UNIVERSITY OF CINCINNATI

June 15 ,2001

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hereby submit this as part of the requirements for the degree of:

Doctor of Philosophy

in Nursing

It is entitled Imposed Work of Breathing and Breathing Comfort of Nonintubated Volunteers Breathing With Three Portable Ventilators and a Critical Care Ventilator

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(FORM B)

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From: Marilyn Sawyer Sommers, Ph.D., R.N.
Committee Chair

Department of: Adult Health Nursing

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has satisfactorily completed the dissertation defense for the doctoral degree.

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
26/Jul/2001	DISSERTATION	

4. TITLE AND SUBTITLE
IMPOSED WORK OF BREATHING AND BREATHING COMFORT OF NONINTUBATED VOLUNTEERS BREATHING WITH THREE PORTABLE VENTILATORS AND A CRITICAL CARE VENTILATOR.

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
LT COL AUSTIN PAUL N

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
UNIVERSITY OF CINCINNATI

8. PERFORMING ORGANIZATION REPORT NUMBER
CI01-204

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
THE DEPARTMENT OF THE AIR FORCE
AFIT/CIA, BLDG 125
2950 P STREET
WPAFB OH 45433

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Unlimited distribution
In Accordance With AFI 35-205/AFIT Sup 1

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE		261	19b. TELEPHONE NUMBER *(Include area code)*

IMPOSED WORK OF BREATHING AND BREATHING COMFORT OF NONINTUBATED VOLUNTEERS BREATHING WITH THREE PORTABLE VENTILATORS AND A CRITICAL CARE VENTILATOR

A dissertation submitted to the

Division of Research and Advanced Studies

of the University of Cincinnati

in partial fulfillment of the

requirements for the degree of

DOCTORATE OF PHILOSOPHY (Ph.D.)

in the College of Nursing

2001

by

Paul N. Austin

B.S.N., The State University of New York at Utica/Rome, 1980

B.S., The George Washington University, 1985

M.S.N., The State University of New York at Buffalo, 1990

Committee Chair: Marilyn Sawyer Sommers, Ph.D., R.N.

ABSTRACT

In spontaneous breathing modes, past laboratory work using a lung model indicated portable ventilators as compared to critical care ventilators may increase inspiratory work of breathing. The purpose of this study was to assess the imposed inspiratory work of breathing and breathing comfort of nonintubated healthy volunteers breathing spontaneously through three portable ventilators and a critical care ventilator in a controlled environment. A physiologic theoretical framework was used for the study. With all subjects having continuous positive airway pressure (CPAP) settings of 0 and 5 cm H_2O and pressure support ventilation (PSV) settings of 0 and 10 cm H_2O, the hypotheses were: 1) Imposed work (WOB_I) and pressure-time product (PTP_I) with the 7200ae (Mallinckrodt, critical care ventilator) will be less than those in the Achieva (Mallinckrodt) ventilator and LTV 1000 (Pulmonetic) ventilator, which will be less than those of the Univent 754 (Impact) ventilator (WOB_I and PTP_I with 7200ae < Achieva = LTV 1000 < Univent 754); 2) breathing comfort (BC) reported by subjects breathing with the 7200ae will be greater than that with the Achieva and LTV 1000, which will be greater than the Univent 754 (BC with 7200ae > Achieva = LTV 1000 > Univent 754). The study used a randomized, single blind repeated measures design using healthy nonobese subjects (n=16). Measured respiratory parameters were saved to a personal computer and subjects recorded BC on a visual analogue scale that had been previously assessed for validity. Control breathing periods were interposed after each fourth study period; maximum inspiratory pressure was the proxy measure for fatigue. Baseline airway pressure was determined in real-time and retrospectively with the differences compared for each ventilator and control period. Repeated measures ANOVA was used

to analyze the data with $\alpha \leq 0.05$. There were no significant differences in the measures during the control breathing periods or in baseline airway pressures. The ventilator was a source of significance for WOB_I, PTP_I, and BC ($p \leq 0.0001$). Tukey's method for comparison of means revealed the WOB_I, PTP_I were greater and BC of subjects was less with the Univent 754. Although the data did not fully support the research hypotheses, the WOB_I, PTP_I, and BC were significantly different in the Univent 754. The other portable ventilators offered no significant increase in WOB_I, and PTP_I nor decrease in BC compared to the critical care ventilator. The differences seen with the Univent 754 were likely due its triggering method, constant inspiratory flow, and intrinsic positive end-expiratory pressure. Further clinical studies are warranted.

ACKNOWLEDGEMENTS

This dissertation is dedicated to my wife, Nancy, and our three children, Matthew, Sarah, and Christopher. Without their support and understanding I never could have started let alone completed this endeavor. I would also like to acknowledge Marilyn S. Sommers, Ph.D., R.N., Theresa A. Beery, Ph.D., R.N., Jay A. Johannigman, M.D., and Paul A. Succop, Ph.D. for their encouragement and expert guidance.

I would also like to sincerely thank Robert S. Campbell, R.R.T., F.A.A.R.C. and Richard D. Branson, B.A., R.R.T., F.A.A.R.C. for their tremendous patience, expertise and encouragement. Without their help, as well as the help received from the staff of the Division of Trauma/Critical Care, University of Cincinnati, this study would not have been possible.

This study was also made possible by the generous financial support received from the American Association of Nurse Anesthetists Foundation and the United States Air Force.

The views expressed in this article are those of the author and do not reflect the official policy or position of the United States Air Force, Department of Defense or the US Government.

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CHAPTER I

INTRODUCTION TO THE STUDY

Introduction to the Problem

Breathing is fundamental to human life. Ancient Eastern and Western philosophers recognized the importance of breathing to sustaining life (Perkins, 1964). There are also references in the Bible to breathing, including Genesis 2:7 "And the Lord God formed man of the dust of the ground, and breathed into his nostrils the breath of life and man became a living soul". The use of mechanical ventilation has become common to meet the needs of those individuals with impaired breathing. Paradoxically these devices, if poorly designed or incorrectly applied, may impair the individual's ability to spontaneously breathe. This discussion examines the factors involved in the proper design and application of portable ventilation.

History of Mechanical Ventilation

The development of mechanical ventilators was aided by advances in equipment developed for the United States Air Corps for supplying pilots with positive pressure ventilation while flying at high altitudes (Barach, Fenn, Ferris, & Schmidt, 1947). Mechanical ventilators were first used with persons suffering ventilatory failure due to paralysis from polio during the 1950's. (Morch, 1990). Advances making mechanical ventilation possible included the use of a tracheostomy and later translaryngeal intubation (Lassen, 1953).

Within a short period of time mechanical ventilators were used to support persons with a variety of other conditions including acute pulmonary edema and acute asthma, in

postoperative patients with poor lung excursion and intraoperative patients when the thorax was opened, and as a ventilation technique when the patient was pharmacologically paralyzed (Motley et al., 1948). In the mid- to late 1960's hospitals in the United States followed the Danes in congregating patients needing high-level care, including mechanical ventilation, into intensive care units (O'Donohue, Baker, Bell, Muren, & Patterson, 1970).

Use of Portable Ventilators Across Settings

Care of ventilator-dependent patients in subacute and home care settings along with the need to transport mechanically ventilated patients sparked the need for portable ventilators (PVs) (Adams, Whitman, & Marcy, 1993; Rouse, Branson, & Semonin-Holleran, 1992). Prior to the introduction of PVs, manual ventilation of patients by a trained provider using a resuscitation bag resulted in shifts in arterial blood gas values and acid-base imbalances. The most notable of these was respiratory alkalosis due to excessive ventilation by the operator (Adams, Branson, & Hurst, 1986; Gervais, Eberle, Konietzke, Hennes, & Dick, 1987; Hurst, Davis, Branson, & Johannigman, 1989). Technological advances, such as PVs, lessened these shifts and helped to remedy this situation, along with employment of monitoring devices to assess exhaled tidal volume and/or end-tidal carbon dioxide. (Weg & Haas, 1989).

In addition to subacute and transport use, there was (and still remains) a military need to provide critical care in hostile environments including field hospitals and during aeromedical evacuation (Dice, 1991; Mabry, Munson, & Richardson, 1993). The demands of PVs for these settings include a simple, robust, battery-powered device (Branson, 1999; Rouse et al., 1992). Additional attractive features include integral flow

generation thereby eliminating a need for a compressed gas source for operation and the capability to use a low pressure oxygen supply, thereby conserving this expensive and hard-to-transport gas. Manufacturers of PVs are faced with the challenge of producing an economical device that will perform at the level of a mechanical ventilator used in a critical care setting.

Use of Portable Ventilators in Spontaneous Breathing Modes

Ventilation modes allowing spontaneous breathing, such as intermittent mandatory ventilation (IMV), synchronized intermittent mandatory ventilation (SIMV), and continuous positive airway pressure (CPAP) present a particular concern to clinicians using PVs (Branson & Davis, 1995; Kacmarek, Stanek, McMahon, & Wilson, 1990). In these ventilation modes the PV supplies the oxygen-containing gas mixture that the patient spontaneously breathes. Compared to critical care ventilators (CCVs), some PVs used in these modes have been found to have the undesirable characteristic of imposing significant inspiratory work of breathing leading to recommendations to modify these ventilators when used in spontaneous breathing modes (Branson & Davis, 1995; Kacmarek et al., 1990). These differences between portable and critical care ventilators are likely due to design decisions intended to simplify and lower the cost of PVs. The concepts of resistance to flow and work of breathing must be explored to understand the issue of spontaneous breathing of people using a PV to help meet their ventilation needs.

Physiologic Framework

A physiologic framework will be used as a basis for the investigation. Of particular importance are the concepts of *resistance to flow* and *work of breathing*. When

used in ventilation modes that allow spontaneous breathing, resistance to gas flow through these devices is produced by a valve that must be opened by the patient's inspiratory effort (the demand valve), as well as the gas pathway in the ventilator, breathing circuit, exhalation valve, CPAP-producing device, and artificial airway. These structures impose resistance to gas flow and the patient must perform work to overcome this resistance to flow (Branson & Davis, 1995).

Work of breathing (WOB) is work the patient accomplishes to move air into and out of the lungs. Because exhalation is normally a passive maneuver due to the elasticity of the lungs and chest wall, WOB is usually confined to work needed for inspiration. Following this convention, in this investigation WOB refers to work needed for inspiration recognizing work may need to be accomplished to exhale by patients with some types of artificial airways and those with pulmonary pathology such as chronic obstructive pulmonary disease.

WOB (also called total work of breathing or WOB_{TOT}) can be broken down into two components: the physiologic work of breathing (WOB_{PHY}) and the imposed work of breathing (WOB_I) (Banner, Jaeger, & Kirby, 1994). WOB_I is influenced by the resistance forces imposed by devices such as an artificial airway and/or mechanical ventilator. WOB_I is the work to overcome these imposed resistances (Banner et al., 1994). An excessive WOB_{TOT} of the patient breathing with the assistance of a mechanical ventilator results in patient discomfort, tachypnea, hypoventilation, increased oxygen demand, and patient-ventilator dyssynchrony (Banner et al., 1994). A drawback of WOB_I is for it to be measured, a change in volume must occur.

Work of breathing is defined as a change in volume that occurs due to a change in pressure. Thus work of breathing can be measured only when there is a change in volume that occurs due to a change in pressure. This presents a problem, as during the time between beginning of inspiration and the start of gas flow from the ventilator, metabolic energy is expended by the respiratory muscles (primarily the diaphragm). However, as no change in volume occurs, work cannot be measured. Nonetheless, the individual has expended energy. In order to account for this, the imposed pressure time product (PTP_I) will be used to supplement the imposed work of breathing as a measure of this expended metabolic energy. PTP_I is defined as the pressure developed by the respiratory muscles as measured at the proximal airway (proximal to the imposed resistances) integrated over the duration of the contraction (Calzia et al., 1998). WOB_I and PTP_I have been studied extensively in the laboratory using spontaneous breathing models.

Prior Laboratory Investigations

Investigators have used a model of spontaneous breathing to examine the WOB_I resulting from resistance to gas flow through devices such as PVs. (Katz, Kraemer, & Gjerde, 1985; Op't Holt, Hall, & Bass, 1982). These spontaneous breathing models typically consist of a two-chambered test lung. A mechanical ventilator (driving ventilator) is attached to one chamber and acts as the respiratory "muscles". The ventilator or other device being studied is attached to other chamber. A pneumotachograph, which is used to measures flow and in turn can be integrated with time to calculate volume, and a pressure transducer is interposed between the ventilator being examined and the test lung. A metal bar is attached to the two chambers so that

when the mechanical ventilator inflates that chamber of the test lung, the other chamber (which is attached to the test ventilator) inflates, mimicking spontaneous breathing (see Figure 1). In this model WOB_I is defined as the area subtended by the pressure-volume curve to the left of the baseline airway pressure (Mador, Walsh, & Tobin, 1993) (see Figure 2).

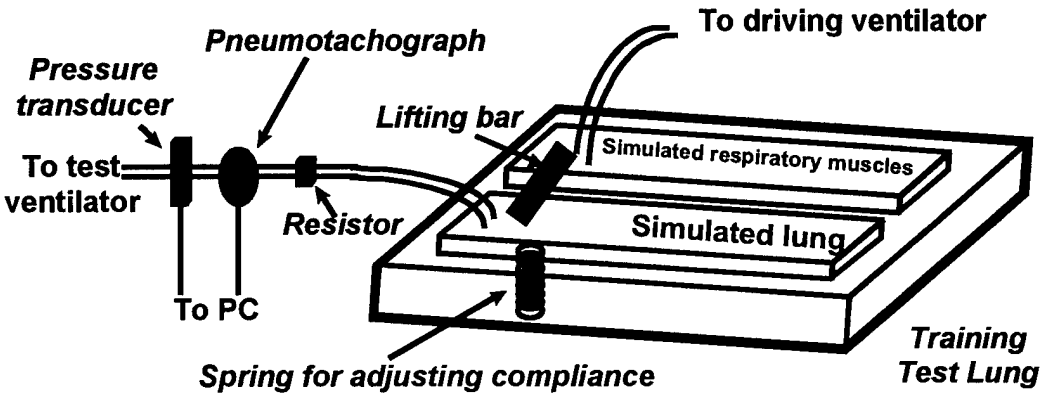


Figure 1. Mechanical model of spontaneous breathing.

