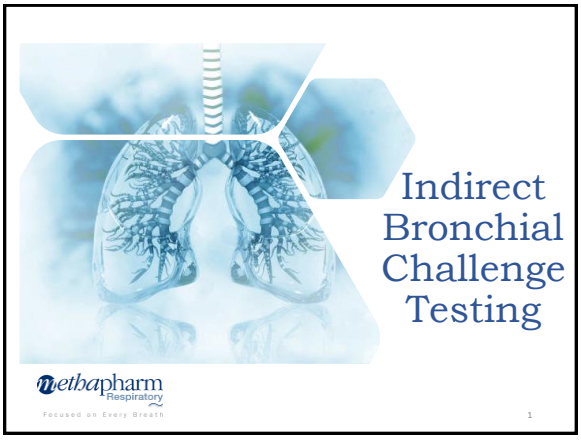
Indirect
Bronchial
Challenge
Testing
methapharm
Respiratory
Focused on Every Breath
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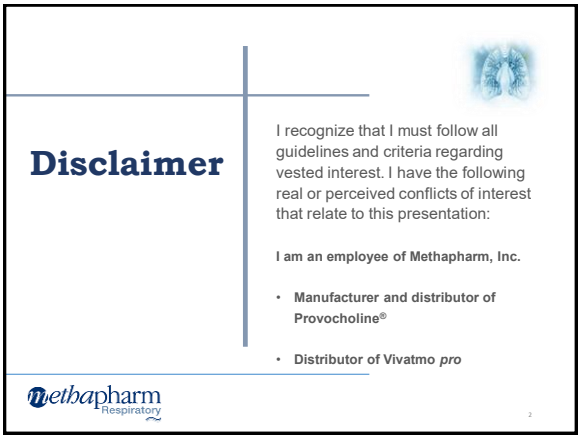
Disclaimer
I recognize that I must follow all guidelines and criteria regarding vested interest. I have the following real or perceived conflicts of interest that relate to this presentation:
I am an employee of Methapharm, Inc.
• Manufacturer and distributor of Provocholine®
• Distributor of Vivatmo pro
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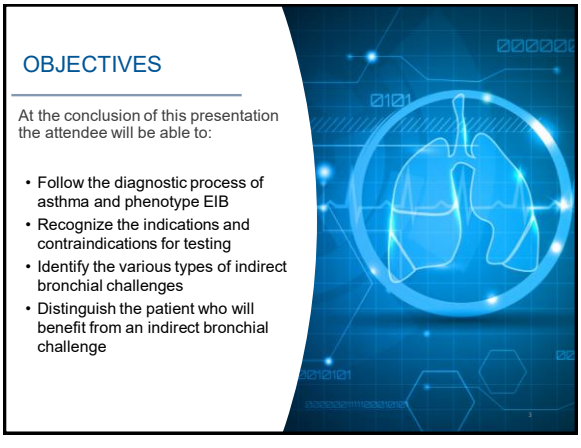
OBJECTIVES
At the conclusion of this presentation the attendee will be able to:
• Follow the diagnostic process of asthma and phenotype EIB
• Recognize the indications and contraindications for testing
• Identify the various types of indirect bronchial challenges
• Distinguish the patient who will benefit from an indirect bronchial challenge
3

3

Patient Presentation

I work, or have worked, in Pulmonary Function Testing.

A. True
B. False

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4

4

Patient Presentation

- 32 year old man comes to primary care physician complaining of chest tightness and wheezing intermittently, causing concerning shortness of breath
- Patient is active, runs 3-4 times a week and swims at least twice a week
- Ran track in high school and was on the swim team
- Works as a real estate agent currently

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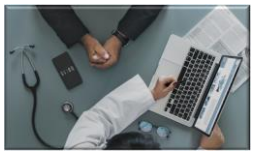
Question 1

Patient Presentation - Primary Care

First step(s) at the initial visit:

A) Gather detailed medical history
B) Physical exam
C) Spirometry
D) All of the above



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Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Full Report 2007 U.S. Department of Health and Human Service National Institutes of Health. National Heart, Lung and Blood Institute.

