Pulmonary Function Testing Guidelines and Controversies

Equipment, Methods, and Normal Values

A Project of the California Thoracic Society

Edited by

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PULMONARY FUNCTION TESTING GUIDELINES AND CONTROVERSIES

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Preface

This volume originated in an ad hoc subcommittee of the California Thoracic Society (CTS) formed to advise the California State Department of Health Services regarding qualifications of laboratory personnel and quality assurance of blood-gas analyses. The combined resources of both technical and medical expertise within the committee were employed to develop recommendations for CTS members concerning methodologies for the various tests performed in pulmonary function laboratories.

The significant differences in test results between laboratories using different equipment, techniques, or normal values led to the conclusion that the more basic technical aspects of testing must first be addressed prior to undertaking meaningful dialogues on the important issues of clinical usefulness, indications for testing, and interpretation of results. (The latter issues will be addressed in another volume, which is currently being developed.)

Chapters in this book were first critically reviewed in a series of committee meetings, revised to reflect committee input, and then subjected to more widespread review when used as the syllabus for a 3-day CTS postgraduate course held in 1980. The guest faculty for this course was selected with the intent of gaining fresh critiques of the recommendations presented in the syllabus. This guest faculty was a rich resource of expertise. We are very appreciative for their helpful comments and suggestions. The faculty included Sonia A. Buist, M.D., Benjamin Burrows, M.D., Edward A. Gaensler, M.D., Reed M. Gardner, Ph.D., Norman L. Jones, M.D., Richard J. Leman, M.D., David A. Mathison, M.D., Alan H. Morris, M.D., Kenneth M. Moser, M.D., Richard M. Peters, M.D., Anton Renzetti, M.D., Joseph R. Rodarte, M.D., John W. Severinghaus, M.D., Gennaro M. Tisi, M.D., Karlman Wasserman, M.D., Ph.D., and Brian Whipp, Ph.D.

Course participants included physicians, technologists, therapists, and repre-

sentatives of manufacturers of pulmonary laboratory equipment. Although many topics sparked considerable differences of opinion, the course was perceived by most participants as an effective and productive interchange of ideas on the technical aspects of testing. The input from the course was then used by each author in preparing the final versions of the chapters.

One of the most heated controversies that developed during the course concerned the appropriateness of including tests that are not established as clinically useful. It was decided that the primary criterion for inclusion of a test in this text was whether or not the test was then being done in a significant number of clinical laboratories. Questions of clinical usefulness will be addressed in the second volume of this project.

This text does not represent an official policy statement of the CTS, nor does every statement represent the unanimous consensus of the committee. As accurately as possible, the material in each chapter represents the authors' synthesis of their own recommendations with those of the committee and course participants. We view this text as the best body of recommendations that can be made based on the current state of the art.

The primary purpose of this book is to maximize the accuracy and precision of pulmonary function testing, and thereby, increase its clinical utility. We hope that the recommendations in this text will help some laboratories improve efficiency, thereby reducing costs, mainly by eliminating unnecessary quality control procedures and unnecessary steps during testing, reducing the need for repeat testing, and decreasing the likelihood of purchasing inappropriate testing equipment and quality control materials.

This text is also intended to give manufacturers guidelines for the development of equipment in accordance with current needs of pulmonary laboratories, as perceived by both laboratory and clinical personnel. As instruments become more automated, it becomes increasingly important that technical and clinical personnel have both a clear understanding of what their instruments do, and input into the design of future instruments. One purpose of the conference was to stimulate increased dialogue between industry and the medical community involved with pulmonary function testing. Thus, conference invitations were sent to all companies we could identify as being involved with pulmonary function testing. In some instances, draft versions of specific chapters were sent to appropriate industrial personnel for their input.

This book is directed primarily at technologists, physiologists, engineers, and physicians who are responsible for clinical application of pulmonary function testing. It should also be of interest to those doing related clinical, physiological, or epidemiological research, and for students and postgraduate trainees in fields involving pulmonary function testing. It may also be of interest to physicians who must interpret pulmonary function tests and therefore wish to better understand the foundations upon which their clinical interpretation of pulmonary func-

tion tests must rest. This book was published to meet the need for a single text containing recommended methodologies for the many pulmonary function tests. Although a number of excellent publications on standardized methodologies are available (see references in Chapter 1), some were developed specifically for research or epidemiological applications, and a number are not readily available in medical libraries. We hope this volume will be useful in the development of more uniform pulmonary function testing.

