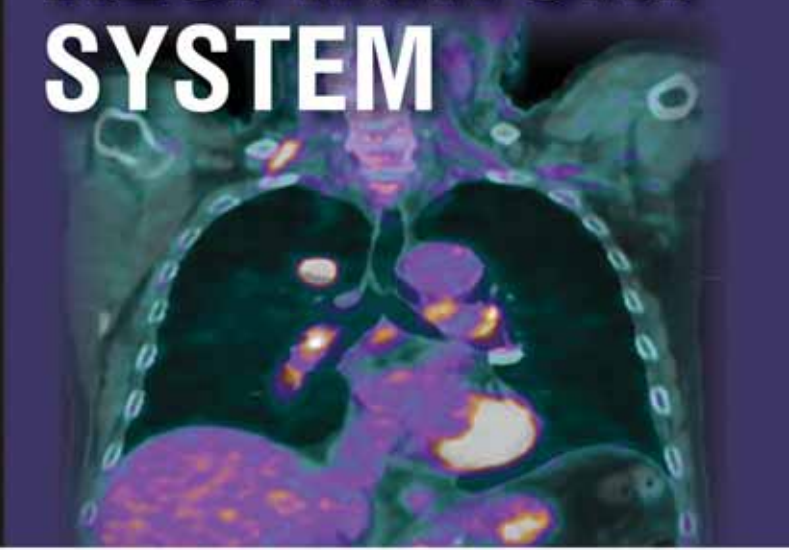
RESPIRATORY SYSTEM

Diagnostic Evaluation of the RESPIRATORY SYSTEM



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Foreword
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Diagnostic Evaluation of the RESPIRATORY SYSTEM

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JAYPEE *The Health Sciences Publisher*
New Delhi | London | Panama

Jaypee Brothers Medical Publishers (P) Ltd

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Email: cservice@jphmedical.com

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Website: www.jaypeebrothers.com
Website: www.jaypeedigital.com

Diagnostic Evaluation of the Respiratory System

First Edition: **2017**

ISBN 978-93-86056-00-9

Printed at

Dedication

To my wife and children,
the reason for my life.
To my mother,
she taught me how to keep my dreams alive.
To my father,
he taught me how to fall and get up.
To Arthur Miles,
an artist, a patient, a friend.
To all the people who fight against respiratory diseases,
never stop doing it, all things are possible for those who believe.

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Foreword

Life is not so short but that there is always time enough for courtesy.

—Ralph Waldo Emerson

I was just asked by the leading author whether I was willing to write a short introduction to the book, and I immediately accepted, in a hot Saturday afternoon of July in Palermo, Italy. I asked myself why I should have done this instead of taking a stroll on the beach or taking my kids to the park. I know why: I know the author, I know his devotion to work, I know his devotion to family, I know his devotion to life. I first met Dr Claudio Sorino about 15 years ago, when he was a student, and I was immediately impressed by his scientific personality and his clear-thinking attitude. He soon showed how work can be exciting when you combine research skills with the ability to solve clinical issues.

I was a member of the Committee on the day of his medical degree with honors and I was his tutor during his specialization in Respiratory Medicine and his PhD in Clinical and Experimental Pulmonology. Today, Dr Sorino is a prominent scientific leader, certainly a rising star in respiratory medicine. When he shared with me his willingness to coordinate the writing of a book on respiratory medicine, I admit I was skeptical about it, but I soon realized that nothing would have stopped him from doing it! Therefore, encouraging him was just an easy task. Now that I have the opportunity to see the final product, I am astonished by the high quality of the book. The practical approach to the diseases, with the scientific rationale always behind it, and the constant presence of the necessary hints make this book a valuable help for young physicians and those who 'feel young'. Indeed, Dr Sorino's experience led him to think that physicians want and need practical information, but they also require solid scientific basis. Therefore, the decision to write such a book was the most appropriate. Moreover, he was never in a hurry to finish it and now I understand why: he wanted to be sure that everything was clear and was in place. I read somewhere—I apologize with the authors for not recalling—a sentence that fully applies to this project: "*Don't start vast projects with half-vast ideas*". If you read this book, I am confident you will enjoy doing it and, most important, profit from it.

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Preface

The idea of creating a guide on the diagnostics of the respiratory system originated from the analysis of needs arising from the undertaking of daily medical activities.

Modern technological progress has made available several diagnostic tests, which may be relatively sophisticated. Some are specific for the respiratory system (e.g. pulmonary function tests), others are more generic (e.g. blood tests, radiological and nuclear medicine tests).

