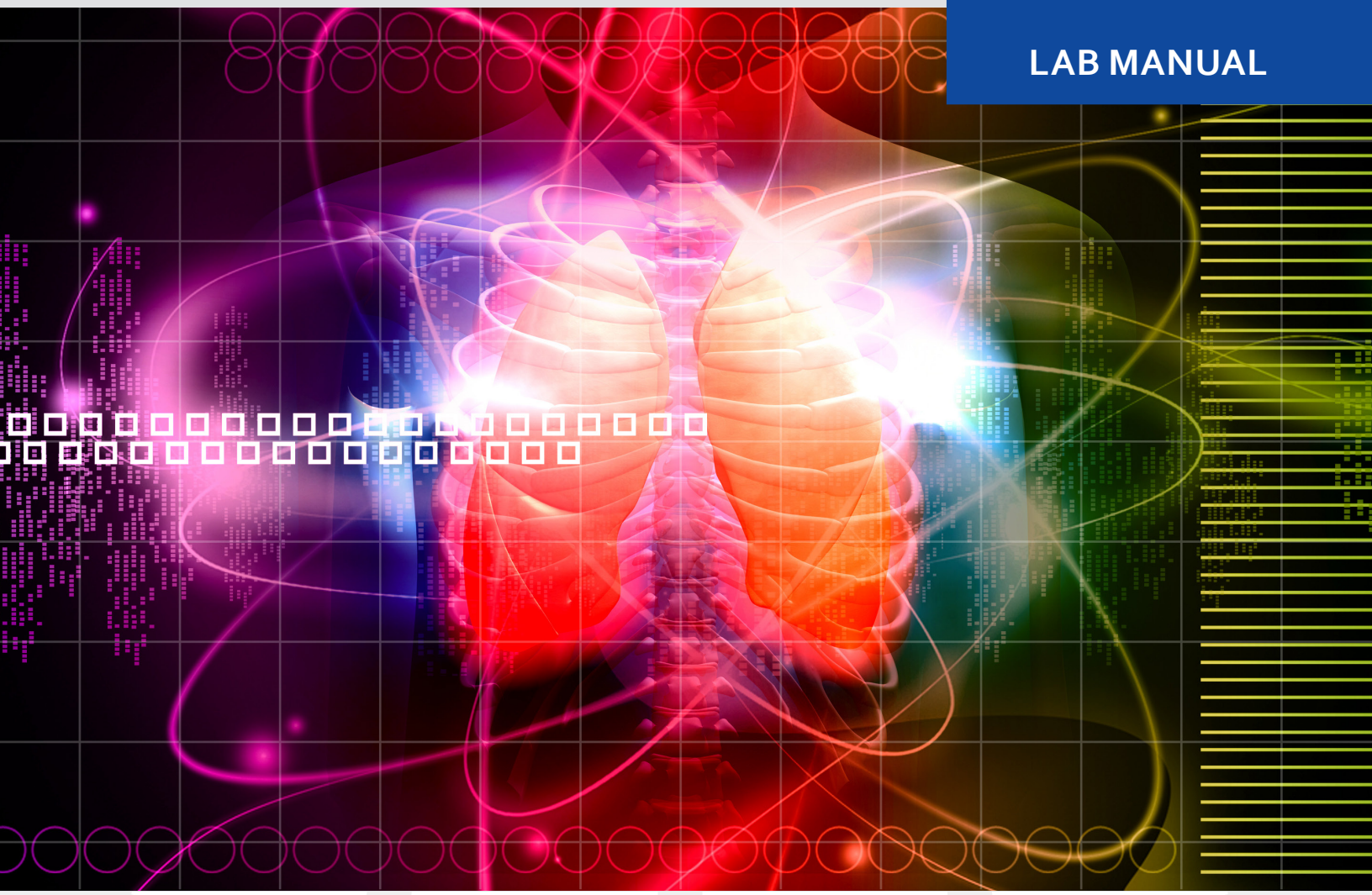
American Thoracic Society

LAB MANUAL



ATS PULMONARY FUNCTION LABORATORY MANAGEMENT AND PROCEDURE MANUAL 3rd EDITION

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ATS Pulmonary Function Laboratory Management & Procedure Manual

Third Edition

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American Thoracic Society
New York

ATS Pulmonary Function Laboratory Management and Procedure Manual, Third Edition

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PREFACE

The idea for this work originated in the American Thoracic Society (ATS) Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories in the 1990's. The first edition was published in 2001, and the second edition in 2004 when the new ATS/ERS recommendations were completed. Since it has been 10 years since the second edition was published, a new update is warranted.

The primary purpose of the ATS Pulmonary Function Laboratory Management and Procedure Manual (ATS Manual) is to provide a tool to help laboratories develop their own pulmonary function laboratory procedure manual. The ATS Manual can be used as-is, or as a template to customize a manual for your laboratory. It is the hope that this tool will also help maximize the accuracy and precision of pulmonary function laboratory data as well as help laboratories improve efficiency and management techniques.

The third edition of the ATS Manual maintains the same general philosophy and purpose as previous editions and has been updated to include the latest ATS/European Respiratory Society (ERS) recommendations. The basic organization of the content has been maintained, but the format has been modified to reflect the new recommendations from the Clinical and Laboratory Standards Institute (CLSI) QM SO2-A6, 6th Edition.

The first five chapters present methods and procedures for the administrative aspects of managing a laboratory. Chapters 6–19 present procedural information on commonly performed pulmonary function tests. Chapter 20 presents information on reference equations and interpretation guidelines, and Chapter 21 contains useful equations and tables.

Most of the material presented here applies to both adult and pediatric pulmonary function laboratories. Where modification of procedures or standards is required, these are specified throughout the Manual. In general, pulmonary function laboratories serving a primarily adult population can perform satisfactory testing on patients in the teenage years, depending on individual maturity, and with attention to age-appropriate reference data. For children of elementary age, appropriate laboratory environment, pediatric-specific protocols, and technicians experienced, comfortable, and competent in working with children are required. Testing of preschool children is best performed in highly specialized pulmonary function laboratories.

The majority of chapters in this third edition were written by Jack Wanger, M.Sc., RRT RPFT FAARC. Chapters 2–6 were written by Carl D. Mottram, B.A., RRT RPFT FAARC. All chapters were then critically reviewed by the members of the ATS Proficiency Standard for Clinical Pulmonary Function Laboratories Committee. The members of the Committee in 2014 included: Bruce H. Culver, M.D., Chair; Allan L. Coates, M.D.; Brian L. Graham, Ph.D.; Teal S. Hallstrand, M.D., M.P.H.; John L. Hankinson, Ph.D.; David A. Kaminsky, M.D.; Neil R. MacIntyre, M.D.; Meredith C. McCormack, M.D., M.H.S.; Jack Wanger, M.Sc.; Margaret Rosenfeld, M.D.; and Daniel J. Weiner, M.D.

The expectation is that this work will be updated periodically. With that in mind, we ask that you send corrections, suggestions, and comments for future editions to: American Thoracic Society, 25 Broadway, 18th Floor, New York, New York, 10004, Attention: Barbara Horner, bhorner@thoracic.org.

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CHAPTER 1

INTRODUCTION AND GENERAL INFORMATION

INTRODUCTION

The American Thoracic Society (ATS) Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories has developed this publication to assist directors and managers in preparing a comprehensive and standardized pulmonary function (PF) laboratory procedure and management manual. Every PF laboratory, physician's office, clinic, or occupational setting that performs PF tests should prepare a comprehensive procedure manual. It is the Committee's hope that this document will be adopted by these health care laboratories or offices, thereby improving standardization of how PF tests are performed and how PF laboratories are managed. Accreditation agencies (e.g., The Joint Commission) require written technical and managerial procedures to ensure the highest level of patient care. This publication will help the PF laboratories and offices meet these requirements.

The specific objectives of this publication are: (*1*) to provide each laboratory with valuable information from the literature and previously written guidelines, (*2*) to improve the technical and procedural quality of lung function testing, (*3*) to assist departments in meeting requirements of the Joint Commission and other accreditation agencies, and (*4*) to assist directors and managers in preparing a useful procedure manual.

The publication is divided into chapters, each detailing management issues or specific test procedures. The material in each chapter is based on previously written guidelines and standardization statements. When such guidelines are not available, the material is extracted from important and pertinent publications.

The publication is designed to be generic, and individual laboratories may modify the procedures to fit their style and circumstances. Every attempt has been made to make the individual chapters as complete as possible; however, there may well be a need to add certain specific information for an individual laboratory. This manual will be reviewed and updated periodically. We encourage comments and suggestions and ask that you send them to:

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This chapter provides general guidelines for preparing the manual including: (*1*) design, (*2*) style, (*3*) format for technical procedures, (*4*) handling of reviews and updates, and (*5*) a glossary of terms and abbreviations.

PROCEDURE MANUAL DESIGN

The design and format of the 3rd Edition of the ATS Pulmonary Function Laboratory Management and Procedure Manual is based on the Clinical and Laboratory Standards Institute (CLSI) guideline QMS02-A6, Quality Management System: Development and Management of Laboratory Documents, 6th Edition (1). This approved guideline is available from CLSI (940 West Valley Road, Suite 2500, Wayne, PA 19087).

While the final form and wording of any procedure manual should be determined by the specific needs and organization of the laboratory or department, the ATS recommends the following as a minimal standard:

1. A loose-leaf notebook designed to allow easy updating, or electronic preparation and storage
2. The use of tabs and a table of contents
3. Process flow charts or tables are strongly recommended
4. Beginning each procedure on a new page
5. Using only current manufacturers' literature (if it is used) and using it only to supplement the written procedure

PROCEDURE MANUAL STYLE

Procedures should be explicit, easy-to-follow, and complete. A uniform style should be established and used throughout. In accordance with CLSI guidelines, the ATS recommends the following:

1. Indicate the page number and the total number of pages at the top or bottom of each page.
2. Include the effective date for the procedure on the first page.
3. Document the date of review of each procedure and include the reviewer's signature.
5. Note if the procedure replaces an earlier one (document history).
6. Retain obsolete or suspended procedures either in the manual or in a separate file, and keep them for at least 2 years.

The procedure manual is also written using the CLSI "Path of Workflow" concept, which is based on a model that is described in the CLSI guideline *Quality Management System A Model for Laboratory Services* (QMS01-A4) (2). This concept recognizes that quality testing incorporates every stage of the testing cycle, which includes the pre-test, test, and post-test phases.

FORMAT FOR TECHNICAL PROCEDURES

The technical procedures should be written in a uniform style and contain the following:

1. **Procedure Name**—concise and descriptive
2. **Purpose or Principle**—written in paragraph form with comprehensive indications and contraindications
3. **Equipment and Supplies**—a listing of what is needed to perform the test (e.g., nose clip, tissue, and mouthpiece)
4. **Patient Preparation (Pre-Test Instructions)**—specific instructions for the patient (e.g., which medications to withhold and for how long)
5. **Assessment of Patients (Pre-Test)**—specific instructions on assuring patient has complied with preparation instructions and has the ability to perform the test procedures
6. **Equipment Preparation and Calibration Checks (Pre-Test)**—directions for preparing the instrumentation and supplies; detailed, stepwise instructions, and frequency and tolerances for calibration

7. **Test Procedures (Pre-Test and Test)**—instructions on patient identification, and detailed step-by-step instructions on the procedure, written using the imperative form (e.g., seal the plethysmograph door); keep these instructions free of extraneous matter (e.g., explanations or justifications)
8. **Review of Test Results (Post-Test)**—policy on final review of test results before entry into patient chart of institution information system
9. **Reporting of Test Results (Post-Test)**—instructions on reporting format (e.g., rounding off procedures, averaging or highest value, and reference values)
10. **Procedure Notes**—information concerning the procedure not included in the purpose/principle section, reasons for special precautions, possible sources of error, helpful hints, pitfalls, clinical situations that can influence the validity of test results, and acceptable turnaround time
11. **References**—manufacturer's product literature, textbooks, standards and guideline publications, and other pertinent publications

This publication contains templates for commonly used procedures performed in PF laboratories. The templates are written in the format shown above, but the exact wording can be altered to meet specific needs.

We have made a strong effort to base the material on published guidelines and standardization statements. In cases in which such guidelines are not available, we have relied on important and pertinent publications. Because we cannot foresee every situation, we encourage that each laboratory customize each chapter as needed. However, the ATS is not responsible for any untoward responses, and laboratories and institutions must take full responsibility for these procedures.

The administrative or nontechnical policies and procedures can be kept in a separate manual. However, this publication has included a few of them with the technical procedures, using the same basic style. Other administration policies and procedures that a laboratory might consider include: attendance and punctuality, dress code, meals and rest periods, staffing plan, charging for tests, scheduling of procedures, patient incidents, smoking, and exposure control plan.

REVIEWS AND UPDATES OF PROCEDURE MANUAL

All technical procedures should be reviewed at least annually, and whenever a change is made in methodology and/or instrumentation. At the time of review, the procedure can be reapproved as written, revised, or retired.

The reviewer(s), who will vary according to administrative structure, should have firsthand knowledge of the procedure and be the director, manager, qualified supervisor, or a delegated committee. However, the medical director should oversee the process and is ultimately responsible for the procedure.

The review should be documented, with the reviewer signing and dating the appropriate section. If there are multiple copies of the procedure, all copies must be reviewed as described.

Obsolete or superseded procedures should be clearly marked as "retired" and stored in a retired file or retired section of the manual. Retired procedures should be kept for a minimum of 2 years.

These review and update recommendations also apply to electronic manuals. Only approved procedures should be available. If the manual is accessible electronically, new or edited material—or material under development—should not be accessible.

GLOSSARY OF TERMS AND ABBREVIATIONS

Important pulmonary terms and abbreviations (3–5)

A	
A	alveolar
a	arterial
an	anatomic
ao	airway opening
ATPD	ambient temperature, barometric pressure, dry
ATPS	ambient temperature, barometric pressure, saturated with water vapor
aw	airway(s)
B	
B	barometric
BE	base excess
BMR	basal metabolic rate
BP	blood pressure
br	bronchial
BSA	body surface area
BTPS	body temperature, barometric pressure, saturated with water vapor
C	
C	compliance, concentration in the blood phase
CL, C_L	compliance of the lung
CL,dyn	dynamic compliance of the lung
c	capillary
c′	pulmonary end-capillary
C.O.	cardiac output
COHb	carboxyhemoglobin concentration
CV	coefficient of variation [(standard deviation/mean) × 100]
D	
D	diffusing capacity
$D_{L_{CO}}$	carbon monoxide diffusing capacity of the lung
d,ds	dead space

di	diaphragm
DM	membrane diffusing capacity
dyn	dynamic
E	
E	elastance
E, exp	expired
EEL	end expiratory level
EPP	equal pressure point
ERV	expiratory reserve volume
F	
F	female
f	frequency (e.g., respiratory)
$FEF_{x\%}$	forced expiratory flow when x% of forced expiratory vital capacity has been exhaled
$FEF_{25-75\%}$	forced mid-expiratory flow
FET	forced expiratory time
FEV_t	forced expiratory volume in t seconds
$FEV_{t\%}FVC$	forced expiratory volume in t seconds as a percentage of the forced vital capacity
FVC, FEVC	forced expiratory vital capacity
FIVC	forced inspiratory vital capacity
FRC	functional residual capacity, method of measurement to be specified
G	
G	conductance
Gaw	airway conductance, the reciprocal of Raw (1/Raw)
Gaw/VL, (sGaw)	specific airway conductance expressed per liter of lung volume at which G is measured
H	
H, ht	standing height
Hb	hemoglobin
I	
I, insp	inspiratory
IC	inspiratory capacity
IRV	inspiratory reserve volume

K	
K_{CO}	concentration fall in alveolar CO per unit of time per unit CO driving pressure
L	
L	length
L	liter
L, l	lung
M	
M	male
m	membrane
max	maximal
mb	multiple breath
min	minute
MEF	maximal expiratory flow
MMEF	maximal mid-expiratory flow
mm Hg	millimeters of mercury
mo	mouth
MVV_f	maximal voluntary ventilation at breathing frequency f
P	
P	pressure
$P_{A_{O_2}}$	alveolar oxygen pressure in mmHg
PCx	provocative concentration of bronchoconstrictor causing x% fall from baseline (e.g., $PC_{20}FEV_1$: provocative concentration causing a 20% fall in FEV_1)
PDx	provocative dose of bronchoconstrictor causing x% fall from baseline
PEF	peak expiratory flow
PEFV curve	partial expiratory flow volume curve
P_{E}max, MEP	maximum expiratory pressure
pH	unit of acidity
phys	physiological
PIF	peak inspiratory flow
P_{I}max, MIP	maximum inspiratory pressure
PIP	peak inspiratory pressure
pl	pleural

pleth	plethysmographic
$P(A–a)O_2$	alveolar-arterial oxygen pressure difference
pulm	pulmonary
Q	
Q	blood volume
R	
R	flow resistance, respiratory
R, RQ	respiratory quotient
Raw	airway resistance
Rrs,int	resistance of respiratory system to gas flow assessed with interruptor technique
Rus	resistance of the airways on the alveolar (upstream) side of the equal pressure point
rb	rebreathing
RHE	respiratory heat exchange
rs	respiratory system
RR	respiratory rate
RV	residual volume
S	
S	saturation
SRaw	specific airway resistance expressed per liter of lung volume at which Raw is measured
Sp_{O_2}	oxygen saturation measured by pulse oximetry
s	second
sb	single breath
sp	spirometric
ss	steady state
st	static
STPD	standard temperature and pressure, dry
T	
T	tidal
t	temperature
t	time
T_L	gas transfer factor for the lung

TL/VA	transfer coefficient (K)
TGV	thoracic gas volume
TLC	total lung capacity
tot	total
tp	transpulmonary
Tr	tracer gas
TV	tidal volume (see VT)
U	
us	upstream
V	
V	gas volume
v	venous
V_L	lung gas volume
V_T	tidal volume during gas exchange formulations instantaneous gas flow
W	
W	weight
W	work
Other Symbols	
Δ	delta: change in variable
θ	specific uptake of CO

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CHAPTER 2

PROCEDURE NAME: PERSONNEL

PURPOSE OR PRINCIPLE

The purpose of this procedure is to ensure appropriate personnel practices. Although personnel issues are typically within the domain of the hospital human resource department, there are several areas for which the American Thoracic Society (ATS) and European Respiratory Society (ERS) have recommendations and/or suggestions, including: qualifications, training, orientation, and competency assessment (1). Their recommendations are directed toward ensuring quality testing in a patient-safe environment by setting guidelines for medical and laboratory staff, including specific job descriptions and competency assessment criteria.

PERSONNEL QUALIFICATIONS

1. Medical Director

1.1. Each pulmonary function (PF) laboratory must have a medical director responsible for the activities and functions of the laboratory (2, 3).

Table 2.1

Medical Director's responsibilities:
1. Supervising the technical staff
2. Overseeing the publishing and review of a procedure manual
3. Determining the specific tests offered
4. Ensuring a safe working and testing environment
5. Ensuring that interpreters of test results are properly qualified
6. Developing and monitoring a system for communicating test results to referring physicians and medical record
7. Assuring the equipment is properly maintained and upgraded
8. Developing appropriate resources for education of staff
9. Assuring a quality control program is in place and functioning

1.2. Board certified or appropriately qualified in pulmonary medicine with acceptable training and experience in PF laboratory management.

2. Manager/Supervisor/Technical Director (4)

2.1. Bachelor's degree in respiratory care or other science is preferred

2.2. At least 4 years of experience in PF testing

2.3. At least 2 years of supervisory experience

2.4. Appropriate credentials, such as from the National Board of Respiratory Care (NBRC) (i.e., Certified or Registered Pulmonary Function Technologist [CPFT or RPFT])

2.5. Experience or education in business because responsibilities include determining appropriate patient charges for tests and for professional interpretation of test results, and interacting with financial management of the institution

3. Technologist

3.1. The importance of the technologist in the PF laboratory has been recognized and has led to several recommendations on education and training (1, 4–8).

3.2. While there are no data specifying the education level necessary to train in the laboratory, the ATS and ERS recommend that completion of secondary education and at least 2 years of college education would be required to understand and fulfil the complete range of tasks undertaken by a pulmonary function technologist (1).

3.3. Technologists should be encouraged to minimally obtain the NBRC pulmonary function testing credential as soon as they meet the examination criteria. Effective June, 2015, the Certification Examination for Entry-Level Pulmonary Function Technologists (CPFT), and the Registry Examination for Advanced Pulmonary Function Technologists (RPFT) will transition to a one-examination, two-cut score examination. If a candidate achieves the lower cut score, they will earn the CPFT credential. If a candidate achieves the higher cut score, they will earn the RPFT credential.

3.3.1. In order to take the examination, an applicant must meet one of the following criteria (9).

1. Be at least 18 years of age
2. Satisfy one of the following:

- Have a minimum of an associate degree from a respiratory therapy education program (*1*) supported or accredited by the Commission on Accreditation for Respiratory Care (CoARC), or (*2*) accredited by the Commission on Accreditation of Allied Health Education Programs (CAAHEP) and graduated on or before November 11, 2009.

OR

- Be a Certified Respiratory Therapist (CRT) or Registered Respiratory Therapist (RRT) credentialed by the NBRC.

OR

- Complete 62 semester hours of college credit from a college or university accredited by its regional association or its equivalent, including college credit level courses in biology, chemistry, and mathematics. A minimum of 6 months of clinical experience in the field of pulmonary function technology is also required prior to applying for the examination. Clinical experience is defined as a minimum of 8 hours per week for a calendar year in pulmonary technology under the supervision of a medical director of a pulmonary function laboratory or a special care area acceptable to the Board. Clinical experience must be completed before the candidate applies for the examination.

TECHNOLOGIST TRAINING AND CONTINUING EDUCATION

1. The duration of training required before an individual is competent to perform testing varies according to background, schooling, and prior experience.
2. One recommendation for training time for a laboratory that trains individuals concurrently to perform arterial blood gases, spirometry, lung volumes, carbon monoxide diffusing capacity of the lung (D_{LCO}), and exercise tests is 6–12 months (4).
3. For troubleshooting problems on PF equipment, it is recommended that the technologist have 1 to 2 years of training time (4).
4. For technologists working in a pediatric PF laboratory, special age-specific training is necessary.
5. Personnel administering PF tests as part of medical surveillance may be required to attend a training course, approved by the National Institute for Occupational Safety and Health (NIOSH) (8).
    - 5.1. The NIOSH training programs are designed to provide basic instruction in spirometry procedures.
    - 5.2. For those who perform medical surveillance and/or epidemiological studies, additional training beyond the NIOSH training program is recommended (8).
6. At the end of the training program, written and practical examinations have been shown to be useful, but are not required (7).
7. Technologists will be required to maintain and improve their knowledge and skills through documented in-services and/or other lectures or seminars.
    - 7.1. These activities will be documented in the employee's department personnel file.

ORIENTATION

1. The organization's human resource department should provide an orientation for new employees within the first 10 days of employment. This orientation usually includes:
    - 1.2. Review of the organizational mission
        - 1.2.1. Governance issues
        - 1.2.2. Payroll and benefits
        - 1.2.3. Various hospital or facility policies and procedures (e.g., infection control and safety).
2. The department will also conduct an orientation during an employee's first three working shifts. This orientation will include information about:
    - 2.1. Department mission and scope of practice
    - 2.2. Department policies and procedures, including dress code, meals, fire and safety, disaster, hazardous materials, and infection control
    - 2.3. The individual's job description
    - 2.4. Performance expectations
    - 2.5. Training objectives
    - 2.6. Department performance improvement program.
3. Attendance and completion of the departmental orientation will be documented using a checklist form (example in Appendix 2.1), which will become part of the employee's department personnel file.

COMPETENCY ASSESSMENT

1. Each technologist will be required to demonstrate competency after orientation or initial training and annually thereafter.
2. An instructional resource notebook/computer file that contains information needed to demonstrate competency will be available (*see* Appendix 2.2).
   2.1 Additional competency assessment tools are available (listed in the related documents section).
3. Identified learning needs will be satisfied and a follow-up competency assessment administered.
4. The medical director, manager, or supervisor may perform the competency assessment.
5. The competency assessment involves three parts:
   5.1. Theory and general information (where the technologist is asked to write some basic information)
   5.2. Equipment and supply preparation
   5.3. Implementation of procedures or techniques (if possible, this will occur using a naive patient).
6. It is not necessary for each technologist to demonstrate competency annually for all tests or procedures performed. The laboratory can choose those areas it deems important. The following areas are recommended for competency evaluation:

Spirometry
Bronchodilator or methacholine administration
Lung volume determination using the body plethysmograph and/or gas dilution/washout techniques
Diffusing capacity
Arterial blood gas collection and analysis
Miscellaneous tests (e.g., cardiopulmonary exercise test, 6-minute-walk)
Emergency procedures if laboratory performs exercise tests and challenges

7. Documentation of the competency assessment will be made using an appropriate form (example in Appendix 2.2), which is stored in the employee's department file.

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APPENDIX 2.1

Departmental New Employee Checklist Form

Department:

Employee Name: Title:

Date of Hire: Date:

Trainer Conducting Orientation:

Item	Date Completed
Department Mission Statement	
Department Organizational Chart	
Tour of Department	
Introduction to Staff	
Department Policies and Procedures	
Department Forms	
ID/Name Badge, Security System , Parking	
Department Meetings and Communication	
Job Description	
Performance Standards and Evaluations	
Department Performance Improvement Program	
Office Equipment (e.g., Fax, Copier, Computer System, and Telephone)	
Safety Issues (e.g., Emergency Preparedness Plan, Chemical Hazards, etc.)	

Manager/Supervisor Signature_____ Date: _____

Employee Signature_____ Date: _____

APPENDIX 2.2

Competency Assessment Form

Percutaneous Collection of Arterial Blood

Employee Name: Title:

Date: Annual ___ Initial ___

Satisfactory ⊙ Identified Learning Need ⊙ Not Applicable

THEORY AND GENERAL INFORMATION

1. Lists at least three concerns or contraindications to performing an arterial puncture.
2. Lists at least three hazards of an arterial puncture.

EQUIPMENT PREPARATION

1. Obtains physician's order.
2. Confirm that there has been no O_2 concentration change for at least 10 minutes, and patient is in a steady state (resting quietly for 10 minutes).
3. Assembles supplies required for arterial puncture.

IMPLEMENTATION

1. Introduces self, identifies patient (two unique identifiers), explains procedure, and asks/ verifies if patient is taking anticoagulation medication.
2. Verifies O_2 flow rate and/or concentration.
3. Selects site for puncture and performs Allen test (if applicable).
4. Uses appropriate barrier protection.
5. Cleanses area with institutionally approved cleansing agent.
6. Properly administers local anesthetic (if applicable).
7. Properly positions patient's arm and obtains sample.
8. Properly removes needle, and applies firm pressure for 5 minutes.
9. Properly removes air and seals syringe.
10. Properly disposes of needle in sharps container.
11. Properly labels syringe and stores on ice (if appropriate), completes arterial blood gas (ABG) form, and transports to lab.
12. Properly disposes of barrier protection and washes hands.
13. Properly documents in patient's chart.

Comments:

Reviewer:

Date of Assessment:

Competency Assessment Resource Material

Percutaneous Collection of Arterial Blood

THEORY AND GENERAL INFORMATION

1. Lists at least three concerns or contraindications to performing an arterial puncture.
   a. Negative results of Allen test indicating reduced patency of ulnar artery
   b. Arterial puncture should not be performed through a lesion or through or distal to a surgical shunt.
   c. Anticoagulation therapy does not necessarily contraindicate arterial puncture but may require special precautions (e.g., compression of the site for extended period).
   d. Clotting disorders
2. Lists at least three hazards of an arterial puncture:
   a. Hematoma
   b. Arteriospasm (reflex constriction of artery)
   c. Thrombosis or embolism
   d. Fainting (vasovagal response)
   e. Allergic reaction to antiseptic solutions or local anesthetics ("caines")

IMPLEMENTATION

1. Introduces self, identifies patient either by asking the patient to state or spell his/her first and last names, and date of birth, and verify the information against ID band and/or requisition. Explains the procedure to the patient, asks if he/she has an allergy to iodine or lidocaine (if applicable), and asks/verifies if he/she is taking anticoagulant medication.
2. If patient is on supplemental O_2, verifies flow rate and/or concentration using appropriate device (e.g., calibrated meter).
3. Selects site for puncture and performs Allen test (if using radial artery).
   a. Radial artery is site of choice, but brachial artery is a reasonable alternative.
   b. Allen test
      1) Have patient make a tight fist to expel blood while technician applies pressure to the radial and ulnar arteries.
      2) The patient opens and closes hand several times.
      3) The patient opens the hand, and the technician releases pressure on the ulnar artery.
      4) If color fails to return quickly to the palm and fingers within 15 seconds, ulnar artery obstruction is indicated and another site should be selected.
4. Uses appropriate barrier protection.
   a. Dons gloves and other protection (e.g., eye goggles), if applicable.
5. Cleanses area with iodine and alcohol.
   a. Adequately scrubs site to ensure aseptic conditions.
6. Properly administers local anesthetic (if applicable).
   a. Verifies patient does not have a "caine" allergy.
   b. Injects 1% or 2% lidocaine without epinephrine into and under the skin, creating a wheal.

c. Slowly probes into the subcutaneous tissue on the sides of the artery, aspirating to ensure that the needle is not in the artery. Injects lidocaine into the periarterial tissue.
d. Uses only a small amount of anesthetic (i.e., 0.5–1.0 ml)
e. Waits 1 to 3 minutes for the anesthetic to become effective before doing the arterial puncture.

7. Properly positions patient's arm and obtains sample.
   a. If heparin solution is used, withdraws a sufficient volume of arterial blood to minimize dilation effect of heparin.
   b. Uses towel or other prop under wrist (radial puncture).
   c. Positions patient's arm to create easy and comfortable access to sampling site.
8. Properly removes needle, and applies firm pressure for 3–5 minutes.
   a. Activate the needle safety feature immediately after specimen collection and discard.
9. Properly removes air, seals syringe, and mixes the specimen thoroughly.
10. Properly labels specimen and immerses in coolant, if applicable.
11. Promptly completes test-request form and transports specimen to lab.
12. Properly disposes of barrier protection and washes hands.
13. Properly documents in patient chart:
    a. Time sample obtained
    b. Puncture site and number of attempts
    c. Results of Allen test
    d. O_2 liter flow, and/or ventilator settings at time of specimen collection

Annual Review

Date	Signature	Date	Signature

Revisions / Document History

Effective Date	Synopsis of Change

Effective Date: 2014
Version #1

CHAPTER 3

PROCEDURE NAME: QUALITY SYSTEM ESSENTIALS FOR GENERAL OPERATIONAL ISSUES

PURPOSE OR PRINCIPLE

The pulmonary function (PF) laboratory intends to provide services that ensure adherence to the quality system model for Respiratory Services, and conform to state, federal, or other regulatory agencies.

The purpose of this procedure is to assure the proper management of a PF laboratory, including establishment of a mission, scope of practice, and organizational structure to provide the foundation of a laboratory's operation. A quality system should be described and implemented to ensure good laboratory practices throughout the path of work flow.

RESPONSIBILITY

The medical director of the PF laboratory and laboratory management staff, if applicable, are responsible for all aspects of ensuring that the system meets the quality objectives required of the department (1).

ORGANIZATION AND ADMINISTRATION

1. Mission statement
   - 1.1. The PF laboratory mission statement should be consistent with the mission, vision, and values of the healthcare system.
   - 1.2. The PF laboratory is responsible for the production of accurate and timely results for all testing performed.
2. Scope of practice
   - 2.1. The PF laboratory staff may be responsible for analyzing and obtaining physiologic specimens, interpreting physiologic data, performing tests of the cardiopulmonary system, monitoring hemodynamic functions, assisting with diagnostic procedures, applying and monitoring medical gases and aerosols, and administering pharmacologic agents related to respiratory care procedures.
   - 2.2. Other duties may include performing cardiopulmonary resuscitation; acquiring, repairing and/or maintaining equipment; assuring quality control, monitoring performance improvement, providing community service and education, charting and record keeping, educating other healthcare providers, and conducting research.
   - 2.3. The age range of laboratory and staff competence should be specified. For example, the PF Laboratory can competently perform testing on adult and pediatric patients (ages 4 and up).

3. Organizational structure
    3.1. The organizational structure of the laboratory depends on the size of the operation, but should include a qualified medical director and well-trained technical staff (1). Larger operations might also require a technical director, manager, and/or supervisor in addition to the testing staff. In addition, there may be computer support staff, administrative assistants (transcriptionist), and/or bioengineers who provide support to laboratory operations.

QUALITY SYSTEMS IN PULMONARY FUNCTION LABORATORIES

The Clinical and Laboratory Standards Institute (CLSI) published an approved guideline outlining a model for quality systems in healthcare in 1999 that was last updated and retitled *Quality Management System: A Model for Laboratory Services (QMS01-A4)* in 2011 (2). Subsequently, in 2002 and updated in 2006, a guideline was published applying the quality management system to respiratory care, titled *Application of a Quality Management System Model for Respiratory Services (QMS07-A2)* (3). Detailed discussion and implementation steps for pulmonary diagnostics may be found in this document and other resources (4). The model outlines twelve essential items or quality-system essentials (QSEs) and the path of workflow for pulmonary diagnostics (*see* Appendix 3.1). Specific recommendations for development of a documentation system are also included. The twelve QSEs should be incorporated into the daily operations. A quality manual includes the PF laboratory's intent to fulfill each of these QSEs as provided in the following example.

1. QSE: Documents and Records: All documents and records are maintained according to standard operating procedures and accreditation or regulatory bodies.
2. QSE: Organization: Each PF laboratory-testing site is committed to providing quality patient care and test performance according to published standards and guidelines.
3. QSE: Equipment: Procedures address selection and installation of equipment. An installation manual is maintained for the life of the equipment.
4. QSE: Process Management: The standard operating procedures in this manual address all test performance issues across the pulmonary diagnostic path of workflow. The laboratory will participate in internal and external assessments.
5. QSE: Personnel: Personnel issues are addressed in the standard operating procedures. All employees are required to complete an approved orientation and training program. In addition, all employees are required to maintain documentation of their training and education.
6. QSE: Purchasing and Inventory: A system to maintain adequate supplies at an acceptable functional level will be maintained and monitored.
7. QSE: Non-conforming Event Management: A problem and resolution log related to equipment is maintained in the calibration log. A system is maintained to record all other occurrences and related actions and/or resolutions.
8. QSE: Assessment (external and internal): Quality indicators will be developed, monitored, and changed as appropriate.
9. QSE: Continual Improvement: Opportunities for improvement may be identified through internal assessment, review of test results, accrediting or regulatory agencies and external assessment.
10. QSE: Customer Focus: A method to evaluate satisfaction with services will be maintained and monitored to identify opportunities.
11. QSE: Facilities and Safety: The environment is designed to provide safety for all and meet all accreditation and regulatory requirements.

12. QSE: Information Management: A method is defined and implemented which maintains the flow of information both internal and external to the PF laboratory that ensures the security of data access and integrity of the flow of information.

PULMONARY DIAGNOSTICS PATH OF WORKFLOW

1. Pre-test
    - 1.1. Patient assessment
    - 1.2. Test request process
    - 1.3. Patient preparation
    - 1.4. Equipment preparation
2. Testing session
    - 2.1. Patient training
    - 2.2. Test performance
    - 2.3. Results review and selection
    - 2.4. Patient assessment for further testing
3. Post-test
    - 3.1. Results report
    - 3.2. Interpretation

DOCUMENTS AND RECORDS

1. Records should be maintained for two years or as defined by institutional policy, or as required for compliance with governmental standards.
2. Records recommended to define and maintain.
    - 2.1. Quality Management Program (5, 6)
    - 2.3. Quality control records
    - 2.4. Performance improvement plan
    - 2.5. Technologist feedback and continual educational plan (1)
    - 2.6. Policy and procedure manuals (5, 6)
        1. Review and update procedures as equipment or procedures are altered.
        2. Medical director or designee review and signature are required annually.
    - 2.7. Medical records
    - 2.8. Staff schedules
    - 2.9. Supervisor logs
    - 2.10. Equipment installation manuals
    - 2.11. Additional records described in the quality management system plan (3).
3. Items in the database may include:
    - 3.1. Patients tested
    - 3.2. Procedure codes (institutional billing code and/or current procedural terminology codes [CPT])
    - 3.3. In-patient or out-patient status
    - 3.4. Third-party payer
    - 3.5. Clinic code or referral site
    - 3.6. Geographic location of patient

3.7. Tests performed
3.8. Time test scheduled, time patient arrived, and time test completed
3.9. Patients who cancel, who reschedule and don't keep appointments.

LABORATORY ENVIRONMENT

1. Temperature
   1.1. The temperature must be maintained within the equipment manufacturer's recommendations (7).
   1.2. The ambient temperature should be maintained higher than 17° C for spirometry unless a manufacturer states that their spirometer will operate accurately at lower ambient temperature (7).
   1.3. Record and report ambient temperature to an accuracy of plus or minus 1° C (7).
   1.4. The temperature should be maintained at a level consistent with patient comfort.
   1.5. Temperature should be measured with a standard thermometer that can be validated for accuracy (5).
   1.6. Record daily the temperature of refrigerators that are used for storage of quality control materials or medications (5). A typical acceptable temperature range is 2–8° C.
2. Barometric pressure
   2.1. The barometric pressure should be accurately measured and recorded daily and should meet equipment and procedure requirements (7).
   2.2. The range of acceptable barometric pressure must be specified by the manufacturer for each piece of equipment (7).
3. Humidity
   3.1. The humidity should be maintained at a level consistent with patient comfort.
   3.3. The humidity must be maintained at a level consistent with appropriate equipment performance.

SCHEDULING OF PATIENTS

1. Tests must be ordered by a physician or appropriate personnel (e.g., nurse practitioner or physician assistant).
   1.1. Verbal orders will be accepted by appropriate personnel working in physician office practices or clinics to schedule outpatients.
   1.2. A written order may be required within a specified time frame (e.g., 24 hours) to confirm verbal orders.
      1. To improve this process, a predefined ordering sheet or form is usually provided (8).
2. Time constraints
   2.1. Laboratory hours of operation: each laboratory should specify their hours of operation.
   2.2. The specific time required to complete the test and associated charting according to the current standards of care (i.e., turnaround time).
      1. The average time required to perform each test should be defined. The American Association for Respiratory Care (AARC) Diagnostic Uniform Reporting Manual (5th Edition 2012, source available on AARC product website) provides guidance for determining and/or calculating relative value units (RVUs).
      2. Pediatric testing generally requires an increase in testing time. The amount of time required generally increases as age decreases. Due to compliance issues with pediatric patients, children should not be scheduled during nap times or following painful tests.

3. Variables that can affect patient scheduling.
   - 3.1. Availability of equipment required to perform the testing
   - 3.2. Number of technologists required for testing
   - 3.3. Patient convenience
     1. Travel distance
     2. School schedules
   - 3.4. Potential infection control issues
     1. Follow Center for Disease Control and Prevention (CDC) guidelines for PF testing (9).
     2. Cystic fibrosis (CF) patients who are *Pseudomonas cepacia* positive should not be scheduled on the same day as other CF patients.
        a. If it is necessary to test *Pseudomonas cepacia* patients with other CF patients on the same day, they must be isolated from each other.
     3. Active *Mycobacterium tuberculosis* patients should be scheduled at specific times to minimize the potential for cross contamination. Most frequently, they will be scheduled as the last patient of the day.
        a. Negative pressure procedure rooms along with personal protective equipment are required by CDC guidelines when testing subjects suspected to have tuberculosis (9).
     4. Consideration may be given to scheduling patients who are immune-compromised or known to have potentially infectious disease.
   - 3.5. Not withholding medications that influence test results for a long enough period of time.
4. In-patient testing should be completed as soon as possible to decrease length of stay.
5. Record required demographic and ordering information.
   - 5.1. Diagnosis and clinical indication for specific tests ordered
   - 5.2. Ordering physician
   - 5.3. Specific test(s) ordered
   - 5.4. Special needs or instructions
     1. A translator may be necessary in some cases.
     2. Accessories for the hearing impaired (e.g. visual aids, hearing enhancement devices, etc.)
     3. Specific medications must be withheld for some tests (e.g., bronchial provocation testing) (7).
     4. Patients on oxygen (O_2) or with a tracheostomy may have additional requirements.
   - 5.5. Date and time of test
   - 5.6. Patient's name and identification number.
6. Provide patient with verbal and written instructions for preparing for tests (example in Appendix 3.2) (4, 8).
   - 6.1. Written instructions should be available at a reading level and language consistent with the patient population.
   - 6.2. Brochures may be provided for specific procedures (e.g., bronchoscopy).
   - 6.3. When indicated, provide a list of medications to withhold and for how long.
   - 6.4. Define appropriate clothing for test(s) (e.g., running or walking shoes for exercise test).
   - 6.5. Provide an approximate amount of time required for completion of the test procedure.
   - 6.6. Provide a brief explanation of the test including purpose and potential benefits.
   - 6.7. Include other preparation instructions as appropriate (e.g. refrain from smoking for 12 hours prior to testing).
   - 6.8. A video or handout could be used to illustrate the procedures the patient will perform.

7. Unusual or special procedures should be referred to the laboratory supervisor or medical director for clarification and scheduling.

PATIENT DEMOGRAPHICS

1. Medical history and medication information
   - 1.1 A respiratory questionnaire may be given to the patient at the time of testing (example in Appendix 3.3), this may also include standardized questionnaires such as the COPD Assessment Test (CAT) or the Medical Research Council (MRC) breathlessness scale.
   - 1.2 Medical history should include: past respiratory problems, occupation, and smoking habits.
   - 1.3 Technologist comments of the patient's condition at the time of testing might include comments about cough, dyspnea, wheeze, cyanosis, anxiety level, and cooperation during the testing session.
   - 1.4 Record the diagnosis and/or reason the test is being performed.
   - 1.5 Verify the absence of contraindications or when suboptimal conditions exist which may affect testing results (1).
     1. Suboptimal conditions for a procedure should be reviewed with the ordering physician and/or medical director prior to test performance.
   - 1.6 Record relevant medications and when last used.
     1. Consideration of each medication and potential effects on test results must be reviewed both during the scheduling of the procedure and in the immediate pre-test period.
   - 1.7 Record date of birth (preferred) or age (in years to nearest tenth [e.g., 8.3 years]) on day of test, gender, race, full name, and billing and medical record numbers.
2. Measuring height and weight
   - 2.1 Measure height with the patient's back against a wall in an upright position without shoes on the day of the test. The patient should be standing up straight and looking forward with their gaze roughly parallel to the ground.
     1. A properly mounted stadiometer provides an accurate method for measuring height. A "physician's" scale should not be used because it can lead to incorrect height measurements.
     2. Record height in inches (in) to nearest ¼ inch or in centimeters (cm) to nearest 0.5 cm (4).
   - 2.2 Accurately obtain and record weight in pounds (lb) to the nearest lb, or kilograms (kg) to the nearest half kg.
3. Estimating standing height for patients with spinal deformities or for those who cannot stand (1, 4).
   - 3.1 Measurement of arm span closely equals standing height for individuals older than 16 years of age.
   - 3.2 Have the patient stretch the arms in opposite directions and obtain the maximal distance between the tips of the middle fingers. Use the following corrections to obtain height:
     1. Height for Caucasian men = arm span/1.03
     2. Height for women = arm span/1.01
     3. Height for African-American men = arm span/1.06
   - 3.3 Pediatric height related to arm span
     1. For boys <9 years the height exceeds arm span.
     2. For girls <12 years the height exceeds arm span.
     3. For boys age 9 to 16 and girls age 12 to 16, the ratio of arm span to height should be linearly interpolated between 1.0 and the appropriate values for adults.
4. Informed consent may be required for some specific tests based on institutional policy (8).
   - 4.1 The informed consent should be written so the patient clearly understands the choices presented and the consequences of their consent.

EQUIPMENT

1. Selection of new or replacement equipment (11, 12)
    1.1. Define the needs of the laboratory and healthcare system.
    1.2. Develop a product evaluation matrix.
    1.3. Develop a list of acceptable vendors based on the defined equipment needs and required specifications.
        1. Consider:
            a. Food and Drug Administration approval
            b. Selected equipment should meet or exceed minimum American Thoracic Society (ATS)/European Respiratory Society (ERS) equipment performance standards (7).
            c. Acceptable limits of accuracy and precision
            d. Specifications for linearity, hysteresis, signal damping and response time
            e. Compatibility of instrument components, costs, limitations, and software or hardware
            f. Frequency and verification standards for software updates
            g. Ease and method of infection control for equipment and accessories
            h. The use of disposable or non-disposable items for measurement of flow or volume parameters
            i. Fixed and variable costs of the system
            j. Availability of supplies
            k. Effect of filters on equipment performance and test results
                1) The total system resistance to airflow must be less than current ATS/ERS equipment recommendation (currently 1.5 cm H_2O/L/s) (7).
            l. Data base management options, which may include:
                1) Patient records and quality control records
                2) Preventive maintenance schedules
                3) Quality assurance programs
                4) Performance improvement indicators
                5) Staff or patient scheduling options
                6) Network and interface options with other systems
            m. Quality control standards and ease of calibration routines
            n. Available reference standards (normal prediction equations)
            o. Training options and costs for operators
            p. Technical support
    1.4. The terms of agreement should include expected response times for service/uptime guarantee.
    1.5. Consider the computer standards for the healthcare system.
    1.6. Verify that calculations included in the software are accurate.
    1.7. Verify that the equipment has been tested by an independent testing agency.
    1.8. The equipment should comply with regulatory agency requirements, for example the National Institute for Occupational Safety and Health (NIOSH), and Social Security Income Administration standards for disability.
    1.9. Warranty and service agreements should be well defined.
    1.10. Perform an on-site evaluation of the equipment.
        1. Simulate normal and abnormal conditions for quality control and patient testing.
        2. Determine if the equipment meets special considerations for the age and population to be tested.
        3. Evaluation tools may include a calibrated syringe and biologic standards (controls).
        4. Complete a biomedical evaluation (safety check).

1.11. Establish cost-per-service versus profit ratios.
1.12. Compare test results between the old equipment and the new equipment.

2. Preparation of equipment for testing
   2.1. New equipment must be validated prior to patient testing (12).
   2.2. Allow for adequate warm-up time for each piece of equipment.
   2.3. Perform quality control as required for each procedure.
   2.4. Verify calibration as indicated for equipment and type of procedure.
   2.5. Attach additional supplies as required for the procedure (e.g., mouthpieces, hoses).

PATIENT PRIVACY

1. Patient privacy during test performance must be maintained to meet regulatory requirements and improve comfort and compliance with testing.
2. Patient confidentiality must be maintained at all times (13).
3. Medical records should be maintained so as to prevent access by unauthorized personnel (13).
   3.1. Medical records and medications should be maintained in locked files or in a locked room to which only authorized personnel have access.

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APPENDIX 3.1

The Quality Management System model takes any laboratory discipline and applies each Quality System Essential (QSE) across the laboratory's path of workflow (courtesy of CLSI QMS01-A4).

APPENDIX 3.2

Example of Patient Preparation Instructions for an Initial Diagnostic PF Test

1. Report to _____ on date:_____.
2. Do not take (if possible) the following medications prior to your appointment:
   A. Inhaled bronchodilators
      - Short-acting for 4–8 hours: (albuterol, salbutamol)
      - Long-acting for 12–24 hours (formoterol, salmeterol)

        Ultra long-acting agents for 24–48 hours (indacterol, vilanterol)

   B. Anticholinergics
      - Short acting for 6 hours (Atrovent)
      - Long-acting for 48 hours (tiotropium)
3. Take as usual the following medications:
   A. Theophylline preparations (Theo-Dur, Slobid, Slo-phyllin, Theolair, Quibron, Uniphyl, etc.)
   B. Inhaled and oral steroid preparations (Advair, Beclovent, Vanceril, Respihaler, Azmacort, Aerobid, Flovent, Pulmocort, Prednisone, Medrol).
4. If you have questions or problems contact the Pulmonary Function Laboratory at ###-####.

APPENDIX 3.3 EXAMPLE OF A QUESTIONNAIRE FOR PF TESTING

Name: _____

Sex: _____ Age today: _____ Date of Birth: _____

Home Phone: _____ Business Phone: _____

Ordering Physician: _____

Your Occupation: _____

1. Have you been tested in this laboratory before: ☐ Yes ☐ No
   If yes, was it under a different name than shown above? ☐ Yes ☐ No
   If yes, what name? _____
   If yes, when approximately? _____

2. Have you ever smoked cigarettes? ☐ Yes ☐ No
   If yes, do you still smoke now? ☐ Yes ☐ No
   If you quit, how long ago?
   If you smoke(d), how many years did you/have you smoked?
   How many packs per day (average)?

3. Have you had a respiratory infection, such as a flu, bronchitis or a chest cold in the last 6 weeks? ☐ Yes ☐ No

4. Have you had more than two cups of caffeinated coffee in the last 2 hours? ☐ Yes ☐ No

5. Have you used an inhaled bronchodilator (e.g., albuterol, Atrovent, Combivent, Proventil, salmeterol, Advair, and Ventolin) in the last 8 hours? ☐ Yes ☐ No

6. Have you taken any bronchodilator pills (e.g., montelukast, theophylline) in the last 8 hours? ☐ Yes ☐ No

7. Have you taken any other medications for your lungs, heart, or blood pressure (e.g., beta-blockers)? ☐ Yes ☐ No

8. Are you currently receiving chemotherapy for the treatment of cancer ☐ Yes ☐ No

APPENDIX 3.3

9. Do you have, or have you ever had tuberculosis (TB)? ☐ Yes ☐ No
   If yes, is it active now? ☐ Yes ☐ No

10. Are you currently being treated for any infectious diseases? ☐ Yes ☐ No
    If yes, what?

11. Do you cough? ☐ Yes ☐ No
    If yes, do you bring up phlegm? ☐ Yes ☐ No

12. Have you had exposure to irritating gases, dusts, or fumes? ☐ Yes ☐ No
    If yes, what? _____

13. Have you ever had an injury or operation affecting your chest? ☐ Yes ☐ No
    If yes, what and when? _____

14. Do you require oxygen therapy? ☐ Yes ☐ No

15. What other medical problems do you currently have? _____

16. Have you done a breathing test in the past? ☐ Yes ☐ No
    If yes, did you experience any problems (including, but not limited to fainting, injury, or other adverse symptoms)? ☐ Yes ☐ No

APPROVAL

Signature: _____Date: _____

Annual Review

Date	Signature	Date	Signature

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CHAPTER 4

PROCEDURE NAME: FACILITIES, HYGIENE, AND SAFETY

PURPOSE AND PRINCIPLE

The pulmonary function (PF) laboratory intends to provide a safe environment for both employees and patients that conform to state and federal regulations and/or those of other regulatory entities (e.g. College of American Pathologists, The Joint Commission). This procedure addresses facilities, hygiene, and safety guidelines for the PF laboratory.

RESPONSIBILITY

The laboratory medical director and management staff are responsible for ensuring a safe work environment for both employees and patients.