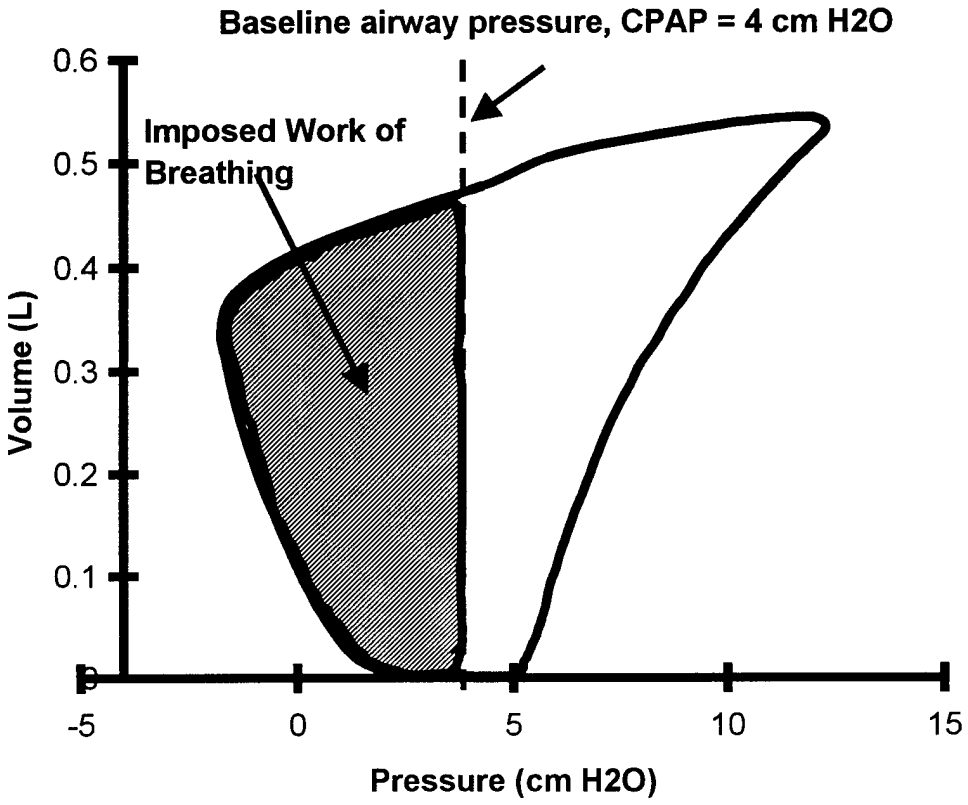


Figure 2. Imposed work of breathing (WOB_I) when using a mechanical model of spontaneous breathing. WOB_I is defined as the area subtended by the pressure-volume curve to the left of the baseline airway pressure.

Kacmarek et al. (1990) and Branson and Davis (1995) used a mechanical model of spontaneous breathing to compare the WOB_I resulting from breathing with a sample of PVs and CCVs. Design features of the PVs tested in these studies that contributed to the increased WOB_I included lack of a demand valve (present on CCVs) whereby the patient must draw gas through an antisuffocation valve, an exhalation valve, or via the air intake of the piston. In recent years the sophistication of PVs has increased with many of these devices now having a demand valve.

A recent laboratory study by Austin, Campbell, Johannigman, and Branson (2001) found the WOB_I of newer PVs to approach that reported for CCVs. The improvement in PVs is likely due to improvement in the design of PVs with widespread use of microprocessors and the incorporation of a demand valve. The present investigation is the first to examine the WOB_I, PTP_I, and breathing comfort using a sample of portable ventilators with human subjects. The use of a model of spontaneous breathing offers benefits to researchers however they are not without drawbacks.

Benefits of a mechanical model of spontaneous breathing include convenience, no risk to human subjects, and the ability to mimic a variety of conditions such as alterations in tidal volume, respiratory rate, airway resistance, and lung compliance. However these models do not challenge the ventilator with breath-by-breath alterations in tidal volume, rate, and inspiratory flow. Also, when a mechanical model is used there is no means to assess a tremendously important parameter: the breathing comfort of the person breathing

through the ventilator. The discipline of nursing is interested in human response to disease and treatment and we must include this subjective measure when investigating phenomena.

Purpose of the Study

The purpose of this study is to assess WOB_I, PTP_I, and breathing comfort of nonintubated healthy volunteers breathing through a sample of portable ventilators (PVs) and a critical care ventilator (CCV) in a controlled environment. A mouthpiece attached to the end of an endotracheal tube will in turn be attached to the ventilator circuit. The subject will place the mouthpiece in his/her mouth. Endotracheal intubation is not necessary as this investigation examines the changes in the above variables imposed by the PVs and CCV, not imposed by endotracheal intubation. Prior investigations have examined the WOB_I (work that must be performed to overcome the resistance to flow through the PV) using a lung model of simulated breathing, however no other investigators have examined the WOB_I, PTP_I and breathing comfort of humans breathing spontaneously through PVs.

A sample of three PVs (one of each model) will be used: Achieva PS (Mallinckrodt, Inc., St. Louis, MO), LTV 1000 (Pulmonetic Systems, Inc., Colton, CA), and Univent 754 (Impact Instrumentation Corp., West Caldwell, NJ). These PVs are selected based on availability, usage patterns, their capability to self-generate compressed air, and their method of producing compressed air (Achieva PS, piston; LTV 1000, turbine; Impact 754, compressor). The CCV selected is the Puritan 7200ae (Mallinckrodt, Inc., St. Louis, MO). This CCV is selected based on its availability, popularity, and level of performance as assessed in a prior investigation (Branson & Davis, 1995).

The following table offers specific design characteristics of these ventilators (see Table 1). These design characteristics are predicted to influence WOB_I, PTP_I and breathing comfort. For example, flow triggering has been suggested to be superior to pressure triggering and placing the exhalation valve in the breathing circuit may be inferior to placing the exhalation valve in the ventilator (Branson, Campbell, Davis, & Johnson, 1994; Sassoon, Giron, Ely, & Light, 1989.

Table 1

Specific Design Characteristics of the Ventilators Used in the Investigation

	Type	Triggering	Location of exhalation valve
Achieva	Portable	Flow	In breathing circuit
LTV 1000	Portable	Flow	In breathing circuit
Univent 754	Portable	Pressure	In breathing circuit
7200 ae	Critical care	Flow	In ventilator

Research Hypotheses

Based on the design characteristics of the ventilators and prior in vitro investigations, when breathing through an 8.0 mm internal diameter endotracheal tube attached to a mouthpiece with an F_IO_2 of 0.4 across the following four combinations of pressure support and CPAP (0 cm H_2O and 0 cm H_2O, 10 cm H_2O and 0 cm H_2O, 0 cm H_2O and 5 cm H_2O, 10 cm H_2O and 5 cm H_2O):

1. The WOB_I with 7200ae < Achieva = LTV 1000 < Univent 754.
2. The PTP_I with 7200ae < Achieva = LTV 1000 < Univent 754.
3. The breathing comfort reported by subjects breathing with the 7200ae > Achieva = LTV 1000 > Univent 754.

Variables

Work of Breathing

WOB_{TOT} can be divided into physiologic work of breathing (WOB_{PHY}) and imposed work of breathing (WOB_I). WOB_{PHY} is comprised of elastic work to overcome the elastic forces during inflation and flow-resistive work to overcome the resistance of the airways and pulmonary tissues to the flow of gas. WOB_I is actually an additional flow-resistive workload. WOB_I is work the patient must perform to move gas through an apparatus such as a PV with accompanying artificial airway. WOB_I along with the physiologic work of breathing (WOB_{PHY}) make up the total work of breathing (WOB_{TOT}) (Banner et al., 1994).

Imposed Pressure Time Product (PTP_I)

PTP_I is used to supplement WOB_I as a quantitative measure of the subject's breathing effort. It estimates metabolic work of the respiratory muscles and increases with imposed resistance to airflow reflecting isometric work that must be done to overcome these imposed resistances (Marini, 1988). As discussed earlier, PTP_I accounts for effort not measured by WOB_I

Breathing Comfort

Investigators have used indices of dyspnea and anxiety as measures of breathing comfort in adult patients weaning from mechanical ventilation (Elliott et al., 1991; Knebel, Janson-Bjerklie, Malley, Wilson, & Marini, 1994). In this subset of patients one can understand why dyspnea and anxiety can be used as measures of breathing comfort although they seem less applicable to measuring breathing comfort in healthy volunteers.

In the present study, breathing comfort will be measured using a visual analogue scale (VAS) to measure breathing comfort in the sample of healthy volunteers. This scale is similar to the method used by Mols et al. in their 2000 investigation.

Portable Ventilator

Portable ventilators include mechanical ventilators designed for prehospital use, intra-hospital transfer, inter-hospital transfer, and for use in subacute settings as well as the home. Authors have proposed PVs possess the following attributes: simple and reliable; have a weight of less than 4 kg; and have a mounting or carrying bracket, a control panel oriented so adjustments can be made from the same plane, and if electrically powered, a battery. (Branson, 1999; Kacmarek & Hess, 1994) Other desirable attributes

include having a built-in method of producing compressed air and the ability to use a low-pressure oxygen source thus reducing uptake of oxygen.

Significance of the Problem

Nurses care for patients who receive ventilatory assistance from PVs in transport, subacute, home care, and in military settings with both stable and critically ill individuals (Goldberg & Frownfelter, 1990; Tobley, 1998). There has been an increase in ventilator-dependent patients in subacute facilities and in the home. In 1992, the number of individuals receiving long-term ventilatory support in long term care facilities in the state of Minnesota doubled from 1986 (Adams et al., 1993). The initiatives to care for ventilator-dependent patients in subacute settings seem to be driven at least in part by the need to control health care costs (Saposnick, 1995).

Nurses are also caring for patients receiving ventilatory assistance from PVs during transport and in military settings (Farmer, 1996; Rouse et al., 1992). With the broadened scope of the patient transport mission, the United States Air Force now faces the challenge of transporting critically ill patients requiring the highest level of ventilatory support (Lyons & Connor, 1995; Mabry et al., 1993). PVs are also becoming increasingly common in military casualty care as doctrine now calls for intensive care capability that is light and mobile and capable of being deployed to locations close to the battlefield (Carlton, 2000). Nurses who care for patients in these settings should have a solid working knowledge of the capabilities and limitations of PVs when used in spontaneous breathing modes.

Results of laboratory investigations suggest PVs may possess an increased

resistance to gas flow resulting in an excessive work of breathing when used in spontaneous breathing modes (Branson & Davis, 1995; Kacmarek et al., 1990). Clinical reports have shown mechanical ventilators possessing an increased resistance to flow result in an increased WOB_I leading to an increased WOB_{TOT}. This may lead the clinician to mistakenly conclude the patient does not have sufficient respiratory muscle strength to be liberated from mechanical ventilation. Increased WOB_{TOT} can also lead to discomfort, respiratory muscle fatigue, and ventilatory failure and needlessly prolong mechanical ventilation with the accompanying time spent in a critical care unit (Kirton, Banner, Axelrod, & Drugas, 1993; Roussos & Macklem, 1977). This investigation, the first using human subject testing with PVs, examines WOB_I, PTP_I and breathing comfort of healthy nonintubated adult volunteers while spontaneously breathing through a PV.

Summary

Breathing is an activity that is basic to sustaining human life. Mechanical ventilation of patients is now accomplished outside of critical care units. Nurses care for these patients during transport, in subacute and home care environments, and in military settings.

Use of PVs with spontaneously breathing patients challenges the patient to work to overcome the resistance to gas flow through the device. The work the patient must do to overcome this resistance to flow is termed the WOB_I. If WOB_{TOT} (the sum of the WOB_{PHY} and WOB_I) is excessive, the result can be patient discomfort, patient-ventilator asynchrony, and respiratory muscle fatigue. In the past this was an impediment to using PVs during spontaneous breathing.

Results of laboratory investigations using models of simulated spontaneous breathing suggest the resistance to flow through some PVs is excessive and may lead to an excessive WOB_I. However the results of recent studies indicate the resistance to flow through newer PVs is low and may approach that of more expensive and complex CCVs. It is anticipated newer PVs will possess WOB_I, PTP_I, and breathing comfort comparable to CCVs. This investigation is the first to compare these variables with healthy nonintubated adult volunteers spontaneously breathing through a sample of PVs and a CCV.

CHAPTER II

REVIEW OF RELATED LITERATURE

Introduction

This section discusses the literature that supports this study and explains the current science in the areas of physiological and psychological responses to mechanical ventilation using spontaneous breathing modes. The section starts with a discussion of the theoretical rationale guiding the investigation including: the mechanics of spontaneous breathing, work of breathing, and breathing comfort. Next, the discussion focuses on the use of PVs in the home, during transport, and in military settings. This section concludes with a discussion of the resistance to airflow though PVs and resultant work of breathing when PVs are used in spontaneous breathing modes.

Theoretical Rationale

The discussion of the theoretical framework that will guide this investigation starts with a review of the mechanics of spontaneous breathing. Following this is a discussion of the concepts of work of breathing and breathing comfort.

The Mechanics of Spontaneous Breathing

Introduction

The components of the respiratory system are the lungs, extrapulmonary airways, diaphragm, and chest wall which includes the costal muscles, bone, and connective tissue. The structures in the respiratory system can be described as tube-like or bag-like. The tube-like structures are the conducting airways such as the upper airway, trachea, and bronchi. The bag-like structures are the alveoli, diaphragm, and abdominal wall (Loring,

1998). Before spontaneous breathing is discussed using these analogies, a brief description of the theoretical rationale of inspiration and expiration is offered.