Despite these innovations, clinical hypothesis is based on the adequate collection of medical history and physical examination, which remain the cornerstone of the diagnostic process. The first therapeutic decisions and the request for further investigation arise from this preliminary evaluation. Clinical reasoning and interpretation of symptoms and signs are, therefore, a key element in avoiding confusion and reducing the risk of diagnostic delays and therapeutic mistakes, as well as reducing the waste of resources: time, energy and money. Indeed, many tests are often performed without a specific clinical basis, with the consequent acquisition of a large amount of data not necessarily relevant to patient symptoms and which can sometimes be misleading.

In the light of this common experience, we have conceived this book with the intention of providing an essential tool for medical practice, including clear, practical and useful suggestions, following evidence-based medical criterion. Key information from the most updated and authoritative guidelines have been included for every topic, in the attempt of providing all the elements needed to make the appropriate choices in each circumstance.

The book has been divided into four major sections: 1. Respiratory system assessment; 2. Evaluation of respiratory function; 3. Diagnostic imaging; 4. Invasive diagnostic procedures. These sections are further divided into chapters, each focusing on the comprehensive needs related to diagnostic technique. Where necessary, pathophysiological aspects have been added to clarify when and how to perform a diagnostic test and how to interpret the results.

Another aspect that this book has addressed is the quality of diagnostic tests and procedures, both in terms of execution and interpretation. Indeed, in order for some diagnostic tests to be as safe as possible, particularly when considering invasive procedures, careful assessment is required regarding not only indications and contraindications, but also their execution. Moreover, the consequences of badly effectuated or misinterpreted tests can be worse than a test which has never been carried out, as it can lead to diagnostic misunderstandings and errors concerning the subsequent treatment plan. The quality of execution is particularly important for tests in which the role of the performer and/or the cooperation of the patient are crucial, such as pulmonary function tests, ultrasound, and invasive diagnostic procedures.

The book aims to be a valuable aid for medical students, pulmonologists and nonrespiratory physicians, who may refer to it for quick answers about the most appropriate choice of investigation in different clinical situations, as well as the correct interpretation of each symptom and test.

We have tried to make the chapters as clear and direct as possible, using a wide iconography and numerous diagrams and algorithms so as to ease understanding and the storage of information.

Our hope is that this book will become a practical guide for physicians and students, stimulating their clinical reasoning in the diverse circumstances they encounter while exercising the medical profession.

The book has been enriched by the contribution and hard work of over 40 international authors. I wish to thank them all. Special thanks are given to Professor Vincenzo Bellia for his suggestions and constant encouragement, Christine Sanders for her language support, Luca Badalamenti for his technical assistance in the creation of images, and the publisher for his support throughout the production process of this book.

Last, but not least, I would like to thank my wife, Maria Rita for her understanding and love during the preparation of the book.

Claudio Sorino MD PhD

Acknowledgments

Kerstin Brauer for her excellent technical assistance in the preparation of the chapter on SPECT.

Domenico Santoro and **Chiara Colombo** from the Division of Infectious Diseases, S. Anna Hospital, Como for their suggestions on the chapter on Tuberculosis Diagnostics.

Raffaella Acconcia from the University of Insubria for the pictures on arterial blood gas analysis.

Radiometer Medical ApS, Denmark for the material supplied to the chapter on Arterial Blood Gas.

Olympus Europe SE & CO. KG for the pictures of the section on Invasive Diagnostic Procedures.

Patrick Morgan for the images in the chapters on Lung Function Testing in Preschool Children.

COSMED for the images in the chapters on Lung Volumes and Cardiopulmonary Exercise Testing.

Pietro Quaretti and **Lorenzo Moramarco** from the Unit of Interventional Radiology, IRCCS Policlinico San Matteo Foundation, Pavia, Italy for the pictures in the chapter on Conventional Pulmonary Angiography.

We would like to thank Mr Jitendar P Vij (Group Chairman), Mr Ankit Vij (Group President), Ms Chetna Malhotra Vohra (Associate Director–Content Strategy), Mr Umar Rashid (Development Editor), and the production team of Jaypee Brothers Medical Publishers (P) Ltd, New Delhi, India for their cooperation in publishing this book.

Contents

Section 1: Respiratory System Assessment

Chapter 7

Displaceable Lung Volumes: Simple Spirometry

Claudio Sorino, Salvatore Battaglia

OVERVIEW OF SIMPLE SPIROMETRY

The mechanical properties of the respiratory system may be affected by several respiratory or systemic diseases. Most of them have consequences upon airway resistance and lung compliance. Simple spirometry is a basic tool for the evaluation of airway function and is commonly the first test performed when a chronic respiratory disease is suspected. By measuring dynamic volumes and flows during forced expiratory and inspiratory maneuvers, it provides a valuable contribute in identifying respiratory diseases associated with some ventilatory defects. It can be used for diagnosing and monitoring respiratory disease, for preoperative risk stratification, and as a tool in epidemiologic and other research studies. The main indications for spirometry are listed in Table 7.1.