FACILITIES

1. Laboratory Design, Space Allocation, and Access

The PF laboratory should work with the organization's facility planning function to develop processes for laboratory building and renovation projects. The design should allow for optimal work process flow and ergonomics (1). The laboratory should ensure that governmental, accreditation, and organizational requirements for current and planned space (e.g., energy sources, lighting, ventilation, water, refuse disposal, etc.) are met. If sample collection is required, the laboratory should have available accommodations for disabled patients and consider comfort, privacy, and safety. Environmental requirements for equipment and patient care are considerations in space allocation and design. Measures are in place to control access to, and use of, examination areas, samples, and supplies.

1.1. The PF laboratory monitors, documents, and controls the environmental conditions as required or when they may influence the quality of results. Such conditions include (as appropriate to technical activities):

- sterility
- electronic interference
- radiation
- humidity
- ventilation duct locations

- electrical supply
- temperature
- sound levels, and
- vibration levels.

1.2. Storage space and conditions are provided to ensure the continuing integrity of the following:

- samples
- reagents
- laboratory supplies
- equipment
- documents
- manuals
- records, and
- files.

2. Testing Environment for Pediatric Pulmonary Function Testing

The testing environment for children should be as child-friendly as possible. Many younger patients do not perform the pulmonary function tests well, or they are apprehensive or uncooperative because of distractions in the testing area. Assure that pain-causing instruments (e.g., needles and syringes) are out of sight and that there are games, pictures, and videos in clear view. Having a fun space for play is helpful. A nearby waiting area for parents is also ideal if the parent is asked to remain outside the testing room.

Assure the child is comfortable in the testing environment. This is achieved through a combination of friendly conversation with the technician, songs, or positive distractions such as a video or book. The level of distraction must be enough to take the child's attention away from his or her breathing, but not so exciting that the child breathes irregularly (2).

GENERAL HYGIENE GUIDELINES

The effects of inadequate hygiene practices have long been recognized as being the causative agent for increasing the incidence of nosocomial infections in hospitalized patients. Poor hygiene practice not only increases patient morbidity (which is also attributed to increased hospital costs) but also increases patient mortality.

To date, there have been no studies reported which directly implicate PF equipment in the spread of disease. This, however, does not suggest that PF equipment does not have the capability of performing such a role, since a number of bloodborne (e.g., HIV, and hepatitis) and airborne pathogens (e.g., tuberculosis [TB], chicken pox, and respiratory syncytial virus [RSV]) pathogens do exist. Some airborne diseases may be inconsequential in most instances, but susceptible or immunocompromised individuals could develop serious health complications. Thus, the possibility exists for transfer of disease via the patient–operator, operator–patient, patient–patient, or the operator–operator interface as well as for patient–instrument or operator–instrument interfaces.

The American Thoracic Society (ATS) and European Respiratory Society (ERS) addressed some hygiene issues in the General Considerations guideline (3). The intent is for the user to understand the goal of hygiene and its relationship to infection control during PF testing.

The goal of infection control in the PF laboratory is to reduce disease transmission through either direct or indirect contact.

***Direct Contact*:** There is the potential for transmission of upper respiratory disease, enteric infections, and bloodborne infections through direct contact. Although hepatitis and HIV transmission are unlikely via saliva, disease transmission is a possibility when there are open sores on the oral mucosa, bleeding gums, or hemoptysis. The most likely surfaces for contact are mouthpieces and the immediate proximal surfaces of valves or tubing (3). Mouthpieces, nose clips, and any other equipment coming into direct contact with mucosal surfaces should be disinfected, sterilized, or, if disposable, discarded after each use. Although the optimal frequency for disinfection or sterilization of tubing, valves, or manifolds has not been established, any equipment surface showing visible condensation from expired air should be disinfected or sterilized before reuse whenever the potential for cross contamination exists.

***Indirect Contact*:** There is potential for transmission of TB, various viral infections, and possibly, opportunistic infections and nosocomial pneumonia through aerosol droplets. The most likely surfaces for possible contamination by this route are mouthpieces and proximal valves and tubing (3).

The Clinical and Laboratory Standards Institute (CLSI) has published a guideline addressing laboratory worker protection from biohazards (4), and the Centers for Disease Control and Prevention (CDC) has published recommendations on how to control nosocomial-acquired pneumonia (5). These documents should be in all PF laboratories and available to interested parties.

Some disease-prevention areas that should be addressed include:

1. Proper hand-washing techniques
2. Disinfection or sterilization of tubing, valves, and manifolds
3. Flushing volume-displacement spirometers between patients
4. Environmental engineering controls
5. Precautions with testing patients having hemoptysis or open sores
6. Precautions with patients with known (or suspected) transmissible infectious diseases
7. Efficacy of in-line filters
8. Manufacturer design of equipment to deal with equipment disinfection issues

1. *Standard Precautions*

   Standard precautions (SP) (as published by the CDC) (5) should be applied in all instances in which there is evidence of contamination with blood (e.g., pneumotachometers and adapters).

   1.1. Although SP do not apply to saliva or mucus, unless it contains blood, other potentially hazardous organisms may be present in these fluids even in the absence of blood, and the appropriate use of barriers and hand washing is recommended (6, 7).

   1.2. Departments should have specific procedures for handling and disposing of articles contaminated with bloodborne pathogens.

2. *Mycobacterium tuberculosis* (TB)

   2.1. *M. tuberculosis* is carried in airborne particles (droplet nuclei) that can be generated when persons who have pulmonary or laryngeal TB sneeze, cough, speak, or sing.

   2.2. Infection occurs when a susceptible person inhales droplet nuclei containing *M. tuberculosis*, and these droplet nuclei then traverse the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli. Once in the alveoli, the organisms are taken up by alveolar macrophages and may be spread throughout the body (8).

   2.3. The risk of nosocomial transmission is higher in areas where patients with TB receive care before diagnosis and initiation of TB treatment and isolation precautions (e.g., clinic waiting areas and emergency departments). In addition, the risk is higher in areas where diagnostic or treatment procedures that stimulate coughing (e.g., PF tests and bronchoscopy) are performed.

2.4. Management of patients who may have active TB in ambulatory-care settings and emergency departments (9):
   1. Vigorous efforts should be made to identify promptly patients who have active TB. Health care workers, who are the first points of contact in facilities that serve populations at risk for TB, should be trained to ask questions that will facilitate identification of patients with signs and symptoms suggestive of TB.
   2. TB precautions should include:
      a. Placing these patients in a separate area apart from other patients, not in open waiting areas.
      b. Giving these patients surgical masks and instructing them to wear the masks.
      c. Giving the patients tissues and instructing them to cover their mouths and noses with the tissues when coughing or sneezing.

2.5. Management of hospitalized patients who have confirmed or suspected TB (8):
   1. Any patient suspected of having or known to have infectious TB should be placed in a TB-isolation room with appropriate ventilation characteristics.
   2. A patient placed in isolation should remain there with the door closed.
   3. Diagnostic procedures (e.g., PF tests) should be performed in the isolation room, if possible, to avoid transporting patients through other areas of the facility.
   4. A patient with infectious TB, who must be transported outside the isolation room for medically essential procedures, should wear a surgical mask that covers their mouth and nose during transport.

2.6. Ventilation recommendations for TB isolation and treatment rooms:
   1. The American Society of Heating, Refrigerating and Air-Conditioning Engineers, Inc. (ASHRAE) recommends a minimum of six air changes per hour (ACH) for TB-isolation and treatment rooms.
   2. Ventilation rates of at least 6 ACH are likely to produce an incrementally greater reduction in the concentration of bacteria in a room than are lower rates (9).
   3. Air from TB-isolation rooms and treatment rooms used to treat patients who have known or suspected infectious TB should be exhausted to the outside in accordance with applicable federal, state, and local regulations.
   4. In cases where recirculation of air into the general ventilation system is unavoidable, high-efficiency particulate air (HEPA) filters should be installed in the exhaust duct leading from the room to the general ventilation system.
   5. Upper-room air ultraviolet germicidal irradiation (UVGI) may be used as an adjunct to general ventilation in the isolation or treatment room. Ultraviolet lamps should be installed properly and maintained adequately and irradiance levels should be monitored.

2.7. Respiratory protection
   1. Respiratory protection approved by the National Institute for Occupational Safety and Health (NIOSH) must be used by persons present during cough-inducing or aerosol-generating procedures on patients with TB.

3. Cystic Fibrosis (CF)
   3.1. All individuals with CF, and their family members and friends, should perform appropriate hand hygiene (with either alcohol-based hand rub or antimicrobial soap and water) when there is a potential for contamination of hands with pathogens (13).
      1. Contamination of hands may occur when entering or exiting a CF clinic, clinic exam room, or hospital room, or from respiratory secretions after coughing performing PF tests, or performing chest physiotherapy (13).
   3.2. Perform pulmonary function testing in one of the following ways to reduce transmission from one person with CF to another person with CF:
      1. Allow at least 30 minutes to elapse between CF patients in the exam room.
      2. Perform PF testing in a negative pressure room (airborne infection isolation room).
      3. Perform PF testing in a room equipped with high-efficiency particulate (HEPA) filters.
      4. Perform PF testing in a room without HEPA filters, allowing at least 30 minutes to elapse between individuals with CF.
   3.3. Isolation Precautions:
      1. The CF Foundation recommends that all healthcare personnel implement Contact Precautions (i.e., wear a gown and gloves) when caring for all people with CF regardless of respiratory tract culture results, in ambulatory and inpatient settings (13).
      2. The CF Foundation recommends that all people with CF, regardless of their respiratory tract culture results, be separated by at least 6 feet (2 meters) from other people with CF in all settings, to reduce the risk of droplet transmission of CF pathogens (13).

CLEANING AND DISINFECTING PROCEDURES AND USE OF FILTERS FOR PF EQUIPMENT

1. Not all PF equipment is designed for easy disassembling and disinfection. Therefore, the laboratory should work in concert with the institution's infection control department to design and implement policies and procedures which describe the method(s) to disinfect PF equipment as well as monitors to ensure effectiveness of disinfection.
2. Disinfection procedures should meet or exceed manufacturer's recommendations.
3. All materials must be cleaned of debris before undergoing the disinfection process. Depending on the type of disinfection processes employed, other preparation issues may need to be addressed (e.g., special wrapping and tape for steam under pressure).
4. Some common methods for sterilization or disinfection include:
   4.1. Heat: Heat is the universally employed and most reliable method of sterilization.
      1. Order of efficiency of sterilization and disinfection (9):
         a. Steam under pressure (autoclave)
            1) Variables involved in the autoclaving process include temperature, pressure, and concentration of steam. Examples of autoclaving cycles include:
               a) 121° C at 15 psi for 15 minutes
               b) 126° C at 20 psi for 10 minutes
               c) 134° C at 29.4 psi for 3 minutes

b. Steam at atmospheric pressure
c. Boiling water
d. Dry heat under pressure
e. Dry heat at atmospheric pressure
f. Water below its boiling point (pasteurization)

4.2. Cold liquid: These generally refer to the group of glutaraldehydes, which kill by binding to amino groups of proteins in microorganisms, thereby interrupting metabolism and reproduction.
1. In general, these agents are bactericidal, tuberculocidal, fungicidal, and viracidal in 10 to 30 minutes and sporicidal in about 10 hours.
2. Healthcare workers can be exposed to elevated levels (> 0.2 ppm) of glutaraldehyde vapor when the cleaning process takes place in poorly ventilated areas or when spills occur. Healthcare workers can also be injured by skin or eye contact.

4.3. Gas: Ethylene oxide (ETO) is the alkylating agent used extensively in gas sterilization. However, this agent is unsafe for the environment and requires stringent material preparation and monitoring.
1. ETO residues may form on substances that have been previously gamma irradiated, a process which produces a tissue-irritating substance: ethylene chlorhydrin.
2. ETO residues are mutagenic for bacteria, and mutagenic and carcinogenic to humans.

4.4. Other liquid disinfectants: alcohol, quaternary ammonium compounds, acetic acid, formaldehyde, phenols, iodine, chlorine, and hydrogen peroxide.
1. Acetic acid solutions, quaternary ammonium compounds, and household bleach may be used for disinfecting respiratory equipment. However, available studies have not been performed to verify the usefulness of these agents (11).
2. Alcohol and hydrogen peroxide may be used for skin cleaning and disinfection (11, 12).

5. The regular use of in-line filters during PF testing are not mandated when appropriate precautions are followed (e.g., regular cleaning, environmental engineering controls, and testing at end of day for those with known transmissible diseases). However, the use of in-line filters in some equipment, particularly multi-purpose testing systems with valve manifolds, may be indicated (3, 10). The effect of these filters on flow measurements is not clear, but they may have an influence. If in-line filters are used, interpretation of the data should allow for the possibility that the filters may affect the data. Further, if filters are used, it is recommended that equipment be calibrated with the filters in place (3). Even when in-line filters are used, the need for regular cleaning and decontamination of lung function equipment is not eliminated.

ACCIDENT, FIRE, AND EVACUATION PROCEDURES

Laboratory management is responsible for maintaining and ensuring a safe working environment (2) and complying with the Occupational Safety and Health Administration (OSHA) and other federal, state, and local regulatory standards. A good hazardous waste and universal precautions program is necessary to meet this need. In addition, policies and procedures should be developed that address patient, visitor, and employee safety issues that comply with institutional edict. Measures should also be described that show how similar mishaps can be prevented (e.g., through education and follow-up, and environmental redesign).

1. Accident
    1.1. Type of Accident: Specific policy and procedure describing what to do, whom to report to, and forms that need to be completed in the event of a(n):
        1. Sharps puncture
        2. Airborne pathogen exposure
        3. Body-fluid exposure
        4. Electrical shock
        5. Chemical exposure
        6. Fall
        7. Other injury (e.g., due to lifting)
    1.2. Follow-up of individual(s) involved in the mishap.
2. Fire
    2.1. There should be a specific policy describing the responsibility of staff regarding:
        1. Rescue of individuals directly involved in a fire
        2. Whom to alert
        3. Containing a fire
        4. Extinguishing a fire
            a. Types of fire-extinguishing tools
                1) Liquids
                2) Chemicals
                3) Blankets
        5. Assuring safety of patients and visitors
3. Evacuation: Addresses issues regarding safe and efficient movement of individuals away from an affected area (e.g., as a consequence of biohazard, fire, or chemical spill)
    3.1. There should be a specific policy describing the responsibility of staff regarding:
        1. Evacuation and rescue of individuals directly involved in an event
        2. Whom to alert
        3. Assuring safety of patients and visitors
        4. Containing a spill
        5. Cleaning up after a spill

COMPRESSED GAS SAFETY

Storage, internal transportation, and use of compressed-gas cylinders require considerations to ensure optimum safety for staff and clients.

1. Store compressed-gas containers in a room or enclosure reserved exclusively for that purpose.
2. Secure all compressed-gas cylinders in accordance with applicable federal, state, and local requirements.
3. Mark containers clearly with the name and concentrations of contents.
4. Use hand-truck or dolly to move large cylinders.

5. Keep connections to piping and regulators tight to prevent leakage. If hose is used, it should be kept in good condition.
6. Prevent sparks or flames from any sources from coming in contact with cylinders and equipment.
7. Close valve when returning empty cylinders, and replace cylinder-valve protective caps before shipping.
8. Never subject any part of any cylinder containing a compressed gas to a temperature >125° F.
9. Keep cylinder valves closed at all times, except when gas is being used.
10. Never attempt to use contents of a cylinder without a suitable pressure-regulating device.
11. After removing valve protection cap and before applying pressure-regulating device, slightly open valve for an instant to clear opening of dust or dirt.
12. When opening valve, point the outlet away from yourself and turn your head so you are looking away from the valve.
13. Before pressure regulating device is disconnected from the cylinder, close the cylinder valve and release all pressure from the device.

ELECTRICAL SAFETY

1. General policies
    - 1.1. All electrical equipment must be properly grounded.
    - 1.2. Bioengineers must check the grounding and leakage current of all electrical instruments every 12 months.
        1. Documentation of these instrument checks should be available.
    - 1.3. Do not touch any electrical instrument with a wet surface.
        1. Do not touch any electrical instrument with wet hands.
    - 1.4. Consider every circuit as "live" and power circuits as potentially dangerous.
    - 1.5. Never use an instrument that has a damaged cord or plug.
        1. Notify the bioengineer and attach a label or tag to the damaged device warning others not to use it.
2. Emergency procedure for electrical shock
    - 2.1. Summon emergency assistance immediately.
    - 2.2. Shut off main power switch, if possible.
    - 2.3. Separate the victim from the power source without endangering yourself.
        1. Use a belt, rope, wooden board, or other non-conducting material to remove the victim safely from the source of the shock.
        2. Make sure your hands are dry and you are standing on a dry surface.
    - 2.4. Administer cardiopulmonary resuscitation (CPR), if needed, when safe to do so.

HAZARD COMMUNICATION PROGRAM

OSHA regulates chemical hazards and communications of hazard information. Both federal and state regulations include specific requirements for:

- Written hazard communication programs
- Labels and other forms of warning

- Material safety data sheets (MSDS)
- Employee information and training

1. Implementing a hazard communication program (HCP) includes (2):
   - 1.1. Identifying responsible staff
     1. Initial and ongoing activities should be the responsibility of the medical director, but may be delegated.
     2. Ultimate accountability remains with the director.
     3. Program must be integrated with the overall facility plan.
   - 1.2. Identify hazardous chemicals in the workplace
     1. List chemicals in the HCP.
        a. Survey entire laboratory to determine which solids, liquids, and gases are present.
     2. Note the location of each chemical and type of hazard.
   - 1.3. Compile MSDS for each chemical
     1. MSDS contain information on each chemical's hazardous effects, chemical and physical characteristics, and about recommendations for protective measures for each chemical.
     2. Distributor/manufacturer must supply replacement sheets.
     3. MSDS must be accessible to employees (e.g., a notebook in the laboratory)
        a. Identify someone in laboratory to maintain and update MSDS
   - 1.4. Develop and implement a written program describing how warnings, MSDS, and employee information and training are being met in your laboratory. For example:
     1. Labels on chemical containers must legible and prominently display the chemical identity and the appropriate hazard warnings.
        a. If chemicals are transferred to other containers (not recommended), they must be labeled appropriately
     2. Employees who may be exposed to hazardous chemicals (accidental or incidental exposures) must be provided information and be trained before working with a hazardous chemical.
     3. The program must cover hazards of non-routine tasks, hazardous chemicals found in pipes, and communication to contract workers.

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ADDITIONAL READING

CLSI Documents

X3–R. Implementing a needlestick and sharps injury prevention program in the clinical laboratory: a report. 2002.

Clinical and Laboratory Standards Institute. QMS02–A4 Quality management system – a model for laboratory services. Clinical and Laboratory Standards Institute; 2011.

APPROVAL

Signature: _____ Date: _____

Annual Review

Date	Signature	Date	Signature

Revisions / Document History

Effective Date	Synopsis of Change

Effective Date: 2014
Version #1

CHAPTER 5

PROCEDURE NAME: QUALITY CONTROL

PURPOSE AND PRINCIPLE

The term "quality control" can be defined as the process of monitoring the precision and accuracy of a test procedure. The term "quality management system" not only encompasses quality control, but includes many other activities, such as: maintaining and calibrating equipment, training personnel and continued competency assessment, reporting results, and record keeping (1, 2).

The purpose of this procedure is to describe the framework for quality control activities needed to ensure that measurements are being made within acceptable limits of accuracy and precision. Specific quality control procedures for the various tests used by the PF laboratory are described in the technical procedure chapters.

Terms and Definitions	
Accuracy	How well the measurement reflects the true or correct value
Precision	Measurement variability (repeatability) and is completely independent of accuracy or truth.
Random errors	Errors that occur without prediction or regularity, tend to decrease precision, and often result from inherent variation in the instrumentation
Systematic errors	Errors within the test system or methodology (e.g., instrument calibration or malfunction) that tend to produce bias
Biologic control (standard)	Healthy nonsmoking individual used in quality control
Mean	The sum of observed values divided by the number of observations
Standard deviation (SD)	A measurement of variability or tendency of values to vary from the arithmetic mean.
Coefficient of variation	A mathematical expression of variability calculated by dividing the SD by the mean

INSTRUMENT MAINTENANCE

1. Preventative maintenance (PM): refers to maintenance performed on a scheduled basis that is usually done by the laboratory staff. The goal of PM should be to anticipate problems before they occur and cause the instrument to malfunction. Examples of PM include:
    - 1.1. Checking volume-displacement spirometers for leaks and linearity
    - 1.2. Cleaning or replacing the flow sensor
    - 1.3. Checking tubing for tears
    - 1.4. Electrical safety.
2. Corrective maintenance (i.e., repairs) is unscheduled action required to correct instrument failure. This is usually done by the manufacturer's representative or by the hospital bioengineer, but can and sometimes is performed by the laboratory staff.
3. PM should be done on a daily, weekly, monthly, or yearly schedule depending on the instrument and the recommendations that are being followed.
4. Maintenance logs should be established and used to indicate which instruments need PM and when, and to record the dates and types of PM procedures performed. If PM identifies a problem and corrective action is taken, the action should be recorded.
5. New instrumentation: Whenever new instruments are purchased and set up, they must undergo verification and validation prior to reporting test results.

INSTALLATION MANUAL

1. The development of an installation manual for new equipment is recommended.
2. The installation manual should be kept for the life of the instrument (2).
3. Essential components
    - 3.1. Vendor/purchaser contract
        - 3.1.1. Equipment model and serial number
        - 3.1.2. Purchase date and cost
        - 3.1.3. Warranty information and/or service contracts
        - 3.1.4. Manufacturer's instrument specifications
    - 3.2. Equipment installation records
        - 3.2.1. Equipment validation performed by the manufacturer
        - 3.2.2. Equipment cleaning instructions
        - 3.2.3. Software version installed, including any updates
        - 3.2.4. Support services and training information
    - 3.3. Installation calibration data obtained by the manufacturer's representative
        - 3.3.1. Results of data generated from a known-volume syringe while in the subject test mode
        - 3.3.2. Results of data on biologic standard(s)
    - 3.4. Calibration data obtained by user
    - 3.5. Results of tests on at least 40 healthy individuals for equipment validation and verification of predicted values may be helpful.

MEASUREMENT PRECISION

1.1. Precision (repeatability) describes the laboratory's ability to get the same result when testing a biologic control or using another type of control (e.g., known-volume syringe).

1.1.1. Precision standards defining a "repeatable" result for individual pulmonary function tests have been established by the American Thoracic Society (ATS) and European Respiratory Society (ERS) (3–5). They are also included in the specific testing chapters in this manual.

1.1.2. Demonstrating repeatability requires at least the following number of acceptable trials for the specific test(s) for which the precision range is being determined:

1.1.2.1. D_{LCO}:

- ≥2 acceptable trials
- Repeatability: within 3 ml CO/min/mm Hg of each other, or within 10% of highest value.

1.1.2.2. Functional residual capacity (FRC) using body plethysmograph:

- >3 acceptable trials
- Repeatability: within 5% (i.e., difference between the highest and lowest acceptable value
  divided by the mean is < 0.05).

1.1.2.3. Airway resistance (Raw):

- >3 acceptable trials
- Repeatability: within 10% of the mean (6)

1.1.2.4. Gas dilution FRC (i.e., FRC_{He}, FRC_{N2}):

- 1 or 2 acceptable trials
- Repeatability (if appropriate): within 10%

1.1.2.5. Spirometry:

- 3 acceptable trials
- Repeatability: FVC within 0.150 L , FEV_1 within 0.150 L; for those with an FVC of ≤ 1.0 L, both these values are 0.100 L.

QUALITY CONTROL ANALYSIS

1. Quality control analysis evaluates an acceptable/repeatable test result versus a standard. Standards can be calibrating syringes, biological controls, or control material(s).
2. In a stable laboratory environment the distribution of the results of the same calibration syringe, biologic control, or control material(s) analyzed a number of times is a Gaussian (normal) distribution.

2.1. In a normal distribution

2.1.1. approximately 65% of the values will be between ±1 SD of the mean

2.1.2. approximately 95% of the values will be between ±2 SD of the mean

2.1.3. approximately 99% of the values will be between ±3 SD of the mean

3. For each quality control parameter you have chosen to use (e.g., spirometer volume with a calibrated syringe, D_{LCO} measurements on a biologic control, etc.), the laboratory should establish a database of mean values and SD by repeated testing of the standard. This generally requires at least 10–20 measurements on different days. An example of a data reporting form is in Appendix 5.1.

4. Thereafter with subsequent testing, the laboratory should use Westgard's rules to enact quality assurance responses (7).
   - 4.1. When one observation exceeds the mean ±2 SD, a "warning" condition exists.
   - 4.2. When one observation exceeds the mean ±3 SD, an "out of control" condition exists.
   - 4.3. When two consecutive standard observations exceed ±2 SD, an "out of control" condition exists.
   - 4.4. When four consecutive standard observations exceed the mean ±1 SD, in the same direction an "out of control" condition exists.
   - 4.5. When 10 consecutive standard observations fall on the same side of the mean, an "out of control" condition exists.
   - 4.6. If an out of control situation exists, the instrument should not be used for patient testing until it has been evaluated to assure it is good working order. Once this evaluation is complete and the instrument considered to be working properly, repeat testing of the control should be done to verify.
5. A reasonable way to record these measurements is with control charts (Levey Jennings Plot).
   - 5.1. Control charts indicate the mean of the distribution and an upper limit (UL) and lower limit (LL), which can be fixed or vary according to the SD. A common approach is to use the mean ± 2SD to represent UL and LL boundaries (see section 2.12 and 4.1 above). This is often termed the 95% confidence interval (95% CI). An alternative approach is to use a fixed percent of the mean (e.g., 95%–105% or 97%–103%) to describe the UL and LL boundaries.
   - 5.2. Figure 5.1 is an example of a control chart using 2 SDs for the UL and LL of data from a biologic control performing the single-breath carbon monoxide diffusing capacity (D_{LCO}) test on one PF device each week.

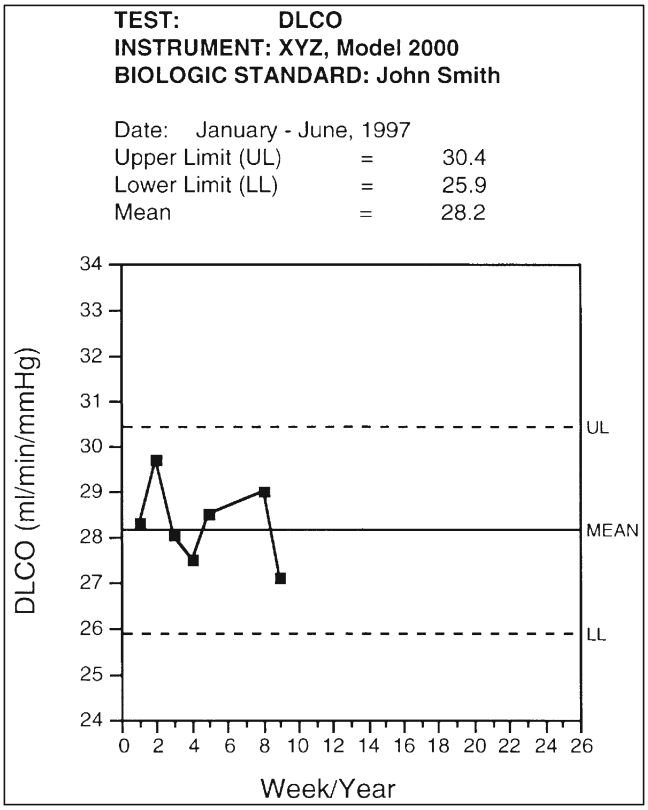

Figure 5.1 An example of a control chart of data collected on a biologic control performing the D_{LCO} test. The data show D_{LCO} values collected each week. In this example, the UL is 30.4 units and the LL is 25.9 units. These limits represent ±2 SD. This control chart is set up for a 6-month time window, but yearly windows can also be used.

5.3. Figure 5.2 is an example of a control chart using a fixed UL and a fixed LL data from daily spirometer calibration using a 3.00-L syringe on one spirometer.
5.4. Control charts are helpful at detecting random and systematic errors.
5.5. The pattern of the data points on a control chart over time also allows the detection of trends.
  5.5.1. One type of trend is the continuous movement of values in one direction over six or more consecutive values.
5.6. Control charts should:
  5.6.1. Be constructed neatly
  5.6.2. Large enough to plot values easily and to present a clear picture
  5.6.3. Contain labels for both axes
  5.6.4. Have the name of the test, instrument, or method; month and year; and the mean, UL, and LL printed on each chart.

CALIBRATION OF CALIBRATORS

1. Calibration devices (e.g., calibration syringes) should be checked regularly and records of checks retained in the quality control log (8, 9).
  1.1. Leak testing (including any tubing) quarterly

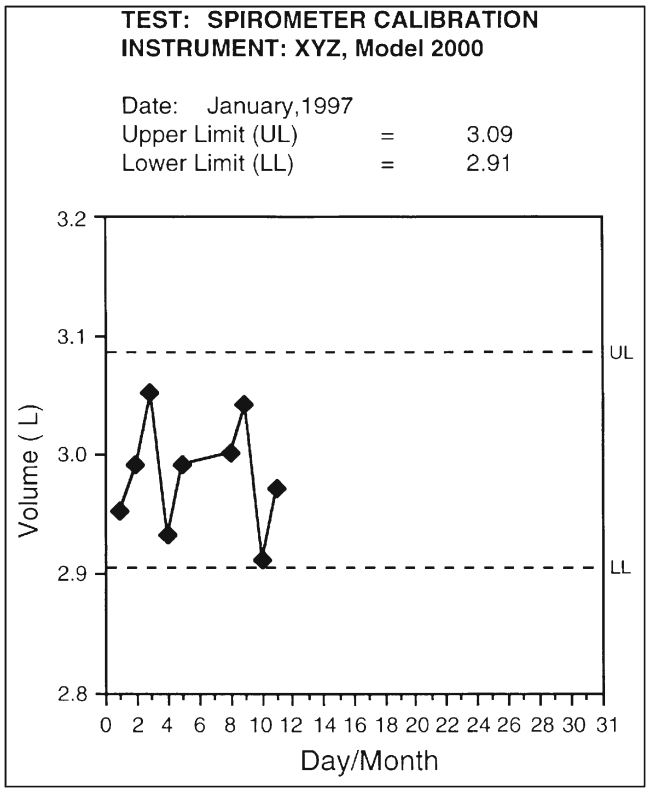

Figure 5.2 An example of a control chart of calibration verification of a spirometer using a 3.00-L syringe. In this example, the UL and LL are fixed at ±3% of the volume of a 3.00-L calibration syringe (i.e., 3.09 L and 2.91 L). The control chart is for a 1-month time window, but others can be used. In addition, this control chart is for one spirometer. If ±3.5% of the volume of a 3.00-L calibration syringe is used (as recommended by more current guidelines), the UL and LL would be 3.11 L and 2.89 L, respectively.

1.2. Accuracy should be checked by having the device revalidated by the manufacturer at a frequency recommended by the manufacturer, or yearly when no specific recommendation is provided.
1.3. When available, the same calibration device should be used regularly on a large number of instruments so that problems with the calibration device can be separated from those of the instrument.

RECORD KEEPING AND LOGS

1. **Problem or Troubleshooting Log:** a log used to document problems, repairs, and revalidation. It should include:
   1.1. Date
   1.2. Problem
   1.3. Remedial action
   1.4. Revalidation data
   1.5. Name of individual solving problem.
2. **Preventive Maintenance (PM) List/Log:** a log used to list all equipment and document PM. It should include:
   2.1. List of instrumentation to be maintained and schedule of when maintenance is to be done
   2.2. Date of PM
   2.3. Problems identified
   2.4. Name of individual performing PM.
3. **Calibration Log:** a log used to document calibration (verification) information. It should include:
   3.1. Date
   3.2. Barometric pressure and ambient or device temperature
   3.3. Humidity, if applicable
   3.4. Section for calibration/validation of calibrators, scales, thermometers, etc.
   3.5. Inspiratory and/or expiratory volume calibration check (for spirometers or volume-measuring devices)
   3.6. Positive and negative pressures (for pressure-measuring devices)
   3.7. Gas analyzer's high and low values
   3.8. Acceptability range and whether instrument met acceptance criteria
   3.9. Name of individual performing calibration.
4. **Quality Control Log:** a log used to document the quality control performed by the laboratory. It should include:
   4.1. Date and time of quality control procedure
   4.2. Quality control method (e.g., known-volume syringe and biologic standard)
   4.3. Name of test and/or instrument or method
   4.4. Acceptability range
   4.5. Control chart
   4.6. Name of individual performing quality control
   4.7. Precision verification data forms
   4.8. Record of calibration of calibrators.
5. Storage of Logs
   5.1. Computer storage of data should have a good system for back-up and be easily retrievable.
   5.2. Installation manual and preventive maintenance log should be kept for the life of the instrument.
   5.3. Problem or troubleshooting log should be kept for at least 3 years.
   5.4. Calibration and quality control logs should be kept for at least 2 years or longer when local law has specific recommendations.

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APPENDIX 5.1

Precision Verification Data Form

Single-Breath Carbon Monoxide Diffusing Capacity (D_{LCO})

D_{LCO} Device Brand/Serial Number: _____

Date	Control ID	D_{LCO} #1	D_{LCO} #2	D_{LCO} #3			Mean D_{LCO}	SD D_{LCO}

Average mean DL_{CO} _____ Average SD DL_{CO} _____

APPROVAL SIGNATURES

Signature: _____ Date: _____

Annual Review

Date	Signature	Date	Signature

Revisions / Document History

Effective Date	Synopsis of Change

Effective Date: 2014
Version #1

CHAPTER 6

PROCEDURE NAME: SPIROMETRY

PURPOSE OR PRINCIPLE

Spirometry is a physiological test that measures inhaled and exhaled volumes of air as a function of time. The primary signal measured in spirometry is volume or flow. Spirometry measures the vital capacity (VC), the largest volume of air that can either be inspired or expired from the lungs. VC measured from a maximal forced exhalation is called the forced vital capacity (FVC). The most commonly measured parameters from the FVC maneuver are the FVC itself and the forced expiratory volume in one second (FEV_1) (1). Various flows can be measured in conjunction with an FVC maneuver, either at specific points (e.g., $FEF_{75\%}$) or across specific intervals ($FEF_{25-75\%}$), but have not been shown to increase diagnostic information or contribute usefully to clinical decision making over and above information from FEV_1, FVC, and FEV_1/FVC ratio (2, 3).

Many of the flow measurements from the forced expiration can also be obtained during forced inspiration (4). The forced inspiratory vital capacity (FIVC) is often measured in conjunction with the FVC, and like the FVC, various inspiratory flows can be measured (e.g., peak inspiratory flow [PIF] and forced inspiratory flow when 50% of the FIVC has been inhaled [$FIF_{50\%}$]).

When the VC is measured in an unforced manner it is called the slow vital capacity (SVC). SVC maneuvers are considered unforced; however, a maximal inspiratory and expiratory effort are still required.

Table 6.1 lists common spirometric terms and measurements (5). Volumes are reported in L (BTPS), and flows are reported in L/s (BTPS) (6).

An additional test, sometimes considered part of spirometry, is the maximal voluntary ventilation (MVV), which is recorded while the patient breathes rapidly and deeply for 12 or 15 seconds. The MVV is reported in L/min (BTPS) (6).

The graphic display of the FVC maneuver (spirogram) is necessary during testing for assessing patient effort and cooperation. The spirogram is also helpful for assessing the quality of the maneuver and for interpretative purposes. Two common spirogram displays are used: volume–time and flow–volume; both should be available to the technician and interpreter.

Since the FVC maneuver includes measurements of both volume and flow, it is useful in the assessment of both restrictive and obstructive diseases. Diseases that interfere with the bellows action of the chest wall or lungs result in a reduction of vital capacity. A reduced FVC or VC, without a disproportionately greater reduction in flows, suggests a restrictive disorder (7). This "restrictive" pattern predicts a reduced total lung capacity (TLC) only about half the time; the absence of the restrictive pattern strongly predicts a normal TLC (8, 9). Measurement of additional lung volumes, such as TLC, may be required to confirm the presence of a restrictive pattern.

Table 6.1

Spirometric terms and measurements		
Term	**Name**	**Description**
VC	Vital capacity	The volume change between the position of full inspiration and complete expiration.
IVC	Inspiratory vital capacity	The maximal volume of air inhaled slowly from the point of maximal exhalation achieved by a slow expiration from end-tidal inspiration.
EVC	Expiratory vital capacity	The maximal volume of air exhaled slowly from the point of maximal inhalation.
FVC	Forced vital capacity	The maximal volume of air exhaled with maximally forced effort from a position of maximal inspiration.
FEV_t	Forced expiratory volume	The maximal volume of air exhaled with maximally forced effort in t seconds; 1 and 6 seconds are the most common.
FEV_t/FVC	Forced expiratory volume in t seconds to forced vital capacity ratio	The ratio of FEV_t to FVC expressed as a percentage; FEV_1/FVC is the most commonly used measure.
$FEF_{x\%}$	Forced expiratory flow	The flow measured during a forceful expiration when x% of the FVC has been exhaled; $FEF_{25\%}$, $FEF_{50\%}$, and $FEF_{75\%}$ are commonly reported.
$FEF_{25-75\%}$	Forced mid-expiratory flow	The average flow measured over the middle 50% of an FVC maneuver.
FET	Forced expiratory time	The time required for the FVC to be expired.
PEF	Peak expiratory flow	The maximal expiratory flow generated during an FVC maneuver.
MVV	Maximum voluntary ventilation	The maximum volume of air one can ventilate over a specified period of time (e.g., 12 seconds).

Spirometry is the diagnostic tool for evaluation of obstructive lung disease. Maximal air flow depends primarily on the elastic recoil of the lungs and the compliance and caliber of the airways (10). During forced expiration from TLC, airflow limitation begins in the large airways (trachea and mainstem bronchi) with the development of turbulent flow. As the forced expiration continues, the site of air flow limitation moves to smaller airways where flow is laminar. Flow is limited by the compression of the airways downstream from the "equal pressure point." As the lungs empty, the equal pressure point moves into smaller airways. Measurements of flow at different lung volumes allows assessment of the status of the airways distal to the "equal pressure point" (11). Loss of elastic recoil (as in emphysema) results in increased compression of the airways and markedly reduced flows at all lung volumes. A decrease in the caliber of the airways (as in asthma or bronchitis) directly limits flow developed for a given driving pressure.

The pattern of flow reduction can be used to assess the site of flow limitation. Large airway obstructions, such as tumors, usually limit flow across a wide range of lung volumes (12). By measuring maximal flows during both inspiration and expiration, the nature of central airway obstruction can often be identified (i.e., fixed versus variable, intrathoracic versus extrathoracic). Measured flows are compared to those of healthy individuals to determine the severity of airway obstruction.

Table 6.2

Indications for spirometry	
Diagnostic	To evaluate symptoms, signs, or abnormal laboratory tests To measure the effect of disease on pulmonary function To screen individuals at risk of having pulmonary disease To assess preoperative risk To assess prognosis To assess health status before enrollment in strenuous physical activity programs
Monitoring	To assess therapeutic intervention To describe the course of diseases affecting lung function To monitor those exposed to injurious agents To monitor for adverse reactions to drugs with known pulmonary toxicity
Disability/Impairment Evaluations	To assess patients as part of a rehabilitation program To assess risks as part of an insurance evaluation To assess individuals for legal reasons
Public Health	Epidemiological surveys Derivation of reference equations Clinical research

Spirometers and procedures should meet the most current ATS/ERS recommendations (6, 13). There are two general groups of spirometers: volume-displacement and flow-sensing.

Volume-displacement spirometers. Some spirometers use a bellows, or cylinder/piston assembly to translate physical displacement into a recording of volume change. Most volume-displacement spirometers use a potentiometer or digital encoder to generate an analog or digital signal proportional to volume change which is processed and stored by a computer (14).

Flow-sensing spirometers. A large number of spirometers measure and integrate gas flow to determine volume. Available flow sensors use various principles including pressure-differential, heated-wire, and ultra-sound. Correction of nonlinear flow signals from these devices is performed automatically, usually by computer. Many flow-sensing spirometers are available in small, portable configurations.

Some indications for spirometry are provided in Table 6.2.

EQUIPMENT AND SUPPLIES

1. Spirometer description (e.g., manufacturer, model, type, accessories, additional features, and software version)
2. Disposable/reusable supplies: mouthpieces, nose clips, large-bore tubing, flow-sensors (pneumotachometers), gas and water absorbers (if applicable). If testing children, appropriately sized mouthpieces should be available.
3. Infection-control supplies: disposable in-line bacteria filters (if used), gloves, gowns, masks, and protective eye wear
4. Computer/printing supplies: paper, pens, and computer media
5. Thermometer, hygrometer (if applicable), barometer [or source of local barometric pressure (PB)] for BTPS correction; stopwatch for checking mechanical recorders

Table 6.3

Relative contraindications for spirometry
Spirometry should not be performed within 1 month of a myocardial infarction (5)
Conditions where suboptimal lung function results or test performance are likely (5): 1. Chest or abdominal pain 2. Oral or facial pain by mouthpiece 3. Stress incontinence 4. Dementia or confused state 5. In ability to follow instructions because of young age (e.g., < 6 years)
Other contraindications and waiting period before spirometry testing include (15): 1. Recent eye surgery (1 week to 6 months depending on type of surgery) 2. Recent brain surgery or injury (3 to 6 weeks) 3. Pneumothorax (2 weeks) 4. Hemoptysis of unknown origin

6. Scales for measuring height, weight, tape measure for arm span
7. Metered dose inhaler (MDI), small-volume nebulizer with compressed gas source, and reservoir (spacer) for bronchodilator/challenge tests.

PATIENT PREPARATION (PRE-TEST INSTRUCTIONS)

1. The patient should refrain from smoking for at least 1 hour before the test (5).
2. The patient's chest expansion should not be restricted by tight fitting clothing (e.g., belts or vests).
3. If reversibility testing is to be performed, the patient should withhold respiratory drugs (with permission of their physician) prior to testing. Guidelines for how long these medications should be withheld prior to reversibility testing include:

Bronchodilator Medication	Length of Abstention
Short-acting beta agonists (e.g., albuterol, salbutamol)	4–6 hours
Ipratropium (Atrovent)	6 hours
Long-acting beta agonists (e.g., formoterol, salmeterol)	12 hours
Ultra long-acting agents (e.g.,tiotropium, indacaterol, vilanterol)	24 hours

When spirometry is done in follow-up to assess ongoing management, it is appropriate to instruct the patient to maintain their daily bronchodilator regimen. The clinician may still request post-bronchodilator testing to look for further acute reversibility. Time of prior dosing of all bronchodilator medications should be noted in the report.

4. A brief history should be obtained (16). Collection of clinical information will enhance the interpretation of spirometric data. The history might include questions about:
   - Breathlessness
   - Cough and sputum production
   - Wheezing or symptoms of asthma

- Smoking history, including years of smoking, packs per day, and current smoking status
- Known lung disease, chest injuries, and chest operations
- Work history, including occupational exposure to dust, and respiratory irritants
- Current medications, dosages, and time last taken.

5. Measure the patient's height in centimeters (cm) to nearest 0.5 cm, or in inches (in) to nearest 0.25 inch while he/she is standing erect, bare-footed or in stocking feet, with their head looking straight ahead. A stadiometer is the ideal device for height measurement.
    5.1. If the patient is unable to stand, or has marked spinal deformity (e.g., kyphoscoliosis), an arm span measurement may be used to estimate standing height. Have the patient stretch the arms in opposite directions and attain the maximal distance between the tips of the middle fingers. For Caucasian men, height = arm span/1.03; for African-American men, height = arm span/1.06; and for women, height = arm span/1.01 (24).
6. The patient's weight should be measured using an accurate scale; weight is not required for most reference values for spirometry but may be useful for interpretive purposes. Weight may be recorded in kilograms (kg) to nearest 0.5 kg, or in pounds (lb) to the nearest lb.
7. The patient's age should be recorded in years as their age on day of testing. Comparison to reference data is more accurate if age is entered by birthday (and converted by software to days to date of test) or years to 0.1 years; this is especially true for children who can have rapid growth (18).
8. Spirometry may be performed with the patient sitting or standing (6). Sitting is preferable for safety reasons to avoid falling due to syncope. If the sitting position is used, the patient should sit up straight and have both feet on the floor. If the standing position is used, a chair with arms and without wheels should be positioned near the patient so they can be quickly and easily eased into a sitting position if he/she becomes light-headed during the testing. The position used for testing should be recorded on the report, and longitudinal studies should consider using the same test position each time.

ASSESSMENT OF PATIENTS

1. Assess each patient for oxygenation status and tolerance to room air if they arrive on supplemental oxygen.
2. Assess each patient for physical and developmental status to determine their ability to perform the test(s) and if special arrangements are required. If there is a language barrier, an interpreter will be used.
3. Record whether or not the patient has complied with the preparation criteria, including:
    3.1. If they have recently smoked, and if so, when;
    3.2. The time of their last meal;
    3.3. Current use of pulmonary medications, dosage, and number of hours taken before the start of testing.
4. Postponement may be necessary if the patient has not complied with the preparation criteria. The ordering physician is to be contacted to determine if rescheduling is necessary.
    4.1. In the event the ordering physician cannot be contacted, the laboratory medical director (or designee) should determine if testing should proceed.
5. Optimally, relevant clinical information including the clinical indication for ordering the test should be provided in writing by the ordering physician.

EQUIPMENT PREPARATION AND CALIBRATION CHECK (VERIFICATION)

1. **Preparation**
   - 1.1. All components should be assembled according to the manufacturer's instructions (i.e., tubing, connectors, flow-sensors, valves, and adapters).
   - 1.2. A new in-line bacteria filter (if used), disposable mouthpiece, or disinfected reusable mouthpiece should be in place; a clean or new flow-sensor should be used (for some flow-based spirometers).
   - 1.3. Turn on the system to ensure adequate warm-up.
   - 1.4. Perform diagnostic spirometry only at ambient temperatures between 17 and 40° C (temperatures outside this range may cause problems for both volume-based and flow-based spirometers).
   - 1.5. Volume-displacement spirometers should be checked for leaks each day of use (6) (application of at least 3 cm H_2O to the system with the outlet occluded should result in a volume change of less than 30 ml/min). Leaks are the most commonly detected problem in volume-displacement spirometers.
   - 1.6. Flow-sensors should be checked for holes in the sensor, clogging, channel plugging, or excess moisture. Care must be taken when "zeroing" a flow-sensing spirometer as zero errors, typically caused by sensor motion or inadvertent air movement, can cause falsely elevated or reduced volumes.
   - 1.7. Environmental data (i.e., internal spirometer temperature or ambient temperature, relative humidity [if applicable] and PB) from an accurate source representative of the laboratory should be entered before calibration checks.
2. **Calibration Check (verification)**
   - 2.1. A 3-L syringe should be used for calibration checks of spirometers; the syringe should have an accuracy of ±15 ml or ±0.5% of full scale (15 ml for a 3-L syringe), whichever is greater (6). The syringe should be checked at least annually to include a leak check and, if appropriate, to ensure the adjustable stop has not moved. A dropped or damaged syringe should be considered out of calibration until it is checked.
   - 2.2. Calibration checks (verification) should be performed at least once for each day of testing; for large-screening surveys or other situations in which a large number of tests are performed, calibration checks (verification) should be repeated more frequently.
   - 2.3. Calibration checks should produce a measured value within 3.5% of the syringe volume (i.e., ±0.105 L for a 3-L syringe). Flow-sensing spirometers that measure flow at the mouth may require separate correction factors for inspiratory and expiratory volumes.
   - 2.4. For flow-based spirometers, the 3-L syringe should be discharged at least three times to give a range of flows varying between 0.5 and 12 L/sec (injections of < 1sec, 3 sec, and 6 sec). The volume achieved at each of these flows should meet the accuracy requirement of ±3.5%. For devices with disposable flow sensors a new and different sensor, taken from those that might be used for patient tests, should be tested each day.
   - 2.5. The calibration syringe should be maintained at the same temperature and humidity as the spirometer (6).
   - 2.6. Spirometers that do not require calibration still need routine accuracy checks.

PROCEDURE

Pre-Test Preparation		
Step	**Action**	
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition.	
	IF	THEN
	Patient unable to provide information	• Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information
	The identifiers do not match	• Contact registration • Resolve discrepancies before proceeding
	The ID band is present but not attached to the patient	• Do not proceed. • Notify patient's nurse or registration desk
2.	Check for a complete physician's order.	
3.	Collect and record demographic information.	
4.	Explain and demonstrate test maneuver and have patient seated comfortably. Advise the patient they will have to remain seated throughout the test. Instruct the patient to keep a tight lip seal and to give maximum effort. A tight-fitting nose clip should be properly in place.	

Slow Vital Capacity	
Step	**Action**
1.	Because of the potential for muscular fatigue and volume history effects, it is preferable that SVC maneuvers be performed before FVC maneuvers.
2.	The VC maneuver may be considered either as an inspiratory vital capacity (IVC) where the patient inhales completely from a position of full expiration, or as an expiratory vital capacity (EVC) where the patient exhales completely from a position of full inspiration.
3.	Instruct the patient to inhale completely (an IVC).
4.	Instruct the patient to exhale slowly and evenly until there is no volume change (< 0.025 L) for a period of 1 second.
5.	Repeat for a minimum of three acceptable maneuvers.
6.	Check repeatability: difference between the largest and next largest VC should be less than 0.150 L. If not met, additional maneuvers should be obtained. Additional maneuvers may be needed to meet repeatability criterion.

FVC Closed-Circuit Testing	
Step	**Action**
1.	Have the patient assume the correct posture.
2.	Attach the nose clip, place mouthpiece in mouth and instruct patient to close lips around the mouthpiece and breathe quietly.
3.	Instruct the patient to inhale completely and rapidly with little or no pause (< 1–2 sec) at TLC.
4.	Instruct patient to exhale maximally until no more air can be expelled.
5.	Repeat instructions as necessary, coaching vigorously during the expiratory maneuver.
6.	Repeat for a minimum of three acceptable test maneuvers, no more than eight are usually required.
7.	Check test session repeatability: the two largest FVC values are to be within 0.150 L of each other, and the two largest FEV_1 values are to be within 0.150 L of each other. If the FVC ≤ 1.00 L, repeatability for both FVC and FEV_1 values is to be within 0.100 L. Perform more test maneuvers as necessary to achieve repeatability.

FVC Open-Circuit Testing	
Step	**Action**
1.	Have patient assume the correct position.
2.	Attach nose clip.
3.	Instruct the patient to inhale completely and rapidly with little or no pause at TLC (< 1 sec).
4.	Instruct the patient to place the mouthpiece in mouth and close lips around the mouthpiece, while holding their lungs full.
5.	Instruct patient to exhale maximally until no more air can be expelled.
6.	Repeat instructions as necessary, coaching vigorously.
7.	Repeat for a minimum of three maneuvers, no more than eight are usually required.
8.	Check test session repeatability: the two largest FVC values are to be within 0.150 L of each other, and the two largest FEV_1 values are to be within 0.150 L of each other. If the FVC ≤ 1.00 L, repeatability for both FVC and FEV_1 values is to be within 0.100 L. Perform more test maneuvers as necessary to achieve repeatability.

