Asthma Masqueraders (adolescents and adults)

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Faculty Disclosures

Stephen Tilles, MD

For the 12 months preceding this CME activity, I disclose the following types of financial relationships:

Honoraria received from:
- Alcon, Merck

Consulted for:
- Hycor, Ista, SRxA, Sunovion

Held Common Stock in:
- None

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- Amgen, Amphastar, Astellas, Aventis, Boehringer Ingelheim, Genentech, Medimmune, Merck, NIH, Novartis, Nutricia, Sunovion, TEVA

I will not be discussing products that are investigational or not labeled for use under discussion.
Objectives

- Understand hallmarks of asthma and how these assist when considering differential diagnosis
- Understand clinical presentation of common asthma masqueraders
- Understand appropriate diagnostic approaches when considering asthma masqueraders
Outline

- Hallmarks of asthma
- Overview of differential diagnosis
  - Distinguishing asthma from COPD
  - Distinguishing asthma from VCD
  - Less common and uncommon masqueraders
- Approaches to reaching the correct diagnosis – clinical scenarios
Hallmarks of Asthma

- Intermittent Symptoms: wheezing, dyspnea, chest tightness, cough
- Symptoms may awaken the patient after midnight
- Triggers
  - Exercise
  - Cold air
  - Viral URIs
  - Allergens
  - Irritants
    - Smoke, chemicals, perfume
  - Emotional stress
  - Weather changes
- Symptoms respond acutely to inhaled bronchodilators
- Symptoms respond subacutely to systemic or inhaled corticosteroids
- Spirometry reveals reversible intrathoracic airflow obstruction
Common Asthma Masqueraders

- COPD
  - Emphysema
  - Chronic bronchitis

- VCD – multiple names *(none particularly accurate)*
  - “VCD” – vocal cord dysfunction
  - “POLO” – periodic occurrence of laryngeal obstruction
  - “PVFM” – paradoxical vocal fold motion
Asthma and COPD in the Elderly

- As world population ages, there is an increased burden of COPD and asthma in the elderly

- Current prevalence
  - Asthma: > 10% in patients > 60 years old
  - COPD: 20-30% in patients > 70 years old

J Allergy 2011; 2011: 843543
Asthma in the Elderly

- Significant overlap with COPD
  - History of smoking is common
  - Late onset asthma usually non-allergic, sometimes neutrophilic

- Methacholine challenge
  - Negative result helpful
  - Positive result more common if FEV-1 is low (i.e. false positives common with COPD)

- Exhaled nitric oxide – utility unclear

Hanania et al JACI 2011;128:S4-24)
## Comparison of Asthma and COPD

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>any age</td>
<td>elderly smokers</td>
</tr>
<tr>
<td>Classic symptoms</td>
<td>wheezing, cough, dyspnea, chest tightness</td>
<td>dyspnea on exertion</td>
</tr>
<tr>
<td>Relation of sx to respiratory Cycle</td>
<td>exhalation &gt; inhalation</td>
<td>exhalation &gt; inhalation</td>
</tr>
</tbody>
</table>

Tilles SA, Nelson HS Current Review of asthma. Current Medicine, 2003
<table>
<thead>
<tr>
<th>Criteria</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXR</td>
<td>hyperinflation</td>
<td>Hyperinflation and hyperlucency</td>
</tr>
<tr>
<td>PFTs</td>
<td>Increased volumes, reversible obstruction, normal or increased DLCO</td>
<td>Increased volumes, irreversible obstruction, decreased DLCO</td>
</tr>
</tbody>
</table>

Tilles SA, Nelson HS Current Review of asthma. Current Medicine, 2003
## Comparison of Asthma and COPD

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>inflammatory cells</strong></td>
<td>Eosinophils</td>
<td>Neutrophils</td>
</tr>
<tr>
<td></td>
<td>Neutrophils</td>
<td>Macrophages</td>
</tr>
<tr>
<td></td>
<td>Mast cells</td>
<td>CD8+ T cells</td>
</tr>
<tr>
<td></td>
<td>CD4+ T cells</td>
<td></td>
</tr>
<tr>
<td><strong>Structural changes</strong></td>
<td>Airway sm muscle +++</td>
<td>Airway sm muscle +</td>
</tr>
<tr>
<td></td>
<td>All airways</td>
<td>Peripheral airways</td>
</tr>
<tr>
<td></td>
<td>No Parenchymal change</td>
<td>Parenchymal destruction</td>
</tr>
<tr>
<td></td>
<td>Epithelial shedding</td>
<td>Epithelial metaplasia</td>
</tr>
<tr>
<td></td>
<td>Fibrosis + (subepithelial)</td>
<td>Fibrosis ++</td>
</tr>
<tr>
<td></td>
<td>Mucous secretion +</td>
<td>(peribronchiolar)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mucous secretion +++</td>
</tr>
</tbody>
</table>

