Complete Summary

GUIDELINE TITLE

Methacholine challenge testing: 2001 revision and update.

BIBLIOGRAPHIC SOURCE(S)

Methacholine challenge testing: 2001 Revision & Update. Respir Care 2001 May;46(5):523-30. [53 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously issued version (Bronchial provocation. Respir Care 1992 Aug;37[8]:902).

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Pulmonary disease

GUIDELINE CATEGORY

Diagnosis
Evaluation
Risk Assessment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Pediatrics
Pulmonary Medicine

INTENDED USERS

Respiratory Care Practitioners

GUIDELINE OBJECTIVE(S)

- To improve the consistency and appropriateness of respiratory care and serve as a guide for education and research.
- To provide clinical practice guidelines on bronchial provocation.

TARGET POPULATION

Children (≥ 5 years of age) and adults with indications for methacholine challenge testing including:

- The need to exclude a diagnosis of airway hyperreactivity (i.e., asthma)
- The need to evaluate occupational asthma
- The need to assess the severity of hyperresponsiveness
- The need to determine the relative risk of developing asthma
- The need to assess response to therapeutic interventions

This clinical practice guideline does not apply to neonatal populations.

INTERVENTIONS AND PRACTICES CONSIDERED

Methacholine challenge test

This guideline does not address other bronchial challenges (e.g., histamine, exercise, occupational exposures, specific antigens, isocapnic hyperventilation.)

MAJOR OUTCOMES CONSIDERED

Results of pulmonary function tests (e.g., spirometry, specific conductance) performed before and after the inhalations associated with the methacholine challenge test.

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultants to the Working Group may review the initial draft of the guideline. After completion by the Working group, the draft is reviewed by the entire Steering Committee and then by a Review Panel, persons engaged in all facets of the delivery of respiratory care who have volunteered to review drafts of the Guidelines before publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Description/Definition:

- The methacholine challenge test is one method of assessing airway responsiveness. In this test, the patient inhales an aerosol of one or more concentrations of methacholine. Results of pulmonary function tests (e.g., spirometry, specific conductance) performed before and after the inhalations are used to quantitate response. This guideline applies to adults and children capable of adequately performing spirometry or body plethysmography and of cooperating during the course of the challenge.
- A positive test is defined as a decrease from the baseline forced expiratory volume in the first second (FEV_1) or of the post-diluent FEV_1 value of 20%, or of a decrease in specific conductance of 35-45% from the baseline or post-diluent value.

Settings:

Possible settings include:

- Pulmonary function laboratory
- Clinic or physician's office
- Field site (e.g., occupational setting or workplace)

Limitations of Method and Validation of Results:

- Limitations of pulmonary function testing used to quantitate response including intralaboratory variability for each pulmonary function test variable:
    - In some patients, spirometry may not be sensitive enough or specific enough to detect response, and other measurements such as airways resistance (R_{aw}) and/or specific conductance (sG_{aw}) may be used. Differences of opinion exist regarding the spirometric values that best track response in particular airways.
    - Deep inspiration taken while performing spirometry variably alters bronchial tone and may result in either bronchoconstriction or bronchodilatation.
    - Poor patient effort during pulmonary function testing can produce false-positive results and make interpretation more difficult or impossible. Results from spirometry should be acceptable according to the most recent American Thoracic Society recommendations, and the quality of the flow-volume curves should be examined after each maneuver.
    - Spirometry should be performed according to the current acceptability guidelines of the American Thoracic Society. Alternatively, the expiratory maneuver can be shortened to about 2 seconds after the methacholine doses are inhaled if forced expiratory volume in the first second (FEV_1) is the only outcome measure. If this shortened expiratory maneuver is used, care should be taken to assure that the inspiration is maximal. After the inhalation of diluent (if used) and of each dose of methacholine, forced expiratory volume in the first second (FEV_1) measurements should be made at 30 and 90 seconds after the last inhalation. The time interval between doses should be standardized at 5 minutes to keep cumulative effect constant.

