Medical Physics Series

# MEASUREMENT IN CLINICAL RESPIRATORY PHYSIOLOGY

Gabriel Laszlo and Michael F Sudlow

# MEASUREMENT IN CLINICAL RESPIRATORY PHYSIOLOGY

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1983

ACADEMIC PRESS

*A Subsidiary of Harcourt Brace Jovanovich, Publishers*

London New York

Paris San Diego San Francisco São Paulo

Sydney Tokyo Toronto

ACADEMIC PRESS INC. (LONDON) LTD.
24/28 Oval Road,
London NW1

*United States Edition published by*
ACADEMIC PRESS INC.
111 Fifth Avenue
New York, New York 10003



*British Library Cataloguing in Publication Data*

Measurement in clinical respiratory physiology.—
(Medical physics, ISSN 0076-5953)
1. Respiratory system—Examination
I. Laszlo, G. II. Sudlow, M. III. Series
616.2'065 RC734.R3

ISBN 0-12-437080-2
LCCCN 83-70715

Printed by W. & G. Baird Ltd., Greystone Press, Antrim, Northern Ireland.

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# PREFACE

This book is intended to be a practical handbook for those working in a respiratory function laboratory. We hope it will be of use in the laboratory and find a place there as well as in the reference library. The authors are all active research workers and we have invited them to contribute because of their practical experience in the topics they discuss.

The book falls into two parts. In the first, we discuss instrumentations; in the second, the assembly of equipment for specific purposes.

In writing, we had in mind the hospital physicist, technician or physiologist who has to equip, organise and run and service a respiratory function laboratory for routine clinical or research purposes. Except for the briefest account in Chapter 1, we have not included any systematic discussion of pulmonary physiology and have avoided details of the interpretation of respiratory function tests or their role in clinical management. Several recent texts listed at the end of Chapter 1 deal with these problems.

We have not attempted a comprehensive review of all the possible measurements of lung function but have dealt with the more important aspects in current practice and emphasized those of growing importance.

We would like to thank all who contributed for their time and effort. Many medical illustrators and secretaries have contributed to the volume, but we particularly thank Claire Douglas, Russell Harvey, Gary James, Anne McAuley, Judy Seward and Morag Wells. We are grateful to Jeanette Dennison for preparing the index.

*May 1983*

*Michael F. Sudlow*
*Gabriel Laszlo*

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# 1. THE WORK OF THE RESPIRATORY LABORATORY

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## INTRODUCTION

Clinical respiratory physiology is concerned with the investigation of pulmonary function when it is disturbed. The investigator may need to:

(1) identify normality or abnormality;
(2) identify the disordered component or components of the respiratory system;
(3) measure the severity of the abnormality identified.

The functions and architectural features of the lungs which may be tested are:

(1) pulmonary ventilation and the work of breathing: the mechanical properties of the lungs;
(2) pulmonary gas exchange and the integrity of the gas exchanging surface;
(3) Neural control of the rate and depth of breathing.

Most respiratory disorders can be diagnosed by clinical means, from the patient's history and medical examination. Occasionally, the condition is complex and a careful study of the components of the respiratory system is required to elucidate the diagnosis fully. Such sessions are not readily repeatable. Many of the procedures described in this book, therefore, are selected for simplicity and repeatability, so that patients can be asked to perform them at intervals to judge the progress of the disorder or the response to treatment. Thus, some tests are chosen for their ability to measure the overall impairment of the system while others, more complex, are designed to reveal more specifically the nature of the abnormality.

## Ventilation

Normal individuals can breathe in and out and thus ventilate the lungs at a much greater rate than is necessary to supply oxygen for most purposes. Severe exercise is normally limited by the ability of the heart and circulation to deliver oxygen to exercising tissues, rather than by the ventilatory capacity. However, a disease may reduce the ventilatory capacity by several mechanisms:

(1) weakness of the respiratory muscles;
(2) narrowing of the air passages, thus reducing maximum rate of air flow than can be achieved;
(3) reduction in lung volume or lung elasticity;
(4) deformity of the thorax.