MVV	
Step	**Action**
1.	Have patient sit at the spirometer.
2.	Attach the nose clip, place mouthpiece in mouth and instruct patient to close lips around the mouthpiece and breathe quietly.

(continues on next page)

MVV (continued from previous page)	
Step	**Action**
3.	After three resting tidal breaths, instruct the patient to breathe as rapidly and deeply as possible. Tongue and teeth must be positioned so as to not obstruct airflow.
4.	Enthusiastically coach the patient throughout the maneuver, and direct the patient to breathe faster or deeper to achieve an ideal rate of between 90 and 110 breaths per minute, though patients with disease may not always be able to achieve this rate. Tidal volume during the maneuver is probably not as important as breathing frequency.
5.	The test interval (e.g., 12 sec) should be noted and reported.
6.	Perform a minimum of two acceptable maneuvers, and check for test repeatability.

REVIEW OF TEST RESULTS

1. Individual spirometry maneuvers are "acceptable" if:
   - 1.1. They are free from artifacts including:
     - Cough or glottis closure during the first second of exhalation
     - Early termination or cutoff
     - Variable effort
     - Leak at the mouth
     - Obstructed mouthpiece
     - Flow signal zeroing error
   - 1.2. Have good starts with extrapolated volume less than 5% of FVC or 0.15 L, whichever is greater. For preschool children, the back extrapolation volume should be ≤ 80 ml or < 12.5% of the FVC (19).
   - 1.3. Have a satisfactory exhalation with reasonable duration or a plateau in the volume–time curve. Reasonable duration is defined as follows: the patient has tried to exhale for at least 3 seconds in children < 10 years of age, and for at least 6 seconds for those over 10 years of age; however, many teenagers will reach a plateau before 6 seconds, so an earlier termination is acceptable if a plateau is demonstrated. A plateau is defined as no change in volume (< 0.025 L) for at least one second. Although patients should be encouraged to achieve maximal effort, they should be allowed to terminate the maneuver on their own at any time especially if they are experiencing discomfort.
     Note 1: *For most adult patients exhalation times longer than 6 seconds are frequently needed. However, exhalation times greater than 15 sec will rarely change clinical decisions.*
     Note 2: *In children and young adults the end exhalation is normally determined by chest wall mechanics rather than by airway closure, so there may be a rapid drop in flow at the end exhalation simulating a cutoff. This pattern should not be misinterpreted as early termination.*
   - 1.4. A maneuver may be considered "usable" if it there is no cough or glottis closure in the first second and have a good start.
2. Between-maneuver repeatability criteria for spirometry (6):
   - 2.1. After a minimum of three acceptable FVC maneuvers have been obtained:
     - The two largest FVC values are within 0.150 L of each other; if the FVC ≤ 1.00 L, repeatability is to be within 0.100 L.
     - The two largest FEV_1 values are within 0.150 L of each other; if the FVC ≤ 1.00 L, repeatability is to be within 0.100 L.

2.2. If both of these criteria are not met, continue testing until
- Both of criteria are met with additional acceptable maneuvers, OR
- A total of eight maneuvers have been performed, OR
- The patient cannot or should not continue.

3. MVV
   3.1. An acceptable maneuver is one in which maximal effort was used without evidence of leak, hesitation, or measurement artifact.
   3.2. The MVV (BTPS) is calculated from the sum of all individual exhalations during the best 12 seconds of the maneuver.
   3.3. There are no clinical studies addressing repeatability; however, additional trials should be considered when the variability between acceptable maneuvers exceeds 20% (6).
4. Final review of data on report should be checked for accuracy and completeness by the individual performing the testing, and/or by the laboratory manager or supervisor.
5. The accuracy of the final report in the hospital information system should be checked periodically.

REPORTING OF TEST RESULTS

1. All volumes and flows are reported at body temperature and pressure saturated with water vapor (BTPS) conditions.
2. The largest VC from at least two acceptable maneuvers is reported; the same value should be used for lung volume calculations.
3. The largest FVC and largest FEV_1 from acceptable maneuvers are reported, even though the values may not come from the same maneuver.
4. The largest PEF obtained is reported.
5. All other flows (e.g., $FEF_{25-75\%}$, $FEF_{50\%}$) are reported from the "best" test. The "best" test is defined as the maneuver with the largest sum of FVC and FEV_1.
6. All inspiratory measurements (e.g., FIVC, PIF, and $FIF_{50\%}$) should be the largest values obtained.
7. If a single volume–time tracing or flow–volume curve is to be included in a final report, it should be the spirogram from the effort with the largest sum of FVC and FEV_1. Expiratory and inspiratory flow–volume curves from different acceptable efforts may be combined to produce a flow–volume loop. Laboratories are strongly encouraged to print (display) at least three acceptable maneuvers.
8. The highest acceptable MVV (L/min) and MVV rate (breaths/min) should be reported. Volume versus time tracings from at least two acceptable maneuvers should be retained and available for inspection.
9. The final report should include:
   - Technologist's comments on patient effort and cooperation, and/or grading scores or codes regarding the acceptability and reproducibility of the data.
   - The instrument's software version.
   - Date, time, and results of most recent calibration.
   - The reference values used.

PROCEDURE NOTES

1. Technologist's qualifications and role
   - 1.1. Individuals performing spirometry should be high school graduates, with at least 6 months supervised training. Individuals responsible for troubleshooting problems should have at least 1 year of training (5, 20).
   - 1.2. Interaction between the technologist and patient are important in obtaining acceptable and repeatable data; technologists should display a high level of motivation in regard to eliciting maximal effort from the patient.
   - 1.3. The laboratory quality assurance program should provide feedback to individual technologists regarding the quality of the data; feedback should include the nature and extent of unacceptable FVC maneuvers, corrective actions to improve quality, and recognition of superior performance (5, 16).
2. Effort dependence of spirometry
   - 2.1. Spirometry (VC, FVC, and MVV) is an effort-dependent test. It requires cooperation, motivation, and understanding by the patient; appropriate patient effort depends on instruction and communication with the technologist.
   - 2.2. Physical and mental impairment, or other conditions may limit the patient's ability to adequately perform the test in an acceptable and repeatable manner.
3. Infection control; there is some risk of infection related to performance of spirometry.
   - 3.1. Cross-contamination between patient and technologist and between patients can occur if the use of gloves, hand washing, and equipment-decontamination procedures are not followed (17).
   - 3.2. Spirometry equipment (e.g., mouthpieces, etc.) contaminated with blood should be handled using universal precautions (UP) (21).
   - 3.3. Patients with known or suspected transmissible diseases (e.g., tuberculosis or TB) should be tested using dedicated equipment or at the end of the day to reduce risk of cross contamination (22).
   - 3.4. The use of in-line bacteria filters may be indicated on multi-use spirometers employing complex valves and circuits. The use of filters may influence the measurement of flows (23).
4. Unacceptable data; it may be necessary to report data which do not meet all criteria for acceptability and repeatability.
   - 4.1. Final report should include technologist's comments regarding unacceptable or non-reproducible data, including a description of the problem (e.g., poor effort, large volume of back extrapolation, and early termination).
   - 4.2. Spirometry data should be reported if at least one acceptable maneuver is obtained after eight attempts; appropriate comments concerning the effect of using data from a single test should be included.
   - 4.3. Spirometry data that are not repeatable (i.e., largest FVC or FEV_1 values not within 0.150 L) may be reported; appropriate comments concerning the possible consequences of the non-repeatable data should be included.
5. Choice of reference equations may affect the final interpretation.

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CHAPTER 7

PROCEDURE NAME: BRONCHODILATOR ADMINISTRATION

PURPOSE

Assessment of airflow-limitation reversibility with drug administration is commonly done as part of pulmonary function (PF) testing. The purpose of this test is to determine whether a patient's lung function can be improved. PF tests (e.g., spirometry) are done before and after (pre-/post-) drug (bronchodilator) administration and the response measured. Many variables affect the bronchodilator response (1). Some patients may respond to one type of bronchodilator but not to another, or they may have a variable response to the same medication at different times. Several factors must be considered in order to standardize assessment of bronchodilator response. These factors are primarily related to the methods used by the laboratory.

Beta-adrenergic aerosols are the most commonly used form of bronchodilator for pre- and post-testing, although the evaluation of other drugs can be conducted as requested by referring physicians. The drug, its dosage, and the means of delivery should be standardized as much as possible.

Evaluating response to bronchodilators requires withholding the usual dose of bronchodilator before testing (2). Recommended times for withholding bronchodilators when the PF test bronchodilator response is to be assessed are presented in Table 7.1.

Table 7.1

Recommended Time Periods for Withholding bronchodilators before Bronchodilator-Response Testing	
Bronchodilator Medication	**Length of Abstention**
Short-acting beta agonists (e.g., albuterol, salbutamol)	4–6 hours
Iprtatriopium (Atrovent)	6 hours
Long-acting beta agonists (e.g., formoterol, salmeterol)	12 hours
Ultra–long-acting agents (e.g.,tiotropium, indacaterol, vilanterol)	24 hours

In most instances, spirometry or plethysmography is performed, followed by administration of a bronchodilator, then the test repeated after an appropriate interval. The delay from pre- to post-test should be determined by the time it takes for the onset of action to peak effect for the drug used. For most short-acting beta-agonists this is a relatively short interval (i.e., ≥10 min) (3). Other drugs, such as short-acting anticholinergics may require a longer interval before retesting (e.g., ≥30 min).

The method of administration of bronchodilators can have a pronounced effect on the results of pre- and post-tests (4, 5). Beta-agonists and anticholinergics are often administered via an inhaler or via a small-volume nebulizer (SVN). Other methods may be used for specific bronchodilator preparations. In order to maximize lung deposition of the bronchodilator, valve-holding chambers (spacers) should be used in conjunction with metered dose inhalers (MDIs) (6).

There is no clear consensus about what constitutes reversibility in patients with airflow limitation. The most common approaches of expressing bronchodilator response are percent of the initial PF test value, percent of the predicted value, and absolute change (7). The most commonly used variables for evaluation of response to bronchodilators are forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), peak expiratory flow (PEF), and sGaw. Other variables (e.g., thoracic gas volume [TGV], isovolume maximal expiratory flows) may identify response to bronchodilators when more conventional measures do not. PF tests that measure parameters that are not flow related (e.g., carbon monoxide diffusing capacity [D_{LCO}], total lung capacity [TLC]) are also sometimes evaluated pre- and post-bronchodilator administration. However, there are few guidelines for these other variables and using them may increase the number of false positives.

Indications and contraindications for bronchodilator response testing are shown in Table 7.2.

EQUIPMENT AND SUPPLIES

1. PF testing instrumentation (e.g., spirometer, plethysmograph).
2. Inhaler or nebulizer and liquid bronchodilator as used by the laboratory. Specify the dosage.
3. A valve-holding chamber or "spacer" for use in conjunction with an MDI should be available. The volume of the spacer should be appropriate for the type of patients tested (i.e., children or adults) (2).

Table 7.2

Indications and Contraindications for Bronchodilator-Response Testing	
Indications	Reversibility of airway obstruction as demonstrated by a reduced FEV_1/FVC ratio or other indicators of flow limitation Evaluation of specific drug regimens in patients with known hyperreactive airways Reversal of bronchospasm induced by bronchial challenge tests Disability determinations when the FEV_1 is less than 70% of predicted Preoperative evaluation when airway obstruction is present
Relative Contraindications	Known or suspected adverse reactions to a specific bronchodilator Unstable cardiovascular status (i.e., serious arrhythmias, significant tachycardia, and elevated blood pressure) that might be aggravated by beta adrenergic stimulation

PROCEDURE

Pre-Bronchodilator Administration Preparation		
Step	**Action**	
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition.	
	IF	THEN
	Patient unable to provide information	• Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information
	The identifiers do not match	• Contact registration • Resolve discrepancies before proceeding
	The ID band is present but not attached to the patient	• Do not proceed. • Notify patient's nurse or registration desk
2.	Check for a complete physician's order. A laboratory-developed protocol that identifies indications for pre- and post-testing may be appropriate.	
3.	Prepare the bronchodilator administration equipment.	
4.	Explain the test to the patient.	
5.	Obtain physiologic data (e.g., pulse rate, blood pressure). This is optional.	

Bronchodilator Administration		
Step	**Action**	
1.	Explain and demonstrate the breathing technique to the patient. The demonstration will be dependent on the device being utilized.	
2.	Administer bronchodilator	MDI The technician should hold MDI 1 to 2 inches from the patient's open mouth. If a valved holding chamber or spacer is used, it should be placed in the patient's mouth (or as recommended by the manufacturer). Have patient exhale below functional residual capacity (FRC), but do not force them to exhale to residual volume (RV). Instruct patient to take a slow, deep breath. While the patient is inhaling from below FRC, activate the MDI; instruct the patient to continue inhaling until they are close to TLC. It is important that the inhalation be slow (i.e., a flow rate of approximately 0.5 L/s or less). Instruct the patient to hold the breath for 5 to 10 seconds, if possible, then exhale slowly (1). Wait approximately 30 seconds, then repeat steps 1 through 4 until the ordered or selected dosage has been delivered. SVN

(continues on next page)

Bronchodilator Administration (Continued from previous page)	
Step	**Action**
	Place the appropriate amount of drug in nebulizer. Adjust airflow as recommended by nebulizer manufacturer. Have the patient take slow, moderately deep breaths (i.e., ~1 L/s for adults) with mouthpiece (preferred) or mask in place. If a thumb-valve is used, the open port should be occluded upon inspiration and then reopened upon exhalation. Continue until prescribed dose is completely nebulized.
3.	Obtain physiologic data (e.g., pulse rate, blood pressure) approximately 5 minutes after bronchodilator has been administered, or earlier if patient complains of symptoms (palpitations, light-headedness, flushing).
4.	Premature discontinuation of bronchodilator administration. If patient complains of symptoms (palpitations, light-headedness, flushing), discontinuation of bronchodilator may be necessary. In the event of serious arrhythmia, tachycardia >120 beats/min, or marked elevation in blood pressure, stabilize the patient and notify the ordering physician or medical director.

Post-Bronchodilator Administration	
Step	**Action**
1.	Wait at least 10 minutes after bronchodilator administration and then repeat spirometry and/or plethysmography (2).
2.	If the bronchodilator is administered after a bronchial challenge, a return to at least 90% of the baseline value should be observed. If the response is less than this, a repeat administration of the bronchodilator may be indicated.

REPORTING RESULTS

1. The percent change after bronchodilator administration is calculated as follows:

$$\% \text{ change} = \frac{\text{post-bronchodilator value} - \text{pre-bronchodilator value}}{\text{pre-bronchodilator value}} \times 100$$

   Pre-bronchodilator values and post-bronchodilator values are any PF variables (e.g., FEV_1). Note that increased flows or volumes will result in a positive number, while decreased flows or volumes result in a negative number.

2. An alternative method (11) of calculating bronchodilator response is:

$$\% \text{ change} = \frac{\text{post-bronchodilator value} - \text{pre-bronchodilator value}}{\text{predicted value}} \times 100$$

3. The ATS/ERS 2005 recommendations (7) suggest the following increases represent significant bronchodilator responses in adult patients:

   FVC: at least 12% *and* 200 ml
   FEV_1: at least 12% *and* 200 ml

   In children the 12% increase is applicable, but without the volume criterion.
4. Other flow measurements (e.g., forced expiratory flow after 50% of the FVC has been expired [$FEF_{50\%}$]) may be reported pre- and post-bronchodilator. Since these flows often depend on lung volume or on expiratory time, they should be corrected to reflect similar volumes (isovolume correction) (12).
5. If flow–volume curves pre- and post-bronchodilator are reported, they should be superimposed at TLC. If static lung volumes are also measured pre- and post-bronchodilator, the curves should be plotted on a common volume axis.
6. The drug, dose, and method of delivery should be noted on the final report (2). Optionally, pulse and respiratory rates pre- and post-bronchodilator delivery can be reported.

PROCEDURE NOTES AND LIMITATIONS

1. Because individuals vary their responses to various bronchodilators, 20% to 30% of responsive patients will respond to one agent but not another (13, 14).
2. The percent change in function after bronchodilator is a function of the degree of baseline airways obstruction (e.g., % predicted FEV_1) (7).
3. Increases in FEV_1 or FVC of less than 8% or 150 ml are generally within the variability of the measurements themselves, and/or may represent a normal reduction in vagally mediated bronchomotor tone (2, 15). The decision to treat patients with bronchodilators is a clinical, not a laboratory decision. Failure to demonstrate a significant response to a single drug on one occasion does not preclude a clinical response to bronchodilator or antiinflammatory therapy (7).
5. Although PEF may be used to evaluate response to inhaled bronchodilators, its inherent variability makes it difficult to interpret.
6. The results from patients who did not perform acceptable or repeatable test maneuvers (either pre- or post-bronchodilator) should be interpreted with caution. However, bronchodilator response may need to be evaluated clinically in lieu of acceptable spirometry or plethysmography. For example, a patient who coughs uncontrollably or has spirometry-induced worsening may not be able to perform acceptable or reproducible spirometry until after administration of a bronchodilator. Post-bronchodilator spirometry that is performed acceptably may indicate significant improvement in this case, even though a percent change cannot be calculated.
7. Although the FEV_1/FVC ratio should be reported pre- and post-bronchodilator, calculating the percent change in this parameter has less use than that of either of its components.
8. For midflow rates ($FEF_{50\%}$ or $FEF_{25-75\%}$), the increases representing a significant response are considerably greater than those for FVC and FEV_1. However, Quanjer and colleagues reported that neither $FEF_{25-75\%}$ nor $FEF_{75\%}$ contribute usefully to clinical decision-making over and above information from FEV_1, FVC, and FEV_1/FVC ratio (16).
9. The $FEF_{25-75\%}$ is a highly variable parameter and is dependent on the FVC. If the FVC changes, post-bronchodilator, the $FEF_{25-75\%}$ is not comparable with that measured pre-bronchodilator (7).

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CHAPTER 8

PROCEDURE NAME: MEASUREMENT OF LUNG VOLUMES

PURPOSE OR PRINCIPLE

The measurement of static lung volumes generally refers to measuring the various lung "capacities" and "volumes." The capacities include: functional residual capacity (FRC), total lung capacity (TLC), vital capacity (VC), and inspiratory capacity (IC).

These four capacities can be divided into sub-volumes, which are also measured and include: inspiratory reserve volume (IRV), expiratory reserve volume (ERV), tidal volume (TV), and residual volume (RV).

FRC is the volume of gas from which a normal breath is taken, or alternatively, the volume of gas present in the lung at end-expiration during tidal breathing. The methods used to measure FRC are body plethysmography (FRC_{pleth}), multiple-breath helium dilution (FRC_{He}), and multiple-breath nitrogen washout (FRC_{N2}). The term "thoracic gas volume" (generally referred to when measuring this volume of gas using the body plethysmograph and abbreviated TGV or V_{TG}) is nonspecific and refers to the absolute volume of air in the thorax at any point in time and at any alveolar pressure, and the use of this term is not recommended and it should be replaced with more specific terminology (e.g., FRC_{pleth}) (1). The gas-dilution techniques (FRC_{He} and FRC_{N2}) measure the gas in the lung communicating with the mouth; plethysmography measures all compressible gas in the thorax. The FRC increases with aging and may also increase in the presence of lung diseases that cause air-trapping (e.g., asthma, chronic bronchitis, and emphysema). Conversely, the FRC can be reduced in the presence of restrictive lung disease processes such as interstitial lung disease (ILD) and pneumonectomy.

TLC is the total or greatest volume of gas in the lung at the end of a full inspiration. TLC is calculated either by summing FRC and IC, or VC and RV. TLC may be normal or increased with obstructive lung diseases, and tends to be reduced with restrictive lung diseases or neuromuscular disorders.

IC is the maximal amount of gas inspired from a normal end-expiration (FRC). It is also the sum of IRV and TV.

VC is the volume change at the mouth between the positions of full inspiration and complete expiration. It is also the sum of TV, IRV, and ERV. As compared to the forced expiratory vital capacity (FVC), the slow vital capacity (SVC) is an untimed maneuver and may also be referred to as the "relaxed vital capacity," or simply as VC. The inspiratory vital capacity (IVC) is also performed in a relaxed manner from a position of full expiration to full inspiration. The VC may be maintained within the normal range with certain pulmonary diseases, but is often reduced in the presence of obstructive lung diseases. It is also reduced in the presence of restrictive lung diseases or neuromuscular disorders.

ERV is the volume of gas that can be maximally exhaled from the end-expiratory level during tidal breathing (i.e., FRC). **TV** (also denoted as V_T) is the volume of gas inhaled or exhaled with the respiratory cycle. If it is measured under conditions other than quiet relaxed breathing, that should be indicated. The **IRV** is the maximal volume of gas that can be inhaled from the end-inspiratory level during tidal breathing.

RV is the volume of gas remaining in the lung after maximal (complete) exhalation regardless of the lung volume at which expiration was started. It requires maximal expiratory efforts and cannot be obtained in non-cooperating subjects. It is indirectly determined by subtracting the ERV from FRC, or VC from TLC. It is usually elevated in obstructive lung diseases and reduced with restrictive lung diseases. While spirometry may suffice in the diagnosis and monitoring response to therapy in obstructive lung diseases such as COPD or asthma, lung volume measurements are essential in the diagnosis of restrictive lung disease and often very helpful in complex or mixed lung conditions.

INDICATIONS AND CONTRAINDICATIONS

Table 8.1

Indications for measuring lung volumes include
Establish or confirm a "restrictive ventilatory defect" or in diagnosing hyperinflation and abnormal distensibility as may occur in patients with emphysema (2).
Differentiating types of lung disease processes characterized by airflow limitation that have similar forced expiratory configurations (2).
Assess response to therapeutic intervention (e.g., drugs, transplantation, radiation, chemotherapy, and lobectomy).
Aid in the interpretation of other lung function tests.
Evaluate cause of pulmonary disability.
Make preoperative assessments in patients with compromised lung function (known or suspected) when the surgical procedure is known to affect lung function.
Quantify the amount of nonventilated lung.

Table 8.2

Relative contraindications for measuring lung volumes include
Relative contraindications for performing static lung volumes include those also considered for spirometry (3): 1. Hemoptysis of unknown origin 2. Pneumothorax 3. Unstable cardiovascular status 4. Thoracic, abdominal, or cerebral aneurysms 5. Recent eye surgery
Presence of an acute disease that might interfere with test performance (e.g., nausea, or vomiting)
Recent surgery of thorax or abdomen
With respect to total-body plethysmography, such factors as claustrophobia, upper-body paralysis, obtrusive casts, or any factor that could limit the patient's access into the chamber is a concern. In addition, temporary interruption of supplemental oxygen (O_2) and intravenous fluids may be contraindicated.
With respect to the multiple-breath dilution or washout methods, in patients with very severe chronic obstructive pulmonary disease (COPD) factors such as depressed ventilatory drive during FRC_{N2} (due to breathing 100% O_2), and induced hypercapnia and/or hypoxemia during FRC_{He} (due to failure to adequately remove carbon dioxide [CO_2] or add O_2), need to be considered and addressed.

EQUIPMENT AND SUPPLIES

1. System description (e.g., XYZ Corp., Model 101 Pulmonary Function System with volume displacement/flow sensing spirometer, infrared helium [He] analyzer [katharometer], and emission-type N_2 analyzer).
2. Compressed-gas cylinder(s) of test gas(es) used by the laboratory (e.g., 100% O_2, or 10% He, 21% O_2 with balance N_2).
3. Appropriate size mouthpiece, tubing, nose clip, CO_2 and O_2 absorbers, and other miscellaneous equipment or supplies needed (e.g., facial tissue).

PATIENT PREPARATION (PRE-TEST INSTRUCTIONS)

1. The patient should refrain from smoking for at least 1 hour before the test (4).
2. The patient should not have had a large meal shortly before testing.
3. Diurnal variation does occur with lung volumes. If serial measurements are anticipated, the time of day should be kept the same (2).
4. The patient's chest expansion should not be restricted by clothing (e.g., brassieres or vests).
5. Medications that affect lung function and volumes (e.g., beta-2 agonists) should be withheld, if clinically feasible. Note: The length of time necessary to withhold various medications varies.

   Guidelines (4) for withholding medications include:

Table 8.3

Recommended times periods for withholding bronchodilators prior to bronchodilator-response testing.

Medication		Length of Abstention
Inhaled bronchodilators	Short-acting	4 to 6 hours
	Long-acting	12 hours
Anticholinergics	Short-acting	6 hours
	Long-acting	24-48 hours
Ultra long-acting agents		24 hours

6. The patient should be seated upright as body position influences lung volumes (5, 6). If another position is used, it should be noted.
7. Interruption of supplemental O_2 is necessary during measurements of static lung volumes. The following considerations must be addressed before initiating testing:
   - 7.1. If FRC_{N2} is to be performed, the patient should not have supplemental O_2 for at least 15 minutes. Breathing room air for > 15 minutes should be adequate in most instances to assure alveolar nitrogen (N_2) is near 80% (2).
   - 7.2. Discontinuation of supplemental O_2 may be contraindicated in some patients with very severe lung disease or hypoxemia. Check with the physician before doing so.

ASSESSMENT OF PATIENTS

1. Assess each patient for physical and developmental status to determine ability to undergo the diagnostic test(s) and if special arrangements are required. If there is a language barrier, an interpreter will be used.
2. Ask each patient if he/she has complied with the preparation criteria, including:
   - 2.1. If they have recently smoked, and if so, when.
   - 2.2. The time of his/her last meal.
   - 2.3. The last time he/she took breathing medications, and what types.
3. Postponement may be necessary if the patient has not complied with the preparation criteria. The ordering physician is to be contacted to determine if rescheduling is necessary.
   - 3.1. In the event the ordering physician cannot be contacted, the laboratory medical director (or designee) should determine if testing should proceed.
4. In order to properly document and interpret the test results, relevant clinical information including the clinical indication for ordering the test must be provided in writing by the ordering physician.

EQUIPMENT PREPARATION AND CALIBRATION CHECKS

1. Equipment Preparation

- 1.1. General Considerations
  1. Turn on the equipment to allow adequate warm-up time.
  2. Ensure the system is leak-free each day.
- 1.2. FRC_{N2} System
  1. Ensure 100% O_2 gas source is adequate for a 10-minute (minimum) test.
  2. Ensure demand valve allows adequate flow with minimal resistance.
  3. Follow manufacturer's instructions in setting up equipment.
- 1.3. FRC_{He} System
  1. Ensure CO_2 and water (H_2O) absorbers are fresh and placed in the proper order.
  2. Ensure fan (to mix and circulate gases) is operational.
  3. Follow manufacturer's instructions in setting up equipment.
- 1.4. Plethysmograph
  1. Ensure mouth occlusion shutter has minimal resistance to opening and closing (i.e., does not stick).
  2. Ensure pressure transducers are correctly aligned.
  3. Ensure adequate door seal.
  4. Follow manufacturer's instructions in setting up equipment.

2. Calibration Check (Verification)

- 2.1. General Considerations
  1. Volume calibration check (verification) using a calibrated syringe (e.g., 3 L) must be performed at least once each day testing is performed; verify calibration of spirometer before patient is tested.
  2. The accuracy of the syringe volume must be considered in determining whether the measured volume is within acceptable limits. For example, if a 3.00-L calibrated syringe with an accuracy of 0.5%, is used, the measured volume should be within 3.5%, or between 2.895 L and 3.105 L.
- 2.2. FRC_{N2}
  1. Two-point (0, and 80% N_2) calibration of the N_2 analyzer should be performed prior to each test. These values should be accurate to within 0.5%.

2.3. FRC_{He}
1. Two-point (zero to full scale) calibration of the He analyzer should be performed at least once each day prior to testing patients.

2.4. Plethysmograph
1. Calibration of mouth pressure and box pressure transducers is performed at least once each day according to manufacturer's instructions prior to testing patients.

PROCEDURE

Pre-Test Preparation

Step	Action	
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition.	
	IF	THEN
	Patient unable to provide information	• Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information
	The identifiers do not match	• Contact registration • Resolve discrepancies before proceeding
	The ID band is present but not attached to the patient	• Do not proceed. • Notify patient's nurse or registration desk
2.	Check for a complete physician's order.	
3.	Collect and record demographic information.	
4.	Explain and demonstrate test maneuver and have patient seated comfortably. Advise the patient they will have to remain seated throughout the test. Instruct the patient to keep a tight lip seal and to give maximum effort. A tight-fitting nose clip should be properly in place.	

Test Procedure for FRC_{pleth}

Step	Action
1.	Set-up and test preparation: • Turn equipment on, allow adequate warm-up time, and calibrate as instructed by the manufacturer. • Adjust the equipment so that the patient can sit comfortably in the chamber and reach the mouthpiece without having to flex or extend the neck. • Seat the patient comfortably, dentures should not be removed. Explain the procedure including that the door will be closed and that the patient's cheeks are supported by both hands, and place the nose clips on the patient's nose. • Close the plethysmograph door and allow ample time (sometimes as much as a minute is needed) for thermal transients to stabilize and the patient to relax.

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Test Procedure for FRC_{pleth} (Continued from previous page)	
Step	**Action**
2.	Instruct the patient to attach to the mouthpiece and breathe quietly until a stable end-expiratory level is achieved (usually 3 to 10 breaths).
3.	When the patient is at or near FRC, close the shutter at end-expiration for approximately 2 to 3 seconds, and instruct the patient to perform a series of gentle pants (approximately ± 10 cm H_2O or 1 kPa) at a frequency between 0.5 and 1.0 Hertz. Panting frequencies greater than 1.5 Hertz may lead to errors, and less than 0.5 Hertz may cause problems with the controlled leak of the body plethysmograph (7).
4.	A series of 3 to 5 technically satisfactory panting maneuvers should be recorded (i.e., on the pressure/volume plot a series of almost superimposed straight lines within the calibrated pressure range of the transducers separated by only a small thermal drift), after which the shutter is opened and the patient performs and ERV maneuver followed by a slow IVC maneuver (or as a second priority an IC maneuver followed by a slow expiratory VC maneuver). If needed, the patient can come off the mouthpiece and rest between TGV/VC maneuvers. Patients with severe dsypnea may have difficulty performing the preferred VC method (i.e., ERV immediately after TGV followed by a slow IVC). To overcome this, the patient can be instructed to take 2 or 3 tidal breaths after the panting maneuver prior to performing the linked ERV and IVC maneuvers.
5.	Obtain at least three separate, acceptable trials (FRC_{pleth} values) that agree within 5% (i.e., the difference between the highest and lowest value divided by the mean is 0.05 or less), and report the mean value. If there is a larger deviation, obtain additional values until 3 values agree within 5% of their mean, and report the mean. The FRC_{pleth} value is rounded to two decimal places (e.g., 4.53 L).

Test Procedure for FRC_{N2}	
Step	**Action**
1.	Set-up and test preparation: • Turn equipment on, allow adequate warm-up time, and calibrate as instructed by the manufacturer. • Ask the patient if he/she has a perforated eardrum (if so, use an earplug). • Seat the patient comfortably; dentures need not be removed. Explain the procedure emphasizing the need to avoid leaks around the mouthpiece during the washout, and place the nose clip on the patient's nose.
2.	Have the patient breathe on the mouthpiece for approximately 30–60 seconds to become accustomed to the apparatus, and to assure a stable end-tidal expiratory level. For young children, testing is best if done while the child watches a video and sits upright in the lap of the parent or someone the child trusts. For very young children, a small face mask that can be sealed with putty is preferred (8).
3.	When breathing is stable and consistent with the end-tidal volume being at FRC, switch the patient into the circuit so 100% O_2 is inspired instead of room air.
4.	Monitor the N_2 concentrations during the washout. A change in inspired N_2 > 1% or a sudden large increase in expiratory N_2 concentrations indicate a leak and the test should be stopped and repeated after a 15-minute period of breathing room air. Commercial software typically will display % N_2 (or log % N_2) plotted against volume or number of breaths.
5.	Testing should be continued until N_2 concentration falls below 1.5% for at least three successive breaths.

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Test Procedure for FRC_{N2} (Continued from previous page)	
Step	**Action**
6.	When N_2 concentration is ≤1.5%, have the patient perform an ERV maneuver and turn the patient out of the system when RV is attained. Remove the mouthpiece and nose clip.
7.	Perform at least one technically satisfactory measurement. If additional trials are performed, allow at least a 15-minute waiting period between trials. In patients with severe obstructive or bullous disease, the time between trials should be at least 1 hour (9). If only one FRC_{N2} measurement is made, caution should be used in interpretations. If more than one measurement is made, report the mean value of technically acceptable results that agree within 10% rounded to two decimal places (e.g., 3.12 L).

Test Procedure for FRC_{He}	
Step	**Action**
1.	Set-up and test preparation: • Turn equipment on, allow adequate warm-up time, and calibrate as instructed by the manufacturer. • Ask the patient if he/she has a perforated eardrum (if so, use an earplug). • Seat the patient comfortably; dentures need not be removed. Explain the procedure emphasizing the need to avoid leaks around the mouthpiece during the washout, and place the nose clip on the patient's nose. • For young children, testing is best if done while the child watches a video and sits upright in the lap of the parent or someone the child trusts. For very young children, a small face mask that can be sealed with putty is preferred (8).
2.	Have the patient breathe on the mouthpiece for approximately 30–60 seconds to become accustomed to the apparatus, and to assure a stable end-tidal expiratory level.
3.	When breathing is stable and consistent with the end-tidal volume being at FRC, switch the patient into the closed breathing circuit.
4.	Adjust the O_2 flow to compensate for O_2 consumption (significant errors in the calculation of FRC can result if O_2 consumption is not adequately accounted for). Note the He concentration every 15 seconds.
5.	He equilibration is considered complete when the change in He concentration is less than 0.02% in 30 seconds. The test rarely exceeds 10 minutes, even in patients with severe gas or exchange abnormalities (10).
6.	Once He equilibration is complete, turn the patient "out" of the system. If the measurements of ERV and IC are to be linked to the FRC measurement, assure that the spirometer has adequate volume for a full ERV and IVC maneuver.
7.	Perform at least one technically satisfactory measurement. If only one measurement is made, caution should be used in interpretation. If more than one measurement is made, the value reported should be the mean of technically acceptable results that agree within 10%, rounded to two decimal places (e.g., 3.12 L). A minimum of 5 minutes should elapse before the test is repeated, with the patient breathing room air. Longer wait times between repeated tests may be necessary if there is significant maldistribution of inspired air to allow elimination of test gas.

Test Procedure for SVC	
Step	**Action**
1.	Immediately after the FRC measurement and without coming off the mouthpiece, instruct the patient to slowly expire as much as possible (ERV maneuver).
2.	Instruct the patient to inhale completely (an Inspired Vital Capacity).
3.	For patients with severe obstructive dysfunction or severe dyspnea who are unable to follow the FRC measurements with a "linked" ERV maneuver, instruct the patient to take a deep breath (IC maneuver).
4.	The patient may come off the mouthpiece between successive "linked" FRC and IC determinations and also between the separate VC maneuvers needed to calculate RV.

REVIEW OF TEST RESULTS

1. Final review of data on report should be checked for accuracy and completeness by the individual performing the testing, and/or by the laboratory manager or supervisor.
2. The accuracy of the final report in the hospital information system should be checked periodically.

REPORTING OF TEST RESULTS

1. Static lung volumes are expressed in liters (L) and reported at body temperature and pressure saturated with water vapor (BTPS).
2. The average FRC value should always be reported (ideally including the variability) with the method used to derive the value (e.g., FRC_{pleth}, FRC_{He}, and FRC_{N2}).
3. The largest VC should be reported.
4. The mean values are reported for IC and ERV.
   - 4.1. The technologist's quality statements should clarify which method was used for reporting IC or ERV and the reason for selecting the method (e.g., "Patient had difficulty providing consistent ERV values, but IC was repeatable").
5. The reported value for RV is the reported value for FRC minus the mean of technically acceptable ERV measurements linked to technically acceptable FRC determinations.
6. The reported value for TLC is the reported value for RV plus the largest of technically acceptable IVCs.

PROCEDURE NOTES

1. Various miscellaneous factors may affect the measurement of lung volumes.
   - 1.1. Perforated eardrums can cause a leak in the dilution/washout lung volume measurement system. The patient can wear earplugs to remedy this problem.
   - 1.2. Diurnal variations in lung function may cause differences, so if serial measurements are to be performed, the time of day when those measurements are made should be held constant.
   - 1.3. The best sequence of lung volumes and spirometry is controversial.
2. Adjustment for altitude is not necessary from sea level up to 1,800 meters (11–13).

3. Interpretation of lung volume data when test acceptability criteria are not met, or only one measurement should be done with caution.
   3.1. When acceptability criteria are not met, data should be reported with the warning that the data are sub-optimal.
   3.2. When only one FRC_{N2} or FRC_{He} is obtained, interpretation should be made with caution.
4. Choice of reference equations may affect the final interpretation.
5. Multiple-breath gas dilution/washout FRC is usually underestimated in individuals with moderate to severe airflow limitation and air trapping.
6. FRC_{pleth} will be overestimated in patients with severe airway obstruction, or induced bronchospasm unless a slow panting speed (i.e., approximately 1 cycle per second) is maintained.
7. Physical and mental impairment, or other conditions may limit the patient's ability to adequately perform the test in an acceptable and reproducible manner.
8. Non-panting measurements (i.e., occlusion during quiet breathing) have been suggested for use in children or other individuals who have difficulty mastering the panting maneuver (14). However, an inspiratory effort that is too slow will not assure adiabatic conditions are maintained in the plethysmograph. Non-panting maneuvers that do not have the rapid inspiratory maneuver in plethysmographs with built-in thermal leaks may invalidate FRC_{pleth} measurements (15).
9. Computer-derived pressure/volume slopes may be inaccurate if the system calculates slopes using a best-fit regression, as erroneous data may be included (16, 17). Technologists should review the computer selection of fit-line to assure correctness.
10. Excessive abdominal gas or panting techniques using accessory muscles may slightly increase the measured FRC_{pleth} value, due to compression effects (18).
11. Patient leaks may not be apparent during the FRC_{He} test.
12. If a bacterial filter is used, and with children especially, the added volume needs to be subtracted from the FRC. Changes in pressure in the lungs are isothermal but in the filter, adiabatic, so efforts to keep the dead volume (e.g., filter and connectors before the body box shutter) as small as possible are important.

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APPENDIX 8.1

Calculations for FRC_{N2}

$$FRC_{N2} = \frac{(\text{gas volume washed out}) \times F_{N2}2 - (N_2 \text{ volume from tissue})}{F_{N2}1 - F_{N2}2}$$

Where: $F_{N2}1$ = fractional concentration of N_2 in the end-tidal air before the 1st breath of washout

$F_{N2}2$ = fractional concentration of N_2 in the volume of gas washed out at the end of the test

Note: FRC_{N2} should be corrected to BTPS conditions and the volume of the equipment dead space subtracted.

$$N_2 \text{ Tissues Excertion } (\text{ml}) = \frac{(\text{BSA} \times 96.5) + 35}{0.8}$$

Where: BSA is body surface area in m^2 and determined by using:

$$\text{BSA}\left(\text{m}^2\right) = 0.007184 \times \text{weight(Kg)}^{0.425} \times \text{height(cm)}^{0.725}$$

APPENDIX 8.2

Calculations for FRC_{He}

The initial Helium content of the apparatus is redistributed to include the subject's lung volume at the time of connection to the apparatus (FRC_{He}) as follows:

$$V_{app} \times F_{He}1 = \left(V_{app} + FRC_{He}\right)\left(F_{He}2\right)$$

Rearranging to solve for FRCHe yields:

$$FRC_{He} = \frac{V_{app}\left(F_{He}1 - F_{He}2\right)}{F_{He2}}$$

Where: Vapp is the known initial volume of the spirometer apparatus, $F_{He}1$ is the initial He fraction, and $F_{He}2$ is the He fraction after equilibration.

1. FRC_{He} should be corrected for BTPS.
2. No corrections for He absorption should be made (1).
3. V_L includes the dead space of the valve and mouthpiece, which must be subtracted.
4. Correction factors for N_2 excretion during the He equilibration and corrections for He concentration when the respiratory quotient differs from 1.0 can be ignored.
5. Switching Error: In practice, patients are not always at FRC when they are switched into the spirometer circuit. Corrections for this should be made from the spirometer trace when reporting FRC_{He}. Some comput-

erized systems report and account for the switch-in-error automatically, but it is still preferable for continuous recordings of spirometry to be available so the computer-computed adjustments for switch-in-errors can be confirmed by the technologist.

APPENDIX 8.3

Calculations for FRC_{pleth}

The simplified calculation for determining FRC using the plethysmograph is:

$$FRC_{pleth} = -(\Delta V/\Delta P) \times P_B$$

Where: $\Delta V/\Delta P$ represents the slope of the simultaneous changes in body volume, which, in a pressure plethysmograph, represents the small changes in pressure within the box calibrated to reflect changes in volume of the patient versus the change in pressure at the mouth.

P_B = barometric pressure

APPROVAL

Signature: _____ Date: _____

Annual Review

Date	Signature	Date	Signature

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CHAPTER 9

PROCEDURE NAME: AIRWAY RESISTANCE AND RELATED INDICES MEASURED BY BODY PLETHYSMOGRAPHY

PURPOSE OR PRINCIPLE

There are three main measurements of resistance of the respiratory system: (*1*) lung resistance, (*2*) airway resistance (Raw), and (*3*) total respiratory resistance (Rtotal). Lung resistance refers to the collective resistance of the lung tissue and airways and is usually determined with an esophageal balloon in place. Raw refers to the flow resistance in the airways between the mouth and alveoli. Rtotal, as determined with forced oscillation or interrupter techniques, is the sum of the chest wall, lung tissue, and Raw.

There are several ways to measure the various resistances including: using an esophageal balloon, forced oscillation, interrupter device, and the body plethysmograph. This procedure describes the measurement of Raw and related indices (specific conductance and specific resistance) using the body plethysmograph and panting technique (1).

Raw can be described mathematically as follows:

$$R = \Delta P/\dot{V},$$

where R is Raw, ΔP is the pressure difference between the alveoli and the mouth, and $\dot{V}$ is the flow during panting.

Raw is most frequently measured while the patient is enclosed in a whole-body plethysmograph, designed to measure pressure changes and flow. Two maneuvers are required: (*1*) panting with the shutter open, and (*2*) panting with the shutter closed. The following explanation assumes a constant-volume type plethysmograph, though other types can be used.

During the open-shutter panting maneuver, the body plethysmograph (body box) pressure (Pbox) and flow are measured and displayed so that the slope of the relationship (i.e., $\Delta\dot{V}/\Delta$Pbox) can be determined. The resulting display is shown in Figure 9.1. Note that during expiration, Pbox decreases because gas in alveoli is compressed by the pressure needed to generate $\dot{V}$.

Immediately after the open-shutter panting maneuver, the shutter in the system is closed and the patient pants against the closed shutter. The change in mouth pressure (ΔPao) and the change in body plethysmograph pressure (ΔPbox) are then measured and displayed so that the slope of the relationship (i.e., ΔPao/ΔPbox) can be determined. The resulting display is shown in Figure 9.2.

The Raw is obtained from the ratio of the two slopes in the following way:

$$\text{Raw} = \frac{\Delta\text{Pao}/\Delta\text{Pbox}}{\Delta\dot{\text{V}}/\Delta\text{Pbox}}$$

or

$$\text{Raw} = \frac{\Delta\text{Pao}}{\Delta\dot{\text{V}}}$$

There is an inverse and hyperbolic relationship between Raw and lung volume. That is, as one takes a bigger breath and lung volume increases, Raw decreases. Conversely, as lung volume decreases, Raw increases.

To adjust for this volume effect, Raw is commonly expressed as the reciprocal form (1/Raw), airway conductance (Gaw). Unlike Raw, there is a direct (almost linear) relationship between lung volume and Gaw. That is, as lung volume increases, Gaw increases in a linear fashion. Conversely, as lung volume decreases, Gaw decreases.

As Raw is most commonly measured in a body plethysmograph, lung volume–adjusted measurements may also be made. The lung volume–adjusted Raw and Gaw measurements are called specific resistance (sRaw = Raw × lung volume) and specific conductance (sGaw = Gaw / lung volume), respectively. Lung volume–adjusted values are important parameters to assess the effects of varying lung volumes and reducing the variability due to differences in lung inflation. For example, in the healthy lung, increasing lung volume will correspond to a decrease in Raw. The sGaw at the increased lung volume would be near the sGaw obtained at functional residual capacity (FRC). However, when individuals with airflow limitation (e.g., asthma, chronic bronchitis, emphysema, and peripheral airways disease), with or without hyperinflation, are instructed to pant, they invariably perform Raw measurements at lung volumes above FRC. The Raw value at the higher lung volume will be lower relative to the Raw at FRC. But unlike in the healthy lung, the lung volume adjusted measurement (sGaw) will be reduced, which indicates airflow limitation (2, 3).

In the United States, most commercial manufacturers supply constant volume, variable-pressure total-body plethysmographs. Because of their design and with resultant frequency–response characteristics, the "panting" method is employed when determining Raw. An alternative technique that measures Raw during quiet breathing may be available on some systems, but is not as well validated as the standard panting technique.

During Raw measurements, the patient is seated with the lips firmly attached to a flow-sensing device, wears a nose clip, and supports the cheeks with fingertips. The patient is instructed to gently pant (moving ≃ 50 to 100 ml of air/breath). The pant frequency is generally in the range of 1.5 to 2 breaths/sec. During this panting phase, $\Delta\dot{\text{V}}/\Delta\text{Pbox}$ is displayed on the computer monitor. When enough technically acceptable pants are obtained (typically three), the shutter is closed and $\Delta\text{Pao}/\Delta\text{Pbox}$ is measured, allowing for the measurement of the lung volume at which Raw was obtained.

Therefore, during Raw measurements performed in a total-body plethysmograph, the patient should be allowed to select the lung volume at which he/she feels most comfortable performing the maneuver (and should not be forced to pant at FRC), since derived values will be lung volume–adjusted (as sRaw and/or sGaw). Having the patient feel comfortable during the testing process will generally result in more consistent (technically acceptable) tests being obtained in a shorter period of time.

Raw is reported in cm H_2O/L/s. Specific conductance is reported in L/s/cm H_2O/L, which is the reciprocal of Raw (1/Raw) divided by the lung volume at which the Raw measurement was made. Raw is generally measured and reported to reflect the mean of both inspiratory resistance (Raw,insp) and expiratory resistance (Raw,exp) values. However, Raw,exp and Raw,insp can be measured and reported separately. As with forced expiratory and forced inspiratory spirometry (flow–volume loops), open-shutter Raw loops have definite shapes (morphologies) that are indicative of specific airway disorders. Because of these specific morphologies

the laboratory should determine whether either Raw,insp or Raw,exp should be included as part of the data in a final report.

Measurements of Raw alone are limited, since lung volume does play such an integral role. Therefore, lung volume–adjusted values should be included when assessing the presence or degree of pulmonary dysfunction. Raw is commonly elevated with active asthma, chronic bronchitis, vocal cord stenosis, airway tumors, and small lung size (e.g., short stature individuals). Raw is often normal in emphysema, peripheral airways diseases, and possibly during asymptomatic asthma. sGaw is reduced in the presence of asthma, chronic bronchitis, peripheral airways disease and is normal in the presence of decreased lung size. Indications for Raw measurement are provided in Table 9.1

Table 9.1

Potential Indications for Raw Include
• Further evaluation of airflow limitation beyond spirometry (4)
• Determining the response to bronchodilator (5)
• Determination of bronchial hyperreactivity in response to methacholine, mannitol or isocapnic hyperventilation (6, 7)
• Differentiating types of obstructive lung diseases having similar spirometric configurations.
• Distinguishing respiratory muscle weakness from obstruction as the cause of low flow rates
• Following the course of disease and response to treatment (4)

Table 9.2

Relative contraindications for Raw Include
• Mental confusion, muscular incoordination, body casts, or other conditions that prevent the patient from entering the plethysmograph cabinet or adequately performing the required maneuvers (i.e., panting against a closed shutter).
• Claustrophobia that may be aggravated by entering the plethysmograph cabinet
• Presence of devices or other conditions, such as continuous intravenous infusions with pumps or other equipment that will not fit into the plethysmograph, that should not be disconnected, or that might interfere with pressure changes (e.g., chest tubes, transtracheal O_2 catheter, or ruptured eardrum)
• Continuous O_2 therapy that should not be temporarily disconnected
• Inability to pant in a smoothly coordinated fashion

EQUIPMENT AND SUPPLIES

1. System description (e.g., XYZ Corp., Model 101 body plethysmograph)
2. Flow and volume measuring device used in the plethysmograph should meet or exceed American Thoracic Society (ATS)/European Respiratory Society (ERS) performance recommendations (8, 9)
3. Either pressure, volume, or flow-type plethysmograph may be used (4)
4. Transducers in the plethysmograph should meet the following specifications (10)

Mouth Pressure:	± 20 to 50 cm H_2O
Box Pressure:	± 2 cm H_2O (with a 500-L box)
Flow:	< 2 L/s

5. Mouthpiece, nose clip, and other equipment or supplies needed (e.g., facial tissue)
6. Calibration supplies

PATIENT PREPARATION (PRE-TEST INSTRUCTIONS)

1. Patients should be asked to refrain from smoking for at least 1 hour before testing. The time of the last smoking event should be recorded.
2. The test should be performed at least 1 hour after eating and physical activity (to avoid bronchospasm).
3. Supplemental oxygen (O_2) and pumping intravenous infusions should be discontinued before entering the plethysmograph.
4. If pre- and post-bronchodilator testing is to be performed, the patient should avoid using bronchodilators prior to testing, using the same schedule as for spirometry.

Assessment of Patients

1. Assess each patient for physical and developmental status to determine ability to undergo the diagnostic test(s) and if special arrangements are required. If there is a language barrier, an interpreter will be used.
2. Ask each patient if he/she has complied with the patient-preparation criteria including:
    2.1. If they have recently smoked, and if they have, the time.
    2.2. Time of his/her last meal.
    2.3. Time he/she took medications for the lungs, and what types.
3. Postponement may be necessary if the patient has not met the preparation criteria. The ordering physician is to be contacted to determine if rescheduling is necessary.
    3.1. In the event the ordering physician cannot be contacted, the laboratory medical director (or designee) should determine if testing should proceed.
4. In order to properly interpret the test results, relevant clinical information (i.e., diagnosis, treatment) and the clinical indication for ordering the test must be provided in writing by the ordering physician.

EQUIPMENT PREPARATION AND CALIBRATION CHECKS

1. Preparation

1.1. Turn on the equipment and allow adequate warm-up time.
1.2. Ensure the door seal is leak free each day of use. Describe your leak-assessment procedure, as noted in the operator's manual.
1.3. Check mouth shutter closing speed and ease of: activation, closure and release. The shutter should not stick or close slowly.

