
M.R. Pinsky · L. Brochard · J. Mancebo · G. Hedenstierna (Eds.)
Applied Physiology in Intensive Care Medicine

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G. Hedenstierna (Eds.)

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With 155 Figures and 27 Tables

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MICHAEL R. PINSKY, MD
University of Pittsburgh Medical Center
Dept. of Critical Care Medicine
Scaife Hall 616
3550 Terrace Street
Pittsburgh, PA 15261
USA

LAURENT BROCHARD, MD
Hôpital Henri Mondor
Dept. Intensive Care Medicine
51 av. Maréchal Lattre de Tassigny
94010 Créteil CX
France

JORDI MANCEBO, MD
Hospital de Sant Pau
Dept. Intensive Care Medicine
Avda. S. Antonio M. Claret, 167
08025 Barcelona
Spain

GÖRAN HEDENSTIERNA, MD
Uppsala University Hospital
Dept. Clinical Physiology
751 85 Uppsala
Sweden

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Introduction

The practice of intensive care medicine is at the very forefront of titration of treatment and monitoring response. The substrate of this care is the critically ill patient who, by definition, is at the limits of his or her physiologic reserve. Such patients need immediate, aggressive but balanced life-altering interventions to minimize the detrimental aspects of acute illness and hasten recovery. Treatment decisions and response to therapy are usually assessed by measures of physiologic function, such as assessed by cardio-respiratory monitoring. However, how one uses such information is often unclear and rarely supported by prospective clinical trials. In reality, the bedside clinician is forced to rely primarily on physiologic principles in determining the best treatments and response to therapy. However, the physiologic foundation present in practicing physicians is uneven and occasionally supported more by habit or prior training than science.

A series of short papers published in Intensive Care Medicine since 2002 under the heading Physiologic Notes attempts to capture the essence of the physiologic perspectives that underpin both our understanding of disease and response to therapy. This present volume combines the complete list of these Physiologic Notes up until February 2009 with the associated review articles over the same interval that also addressed these central issues. This volume was created to address this fundamental unevenness in our understanding of applied physiology and underscore what is known and how measures and monitoring interact with organ system function and response to therapy. This collection of physiologic perspectives and reviews, written by some of the most respected experts in the field, represent an up-to-date and invaluable compendium of practical bedside knowledge essential to the effective delivery of acute care medicine. Although this text can be read from cover to cover, the reader is encouraged to use this text as a reference source reading individual Physiologic Notes and Review articles as they pertain to specific clinical issues. In that way the relevant information will have immediate practical meaning and hopefully become incorporated into routine practice.

We hope that the reader finds these papers and reviews useful in their practice and enjoy reading them as much as we enjoyed editing the original articles that it comprises.

Michael R. Pinsky, MD
Laurent Brochard, MD
Jordi Mancebo, MD
Göran Hedenstierna, MD

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Contributors

Jérôme Aboab

Réanimation Médicale
Hôpital Henri Mondor
Créteil, France

Lars Algotsson

Department of Anaesthesiology–
Heart-Lung Division
University Hospital of Lund,
22185 Lund, Sweden

Peter J.D. Andrews

Department of Anaesthetics, Intensive
Care and Pain Medicine
University of Edinburgh, Western General Hospital
Crewe Road, EH4 2XU Edinburgh, Scotland, UK

Michel Aubier

INSERM U 700 and IFR 02, Facult Xavier Bichat
16 rue Henri Huchard, 75018 Paris, France

Elie Azoulay

Department of Clinical Immunology,
and Hôpital Saint-Louis, Medical ICU, AP–HP,
University Paris-7 Diderot, UFR de Médecine,
1 avenue Claude Vellefaux, 75010 Paris, France

Andreas Bacher

Department of Anesthesiology
and General Intensive Care
Medical University of Vienna, AKH
Währinger Gürtel 18–20, 1090 Vienna, Austria

Jan Bakker

Department of Intensive Care, Erasmus MC
University Medical Center Rotterdam
P.O. Box 2040, 3000 CA
Rotterdam, The Netherlands

Rinaldo Bellomo

Department of Intensive Care
and Division of Surgery
Austin & Repatriation Medical Centre
3084 Heidelberg, Melbourne, Victoria, Australia

Karim Bendjelid

Surgical Intensive Care Division,
Geneva University Hospitals
1211 Geneva 14, Switzerland

Anuj Bhatia

Department of Anaesthesia,
Addenbrooke's Hospital,
Hills Road, CB2 2QQ Cambridge, UK

Luis Blanch

Critical Care Center
Hospital de Sabadell
Parc Taulis/n, 08208 Sabadell, Spain

Frank Bloos

Klinik für Anästhesiologie und Intensivtherapie
Klinikum der Friedrich-Schiller-Universität
Erlanger Allee 101, 07747 Jena, Germany

Jorge Boczkowski

INSERM U 700 and IFR 02, Facult Xavier Bichat
16 rue Henri Huchard, 75018 Paris, France

Alain F. Broccard

Medical Intensive Care Unit,
Regions Hospital Pulmonary and Critical Care Division,
Regions Hospital, St Paul,
MN 55101-2595, USA

Laurent Brochard

Réanimation Médicale
Hôpital Henri Mondor,
Université Paris 12, INSERM
U651, 94010 Créteil, France

Sophie Buyse

Department of Clinical Immunology,
and Hôpital Saint-Louis, Medical ICU,
AP–HP, University Paris-7 Diderot, UFR de Médecine,
1 avenue Claude Vellefaux, 75010 Paris, France

Belen Cabello

Hospital Santa Creu i Sant Pau,
Servicio de Medicina Intensiva
Av/ Sant Antoni Maria Claret 167,
CP 08025 Barcelona, Spain

Enrico Calzia

Sektion Anästhesiologische Pathophysiologie
und Verfahrensentwicklung Universitätsklinik
für Anästhesiologie, Universität Ulm
Parkstrasse 11, 89070 Ulm, Germany

Giuseppe Citerio

Neuroranimazione, Dipartimento
di Anestesia e Rianimazione
Nuovo Ospedale San Gerardo
Via Donizetti 106, 20052 Monza, Italy

Caroline Créput

Department of Clinical Immunology,
and Hôpital Saint-Louis, Medical ICU, AP-HP,
University Paris-7 Diderot, UFR de Médecine,
1 avenue Claude Vellefaux, 75010 Paris, France

Jacques Creteur

Department of Intensive Care,
Erasme University Hospital, Free
University of Brussels
Route de Lennik 808, 1070 Brussels, Belgium

Daniel De Backer

Department of Intensive Care,
Erasme University Hospital
Free University of Brussels
Route de Lennik 808, 1070 Brussels, Belgium

Lisa L. Dever

UMDNJ-New Jersey Medical School,
VA New Jersey Health Care System
385 Tremont, East Orange, NJ 07018, USA

Ioanna Dimopoulou

Second Department of Critical Care Medicine,
Attikon Hospital, Medical School National
and Kapodistrian University of Athens
2 Pasmazoglou Street, 14561
Kifissia, Athens, Greece

Andrew Durward

Evelina Children's Hospital, Guy's and
Saint Thomas' NHS Trust,
Paediatric Intensive Care Unit,
SE1 7EH London, UK

Lennart Edmark

Department of Anesthesia and Intensive Care
Central Hospital
72335 Vasteras, Sweden

Jean-François Enrico

Former Chief of Intensive Care Unit
Hôpital des Cadolles,
Neuchâtel, Switzerland

Timothy W. Evans

Imperial College School of Medicine
Department of Intensive Care Medicine
Royal Brompton Hospital, London, UK

Konrad J. Falke

Klinik für Anaesthesiologie und
operative Intensivmedizin Berlin
Campus Virchow Klinikum, Charite,
Berlin, Germany

François Feihl

Division of Clinical Pathophysiology,
University Hospital (CHUV)
and Lausanne University (UNIL),
1011 Lausanne, Switzerland

