The Annual General Pediatric Review & Self Assessment

Nicklaus Children's Hospital

Pulmonology

Maria Franco, MD

Pediatric Pulmonology
Nicklaus Children's Hospital
Miami, FL

Nicklaus Children's Hospital

Disclosure of Relevant Relationship

Dr. Franco disclosed relevant conflicts of interests (COIs) and/or financial relationships in the past 24 months with the following ineligible companies:

Ineligible Company(ies)	Role/ Type of Relationship
Vertex Pharmaceutical	Research Support
PTC 124	Contracted Research

All COIs have been mitigated prior to this activity

Dr. Franco will support this presentation and clinical recommendations with the "best available evidence" from medical literature.

Dr. Franco does not intend to discuss an unapproved/investigative use of a commercial product/device in this presentation.

General Signs and Symptoms

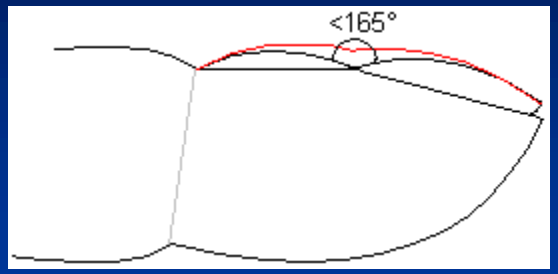
Cough

- Acute:
  - Infection, aspiration, foreign body
- Recurrent
  - Reactive airways, CF, reflux, aspiration, anatomic abnormality, passive smoking
- Chronic (> 3 weeks)
  - RAD, CF, GER, Pertussis, anatomic abnormality, smoke exposure, psychogenic (often after a URI, does not occur at night)

Tachypnea

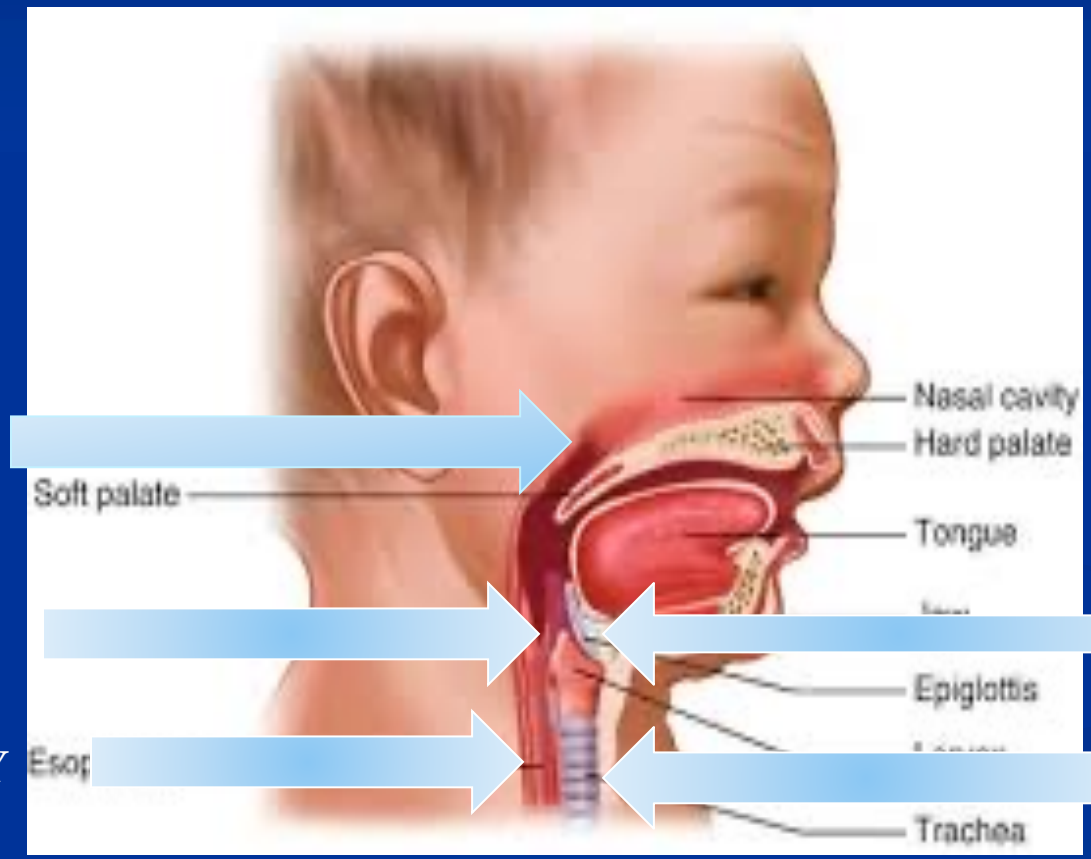
- WHO definition:
  - 0-2 mos > 60 bpm
  - 2-12 mos > 50 bpm
  - 12 months- 5 years of age > 40 bpm
  - > 20 bpm in older children and adolescents

Clubbing



- CF
- Bronchiolitis obliterans
- Primary Ciliary Dyskinesia
- Congenital heart disease
- Biliary atresia, IBD, alpha1antitrypsin
- Thyrotoxicosis, hypothyroid
- Idiopathic, hereditary

Sites & Sounds of Airway Obstruction



Definitions of obstructive noises

Stertor : respiratory sound characterized by heavy snoring or gasping

- Low-pitched
- Inspiratory
- Nasopharynx, oropharynx, nasal passage
- Loudest over neck, cheeks

(A heavy snoring inspiratory sound occurring in coma or deep sleep, sometimes due to obstruction of the larynx or upper airways)

Stertor (…Snoring)

Causes

- Choanal atresia
- Mandibular hypoplasia
- Macroglossia
- Nasal congestion
- Adenotonsillar hypertrophy
- Pharyngeal insufficiency
- Encephalocele
- Dermoid of base of tongue
- Thyroglossal duct cyst
- Lingual thyroid

Definitions of obstructive noises

STRIDOR : Harsh noise caused by turbulent flow

- Inspiratory = larynx
- Expiratory = trachea
- Biphasic = fixed lesion in subglottic region

Inspiratory Stridor

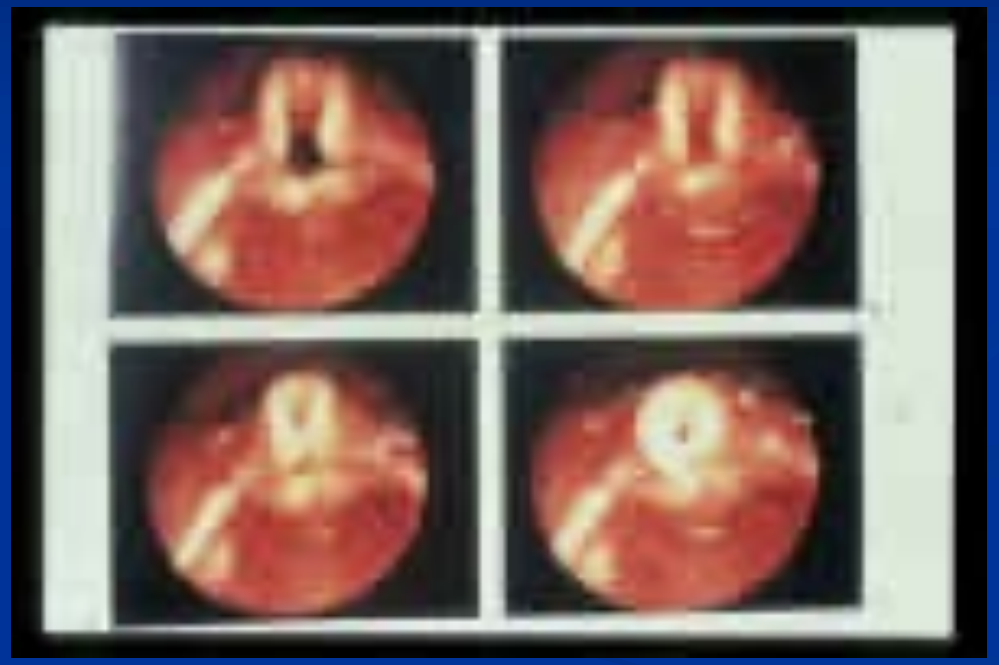
Causes

- Laryngomalacia
- Vocal cord paralysis
  - Unilateral – left (recurrent laryngeal nerve)
  - Bilateral – brainstem
- Laryngotracheoesophageal cleft
- Laryngocele
- Laryngeal polyp
- Abscess
- Hypotonia
- Vocal Cord Dysfunction

Inspiratory Stridor

Laryngomalacia

- 60% of insp. stridor
- 90% require no intervention
- Improves when prone (sleep)
- Worsens with activity and with presence of GERD
- Worsens over first 1-6mos, then improves
- Watch for FTT, apnea, cyanosis
- Bronchoscopy if does not follow classical history