2. Calibration Check (Verification)

2.1. Equipment calibration should be performed at least once each day before testing patients and every four hours during use (4, 8)
   1. Calibration of multiple pressure transducers is necessary. The technologist should use a water manometer (or equivalent method) that is capable of accurately providing a pressure of ±20 cm H_2O (for calibration of mouth pressure transducer), a 30- to 50-ml sine-wave pump (for calibration of box pressure) and a method for calibration of the flow-sensing device (4).
   2. On some systems, the calibration syringe is used to calibrate (verify) flow

2.2. Volume-measuring device calibration verification with a 3.00-L calibrating syringe should be performed each day testing is performed (8, 11).
   1. The accuracy validation limit for recovered volume is ±3.5% of the syringe standard.

PROCEDURE

Pre-Test Preparation		
Step	**Action**	
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition.	
	IF	THEN
	Patient unable to provide information	• Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information
	The identifiers do not match	• Contact registration • Resolve discrepancies before proceeding
	The ID band is present but not attached to the patient	• Do not proceed. • Notify patient's nurse or registration desk
2.	Check for a complete physician's order.	
3.	Collect and record demographic information.	
4.	Explain and demonstrate test maneuver and have patient seated comfortably. Advise the patient they will have to remain seated throughout the test. Instruct the patient to keep a tight lip seal and to give maximum effort. A tight-fitting nose clip should be properly in place.	

Test Procedure	
Step	**Action**
1.	Explain and demonstrate the procedure to the patient. Emphasize the following: a. The importance of relaxing and breathing "normally" between measurements b. The need to "pant" while supporting the cheeks with the fingertips. The panting maneuver (during open and closed shutter) requires that the breaths are: • Small (≃ 50 to 100 ml) • Slow (Raw ≃ 1.5 to 2.0 breaths/s) • Uniform (equal volume in and out) Use descriptive phrases such as • Open shutter: panting like a "little piston," or "like a dog" • Closed shutter: "like panting with your hand over your mouth" Reassure the patient constantly, to reduce anxiety associated with the test or from sitting in the closed booth, emphasizing that the test should take less than 5 minutes. If the patient desires, the test can be stopped at any time and the door opened to allow him/her to relax before subsequent measurements are made. The door may be released from the inside at any time (manufacturer specific). Assure the communication device is operational (manufacturer specific). Close the plethysmograph door and allow thermal equilibration. Observe the plenum (or similar device) to assure thermal equilibration (4).
2.	Instruct the patient to insert the mouthpiece into the mouth, assuring the tongue and/or teeth are not blocking the mouthpiece port. Have the patient apply the nose clip on the nose, support the cheeks using the fingertips, and relax the shoulders and breathe "normally."
3.	Activate the computer
4.	Instruct the patient to begin panting small (≃ 50 to 100 ml/pant), uniform pants and at a frequency between 1.5 and 2.0 breaths/s. Open-shutter loops should be closed (or nearly so), and linear (non-elliptical), particularly within the range of +0.5 to -0.5 L/s (*see* Figures 9.3–9.5). The entire tracing should be visible and within the calibrated pressure range. Once two to three acceptable open-shutter loops have been collected, close the mouth shutter and instruct the patient to continue panting. The displayed Pao/Pbox loop should be closed or nearly so. Acceptable pressure changes should be within the calibrated pressure range of each transducer. The entire tracing should be visible. Pressure changes that are too large or too small may yield erroneous results. During closed-shutter loop data collection, the shutter should be closed for only a brief period of time (e.g., ≃ 2 seconds) as longer time may cause undue patient discomfort.
5.	Repeat open- and closed-shutter panting maneuvers until four or five technically acceptable tests are obtained. Assure the patient returns to tidal breathing between maneuver performance. Discourage deep inspiration as lung inflation could provide a bronchodilatory or bronchoconstrictive effect. Encourage patient's performance during each attempt, offering suggestions on how to improve on subsequent maneuvers (e.g., "slow the panting frequency," "pant using smaller volumes," "do the same on the next attempt"). Ask the patient if he/she is able to continue or does he/she need a rest period.
6.	Visually inspect each maneuver to ensure it meets acceptability criteria, there was no evidence of thermal drift and the panting frequencies were similar. Some individual's Raw values get worse at higher panting frequencies, possibly because of uneven time constants within the airways ("frequency dependence of resistance") (13) If serial measurements are to be performed, the panting frequency should be kept the same to aid in the interpretation (4).
7.	Adjust computer measured open- and closed-shutter slopes, if necessary.

REVIEW AND REPORTING RESULTS

1. The reported Raw and related indices
   - 1.1. Should be calculated from the ratio of open- and closed-shutter tangents for each maneuver (14).
   - 1.2. Should be averaged from three to five separate, acceptable maneuvers (which may require as many as 8 to 10 trials) (15).
   - 1.3. Should have the open shutter tangent ($\dot{V}$/Pbox) measured between flows of +0.5 to −0.5 L/s (4). For loops that display hysteresis, the inspiratory limbs may be used and the report should contain a comment noting this (14).
2. Report of test results should contain a technologist's statement about test quality, patient's understanding of testing process, and, if appropriate, which criteria were not achieved (4, 8, 9, 16).

PROCEDURE NOTES

1. Various miscellaneous factors may affect this test.
   - 1.1. Certain pathologic conditions can cause a leak in the lung measurement system (e.g., leak around mouthpiece).
   - 1.2. Diurnal variations in lung function may cause differences (particularly in the patient with asthma). Thus, if serial measurements are to be performed, the time of day that measurements are made should be held constant (16).
   - 1.3. Raw measurements should precede forced expiratory maneuvers, which may cause bronchospasm and alter resting values.
     - 1.3.1. Other confounding factors that could influence resting Raw values include exposure to environmental pollution, cold air, allergen, exercise, or the type of medication the patient is taking (e.g., bronchodilators and steroids).
   - 1.4. The patient with asthma should refrain from performing deep inspirations, which could alter Raw values (17, 18).
   - 1.5. Physical and mental impairment, or other conditions, may limit the patient's ability to perform the test adequately in an acceptable and repeatable manner (4).
     - 1.5.1. Claustrophobia may be aggravated by entering the plethysmograph cabinet (4).
2. Some patients are unable to perform the necessary panting maneuver required for Raw determination.
3. Choice of reference equations may affect the final interpretation (1, 19).
   - 3.1. Interpretation of test data that are not acceptable should be reported with a warning that data are suboptimal.
4. Non-panting measurements have been suggested for use in children or others who have difficulty mastering the panting maneuver (20). Non-panting maneuvers in plethysmographs with built-in thermal leaks may invalidate thoracic gas volume (TGV) measurements (21). In addition, non-panting (tidal breathing) technique has been reported to overestimate sRaw compared to panting in children (23).
5. Computer-derived TGV slopes may be inaccurate if the system calculates slopes using a best-fit regression, as erroneous data may be included (22).
6. Bacterial filters cause a small difference in Raw in children, but it is not considered clinically significant (24).

Pediatric Considerations

As a tidal breathing maneuver, sRaw may be measured as young as the preschool years, though commercial devices generally lack incentives to aid the child in breathing gently and regularly. A parent may accompany the child into

the plethysmograph to improve cooperation. The technique is feasible in approximately 80% of 3- to 6-year-olds and nearly 100% of 5- to 6-year-olds (25). A specially adapted facemask may be used to prevent nasal breathing. However, equal success has been demonstrated in 3- to 6-year-olds when using a nose clip and mouthpiece (25).

In contrast to infant lung function and preschool spirometry, there exists no consensus with respect to sRaw measurement conditions, quality control, methods of analyzing and reporting results, or outcome measures for young children (26).

Current default values for reference equations in commercially available equipment are based on data collected under BTPS conditions, rather than the electronic thermal compensation that is now applied. These equations generally under-estimate values observed in healthy children, and thus over-estimate morbidity in those with lung disease. In addition, the existing reference equations were developed from measurements with methodological differences, so that reported mean (SD) predicted values in young children range from 0.55 (0.18) to 1.29 (0.30) kPa·s (27). Although sRaw is relatively constant during the preschool years, it appears to decrease slightly with age and is also lower in girls than boys, such that predicted values and the upper limit of normal should ideally be derived from reference equations rather than a fixed threshold (27). In contrast to spirometric parameters, ethnic group does not appear to influence measures of sRaw, as this variable is internally adjusted for lung volume.

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APPENDIX 9.1

Checklist for Acceptable Test and Repeatability Criteria for Raw Measurements (7)

1. Use of equipment that has undergone quality control.
2. Proper positioning of patient, assuring mouthpiece and nose clip are positioned appropriately, with cheeks supported with fingertips.
3. Panting frequency between 1.5 to 2.0 pants/s with entire open- and closed-shutter loops displayed within calibrated range.
   3.1 Open-shutter loops are linear, non-elliptical and closed (or nearly closed).
4. Adjustment of open shutter loops between +0.5 L/s and −0.5 L/s.
5. Closed shutter loops (for determining TGV) adjusted as center fit.
6. Perform at least four to five technically acceptable trials.
7. The average of at least four to five technically acceptable trials that agree within ≤10% of the mean value is reported.
8. Technologist's quality statements about patient's understanding of test instructions, his/her level of participation in testing process, and notation if the reported results do not comply with laboratory standardization criteria.

APPENDIX 9.2

Examples of Open- and Closed-Shutter Loops for Raw Measurements

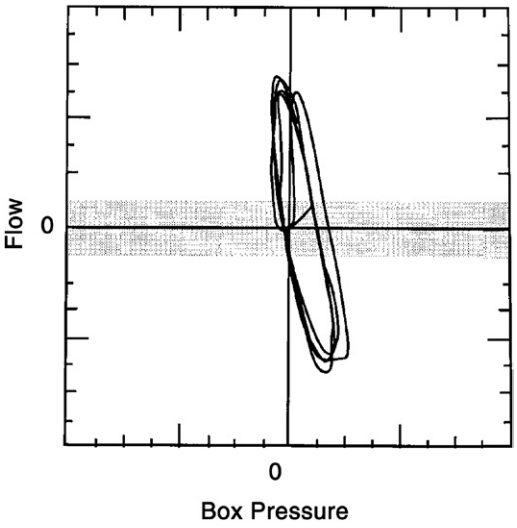

Figure 9.1 Open-shutter loop. Graphic representation of an open-shutter Raw loop whereby ΔBox Pressure are plotted against ΔFlow.

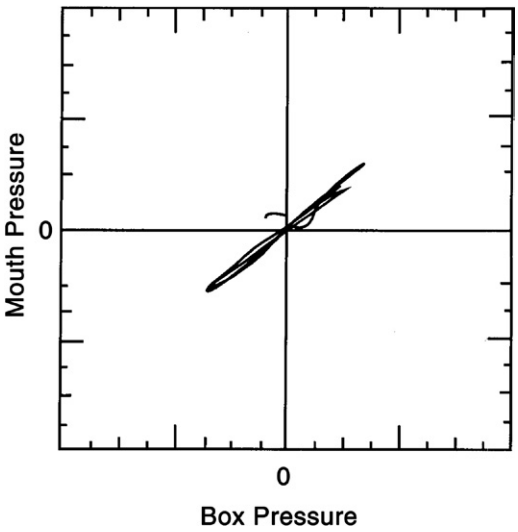

Figure 9.2 Closed-shutter loop. Depiction of tracing derived when the mouth shutter closes and the patient pants against it, alternately compressing and decompressing the thoracic gas, with resultant ΔMouth Pressure plotted against ΔBox Pressure.

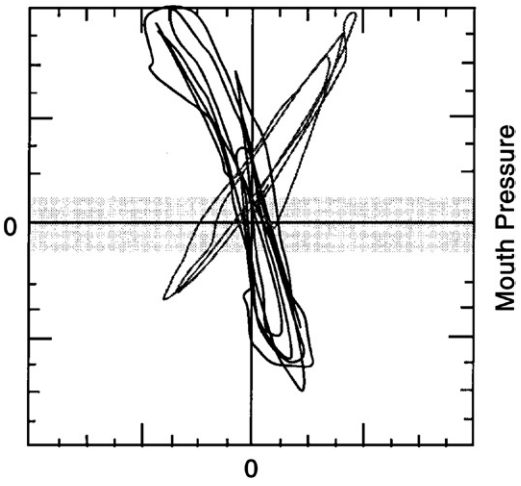

Figure 9.3 Open- and closed-shutter loops. Representation of the combined loops (superimposed) as commonly depicted with commercially available Raw measurement software. Absolute configurations are dependent upon the specific manufacturer.

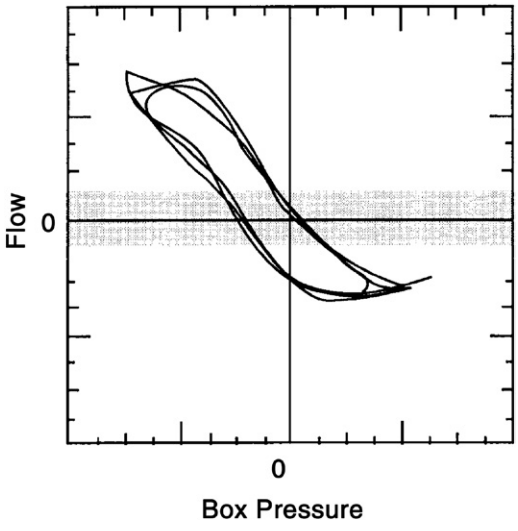

Figure 9.4 "Too slow." Graphic representation of open-shutter loops with a patient panting too slowly. Generally, this pattern occurs when the panting rate is less than 1.5 cycles/s. This is easily corrected by having the patient increase the panting speed without changing the volume per pant. However, a similar pattern is commonly encountered with patients having large amounts of trapped gas which, despite increasing the pant frequency, will not result in loop closure.

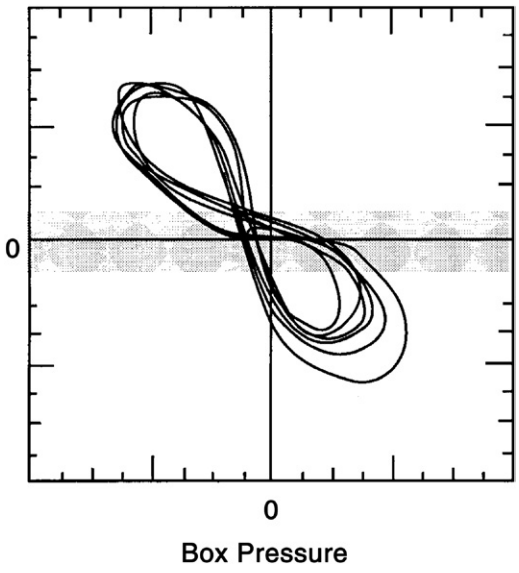

Figure 9.5 "Too fast." Graphic representation of the patient panting too rapidly and either exceeding the frequency response characteristics of their plethysmograph or inhomogeneity of time constants between lung units. This situation is commonly remedied by instructing the patient to slow down panting frequency. Use of a metronome or similar device helps the technologist develop the optimal panting frequency.

APPENDIX 9.3

Calculations

Raw:

$$\text{Raw} = \frac{\text{slope of closed} - \text{shutter panting}}{\text{slope of open} - \text{shutter panting}} - \text{Rapp}$$

or

$$\text{Raw} = \frac{\Delta\text{Pao}/\Delta\text{Pbox}}{\Delta\dot{\text{V}}/\Delta\text{Pbox}} - \text{R}_{\text{app}}$$

Where: R_{app} = Correction factor for the resistance of the apparatus (determined by the laboratory or supplied by the manufacturer)

TGV:

$$\text{TGV} = \text{PB} \times \frac{1}{\text{closed} - \text{shutter panting}} \times \frac{\text{Pbox calibration factor}}{\text{Pao calibration factor}}$$

Where: PB = Barometric pressure minus water vapor pressure at 37° C (in cm H_2O)

Note: 1.36 converts mmHg to cm H_2O

$$\text{slope} = \Delta\text{Pao}/\Delta\text{Pbox}$$

$$\text{Specific resistance} : \text{sRaw} = \text{Raw} \times \text{TGV}$$

$$\text{Specific conductances} \text{Gaw} = \text{Gaw}/\text{TGV}\ , \quad \text{where Gaw} = \frac{1}{\text{Raw}}$$

APPENDIX 9.4

Sample Raw Calculation

Conditions

Calibration (cal) and calculation factors:

Flow $\dot{V}$ = 1.0 L/s/cm
Mouth pressure (Pao) = 2.5 cm H_2O/cm
Body box pressure (Pbox) = 10 ml/cm
Body Box breathing system resistance (Rapp) = 0.2 cm H_2O/L/s
PB (corrected for water vapor pressure at 37° C) = 970 cm H_2O

Step 1: Calculate Raw

$$\text{Raw} = \frac{\text{slope of closed} - \text{shutter panting maneuver}}{\text{slope of open} - \text{shutter panting maneuver}} \times \text{cal factors} - \text{Rapp}$$

$$\text{Raw} = \frac{\Delta\text{Pao}/\Delta\text{Pbox}}{\Delta\dot{V}/\Delta\text{Pbox}} \times \frac{\text{Pao cal factor/Pbox cal factor}}{\text{V cal factor/Pbox cal factor}} - \text{Rapp}$$

The slopes can be measured as the tangent of the angle. The slope of the open-shutter panting maneuver is measured to be 55°, resulting in a tangent of 1.428. The slope of the closed-shutter panting maneuver is measured to be 45°, resulting in a tangent of 1.000. Substituting these values and the calibration factors yields:

$$\text{Raw} = \frac{1.000}{1.428} \times \frac{\frac{2.5 \text{ cm } H_2O/\text{cm}}{10 \text{ ml/cm}}}{\frac{1 \text{ L/s/cm}}{10 \text{ mL/cm}}} - \text{Rapp}$$

$$\text{Raw} = 0.700 \times 2.5 \text{ cm } H_2O/\text{L/s} - 0.2$$

$$\text{Raw} = 1.55 \text{ cm } H_2O/\text{L/s}$$

Step 2: TGV

$$\text{TGV} = \text{PB} \times \frac{1}{\text{slope of closed} - \text{shutter panting}} \times \frac{\text{Pbox cal factor}}{\text{Pao cal factor}}$$

$$\text{TGV} = 970 \text{ cm } H_2O \times \frac{1}{1.00} \times \frac{10 \text{ ml/cm}}{2.5 \text{ cm } H_2O/\text{cm}}$$

$$\text{TGV} = 970 \text{ cm } H_2O \times 4 \text{ ml/cm } H_2O$$

$$\text{TGV} = 3,880 \text{ ml}, \text{ or } 3.88 \text{ L}$$

Step 3: Calculate Gaw, sGaw, and sRaw

Use the Raw and TGV results to calculate lung volume–adjusted Raw values: Gaw, sGaw, and sRaw

$$\text{Gaw} = \frac{1}{\text{Raw}} = \frac{1}{1.55} = 0.65$$

$$\text{sGaw} = \frac{\text{Gaw}}{\text{TGV}} = \frac{0.65}{3.88} = 0.17 \text{ cm } H_2O/\text{L/s/L}$$

$$\text{sRaw} = \text{Raw} \times \text{TGV} = 1.55 \times 3.88 - 6.01$$

APPROVAL

Signature: _____ Date: _____

Annual Review

Date	Signature	Date	Signature

Revisions / Document History

Effective Date	Synopsis of Change

Effective Date: 2017
Version #2

CHAPTER 10

PROCEDURE NAME: SINGLE-BREATH CARBON MONOXIDE UPTAKE IN THE LUNG (DIFFUSING CAPACITY [D_{LCO}], TRANSFER FACTOR [T_{LCO}])

PURPOSE OR PRINCIPLE

The diffusing capacity of the lung for carbon monoxide (D_{LCO}), also referred to as the transfer factor of the lung for carbon monoxide (T_{LCO}), is used to evaluate the transfer of gas from the alveolar air spaces into the pulmonary capillaries. It can be measured when known and very low concentrations of carbon monoxide (CO) are inspired. The rate of CO disappearance is calculated from the ratio of the CO concentrations of the inspired and expired gas and then expressed as a function of the driving pressure (ml CO/min/mm Hg). This can be expressed in the equation below:

$$D_{LCO} = \dot{V}_{CO} / \left(P_{ACO} - \overline{P}C\,CO\right)$$

Where: $\dot{V}_{CO}$ is the uptake of CO in ml of CO at STPD conditions per minute

P_{ACO} is the average partial pressure of CO in alveoli

$\overline{P}C$ CO is the average partial pressure of CO in the pulmonary capillary plasma

Because hemoglobin (Hb) has a very high affinity for CO, the partial pressure of CO in the plasma ($\overline{P}C$) can be considered zero when the carboxyhemoglobin (COHb) concentration is low (1 to 3%). The equation then becomes:

$$D_{LCO} = \dot{V}_{CO} / P_{ACO}$$

Thus, all physiologic methods of assessing D_{LCO} involve two steps: (1) measuring the rate of CO uptake, and (2) estimating CO driving pressure (1). Carbon monoxide uptake is usually measured as the product of a concentration change over time multiplied by alveolar volume (V_A); CO driving pressure is calculated by multiplying the inhaled CO concentration times the ratio of inspired volume (V_I) to the V_A, and the barometric pressure.

The 10-second, single-breath breath-holding technique is the most widely used. It was introduced by Marie Krogh (2) in 1915, and later refined by Forster and coworkers (3), Ogilvie and coworkers (4), and McGrath and Thomson (5). Two alveolar gas sampling techniques following the 10-second, single-breath have emerged: (*1*) an

alveolar gas sample in a bag/chamber, and (*2*) measuring exhaled gas concentrations continuously during exhalation using a rapid response gas analyzer.

Breath-hold with alveolar sample bag/chamber: In this technique, the patient inhales a volume of test gas usually containing 10% helium (He) or 0.3% methane (CH_4) as a tracer gas, 0.3% CO, and 21% oxygen (O_2) with the balance nitrogen (N_2). The test gas is held in the lungs for approximately 10 seconds, and after enough gas is exhaled to wash out the mechanical and anatomical dead space a gas sample is collected in a bag or chamber for analysis.

Breath-hold with a rapid response gas analyzer: In this technique, the patient inhales a volume of test gas containing 0.3% methane or other tracer gas, 0.3% CO, 21% O_2, and the balance N_2. Again the test gas is held in the lungs for approximately 10 seconds, and then during exhalation the tracer gas and CO concentrations are analyzed continuously by a rapid response gas analyzer, eliminating the need to collect gas in a sample bag or chamber (6).

While using a single D_{LCO} value to summarize individual CO uptake properties of millions of lung units is a limitation of this test, measuring an "overall" CO uptake has proved to be clinically useful. In the presence of various systemic disease processes and lung abnormalities that affect alveolar–capillary gas transport, D_{LCO} can be increased or decreased (7).

Increases in D_{LCO} occur in:

- Polycythemia
- Pulmonary hemorrhage
- Diseases associated with increased pulmonary blood flow
- Exercise
- Asthma
- Mueller maneuver

Decreases in D_{LCO} occur in:

- Emphysema
- Parenchymal lung diseases (e.g., interstitial pulmonary fibrosis)
- Pulmonary involvement in systemic diseases
- Diseases or conditions that result in reduced effort or respiratory muscle weakness
- Cardiovascular diseases
- Pulmonary embolism
- Anemia
- Hemoglobin binding changes (e.g., increased COHb)
- Valsalva maneuver
- Pulmonary edema, vasculitis, or hypertension

INDICATIONS AND CONTRAINDICATIONS

Some indications for D_{LCO} are provided in Table 10.1.

There are no significant contraindications for the D_{LCO} test other than the considerations listed under "Special safety precautions" below.

EQUIPMENT AND SUPPLIES

1. System description (e.g., manufacturer, model, type, accessories, additional features, and software version). The system should meet or exceed recommendations made in the latest ATS/ERS standardization document on D_{LCO} (7).
2. Cylinder of test gas appropriate for the testing system.

Table 10.1

Indications for D_{LCO} include (8, 9)
• Evaluation and monitoring of diseases which involve lung parenchyma (e.g., those associated with dusts, drug reactions, or sarcoidosis)
• Evaluation and monitoring of emphysema
• Differentiating among chronic bronchitis, emphysema, and asthma
• Evaluation and monitoring of pulmonary involvement in systemic disease
• Evaluation of cardiovascular diseases
• Prediction of arterial desaturation during exercise in some patients with lung disease
• Evaluation and quantification of impairment and disability associated with interstitial lung diseases and emphysema
• Evaluation of the pulmonary effects of chemotherapy agents or other drugs known to induce pulmonary dysfunction
• Evaluation of pulmonary hemorrhage

3. Mouthpiece, nose clip, carbon dioxide (CO_2) and water absorbers (if applicable), and other miscellaneous supplies needed (e.g., tissues).
4. Infection control supplies: disposable in-line filters (if used), gloves, gowns, masks, and protective eye wear (if applicable).
5. Computer/printer supplies.

PATIENT PREPARATION (PRE-TEST INSTRUCTIONS)

1. The patient should refrain from smoking or other CO exposures on the day of the test. The time of the last cigarette smoked should be recorded and noted in interpretation. Because air pollution may also result in higher COHb, exposure to high levels of air pollution should be noted. A correction for CO back-pressure should be made for recent or heavy cigarette smoking.
2. Measure patient's height in centimeters (cm) to nearest cm, or in inches (in) to nearest ½ in, while he/she is standing erect, without shoes.
3. The patient's weight should be measured using an accurate scale: weight is not required for reference values for D_{LCO}, but may be useful for interpretive purposes. Some systems use weight to estimate the anatomic dead space.
4. The patient's age should be recorded as age on day of test.
5. The D_{LCO} test should be done in the sitting position, with the patient sitting quietly for at least 5 minutes before testing and remaining seated throughout the procedure.
6. The patient should refrain from heavy exercise immediately before the test and refrain from having a large meal for at least 2 hours before the test.
7. Ingestion of ethanol has been reported to decrease D_{LCO} (18, 29). The mechanisms involved are not clear, although it is known that some fuel-cell CO analyzers are sensitive to exhaled ethanol and ketones. One suggestion is to have the patient refrain from drinking alcohol for at least 4 hours before testing.

8. If clinically acceptable, supplemental O_2 should be discontinued for 10 minutes before beginning the test. If this cannot be done safely, O_2 should be adjusted appropriately and recorded so that the results can be interpreted accordingly.
9. The patient's race or ethnicity should be determined from questioning the patient. While not currently included in published reference equations (which are usually based on Caucasian populations), it can be useful for interpretive purposes.

ASSESSMENT OF PATIENTS

1. Assess each patient for physical and developmental status to determine ability to perform the diagnostic test and if special arrangements are required. If there is a language barrier, an interpreter will be used.
2. Patients should be asked if they have complied with the preparation criteria including:
   - 2.1. If they have recently smoked, and if so, what was the time?
   - 2.2. If they have consumed alcohol within 4 hours of test starting time.
   - 2.3. If they have eaten within 2 hours of test starting time.
   - 2.4. If they have exercised within an hour of test starting time.
3. Postponement may be necessary if the patient has not complied with the preparation criteria. The ordering physician is to be contacted to determine if rescheduling is necessary.
4. In order to properly interpret the test results, relevant clinical information should be provided in writing by the ordering physician (i.e., diagnosis and type of treatment). A recent measurement of hemoglobin concentration should also be obtained. Information on use of respiratory medications in the past 24 hours should also be noted. If the D_{LCO} is measured following the administration of bronchodilators for spirometry testing, this should be noted as well.

SPECIAL SAFETY PRECAUTIONS

The following may pose a relative danger to the patient and/or affect the validity of the test:

1. More than five maneuvers will likely increase the COHb level by approximately 3.5% (10), which in turn will likely decrease the D_{LCO} value by approximately 3–3.5%, and is not recommended (7).
2. A large meal or vigorous exercise immediately before the test (unless using exercise to assess D_{LCO} "recruitability").
3. Mental confusion or poor muscular coordination that prevent the patient from adequately performing the maneuver or the inability to adequately seal their lips on the instrument mouthpiece.

EQUIPMENT PREPARATION AND CALIBRATION CHECKS

1. Preparation

- 1.1. Ensure CO_2 and H_2O absorbers (if applicable) are replaced at a frequency recommended by the manufacturer, when saturated (as indicated by color change), or sooner. Additionally, they should be placed in the proper order (i.e., the CO_2 absorber should precede H_2O absorber). If selectively permeable tubing is used, ensure it has been replaced at appropriate intervals as recommended by the manufacturer.
- 1.2. Turn on the equipment to ensure adequate warm-up time, usually at least 30 minutes.
- 1.3. For D_{LCO} systems using a volume-type spirometer, a leak test of the spirometer should be done according to the manufacturer's specifications.

1.4. Check inspiratory flow from the demand valve (if applicable, the maximal inspiratory pressure required for a 6 L/s inspiratory flow should be less than 10 cm H_2O).

1.5. Ensure gas chromatograph columns, or elements of the gas measuring system with limited life span are replaced at the frequency recommended by the manufacturer.

2. Calibration Check (Verification)

2.1 Each day, prior to testing, there must be a volume calibration check with a 3-L syringe discharged at least three times to give a range of flows varying between 0.5 and 12 L/s (with 3-L injection times of ~6 s and ~0.5 s). The volume at each flow must meet the accuracy requirement of ≤2.5% error. For devices using disposable flow sensors, a new sensor from the supply used for patient tests must be tested each day. The calibration check may need to be repeated during the day if ambient conditions change. Newer systems monitor ambient conditions and make adjustments as necessary or produce a calibration alert when necessary. Older systems may require a calibration check if room temperature changes by more than 3°C or relative humidity changes by more than 15% (absolute).

Operators should also perform a calibration check whenever they notice significant discrepancies between inspired volume (V_I) and VC, or VA and total lung capacity (TLC) that might suggest volume calibration problems.

2.2 Prior to each maneuver, flow and gas analyzers must be zeroed. After each maneuver, a new zeroing procedure must be carried out to account for analyzer drift during the maneuver.

2.3 On a weekly basis, and whenever problems are suspected, the following procedures must be followed:

2.3.1 Perform a D_{LCO} test with a calibrated 3.0-L syringe by attaching the syringe to the instrument in the normal patient test mode. The syringe is emptied and then filled with three liters of test gas. The syringe is then emptied into the mouthpiece after the 10-s breath hold. The calculation of VA must be within 300 ml of 3 L times the STPD to BTPS correction factor, which is 863/(PB-47). Note that a 3-L calibration syringe will have an additional dead space, which, depending on the connection to the mouthpiece, is typically ~50 ml, which must be considered in the VA calculation. The absolute value of the calculated D_{LCO} must be <0.5 ml/min/mm Hg or <0.166 mmol/min/kPa.

2.3.2 A D_{LCO} test should be performed on a "standard subject" (biological control) or simulator. Standard subjects are nonsmokers who have been found to have a consistently repeatable D_{LCO} (e.g., healthy laboratory personnel). If the D_{LCO} in a standard subject varies either by >12% or by >3 ml/min/mm Hg (1 mmol/min/kPa) from the mean of previous values, the test must be repeated. A study of the long-term intersession variability of D_{LCO} found that biological control deviations either >12% or >3 ml/min/mm Hg from the average of the first six tests indicate that the instrument is not within quality control limits and must be carefully evaluated before further patient testing (30).

2.4 Gas-analyzer linearity should be assessed every month. A straightforward approach is to measure known serial dilutions of the test gas, or measure the concentration of a separate high-precision test gas having a certificate of analysis. For systems with independent measurements of CO and tracer gas, the analyzer linearity may also be assessed by comparing the ratio of CO and tracer gas concentrations over arbitrary dilutions of test gas with room air. An alternate linearity check using a calibration syringe is described in the 2017 ATS/ERS guideline (7).

PROCEDURE

Pre-Test Preparation		
Step	**Action**	
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition.	
	IF	THEN
	Patient unable to provide information	• Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information
	The identifiers do not match	• Contact registration • Resolve discrepancies before proceeding
	The ID band is present but not attached to the patient	• Do not proceed. • Notify patient's nurse or registration desk
2.	Check for a complete physician's order.	
3.	Collect and record demographic information.	
4.	Explain and demonstrate test maneuver and have patient seated comfortably. Advise the patient they will have to remain seated throughout the test. Instruct the patient to keep a tight lip seal and to give maximum effort. A tight-fitting nose clip should be properly in place.	

Test Procedure	
Step	**Action**
1.	Instruct the patient to put mouthpiece in mouth and nose clip on nose and breathe quietly.
2.	Activate computer software.
3.	After at least three breaths, instruct patient to exhale slowly (unforced) to residual volume (RV). In obstructive lung disease, where exhalation to RV may require a prolonged period, a reasonable recommendation is that this portion of the maneuver must be limited to <12 s.
4.	When at or near RV, activate the valves using computer and instruct patient to inhale rapidly to total lung capacity (TLC) with a sufficiently high flow so that 90% of the V_I is inspired in less than 4 seconds. V_I must be at least 90% of the largest VC in the same pulmonary function testing session. However, a maneuver may be deemed to be acceptable if V_I is within 85% of the largest VC and the VA is within 200 ml or 5% (whichever is greater) of the highest VA among acceptable DL_{CO} maneuvers.
5.	Coach the patient to hold his/her breath with the lungs held full for 10 ±2 seconds.
6.	Instruct the patient to exhale at a moderate speed.
7.	After an appropriate washout volume has been expired to clear dead space (0.75 – 1.0 L in classical systems and in rapid gas analyzer systems determined by visual inspection or software objective algorithm), collect a gas sample (alveolar sample) or measure the mean exhaled gas concentration over a comparable volume change (rapid gas analyzer systems).
8.	Instruct the patient to come off the mouthpiece, but remain seated.

(continues on next page)

Test Procedure (continued from previous page)	
Step	**Action**
9.	Perform at least two acceptable maneuvers that agree within 2 ml/min/mm Hg (0.67 mmol/min/kPa) of each other.
10.	At least 4 minutes should be allowed between each test maneuver for classical systems. For rapid gas analyzer systems, washout may be complete when the end-expiratory tracer gas concentration is <2% of the tracer gas concentration in the test gas, which may take less than 4 minutes.

REVIEW OF TEST RESULTS

1. Individual test maneuvers are considered acceptable if:
   - 1.1. Properly quality controlled instrumentation was used.
   - 1.2. Inspired volume of test gas (V_I) was at least 90% of largest VC measured in the same pulmonary function test session, and 85% of the V_I was inspired within 4 seconds.
   - 1.3. A stable calculated breath-hold time of 10 ±2 seconds (8 to 12 seconds).
   - 1.4. No evidence of leaks or Valsalva or Mueller maneuvers during the breath hold.
   - 1.5. The appropriate clearance of dead space during the exhalation after the breathhold.

   Note: tests outside the limits set in 1.3–1.5 may still have clinical utility, but deviations from the standard acceptability criteria should be noted and possible impact considered.
2. Assure that anatomical and mechanical dead space are cleared before the alveolar sample is collected. With classical systems, dead space washout volume should be 0.75 to 1.0 L (7). If a patient's VC is less than 2.0 L, the washout volume may need to be reduced to 0.5 L. Sample volume is 50–100 ml (or less than 50 ml if VC is less than 2.0 L). Using a rapid gas analyzer with visual display, these washout and sample volumes can be manually adjusted using the phase 2 to phase 3 transition of the tracer gas concentration to assure an appropriate sample for analysis.
3. Assure that there were at least 4 minutes between maneuvers for classical systems, or for rapid gas analyzer systems washout may be complete in less than 4 minutes and the end-expiratory tracer gas concentration should be <2% of the tracer gas concentration in the test gas.
4. Assure that at least two acceptable maneuvers have been performed.
5. Assure that the Jones-Mead method (11) of calculating breath hold time was used. See Figure 10.1.
6. Assure between maneuver repeatability criteria has been met. The repeatability criteria is at least two acceptable maneuvers agree within 2 ml/min/mm Hg (0.67 mmol/min/kPa) of each other.
7. Adjustments for Hb, COHb, and inspired P_{O_2} should be made prior to interpretation. Hb correction should use the equations of Cotes (*see* Appendix 1) (12).

REPORTING OF TEST RESULTS

1. The average of at least two acceptable maneuvers that meet the repeatability requirement should be reported (i.e., outliers need to be excluded) (7).
2. The report should always include (7):
   - 2.1. Measured uncorrected $D_{L_{CO}}$ and K_{CO} (the use of the term $D_{L_{CO}}$/VA is discouraged)
   - 2.2. Measured $D_{L_{CO}}$ adjusted for barometric pressure
   - 2.3. Predicted $D_{L_{CO}}$ and K_{CO} with the lower limit of normal and z-score
   - 2.4. Percent predicted $D_{L_{CO}}$ and K_{CO}

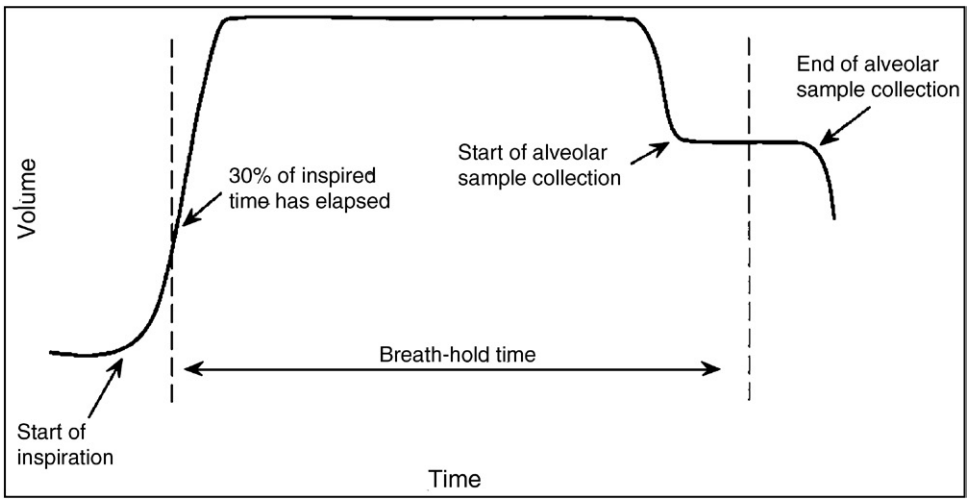

Figure 10.1 Graphic illustration of the Jones-Meade method for calculating the breath-hold time during the D_{LCO} maneuver. The breath-hold time starts after 30% of the time it takes to inspire the test gas has elapsed, and ends halfway into the alveolar sample collection. The beginning of inspiration is determined using the back extrapolation technique, although it has been recently reported that there are no significant differences between the visual and extrapolation approaches (11).

3. Any adjustments (e.g., Hb, COHb, P_{O_2}) should also be reported separately along with the data used to make the adjustment (7).
4. The average V_A (BTPS) should be reported along with the predicted V_A (the predicted TLC minus predicted dead space) and % predicted V_A.
5. The average V_I at BTPS should be reported.

PROCEDURE NOTES

1. Various miscellaneous factors may affect this test.
   1.1. A diurnal variation (1.2–2.2% fall/h from 9:30 A.M. to 5:30 P.M.) has been reported in D_{LCO} (14). However, this fall can be partially explained by increasing COHb and decreasing Hb concentrations (10).
   1.2. A 13% change in D_{LCO} during the menstrual cycle has been reported (17) The highest D_{LCO} values were observed just before and during menses and the lowest D_{LCO} values were observed during week 3 (25).
   1.3. A 15% reduction 90 minutes after ingesting ethanol has been reported on some analyzers (18).
   1.4. Cigarette smoking alters the outcome of this test.
2. An adjustment for COHb is not required but is recommended for interpretation purposes when COHb is clinically elevated. COHb-adjusted D_{LCO} = measured D_{LCO} (1 + %COHb / 100) (7).
3. D_{LCO} increases with increasing altitude (reflects decreased P_{IO_2}) (13). Adjustment equation for altitude-induced changes (i.e., P_{O_2}) is:

   D_{LCO} adjusted for altitude = Measured $D_{LCO} \times [1 + 0.0031(P_{IO_2} - 150)]$, where estimated $P_{IO_2} = 0.21$ (barometric pressure −47), or you can adjust the predicted value:

   D_{LCO} predicted for altitude = D_{LCO} predicted / $[1 + 0.0031(P_{IO_2} - 150)]$
4. When test specifications are not met, such data should be reported with the warning that the data are suboptimal.
5. Small increases in COHb (about 0.7% per inhalation of test gas) occur when CO is inspired during the D_{LCO} test.

6. An adjustment for Hb concentration should be done whenever possible (Appendix 1).
7. Valsalva or Mueller maneuvers during the breath-hold alter D_{LCO}. The Valsalva maneuver will decrease the D_{LCO} by decreasing capillary blood volume. The Mueller maneuver will increase the D_{LCO} by increasing capillary blood volume.
8. Pregnancy (first trimester) has been reported to be associated with an increased D_{LCO} (14). However, two other studies have reported no change during pregnancy (15, 16). Thus, it is unclear whether D_{LCO} changes during early pregnancy.
9. Bronchodilators may affect D_{LCO} (26). The D_{LCO} report should note if the test was done before or after bronchodilator administration.
10. The choice of reference equations may affect the final interpretation. Each laboratory should select reference equations that are appropriate for the methods used and the population tested. One approach is to test 30–100 normal subjects over a range of ages and compare their results to currently available prediction using least square techniques. This is a critical element because large differences have been observed among different reference equations and among different laboratories (27).
11. The choice of reference equation for the pediatric population has been particularly challenging. As of 2015, the most rigorous equations are those of Kim and colleagues (28).
12. The Global Lung Function Initiative reference values for D_{LCO} for ages 6 to 90 years of age will become available in 2017 (*see* www.lungfunction.org).

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APPENDIX 10.1

D_{LCO} Adjustment for Hemoglobin

Because CO-Hb binding is such an important factor in CO transfer, D_{LCO} changes can be substantial as a function of hemoglobin concentration (19–24). The equation for adjusting predicted D_{LCO} in adolescents and adult men is (assuming Hb is in g/dL):

$$D_{LCO} \text{ predicted for Hb} = D_{LCO} \text{ predicted } 1.7 \text{ Hb}/(10.22 + \text{Hb})$$

The equation for adjusting predicted D_{LCO} in children under 15 yr of age and women is:

$$D_{LCO} \text{ predicted for Hb} = D_{LCO} \text{ predicted } 1.7 \text{ Hb}/(9.38 + \text{Hb})$$

The equation for adjusting measured D_{LCO} in adolescents and adult men is:

$$D_{LCO} \text{ adjusted for Hb} = \text{Measured } D_{LCO} \times (10.22 + \text{Hb}) / (1.7 \times \text{Hb})$$

The equation for adjusting measured D_{LCO} in children under 15 yr of age and women is:

$$D_{LCO} \text{ adjusted for Hb} = \text{Measured } D_{LCO} \times (9.38 + \text{Hb}) / (1.7 \times \text{Hb})$$

Please note that these equations assume that Hb is 13.4 g/dL in females and children, and 14.6 g/dL in males over age 15. These are approximate Caucasian value, but Hb levels vary significantly from these values with age and ethnicity (31).

Example of measured D_{LCO} adjustment for Hb for an adult man with a measured D_{LCO} of 40.37 ml/min/mm Hg and Hb of 15.7 g/dL:

$$D_{LCO} \text{ adjusted for Hb} = \text{Measured } D_{LCO} \times (10.22 + \text{Hb}) / (1.7 \times \text{Hb})$$

$$D_{LCO} \text{ adjusted for Hb} = 40.37 \times (10.22 + 15.7) / (1.7 \times 15.7)$$

$$D_{LCO} \text{ adjusted for Hb} = 40.37 \times 0.9712$$

$$D_{LCO} \text{ adjusted for Hb} = 37.33 \text{ ml/min/mmHg}$$

APPROVAL

Signature: _____ Date: _____

Annual Review

Date	Signature	Date	Signature

Revisions / Document History

Effective Date	Synopsis of Change

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Effective Date: 2014
Version #1

CHAPTER 11

PROCEDURE NAME: MAXIMUM RESPIRATORY PRESSURES

PURPOSE OR PRINCIPLE

The measurement of respiratory muscle forces (or strength), maximum inspiratory pressure (MIP or PImax), and maximum expiratory pressure (MEP or PEmax), are direct tests that are simple to perform, and are well tolerated by patients. The test assesses the aggregate force or pressure that respiratory muscles can generate against an occlusion at the mouth (1). PImax is an index of diaphragm strength, while PEmax measures the strength of abdominal and intercostal muscles (1, 2). The most commonly reported method of measuring respiratory muscle force is that reported by Black and Hyatt (3). The equipment required is a pressure gauge, manometer, or transducer that can be a handheld device, or part of a more complex pulmonary function (PF) system. The technician must be a motivating coach and encourage the patient to give maximal efforts on a test that is very effort-dependent and may be uncomfortable (2). PEmax is measured at or near total lung capacity (TLC), and PImax is measured at or near residual volume (RV).

INDICATIONS AND CONTRAINDICATIONS

Some indications for measuring maximum respiratory pressures are provided in Table 11.1.

Table 11.1

Indications for Maximum Respiratory Pressures
• Assess and quantify the degree of respiratory muscular weakness that may occur with neuromuscular diseases (e.g., amyotrophic lateral sclerosis, myasthenia gravis, Guillain-Barré syndrome, muscular dystrophy, stroke, and polymyositis), obstructive lung disease causing hyperinflation (e.g., emphysema, chronic bronchitis, and cystic fibrosis), and conditions requiring chronic steroid use, conditions with chest deformities, and unexplained dyspnea (3).
• Abnormal diagnostic test results (e.g., decreased forced vital capacity [FVC], peak flow, maximal voluntary ventilation [MVV], or abnormal chest radiograph).
• The PEmax gives information about the potential for effective cough and ability for secretion clearance (4).
• Diagnosis and management of a patient with actual or suspected injury to the diaphragm or other respiratory muscles (4).
• Evaluate the effectiveness of therapy designed to improve respiratory muscle strength.

Table 11.2

Contraindications for Performing Maximum Respiratory Pressures	
Absolute Contraindications	• Unstable angina • Recent myocardial infarction (within the previous 4 weeks) or myocarditis • Recent pneumothorax • Uncontrolled systemic hypertension • Lung biopsy within previous week
Relative Contraindications	• Resting diastolic blood pressure >110 mm Hg or resting systolic blood pressure >200 mm Hg • Recent spinal injury • Recent eye surgery • Non-compliant patient or one who is not capable of performing the test because of weakness, pain, fever, dyspnea, lack of coordination, or psychosis.

Contraindications for performing maximum respiratory pressures are provided in Table 11.2.

EQUIPMENT AND SUPPLIES

1. Several equipment options are commercially available. Equipment can also be fabricated in the laboratory with parts available from several sources. System description (e.g., manufacturer, model, type, accessories, additional features, and software version) should be included here. An example of a device is provided below.
    1.1. Portable handheld system with two diaphragm gauges connected to a large-bore metal "T" or "Y" valve. The gauges, scaled in cm H_2O, attach to a pressure tap in the distal end of the cylinder with rigid plastic tubing: one gauge records positive pressure; the other gauge records negative pressure. The distal end of the unit is closed, except for a small opening (a "controlled leak" 1 to 2 mm inside diameter, 15 mm long). The purpose of the small opening is to help prevent glottic closure and to prevent facial muscles from producing significant additional pressures (1, 3).
2. Disposable/reusable supplies: flanged mouthpiece, nose clip, and other miscellaneous equipment or supplies.

PATIENT PREPARATION (PRE-TEST INSTRUCTIONS)

1. The patient should refrain from heavy exercise immediately before testing.
2. The effect of smoking is unclear, but ask the patient if he/she has recently smoked.
3. Explain and demonstrate the procedure.

ASSESSMENT OF PATIENTS

1. Assess each patient for physical and developmental status to determine ability to undergo the diagnostic test(s) and if special arrangements are required. If there is a language barrier, an interpreter will be used.
2. Ask each patient if he/she has complied with the preparation criteria, including:
    2.1. If they have recently smoked, and if so, when.
    2.2. The time of his/her last meal.
    2.3. The last time he/she took medications for the lungs, and what types.

3. Postponement may be necessary if the patient has not complied with the preparation criteria. The ordering physician is to be contacted to determine if rescheduling is necessary.
   3.1. In the event the ordering physician cannot be contacted, the laboratory medical director (or designee) should determine if testing should proceed.
4. In order to properly document and interpret the test results, relevant clinical information, including the clinical indication for ordering the test, must be provided in writing by the ordering physician.

SPECIAL SAFETY PRECAUTIONS

1. Indications for immediate termination of testing
   1.1. Syncope
   1.2. Angina
   1.3. Lightheadedness not relieved by rest
   1.4. Request from patient to terminate test
2. Abnormal responses that may require discontinuation of testing
   2.1. Mental confusion or headache
   2.2. Nausea or vomiting
   2.3. Muscle cramping
3. Hazards associated with maximal respiratory force testing
   3.1. Ruptured ear drum
   3.2. Exacerbation of hemorrhoids
   3.3. Syncope
   3.4. Conjunctival hemorrhage

EQUIPMENT PREPARATION AND CALIBRATION CHECKS

1. Check the calibration of the measurement system according to manufacturer's instructions each day of use. Ideally, the pressures can be verified using an oil or water manometer.

PROCEDURE

Pre-Test Preparation		
Step	**Action**	
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition.	
	IF	THEN
	Patient unable to provide Information	• Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information
	The identifiers do not match	• Contact registration • Resolve discrepancies before proceeding
	The ID band is present but not attached to the patient	• Do not proceed. • Notify patient's nurse or registration desk
2.	Check for a complete physician's order.	

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Pre-Test Preparation (Continued from previous page)	
Step	**Action**
3.	Collect and record demographic information.
4.	Explain and demonstrate test maneuver, including correct posture while in the sitting position. Advise the patient that the maximal expiratory maneuvers may make the ears "pop." Instruct the patient to keep a tight lip seal and to give maximum effort. A tight-fitting nose clip should be properly in place.

Maximal Inspiratory Pressure	
Step	**Action**
1.	Place a rubber-flanged mouthpiece, a circular non-flanged rubber mouthpiece or other rigidly constructed tube firmly onto the mouthpiece adapter.
2.	Patients are normally seated and a nose clip is not required, but may be used.
3.	Instruct the patient to exhale slowly and completely (to RV), seal his/her lips firmly around the mouthpiece, and then inhale with as much force as possible.
4.	Strong encouragement is necessary, and the patient should be urged to "suck real hard" or "pull in hard" for at least 1.5 seconds (5).
5.	Obtain at least three efforts with a maximum of eight efforts.
6.	A goal for repeatability should be that the two highest values agree within 10%. If the final effort is the highest value, obtain an additional effort (6–8).
7.	Allow the patient to rest for 30 to 60 seconds between efforts (3, 6, 8).

Maximal Expiratory Pressure	
Step	**Action**
1.	Place a rubber-flanged mouthpiece, a circular non-flanged rubber mouthpiece or other rigidly constructed tube firmly onto the mouthpiece adapter.
2.	Patients are normally seated and a nose clip is not required, but may be used. Patients often need coaching to prevent air leaks around the mouthpiece and to support the cheeks during the expiratory efforts. One approach is to have the patient pinch their lips around the mouthpiece (5).
3.	Instruct the patient and demonstrate correct placement of the rubber mouthpiece or tube held firmly against pursed lips (not inside the mouth like other mouthpieces). If the patient can't perform the test acceptably, switch to a different style of mouthpiece or interface.
4.	Instruct and urge the patient to inhale completely (to TLC), press the mouthpiece firmly against his/her lips, and then to exhale with as much force as possible against the mouthpiece for at least 1.5 seconds (5).
5.	Watch the patient closely to ensure there are no leaks.
6.	Obtain at least three efforts with a maximum of eight efforts.