Evans R. Fernández Pérez

Mayo Clinic College of Medicine
Rochester, MN 55905, USA

Lionel Galicier

Department of Clinical Immunology,
and Hôpital Saint-Louis, Medical ICU, AP-HP,
University Paris-7 Diderot, UFR de Médecine,
1 avenue Claude Vellefaux, 75010 Paris, France

Jean-Roger Le Gall

Department of Intensive Care Medicine
Saint-Louis University Hospital, Paris, France

Luciano Gattinoni

Istituto di Anestesia e Rianimazione
Fondazione IRCCS Ospedale Maggiore Policlinico
Mangiagalli, Regina Elena di
Milano, Università degli Studi
Via Francesco Sforza 35, 20122 Milan, Italy

Ian S. Grant

Department of Anaesthesia,
University of Edinburgh,
Western General Hospital, Edinburgh,
Scotland, UK

Claude Guerin

Hôpital de la Croix Rousse and Université de Lyon,
Service de Réanimation Médicale,
103 Grande Rue de la Croix Rousse,
69004 Lyon, France

Arun Kumar Gupta

Department of Anaesthesia,
Addenbrooke's Hospital, Hills Road,
CB2 2QQ Cambridge, UK
and
Neuroscience Critical Care Unit,
Addenbrooke's Hospital, Hills Road,
CB2 2QQ Cambridge, UK

Göran Hedenstierna

Clinical Physiology, Department of
Medical Sciences, University Hospital
75185 Uppsala, Sweden

Rolf D. Hubmayr

Mayo Clinic College of Medicine
Rochester, MN 55905, USA

François Jardin

Hôpital Ambroise Paré,
Service de Réanimation Médicale,
9 avenue Charles de Gaulle,
92104 Boulogne, France

Waldemar G. Johanson †

UMDNJ-New Jersey Medical School
185 South Orange, Newark, NJ 07018, USA

Björn Jonson

Department of Clinical Physiology
University Hospital of Lund
22185 Lund, Sweden

Amal Jubran

Division of Pulmonary and Critical Care Medicine
Edward Hines Jr. Veterans Affairs Hospital
Route 111 N, Hines, IL, 60141, USA

Peter Karpati

Department of Anaesthesiology
and Critical Care Medicine
Hopital Lariboisier, 2 Rue Ambroise Pare
75475 Paris Cedex 10, France

Brian P. Kavanagh

Department of Critical Care Medicine,
Hospital for Sick Children
555 University Avenue, Toronto,
ONT, M5G 1X8, Canada

John A. Kellum

Division of Critical Care Medicine, Scaife Hall
University of Pittsburgh Medical Centre,
Terrace Street, Pittsburgh, PA 15260, USA

Ioanna Korovesi

Department of Critical Care & Pulmonary
Medicine and "M. Simou" Laboratory
Medical School, University of
Athens, Evangelismos Hospital
45-47 Ipsilandou St., 10675 Athens, Greece

John G. Laffey

Department of Anaesthesia,
University College Hospital
Galway and Clinical Sciences Institute,
National University of Ireland, Galway, Ireland

Sophie Lanone

INSERM U 700 and IFR 02, Facult Xavier Bichat
16 rue Henri Huchard, 75018 Paris, France

Alexandre Lima

Department of Intensive Care, Erasmus MC
University Medical Center Rotterdam
P.O. Box 2040, 3000 CA
Rotterdam, The Netherlands

Bruno Louis

Inserm Unit 651
Department of Medicine Paris 12
Créteil, France

Umberto Lucangelo

Department of Perioperative Medicine,
Intensive Care and Emergency, Cattinara
Hospital, Trieste University School of Medicine
34139 Trieste, Italy

Jordi Mancebo

Hospital Santa Creu i Sant Pau,
Servicio de Medicina Intensiva
Av/ Sant Antoni Maria Claret 167,
CP 08025 Barcelona, Spain

Alexandre Toledo Maciel

Department of Intensive Care,
Erasmé University Hospital, Free
University of Brussels
Route de Lennik 808, 1070 Brussels, Belgium

Carol S. A. Macmillan

University of Dundee, Department of Anaesthesia
Ninewells Hospital, Dundee DD1 9SY, UK

Manu L. N. G. Malbrain

Medical Intensive Care Unit,
ACZA Campus Stuivenberg
Lange Beeldekenstraat 267, B-
2060 Antwerpen, Belgium

Paul E. Marik

Department of Critical Care Medicine
University of Pittsburgh Medical Center
640A Scaife Hall, 3550 Terrace
Street, Pittsburgh, PA, 15261, USA

George M. Matuschak

Division of Pulmonary, Critical Care
and Occupational Medicine
Departments of Internal Medicine and
Pharmacological and Physiological Science
School of Medicine
Saint Louis University, 3635 Vista Ave.,
Saint Louis, MO 63110-0250, USA

Irene Mavrommati

Department of Critical Care & Pulmonary
Medicine and "M. Simou" Laboratory
Medical School, University of
Athens, Evangelismos Hospital
45-47 Ipsilandou St., 10675 Athens, Greece

Paul McLoughlin

Department of Physiology,
University College Dublin
Dublin, Ireland

Alexandre Mebazaa

Department of Anaesthesiology
and Critical Care Medicine
Hopital Lariboisière, 2 Rue Ambroise Pare
75475 Paris Cedex 10, France

L. Joanne Meyer

Department of Medicine,
St. Joseph's Hospital
Toronto, Canada

Xavier Monnet

Hôpital de Bicêtre, AP-HP,
Service de réanimation médicale,
78 rue du Général Leclerc,
94270 Le Kremlin-Bicêtre, France
and
Université Paris-Sud, Equipe d'accueil EA 4046,
Faculté de Médecine Paris-Sud,
94270 Le Kremlin-Bicêtre, France

Robert Naeije

Department of Physiology,
Faculty of Medicine of the Free University
of Brussels, Erasme Campus
808 Route de Lennik, CP 604,
1070 Brussels, Belgium

Luis J. Noronha

Division of Pulmonary, Critical Care
and Occupational Medicine
Departments of Internal Medicine and
Pharmacological and Physiological Science
School of Medicine
Saint Louis University, 3635 Vista Ave.,
Saint Louis, MO 63110-0250, USA

Donall O'Croinin

Department of Physiology,
University College Dublin
Dublin, Ireland

Stylianos E. Orfanos

2nd Department of Critical Care,
University of Athens Medical
School, Attikon Hospital
1, Rimini St., 12462 Haidari (Athens), Greece

Sairam Parthasarathy

Division of Pulmonary and Critical
Care, Medicine Edward Hines Jr.
Veterans Administrative Hospital, Loyola
University of Chicago Stritch School of Medicine
Route 111 N, Hines, IL 60141, USA

Michael Piagnerelli

Department of Intensive Care,
Erasme University Hospital
Free University of Brussels
808 route de Lennik, 1070 Brussels, Belgium

Claude Perret

Former Chief of Intensive Care Department
University Hospital of Lausanne, Switzerland
Ruelle des Halles 4, CH-1095 Lutry, Switzerland

Antonio Pesenti

Dipartimento di Medicina
Perioperatoria e Terapia Intensiva
A.O. Ospedale S.Gerardo
Monza, Università degli Studi
Milan-Bicocca, Italy

Michael R. Pinsky

Department of Critical Care Medicine
University of Pittsburgh Medical Center,
604 Scaife, 3550 Terrace Street,
Pittsburgh, PA 15261, USA

Murugan Raghavan

Conemaugh Memorial Medical Center
Johnstown, Pennsylvania, USA

Peter Radermacher

Sektion Anästhesiologische Pathophysiologie
und Verfahrensentwicklung Universitätsklinik
für Anästhesiologie, Universität Ulm
Parkstrasse 11, 89070 Ulm, Germany

Konrad Reinhart

Klinik für Anästhesiologie und Intensivtherapie
Klinikum der Friedrich-Schiller-Universität
Erlanger Allee 101, 07747 Jena, Germany

Estelle Renaud

Department of Anaesthesiology
and Critical Care Medicine
Hopital Lariboisie`re, 2 Rue Ambroise Pare
75475 Paris Cedex 10, France