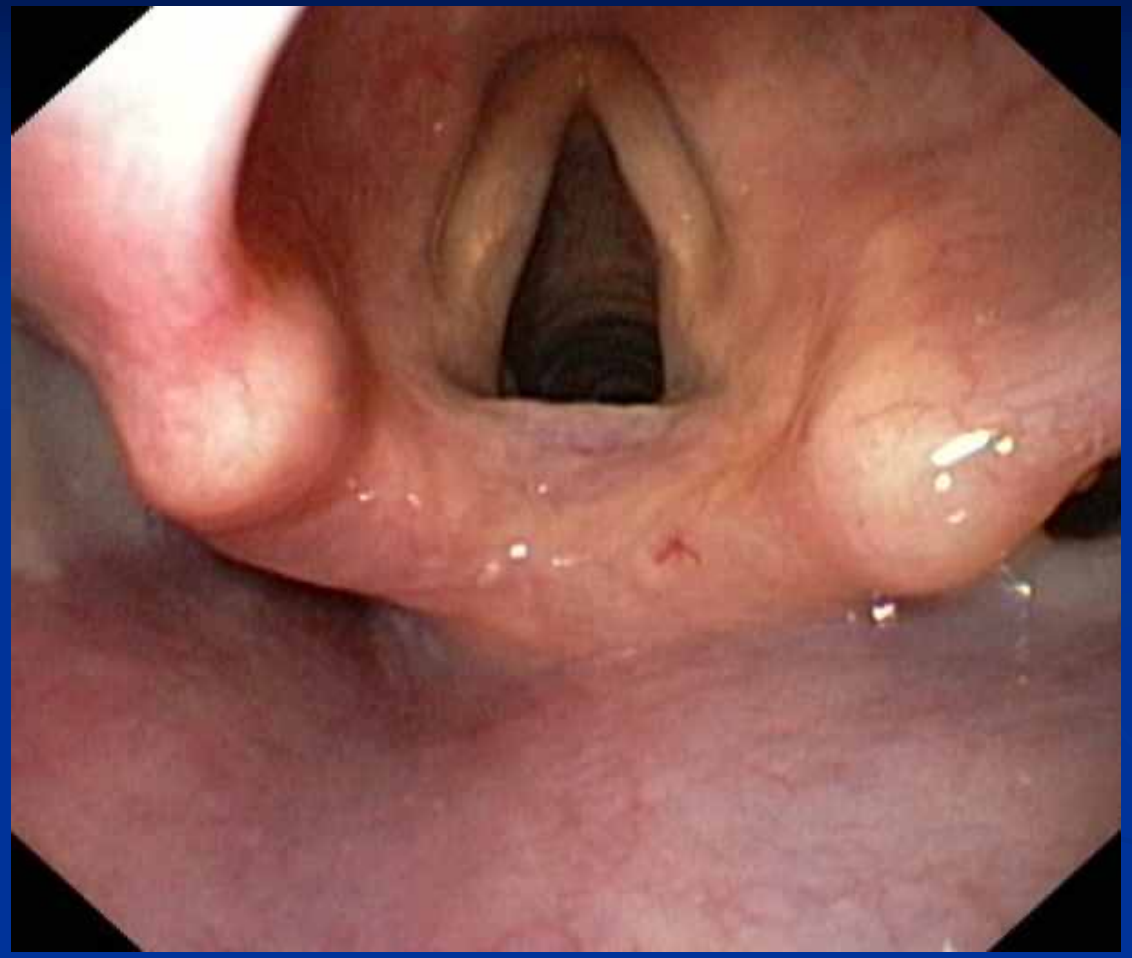


Laryngomalacia

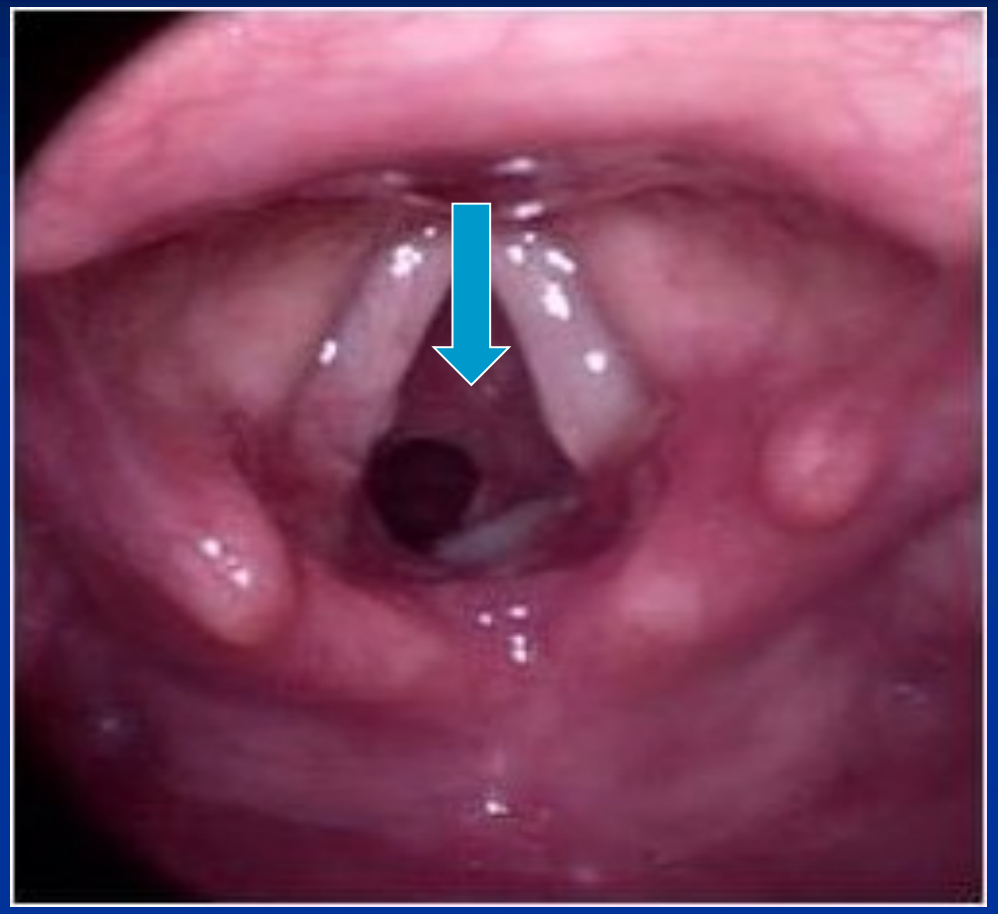
Biphasic Stridor

Causes

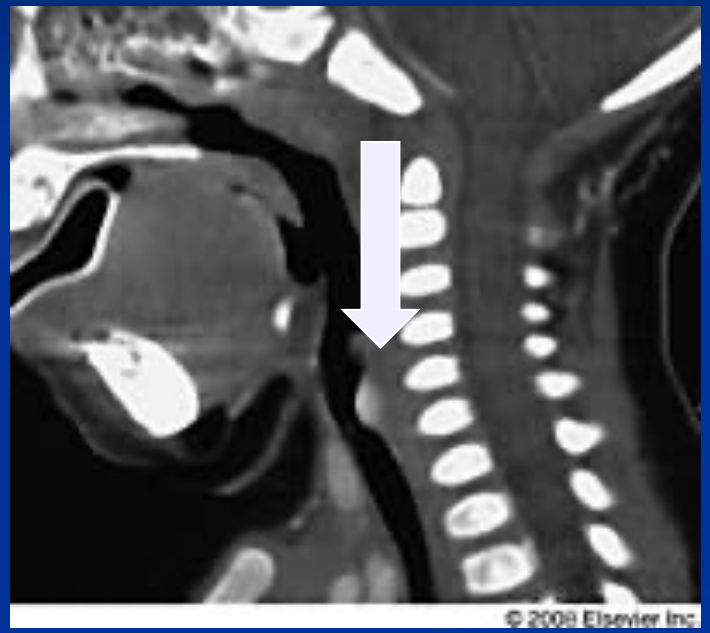
- Subglottic stenosis
  - Congenital
  - Acquired – intubation, croup
- Subglottic hemangioma
- Laryngeal web
- GERD



NORMAL LARYNX



SUBGLOTTIC STENOSIS



SUBGLOTTIC HEMANGIOMA

Biphasic Stridor

Causes

- **Croup** – acute barky cough, stridor, resp. distress
  - Low grade fever
  - Rhinorrhea
  - Worse at night
  - 3mos-3yrs
  - Parinfluenza 1-3, RSV, Influenza
  - Fall/Winter

Biphasic Stridor

Causes

- **Recurrent Croup**
  - Consider underlying airway anomaly
  - GERD
  - Spasmodic (reactive airways)

Definitions of obstructive noises

Wheeze : Higher-pitched expiratory noise

- Monophonic, homophonous = large airway

  = expiratory stridor

- Polyphonic, heterophonous, musical = small airways

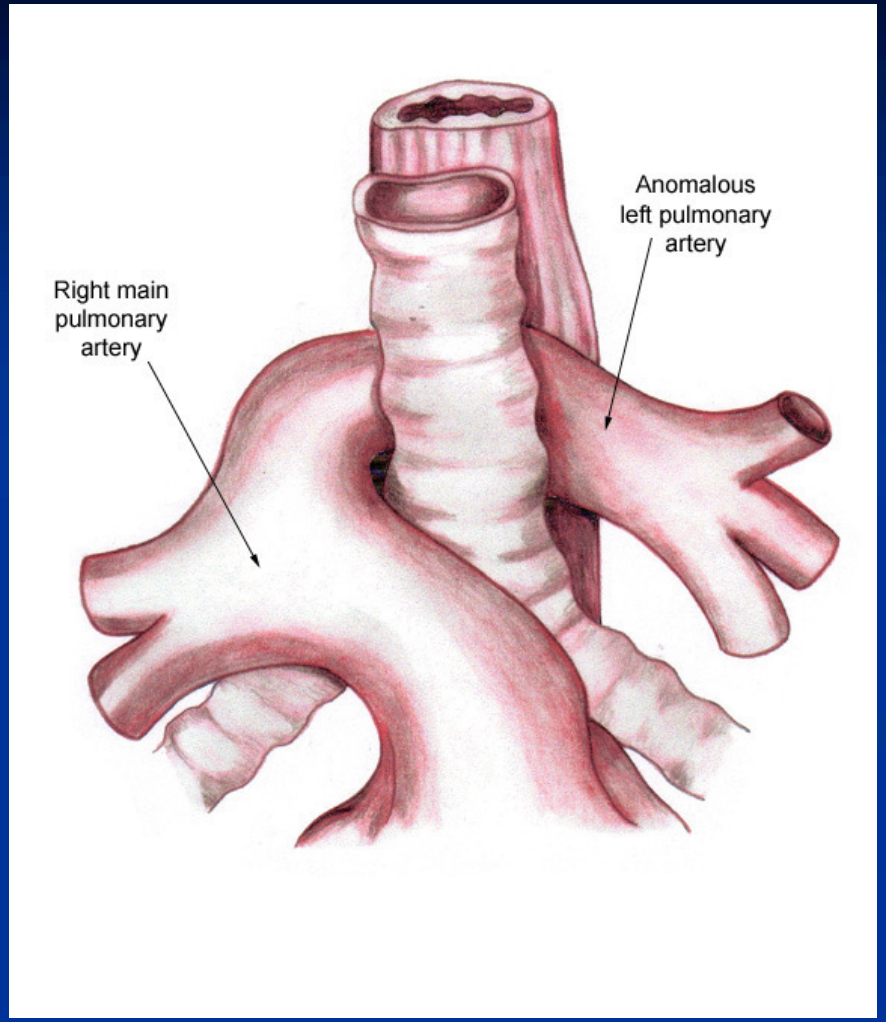
Homophonous Wheezing – Expiratory Stridor