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Maximal Expiratory Pressure (Continued from previous page)	
Step	**Action**
7.	A goal for repeatability should be that the two highest values agree within 10%. If the final effort is the highest value, obtain an additional effort (6–8).
8.	Allow the patient to rest for 30 to 60 seconds between efforts (3, 6, 8).

REVIEW OF TEST RESULTS

1. Final review of data on the report should be checked for accuracy and completeness by the individual performing the testing, and/or by the laboratory manager or supervisor.

REPORTING OF TEST RESULTS

1. PImax should be a negative value, reported in cm H_2O. Report the most negative value.
2. PEmax should be a positive value, reported in cm H_2O. Report the most positive value.
3. Report the number of efforts, degree of repeatability, percent of predicted, and lower limit of normal.
4. To adjust for differences in body size and varied levels of lung capacity, caused by disease states, pressures can be presented as percent of predicted TLC at which they were measured. This is not possible with handheld devices.
5. To facilitate the above corrections, it is preferable to perform lung volume testing at the same time as the maximal respiratory pressures, using a body plethysmograph to obtain functional residual capacity (FRC_{pleth}). This allows correlation of respiratory muscles forces with the degree of hyperinflation at which they were generated, which can be especially important with patients with obstructive lung disease (1). However, the body plethysmograph makes coaching more difficult and the flanged mouthpiece may not be optimal for measuring at the same visit with the respiratory pressures measured outside the body plethysmograph.
6. Maximum respiratory pressures can usually be incorporated into the pulmonary function test report. If using a separate report, include demographic information.

PROCEDURE NOTES

1. Handheld devices have been developed for quick and easy use at many clinical settings.
2. If handheld devices without recorders are used, values cannot be corrected for lung volumes.
3. It may be difficult to distinguish between poor patient effort and neuromuscular disease. More invasive tests such as twitch Pdi with phrenic nerve stimulation, or esophageal and gastric balloon placement may be required in these patients (9–11).
4. If testing is not performed with the patient in an upright sitting position, make a note on the report.
5. If the values observed are less than predicted, reassess the patient for cooperation and technique. If there is a physical reason for abnormal results, such as back injury or lip-seal leak, note those factors (4).
6. Note if the patient appears not to understand the directions or does not appear to give a maximal effort.
7. If results are questioned, check the system calibration, and/or the technicians can test themselves. This serves the purpose of demonstrating the procedure again for the patient and comparing a known patient's results to validate the instrument.

8. If the patient cannot maintain a tight lip seal, another person can use their fingers to secure the patient's lips. Facial muscle weakness, which is often associated with generalized neuromuscular disease, can cause problems in this test. Technician-aided lip compression has been reported to produce higher PEmax than lip compression done by the patient (12).
9. Patients may obtain higher values when incorrect procedures are performed. "Cheating" can occur on PImax when a patient "sucks in" forcefully with a closed glottis. The pressure is generated by the oral/facial muscles and can be higher than pressures generated by respiratory muscles. Conversely, in the PEmax maneuver, pumping the cheeks against a closed glottis may produce higher pressures inappropriately. Clear instructions with proper demonstration by the technician help to standardize the technique and obtain accurate results (12).
10. Several studies have reported maximum static airway pressures in healthy adults and adolescents (3, 7, 8, 14–18). The range in reported healthy values is broad, likely due to population and methodology differences, and the coefficient of variation when performing this test in healthy patients is approximately 10%. Appendix 11.1 lists some values reported in healthy individuals.
11. Respiratory muscle force may also be assessed by measuring changes in pleural pressure with an esophageal catheter.
12. Assessment of diaphragm strength can be made by measuring abdominal and esophageal pressures via balloon-tipped catheters placed in the stomach and esophagus, and then calculating transdiaphragmatic pressure (Pdi).
13. Different mouthpiece interfaces do not result in significant differences in PImax and PEmax (19).

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APPENDIX 11.1

Reported PImax and PEmax Values in Healthy Patients				
Reference Study	**Gender**	**Age Range (*years*)**	**PImax (cm H_2O ±SD)**	**PEmax (cm H_2O ±SD)**
Black, Hyatt (3)	M F	20 to 54 20 to 54	124 ± 22 87 ± 16	233 ± 42 152 ± 27
Ringqvist (13)	M F	18 to 83 18 to 83	130 ± 32 98 ± 25	237 ± 46 165 ± 30
Vincken, *et al.* (6)	M F	16 to 79 16 to 79	105 ± 25 71 ± 23	140 ± 38 89 ± 24
Wilson, *et al.* (15)	M F	19 to 65 18 to 65	106 ± 31 73 ± 22	148 ± 34 93 ± 17
Enright, *et al.* (7)	M F	65 to 85 65 to 85	83 ± 27 58 ± 22	175 ± 46 118 ± 37

APPROVAL

Signature: _____ Date: _____

Annual Review

Date	Signature	Date	Signature

Revisions / Document History

Effective Date	Synopsis of Change

Effective Date: 2018
Version #2

CHAPTER 12

PROCEDURE NAME: METHACHOLINE CHALLENGE TEST

PURPOSE OR PRINCIPLE

Asthma is a chronic inflammatory disorder of the airways. The airway inflammation contributes to airflow limitation, bronchial hyperresponsiveness, respiratory symptoms, and disease chronicity. The airflow limitation (or airway narrowing) is reversible either spontaneously or with treatment. There is also an associated increase in existing bronchial hyperresponsiveness to a variety of stimuli (1, 2).

Improvement in airflow following inhalation of a bronchodilator is generally accepted as indicative of reversible airway obstruction. However, the evaluation of bronchial hyperresponsiveness is often indicated, especially in patients with unclear or nonspecific symptoms (e.g., symptoms of asthma with normal spirometry and no bronchodilator response). Bronchial provocation (challenge) testing may be performed with a variety of stimuli that can be divided into two groups: direct and indirect agents.

Direct stimulants provoke airway constriction by acting directly on the bronchial smooth muscle receptors, bronchial vascular endothelial cells, and mucus-producing cells. Direct stimulants include methacholine and histamine.

Indirect stimulants provoke airway constriction indirectly by releasing a number of mediators from inflammatory cells within the airway. These mediators then stimulate specific receptors on bronchial smooth muscle. Indirect stimulants include exercise, eucapnic hyperventilation, mannitol, adenosine, allergens, and hypertonic and hypotonic aerosols.

The 1999 ATS Guideline for methacholine challenges recommended the 2-minute tidal breathing method and the 5-breath dosimeter method (3). Although calculations estimated that the dose of methacholine delivered at each step would be twice as high with the tidal breathing method, it was expected that deep breaths with a 5-second breath-hold at total lung capacity (TLC) would allow better distribution and retention of the aerosol and early studies did suggest that the two delivery methods gave similar results (3). More recent studies show small differences, consistent with those dose-delivery considerations, in patients with more severe asthma, reacting to low levels of methacholine, but results are less comparable in patients with less airway hyperresponsiveness (4–6). This means that patients who would be considered to have mild hyperresponsiveness by the 2-minute tidal breathing method will be considered normal by the dosimeter method. This false negative rate was 25% of all tests and 50% of those with mild-moderate airway hyperresponsiveness in one series (7). This effect is seen in those considered normal and those with mild asthma, but is lost with more severe disease (6–9). For these reasons, methods requiring deep inhalations to TLC during aerosol delivery are no longer recommended, and only the tidal breathing method will be described in this procedure (10).

INDICATIONS AND CONTRAINDICATIONS

Indications for the methacholine challenge test are provided in Table 12.1, with a list of relative contraindications presented in Table 12.2.

EQUIPMENT AND SUPPLIES

1. Methacholine (acetyl-β methylcholine chloride)
   - 1.1. Methacholine (Provocholine®) approved by the Food and Drug Administration (FDA) and/or United States Pharmacopieia (USP) can be obtained in 100-mg pre-measured sealed containers from:
     Methapharm, Inc.
     19 Isabel Drive
     RR 4, Brantford, ON
     N3T 5L7, CANADA
     1-800-287-7686
     www.methapharm.com
   - 1.2. Industrial methacholine is available in bulk quantities from chemical supply companies, but is not FDA approved. While industrial methacholine has been shown to be clinically and structurally similar to the FDA-approved product (12), its use is not recommended by the most current ATS/ERS guideline (10).
   - 1.3. Where methacholine is formulated locally, the laboratory must be assured that it meets good manufacturing practices for quality, purity, and consistency.
   - 1.4. Sealed prepackaged vials of Provocholine have a shelf life of 2 to 3 years when stored at ambient temperature.

Table 12.1

Indications for Methacholine Challenge Testing (10)
Clinical Indications for Testing Include Evaluation of:
• Confirm or exclude a suspected diagnosis of asthma • Screening applicants for situations where asthma would present a high safety risk (e.g., commercial diving, submarine service, and some occupational exposures) • Assess response to therapeutic interventions

Table 12.2

Relative Contraindications for Performing Methacholine Challenge Testing (10)
Relative Contraindications for Testing Include:
• Low FEV_1 (Less than 60% of predicted or 1.5 L in adults) • Inability to perform acceptable and repeatable spirometry (11) • Uncontrolled hypertension, recent heart attack or stroke, arterial hypoxemia • Recent eye surgery, or any condition where raised intracranial pressure (caused by forced exhalation) is a contraindication • Pregnancy and nursing mothers: methacholine is a pregnancy category C drug, meaning no animal reproductive studies have been performed to determine if methacholine chloride is associated with fetal abnormalities, or whether it is excreted in breast milk. • Current use of cholinesterase inhibitor medication (e.g., myasthenia gravis)

2. Diluent
   - 2.1. Methacholine should be diluted using a sterile sodium chloride (NaCl) solution (0.9%) with or without 0.4% phenol. There is no evidence that adding a preservative such as phenol to sterile NaCl diluent is necessary (13), nor is there evidence that use of phenol adversely affects the methacholine challenge test. The potential benefit of adding phenol is reducing the potential for bacterial contamination (10).
   - 2.2. The use of a buffer had previously been recommended (14), but may render the solution too alkaline, which may lead to methacholine decomposition (15, 16).
3. Methacholine Solution Preparation
   - 3.1. Methacholine powder is very hygroscopic, meaning it readily absorbs moisture. If bulk quantities of methacholine are kept, the powder should be stored in a dry container (desiccator) in a refrigerator or freezer (17).
   - 3.2. Methacholine solutions should be mixed by a pharmacist or other qualified, well-trained individual using sterile technique and following the manufacturer's instructions (10).
   - 3.3. The recommended approach is to use the sealed 100 mg Provocholine vials. The dilution schemes for two dosing schedules using the 100 mg Provocholine vials are shown in Tables 12.3 and 12.4 (10). An example of a dosing protocol is shown in Appendix 12.5.

Table 12.3

Dilution Schedule for Doubling Doses			
Label Strength	**Take**	**Add Diluent**	**Obtain Dilution**
100 mg	100 mg	6.25 ml	16 mg/ml
	3 ml of 16 mg/ml	3 ml	8 mg/ml
	3 ml of 8 mg/ml	3 ml	4 mg/ml
	3 ml of 4 mg/ml	3 ml	2 mg/ml
	3 ml of 2 mg/ml	3 ml	1 mg/ml
	3 ml of 1 mg/ml	3 ml	0.5 mg/ml
	3 ml of 0.5 mg/ml	3 ml	0.25 mg/ml
	3 ml of 0.25 mg/ml	3 ml	0.125 mg/ml
	3 ml of 0.125 mg/ml	3 ml	0.0625 mg/ml
	3 ml of 0.0625 mg/ml	3 ml	0.031 mg/ml
	3 ml of 0.031 mg/ml	3 ml	0.015625 mg/ml

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

3.4. Storage of diluted methacholine solutions

3.4.1. Methacholine solutions should be stored in a refrigerator (4° C). At this temperature, higher concentrations (i.e., >1.25 mg/ml) have been reported to be stable for at least 15 weeks (15–19).

3.4.2. According to the package insert, Provocholine® solutions are stable for up to 2 weeks when stored at 36° to 46° F (2° to 8 ° C). If using Provocholine®, the package insert instructions should be followed.

3.4.3. Each vial of methacholine solution should be clearly labeled with the drug name, concentration of the diluent, date prepared, date expired, and initials of individual preparing the solution. For example:
Methacholine
2.5 mg/ml
Diluent: 0.9% NaCl
Prepared: 12/16/17 by XYZ (initials of person making solutions)
Expires: 12/30/17

RECOMMENDED EQUIPMENT FOR TIDAL BREATHING METHOD (10).

The 1999 ATS guidelines (3) recommended the English Wright nebulizer for the tidal breathing technique and the DeVilbiss 646 for the 5-breath dosimeter method. Both these devices would be considered obsolete by modern standards. Furthermore, the bronchodilator effect of the inspiration from FRC to TLC with the 5-breath dosimeter technique has been shown to blunt the response to methacholine and give rise to false negative results (7). When comparing the results from one nebulizer to another, the dose delivered to the lung gives rise to similar results, which is not the case with the concentration used, which favors the use of the cumulative dose of methacholine that causes a fall of 20% for the FEV_1. There are data that allow the comparison of the English Wright to a breath-actuated nebulizer, and manufacturers should be able to supply data allowing the calculation of the dose delivered to the lungs for each concentration.

4.1. Nebulizer

4.1.1. Use a high-quality nebulizer that generates aerosols with a particle size of ≤ 5 μm. The performance characteristics must be measured and both the technique and results reported by the manufacturer (10).

4.1.2. Use the same nebulizer throughout a challenge because of inter-nebulizer output variability.

4.1.3. The use of disposable nebulizers that are discarded after use is recommended. The re-use of disposable nebulizers may give rise to cross contamination. The manufacturers of good-quality nebulizers can provide output specifications, and based on particle size and the ratio of inspiratory time to total breathing time (Ti/Ttot), the dose can be calculated.

4.3. Compressed gas source, flow meter, and tubing

4.4. Pulmonary function testing system (e.g. spirometers)

4.5. Timer

4.6. Bronchodilator (e.g., inhaled albuterol) for reversal, and oxygen source

4.7. Mouthpiece for nebulizer

4.8. Stethoscope, sphygmomanometer, and pulse oximeter are optional.

PATIENT PREPARATION (PRE-TEST INSTRUCTIONS)

1. Medications

1.1. Patients should be instructed not to take drugs that affect airway caliber and/or are considered antagonists to methacholine for an interval that exceeds their duration of action. These medications and the time period for withholding them prior to the test are presented in Table 12.5.

1.2. Beta-adrenergic blocking agents: The Provocholine® package insert states methacholine inhalation challenge should not be performed in patients receiving any beta-adrenergic blocking agent because in such patients responses to methacholine chloride can be exaggerated or prolonged, and may not respond as readily to accepted modalities of treatment. Withholding of beta-adrenergic blocking agents or performing the challenge in patients taking such agents should be performed with caution and only upon specific orders from the ordering physician.

2. Caffeine and caffeine-related products have been shown to have no effect of clinical significance (21).

Table 12.5

Medication Withholding Recommendations for Methacholine Challenge Test.	
Medication	**Length of Abstention**
Short-acting inhaled beta agonists in conventional doses (e.g., albuterol 200 μg)	6 hours
Long-acting inhaled beta agonists (e.g., salmeterol)	36 hours
Ultra–long-acting beta agonists (e.g., indacterol, vilanterol)	48 hours
Short-acting anticholinergics (e.g., Atrovent 40 μg)	12 hours
Long-acting anticholinergics (e.g., Tiotropium)	At least 168 hours
Oral theophylline	12–24 hours
Cromones	Do not need to be withheld
Leukotriene modifiers	Do not need to be withheld (20)
Corticosteroids (inhaled, oral)	Not usually withheld
Antihistamines	Not usually withheld for methacholine challenge

3. Suggestion
    3.1. Both bronchoconstriction and bronchodilatation can be induced by suggestion (22–24). Tell patients they will be inhaling a mist that could make them feel worse, feel better, or cause no change (25). Avoid giving them too much information.
4. Informed consent and pre-test questionnaire
    4.1. A consent form describing the procedure should be carefully read and signed by the patient or parent/legal guardian of the patient prior to the challenge.
    4.2. The consent form should not provide information that will suggest a specific outcome.
    4.3. An example consent form is presented in Appendix 12.1.
    4.4. A pre-test questionnaire should be administered and may alert the technician to important issues, including contraindications for testing, recent exposures or viral infections, and medications that may alter airway responsiveness (10). See Appendix 12.2 for an example.
5. Instructions
    5.1. Before the challenge, the technician will explain and demonstrate the test requirements to the patient including inhalation of the test solutions and performance of pulmonary function (PF) tests.

ASSESSMENT OF PATIENTS

1. The patient's medical history should be reviewed by a trained physician or professional including current medications, current symptoms, clinical diagnosis, and reason for the test.
2. Assess each patient for physical and developmental status to determine ability to undergo the diagnostic test(s) and if special arrangements are required. If there is a language barrier, an interpreter will be used.
3. Ask each patient if he/she has complied with the preparation criteria, including:
    3.1. Withholding the medications that may affect the outcome of the test
    3.2. Any recent serious illnesses (e.g., myocardial infarction).
4. Postponement may be necessary if the patient has not complied with the preparation criteria. The ordering physician is to be contacted to determine if rescheduling is necessary.
    4.1. In the event the ordering physician cannot be contacted, the laboratory medical director (or designee) should determine if testing should proceed.
5. In order to properly document and interpret the test results, relevant clinical information including the clinical indication for ordering the test must be provided in writing by the ordering physician.

EQUIPMENT PREPARATION AND CALIBRATION CHECKS

1. Preparation
    1.1. Remove the methacholine solutions from refrigerator and allow them to equilibrate to room temperature (approximately 30 minutes) because the temperature of the solution affects nebulizer output.
    1.2. Check the nebulizer and compressed gas systems to ensure they are working properly
2. Calibration
    2.1. Calibrate the PF testing system each day of use and before the challenge.

PROCEDURE

Pre-Test Preparation	
Check patient identification	Identify patient using an institutionally approved process.
Orders	Check for a complete physician's order.
Demographics	Collect and record demographic information
Test explanation and patient training	Review preparation guidelines, recording all drug therapy and time of last dose, and responses to questions about exposures and illnesses. A pre-test questionnaire may be used (Appendix 12.2). Explain the procedure to the patient and obtain informed consent.
Other	Remove methacholine solutions from the refrigerator and allow them to equilibrate to room temperature for at least 30 minutes. The solutions should be placed out of the view of patients, so they will not know which concentration they receive. Ensure that bronchodilators and O_2 are available and ready to use.

Test Procedure	
Baseline (Pre-Challenge) Step	Spirometry should be performed according to the most recent ATS/ERS recommendations (3) with at least three acceptable maneuvers and the two highest FVC values and two highest FEV_1 values agreeing within 0.150 L. For small children or patients who cannot perform spirometry, alternative assessment techniques include: forced oscillation, peak expiratory flow (PEF), and body plethysmography. Determine if there are any absolute or relative contraindications, regarding airflow obstruction, to performing the test. If there are, notify the ordering physician and obtain permission to proceed. It is not recommended to perform the challenge when the FEV_1 is less than 60% of predicted or less than 1.5 L (10).
Diluent Step	Select the nebulizer to be used for the diluent and methacholine steps (the same nebulizer should be used for all steps in a challenge test). The practice of administering the diluent alone before the first methacholine stage has been questioned (26), but remains the preferred and recommended method (10). Withdraw 2–3 ml or appropriate amount of diluent and place it in the nebulizer. Connect the nebulizer tubing to the source of compressed air and assure nebulizer is working properly. Apply the nose clip and instruct the patient to relax and breathe quietly (tidal breathing) on the mouthpiece for the appropriate time for the specific nebulizer (e.g., 2 minutes for a low output nebulizer or 60 seconds for a higher output nebulizer). Ask the patient to hold the nebulizer upright with the mouthpiece in his/her mouth. Start timer.

(continues on next page)

	Test Procedure (Continued from previous page)
Diluent Step	Watch the patient to ensure that he/she is breathing comfortably and quietly, and not tipping the nebulizer. After the appropriate time or breath number for that nebulizer, turn off the compressed air source and take the nebulizer from the patient. Perform post-diluent spirometry at 30 and 90 seconds after nebulization is completed. Obtain acceptable quality FVC test maneuvers at each time point. This may require repeated attempts. Full FVC efforts lasting at least 6 seconds should be performed after administration of the diluent. Calculate a target FEV_1 that indicates a 20% fall in FEV_1 (i.e., $FEV_1 \times 0.80$) using the post-diluent data. The diluent should not cause significant change from the pre-challenge testing spirometry. If the FEV_1 has changed by less than ±10% from the pre-challenge FEV_1, proceed to administer the first dose of methacholine in the same manner the diluent was administered. If the FEV_1 has increased or decreased at least 10% after diluent, repeat the diluent step. If the FEV_1 has decreased by 20% or more after diluent, the challenge should be cancelled.
First Dose of Methacholine Aerosolization Step	Empty the remaining diluent from the nebulizer by shaking excess diluent into wastebasket or sink. Withdraw 2–3 ml or appropriate amount of the starting concentration of methacholine, and place it in the same nebulizer used for the diluent. A starting dose of 1–3 μg is considered safe in the routine testing environment where patients have normal or near-normal spirometry and no significant bronchodilator response. With nose clip in place, aerosolize the methacholine using the same nebulizer used for diluent. Nebulization time should be the same for each step and appropriate for the chosen nebulizer (e.g., 2 minutes, or 60 seconds). Start timer. Perform post-methacholine spirometry at 30 and 90 seconds after nebulization is completed. Obtain an acceptable quality FEV_1 at each time point. Perform no more than 3 or 4 test maneuvers after each dose. Obtaining a full FVC is not required if FEV_1 is the only outcome. If abbreviated expiratory time is used, care should be taken to assure the inspiration is complete. If other spirometric outcome variables are used or if vocal cord dysfunction is suspected, full FVC maneuvers including inspiration should be performed throughout the test. In order to keep the cumulative effect of methacholine relatively constant, the time interval between the commencement of two serial concentrations is important and should be kept constant at 5 minutes. At each dose, report the highest FEV_1 from acceptable test maneuvers. If the highest post-methacholine FEV_1 falls less than 20% from the post-diluent value (i.e., above target value) go to next step.

(continues on next page)

	Test Procedure (Continued from previous page)
Next and Remaining Doses of Methacholine Steps	If the FEV_1 falls less than 20% from the post-diluent value, empty the nebulizer by shaking excess solution into wastebasket or sink. Withdraw 2 ml or appropriate amount of the starting dose of methacholine, and place it in the same nebulizer used for the diluent. With nose clip in place, aerosolize the methacholine using the same nebulizer used for diluent. Start timer. Perform post-methacholine spirometry at 30 and 90 seconds after nebulization is completed. Obtain an acceptable quality FEV_1 at each time point. As noted above, obtaining a full FVC is not required if FEV_1 is the only outcome. If abbreviated expiratory time is used, care should be taken to assure the inspiration is complete. Perform no more than 3 or 4 test maneuvers after each dose. In order to keep the cumulative effect of methacholine relatively constant, the time interval between the commencement of two serial concentrations is important and should be kept constant at 5 minutes. At each dose, report the highest FEV_1 from acceptable test maneuvers. If the highest post-methacholine FEV_1 falls less than 20% from the post-diluent value go to next step (next highest concentration of methacholine). If the highest post-methacholine FEV_1 falls more than 20% from the post-diluent FEV_1 or the highest concentration has been administered, give no further methacholine, note signs and symptoms, and administer an inhaled bronchodilator.
Bronchodilator Administration	If the highest post-methacholine FEV_1 from any dose falls 20% or more from the post-diluent FEV_1, administer a bronchodilator (e.g., 0.5 ml of albuterol in 1 ml of normal saline by small volume nebulizer, or 2 puffs from a metered dose inhaler). Wait 5–10 minutes and repeat PF tests. If the post-bronchodilator $FEV_1 \geq 90\%$ of the highest pre-challenge FEV_1, the patient can leave the laboratory. If the post-bronchodilator $FEV_1 < 90\%$ of the highest pre-challenge FEV_1 or the patient is symptomatic, administer a second bronchodilator or ipratropium bromide treatment and repeat PF tests after a waiting period of 10 minutes. If the post-bronchodilator FEV_1 is still < 90% of the highest baseline, notify ordering physician before letting patient leave the laboratory.

REVIEW OF TEST RESULTS

1. Assure acceptable and repeatable spirometry data at pre-challenge and post-diluent stages.
2. Assure an acceptable maneuver at each time point of each stage.
   2.1. Repeatability of FEV_1 (i.e., two highest within 0.150 L) may be difficult to obtain once methacholine is administered.
3. Assure FEV_1 is less than or equal to 80% of post-diluent FEV_1 value for a positive test.
4. Assure bronchodilator has been administered (if applicable) and post-bronchodilator spirometry performed, and FEV_1 is at least 90% of baseline.

REPORTING OF TEST RESULTS

1. Data should be expressed as a percent decrease in FEV_1 from the post-diluent value (or pre-challenge value if a diluent step is not used) in relationship to the calculated final dose.
2. If more than one diluent stage is used, the percent change is calculated from the final post-diluent stage.
3. Data should be presented for each step in the protocol, including post-bronchodilator spirometry.
4. For spirometry, report the FEV_1, and FVC and FEV_1/FVC ratio (if complete FVC maneuvers were performed). Also include: bronchodilator administered and dose, display of best flow–volume and/or volume–time curve from each step, PD_{20}, or include a dose–response curve, and signs and symptoms after final dose.
5. For plethysmography measurements, report sGaw or specific resistance (sRaw).
6. Express the concentration as mg/ml and dose as cumulative dose units of methacholine (CUM).
7. Cumulative dose units
   7.1. Methacholine has been shown to accumulate between concentrations because it is metabolized somewhat slowly (27).
8. Graphic and tabular displays showing percent change and absolute values should be presented in the report.
9. Technician comments should include evaluations of patient effort and cooperation, whether coughing occurred, and patient response to specific queries concerning the presence of shortness of breath, wheezing, and other symptoms that can be used to confirm the response.
10. If FEV_1 does not fall by at least 20% following the highest dose, then PD_{20} should be reported as "greater than final dose given." If FEV_1 falls by >20% following inhalation of diluent, a PD_{20} is not reported. Instead, state, "there was a significant decrease in lung function following inhalation of the diluent and methacholine was not given."

PROCEDURE NOTES

1. Shortening the test procedure
   1.1. Doubling concentrations are recommended for research protocols and are mathematically attractive. However, the use of doubling concentrations requires more steps and increases the time for the test. Fewer concentrations have been used by investigators in order to save time without any apparent increase in risk or severe bronchospasm (28, 29). Quadrupling increments is recommended for clinical testing, but if the test is used to determine changes in airway reactivity following therapy in patients known to have asthma, using doubling doses will give more precise PD_{20} values. The quadrupling dose schedule will result in a lower cumulative dose, but since the increase in dose is logarithmic, only the last one or two concentrations has a major effect on the PD_{20}s.

2. Interpretation
   - 2.1. Commonly, the methacholine challenge is interpreted categorially as either demonstrating airway hyperresponsiveness or not.
   - 2.2. Based on the 1999 ATS guideline, and for the 2-minute tidal breathing technique using twofold increases in concentrations, the PC_{20} FEV_1 cutoff between hyperresponsive and nonhyperresponsive airways ranges from 4 to 16 mg/ml (30–34).
   - 2.3 Recommendations from 2017 ERS guideline (10) using PD_{20}, and based on 2 minutes of nebulization using English Wright nebulizer are as follows:

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.

3. Safety and Training
   - 3.1 The technician performing the methacholine challenge should:
     1. Be trained in spirometry and performing the challenge
     2. Receive approximately 4 days of hands-on training and perform at least 20 supervised tests to become proficient
     3. Be familiar with safety and emergency procedures
     4. Wash their hands before and after handling the equipment and testing
     5. Minimize exposure to aerosolized methacholine and strongly consider not performing this test if they have asthma or symptoms suggestive of hyperreactive airways. The use of a breath-actuated nebulizer will minimize environmental methacholine since aerosol is produced only during inspiration.
   - 3.2 The medical director of the laboratory, another physician, or another person appropriately trained to treat acute bronchoconstriction, including appropriate use of resuscitation equipment, must close enough to respond quickly to an emergency.
   - 3.3 Patients should never be left unattended during the test procedure.
   - 3.4 O_2 and appropriate O_2 tubing will be readily available in the testing room. Also, a stethoscope and sphygmomanometer to auscultate the chest and to measure blood pressure, and a pulse oximeter to ensure adequate O_2 delivery should be available.
   - 3.5 Medications to treat an acute bronchospasm attack should also be present in the testing room, including epinephrine for subcutaneous injection, and albuterol and ipratropium bromide in metered dose inhaler and/or in premixed solutions.

3.6 The testing room must have adequate ventilation (i.e., at least two air exchanges/hour).
3.7 Other optional methods to reduce methacholine exposure for the technician include using low-resistance filters, supplemental local exhaust ventilation, and/or a HEPA room air cleaner.

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APPENDIX 12.1

Sample Consent Form for Methacholine Challenge Test

Procedure

The purpose of a methacholine challenge test is to determine the amount of airway irritability of a patient. You (or your child) will be asked to inhale a mist that contains different concentrations of a medication called methacholine or a placebo. The mist is produced by a device called a nebulizer, and you inhale the mist through a mouthpiece. Before the test begins and after each period of inhalation, you or your child will be asked to blow forcefully into a spirometer, a device that measures how much air you can blow out and how fast. The test will take approximately 60 minutes. The results from the test can help your doctor to decide which treatments are likely to work best for you or your child.

Discomforts and Risks

This test does not cause an asthma attack, but the inhalation of the mist may be associated with mild shortness of breath, cough, chest tightness, wheezing, chest soreness, or headache. Many patients do not have any symptoms at all. These symptoms (if they occur) are mild, last only a few minutes, and disappear following the inhalation of a bronchodilator medication, which we will give to you if indicated. The test is carried out in such a way that the danger of a severe asthmatic reaction is minimized; however, there is still a very small possibility of severe narrowing of your airways. If this occurs, you or your child will be treated immediately and all medication necessary to treat you will be immediately available.

Your signature below indicates you have read the above information and understand the purpose of the test and the associated risks.

With this knowledge I agree to having this test performed on me or my child.

_____	_____	_____
Patient or Guardian	Date	Witness

APPENDIX 12.2

Sample Methacholine Challenge Pre-Test Questionnaire

Patient name: _____ Date of birth: _____

Medical Record or ID Number: _____

1. List all medications you have taken in the last 3 days for asthma, hay fever, heart disease, blood pressure, allergies, or stomach problems, and the number of hours or days since your last dose for each medication.

Drug	Date/Time Taken	Drug	Date/Time Taken
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____

2. Has a physician told you that you have asthma? ☐ Yes ☐ No
3. Have you ever been hospitalized for asthma? ☐ Yes ☐ No
4. Did you have respiratory disease as a child? ☐ Yes ☐ No
5. Have you experienced asthma symptoms such as wheezing, chest tightness, or shortness of breath within the last two weeks? ☐ Yes ☐ No
6. If you are a smoker, give the time of your last cigarette_____
7. Have you had a respiratory infection in the last 6 weeks? ☐ Yes ☐ No
8. Have you had a heart attack or stroke within the last 3 months? ☐ Yes ☐ No
9. Are you pregnant or nursing? ☐ Yes ☐ No
10. Do you have high blood pressure? ☐ Yes ☐ No
11. Do you have an aortic aneurysm? ☐ Yes ☐ No
12. Have you had recent eye surgery? ☐ Yes ☐ No

APPENDIX 12.3

Calculation of Percent Change in Lung Function

Calculation of percent change in lung function (e.g., FEV_1) is accomplished by using the highest value associated with a specific dose.

$$\%\ \text{change} = \frac{\text{highest post-diluent } FEV_1 - \text{highest post-methacholine } FEV_1}{\text{highest post-diluent } FEV_1} \times 100$$

Example calculation of percent change between the post-diluent FEV_1 and the starting dose of methacholine FEV_1, using the highest value from three FVC test maneuvers at each stage.

	1	2	3
Baseline FEV_1 (L)	3.20	3.24	3.30
Post-diluent FEV_1 (L)	3.27	3.24	3.29
Post-dose FEV_1 (L)	2.94	2.98	3.03

$$\%\ \text{change} = (3.29 - 3.03)/3.29$$

$$\%\ \text{change} = \text{decrease of } 7.9\,\%$$

APPENDIX 12.4

Calculation of the Provocative Dose (PD)

1. Responsiveness is expressed as the dose of inhaled methacholine that causes a threshold response.
2. The term $PD_{20}FEV_1$ is defined as the dose that causes a 20% fall in FEV_1. The term PD_{40}sGaw is defined as the dose that causes a 40% fall in sGaw.
3. The PD_{20} is obtained by linear interpolation between the final two doses. The formula is as follows:

$$PD_{20}FEV_1 = \text{antilog}\left[\log D1 + \frac{(20 - R1)\,(\log D2 - \log D1)}{(R2 - R1)}\right]$$

where: D1 = next-to-last dose of methacholine
D2 = final dose of methacholine
R1 = percent fall in FEV_1 after D1
R2 = percent fall in FEV_1 after D2

Example calculation of $PD_{20}FEV_1$, using the highest FEV_1 value from the two FVC tests at 150 and 210 seconds.

	150 s	210 s
Baseline FEV_1	3.24	3.30
Post-diluent FEV_1	3.24	3.29
Post 0.03 mg/ml FEV1 (Cum Dose = 1.275 µg)	3.24.	3.29
Post 0.06 mg/ml FEV_1 (Cum Dose = 3.825 µg)	2.98	3.03*
Post 0.125 mg/ml FEV_1 (Cum Dose = 9.138 µg)	2.53	2.55**

*percent fall in FEV_1 from diluent = 7.9%
**percent fall in FEV_1 from diluent = 22.5%

$$PD_{20}FEV_1 = \text{antilog}\left[\log D1 + \frac{(20 - R1)\,(\log D2 - \log D1)}{(R2 - R1)}\right]$$

$$PD_{20}FEV_1 = \text{antilog}\left[\log 3.825 + \frac{(20 - 7.9)\,(\log 9.138 - \log 3.825)}{(22.5 - 7.9)}\right]$$

$$PD_{20}FEV_1 = \text{antilog}\left[0.5826 + \frac{(12.1)\,(0.9609 - 0.5826)}{(14.6)}\right]$$

$$PD_{20}FEV_1 = \text{antilog}\ 0.8961$$

$$PD_{20}FEV_1 = 7.872\ \mu g$$

APPENDIX 12.5

Example of Doubling and Quadrupling Dose Protocols for Methacholine Challenge Test (one minute)

1. The table below provides doubling and quadrupling dosing protocols for using the AeroEclipse® Breath Actuated Nebulizer with **one minute** of tidal breathing.
2. AeroEclipse® Breath Actuated Nebulizer characteristics and related calculations:
   - 2.1. Rate of output from breath simulator using 16 mg/ml solution of methacholine:
     2.70 mg/min divided by 16 mg/ml = 0.16875 ml/min
   - 2.2 Respirable fraction (RF, droplets < 5 m): 76% or 0.76
   - 2.3 Ti/Ttot: 0.4
   - 2.4 Breathing 16 mg/ml for one minute, the delivered dose would be:
     Output × RF = 0.16875 ml/min × 0.76 = 0.12825 ml/min
   - 2.5 For other dilutions:
     Dose (µg) = concentration in nebulizer in mg/ml × 0.12825 ml/min × 1 min × 1,000

Doubling Dose Protocol		Quadrupling Dose Protocol	
Concentration (mg/ml)	**Dose (µg)**	**Concentration (mg/ml)**	**Dose (µg)**
0.015625	2	0.015625	2
0.03125	4	0.0625	8
0.0625	8	0.25	32
0.125	16	1	128
0.25	32	4	512
0.5	64		
1	128		
2	256		
4	512		

APPROVAL

Signature: _____ Date: _____

Annual Review

Date	Signature	Date	Signature

Revisions / Document History

Effective Date	Synopsis of Change

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Effective Date: 2014
Version #1

CHAPTER 13

PROCEDURE NAME: MANNITOL CHALLENGE TEST

PURPOSE OR PRINCIPLE

Airway hyperresponsiveness can be assessed by bronchial provocation tests (bronchial challenges) using direct or indirect stimuli. Challenges with direct stimuli (e.g., methacholine) act directly on the airway smooth muscle causing airway narrowing. Challenges with indirect stimuli, such as mannitol, adenosine, specific allergens, and exercise, act by causing a release of mediators from inflammatory cells (e.g., prostaglandins, leukotrienes, and histamine) and neuropeptides from sensory nerves, which in patients with asthma causes exaggerated airway narrowing and airflow limitation.

The use of mannitol as a bronchial challenge agent was first described by Anderson and colleagues in the late 1990s (1). Mannitol challenges have been found to be safe and useful in identifying patients with asthma responsive to hypertonic saline, eucapnic hyperventilation, and exercise (2). Mannitol is considered to be more specific, but less sensitive than methacholine for asthma.

Mannitol is a naturally occurring sugar hexahydric alcohol found in most vegetables. The formulation prepared for bronchial challenges is a white crystalline powder contained within gelatin capsules. It is sold as Aridol by Pharmaxis Ltd, Australia, and supplied in a kit containing the necessary capsules to complete one challenge along with the inhaler. The capsules are color coded in doses of 5, 10, 20, and 40 mg. Also included is a 0-mg clear capsule administered as a control.

INDICATIONS AND CONTRAINDICATIONS

The indications for the mannitol challenge testing are provided in Table 13.1, with the relative contraindications in Table 13.2. The list of possible contraindications may not be all-inclusive and therefore is not a substitute for clinical judgment.

Table 13.1

Indications for Mannitol Challenge Test
Indications for testing include:
• Assess pre-test probability of asthma in those with asthma-like symptoms (3) • Monitor asthma treatment response • Determine level of airway inflammation • Determine effectiveness of inhaled corticosteroid therapy (4) • Predict whether or not inhaled corticosteroid dose can be reduced (5, 6)

Table 13.2

Relative Contraindications for Mannitol Challenge Test (7)
Relative contraindications for testing include:
• The test should not be performed on those with known hypersensitivity to mannitol or to the gelatin used to make the capsules • Inability to perform acceptable-quality spirometry • Moderate or more severe airflow limitation (i.e., FEV_1 < 70% predicted) • A ≥10% reduction in FEV_1 from pre-challenge FEV_1 after administration of the 0-mg capsule • The test should not be performed on those with conditions such as: severe cough, ventilatory impairment, spirometry-induced bronchoconstriction, hemoptysis of unknown origin, pneumothorax, recent abdominal, thoracic or eye surgery, unstable angina, or active upper or lower respiratory tract infection. • History of cardiovascular problems • Pregnancy or nursing mothers

EQUIPMENT AND SUPPLIES

1. Bronchial challenge test kit (mannitol capsules, inhaler, instructions)
2. Spirometer, mouthpiece, and nose clip
3. Timer and calculator
4. Short-acting bronchodilator (e.g., albuterol)
5. Medication and emergency equipment in testing area

PATIENT PREPARATION (PRE-TEST INSTRUCTIONS)

1. The patient should refrain from taking medications that can influence their airway responsiveness to the mannitol challenge test. The medications and time period for withholding them prior to the test are listed in Table 13.3.

ASSESSMENT OF PATIENTS

1. The patient's medical history should be reviewed by a trained physician or professional. This should include:
   - 1.1. Current medications (e.g., bronchodilator and medications for control of blood pressure)
   - 1.2. Other test results including pulmonary function tests, blood gas data, chest radiograph, and blood chemistry
   - 1.3. Current symptoms, including chest pain, discomfort or wheezing, shortness of breath, and dyspnea on exertion
   - 1.4. The clinical diagnosis and reason for the test.
2. Assess each patient for physical and development status to determine ability to perform the diagnostic procedure and if special arrangements are required. If there is a language barrier, an interpreter will be used.
3. Ask each patient if they have complied with the preparation procedures, including:
   - 3.1. If they have eaten recently and, if so, when.
   - 3.2. If they have taken any medications for their breathing.

Table 13.3

Medication Withholding Recommendations	
Medication	**Withhold Time**
Inhaled beta-agonists in conventional doses	
• Short-acting (e.g., albuterol)	6–8 hours
• Long-acting (e.g., salmeterol)	36 hours
Inhaled anticholinergics	
• Short-acting (e.g., ipratropium)	12 hours
• Long-acting (e.g., tiotropium)	48 hours
Antihistamines	
• Short-acting	48 hours
• Long-acting	3 days
Cromones	6–8 hours
Inhaled corticosteroids	12 hours
Leukotriene modifiers	4 days
Inhaled corticosteroids + long acting beta agonists	36 hours

4. Postponement may be necessary if the patient has not complied with the preparation criteria. The ordering physician is to be contacted to determine if rescheduling is necessary.
5. In order to properly interpret the test results, relevant clinical information should be provided in writing by the ordering physician (i.e., diagnosis, and type of treatment).

EQUIPMENT PREPARATION AND CALIBRATION

1. Assure spirometer has been checked for accuracy.
2. Open Bronchial Challenge Test Kit and remove blister packs and inhaler. There are three blister packs numbered consecutively and containing 19 capsules.
   - 2.1. Blister Pack 1 contains four capsules:
     - Marked 1 – 1 × empty clear capsule
     - Marked 2 – 1 × 5 mg white clear capsule
     - Marked 3 – 1 × 10 mg yellow clear capsule
     - Marked 4 – 1 × 20 mg pink clear capsule
   - 2.2. Blister Pack 2 contains 7 capsules:
     - Marked 5 – 1 × 40 mg red clear capsule
     - Marked 6 – 2 × 40 mg red clear capsules
     - Marked 7 – 4 × 40 mg red clear capsules
   - 2.3. Blister Pack 3 contains 8 capsules:
     - Marked 8 – 4 × 40 red clear capsules
     - Marked 9 – 4 × 40 mg clear capsules

PROCEDURE

Pre-Test Preparation		
Step	**Action**	
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition.	
	IF	THEN
	Patient unable to provide information	• Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information
	The identifiers do not match	• Contact registration • Resolve discrepancies before proceeding
	The ID band is present but not attached to the patient	• Do not proceed. • Notify patient's nurse or registration desk
2.	Check for a complete physician's order.	
3.	Collect and record demographic information.	
4.	Explain and discuss the test procedure, and what will be required of the patient, including performing acceptable and repeatable spirometry, type of inhalation flow required for the inhaler, and demonstrations as required.	
5.	Patient should be seated for the test. If the patient needs to use the toilet, they should do so before starting the test. Enter patient demographic information into spirometer, as applicable.	
6.	**Pre-challenge spirometry:** Have patient perform spirometry according to ATS/ERS guidelines (8). Check for any contraindications (e.g., patient's FEV_1 should be ≥ 70% of predicted, and patient should be able to perform acceptable-quality spirometry).	

Test Procedure for Mannitol Challenge Test (7)	
Step	**Action**
1.	**Determine Baseline FEV_1** 1.1. Remove the 0 mg mannitol capsule from foil, twist open the inhaler, place capsule inside inhaler, and close inhaler, 1.2. Pierce the capsule only once by fully depressing both piercing buttons on the sides of the inhaler simultaneously. 1.3. Instruct the patient to attach nose clip. Have patient hold inhaler and tilt inhaler at a 45 degree angle (mouthpiece down), exhale away from inhaler, seal lips tightly around inhaler mouthpiece and to take a controlled and deep inhalation. During a successful inhalation, a rattling sound should be heard as the capsule spins within the inhaler.

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Test Procedure for Mannitol Challenge Test (7) (Continued from previous page)	
Step	**Action**
	1.4. Start the timer for 60 seconds at the end of inhalation and ask the patient to hold their breath for about 5 seconds after inhalation. 1.5. When 5 seconds has elapsed, instruct the patient to exhale through their mouth away from the inhaler, remove the nose clip, and to breathe normally. 1.6. At 60 seconds, perform spirometry on patient and obtain two FEV_1 values. The highest FEV_1 is retained as the Baseline FEV_1. 1.7. If the highest FEV_1 is ≥ 10% lower than the pre-challenge FEV_1, the test should be stopped.
2.	**Calculate the target FEV_1** 2.1. Multiply Baseline FEV_1 by 0.85 and record this target value. 2.2. A positive challenge test is achieved when the patient's FEV_1 falls ≥15% from their baseline FEV_1.
3.	**Administer the 5 mg capsule** 3.1. Insert the 5 mg capsule into the inhaler and pierce the capsule as in Step 1.2. 3.2. Repeat steps 1.3–1.5. 3.3. Following inhalation, remove the capsule from the inhaler and check to ensure it has been emptied sufficiently; if not, a second inhalation will be required immediately. 3.4. Load the 10-mg capsule to prepare for the next dose. 3.5. At 60 seconds following inhalation, perform spirometry on patient and obtain two FEV_1 values. Acceptability criteria must be met. Use the highest value to calculate the change in FEV_1. Since FEV_1 is the only endpoint, a full FVC lasting at least 6 seconds or until a plateau is achieved may not need to be done. 3.6. Compare the FEV_1 value at this dose to the target FEV_1. If the FEV_1 is equal to or below the target value, or there has been an incremental fall of at least 10% from the previous dose, the challenge is positive and complete. If not, immediately proceed to the next dose.
4.	**Administer the 10-mg capsule**, following the directions given in Step 3.
5.	**Administer the 20-mg capsule**, following the directions given in Step 3.
6.	**Administer the 40-mg capsule**, following the directions given in Step 3.
7.	**Administer 80-mg dose (2 × 40-mg capsules).** 7.1. Insert and pierce the first of the two 40-mg capsules that comprise the 80-mg dose. 7.2. The patient should inhale the dose in the same manner as previous doses, hold their breath for the 5 seconds, and then exhale. 7.3. Remove the first 40-mg capsule from the inhaler and check to ensure it has been emptied sufficiently; if not, a second inhalation will be required immediately. Do this check following the inhalation of the contents of each capsule. 7.4. Following inhalation, load the second 40-mg capsule and administer it immediately following the exhalation after the first 40-mg capsule.

(continues on next page)

Test Procedure for Mannitol Challenge Test (7) (Continued from previous page)	
Step	**Action**
	7.5. Instruct the patient to inhale the contents of the second capsule immediately to endure that the osmotic effect of mannitol is cumulative. 7.6. Set the timer for 60 seconds when the contents of second 40-mg capsule has been inhaled. 7.7. Instruct the patient to hold their breath for 5 seconds before exhaling. 7.8. At 60 seconds following inhalation of the contents of the second capsule, perform spirometry on patient and obtain two FEV_1 values. Acceptability criteria must be met. Use the higher of these two values to calculate the change in FEV_1. 7.9. Compare the FEV_1 value at this dose to the target FEV_1. If the FEV_1 is equal to or below the target value, or there has been an incremental fall of at least 10% from the previous dose, the challenge is positive and complete. If not, immediately proceed to the next dose.
8.	**Administer first 160-mg dose (4 × 40-mg capsules)** 8.1. Insert and pierce the first of the four 40-mg capsules that comprise the 160-mg dose. 8.2. The patient should inhale the dose in the same manner as previous doses, hold their breath for the five seconds then exhale. 8.3. Remove the capsule from the inhaler and check to ensure it has been emptied sufficiently; if not, a second inhalation will be required immediately. Do this check following the inhalation of the contents of each capsule. 8.4. Following inhalation, load the second 40-mg capsule and administer it immediately following the exhalation after the first 40-mg capsule. 8.5. The patient should hold their breath for 5 seconds, then exhale. 8.6. Following inhalation, load the third 40-mg capsule and administer it immediately following exhalation. 8.7. The patient should inhale the contents of the third capsule, hold their breath for 5 seconds, then exhale. 8.8. Immediately following inhalation, load the fourth 40-mg capsule and give to the patient immediately following exhalation. 8.9. Instruct the patient to inhale the fourth capsule immediately to ensure the osmotic effect of mannitol is cumulative. 8.10. Set the timer for 60 seconds when the contents of fourth 40-mg capsule has been inhaled. 8.11. Instruct the patient to hold their breath for 5 seconds before exhaling.
	8.12. At 60 seconds following inhalation of the contents of the fourth capsule, perform spirometry on patient and obtain two FEV_1 values. Acceptability criteria must be met. Use the higher of these two values to calculate the change in FEV_1. 8.13. Compare the FEV_1 value at this dose to the target FEV_1. If the FEV_1 is equal to or below the target value, or there has been an incremental fall of at least 10% from the previous dose, the challenge is positive and complete. If not, immediately proceed to the next dose.
9.	**Administer second 160-mg dose (4 × 40-mg capsules)** 9.1. Administer the second 160-mg dose following the directions in Step 8.

(continues on next page)

Test Procedure for Mannitol Challenge Test (7) (Continued from previous page)	
Step	**Action**
10.	**Administer third 160-mg dose (4 × 40-mg capsules)** 10.1. Administer the third 160-mg dose following the directions in Step 8.
11.	**End of challenge** 11.1. following completion of the mannitol challenge test with a positive result or significant respiratory symptoms (e.g., wheezing, dyspnea, cough), administer a short-acting inhaled beta-agonist and monitor patient until fully recovered to within baseline. In the case of a negative outcome, if the patient has significant respiratory symptoms, administer a short-acting inhaled beta-agonist.

Calculations

Positive responses are determined by a change in FEV_1 from the post–0-mg dose, or if there is a fall of at least 10% in FEV_1 between consecutive doses. Below is the formula to calculate the percent change for mannitol challenges using the 0-mg and 5-mg doses as an example.

$$\%\ \text{change} = \frac{\text{Post 0-mg } FEV_1 - \text{Post 5-mg } FEV_1}{\text{Post 0-mg } FEV_1} \times 100$$

If:

Post 0-mg FEV_1 = 3.30 L
Post 5-mg FEV_1 = 3.10 L
The % change = −6.1%

REPORTING OF TEST RESULTS

The response for the mannitol challenge is expressed as the cumulative dose and a provocative dose (PD) causing a 15% reduction in FEV_1 (PD_{15}) value is reported. The PD_{15} is determined by linear interpolation in a similar manner as used to calculate PC_{20} for the methacholine challenge.

Reactivity to mannitol is expressed as percent decrease in FEV_1 at the end of the challenge divided by the cumulative dose of mannitol administered to induce that decrease in FEV_1 (1, 3).

PEDIATRIC CONSIDERATIONS

The Mannitol challenge test should not be performed in children under 6 years of age according to the product information page. There is limited information on the use of Mannitol in patients 6 to 18 years of age (9), and children under age 6 may not be able to perform acceptable and repeatable spirometry to conduct the challenge properly.