Inspiration and Expiration

During spontaneous breathing, the diaphragm is the major respiratory muscle. During inspiration, the diaphragm contracts, thereby resulting in downward displacement of the abdominal contents enlarging the vertical dimensions of the chest. Also the rib margins are moved upward and outward, increasing the transverse diameter of the chest. Contraction of the external intercostal muscles also causes the ribs to rise, increasing the anteroposterior diameter of the chest. During strenuous breathing the accessory muscles of respiration contribute to inspiration. These include the scalene muscles and the sternocleidomastoid muscles. Expiration is normally a passive maneuver as the energy for expiration is stored in the elastic properties of the lung and chest wall (Agostoni, 1964). This investigation examines solely inspiratory work. Boyle's Law helps explain air flow during inspiration.

Boyle's Law and inspiration.

The increase in vertical and anteroposterior dimensions of the chest during inspiration cause a decrease in intrapleural pressure, following Boyle's Law. Boyle's Law states at a constant temperature, the pressure (P) of a given mass of gas is inversely proportional to its volume (V). The equation below describes Boyle's Law:

$$P_1V_1 = P_2V_2$$

The kinetic theory of gases offers an explanation as to why this occurs. The molecules of a gas are in continuous random motion. These molecules are deflected off course by striking other molecules or the walls of a container. Pressure results from these molecules striking the walls of the container. The magnitude of pressure these molecules exert on the walls of the container is dependent on the number of molecules present, their mass, and their speed. As the volume of the intrapleural space increases, the molecules of gas present in the intrapleural space less frequently strike the structures making up the boundaries of the intrapleural space (West, 2000).

With this increase in intrapleural volume and decrease in intrapleural pressure, a pressure gradient is established between the air in the alveoli and the more negative intrapleural space. This causes inflation of the alveoli with the establishment of a pressure gradient between the air in the alveoli and the air in the conducting airways. This gradient causes airflow to occur from the area of greater pressure (airways) to the area of more negative pressure (alveoli).

$$P_2 \longrightarrow \dot{V} \longrightarrow P_1$$

Air (comprised primarily of oxygen and nitrogen) flows into the alveoli until this pressure gradient disappears with the distention of the alveoli, which causes the alveoli to inflate. There is then set up a pressure gradient between the gas in the alveoli and gas that is distal to the alveoli. This pressure gradient produces flow of gas through the airways

into the alveoli. Gas diffuses from the alveoli into the blood in the pulmonary capillary. The factors influencing the rate of gas exchange between the alveoli and blood in the pulmonary capillary include the difference in the pressure of the gas in the alveoli and capillary, solubility of the gas, the cross sectional area of the fluid, distance the gas must diffuse, molecular weight of the gas, and temperature of the gas (Guyton & Hall, 2000). Expiration is normally a passive maneuver as the lungs and chest wall are elastic and energy for expiration is stored in these structures and expended during expiration (Mead & Agostoni, 1964).

The discussion of the theoretical rationale guiding this investigation now continues using the analogies introduced earlier.

Tube-Like and Bag-Like Structures

Introduction.

The tube-like structures described above are the conduits for air in the lungs. Their mechanics can be characterized by the relationship between gas flow through the tube. This relationship can been illustrated by plotting the change in volume resulting from a given change in pressure (see Figure 3). The bag-like inflatable structures contain gas and their mechanics are characterized by the relationship between the contained gas volume (V) and the pressure difference displacing the wall (see Figure 4) (Loring, 1998). These analogies can be used to discuss pulmonary compliance and resistance.

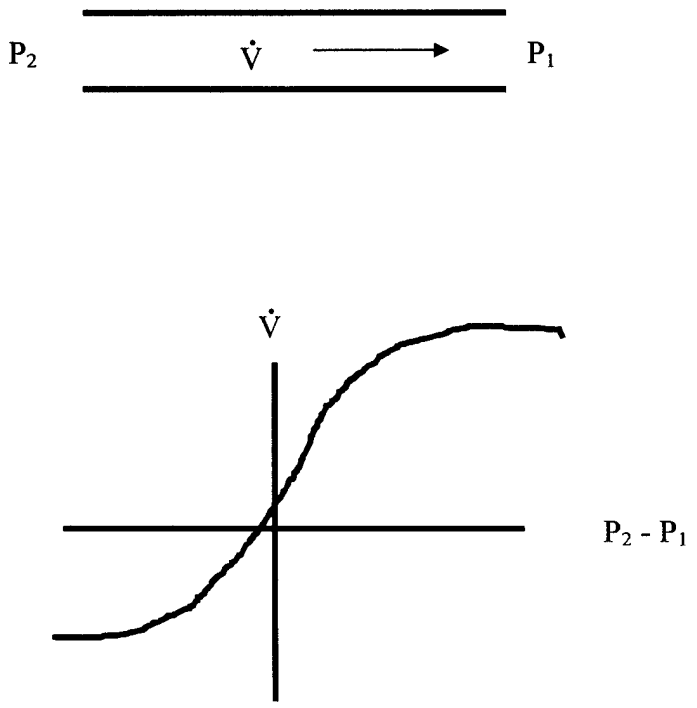


Figure 3. Relationship between pressure (P) and flow ($\dot{V}$) for a tube. (Redrawn from Loring, 1998.)

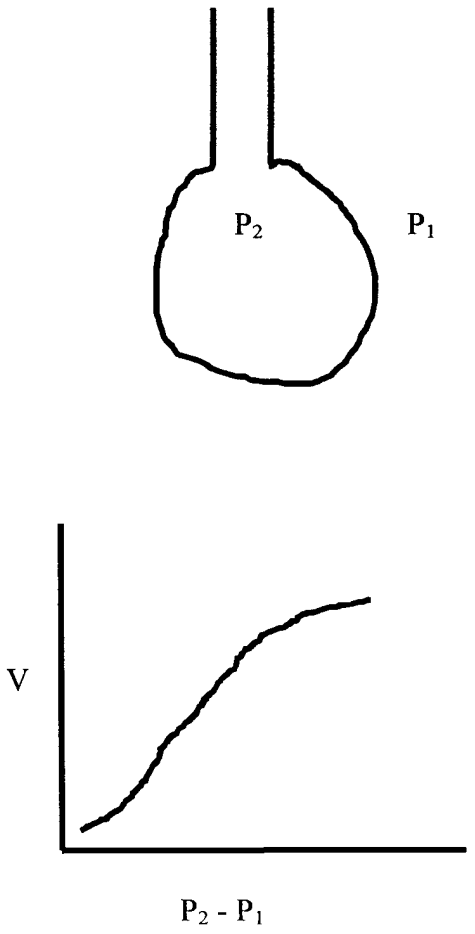


Figure 4. Relationship between pressure (P) and volume (V) for a hypothetical bag-like structure. (Redrawn from Loring, 1998.)

Compliance

Introduction.

Compliance is a concept that applies to bag-like structures such as the lungs. Compliance (C) is defined as a change observed in volume (V) per change in pressure (P).

$$C = \Delta V/\Delta P$$

For the lung, compliance (C_L) is described as the change in lung volume (ΔV_L) seen with a change in the elastic recoil pressure of the lung, which is the pressure across the lung tissue (ΔP). The elastic recoil pressure across the lung is in turn defined as the difference between the pressure of the alveolus (P_{alv}) and the intrapleural space (P_{pl}) (Loring, 1998). See the following equation.

$$C_L = \Delta V_L/\Delta P$$

$$\Delta P = (P_{alv} - P_{pl})$$

The compliance of the lungs is reduced by diseases that cause an increase of fibrous tissues in the lung. Compliance is also reduced by edema in the alveolar spaces. The compliance of the lung is increased with the loss of elastic tissue in both pulmonary emphysema and with increases in age. The compliance of the lung also depends on the size

of the lung. That is, at lower lung volumes, compliance is reduced.

The elastic nature of the lung is due to anatomy of the lung and surface tension of the liquid film lining the alveoli. The lung contains stretchable elastin fibers and collagen fibers that are not easily stretched. The elastic behavior of the lung is not due solely to the presence of elastin fibers but due to their geometric arrangement in the lung. The stretching of the lung is probably due to the distortion of the geometrical arrangement of the elastin and collagen fibers (West, 2000).

Role of surfactant in determining compliance.

Surface tension is defined as the force acting across an imaginary line 1 cm long in a liquid surface. Tension develops because the cohesive forces between the adjacent liquid molecules are greater than the forces between the molecules of the liquid and gas outside the surface. The Law of LaPlace describes the relationship between pressure (P), tension (T), and radius (r) for spherical structures, such as alveoli:

$$P = 2T/r$$

That is, the pressure in the alveolus is equal to twice the tension divided by the radius. In the absence of surfactant, which acts to decrease surface tension, the pressure developed in a smaller alveolus will be greater than the pressure in the larger alveolus. This would result in the volume contained in the smaller alveolus emptying into the larger alveolus. If this situation were present, the lung would be very unstable. However surfactant is present and lines the inside of the alveoli. Surfactant acts to reduce the surface tension of

the alveoli resulting in lesser tendency for smaller alveoli to empty into larger alveoli (West, 2000). The presence of surfactant also helps explain most of the hysteresis of the intact lung. In a pressure-volume curve of the lung (see Figure 5), hysteresis refers to the inflation limb of the curve appearing different than the deflation limb of the pressure-volume curve (Loring, 1998).

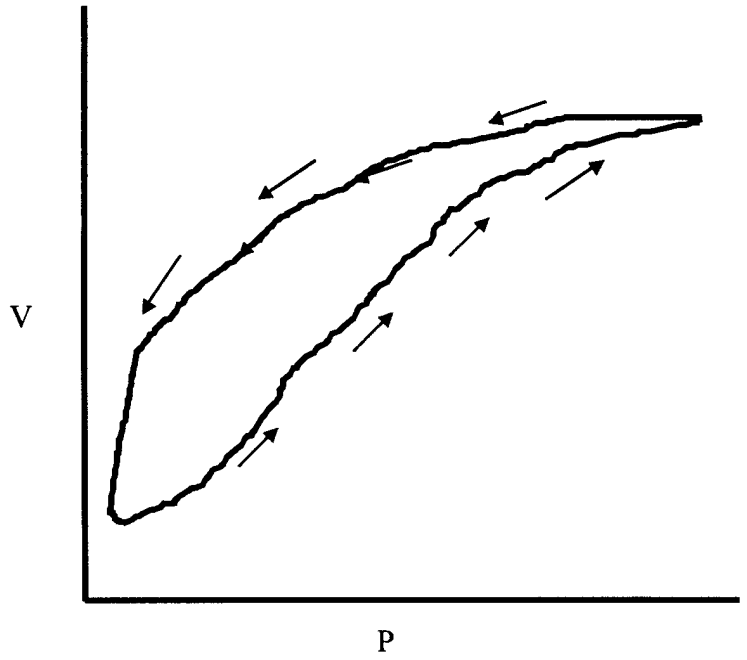


Figure 5. Pressure (P) - volume (V) curve of the lung illustrating hysteresis. (Redrawn from Loring, 1998).

The lungs are more compliant in the presence of surfactant; thus the work to expand the lungs with each breath is reduced in its presence. As noted above, the alveoli are more stable in the presence of surfactant. Finally surfactant helps to keep the lungs dry by lessening the tendency of water to be pulled across the alveolar-capillary membrane into the lumen of the alveoli.

Elastic properties of the chest wall and compliance.

The elastic properties of the chest wall must be addressed when discussing compliance. The chest wall has the tendency to expand while the lungs have the tendency to contract. Because of the relationship between these structures and the pleural space (a closed space), the tendency of the chest wall to spring outward helps to expand the lungs while the tendency of the lungs to contract acts to pull the chest wall inward. The interaction between the elasticity of the chest wall and the lung can be summarized in a relaxation pressure-volume diagram.

Relaxation pressure-volume diagram.

The relaxation pressure is the airway pressure obtained when the subject is completely relaxed, not attempting to inflate or deflate his/her lung and chest wall by muscle activity. If the relaxation pressure-volume of the curve and chest wall is examined at the functional residual capacity (FRC), the relaxation pressure is zero. That is, at FRC the pressure produced by the lungs attempting to contract is balanced by the pressure produced by the chest wall attempting to expand. As the volume of the lung is increased, the relaxation pressure becomes positive as the lung and chest wall tend to return to

equilibrium FRC position The relaxation pressure is about 30 cm H_2O at total lung capacity. As lung volume drops below FRC, the residual volume is gradually approached and relaxation pressure is quite low. Under these conditions the lungs and chest wall tend to spring outward when the expiratory muscles relaxed. This generates the negative relaxation pressure (Agostoni & Mead, 1964). This reference along with Campbell (1958), Dubois (1964), Mead and Agostoni (1964), and Otis (1964) represent the classic works in the field of pulmonary mechanics.

If the relaxation pressure-volume curve for the lung alone is examined (with the lung removed from the thorax and inflated with positive pressure as in experimental preparation), it is noted at FRC a positive pressure of about 5 cm H_2O is developed as the lung tries to collapse. At total lung capacity about 25 cm H_2O of positive pressure is developed. If the lung is inflated to a volume below FRC the relaxation pressure falls to zero (Agostoni & Mead, 1964).

When the relaxation pressure-volume curve (see Figure 6) for the chest wall alone is examined (if this could be done for the chest wall with the lungs removed) at FRC, the chest wall develops a negative relaxation pressure. That is, the chest wall tends to spring out at FRC at the same time the lung is collapsing inward. The negative relaxation pressure of the chest wall and the positive relaxation pressure of the lung are identical; thus this is the equilibrium position for the lung and chest wall together. At any volume, the curve for the combined lung and chest wall can be explained by the addition of the individual lung and chest wall curves. Finally at about 70% of vital capacity, the chest wall no longer tends to spring out. At volumes above this, the chest wall tends to collapse

inward resulting in positive relaxation pressures (Agostoni & Mead, 1964).

Compliance describes the relationship between pressure and volume. As will be revealed below, resistance describes the relationship between pressure and flow.