Causes

- Tracheobronchomalacia
  - Deficient cartilage rings
  - Worse with exertion, agitation
  - Prolonged expiratory phase
  - Narrow trachea on expiratory lateral films
  - Primary vs. Secondary
    - BPD, TEF, vascular anomalies

Vascular Rings

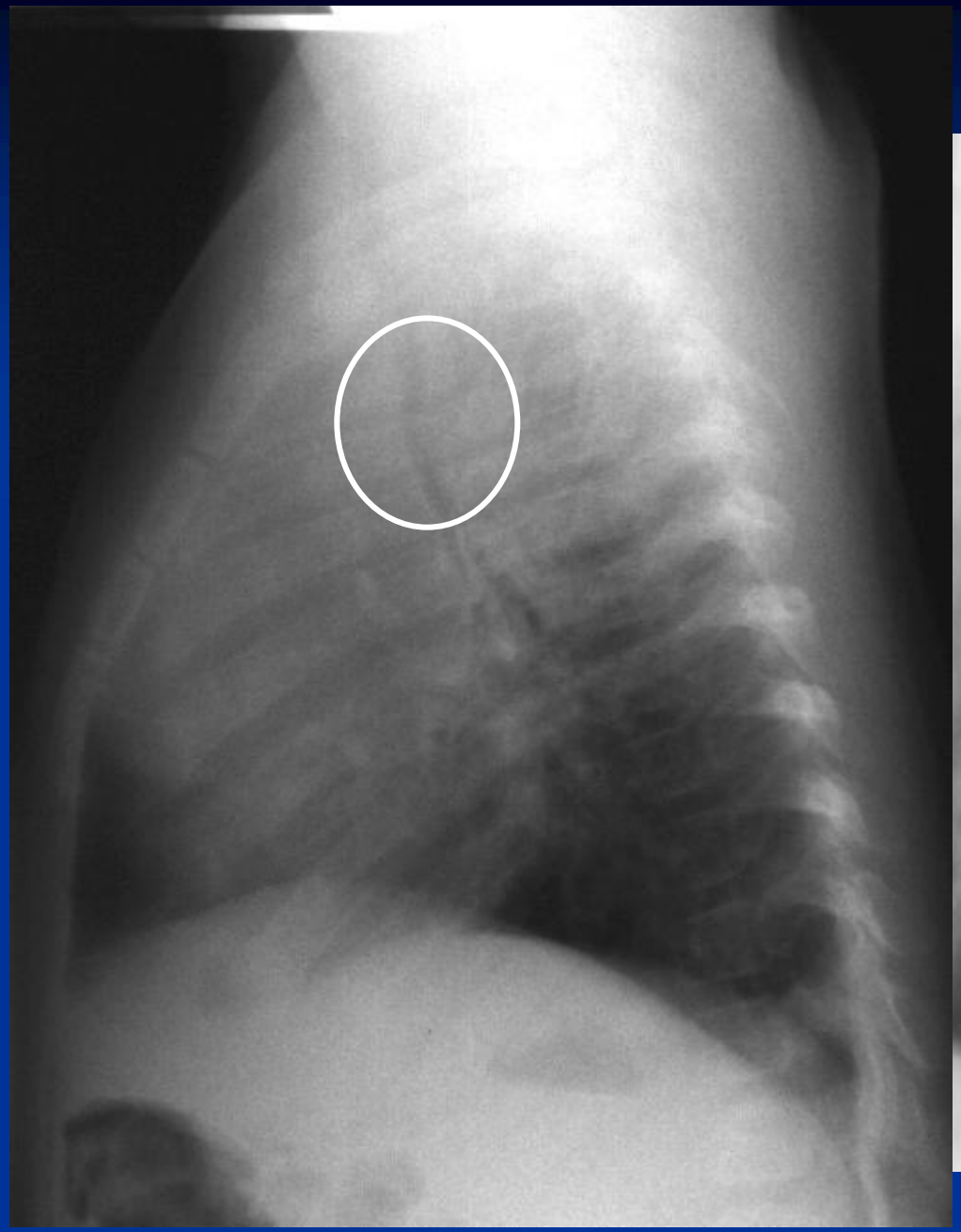
- Tracheal or tracheobronchial malacia and stenosis may develop in association with some of these lesions in the areas where the greatest degree of compression exists. This is particularly true in cases of anomalous left pulmonary artery.

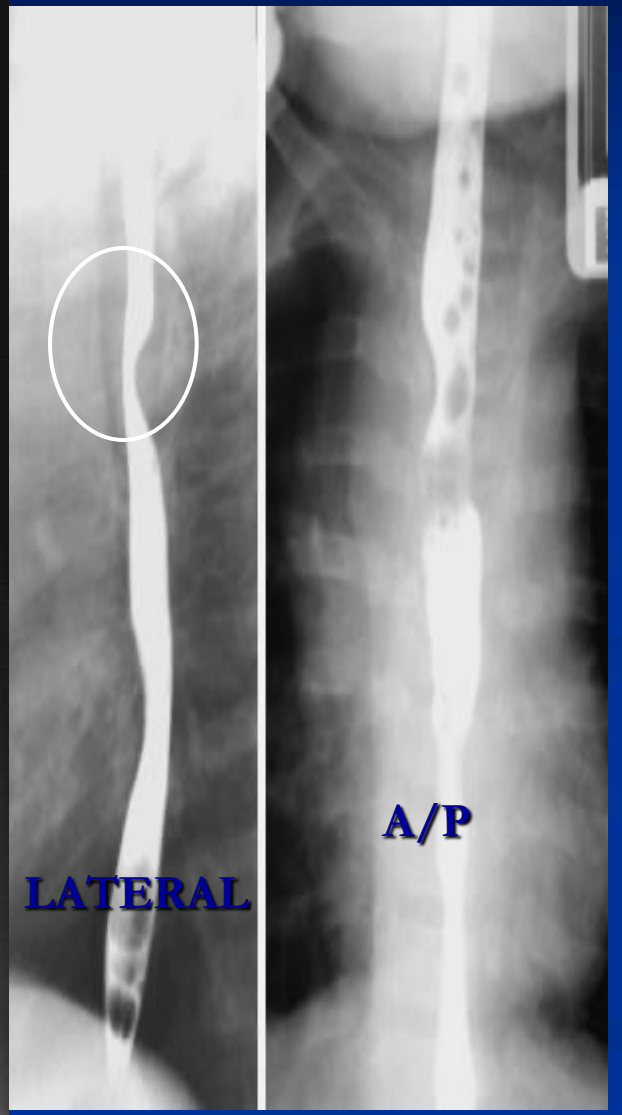


Aberrant left pulmonary artery or pulmonary artery sling.

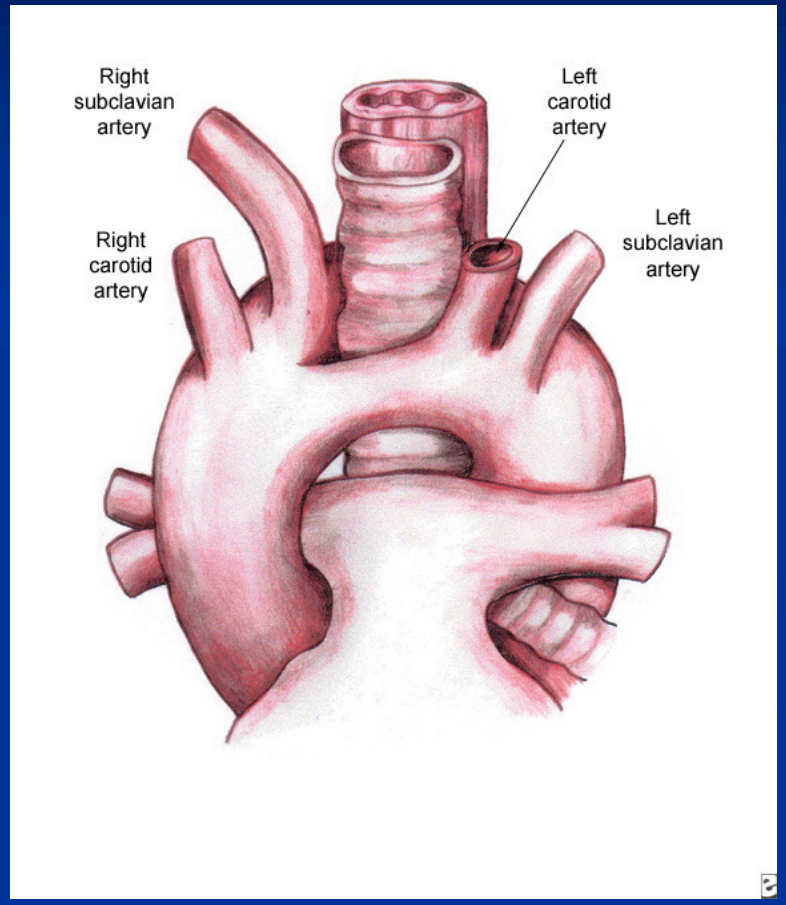
Most patients are symptomatic by 1 month after birth.

