New Developments in Bronchial Challenge Testing

KSRC 2012

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Sponsored by Pharmaxis
Who are you?

- Night shift 8’s or 12’s?
- Any 8 hr Evening? 8 or 12’s on Days?
- Neonatal ICU?
- Managers/Supervisors?
- Home Care?
- Students?
- PFT? CPFT? RPFT?
- > 25 years in profession? 30 yrs? 40 yrs?
- English majors?
- Drummers?
Conflict of interest

- Speaker’s bureau: Boehringer Ingelheim, Sunovion, Pharmaxis
- Trainer: Hill–Rom, Pharmaxis
Objectives

- Understand the indications and contraindications for bronchial challenge testing (BCT)
- Explain the pre-test preparation and equipment/supplies needed for various tests
- Review the testing procedures and define a positive test
- Discuss a new challenge test using Mannitol
Definition of Bronchial Hyperresponsiveness (BHR)

- BHR – exaggerated bronchoconstriction
  - Allergens: dust mites, pollen, dander, mold, cockroach
  - Pollutants: exhaust fumes, smog
  - Irritants: tobacco or wood smoke, chemicals
  - BHR also linked to exercise, cold air, sulphur dioxide, non-isotonic aerosols.
- These stimuli all act to cause the airways to narrow.
- BHR is the acute pathology in asthma and is linked to the inflammatory process
Airway inflammation is the underlying pathology in asthma

Inflammation leads to:
- Airway hyperresponsiveness – rapid and exaggerated response to triggers
- Obstruction due to bronchoconstriction – usually at least partially reversible
- Symptoms – cough, wheeze, dyspnea, chest tightness
- Further inflammation, airway remodeling

Symptoms are easily appreciated, but inflammation is often overlooked

http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf
Pre–post F/V loops and V/T curves
Spirometry and symptoms may give clear clues for asthma.....
Significant response to SABA:
FVC (+) 620 ml, 25%
FEV1 (+) 550 ml, 35%
Asthma is often misdiagnosed
No blood test, X-ray, lab test
Many things mimic asthma (CHF, VCD, COPD, etc)
Subjective estimates of asthma correlate poorly to objective measures
Treatment is often not “EBM” (NIH > NHLBI > NAEPP > EPR–3)
  ◦ No ICS, no ICS/LABA, relying on SABA only
BCT helps to rule in or rule out asthma (but it is still not a definitive test)
When is BCT needed?

- Symptoms suggest asthma but a normal PFT...
  - Questionable case (EIB, cough variant asthma)
- Asthma needs to be confirmed objectively and treated effectively at the lowest cost
  - Occupation or recreational activity where BHR could be a potential problem
  - May be useful to “step down” in treatment
  - Following exposure to an occupational irritant or allergen that has induced symptoms of asthma
2 types of BCT

- Direct tests: acts directly on the bronchial smooth muscle to cause bronchoconstriction.
  - Process uses: Inhaled methacholine or histamine to cause a measurable change
  - Direct test tends to RULE OUT asthma

- Indirect tests: cause a change in the airway and this affects mast cells
  - Release of histamine, leukotrienes, prostaglandins, etc.
  - Indirect tests tend to RULE IN asthma
    - Process uses: Exercise–induced bronchospasm (EIB), Eucapnic voluntary hyperventilation (EVH)
    - Process uses: Inhaled agents (mannitol, hypertonic saline, adenosine monophosphate)

Mast Cells & eosinophils as source of mediators that cause Bronchial Smooth Muscle to contract

Indirect means the stimulus comes from cells e.g. the mast cell eosinophil

Direct methacholine acts directly on the receptors on smooth muscle

Allergen

Increase in osmolarity by mannitol

Histamine

Prostaglandins

Leukotrienes

Eosinophils

Bronchial smooth muscle
Respiratory Water Loss

Mucosal Dehydration

Increase in [Na\(^+\)], [Cl\(^-\)], [Ca\(^{2+}\)], [K\(^+\)]

Increase in osmolarity

Airway surface liquid

Epithelial Cells

Submucosa

of Airway inflammation (eosinophils, mast cells)

Mediators Release from Inflammatory Cells

Bronchial smooth muscle contraction

in those with hyperresponsive airways

Cough

Sensory Nerves

Exercise / Eucapnic Voluntary Hyperpnea

Inhaled Mannitol

Methacholine
Bronchial Challenge Tests

- Methacholine
- Exercise
- Eucapnic voluntary hyperventilation (EVH)
- Mannitol
- Cold air
- Hypertonic saline
Check List: applies to all challenge protocols