PROCEDURE NOTES

1. The inhaler is for single patient use (i.e., one inhaler per challenge test).
2. Pierce the capsule only once by fully depressing both piercing buttons on the sides of the inhaler simultaneously. A second puncture may cause the capsule to split or fragment.
3. Using rubber/latex gloves when administering the test and handling mannitol capsules may increase static and inhibit capsule movement within the inhaler.

4. Inhalation of mannitol may cause coughing and/or dry throat. You can offer the patient water to sip during and after the challenge test.
5. The mannitol challenge test is time critical and requires an osmotic gradient to be established and maintained. Prolonged intervals between doses may affect the validity of the test results and should be avoided.

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APPROVAL

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Annual Review

Date	Signature	Date	Signature

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CHAPTER 14

PROCEDURE NAME: EXERCISE CHALLENGE TEST

PURPOSE OR PRINCIPLE

The purpose of this airway challenge test is to determine whether the patient has exercise-induced airway narrowing. The identification of hyperreactive airways using an exercise stimulus can play an important role in the diagnosis and management of asthma (1–3). The preferred term for bronchoconstriction that occurs during or after short-term exercise is exercise-induced bronchoconstriction (EIB). Although historically referred to as exercise-induced asthma (EIA), it is probably more appropriate to call this condition EIB, because the response to exercise is actually bronchoconstriction and not all people with asthma have EIB (4–6). However, EIB has been reported to occur in up to 90% of children with asthma in some selected series (1, 7, 8), but population-based studies indicate a prevalence of about 50% (9). Several cross-sectional screening studies have found rates of EIB between 10 and 18% in the general population (10, 11). Data from published studies suggest that the severity of asthma correlates with the severity and degree of EIB (1–3). Atopy is a recognized risk factor for EIB, suggesting that patients with allergic rhinitis or atopic dermatitis with exercise-related symptoms may have EIB (12–14).

The pathophysiology of the airway response to exercise has been highly debated (1, 2, 15–17). One theory postulates that the initiating stimulus for bronchoconstriction is the increased ventilation induced by exercise, which induces airway heat loss due both to convection and evaporation. Convective heat loss is related to the heat capacity of gas, and evaporative heat loss is related to the heat of vaporization of water (18). Direct measurements have demonstrated temperature changes in the airway mucosa in humans during exercise (19, 20).

There is also strong evidence that EIB is a manifestation of airway inflammation, since patients with EIB, relative to individuals with asthma without this syndrome, have higher levels of cysteinyl leukotrienes and 8-isoprostanes (21–23, 82). The level of exhaled nitric oxide (eNO) is also correlated with the severity of EIB (24–29). Some studies indicate that EIB may result from injury to the airways, since this syndrome occurs frequently in elite athletes, without prior history of asthma, after exposure to training environments in which they inspire large volumes of cold dry air (30–35).

INDICATIONS

The indications for exercise challenge testing are provided in Table 14.1, and the relative contraindications are presented in Table 14.2.

The list of possible contraindications may not be all-inclusive and therefore is not a substitute for clinical judgment.

Table 14.1

Indications for Exercise Challenge Testing
Clinical Indications for testing include evaluation of (6, 36):
• To diagnose EIB in those with a history of breathlessness or wheezing during or after exercise • To quantify the severity of the airway response to exercise • To assess those engaged in demanding or lifesaving work (e.g., military, police, or firefighting work) • To examine the effectiveness of acute or chronic medication or other therapeutic modalities in the prevention of EIB

Table 14.2

Relative Contraindications for Performing Exercise Challenge Test
Relative contraindications for testing include (6, 36–41):
• Airflow limitation (i.e., FEV_1 < 75% predicted) • Pulse oximetry O_2 saturation of < 94% • Significant cardiovascular disease such as inducible cardiac ischemia, uncontrolled hypertension, aortic aneurysm or life threatening arrhythmias. • Pregnancy due to risk to the fetus • Inability to perform acceptable spirometry; relative contraindications for spirometry (e.g., recent abdominal, thoracic, or eye surgery) should be considered.

EQUIPMENT AND SUPPLIES

1. Treadmill
   - 1.1. Electrically driven
   - 1.2. Speed range 0 to 8 mph (0 to 15 mph for healthy, physically active patients and those who are competitive athletes)
   - 1.3. Grade range, 0% to 20%
   - 1.4. Emergency stop button
   - 1.5. Padded hand rails (front and sides)
2. Cycle ergometer
   - 2.1. Mechanical or electromagnetically braked
   - 2.2. Capable of calibration
   - 2.3. Handlebars and seat that adjust to height
3. ECG system
   - 3.1. Instrumentation should meet the specification set by the American Heart Association (AHA) (42, 43)
   - 3.2. Continuous oscilloscopic monitoring of a minimum of three leads
   - 3.3. 12-lead printed-copy capacity
4. Blood pressure (44)
   - 4.1. Assorted cuff sizes
   - 4.2. Calibrated Bourdon pressure gauge

5. Appropriate standard precautions (SP) attire and gloves for the technician (45)
6. Resuscitation cart (6, 37, 46)
   - 6.1. Airway-management equipment
   - 6.2. Defibrillator
   - 6.3. Suction
   - 6.4. Emergency medications (e.g. epinephrine and lidocaine)
   - 6.5. Bronchodilators (6)
   - 6.6. Oxygen (O_2) equipment and delivery systems (6)
7. Pulse oximeter with a variety of appropriate probes (e.g. ear, finger, reflectance)
8. Chart displaying the ratings of perceived exertion (RPE) scale also known as the Borg scale (47)
9. Inhalant
   - 9.1. Because the tendency to elicit airway narrowing is enhanced when the inhalant is cool and/or dry, special attention to the inhalant is needed.
   - 9.2. If possible, the absolute water content of the inspired air should be below 10 mg/L or relative humidity (RH) less than 50% between 20 and 25° C (6, 36, 48).
   - 9.3. Inhaled gases other than room air can be used but are not required.
   - 9.4. If not using room air, a dry gas source (e.g., compressed air cylinder) with reservoir bag, valves and tubing, or demand valve (48).
   - 9.5. Cold air can be added using a cold-air generating device when the patient's complaints specifically relate to symptoms induced by cold air inhalation; however, cold air is generally not necessary to elicit bronchoconstriction (18, 48).

PATIENT PREPARATION (PRE-TEST INSTRUCTIONS)

1. The patient should be instructed to wear loose-fitting, comfortable clothing and shoes suitable for exercise.
2. The patient should abstain from eating a heavy meal, smoking cigarettes, and consuming alcohol 3 hours prior to test (43, 46, 49–51).
3. The patient should refrain from heavy exercise for at least 4 hours, as this has been found to exert a protective effect (52).
4. The patient should refrain from taking medications that can influence their airway responsiveness to exercise (6, 48–51, 53–55). The medications and the time period for withholding them prior to the test are listed in Table 14.3.
5. There should be a brief explanation of the procedure and the patient's questions should be answered before the test (36, 46, 51).
6. Informed consent should be obtained and witnessed by personnel who can accurately describe the test and potential risks (37, 38, 49, 56) (*see* Appendix 14.1).
7. Other variables that could affect the diagnostic value of the procedure include:
   - 7.1. Regular use of bronchodilators increases the severity of EIB (57, 58).
   - 7.2. A recent study demonstrated a preventative effect of a single high dose of an inhaled corticosteroid prior to exercise and eucapnic hyperventilation challenge (59, 60).

Table 14.3

Medication Withholding Recommendations	
Medication	**Length of Abstention**
Inhaled beta-agonists in conventional doses	
• Short-acting (e.g., albuterol)	6 hours
• Long-acting (e.g., salmeterol)	36 hours
Inhaled anticholinergics	
• Short-acting (e.g., ipratropium)	12 hours
• Long-acting (e.g., tiotropium)	48 hours
Antihistamines	
• Short-acting	48 hours
• Long-acting	3 days

Note: Cromones, inhaled low-dose corticosteroids, and leukotriene modifiers have little or no effect in single dose and do not need to be withheld unless the intent is to offload an anti-inflammatory effect, in which case the withhold time should be weeks. Caffeine and caffeine-related products (e.g., chocolate) have no effect of clinical significance. Influenza vaccination, the menstrual cycle, and oral contraceptives do not significantly affect airway responsiveness.

ASSESSMENT OF PATIENTS

1. The patient's medical history should be reviewed by a trained physician or professional (5). This should include:
    1.1. The current medications (e.g., bronchodilator and medications for control of blood pressure)
    1.2. Tests including pulmonary function tests, blood gas data, chest radiograph, and blood chemistry results
    1.3. Current symptoms, including chest pain, discomfort or wheezing, shortness of breath, and dyspnea on exertion
    1.4. The patient's exercise limitations and activities of daily living
    1.5. The clinical diagnosis and reason for the test.
2. Assess each patient for physical and development status to determine ability to perform the diagnostic procedure and if special arrangements are required. If there is a language barrier, an interpreter will be used.
3. Ask each patient if they have complied with the preparation procedures, including:
    3.1. If they have eaten recently and, if so, when.
    3.2. If they have taken any medications for their breathing.
    3.3. If they have recently exercised, if so, when.
4. Postponement may be necessary if he/she have not complied with the preparation criteria. The ordering physician is to be contacted to determine if rescheduling is necessary.
5. In order to properly interpret the test results, relevant clinical information should be provided in writing by the ordering physician (i.e., diagnosis, and type of treatment)

EQUIPMENT PREPARATION AND CALIBRATION

1. Room specifications (46, 50, 56)
   - 1.1. Large enough to accommodate equipment, personnel and emergencies
   - 1.2. Room temperature between 20 and 25° C
   - 1.3. Relaxed, pleasant atmosphere
   - 1.4. If not using a dry gas source the absolute water content of the inspired air should be below 10 mg/L or RH less than 50% between 20 and 25° C.
2. Treadmill
   - 2.1. Calibrate speed and grade every 3 to 6 months (50).
     - 2.1.1. To calibrate speed:
       - Measure length of belt and place a mark on the belt.
       - Using stopwatch, count the number of laps made by the mark per minute.
       - Recheck with average size patient on the treadmill.
     - 2.1.2. To calibrate grade:
       - The grade can be calibrated by measuring treadmill height from the ground versus the length of the treadmill. A carpenter's square and level are helpful.

$$\%\ \text{grade} = \frac{\text{vertical height of elevation}}{\text{length of the treadmill}} \times 100$$

3. Cycle ergometers (mechanically and electrically braked)
   - 3.1. Mechanically braked cycles are less expensive but require a constant pedal frequency to maintain constant power output.
   - 3.2. Electrically braked cycles are more expensive; however, the power output of the ergometer is more accurate at varying pedal frequencies.
   - 3.3. Calibrate every 3 to 6 months (50).
   - 3.4. Verify pedal frequency with a stopwatch.
   - 3.5. Static calibration with weights allows the user to perform checks of the internal force transducer, although it does not check the internal resistance of the cycle.
   - 3.6. Dynamic calibration requires a means of externally turning the crank of the cycle while measuring the torque (61, 62). Some manufacturers may loan or rent calibrators for validation studies.
   - 3.7. Electronically braked cycles may lose their calibration, if they are not carefully handled when moved.
4. Pulse oximetry
   - 4.1. Refer to manufacturer's operation manual to obtain quality assurance instructions for the particular brand and model.
   - 4.2. Have several optional probes available (e.g. finger, ear, reflectance, etc.)
5. Resuscitation Cart and Training
   - 5.1. Check daily or weekly, according to institution policy (37, 46).
   - 5.2. An inventory checklist should accompany the cart.
   - 5.3. Check for missing or outdated medications.
   - 5.4. Check operation of airway-management equipment.
   - 5.5. Check the function of the defibrillator.
   - 5.6. An emergency-response plan should be available and understood by all personnel.
   - 5.7. Testing personnel should be knowledgeable in basic ECG arrhythmia recognition and basic life support (63). It is strongly encouraged that they be trained in advanced cardiac life support (46).

6. Recommendations for additional equipment and set-ups have been reported (48, 63).
   6.1. Dry inspired air via a reservoir bag; connecting tubing, one-way valve or demand valve may be used to accentuate the response (48). This additional equipment can also be used if the water content of the room is more than 10 mg/L (20 to 23° C, 50% RH).
   6.2. Cold dry air using a heat exchanger may be used to accentuate the response (18, 48). This device may be advantageous because it shortens the duration of the challenge portion of the test needed to induce bronchoconstriction in some studies.

PROCEDURE

Several attempts have been made to standardize the exercise challenge testing procedure, but the methodology is still inconsistent (4–6, 36, 48, 54, 64, 65). Some of the difficulty of standardization can be attributed to the different populations being tested. Silverman and Anderson (4) and others have recommended exercise guidelines specific for children with asthma (54, 55). Others have recommended protocols that relate to a broad spectrum of adult populations (36, 53, 64, 65). Debate remains ongoing regarding the preferred type of exercise device. An early study demonstrated that treadmill exercise is more provocative than cycle testing. This same study reported a higher degree of response associated with free-running versus running on a treadmill, which could be possibly related to environmental factors or the level of exercise achieved (66). Currently, several authors recommend the use of cycle ergometers because it is easier to determine work rates and to monitor additional variables (53, 64). Selection of the exercise device and the type of exercise will likely be related to the availability of the equipment, staff preferences, and the clinical presentation and abilities of the patient.

The test that has been extensively validated using a rapid ramp to 85% maximum HR and then a plateau phase at that work level for an additional 6 minutes. Safety concerns, especially in older adults, have led to a slower ramp up to the 85% target.

1. Pulmonary Function (PF) Test Evaluation Methodology

PF tests are used to assess the airway function and responsiveness before and after exercise.

1.1. The type of measurement can be specific for the clinical presentation of the patient or the sophistication of the laboratory, but spirometry is the standard mode of testing.

1.2. Spirometry is performed according to ATS/ERS recommendations prior to and after the exercise period (67). However, two acceptable spirometric test maneuvers (instead of the usual three) may be used for time considerations.

1.3. Peak expiratory flow rate (PEFR) using a peak flow meter can be used. However, while the instrumentation is less expensive than a spirometer, the PEFR measurement using a peak flow meter is more variable, more effort dependent, has poor quality control, and is less sensitive.

1.4. Airways resistance (Raw) can be a sensitive indicator of airway responsiveness (5, 68).

1.5. Static lung volume measurements can be performed to assess air trapping (6).

1.6. PF test equipment should be calibrated according to manufacturer's and ATS/ERS recommendations (67).

2. Exercise Intensity

2.1. Several authors recommend an exercise intensity based on the heart rate response (5, 6, 15, 48, 63, 69). Using the heart rate as an indicator of exercise intensity allows use of the treadmill or various ergometers and adjustment of the work rate based on the patient's aerobic capacity.

2.1.1. A wide range of recommended heart rate levels are reported in the literature (5, 6, 15, 48, 63, 69). Achieving 85% (adults), and 90% (children) of the predicted maximal heart rate for the patient is the most common approach.

2.1.2. Two simple equations have been described for predicting maximum heart rate (Max HR) (39, 40, 49):

1. Max HR = 210 − [0.65 × (age)]
2. Max HR = 220 − age.

2.1.3. Predicted Max HR can be affected by medication (e.g. beta-blockers) (37)

2.1.4. Multiply predicted Max HR times 0.85 to obtain target heart rate.

2.2. Minute ventilation ($\dot{V}E$) can also be monitored; however, this requires monitoring expired gas during exercise. Exercise intensities can be chosen to target 40 to 60% (80% in elite athletes) of the measured or calculated maximum voluntary ventilation (MVV) (36, 48).

2.2.1. Calculated MVV equals 35 to 40 times the measured FEV_1 (49).

2.2.2. Multiply MVV times 0.4 to 0.6, or 0.8 for elite athletes.

2.3. Using 60 to 80% of the predicted maximum O_2 consumption ($\dot{V}O_2max$) has also been reported (19, 53, 69), but determination of O_2 uptake may be more complicated and impractical.

2.3.1. Calculate predicted $\dot{V}O_2max$; one set of regression formulas (39) is:

1. Males: [60 − 0.55(age)] × (weight in kg)
2. Females: [48 − 0.37(age)] × (weight in kg)

2.3.2. Multiply predicted $\dot{V}O_2max$ times 0.60 to 0.80 to obtain target $\dot{V}O_2$.

2.4. Treadmill protocols

2.4.1. Several standardized treadmill protocols state the work rate relationship at each stage to a corresponding MET (metabolic equivalent) (70–72).

2.4.2. To calculate the $\dot{V}O_2$ for a target work rate:

1. Calculate the target $\dot{V}O_2$.
2. Divide target $\dot{V}O_2$ by the patient's body weight in kg.
3. Divide $\dot{V}O_2$/kg by 3.5 to obtain MET value.
4. Use the work rate that corresponds to this MET value to determine highest exercise level.

2.5. Cycle ergometer protocol

2.5.1. To calculate the $\dot{V}O_2$ for a given work rate:

1. Calculate the target $\dot{V}O_2$.
2. ($\dot{V}O_2$,target – $\dot{V}O_2$,unloaded)/10 = work rate, where work rate is in watts, $\dot{V}O_2$ in ml/min (73).
3. Use this work rate to determine highest exercise level.

Pre-Test Preparation	
Step	**Action**
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition. IF / THEN Patient unable to provide information → • Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information The identifiers do not match → • Contact registration • Resolve discrepancies before proceeding The ID band is present but not attached to the patient → • Do not proceed. • Notify patient's nurse or registration desk
2.	Check for a complete physician's order.
3.	Collect and record demographic information.
4.	Explain the test procedure and what will be required of the patient.
5.	Place ECG electrodes • The modified 10-electrode (Mason-Likar) configuration is the preferred method (42, 43). • A modified 5-lead configuration may be used in patients under the age of 35 with no history of cardiovascular disease (a 3-lead system has also been reported in patients without cardiovascular risk) (6). • In some cases (young and otherwise healthy individuals), the pulse oximeter can be used to monitor heart rate. • Skin preparation is essential to reduce surface resistance and ensure a good ECG signal (37, 46, 51). • Shave hair when applicable. • Use an alcohol wipe to remove surface oils. • Abrade skin with fine emery cloth (sandpaper, 240 grid) or mechanical skin-preparation device (Note: commercial skin preps that include an abrasive and alcohol are available). • Implementing a method for cable stabilization is important to reduce motion artifact (46).

6.	Discuss test performance with patient
	• Explain the purpose of the test. The patient will perform PF tests before and after exercise. The patient will exercise at a moderate to heavy intensity level for approximately 6 to 8 minutes.
	• Explain the end-points (5), which include but are not limited to:
	  ○ Attainment of predetermined heart rate or ventilation level
	  ○ Development of limiting symptoms (e.g., wheezing, chest tightness, and chest pain)
	  ○ Severe blood pressure elevation or blood pressure fall
	  ○ ECG abnormalities
	• Explain Borg scale.

7.	Perform pre-exercise PF tests • Spirometry with the measurement of FEV_1 is considered the most useful and reproducible test (5, 6, 22, 30). It should be performed using ATS/ERS methodology with at least three acceptable forced vital capacity (FVC) maneuvers (67). • Static lung volumes to evaluate hyperinflation (air-trapping) may be useful in some cases (6). • Raw measured via plethysmography is more sensitive and less effort-dependent but may be more variable (5, 68).

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Pre-Test Preparation (Continued from previous page)	
Step	**Action**
8.	Determine exercise intensity • Several methods of determining the exercise intensity for the test are reviewed above (see **Exercise Intensity).** • The most common approach is to multiply predicted Max HR times 0.85 to obtain target heart rate.

Test Procedure for Exercise Challenge Test	
Step	**Action**
1.	Position patient on treadmill or cycle ergometer

2.	Treadmill Instructions:
	• Instruct the patient to keep hands at side.
	  ○ If railings are used, the back of the hands can be used for balance or light touch.
	  ○ Arm support decreases the effective work rate (6). Arm support also increases the muscle artifact in the ECG tracing (35).
	• A brief trial walk may be appropriate both to familiarize the patient with the equipment and to check the ECG signal for motion artifact.
	• For the patient's safety, a spotter at the rear of the treadmill may be appropriate.

3,	Cycle Ergometer Instructions: • Adjust handlebar and saddle height. • When pedal is at bottom dead center, leg extension should be about 20° at the knees. • Instruct patient on pedal speed (*see* ergometer manual for linearity tolerance). • A brief trial with little or no power output may be appropriate both to familiarize the patient with the equipment and to check the ECG signal for motion artifact.
4.	Instruct patient on use of Borg scale (47, 74) or other rating scales (e.g., chest pain, chest tightness, light-headedness, etc).
5.	Place nose clip on the patient just prior to starting exercise and leave in place during the exercise test (5, 6, 36, 48, 73). • Nose clip is recommended to maximize the drying of the airways. • Use of a nose clip also ensures the same breathing strategy (mouth-breathing) throughout exercise.
6.	Place pulse oximeter probe: • Select probe (e.g. finger, ear probe, or reflectance). • Prep the site, if applicable, according to oximeter manual instructions.
7.	Obtain resting ECG. Results may differ morphologically (e.g. T-wave inversion) from standard ECG performed in the supine position with limb-lead configuration (37, 46).
8.	Obtain resting blood pressure measurement and assess results for contraindications.
9.	Obtain resting RPE and/or other subjective information (e.g., shortness of breath, chest tightness, wheezing, chest pain). A 0–4 scale can be used, where 0 is nothing at all, and 4 is severe (74).

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Test Procedure for Exercise Challenge Test (Continued from previous page)	
Step	**Action**
10.	Exercise Protocol: • General consensus is that the overall exercise time be 6 to 10 minutes (1, 2, 4–6, 36, 48, 53, 54, 64, 65, 69) • If the target workload is overestimated, the work rate can be reduced during the test to maintain the exercise response in the desired range. • Two methods of achieving the desired exercise level are (5, 64): ○ Rapid increase in the work rate over the first 1 to 2 minutes to the pre-determined work rate, then continue for 6 to 8 minutes. ○ In adults it is recommended for safety reasons that the high-work plateau be approached in three steps to allow for careful observations of the cardiopulmonary response (64). × 2 minutes warm-up at a low intensity × 2 minutes at a moderate work rate × 5 to 8 minutes at the target work rate
11.	Start exercise using selected protocol • Obtain ECG, blood pressure, subjective measurements (i.e., RPE, asthma symptoms) at rest, during and immediately after exercise. • Blood pressure is often difficult to measure accurately during exercise (75). • Auscultation of the chest can be performed before, during and after exercise (5).
12.	Exercise to predetermined end-point or early termination criteria • *See* sections Exercise Intensity for target • *See* Table 14.4

Post-test Procedure	
Step	**Action**
1.	Post-exercise phase: • There should be a brief cool-down phase at a reduced work rate for 1 to 2 minutes. • An ECG should be recorded every minute until discontinuation of test. Monitoring of physiologic variables should continue until abnormal ECG or blood pressure results are resolved (46).
2	Post-exercise PF tests: • Performed serially for approximately 30 minutes (5, 6, 48, 63–65). • Many laboratories conduct the first PF test immediately after exercise, and then 3, 6, 10, 15, and 30 minutes after exercise is stopped. Performing PF tests immediately after exercise is stopped may be artificially low due to exhaustion. • Another appropriate post-exercise testing schedule is 5, 10, 15, 20, and 30 minutes after cessation of exercise (52). • Following patients for more than 30 minutes is controversial (76, 77).
3.	Spirometry: • Performed according to ATS/ERS recommendations (67). • At least two and preferably three acceptable tests should be obtained at each testing interval. • As a goal, the highest and second highest FEV_1 values should differ by no more than 0.150 L. • The highest of the acceptable FEV_1 values is selected as the representative value at each interval. • If FEV_1 has returned from its nadir (low-point) to the baseline level or greater, spirometry testing can be terminated at 20 minutes post-exercise.

(continues on next page)

Post-test Procedure (Continued from previous page)	
Step	**Action**
4.	If EIB is documented by PF tests: • Administer bronchodilator(s) as needed. • Typically 0.5 ml of albuterol in 1 ml of normal saline is administered by small-volume nebulizer, or two inhalations of albuterol from a metered dose inhaler can be used. • Wait 10 minutes and re-measure PF tests after the bronchodilator to ensure the patient's FEV_1 is at least 90% of baseline before the patient leaves the laboratory.

Calculations

1. For each interval of spirometric measurements performed after exercise, the highest repeatable FEV_1 should be reported (52). The severity of the response is assessed by taking the interval with the lowest FEV_1 observed after exercise (i.e., interval with the greatest drop), subtracting it from the pre-exercise value, and expressing it as a percentage of the pre-exercise level (4, 36, 48). This is applicable whether using PEFR, FEV_1, or Raw.

$$\%\ change = \frac{pre\ exercise - post\ exercise}{pre\ exercise} \times 100$$

2. Some laboratories measure FEV_1 or PEFR during exercise, especially if airflow obstruction is present at rest. A lability index can then be derived by taking the highest value recorded during exercise, subtracting the lowest reproducible value observed after exercise, and expressing it as a percentage of the pre-exercise level (4, 37).

$$Lability\ \% = \frac{highest\ during\ exercise - lowest\ post\ exercise}{pre\ exercise} \times 100$$

REPORTING OF TEST RESULTS

1. The units that apply to the measurement of the PF tests are:
   - 1.1. FVC is expressed in L (BTPS)
   - 1.2. FEV_1 is expressed in L (BTPS)
   - 1.3. PEFR is expressed in L/s (BTPS)
   - 1.4. Raw is recorded in cm H_2O/L/sec
2. The fewest values that constitute an adequate report are the pre-exercise value, the lowest repeatable post-exercise value, and the percent change.
3. Other variables that need to be recorded are:
   - 3.1. Type of exercise device
   - 3.2. Sustained work rate and ventilation, if available
   - 3.3. Total exercise time
   - 3.4. Max HR and length of time at target HR
   - 3.5. Interpretation of the ECG
   - 3.6. O_2 saturation via pulse oximetry, if measured

3.7. Environmental factors: room temperature, relative humidity, and barometric pressure
3.8. Additional provocations, if applicable
- Dry air
- Cold air
- Delivery method (e.g. reservoir bag, and demand valve)

3.9. Clinical signs and symptoms (e.g., wheezing and cough)
3.10. Bronchodilator(s) or other medication(s) administered after exercise, if applicable. Spirometry data from post-bronchodilator stage should be reported.

PROCEDURE NOTES

1. Several factors may influence the test results.
1.1. Repeatability of the PF tests
1.1.1. If the patient cannot perform repeatable maneuvers, the test is invalid.
1.2. Any exercise preceding the test can cause a refractory period to EIB up to several hours (48, 63).
1.3. The temperature and RH of the inhaled gas can affect the level of response (6, 36, 48, 54, 55).
1.4. The addition of dry air from a compressed gas cylinder may cause a greater response in some individuals (48, 63, 78).
1.5. The addition of cold air (compared to dry air) may cause a greater response in some individuals (19).
1.6. Medications (if not withheld) can affect the test outcome.
1.7. Exercise device selection and usage
1.7.1. Patient performance, coordination, physical limitation with a particular exercise device can affect results. These include:
- Inability to walk on treadmill
- Weight support on handrails
- Inability to coordinate pedaling effort
- Orthopedic constrains

1.8. The use of arm ergometry for this test is not recommended because the obtained level of ventilation is usually not high enough.
1.9. Interpretation: a decrease in FEV_1 from baseline of at least 10% is suggestive of EIB (79, 80). However, the specificity is higher with a decrease of ≥15% from baseline.
1.10. When the purpose of this test is to evaluate pharmacotherapy (i.e., which drug[s] and what dose will block or attenuate the response), the drug(s) being evaluated should be administered long enough before exercise to ensure they have taken effect. PF tests can be measured before and after the administration of the drug(s), although the essential measurement is after administration and just prior to exercise (81).
1.11. The use of a facemask to deliver dry and/or cold air is not recommended because of the warming and humidification effect.
1.12. Patient Safety: The most common problem encountered in exercising a patient with asthma is severe bronchoconstriction that can usually be treated rapidly and successfully by administering nebulized bronchodilator with O_2. The approach to monitoring will vary depending on the setting and the risk of the patient. A hospital setting may be more appropriate for higher risk patients since a resuscitation team may be readily available. In contrast, a young relatively healthy patient can be tested in a laboratory with minimal monitoring, an experienced technologist present and a physician in the immediate area. In a setting with less support and a higher risk patient, more intense monitoring by individuals with the skills to appropriately diagnose and treat adverse events would be necessary (52).

Table 14-4

Indications for stopping an exercise test (5, 37, 41, 50, 51)	
Cardiac signs and symptoms	Progressive angina (3 on 1–4 scale)
	Ventricular tachycardia
	>2 to 4 mm horizontal or down-sloping ST depression
	A significant drop (>20 mm Hg) in blood pressure or failure of the blood pressure to rise over several minutes of exercise.
	Onset of second or third degree heart block
	Exercise-induced left bundle branch block
	Sustained supraventricular tachycardia
Other Symptoms	Lightheadedness, confusion, nausea, ataxia, pallor, etc.
	Patient complains of severe chest tightness or wheezing
	Volitional termination by the patient (i.e., cannot continue)
Monitoring	Failure of the ECG or blood-pressure monitoring system

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APPENDIX 14.1

Example of Informed Consent for Exercise Challenge Test

To determine the nature and severity of your pulmonary disease, you are being asked to voluntarily agree to engage in an exercise test. The test will be conducted on an appropriate exercise device (e.g., treadmill). You will be asked to wear a nose clip and we will monitor your heart, blood pressure, and oxygen saturation. The exercise intensity will be increased until you are at about 80% of your maximum and we will ask you to continue to exercise for about 10 minutes. We will have you blow into a spirometer to measure your lung function before and several times after the exercise period.

The information obtained will be used to help your doctor understand more about the effect of exercise on your breathing. The test including the electrocardiogram (ECG) and blood pressure will be monitored by a trained professional and precautions for your safety will be observed.

Risks of the testing procedure are modest and complications from the test are rare. But they do include the following: fainting, falling, irregularities of heartbeat, wheezing and shortness of breath, and, very rarely, heart attack or death (less than 1 in 10,000 cases).

Physical injury can occur because of the unfamiliarity with the equipment on the part of the patient. Every effort will be made to explain the nature of the exercise equipment prior to starting the test.

Professional staff will be present and necessary equipment available for emergency treatment, if any problems should arise.

I have read and fully understand the above and voluntarily consent to perform this exercise test at the _____ _____ hospital/clinic.

Patient Name (Print) _____

Patient or legal guardian signature _____

Date _____

Witness _____

Physician supervising the test _____

APPROVAL

Signature: _____ Date: _____

Annual Review

Date	Signature	Date	Signature

Revisions / Document History

Effective Date	Synopsis of Change

Effective Date: 2014
Version #1

CHAPTER 15

PROCEDURE NAME: PERCUTANEOUS ARTERIAL BLOOD SAMPLING

PURPOSE OR PRINCIPLE

Every individual performing arterial punctures must know the dangers of the procedure and the precautions that minimize hazards to the patient, or healthcare worker, and the factors that alter the test results. Related policies that define qualifications, training, and competency reviews for individuals who obtain arterial blood specimens and analyze them for blood gas or related values must be followed. All individuals approved for this procedure are required to successfully complete a structured and documented training program that is specifically designed for this procedure. Records of such training and certification will be kept on file as required by the College of American Pathologists (CAP), Joint Commission on the Accreditation of Hospitals (JCAHO), and The Clinical Laboratory Act of 1988 (CLIA'88). All training and certification must be under the guidance and direction of the laboratory medical director. Only personnel certified by the laboratory medical director should perform arterial punctures.

The physician's order should be validated by referring to the patient's chart. Blood is drawn anaerobically from a peripheral artery (radial or brachial) via a single percutaneous needle puncture. This provides a blood specimen for direct measurement of the partial pressure of arterial carbon dioxide (Pa_{CO_2}) and the partial pressure of arterial oxygen (Pa_{O_2}), hydrogen ion activity (pH), total hemoglobin (tHb), oxyhemoglobin (O_2Hb), and the dyshemoglobins, carboxyhemoglobin (COHb) and methemoglobin (MetHb). Additional analytes may also be obtained from whole blood specimens (e.g., electrolytes).

The proper collection of specimens is the first step to reliable test results. The specimen for blood gas analysis should be collected in a suitable heparinized plastic syringe. The blood must be anticoagulated to prevent clotting within the analyzer. For convenience, kits are available that contain a preheparinized syringe, needle, needle protection guard to avoid recapping, syringe cap, skin preparation solutions, gauze sponge, adhesive bandage, specimen labels, and transport bag.

Not all brands of blood gas syringes are compatible with all blood gas analyzers. The preheparinized syringes are evaluated by the blood gas analysis device manufacturer for anticoagulation effectiveness and analyte interference. Thus, it is important to follow the analyzer manufacturer's recommendation for heparin compatibility with the analytes being measured.

Before plastic syringes became customary, glass syringes were used for blood gas specimen collection. The syringe was immersed in an ice-water bath to slow the white blood cell metabolism, thereby retarding oxygen (O_2) consumption. Syringes made of plastic are more gas permeable than glass, and when cooled they can accelerate a

flux that can artificially elevate Po_2 results. Therefore, it is strongly recommended that specimens obtained in plastic syringes for blood gas measurements be stored at room temperature. If analysis is anticipated to be delayed by more than 30 minutes, the blood should be collected in a glass syringe and placed in an ice water bath (1, 2).

Proper specimen labeling is critical to assuring appropriate interpretation of results and adhering to good laboratory practice standards. The key components of proper documentation are: patient's name, identification number, location, body temperature, respiratory rate, date, time of sampling, sampling site, results of a modified Allen test, name or initials of person who obtained the specimen, name of physician requesting the test, and any therapeutic interventions (e.g., mechanical ventilation settings, supplemental O_2 flow rate, and delivery system) (1).

INDICATIONS AND CONTRAINDICATIONS

Indications for arterial blood sampling are provided in Table 15.1.

The American Association for Respiratory Care and the Clinical and Laboratory Standards Institute have published guidelines for percutaneous arterial blood sampling. This procedure includes the most recent recommendations (1, 3).

A list of relative contraindications is presented in Table 15.2.

EQUIPMENT AND SUPPLIES

All equipment should be used in accordance with the manufacturer's instructions.

The following equipment is required to collect an arterial blood specimen:

1. Collection Device
   - 1.1. For percutaneous arterial blood sampling a 1-, 3-, or 5-ml, self-filling, plastic, disposable syringe, prefilled with an appropriate amount and type of lyophilized heparin salt or other suitable coagulant, is most common (1, 2).
   - 1.2. Follow manufacturer recommendations for use of different types of syringes (e.g., pre-set or self-filling syringes, and aspiration-type syringes).
2. Hypodermic needles

Table 15.1

Indications for Arterial Blood Sampling (3)
Clinical Indications for arterial blood sampling:
• Evaluation of adequacy of ventilation, acid–base status, oxygenation status, and the O_2-carrying capacity of blood • Quantification of the patient's response to therapeutic intervention and/or diagnostic evaluation • Monitor the severity and progression of a documented disease process

Table 15.2

Relative Contraindications for Performing Arterial Blood Sampling (2)
Relative contraindications for arterial blood sampling include:
• A negative Allen test for a radial puncture site (*see* Patient Preparation, section 7) • Performance of a puncture through a lesion or through or distal to a surgical shunt • Coagulapathy or medium-to-high-dose anticoagulation therapy (relative)

2.1. Preferably short-bevel, 20- to 25-gauge needles with length from 5/8 to 1½ inch, (depending on sampling site) are acceptable for arterial puncture (1).
2.2. Smaller gauge needs (e.g., 25 gauge) may require gentle aspiration (4).

3. Anticoagulant
   3.1. The choice and type of heparin depends on the specific analytes to be measured and the method analysis (1).
4. Antiseptic supplies (e.g. isopropanol sponges) are required for cleansing the puncture site (1).
5. Specimen label adequate for unique specimen identification (1)
6. Sterile gauze pads (1)
7. Engineered sharps: equipment with engineered sharps injury protections that allow for one-handed removal of the needle, or other suitable capping device for the blood specimen syringe or collection device (1)
8. Coolant (e.g., container of ice water or other coolant capable of maintaining a temperature of 1 to 5° C and large enough to allow for immersion of the barrel of the syringe or collection device if the specimen is not expected to be analyzed within 30 minutes [1])
9. Disposal container: a puncture-resistant disposal container in which to place used needles and syringes (1)
10. Barrier protection: standard precautions need to be diligently followed to protect the health practitioner from biohazard infections. These Standard Precautions are accepted standards that are dictated by the Occupational Safety and Health Administration (OSHA), the Centers for Disease Control and Prevention (CDC), and all organizations that oversee best practices for laboratory safety. Standards include: hand washing, donning barrier protective clothing (e.g., gloves at minimum), and the avoidance of recapping needles.

PATIENT PREPARATION

1. Identify the patient using institutionally-approved process.
2. Validate the physician's order.
   2.1. Confirm absence of allergy to antiseptic (1).
3. Verify that any supplemental oxygen (O_2) has been stable for ≥15 minutes prior to sampling.
4. Assess and verify stability of patient conditions which may influence results (e.g., body temperature, respiratory rate, ventilator settings, supplemental O_2).
5. Assess the patient for physical and developmental status to determine if special arrangements are required. If there is a language barrier, an interpreter is to be utilized.
6. Explain the procedure to the patient, answering any questions and attempting to allay any fears.
7. The patient may be either seated or supine for radial or brachial punctures.
8. Perform a modified Allen test to confirm presence or absence of radial artery occlusion.
   8.1. The Allen test was originally described in 1929 for confirming the presence of radial artery occlusion (5). The modified Allen test is now used to assess collateral circulation to the hand (4).
   8.2. Modified Allen test: ask patient to close fist tightly to force most of the blood from the hand. Apply pressure at wrist to compress and obstruct radial and ulnar arteries. Ask patient to unclench fist and then remove pressure from only the ulnar artery. Observe the inside of the palm for flushing of palm, fingers, and thumb for 15 seconds. Flushing within 15 seconds indicates a positive modified Allen test. Negative results must prompt assessment of alternative sites.

8.3. Limitations of the modified Allen test include (6):
   1. It cannot be performed properly on unconscious patients, or those with wrist or palm burns.
   2. Patients in shock, deeply jaundiced, or pallid present a problem with evaluation of reperfusion.

9. Site preparation

9.1. The puncture site and an area at least 2 inches in diameter surrounding the site should be prepared by scrubbing it with an antiseptic. If the technologist is unable to obtain a specimen from a site and another site is chosen, the new site should be prepared in the same way. A new, appropriately sized, sterile needle should be used for each puncture attempt.

10. Sample size depends on the amount and type of anticoagulant and the specific analyzer. A volume smaller than 0.5 ml can be analyzed for pH, Pa_{CO_2}, and Pa_{O_2}, but may give false results due to dilution if liquid sodium heparin is used (1, 7).

10.1. Sample size for infants weighing less than 10 kg is no more than 0.5 ml.

ASSESSMENT OF PATIENTS

1. Assess each patient for physical and developmental status to determine if the ability to undergo the test and if special arrangements are required. If there is a language barrier, an interpreter is to be utilized.
2. Ask each patient if he/she has complied with the preparation criteria, or check medical record to assure the preparation criteria have been met.
3. Postponement may be necessary if the patient has not complied with the preparation criteria. The ordering physician is to be contacted to determine if rescheduling is necessary.
4. In order to properly interpret the test results, relevant clinical information (i.e., diagnosis and type of treatment) must be provided in writing by the ordering physician.

SELECTION OF SITE

The site of preference is the radial artery (4). Should the radial arteries be ruled out, the brachial artery is the next choice, with the femoral artery the last choice. The radial artery site should not be used if the modified Allen test demonstrates poor ulnar blood flow. Other reasons for excluding the radial artery include inaccessibility due to dressings, casts, and IV lines; hematomas or laceration of tissue due to multiple radial punctures, or the inability to adequately palpate the vessel; or patient statement of previous difficulties with radial punctures.

1. Radial artery

1.1. Although small, it is easily accessible in most patients and the most commonly used site in clinical situations (1).

1.2. Is easily compressed over the firm ligaments of the wrist, and incidence of hematomas is relatively low (1).

1.3. Collateral circulation to the hand is normally provided by the ulnar artery, and the Modified Allen test may be helpful in evaluating this collateral circulation (4).

2. Brachial artery

2.1. May be preferred for larger volumes, but may be more difficult to puncture due to deeper location between muscles and connective tissue (1).

2.2. Proper positioning of arm with hyperextension improves the position of the artery for puncture.

2.3. May be difficult to palpate in obese patients (1).

2.4. Effective compression of the puncture site is more difficult because of the deep location, and incidence of hematoma formation may be more common than the radial site (1).

2.5. Not commonly selected as a site in infants and children because of issues with palpation and lack of collateral circulation (1).

3. Femoral artery
   3.1. Large vessel that is easily palpated and punctured (1).
   3.2. Generally, this is the last site selected in clinical practice because of poor collateral circulation to the leg, and increased chance of infection if the site is not thoroughly cleansed (1).
4. Age limits for the performance of arterial punctures versus capillary samples should be defined by each medical director.

Hazards/Complications of Arterial Puncture (1)

1. Vasovagal response, which can result in a loss of consciousness. If patient has fainted or is unexpectedly nonresponsive you should:
   1.1. Notify the designated first-aid-trained personnel.
   1.2. Where practical, lay the patient flat or lower his/her head and arms (if sitting) and loosen tight clothing.
2. Arteriospasm
   2.1. A reflex constriction of the artery in response to pain or other stimuli.
   2.2. May make it impossible to obtain blood even though needle is properly located in the lumen.
3. Hematoma
4. Thrombosis and embolism
   4.1. Most likely to happen if a needle or cannula is left in place for some time.

PROCEDURE (1, 4)

Pre-Test Preparation		
Step	**Action**	
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition.	
	IF	THEN
	Patient unable to provide information	• Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information.
	The identifiers do not match	• Contact registration. • Resolve discrepancies before proceeding.
	The ID band is present but not attached to the patient	• Do not proceed. • Notify patient's nurse or registration desk.
2.	Check for a complete physician's order.	
3.	Collect and record demographic information, verify clinical indication for arterial sampling, verify ventilatory status, F_{IO2}, and delivery system.	
4.	Explain the specimen collection procedure and have patient seated or lying comfortably.	

Test Procedure for Radial Artery Puncture	
Step	**Action**
1.	Set-up and preparing for specimen collection • Before this site is selected, the presence of adequate collateral circulation via the ulnar artery should be assessed by a modified Allen Test, or with a Doppler ultrasonic flow indicator, or both. • If the Allen test indicates adequate collateral circulation, the radial artery may be punctured. • The arm should be rotated (abducted) with the palm facing up and the wrist extended about 30° to stretch and fix the soft tissue over the ligaments and bone. A rolled towel or other wrist support can used to support the wrist. • Locate the artery and exact puncture site by palpating the radial artery with the fingers of one hand.
2.	Prepare the puncture site aseptically. Be certain that after cleansing, the puncture site is not touched again except with gloved fingers.
3.	Hold the collection device in one hand as one would hold a dart or pencil and place a finger of the other hand over the artery at the exact point where the needle should enter the artery (not the skin). Puncture the skin about 5 to 10 mm distal to the finger directly over the artery with the bevel of the needle up, at an angle of approximately 30 to 45 ° against the blood stream.
4.	Advance the needle under the skin, aiming for the artery just under the finger. When the artery is entered, blood will enter the flashback chamber spontaneously and blood will flow into the collection chamber.
5.	After the required amount of blood has been obtained, placed a dry gauze sponge over the puncture site, while simultaneously quickly withdrawing the attached needed and collection device.
6.	Manually compress the artery at the puncture site immediately with firm pressure for a minimum of 3–5 minutes. While applying pressure to the artery with one hand, check the syringe or collection device immediately for air bubbles and carefully expel any trapped bubbles, following the manufacturer's recommended procedure. In order to prevent potential worker exposure, the needle safety feature should be activated immediately after specimen collection and discarded.
7.	Mix the specimen thoroughly by rotating or inverting specimen several times ensuring adequate anticoagulation in order to prevent clots from being introduced into the specimen. • If the patient is on anticoagulant therapy or has a prolonged clotting time, hold pressure on the site for a longer period of time.
8	After relieving pressure, immediately assess the puncture site • If hemostasis has not occurred or a hematoma is developing, reapply pressure. • Continue to assess the puncture site and hold pressure until hemostasis has occurred. • If hemostasis has not occurred within a reasonable time, obtain medical assistance.

Test Procedure for Brachial Artery Puncture	
Step	**Action**
1.	Set-up and preparing for specimen collection • The arm should be fully extended and the wrist rotated until the maximum pulse is palpated just above the skin crease in the atecubital fossa. A rolled towel can be used to facilitate positioning of the extremity. • Skill and good technique are required to avoid hitting the median nerve, which lies very close to the brachial artery.

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Test Procedure for Brachial Artery Puncture (Continued from previous page)	
Step	**Action**
2.	Prepare the puncture site aseptically. Be certain that after cleansing, the puncture site is not touched again except with gloved fingers.
3.	Spread two fingers along the course of the artery which may be located by palpating the pulsations. Enter the skin just below your finger and aim the needle along the line connecting the two fingers using a 45° angle of insertion with the bevel up. The artery lies deep in the tissue, especially in obese patients.
4.	Advance the needle under the skin, aiming for the artery just under the finger. When the artery is entered, blood will enter the flashback chamber spontaneously and blood will flow into the collection chamber.
5.	After the required amount of blood has been obtained, placed a dry gauze sponge over the puncture site, while simultaneously quickly withdrawing the attached needed and collection device.
6.	Manually compress the artery at the puncture site immediately with firm pressure for a minimum of 5 minutes, in order to stop bleeding. While applying pressure to the artery with one hand, check the syringe or collection device immediately for air bubbles and carefully expel any trapped bubbles, following the manufacturer's recommended procedure. In order to prevent potential worker exposure, the needle safety feature should be activated immediately after specimen collection and discarded.
7.	Mix the specimen thoroughly by rotating or inverting specimen several times ensuring adequate anticoagulation in order to prevent clots from being introduced into the specimen. • If the patient is on anticoagulant therapy or has a prolonged clotting time, hold pressure on the site for a longer period of time.
8	After relieving pressure, immediately assess the puncture site • If hemostasis has not occurred or a hematoma is developing, reapply pressure. • Continue to assess the puncture site and hold pressure until hemostasis has occurred. • If hemostasis has not occurred within a reasonable time, obtain medical assistance.

Test Procedure for Capillary Sampling	
Step	**Action**
1.	Set-up and preparing for specimen collection • When blood is collected for pH and blood gas determinations, the site must be properly warmed prior to puncture. A warm moist towel or other warming device at a temperature no higher than 42° C may be used to cover the site for 3–5 minutes. This technique increases arterial blood flow to the site significantly, does not burn the skin, and does not result in significant changes in analytes. • It is difficult to obtain arterial specimens using the capillary method of sampling because the specimens may be contaminated with room air or interstitial fluid. • Blood may be obtained from the palmar surfaces of fingers, the plantar surface of the heel, and the plantar surface of the big toe. Heel puncture is generally performed in infants less than 1 year of age. Heel punctures must not be made through a previous puncture site, the posterior curvature of the heel, or the central area of the foot.
2.	Prepare the puncture site aseptically. Be certain that after cleansing, the puncture site is not touched again except with gloved fingers.

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Test Procedure for Capillary Sampling (Continued from previous page)	
Step	**Action**
3.	The heel should be punctured with a sterile lancet, or with an automated lancet device to a depth of approximately 2 mm.
4.	The specimen should be collected in a heparinized capillary tube and must not contain air bubbles. Exposure of blood to air even for short periods can result in significant changes. Thus, the specimen is to be kept anaerobic (i.e., capillary ends sealed) at all times.
5.	After collecting a specimen in the capillary tube, seal one end immediately with a cap or putty. Place a small magnetic stirring bar (also called "flea") into the tube and seal the other end. With the stirring bar in the tube, the blood can be mixed by moving the magnet back and forth along the entire length of the outside of the tube.
6.	Apply mild pressure to the site using dry gauze, until hemostasis occurs.

Post Collection Procedure	
Step	**Action**
1.	Initial Handling • Properly identify and label the specimen according to institutional procedures. If the specimen is to be immersed in coolant, the label must remain legible after immersion. • Specimens obtained in plastic syringes for blood gas measurements should be stored at room temperature. If analysis is anticipated to be delayed by more than 30 minutes, the blood should be collected in a glass syringe and placed in an ice water bath (1, 2). • Coolant: if it necessary to cool the specimen, a container with a mixture of crushed ice and water or other coolant, large enough to permit immersion of the entire barrel of the syringe or collection device, should be prepared before the specimen is obtained. Immerse the specimen in the coolant immediately after it has been securely closed and labeled.
2.	Samples for blood gas and pH analysis: • If prompt analysis occurs within 30 minutes of collection, the use of a plastic syringe is recommended, and specimen does not need cooling. • If analysis is delayed (i.e., >30 minutes after collection), the specimen should be immersed in coolant as soon as possible after collection.
3.	Transportation to laboratory: • The entire container (including coolant, if used) and the specimen should be taken to the laboratory and analyzed as soon as possible. • A requisition or test-request form must accompany the specimen and include a unique specimen identification, date and time of specimen collection, and additional information as referred to in Patient Preparation section.

PROCEDURE NOTES

1. Safety and infection control
    - 1.1. Standard precautions (SP) are followed when collecting blood specimens (8–10).
        - 1.1.1. Barrier protection must be used to prevent contamination with body fluids to which SP apply. This means gloves must be worn for an arterial puncture. Eye covering or face shield should be worn, if there is likelihood for splattering.
    - 1.2. Hands or other skin surfaces should be washed immediately, if contaminated with blood (1).
    - 1.3. Unintentional injuries caused by needles must be immediately reported (1).
    - 1.4. Workers with exudative lesions or weeping dermatitis should refrain from patient contact (1).
    - 1.5. Proper blood collection techniques must be used.
    - 1.6. Adhere to current Occupational Safety and Health Administration (OSHA) guidelines at all times.
    - 1.7. Dispose of needles, syringes, and blood specimens in puncture-resistant containers (2).
    - 1.8. Workers should receive the Hepatitis B vaccine, or sign a waiver refusing to do so.
2. The use of local anesthesia is optional. If used, 1% lidocaine without epinephrine is recommended (1).

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CHAPTER 16

PROCEDURE NAME: BLOOD GAS, pH, AND HEMOXIMETRY ANALYSIS

PURPOSE OR PRINCIPLE

This chapter addresses the analysis of blood for blood gases, pH, and hemoximetry (i.e., hemoglobin, hemoglobin fractions, O_2 content, and hemoglobin-O_2 saturation). It is limited to the measurement of these parameters *in vitro* using a single specimen. Arterial blood is the most common type of blood sample analyzed for these parameters, but it can also apply to capillary or venous blood samples.