Tzortzaki EG, et al J Allergy 2011; 2011:843543
# Comparison of Asthma and COPD

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response to corticosteroids</td>
<td>good</td>
<td>poor</td>
</tr>
<tr>
<td>Response to bronchodilators</td>
<td>good</td>
<td>modest</td>
</tr>
</tbody>
</table>

Tilles SA, Nelson HS Current Review of asthma. Current Medicine, 2003
Hallmarks of VCD
NHLBI EPR3 2008

- Intermittent Symptoms: dyspnea, throat tightness, chest tightness, wheezing
- Triggers
  - Exercise
  - Cold air
  - Irritants
    - Smoke, chemicals, perfume
  - Emotional stress
- Symptoms typically do not respond acutely to inhaled bronchodilators
- Symptoms typically do not respond subacutely to systemic or inhaled corticosteroids
- Spirometry during symptoms often reveal extrathoracic airflow obstruction
Vocal Cord Dysfunction

- VCD can mimic asthma, but it is a distinct disorder
- VCD may coexist with asthma
- Asthma medications typically do little, if anything, to relieve VCD symptoms
- Variable flattening of the inspiratory flow volume loop on spirometry is strongly suggestive of VCD

Guidelines for the Diagnosis and Management of Asthma
NHLBI NAEPP EPR 3
November, 2007
Vocal Cord Dysfunction

- Diagnosis of VCD is from indirect or direct vocal cord visualization during an episode, during which abnormal adduction can be documented.
- VCD should be considered in patients with difficult-to-treat, atypical asthma and in elite athletes who have exercise related breathlessness unresponsive to asthma medication.

Guidelines for the Diagnosis and Management of Asthma
NHLBI NAEPP EPR 3
November, 2007
### Spirometry and Flow Volume Loops

<table>
<thead>
<tr>
<th>Metric</th>
<th>Normal</th>
<th>Reversible intra-thoracic obstruction</th>
<th>Variable extra-thoracic obstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁</td>
<td>4.36 (100%)</td>
<td>2.27 → 2.71 (16%)</td>
<td>3.65 (99%)</td>
</tr>
<tr>
<td>FVC</td>
<td>5.04 (108%)</td>
<td>3.20 → 3.58 (11%)</td>
<td>3.71 (96%)</td>
</tr>
<tr>
<td>FEV₁ / FVC</td>
<td>.86</td>
<td>.71 → .76 (6%)</td>
<td>.98</td>
</tr>
<tr>
<td>FEF₂₅-₇₅</td>
<td>4.77 (108%)</td>
<td>1.63 → 2.13 (23%)</td>
<td>6.15 (155%)</td>
</tr>
<tr>
<td>FEF₅₀ / FIF₅₀</td>
<td>0.84</td>
<td>0.38 → 0.30 (23%)</td>
<td>4.33</td>
</tr>
</tbody>
</table>
Clinical and Lung Function Variables Associated with VCD

Watson et al. Respiratory Care 2009 54(4):467-473

- Comparison of spirometry and laryngoscopic findings in 226 patients evaluated for VCD
  - Included retrospective flow volume loop interpretation by 3 pulmonologists blinded to laryngoscopy result
Clinical and Lung Function Variables Associated with VCD

Watson et al. Respiratory Care 2009 54(4):467-473

RESULTS

- 100 confirmed to have VCD via laryngoscopy
- Majority of confirmed cases did not have abnormal inspiratory flow volume loop
- Authors’ conclusions:
  - VCD remains difficult to predict with spirometry or flow-volume loops.
  - If VCD is suspected, normal flow-volume loop patterns should not influence the decision to perform laryngoscopy
Proposed Etiologies for VCD