6

6

Case Study

Initial work up

Medical history and physical
- no Hx of asthma
- no Hx of heart disease

Vital Signs
- HR 70 at rest,
- RR 16 comfortable,
- BP 108/76 SaO2 96% on R/A
- Breath Sounds – clear and equal bilaterally

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Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018].

7

7

Diagnosing Asthma

Guidelines - Expert Panel Report

- Gather detailed medical history
- Physical exam
- Spirometry to demonstrate obstruction and assess reversibility
- Additional studies if necessary to rule out alternate diagnosis

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Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Full Report 2007 U.S. Department of Health and Human Service National Institutes of Health. National Heart, Lung and Blood Institute

8

8

Case Study

Follow Up

- Spirometry is inconclusive
- Patient is still experiencing symptoms that look like asthma
- Reports no chronic issues with breathing, can run and play sports without incident
- Upon further questioning patient reports he noticed the shortness of breath seemed to happen on the days he worked out, although he had no difficulty while working out

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Question 2

Follow Up Steps

Now what should the doctor do?

A) Chest x-ray
B) CBC
C) 6 min walk test
D) Bronchoprovocation challenge

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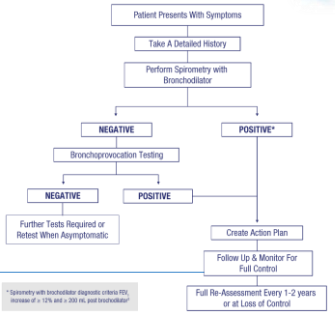
Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018].

Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Full Report 2007U.S. Department of Health and Human Service National Institutes of Health. National Heart, Lung and Bloodinstitute.

10

Diagnosing Asthma

Example Algorithm



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What is a Bronchial Challenge?

Stimulation of the airway by either a direct stimulus or an indirect stimulus to cause the airways to show an onset of hyperreactivity as seen in asthma.

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Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018

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Types of Bronchial Challenge Tests

Direct	Indirect
• Methacholine Challenge • Histamine	• Exercise • Eucapnic Voluntary Hyperpnea • Cold Air • Mannitol • Hypertonic Saline
Diagnostic Purpose: To rule **out** asthma	Diagnostic Purpose: To rule **in** asthma

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Direct or Indirect Challenge

Comparing Tests

Direct stimuli act directly on the bronchial smooth muscle to cause bronchoconstriction in susceptible individuals (i.e. methacholine)

Indirect stimuli (via the release of inflammatory mediators act indirectly) to cause bronchoconstriction in susceptible individuals (i.e. Exercise Challenge, EVH, mannitol)

Bronchoconstriction is measured by performing spirometry to measure lung function (FEV_1)

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Value of Indirect Challenge Testing

1. High specificity
2. Confirms AHR (as seen in asthma)
3. Helps to define if symptoms represent EIB, rather than dysfunctional breathing or airflow obstruction
4. Assists in evaluating potential responsiveness to ICS

methapharm Respiratory

Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challengetesting: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018

Brannan JD and Lougheed D. Airway hyperresponsiveness in asthma: mechanisms, clinical significance and treatment. Frontiers in Physiology 2012 Vol 3

15

15

ATS Guideline Recommendations

- The diagnosis of EIB is established by changes in lung function provided by exercise, not on the basis of symptoms alone.
- Serial lung function measurements after a specific exercise or hyperpnea challenge are used to determine if EIB is present and to quantify the severity of the disorder.

methapharm Respiratory

Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respi Crit Care Med Vol 187, Iss. 9, pp 1016-1027, May 1, 2013

16

16

Question 3

Mechanism of Action

Indirect challenges cause increased fluid osmolarity in the airways in everyone regardless of diagnosis of asthma.

A) True
B) False

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Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J. 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018].

