Disclosures

NONE

ZERO
OBJECTIVES

• To encourage better history taking when seeing patients to broaden the scope of possibilities of the causation of symptoms of exertional shortness of breath.

• Make students aware of the useful physical findings and useful observations as well as how they can incorporate into their practice.

• Provide examples and comparisons of new as well as old tests for EIB which will permit them to decide which modalities they would like to pursue.

• Provide encouragement as to potential outcomes that can be achieved.
Eugene Legends

Who is that guy??
It has long been recognized, even during biblical times, that physical exercise may induce asthma symptoms in susceptible individuals.\(^1\) Nevertheless, the term exercise-induced asthma (EIA) only became popular in the 1960s and 1970s when several reports addressed the pattern of airway response to exercise and the influence of drugs on EIA, particularly in children.\(^2,3\) Subsequently, reports of studies of the mechanisms causing EIA\(^4\) often asserted that EIA
EIA vs. EIB vs. EID

A = Asthma
B = Bronchospasm
D = Dyspnea
EIA vs. EIB vs. EID

- **EIA:**
  Exercise induces symptoms in patients who have asthma\(^1\).

- **EIB:**
  Airway obstruction occurring without regard to the presence of chronic asthma\(^1\).

- **EID:**
  Dyspnea with exercise without airway obstruction\(^2\).


2. Jack M. Becker, ACAAI, November, 2006
EIA vs. EIB vs. EID

A = Assuring *
B = BAD
D = Difficult or Demanding

*343 EIA patients in our clinic, with 95% doing very well
Exercise Induced Asthma (EIA)

• Present in the vast majority of asthmatics (90%).

• Follows a pattern more closely than EIB or EID.

• Eosinophilic inflammation that responds well to anti-inflammatory and bronchodilator therapy.

Clinical Presentation of EIA

After 6-8 Minutes of Strenuous and Continuous Aerobic Exercise

- Cough*
- Wheeze
- Chest tightness*
- Excess mucus
- Unusual shortness of breath

Other Features of EIA

- Cold weather and endurance events more likely to trigger.
- Responds well to SABA and LABA.
- A 10-15 minute warm up at 50-60% maximum heart rate helps prevent EIA.
- A refractory period of 2-3 hours after EIA.
EIB in Athletes

- Poorly predicted by baseline PFT’s.
- Less responsive to inhaled corticosteroids than EIA.
- Peculiar mechanisms including osmotic, thermal and mechanical are linked to hyperpnea.
- Often associated with neutrophilic rather than eosinophilic inflammation.
- Exercise challenge, eucapnic voluntary hyperventilation, or manitol are better diagnostic indicators than methacholine or histamine challenge.

50% of EIB isn’t!

Ray Davis, Susan Brugman, Gary Larsen, JACI, 118, 6, 1329-31 June, 2007
Vocal Cord Dysfunction (VCD)
Exercise Induced Laryngeal Dysfunction (EILD)
Paradoxical Vocal Fold Movement (PVFM)

1. VCD
2. Exercise laryngeal prolapse
3. Exercise laryngomalacia
Exercise Testing

• Methods:
  High intensity exercise with 6 - 8 minute duration.
  Spirometry at 3, 5, 7, 10 & 15 minutes post exercise.
  **Consistent with EIB if FEV$_1$ drops $\geq$ 10%**

• In the lab:
  Choice limited to 2 or 3 ergometers.
  Neutral air conditions.
  **False negative tests** (*Rundell et al. 2000*)

• In the field:
  Recommended, but not always feasible.
  **Need surrogate challenges**
1. Methods:
High intensity exercise with 6 - 8 minute duration. Spirometry at 3, 5, 7, 10 & 15 minutes post exercise. Consistent with EIB if FEV₁ drops ≥ 10%

2. In the lab:
Choice limited to 2 or 3 ergometers. Neutral air conditions. False negative tests *(Rundell et al. 2000)*

3. In the field:
Recommended, but not always feasible. Need surrogate challenges
Mannitol

Advanced Drug Delivery Reviews
Volume 133, August 2018, Pages 45-56
Mannitol dry powder increases osmolarity at the airway surface to cause mediator release from mast cells & eosinophils.

