Performing a Methacholine Challenge Test

Provocholine®
(methacholine chloride USP)
powder for solution, for inhalation

*Provocholine is a registered trademark of Methapharm Inc. © Copyright © Methapharm Inc. 2016. All rights reserved. Healthcare professionals should consult the Provocholine package insert for the complete product safety information. A sterile 0.22 µm bacterial retentive filter (e.g., Millex GV®) should be used when transferring a solution to the nebulizer. Warning: Provocholine is a bronchoconstrictor agent for diagnostic purposes only and should not be used as a therapeutic agent. Provocholine inhalation challenge should be performed only under the supervision of a physician trained in and thoroughly familiar with all aspects of the technique of methacholine challenge, all contraindications, warnings and precautions, and the management of respiratory distress. Emergency equipment and medication should be immediately available to treat acute respiratory distress. For complete prescribing information, please consult the Product Insert which is available for download at www.provocholine.com or on request by calling Methapharm Medical Information at 1-800-287-7686 | +1-519-751-3602 ext. 7804 or faxing us at +1-519-751-9149.

This information is provided as a professional courtesy, and it is intended to provide data available to us that may assist you in deriving your own conclusions and opinions. This information is not intended to advocate any indications, dosage, or other claim that is not described in the package insert.
Technologist Qualification

1. Be familiar with the guidelines and test procedure.
2. Understand and manage the equipment including set-up, quality control, maintenance, and cleaning.
3. Have established competence with spirometry performance.
4. Know contraindications to methacholine challenge testing (MCT).
5. Be competent to perform emergency procedures and understand the safety procedures.
6. Know when to continue or stop testing.
7. Have established competence in the administration of inhaled bronchodilators and evaluation of the response.
Patient Safety

1. A physician or individual qualified to treat acute bronchospasm should be close enough to respond to an emergency.
2. Patients should never be left unattended.
3. Medications to treat severe bronchospasm must be available in the testing room.
4. Oxygen must be available.
5. Additional required equipment includes a nebulizer, stethoscope, sphygmomanometer and pulse oximeter.
Technologist Safety

1. Minimize exposure to the methacholine chloride.
2. Consider additional precautions if the technologist has asthma.
Overview

1. Pre-Test
   • Provocholine Preparation
   • Equipment Preparation
   • Patient Preparation

2. Test
   • Administration of Provocholine
   • Spirometry Testing

3. Post-Test
   • Return Patient to Baseline Pulmonary Function
   • Evaluate Results
1 Provocholine Preparation

For instructions on the preparation of the Provocholine solutions for the methacholine challenge test, please view the Mixing Methacholine Dilutions for Bronchoprovocation Challenge Testing video.
1 Provocholine Preparation

Be sure to remove the Provocholine dilutions from the refrigerator 30 minutes prior to testing to allow it to warm to room temperature.
1 Equipment Preparation

- Nebulizer
- Spirometer

It is important to ensure that you have bronchodilators, oxygen, and emergency equipment available.
Nebulizer must deliver aerosol with particle mass median diameter (MMD) between 1.0 and 3.6 µm

Avoid nebulizers with particle MMD < 1.0 µm
Nebulizer – Tidal Breathing

- Flow meter should be adjusted to deliver an output within 10% of 0.13 mL/minute
- Nebulizers should be properly calibrated in order to determine the flow meter setting
Nebulizer – Dosimeter Method

- Flow meter should be adjusted to deliver an output of 0.009 mL + / - 10% of the solution per 0.6 seconds of actuation during inhalation
1 Patient Preparation

- Medication Withholding
- Contraindications
## 1 Medication Withholding

<table>
<thead>
<tr>
<th>Medication</th>
<th>Withholding Time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inhaled agents</strong></td>
<td></td>
</tr>
<tr>
<td>Short acting bronchodilators</td>
<td>8 hrs</td>
</tr>
<tr>
<td>Anticholinergic bronchodilators</td>
<td>24 hrs</td>
</tr>
<tr>
<td>Long acting bronchodilators</td>
<td>48 hrs</td>
</tr>
<tr>
<td><strong>Oral Bronchodilators</strong></td>
<td></td>
</tr>
<tr>
<td>Theophylline</td>
<td>12 hrs</td>
</tr>
<tr>
<td>Intermediate theophylline</td>
<td>24 hrs</td>
</tr>
<tr>
<td>Long acting theophyllines</td>
<td>48 hrs</td>
</tr>
<tr>
<td>Standard B-agonist</td>
<td>12 hrs</td>
</tr>
<tr>
<td>Long acting B-agonist</td>
<td>24 hrs</td>
</tr>
<tr>
<td><strong>Other Medications</strong></td>
<td></td>
</tr>
<tr>
<td>Hydroxazine, Cetirazine</td>
<td>3 days</td>
</tr>
<tr>
<td>Leukotriene modifiers</td>
<td>24 hrs</td>
</tr>
<tr>
<td>Nedocromil</td>
<td>48 hrs</td>
</tr>
<tr>
<td>Cromolyn sodium</td>
<td>8 hrs</td>
</tr>
</tbody>
</table>