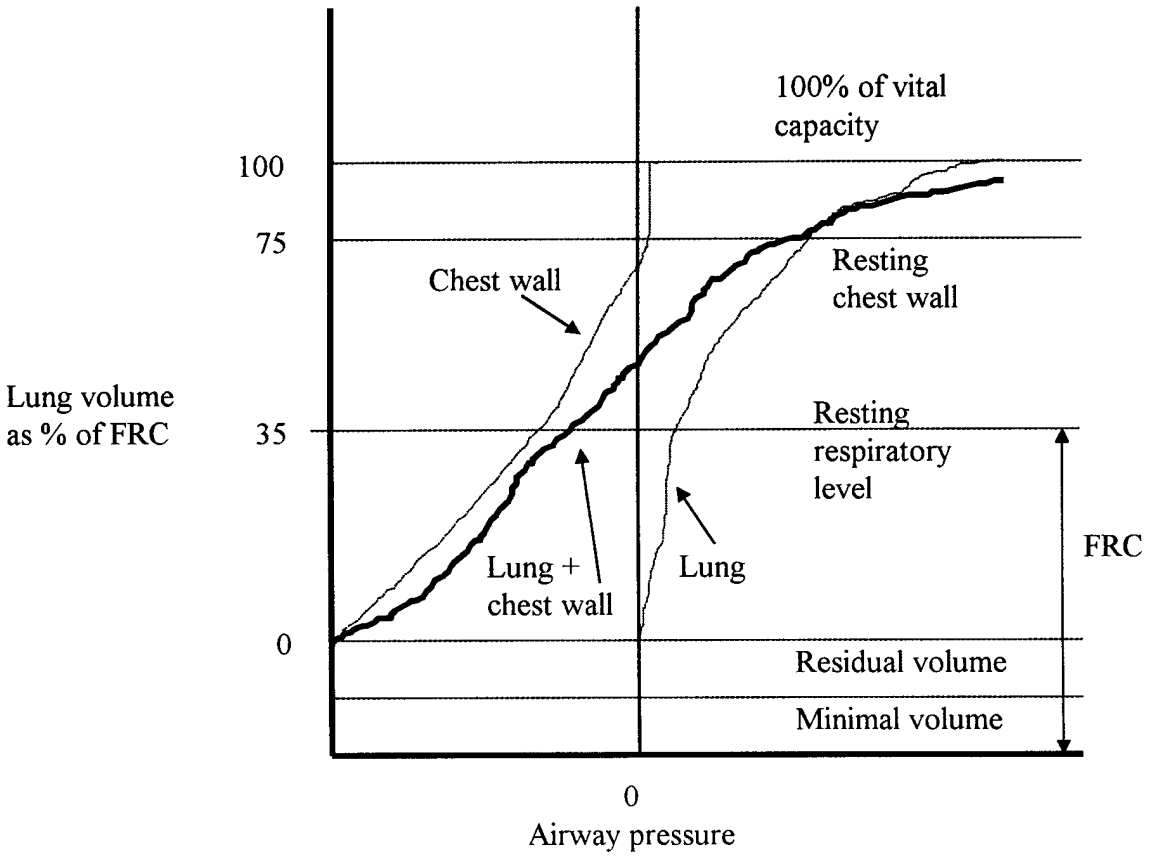


Fig 6. Relaxation pressure-volume curve of the lung and chest wall. (Redrawn from Loring, 1998.)

Resistance

Introduction.

Resistance (R) is defined as the ratio of driving pressure (ΔP) for a gas across a system to the resulting flow ($\dot{V}$).

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

This change in pressure is also known as resistive pressure (P_R) and is the pressure dissipated across the airways and parenchyma to overcome the frictional forces generated with gas flow. Resistances add in series so the resistance of the respiratory system (R_{RS}) is the sum of its components: the resistance of the lung (R_L) and chest wall (R_{CW}).

$$R_{RS} = R_L + R_{CW}$$

Factors changing resistance.

Resistance varies with the phase of breathing, lung volume, and gas flow rate. Resistance is greater on expiration especially in those persons with obstructive lung disease. Resistance is less at high lung volumes due to the alteration of airway diameter resulting from the tethering action of lung parenchyma on the airways. Velocity (flow rate through the tube) is important in the study of resistance. The relationship of pressure and

resistance to flow rate is linear at low flow rates. However at higher flow rates when turbulence and thus friction pressure losses are increased the relationship of pressure and resistance to flow rate is exponential. That is, at higher flow rates flow can be changed from laminar to turbulent. Thus comparisons should be made at similar flow rates and lung volumes.

Resistance during laminar flow.

Laminar flow through a tube occurs when flow is parallel to the tube walls in concentric layers with linear velocities that increase towards the center of the tube. Laminar flow is more likely with flow through a straight smooth tube. With turbulent flow there is formation of currents and eddies resulting in chaotic movement of gas molecules. Turbulent flow is more likely if the tube is curved and the inside surface of the tube is rough compared to if the tube is straight and the inside surface of the tube is smooth. In the pulmonary system turbulent flow of gas is more likely in trachea while laminar flow is more likely in the smaller conducting airways. (Dubois, 1964; MacIntyre & Branson, 2001).

At flow rates resulting in laminar flow, Poiseulle's Law describes the pressure-flow characteristics. That is, in smooth straight circular tubes, the flow is described by the following equation:

$$\dot{V} = \Delta P \pi r^4 / 8nl$$

In this equation, ΔP is the driving pressure, r is the radius of the tube, n is the viscosity of the fluid in the tube, and l is the length of the tube. Thus driving pressure is proportional to flow rate or:

$$\Delta P = \dot{V}K$$

$$\text{Where } K = 8l/\pi r^4 * n$$

Since resistance to flow is driving pressure divided by flow, resistance is directly proportional to the viscosity of the fluid (n) and length of the tube (l) and inversely proportional to the radius of the tube.

$$R = 8nl/\pi r^4$$

Thus when the radius of the tube is halved the resistance increases 16 fold. But if length is doubled then resistance is only doubled (Dubois, 1964; Guyton & Hall, 2000).

Resistance during turbulent flow.

Turbulent flow has different properties than laminar flow. Pressure during turbulent flow is not proportional to flow rate but, approximately, to its square as shown in the equation below.

$$P = K\dot{V}^2$$

$$\text{Where } K = fl/\pi^2 r^5$$

In the equation above, f is a friction factor that depends on the Reynold's number that is a measure of laminar or turbulent flow. Also during turbulent flow the viscosity of the fluid is less important but an increase in gas density increases the pressure drop for a given flow (Dubois, 1964).

Sources of resistance in the respiratory system.

The airways and nonelastic deformation of tissue offer the major resistance to gas flow in the lungs. The chief location of airway resistance are the medium-size bronchi. While the small bronchi do individually have smaller radius, they are collectively arranged in parallel with a small combined resistance. Lung volume is an important determinant of airway resistance as the bronchi run within and are tethered by the lung parenchyma. As the lung expands, caliber of the airway increases. The tone of the bronchial smooth muscle is another important determinant of airway resistance. As the small bronchi constrict due to overriding parasympathetic tone, the resistance to gas flow increases. The density and viscosity of the gas being breathed also determines resistance to gas flow. Gas flow in the lungs of individuals with severe asthma can be increased by having the individual breathe a mixture of oxygen and helium since helium is a gas with a very low density (Dubois, 1964; Guyton & Hall, 2000).

Imposed sources of resistance.

There are additional sources of flow resistance if the subject is spontaneously breathing through an apparatus. The apparatus may be an artificial airway such as an endotracheal tube or a tracheostomy tube. Other components of the apparatus include a

ventilator with its associated breathing circuit. Appendix A discusses the classification of modes of ventilation.

One source of imposed resistance is an endotracheal tube as the radius of the natural airway is greater than the radius of an appropriately sized endotracheal tube. Bolder, Healy, Bolder, Beatty and Kay (1986) found over a range of simulated breathing patterns flow through endotracheal tubes between 5.0 and 10.0 mm internal diameter (ID) was turbulent. Thus the imposed resistance can be described by the equation

$$P = K\dot{V}^2$$

$$\text{Where } K = fl/\pi^2 r^5$$

Replacing the natural airway with an endotracheal tube will increase resistance to gas flow as the endotracheal tube is a smaller diameter than the natural airway. Resistance to gas flow is also increased in the intubated human due to reflex airway constriction distal to the endotracheal tube. Gal and Suratt (1980) examined airway resistance of six healthy males when they breathed through an 25 mm ID mouthpiece (control); an externally held 8 mm ID endotracheal tube, 25 cm in length; and when they were intubated with the same size endotracheal tube using topical anesthesia. Airway resistance increased from a mean control value of 0.99 cm H_2O/L/sec to mean resistance of 2.34 H_2O/L/sec with the externally held endotracheal tube. Mean resistance after intubation was 2.75 H_2O/L/sec. These investigators concluded not only did the endotracheal tube increase mean airway

resistance primarily due to the diameter of the endotracheal tube being smaller than the diameter of the natural airway but also with intubation there was a decrease in the caliber of the airways distal to the endotracheal tube due to the irritation by the endotracheal tube. Tracheostomy tubes differ from endotracheal tubes in terms of resistance to flow.

Tracheostomy tubes offer less resistance to flow than do endotracheal tubes. The decreased length and rigidity of tracheostomy tubes explain this. Unlike pliant endotracheal tubes whose radius decreases once placed in situ at body temperature, rigid tracheostomy tubes maintain their radius at body temperature. Using a model of spontaneous breathing, Davis, Branson, and Poremka (1994) examined the pressure drop across a variety of endotracheal tubes and tracheostomy tubes along with the imposed work of breathing. These measures reflected the resistance to flow offered by the artificial airways. The investigators suggested the resistance to flow offered by an endotracheal tube is greater than a tracheostomy tube of a similar diameter. As flow through an endotracheal tube is usually turbulent, Poiseulle's Law does not totally explain the decreased resistance seen with this artificial airway. Since often these artificial airways are used with mechanical ventilators, the resistance to flow offered by mechanical ventilators must be examined.

Mechanical ventilators with their breathing circuits are sources of resistance to gas flow when used in spontaneous breathing modes e.g., synchronized intermittent mandatory ventilation (SIMV), pressure support ventilation (PSV), continuous positive airway pressure (CPAP) (Bersten, Rutten, Vedig, & Skowronski, 1989). These ventilation modes require the ventilator to supply a flow of gas for the patient to breathe. Two

techniques can be used to supply this flow of gas: continuous and demand flow.

In continuous flow systems, a high flow of gas passes from an air-oxygen blender through a reservoir bag, humidifier, and breathing circuit to the patient. With a demand-flow-system, a regulating device on the inspiratory limb (usually part of a mechanical ventilator) controls the airflow. The challenge is to supply the patient with sufficient inspiratory flow though a low resistance device to satisfy his/her inspiratory requirements. Drawbacks of continuous flow systems include the expense of continuous high gas flows and the difficulty in measuring inspired volumes.

Early demand-flow systems offered higher resistance to gas flow than continuous-flow systems (Gibney, Wilson, & Pontoppidan, 1982). Some individuals failed to wean from mechanical ventilators that used a demand-flow system when the ventilators were used in spontaneously-breathing modes. However if a ventilator was used that contained a continuous flow system there was a greater likelihood weaning would be successful. By comparing the inspiratory work of subjects breathing through demand-flow and continuous-flow devices, Gibney et al. concluded the demand flow devices offered a higher resistance to flow as reflected by higher inspiratory work of breathing.

Using a model of spontaneous breathing, Katz et al. (1985) examined the inspiratory work resulting from simulated spontaneous breathing through a group of newer ventilators, comparing the inspiratory work of breathing with a continuous-flow device. They found the demand-flow systems of some of the newer CCVs offered less resistance to gas flow than did some continuous-flow systems. These investigators concluded demand-flow systems vary widely in the resistance they offer to flow.

Resistance to breathing, either due to a narrowing of the individual's airways or due to breathing through an artificial airway and ventilator increases the individual's work of breathing. Understanding the mechanics of spontaneous breathing is integral to comprehending the next concept, work of breathing.

Work of Breathing

Introduction

Work is performed by the respiratory muscles during spontaneous breathing. By definition work (W) is performed when a force (F) moves its point of application over a given distance (D). This is described by the following equation:

$$W = F \times D$$

In a fluid system, such as the respiratory system, work (W) is performed when a pressure (P) changes the volume (V) of the system (Otis, 1964).

$$W = P \times V$$

The Systeme International d'Unites (SI) unit for work is the joule (J) which equals 0.1 kg * m. By convention, the work of breathing is normalized to volume and reported as J/L. Power is work performed per unit time and reported as J/min. Normal inspiratory work of breathing for healthy subjects is about 0.3 to 0.6 J/L not breathing through any

sort of an apparatus (Otis, 1964). Marini, Capps, and Culver (1985) reported the inspiratory work of breathing of healthy subjects breathing spontaneously through a ventilator was 0.54 J/L (trigger sensitivity -2 cm H_2O) to 0.79 J/L (trigger sensitivity -5 cm H_2O).

This section discusses inspiratory and expiratory work, pressure-time product (PTP), components of the work of breathing, and methods used to examine the work of breathing. Discussed in detail is the work of breathing due to imposed forces. The discussion concludes with a review of the consequences of increased work of breathing.

Inspiratory and Expiratory Work

An examination of the equation above reveals work only occurs when a change in volume results from a change in pressure. Inspiration results from the contraction of the muscles of ventilation such as the diaphragm. That is, these muscles perform work when they contract. It must be kept in mind that these muscles expend energy when they contract but inspiration does not occur (isometric contraction). This can occur with a spontaneously ventilating patient and a demand-flow system on a ventilator. Here the patient's inspiratory effort opens the demand valve. The demand valve may not open immediately in response to inspiration. Thus the patient's respiratory muscles are generating pressure but for a short time no change in volume results. By definition no work is done however the respiratory muscles still consume energy. Energy consumption that does not result in a volume change can be measured using the pressure-time product (PTP).