These may be identified by measuring air movement in relation to maximum effort, or by examining the relationship between pressure generated by the respiratory muscles and movement of air in and out of the thorax achieved as a result of these pressure changes. A large section of this book, therefore, is concerned with the techniques which have been developed to examine the relationship between air flow and the effort of the respiratory muscles.

The simplest tests of ventilation are those derived from the *timed forced vital capacity*. The vital capacity is the maximum volume of air which can be delivered during expiration after a full inspiration. This test identifies the reduction in the size of the accessible portion of the lung and the patency of the airways (Chapter 9).

Normally, 80% of the vital capacity can be exhaled forcibly in one second. If the vital capacity is normal but the ratio that can be exhaled in one second is reduced, we deduce that obstruction to air flow is present.

If the vital capacity is small, it is necessary to distinguish between several causes of this abnormality:

(1) Premature closure of airways because of obstruction. In this situation, the total lung volume is normal and the air left in the lungs at the end of a full expiration (residual volume) is increased.
(2) So-called *restrictive* diseases in which the total lung volume is reduced after maximal inspiratory effort. There are three main types of abnormality which produce this result:
    (a) reduced numbers of alveoli;
    (b) increase in the density of the lung tissue in relation to the volume of air within the lungs;

(c) deformity of the thoracic cage;
(d) weakness of the inspiratory muscles.

The last two may often be recognized by examination of the patient. These conditions are not easy to investigate physiologically but may be distinguished by the measurement of pressure within the thorax (oesophageal pressure, Chapter 9) in relation to lung volume. In the case of (b), relaxation pressure is increased in relation to lung size, whereas in (a), (c) and (d) it is normal. The distending pressure of the thorax as distinct from the lungs is best measured under an anaesthetic by relating lung volume to pressure, but under certain circumstances it may be measured if the patient can learn to relax all the respiratory muscles while expiration is obstructed at the mouth. Weakness of the respiratory muscles may be shown by the inability of the patient to generate the normal negative inspiratory and positive expiratory pressures while the breathing is obstructed.

The inspiratory muscles work by enlarging the thoracic volume and distending the lungs. The *diaphragm* forms the floor of the thorax. When it contracts, it generates a positive pressure within the abdomen and a negative pressure in the chest. The difference between these pressures, measured in the stomach and oesophagus respectively, reflect the force of diaphragmatic contraction.

Knowledge of the *lung volumes* is an important component of physiological interpretation of ventilatory tests. These may be measured by introducing a known volume of an insoluble foreign gas into a closed breathing circuit and measuring its dilution. Alternatively, there is a technique using Boyle's law to study the changes of pressure as the subject pants against an obstruction at the mouth in a body plethysmograph (Chapters 9 and 14).

## Gas Exchange

Within the lungs, oxygen and carbon dioxide are exchanged by diffusion across a thin *alveolar membrane*. Gas exchange is affected by: by:

(1) pulmonary ventilation;
(2) diffusion of gases within the airways and alveoli;
(3) diffusion of gases across the alveolar walls;
(4) the distribution of pulmonary blood flow in a uniform manner to match to pulmonary ventilation.

In normal subjects, the rate and depth of breathing is relatively shallow in comparison to the lung volume, and the inspired air is only

drawn into the most proximal air spaces. This air, rich in oxygen and free from carbon dioxide, exchanges with the alveolar gas by a rapid diffusion within the intra-pulmonary air spaces. Moreover, there are control mechanisms within the pulmonary circulation which ensure that the major portion of the pulmonary blood flow is directed to those portions of the lungs which are well ventilated, since shortage of oxygen at their surface causes narrowing of individual pulmonary blood vessels.