- Spirometer calibration checked
- **Medications withheld for the appropriate period of time**
- No vigorous exercise in last 4 hrs & no excess caffeine
- No sign of upper or lower respiratory infection
- Spirometry done as first step. FEV₁ at baseline ≥ 70% predicted (don’t test if obstruction is present)
- FEV₁ for each step is reproducible and performed to ERS/ATS criteria
- Bronchodilator and oxygen available if required
- All positive tests should check for return to baseline before discharging the patient (reverse bronchospasm with SABA)
<table>
<thead>
<tr>
<th>Withholding Time</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 hours</td>
<td><strong>Short-Acting Bronchodilators</strong></td>
</tr>
<tr>
<td></td>
<td>Albuterol, terbutaline sulfate</td>
</tr>
<tr>
<td>12-24 hours</td>
<td><strong>Inhaled Corticosteroids</strong></td>
</tr>
<tr>
<td></td>
<td>beclomethasone dipropionate, budesonide, fluticasone propionate, mometasone</td>
</tr>
<tr>
<td></td>
<td><strong>Anticholinergic Bronchodilators</strong></td>
</tr>
<tr>
<td></td>
<td>ipratropium bromide</td>
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<tr>
<td></td>
<td><strong>Phosphodiesterase Inhibitors/Adenosine Receptors</strong></td>
</tr>
<tr>
<td></td>
<td>Theophyllines</td>
</tr>
<tr>
<td>24-48 hours</td>
<td><strong>Long-Acting Bronchodilators</strong></td>
</tr>
<tr>
<td></td>
<td>salmeterol xinafoate, formoterol fumarate</td>
</tr>
<tr>
<td></td>
<td><strong>Inhaled Corticosteroids And Long-Acting Beta2 Agonist Combination</strong></td>
</tr>
<tr>
<td></td>
<td>fluticasone propionate and salmeterol xinafoate; budesonide and formoterol fumarate dehydrate</td>
</tr>
</tbody>
</table>
## Withholding medications

<table>
<thead>
<tr>
<th>Withholding Time</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>72 hours</strong></td>
<td><strong>Long-lasting Anticholinergics</strong>&lt;br&gt;triotropium bromide</td>
</tr>
<tr>
<td><strong>4 days</strong></td>
<td><strong>Antihistamines: Over-the-Counter &amp; Prescription</strong>&lt;br&gt;brompheniramine maleate (Dimetapp®); diphenhydramine (Benadryl®); loratadine (Claritin®); cetirizine (Zyrtec®); fexofenadine (Allegra®); levocetirizine dihydrochloride (Xyzal®)</td>
</tr>
<tr>
<td><strong>Day of Test</strong></td>
<td><strong>Leukotriene-Receptor Antagonists</strong>&lt;br&gt;montelukast sodium (Singulair®)</td>
</tr>
<tr>
<td></td>
<td><strong>Refrain from the following:</strong>&lt;br&gt;* Caffeine-containing foods: coffee, tea, cola, chocolate, etc.&lt;br&gt;* Vigorous exercise&lt;br&gt;* Smoking at least six hours prior to testing</td>
</tr>
</tbody>
</table>
Methacholine Challenge Test (MCT)

- 2 methods of doing the test
  - 2 minute tidal breathing: timed interval of tidal volume breathing while inhaling aerosolized methacholine
  - 5 breath-breath dosimeter method: 5 slow, deep breaths while inhaling aerosolized methacholine

- Measure FEV₁ at 30 seconds and 90 seconds after the dose is given
  - Positive test– 20% decrease in FEV₁ from baseline (PC₂₀)
  - Negative test – entire schedule of drug is given without a 20% decrease in FEV₁
  - Each method uses increasing doses of methacholine
Methacholine dosing regimen

2 minute tidal breathing

- Baseline (3 ml NaCL)
- 0.031 mg/ml
- 0.0625 mg/ml
- 0.125 mg/ml
- 0.25 mg/ml
- 0.5 mg/ml
- 1.0 mg/ml
- 2.0 mg/ml
- 4.0 mg/ml
- 8.0 mg/ml
- 16.0 mg/ml

5-breath dosimeter

- 0.0625 mg/ml
- 0.25 mg/ml
- 1.0 mg/ml
- 4.0 mg/ml
- 16.0 mg/ml

Dry methacholine is mixed with 0.9% NaCl by a pharmacist using sterile technique. Each dose must be clearly labeled. May be mixed ahead and stored under refrigeration. Must be at room temperature for test.
Dosimeter and nebulizer