Pressure-Time Product and Imposed Pressure Time Product

The PTP is generally thought of as a better measure of oxygen consumption of the respiratory muscles than work of breathing as it measures the pressure developed by the respiratory muscles regardless of a lung volume change. PTP is defined as the pressure developed by the respiratory muscles (P_{mus}) integrated over the duration of the contraction (T_I). Usually the PTP is calculated over one minute. Below is the equation for PTP.

$$PTP = \int_0^{T_I} P_{mus} * dt$$

The P_{mus} is estimated for the inspiratory muscles as the intraesophgeal pressure (P_{es}) minus the chest wall pressure (P_{cw}) or:

$$P_{mus} = P_{es} - P_{cw}$$

Using a model of spontaneous breathing, Sassoon and Gruer (1995) found there was a direct relationship between the time delay of the opening of the demand valve and PTP. PTP also varies directly with inspiratory resistance. Collett, Perry, and Engel (1985) found a direct relationship between PTP and the amount of oxygen needed to accomplish the work of breathing of subjects breathing spontaneously through an inspiratory resistance. Others have used PTP as a measure of the oxygen consumption of

the respiratory muscles using both humans and a model of spontaneous breathing (Calzia et al., 1998; Marini, Smith, & Lamb, 1988; Sassoon & Gruer, 1995). The upper limit of normal for PTP in health subjects is 120 cm H_2O * secs/min (Barnard & Levine, 1986).

In their 1998 investigation, Calzia et al. also examined the imposed pressure-time product or PTP_I. PTP uses pressure measured in the esophagus during inspiration hence accounts for the effects on this pressure of the compliance of the lungs and chest wall and the resistance of the airways, both physiologic and imposed. On the other hand, PTP_I uses pressure measured proximally to any imposed resistances, such as an airway and ventilator. Thus PTP_I reflects the effect of imposed resistances on oxygen consumption of the respiratory muscles.

Components of the Work of Breathing

There are five main types of forces that must be overcome by the respiratory muscles. These are (a) elastic forces that develop in the tissues of the lungs and chest when a change in volume occurs, (b) flow-resistive forces offered by the airways to the flow of gas and by the nonelastic deformation of tissue, (c) inertial forces that depend on the mass of tissues and gases, (d) gravitational forces that can be considered part of the inertial forces but in practice are included in the measurement of elastic forces, and (e) distorting forces of the chest wall observed at relatively high rates of ventilation or when breathing through resistances (Rousso & Campbell, 1986). A sixth force, imposed resistive forces can be added to this list if the patient is spontaneously breathing through an apparatus such as an artificial airway and/or ventilator with associated breathing circuit (Banner, Jaeger, & Kirby, 1994). The increase in the WOB due to increased imposed

forces has been termed imposed WOB (WOB_I).

Methods of Measuring Work of Breathing

Two methods have been used to measure the work of breathing. These are determining the oxygen cost of breathing (O_2COB) and measurement of the mechanical work of breathing.

O_2COB

The O_2COB measures the oxygen uptake by the respiratory muscles during spontaneous breathing. This is done by calculating the difference between total body oxygen uptake (VO_2) during controlled ventilation (with no spontaneous breathing effort) and VO_2 during spontaneous breathing. Using a value to account for the efficiency of such work, one can calculate the O_2COB. Problems with this method include measuring VO_2. This method is seldom used as a measure of WOB (Sassoon & Mahutte, 1998).

Measurement of the Mechanical Work of Breathing

Here WOB is estimated by measuring pressure and volume changes over time. Work is calculated by measuring the change in pressure with respect to time. Esophageal pressure (P_{es}) is typically used as an estimate for intrapleural pressure (P_{pl}). Transpulmonary pressure is calculated as the difference between P_{es} and airway pressure (P_{AW}). The aspect of the work being measured is determined by the pressure being integrated. For example, airway pressure includes work done on the lungs, chest wall, and respiratory apparatus; transpulmonary pressure work done on the lungs alone; and transthoracic pressure (atmospheric pressure (P_{ATM}) - P_{PL}) work performed on the chest wall (French. 1999).

E.J.M. Campbell published the classic method of measuring mechanical work of breathing in spontaneously breathing subjects in 1958. Fundamental to this method is construction of a pressure-volume diagram referred to as the Campbell diagram. Pressure multiplied by volume equals work. Thus the areas on such a diagram can be used to calculate WOB.

The relaxation pressure-volume curves (see Figure 7) must be reviewed to understand the construction of a Campbell diagram. These curves are constructed by the subject inspiring or expiring to a certain volume. The airway is then occluded and the subject relaxes his/her respiratory muscles and the resultant pressure is recorded.

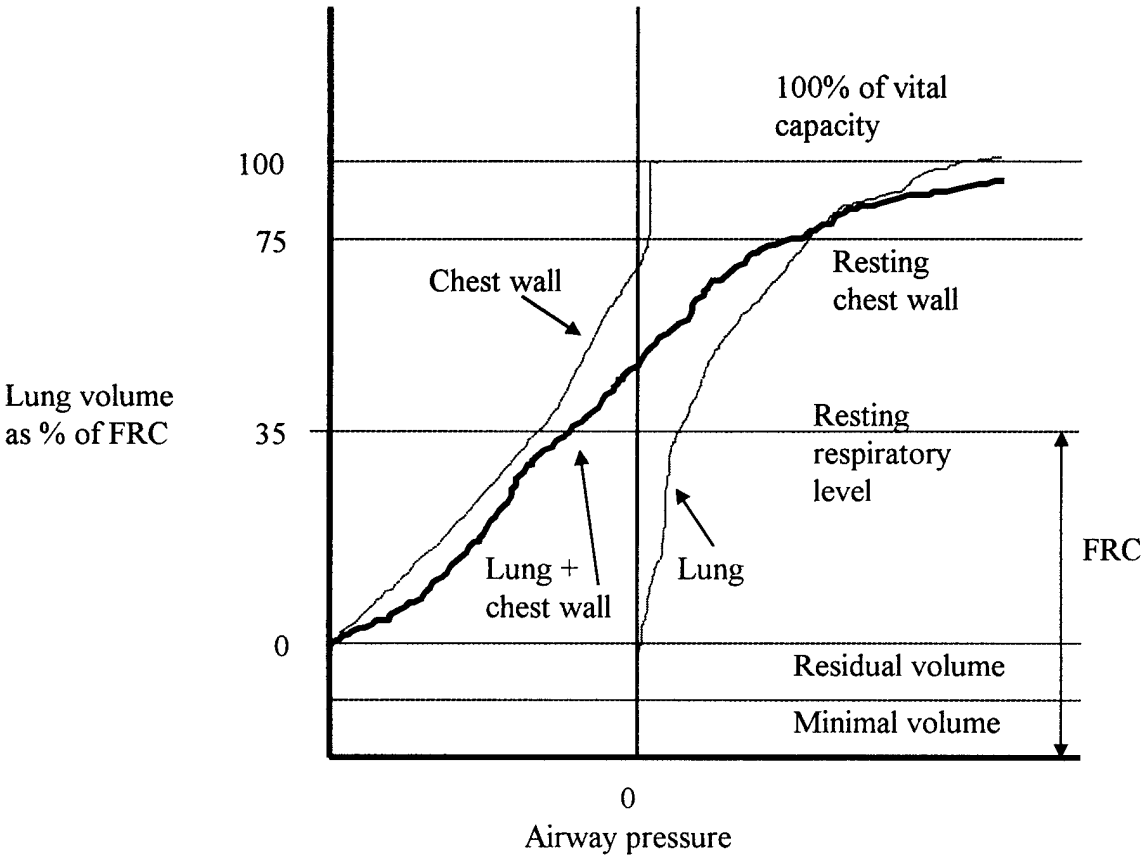


Figure 7. Relaxation pressure-volume curve of the lung and chest wall.

(Redrawn from Loring, 1998)

As can be seen from Figure 7, these curves are linear about the functional residual capacity (FRC) such that their slopes can be represented by a simple linear function. This linear function can be defined as the change in volume produced by a unit change in pressure (ml/cm H_2O). Three compliance values can be derived: compliance for the total respiratory system (C_{TOT}), compliance of the lung (C_L) and compliance of the chest wall (C_{CW}) (Loring, 1998).

These linear portions of the relaxation pressure-volume curves are illustrated in Figure 8. The linear portion of the static intrathoracic pressure (P_{TS}) is added to the diagram. The intrathoracic pressure when alveolar pressure is zero is defined as the P_{TS}. At this point there is no airflow. The P_{TS} is produced by the elastic recoil of the lung pulling inward on the chest wall. This pressure under conditions where there is no airflow is equal and opposite to the pressure of the lung such that $P_{TS} + P_{EL}{}^{L} = 0$. The P_{TS} curve and the lung relaxation curves ($P_{EL}{}^{L}$) are then mirror images. This fact is used in the construction of the Campbell diagram.

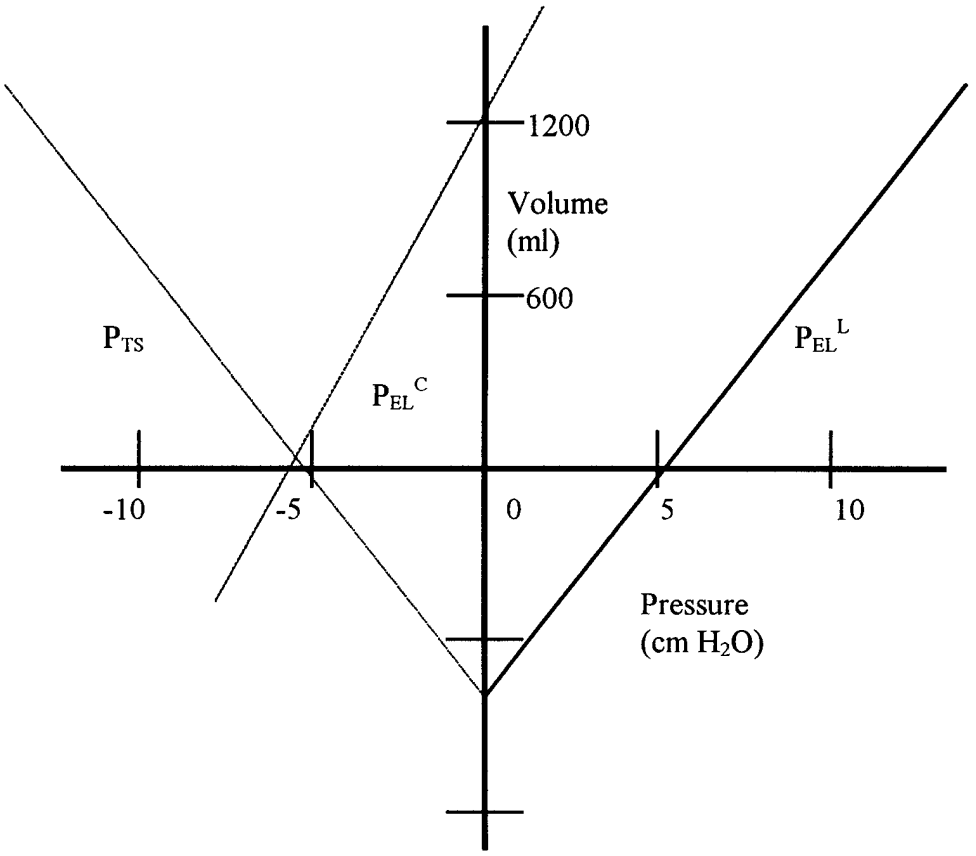


Figure 8. Pressure-volume diagram of the lungs and chest wall. P_{TS} is the static intrathoracic pressure, P_{EL}^{L} is the relaxation pressure curve of the lung, and P_{EL}^{C} is the relaxation pressure curve of the chest wall. Volume represents volume above FRC. 0 cm H_2O represents atmospheric pressure. It is important to note P_{TS} is a mirror image of P_{EL}^{L}. (Redrawn from Campbell, 1958.)

Construction of the Campbell Diagram.

Campbell first published the diagram in 1958. Key to this construction is the fact $P_{EL}{}^{L} = -P_{TS}$. Therefore a diagram can be constructed where pressures and hence work on the lung appear on the same side of the ordinate as those performed in the chest wall. Quiet inspiration is depicted in Figure 9 and quiet expiration is depicted in Figure 10. "Volume" in the diagrams refers to volume above FRC.

Below is the work performed during quiet inspiration as depicted in Figure 9.

1. The area bounded by AIBA represents the flow-restrictive work performed during inspiration. The amount of flow-resistive work depends on flow resistance and the rate of movement of gas and tissues.

2. The area bounded by ABCA represents elastic work during inspiration. Some of this elastic work is stored as potential energy to be used during expiration. This potential energy also provides the forces required for the flow-resistive work of expiration and for the negative (also termed pliometric) work being performed on the inspiratory muscles.

Below is the work performed during quiet expiration as depicted in Figure 10.

1. The area bounded by ABEA is the flow-resistive work performed during expiration.

In Figures 9 and 10, the area bounded by ABCA negate each other with no net work performed. However there is a metabolic cost. The area ACDFA illustrates the work performed by the chest wall on the lungs during inspiration and by the lungs on the chest wall during expiration. Here again there is no net work performed however there is

no metabolic cost incurred.

Figure 11 combines Figures 9 and 10. Here the area bounded by AIBCA describes the total metabolic cost in joules. Thus it can be seen if one only measures the area enclosed within a pressure-volume, curve work of breathing will be significantly underestimated as only the flow-resistive work of inspiration and expiration will be determined. If only the area enclosed within a pressure-volume curve is measured, the majority of area AIBCA is not calculated and only a small part of the total elastic work is measured. The chest wall relaxation pressure curve should be measured in the clinical setting as it will vary in cases such as obesity, tight thoracic dressings, and chest wall scarring. While some investigators insist the chest wall relaxation curve should be measured, many use 200 ml/cm H_2O as the chest wall compliance for a normal adult (Banner, Jaeger, & Kirby, 1994).

