06Name of Policy:	**Methacholine Challenge Test**
Policy Number:	3364-136-PF-06
Department:	Pulmonary Services
Approving Officer:	Senior Hospital Administrator
Responsible Agent:	Director, Pulmonary Services
Scope:	The University of Toledo Medical Center Pulmonary Services Department

THE UNIVERSITY OF TOLEDO MEDICAL CENTER

Effective Date: May 17, 2023
Initial Effective Date: July 1, 1978

_____ New policy proposal	_____ Minor/technical revision of existing policy
X Major revision of existing policy	_____ Reaffirmation of existing policy

(A) Policy Statement

The approved procedure for challenge tests will be followed by all Pulmonary Function staff members. The procedure is based on The American Thoracic Society Guidelines. The Pulmonary Function therapist performing the procedure will ensure safety measures are followed: minimization of aerosol exposure, availability of oxygen, a stethoscope, sphygmomanometer, and other emergency equipment as needed.

(B) Purpose of Policy

1. To standardize the testing procedure, thereby providing the greatest possible accuracy and reproducibility of test results.
2. Methacholine is used to assist in making a positive diagnosis of asthma as well as documenting severity and following changes.
3. To confirm a diagnosis of bronchial hyper-reactivity in subjects who do not have clinically apparent asthma (FEV1 of at least 60% predicted value) yet do have chronic cough, recurrent respiratory infection, and history of wheezing with objective clinical documentation.

(C) Procedure

Patient Preparation

1. Power, warm up and calibrate Pulmonary Function Testing system.

2. Gather material needed: Special methacholine administration kit; properly labeled dosages of methacholine from Pharmacy. Source of pressurized oxygen. Albuterol unit dose with a high-quality nebulizer (output with verified particle size of at least five (5) μm). Review and confirm physician's order. Maintain appropriate infection control maneuvers. Ensure the medication equilibrates to room temperature for at least 30 minutes.

3. Pharmacy will mix and label the solution in the following concentrations according to the ATS Dilution Schedule for Quadrupling Concentrations:

Table 12.4

Dilution Schedule for Quadrupling Concentrations			
Label Strength	**Take**	**Add Diluent**	**Obtain Dilution**
100 mg	100 mg	6.25 ml	16 mg/ml
	3 ml of 16 mg/ml	9 ml	4 mg/ml
	3 ml of 4 mg/ml	9 ml	1 mg/ml
	3 ml of 1 mg/ml	9 ml	0.25 mg/ml
	3 ml of 0.25 mg/ml	9 ml	0.0625 mg/ml

4. Reconcile current patient medications. If they include any of the medications listed in Appendix I and have not been held for the recommended interval, inform the patient's physician. Explain that such drugs may interfere with the challenge and possibly reschedule test. Smoking and drinking beverages that contain caffeine (such as cola or chocolate) should be refrained from at least six (6) hours prior to testing. Exercise and exposure to cold air should be avoided for at least two (2) hours before test.

5. Educate patient regarding testing procedure.

Testing Procedure

Perform methacholine challenge testing according to Appendix II

Contraindications

1. Baseline pulmonary function tests with FEV1 less than 1.5 liters or less than 60% of the predicted values.
2. Females of childbearing age: challenge should be performed either within ten days following the onset of menses or within two weeks of a negative pregnancy test. Nursing mothers should also be included in this group due to the category C status of the drug, meaning no animal reproductive studies have been performed to ensure fetal or infant safety.
3. Inability to understand the procedure and/or perform acceptable and repeatable spirometry.
4. Uncontrolled hypertension, recent heart attack or stroke, arterial hypoxemia
5. Recent eye surgery, or any condition where raised intracranial pressure (due to forced exhalation) is a contraindication.
6. Current use of cholinesterase inhibitor medication (e.g., myasthenia gravis treatment)

Possible Side Effects

1. Chest tightness
2. Mild cough
3. Mild wheezing
4. Dizziness, lightheadedness, and chest pain associated with spirometry maneuver

APPENDIX I:

FACTORS THAT DECREASE BRONCHIAL RESPONSIVENESS

Medications	**Minimum Time Interval from Last Dose to Study**
Short-acting inhaled bronchodilators Such as isoproterenol, isoetharine, Metaproterenol, albuterol, terbutaline	8h
Medium-acting bronchodilators Such as ipratropium	24h
Long-acting bronchodilators Such as salmeterol, formoterol, tiotropium	48h (perhaps 1wk for tiotropium)
Oral bronchodilators	
Liquid theophylline	12h
Intermediate-acting theophylline	24h
Long-acting theophylline	48h
Standard Beta $_2$ agonist tablets	12h
Long-acting Beta $_2$ agonist tablets	24h
Cromolyn sodium	8h
Nedocromil (Tilade)	48h
Hydroxazine, Cetirizine	3d
Leukotriene modifiers	24h

APPENDIX II:

Procedure to perform Challenge test

1. Parameters to be measured:
    a. Flows and volumes from a forced expiratory maneuver and/or
    b. Specific airway conductance (GAW/VL)

2. Nebulization method: Special methacholine nebulizer set-up. Run the 5ml solution at 6-8LPM for two (2) minutes.

3. Threshold Response Criteria for Airway Hyperresponsiveness Criteria (AHR):

PD_{20}		PC_{20}	
(µmole)	µg	(mg/ml)	Interpretation
>2	>400	>16	normal AHR
0.5–2.0	100–400	4–16	borderline AHR
0.13–0.5	25–100	1–4	mild AHR
0.03–0.13	6–25	0.25–1	moderate AHR
<0.03	<6	<0.25	marked AHR

AHR = airway hyperresponsiveness.

4. Drug Concentrations for methacholine challenge of 100 mg label strength:
   0.0625 mg/ml, 0.25 mg/ml, 1 mg/ml, 4 mg/ml, 16 mg/ml

5. Performance Steps
   a. Measure baseline parameters.
   b. Nebulize diluent (sodium chloride) in which methacholine is dissolved. Patient is asked to wear a nose clip and breathe normally through the mouthpiece of a nebulizer.
   c. Perform measurements at 30 and 90 seconds after inhalation.
   d. If the FEV1 falls by greater than 20% from the baseline measurement, terminate procedure since the subsequent response to the pharmacologic agent is uninterpretable. Following insignificant response to control continue with following steps.
   e. Empty contents of left-over medication into wastebasket or sink.
   f. Withdraw 2-3ml or appropriate amount of the starting concentration of methacholine and place it in the nebulizer with the diluent.
   g. Nebulize the drug for two (2) minutes.
   h. Repeat measurements as in step d.
   i. Administer the 2-minute inhalations in ascending order of the serial concentrations, repeating steps d, f, and g until threshold response is achieved.
   j. Periodic auscultation, pulse rate and /or blood pressure may be monitored to assist in patient assessment and test interpretation.

   k. After completion of Methacholine challenge delivery, bronchoconstriction is then reversed:
      1. Administer Albuterol unit dose (2.5 mg Albuterol / 0.5 mL)
      2. Repeat measurements.
      3. In the event of a positive response, measure parameters until return to near baseline values.

Data Presentation

1. The results are reported as a percent decrease in FEV1 from baseline (or post diluent if diluent step is used).
2. Data should be presented for each step of protocol, including the post bronchodilator test.
3. The highest FEV1 value from acceptable tests is selected for outcome variable.
4. The PC20 (20% change) is calculated from change/decline in FEV1.

Variability of Test

1. Patients with excessive variability in measured baseline values (greater than 5% of the FEV1) should not be tested.

Reference:

Am J Respir Crit Care Med Vol 161. pp 309-329, 2000
"Methacholine Challenge Test" ATS Pulmonary Function Laboratory Management and Procedure Manual 3rd Edition, Version #2. pp 122-134
"Guidelines for Methacholine and Exercise Challenge Testing- 1999" Official statement of the American Thoracic Society- July 1999, Amer J Respir Crit Care Med Vol 161. pp 309 – 329, 2000
www.atsjournals.org

Approved by:		**Review/Revision Date:**	
		01/01/1981	08/05/2008
		06/24/1984	06/30/2011
/s/	5/23/2023	07/08/1987	02/28/2014
Michael Taylor	Date	06/06/1990	05/01/2017
Director, Pulmonary Services		06/06/1993	06/01/2020
		09/05/1996	05/18/2023
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Russell Smith	Date	08/11/2005	
Senior Hospital Administrator			
Review/Revision Completed By:		**Next Review Date:** May 2026	
Director, Pulmonary Services			
Policies Superseded by This Policy:			

It is the responsibility of the reader to verify with the responsible agent that this is the most current version of the policy.