KoKo Dosimeter

Devilbiss 646 nebulizer
Bronchial challenge testing - positive methacholine test
Bronchial challenge testing—positive methacholine test

Baseline 0.0625 0.25

PC 20 FEV1 0.109
*Airway responsiveness to inhaled methacholine or histamine in a normal subject, and in asthmatics with mild, moderate, and severe airway hyperresponsiveness. Asthmatics have an increased sensitivity and an increased maximal broncho-constrictor response to the agonist. The response to the agonist is usually expressed as the provocative concentration causing a 20% decline in FEV₁ (PC20).
Issues with Methacholine

- **Clinical Aspects:**
  - Positive response is not predictive of having EIB or its severity
  - Positive response not specific for asthma
  - Negative response is helpful to rule out asthma
  - Positive response is not predictive of benefit from ICS

- **Safety Aspects:**
  - High concentrations of methacholine may be needed for positive response and may cause unwanted side effects
Issues with Methacholine

- Technical Aspects
  - Several nebulizers may be required and need to be cleaned & calibrated
  - Different protocols have different cut off points for AHR
  - Solutions needed to be made up by pharmacist, refrigerated & regularly discarded
  - Negative test takes 40 min using 2 minute tidal breathing protocol which is now the most highly recommended by advocates
Exercise Challenge

Usefulness:

◦ May be able to use the actual stimulus that produces the symptoms
◦ High positive predictive value for asthma
◦ Likely to be the most common trigger of an attack
◦ Appropriate for assessing drug effects
Exercise Protocol

- 6 to 8 minutes at high level of exercise
  - Targeting a percentage of max HR based on age
- Monitor continuous ECG and SpO2
  - Some labs monitor F/V loops, minute ventilation and tidal volume during exercise to assess workload
- Environmental conditions should be controlled:
  - Temp <25°C (77°F), relative humidity ≤50%
  - Nose clips needed to reduce gas conditioning by nose
- Spirometry recorded at 1 to 2 minutes post exercise then at 5, 10, 15, 20, and 30 minutes
- Positive test: 10% to 15% drop in FEV$_1$ from baseline
Exercise Challenge

Limitations:
- Exercise choice is limited
- Unable to exercise for the test?
- Elite athletes may be difficult to reach max exercise
- Exercise may need to be sports specific (rowing vs ski)
- ‘Dry’ air for best results
- Safety issues
  - May have severe bronchospasm post exercise (greater risk for large falls in FEV₁)
  - If using a treadmill – required speeds are high...safety?
- Cost and resources
Eucapnic Voluntary Hyperventilation (EVH)

- **Usefulness**
  - High sensitivity to identify EIB
  - Protocol and inspired air conditions can be adjusted to simulate conditions of a specific sport (e.g. rowing, cross country skiing, cycling)
  - Negative test = low risk of EIB
  - Mediators the same as for EIB
  - Equipment less expensive compared with exercise
Protocol for EVH

- Cold air (relative humidity near 0%) breathed at high level of ventilation
  - Target ventilation is between 30 to 70% of the MVV
- CO₂ levels kept stable by using special gas mixture
  - ~5% CO₂ 21% O₂ balance N₂
- Hyperventilation maintained for 4 to 6 minutes
- Spirometry measured at 1, 5, 10, 15, 20 minutes post exercise
- 15% decrease in FEV₁ from baseline is positive
EVH testing during
Olympics in Athens 2004
EVH Limitations

- Special gas mixture needed (~5% CO₂ 21% O₂ balance N₂)
- Less sensitive if <6 minutes or if $V_E < 30 \times FEV_1$
- 6-min protocol 30 x FEV₁ can provoke severe fall in FEV₁
Mannitol (Aridol) Bronchial Challenge Test
Indications for mannitol BCT

- The assessment of bronchial hyperresponsiveness (BHR) in patients 6 years of age and older who do not have clinically apparent asthma.

