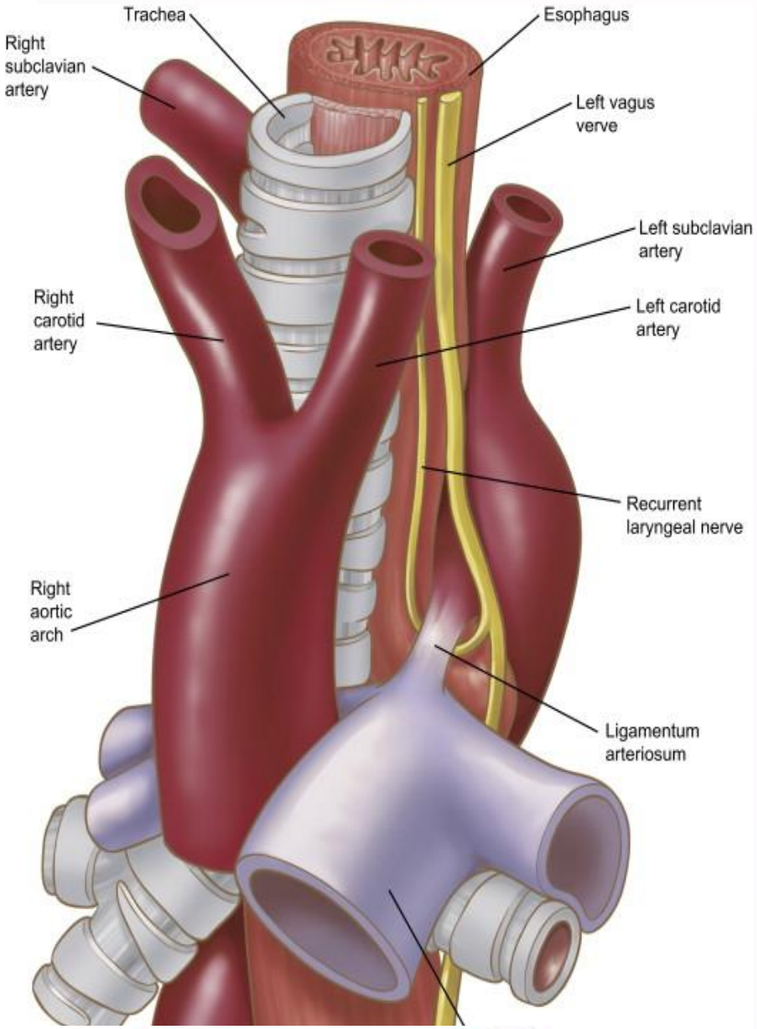
Compression of airways by abnormal vascular structures

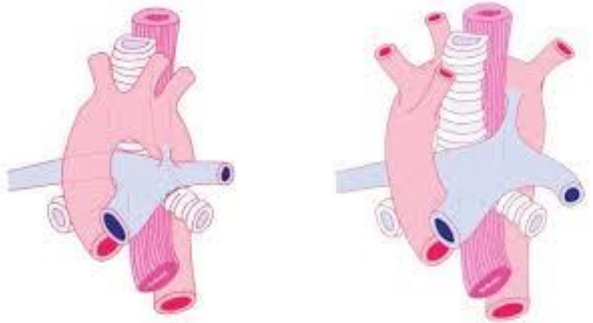
Tracheoesophageal Fistulae

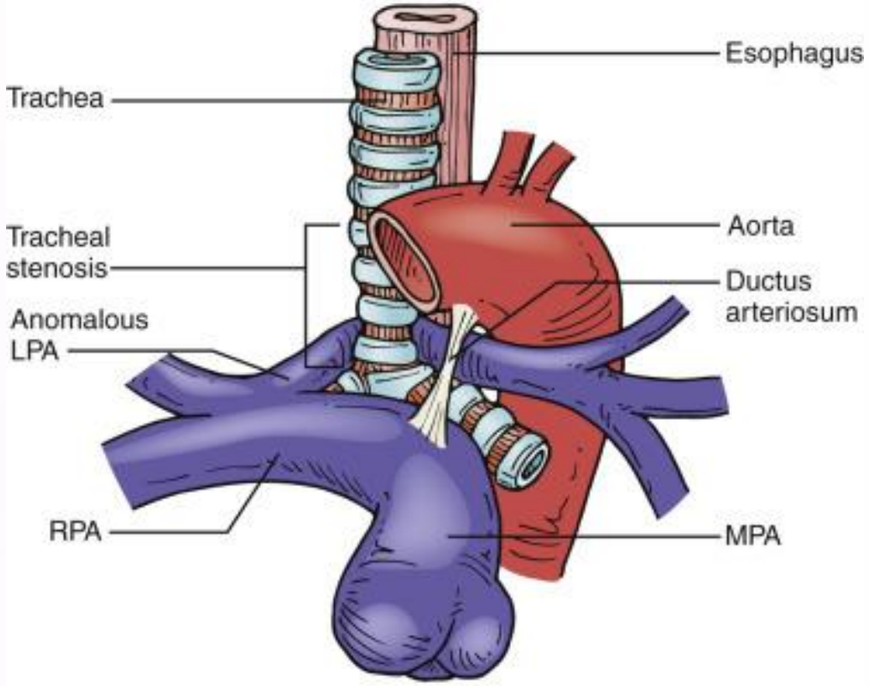
Abnormal connections between trachea and esophagus