Diffusion of oxygen into the red blood corpuscle and carbon dioxide out of it is normally very rapid because the membrane dividing the alveolar gas and the red blood corpuscle is very thin, and the surface area for gas exchange is very large. Damage to the gas-exchanging surface of the lung may cause increased thickness of the diffusion pathway or, much more commonly, a reduction of the surface area available for gas exchange. As indicated above, the latter may be caused by reduction in the numbers of alveoli, or by failure of the inspired gas to reach some of the patent alveoli because the airways connecting them are narrowed.

The presence of these types of abnormality may most easily be detected by a reduction in the uptake in carbon monoxide under standard conditions (Chapter 11). Carbon monoxide in trace quantities has a very high affinity for haemoglobin within the red blood corpuscles, much greater than that of oxygen. This means that the uptake of carbon monoxide is limited by the amount of haemoglobin that is in close contact with the inspired gas during the test, rather than by its removal in the circulation, since the red cells do not achieve sufficiently great partial pressure of carbon monoxide during the test to limit uptake. This remains true, regardless of whether the red cells are moving or not. CO uptake is therefore "diffusion limited" rather than circulation limited, which is the case for oxygen.

Even if total pulmonary ventilation and blood flow are virtually normal, it is necessary for efficient gas exchange that they should be matched evenly within the lungs. Mismatching of ventilation and perfusion results in two types of abnormality:

(1) alveoli having an abnormally high ventilation:perfusion ratio;
(2) alveoli with a low ventilation:perfusion ratio.

The first type of abnormality results in wasted ventilation because work has to be done to move air in and out of these alveoli without much gas exchange taking place within them.

The second type of abnormality results in lower than normal content of oxygen within the blood leaving the lungs and being distributed to the tissues, as a result of the phenomenon known as the *shunt effect*. This is most easily explained by considering the extreme case where

blood reaches alveoli which are totally obstructed and have no fresh air reaching them at all during ventilation. Such blood passes straight through the lungs, taking with it haemoglobin with an excess of free oxygen receptors ("shunted" blood). Ventilation and perfusion are normally arranged so that haemoglobin is almost fully saturated in the blood leaving normal alveoli. In the presence of "shunted" blood, the mixed arterial blood has an abnormal amount of reduced haemoglobin in it. Diffusion must also be matched to blood flow for efficient gas exchange. These abnormalities may be identified by measurements of arterial blood oxygen saturation, content or partial pressure (Chapters, 5, 6).

Wagner and West (1980) have developed an elegant approach to the problem by analysing the clearance by the lungs of an intravenous infusion of gases at different solubilities.

## Control of Ventilation

For any given delivery to the lungs of carbon dioxide and reduced haemoglobin the pulmonary circulation to the lungs, the pulmonary gas exchange will be determined by the rate of ventilation. Briefly, if ventilation is high in relation to perfusion, the expired air will resemble closely room air and the partial pressure of carbon dioxide in it will be low. The less the ventilation, the greater will be the partial pressure of carbon dioxide.

Blood is a buffered system and carbon dioxide in solution as carbonic acid has a p$K$ (7.1) close to the pH of normal blood (7.4). To maintain the pH within normal limits required for optimal functioning of metabolism within the tissues, ventilatory control mechanisms have evolved which maintain $P_{CO_2}$ at a level of 5.5 kPa (40 mmHg). These control mechanisms are tuned so that, as the metabolic rate increases with increasing activity, ventilation increases in proportion, thus maintaining a constant mean $P_{CO_2}$ within the alveoli. Thus, $P_{CO_2}$ varies very little under normal circumstances.

An elevated arterial $P_{CO_2}$ therefore indicates *alveolar under-ventilation*. This may occur either because of impairment of the ventilatory mechanisms or because the control mechanisms are in some way at fault. *Alveolar hyper-ventilation*, or over-breathing, is a manifestation of a variety of states, not all abnormal:

(a) Increased *chemo-receptor* drive. There are oxygen and hydrogen ion sensors within the brain and peripheral circulation which recognize low arterial $P_{O_2}$ and pH and stimulate, by a reflex, an increase in the rate and depth of breathing. These mechanisms are of great importance in normal subjects and animals at altitude where the inspired oxygen pressure is lower than at sea-level.