Most patients can easily perform spirometry when coached by an appropriately trained technician or other health care provider. The test can be performed in the ambulatory setting, physician's office, emergency department, or inpatient setting. Since several steps should be followed from the preparation to the running of the test, the use of a checklist may be useful to ensure not to overlook some important factors (Table 7.2).

Table 7.1: Main indications for running simple spirometry.

Unexplained, recurrent or persistent respiratory symptoms: dyspnea, cough, or wheezing
Suspected obstructive disease: asthma or chronic obstructive pulmonary disease (COPD)
Presence of risk factors for respiratory diseases (congenital or acquired)
Suspected restrictive disease: suspected interstitial lung disease; chest wall disorders
Assessment of therapy response
Disease follow-up (lung function decline)
Preoperative evaluation of lung function, if indicated

Table 7.2: Example of checklist usable when a spirometry is performed.

• Check the accuracy of the spirometer (daily calibration)
• Record subject's key anthropometric data (gender, date of birth or age, race, standing height, weight).
• Assess if there are contraindications to performing the test (Table 7.3)
• Assess if there are contraindications to administering bronchodilators (Table 7.4)
• Assess which drugs are being used at the present and when they were last taken
• Assess for active smoking (avoid to perform spirometry within 2 hours from the last smoked cigarette).
• Ask the patient to sit for the test
• Ask the patient to loosen restrictive clothing
• Explain the procedure carefully and demonstrate the maneuvers
• Attach nose clip
• Place mouthpiece in mouth and ask the patient to close lips around the mouthpiece
• Ask the patient to inhale quickly and completely (to total lung capacity), then to exhale forcefully without hesitation until no more air can be expelled
• Repeat for a minimum of three valid maneuvers
• Assess the attainment of FEV1 and FVC repeatability, otherwise perform additional maneuvers (up to eight in total)

PREPARATION OF THE EQUIPMENT

Properly calibrated and accurate spirometers are a key element for the correct measurement of respiratory function.

One disadvantage of the new generation of spirometers is that flow sensors can lose accuracy over time, so that calibration checks are needed each day the spirometer is to be used. A 3-liter calibration syringe should be used for this verification. It should be stored near the spirometer so that the two devices remain at the same temperature.

The syringe should be periodically checked for leaks. This can be done by filling the syringe with air, holding the palm against the outlet snout and trying to empty the syringe.

In order to minimize the risk of cross-contamination, the disposable mouthpiece must always be replaced between patients. Moreover, routine hand washing, and proper cleaning of permanent flow sensors are recommended.

PREPARATION OF THE PATIENT AND PRECAUTIONS BEFORE TESTING

Before performing spirometry, the physician should verify that it is safe for the patient. There are absolute and relative contraindications to the spirometry. As shown in Table 7.3, some of these are pathological conditions which are potentially worsened by a forced expiratory maneuver and that may require the postponement of the test until they are resolved (e.g. recent myocardial infarction, pulmonary embolism, pneumothorax, stroke, thoracic, abdominal or eye surgery, uncontrolled hypertension). Other relative

Table 7.3: Absolute and relative contraindications to perform simple spirometry and reasons for this.

Conditions	
Absolute	*Reason: Unsafe for the patient*
Hemoptysis of unknown origin	Risk of exacerbation of the underlying condition with major hemorrhage Possible active pulmonary tuberculosis and consequent risk of cross-infection due to contamination of equipment
Unresolved pneumothorax	Forced expiration may aggravate the problem
Unstable angina or recent myocardial infarction or pulmonary embolism (in the last month)	Risk of precipitating acute coronary syndrome or massive pulmonary embolism, mainly as a consequence of blood pressure changes
Recent thoracic or abdominal surgery (in the last 3 months)	Forced expiration raise intracranial, intrathoracic and intra-abdominal pressures, can cause pain, incisional hernias
Recent eye surgery, e.g. cataract (in the last 3 months)	Forced expiration may cause undesirable raised intraocular pressure
Recent stroke (in the last 3 months)	Risk of recurrence
Uncontrolled arterial hypertension	Risk of dangerous further increase in blood pressure
History of hemorrhagic cerebrovascular events	Precipitation of cerebral bleed
Fractured ribs	Risk of pneumothorax, painful maneuver
Thoracic, abdominal, or cerebral aneurysms	Danger of aneurysm rupture due to increased thoracic pressure
Relative	*Reason: Unsafe for others*
Known or suspected respiratory infection and hemoptysis of unknown origin	Risk of cross-infection due to contamination of equipment Potentially impaired meaning of the results
Relative	*Reason: Suboptimal results*
Nausea, vomiting, or pain	They can affect the patient's ability to perform the test
Confusion, cognitive impairment	Inability to comply with instruction
Oral or facial pain exacerbated by a mouthpiece	The test can be uncomfortable
Stress incontinence	The test can be uncomfortable
Extreme shortness of breath	The test can be uncomfortable
Presence of cough during the test	The test can be unreliable

contraindications are just conditions that may affect the reliability of spirometry measurements (e.g. cognitive impairment, extreme shortness of breath or cough, oral or facial pain, nausea, vomiting).