- A limitation of the method is the variability due to the effects of various factors including medications, time of day, and differences in technique and equipment.
- Inconsistencies in technique and equipment can affect the amount of agonist reaching the airways and, thus, the subject's response--making meaningful interpretation difficult or impossible. Factors influencing response that must be controlled and held constant across testing include nebulizer output and particle size, volume inhaled, length of breath-hold, and inspiratory flow.
- If clinical suspicions are not confirmed by one test, additional tests may be indicated.
- The final test report should include:
    - $PC_{20}FEV_1$ (i.e., the provocative concentration that causes a 20% fall in forced expiratory volume in the first second);
    - Comment on the adequacy of spirometric effort and quality of other measurements;
    - Notation regarding medications known to confound interpretation of results taken by the patient prior to testing;
    - Presence or absence of other factors known to confound interpretation of results;
    - Clinical signs and symptoms and clinical appearance during the course of the test and after final dose;
    - Bronchodilator and dose administered at end of challenge;
    - Tabular display of data for each test phase including response to bronchodilator at end of challenge.

Assessment of Need:

Need is established by documenting in a subject the presence of one or more of the listed indications or as established by progression through the institution's or the laboratory's protocol decision tree.

Assessment of Test Quality and Validity of Results:

The consensus of the committee is that all diagnostic procedures should follow the quality model described in the NCCLS GP26-A A Quality System Model for Health Care (NCCLS, 940 West Valley Road, Ste. 1400, Wayne, PA 19087-1898; Web site: www.nccls.org). The document describes a laboratory path of workflow model that incorporates all the steps of the procedure. This process begins with patient assessment and the generation of a clinical indication for testing through the application of the test results to patient care. The quality system essentials defined for all health care services provide the framework for managing the path of workflow. A continuation of this model for respiratory care services is further described in NCCLS HS4-A A Quality System Model for Respiratory Care (NCCLS, 940 West Valley Road, Ste. 1400, Wayne, PA 19087-1898; Web site: www.nccls.org). In both quality models the patient is the central focus.

- General considerations include:
    - As part of any quality assurance program, indicators must be developed to monitor areas addressed in the path of workflow.
    - Each laboratory should standardize procedures and demonstrate intertechnologist reliability. Test results can be considered valid only if

they are derived according to and conform to established laboratory quality control, quality assurance, and monitoring protocols.
    - Documentation of results, therapeutic intervention (or lack of) and/or clinical decisions should be placed in the patient's medical record.
    - The type of medications, dose, and time taken prior to testing and the results of the pretest assessment should be documented.
    - Report of test results should contain a statement by the technician performing the test regarding test quality (including patient understanding of directions and effort expended) and, if appropriate, which recommendations were not met.
    - Test results should be interpreted by a physician, taking into consideration the clinical question to be answered.
    - Personnel who do not meet annual competency requirements or whose competency is deemed unacceptable as documented in an occurrence report should not be allowed to participate, until they have received remedial instruction and have been re-evaluated.
    - There must be evidence of active review of quality control, proficiency testing, and physician alert, or 'panic' values, on a level commensurate with the number of tests performed.
- Calibration and quality control measures specific to equipment used in methacholine challenge include:
    - The size of the dose received and, thus, the response and its interpretation include nebulizer output, particle size, inspiratory flow, lung volume at beginning of inspiration, and breath-hold time (These factors must be held constant across the testing procedure and from one test to another.);
    - Excessive variability in measured values including a nonreproducible baseline [forced expiratory volume in the first second (FEV_1) variation of more than 0.2 L after repeated efforts] makes test results more difficult to interpret.
- Recommendations related to equipment maintenance and calibration made in the AARC clinical practice guidelines for spirometry and measurement of specific conductance should be addressed.

Resources:

- Equipment:
    - Spirometers must meet or exceed American Thoracic Society requirements and be calibrated appropriately. All other equipment must be appropriately calibrated and maintained.
    - A high quality nebulizer with consistent output should be used to produce the aerosol. The particles produced by the nebulizer should have a mass median aerodynamic diameter (MMAD) of 1-4 microns. If more than one nebulizer is used in the testing of a given subject, nebulizer output should be measured for each nebulizer to assure a consistent dose. If output measurement is not possible, we recommend the use of the same nebulizer to deliver all concentrations to a given patient.
    - The gas powering the nebulizer and/or dosimeter should be at the correct driving pressure or flow (as specified by the manufacturer) and should be maintained at that pressure or flowrate consistently throughout the test.