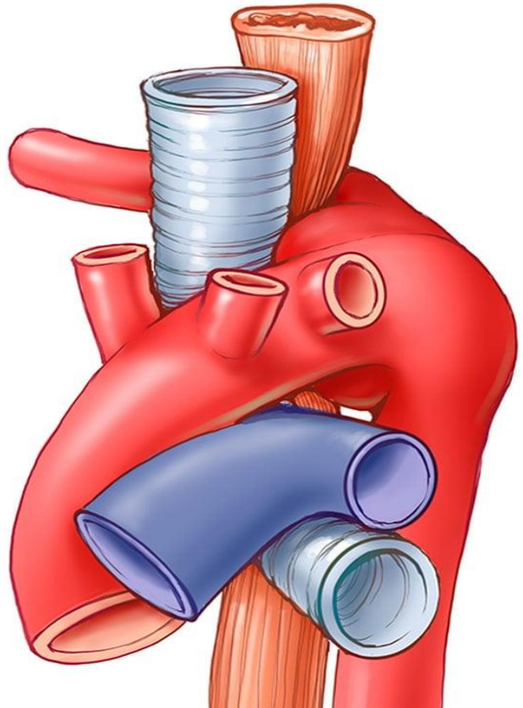
46% of children ages 7-14 months with poor response to asthma therapy had central airway malacia











Double aortic arch2

More Structural Causes

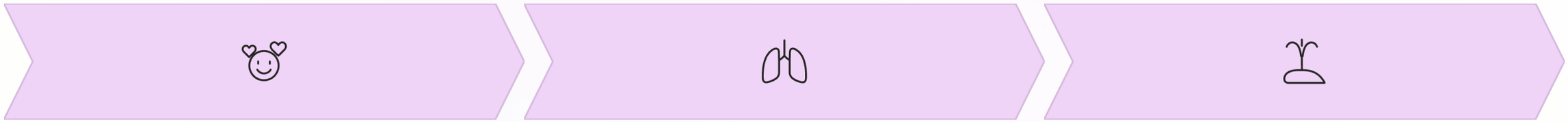
Mediastinal Masses

- *Tumors*
- *Thymic lesions*
- *Bronchogenic cysts*
- *Angiomatous lesions*
- *Enlarged lymph nodes*

Cardiovascular Causes

- *Pulmonary artery dilation*
- *Large left-to-right shunts (VSD, ASD)*
- *Pulmonary hypertension*
- *Left atrial enlargement*
- *Poor left ventricular function*

Cardiovascular Causes of Wheezing



Overcirculation

Most common cardiac cause of wheezing

Pulmonary Vascular Bed

Distension and bronchiolar wall edema

Increased Airway Resistance

Results in wheezing

Important: Cardiac findings including cardiomegaly and murmurs may be absent in some infants

Functional Causes of Wheezing

Aspiration Syndromes

Gastroesophageal Reflux

- *Chronic microaspiration*
- *Mucosal edema and inflammation*
- *May not report typical reflux symptoms*
- *Nocturnal symptoms, hoarseness*

Swallowing Disorders

- *Neurologic/muscular dysfunction*
- *Impaired swallowing*
- *Incomplete glottic closure*
- *Depressed cough reflex*
- *May be "silent" aspiration*

More Functional Causes

Bronchopulmonary Dysplasia

Important cause in preterm newborns, especially birth weight <1250g

Inducible Laryngeal Obstruction(VCD)

Inappropriate vocal fold adduction during inspiration; typically in teenagers

Exercise-Induced Laryngeal Obstruction

ILO restricted to exercise; can mimic asthma symptoms

Less Common Causes

Cystic Fibrosis

50% of young CF patients have wheezing; airway hyperreactivity common

Primary Ciliary Dyskinesia

Rare disease (1:10,000-30,000); typically presents with wet cough

Inborn Errors of Immunity

Recurrent infections leading to bronchiectasis and wheezing

Bronchiolitis Obliterans

Causes

- *Epithelial injury to lower respiratory tract*
- *Chemical, infectious, or immunologic injury*
- *Postviral bronchiolar damage (adenovirus most common)*
- *Lung transplant rejection*