Esophagram



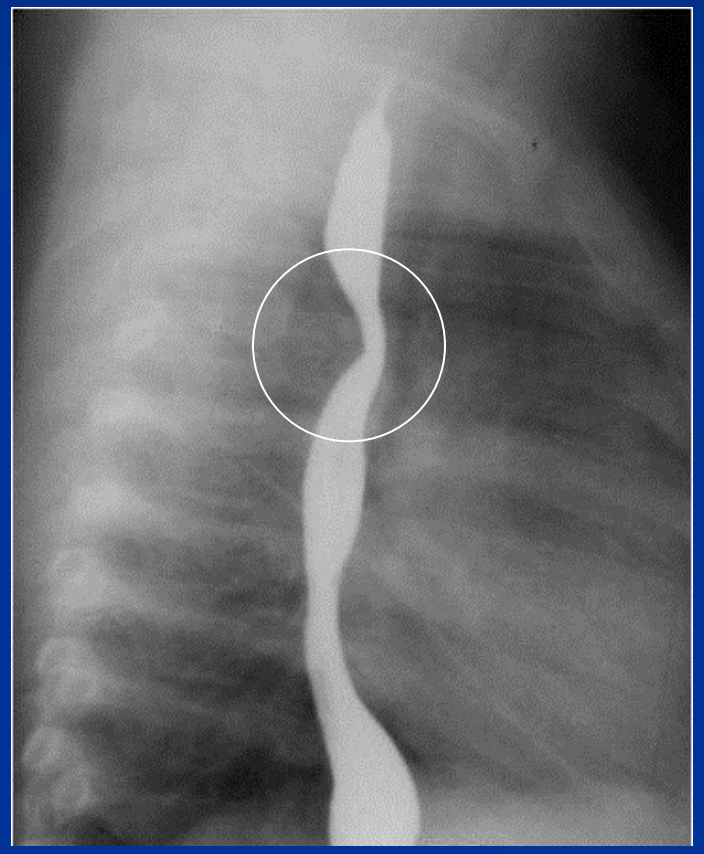


Double aortic arch



The double aortic arch forms a ring around the trachea and esophagus, compressing both of these structures. Tracheoesophageal compression typically results in early symptoms

Double Aortic Arch



Mediastinal Mass

Bronchogenic Cyst
In a 12 month old
Evaluated for chronic wheezing

Heterophonous Wheezing

Causes

- Asthma
- Bronchiolitis
- Pneumonia (Mycoplasma)
- GERD – inflammation, bronchospasm
- Heart Failure – often presents around 2 mos
- Cystic Fibrosis
- Ciliary Dyskinesia
- Food Allergy

ASTHMA

Asthmatic Inflammation

Asthma Is a Chronic Inflammatory Disease

- Asthma is a chronic inflammatory disease.
- Airway inflammation leads to:
  - Hyperresponsiveness—responses to triggers
  - Obstruction—usually reversible
  - Symptoms—cough, wheezing, dyspnea

NAEPP. *Clinical Practice Guidelines: Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma.* June 2002. NIH publication 02-4051.

ASTHMA

Most common chronic pediatric disorder

ATOPIC WHEEZING ASTHMA

- MORE THAN ½ OF ALL CASES OF PERSISTENT ASTHMA START BEFORE AGE 3.
- 80% START BEFORE 6 YEARS OF AGE

ASTHMA DIAGNOSIS

Consider asthma if:

- History of chronic dry cough
- Cough during exercise
- Wheezing
- Wheezing with upper respiratory infections and or with exercise.

GOALS OF ASTHMA THERAPY

- Lack of symptoms
- Diminished response to triggers
- Full participation in usual activities
- Normal pulmonary function
- Use of as little medication as possible but as much as necessary

Pharmacologic Therapy

Quick-relief medications: ACUTE

- **Short-acting Beta2-agonists:** Bronchodilatation

  Albuterol

  Levalbuterol
- **Oral Corticosteroids** : Anti-inflammatory

  Up to 10 days of therapy no need for tapering dose.
- **Ipratropium Bromide** : Add on severe asthma

Pharmacologic Therapy

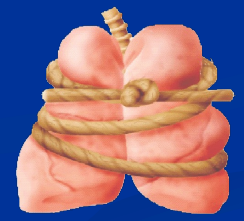
LONG TERM CONTROL MEDICATION

- Cromolyn Sodium
- Nedocromil
- Leukotriene Modifiers
- Long Acting Beta2-agonists
- Sustained-released theophylline
- Oral Steroids
- Inhaled Steroids
- Inhaled Steroids + Long Acting Beta2-agonists
- Biologics

- All medications decrease airway hyperactivity
- Cromolyn, Nedocromyl, Steroids and Leukotriene Modifiers also decrease inflammatory component of the airway.

ICS Safety Includes …

- Data demonstrating no effect on final adult height at recommended doses
- Minimizing effects of chronic inflammation in the lung
- Protection of lung function
- Reducing risk of death, hospitalizations, and emergency room visits for asthma
- Significant reduction in asthma symptoms and exacerbations



"RULES OF TWO™"*

Patients Are Candidates for Maintenance Therapy If …

- They are using a quick-relief inhaler more than 2 times per week
- They awaken at night due to asthma more than 2 times per month
- They refill a quick-relief inhaler prescription more than 2 times per year

*"RULES OF TWO™" is a trademark of the Baylor Health Care System.

Rule of Twos

- ≥ 2 days/week but not daily, ≥ 2 nights/month → Mild persistent
  - Treatment: Low-dose inhaled corticosteroid
    Leukotriene Modifiers
- Daily daytime symptoms, > 1 night/week → Moderate persistent
  - Treatment: **Low-dose ICS + LABA, OR medium-dose ICS**
- Continual symptoms → Severe persistent
  - Treatment: High-dose ICS + LABA, and OCS
    Or Biologics (monoclonal antibodies)

Exercise can trigger asthma

- Symptoms are worse with cold, dry air
- However, exercise helps lungs function better and prevents obesity
- As long as asthma is well-controlled and a short-acting bronchodilator (rescue medicine) is used beforehand, children with asthma should be able to do sports
- Pulmonary function testing best first test; then exercise testing.

Bronchiolitis

Bronchiolitis

- Most common cause is RSV.
- Most common cause of first episode of wheezing in infants.
- Diagnosed by RSV antigen by nasal wash.
- For treatment steroids or bronchodilators are not recommended.
- Observation and close monitoring during hospitalization. Hydration when necessary.
- Nasal Suction prior feedings to avoid aspiration.

Acute Respiratory Failure

- Increased Respiratory Drive
  - Tachypnea – increased RR
  - Dyspnea – breathlessness
  - Retractions
  - Accessory muscle use
- Decreased Respiratory Drive
  - Decreased RR
  - Lethargy
  - Confusion
  - Snoring

Increase CO_2 is always the most clear sign of respiratory failure

Normal CO_2 is from 40 to 45 mm Hg

Acute Respiratory Failure

- Respiratory Muscle Fatigue
  - Paradoxic “see-saw” respirations
  - Grunting
  - Uncoordinated breathing
- Hypoxemia – $PaO_2 < 60$
- Hypercapnea – $PaCO_2 > 50$