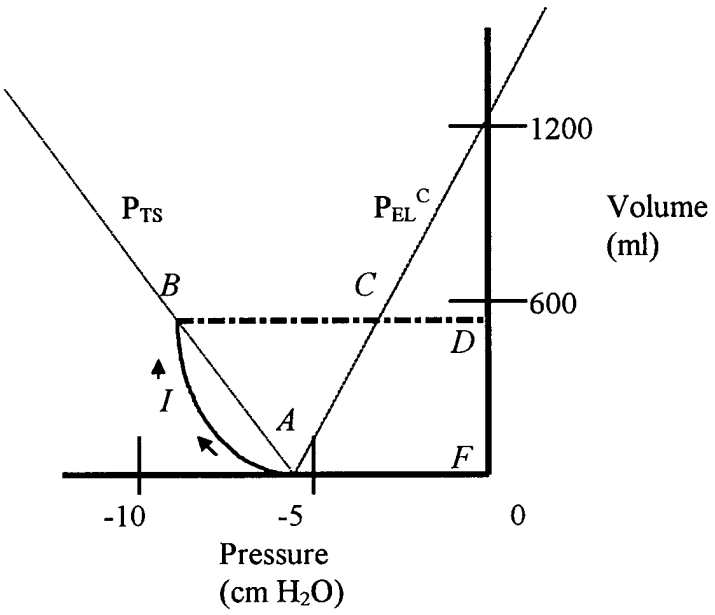


Figure 9. Pressure-volume curve during quiet inspiration. The area bounded by AIBA represents the flow resistive work of inspiration. The area bounded by ABCA represents the elastic work performed by the respiratory muscles. This is partly used for inspiration and also stored as potential energy for used during expiration. (Redrawn from Campbell, 1958.)

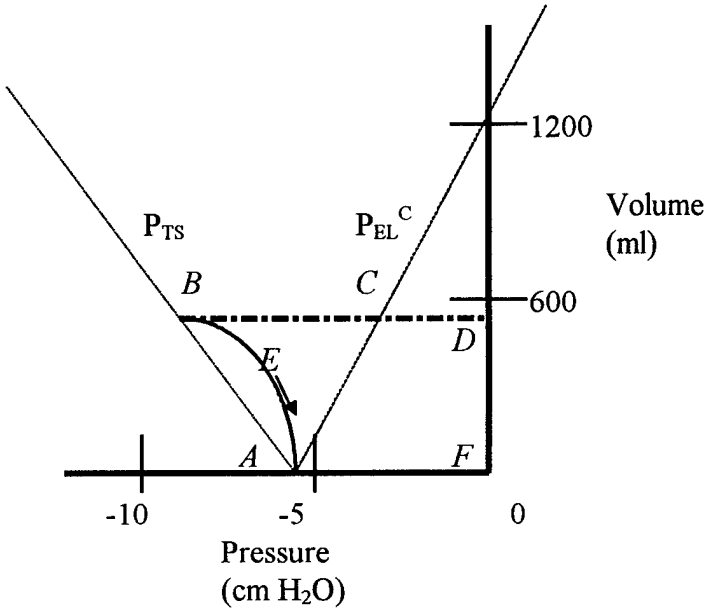


Figure 10. Pressure-volume curve during quiet expiration. The area bounded by ABEA represents the flow resistive work of expiration. This work is performed by the potential energy stored in the chest wall and the lung (which were stretched during inspiration). If the area bounded by ABEA extends beyond the relaxation pressure curve of the chest wall ($P_{EL}{}^{C}$), then additional work is must be performed by the expiratory muscles. (Redrawn from Campbell, 1958.)

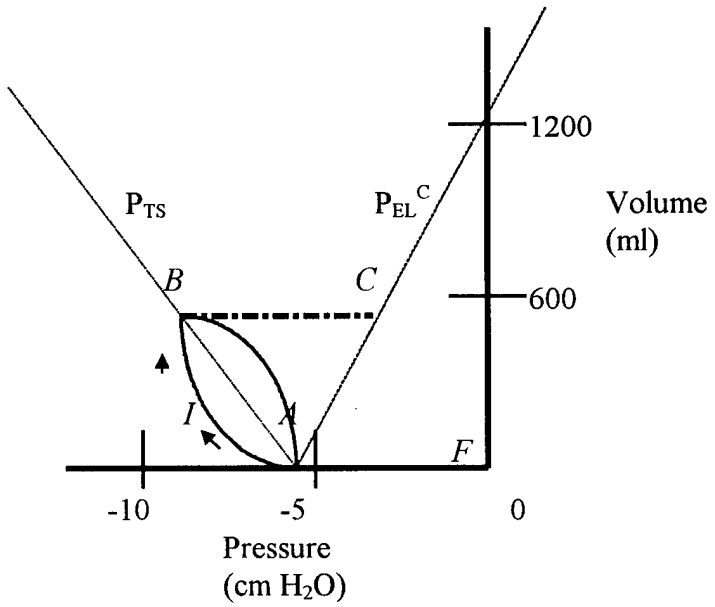


Figure 11. The Campbell diagram that combines Figures 7 and 8. The total metabolic cost of breathing is represented by area AIBCA. (Redrawn from Campbell, 1958.)

Disadvantages of the Campbell Diagram.

There are four main disadvantages of using the Campbell diagram to estimate WOB. These are (a) its reliance on the estimation of intrapleural pressure from intraesophageal pressure, (b) it neglects the nonelastic resistance of the chest wall, (c) it neglects the additional elastic work required as a result of distortion of the chest wall from its resting configuration, and (d) it neglects the effects of inertial forces and thoracic gas compressibility (French, 1999).

The measurement of intrapleural pressure is highly invasive requiring placement of an intraesophageal balloon. Using intraesophageal pressure as an estimate of pleural pressure was first suggested 70 years ago. P_{es} reflects changes in pleural pressure as long as the subject is not in the supine position. The position of the esophageal balloon is important when using intraesophageal pressure. The balloon should be placed in the distal third of the esophagus. This position can be confirmed nonradiographically by performing the "occlusion test" described by Baydur, Behrakis, Zin, Jaeger, and Milic-Emili (1982). Here the esophageal balloon is positioned such that the ratio of the change in esophageal pressure and mouthpiece pressure is close to 1.0 when the subject inspires against an occluded airway.

There is no method currently available to measure the non-elastic resistance of the chest wall in a spontaneously breathing subject. The reason is because the muscles that perform the work constitute part of the chest wall and therefore can not be separated from the load upon which they work. Thus non-elastic work performed on the chest wall has been ignored in work of breathing studies (French, 1999).

The Campbell diagram also does not measure work performed in overcoming inertial forces. Inertial forces of the respiratory system appear to be small with their magnitude greatest at the extremes of volume and flow changes. Inertial work is generally ignored in work of breathing studies (Guyton & Hall, 2000; Otis, 1964).

Goldman, Grimby, and Mead (1976) compared the work of breathing estimated from the Campbell diagram with mechanical work derived from separate rib cage and abdominal volume-pressure tracings. These investigators found at low ventilation the chest wall configuration is similar to the passive configuration and there is little distortion of the chest wall. Thus estimation of work of breathing using a Campbell diagram compared favorably with that obtained from separate volume-pressure tracings of the rib cage and abdomen. If ventilation is increased to levels such as 50 - 100 L/min, such as during exercise, the Campbell diagram may underestimate work of breathing.

Imposed work

The imposed work is due to the flow resistive forces of the artificial airway and mechanical ventilator with the associated breathing circuit. The imposed work is due to the flow resistive forces of the artificial airway and mechanical ventilator with associated breathing circuit. Figure 12 illustrates the Campbell diagram of a patient with imposed work of breathing.

Use of the Campbell diagram to examine imposed work requires the placement of an esophageal balloon. Placement of an esophageal balloon adds discomfort and risk to the participant as well as cost and complexity to the investigation. There are two other reasons it is not necessary to use the Campbell diagram to measure imposed work in this

investigation. First, the purpose of the investigation is to examine the effects (WOB_I, PTP_I, and breathing comfort) imposed by the ventilators, not the physiologic WOB and PTP. The concept of imposed work has been used by others when examining ventilators and other devices (Austin et al., 2001; Bolder et al., 1986; Branson, Campbell, Davis, & Johnson, 1994; Branson, & Davis, 1995; Calzia et al., 1998; Kacmarek et al., 1990; Katz et al., 1985). Second, the normal physiologic work of breathing and pressure time product have been described in the literature as 0.3 to 0.6 J/L and up to 120 cm H_2O * secs/min, respectively (Banner et al., 1994; Barnard & Levine, 1986; Otis, 1964). The risks of using the Campbell diagram to measure imposed work (necessitating placement of an esophageal catheter) outweigh the benefits of measuring imposed work by this method. Therefore in the present study, imposed work will be examined as described below.

As stated earlier, work in a fluid system such as the respiratory system is performed when a pressure changes the volume of the system as shown in Figure 12 (Mador et al., 1993; Otis, 1964). This concept is used when examining work due to imposed resistances of artificial airways, ventilators, and other devices both in investigations using lung models and human subjects (see Figure 13) (Austin et al., 2001; Bolder et al., 1986; Branson et al., 1994; Branson, & Davis, 1995; Calzia et al., 1998; Kacmarek, Stanek, McMahon, & Wilson, 1990; Katz et al., 1985). In these studies as in the current investigation, WOB_I is determined using the pressure at the proximal airway which is distal to the resistance imposed by the endotracheal tube and mechanical ventilator rather than pleural pressure. Sources of imposed work are discussed below.

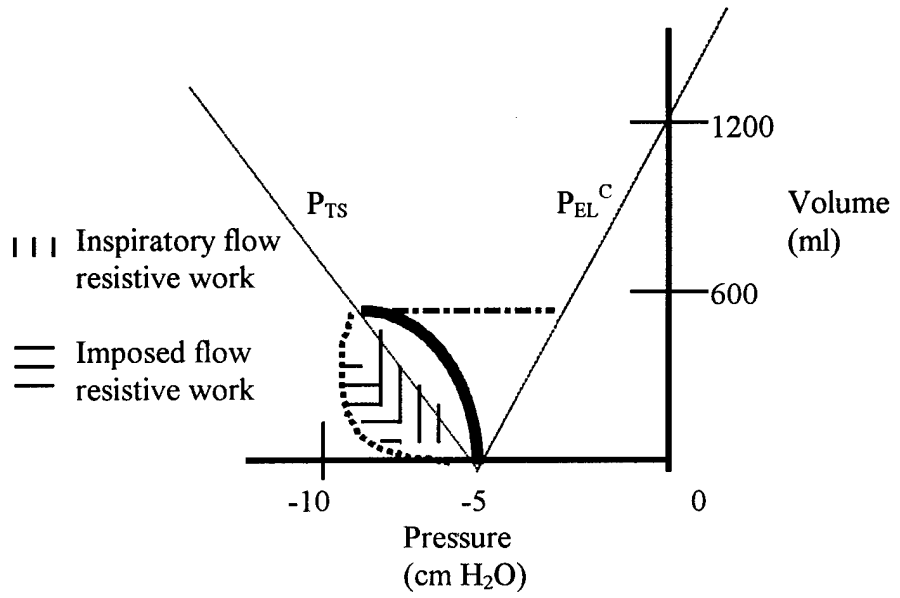


Figure 12. The Campbell diagram illustrating WOB_I. (Redrawn from Banner, Jaeger, & Kirby, 1994.)

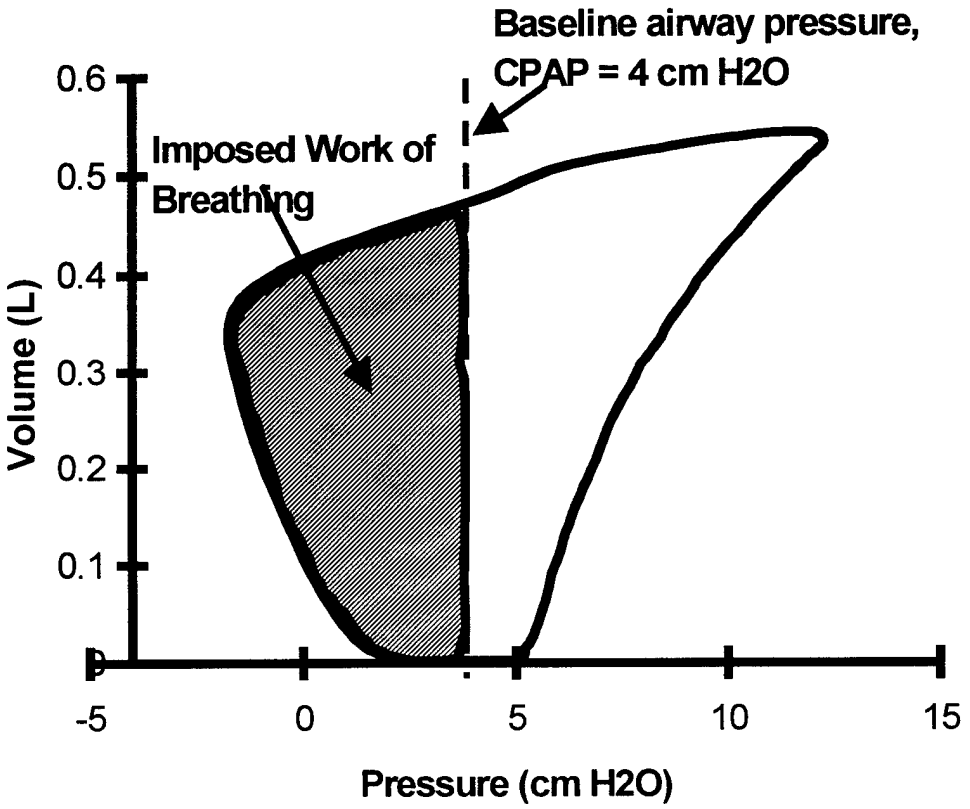


Figure 13. WOB_I is defined as the area subtended by the pressure-volume curve to the left of the baseline airway pressure.

Artificial airway.

Sources of imposed work include the artificial airway such as an endotracheal tube or tracheostomy tube. WOB_I is inversely proportional to the radius of the endotracheal tube. WOB_I is directly proportional to the length of the tube but this factor plays a minor role compared to the radius. WOB_I due to an endotracheal tube may be underestimated when measured in vitro compared to being measured in vivo. When measured in vivo, the endotrachael tube curves to conform to the individual's anatomy and becomes softer due it being warmed by the individual. These two factors combined with the presence of secretions change the resistance characteristics of the endotracheal tube (Bolder et al., 1986; Wright, Marini, & Bernard, 1989).