Hicks M, Brugmen SM, Katial R Primary Care Clinics 2008; 35(1): 81-103

- Upper airway hyperresponsiveness (irritable larynx syndrome) secondary to
  - Laryngopharyngeal reflux
  - Inflammatory upper airway disease
  - Toxic inhalation (occupational, accidental)

- Exaggerated glottic closure reflex
- Autonomic dysfunction of the larynx
- Primary psychiatric disorder
A word about Phenotypes

**Asthma**
- 4 year old with itchy eyes, runny nose, sneezing and wheezing in late spring during the peak of grass pollen
- 48 year old without prior atopy who has severe respiratory infection followed by chronic wheezing, dyspnea, and reversible airflow obstruction controlled by the combination of continuous ICS and PRN SABA

**VCD**
- 15 year old non-atopic elite soccer player with episodic exercise-induced stridor
- 45 year old with history of chronic anxiety/depression and recurrent dramatic episodes of dyspnea, stridor and multiple intubations
VCD adult phenotype: National Jewish Adult VCD Series
Newman et al AJRCCM 152:1382 1995

- All VCD patients from 1984 to 1991 (95)
  - 42 VCD alone
  - 53 VCD + asthma
  - 42 control subjects with severe asthma
### VCD: National Jewish Series


<table>
<thead>
<tr>
<th></th>
<th>VCD</th>
<th>VCD + Asthma</th>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of Sx</td>
<td>4.8 +/- 5.2</td>
<td>14.1 +/- 13.9</td>
<td>15.7 +/- 13.8</td>
</tr>
<tr>
<td>Prednisone dose</td>
<td>29.2 +/- 28.7</td>
<td>21.31 +/- 23.6</td>
<td>25.5 +/- 25.3</td>
</tr>
<tr>
<td>Years of prednisone</td>
<td>4.3 +/- 10.9</td>
<td>4.0 +/- 4.1</td>
<td>3.3 +/- 5.4</td>
</tr>
<tr>
<td>ER visits in prev. yr</td>
<td>9.7 +/- 7.9</td>
<td>5.5 +/- 6.2</td>
<td>4.5 +/- 4.8</td>
</tr>
<tr>
<td>Admits in prev. yr</td>
<td>5.9 +/- 6.1</td>
<td>6.7 +/- 11.9</td>
<td>3.1 +/- 4.7</td>
</tr>
<tr>
<td>Intubated</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

**Note:** The values are presented in units of years or units per year.
Psychiatric Disturbance in 42 VCD patients without asthma

- 73% axis I diagnosis (38% abused)
- 37% axis II diagnosis
- 21% psychiatric Hospitalization

Only psychiatric hospitalizations were significantly different from controls
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Presentation</th>
<th>Diagnostic Keys</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF</td>
<td>DOE, PND</td>
<td>PE: rales, edema, S3</td>
</tr>
<tr>
<td></td>
<td>Occasional wheezing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Occasional BHR</td>
<td>CXR, ECG, echo</td>
</tr>
<tr>
<td></td>
<td>Cardiac risk factors</td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Dyspnea, occasional wheezing</td>
<td>PE: unilateral rales, leg edema, cord</td>
</tr>
<tr>
<td>embolism</td>
<td>PE risk factors</td>
<td>V/Q scan; chest CT</td>
</tr>
</tbody>
</table>
# Less Common Asthma Masqueraders

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Presentation</th>
<th>Diagnostic Keys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic Fibrosis</td>
<td>Dyspnea, cough, GI complaints</td>
<td>Sweat chloride screen</td>
</tr>
<tr>
<td></td>
<td>Airflow obstruction</td>
<td>DNA analysis</td>
</tr>
<tr>
<td></td>
<td>Infertility</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Poor growth</td>
<td></td>
</tr>
<tr>
<td>Bronchiolitis obliterans</td>
<td>Cough, dyspnea</td>
<td>Bronch with BAL, Bx</td>
</tr>
<tr>
<td></td>
<td>Irreversible obstruction</td>
<td>Chest CT</td>
</tr>
</tbody>
</table>
## Less Common Asthma Masqueraders