Limitations of Use: mannitol is not a standalone test or a screening test for asthma. Mannitol should be used only as part of a physician’s overall assessment of asthma.
All bronchial challenge tests, including mannitol, have Boxed Warnings

- WARNING: RISK OF SEVERE BRONCHOSPASM

- See Full Prescribing Information

- Mannitol, the active ingredient in ARIDOL, acts as a bronchoconstrictor and may cause severe bronchospasm. Bronchial challenge testing with ARIDOL is for diagnostic purposes only. Bronchial challenge testing with ARIDOL should only be conducted by trained professionals under the supervision of a physician familiar with all aspects of the bronchial challenge test and the management of acute bronchospasm. Medications (such as short acting inhaled beta-agonist) and equipment to treat severe bronchospasm must be present in the testing area. If severe bronchospasm occurs it should be treated immediately by administration of a short acting inhaled beta-agonist. Because of the potential for severe bronchoconstriction, bronchial challenge testing with ARIDOL should not be performed in any patient with clinically apparent asthma or very low baseline pulmonary function tests (e.g., FEV₁ <1–1.5 liters or <70% of the predicted values).
Clinical application

- Use in patients with an FEV$_1$ $\geq$ 70% of predicted.
- Should be used:
  - As part of a physician’s overall assessment of asthma
  - To detect exercise-induced bronchoconstriction [EIB]
  - To evaluate unspecified chronic cough
  - To test patients who have issues performing other challenge tests
Mannitol protocol

**PROGRESSIVE PROTOCOL**
- Inhaled doses: 0, 5, 10, 20, 40, 80*, 160*, 160*, 160* mg

**MEASUREMENTS**
- Two FEV₁: 1 minute post dose. Pick the best
- After each FEV₁ maneuver, the next dose is immediately administered followed again by two FEV₁ maneuvers one minute later.
- Each dose is to follow on as soon as possible after the last to maintain the osmotic gradient. A negative test result may not be valid if time exceeds 35 min.

* 2 to 4 capsules used for inhalation (40 mg dose)
POSITIVE TEST
- A positive response is achieved when the patient experiences either:
  - 15% fall in FEV₁ from baseline (0 mg dose)
  - 10% incremental fall in FEV₁ between doses

NEGATIVE TEST
- A cumulative dose of 635 mg of mannitol has been administered and a positive response has not been met
### ARIDOL BRONCHIAL CHALLENGE TEST

Enter the "best of two" FEV₁ values for each Aridol dose in the shaded boxes below:

The % change in FEV₁ is automatically calculated from 0 mg dose and between doses and between Pre-test FEV₁ and 0 mg dose.

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>Total Dose (mg)</th>
<th>Pre-test FEV₁</th>
<th>% Change Between Doses</th>
<th>% Change from 0 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>3.24</td>
<td>-0.61</td>
<td>-0.61</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>3.2</td>
<td>-1.2</td>
<td>-1.23</td>
</tr>
<tr>
<td>10</td>
<td>15</td>
<td>3.17</td>
<td>-0.9</td>
<td>-2.15</td>
</tr>
<tr>
<td>20</td>
<td>35</td>
<td>3.16</td>
<td>-0.3</td>
<td>-2.47</td>
</tr>
<tr>
<td>40</td>
<td>75</td>
<td>3.15</td>
<td>-0.3</td>
<td>-2.78</td>
</tr>
<tr>
<td>80</td>
<td>155</td>
<td>3.13</td>
<td>-0.6</td>
<td>-3.40</td>
</tr>
<tr>
<td>160</td>
<td>315</td>
<td>3.1</td>
<td>-1.0</td>
<td>-4.32</td>
</tr>
<tr>
<td>160</td>
<td>635</td>
<td>3.01</td>
<td>-0.7</td>
<td>-7.10</td>
</tr>
</tbody>
</table>

**Positive Test:**
- ≥15% fall in FEV₁ from 0 mg dose
- ≥10% fall in FEV₁ between two consecutive doses

**Negative Test:**
- 63.5 mg [all capsules] are administered WITHOUT:
  - ≥15% fall in FEV₁
  - ≥10% fall in FEV₁ between two consecutive doses

For further information contact Pharmaxis Medical Affairs at 610-363-5120 extension 110.

The PD₁₅ is automatically calculated below:

- Cumulative dose (mg)
- % change in FEV₁, prior to -15% change (% dose from 0 mg dose)
- Cumulative dose (mg)
- % change in FEV₁, prior to -15% change (% dose from 0 mg dose)
- First (-) change in FEV₁ ≥-15%
- PD₁₅, Mannitol (mg):
  - Response/dose ratio:
  - PD₁₅ = provocative dose to cause a 15% fall in FEV₁
## ARIDOL BRONCHIAL CHALLENGE TEST

Enter the "best of two" FEV₁ values for each Aridol dose in the shaded boxes below:
The % change in FEV₁ is automatically calculated from 0 mg dose and between doses and between Pre-test FEV₁ and 0 mg dose.