Receptors on smooth muscle are stimulated by the mediators so it contracts & the airways narrow in those with currently active asthma.

Mannitol dry powder increases osmolarity of the periciliary fluid layer and water moves to the lumen enhancing clearance of mucus.

$H_2O$ from submucosa rehydrates airway surface liquid.
Mannitol Inhaled Challenge

Oregon Allergy Associates
1488 Oak Street
Eugene, OR 97401
(541) 683-1577

Test, Test  ID: 1234  Age: 29 (10/2/1989)
Gender  Female
Ethnicity  Caucasian
Height  66 in
Weight  --
BMI  --

Provocation, FVC (ex only)
Test Date  6/27/2019 1:15:31 PM
BTPS (IN/EX)  1.12/1.02
Predicted  Hankinson (NHANES III), 1999

Provocation - Mannitol

<table>
<thead>
<tr>
<th>Dose</th>
<th>Total</th>
<th>Administer Time</th>
<th>FEV1</th>
<th>Test Time</th>
<th>Δ Step [%]</th>
<th>Δ Base [%]</th>
</tr>
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<tbody>
<tr>
<td>0 mg</td>
<td>0 mg</td>
<td>1:15 PM</td>
<td>2.69 L</td>
<td>1:16 PM</td>
<td>-0.9 %</td>
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<td>5 mg</td>
<td>5 mg</td>
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<td>2.67 L</td>
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<td>10 mg</td>
<td>10 mg</td>
<td>1:20 PM</td>
<td>2.73 L</td>
<td>1:20 PM</td>
<td>-0.9 %</td>
<td>-0.9 %</td>
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<td>20 mg</td>
<td>20 mg</td>
<td>1:21 PM</td>
<td>2.75 L</td>
<td>1:21 PM</td>
<td>-0.9 %</td>
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<td>40 mg</td>
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<td>2.80 L</td>
<td>1:22 PM</td>
<td>-0.9 %</td>
<td>-0.9 %</td>
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<tr>
<td>80 mg</td>
<td>80 mg</td>
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<td>2.78 L</td>
<td>1:23 PM</td>
<td>-0.9 %</td>
<td>-0.9 %</td>
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<tr>
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<td>160 mg</td>
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<td>2.46 L</td>
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<td>-0.9 %</td>
<td>-0.9 %</td>
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<td>320 mg</td>
<td>320 mg</td>
<td>1:25 PM</td>
<td>2.34 L</td>
<td>1:25 PM</td>
<td>-0.9 %</td>
<td>-0.9 %</td>
</tr>
</tbody>
</table>

Response / Dose ratio: 0.0246

15% fall from baseline

Cumulative dose of Mannitol [mg]

Flow [L/min]

Volume [L]
Eucapnic Voluntary Hyperventilation

- 6 minutes of hyperpnea
  - dry air
  - 4.9% CO₂

- 10% fall in FEV₁

- Specific for diagnosis of EIA
  Rundell et al. 2004

- Recommended by the IOC

Courtesy Dr. P. Kippilen
47 Exercise Challenges
Our Experience

Average age of 16 years; 32 female and 15 male.