Presentation

- *Tachypnea*
- *Dyspnea*
- *Persistent cough*
- *Wheezing unresponsive to bronchodilators*
- *Hypoxemia in severe cases*

Evaluation of Wheezing

Clinical History & Physical Examination

Often allow accurate diagnosis

Therapeutic Trial

Bronchodilators to evaluate reversible airway obstruction

Additional Testing

Radiography, PFTs, bronchoscopy, laboratory studies as needed

Clinical History: Key Questions

Is it really wheezing?

"Wheezing" often used to describe various noisy breathing

Age at onset?

Structural abnormalities typically present in infancy

Acute or gradual onset?

Acute: infection, FBA; Gradual: structural, chronic

Persistent or intermittent?

Persistent early in life suggests congenital abnormality

More History Elements

Association with viral infections?

Common in first few years; 30% of children <2 years

Associated cough?

Wet vs. dry cough provides diagnostic clues

Response to medications?

Response to bronchodilators suggests asthma

Features Favoring Asthma Diagnosis

1

Intermittent Episodes

With common triggers (URIs, weather, exercise, allergens)

2

Seasonal Variation

Symptoms worsen during specific seasons

3

Family History

Asthma and/or atopy in family members

4

Medication Response

Good response to asthma medications

5

Positive API

Asthma Predictive Index suggests future asthma

Features Suggesting Alternative Diagnosis

Poor Response to Medications

Minimal improvement with bronchodilators or steroids

Symptoms Since Birth

Suggests congenital abnormality

Feeding-Associated

Wheezing with feeding or vomiting (GER, aspiration)

Choking History

Suggests foreign body aspiration

Wheezing with Little Cough

Suggests mechanical obstruction

Position-Dependent

Symptoms vary with position changes

Poor weight gain + recurrent infections may suggest CF, immunodeficiency, or ciliary dysfunction

Physical Examination

General Assessment

Weight, height, vital signs, oxygen saturation

Chest Examination

Complete lung and chest exam, digital inspection

Extrapulmonary Findings

Cardiac exam, skin (eczema), nasal exam

Cyanosis or clubbing suggests diagnosis other than asthma

Chest Examination Focus

- **Inspection**

  Respiratory distress, tachypnea, retractions, structural abnormalities

- **Palpation**

  Lymphadenopathy, tracheal deviation

- **Percussion**

  Diaphragm position, differences in resonance

- **Auscultation**

  Characteristics and location of wheezing, air entry variations

Prolonged expiratory phase suggests airway narrowing

Auscultation Findings

Wheezing Characteristics

- *Constant acoustic character = large airway*
- *Varying acoustic character = small airways*
- *Persistent focal wheezing = structural abnormality*

Crackles

- *Can be present with wheezing in asthma*
- *Early inspiratory = secretions/closed airways*
- *Late inspiratory = ILD, heart failure*

Radiography

When to Obtain

New-onset wheezing of undetermined etiologyChronic, persistent wheezing not responding to therapy

What It Shows

Large airwaysDiffuse vs. focal diseaseHyperinflationParenchymal diseaseAtelectasisBronchiectasis

Cardiac Findings

CardiomegalyEnlarged pulmonary vesselsPulmonary edemaSigns of heart failure

Additional Imaging Studies

Chest CT

Detailed anatomy of mediastinum, airways, lung parenchyma

MRA/MDCT

Study of choice for suspected vascular ring or sling

Barium Swallow

Helps identify vascular rings, swallowing dysfunction, GER

Videofluoroscopic swallowing study suggested in children <2 years with recurrent wheezing unresponsive to therapy

Pulmonary Function Tests

Older, Cooperative Children

- *Flow-volume loops*
- *Determines presence, degree, location of obstruction*
- *Measures response to bronchodilators*
- *Methacholine challenge testing*
- *Exercise testing*

Infant PFT

- *Requires sedation*
- *Assesses airway obstruction*
- *Quantifies bronchodilator response*
- *Reserved for selected patients*

Response to Treatment

Bronchodilator Trial

Confirms reversible airway disease

Partial/Negative Response

Doesn't rule out asthma

Inhaled Steroids + Bronchodilators

2-week trial if asthma still suspected

Further work-up indicated if response inadequate or comorbid condition suspected

Laboratory Studies

Few laboratory tests useful in initial evaluation

Complete Blood Count

Important in patients with chronic/systemic symptoms

Eosinophilia supports allergic process

Specific Tests

Based on suspected diagnosis

Confirm diagnosis or rule out other conditions

Infectious Work-up

Viral Studies

- *Paramyxoviridae family (RSV, parainfluenza)*
- *Picornavirus family (rhinovirus)*
- *Metapneumovirus*
- *Helpful in confirming bronchiolitis etiology*
- *Not routinely recommended*