Jean-Christophe Richard

Hôpital de la Croix Rousse and Université de Lyon,
Service de Réanimation Médicale,
103 Grande Rue de la Croix Rousse,
69004 Lyon, France

Charis Roussos

Department of Critical Care & Pulmonary
Medicine and “M. Simou” Laboratory
Medical School, University of
Athens, Evangelismos Hospital
45–47 Ipsilandou St., 10675 Athens, Greece

Josep Roca

Servei de Pneumologia, Hospital Clínic
Institut d’Investigacions Biomèdiques
August Pi i Sunyer, Universitat de Barcelona
Villarroel 170, 08036 Barcelona, Spain

Robert Rodríguez-Roisin

Servei de Pneumologia, Hospital Clínic
Institut d’Investigacions Biomèdiques
August Pi i Sunyer, Universitat de Barcelona
Villarroel 170, 08036 Barcelona, Spain

Jacques-André Romand

Surgical Intensive Care Division,
Geneva University Hospitals
1211 Geneva 14, Switzerland

Claudio Ronco

Divisione di Nefrologia, Ospedale San Bortolo
Via Ridolfi, 36100 Vicenza, Italy

Frédérique Schortgen

Réanimation Médicale et Infectieuse
Hôpital Bichat-Claude Bernard
75018 Paris, France

Suveer Singh

Chelsea and Westminster Hospital
Department of Intensive Care Medicine
369 Fulham Road, SW10 9NH London, UK

Arthur S. Slutsky

Queen Wing, St. Michael’s Hospital
30 Bond St., Toronto, ONT, M5B 1W8, Canada

Pierre Squara

CERIC Clinique Ambroise Pare
27 Boulevard Victor Hugo, 92200
Neuilly-sur-Seine, France

Camille Taillé

INSERM U 700 and IFR 02, Facult Xavier Bichat
16 rue Henri Huchard, 75018 Paris, France

Jukka Takala

Department of Intensive Care Medicine,
University Hospital Bern (Inselspital),
University of Bern, 3010 Bern, Switzerland

Jean-Louis Teboul

Hôpital de Bicêtre, AP-HP,
Service de réanimation médicale,
78 rue du Général Leclerc,
94270 Le Kremlin-Bicêtre, France
and
Université Paris-Sud, Equipe d’accueil EA 4046,
Faculté de Médecine Paris-Sud,
94270 Le Kremlin-Bicêtre, France

Shane M. Tibby

Paediatric Intensive Care Unit,
Evelina Children’s Hospital,
Guy’s and Saint Thomas’ NHS Trust,
SE1 7EH London, UK

Martin J. Tobin

Division of Pulmonary and Critical Care Medicine
Edward Hines Jr. VA Hospital, 111N
5th Avenue and Roosevelt Road
Hines, Illinois 60141, USA

Lorraine N. Tremblay

Department of Surgery
Sunnybrook and Women's Health Sciences Center
Toronto, Ont., Canada

Stylios Tsagarakis

Department of Endocrinology, Athens Polyclinic
Athens, Greece

Michel Vanhaeverbeek

Experimental Medicine Laboratory,
André Vésale Hospital
Montigny-le-Tilleul, Belgium

Theodoros Vassilakopoulos

Department of Critical Care and Pulmonary Services,
University of Athens Medical School,
Evangelismos Hospital,
45–47 Ipsilandou Street, 10675 Athens, Greece

and

Critical Care Department,
Evangelismos Hospital,
45–47 Ipsilandou Strasse, 10675 Athens, Greece

Antoine Vieillard-Baron

University Hospital Ambroise Paré,
Assistance Publique Hôpitaux de Paris
Medical Intensive Care Unit
9 avenue Charles de Gaulle, 92104
Boulogne Cedex, France

Jean-Louis Vincent

Department of Intensive Care,
Erasmus University Hospital
Free University of Brussels
Route de Lennik 808, 1070 Brussels, Belgium

Peter D. Wagner

Department of Medicine, Division of Physiology,
University of California, San Diego, 9500 Gilman Drive,
Dept. 0623A, La Jolla CA 92093-0623A, USA

Karim Zouaoui-Boudjeltia

Experimental Medicine Laboratory,
André Vésale Hospital
Montigny-le-Tilleul, Belgium

1.1. Pulmonary

1.1.1 Respiratory Mechanics

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Intrinsic (or auto-) PEEP during controlled mechanical ventilation

Introduction

Extrinsic positive end-expiratory pressure (PEEP) applied to the patient at the airway opening is used artificially to increase end-expiratory lung volume. Extrinsic PEEP is increased or decreased in small increments in ventilator-dependent patients because of its marked effects on cardiorespiratory status. Unintentional or unmeasured end-expiratory hyperinflation, called intrinsic or auto-PEEP, can also occur and have similarly marked profound cardiorespiratory effects in ventilator-dependent patients during controlled mechanical ventilation. Ventilatory settings can interact with the passive process of expiration and generate intrinsic or auto-PEEP [1, 2].

What is intrinsic (or auto-) PEEP?

During passive expiration of the lungs the elastic forces of the respiratory system are the driving forces and can be described by the relationship between lung volume and the elastic recoil pressure of the respiratory system. The lower the elastic forces, or the higher the resistive forces, the longer will be the time needed to fully expire the inspired tidal volume. In a single-compartment model of the lung in which the lung behaves as if it has a single resistance and compliance, the volume at any given time during expiration (V) is described by the monoexponential equation, $V=V_o-Ve^{-kt}$, where k is the time constant of the equation and is the product of resis-

tance times compliance (the reverse of elastance), and V_o is the end-inspiratory volume. In practical terms a time constant is the time required for the lungs to expire 63% of their initial volume. Thus the time needed passively to expire the inspired tidal volume is determined by the two main characteristics of the respiratory system: elastance and resistance. If expiration is interrupted before its natural end, i.e., by occurrence of the next inspiration, end-expiratory lung volume is higher than the so-called relaxation volume of the respiratory system, usually referred to as functional residual capacity. As a result the alveolar pressure at the end of expiration is higher than zero (zero being the atmospheric pressure), as predicted by the relationship between lung volume and the elastic recoil pressure of the respiratory system. This process is called dynamic hyperinflation, and the positive end-expiratory alveolar pressure associated with a higher than resting lung volume, is called intrinsic or auto-PEEP. Importantly for the clinician, this pressure is not directly measured at the airway opening and is thus not shown on the pressure dial of the ventilator. What the ventilator measures is the pressure in the ventilator circuit. Because the direction of the flow is still expiratory, the pressure measured by the ventilator at the end of expiration reflects only the relationship between flow and the resistance of the expiratory line, above the set PEEP. It does not give the clinician any information about the real alveolar pressure.

How one can suspect the presence of intrinsic (or auto-) PEEP

The presence of a positive alveolar pressure higher than the atmospheric pressure or higher than the external PEEP set on the ventilator (which is a new “reference pressure” for the lungs) can be identified by inspection of the expiratory flow-time curve. When the expiratory time is sufficient for lung emptying, expiratory flow de-

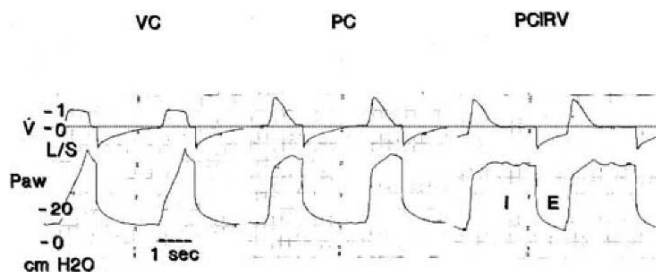


Fig. 1 Tracings of flow (\dot{V}) and airway pressure (P_{aw}) at the airway opening during volume controlled (VC), pressure-controlled (PC), and pressure-controlled inverse ratio ventilation (PCIRV). In the first two situations the expiratory flow declines gradually to zero; in the third case inspiration is lengthened by the inverse ratio setting and expiration shortened; the expiratory flow is abruptly interrupted, indicating the presence of dynamic hyperinflation and intrinsic or auto-PEEP. (From Lessard et al. [3])

clines from a maximum to zero or to the set PEEP. An interruption in this process results in an abrupt change in the slope of this curve, immediately continued by the next inspiratory flow. In other words, the next “inspiration” starts during “expiration.” Since the ventilator, which cannot generate flow into the patient’s lungs until the pressure at the airway opening exceeds the end-expiratory alveolar pressure, one way in which to measure intrinsic or auto-PEEP is to determine the airway pressure at the exact time of inspiratory flow. One can measure the intrinsic PEEP level by simultaneously recording airway pressure and flow data using a high-speed tracing. Figure 1 illustrates how shortening the expiratory phase generates such dynamic hyperinflation [3].