Blood Gases

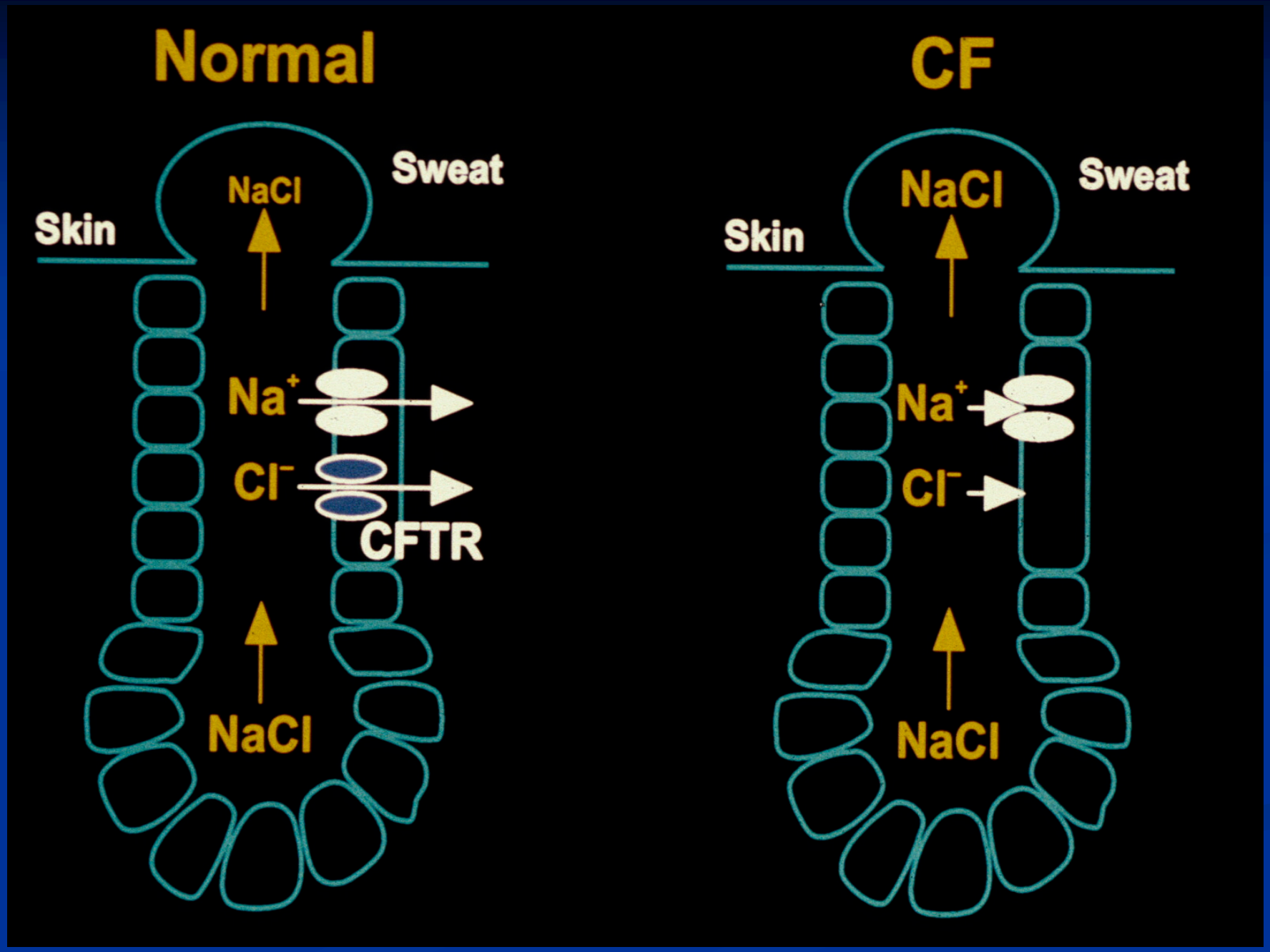
pH	PCO2	PO2	HCO3	
7.24	60	50	24	ARF
7.35	60	50	34	CRF
7.40	40	70	24	Normal

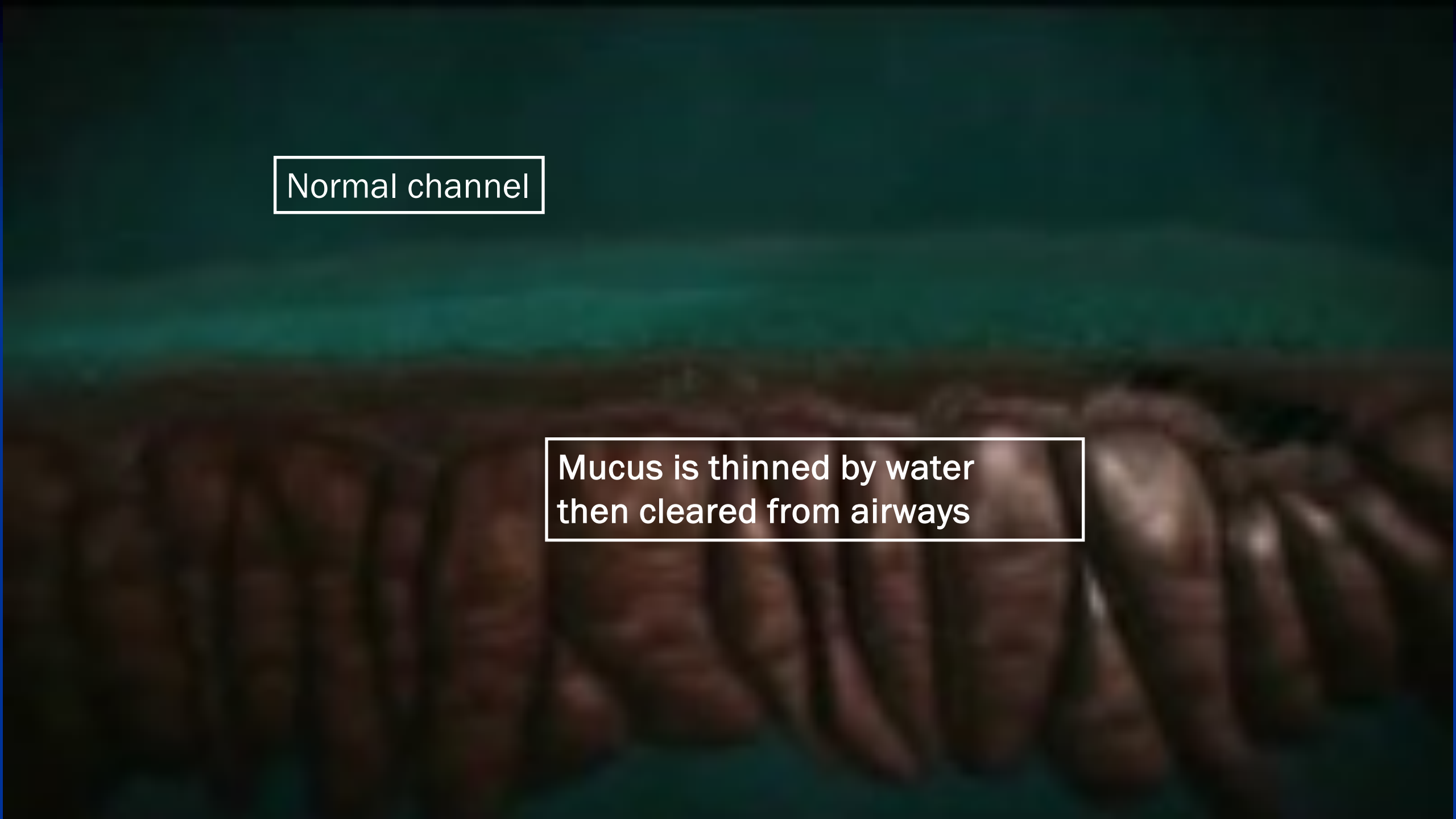
CYSTIC FIBROSIS

- Chronic, progressive and life limiting autosomal recessive genetic disease characterized by chronic respiratory disease, pancreatic insufficiency, elevation of sweat electrolytes and male infertility

CF

- CF is caused by a mutation in a gene located in the long arm of chromosome # 7.
- Gene called CFTR (cystic fibrosis transmembrane conductance regulator)
- Membrane protein, epithelial chloride channel