Moreover, the patients should not have eaten a hearty meal within 2 hours prior to the test (since a full stomach may restrict movement of the diaphragm and cause an underestimation of lung volumes), smoked in the last 2 hours prior to the test or consumed alcohol 4 hours prior to the test (above all if gas transfer or static lung volume measurement are required), undertaken vigorous exercise within 30 minutes prior to the test (since this may affect the quality of spirometry mainly for the measurement of effort-dependent parameters), taken a short-acting bronchodilator within 4 hours prior to the test or long-acting bronchodilator within 12 hours prior to the test (in order to allow the correct measurement of pre- and postbronchodilator values).

Anthropometric data of the patient (race, age, height and weight) are needed for the calculation of predicted values. Height should be accurately measured without shoes, with the feet together, standing as tall as possible with the eyes level looking straight ahead (Fig. 7.1).

Any systemic or inhaled drug able to alter lung function should be recorded, together with its dosage and last intake.

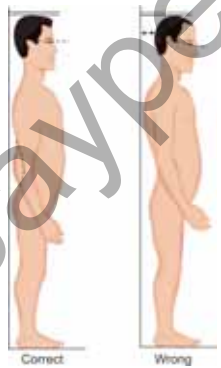


Fig. 7.1: Correct position for the measurement of the height.

TEST EXECUTION

The technician should explain and demonstrate the appropriate technique. Instruction should be detailed but simple and age-appropriate. It is preferable that the patient is sitting, using a chair with arms and without wheels for safety reasons in order to avoid falling due to syncope. When you believe that the patient has understood the instructions, the breathing tube is inserted into his/her mouth, making sure the lips are sealed around the mouthpiece and that the tongue does not occlude it. The use of a nose clip or manual occlusion of the nostril is recommended.

The three key step of a forced expiratory maneuver are the following:

1. Maximal inspiration: the subject should inhale rapidly and completely from functional residual capacity (FRC) to total lung capacity (TLC).
2. Strong exhalation: it is important to prompt the subject to "blast," not just "blow," the air from the lungs.
3. Continued complete exhalation: the subject should be encouraged to fully exhale until the complete emptying of the lung, or at least until the amount of air which exits from the lungs is negligible (*see* end of test criteria).

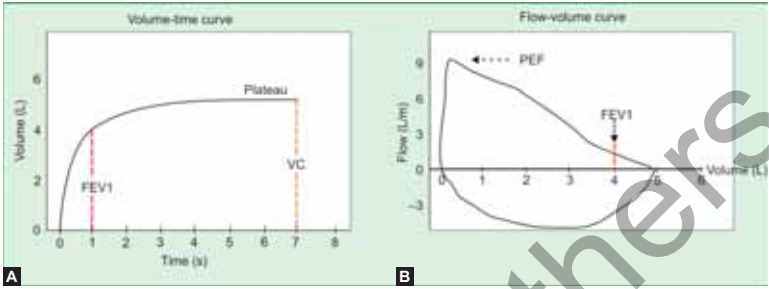
Reductions in PEF and FEV1 have been observed when inspiration is slow and/or there is a pause higher than 4 seconds at TLC before beginning exhalation. Consequently, it is important that the preceding inspiration is fast and any pause at full inspiration be minimal (ideally only for 1–2 seconds).

The patient's trunk and neck should remain erect during the maneuver, the patient looking straight forward during the entire test without bending over (the latter not only affects the way the trachea is stretched, but may also lead to saliva dripping into the filter mouthpiece and equipment).

In order to more accurately assess the vital capacity (VC), the forced maneuvers can be preceded by two or more slow maneuvers. This can be done in two different ways: (1) starting from end-tidal volume, the subject expires maximally and then makes a full inspiration [inspiratory vital capacity (IVC)] or (2) the subjects make a full inspiration and then exhales maximally [expiratory vital capacity (EVC)].

QUALITY ASSESSMENT OF SPIROMETRY

Before interpreting any spirometry maneuver, it is necessary to evaluate its quality. The reading of the numerical



Figs. 7.2A and B: (A) Volume-time curve and (B) Flow-volume curve recorded during a well-performed spirometry in a healthy subject.

data without a review of the quality of the test, as well as the automatic interpretation by the computer, is common sources of interpretation mistakes.

The American Thoracic Society (ATS) criteria, which are the most widely used, suggest to achieve three acceptable maneuvers and verify the repeatability of the main parameters (FEV1 and FVC). They consider the acceptability of the start and the end of each forced spirometric maneuver and repeatability criteria, as discussed below in details.