Is the level of intrinsic (or auto-) PEEP predictable?

If one assumes the respiratory system to be homogeneous and behave as a single compartment, a monoexponential equation can be used. By simple mathematics it takes three time constants (one being the product of resistance and compliance) to expire 96% of the inspired tidal volume. Therefore any longer expiratory time minimizes or fully avoids incomplete emptying. For instance, a resistance of $10 \text{ cmH}_2\text{O}\cdot\text{l}^{-1}\cdot\text{s}^{-1}$ and a compliance of $100 \text{ ml}\cdot\text{cmH}_2\text{O}^{-1}$ ($0.1 \text{ l}\cdot\text{cm H}_2\text{O}^{-1}$) results in a time constant of 1 s. Thus 3 s represents the minimal expiratory time needed to avoid intrinsic or auto-PEEP. Unfortunately, the diseased lungs are not only frequently inhomogeneous, making this calculation overly simplistic, but the presence of small airway collapse during expiration, also referred to as expiratory flow limitation, makes this even more complicated. Because of an abnormal structure of the small airways, when the pressure surrounding these conducts becomes higher than the pressure inside the airway, these small conducts collapse. The relationship between the “driving pressure” (pres-

sure in the alveoli minus pressure at the airway opening) on which is based the equation, disappears. In the setting of expiratory flow-limitation, the expiratory time required to minimize intrinsic PEEP is much longer than predicted by the time constant alone. By minimizing inspired minute ventilation the clinician can minimize intrinsic (auto-) PEEP.

Can intrinsic (or auto-) PEEP be reliably measured?

Since the reason for the presence of intrinsic PEEP is flow-dependent pressure gradients from the alveolus to the airway opening, occluding of the expiratory port of the ventilator at the exact end of expiration causes airway pressure to equilibrate rapidly with alveolar pressure and reliably measure the end-expiratory alveolar pressure. This occlusion takes place at the exact time where the next inspiration should start and is now available on most modern ventilators (“expiratory hold or pause”). If the patient is fully relaxed, this pressure measurement reflects the mean alveolar pressure at the end of expiration. Most of the time a plateau is reached after less than 1 s, but in the case of inhomogeneous lungs this pressure may require a few seconds to also reflect some very slow compartments. This airway occlusion pressure may not be homogeneously present in the whole lung but represents an average pressure of all regional levels of end-expiration alveolar pressure. Usually the difference between the expiratory pause airway pressure and the set external PEEP is called intrinsic or auto-PEEP, while the measured pressure is referred to as total PEEP.

Can the set external PEEP influence the total PEEP in the case of dynamic hyperinflation?

A frequent confusion is the belief that external PEEP could be useful in reducing the level of dynamic hyperinflation because it helps to reduce the value of auto- or intrinsic PEEP. Obviously this is not the case. The effect of external PEEP is to minimize the difference between the alveolar and the ventilator proximal airway pressure. This difference being called intrinsic or auto-PEEP, external PEEP application results in a decreased intrinsic or auto-PEEP. The level of dynamic hyperinflation, however, depends on the level of total PEEP and is either not influenced by external PEEP when external PEEP is less than intrinsic PEEP or is even worsened if external PEEP is set higher than the minimal level of regional intrinsic PEEP.

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Intrinsic (or auto-) positive end-expiratory pressure during spontaneous or assisted ventilation

Introduction

The mechanisms generating intrinsic or auto-positive end-expiratory pressure (PEEP) during controlled mechanical ventilation in a relaxed patient also occur during spontaneous breathing or when the patient triggers the ventilator during an assisted mode [1, 2]. These include an increased time constant for passive exhalation of the respiratory system, a short expiratory time resulting from a relatively high respiratory rate and/or the presence of expiratory flow limitation. Whereas dynamic hyperinflation and intrinsic or auto-PEEP may have haemodynamic consequences, this is not frequently a major concern in spontaneously breathing patients or during assisted ventilation because the spontaneous inspiratory efforts result in a less positive or more negative mean intrathoracic pressure than during controlled mechanical ventilation. The main consequence of dynamic hyperinflation during spontaneous and assisted ventilation is the patient's increased effort to breathe and work of breathing [1, 2].

To what extent does intrinsic (or auto-) positive end-expiratory pressure influence work of breathing?

For air to enter the lungs, the pressure inside the chest has to be lower than the pressure at the mouth (spontaneous breathing) or at the airway opening (assisted ventilation). In the case of intrinsic (or auto-) PEEP, by definition, the end-expiratory alveolar pressure is higher than the pressure at the airway opening. When the patient initiates the breath, there is an inevitable need to reduce airway pressure to zero (spontaneous breathing) or to the value of end-expiratory pressure set on the ventilator (assisted ventilation) before any gas can flow into the lungs. For this reason, intrinsic or (auto-) PEEP has been described as an inspiratory threshold load. In patients with chronic obstructive pulmonary disease (COPD) this load has sometimes been measured to be the major cause of increased work of breathing [3].

During assisted ventilation, is the trigger sensitivity important to reduce intrinsic (or auto-) positive end-expiratory pressure?

Because the problem of intrinsic or (auto-) PEEP has to do with the onset of inspiration, one may reason that increasing the inspiratory trigger sensitivity to initiate a breath with a lower pressure or flow deflection should reduce the work of breathing induced by hyperinflation. These systems are based on the detection of a small pressure drop relative to baseline (pressure-triggering system) or on the presence of a small inspiratory flow (flow-triggering systems). Unfortunately, increasing the trigger sensitivity induces only a small reduction in the total work of breathing. The reason for this lack of effect relates to the need for the inspiratory trigger to sense changes in airway pressure or in inspiratory flow. Thus, intrinsic PEEP needs to be counterbalanced first by the

effort of the inspiratory muscles, in order for this effort to generate a small pressure drop (in the presence of a closed circuit) or to initiate the inspiratory flow (in an open circuit) [4]. The consequence of intrinsic or (auto-) PEEP is that the inspiratory effort starts during expiration. This is easily identified by inspection of the expiratory flow-time curve [1]. As a consequence, it cannot be detected by any of the commercially available trigger systems.

Can the set external positive end-expiratory pressure reduce dynamic hyperinflation and work of breathing?

Responses to these two questions are the same as during controlled mechanical ventilation in a relaxed patient [1]. Their consequences are, however, very different. External PEEP reduces the difference between the alveolar and the ventilator proximal airway pressure, i.e., intrinsic (or auto-) PEEP. The inspiratory threshold load resulting from intrinsic (or auto-) PEEP is thus reduced by addition of external PEEP. Thus, the total work of breathing is reduced, especially in patients with high levels of intrinsic (or auto-) PEEP, such as those subjects with COPD [5, 6].

Although external PEEP reduces work of breathing, it does not minimise hyperinflation. The level of dynamic hyperinflation is not modified by external PEEP, unless this PEEP is set higher than the minimal level of regional intrinsic PEEP, and then hyperinflation increases. Increasing hyperinflation can aggravate the working conditions of the respiratory muscles by placing them at a mechanical disadvantage and can result in significant haemodynamic compromise by decreasing venous return and increasing right ventricular outflow resistance. Hyperinflation in excess of intrinsic (or auto-) PEEP occurs usually when the set PEEP is positioned at values above 80% of the mean "static" intrinsic PEEP [7]. For this reason, titration of external PEEP based on measuring intrinsic (or auto-) PEEP would be desirable. Unfortunately, a reliable measurement of intrinsic (or auto-) PEEP in the spontaneously breathing subject is much more difficult to obtain than in passive positive-pressure ventilation conditions.