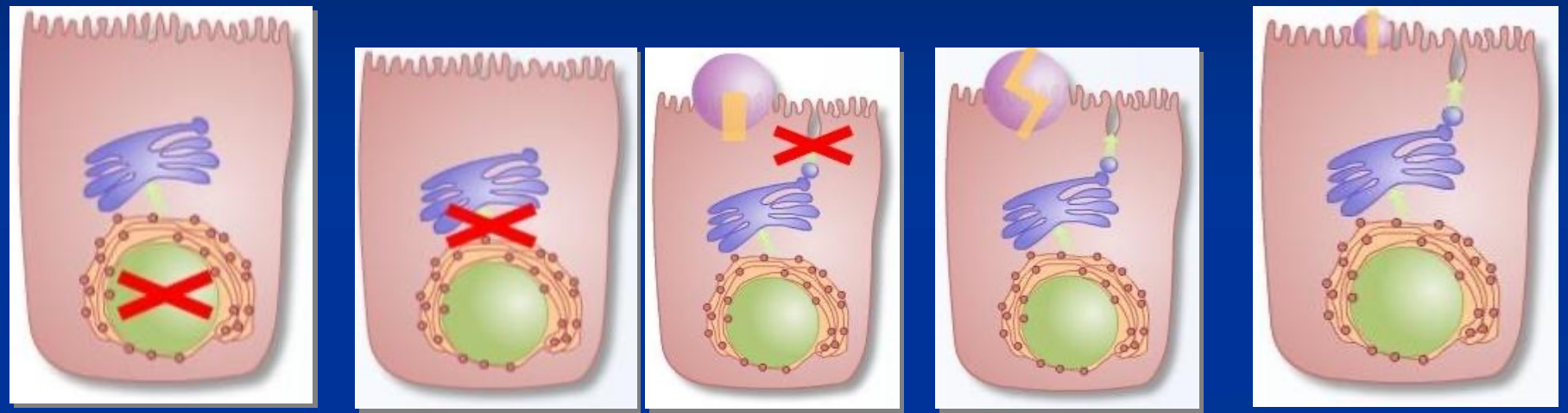

Normal
Sweat
NaCl
Skin
Na+
Cl−
CFTR
NaCl
CF
Sweat
NaCl
Skin
Na+
Cl−
NaCl


Normal channel
Mucus is thinned by water
then cleared from airways

Absent or defective channel

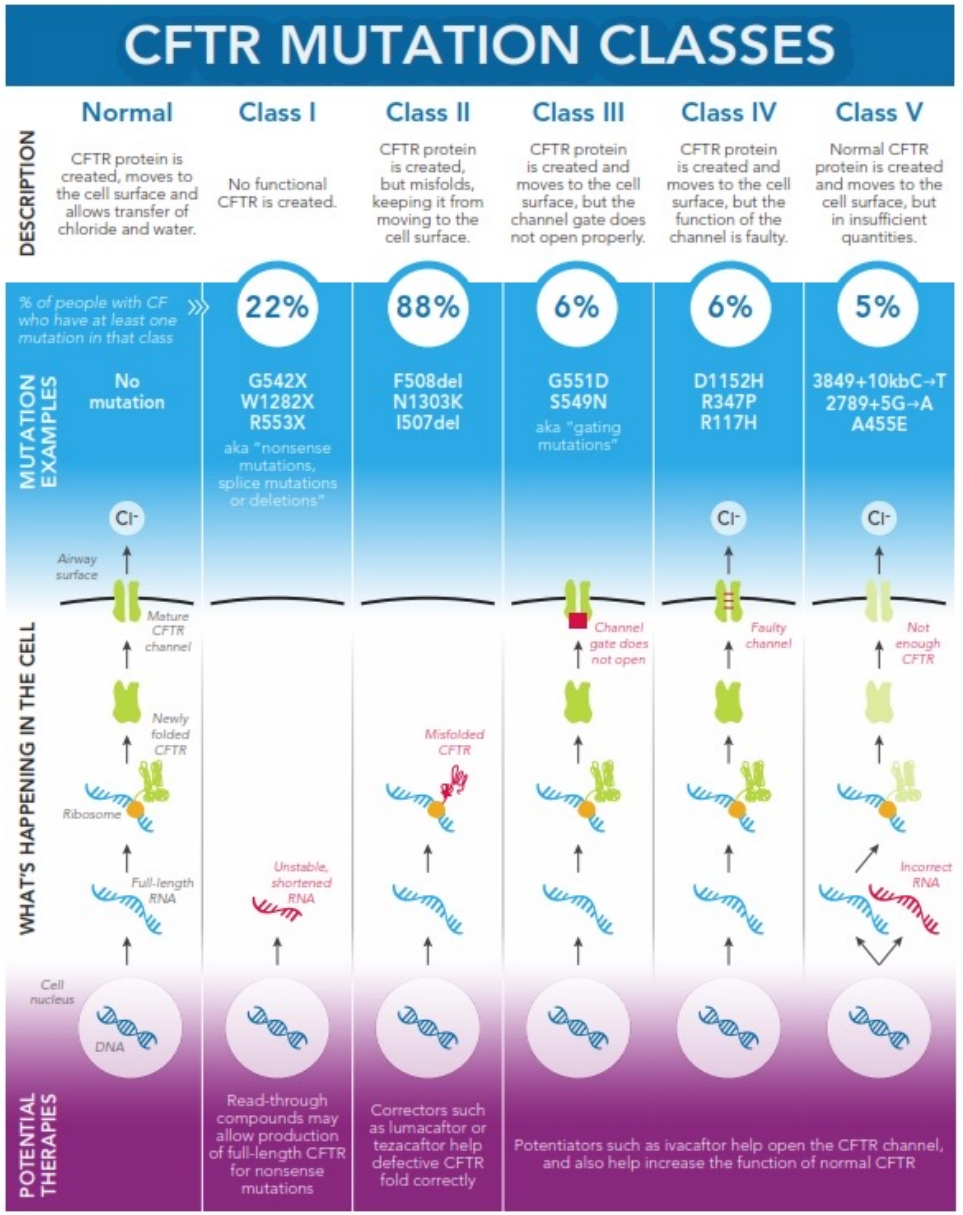
Lack of chloride ions means less water;
mucus becomes sticky and difficult to clear

5 Classes of CFTR Mutations



I	II	III	IV	V
Defective Protein Production	Defective Protein Processing	Defective Protein Regulation	Defective Protein Conductance	Reduced Amounts CFTR protein

CF Mutations can be classified by the effect they have on the CFTR protein.


CFTR MUTATION CLASSES
Normal
Class I
Class II
Class III
Class IV
Class V
DESCRIPTION
CFTR protein is created, moves to the cell surface and allows transfer of chloride and water.
No functional CFTR is created.
CFTR protein is created, but misfolds, keeping it from moving to the cell surface.
CFTR protein is created and moves to the cell surface, but the channel gate does not open properly.
CFTR protein is created and moves to the cell surface, but the function of the channel is faulty.
Normal CFTR protein is created and moves to the cell surface, but in insufficient quantities.
% of people with CF who have at least one mutation in that class
22%
88%
6%
6%
5%
MUTATION EXAMPLES
No mutation
G542X
W1282X
R553X
aka "nonsense mutations, splice mutations or deletions"
F508del
N1303K
I507del
G551D
S549N
aka "gating mutations"
D1152H
R347P
R117H
3849+10kbC→T
2789+5G→A
A455E
WHAT'S HAPPENING IN THE CELL
Cl-
Airway surface
Mature CFTR channel
Newly folded CFTR
Ribosome
Full-length RNA
Cell nucleus
DNA
Unstable, shortened RNA
Misfolded CFTR
Channel gate does not open
Faulty channel
Not enough CFTR
Incorrect RNA
POTENTIAL THERAPIES
Read-through compounds may allow production of full-length CFTR for nonsense mutations
Correctors such as lumacaftor or tezacaftor help defective CFTR fold correctly
Potentiators such as ivacaftor help open the CFTR channel, and also help increase the function of normal CFTR

CF mutations

- There about 1700 known mutations of the CF gene
- The most common Delta F 508

(a type II mutation)

CF: Genetics

- More than 80 percent of patients are diagnosed by age three; however, nearly 10 percent of newly diagnosed cases are age 18 or older.

- Newborn screening Only Detects 10% of the cases

Presentation (CF PANCREAS)

C Chronic respiratory disease

F Failure to thrive

P Polyps

A Alkalosis, metabolic

N Neonatal intestinal obstruction

C Clubbing of fingers

R Rectal prolapse

E Electrolyte ↑ in sweat

A Aspermia / absent vas deferens

S Sputum – S.aureus/P.aeruginosa

CF: Symptoms

- Chronic sino-pulmonary disease
  - Chronic Sinusitis
  - Nasal Polyps
- Gastrointestinal/nutritional problems
- Salt-loss syndromes
- Normal intellect
- Life span about 30+ years
- If pancreatic sufficient, life span 56 years

SYMPTOMS

- People with CF have a variety of symptoms including:
  - Very salty-tasting skin
  - Persistent coughing, at times with phlegm; wheezing or shortness of breath
  - Excessive appetite but poor weight gain; and greasy, bulky stools.
  - Symptoms vary from person to person

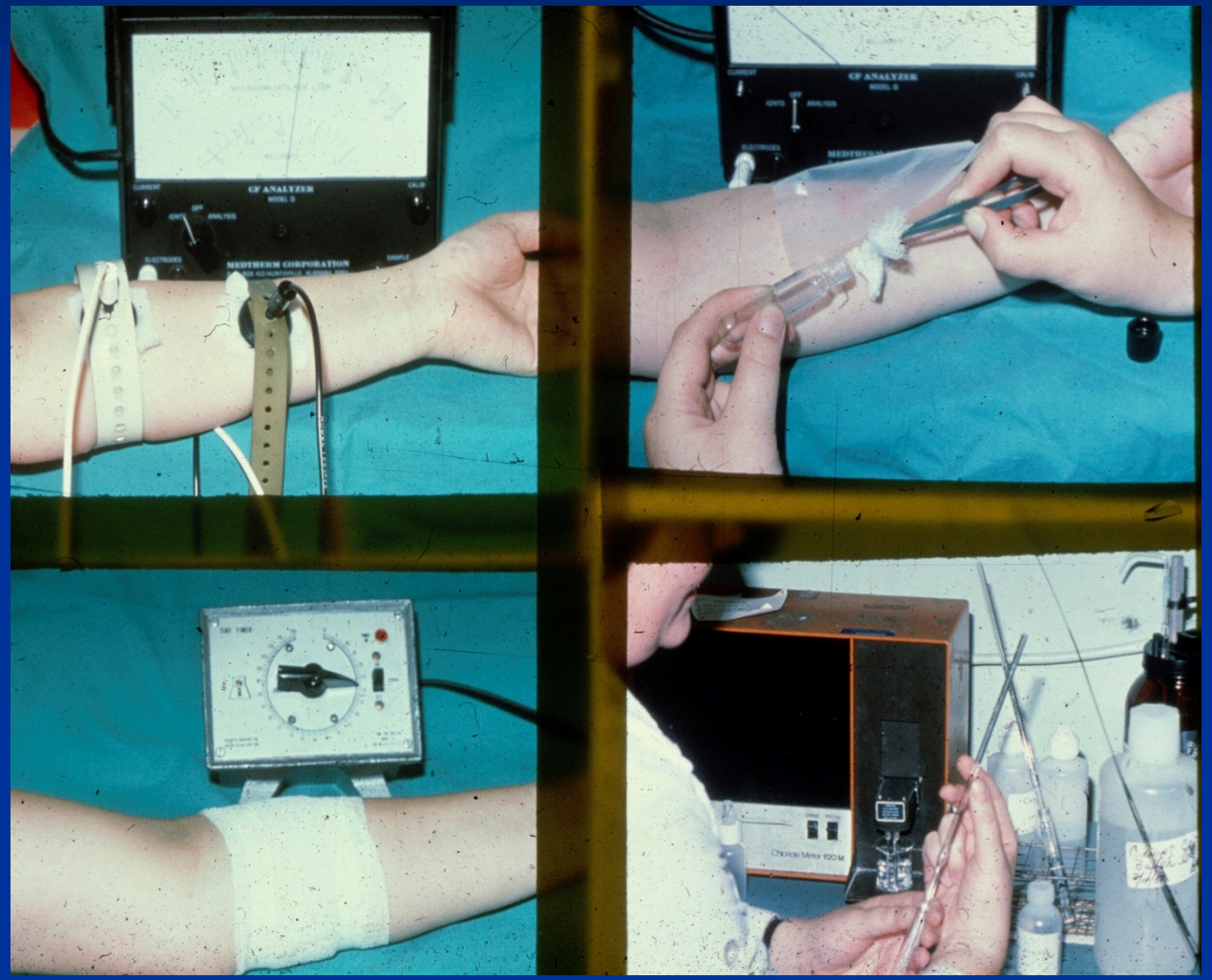
CF: Gastrointestinal Disease

- Pancreatic insufficiency/malabsorption
- Neonatal intestinal obstruction Meconium Ileus(15%)
- Lipo-soluble vitamin deficiency
- Failure to thrive
- Recurrent distal intestinal obstruction
- Biliary stasis