The first six chapters present general overviews of subjects that interrelate to each of the subsequent chapters. The remaining chapters deal with more specific testing procedures and, wherever possible, were organized in the following format:

The *Introduction* includes a brief review of the clinical applications of the test. The summary of indications for each test does not represent a critical assessment of the clinical usefulness, but is intended to give readers a general perspective. Only a brief review of the pathophysiological basis of the test is included. Greater detail is available in numerous physiological texts and articles.

The *Equipment* sections outline what equipment is necessary and, wherever possible, what the minimal performance characteristics should be. Every effort was made to describe equipment in generic terms.

The *Quality Control* sections present the recommended procedures for assuring the accuracy and precision of clinical tests. The selection of optimal quality control procedures is so dependent on instrument characteristics, however, that in many cases quality control procedures different than those recommended may be required.

In the *Procedures* section, we have emphasized the critical aspects of the testing procedures, including those instructions to the patients that are necessary for optimal test results. The necessity for active patient participation is one of the critical differences between tests performed in pulmonary function laboratories and those conducted in clinical pathology laboratories.

The *Calculations* sections, in addition to presenting the formulas used in data calculations, present sample calculations, which were included to prevent problems in the expression of data in the wrong units, the use of incorrect factors, or the erroneous application of algebraic logic.

The recommendations for *Normal Predictive Values* represent the outcome of considerable thought and committee discussion. Although our goal was to recommend a single set of normal reference values for each test, in very few cases was there sufficient evidence to permit the conclusion that a particular study was "the best." One of the most interesting outcomes from the committee was the appreciation of the diversity of normal values that we chose to use in our own laboratories. In almost every chapter, the selection of optimal reference values remains an unresolved controversy. Chapter 6 presents the important general characteristics of studies of normal subjects that must be considered in selecting

the most appropriate set of reference values. In most of the chapters dealing with specific tests, we have presented a number of studies of normal values so that laboratories can evaluate and select the study most appropriate for their particular instrumentation and patient population. When specific sets of normal values were recommended, they usually reflected the opinion of the chapter authors rather than the unanimous consensus of the committee. Clearly one of the more challenging future tasks is the identification or development of prediction equations for normal values that are of maximal clinical usefulness. As greater uniformity in testing procedures is achieved, this task will be easier.

We presented data on *Expected Reproducibility* because we believe that this information is useful for confirming that the precision of a laboratory's own testing methods is adequate. This information is also of obvious importance in interpreting the clinical significance of measurements that differ from those predicted for or previously obtained from the same patient. For comparison with normal values, the within-day reproducibility is most pertinent; for serial measurements, the between-day variability is more appropriate.

In the *Troubleshooting* sections we present what we feel would be the most useful information on sources of error. No attempt was made to include all possibilities. For further information, readers are encouraged to review the excellent instrument-specific publications available from most manufacturers of equipment and quality control products.

The *Controversies* sections attempt to identify and sometimes briefly discuss those testing aspects for which we felt there is insufficient scientific evidence on which to base a recommendation. Because these are issues that usually need further investigation, studies related to these issues will be of obvious interest in the future. Resolution of these controversies will be a key step toward achieving more uniform testing procedures.

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The financial and administrative support of the California Thoracic Society (CTS) and the California Chapter of the American Lung Association was essential to the development of this text. The considerable administrative support of Elma Plappert, Executive Secretary of the CTS, is particularly appreciated. Dr. Philip Gold was the committee chairman when this project was initiated and later served as president of the CTS. He was a key factor in the development and continued support of this project.

Numerous people contributed very helpful suggestions and corrections to the original course syllabus. They include associates at the various institutions represented by the authors of this text, colleagues within the CTS and other participants in the 1980 postgraduate course. Most useful and appreciated were the detailed suggestions given to us by the guest faculty, as well as the detailed reviews by Barbara Corbett and Paul Koenig. Jan Evans made essential contributions in the typing and communications between myself, the authors, and the publishers. Her cheerful input into this project is gratefully acknowledged. The contributions of Linda Zarins as assistant editor extended well beyond her careful technical documentation and are greatly appreciated.

I enjoyed the privilege of editing this text and assume responsibility for any errors or omissions. Suggestions and corrections will be received with interest and gratitude.

Terms and Abbreviations

The variety of abbreviations used in clinical pulmonary function reports (e.g., MEF 50%, FEF 50%, Vmax 50%, and $\dot{V}$ 50%) often leads to considerable confusion, especially for physicians without specific training in pulmonary medicine. Although not perfect, the terminology and abbreviations suggested by an American College of Chest Physicians/American Thoracic Society (ACCP/ATS) joint committee are the best available and should be used whenever possible. Those most relevant to subsequent chapters are given below. Abbreviations marked with an asterisk were not cited by the ACCP/ATS joint committee, but are used in this book.