• 21 positive for **EIB** (44%)
• 11 **Tachycardia** (23%)
  • 7 Pubertal, all female
  • 3 Inappropriate Tachycardia (2 taking Ritalin)
  • 2 **WPW** (both treated with ablation)
• 8 **VCD** – “**EILD**” (Laryngoscopy) (17%)
• 2 Hypertrophic **cardiomyopathy** (one fatal)
• 1 **Patent foramen ovale** (PFO)
• 1 **Thyroid cancer** with multiple metastasis
CASE 1
19 year old male with “EIB”

- 1 year history of sudden and extreme SOB while playing tennis and jogging home.
- Albuterol MDI of no benefit.
- Attacks became more frequent, more severe and occurred with less exertion.
- Felt like he was going to “black out.”
- Sense of impending doom.
Exam

- Great shape
- 72 inches
- 150 pounds
- Oxygen saturation 99%
- BP 104/64
- HR 78
- Grade I/VI SEM base, very soft
Evaluation

• **Spirometry**
  
  FEV1   4.87 L   106%
  
  FVC    5.67 L   107%
  
  FMF    5.42 L/M 106%
  
  Normal FVLP

• **Chest x-ray** normal
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Name</td>
<td>Male</td>
<td>Affiliated Physicians Northwest</td>
</tr>
<tr>
<td>Age</td>
<td>19 years</td>
<td>Normal sinus rhythm with marked sinus arrhythmia</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Caucasian</td>
<td>Voltage criteria for left ventricular hypertrophy</td>
</tr>
<tr>
<td>Height</td>
<td>72in</td>
<td>Inferior infarct, age undetermined</td>
</tr>
<tr>
<td>Weight</td>
<td>150lbs</td>
<td>Marked ST abnormality, possible lateral subendocardial injury</td>
</tr>
<tr>
<td>Vent. rate</td>
<td>80 bpm</td>
<td>Abnormal ECG</td>
</tr>
<tr>
<td>PR interval</td>
<td>132 ms</td>
<td></td>
</tr>
<tr>
<td>QRS duration</td>
<td>100 ms</td>
<td></td>
</tr>
<tr>
<td>QT/QTc</td>
<td>368/424 ms</td>
<td></td>
</tr>
<tr>
<td>P-R-T axes</td>
<td>69-53 134</td>
<td></td>
</tr>
</tbody>
</table>

Tests conducted by JM
Test Info: BASELINE

Meds: NONE

Ref. by: KWJ

Confirmed By:
Hypertrophic obstructive cardiomyopathy with severe hypertrophy of the interventricular septum and small end systolic cavity
27 year old female with “EIB”

- SOB with any exercise including aerobics, kickboxing and dance.
- Chest is “on fire” and heart pounds with activity of 5 minutes or less.
- Albuterol MDI made symptoms worse with less exercise tolerance.
- Symptoms of GERD treated with Prevacid without effect on chest symptoms.
Exam

- Great Shape
- 62 inches
- 130 pounds
- Oxygen saturation 96%
- BP 98/64
- HR 87 (resting)
- Normal physical exam
Evaluation

• **Spirometry**

  FEV1  2.97  93%
  FVC  3.51  95%
  FMF  3.08  79%

  Normal FVLP

• **No bronchodilator** therapy due to history of worsening symptoms when given.
27 years
Female Caucasian
63 in 130 lbs

Vent. rate 68 bpm
PR interval 160 ms
QRS duration 80 ms
QT/QTc 372/396 ms
P-R-T axes 75 101 40
BP: 98/64

Normal sinus rhythm with sinus arrhythmia
Rightward axis
Borderline ECG

Technician: JR
Test ind.: BASELINE
Meds: NO MEDICATIONS

Ref. by: KWJ
Confirmed By:

190hz 25mm/s 10mm/mV
MAX 001D 12SL v84
• Thyroid tests normal
• VMA normal
• Metanephrines normal
• Echocardiogram normal

Diagnosis: Inappropriate Tachycardia

History of Patient H-H

• Symptoms:
  Early and severe shortness of breath with exercise.
  Symptoms resolve with rest.
  Taking Ritalin for ADHD and Yasmin for dysmenorrhea.