Evaluation of the Technique and Graphs

Several errors in the patient's execution technique may compromise the interpretation of a spirometry. A careful observation of the patient during the test is essential to assess the adequacy of the technique, in particular of the patient's forced expiratory effort. A correctly performed maneuver should appear to be delivered with maximal effort, starting from the level of maximum inspiration. Forced expiration should start instantaneously and the effort should be sustained at least for one-third of VC. Exhalation should continue until reaching the residual volume, without cough or other interruptions, without evidence for leaks at the mouthpiece, obstruction at the mouth opening due to the tongue or biting the mouthpiece, or to bad-fitting dentures.

The inspection of the volume-time and flow-volume curves is another key element for the quality assessment of a spirometry test. The *volume-time curve* plots volume (in liters) on the vertical axis and time (in seconds) on the horizontal (Fig. 7.2A). The trace must curve upward, be smooth, free of irregularities, and must plateau for at least one second. The *flow-volume curve* plots flow rate (in liters per second or minute) on the vertical axis and volume (in liters) on the horizontal (Fig. 7.2B). The trace should rise almost vertically to a peak flow, then it should go down and merge smoothly with the horizontal axis at FVC at the end of the blow.

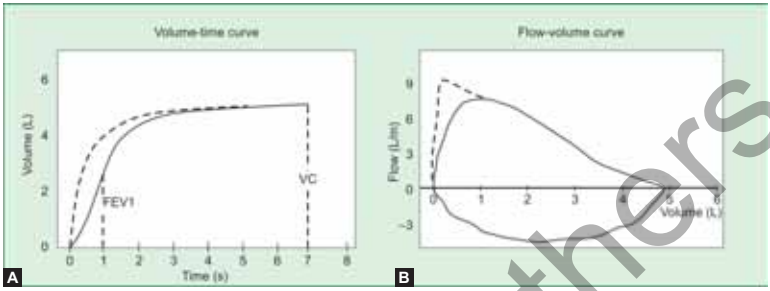
A slow start to the forced maneuver often results in a reduced FEV1. In such a case, the volume-time curve has an "S" shape at the start (Fig. 7.3A), whereas the flow-volume curve does not rise steeply (Fig. 7.3B).

When a forced maneuver is performed without enough effort during the initial phase of exhalation, a reduced peak flow can be observed. Moreover, this may result in slightly larger flow rates at middle lung volumes and a higher FEV1, usually due to a reduced gas compression and a lack of sensitivity to lung volume changes when flow is measured at the mouth.

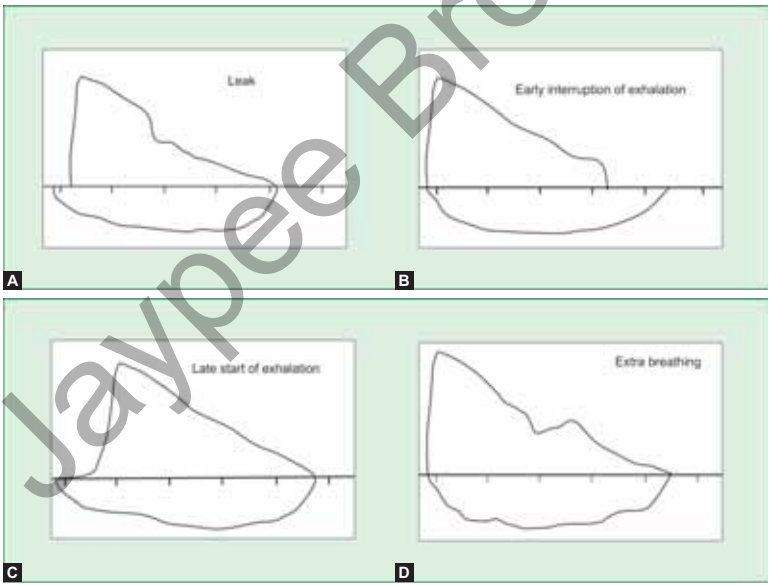
If a maneuver has an obviously hesitant start, the technician may terminate the trial early to avoid an unnecessary prolonged effort. A sudden drop of flow to zero usually suggests a glottis closure or other early interruption of the exhalation, resulting in inaccurate measurement of VC.

Some events that may affect the proper performance and interpretation of spirometry can be easily recognized by observing the graphs (Figs. 7.4A to F).

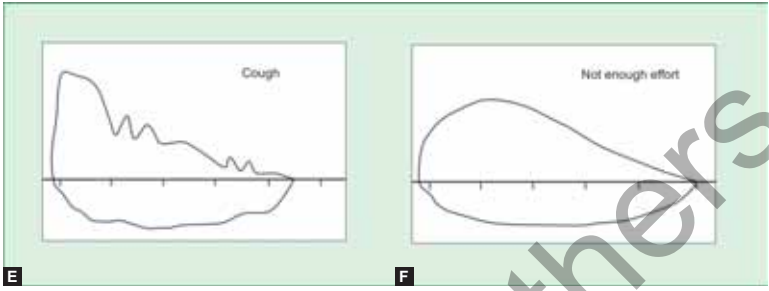
Even a nonoptimal test can provide useful information. For example, the early interruption of exhalation



Figs. 7.3A and B: Slow start of forced expiration on the (A) Volume-time and (B) Flow-volume curve. The dashed line indicates the predicted path of the curve without artifacts.