Can standard ventilatory settings influence intrinsic (or auto-) positive end-expiratory pressure?

During assisted ventilation, the patient is supposed to determine the respiratory rate freely, and one may suppose that he/she will govern his/her respiratory rate to control expiratory time and minimise hyperinflation. Unfortunately, most patients will not be able to counteract fully the effects of a ventilator inspiratory time longer than

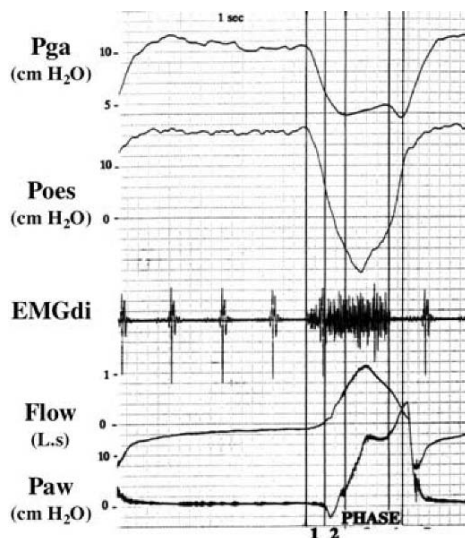


Fig. 1 Tracings of gastric (P_{ga}), oesophageal (P_{oes}) and airway (P_{aw}) pressures, flow and diaphragmatic electromyographic activity (EMG_{di}) during an assisted breath (pressure-support ventilation). The vertical lines help to delineate the different phases of the inspiratory effort. During phase 1, the flow is still expiratory: the start of EMG_{di} and the abrupt decrease in both P_{es} and P_{ga} all indicate that the patient performs an active inspiratory effort against intrinsic positive end-expiratory pressure (PEEP) at the same time that his/her expiratory muscles relax. Phase 2 is the triggering of the ventilator and occurs once intrinsic (or auto-) PEEP has been counterbalanced

their own inspiratory time [8]. Although some compensatory mechanism may exist, it will frequently be insufficient. Every setting influencing the ventilator inspiratory time may thus influence the level of dynamic hyperinflation.

Is intrinsic (or auto-) positive end-expiratory pressure always synonymous with dynamic hyperinflation?

In patients with spontaneous respiratory activity, recruitment of the expiratory muscles frequently participates in generating intrinsic (or auto-) PEEP independently of dynamic hyperinflation. In the case of airflow obstruction, the main consequence of an activation of the expiratory muscles is to augment intrathoracic pressure, whereas their effects on expiratory flow may be very modest, especially in the case of airflow limitation, thus promoting small airways to collapse. The activation of the expiratory muscles results from an increase in respiratory drive. Many patients with COPD already have a recruitment of their expiratory muscles at rest. This expiratory muscle recruitment results in a measurable increase in alveolar pressure. However, such expiratory muscle recruitment, although creating an intrinsic (or au-

to-) PEEP, does not contribute to the inspiratory threshold load and the increased work of breathing. Indeed, at the same time that the inspiratory muscles start to decrease intrathoracic pressure, the expiratory muscles relax and their release almost immediately abolishes this part of intrinsic (or auto-) PEEP due to the expiratory muscles [9]. This is illustrated in Fig. 1.

Can intrinsic (or auto-) positive end-expiratory pressure be reliably measured?

The commonly applied end-expiratory airway occlusion method that measures intrinsic (or auto-) PEEP in patients on controlled ventilation cannot be readily applied to the patient making spontaneous inspiratory efforts. For example, it is not possible to determine which amount of measured positive airway occlusion pressure, if not all, is due to expiratory muscle activity [9]. Setting the external PEEP based on this measurement could induce considerable mistakes by overestimating intrinsic (or auto-) PEEP. The only readily available and reliable method of measuring intrinsic (or auto-) PEEP in the spontaneously breathing subject is to measure the drop in oesophageal pressure occurring before flow becomes inspiratory, and sub-

sequently subtract the part due to expiratory muscle activity determined from an abdominal pressure signal [9]. The reasoning is as follows: any rise in abdominal pressure occurring during expiration is transmitted to the intrathoracic space and increases alveolar pressure.

Intrinsic PEEP is measured from the abrupt drop observed on the oesophageal pressure signal until flow becomes inspiratory (phase 1 on Fig. 1). Part of this drop in oesophageal pressure is caused by the relaxation of the expiratory muscles. This part needs to be subtracted from the oesophageal pressure drop, in order to evaluate a "corrected" intrinsic PEEP due to hyperinflation. Two main possibilities exist: to subtract the rise in gastric pressure that occurred during the preceding expiration [9] or to subtract the concomitant decrease in gastric pressure at the onset of the effort [10]. Because the correction of intrinsic (or auto-) PEEP for expiratory muscle activity has not been used in early studies, one can hypothesise that the magnitude of intrinsic (or auto-) PEEP has often been overestimated. This combined oesophageal and gastric pressure measuring technique requires the insertion of a nasogastric tube equipped with both oesophageal and gastric balloon catheters. This technique is often used for research purposes but cannot be easily used at the bedside for routine clinical monitoring.

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Introduction

The main goal of mechanical ventilation is to help restore gas exchange and reduce the work of breathing (WOB) by assisting respiratory muscle activity. Knowing the determinants of WOB is essential for the effective use of mechanical ventilation and also to assess patient readiness for weaning. The active contraction of the respiratory muscles causes the thoracic compartment to expand, inducing pleural pressure to decrease. This negative pressure generated by the respiratory pump normally produces lung expansion and a decrease in alveolar pressure, causing air to flow into the lung. This driving pressure can be generated in three ways: entirely by the ventilator, as positive airway pressure during passive inflation and controlled mechanical ventilation; entirely by the patient's respiratory muscles during spontaneous unassisted breathing; or as a combination of the two, as in assisted mechanical ventilation. For positive-pressure ventilation to reduce WOB, there needs to be synchronous and smooth interaction between the ventilator and the respiratory muscles [1, 2, 3]. This note will concentrate on how to calculate the part of WOB generated by the patient's respiratory muscles, especially during assisted ventilation.

Esophageal pressure and the Campbell diagram

Measuring WOB is a useful approach to calculate the total expenditure of energy developed by the respiratory

muscles [4]. In general, the work performed during each respiratory cycle is mathematically expressed as $WOB = \int \text{Pressure} \times \text{Volume}$, i.e. the area on a pressure–volume diagram. Esophageal pressure, which is easily measured, is usually taken as a surrogate for intrathoracic (pleural) pressure. The dynamic relation between pleural pressure and lung volume during breathing is referred to as the Campbell diagram [5] (Fig. 1). Esophageal pressure swings during inspiration are needed to overcome two forces: the elastic forces of the lung parenchyma and chest wall, and the resistive forces generated by the movement of gas through the airways. One can calculate these two components (elastic and resistive) by comparing the difference between esophageal pressure during the patient's effort during the breath and the pressure value in passive conditions, represented by the static volume–pressure curve of the relaxed chest wall. This passive volume–pressure curve is a crucial component of the Campbell diagram. It is calculated from the values of esophageal pressure obtained over lung volume when the airways are closed and the muscles are completely relaxed. Unfortunately, as this is difficult to do (because it requires passive inflation and often muscle paralysis), a theoretical value for the slope of this curve is frequently used. However, if a patient is passively ventilated and an esophageal balloon is placed, a true value for the volume–pressure relationship of the chest wall during passive tidal breathing can be obtained [6]. This passive pressure–volume relationship can be used as a reference value for subsequent calculations when the patient develops spontaneous inspiratory efforts.