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Presentation</th>
<th>Diagnostic Keys</th>
</tr>
</thead>
<tbody>
<tr>
<td>bronchiectasis</td>
<td>Cough, dyspnea unresponsive to bronchodilator or corticosteroids</td>
<td>Chest CT</td>
</tr>
<tr>
<td>Hypersensitivity pneumonitis</td>
<td>Dyspnea after chronic exposure to organic antigen Spiro - restriction</td>
<td>Precipitating antibodies Chest CT</td>
</tr>
</tbody>
</table>
## Less Common Asthma Masqueraders

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Presentation</th>
<th>Diagnostic Keys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration/GERD</td>
<td>h/o heartburn and/or regurgitation</td>
<td>Esophageal pH probe</td>
</tr>
<tr>
<td></td>
<td>Recurrent pneumonia, Restrictive spirometry</td>
<td>Barium swallow</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chest CT</td>
</tr>
<tr>
<td>Central airway obstruction</td>
<td>Dyspnea, expiratory wheezing</td>
<td>Improves with heliox</td>
</tr>
<tr>
<td></td>
<td>Not episodic</td>
<td>bronchoscopy</td>
</tr>
<tr>
<td></td>
<td>No nocturnal worsening</td>
<td></td>
</tr>
</tbody>
</table>

- **Aspiration/GERD**
  - h/o heartburn and/or regurgitation
  - Recurrent pneumonia, restrictive spirometry

- **Central airway obstruction**
  - Dyspnea, expiratory wheezing
  - Not episodic
  - No nocturnal worsening
Causes of Central Airway Obstruction

- Broncholithiasis
- Endobronchial granulomatous disease (TB, Sarcoid)
- Bronchomalacia
- Foreign body
- Web or stricture
- Vascular ring
- Tumor
- Relapsing polychondritis
- Extrinsic compression (tumor, vascular structure)
# Less Common Asthma Masqueraders

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Presentation</th>
<th>Diagnostic Keys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extrathoracic</td>
<td>Dyspnea, stridor, inspiratory wheezing, truncation of insp FVL</td>
<td>Laryngoscopy</td>
</tr>
<tr>
<td>obstruction</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Causes:**

- VCD, vocal cord paresis, cricoarytenoid joint arthritis,
- lymph node enlargement, tumor, tracheomalacia, epiglotitis,
- extrinsic compression (edema, hemorrhage, thyroid enlargement, tumor)
Uncommon Asthma Masqueraders

- Pulmonary infiltrates with eosinophilia
  - Tropical eosinophilia
  - Loffler’s syndrome
  - Chronic eosinophilic pneumonia
  - Idiopathic hypereosinophilic syndrome
  - ABPA
  - Churg-Strauss syndrome

Tilles SA, Nelson HS Current Review of asthma. Current Medicine, 2003
Uncommon Asthma Masqueraders

- Metastatic carcinoid
- Systemic mastocytosis
- Lymphangioleiomyomatosis
- Amyloidosis

Tilles SA, Nelson HS Current Review of asthma. Current Medicine, 2003
Outline

- Hallmarks of asthma
- Overview of differential diagnosis
  - Distinguishing asthma from COPD
  - Distinguishing asthma from VCD
  - Less common and uncommon masqueraders
- Approaches to reaching the correct diagnosis – clinical scenarios
Clinical Scenario #1 - Megan

- 13 year old “crossfire” soccer player
- 8 month history of dyspnea, chest tightness during exercise
  - Upper chest “tightness” after 10 min of exercise, followed by wheezing and difficulty breathing in
  - No triggers other than exercise
  - Refractory to treatment with:
    - prophylactic inhaled albuterol
    - twice daily fluticasone 250 ug/salmeterol 50 ug
    - Once daily montelukast 10 mg
CASE - Megan

- PMH  Acne, Mild eczema
- SH
  - Supportive parents; 1 sibling
  - no history of anxiety, depression, major psychological trauma
  - 3.5 GPA
- PE  62”, 111 lb; Exam normal
Case – Megan: spirometry

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>3.12 (100%)</td>
</tr>
<tr>
<td>FEV-1</td>
<td>2.90 (97%)</td>
</tr>
<tr>
<td>FEV-1/FVC</td>
<td>0.93</td>
</tr>
<tr>
<td>FEF50/FIF50</td>
<td>0.80</td>
</tr>
</tbody>
</table>
EIB: The Response

Standardization of Exercise Tests in Asthmatic Children
Silverman M, Arch Dis Childhood 1972; 47:882
EIB: Refractory Period