Figs. 7.4A to D



Figs. 7.4A to F: Examples of incorrect maneuvers that can be identified by looking at the graphs.

makes the measurement of FVC unreliable, but it does not affect the measurement of FEV1. In contrast, a weak start of exhalation may prevent a correct calculation of FEV1, but VC can still be measured if the patient completed the lungs emptying.

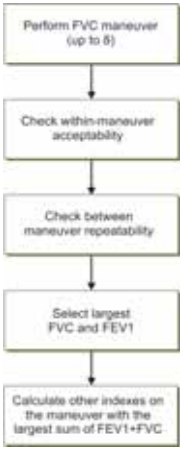
To ensure a reliability of the spirometry results, the maneuvers must be acceptable and reproducible (*see* below). If all the criteria for acceptability and repeatability are not fully met, the interpreter should comment on the test, pointing out the problems, the direction and magnitude of potential errors.

Within-Maneuver Evaluation (Acceptability)

The acceptability criteria should be applied before reproducibility is checked (Flowchart 7.1). The acceptability is established through "start of test" and "end of test" criteria, which are summarized, together with the repeatability criteria in Table 7.4.

The "start of test" refers to the beginning of forced expiration that should be carried out with the maximal effort and without hesitation. The effective start of timed measurements is determined by the *back extrapolation* method, which provides a new "time zero", and is essential for the accurate calculation of many parameters. In order to achieve an accurate time zero and assure that the FEV1 comes from a maximal effort curve, the EV (back extrapolated volume) must be less than 5% of the FVC or less than 150 mL, whichever is greater. A time to peak expiratory flow (time-to-PEF) less than 120 seconds is an additional start of test criterion. A rapid computerized feedback to the technician is usually given when these criteria are not met.

Flowchart 7.1: Suggested steps for the performance and interpretation of spirometry to obtain a satisfactory quality of the test and accuracy of results



The main end of test criterion is the achievement of a minimum exhalation time of 6 seconds, unless the volume time curve shows a previous clear plateau (i.e. no volume change or <25 mL) of reasonable duration (at least

Table 7.4: Summary of the acceptability and repeatability criteria.

Acceptability
Start of Test
Extrapolated volume <5% of the FVC or <150 mL No hesitation or false start Rapid start to rise time No cough during the first second of the maneuver
End of Test
No early termination of exhalation Exhalation time ≥6 seconds or plateau ≥1 second
Repeatability
Difference of FEV1 from the largest FEV1 <150 mL* Difference of FVC from the largest FVC <150 mL*
* 100 mL if the FVC is <1.0 L

Table 7.5: Stratification of the degree of acceptability and repeatability.

Characteristic	*Grade*	*Criterion*
Acceptability	A	≥3 acceptable maneuvers
	B	2 acceptable maneuvers
	C	Only 1 acceptable maneuver
	D	No acceptable maneuvers
FEV1 repeatability	A	Two largest values match within 100 mL
	B	Two largest values match between 101 mL and 150 mL
	C	Two largest values match between 151 mL and 200 mL
	D	Two largest values do not match (difference >200 mL)
FVC repeatability	A	Two largest values match within 100 mL
	B	Two largest values match between 101 mL and 150 mL
	C	Two largest values match between 151 mL and 200 mL
	D	Two largest values do not match (difference >200 mL)
PEF repeatability	A	Two largest agree within 5%
	B	Two largest agree between 6% and 10%
	C	Two largest agree between 11% and 15%
	D	Two largest do not agree (difference >15%)

1 second). Indeed, some young and healthy people (especially females) complete exhalation and reach a plateau before 6 seconds.

An early interruption of expiration causes an underestimation of FVC (and overestimation of the parameters in which the FVC is the denominator, e.g. FEV1/FVC). However, no maneuver should be eliminated solely because of early termination, since the FEV1 from such maneuvers may be valid.

In addition to the above criteria, no cough (usually revealed by a 50% drop in flow) should be noticed, especially during the first second of the exhalation, and there should not be artifacts, glottis closure, leak at the mouth or obstruction of the mouthpiece by the tongue or teeth.

A minimum of three technically acceptable forced maneuvers are required. If a subject is unable to perform a single acceptable maneuver after eight attempts, testing may be discontinued.

Between-Maneuver Evaluation

After obtaining a minimum of three acceptable FVC maneuvers, *repeatability* (sometimes indicated as reproducibility) should be assessed.