17

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Exercise-Induced Bronchoconstriction

Formerly Exercise-Induced Asthma

- Narrowing of the airways causing asthma like symptoms after exercise
- Symptoms typically present 15 minutes after exercise and self resolves within 60 min

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Smoliga, James M., Prima Weis, Kenneth W Rundell. Exercise induced bronchoconstriction in adults: evidence based diagnosis and management. BMJ 2016;352:h6951 doi: 10.1136/bmj.h6951 (Published 13 January 2016)

EPR-3. Expert panel report 3: Guidelines for the diagnosis and management of Asthma (EPR3-2007). Department of Health and Human Services, National Institute of Health; National Heart, Lung and Blood Institute; National Asthma Education and Prevention Program 2001.

18

18

EIB is an Asthma Phenotype

Clinical Symptoms:

- Chest tightness
- Cough
- Wheezing
- Dyspnea

EIB is commonly misdiagnosed because its symptoms are neither sensitive nor specific

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Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respir Crit Care Med Vol 187, Iss. 9, pp 1016–1027, May 1, 2013

Smoliga et al. Exercise induced bronchoconstriction in adults: evidence based diagnosis and management. BMJ 2016;352:h6932

19

19

EIB Prevalence

Among Athletes

EIB is common in athletes of all levels

- Competitive and recreational athletes
- Elite Athletes
  - 0-61% reported, varies on sport and environment, eg skaters and cross-country skiers, swimmers
- Typically higher in female athletes

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Weiler, John M et al. Exercise-induced bronchoconstriction update-2016. American Academy of Allergy, Asthma & Immunology, American College of Asthma, Allergy & Immunology

20

20

EIB Prevalence

General Population

Children
- 10-20%
- Shown to be more prevalent in girls vs boys
- Higher in urban settings than rural

Adults
- 19.4% shown to have EIB without a history of asthma

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Weiler, John M et al. Exercise-induced bronchoconstriction update-2016. American Academy of Allergy, Asthma & Immunology, American College of Asthma, Allergy & Immunology

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21

Identifying EIB

Who should be Tested for EIB?

Patient experiences signs and symptoms of asthma while exercising and has

- No clinical history of asthma
- Normal or near normal lung function during spirometry

methapharm Respiratory

Fitch et al. Asthma and the elite athlete: Summary of the International Olympic Committee's Consensus Conference, Lausanne, Switzerland,January 22-24, 2008. J Allergy Clin Immunol Aug 2008

Weiler, John M et al. Exercise-induced bronchoconstriction update-2016. American Academy of Allergy, Asthma & Immunology, American College of Asthma, Allergy & Immunology

22

22

Question 4

Diagnosing EIB

Why should the physician **not** skip the challenge test and start the patient on bronchodilator therapy?

A) Symptoms could be from a cardiac issue
B) Symptoms could be from a vocal cord issue
C) A challenge test could help direct precision therapy
D) All of the above

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Aaron, S.D., Vandemheen, K.L., FitzGerald, J.M., Ainsle, M, Gupta, S, Lemiere, C., ...Boulet, L. (2017). Reevaluation of Diagnosis in Adults with Physician-Diagnosed Asthma. Jama, 317(3):269-279. doi 10.1001/jama.2016.19627

23

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Diagnosing EIB

Guideline Recommendations

EIB should be diagnosed with objective testing

- Pre and post bronchodilator spirometry

If spirometry is inconclusive use bronchial challenge testing

- Exercise challenge
- Eucapnic voluntary hyperpnoea (EVH) challenge
- Hypertonic saline challenge
- Mannitol challenge

methapharm Respiratory

Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respi Crit Care Med Vol 187, Iss. 9, pp 1016-1027, May 1, 2013.

Wanger, J. ATS Pulmonary function laboratory management & procedure manual, 3rd ed. New York, NY: American Thoracic Society, 2016.

24

24

Question 5

Additional Testing

When the physician learns the patient has symptoms after exercise, he suspects EIB.

Which type of bronchoprovocation test should the physician order?