(b) A variety of mechanical abnormalities. Respiratory discomfort associated with certain lung diseases may stimulate hyperventilation even without a reduction of arterial $P_{O_2}$.
(c) Other physical discomforts such as pain, external heat or cold, excitement, anxiety and prolonged talking or laughing result in a low arterial $P_{CO_2}$.

## SYMPTOMS OF RESPIRATORY DISEASE

Most of the patients attending for investigation in the pulmonary function laboratory will be suffering from *shortness of breath,* usually on exertion. The principal mechanisms involved are:

(1) *Respiratory discomfort.* Often, because of narrowing of the airways or reduction in the size of the lungs, the normal pattern of breathing during exercise is disturbed and the patient feels the sensation of discomfort. The abnormality may be chronic or it may occur transiently as a result of exercise.
(2) *Increased ventilatory requirement.* Ventilation normally increases in proportion to the increased oxygen uptake required to perform any task. This may result in a disproportionate ventilatory requirement, if a large portion of the ventilation is wasted in under-perfused parts of the lung because of ventilation perfusion mismatching, *or* if there is oxygen lack or some other stimulus to hyper-ventilation which is made worse during exercise. These may readily be identified by measurements of ventilation, $P_{CO_2}$ and oxygen content or saturation during exercise (Chapter 13).

Other symptoms are of importance to physicians because they indicate the presence of bronchial or pulmonary disease. They include:

(1) *Coughing.* A cough is a paroxysm of repeated forced expirations with the vocal cords intermittently closed to produce a rapid expulsive movements of air. It is stimulated by irritation of the throat and trachea and its purpose is to expel inhaled foreign material or accumulated mucus. It is stimulated uselessly in a variety of inflammatory disorders where no foreign material is present.
(2) *Sputum production.* Sputum is excessive mucus, or pus, in the air passages. It is the result of inflammation of the airways and may occur because of infection, or irritation by cigarette smoke and other agents.
(3) *Haemoptysis or blood spitting.* This is often of no serious signi-

ficance but is important because it may be a manifestation of pulmonary tuberculosis, cancer of the lung, or other diseases. No patient with heavily infected or blood-stained sputum should have breathing tests until a chest X-ray has been taken which confirms that he is not suffering from pulmonary tuberculosis, because of the risk of infection to others.

(4) *Pain in the chest.* Pain rarely arises from the lungs but may be sensed in the heart, the digestive system, the blood vessels within the lungs, or the pleura and chest wall. It is very difficult to obtain useful measurements of pulmonary function in individuals who are suffering from chest pain at the time of the test. An electrocardiograph at the time of chest pain may be valuable to confirm or exclude a cardiac cause.

## SCOPE OF THIS BOOK

This volume is concerned with describing techniques for the measurement of the overall integrity and efficiency of the ventilatory, gas exchanging and control functions of the respiratory system, employing measurements of pressure, air flow and gas analysis.

The first half of the book describes the basic equipment required for the analysis of flow rate, volume and composition of respiratory gases, and for the measurement of the respiratory properties of blood. Subsequent chapters are devoted to the various assemblies of these basic components which are used to make measurements of pulmonary function in conscious human subjects.

This is a physiological cook-book. We have assembled a distinguished team of contributors, all of whom are actively concerned in making measurements and we have asked them to describe their techniques as one might to a qualified physicist, physiologist or technician who had not previously worked in a respiratory laboratory. The contributors have concentrated most attention on those aspects which are not well covered in standard texts, in which they have made major contributions or which require skill to produce good results.

No attempt will be made to describe the radionucleide investigation of the distribution of ventilation in perfusion or lung particle clearance. The metabolic functions of the lung and its role in defence against infection will not be discussed, nor have we included a section on the deposition and clearance of inhaled particles. Sections on the clinical interpretation of the tests that we have described would have been interesting, but their inclusion would make the book far too long and the reader is referred to the volumes listed at the end of this chapter. An elementary account is given by Hughes and Empey (1981). The indis-