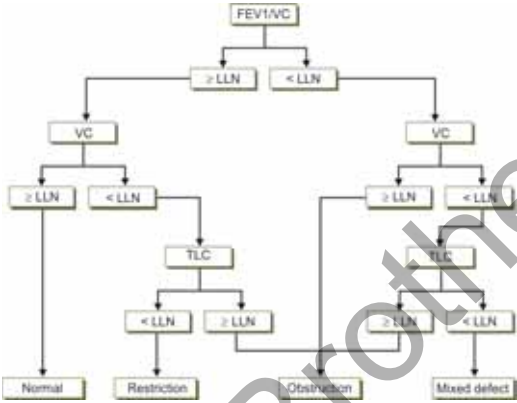
A good repeatability is achieved when the difference between the largest and the next largest FVC is smaller than or equal to 150 mL and the difference between the largest and next largest FEV1 is less than or equal to150 mL. If the FVC is 1.0 L or less, both these values are 100 mL. If these criteria are not met in three maneuvers, additional trials should be attempted, up to, but usually no more than eight maneuvers. Large variability among tests is often due to incomplete inhalations. Some patients may require a brief rest period between maneuvers. Some individual may show a progressive reduction in FEV1 or FVC with each subsequent blow as an expression of high bronchial reactivity. If the cumulative drop exceeds 20% of start value, the test procedure should be terminated in the interest of patient safety.

An overall assessment of the quality of spirometry may be done by assigning a value of acceptability and repeatability, as shown in Table 7.5.

INTERPRETATION OF TEST

The interpretation of spirometry requires the comparison of the parameters measured in the patient with those

Flowchart 7.2: Algorithm for the interpretation of the simple spirometry.



obtained by adequate reference equations. These equations are derived from large cohorts of healthy subjects and allow to calculate the "theoretical" value (or "predicted") for each parameter, as well as the normal ranges with the limits beyond which a result can be considered as pathological. The predicted values are specific for each subject, and vary primarily with gender, age, ethnicity and height of the individual.

On the basis of spirometric parameters, it is possible to identify two large groups of pulmonary disease: obstructive airway diseases, in which there is an expiratory airflow limitation due to a narrowing of the airways [asthma, chronic obstructive pulmonary disease (COPD), etc.] and restrictive lung diseases, characterized by a decrease in lung volumes or in the patient's ability to expand the lungs (obesity, interstitial lung diseases, myopathy, etc.).

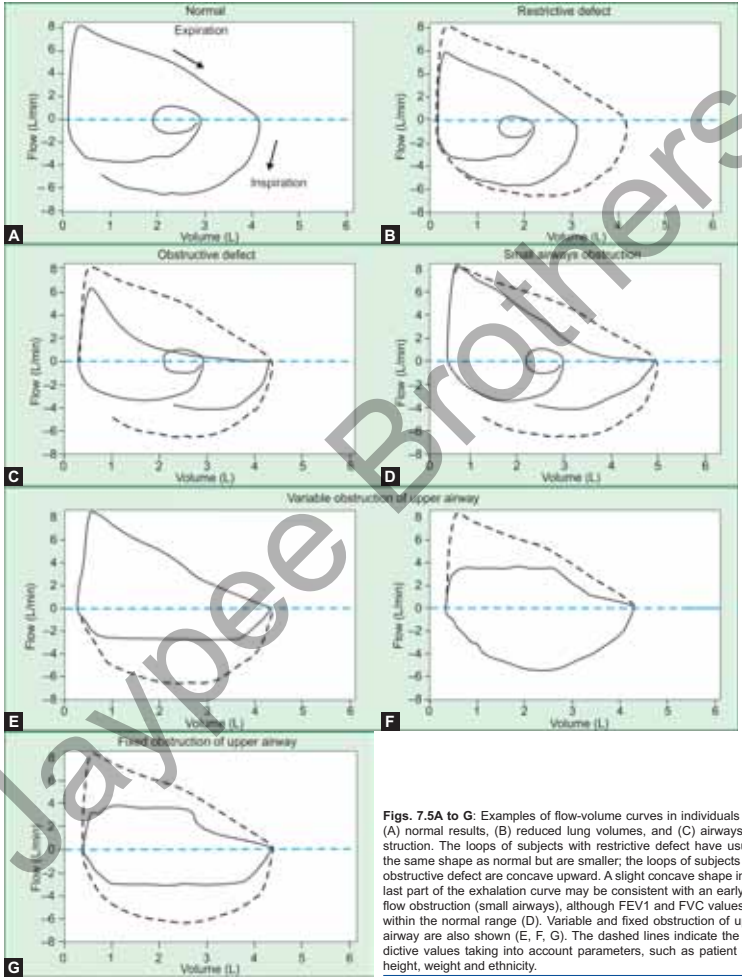
The diagnosis of bronchial obstruction require a reduction of FEV1 and of its relationship with the VC or forced vital capacity (FVC) (Tiffeneau Index) at values lower than their respective lower limits of normal (LLN). Lung restriction may be only suspected though a simple spirometry if VC is lower than LLN; its confirmation require the measurement of nondisplaceable lung volumes, showing a reduction of the TLC. Flowchart 7.2 shows a diagnostic algorithm useful for the evaluation of lung function; Figures 7.5A to G show the morphology of the flow-volume curves in normal and pathological conditions.