Weiler-Ravell D, JACI 1981; 67:391
Inspiratory Stridor in Elite Athletes
Rundell KW et. al. Chest 2003 123:468-474

- 370 athletes performed exercise challenge in cold, dry conditions*:
  - 5% developed inspiratory stridor
  - 30% developed EIB

<table>
<thead>
<tr>
<th>Stridor +</th>
<th>EIB +</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>male</td>
</tr>
<tr>
<td>1</td>
<td>53</td>
</tr>
<tr>
<td>female</td>
<td>female</td>
</tr>
<tr>
<td>18</td>
<td>58</td>
</tr>
</tbody>
</table>

* no laryngoscopies performed
# Adolescents with VCD Mimicking EIB

<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>Presenting Symptoms</th>
<th>Sport</th>
<th>EIB</th>
<th>Psychiatric Diagnosis</th>
<th>Academic Achievement</th>
</tr>
</thead>
<tbody>
<tr>
<td>16/F</td>
<td>Throat tightness, Dyspnea</td>
<td>BB, VB, Tr</td>
<td>No</td>
<td>----</td>
<td>A</td>
</tr>
<tr>
<td>12/F</td>
<td>Throat tightness, Dyspnea</td>
<td>Sw, Ch</td>
<td>Yes</td>
<td>Anxiety</td>
<td>A</td>
</tr>
<tr>
<td>14/F</td>
<td>Throat tightness, Cough</td>
<td>Tae Kwon Do</td>
<td>No</td>
<td>Anxiety &amp; Depression</td>
<td>A</td>
</tr>
<tr>
<td>12/F</td>
<td>Throat/Chest tightness</td>
<td>S, SB</td>
<td>No</td>
<td>----</td>
<td>A</td>
</tr>
<tr>
<td>15/M</td>
<td>Throat/Chest tightness</td>
<td>Tr, FB</td>
<td>No</td>
<td>----</td>
<td>A</td>
</tr>
<tr>
<td>16/F</td>
<td>Voice changes, Wheezing</td>
<td>Sw, Tr</td>
<td>No</td>
<td>Depression</td>
<td>A</td>
</tr>
<tr>
<td>18/F</td>
<td>Throat tightness, Wheezing</td>
<td>VB</td>
<td>No</td>
<td>----</td>
<td>A</td>
</tr>
</tbody>
</table>

---

Landwehr et al, Pediatrics 1996; 88:971
Pediatric Paradoxical Vocal Fold Motion: Presentation and Natural History


- Retrospective chart review
  - 59 patients (average age 13.6; female: male = 3:1)
    - “PVFM” diagnosis based on clinical history (some had laryngoscopy)
  - 10% known anxiety or depression (ultimately diagnosed in 30%)

- Speech therapy
  - 45/59 had symptom resolution after average of 3.7 sessions
Reasonable Approaches When VCD Suspected

1. Empiric speech therapy
   - Must be wary of atypical asthma, anaphylaxis, or other dangerous Dx
   - Speech pathologist must be familiar with VCD

2. Methacholine challenge
   - Should only be performed if suspected not to have asthma or if attempting to provoke symptoms for laryngoscopy
   - If methacholine challenge negative, refer for speech therapy
Reasonable Approaches When VCD Suspected

3. Baseline laryngoscopy or refer for laryngoscopy before speech therapy
   ▪ Will confirm the absence of anatomic deformity, tumor, etc.
   ▪ May identify indirect signs of chronic laryngopharyngeal acid reflux
   ▪ Must be sure that otolaryngologist has knowledge of non-organic laryngeal syndromes such as VCD/PVFM

4. Symptom provocation with spirometry, laryngoscopy
   ▪ Methacholine, exercise, irritant
   ▪ Advantage: minimizes guesswork; high patient and referring MD satisfaction
   ▪ Disadvantage: expensive; limited availability
Normal Larynx

1. Vocal cords
2. False vocal cords
3. Arytenoids
4. Interarytenoid space
5. Epiglottis
VCD provoked during free-running exercise challenge

Resting breathing (inspiration)
during exercise-induced dyspnea, throat tightness (inspiration)
CASE – Megan : Baseline Laryngoscopy
### Megan : Free-run Exercise challenge