A) Direct
B) Indirect

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Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respir Crit Care Med Vol 187, Iss. 9, pp 1016-1027, May 1, 2013

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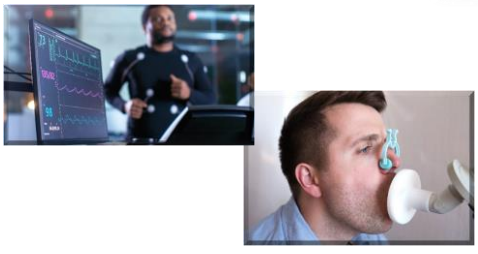
Indirect Bronchial Challenge



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Test Options

Indirect challenge tests cause an increase in osmolarity of the small airways resulting in inflammation, potentially leading to bronchoconstriction

- Exercise
- Eucapnic Voluntary Hyperpnea (EVH)
- Cold Air
- Hypertonic Saline
- Mannitol

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Indirect Bronchial Challenge

Indications

- Assess Bronchial Hyperresponsiveness (AHR) in the presence of exercise
- Assess ICS effectiveness of preventing asthma exacerbations
- Stepping down ICS therapy

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Joos GF, O'Connor B, Anderson SD, et al. Indirect airway challenges. Eur Respir J 2003; 21: 1050–1068.

Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018].

Anderson D. and Brannan JD, Methods for "Indirect" Challenge Tests Including Exercise, Eucapnic Voluntary Hyperpnea,and Hypertonic Aerosols. Clinical Reviews in Allergy & Immunology, 2003, Vol 24

28

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Potential Use

For Assessment of ICS Therapy

- ICS is a second step in treating EIB when SABA's are used daily or not effective
- ICS will decrease responsiveness of the airway to an Indirect Bronchial Challenge
- ICS therapy takes up to 4 weeks to be effective at obliterating response to Indirect Bronchial Challenge
- Consider stepping down ICS therapy in asthmatics who do not respond to Indirect Bronchial Challenge.

methapharm Respiratory

Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018]

EPR-3. Expert panel report 3: Guidelines for the diagnosis and management of Asthma (EPR3-2007). Department of Health and Human Services, National Institute of Health, National Heart, Lung and Blood Institute, National Asthma Education and Prevention Program 2001.

29

29

Contraindications

All Indirect Challenges

- Inducible cardiac ischemia
- Uncontrolled hypertension
- Aortic aneurysm
- Life threatening arrythmias
- Recent surgeries
- Respiratory tract infections that may be impacted by irritation of airway

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Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018].

Aridol US Package Insert (available for download at aridolchallenge.com

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Contraindications continued

When to Reconsider Challenge Testing

Baseline FEV1
- ≤ 75% for EC and EVH
- ≤ 65% for Cold Air Challenge
- ≤ 70% for Hypertonic Saline and mannitol

Mannitol only
- Allergy to mannitol
- Allergy to gelatin used for capsules

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Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018].
Aridol US Package Insert (available for download at aridolchallenge.com

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Pre-Challenge Spirometry

All Challenge Tests

- Obtain 3 reproducible FVC maneuvers
- Determine the patient's FEV_1 percentage of predicted

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Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respi Crit Care Med Vol 187, Iss. 9, pp 1016-1027, May 1, 2013
Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018].

32

32

Exercise Challenge

- High intensity exercise to replicate the physiological response specific to individual sport
- Gives a real-life look at cause of symptoms
- Guidelines are well defined and current
- Used in pediatric and adult patients

methapharm Respiratory

Smoliga, James M, Pnina Weis, Kenneth W Rundell. Exercise induced bronchoconstriction in adults: evidence based diagnosis and management. BMJ 2016;352:h6951 doi: 10.1136/bmj.h6951 (Published 13 January 2016)
Brannan, John D. and Celeste Porsbjerg. Immunol Allergy Clin N Am 38 (2018) Testing for Exercise-Induced Bronchoconstriction pp 215–229

33

33

Exercise Challenge

Performing the Test

Patient exercises until a specific heart rate or respiratory rate has been maintained for 4-6 minutes

Required Equipment:

- Treadmill **or** electromagnetically braked cycle ergometer
- EKG (three lead if uncomplicated, 12 lead for complicated)
- Dry air source
- Nose clip
- Pulse oximeter (optional)

methapharm Respiratory

American Thoracic Society Guidelines for Methacholine and Exercise Challenge Testing – 1999 (Published in American Journal of Respiratory & Critical Care Medicine, Vol. 161:1, January 2000.