Bacterial Studies

- *Sputum Gram stain and cultures*
- *Tuberculin skin testing*
- *Specific serologic assays*
- *Mycoplasma serologic testing*

Mycoplasma is increasingly recognized cause of wheezing

Immunologic Evaluation

Immunoglobulin Levels

Screen for humoral immunodeficiencies

Detailed Immunologic Work-up

If high suspicion of immunodeficiency

IgE Levels

Elevated IgE indicates allergic process

Allergen Testing

Skin prick or in vitro testing for environmental allergies

Sweat Chloride Test

When to Obtain

Low threshold in patients with:

- *Persistent/recurrent pulmonary symptoms*
- *No improvement on asthma therapies*
- *Chronic, productive cough with wheezing*

Important Considerations

- *Should be done at facility with substantial experience*
- *Be aware of other conditions causing elevated sweat chloride*
- *Major implications for patient, family, future reproductive decisions*

Primary Ciliary Dyskinesia Work-up

Genetic Testing

Identifies mutations in genes affecting ciliary function

Nasal Nitric Oxide

Low levels suggest PCD

Ciliary Analysis

Motion and ultrastructural analysis of cilia

Consider in patients with wet chronic cough, chronic sinusitis, and recurrent otitis media

Endoscopy

Rigid Bronchoscopy

- *Used for suspected foreign body aspiration*
- *Sudden onset of wheezing*
- *Therapeutic removal of foreign body*

Flexible Bronchoscopy

- *Identifies structural airway abnormalities*
- *Evaluates airway malacia*
- *Bronchoalveolar lavage for cytology*
- *Helps identify asthma phenotype*

Structural abnormality identified in up to 33% of infants with chronic wheezing not responsive to asthma therapies

GER Evaluation

When to Consider

Common in children <2 years with recurrent wheezingPoor response to asthma therapiesSuggestive symptoms (burping, emesis, post-meal cough)

24-hour pH Monitoring

Preferred over upper GI series or scintigraphyGold standard for GER diagnosis

Multichannel Intraluminal Impedance

Measures all reflux episodes (acidic and non-acidic)Often combined with pH monitoringDetects reflux events causing symptoms twice as often as pH alone

Diagnostic Algorithm

Systematic approach to diagnosis based on clinical presentation, response to therapy, and targeted testing

Key Takeaways

1 **Wheezing is Common**

1 in 3 children experience wheezing before age 3

2 **Asthma Most Likely**

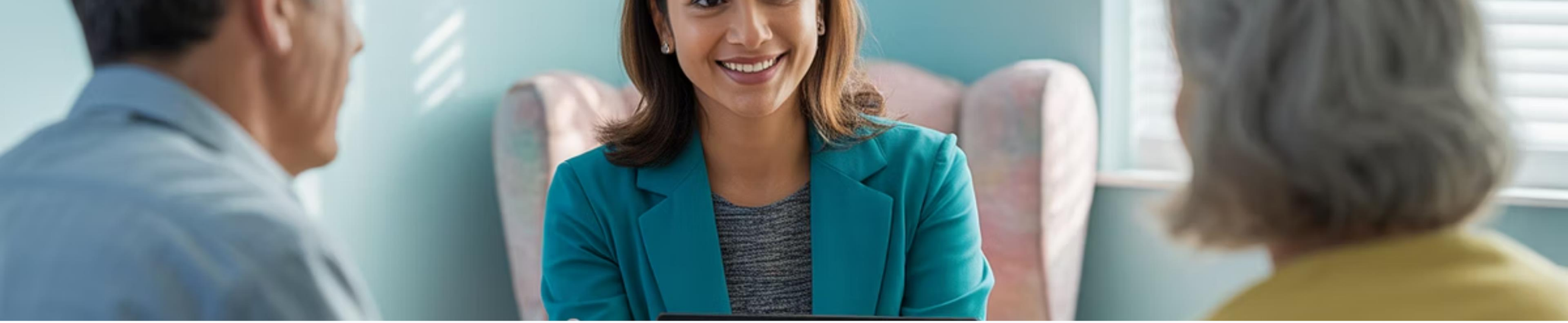
But consider other diagnoses, especially with poor treatment response

3 **History and Exam Critical**

Often allow accurate diagnosis before additional testing

4 **Targeted Testing**

Based on suspected diagnosis and clinical presentation



Thank You

Questions?

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