<table>
<thead>
<tr>
<th>Time</th>
<th>Exercise</th>
<th>Pulse</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td>75</td>
<td>none</td>
</tr>
<tr>
<td>1.5 min</td>
<td>Jogging (warm-up)</td>
<td>170</td>
<td>none</td>
</tr>
<tr>
<td>3.5 min</td>
<td>Six 30 meter sprints at ¾ effort</td>
<td>180</td>
<td>none</td>
</tr>
<tr>
<td>7 min</td>
<td>3 sets sprinting lines (30 sec each)</td>
<td>200</td>
<td>“6/10” inspiratory upper chest tightness</td>
</tr>
</tbody>
</table>
CASE – Megan: Post-exercise inspiratory “6/10” upper chest tightness

Paradoxical motion of arytenoids
No paradoxical motion of vocal cords
CASE – Megan: Post-exercise inspiratory “6/10” upper chest tightness

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Immediately Post-exercise</th>
<th>10 min post exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>3.12 (100%)</td>
<td>3.03 (97%)</td>
<td>2.86 (91%)</td>
</tr>
<tr>
<td>FEV-1</td>
<td>2.90 (97%)</td>
<td>2.91 (98%)</td>
<td>2.73 (92%)</td>
</tr>
<tr>
<td>FEV-1/FVC</td>
<td>0.93</td>
<td>0.96</td>
<td>0.96</td>
</tr>
<tr>
<td>FEF50/FIF50</td>
<td>1.30</td>
<td>1.48</td>
<td>1.00</td>
</tr>
</tbody>
</table>
“Anatomic” Phenotypes for VCD: depends on how VCD is defined

- **Strict definition of VCD:** requirement for anterior adduction of vocal cords with posterior chink during symptoms (very specific; poor sensitivity)

- **Broad definition:** spectrum of non-organic disorders involving symptoms related to dysfunction of the larynx and/or periglottic structures (more sensitive; less specific)
VCD “anatomic” Phenotype Examples

#1

exhalation

#2

inhalation
5 case reports of patients who had been referred by an asthma specialist to the NAAC VCD Clinic with suspected exercise-induced VCD

H&P, PE, baseline laryngoscopy performed on all patients

In 2 patients the diagnosis was suggested by baseline laryngoscopy

3 patients underwent exercise challenge
16 yo High School Varsity Football Player (wide receiver) with history of stridor during wind sprints

JACI 2009;124:277

**Laryngoscopy**

**Flow Volume Loop**

**Spirometry**

- FVC: 3.85 (96%)
- FEV₁: 3.65 (98%)
- FEV₁/FVC: 0.95 (103%)
- FEF₅₀/FIF₅₀: 1.66

*Fig E1. Left Laryngoscopy photograph for patient 2 shows obstruction of the glottic opening by abnormal positioning of the right arytenoid. Middle, Truncation of the inspiratory portion of the flow volume loop in patient 2, suggesting extrathoracic obstruction. Right, Patient 2 spirometry findings include an abnormally elevated ratio of forced expiratory to forced inspiratory flow at 50% of forced vital capacity (FEF₅₀/FIF₅₀), suggesting extrathoracic obstruction.*
37 year old Caucasian female with 2.5 year history of exertional dyspnea, wheezing – CXR, chest CT normal; no response to albuterol, ICS, LABA, LTRA

JACI 2009;124:277

Height: 67 inches
Weight: 123 lb

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Percentage</th>
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<td>FVC</td>
<td>3.82</td>
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<td>FEV-1</td>
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<td>FEV-1/FVC</td>
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<tr>
<td>FEF50/FIF50</td>
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Subglottic Stenosis

Airway significantly compromised due to membranous stenosis

39 yo female with 1 yr h/o SOB, throat tightness running on treadmill: serial spirometry in clinic

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<th>Date</th>
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*in VCD clinic*
History: symptom onset age 4; expiratory symptoms

Baseline spirometry normal

Prior work-up: echocardiogram normal

Prior unsuccessful Rx:
- albuterol MDI, ICS/LABA
- Speech therapy

Exercise challenge - expiratory “hissing” and chest tightness with normal spirometry and laryngoscopy during symptoms
Anomalous bronchi with stenotic left mainstem bronchus

JACI 2009;124:277

Fig E2. Patient 3: bronchoscopy photograph taken from the proximal trachea showing tracheal origin of the right upper lobe bronchus and stenosis of the distal trachea.