



Provocholine[®]

[methacholine chloride USP]

powder for solution, for inhalation

Performing a Methacholine Challenge Test

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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.

1 Nebulizer – Tidal Breathing

- **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**

1 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

1 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

	Medication	Withholding Time
Inhaled agents	Short acting bronchodilators	8 hrs
	Anticholinergenic bronchodilators	24 hrs
	Long acting bronchodilators	48 hrs
Oral Bronchodilators	Theophylline	12 hrs
	Intermediate theophylline	24 hrs
	Long acting theophyllines	48 hrs
	Standard B-agonist	12 hrs
	Long acting B-agonist	24 hrs
Other Medications	Hydroxazine, Cetirazine	3 days
	Leukotriene modifiers	24 hrs
	Nedocromil	48 hrs
	Cromolyn sodium	8 hrs

*Crapo R, Casaburi R, Coates A, et al. Guidelines for methacholine and exercise challenge testing - 1999. Am J Respir Crit Care Med 2000 : 161(1):309-29.

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**

1 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 ($FEV_1 < 50\%$ predicted or $FEV_1 < 1.0$ L)***
- **Heart attack (myocardial infarction) or stroke (CVA) within the previous 3 months**

*Crapo R, Casaburi R, Coates A, et al. Guidelines for methacholine and exercise challenge testing - 1999. Am J Respir Crit Care Med 2000 : 161(1):309-29.

1 **Contraindications - Absolute**

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

1 **Contraindications - Relative**

- **Airflow limitation (reduced FEV₁/FVC ratio) and FEV₁ < 60% predicted or < 1.5 L***
- **Inability to perform acceptable/repeatable spirometry at baseline**
- **Pregnant or nursing mothers**
- **Current use of cholinesterase inhibitor medication**

*Crapo R, Casaburi R, Coates A, et al. Guidelines for methacholine and exercise challenge testing - 1999. Am J Respir Crit Care Med 2000 : 161(1):309-29.

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**

1 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.

1 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**

1 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**

2 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 FEV₁ drops at least 20% from the post-diluent baseline or highest concentration has been administered**

2 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 FEV₁ 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 FEV₁**
- **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, FEV₁, and the FEV₁/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:

C₁ = methacholine concentration preceding **C₂**

C₂ = methacholine concentration causing a $\geq 20\%$ drop in **FEV₁** from baseline

R₁ = percent fall in **FEV₁** after **C₁**

R₂ = percent fall in **FEV₁** after **C₂**

3 Interpreting Results

Categorization of Bronchial Responsiveness (ATS)

PC ₂₀ Results	Interpretation*
>16 mg/mL	Normal bronchial responsiveness
4-16 mg/mL	Borderline bronchial hyper-responsiveness (BHR)
1-4 mg/mL	Mild BHR
<1 mg/mL	Moderate – Severe BHR

* This method of interpretation assumes:

- baseline airway obstruction is absent
- spirometry quality is good
- there is substantial post-challenge FEV₁ recovery

3 Reporting Results

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

Where:

PC_{20} = Provocative concentration to elicit 20% drop in FEV₁

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