### Dose (mg) | Total Dose (mg) | FEV₁ | % change Between Doses | % change from 0 mg
---|---|---|---|---
0 | 0 | 3.2 | -1.84 | -1.84
5 | 5 | 3.17 | -0.94 | 0
10 | 15 | 3.13 | -1.3 | -2.19
20 | 35 | 3.1 | -1.0 | -1.6
40 | 75 | 2.96 | -4.5 | -7.5
80 | 155 | 2.7 | -8.8 | -15.63
160 | 315 | #N/A | #N/A | #N/A
160 | 475 | #N/A | #N/A | #N/A
160 | 635 | #N/A | #N/A | #N/A

### Positive Test:
- ≥15% fall in FEV₁ from 0 mg dose
- ≥10% fall in FEV₁ between two consecutive doses

**Positive test value will appear in RED**

### Negative Test:
- 635 mg [all capsules] are administered WITHOUT:
  - ≥15% fall in FEV₁
  - ≥10% fall in FEV₁ between two consecutive doses

For further information contact Pharmaxis Medical Affairs at 610-363-5120 extension 110.

### The PD₁₅ is automatically calculated below:
- Cumulative dose (mg) Prior to change in FEV₁ of ≥15%
- % change in FEV₁ prior to ≥15% change (at above dose)

- Cumulative dose (mg) At ≥15% change in FEV₁
- First (1st) change in FEV₁ ≥15%
- PD₁₅ Mannitol (mg): 147
- Response/dose ratio: 0.101

PD₁₅ = provocative dose to cause a 15% fall in FEV₁

### % change from 0 mg

[Graph of % change from 0 mg]

1. Guidelines
Levels of Bronchial hyperresponsiveness to mannitol

Cumulative dose of mannitol (mg)

Severe BHR  Moderate BHR
< 35mg      < 155mg

Mild BHR
> 155mg

% Fall FEV1

Airway response to mannitol between asthmatic and non-asthmatic subjects

Asthmatic subjects experienced a 15% or greater fall in FEV₁

Non-asthmatic subjects did not experience a 15% fall in FEV₁

Anderson SD et al AJRCCM 1997 156:758
Dry powder inhaler – single patient use, disposable
All doses of mannitol are in this kit and ready to use
Performing the Mannitol Challenge Test

A quick summary

**Load** and pierce the capsule

**Tilt** head and hold inhaler at a 45° angle

**Inhale** – controlled and deep

**Start** 60 sec. timer & have pt. hold breath 5 sec.

**Exhale** away from the inhaler at end of the

5 sec. breath hold

**Check** that capsule is empty after each inhalation

**Record** (2) FEV₁ maneuvers. Stop or go on as indicated
# Comparison of Bronchial Provocation Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Equip</th>
<th>Cost</th>
<th>Convenience</th>
<th>Safety</th>
<th>Test time</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold Air</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+/−</td>
<td>−</td>
<td>+/−</td>
<td>+/−</td>
</tr>
<tr>
<td>EVH</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+/−</td>
<td>+/−</td>
<td>+/−</td>
<td>+/−</td>
</tr>
<tr>
<td>Exercise</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+/−</td>
<td>+/−</td>
<td>+/−</td>
</tr>
<tr>
<td>Methacholine</td>
<td>+/−</td>
<td>+/−</td>
<td>+/−</td>
<td>−</td>
<td>+/−</td>
<td>−</td>
<td>+/−</td>
</tr>
<tr>
<td>Mannitol</td>
<td>+</td>
<td>+</td>
<td>+/−</td>
<td>+</td>
<td>+</td>
<td>+/−</td>
<td>+/−</td>
</tr>
</tbody>
</table>

Symbols: + superior, +/- intermediate, − inferior

The mannitol challenge test has the following advantages over other indirect bronchoprovocation tests:

- a standardized test kit,
- minimal required equipment,
- relatively low cost,
- ease of administration,
- a consistent dose response,
- enhanced safety,
- and ease of performance.

Mannitol “A−305”

Methods

◦ 509 subjects enrolled. The intent-to-treat population was 391 subjects.
◦ 375 subjects (aged 6–50 years) completed all 4 study tests.
◦ Subjects had signs and symptoms suggestive of asthma according to the NAEPPII questionnaire, but without a firm diagnosis or exclusion of asthma as a diagnosis.
Mild asthmatics comprised the study population of A–305

- No definitive diagnosis
  - NAEPPII scores (mean 1.2 on scale 1 to 4) helped support that these subjects had an unconfirmed diagnosis.