CF: Pancreas-malabsorption

DIAGNOSIS

The sweat test (Chloride)



Negative ***(02/2017)***

Under 30 mEq/L

Past was less than 40

Borderline

30-59 mEq/L

Positive

Over 60 mEq/L

J. Peds Volume 181, Supplement, February 2017, Pages S4–S15.e1

MACRODUCT SYSTEM

Start at 2 weeks of age

Blood Gases Patient with CF

- **Ph Metabolic Alkalosis**
  - Low Sodium
  - Normal Potassium
  - Low Chloride
  - High Bicarbonate
  - Normal BUN

One frequent differential Diagnosis

- **Ciliary Dyskenesia Primary**:
  - Recurrent Otitis Media
  - Chronic Sinusitis
  - Productive cough
  - Bronchiectasis
  - Recurrent Pneumonia
  - Situs Inversus (Kartagener's Syndrome)

Differential Diagnosis for Wheezing

FOREIGN BODY ASPIRATION

Upper Airway Laryngeal area

- Acute episode of: +/-
  Hoarse voice
  Cough
  Wheezing
  Respiratory distress
  No fever
  With or without history of choking episode.

Airway Symptoms Lower

- Persistent paroxysmal cough after choking episode.
- Localized wheezing does not improve with bronchodilators.
- Chest x-ray shows one side hyperinflation during inspiration and expiration from the side where the foreign body is located.
- Treatment Bronchoscopy.

Pneumothorax

- Primary spontaneous – Teens and young adults, esp. tall thin males, Ehlers-Danlos, and Marfan.
- Secondary spontaneous – underlying conditions: pneumonia, empyema, cyst, Foreign body, asthma. Not due to trauma.
- Iatrogenic
- Catamenial pneumothorax – associated with menses, passage of intra-abdominal air through diaprhagmatic defects.

PNEUMOTHORAX

- **ACUTE ONSET OF CHEST PAIN, RESPIRATORY DISTRESS IN A PATIENT WITH ASTHMA**
- **TRAUMA**
- **ACUTE DECOMPENSATION IN A PATIENT ON MECHANICAL VENTILATION**

ALWAYS DECREASE BREATH SOUNDS IN THE LUNG WITH THE PNEUMOTHORAX

Pneumothorax

- Rx: <5% is “small”, may resolve spontaneously, give 100%O2,
- >20% = “large” pneumos need chest tube
- Tension pneumos need immediate decompression.

Hemoptysis

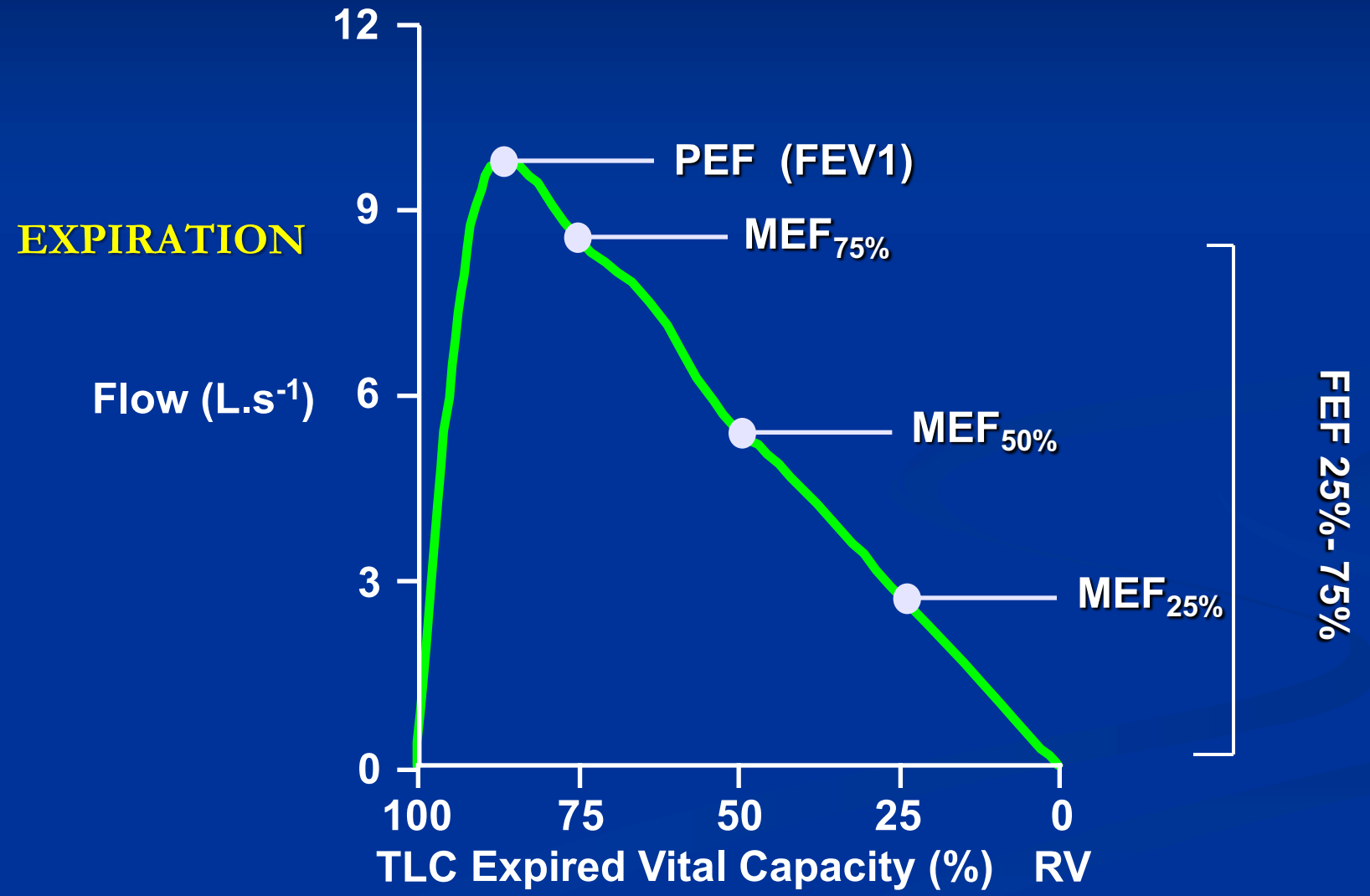
- The leading causes of hemoptysis in children are cystic fibrosis, congenital heart disease (CHD), and trauma.
- Infection, tracheostomy-related, bronchiectasis, foreign body, A-V Malformation, trauma, tumor.
- Pulmonary hemosiderosis, Goodpasture syndrome, Wegener granuloma

Epistaxis

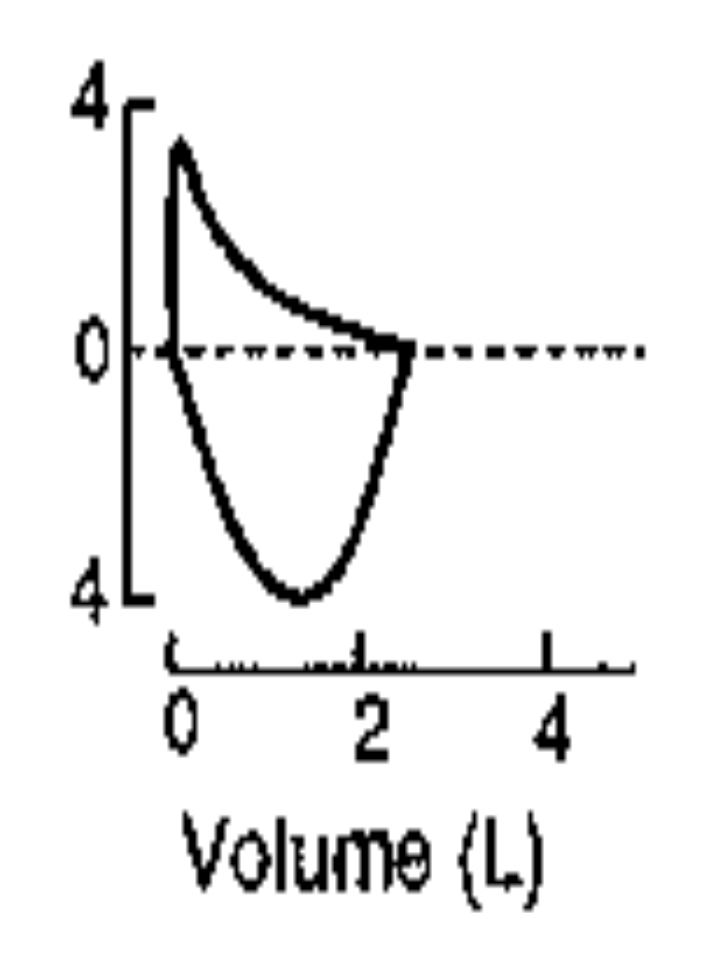
- Most Common Cause is: digital trauma
- Adolescents – question about drug abuse.
- Kiesselbach plexus
- Order coagulation and hematologic studies only if prolonged, severe, or family history.