34

34

Exercise Challenge

Monitoring

- Measure FEV_1 immediately and at 3, 6, 10, 15, & 30 min
- Continue to measure FEV_1 all the way to 30 min to capture severity of bronchoconstriction
- A 10% drop of FEV_1 from baseline = positive test
  - Administer a SABA if the patient experience severe reactions or if the FEV1 has not returned to within 10% of baseline at discharge

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Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033

35

35

Exercise Challenge

Potential Limitations

- Type, duration and intensity of exercise
- Humidity level
- Sustaining high respiratory rate
- Recent exercise
- Access to quality testing
- Reproducibility
- Sensitivity
- Safety
- Staffing

methapharm Respiratory

Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respir Crit Care Med Vol 187, Iss. 9, pp 1016-1027, May 1, 2013

Anderson SD. "Indirect" Challenges from Science to clinical practice. Eur Clin Respir J. 2016;3:31096

36

36

Eucapnic Voluntary Hyperventilation (EVH)

- Creates response similar to exercise without stress of exercise
- Yields faster results then an exercise challenge through the patient's voluntary maximum ventilation efforts
- False-negative tests are unlikely
- Does not require space for exercise equipment

methapharm Respiratory

Brannan, John D. and Celeste Porsbjerg. Immunol Allergy Clin N Am 38 (2018) Testing for Exercise-Induced Bronchoconstriction pp 215–229
Anderson SD. "Indirect" Challenges from Science to clinical practice. Eur Clin Respir J. 2016;3:31094
Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-Induced Bronchoconstriction. Am J Respi Crit Care Med Vol 187, Iss. 9, pp 1016-1027, May 1, 2013.
37

37

Eucapnic Voluntary Hyperventilation (EVH)

Required Equipment

- Compress gas containing 21% O2, 5% CO2, balance N2
- Gas cylinder with a direct demand valve or Douglas bag/balloon
- High pressure tubing
- Mouthpiece
- Nose clip
- 3 cm tubing
- Stop clock
- Dry gas meter
- Bronchodilator
- Emergency response equipment

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Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respi Crit Care Med Vol 187, Iss. 9, pp 1016-1027, May 1, 2013.
Hull, JH, Ansley, L, Price, O.J., Dickinson, J.W., Bonini, M; Eucapnic Voluntary Hyperpnea: Gold Standard for Diagnosing Exercise-Induced Bronchoconstriction in Athletes?: Sports Med, 2016 Aug 46 (8) 1083-93 doi: 10.1007/s40279-016-0491-3
38

38

Eucapnic Voluntary Hyperventilation (EVH)

Performing the Test

- Patient breaths dry air containing 5% CO2 at 85% MVV for 6 minutes
- FEV_1 is measured immediately post-test and at 3,6,10,15 and 30 minutes
- Positive EVH if FEV_1 falls ≥ 10% from baseline
- Administer a SABA if the patient experiences severe reactions or if the FEV_1 has not returned to within 10% of baseline at discharge

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Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018].
39

39

Eucapnic Voluntary Hyperventilation (EVH)

Potential Limitations

- Variable sensitivity and specificity
- Requires highly trained staff
- Requires specialized equipment
- Specialized gas at specific temperatures and mixture:
  - 21% O2
  - 4.9-5% CO2
  - nitrogen for the remaining gas

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Hull, JH, Ansley, L, Price, O.J., Dickinson, J.W., Bonini, M; Eucapnic Voluntary Hyperpnea: Gold Standard for Diagnosing Exercise-Induced Bronchoconstriction in Athletes?: Sports Med, 2016 Aug 46 (8) 1083-93 doi: 10.1007/s40279-016-0491-3

Anderson SD. "Indirect" Challenges from Science to clinical practice. Eur Clin Respir J. 2016;3:31096

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Cold Air Challenge

- Cold air is added to the exercise challenge or EVH
- Cold air may require less time than EC or EVH alone
- A cold air generator is used to create temperatures of 14 -˜4F -10 to -20 C

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Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018].