1 Medication Withholding

- The ATS does not recommend routinely withholding oral or inhaled corticosteroids, but their anti-inflammatory effect may decrease bronchial responsiveness.
- Antihistamines are generally not withheld.
Medication Withholding

- Withholding beta-adrenergic blocking agents or performing MCT with these agents should be done with caution and ONLY on specific orders of the ordering physician.

1 Contraindications

- Absolute
- Relative
1 Contraindications - Absolute

- Known hypersensitivity to methacholine chloride or other parasympathomimetic agents
- Severe airflow limitation (FEV₁ < 50% predicted or FEV₁ < 1.0 L)*
- Heart attack (myocardial infarction) or stroke (CVA) within the previous 3 months

1 Contraindications - Absolute

- Uncontrolled hypertension (systolic BP > 200 and/or diastolic BP > 100 mm Hg)
- Known arterial aneurysm
Contraindications - Relative

- Airflow limitation (reduced FEV$_1$/FVC ratio) and FEV$_1$ < 60% predicted or < 1.5 L*
- Inability to perform acceptable/repeatable spirometry at baseline
- Pregnant or nursing mothers
- Current use of cholinesterase inhibitor medication

1 Contraindications - Relative

- Significant response to diluent (i.e. FEV₁ falls > 10% from baseline after administration of saline solution not containing any methacholine chloride)
- Upper or lower respiratory-tract infection within previous 2-6 weeks
- Patients receiving any beta-adrenergic blocking agent
Patient Preparation

Introduce yourself as the patient enters the room.
1 Patient Preparation

Briefly explain the test that you are about to perform to the patient and any family members who may be present, including the inhalation of the product and the required pulmonary function testing.
Patient Preparation

Encourage the patient to ask any questions he or she may have about the test, and answer those questions in simple words and phrases, avoiding the use of technical terms and acronyms.
1 Patient Preparation

- Confirm patient identification, physician order, clinical history, and indication for testing
- Assess each patient’s ability to perform the MCT
- Ensure the patient has complied with the preparation criteria including recent illnesses and withholding medications as required
Baseline Spirometry

- Perform baseline spirometry according to the most recent ATS/ERS criteria
- Evaluate the presence of absolute and relative contraindications:
  - If absolute contraindications are present do not proceed with the methacholine challenge test
  - If relative contraindications are present please contact the referring physician
2 Administration of Provocholine

- Tidal Breathing Method
- Dosimeter Method
Tidal Breathing

Demonstrated with:

AeroEclipse II Breath Actuated Nebulizer (BAN)
2 Tidal Breathing

- Dispense the diluent into the nebulizer
- Attach the nose clip and exhalation filter (Optional)
- Perform spirometry after inhalation of the diluent is complete
2 Tidal Breathing

- If the highest post-diluent FEV₁ is:
  - > 90% of the highest baseline, empty and clean nebulizer thoroughly, and begin to administer the first dose of Provocholine
  - < 90% and > 80% of the highest baseline, repeat the diluent step
  - < 80% of the highest baseline, contact the ordering physician
2 Tidal Breathing

- Dispense the lowest concentration of Provocholine into the nebulizer
- Perform spirometry after inhalation of the Provocholine is complete
2 Tidal Breathing

- Repeat the process until either FEV$_1$ drops at least 20% from the post-diluent baseline or highest concentration has been administered.
Dosimeter

Demonstrated with:

DeVilbiss model 646 nebulizer
2 Dosimeter

- Dispense the diluent into the nebulizer
- Attach the nose clip and exhalation filter (Optional)
- Actuate the dosimeter 2 times to prime the nebulizer and observe adequate nebulization
2 Dosimeter