A	Alveolar
a	Arterial
an	Anatomic
ATPD	Ambient temperature and pressure, dry
ATPS	Ambient temperature and pressure, saturated with water vapor at these conditions
B	Barometric
BTPS	Body conditions: Body temperature, ambient pressure, and saturated with water vapor at these conditions
C	A general symbol for compliance, volume change per unit of applied pressure
c	Capillary
C/V_L	Specific compliance
CD*	Cumulative inhalation dose. The total dose of an agent inhaled during bronchial challenge testing; it is the sum of the products of concentration multiplied by the number of breaths at that concentration
C_{dyn}	Dynamic compliance, compliance measured at point of zero gas

	flow at the mouth during active breathing. The respiratory frequency should be designated; e.g., $C_{dyn}40$
C_{st}	Static compliance, compliance determined from measurements made during conditions of prolonged interruption of air flow
D	Dead space or wasted ventilation (qualifying symbol, e.g., V_D)
D/V_A	Diffusion per unit of alveolar volume
D_k	Diffusion coefficient or permeability constant as described by Krogh; it equals $D \cdot (P_B - P_{H_2O})/V_A$
D_m	Diffusing capacity of the alveolar capillary membrane (STPD)
D_x (or $D_{L_{CO}}$)	Diffusing capacity of the lung expressed as volume (STPD) of gas (x) uptake per unit alveolar-capillary pressure difference for the gas used. Unless otherwise stated, carbon monoxide is assumed to be the test gas, i.e., D is D_{co}. A modifier can be used to designate the technique, e.g., D_{SB} is single breath carbon monoxide diffusing capacity and D_{SS} is steady state CO diffusing capacity. (Editor's note: This recommendation has not widely been accepted. $D_{L_{CO}}$, $D_{L_{CO}SB}$, and $D_{L_{CO}SS}$ are still the most commonly used abbreviations.)
E	Expired
ERV	Expiratory reserve volume; the maximal volume of air exhaled from the end-expiratory level
est	Estimated
f	Respiratory frequency per minute
F	Fractional concentration of a gas
FEF_{max}	The maximal forced expiratory flow achieved during an FVC
$FEF_{25-75\%}$	Mean forced expiratory flow during the middle half of the FVC (formerly called the maximum mid-expiratory flow rate)
$FEF_{75\%}$	Instantaneous forced expiratory flow after 75% of the FVC has been exhaled
$FEF_{200-1200}$	Mean forced expiratory flow between 200 ml and 1200 ml of the FVC (formerly called the maximum expiratory flow rate)
FEF_x	Forced expiratory flow, related to some portion of the FVC curve. Modifiers refer to the amount of the FVC already *exhaled* when the measurement is made
FET_x	The forced expiratory time for a specified portion of the FVC; e.g., $FET_{95\%}$ is the time required to deliver the first 95% of the FVC and $FET_{25-75\%}$ is the time required to deliver the $FEF_{25-75\%}$
$FEV_t/FVC\%$	Forced expiratory volume (timed) to forced vital capacity ratio, expressed as a percentage
FIF_x	Forced inspiratory flow. As in the case of the FEF, the appropriate modifiers must be used to designate the volume at which flow is

	being measured. Unless otherwise specified, the volume qualifiers indicate the volume inspired from RV at the point of the measurement
FRC	Functional residual capacity; the sum of RV and ERV (the volume of air remaining in the lungs at the end-expiratory position). The method of measurement should be indicated as with RV
G_{aw}	Airway conductance, the reciprocal of R_{aw}
G_{aw}/V_L	Specific conductance, expressed per liter of lung volume at which G is measured (also referred to as SG_{aw})
I	Inspired
IRV	Inspiratory reserve volume; the maximal volume of air inhaled from the end-inspiratory level
IC	Inspiratory capacity; the sum of IRV and V_T
L	Lung
max	Maximal
MIP*	Maximal inspiratory pressure
MEP*	Maximal expiratory pressure
MVV_x	Maximal voluntary ventilation. The volume of air expired in a specified period during repetitive maximal respiratory effort. The respiratory frequency is indicated by a numerical qualifier; e.g., MVV_{60} is MVV performed at 60 breaths per minute. If no qualifier is given, an unrestricted frequency is assumed
p	Physiological
P	Pressure, blood or gas
PA*	Pulmonary artery
PD*	Provocative dose; the dose of an agent used in bronchial challenge testing which results in a defined change in a specific physiologic parameter. The parameter tested and the percent change in this parameter is expressed in cumulative dose units over the time following exposure that the positive response occurred. For example, $PD_{35}SG_{aw}$ = x units/y minutes, where x is the cumulative inhalation dose and y the time at which a 35% fall in SG_{aw} was noted
PEF	The highest forced expiratory flow measured with a peak flow meter
P_{st}	Static transpulmonary pressure at a specified lung volume; e.g., $P_{st}TLC$ is static recoil pressure measured at TLC (maximal recoil pressure)
Q_c	Capillary blood volume (usually expressed as V_c in the literature, a symbol inconsistent with those recommended for blood volumes). When determined from the following equation, Q_c represents the effective pulmonary capillary blood volume, i.e.,