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Cold Air Challenge

Performing the Test

- Obtain baseline spirometry
- Place nose clips
- Have patient breathe comfortably on equipment X 1 min
- Breathe at target ventilation x 3 min
- Begin serial FVC maneuvers @ 5 min intervals x 20 min
- Stop and reverse when a 10-15% drop in FEV_1 is achieved

methapharm Respiratory

Bauer I, Weisner MD. Cold air bronchial provocation. Technical issues and protocol. Copyright 1998, Equilibrated Bio Systems Inc.

42

42

Cold Air Challenge

Potential Limitations

- Low sensitivity
- Best use is with patients who complain of shortness of breath specifically while in cold air
  - Sometimes shortness of breath is thought to be caused by the face being exposed to cold air
- Requires specialized equipment

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Anderson D. and Brannan JD, Methods for "Indirect" Challenge Tests Including Exercise, Eucapnic Voluntary Hyperpnea,and Hypertonic Aerosols. Clinical Reviews in Allergy & Immunology, 2003, Vol 24

43

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Interpretation

Severity Specific to EC,EVH,CAC

The severity of EIB can be graded as mild, moderate, or severe if fall in FEV1 from the pre-challenge level is

- ≥ 10% but < 25%
- ≥ 25% but < 50%
- > 50%

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Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respir Crit Care Med Vol 187, Iss. 9, pp 1016-1027, May 1, 2013

44

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Indirect Bronchial Challenge

Special Consideration

Dose response tests such as mannitol and hypertonic saline are recommended for patients with known asthma, as some of the other indirect tests can potentially cause a more significant fall in FEV_1.

methapharm Respiratory

Weiler et al. Exercise-induced bronchoconstriction update – 2016. J Allergy Clin Immunol Nov 2016

45

45

Hypertonic Saline Challenge

- Incremental indirect challenge
- Quick and simple
- Does not require capital equipment e.g. treadmill or stationary bike
- Used in pediatrics and adults

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Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respir Crit Care Med Vol 187, Iss. 9, pp 1016-1027, May 1, 2013.

Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018].

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Hypertonic Saline Challenge

Performing the Test

- 4.5% hypertonic saline is delivered via ultrasonic nebulizer for increasing periods of time
- Breathing time is 30 seconds, 1, 2, 4 and 8 minutes
- FEV_1 is monitored after each delivery step at 30 and 90 seconds
- If FEV_1 decreases > 15% from baseline, the test is considered positive
- If the FEV_1 decreases 10-15% from baseline during test, dose is repeated

methapharm Respiratory

Coates AL, Wanger J, Cocroft DW, et al. ERS technical standards on bronchial Challenge testing: general considerations and performance of methacholine Challenge tests. Eur Respir J 2017; 49: 1601526

47

47

Hypertonic Saline Challenge

Potential Limitations

- Nebulizer
  - Must be ultra sonic nebulizer
  - Known particle size
- Piezo-electrodes do not produce stable size of aerosol over time
- Disinfecting machine to reduce bacterial growth
- Excessive salivation, a saliva collection reservoir is recommended

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Anderson SD. "Indirect" Challenges from Science to clinical practice. Eur Clin Respir J. 2016;3:31096

Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018]

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Interpretation

Specific to Hypertonic Saline

AHR is classified using the volume of Hypertonic Saline administered during the challenge.

PD15	Classification
<2 ml	Severe
2.1 – 6.0 ml	Moderate
6.0 ml	Mild

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Anderson D. and Brannan JD, Methods for "Indirect" Challenge Tests Including Exercise, Eucapnic Voluntary Hyperpnea,and Hypertonic Aerosols. Clinical Reviews in Allergy & Immunology, 2003, Vol 24