- Instruct the patient to inhale slowly from Functional Residual Capacity (FRC) to total lung capacity (TLC) and hold the breath at TLC for approximately 5 seconds.
- Alternatively, inhalation to 50-60% of inhalation capacity.
2 Dosimeter

- Repeat the maneuver until five breaths have been completed, within 2 minutes
- Start the timer after the fifth breath has been completed
- Perform spirometry at 30 and 90 seconds after inhalation of the diluent is complete
2 Dosimeter

- If the highest post-diluent FEV₁ is:
  - > 90% of the highest baseline, empty and clean nebulizer thoroughly, and begin to administer the first dose of Provocholine
  - < 90% and > 80% of the highest baseline, repeat the diluent step
  - < 80% of the highest baseline, contact the ordering physician
2 Dosimeter

- Dispense the lowest concentration of Provocholine into the nebulizer
- Always prime the dosimeter 2 times
- Repeat inhalation and spirometric maneuvers
2 Dosimeter

- Repeat the process until either FEV$_1$ drops at least 20% from the post-diluent baseline or highest concentration has been administered.
3 Return Patient To Baseline

- When the FEV$_1$ is $\leq$ 80% of the highest post-diluent FEV$_1$, administer a bronchodilator
- Wait 10 min and repeat spirometry, ensuring FEV$_1$ $\geq$ 90% of baseline prior to sending patient home
- A second bronchodilator may be administered if the FEV$_1$ $\leq$ 90%
3 Reporting Results

- Primary Outcome:
  - Change in $\text{FEV}_1$
  - Evaluate the flow volume loop
3 Reporting Results

- Technologist should always include their observations:
  - Did the test meet ATS/ERS criteria for performing an MCT? Why or why not?
  - Any evidence of medication, technique, or history that could impact the reliability of the test results?
  - Were symptoms present? If yes, were the symptoms similar to the initial complaint?
3 Reporting Results

- Include technologist comments concerning cooperation, effort, cough response, wheezing, shortness of breath, or other symptoms
3 Reporting Results

- Present data for each step of the test including the bronchodilator
- Express each dose in mg/mL
- For spirometry, report FVC, FEV$_1$, and the FEV$_1$/FVC ratio
- Express data as percent of baseline or the post-diluent result
- For plethysmography, report sGaw or sRaw
3 Reporting Results

- $PC_{20}$
- $PD_{20}$
- $PC_{40} SG_{aw}$
3 Reporting Results

\[
PC_{20} = \text{antilog} \left( \log C_1 + \frac{(\log C_2 - \log C_1) (20-R_1)}{R_2 - R_1} \right)
\]

Where:

- \(C_1\) = methacholine concentration preceding \(C_2\)
- \(C_2\) = methacholine concentration causing a \(\geq 20\%\) drop in \(FEV_1\) from baseline
- \(R_1\) = percent fall in \(FEV_1\) after \(C_1\)
- \(R_2\) = percent fall in \(FEV_1\) after \(C_2\)

### Categorization of Bronchial Responsiveness (ATS)

<table>
<thead>
<tr>
<th>PC&lt;sub&gt;20&lt;/sub&gt; Results</th>
<th>Interpretation*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;16 mg/mL</td>
<td>Normal bronchial responsiveness</td>
</tr>
<tr>
<td>4-16 mg/mL</td>
<td>Borderline bronchial hyper-responsiveness (BHR)</td>
</tr>
<tr>
<td>1-4 mg/mL</td>
<td>Mild BHR</td>
</tr>
<tr>
<td>&lt;1 mg/mL</td>
<td>Moderate – Severe BHR</td>
</tr>
</tbody>
</table>

* This method of interpretation assumes:
  - baseline airway obstruction is absent
  - spirometry quality is good
  - there is substantial post-challenge FEV<sub>1</sub> recovery

3 Reporting Results

PD_{20} = PC_{20} \times neb \ output \times t

Where:

PC_{20} = Provocative concentration to elicit 20% drop in FEV_{1}

neb output = flow rate for the nebulizer

t = actuation time
Summary

1. Pre-Test
   - Provocholine Preparation
   - Equipment Preparation
   - Patient Preparation

2. Test
   - Administration of Provocholine
   - Spirometry Testing

3. Post-Test
   - Return Patient to Baseline Pulmonary Function
   - Evaluate Results
Questions or Concerns

Contact Methapharm at 1-800-287-7686