- A very mild group of patients
  - All had normal FEV$_1$
  - Only 7.5% (28) subjects were reversible to $\beta_2$ agonists.
  - In patients with an EPR–2 score of 1–2, physicians cannot rely on reversibility to diagnose asthma.

- 22% of patients non–atopic
  - This was the first large study of mannitol to include a significant number of non–atopic patients.
A–305 Results: A positive challenge test in half the time

Time to perform a positive challenge

<table>
<thead>
<tr>
<th></th>
<th>Aroidol (N=168)</th>
<th>Methacholine (N=156)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minutes to perform test</td>
<td>19.9 (SE 0.9) min</td>
<td>44.5 (SE 1.4) min</td>
</tr>
</tbody>
</table>

Time to perform a positive mannitol test was shorter than a positive methacholine test by ~25 minutes

19.9 (SE 0.9) min vs. 44.5 (SE 1.4) min

Positive subjects from the per-protocol population
Safety: Fewer patients experienced a > 30% fall in FEV$_1$

Number of subjects who had a ≥30% fall in FEV$_1$ after challenge

- **ARIDOL**: 2 patients (1.2%)
- **Exercise**: 25 patients (15.3%)
- **Methacholine**: 46 patients (29%)

N = 375, PPP

Anderson SD et al. Respiratory Research 2009, 10:4
A-305 Results: Not all bronchial challenge tests produce large falls in FEV<sub>1</sub>

No patients experienced a > 60% fall in FEV<sub>1</sub> during the mannitol or exercise challenges

Percent of subjects that experienced a > 60% fall in FEV<sub>1</sub>

<table>
<thead>
<tr>
<th></th>
<th>ARIDOL</th>
<th>Exercise</th>
<th>Methacholine</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>0%</td>
<td>1%</td>
<td></td>
</tr>
</tbody>
</table>

N = 375, PPP
Comparison of mannitol to methacholine in sensitivity and specificity against BHR from exercise

- Sensitivity:
  - ARIDOL: 58.6%
  - Methacholine: 55.2%

- Specificity:
  - ARIDOL: 65.2%
  - Methacholine: 68.9%

N = 375, PPP

Methacholine PC$_{20}$ = 16 mg/ml
Drug and CPT Coding

- **Product Reimbursement : HCPCS Code**
  - J7665 Aridol approved effective Jan 1, 2012

- **Bronchial Challenge Testing: CPT Codes**
  - 95070 Inhaled bronchial challenge testing (not including necessary PFTs) with histamine, methacholine, or similar compounds
  - 94070 Bronchospasm provocation evaluation, multiple spirometric determinations with administered agents (eg with antigens, cold air, methacholine)
  - 94640 Pressurized or nonpressurized inhalation treatment for acute airway obstruction or sputum induction for diagnostic purposes (eg with nebulizer, MDI, or IPPB)
Drug and CPT Coding

- Evaluation and Management: CPT Codes
  - 99201–99205  Eval and Mgt... new patient visit
  - 99211–99215  Eval and Mgt ... Established patient visit
  - 99241–99245  Eval and Mgt... Outpatient consultation
ARIDOL® (mannitol inhalation powder)

Bronchial Challenge Test Kit
Customer Training Opportunities

US-A-3-12-155
March 2012
The training opportunities available to ARIDOL customers by Pharmaxis, Inc.

As part of our partnership and commitment to train healthcare professionals on how to properly conduct an ARIDOL Bronchial Challenge Test, Pharmaxis, Inc. is pleased to offer you the following training opportunities:

**On-site training by the ARIDOL Training Team**
The ARIDOL Training Team is available by request to any customer who purchases ARIDOL. This team of trained nurses, pharmacists, respiratory therapists and certified asthma educators is available for on-site, one-on-one training. Just call a Regional Customer Specialists to schedule.

**Training and coaching by telephone**
The ARIDOL Training Team is also available for training and coaching by telephone.

**The ARIDOL Flipchart**
A step-by-step guide on how to conduct the ARIDOL Bronchial Challenge Test.

**www.ARIDOL.info**
An informative website to learn more about ARIDOL and the proper conduct of an ARIDOL Bronchial Challenge Test.

For more information, contact a Pharmaxis Regional Customer Service Specialists at 888-416-1828
Thanks for listening!

- [www.thoracic.org/statements](http://www.thoracic.org/statements)
  - Pulmonary Function and Exercise Testing

Questions about mannitol (Aridol) for BCT …
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