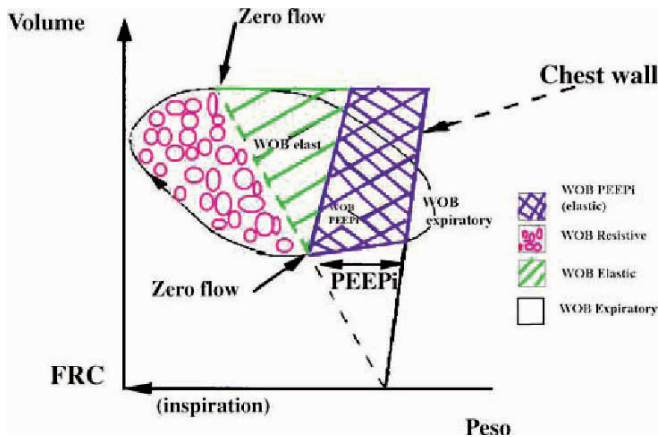


Fig. 1 Campbell's diagram. Work of breathing measured by the esophageal pressure: resistive WOB (W_{resist}), elastic WOB (W_{elast}), WOB related to active expiration ($WOB_{expiratory}$) and WOB related to intrinsic PEEP (W_{PEEPi}). *Chest wall*: this thick line (the chest wall compliance) represents the pleural (esophageal) pressure obtained when muscles are totally relaxed and lung volume increases above functional residual capacity, measured in static conditions

The WOB is normally expressed in joules. One joule is the energy needed to move 1 l of gas through a 10-cmH₂O pressure gradient. The work per liter of ventilation (J/l) is the work per cycle divided by the tidal volume (expressed in liters). In a healthy subject the normal value is around 0.35 J/l [7]. Lastly, WOB can be expressed in work per unit of time, multiplying joules per cycle by the respiratory rate (expressed in breaths per minute) to obtain the power of breathing (joules/minute). In a healthy subject the normal value is around 2.4 J/min [7]. As illustrated by the Campbell diagram, two other phenomena affect the WOB: intrinsic PEEP (positive end-expiratory pressure, or PEEP_i) and active expiration.

PEEP_i and active expiration

The distending pressure of the lungs is called the transpulmonary pressure and it can be estimated as the difference between airway and esophageal (pleural) pressure. At the end of a normal expiration, alveolar and airway pressures are zero relative to atmosphere, and esophageal pressure is negative, reflecting the resting transpulmonary pressure (around 5 cmH₂O in normal conditions). However, in the presence of PEEP_i, the alveolar pressure remains positive throughout expiration, because of either dynamic airway collapse or inadequate time to exhale [8]. This implies that some degree of dynamic hyperinflation does exist (lung volume at end-expiration is higher than passive functional residual capacity). Importantly, for lung volume to further increase in a patient with PEEP_i, the inspiratory muscles contract to an amount equal to PEEP_i before any volume is displaced.

PEEP_i can be quite high in patients with chronic obstructive pulmonary disease (COPD) and may represent a high proportion of the total WOB [9]. For example, a patient who displaces 0.5 l of tidal volume through a 7-cmH₂O pressure gradient will perform an amount of work of 0.35 J/cycle. If nothing else changes except that this patient develops 5 cmH₂O of PEEP_i, 0.25 J will be required to counterbalance this, meaning that the total WOB will be 0.60 J (0.35 + 0.25), which represents around 40% of the total work required for the inspiration. The PEEP_i value is measured as the drop in esophageal pressure occurring during expiration when the inspiratory muscles start contraction, until the flow reaches the point of zero (see Fig. 1).

In the case of ineffective respiratory efforts, that is, muscle contraction without volume displacement, WOB cannot be measured from the Campbell diagram, since this calculation is based on volume displacement. In this situation, measurement of the pressure–time product (PTP) may more accurately reflect the energy expenditure of these muscles. The PTP is the product of the pressure developed by the respiratory muscles multiplied by the time of muscle contraction, expressed in cmH₂O per second. The relevant pressure is again the difference between the measured esophageal pressure and the static relaxation curve of the chest wall.

Expiration normally occurs passively. However, the co-existence of PEEP_i and active expiration is common, especially in COPD patients [10]. Positive expiratory swings in gastric pressure are observed during active expiration as a consequence of abdominal muscle recruitment. When the patient starts contracting the inspiratory muscles, the expiratory muscles also start to relax. The drop in esophageal pressure used to estimate PEEP_i is therefore also due to the relaxation of the expiratory muscles. To avoid overestimating the value of PEEP_i, the abdominal pressure swing resulting from the active expiration must thus be subtracted from the initial drop in esophageal pressure [10].

Technical aspects of WOB calculation

Two other calculations can be obtained from pressure and volume measurements: airway pressure WOB and transpulmonary pressure WOB. The airway pressure WOB displays the energy dissipated by the ventilator to inflate the respiratory system. The transpulmonary pressure WOB shows the energy needed to inflate the lung parenchyma and reflects the mechanical characteristics of the pulmonary tissue. The limitation of these two measurements is that the amount of WOB performed by the patient's respiratory muscles is ignored.

The main tools used to measure the WOB are a double-lumen polyethylene gastro-esophageal catheter–balloon system and a pneumotachygraph. The catheter has an esophageal and a gastric balloon, usually filled with

0.5 and 1 ml of air to measure the esophageal and gastric pressures, respectively. Correct positioning of the esophageal balloon is assessed by an occlusion test: when the airways are closed at the end of expiration and an active inspiration occurs, a drop in esophageal pressure occurs. In this scenario, there are no changes in lung volume and the decrease in esophageal pressure equals the decrease in airway pressure (because in the absence of volume displacement, the transpulmonary pressure has to be nil) [11]. The catheter–balloon system should be placed to obtain a ratio between airway pressure and esophageal pressure changes as close as possible to 1. Also, the correct positioning of the gastric balloon needs to be checked [12].

Limitations

The calculation of WOB has several limitations. The first is that it requires insertion of a double-balloon gastro-esophageal catheter system. The second is the validity of the esophageal pressure value. Since pleural pressure is influenced by gravity, it can be modified by the weight of the thoracic content and by the posture. In the supine position, end-expiratory esophageal pressure is usually positive because of the weight of the heart and mediastinum on the esophagus. However, the amplitude of the changes in esophageal pressure is not usually affected. The third limitation is that the theoretical value for chest wall compliance is often used rather than a true measured

value. Furthermore, chest wall deformation can occur if levels of ventilation are high [13]. Lastly, it is difficult to determine what the optimal WOB level should be for each patient on clinical grounds.

Conclusion

From the standpoint of clinical research, the measurement of WOB is extremely useful in the field of mechanical ventilation, having contributed to important progress in the management of patients for optimizing and understanding the effects of ventilator settings such as trigger, external PEEP, peak inspiratory flow, etc. WOB has also been used to evaluate the physiological effects of a number of agents such as helium and bronchodilators [9, 14, 15, 16, 17, 18, 19]. Studies on WOB have given us greater insight into the pathophysiology of weaning failure [3] and have also contributed to the progress made in the field of non-invasive mechanical ventilation [20, 21]. Bedside measurements of WOB in clinical practice, however, should be reserved for individuals in whom assessment of this parameter can provide further insight into the patient ability to breath and the patient–ventilator interactions.

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Abstract Most mechanical ventilators display tracings of airway pressure (P_{aw}) volume (V) and flow (\dot{V}). In volume preset modes, P_{aw} informs about the mechanical properties of the respiratory system and about the activity of respiratory muscles acting on the system. When monitoring ventilator waveforms, it

is important to appropriately scale the tracing so that nuances in time profiles may be appreciated. In this short monograph, we offer three examples of how clinicians may use this information for patient assessment and care.