- Reagents:
    - The Food and Drug Administration (FDA) approved form of methacholine powder (Provocholine) is available in prepackaged vials ready for dilution.
    - The recommended diluent used to dissolve the methacholine is sterile normal saline (0.9% sodium chloride) with or without a preservative (e.g., 0.4% phenol).
    - Various strategies have been described for dosing schemes. The range of doses is 0.02-25.0 mg/mL, generally given in doubling doses (i.e., 0.02 mg/mL, 0.04 mg/mL, 0.08 mg/mL.). The dosing scheme most recently recommended by the American Thoracic Society is: diluent, 0.03, 0.06, 0.125, 0.25, 0.5, 1, 2, 4, 8, and 16 mg/mL. If a shortened dosing protocol is desired, the American Thoracic Society recommends: diluent, 0.06, 0.25, 1, 4, and 16 mg/mL. Caution should be used with the shortened protocol when testing small children with asthma symptoms. The use of the diluent step is optional.
    - In general, higher concentrations of methacholine solution (i.e., >1.25 mg/mL) are stable for at least 4 months when stored at 4 degrees C. The package insert for Provocholine recommends that solutions >0.25 mg/mL be stored for no longer than 2 weeks, with weaker solutions mixed on the day of testing.
    - A pharmacist or other well-trained individual should prepare the methacholine reagents according to the manufacturer's recommendations, using sterile technique.
    - Reagents should be clearly labeled with dose, date prepared, and expiration date.
    - The test should be administered in a well-ventilated room (with at least 2 complete air exchanges per hour). A filter to collect excess particles or an exhaust system to remove provocative material from the room may be desirable.
    - Oxygen, bronchodilators, and resuscitation equipment should be readily available.
    - The need for written consent should be determined within the specific institution.
    - A pretest questionnaire should be used. An example of a questionnaire can be found in the American Thoracic Society Methacholine Challenge Guideline.
- Personnel:
    - Methacholine challenge tests should be performed under the direction of a physician trained in pulmonary function testing and experienced in bronchial provocation. Personnel performing the test should be experienced in patient assessment, knowledgeable of and have demonstrated competency in performing this challenge (including reversal of methacholine response), know the associated hazards, and be certified in basic life support. Attainment of the Entry Level Pulmonary Function Technologist (CPFT) and/or Advanced Pulmonary Function Technologist (RPFT) credentials is recommended.
    - During the testing procedure, a physician knowledgeable in provocation testing procedures and trained to treat acute bronchospasm and use resuscitation equipment must be close enough to respond in an emergency.

Patient Monitoring:

- The forced expiratory volume in the first second (FEV_1) is the primary variable to be monitored, and the results of spirometry should meet acceptability and reproducibility recommendations proposed by the American Thoracic Society. A shortened expiratory maneuver can be used in some situations and may be acceptable, and reproducibility after inhalation of some methacholine concentrations may be difficult.
- The test should be administered according to the specific protocol, with the number of breaths and the breathing pattern documented.
- Breath sounds, pulse rate, pulse oximetry, and/or blood pressure may be monitored to assist in patient evaluation and test interpretation. Patients should not be left unattended during the procedure.
- In the case of a positive response to provocation (i.e., greater than or equal to 20% fall in forced expiratory volume in the first second), bronchodilator may be administered to speed recovery. Spirometry should be repeated after bronchodilator administration to ensure that ventilatory function has returned to near baseline (i.e., at least 85% of baseline).

Frequency:

- To ensure that a previous methacholine challenge test does not affect a later test, 230 minutes should be allowed to elapse before the test is repeated. Tolerance of methacholine may occur in patients who are not asthmatic when tests are repeated at less than 24-hour intervals.
- When a test is to be repeated, medications, exposures, time of day, and nebulizer employed should be held constant, if possible.

Infection Control:

- The staff, supervisors, and physician-directors associated with the pulmonary laboratory should be conversant with the "Guideline for Isolation Precautions in Hospitals" made by the Centers for Disease Control and Prevention and the Hospital Infection Control Practices Advisory Committee (HICPAC), and develop and implement policies and procedures for the laboratory that comply with its recommendations for "Standard Precautions" and "Transmission-Based Precautions."
- The laboratory's manager and its medical director should maintain communication and cooperation with the institution's infection control service and the personnel health service to help assure consistency and thoroughness in complying with the institution's policies related to immunizations, post-exposure prophylaxis, and job- and community-related illnesses and exposures.
- Primary considerations include adequate handwashing, provision of prescribed ventilation with adequate air exchanges, careful handling and thorough cleaning and processing of equipment, and the exercise of particular care in scheduling and interfacing with the patient in whom a diagnosis has not been established.
- Sterility of reagents should be maintained by proper storage and aseptic handling.

Age-Specific Issues:

Test instructions and techniques should be given in a manner that takes into consideration the learning ability and communication skills of the patient being tested.