PULMONARY FUNCTION TEST

Forced Expiratory Flow-Volume Curve



Obstructive Disorders



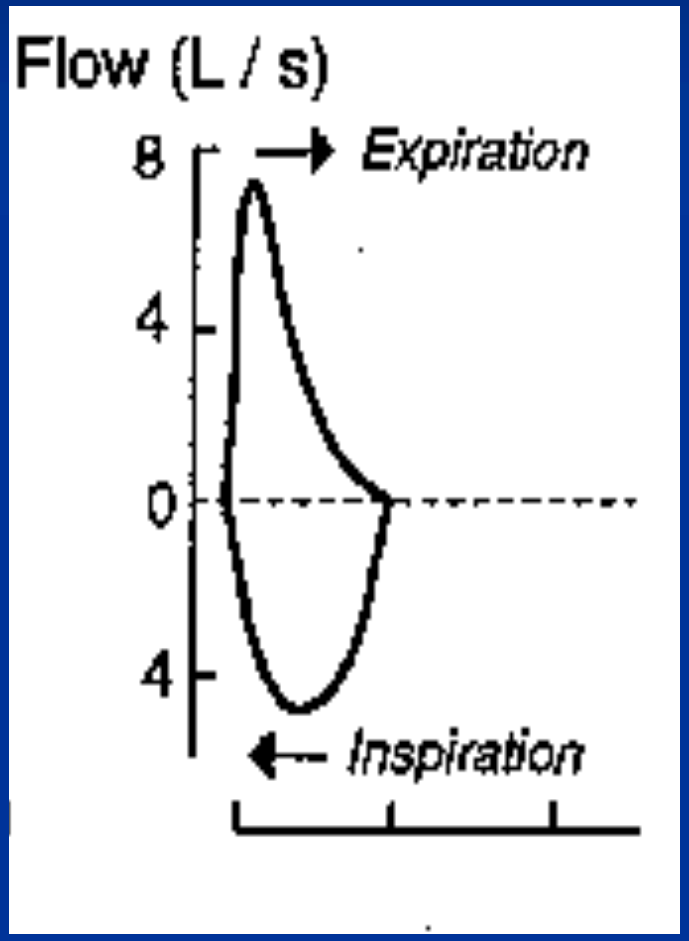
- Characterized by a limitation of expiratory airflow
  - Examples:

    Asthma, COPD
- Decreased:

  FEV_1, FEF_{25-75},

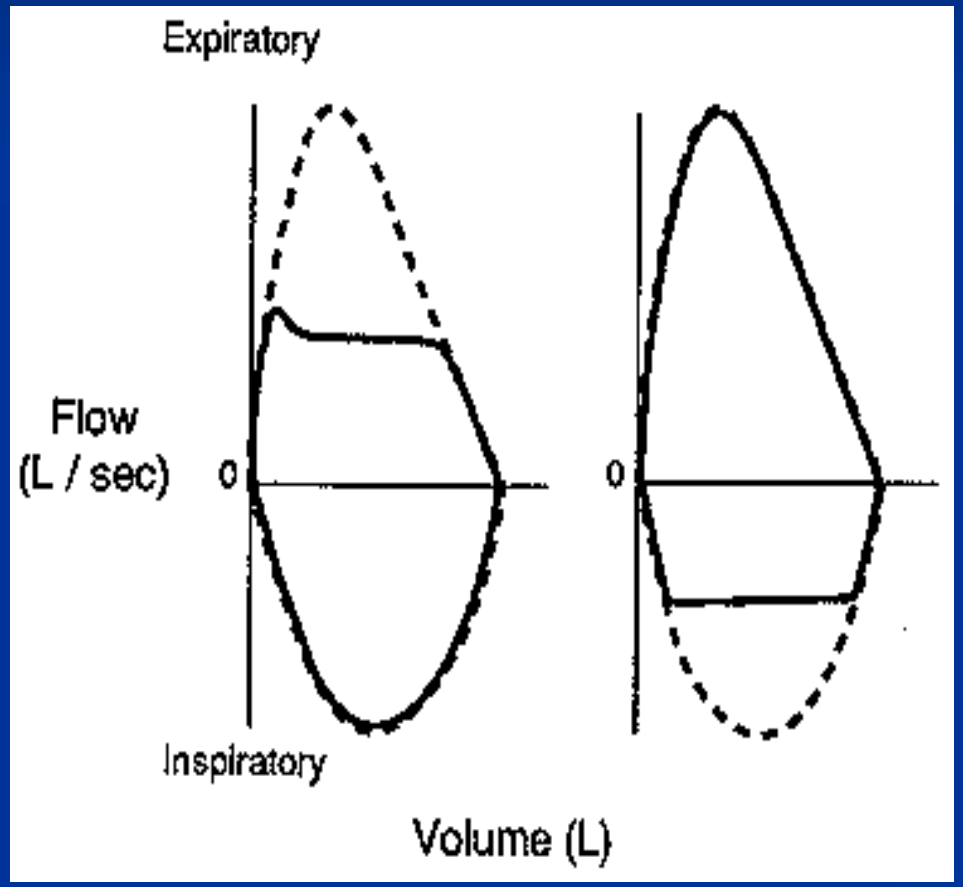
  FEV_1/FVC ratio (<0.8)
- Increased or Normal: TLC
- Normal Diffusion Capacity

Restrictive Lung Disease



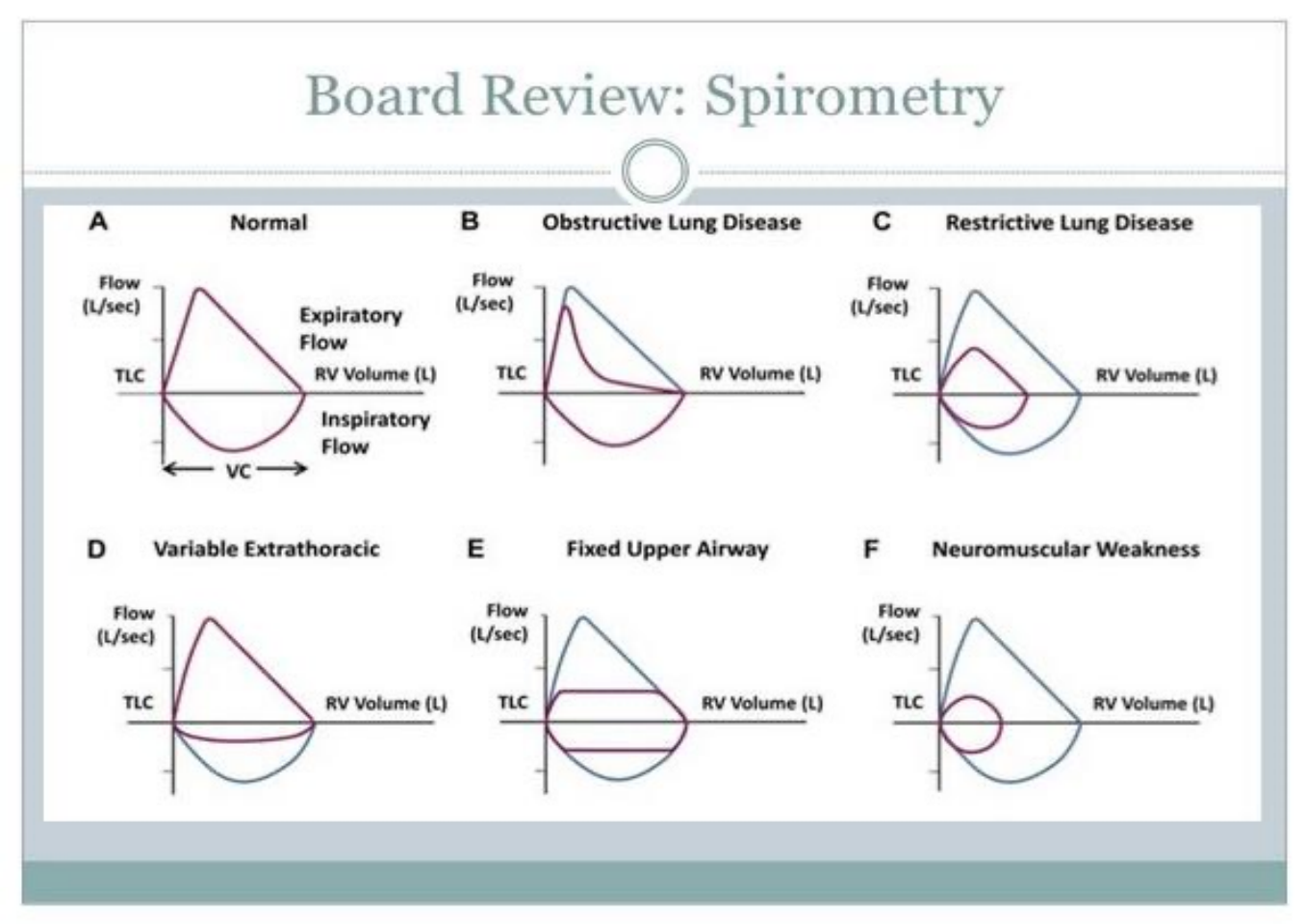
- Characterized by diminished lung volume due to:
  - change in alteration in lung parenchyma (interstitial lung disease)
  - disease of pleura, chest wall (e.g. scoliosis), or neuromuscular apparatus (e.g. muscular dystrophy)
- Decreased TLC, FVC
- Normal or increased: FEV_1/FVC ratio
- Diffusion capacity could be altered

Large Airway Obstruction



- **Characterized by a truncated inspiratory or expiratory loop**

Spirometry Loops



Thank you !!!

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GOOD LUCK!!!