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Mannitol Challenge

- Incremental dose response challenge
- Patient is not required to exercise
- No capital equipment, treadmill, bike needed
- Useful to establish treatment and step up/down of ICS*
- Is an established challenge for exercise induced bronchoconstriction

methapharm Respiratory

Anderson SD. "Indirect" Challenges from Science to clinical practice. Eur Clin Respir J. 2016;3:31096Hallstrand TS, Leuppi JD, Joos G, et al. ERS technical standard on bronchial challenge testing: pathophysiology and methodology of indirect airway challenge testing. Eur Respir J 2018; 52:1801033 [https://doi.org/10.1183/13993003.01033-2018]

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50

Mannitol Challenge

Equipment Needed

- Mannitol Bronchial Challenge Test Kit
- Spirometer
- Nose Clips (optional)
- Timer (optional)
- Calculator (or spirometer software)
- Bronchodilator
- Oxygen + Emergency Equipment
- Water for the patient to sip

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Aridol US Package Insert (available for download at aridolchallenge.com)
Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-induced Bronchoconstriction. Am J Respir Crit Care Med Vol 187, Iss. 9, pp 1016-1027, May 1, 2013

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51

Mannitol Challenge

Performing the Test

Progressive Protocol:
- 0 mg (baseline) 5,10,20,40,80,160,160,160 (635 mg accumulative)

Measurement
- FEV_1 60 seconds post each dose
- Two maneuvers are attempted with each level and the highest FEV_1 is reported

methapharm Respiratory Aridol US Package Insert (available for download at aridolchallenge.com)

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Mannitol Challenge

End of Test Criteria

- Test ends when FEV_1 falls
  15% from baseline
  OR
  10% between doses
- If a cumulative dose of 635mg has been inhaled without a 15% fall from baseline (0mg), the challenge is considered negative and complete
- Administer post-test bronchodilator as per protocol
- Patients should be monitored until FEV_1 has returned to 5% of pre-challenge level

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Mannitol Challenge

Potential Limitations

- Improper inhalation technique can cause coughing
- Patients who can not perform multiple spirometry maneuvers

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Interpretation

Specific to Mannitol

PD15	Classification
< 35 mg	Severe
35- 155 mg	Moderate
155 mg	Mild
No Response	No AHR

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Brannan, J.D., Porsbjerg, C. Testing for Exercise-Induced Bronchoconstriction. Immunol Allergy Clin N Am 38 (2018) https://doi.org/10.1016/j.iac.2018.01.010

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Negative Results

Alternative Diagnosis

If patient does not respond to indirect bronchial challenge potential alternative causes to consider:

- Exercise-induced laryngeal dysfunction
- Exercise-induced hyperventilation/dyspnea – health obese
- Obstructive/Restrictive lung disease
- Obesity
- Skeletal Defects
- Diaphragmatic Paralysis
- Interstitial fibrosis
- Exercise-induce anaphylaxis
- Underlying cardiovascular mechanism
- Underlying gastrointestinal mechanism
- Exercise-induced dyspnea age appropriate
- Exertional GERD
- Mitochondrial enzyme deficiency
- Psychological

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Weiler, John M et al. Exercise-induced bronchoconstriction update-2016. American Academy of Allergy, Asthma & Immunology, American College of Asthma, Allergy & Immunology.

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Case Study

Patient Outcome

- The patient went to Pulmonary Function Lab and had an Indirect Bronchial Challenge.
- Challenge was positive.
- Patient diagnosed with moderate EIB.
- SABA ordered and patient to take it 15-20 min before exercise.
- Reports some improvement in symptoms but not complete resolution.

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Question 6

What should the physician do now?

A) Tell the patient to stop running and swimming
B) Ask the patient to increase use of SABA to Q4 W/A
C) Start on ICS therapy
D) All of the above

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Parsons et al. An Official American Thoracic Society Clinical Practice Guideline: Exercise-Induced Bronchoconstriction. Am J Respir Crit Care Med Vol 187, Iss. 9, pp 1016-1027, May 1, 2013

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Indirect Bronchial Challenge

Summary

- Stimulus which cause the inflammatory pathways to activate and cause bronchoconstriction
- Highly specific tests, used to *CONFIRM AHR and EIB*
- Useful to help initiate and titrate ICS therapy
- Multiple options – which one works best for you

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Thank you!

Questions?

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