Exhalation and PEEP valves.

The flow resistance of exhalation valves and devices that produce PEEP can also add increased WOB during both inspiration and expiration. External exhalation valves may require more work to close at the beginning of inhalation, increasing WOB_I and WOB_{TOT}. Kacmarek, Mang, Barker, and Cycyk-Chapman (1994) found the high flow resistance of some PEEP valves resulted in an increased amount of inspiratory work. Also overdistention of the thorax will place the inspiratory muscles at a mechanical disadvantage and increase inspiratory WOB.

Ventilator design and settings.

Ventilator design and settings can increase WOB. Important determinants of WOB_I include trigger method (flow versus pressure), trigger sensitivity, peak inspiratory

flow rate and initial rate of gas flow when PSV is used, and level of PSV. When the patient must generate more negative inspiratory pressure or inspiratory flow to initiate the flow of gas (less sensitive trigger), the patient performs more work (Marini, Rodriguez, & Lamb, 1986a). If auto-PEEP is present, trigger sensitivity will diminish even more as the inspiratory muscles will have to overcome the PEEP plus the set trigger sensitivity before flow is delivered (Smith & Marini, 1988). Flow triggering results in less WOB_I compared to pressure triggering as suggested by the findings of investigations conducted by Branson, Campbell, Davis, and Johnson (1994) and Sassoon, Giron, Ely, and Light (1989). The set sensitivity and degree of auto-PEEP are probably major determinants of the WOB_I during the period of time the patient is triggering flow (Sassoon, 1992).

Once the patient has triggered flow, the WOB_I is governed by the patient's demand for flow and the capability of the ventilator to supply that demand (Sassoon & Gruer, 1995, Sassoon & Mahutte, 1995). The flow delivered from the ventilator depends on the feedback pressure signal to the ventilator's pressure-flow control algorithm. The feedback pressure signal is the gradient between the pressure sensed within the ventilator circuit as a result of patient effort and a target pressure relative to the CPAP level. The larger the pressure gradient, the greater the flow the ventilator delivers to the patient. The feedback pressure gradient can be increased by increasing the target pressure by applying pressure support or by lowering the sensed pressure within the ventilator circuit by methods such as sensing pressure at the carinal end of the endotracheal tube (Banner, Kirby, & Blanch, 1992).

The set peak inspiratory flow rate will influence WOB_I. If the peak inspiratory

flow rate is the same or lower than the patient's inspiratory flow demand, the patient will perform increased work in an attempt to satisfy their flow demand (Marini, Rodriguez, & Lamb, 1986b). If the peak inspiratory flow rate is set excessively high, the patient may become agitated resulting in patient-ventilator asynchrony (Puddy & Younes, 1992). If PSV is being used, WOB_I is lessened if the rate of initial flow delivery is sufficient such that the desired level of PSV is promptly attained (MacIntyre & Ho, 1991).

Based on the above discussion, it is predicted subjects breathing through the 7200ae will have the least WOB_I and PTP and greatest breathing comfort across the study conditions in the present investigation. The 7200ae is flow triggered and has an internal exhalation valve. In a bench study, Branson and Davis (1995) found the WOB_I of this ventilator was 0.07 J/L using a simulated tidal volume of 0.4 L and inspiratory flow rate of 60 L/min. This was significantly lower than the WOB_I under the same conditions of the Aequitron LP-10, a portable ventilator that does not have a demand valve and uses an external exhalation valve (0.19 J/L, $p<0.001$). It is predicted subjects breathing through the Achieva and LTV 1000 will have a greater WOB_I and PTP_I and less breathing comfort compared to when breathing through the 7200ae but less WOB_I and PTP_I and greater breathing comfort compared to breathing through the Univent 754. The Achieva and LTV 1000 are flow triggered but have an external exhalation valve. The Univent 754 is pressure triggered and has an external exhalation valve.

PSV and WOB_I.

WOB_I is inversely proportional to the set level of PSV (Brochard, Harf, Lorino, & Lemaire, 1989; Brochard, Rua, Loino, Lemaire, & Harf, 1991; MacIntyre & Leatherman,

1990). In fact, high levels of PSV can completely unload the respiratory muscles (Slutsky, 1994). By titrating the level of PSV, Banner, Kirby, Blanch, & Layon (1993) were able to reduce WOB_I to zero from 0.6 J/L. In another study, they were able to reduce total WOB to zero by further upward titration of the PSV level (Banner, Kirby, Gabrielli, Blanch, & Layon 1994).

Effects of Increased WOB

Respiratory muscle fatigue.

Respiratory muscle fatigue is defined as "a condition in which there is a loss in the capacity for developing force and/or velocity of a muscle, resulting from muscle activity under load and which is reversible by rest" (National Heart, Lung, and Blood Institute, 1990). Respiratory muscle weakness, in contrast, is not reversible by rest. Roussos and Macklem (1977) were the first to confirm that fatigue occurred in respiratory muscles as it does in skeletal muscles. Other investigators substantiated these findings (Aldrich, Shander, Chaudhry, & Nagashima, 1986; Aubier, Trippenbach, & Roussos, 1981; Hussain, Simkus, & Roussos, 1985).

A framework to examine respiratory muscle fatigue.

A framework based on the command chain for the respiratory muscles is often used to examine respiratory muscle fatigue as illustrated in Figure 14 (Roussos & Moxham, 1985) . In this framework, respiratory muscle fatigue can be caused by central events when the respiratory center in the central nervous system fails to signal the diaphragm. This may protect the diaphragm from damage due to contracting in the face of an unsustainable load (Bellemare & Bigland-Ritchie, 1987). Transmission fatigue

occurs when the signal from the CNS fails to reach the muscle fiber possibly due to axonal conduction failure, inadequate neurotransmitter release, and reduced sensitivity of the cell membrane (Aldrich, 1987). Finally contractile failure can occur if the proper signal is produced and transmitted to the muscle fiber but does not result in a contraction. This may be due to impaired excitation-contraction coupling and build up of adenosine triphosphate breakdown products (Roussos & Zakynthinos, 1996).

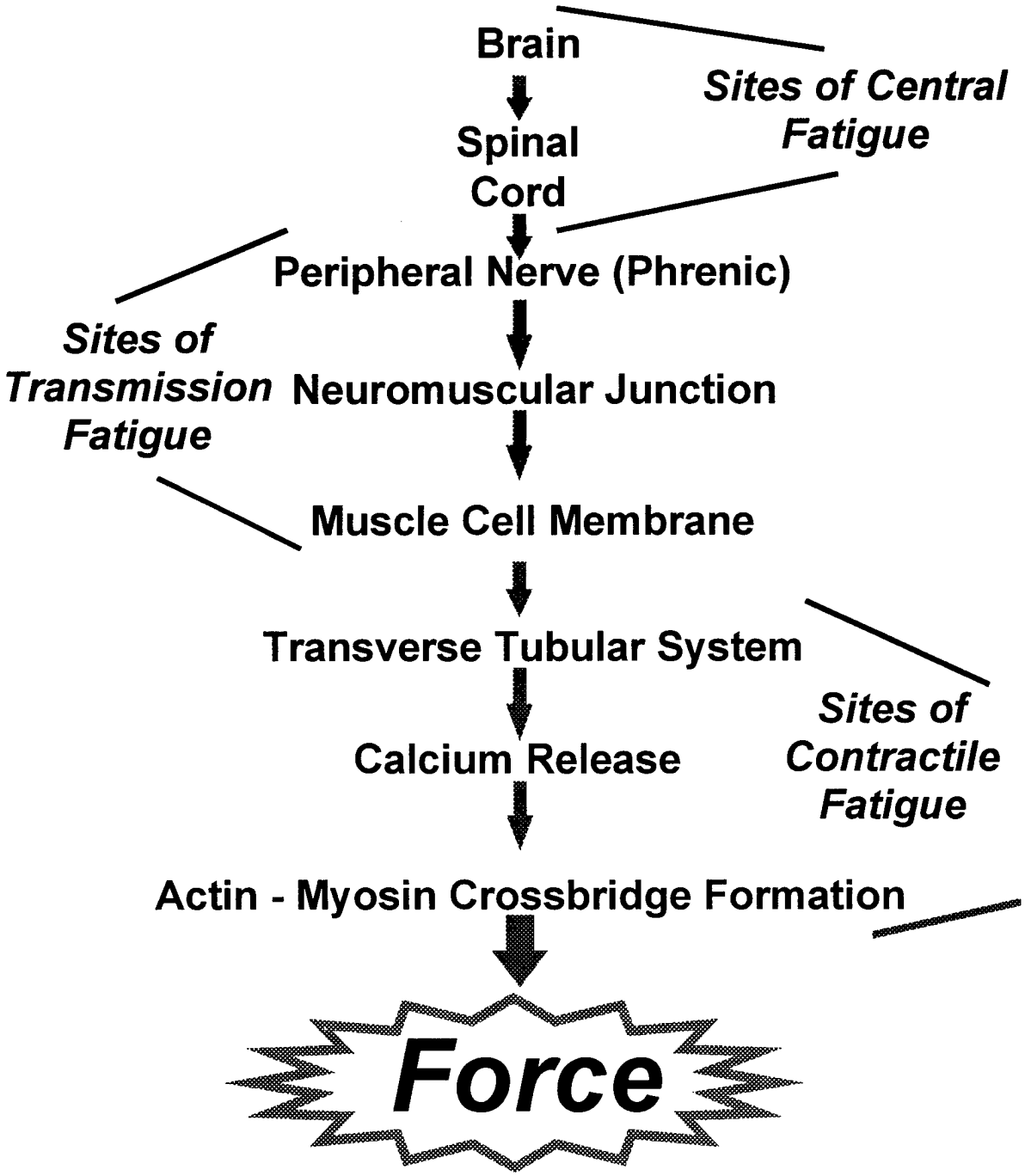


Figure 14. Framework for examining respiratory muscle fatigue. (Redrawn from Roussos & Moxham, 1985.)

The relationship between WOB and respiratory muscle fatigue.

The relationship between WOB and respiratory muscle fatigue is as follows: an excessive work of breathing may tip the balance of respiratory muscle energy supply and demand (see Figure 15). Energy demand outstrips supply resulting in respiratory muscle fatigue. There is a second paradoxical relationship between these two phenomena. If respiratory muscles are completely rested (decreased or no WOB) for an extended period of time such as during mechanical ventilation, atrophy of the diaphragm results. When spontaneous breathing resumes, the diaphragm is weakened and respiratory muscle fatigue may result (Roussos, 1982; Roussos & Zakynthinos, 1996). In summary, respiratory muscle fatigue may result from an excessive WOB and weakening of the respiratory muscles may occur with total resting of these muscles resulting in respiratory muscle fatigue once spontaneous breathing resumes.

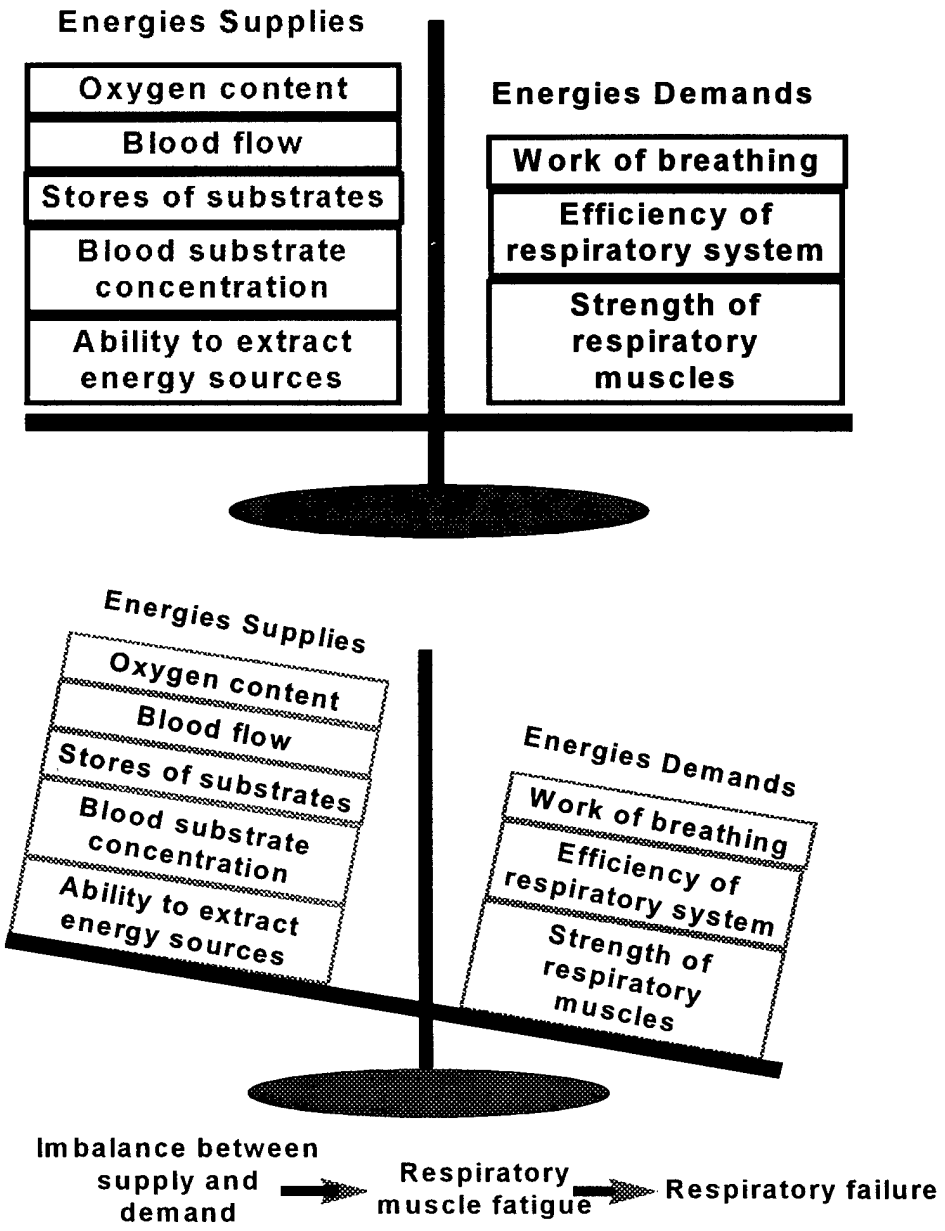


Figure 15. Work of breathing as a determinant of respiratory muscle demand and the result of increased respiratory muscle demand. (Redrawn from Roussos & Zakynthinos, 1996).