The P_{aw} waveform

The interactions between a ventilator and a relaxed intubated patient can be modeled as a piston connected to a tube (flow-resistive element) and balloon (elastic element). Accordingly, at any instant in time (t), the pressure at the tube inlet reflects the sum of a resistive pressure (P_{res}) and an elastic pressure (P_{el}) [1]. P_{res} is determined by the product of tube resistance with \dot{V} , while P_{el} is determined by the product of balloon elastance (a measure of balloon stiffness) with volume [1]. In this model, the resistive element reflects the properties of the intubated airways, while the elastic element reflects those of lungs and chest wall. When applied to volume preset ventilation with constant inspiratory \dot{V} and a short post-inflation pause, the resulting P_{aw} tracing has three distinct components: (1) an initial step change proportional to P_{res} ; (2) a ramp that reflects the increase in P_{el} as the lungs fill to their end-inflation volume; and (3) a sudden decay from a pressure maximum (P_{peak}) to a plateau (P_{plat}) that reflects the elastic recoil (P_{el}) of the relaxed respiratory system at the volume at end-inflation. Since in this example flow is held constant throughout inflation,

P_{res} must remain constant unless flow resistance changes volume and time. Consequently, the initial step change in P_{aw} and its decay from P_{peak} to P_{plat} are of similar magnitude. Fig. 1a demonstrates these features. Since, in pneumatic systems, there are invariable delays in the pressure and flow transients, in practice the step changes in pressure are never as sudden as they are depicted in Fig. 1a [2]. Nevertheless, the amplitude of transients can be easily estimated by extrapolating the tracing relative to the slope of the pressure ramp. Finally, while the principles that govern the interactions between pressure, volume and flow apply to all modes of mechanical ventilation, the specific pressure waveforms depicted in Fig. 1 refer only to constant flow inflation (square wave) and look very different when other flow profiles (e.g., decelerating, sine wave) are used. Our use of square wave profiles in Fig. 1 should not be interpreted as an endorsement of a specific mode, but rather as the most convenient means to present this information.

The tracing in Fig. 1b differs in several important respects: the P_{aw} ramp is steeper and it is nonlinear with respect to time. Since \dot{V} is constant the nonlinearity between P_{aw} and t means that the relationship between P_{aw} and V

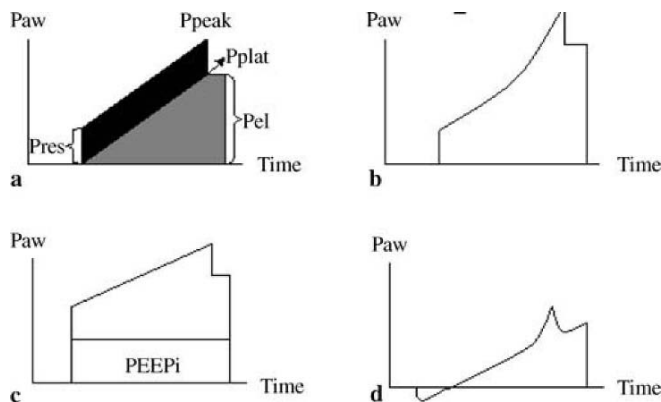


Fig. 1 Schematic illustration of the P_{aw} profile with time during constant-flow, volume-cycle ventilation. **a** Passive respiratory system with normal elastance and resistance. Work to overcome the resistive forces is represented by the *black shaded area*, and the *gray shaded area* represents the work to overcome the elastic forces. **b** Up-sloping of the P_{aw} tracing representing increased respiratory system elastance. **c** P_{aw} tracing in the presence of inadvertent PEEP. **d** scalloping of the P_{aw} tracing generated by a large patient effort (P_{aw} airway pressure, P_{el} elastic pressure, P_{peak} pressure maximum, P_{plat} pressure plateau, $PEEP_i$ inadvertent PEEP, P_{res} resistive pressure)

must be nonlinear as well. Assuming identical ventilator settings as in Fig. 1a the increased steepness of the ramp and its convexity to the time axis indicates a stiffening of the respiratory system with volume and time and suggests that the lungs may be overinflated to volumes near or ex-

ceeding their capacity. At the bedside, such an observation should raise concern for injurious ventilator settings [2].

The tracing in Fig. 1c is characterized by a larger-than-expected initial step change in P_{aw} that exceeds the peak-to-plateau pressure difference. In an otherwise relaxed patient, such an observation should raise suspicion for dynamic hyperinflation and inadvertent PEEP ($PEEP_i$). If P_{el} at end-expiration is greater than P_{aw} at that time (i.e., $PEEP_i$ is present), then gas will flow in the expiratory direction. The step change in P_{aw} during the subsequent inflation will therefore not only reflect P_{res} but also $PEEP_i$ that must be overcome to reverse flow at the tube entrance [1]. Tracings like the one in Fig. 1c should therefore alert the clinician to the presence of dynamic hyperinflation and provide an estimate of the extrinsic PEEP necessary to minimize the associated work of breathing. $PEEP_i$ is invariably associated with a sudden transient in expiratory flow prior to ventilator-assisted lung inflation [3]. However, this flow transient need not be associated with dynamic hyperinflation, because it is also seen in patients with increased respiratory effort and active expiration.

The tracing in Fig. 1d represents a significant departure from relaxation patterns. There is no initial step change in P_{aw} ; the ramp is nonlinear, and the end-inspiratory pressure plateau is lower than expected. This tracing suggests that the inspiratory muscles are active throughout machine inflation and that their work represents a considerable fraction of the work performed on the respiratory system. This pattern should alert clinicians to the presence of a potentially fatiguing load.

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Measurement of respiratory system resistance during mechanical ventilation

Abstract *Background:* The measurement of respiratory system resistance during mechanical ventilation is important to ascertain the causes of increase in airway pressure during volume-controlled ventilation, which may include airways resistance and decreased respiratory system compliance. *Discussion:* Separation of total resistance from compliance of the respiratory system can be assessed by the end-inspiratory hold maneuver that separates peak pressure from plateau pressure.

Conclusions: Although this method assumes a homogeneous respiratory system, it has proven useful clinically to separate flow-dependence issues such as bronchospasm or endotracheal tube obstruction from stiff lungs (acute lung injury) or decrease chest wall (abdominal distension) compliance.

Keywords Airway pressure · Mechanical ventilation · Respiratory system compliance · Respiratory system resistance

Introduction

Change in the resistance of the respiratory system to gas flow (R_{rs}) commonly occurs in critically ill patients and is manifest in mechanically ventilated patients on volume-controlled ventilation as an increase in airway pressure (P_{aw}). Increases in P_{aw} commonly occur with many processes and can profoundly alter gas exchange and cardiovascular function. Inspiratory gas flowing from the ventilator must overcome two primary components of R_{rs} before it can distend the alveoli. These include airway resistive forces needed to cause airflow associated with the endotracheal tube (ETT) and airways and elastic forces needed to distend the tissues associated with baseline positive end-expiratory pressure (PEEP_t) and tidal volume (V) as they interact with the combined lung and chest wall tissue elastance. In patients receiving noninvasive mechanical ventilation the upper airways are an important, but difficult to assess [1] contributing factor to R_{rs} . At any given time t during mechanical inflation P_{aw} can

be described by the equation of motion that reflects the sum of resistive (P_{res}) and elastic (P_{el}) forces at that moment:

$$\begin{aligned} P_{aw}(t) &= PEEP_t + P_{res}(t) + P_{el}(t) \\ &= PEEP_t + V'(t) \times R + V(t) \times E \end{aligned} \quad (1)$$

where V' is inflation flow, R and E resistance and elastance of the respiratory system. Although Eq. 1 depicts the behavior of the respiratory system as a single-compartment model (Fig. 1a), this approach tends to describe respiratory function under most conditions. However, the model described in Eq. 1 also assumes both R and E are constant as V and V' change, which is incorrect. For example, airway resistance (R_{aw}) decreases with increasing V [2]. More refined models have therefore been described (Fig. 1b) [3, 4]. In particular, such complex models are needed to take into account the V' dependence of R_{rs} [5]. An immediate practical implication of this is that any value of R_{rs} must be referred to the levels of V' set on the ventilator.