• ECG:
  Tachycardia with 102 bpm at rest, otherwise normal.
Spirometry

Pre-bronchodilator

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Percentage</th>
</tr>
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<td>3.62 L</td>
<td>106%</td>
</tr>
<tr>
<td>FVC</td>
<td>4.31 L</td>
<td>121%</td>
</tr>
<tr>
<td>FMF</td>
<td>3.80 L</td>
<td>101%</td>
</tr>
</tbody>
</table>

Minimal reversibility post-bronchodilator
Exercise Challenge

• Pre challenge ECG

• Pre and post PFT’s at 1, 5, 10 minutes

• Heart rate monitor

• 6 - 8 minutes at 85% max heart rate
Exercise Challenge #1

- Difficult to control heart rate in order to begin testing.
- Rapid increase in heart rate.
- Inability to sustain exercise for testing period.
- No decrease in PFT’s.
## Spirometry

### Pre- exercise

<table>
<thead>
<tr>
<th></th>
<th>FEV1</th>
<th>%</th>
<th>FVC</th>
<th>%</th>
<th>FEV(_1)/FVC</th>
<th>%</th>
<th>FMF</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.81</td>
<td>112</td>
<td>4.53</td>
<td>127</td>
<td>0.86</td>
<td>100</td>
<td>4.22</td>
<td>112</td>
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</tbody>
</table>

### Post- exercise

<table>
<thead>
<tr>
<th></th>
<th>FEV1</th>
<th>%</th>
<th>FVC</th>
<th>%</th>
<th>FEV(_1)/FVC</th>
<th>%</th>
<th>FMF</th>
<th>%</th>
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<tbody>
<tr>
<td></td>
<td>3.92</td>
<td>115</td>
<td>4.30</td>
<td>121</td>
<td>0.91</td>
<td>106</td>
<td>4.96</td>
<td>132</td>
</tr>
</tbody>
</table>
Plan

- Stop Ritalin®
- Start Strattera®
- Return visit in 3 weeks.
- Repeat exercise challenge in 6 months.
Follow-up 3 weeks later…

- HR 47 bpm (resting).
- Reported increased exercise tolerance.
- 4 - 5 minutes to peak.
- Longer exercise tolerance of 8 minutes.
CASE 4
Ms. Smith returns today for a followup after her catheter ablation of WPW.

Since her ablation of March 12, Ms. Smith has done very, very well. She has had no difficulty with her leg, and she is exercising at a high level. She recently ran the Rogue River Trail, 41 miles, without any difficulty. She feels more confident in things now, she is getting back to her very high level of fitness.

PHYSICAL EXAMINATION:
GENERAL: She is in no distress.
VITAL SIGNS: Weight is 66.1 kg. Blood pressure is 104/78. Pulse is 52 beats per minute and regular.
NECK: Thyroid is normal.
CHEST: Clear to auscultation and percussion.
HEART: Regular rate and rhythm. Normal S1 and S2; there is no S3, S4, or murmur. PMI is nondisplaced. Carotid upstrokes and jugular venous distention are normal.

ELECTROCARDIOGRAM: EKG shows normal sinus rhythm with a single PAC. There is no pre-excitation.

IMPRESSION/PLAN:
1. WPW, status post ablation. She is doing well. I have not made a return appointment but have let her know that she can call or write at any time she has questions or concerns.
CASE 5
38 year old Female

- History of exertional SOB.
- No relief from SABA.
- ECG normal.
- Pre-Post and FVLP spirometry normal.
- Laryngoscopy normal.
- Exam normal except for fixed split S2.
- Positive diagnostic echocardiogram.
Patent Foramen Ovale

Conclusions

Injection of contrast documented an interatrial shunt with valsala. A patent foramen ovale is present. The left ventricle is normal in size. Left ventricular systolic function is normal. The left ventricular ejection fraction is approximately 60 - 64%. There is mild aortic regurgitation. The right ventricle is normal in size and function. The relatively large amount of shunting indicates a substantial patent foramen ovale. A small secundum type atrial septal defect cannot be excluded. Consider transesophageal echo to better evaluate, if clinically indicated.
Questions?