The analysis of blood for hydrogen ion concentration (pH), partial pressure of oxygen (Pa_{O_2}) and partial pressure of carbon dioxide (Pa_{CO_2}) are required to assess and revise therapeutic interventions to maintain acid-base and/or respiratory homeostasis. The evaluation of acid-base status is based on the direct measurement of pH and Pa_{CO_2}. The pH is measured using two chemical half-cells to measure the potential difference between solutions with different hydrogen ion [H^+] concentrations. The measuring half-cell is a Sanz electrode. The reference half-cell is composed of an electrode that supplies a constant reference voltage and is in a housing composed of potassium chloride solution (1). In traditional systems the Pa_{CO_2} is measured with a Severinghaus electrode. The Pa_{O_2} is measured with a Clark electrode. Base excess, standard bicarbonate, and total carbon dioxide may be calculated using the measured parameters. Hemoximetry, also known as whole blood CO-oximetry, is the spectrophotometric analysis of the concentration of total hemoglobin (tHb) and percent saturations of the hemoglobin derivatives: oxyhemoglobin (O_2Hb), reduced or deoxyhemoglobin (HHb), carboxyhemoglobin (COHb), and methemoglobin (MetHb). Hemoximetry of arterial blood is the only clinical laboratory test for the evaluation of anemic hypoxia, including carbon monoxide toxicity, methemoglobinemia, and sulfhemoglobinemia.

The analyzer used for these measurements must be maintained and operated in a manner that provides accurate and precise measurements in an acceptable time frame. Blood gases, pH, and hemoximetry analyses must also meet current regulatory standards.

INDICATIONS AND CONTRAINDICATIONS

Indications for blood gas, pH, and hemoximetry analysis are provided in Table 16.1, and a list of relative contraindications is presented in Table 16.2.

Table 16.1

Indications for Performing Blood Gas and pH Analysis (2)
Clinical indications for blood sampling:
• Evaluation of adequacy of ventilation, acid-base, oxygenation status, and the O_2-carrying capacity of blood • Quantification of the patient's response to therapeutic intervention and/or diagnostic evaluation • Monitor the severity and progression of documented disease processes

Table 16.2

Relative Contraindications for Performing Blood Gas, pH, and Hemoximetry Analysis (2)
Relative contraindications for blood analysis include:
• Improperly functioning blood gas analyzer (non-calibrated and/or non-linear) • A blood gas analyzer that has not had functional status validated using commercially prepared quality control products, tonometered whole blood, or as part of a proficiency testing program. • A specimen containing visible air bubbles • A specimen in a plastic collection device that has been stored at room temperature for longer than 30 minutes • The specimen does not have a complete requisition that includes: patient's name or other unique identifier, birth date or age, date and time of sampling, location of patient, name of ordering physician, clinical indication, blood sampling site or source, respiratory rate, $F_{I_{O_2}}$ or O_2 flow rate, body temperature, ventilator settings for mechanically ventilated patients, signature or initials of individual who obtained the sample.

CALIBRATION OF BLOOD GAS ANALYZER

There are numerous blood gas analyzers available and each has specific manufacturer recommendations for calibration. Laboratories must follow these recommendations including use of proper calibration materials and frequency of calibration. The manufacturer's calibration materials should be traceable to certified reference materials issued by national or international metrology institutes, or natural occurring standards (3).

Calibration traceability shall be documented for all materials used to perform internal and external calibration on blood gas analyzers. Documentation should include a statement by the manufacturer regarding traceability, and a certificate of analysis.

Traditional systems for measurement of blood gases are calibrated with humidified gas mixtures and require correction for ambient barometric pressure to derive the partial pressure of O_2 and CO_2 in the mixtures, according to Dalton's Law. In modern systems an internal electronic barometer is used to measure and correct for ambient barometric pressure. The function of the internal barometer should be checked regularly by comparing its reading to a reliable independent measurement. The manufacturer's recommendations for barometric checks should be followed. Barometric pressure readings should be local conditions and not adjusted to sea level (3).

PREANALYTIC PHASE

The preanalytic phase of testing encompasses procedures prior to analysis, including identification of patient, supplies, arterial puncture and sampling, storage, transport, and handling of samples. The laboratory must have policies and procedures in place describing the process from the time of sample collection to the reporting of results (4). The preanalytical phase includes patient identification, patient assessment, sample collection and labeling, handling of the sample once it has been obtained, transportation of the sample to the laboratory, and handling of the sample in the laboratory.

Patient Identification

Prior to sample collection, a formal process of ensuring positive identification of the patient is required. At least two unique identifiers (e.g., date of birth, patient's full name) should be used (5, 6). The patient's room number or location are not acceptable identifiers.

Patient Assessment

Urgent blood gas analysis is needed in many situations and these require immediate collection of the specimen. Patients on ventilators may need to achieve a "steady state" before collecting the arterial blood sample. A period of 20–30 minutes may be required to achieve steady state in cases of acute respiratory failure, positive end expiratory pressure (PEEP) or ventilator modalities intended to promote alveolar patency, postural changes, or post-bronchodilator/airway clearance procedures. Patients with communication deficits or language barriers may need assistance from an interpreter to understand the procedure and provide consent (3).

Collection, Labeling, Storage, Transport, and Handling

The specimen for blood gas analysis should be collected in a suitable heparinized plastic syringe, or capillary tube (*see* Chapter on percutaneous arterial blood sampling).

The specimen must be properly labeled with the patient's full name, a second identifier (e.g., medical record or clinic number, or date of birth) according to the institutional policy, date and time of collection, signature or initials of person collecting the specimen (3). In addition, the following information should be recorded in the medical record:

- Age and location of patient
- Body temperature
- Time of sampling
- $F_{I_{O_2}}$ or flow rate and mode of supplemental O_2 delivery, PEEP, or CPAP
- Ventilatory status (e.g., assisted or controlled ventilation, spontaneously breathing)
- Site of sampling
- Position of patient and activity (i.e., rest or exercise)

If analysis of specimen is expected to occur within 30 minutes the specimen should be stored at room temperature. If analysis is anticipated to be delayed by more than 30 minutes, the specimen should be collected in a glass syringe and placed in an ice water coolant. Blood specimens that will also be analyzed for potassium should not be cooled. Cooling of these samples can hemolyze the red blood cells and produce erroneously high potassium results.

Immediate transport of the sample to the blood gas laboratory is essential to avoid variability in analyte results. When the specimen is received in the laboratory, the analysis should be conducted as soon as possible. If air bubbles are not removed from the collection device, vibrations and movement (e.g., those that occur in pneumatic transport) of the air within the sample can accelerate gas equilibrium producing erroneous results.

The blood sample must be thoroughly mixed immediately prior to analysis to achieve a uniform distribution of red blood cells and plasma. Improperly mixed blood may produce variable results, specifically if hemoglobin and/or hematocrit are measured. The laboratory must have a detailed written procedure for specimen mixing prior to analysis. The specimen should be gently rotated either manually or using a mechanical device that rotates the specimen through two axes for a minimum of one minute immediately prior to analysis (3). Capillary tube samples that contain a stirring bar or rod ("flea") should be mixed by applying an external magnate and moving the flea from end to end for at least five seconds (3). The manufacturer's instructions should be followed carefully when introducing samples into blood gas analyzers. Incorrect introduction of blood into the analyzer can result in erroneous results. When blood samples are aspirated into the analyzer, an air bubble may form in the syringe due to fluid displacement, and should be removed immediately in case repeat analysis is necessary.

An analysis should be repeated immediately (ideally on another analyzer) if the results are:

- Inconsistent with the patient's past results and/or conditions (3)
- Physiologically inconsistent values (3) (e.g., Pa_{O_2} >120 mm Hg for patients breathing room air)
- At the extremes of the range of expected values (3).

ANALYTIC PHASE

The technology used to analyze pH and blood gases has developed to permit expanded utility and ease of instrument operation, but methodology has remained relatively unchanged. Modifications of current design have also allowed for miniaturization of the electrodes, which has enabled point of care (POC) testing.

Before introduction of blood samples, the analyzer's electrode outputs are evaluated with known high and low concentrations of buffer, solutions, and gases. If required, the analyzer is recalibrated. Some analyzers are calibrated before each test, and other instruments internally verify calibration at least every 30 minutes. Calibrations are usually referred to as one or two point, where the electrode response is adjusted at one level or at two levels (7). Because there are so many different designs, protocols, and recommendations from manufacturers regarding calibration, the laboratory must adhere to the manufacturer's recommendations.

The measurement of barometric pressure must be considered and is integrated into the calibration equation of the instrument. To ensure accurate calibration of the blood gas electrodes, the internal instrument barometer should be verified for accuracy at least annually against a National Institute of Standards and Technology traceable barometer and be documented.

Analyte analysis begins when a blood specimen is injected or aspirated into the sample chamber for measurement. Because temperature changes affect measured results, the electrodes systems and the sample chamber are located inside a temperature-controlled block maintained at 37° C. Typically, when the blood sample contacts the electrodes in the chamber, it produces an electrical output that corresponds to a pH, partial pressure, or hematocrit value. Blood gas analyzers monitor the electrodes' response continuously and, after a predetermined stabilization period, the instrument will display and/or print the measured results. When analysis is complete, the blood specimen is disposed of and the electrode-sensor system is flushed with a rinse solution (7).

POSTANALYTIC PHASE

The postanalytic phase of testing primarily encompasses reporting results. Accurate and complete documentation, whether performed manually or electronically, is extremely important. All patient results should be reported with the analyzer's normal range as documented in the blood gas laboratory's policy and procedure manual. When applicable, communication to the medical staff of critical or alert values needs to occur in a timely fashion.

In addition to the blood gas results, a complete report should include the collection time, source of sample, F_{IO_2} level, any ventilator settings, the type and location of any fluid infusion, the collection site, and patient posture (3).

Critical values or alert values are defined as test results that are markedly outside normal range and associated with impending morbidity or mortality. The blood gas laboratory policy and procedure manual should describe the procedure for reanalysis of the specimen when values are outside the critical value range. For example, the specimen should be analyzed on a different instrument (if possible) to verify results. The policy and procedure manual should also describe the protocol for how to rapidly communicate critical values to the medical staff. Documenting this communication (e.g., name of the physician or nurse contacted, as well as the person making the contact should be written on the blood gas report) is an essential component of the standards that regulate laboratories (3).

Error messages received during the analytic phase of testing and potential erroneous results need to be evaluated and recorded. In addition, the names of all individuals associated with the blood gas test need to be recorded in case questions related to the results are investigated (7).

Comments regarding quality of the specimen when it was received, transportation delays, and improper storage should also be documented. This information is helpful to the operator of the analyzer in judging the quality of the results, and the clinician in evaluating the relevance to the patient (3).

The laboratory's policy and procedure manual should include the procedure for handling blood gas specimens of questionable quality on delivery (2, 3, 8). Improperly labeled or transported specimens received from within the healthcare system may be refused. The ordering physician or the nurse directly responsible for the patient's care should be notified of the problem by the laboratory and asked if another specimen is required. If the specimen is analyzed, the results should be reported, but marked to show the questionable nature of the values.

Rejected specimens, whether due to temperature storage, air bubble contamination, or improper labeling, require immediate notification and documentation for rectification and/or repeat sample collection. The individual or department responsible for collecting the specimen should be contacted by phone, informed of the concerns, and given the opportunity to provide another specimen, if appropriate.

The laboratory's policy and procedure manual should describe how to handle unacceptable or questionable blood gas results (3, 8). When results are incorrectly reported due to clerical error, operator mistake, or equipment failure the problem should be remediated by reporting the correct results in a timely fashion. A "Revised Report" or "Revised Data" should be recorded on the blood gas report form, including the date the revision was made. The ordering physician and nursing unit should be notified. The individual reporting the correct results will note on the report the date, time, and individual to whom the correct results were reported.

QUALITY MANAGEMENT OF THE BLOOD GAS LABORATORY

A laboratory quality management system is an integration of policies and procedures that transform a physician's order into laboratory information. The objectives of a quality management system are to provide quality, accurate diagnostic test results and reduce the potential for medical errors (9). The quality management system includes: policy and procedure manual, quality control, proficiency testing, system audits, training and competency certification, and inventory management.

POLICY AND PROCEDURE MANUAL

The policy and procedure manual is a set of documents that clearly describe the guidelines related to all testing as defined by the institution. An annual review of the manual and revisions, if appropriate, are required by the medical director named on the CLIA license (9).

QUALITY CONTROL

A robust quality control (QC) program assures that the instruments used for patient testing meet the manufacturers' specifications for optimal performance. Periodic monitoring of QC provides data and trend analysis of the test system's function.

Some instruments are equipped with a self-contained QC test that checks the integrity of the electronic circuitry of the analyzer. These systems are known as Internal or Electronic QC tests. Commercial external controls, known as Liquid Quality Controls, are also available and are manually introduced into the analyzer by the operator. Liquid Quality Control tests evaluate the entire system performance, analyzer function, reagent or sensor accuracy, and operator technique.

The blood gas laboratory's policy and procedure manual should describe in detail the QC program including type of controls and how often they are to be analyzed.

PROFICIENCY TESTING

Proficiency testing is a comprehensive tool in the quality management system that evaluates the entire blood gas test. It involves the analysis of specimens with unknown values and statistically compares the results with a peer group. A minimum of 10 laboratories from a regional geographical area comprise a peer group. The reporting facilities in the peer group must use the same model device and test at a similar altitude. Proficiency test samples must be analyzed as patient tests within the environment where testing occurs. The proficiency testing providers assess the individual site's data and notify the laboratory of how their results compared to the peer group.

All analytes defined by CLIA as "regulated" must participate in a proficiency testing program. Typically proficiency testing programs supply five samples at various levels or concentrations of analytes. A satisfactory performance is set at 80% for each individual testing event. This allows for one unacceptable result or deficiency. When a deficiency is cited by the proficiency testing provider, the site must investigate and document its findings.

SYSTEM AUDITS

System audits are an essential part of every blood gas laboratory. They allow for closer examination of the policies and procedures and can identify possible sources of error before they occur. Auditors should be familiar with the test system but not involved with the development of the polies or procedures. The audits should involve: patient identification, sample collection and handling, instrument operation and maintenance, QC data analysis, results reporting, proficiency testing, and noncompliance management.

OPERATOR TRAINING AND COMPETENCY CERTIFICATION

Annual training is required by all regulatory bodies and should entail a review of the laboratory's policy and procedure manual. The training documentation can include a written assessment, direct observation of specimen testing, and certification with a skills checklist. The skills checklist should include: obtaining a sample, performing an analysis, reporting results, correctly managing critical values, and identifying the location of the policy and procedure manual.

INVENTORY MANAGEMENT

The date when reagents and supplies are received is documented to assist with inventory management. It is also necessary to note when supplies or reagents are removed from temperature-controlled storage units. Daily temperature monitoring and recording of the instrument's environment, reagents, and quality control material is mandatory.

PROCEDURE

Preanalytic Phase	
Step	**Action**
1.	Check arriving specimen for proper labeling and documentation of the following information: • Patient's name • Identification number • Date and time of sample • Age and location of patient • Body temperature • FI_{O_2} or flow rate and mode of supplemental O_2 delivery, PEEP or CPAP • Ventilatory status (e.g., ventilator or spontaneously breathing) • Site of sampling • Position of patient and activity
2.	Record the date and time of the receipt of the specimen in the laboratory (3, 8).
3.	Assure specimen has been transported appropriately and in a timely manner.
4.	Accept or reject the specimen. A specimen may be rejected for analysis when improperly labeled, transported, or stored (2, 3, 8). However, it is preferable to call the submitter and describe the problem. Questionable specimens may be processed and reported as described in the laboratory's policy and procedure manual.
5.	Mix the blood sample thoroughly immediately prior to analysis.
6.	Assure analyzer is calibrated and operating properly

Analytic Phase	
Step	**Action**
1.	Follow the manufacturer's step-by-step instructions for sample introduction and analysis.
2.	Verify the measured values are consistent with a stable reading.
3.	Repeat the analysis if the results are: • Inconsistent with the patient's past results and/or conditions • Physiologically inconsistent • At the extremes of the range of expected values
4.	When analysis is complete dispose of the sample appropriately.

Postanalytic Phase	
Step	**Action**
1.	Review all specimen results to assure accuracy. If results are questioned, reprocess the specimen immediately.
2.	If results fall into the alert value range, notify the medical staff immediately, and document who was notified and when.
3.	Record and evaluate any error messages were received during the analysis.
4.	Record/report the results in the institution information system including: • Blood gases, pH, and Hemoximetry results • Date and time of sample • Source of sample • FI_{O_2} or flow rate and mode of supplemental O_2 delivery, PEEP or CPAP • Ventilator settings, if applicable • Collection site • Patient posture • Comments regarding quality of specimen including transportation delays or improper storage.
5	Verify results have been received/printed/viewed.

PROCEDURE NOTES

1. Turnaround time for specimen analysis and reporting must be defined in each laboratory for STAT and routine samples. Selected parameters should meet the needs of the clinical situation and specimen-storage requirements (8). For example, specimens defined as STAT will be analyzed within 10 minutes and routine specimens are analyzed within 20 minutes.
2. Critical values are defined as results that are markedly outside normal or expected range and may represent life-threatening conditions.

3. Normal values and an example of critical or alert value ranges for arterial blood gas analysis:

	Normal (7)	Critical (7)
pH	7.35 to 7.45	≤7.20 or ≥7.60
Pa_{CO_2}	35–45 mm Hg	≤ 20 or ≥70 mm Hg*
Pa_{O_2}	83–108 mm Hg**	≤40 mm Hg

*Only in cases with a marked decrease in pH
**Breathing room air at sea level; declines with age

4. All documentation of completion of maintenance, quality control, and specimen results is maintained for a minimum of two years or as otherwise required by regulatory agencies (3).

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APPROVAL

Signature: _____ Date: _____

Annual Review

Date	Signature	Date	Signature

Revisions / Document History

Effective Date	Synopsis of Change

Effective Date: 2014
Version #1

CHAPTER 17

PROCEDURE NAME: EXERCISE TEST FOR THE ASSESSMENT OF DESATURATION

PRINCIPLE OR PURPOSE

In healthy individuals the partial pressure of arterial oxygen (Pa_{O_2}) and arterial oxygen saturation (Sa_{O_2}; Sp_{O_2}, if measured by pulse oximetry) remain mostly unchanged or increase during exercise. In individuals with substantial pulmonary disease, the Pa_{O_2} and Sa_{O_2} (Sp_{O_2}) fall with exercise, indicating oxygen (O_2) desaturation. This desaturation can be defined as a decrease in Sa_{O_2} (as measured from arterial blood samples by CO-Oximetry) of at least 2% compared to rest, an Sa_{O_2} of less than 88% during exercise, and/or a Pa_{O_2} of less than or equal to 55 mm Hg during exercise (1, 2). It is generally accepted that a 3 to 4% fall in Sp_{O_2} is considered significant when using a pulse oximeter. Oxyhemoglobin desaturation with exercise implies that diffusion cannot be increased to accommodate for a shorter pulmonary capillary transit time.

The exercise test used to determine if desaturation occurs can be performed as a component of a maximal cardiopulmonary exercise test (CPET), or as a less sophisticated test using a submaximal exercise test on a treadmill, cycle ergometer, or simply by having the patient climb stairs or walk in a hall corridor. The process of elucidating exercise desaturation during a maximal CPET is not addressed in this chapter. Exercise duration can vary from institution to institution, but is commonly less than 10 minutes. However, it is recommended that steady-state exercise be of at least 3 minutes duration. Shorter-duration exercise may lead to both false-positive and false-negative results. The treadmill, cycle, or stair unit have the advantage of providing an environment for better monitoring, and require less space than hallway corridor walking. Walking in the hallway or using a stair unit with railing allows the patient to adjust the pace easily, pause to rest if necessary, and have fewer concerns about falling (3). The major disadvantage of these informal treadmill, stairs, or corridor walks (i.e., without sophisticated physiologic measuring and monitoring instrumentation) is the lack of information about the subtle physiologic changes during exercise, or about the relationship of work rate to desaturation (1).

OXYGEN (O_2) TITRATION

O_2 titration refers to the process of determining the appropriate level of supplemental O_2 required by the patient to prevent or attenuate desaturation. The goal usually is to determine the lowest level of supplemental O_2 the patient needs to maintain Sa_{O_2} or Sp_{O_2} at an acceptable level at rest and during exertion.

During exercise, there are two approaches to determine the lowest O_2 flow rate required to keep a patient's Sa_{O_2} above a specific threshold (e.g., 90%): (*1*) adjusting while the patient continues to exercise; and (*2*) stopping the exercise, adjusting flow rate, and then restarting the exercise after equilibration.

The first method is quicker and simpler. It only requires the technologist to increase the O_2 flow rate after desaturation is observed while the patient continues exercising. The disadvantage of this approach is that the O_2 flow rate needed to keep the patient adequately oxygenated during exercise, starting from rest, may not be accurately determined.

The second approach requires that the exercise be stopped when desaturation is observed and the patient allowed to rest (seated or standing). The O_2 flow rate is increased, and after 5 to 10 minutes to allow equilibration, the exercise is restarted. This approach may require several exercise sessions and O_2 flow-rate changes to achieve the desired information. It is to be noted that measuring O_2 saturation immediately after exercise is not acceptable. In hypoxemic patients O_2 saturation generally increases rapidly after the cessation of exercise.

INDICATIONS AND CONTRAINDICATIONS

The indications and contraindications for performing the exercise test for the assessment of desaturation are provided in Tables 17.1 and 17.2, respectively.

Table 17.1

Indications for Performing an Exercise Test for the Assessment of Desaturation
• Assess and quantify the adequacy of Sa_{O_2} at rest and during exercise in patients who are clinically suspected of desaturation (e.g., dyspnea on exertion, pulmonary disease, decreased carbon monoxide diffusing capacity [D_{LCO}], decreased Pa_{O_2} at rest). • Titrate or adjust supplemental O_2 to treat hypoxemia or desaturation during activity. • Assess preoperatively for lung resection or transplant. • Assess the degree of impairment for medico-legal disability evaluation (e.g., pneumoconiosis, or asbestosis). • Ensure that oxygenation is maintained during anesthesia or operative procedures.

Table 17.2

Contraindications for Performing an Exercise Test for the Assessment of Desaturation	
Absolute contraindications	• Unstable angina • Uncontrolled systemic hypertension • Recent systemic or pulmonary embolism
Relative contraindications	• For adults, a resting diastolic blood pressure >110 mmHg or resting systolic blood pressure >200 mm Hg (1). • If Sp_{O_2} <85% with patient breathing room air, do not perform a room-air assessment. • If a resting room air arterial blood gas (ABG) analysis results in any of the following: ◦ pH <7.30 or >7.50 ◦ Pa_{CO_2} >50 mm Hg and with pH <7.30 ◦ Pa_{O_2} <55 mm Hg at sea level* ◦ Sa_{O_2} <87%* ◦ Carboxyhemoglobin (COHb) >8% ◦ Methemoglobin (METHb) >5% ◦ Total hemoglobin (tHb) <8 • Unstable (fluctuating) pulse oximetry reading or the oximeter does not display quality signal indicators as described in the manufacturers manual • Sustained tachydardia (e.g., in adults, a resting heart rate greater than 120 beats/minute after 10 minutes) • Non-compliant patient or one not capable of performing the test because of weakness, pain, fever, dyspnea, lack of coordination, or psychosis. • Recent (within the previous 4 weeks) myocardial infarction (MI) is a relative contraindication. However, the test may be indicated in MI patients with coexisting lung disease to ascertain the need for supplemental O_2 during ambulation.

*If values are less than the listed values, perform the exercise test with supplemental O_2.

EQUIPMENT AND SUPPLIES

1. Treadmill
   - 1.1. Electrically driven
   - 1.2. Speed range should allow for very slow walking (e.g., 0.5 or 1 mph)
   - 1.3. Emergency stop button
   - 1.4. Padded hand rails (front and sides)
2. Cycle ergometer
   - 2.1. Mechanical or electromagnetically braked
   - 2.2. Handlebars and seat that adjust to height
3. Stair unit
   - 3.1 Two, three, or four steps with railing on both sides.
4. Blood pressure (4)
   - 4.1. Assorted cuff sizes
   - 4.2. Calibrated analog pressure gauge
5. Nasal cannula or other O_2 delivery device with O_2 source (i.e., gas cylinder, liquid or wall O_2)
6. Stop watch or timer
7. Borg dyspnea scale, or Visual analog dyspnea scale (Appendix 17.1) (5, 6)
8. Exercise form (to document results)
9. Appropriate standard precautions (SP) attire and gloves for the technician (7)
10. Pulse oximeter with a variety of appropriate probes (e.g., ear, finger, reflectance)

PATIENT PREPARATION (PRE-TEST INSTRUCTIONS)

Pre-Test Instructions

- Patients will be instructed to wear loose-fitting, comfortable clothing and shoes suitable for exercise.
- The patient should be instructed to refrain from smoking and from inhaling second-hand smoke on the day of the test.
- The patient should be instructed to refrain from eating a large meal for 1 hour prior to the test time. A light meal is acceptable
- Patients with respiratory and/or cardiac disease are instructed to use all regular medications as ordered on the normal daily schedule

ASSESSMENT OF PATIENT

1. Assess each patient for physical and development status to determine ability to perform the diagnostic procedure and if special arrangements are required.
   - 1.1. If there is a language barrier, an interpreter will be used.
2. Ask each patient if he/she has complied with the pre-test instructions. The test may be postponed if the patient has not met the criteria. Contact the ordering physician or medical director to determine if rescheduling is necessary.
3. In order to properly interpret the test results, relevant clinical information (i.e., diagnosis and type of treatment) should be provided in writing, or electronically by the ordering physician.

PROCEDURE

Pre-Test Preparation		
Step	**Action**	
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition.	
	IF	THEN
	Patient unable to provide information	• Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information
	The identifiers do not match	• Contact registration • Resolve discrepancies before proceeding
	The ID band is present but not attached to the patient	• Do not proceed. • Notify patient's nurse or registration desk
2.	Check for a complete physician's order.	
3.	Collect and record demographic information.	
4.	Explain the purpose of the test, including but not limited to: exercise methodology, use of the pulse oximeter, O_2 delivery device, subjective scales, and exercise end-points	
5.	The results from a resting ECG done during the previous 6 months will be reviewed by the ordering physician or laboratory medical director. Stable exertional angina is not an absolute contraindication but patients with this disorder will perform the test with their anti-angina medication.	
6.	Medications to treat asthma and angina will be available, including supplemental O_2, sublingual nitroglycerine, aspirin (not-enteric coated), and albuterol (metered dose inhaler or solution for nebulizer). A telephone or other means will be readily available to enable a call for help, and the medical director will establish the appropriate location for the crash cart.	
7.	Physicians are not required to be present during all tests. The physician ordering the test, supervising laboratory physician, or the laboratory's standard operating procedure should define whether physician attendance at a specific test is required.	
8.	Technologists should be trained in at least Basic Life Support by attending an American Heart Association accredited program. Advanced cardiac life support training is desirable.	

Test Procedure for Exercise Test for Assessment of Desaturation	
Step	**Action**
1.	Set-up and preparation: • Re-explain the test method, if necessary, and patients are then asked to repeat the gist of the instructions to validate understanding. • Ask the patient not to talk during the exercise testing unless necessary to inform the technician of adverse symptoms.
2.	Position patient on the treadmill, cycle, in the hallway, or at foot of stairs unit. • Hall corridor or stair unit ◦ Define course end-points ◦ Define rate or cadence of stair climbing ◦ Treadmill ◦ Explain or demonstrate treadmill-walking techniques. ◦ A brief trial walk may be appropriate to familiarize the patient with the equipment • Cycle ergometer ◦ Adjust handlebar and saddle height to the appropriate level ◦ Give instructions to the recommended cycling rate (RPMs)
3.	Place pulse oximeter • Select appropriate probe (e.g. finger, ear probe, or reflectance). • Prep the site according to oximeter manual instructions. • Physical rubbing to ensure good blood flow may be required when using a peripheral site probe (e.g., finger or ear). • Allow the instrument to search for and lock onto the pulsatile portion of the perfusion, then evaluate the accuracy of capture by comparing the palpated pulse to the reported heart rate on the device. • Lightweight pulse oximeters (e.g., finger clip-on units) can be used so the patient is not carrying any extra load.
4.	Record resting (standing) parameters • Record a resting Borg or visual analog scale score. • Standing Sp_{O_2} (oximeter) • If resting Sp_{O_2}, is less than 88%, do not exercise on room air ◦ Contact the ordering physician or laboratory medical director. ◦ If O_2 titration is ordered, place patient on O_2 and titrate 1. Increase O_2 in 0.5–1.0 L/min increments until the Sp_{O_2} just exceeds 90% 2. Observe for Sp_{O_2} stability 3. Arterial blood gases may be warranted to correlate pulse oximeter readings and to rule out progressive hypercapnea. • Record Sp_{O_2}, whether on room air or on O_2 with liter flow, mode of delivery, time on O_2, heart rate, and blood pressure, if measured.

(continues on next page)

Test Procedure for Exercise Test for Assessment of Desaturation (Continued from previous page)	
Step	**Action**
5.	Exercise protocol: • Exercise duration is typically 5–10 minutes in depending on the laboratory's protocol. A minimum of 3 minutes of exercise is recommended. • Hall corridor or stairs 1. Have the subject walk at a vigorous pace or one they can maintain for 5–10 minutes 2. Have the subject walk on the stairs at the pre-determined walking cadence. • Treadmill 1. Speed and grade can be determined by the technologist based on the activity level that elicits dyspnea in a given patient. 2. Typically this is 1 mile per hour (mph), but may vary. 3. Increase or decrease the speed and grade as tolerated by the patient. • Cycle ergometer 1. Beginning workload: 40–80 RPMs at 15–20 watts 2. Increment workload as tolerated by the patient.
6.	Record the post-exercise parameters: • Total exercise time • End-exercise Sp_{O_2} • End-exercise heart rate • Blood pressure, if appropriate • Borg or Visual Analog Scale score • Any symptoms (e.g. chest pain, chest tightness, lightheadedness, etc.)
7.	Exercise end points: • Completing the pre-determined exercise time • Sp_{O_2} < 88% • Adverse symptoms • Patient complains of severe chest angina, tightness or wheezing • Lightheadedness, confusion, nausea, ataxia, pallor, etc. • Inappropriate tachycardia (> 160 bpm) • Volitional termination by the patient (i.e., cannot continue)
8.	O_2 titration with exercise: • Have the patient rest for 10 minutes prior to test. • Use the patient's resting O_2 flow rate if already titrated at rest, and/or start O_2 at 1–2 L/min. • Start the exercise protocol (*see above*) • Adjust the O_2 flow rate to maintain a Sp_{O_2} between 90–92% using one of the two approaches mentioned under "Oxygen Titration" above. • Titration of patients on supplemental O_2 and using an O_2 conserving device can be a combination of adjustments to both O_2 flow rate and conserving device settings. • Exercise endpoints: 1. Same as above 2. Sp_{O_2} <88% with an O_2 flow rate of 6 L/min.

Post-test Procedure	
Post exercise phase	Monitor the patient for 3–5 minutes for adverse symptoms: • Patient complains of severe chest angina, tightness or wheezing • Lightheadedness, confusion, nausea, ataxia, pallor, etc. • Inappropriate tachycardia (> 160 bpm) May be appropriate to educate the patient on the general use of O_2 therapy devices.

REPORTING OF TEST RESULTS

The physician's order and pulse-oximeter results obtained should be documented in the medical record with the date and time of measurement. The patient's position and activity level should be noted.

1. The supplemental O_2 flow rate and delivery device should be documented (8).
2. The type and duration of exercise, and perceived exertion scale should be noted.
3. The oximeter type (if more than one type is available), probe type, and placement should also be noted.
4. The results of ABG analysis and directly measured saturations of O_2Hb, COHb, and MetHb should be recorded or referenced, if simultaneously measured.
5. The stability of readings, length of observation, and range of fluctuation of readings should be included (8).
6. The clinical appearance of the patient should be included, if significant, including peripheral perfusion, skin temperature, cyanosis and other signs and symptoms (8).
7. Correlation of the heart rate readout on the oximeter with the actual palpated heart rate should be noted, but good agreement with the heart rate does not guarantee valid Sp_{O_2} results (8, 9).

PROCEDURE NOTES

1. To assure accuracy and consistency of reported results, it is ideal to standardize oximeter types throughout the testing continuum. If various oximeter brands are available in an institution, the same type of device should be used for serial measurements on a patient, since there are differences in accuracy among devices (7).
2. The pulse-oximeter probe should be compatible with the instrument used and the appropriate site used for the probe type.
3. Comply with all manufacturers' recommendations for patient safety and device application.
4. Pulse oximetry may be used to check for desaturation during exercise (change in Sp_{O_2}). Absolute values are less reliable when compared to CO-oximetry values (10, 11).
5. Situations or outside interference may affect pulse-oximeter readings, limit precision or limit the performance of a pulse-oximeter instrument (8, 9).
    5.1. Motion artifact can interfere with pulse oximeter measurements (8, 9, 12–15). Some pulse oximeters are better than others at rejecting motion artifact.

5.2. Dyshemoglobins: COHb falsely elevates Sp_{O_2} values; MetHb absorbs light at both oximeter wavelengths, and at high levels tends to force the Sp_{O_2} reading towards a value of 85% (9, 13, 14, 16–18).
5.3. Intravascular dyes, including methylene blue, indigo carmine, and indocyanine green have been reported to lower Sp_{O_2} measurements (8, 9).
5.4. Exposure of measuring probe to ambient light during measurement (8, 9, 12, 14, 17).
5.5. Low perfusion states, from vasoconstriction or hypothermia (8, 9, 14, 16, 17, 19, 32).
5.6. Nail polish, mood-type nail polish, or acrylic nail coverings can alter oximetry readings when a finger probe is used; black or brown nail polish significantly lower readings (20). Tattoos can also be a source of error and the probe should be located where tattoos do not exist. It is recommended that any nail polish be routinely removed before finger probes are used for pulse oximetry (8, 9, 21).
5.7. Inability to detect saturations below 83% with the same degree of accuracy and precision as at higher saturations (8, 9, 22, 23).
5.8. Inability to quantify the degree of hyperoxemia present (9, 24).
5.9. Hyper-bilirubinemia has been shown NOT to affect the accuracy of Sp_{O_2} readings (25–27).
5.10. Skin pigmentation can be a source of error, but this has not been consistently proven (8, 9, 13).
5.11. Venous pulsations: venous blood volume can also pulsate in some settings, producing erroneously low Sp_{O_2} readings and an inaccurate PR (28, 29).

6. To validate pulse-oximeter readings, direct measurement of Sa_{O_2} may be made on a CO-oximeter. The correlation of Sp_{O_2} to Sa_{O_2} should be done simultaneously with initial testing of the patient, then periodically re-evaluated if the patient's clinical status has changed (9, 13, 16, 17, 22, 30).
7. A normal Sp_{O_2} in the presence of an elevated inspired O_2 concentration provides little or no information on the adequacy of patient ventilation. Pulse oximetry alone should not be relied upon as the sole monitor for patient status in situations such as bronchoscopy, intubation, or cardiac arrest (31).

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APPROVAL SIGNATURES

Signature: _____ Date: _____

Annual Review

Date	Signature	Date	Signature

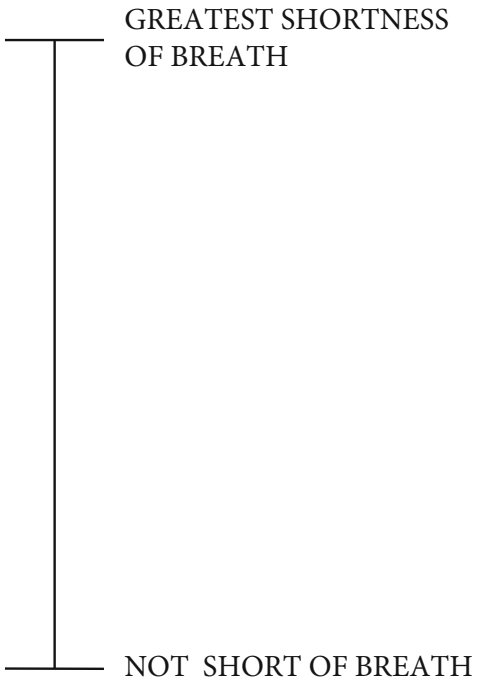
Revisions / Document History

Effective Date	Synopsis of Change

APPENDIX 17.1

Visual Analog Dyspnea Scale

Visual Analog Scale



APPENDIX 17.2

Worksheet and Report Example

Patient Name: _____ Patient ID#:

Walk #: _____ Test Administrator: _____ Date:

Gender: M F Age: ___ Race: __ Height: _____ inches____cm

Weight: _____ lbs____kg Resting Blood pressure:

Medications taken prior to test (dose and time):

Supplemental O_2 during test: No Yes: flow _____ L/min Delivery device:

	Baseline	End of Test
Time		
Pulse rate		
Dyspnea score (Borg scale)		
Sp_{O_2}		

Stopped or paused before predetermined time: No Yes, reason
Other symptoms at end of exercise: angina dizziness hip leg calf pain
Comments:
Interpretation:

Effective Date: 2014
Version #1

CHAPTER 18

PROCEDURE NAME: 6-MINUTE-WALK TEST

PURPOSE OR PRINCIPLE

In the assessment of functional capacity in patients with respiratory disease, objective measures are considered better than questioning patients about their abilities to perform activities (such as asking the number of blocks that can be walked). The 12-minute-walking test, originally described by Cooper (1) in 1968, was adapted to assess disability in patients with chronic bronchitis (2). However, the 12-minute-walk was found to be too exhausting for patients with some respiratory diseases, and the 6-minute-walk was shown to provide as good discrimination and repeatability as the 12-minute-walk (3).

The 6-minute-walk test (6MWT) is a practical simple test to perform that does not require exercise equipment. The 6MWT measures the distance that a patient can walk quickly on a flat hard surface in a period of 6 minutes (the 6MWD). The 6MWT evaluates the global and integrated responses of all body systems involved during exercise. It does not provide specific information on the function of each of the different organs and systems involved as is possible with the cardiopulmonary exercise test. Most patients do not achieve maximal exercise capacity during the 6MWT, and instead, choose their own level of intensity.

The most common use of the 6MWT is to measure the response to therapy in patients with a severe cardiopulmonary disease. The patient's pre-treatment 6MWD is compared with their post-treatment value (4–8). The 6MWT is also used as a one-time measure of the functional status of patients with COPD (9, 10). Although it is not a required element of the test, other measures including the change in oxygen saturation during the walk test have been used as functional measures. Table 18.1 presents the reported uses for the test.

The contraindications for performing the 6MWT are presented in Table 18.2 (11).

EQUIPMENT, SUPPLIES AND LOCATION

The 6MWT will be performed indoors, along a flat, long, straight, corridor with a hard surface and with little traffic. The walking course should be approximately 30 meters (100 feet) in length (11). The course will be marked with visible markers (e.g., traffic cones). A starting line, which marks the beginning and end of each 60 meter lap, will be marked on the floor. Incremental markers of distance on the floor or wall (e.g., every 10 meters) help to measure the distance walked.

Table 18.1(11)

Reported uses of performing the 6MWT	
Pretreatment and post-treatment comparisons	• Lung transplantation • Lung resection • Lung volume reduction surgery • Pulmonary rehabilitation • COPD • Pulmonary hypertension • Heart failure
Functional status (single measurement)	• COPD • Cystic fibrosis • Heart failure • Peripheral vascular disease • Fibromyalgia • Older patients
Predictor of morbidity and mortality	• Heart failure • COPD • Primary pulmonary hypertension • Idiopathic pulmonary fibrosis

Table 18.2

Contraindications for performing the 6MWT:	
Absolute contraindications	Unstable angina in the previous month Myocardial infraction in the previous month
Relative contraindications	Resting diastolic blood pressure >100 mm Hg or resting systolic blood pressure >180 mm Hg. Resting pulse rate >120

The following equipment is used for the 6MWT:

1. A stopwatch
2. Mechanical counter or other method to count laps
3. Markers to identify the course
4. Borg dyspnea scale (12) (a Visual Analog Scale can also be used; *see* Appendix 1)
5. Chair or wheel chair
6. Pad of worksheets on a clipboard
7. Sphygmomanometer and appropriately sized cuffs (13)
8. Access to an automatic electronic defibrillator
9. Telephone
10. Pulse oximeter, if requested (pulse oximetry is not a required element) (11)

PATIENT PREPARATION (PRE-TEST INSTRUCTIONS)

Pre-Test Instructions
• Patients will be instructed to wear loose-fitting, comfortable clothing and shoes suitable for exercise. • Patients should use their usual waking aids during the test (cane, walker, etc.). • A light meal is acceptable before early morning or early afternoon tests. • Patients with respiratory and/or cardiac disease are instructed to use all regular medications as ordered on the normal daily schedule.

PROCEDURE

Pre-Test Preparation	
Step	**Action**
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition.
	IF: Patient unable to provide information THEN: • Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information.
	IF: The identifiers do not match THEN: • Contact registration. • Resolve discrepancies before proceeding.
	IF: The ID band is present but not attached to the patient THEN: • Do not proceed. • Notify patient's nurse or registration desk.
2.	Check for a complete physician's order.
3.	Collect and record demographic information.
4.	Explain the test to the patient.
5.	The results from a resting ECG done during the previous 6 months will be reviewed by the ordering physician or laboratory medical director. Stable exertional angina is not an absolute contraindication for the 6MWT, but patients with this disorder will perform the test with their anti-angina medication.
6.	Medications to treat asthma and angina will be available, including supplemental O_2, sublingual nitroglycerine, aspirin (not-enteric coated), and albuterol (metered dose inhaler or solution for nebulizer). A telephone or other means will be readily available to enable a call for help, and the medical director will establish the appropriate location for the crash cart.
7.	Physicians are not required to be present during all tests. The physician ordering the test, supervising laboratory physician, or the laboratory's standard operating procedure should define whether physician attendance at a specific test is required.
8.	Technologists should be trained in at least Basic Life Support by attending an American Heart Association accredited program. Advanced cardiac life support training is desirable.

Test Procedure for 6 MWT	
Step	**Action**
1.	Set-up and test preparation: • Measure blood pressure. • Check for contraindications to testing. • Have the patient stand at the starting point. • Explain the Borg scale (12) to the patient, and record a resting score. • Place pulse oximeter and record resting Sp_{O_2} and pulse rate, if requested. • If pulse oximeter is used the technologist should be trained in pulse oximetry applications, quality assurance and limitations (14, 15). • Complete the first part of the worksheet/report (Appendix 18.2). • Set the lap counter to zero and timer to 6 minutes. • Instruct the patient as follows (hearing impaired patients may benefit from written as well as verbal instructions): *"The object of this test is to walk as far as possible for 6 minutes. You will walk back and forth in this hallway. Six minutes is a long time to walk, so you will be exerting yourself. You will probably get out of breath or become exhausted. You are permitted to slow down, to stop, and to rest as necessary. You may lean against the wall while resting, but resume walking as soon as you are able.* *You will be walking back and forth around the markers. You should turn briskly around the markers and continue back the other way without hesitation. Now, I'm going to show you. Please watch the way I turn without hesitation.* • Demonstrate by walking one lap yourself, starting at the starting line and tell patient: *"Are you ready to do that? I am going to use this counter to keep track of the number of laps you complete. I will click it each time you turn around at this starting line. Remember that the object is to walk AS FAR AS POSSIBLE for 6 minutes, but don't run or jog. When the 6 minutes are up I will tell you to stop. I want you to stop right where you are and I will come to you. Start now, or whenever you are ready."*
2.	As soon as the patient starts to walk, start the timer. Do not walk with the patient.
3.	During the walk, do not talk to anyone else except the patient. Use an even tone of voice when using the standard phrases of encouragement. Watch the patient and do not get distracted. Each time the patient returns to the starting line, click the lap counter once (or mark the lap on the worksheet). Let the patient see you do this.
4.	Standard phrases of encouragement: After the first minute, tell the patient: *"You are doing well. You have 5 minutes to go"* When the timer shows 4 minutes remaining, tell the patient: *"Keep up the good work. You have 4 minutes to go."* When the timer shows 3 minutes remaining, tell the patient: *"You are doing well. You are halfway done."* When the timer shows 2 minutes remaining, tell the patient: *"Keep up the good work. You have only 2 minutes left."* When the timer shows only 1 minute remaining, tell the patient: *"You are doing well. You have only 1 minute to go."* When the timer is 15 seconds from completion, say: (continues on next page)

Test Procedure for 6 MWT (Continued from previous page)	
Step	**Action**
	"In a moment I'm going to tell you to stop. When I do, just stop right where you are and I will come to you." When the timer rings, say: *"Stop!"* Walk over to the patient (consider taking a chair if he/she looks exhausted). Mark the spot where the patient stopped by placing a bean bag or piece of tape on the floor. Note: If the patient stops during the test, and needs to rest, say, "You can lean against the wall if you would like; then continue walking whenever you feel able." Do not stop the timer. If the patient stops before the 6 minutes are up and refuses to continue (or you decide that they should not continue), take a chair over the patient to sit on, discontinue the walk, and note on the worksheet the distance, the time stopped, and reason for stopping prematurely.
5.	If using a pulse oximeter the Sp_{O_2} and pulse rate should be continuously monitored.
6.	Record the post-walk dyspnea score using the Borg scale.
7.	Congratulate the patient on good effort, and offer a drink of water.
8.	Record the number of laps from the counter (or tick marks on the worksheet) and the additional distance covered (the number of meters in the final partial lap) using incremental markers on the wall or floor as distance guides.
9.	When patient is fully recovered and all data collected, the patient can leave.

Table 18.3

Reasons for immediately stopping the test
Chest pain
Intolerable dyspnea
Leg cramps, staggering
Diaphoresis, pale or ashen appearance

The indications for stopping the 6MWT are presented in Table 18.3.

Technologists must be trained to recognize the signs and symptoms in Table 18.3 and know the appropriate responses. If a test is stopped for any of the reasons noted in Table 18.3, the patient should sit or lie supine as appropriate depending on the severity of the event and the technologist's assessment of the severity of the event. Activation of the institution's emergency rapid response system may be required. The following should be obtained based on the judgement of the technologist: blood pressure, pulse rate, O_2 saturation, and a physician evaluation. Oxygen should be administered as appropriate.

REPORTING OF TEST RESULTS

1. Results should include the following:
    - 1.1. Demographic information
    - 1.2. Resting variables
        - 1.2.1. Blood pressure, heart rate, Borg scale, and Sp_{O_2}

1.3. Exercise variables
- 1.3.1. Total distance walked reported in meters or feet
- 1.3.2. Oxygen usage, if applicable
  - 1.3.2.1. Liter flow (continuous or pulsed)
  - 1.3.2.2. Delivery device (nasal cannula, oxygen pendent)
  - 1.3.2.3. Mode of transport (carried shoulder unit or pushed/pulled tank)
- 1.3.3. Dyspnea using Borg scale scores, or Visual Analog Scale scores
- 1.3.4. Reason for early termination, if applicable
- 1.3.5. Heart rate response including recovery
- 1.3.6. Oxygen saturation (Sp_{O_2})

PROCEDURE NOTES

1. Sources of Variability

There are many sources of variability in this test, including height, age, weight, disease, and musculo-skeletal disorders. Procedural sources of variability will be controlled as much as possible.

2. Learning Effect

There is strong evidence of a learning effect for the 6MWD when two or more tests are conducted. Most reports indicate that the second 6MWD is somewhat higher than the first (16–19). One large study reported a 95% confidence interval for the learning effect of 24–29 meters (20). The learning effect appears to be moderated by test repetition and practice, at least in the short term. Three studies reported that there was a statistically significant increase in 6MWD between walks 1 and 3 on a single day; however, one of these studies reported no significant difference in 6MWD for walks 2 and 3 (17, 21, 22). After three walks, further repetition did not consistently improve 6MWD (17, 22). A practice test is not needed in most clinical settings, but can be considered by the medical director of the laboratory.

3. Technologist Training and Experience

Technologists who perform 6MWTs will be trained using this standard protocol, and then supervised by the laboratory lead or medical director for several tests before performing them alone.

4. Instructions and Encouragement

The script provided in this document will be used to explain the test and instruct the patient. Standardized phrases of encouragement will be used each minute during the test.

5. Supplemental O_2

If supplemental O_2 is needed during the walks, and serial tests are planned, then during all walks by that patient, O_2 will be delivered in the same way with the same flow. If the flow must be increased during subsequent visits due to worsening gas exchange, this should be noted on the worksheet, and considered during interpretation of the change noted in the 6MWD. The type of O_2 delivery device will also be noted on the report (e.g., patient carried liquid oxygen container).

6. Course Location and Layout

While the standardized straight track length is 30 meters (100 feet), not all sites have space for this. The effect of track length has been examined, with varying results. One study in patients with severe COPD found no differences in average 6MWD between track lengths of 15 and 60 meters (19). However, another study comparing track lengths of 10 and 30 meters in patients with moderate COPD reported a mean increase in 6MWD of 49.5 meters on the longer course (23).

7. Oxygen Saturation Measurements

Although the 6MWT may be safe without continuous monitoring of Sp_{O_2}, continuous monitoring is needed to obtain an accurate measure of desaturation (24, 25).

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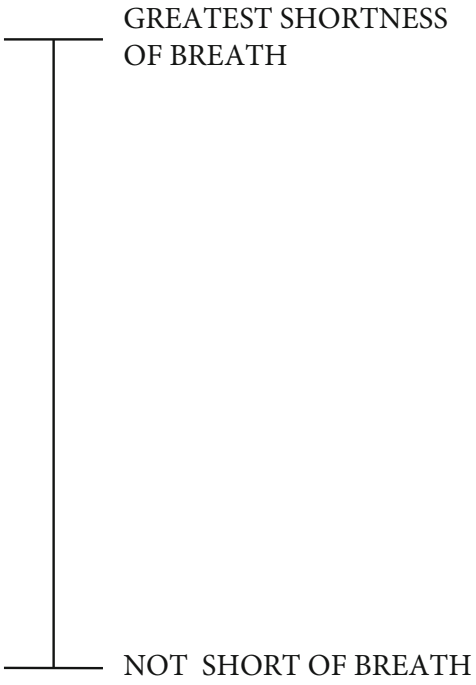
APPENDIX 18.1

Visual Analog Dyspnea Scale

Visual Analog Scale



APPENDIX 18.2

Worksheet and Report Example

Patient Name: _____ Patient ID#:

Walk #: _____ Test Administrator: _____ Date:

Gender: M F Age: ___ Race: __ Height: _____ inches____cm

Weight: _____ lbs____kg Resting Blood pressure:

Medications taken prior to test (dose and time):

Supplemental O_2 during test: No Yes, flow _____ L/min Delivery device:

	Baseline	End of Test
Time		
Pulse rate		
Dyspnea score (Borg scale)		
Sp_{O_2}		

Sp_{O_2} nadir (lowest point): _____

Stopped or paused before 6 minutes: No Yes, reason

Other symptoms at end of exercise: angina dizziness hip leg calf pain

Number of laps: (X meters/feet) = _____ Final partial lap: _____ meters/feet

Total distance walked in 6 minutes: _____ meters or feet

Comments:

Interpretation:

APPROVAL SIGNATURES

Signature: _____ Date: _____

Annual Review

Date	Signature	Date	Signature

Revisions / Document History

Effective Date	Synopsis of Change

Effective Date: 2014
Version #1

CHAPTER 19

PROCEDURE NAME: CARDIOPULMONARY EXERCISE TEST

PURPOSE OR PRINCIPLE

The cardiopulmonary exercise test (CPET) involves the assessment of cardiopulmonary function during incremental exercise and combines the routine measurements of the electrocardiogram (ECG), blood pressure and power output with the analysis of exhaled gases (1, 2). It is useful in a wide spectrum of clinical settings and helpful in clinical decision making. In practice, CPET is considered when specific questions persist after consideration of basic clinical data (e.g., physical examination, chest radiograph, pulmonary function tests, and ECG).