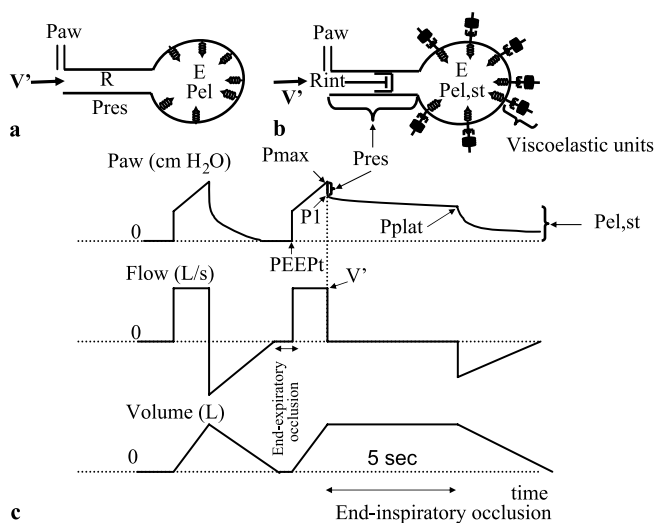


Fig. 1 a Single-compartment model of respiratory system with a standard resistance (dashpot R) and elastance (spring E). b Multiple-compartment model of respiratory system comprising the standard resistance (dashpot R_{int}) and the standard elastance (spring E), both arranged serially, and the viscoelastic units which are arranged in parallel around E . The viscoelastic units comprise a dashpot and a spring that are arranged serially. c Interrupter technique during mechanical ventilation with constant flow inflation. From top to bottom, schematic drawing of airway pressure (P_{aw}), flow and change in lung volume against time. At the end of a baseline breath the airways are occluded for 5 s (second horizontal double arrow). After occlusion the sudden pressure drop from maximal pressure (P_{max}) to pressure at first zero flow (P_1) is the pure resistive pressure drop ($Pres$). The slow decay from P_1 to the plateau pressure (P_{plat}) is the pressure dissipation into the viscoelastic units. The elastic pressure (Pe_l) is above the static elastic end-expiratory pressure ($PEEP_t$) obtained from end-expiratory occlusion (first horizontal double arrow)

Techniques of measurement of R_{rs}

Although more complex methods exist, a simple bedside approach to measuring R_{rs} and its components appears to also be accurate. The first method is based on the rapid interruption of V' at the airways while measuring P_{aw} downstream the location of occlusion as described 80 years ago [6] and validated in mechanically ventilated patients 40 years ago [7]. The occlusion is performed at end-inflation during constant V' and V conditions. One observes the resultant P_{aw} behavior. This end-inspiratory hold maneuver results in the P_{aw} rapidly decreasing from a peak P_{aw} , called P_{max} , at end-inspiration to P_1 (Fig. 1c) and then by a slow decay from P_1 to plateau pressure (P_{plat}), as end-inspiratory lung volume is held constant. P_{plat} represents the static elastic end-inspiratory recoil pressure of the respiratory system (Pe_l, st). By dividing $(P_{max}-P_1)$ by the V' immediately preceding the occlusion, the interrupter resistance ($R_{int, rs}$) can be computed. By dividing (P_1-P_{plat}) by the same V' the additional viscoelastic resistance (ΔR_{rs}) can be obtained. R_{rs} is the

sum of $R_{int, rs}$ and ΔR_{rs} . $R_{int, rs}$ mainly reflects airway resistance [8] and ΔR_{rs} dynamic pressure dissipation due to tissue viscoelastic properties in normal lung [4] and time-constant inequality in diseased lungs [9, 10]. The technique is easy to do by instructing the ventilator to perform an inspiratory hold maneuver of 3 s [11]. This diagnostic technique is often an automated function on many ventilators. The accuracy of the results requires patients to not be actively participating in inspiratory efforts and thus works best in those patients in synchrony with the ventilator, including those deeply sedated and/or paralyzed.

The second method of assessing R_{rs} is based on the forced oscillation technique introduced 50 years ago [12]. This method determines the respiratory input impedance (Z), which is the response of the respiratory system to an external oscillatory stimulus at various respiratory frequencies usually between 0.5 and 20 Hz. Z is computed as the ratio of the Fourier transform of P_{aw} to the Fourier transform of V' . The resultant Z has two components, a “real” part that is related to R_{rs} and an imaginary part, or reactance, which is related to elastance. This method can be used in patients receiving invasive [13] or noninvasive mechanical ventilation [14] but requires additional equipment. Accordingly, it is not routinely used in most ICUs to assess R_{rs} even though it is accurate.

Airway and endotracheal tube resistance

In normal subjects under mechanical ventilation $R_{int, rs}$ amounts to $2.2 \text{ cmH}_2\text{O l}^{-1} \text{ s}^{-1}$ at V' of 0.6 l s^{-1} , whereas greater values have been measured in various diseased conditions [9, 10, 15, 16]. $R_{int, rs}$ is V' dependent, linearly increasing with V' for a constant V , in both normals [4] and in patients with lung disease [9, 10]. In the mechanically ventilated patient P_{aw} is usually measured at the proximal tip of the ETT. Thus the measured $R_{int, rs}$ reflects both R_{aw} and ETT resistance. The pressure drop across the ETT depends highly on V' and ETT size such that the higher the V' and smaller the ETT size, the higher is ETT flow resistance. This relationship can be described by the model proposed by Rohrer [17] as:

$$Pres = K_1 V' + K_2 V'^2 \quad (2)$$

where K_1 and K_2 are constants. Although the physiological meaning of K_1 and K_2 is not clear, the presence of K_2 underlines the nonlinear V' dependence of $Pres$. This nonlinear $Pres-V'$ relationship has been described with other models based on the physical characteristics of the conducts and of the gas (Reynolds number, Blasius equation). Although beyond the scope of this note, it is important to bear in mind that V' can change from laminar to fully turbulent, explaining this nonlinearity in the $Pres-V'$ relationship. This has important consequences

for V' delivery during inhaled therapy or justifies to change the nature of the gas such as helium in case of highly turbulent conditions. Equation 2 is used in many ventilators as an "automatic tube compensation mode" (ATC) during pressure support breathing to compensate for the resulting additional work of breathing due to the ETT [18]. ATC may also use equation as $Pres = V'^b$ where b , which depends on the size of the ETT tube, is usually slightly lower than 2.

component the dominate factor in increasing ΔRrs [19]. ΔRrs also exhibits V' dependence in both normals [4] and patients [9, 10]. However, unlike $Rint$, rs , ΔRrs decreases progressively with increasing V' [2]. Thus Rrs depends on the respective contributions of $Rint$, rs and ΔRrs . From the clinical perspective Rrs is maximal at low V' and decreases with increasing V' to a minimal value that occurs at V' of about 1 l s^{-1} in both COPD [10] and ARDS [9, 20] patients.

Tissue resistance

The tissue resistance ΔRrs is equal to or slightly greater than $Rint$, rs . Tissue resistance has two components, lung parenchyma and chest wall, which includes the diaphragm. In patients with chronic obstructive lung disease (COPD) the contribution of chest wall to Rrs is modest [10], whereas in patients with the acute respiratory distress syndrome (ARDS) the lung and chest wall contribution to ΔRrs is highly variable and depends to a great degree on whether lung injury is the primary cause of ARDS (primary) or secondary. In secondary ARDS abdominal distension often increases intra-abdominal pressure limiting chest wall expansion making the chest wall

Clinical Implications

Assessing Rrs during mechanical ventilation is important in order to: (a) attribute to increased Rrs an increase in Paw during volume-controlled mode or a decline in tidal volume during pressure-controlled mode, (b) identify the mechanism of increased Rrs as an increase in resistance of ETT or Raw or tissue resistance, (c) assess the effects of bronchodilating agents, and (d) detect ETT obstruction. Rrs can easily be measured with the interrupter technique in patients receiving invasive mechanical ventilation in ICU from the values of $Pmax$, $Pplat$, and V' provided by the ventilator. Clinicians must have in mind the V' dependence of the values of Rrs when interpreting the results.

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