	capillary blood volume in intimate association with alveolar gas: $1/D = 1/D_m + 1/(\Theta \cdot Q_c)$
R	A general symbol for resistance, pressure per unit flow
R_{aw}	Airway resistance
rb	Rebreathing
RQ*	Respiratory quotient
R_{us}	Resistance of the airways on the alveolar side (upstream) of the point in the airways where intraluminal pressure equals Ppl, measured under conditions of maximum expiratory flow
RV	Residual volume; that volume of air remaining in the lungs after maximal exhalation. The method of measurement should be indicated in the text or, when necessary, by appropriate qualifying symbols
SBN*	Single breath nitrogen test; a test in which plots of expired N_2 concentration versus expired volume after inspiration of 100% O_2 are recorded. The closing volume and slope of Phase III are two parameters measured by this test
STPD	Standard conditions: temperature 0° C, pressure 760 mm Hg, and dry (0 water vapor)
t	Time
T	Tidal
TGV*	Thoracic gas volume; the volume of gas within the thoracic cage as measured by body plethysmography
TLC	Total lung capacity; the sum of all volume compartments or the volume of air in the lungs after maximal inspiration. The method of measurement should be indicated, as with RV
V	Gas volume. The particular gas as well as its pressure, water vapor conditions, and other special conditions must be specified in text or indicated by appropriate qualifying symbols
v	Venous
$\bar{v}$	Mixed venous
$\dot{V}_A$	Alveolar ventilation per minute (BTPS)
$\dot{V}_{CO_2}$	Carbon dioxide production per minute (STPD)
$\dot{V}_D$	Ventilation per minute of the physiologic dead space (wasted ventilation), BTPS, defined by the following equation: $\dot{V}_D = \dot{V}_E(PaCO_2 - P_ECO_2/(PaCO_2 - P_ICO_2)$
V_D	The physiologic dead-space volume defined as $\dot{V}_D/f$
$V_D$an	Volume of the anatomic dead space (BTPS)
$\dot{V}_E$	Expired volume per minute (BTPS)
$\dot{V}_I$	Inspired volume per minute (BTPS)
VisoV̇*	Volume of isoflow; the volume when the expiratory flow rates

become identical when flow-volume loops performed after breathing room air and helium-oxygen mixtures are compared

$\dot{V}_{O_2}$ Oxygen consumption per minute (STPD)

$\dot{V}_{max}X$ Forced expiratory flow, related to the total lung capacity or the actual volume of the lung at which the measurement is made. *Modifiers refer to the amount of lung volume remaining when the measurement is made.* For example: $\dot{V}_{max}$ 75% is instantaneous forced expiratory flow when the lung is at 75% of its TLC. $\dot{V}_{max}3.0$ is instantaneous forced expiratory flow when the lung volume is 3.0 liters. [Editor's note: It is still common to find reports in which modifiers refer to the amount of VC remaining.]

V_T Tidal volume; TV is also commonly used

X_A or Xa A small capital letter or lowercase letter on the same line following a primary symbol is a qualifier to further define the primary symbol. When small capital letters are not available on typewriters or to printers, large capital letters may be used as subscripts, e.g., $X_A = X_A$

Blood-Gas Measurements

Abbreviations for these values are readily composed by combining the general symbols recommended earlier. The following are examples:

$PaCO_2$ Arterial carbon dioxide tension

$C(a-v)O_2$ Arteriovenous oxygen content difference

CcO_2 Oxygen content of pulmonary end-capillary blood

F_ECO* Fractional concentration of CO in expired gas

$P(A-a)O_2$ Alveolar-arterial oxygen pressure difference; the previously used symbol, $A\text{-}aDO_2$ is not recommended

SaO_2 Arterial oxygen saturation of hemoglobin

Q_{SP} Physiologic shunt flow (total venous admixture) defined by the following equation when gas and blood data are collected during ambient air breathing:

$$Qsp = \frac{CcO_2 - CaO_2}{CcO_2 - CvO_2} \cdot Q$$

$P_{ET}O_2$ PO_2 of end tidal expired gas

$TCPO_2$ Transcutaneous PO_2

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