- Neonatal: This clinical practice guideline does not apply to neonatal populations.
- Pediatric: This clinical practice guideline is appropriate for children who can perform good quality spirometry or body plethysmography aged 5 years and older).
- Geriatric: This clinical practice guideline is appropriate for the geriatric population.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Not specifically stated for each recommendation.

The guideline is developed from a thorough review of the literature, surveys of current practice, and the expertise of the members of the Working Group.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate utilization of methacholine challenge testing may help to exclude a diagnosis of airway hyperreactivity (i.e., asthma); evaluate occupational asthma; assess the severity of hyperresponsiveness; determine the relative risk of developing asthma; and assess response to therapeutic interventions.

POTENTIAL HARMS

The following possible hazards or untoward reactions may occur:

- Bronchoconstriction, hyperinflation, severe coughing
- Hazards associated with spirometry, such as dizziness, light-headedness, chest pain
- Possible exposure of technicians to provocative substances

CONTRAINDICATIONS

CONTRAINDICATIONS

- Absolute contraindications are:

    - Ventilatory impairment: forced expiratory volume in the first second (FEV_1) <50% of predicted or <1.0 L [This may be a relative contraindication depending on the age or size of the patient or on the presence of a restrictive lung disorder (reduced forced vital capacity, or FVC, with a relatively normal FEV_1/FVC)]
    - Heart attack or stroke within the previous 3 months
    - Known aortic or cerebral aneurysm
    - Uncontrolled hypertension (the American Thoracic Society suggests systolic pressure >200 and/or diastolic pressure >110 mm Hg)
- Relative contraindications are:
    - Ventilatory impairment: forced expiratory volume in the first second (FEV_1) >50% or >1.5L but <60% of predicted
    - Inability to perform spirometry of acceptable quality
    - Significant response to the diluent, if administered (i.e., >10% fall in forced expiratory volume in the first second (FEV_1) from baseline)
    - Upper- or lower-respiratory-tract infection within previous 2 to 6 weeks
    - Current use of cholinesterase-inhibitor medication (for myasthenia gravis)
    - Pregnancy (the effect of methacholine on the fetus is unknown)
    - Lactation
- Failure to withhold medications may affect the methacholine challenge test. Recommended periods for withholding medications are generally based on their duration of action. Laboratories may choose to develop a simplified withholding schedule that makes allowances for agents used by the patient. (A list of agents and recommended withholding times are listed in the original guideline document).
- Foods: Ingestion of coffee, tea, cola drinks, chocolate, or other foods containing caffeine may decrease bronchial responsiveness. These substances should be withheld on the day of test.
- Other factors that may confound results include:
    - Smoking
    - Occupational sensitizers
    - Respiratory infection
    - Specific antigens
    - Vigorous exercise (Performing other bronchial challenge procedures or exercise testing immediately prior to methacholine challenge may affect interpretation.)

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guideline applies to adults and children (5 years of age and older) capable of adequately performing spirometry or body plethysmography and of cooperating during the course of the challenge.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Methacholine challenge testing: 2001 Revision & Update. Respir Care 2001 May;46(5):523-30. [53 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 May

GUIDELINE DEVELOPER(S)

American Association for Respiratory Care - Professional Association

SOURCE(S) OF FUNDING

American Association for Respiratory Care (AARC)

GUIDELINE COMMITTEE

Pulmonary Function Testing Clinical Practice Guidelines Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Jack Wanger MS RRT RPFT; Susan Blonshine BS RRT RPFT; Catherine M Foss, BS RRT RPFT; Carl Mottram, BA RRT RPFT, Chair; Gregg Ruppel MEd RRT RPFT

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously issued version (Bronchial provocation. Respir Care 1992 Aug;37[8]:902).

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Association for Respiratory Care (AARC) Web site.

Print copies: Available from AARC, CPG Desk, 11030 Ables Ln, Dallas, TX 75229-4593.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on November 30, 1998. The information was verified by the guideline developer on December 15, 1998. This summary was updated by ECRI on August 24, 2001. The updated information was verified by the guideline developer as of October 17, 2001.

COPYRIGHT STATEMENT

Interested persons may copy the guidelines for noncommercial purposes of scientific or educational advancement. Please credit The American Association for Respiratory Care (AARC) and Respiratory Care Journal.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx.

NGC, AHRQ, and its contractor ECRI make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2006 National Guideline Clearinghouse

Date Modified: 9/25/2006