Forced vital capacity is often used in place of VC because obtained in the same forced expiratory maneuver. However, most recommend to use the largest VC available, which can be obtained either during inspiration (IVC), slow expiration (SVC), or forced expiration (FVC). FVC is usually reduced more than IVC and SVC in airway obstruction. The forced expiratory volume at 6 seconds (FEV6) may be used as a surrogate of VC in subject who cannot complete the exhalation; this requires the use of appropriate LLN for FEV1/FEV6.

The advantages of the use of flow-volume loops include the possibility to identify the probable anatomical location of airway obstruction. An obstructing lesion located in the extrathoracic upper airway (larynx, trachea) can limit airflow in a fixed way and may be identified during the inhalation component on the flow-volume loop.

BRONCHODILATOR REVERSIBILITY TEST

A bronchial reversibility test is always indicated when spirometry reveals airway obstruction (both FEV1 and FEV1/FVC <LLN). After performing a simple spirometry, the patient is asked to inhale a bronchodilator with rapid onset of action (usually 400 mcg of Salbutamol by metered dose inhaler, preferably with a spacer). The forced expiratory maneuver is then repeated about 20 minutes after such an inhalation.



Figs. 7.5A to G: Examples of flow-volume curves in individuals with (A) normal results, (B) reduced lung volumes, and (C) airways obstruction. The loops of subjects with restrictive defect have usually the same shape as normal but are smaller; the loops of subjects with obstructive defect are concave upward. A slight concave shape in the last part of the exhalation curve may be consistent with an early airflow obstruction (small airways), although FEV1 and FVC values are within the normal range (D). Variable and fixed obstruction of upper airway are also shown (E, F, G). The dashed lines indicate the predictive values taking into account parameters, such as patient age, height, weight and ethnicity.

The single administration of inhaled bronchodilators for the reversibility test is generally safe. Hypersensitivity to atropine-like substances is the only rare contraindication to the use of anticholinergics. In some situations, the use of an anticholinergic instead of a β2-sympathomimetic may be a prudent choice. These include thyrotoxicosis, heart failure, hypertension, and diabetes mellitus with poor glycemic control.

Potentially serious hypokalemia and consequent cardiac arrhythmia may result from b2-agonist administration, but the risk concerns mainly patients receiving high doses for therapeutic purposes, especially if endovenous. Caution is advised in patients with hypoxia, concomitant use of heart glycosides (e.g. digoxin, digitalis), xanthine derivatives (e.g. theophylline aminophylline), steroids, diuretics.

β2-sympathomimetic may increase blood sugar levels, and if a diabetic patient is unable to compensate for this, ketoacidosis may occur.

Before undertaking bronchodilator testing, the patient should stop short-acting bronchodilators for 6 hours, long-acting bronchodilators for 12 hours and theophylline for 24 hours.

Test performance is affected by the day of testing, the severity of baseline lung-function impairment. The test is considered positive when it shows an increase in FEV1 and/or FVC or VC of at least 12%, with a simultaneous change in their absolute values of more than 200 mL.

In the past, bronchodilator reversibility has been widely used to differentiate COPD from asthma, since airflow obstruction was thought to be little or no reversible in patients with COPD, and fully reversible in patients with asthma. In effect, no clear cut-off exists between asthmatic and COPD patients. Furthermore, the test is scarcely reproducible over time in the same patient.

Despite this, bronchoreversibility testing is largely used in clinical practice to guide the clinician through the diagnostic and follow-up process. Large increments in the FEV1 from baseline (>400 mL) after the administration of salbutamol support the diagnosis of asthma in patients with a history compatible with the disease.

The presence of chronic airway inflammation may mask the acute reversibility, especially in the elderly; in such cases, if there is a strong clinical suspicion of bronchial asthma, to run a "chronic reversibility test" (or "steroid reversibility test") can be useful. This method, still not well standardized, requires a few weeks period of therapy with oral corticosteroids (e.g. 25 mg of prednisone daily or equivalent for 2 weeks) and/or inhaled corticosteroids (e.g. 200 mcg of beclometasone daily or equivalent inhaled corticosteroid for 6–8 weeks). After this trial, the spirometry is repeated, using criteria for the evaluation response identical to those of acute reversibility.

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