Cellular respiration involves the oxidation of carbohydrates, fats, and glycogen stores using both aerobic and anaerobic metabolic pathways (3, 4). The volume of oxygen (O_2) taken up each minute by the muscles for the oxidative process ($\dot{V}O_2$), increases during exercise proportionate to the work rate that is being performed (5). In order to satisfy the increased metabolic needs of the exercising muscle, the lungs, heart, pulmonary circulation, and peripheral circulation must respond in a coordinated fashion appropriate to the increase in metabolic demand (3). As exercise intensity increases, one or more of these essential systems may reach its maximal response, imposing a limitation to exercise. The assessment of maximum O_2 consumption ($\dot{V}O_2max$) and determination of any limitations to increases in $\dot{V}O_2$ are important diagnostic tools. The quantification and physiologic response of $\dot{V}O_2$, carbon dioxide (CO_2) production ($\dot{V}CO_2$), and the minute ventilation ($\dot{V}_E$) and other cardiopulmonary variables measured during a CPET allows the clinician to study the response of these systems under controlled metabolic stress (1, 3, 6–8).

INDICATIONS AND CONTRAINDICATIONS

The indications and contraindications for performing the CPET are provided in Tables 19.1 and 19.2, respectively.

Table 19.1

Indications for Performing the CPET (2, 9–13)
• Determination of the exercise capacity • Determination of the cause of a cardiopulmonary limitation to exercise • Identification of abnormal cardiopulmonary responses to exercise • Detection of coronary artery disease in patients with chest pain (chest discomfort) syndromes or potential symptom equivalents • Exercise prescription and monitoring response to exercise for training and rehabilitation • Evaluation of results of therapeutic intervention • Pre-operative evaluation • Impairment/disability evaluation • Selection of patients for cardiac transplantation • Evaluating unexplained dyspnea when initial cardiopulmonary testing is nondiagnostic

Table 19.2

Contraindications for Performing the CPET (2, 9–13) (However, this List Should not Replace Good Clinical Judgment)	
Absolute contraindications	• Acute myocardial infarction, within past 2 days • Symptomatic severe aortic stenosis • Ongoing unstable angina • Uncontrolled cardiac arrhythmias with hemodynamic compromise • Acute pulmonary embolism, pulmonary infarction, or deep vein thrombosis • Active endocarditis • Decompensated heart failure • Acute myocarditis or pericarditis • Acute aortic dissection • Physical disability that precludes safe and adequate testing
Relative contraindications	• Resting hypertension. Resting systolic >200 mm Hg, diastolic >110 mm Hg • Tachyarrhythmias • Known obstructive left main coronary artery stenosis • Moderate to severe aortic stenosis with uncertain relation to symptoms • Acquired advanced or complete heart block • Known electrolyte abnormalities (e.g., hypokalemia and hypomagnesemia) • Recent stroke or transient ischemic attack • Hypertrophic obstructive cardiomyopathy with severe resting gradient • Uncorrected medical conditions, such as significant anemia, important electrolyte imbalance, and hyperthyroidism

PATIENT SAFETY

1. Monitored exercise testing is considered relatively safe with a reported complication rate of < 1 to 5 per 10,000 tests (14–19), and death has occurred in approximately 0.5 per 10,000 tests.
2. Criteria for immediately stopping the exercise test (9, 13):

   In the vast majority of CPETs, patients should be verbally encouraged before and during the test, to give a maximal effort with the goal of achieving physiologic limitation. Exceeding a preset heart rate criterion is not a useful criterion for stopping exercise. Absolute indications for exercise termination are:

   2.1. Moderate to severe angina
   2.2. ST-segment elevation (>1.0 mm) in leads without preexisting Q waves because of prior MI
   2.3. Central nervous system symptoms (e.g., ataxia, dizziness, near syncope)
   2.4. Signs of poor perfusion (cyanosis or pallor)
   2.5. Fall in systolic blood pressure >10 mm Hg, despite an increase in workload, when accompanied by any other evidence of ischemia
   2.6. Severe desaturation: $Sp_{O_2} \leq 80\%$ when accompanied by symptoms and signs of severe hypoxemia
   2.7. Sustained ventricular tachycardia or other arrhythmia, including second or third degree atrioventricular block, that interferes with normal maintenance of cardiac output during exercise
   2.8. Technical difficulties in monitoring the ECG or systolic blood pressure
   2.9. Patient's request to stop
   2.10. Exaggerated hypertensive response (e.g., for adults, systolic blood pressure >250 mm Hg or diastolic blood pressure > 115 mm Hg)

In situations in which the exercise is terminated because of the above criteria, the patient should be observed until the patient is stable and physiologic variables have returned to baseline conditions.

3. Personnel Qualifications (9):
   - 3.1. The director of the laboratory performing the CPET should be a physician, preferably a pulmonologist or cardiologist certified in advanced cardiovascular life support, with knowledge of exercise physiology and with training in calibration, quality control, performance, and interpretation of CPET.
   - 3.2. The director, based on the clinical situation and clinical judgment, should determine whether a physician needs to be present during the actual test or whether it is sufficient for the physician to be physically available in the proximity of the exercise laboratory, so as to be able to respond immediately in case of emergency.
   - 3.3. The technicians should be trained in the field related to CPET such as exercise physiology, respiratory therapy, or pulmonary function testing. The technicians must have the basic knowledge of normal and abnormal exercise responses and be certified in basic cardiac life support (advanced cardiac life support preferred). They should be able to recognize an abnormal rhythm and ST depression on and ECG. The technician must have a minimum of 3 months of experience or internship in CPET before being given full responsibility for conduct of tests, and be competent in calibrating the equipment, and performing quality control procedures.

EQUIPMENT AND SUPPLIES

1. Treadmill (20, 21)
   - 1.1. Electrically driven
   - 1.2. Speed range 0.5 to 8 mph (0.5 to 15 mph for healthy physically active and competitive athletes)
   - 1.3. Grade range 0% to 20%
   - 1.4. Accommodate body weights up to 350 lb
   - 1.5. Emergency stop button
   - 1.6. Padded hand rails, front and sides
2. Cycle ergometer (20, 21)
   - 2.1. Electromagnetically braked
   - 2.2. Capable of calibration
   - 2.3. Handlebars and seat that adjust to height
3. ECG system
   - 3.1. Instrumentation should meet the most current specifications set by the American Heart Association (AHA)
4. Blood pressure
   - 4.1. Sphygmomanometer (cuff measurement method)
     1. Assorted cuff sizes
     2. Mercury column or calibrated pressure gauge
   - 4.2. Direct method using in-dwelling arterial catheter
     1. Pressure transducer
     2. Recorder
     3. Intravenous (IV) administration set and associated pressure tubing
     4. 500-ml IV bag of heparinized saline solution with 1,000 units of heparin (2 units/ml) to be put under pressure for catheter flushing apparatus.

5. Pre-heparinized (dry heparin) syringes for arterial blood gas (ABG) harvesting
6. Appropriate standard precaution (SP) attire and gloves for technicians
7. Gas analyzers (O_2 and CO_2)

   Modern CPET systems contain rapidly responding O_2 and CO_2 sensors that allow for the calculation of oxygen uptake and carbon dioxide output at rest, during exercise, and during recovery, as frequently as breath by breath. Although manufacturers' recommendations vary considerably regarding calibration, all CPET systems should be calibrated immediately before each exercise test (22).
8. A flow measurement device (e.g., pneumotachograph, mass flow sensor, pitot tube, or turbine) are included in CPET systems to measure ventilated volume. Some systems include directional valves and tubing as well. All flow measurement devices should be validated before testing by assuring a stable zero flow signal, and by using a known-volume calibration syringe.
9. Data-acquisition computer, monitor, and keyboard
10. Resuscitation cart (20, 23)
    - 10.1. Airway management equipment
    - 10.2. Defibrillator
    - 10.3. Airway suction apparatus, tubing and disposable ends
    - 10.4. Emergency medications (e.g., epinephrine, lidocaine, and nitroglycerine)
11. Supplemental O_2 equipment and delivery systems
12. Pulse oximeter with appropriate probes
13. Chart displaying the ratings of perceived exertion (RPE) scale (24) or visual analog scale (VAS) (25)
14. Other optional tests require specific equipment
    - 14.1. Cardiac output determination using either CO_2 equilibration or foreign gas uptake techniques
    - 14.2. Spirometer for flow–volume curves before, during, and after exercise
15. Barometer (or other valid method to obtain barometric pressure) and accurate thermometer

PATIENT PREPARATION (PRE-TEST INSTRUCTIONS)

1. Patient instructions
   - 1.1. Loose-fitting and comfortable clothing and shoes suitable for exercise (3, 22, 23, 26)
   - 1.2. The patient should abstain from smoking and from consuming alcohol at least 4 hours prior to test, and should not eat for 3 hours prior to test (3, 9, 10, 13, 16).
   - 1.3. Typically, no medications are withheld prior to the CPET, however if testing is performed for the diagnosis of ischemia, some medications (beta-blockers) may be held if they attenuate heart rate and blood pressure responses to exercise. All medications taken on day of test should be recorded.
2. The patient should receive a detailed description of the exercise procedure and purpose of the test (13, 20). Protocols for maximal cardiopulmonary exercise testing generally include an initial warm-up period (no or low workload), followed by progressive graded exercise with increasing workloads, and a post exercise period at no or low workload (13).
3. Obtain informed consent (if applicable in the institution) by personnel who can accurately describe the test and potential risks, and have it witnessed (3, 20, 23).

4. Patient assessment and history review at the time of the test
5. A resting supine standard 12-lead ECG should be obtained before exercise to compare to previously obtained ECGs to determine if changes have occurred over time (13). This should be followed by a standing or sitting (if using cycle) ECG with limb electrodes on the trunk of the body to minimize motion and muscle artifact during exercise.
6. ECG electrode placement
   - 6.1. The modified 10-electrode (Mason-Likar) configuration is the preferred method of electrode placement for obtaining a 12-lead ECG (20, 23, 27).
     1. The positions of the precordial leads are in the standard locations. The right arm (RA) and left arm (LA) limb electrodes are usually placed slightly below the right and left clavicle. The right leg (RL) and left leg (LL) limb electrodes are usually placed at the lower edge of the rib cage, or alternatively, at the level of the umbilicus at the mid-clavicular line.
   - 6.2. Skin preparation is essential to reduce surface resistance and ensure a good ECG signal (20, 23).
     1. Shave hair in the areas of the electrode application, when applicable.
     2. Use alcohol wipe to remove surface oils.
     3. Abrade skin with fine emery cloth (240 grit sandpaper or mechanical skin preparation device). There are commercially available skin preps which include an abrasive and alcohol.
7. If arterial blood gases are indicated, arterial line placement to obtain multiple arterial blood samples may be required to fully assess gas exchange (2, 3). Alternately, in some situations, a single arterial blood sample may be taken during heavy exercise by radial artery puncture.
8. Pulmonary function tests
   - 8.1. Obtain pre-exercise spirometry, including maximum voluntary ventilation (MVV). The results of this test can be used for:
     1. Determining ventilatory capacity and therefore breathing reserve for assessing ventilatory limitations (3, 28)
     2. The assessment of airway function pre- and post-exercise (although it appears that the incremental exercise protocol used for CPET is less sensitive than a constant work protocol for the detection of exercise-induced bronchoconstriction) (29)
   - 8.2. Results from other PF tests such as D_{LCO} will help determine which outcome measures are most appropriate.
9. Pulse oximetry
   - 9.1. Prepare probe site according to manufacturer's instructions.
   - 9.2. Ensure a good baseline reading for any probe by noting that the instrument indicates an adequate signal, pulsing with the heartbeat, and that heart rate measured by pulse oximeter agrees with ECG readings.

PATIENT ASSESSMENT AND HISTORY

1. The patient's medical history, clinical diagnosis, and reason for the test should be reviewed by a physician or trained professional. A questionnaire can aid this process (example in Appendix 19.1) and would likely include asking about:
   - 1.1. Current medications (e.g., bronchodilator, medications for control of blood pressure, and beta-blockers)

1.2. Pulmonary function tests, blood gas data, chest radiograph, blood chemistry results, etc.
1.3. Current symptoms including chest pain, discomfort, or wheezing
1.4. The patient's usual exercise program, exercise limitations and activities of daily living

2. Assess each patient for physical and development status to determine ability to perform the diagnostic procedure. Postponement may be necessary if the patient has not complied with the preparation criteria. Contact the ordering physician to determine if rescheduling is necessary.
3. If there is a language barrier an interpreter should be used.
4. Ask each patient if he/she complied with the preparation procedures.
   4.1. Time of the last meal
   4.2. Medication was taken as instructed
   4.3. If they exercised recently

QUALITY CONTROL

A quality control program starts with routine equipment calibration and maintenance, with appropriate documentation. In addition, a biological control program is highly recommended to both document the accuracy of equipment and early detection of problems.

1. Biologic controls (BioQC; one or two healthy, non-smoking laboratory personnel)
   1.1. Obtain consent to repeated testing.
   1.2. Test weekly (or at least monthly) depending on the volume of testing performed (30, 31).
   1.3. The biologic standards should initially perform a maximal study, then use 40 to 50% of the maximum workload as their steady-state work rate. As long as the subject is in a steady state, $\dot{V}O_2$ and other parameters should be reproducible.
   1.4. For the steady-state tests, collect gas exchange and work intensity data on each biologic control as 6 minutes of constant work rate is performed.
   1.5. If the $\dot{V}O_2$ or $\dot{V}CO_2$ value obtained by averaging the last 2 minutes of the 6-minute test are outside the 95% confidence limits (i.e., mean ±1.96 × SD) for a historical average for a particular biologic control, repeat the test or use another biologic control. Another approach for the limits of variation have been reported by the AHA (22) and are:

O_2 uptake	±5.0%
CO_2 output	±6.0%
Minute ventilation	±5.5%
RER	±3.0%

   1.6. Take corrective action if the repeat values or other biologic control's values are also outside the 95% confidence limits, and repeat the test of the biologic standard to verify adequacy of the corrective procedure.
   1.7. Add data to the quality control database only after the system is again performing properly. Recalculate averages and SD to obtain updated values for the 95% confidence limits.
   1.8. The time of day used to test the biologic control should be consistent from session to session.
   1.9. These procedures test the reproducibility, but not the accuracy of the gas exchange measurements.

2. Mechanical simulators (32) are available for routine quality checks and reproducibility checks. However, these calibrators have not been extensively validated, do not add water vapor in "expired" gas, and do not change temperature from inspiration to expiration. Thus, they do not test the integrity of the gas-sample drying circuit and the ability to compensate for temperature difference of expired gas (31). They do, however, test system accuracy and are capable of detecting smaller errors than can be detected by biologic calibration.
3. Collection of exhaled gases: utilizing appropriate valving, a 1- to 2-minute collection of exhaled gas can be obtained while a subject is in the steady state of exercise. Assessment of gas sample for volume and fractional concentrations of O_2 and CO_2 can be used to calculate $\dot{V}O_2$, $\dot{V}CO_2$, and $\dot{V}E$. Though technically challenging, this method may be considered the gold standard validation method (9).
4. Establish mean and SD by repeated testing and apply rules for adequate quality assurance responses.

PROCEDURE

Pre-Test Preparation

Step	Action	
1.	Check patient identification. Ask the patient to state or spell his/her first and last names, and date of birth. Verify the spelling and date of birth against ID band, and/or requisition.	
	IF	THEN
	Patient unable to provide information	• Get information from family member or caregiver, if present. • Notify person in charge, if a family member or caregiver is not present to provide the information
	The identifiers do not match	• Contact registration • Resolve discrepancies before proceeding
	The ID band is present but not attached to the patient	• Do not proceed. • Notify patient's nurse or registration desk.
2.	Check for a complete physician's order.	
3.	Collect and record demographic information.	
4.	Explain the test: • The purpose of the test • That it is a maximum exercise stress test, and that the mouthpiece or mask must be in place for the duration of the test. • Explain the end-points (attainment of maximal heart rate, development of limiting symptoms, or blood pressure, ECG, or O_2 saturation out of range) and reassure the patient about safety. • Instruct the patient about the use of symptom scales: a. RPE (Borg scale) for rating perceived exertion b. Other symptom scales (e.g., visual analog scale to score breathlessness); chest pain, chest tightness, asthma score, lightheadedness, leg fatigue, and shortness of breath on a 0 to 4 scale with 1 being a slight presence and 4 being severe.	

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Pre-Test Preparation (Continued from previous page)	
Step	**Action**
5.	Determine exercise protocol: • Determine exercise device and protocol based on the history, physical exam, exercise limitations, type of available equipment, and patient age (9, 33, 34). • Treadmill 1. Maximal incremental protocols are based on the Bruce, Balke, and Naughton protocols (35–37). Modification of protocols may be necessary to meet the exercise limitations of the patient, though any modification should be documented. A linear treadmill ramp protocol can also be used (38). A complete set of protocols is available from the American College of Sports Medicine guide for exercise prescription and training (23). 2. Exercise protocols designed to determine $\dot{V}O_2$max as one end point typically last about 10 minutes (39) (protocol may be modified with this total expected exercise time in mind). 3. Ramp protocols start the patient at a low speed, which is increased gradually until the patient has a good stride. The grade is increased progressively at fixed intervals (e.g., 10 to 60 seconds) or continuously starting at 0% grade. The increase in grade is calculated so that the exercise is completed in 6 to 12 minutes (13). • Cycle ergometer 1. Standardized protocols: Jones (40), Astrand (41), James (42) 2. Maximal incremental protocol a. 3 minutes of unloaded pedaling b. Increase work rate in 10 to 25 Watt increments every minute until patient reaches volitional exhaustion, or test is terminated by the medical monitor. c. With computer-controlled cycle ergometers, it is possible to increase the work rate continuously, usually every 1 to 2 seconds in a ramp-like fashion (ramp protocol). However, the total increment per minute should be 5 to 25 W/minute (9). d. To determine an appropriate work rate increment to yield a test whose incremental exercise period is approximately 10 minutes in duration: • ($\dot{V}O_2$max,predicted – $\dot{V}O_2$unloaded)/10 = estimated increments in power output (in Watts/minute) (where $\dot{V}O_2$ is in ml/min) • Reduce the work rate increment for patients suspected of having reduced exercise tolerance. • Increase the work rate increment rate for very fit patients.
6.	Position patient on exercise device: • **Treadmill** 1. Hands at side 2. If railings are used, the back of the hands can be used for balance or light touch. a. Avoid weight support which has an effect on $\dot{V}O_2$max and exercise time (22, 34). b. Use of upper extremities increases the muscle artifact in the ECG tracing. 3. Instruct the patient about walking on the belt. a. A brief trial walk may be appropriate to familiarize the patient with the equipment and to check the ECG signal for motion artifact. 4. For the safety of the patient, a spotter at the rear of the treadmill may be appropriate (20). • **Cycle ergometer** 1. Adjust handlebar and saddle height. a. When the pedal is at bottom center, knee flexion should be about 20°. 2. Instruct the patient on pedal speed (appropriate to ergometer); 60 rpm is the usual target. a. A brief trial with little or no power output is appropriate to familiarize the patient with the equipment and to check the ECG signal for motion artifact.

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Pre-Test Preparation (Continued from previous page)	
Step	**Action**
7.	Attach patient to mouthpiece/mask • Place mouthpiece in patient's mouth or attach mask and apply nose clip. Although sometimes uncomfortable, the mouthpiece is preferred to the mask, since leaks could occur with the mask and cause erroneous results. • Instruct the patient to maintain a tight seal around the mouthpiece to reduce the incidence of air leak. If the patient is using a mask, ensure that it fits tightly. • Instruct the patient to breathe quietly for 2 to 3 minutes; feedback may be needed to avoid inappropriate breathing patterns (e.g., hyperventilation).
8.	Pulse oximeter • Place pulse oximeter, if applicable. • Reflectance, finger, or ear probe can be used. The ear probe is preferred over finger because the contraction of the hand muscles while holding the handlebar of the cycle can alter blood flow to the finger. • If the ear is used, prep the site by rubbing to ensure good blood flow. • Pulse oximetry may or may not be accurate in exercise testing (43–45) (check pulse tracing to assess quality of signal if O_2 saturation reading seems inappropriate).

Resting Measurements	
Step	**Action**
1.	**ECG:** Obtain resting ECG, which may differ morphologically (e.g., T-wave inversion) from standard ECG performed in the supine position with limb-lead configuration (10). Obtaining supine, upright, and hyperventilation ECGs have been recommended to document morphological changes (20, 23).
2.	**Blood Pressure:** Obtain resting blood pressure and assess for absolute or relative contraindication for testing. • Cuff blood pressure measurement 1. The AHA recommends that the width of the bladder should be 40% of the circumference of the arm and the length of the bladder should be at least 80% of the arm circumference (46). 2. Mercury manometer or Bourdon gauge should be at eye level to avoid parallax (46). 3. Measure blood pressure with the patient's arm relaxed and not grasping treadmill bar or cycle handlebar (23). 4. Automated blood pressure units are available but may be unreliable at higher power outputs, likely because of motion artifact (3, 20, 30). • Direct measurements of blood pressure are available with an arterial catheter (47). 1. Pre-flush gauge and tubing with heparinized solution, clearing all bubbles. 2. View pulse wave-form to detect overdamping or underdamping of the signal. 3. Mount the pressure gauge at the left atrium level and set electrical output to read zero when gauge is opened to atmosphere (47).
3.	**RPE (Ratings of Perceived Exertion):** • Obtain resting RPE and other subjective information from the patient (e.g., chest pain).
4.	**Flow–Volume Loop:** If exercise flow–volume loops are assessed, obtain a resting maximal flow–volume loop (48).

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Resting Measurements (Continued from previous page)	
Step	**Action**
5.	**Blood Samples:** Harvest arterial blood for analysis (e.g., blood gases and lactate) using appropriate technique at rest and throughout exercise per laboratory procedure.
6.	**Other Assessments:** Perform any additional tests (e.g., cardiac outputs) at rest per laboratory procedure.

Exercise Measurements	
Step	**Action**
1.	Start exercise using selected protocol.
2.	Obtain 12-lead ECG and blood pressure at 1 to 2 minute intervals during exercise. Subjective measurements (e.g., RPE) are measured at rest and immediately post exercise. Perform ECG and blood pressure at the maximal work rate, if possible.
3.	Encouragement may be needed with certain individuals to obtain a maximal effort.
4.	Obtain arterial blood for analysis using appropriate technique throughout exercise per laboratory procedure.
5.	Monitor and record exercise flow–volume loops with periodic inspiratory capacity maneuvers during exercise in order to properly position the exercise flow–volume loops within the resting maximal flow–volume loop.
6.	At the termination of exercise ask the patient the reason for stopping the test (e.g., legs hurt, shortness of breath, or fatigue). This may assist in the determination of maximal effort and help the clinician understand the patient's exercise limitations. Indications to terminate exercise are described in Patient Safety section.

Post Exercise Measurements	
Step	**Action**
1.	**Cool down:** Recovery should include a cool-down phase at a reduced work rate (e.g., unloaded pedaling) for 2 to 4 minutes, followed by 2 to 6 minutes of rest with ECG and symptom monitoring (20, 22).
2.	**ECG**: 12-lead ECG should be monitored continuously for 10 minutes and recorded for 10 seconds every 2 minutes. This may not be necessary when the ECG is unremarkable during exercise.
3.	**Blood Pressure:** Blood pressure should be measured every 1 to 2 minutes, as appropriate.
4.	**Discontinue Monitoring**: Monitoring should continue for 6 to 8 minutes after exercise, or longer if the patient is symptomatic or if blood pressure, heart rate, or ST segment change have not returned to near pre-exercise values (13).

CALCULATIONS

Calculations are usually performed by a computerized data acquisition system and include the following terms (49):

1.	$\dot{V}_{O_2}$ max	Maximal O_2 uptake
2.	$\dot{V}_E$	Minute ventilation (expired)
3.	$\dot{V}_{CO_2}$	CO_2 output
4.	$\dot{V}_{O_2}/HR$	O_2 pulse
5.	$\dot{V}_E/\dot{V}_{O_2}$	Ventilatory equivalent for oxygen
6.	$\dot{V}_E/\dot{V}_{CO_2}$	Ventilatory equivalent for carbon dioxide
7.	AT, VT, GET	Anaerobic, ventilatory, or gas exchange threshold
8.	RER, RQ, R	Respiratory exchange ratio, $\dot{V}_{CO_2}/\dot{V}_{O_2}$
9.	V_D/V_T%	Dead space to tidal volume ratio as a percent
10.	Pa_{O_2}	Arterial partial pressure of O_2
11.	Pa_{CO_2}	Arterial partial pressure of CO_2
12.	$P_{ET_{CO_2}}$	End-tidal partial pressure of CO_2
13.	$P_{ET_{O_2}}$	End-tidal partial pressure of O_2

Though the precise form of equations will vary depending on the technique used, the equations should conform to the following general guidelines:

1. $\dot{V}_E$ is calculated from the timed collection of expired gas, with gas volumes being corrected to BTPS conditions:

$$\dot{V}_E\text{, BTPS} = \frac{\dot{V}_E\text{, ATPS} \times \text{(ATPS to BTPS factor)}}{t\ \text{(min)}}$$

where:

$\dot{V}_E$,BTPS = expired minute ventilation in L/min at BTPS

$\dot{V}_E$,ATPS = expired volume (L) at ambient temperature and pressure conditions collected over sampling time (t).

ATPS to BTPS factor = conversion from ATPS to BTPS conditions

$$\text{ATPS to BTPS factor} = \frac{(PB - PH_2O) \times (310)}{(PB - 47) \times (TA + 273)}$$

where:

PH_2O = water vapor pressure at the ambient temperature (TA). Must be obtained from tables of water vapor pressure versus temperature.

PB = barometric pressure.

2. Inspired volume ($\dot{V}_I$) is needed for other calculations, and if room air is inspired, can be obtained from:

$$\dot{V}_I = \dot{V}_E \times \frac{1 - F_{E_{O_2}} - F_{E_{CO_2}}}{0.7904}$$

where:

$F_{E_{O_2}}$ = mixed expired O_2 concentration.

$F_{E_{CO_2}}$ = mixed expired CO_2 concentration.

3. $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ are calculated from timed gas collection and concentration of mixed expired gases (either direct measurement of a mixed expired gas sample, or calculated from analysis of expired gas flow and concentration), corrected to ml/min at STPD conditions (40):

$$\dot{V}_{O_2} = \left[\left(\dot{V}_I\,,\ BTPS \times F_{I_{O_2}}\right) - \left(\dot{V}_E\,,\ BTPS \times F_{E_{O_2}}\right)\right] \times \frac{PB - 47}{0.863}$$

$$\dot{V}_{CO_2} = \left[\left(\dot{V}_I\,,\ BTPS \times F_{I_{CO_2}}\right) - \left(\dot{V}_E\,,\ BTPS \times F_{E_{CO_2}}\right)\right] \times \frac{PB - 47}{0.863}$$

where:

$\dot{V}_E$ and $\dot{V}_I$ are calculated above

0.863 = conversion from L/min to ml/min and the ratio of (760 × 310/273) × 0.001 is the factor for the conversion from BTPS to STPD conditions.

$F_{I_{O_2}}$ = fractional concentration of inspired O_2

$F_{I_{CO_2}}$ = fractional concentration of inspired CO_2

$F\bar{E}_{O_2}$ = fractional concentration of mixed expired O_2

$F_{E_{CO_2}}$ = fractional concentration of mixed expired CO_2

4. There are variables of interest that are derived from $\dot{V}_E$, $\dot{V}_{CO_2}$, $\dot{V}_{O_2}$ and heart rate (HR): the ventilatory equivalents ($\dot{V}_E/\dot{V}_{O_2}$, and $\dot{V}_E/\dot{V}_{CO_2}$), the oxygen pulse ($\dot{V}_{O_2}$/HR), and the gas exchange ratio or respiratory exchange ratio (RER = $\dot{V}_{CO_2}/\dot{V}_{O_2}$) (3, 8, 50).

5. Measures of pulmonary dead space to tidal volume ratio can be done either with analysis of arterial blood gases using the classic Bohr equation (which gives the physiological dead space exactly) (51):

$$V_D/V_T\,\% = [(Pa_{CO_2} - P_{E_{CO_2}})/Pa_{CO_2}] - (V_D, \text{valve}/V_T)] \times 100,$$

where

$P_{E_{CO_2}}$ = mixed expired partial pressure of CO_2

V_D,valve = respiratory valve and mouthpiece dead space, or by a calculation erroneously called "non-invasive V_D/V_T" is made by assuming that $P_{ET_{CO_2}}$ reflects the partial pressure of CO_2 in arterial blood.

$$\text{Non} - \text{invasive } V_D/V_T\,\% = [(P_{ET_{CO_2}} - P_{E_{CO_2}})/P_{ET_{CO_2}}] - (V_D\,,\ \text{valve}/V_T) \times 100$$

The latter equation is usually misleading and can lead to radically wrong V_D/V_T values because $P_{ET_{CO_2}}$ can be considerably different than Pa_{CO_2} in the presence of significant gas exchange abnormalities which yield alveolar dead space (52). Utilization of "non-invasive V_D/V_T" is inappropriate in CPET.

6. Anaerobic threshold (AT), ventilatory threshold (VT), and gas exchange threshold (GET), are alternative names for the same measurement and are determined from graphical analysis of data (53).
   6.1. The conventional method (51) for determining AT uses ventilatory equivalents plotted against $\dot{V}O_2$. Usually, data are smoothed or averaged to reduce breath-by-breath variability, facilitating location of the AT. The AT coincides with the minimum of $\dot{V}O_2$. The $\dot{V}E/\dot{V}CO_2$ should either be constant or declining in the region around the AT. An increasing $\dot{V}E/\dot{V}CO_2$ suggests the increase in both parameters is due simply to hyperventilation rather than to a change caused by lactic acidosis.
   6.2. AT can also be located using V-slope analysis (54, 55), where the $\dot{V}CO_2$ (vertical axis) is plotted versus the $\dot{V}O_2$ (horizontal axis). The AT is the point where the slope of $\dot{V}CO_2$ versus $\dot{V}O_2$ increases; this can be located either manually or by using computerized analytic routines. If computerized analysis routines are used, the AT should always be verified by visual inspection of the data.
   6.3. Another approach is to plot the lactate concentration values in arterial blood against $\dot{V}O_2$ (using either manual or computerized data analysis routines). The AT is the point where the rate of rise in lactate increases or the total lactate concentration exceeds a threshold value (usually about 2 mEq/L). Presenting the log(lactate) versus log($\dot{V}O_2$) amplifies the change in slope, allowing easier identification of the threshold (56).
7. The normal alveolar–arterial O_2 gradient [$P(A\text{-}a)O_2$] increases with age and during exercise. At 20 to 39 years of age, the mean $P(A\text{-}a)O_2$ is 8 mm Hg at rest, and 15 mm Hg at maximal exercise. At 40 to 69 years of age, the mean $P(A\text{-}a)O_2$ is 13 mm Hg at rest, and 19 mm Hg at maximal exercise. In this older group, at maximum exercise the upper limit of normal (i.e., 95% confidence interval) is 28 mm Hg (3). A general guideline for the upper limit of adults is a $P(A\text{-}a)O_2$ <35 mm Hg (8).

REPORTING RESULTS

1. Typically data from several representative work rates are reported in tabular format. In some laboratories, data from all work rates are reported.
   1.1. The patient's response, the physician interpreting the results, or the laboratory practice may influence which variables are chosen for the report.
   1.2. At a minimum, data should be reported from: (*1*) rest; (*2*) near or at AT, if identifiable; and (*3*) maximal power output.
2. Report $\dot{V}O_2$max and $\dot{V}CO_2$ at STPD conditions in L/min
   2.1. $\dot{V}O_2$max may also be normalized for body weight (ml/min/kg). However, this may be misleading in obese individuals (57).
   2.2. Report $\dot{V}O_2$max using one of several approaches to process the individual data points.
      1. All the breaths within a specific interval of time
      2. Middle 5 of 7 breaths
      3. Median of 7 breaths
      4. Average of 8 breaths
   2.3 The automated systems allow several options for averaging the individual data points. Because of the noise observed in the breath-by-breath measurements and the fact that the units of the cardiopulmonary variables are L/min, it is recommended that the data be reported in 0.5-minute intervals. The minimum acceptable would be 20-second intervals.
3. $\dot{V}E$ is reported at BTPS conditions in L/min.
4. Pa_{O_2}, Pa_{CO_2} (if obtained), $P_{ET_{O_2}}$, and $P_{ET_{CO_2}}$ are reported in mm Hg.
5. Sp_{O_2} and Sa_{O_2} (from CO-oximetry) are reported as percent.

PROCEDURE NOTES

1. Several factors may influence the test results.
   - 1.1. Patient effort
     - 1.1.1. Patient should be encouraged to give a maximal performance, unless early termination is warranted (40, 50).
     - 1.1.2. Variables to detect a maximal performance (30).
       1. HR must be close to the maximal predicted:
          predicted HR = 210 − 0.65 × (age), (preferred), or 220 − age (3, 30, 50)
       2. $\dot{V}_E$,max: between 60 and 80% of ventilatory capacity (3, 28)
          Ventilatory Capacity = MVV or $FEV_1 \times 35$ to 40
       3. Metabolic work: RER equal to or greater than 1.10 to 1.15; lactate equal to or greater than 7 mMol
       4. Supervising clinician's observation of apparent effort
   - 1.2. Medications
     1. Beta-blockers, calcium channel blockers, and similar medications may affect the heart rate response.
     2. Bronchodilators may affect the ventilatory response.
   - 1.3. Exercise device selection and usage
     - 1.3.1. Patient performance, coordination, and physical limitation with a particular exercise device can affect results:
       1. Inability to walk on treadmill
       2. Weight support on handrails
       3. Inability to coordinate pedaling effort
       4. Orthopedic constraints
     - 1.3.2. Exercise device calibration
       1. A poorly calibrated exercise device will affect reported work rate but not the overall $\dot{V}O_2$max.
     - 1.3.3. In untrained patients without heart or lung disease, higher $\dot{V}O_2$max is usually obtained on a treadmill (20, 22). In trained patients, their usual form of exercise may produce the highest $\dot{V}O_2$max.
2. Clinical exercise testing using an arm ergometer (20, 23)
   - 2.1. Useful alternative for diagnostic exercise testing in patients with lower extremity impairment
   - 2.2. Performed for occupational evaluation in patients whose work primarily involves upper body activity
   - 2.3. Arm ergometers can be either mechanically or electronically braked.
     1. Calibration should be performed according to the manufacturer's suggested guidelines (20).
   - 2.4. Exercise protocols can be continuous, incremental, or discontinuous (23).
     1. 10- to 25-Watt increments in 2-minute intervals are suggested (20, 23).
   - 2.5. $\dot{V}O_2$max for arm exercise is generally equal to about 70% of that for leg exercise (58).
3. Cardiopulmonary exercise testing should be performed under the supervision of a physician appropriately trained to conduct clinical exercise tests and certified in advanced cardiac life support. The degree of supervision will be determined by the clinical condition of the patient being tested. It is recommended that the physician be present when patients are tested.

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APPENDIX 19.1

Example of Pre-Exercise Test Questionnaire

Name: ID No.: Date:
Ordering M.D.: Test Indication:
Medications (include time last taken and dose)
Chest Pain: Yes No If yes, when:
Do you use oxygen? Yes No Usage:
Medical History:
Cardiac History:
Smoking History:
When and what did you last eat?
Exercise Tolerance:
Can walk_____ steps/flights of stairs without resting
Can walk_____ blocks without resting
Can run/walk____ miles without resting (___ minutes per mile)
Regular exercise or activity includes:
Comments:
Name of individual completing questionnaire:

APPENDIX 19.2

Example of Informed Consent for Exercise Testing

To determine your cardiopulmonary response to exercise, you are being asked to voluntarily agree to engage in an exercise test. The information obtained will be used to help your doctor understand more about any problems related to your heart or lungs. The test will measure your tolerance of exercise until fatigue, breathlessness, chest discomfort, other symptoms occur, or a specific period time expires, which will stop the test. The test, including the electrocardiogram (ECG) and blood pressure will be monitored by a physician and precautions for your safety will be observed.

Risks of the testing procedure are minimal and complications from the test are rare, but they do include the following: fainting, falling, irregularities of heart beat, and, very rarely, heart attack or death (less than 1 in 10,000 cases).

Physical injury can occur because of the unfamiliarity with the equipment on the part of the patient. Every effort will be made to explain the nature of the exercise equipment prior to starting the test.

Professional staff will be present and necessary equipment available for emergency treatment if any problems should arise.

I have read and fully understand the above and voluntarily consent to perform this exercise test at the _____ hospital.

Patient signature: _____ Date:

Witness:

Physician supervising the test:

APPROVAL SIGNATURES

Signature: _____ Date: _____

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CHAPTER 20

PROCEDURE NAME: REFERENCE EQUATIONS AND INTERPRETATION GUIDELINES

PURPOSE

Interpretation of pulmonary function (PF) tests involves comparisons of measured values with respect to a healthy reference population and assessment of data reliability. The policies and processes for selection of reference values and interpretation of data provide consistency. The consequences of false-positive and false-negative errors are considered in the interpretative process. The referring physician should not be led to infer a change in the condition of the patient because of a change in the approach to the interpretation of the data. The measured lung function values are integrated by the requesting physician into the diagnosis, therapy, and prognosis for an individual patient.

RESPONSIBILITY

The PF laboratory medical director is responsible for selecting the appropriate reference values and developing the process and procedures for interpretation of lung function tests.

SELECTION OF APPROPRIATE REFERENCE VALUES

1. Criteria for selection (1–4)
    - 1.1. Obtain reference values from studies that used equipment that meets or exceeds American Thoracic Society (ATS)/European Respiratory Society (ERS) recommendations, if possible.
    - 1.2. Selected studies should represent data obtained by technicians and protocols with performance standards that are consistent with ATS/ERS recommendations.
    - 1.3. The reference population should match the test population as closely as possible, with respect to age, gender, height, and ethnic composition.
    - 1.4. The technical aspects of the testing for the reference population study (instrumentation and procedures) should be comparable to those used in the laboratory.
    - 1.5. Select all equations from the same reference set, so that one reference study is used for all parameters, if possible.

2. Selection and verification of published reference equations (1)
    2.1. The European Community for Coal and Steel (ECCS) published a comprehensive list of equations from studies published prior to 1983 (5). A more recent list of equations was published in the 2005 ATS/ERS Interpretative strategies for lung function tests (4).
    2.2. As new reference equations are published, review the equations chosen by the laboratory.
    2.3. Spirometry: When testing patients in North America, ages 8 to 80, it was recommended in the 2005 ATS/ERS recommendations (4) that the NHANES III reference equations (7) be used. The NHANES III reference equations are based on a random sample in the United States. Equations for predicted values and lower limits of the reference range are provided for individuals ages 8 to 80, three ethnic groups, and includes two new spirometric variables (FEV_6 and FEV_1/FEV_6). Other reference equations may be used if they provide better comparisons for a specific laboratory or patient group. One important and recent addition for spirometry are the data from the Global Lung Function Initiative (www.lungfunction.org) which extend the age ranges down to age 3.5 and up to age 95, but include data from non-U.S. populations (6).
    2.4. There are no specific recommendations on reference equations for D_{LCO} and lung volumes.
    2.5. Reference equations should be updated on a regular basis (e.g., every 10 years), taking into account the applicability of the newer reference equations and the effect on interpretation of longitudinal patient follow up (4).
3. Validation of selection
    3.1. Compare the results of at least 40 local reference subjects (i.e., healthy, non-smoking male and female subjects with a wide range of ages and heights) to the intended reference equations.
    3.2. If more than 30% of the people studied fall outside the 95% confidence interval for normal limits, review all aspects of the testing procedure and then select another equation set (8).
    3.3. Jensen and coworkers (7) reported that 20 to 40 subjects may not be enough to consistently confirm the selection of appropriate reference values and this method should be used cautiously. Quanjer and coworkers found that at least 150 males and 150 females would be necessary to validate values (9).
4. Limitations of available equations (1)
    4.1. Data may be limited for some ethnic groups, and even within some ethnic groups, differences may exist (10).
5. Epidemiologic issues (1)
    5.1. Healthy subject reference equations that include hospital patients should not be used.
    5.2. Select studies from a population free of respiratory symptoms and diseases.
    5.3. Base the reference equations on a nonsmoking population.
    5.4. Consider the effect of altitude on values for D_{LCO} and spirometric flows.
6. Statistical considerations (1)
    6.1. Age and height should be the primary independent variables.
    6.2. Linear equations may over-predict lung function in young adults and adolescents, and either over-predict or under-predict lung function values in the elderly.
    6.3. Reference value studies should provide appropriate limits of the healthy reference range. For spirometric values, only lower limits of the reference range are appropriate since the question being asked is almost always: Is the measured value too low? For lung volumes and D_{LCO}, upper and lower limits of the reference range are recommended because the question being asked may be either: Is the measured value too low? Or, is the measured value too high?

6.4. Use caution when extrapolating equations for patients of ages or heights not covered in data generated by the reference set.
6.5. Consider the ethnic origin of the subject being tested.

7. Upper and lower limits of reference ranges (1)
   7.1. Reference ranges may be based on either upper or lower 5th percentiles or 95% confidence intervals. These can also be expressed as standard deviation (Z) scores (i.e., the 5th percentile corresponds to a Z = −1.645). Percentiles provide appropriate limits for reference ranges regardless of the distribution of the values. They do require a relatively large sample size (at least 120 subjects per grouping) to provide accurate estimates of the reference range limits. Confidence intervals may be accurate with smaller sample sizes but should only be used when the distribution of the measured values is Gaussian.
   7.2. The limits of reference ranges are inherently variable; so interpret results close to limits with caution.
   7.3. A fixed percent of predicted for the lower limit of normal (e.g., 80%) may be misleading and varies according to the parameter being considered (i.e., LLN for FEV_1 may be approximately 80%, but LLN for $FEF_{25-75\%}$ may be much lower) and subject characteristics including age and gender.
8. Cite the source (i.e., author and year) of reference values for each test on the final report (1). If a mathematical adjustment for ethnic group is used, specify the percentage.

INTERPRETATION OF LABORATORY DATA

1. General principles and guidelines (1)
   1.1. Define the lower and/or upper limits of the reference range for each lung function parameter.
   1.2. Begin the interpretation with a statement about test quality (1, 11).
      1.2.1. If test quality is poor, the interpretation should deal with the effect of test quality problems on the results.
   1.3. Consider the clinical question asked.
   1.4. Use a conservative approach when suggesting a diagnosis based on PF tests alone. Diagnostic statements usually require clinical information in addition to lung function data.
   1.5. When possible, the interpretation should reflect an understanding of the statistical distribution of measured results in disease states and the prior probability of the disease.
   1.6. False-positive results increase as the number of indices used in the interpretation increases.
   1.7. The primary indices to be used for spirometric interpretation are VC (FVC) or slow VC, FEV_1, and FEV_1/VC.
   1.8. An individual familiar with pediatric lung function should interpret PF tests performed on children.
   1.9. The individual(s) performing the interpretation should have documented training and competency verification. If more than one individual performs interpretation of test results, a system should be employed to ensure consistency of interpretation.
2. Consider the effect of race and ethnic group on test results (1, 8). The use of race and ethnicity in interpreting lung function tests presents significant challenges (12) that should be understood by those interpreting tests.
   2.1. For African Americans, the actual values for total lung capacity (TLC), FEV_1, and FVC may be about 12% lower than Caucasians with the same standing height (1).
   2.2. For African Americans, the actual values for functional residual capacity (FRC) and residual volume (RV) may be 7% lower (1).

2.3. Use ethnic group specific reference equations whenever possible. Each patient should determine their own ethnic grouping; technicians should not determine ethnic group based on physical characteristics of the patient such as skin color, or language. This approach is known to lead to errors. In addition, asking individuals to specify their race/ethnic group conforms to the NHANES III method and therefore establishes a better link to the use of the NHANES III equations.

2.3.1. The use of race/ethnic specific reference studies is the preferred method. Problems with this approach include:

a. Finding a good reference study for each specific ethnic group
b. Dealing with patients of multi-ethnic background.

2.3.2. The problems in applying racial/ethnic adjustment factors to equations based on Caucasian subjects include:

a. One factor may not be appropriate for all PF test values;
b. Knowing or determining correction factors for different ethnic groups;
c. Knowing how a specific computer program has modified the reference values for an ethnic difference (if applicable to the specific device used for testing);
d. Dealing with patients of multi-ethnic background.

2.3.3. Use the laboratory's chosen reference equations and indicate the possible effects of ethnic group when interpreting results.

3. Test "turnaround time" (8)

3.1. An interim, uninterpreted report is available immediately post-test.
3.2. An interpreted copy of the test results is available within 48 hours.

4. Summary interpretation and/or impression

4.1. One approach is to assess or interpret the values (low, normal, high, etc.), and then form an impression as to what the values mean. Suggest characteristic patterns of dysfunction (i.e., obstructive versus restrictive).
4.2. Observe the patterns in relation to all tests performed.
4.3. Compare present results to previous test results (if applicable) (13).

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CHAPTER 21

PROCEDURE NAME: USEFUL EQUATIONS AND TABLES

PURPOSE

The purpose of this chapter is to provide the pulmonary function laboratory with useful equations and tables that are used to calculate or convert many of the values.

Table 21.1

Water Vapor Pressure: Table of the Vapor Pressure of Water (PH_2O) in 1°C Increments from 10°C to 40°C. Pressure is in mm Hg and kPa Units (To Convert mm Hg to kPa, Multiply kPa by 7.5006) (1).					
°C	PH_2O (mm Hg)	PH_2O (kPa)	°C	PH_2O (mm Hg)	PH_2O (kPa)
10	9.2	1.23	26	25.2	3.36
11	9.8	1.31	27	26.7	3.57
12	10.5	1.40	28	28.3	3.78
13	11.2	1.50	29	30.0	4.01
14	12.0	1.60	30	31.8	4.25
15	12.8	1.71	31	33.7	4.50
16	13.6	1.82	32	35.7	4.76
17	14.5	1.94	33	37.7	5.03
18	15.5	2.06	34	39.9	5.32
19	16.5	2.20	35	42.2	5.63
20	17.5	2.34	36	44.6	5.95
21	18.6	2.49	37	47.1	6.28
22	19.8	2.64	38	49.7	6.63
23	21.1	2.81	39	52.4	7.00
24	22.4	2.99	40	55.3	7.38

The equation used to calculate PH_2O is (2):

$$\left[\frac{6.36\,(T-37)}{232+T}\right]$$

$$PH_2O = 47.07 \times 10\,,$$

where: T = temperature in °C

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Table 21.2

Conversion Equations for Gas Volumes (1)		
To Convert from	**To**	**Multiply by**
ATPS	STPD	$\frac{PB - PH_2O}{760} \times \frac{273}{273 + T}$
	BTPS	$\frac{PB - PH_2O}{PB - 47} \times \frac{310}{273 + T}$
	ATPD	$\frac{PB - PH_2O}{PB}$
ATPD	STPD	$\frac{PB}{760} \times \frac{273}{273 + T}$
	BTPS	$\frac{PB}{PB - 47} \times \frac{310}{273 + T}$
	ATPS	$\frac{PB}{PB - PH_2O}$
BTPS	STPD	$\frac{PB - 47}{760} \times \frac{273}{310}$
	ATPS	$\frac{PB - 47}{PB - PH_2O} \times \frac{273 + T}{310}$
	ATPD	$\frac{PB - 47}{PB} \times \frac{273 + T}{310}$
STPD	BTPS	$\frac{760}{PB - 47} \times \frac{310}{273}$
	ATPS	$\frac{760}{PB - PH_2O} \times \frac{273 + T}{273}$
	ATPD	$\frac{760}{PB} \times \frac{273 + T}{273}$

where: PB = barometric pressure (mm Hg)

T = ambient temperature °C

PH_2O = ambient water vapor pressure

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Table 21.3

International System of Units (SI)			
Physical Quantity	**Conventional Unit**	**SI Unit**	**Conversion Factor**
Mass	pound (lb)	kilogram (kg)	0.4545
Length	inch (in)	meter (m)	0.0254
Pressure	cm H_2O	kilopascal (kPa)	0.09806
	mm Hg (Torr)	kPa	0.1333
	pounds/in^2 (psi)	kPa	6.895
Work	kilogram meter (kgm)	joule (J)	9.807
Energy	kg · m/min	J	0.1634
Compliance	L/cm H_2O	L/kPa	10.20
Resistance	cm H_2O/L/sec	kPa/L/sec	0.09806

This appendix contains a listing of conventional and SI units for commonly used physical quantities in the pulmonary function laboratory. To convert a conventional unit to an SI unit, multiply the conventional unit by the conversion factor. To convert an SI unit to a conventional unit, divide by the conversion factor.

Table 21.4

Temperature Scales			
°C	**°K**	**°F**	**Description**
100	373	212	Boiling point of water
0	273	32	Freezing point of water
−273	0	−459	Absolute zero

Table 21.5

Temperature Conversion Formulas °F and °C comparisons (1)							
°F	**°C**	**°F**	**°C**	**°F**	**°C**	**°F**	**°C**
32	0	52	11	72	22	91	33
34	1	54	12	73	23	93	34
36	2	55	12	75	24	95	35
37	3	57	14	77	25	97	36
39	4	59	15	79	26	99	37
41	5	61	16	81	27	100	38
43	6	63	17	82	28	102	39
45	7	64	18	84	29	104	40
46	8	66	19	86	30		
48	9	68	20	88	31		
50	10	70	21	90	32		

$$°K = °C + 273 \text{ or } °C = °K - 273$$

$$°F = \frac{9}{5}(°C) + 32 \text{ or } °C = (°F - 32)\frac{5}{9}$$

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Table 21.6

Alveolar Air Equation
$P_{A_{O_2}} = F_{I_{O_2}} (PB - 47) - Pa_{CO_2} [F_{I_{O_2}} + (1 + F_{I_{O_2}}/R)]$,
where: $P_{A_{O_2}}$ = partial pressure of oxygen (O_2) in the alveoli $F_{I_{O_2}}$ = fractional concentration of inspired O_2 PB = barometric pressure (mm Hg) Pa_{CO_2} = arterial carbon dioxide tension R = respiratory exchange ratio (respiratory quotient)
Notes: 1. If the $F_{I_{O_2}}$ is 1.00, the entire term in the right-hand parentheses becomes 1 and can be ignored. 2. R varies between 0.6 and 1.2. If not measured, it is usually assumed to be 0.8. 3. A simplified version of the alveolar air equation often used clinically is: $P_{A_{O_2}} = F_{I_{O_2}} (PB - 47) - (Pa_{CO_2}/0.8)$

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