Consequences of respiratory muscle datigue due to an increased WOB.

As stated earlier, the imposed work is due to the flow-resistive forces of the artificial airway and mechanical ventilator with associated breathing circuit. Kirton et al. (1993) reported the failure to wean two individuals from mechanical ventilation due to an increase in WOB_I. Both individuals were ventilated using SIMV. In the first patient, this increase in WOB_I was due to malfunction of the ventilator's demand-flow system. The WOB_I decreased from 3.5 J/L when the demand-flow system was malfunctioning to 2.1 J/L after the problem was remedied. In the second patient, the total WOB was 1.8 J/L. This increased WOB was thought to be due to the use of a 7.5 mm internal diameter endotracheal tube for this robust 95 kg, 30 year old male. The patient was extubated resulting in normal ventilation parameters. "Nosocomial respiratory failure" and "iatrogenic ventilator dependency" are terms that have been used to refer to cases such as these where the patient appears to need further ventilatory support not due to physiologic alterations but due to increases in resistance to air flow through the artificial airway and ventilator (Civetta, 1993).

Breathing Comfort

Introduction

While there is a tremendous amount of work addressing the objective quantitative measurement of work expended while breathing spontaneously through an artificial airway and mechanical ventilator, there is a paucity of work addressing the comfort of individuals spontaneously breathing through such devices (MacIntyre, 1995).

Investigations Examining Breathing Comfort

Subjects with pulmonary disease described their feelings when their breathing was troubling them as dyspnea and anxiety (Elliott et al., 1991; Knebel et al., 1994). Based on these findings, Knebel, Janson-Bjerklie, Malley, Wilson, and Marini (1994) assessed breathing comfort using indices of dyspnea and anxiety in 21 adult individuals weaning from mechanical ventilation using SIMV with and without PSV. Horizontal visual analogue scales (VASs) of dyspnea and anxiety were used by these investigators. Knebel et al. found positive correlation between dyspnea and anxiety ($r = 0.55$ and $r = 0.61$ during SIMV and PSV weaning, respectively).

Manning, Molinary, and Leiter (1995) used a VAS to assess breathing discomfort of ten healthy volunteers who were mechanically ventilated. Tidal volume, respiratory rate, and inspiratory flow rate were adjusted until the subjects indicated they were maximally comfortable. At that point inspiratory flow rate was adjusted above and below this point and the blinded volunteers were asked to record breathing discomfort on the VAS. Discomfort scores were higher at the extremes of inspiratory flow with a mean discomfort score of 12.1 at the lowest inspiratory flow and 8.2 at the highest inspiratory flow. These scores were significantly higher than the discomfort scores (mean 4.4) obtained when the inspiratory flow was set at maximally comfortable ($p<0.05$)

Guttmann et al. (1997) examined respiratory comfort of ten healthy volunteers breathing spontaneously through a 7.5 mm internal diameter endotracheal tube fixed to a mouthpiece (i.e., the subjects were not endotracheally intubated) and a mechanical ventilator. The aim of the study was to assess the subject's respiratory comfort when

breathing through three spontaneous breathing modes: inspiratory automatic tube compensation, inspiratory and expiratory automatic tube compensation, and PSV. The blinded subjects were asked to rate breathing comfort immediately following the transition between the breathing modes as better, unchanged or worse. The assessment of respiratory comfort immediately after the transition between modes was selected as Puddy and Younes (1992) found the ventilatory response (change in ventilatory rate) following a transition in inspiratory flow rate was complete by the second breath after the transition. Guttmann et al. found the majority of volunteers perceived the transition from PSV to either type of automatic tube compensation as increasing comfort whereas the opposite transition from automatic tube compensation to PSV was perceived negatively as decreasing comfort ($p<0.01$).

In a randomized, double blind study, Mols et al. (2000) examined the respiratory comfort of fifteen healthy non-intubated volunteers when they breathed spontaneously though a ventilator with proportional assist ventilation (PAV) or PSV. The chest wall compliance was reduced by banding the subject's chest. The subjects were asked to compare breathing comfort using a visual analogue scale when breathing with PAV or PSV to when they were not breathing through the ventilator with their chest not banded. In the second part of the study, the subjects were exposed to shifts in the breathing mode (PAV or PSV) and asked if the change was better, the same, or worse than the prior mode. The investigators found under these conditions respiratory comfort was higher with PAV than for PSV. Mean comfort score breathing with PAV of 8 cm H_2O/L was 9.0 while the mean comfort score with PSV of 10 cm H_2O was 6.5 ($p<0.001$).

Summary

The work accomplished by the individual to breathe is described as the *work of breathing* or WOB. Forces the individual must overcome to breathe include elastic forces, flow-resistive forces, inertial forces, gravitational forces, and distorting forces. Additional flow-resistive forces are present if the individual is breathing through an artificial airway and mechanical ventilator. The work of breathing the individual must perform to overcome these imposed forces is termed the *imposed work of breathing* or WOB_I.

An increased WOB can lead to respiratory muscle fatigue regardless of the cause. This increased WOB can be due to increased elastic, flow-resistive, inertial, gravitational, distorting forces, and/or imposed flow-resistive forces. The practitioner is able to alter the imposed flow-resistive forces by altering the characteristics of the artificial airway, the exhalation and/or PEEP valves, the ventilator design and settings, and presence of pressure support. CCVs have evolved and impose little work due to flow-resistive forces. But what about the flow resistive forces imposed by portable ventilators?

Before this area can be explored, the use of PVs in subacute, transport, and military settings must be described. This discussion will offer a brief history and rationale for use of the PV in each of these settings. Subsequent to this discussion, the concluding section will explore the topic of flow resistive forces imposed by portable ventilators.

Use of PVs in the Home, During Transport, and in Military Settings

Introduction

The use of mechanical ventilators is widespread in modern critical care units. Common indications for mechanical ventilation include real or impending hypoxemic respiratory failure and/or hypercapneic respiratory failure. Broad causes of hypoxemic (defined as a PaO_2 less than 50 torr with an F_IO_2 of 0.5) respiratory failure include hypoventilation, right-to-left shunt, ventilation-perfusion mismatch, and/or incomplete diffusion equilibrium. Etiologies of hypercapneic respiratory failure ($PaCO_2$ >45 torr) can be inadequate central drive, inadequate inspiratory muscle performance, and/or excessive respiratory workload (Aldrich & Prezant, 1994).

Mechanical ventilation was used first to support individuals who were paralyzed due to polio. These patients were cared for in specialized critical care units. Mechanical ventilation soon was used with other individuals including those with lung conditions such as asthma, recovering from surgery, and in the operating room during open-chest procedures. During the 1970's and remainder of the 20th century, mechanical ventilation was used in the home, during transport of ventilator dependent individuals, and in military settings.

Critical care ventilators (CCVs) are typically large, complex, and dependent on a compressed gas source and an external power supply. These attributes hinder their use in the subacute setting, during transport, and in military settings (Branson, 1999). Thus the need for portable ventilators (PVs) was established for use in these settings.

History of Mechanical Ventilation in the Subacute Setting

The first reports of the use of positive pressure ventilation outside of the acute care setting in the United States were in the 1980's (Fisher & Prentice, 1982; Gilmartin & Make, 1983; Sivak, Cordasco, & Gipson, 1983; Sivak, Cordasco, Gipson, & Mehta, 1986; Splaingard, Frates, Harrison, Carter, & Jefferson, 1983). An even earlier program was the Responaut Program in Great Britain, organized by Dr G. Spencer at St. Thomas' Hospital in London. Initially made up of polio survivors in 1965, the program prepared ventilator-dependent individuals (VDIs) for discharge to the home or a variety of community alternatives (Goldberg & Faure, 1984). Similar programs existed in other countries including France and Canada (Goldstein, Psek, & Gort, 1995; Lurie, 1999).

Prevalence and Advantages of Caring for VDIs in the Home

The number of VDIs appears to be increasing with Adams et al. reporting in 1993 there was a 110% increase in VDIs cared for outside of an acute care hospital in Minnesota from 1986 to 1992. Goldberg and Frownfelter (1990) reported 453 VDIs in the state of Illinois. Extrapolating from those data; Bach, Intintola, Alba, and Holland (1992) estimated in the early 1990's there were greater than 11,000 VDIs in the United States.

There are a number of advantages in caring for the VDI in the home. These include decreased risk of nosocomial infection, increased mobility, and improved nutritional status (Banaszak, Travers, Frazier, & Vinz, 1983; Lehner, Ballard, Figueroa, & Woodruff, 1980; Sivak, Cordasco, & Gipson, 1983). Results of investigations examining the psychosocial aspects of home care suggest both the VDIs and their families have

higher morale and an increased sense of control when the VDI is cared for in the home compared to institutional care (Frace, 1986; Gipson, Sivak, & Gulledge, 1987). There are fiscal advantages as well. Adams et al. (1993) reported the cost of caring for a VDI in the home was $6,557 per month compared to approximately $64,513 per month for caring for a VDI in a critical care unit (1986 dollars). Scheinharon, Artinian, and Catlin (1994) reported the cost of caring for a VDI in the home was $405 per day compared to $600 per day for caring for the VDI in an extended care facility.

Challenges of Transporting the VDI

Individuals requiring ventilation during transport present unique challenges to health care professionals. These challenges include not only assuring effective ventilation but also the requirement for vigilant management of the myriad of other monitoring and life-sustaining devices attached to or accompanying these individuals. Complications that may occur during transport of the individuals who require ventilation include accidental extubation, intubation of a mainstem bronchus, disconnection of the oxygen source, battery failure, infiltration of intravenous infusions, poorly controlled fluid management, and inadequate chest tube functioning (Stearley, 1998). Transport of a mechanically ventilated individual is therefore quite complex. Given the potential for adverse events during transport, a safe and reliable system to maintain ventilation, and thereby effective airway and breathing, is essential.

Mechanical Versus Manual Ventilation During Transport

Investigators have examined the effects on blood gas values of manual ventilation with a self-inflating resuscitation bag compared to a PV in individuals during transport.

Braman, Dunn, Amico, and Millman (1987) found 14 out of 20 individuals ventilated using a manual resuscitation bag during transport had changes in $PaCO_2$ greater than 10 torr and changes in pH greater than 0.05. These changes occurred both above and below the baseline values. There were significantly less swings in these parameters when a PV was using during transport ($p < 0.01$). The authors did not speculate why there were shifts in these parameters in both directions. The subjects were not randomized nor were the study personnel blinded. The authors concluded proper monitoring of ventilation must be done during patient transport.

Gervais et al. (1987) reported the findings of a randomized study where 30 critically ill individuals were ventilated during intrahospital transport via one of three methods: using a PV, using a self-inflating bag with the rate and tidal volume delivered governed by the judgment of the operator, or by using a self-inflating bag with an accompanying volumeter. The investigators suggested individuals ventilated with a manual self-inflating bag with no objective tidal volume measurement tended to be hyperventilated. The mean $PaCO_2$ was 34 torr after ventilation with this method compared to a mean $PaCO_2$ of 41 torr prior to transport while ventilated with a CCV ($p < 0.05$). Hyperventilation with accompanying alkalemia produces a shift of the oxyhemoglobin curve to the left risking decreased oxygen availability to the tissues. Other results of acute respiratory alkalosis due to hyperventilation include dysrhythmias, tachycardia, decreased myocardial contractility and stroke volume, and reduced myocardial and cerebral blood flow. These authors concluded safe manual ventilation during patient transport is possible with monitoring of tidal volume but did not comment

in respiratory rate.

These findings were confirmed by Hurst et al. (1989). In this study, 28 critically ill individuals were randomly assigned to be ventilated during transport with a self-inflating resuscitation bag operated by an experienced critical care nurse or respiratory therapist without objective measurement of delivered VT or ventilated with a PV. Those individuals who were manually ventilated exhibited blood gas values compatible with acute respiratory alkalosis with a mean pH of 7.51 compared to a pH of 7.40 after ventilation with a PV ($p < 0.05$). These authors recommended using a mechanical ventilator during transport or using manual ventilation with monitoring of tidal volume.

In contrast to the findings of the investigations discussed above, Weg and Haas (1989) reported no significant changes in blood gas values when individuals were manually ventilated during intrahospital transport. In this nonrandomized, nonblinded study, 20 critically ill individuals were manually ventilated with a resuscitation bag during transport with arterial blood gas specimens obtained before, during, and after transport. The operator of the manual resuscitation bag was an experienced respiratory therapist and did not use any tidal volume monitor. Only one of these 20 subjects was found to have acute respiratory alkalosis with manual ventilation. However, overall there was a tendency for pH to rise and $PaCO_2$ to fall during transport. These authors concluded mechanical ventilation is expensive and unnecessary for the intrahospital transport if the operator of the manual resuscitation bag is experienced and aware of the tidal volume delivered with each resuscitation bag deflation.

Advantages of Mechanical Ventilation During Transport

Overall these studies provide information on two primary advantages of mechanical ventilation during transport: the potential for less alterations in ventilation as evidenced by changes in arterial blood gases and liberation of one of the transport team members from the duty of manual ventilation. In addition, ventilation can be better assured when the patient is transported through narrow doorways, elevators, and other locations where the provider may not have ready access to the manual resuscitation bag. The disadvantages of using a PV during transport include expense and reliance on a complex mechanical device that is costly and requires personnel to be trained in its use.

Mechanical Ventilation During Pre-, Intra-, and Interhospital Transport

Mechanical ventilation can be used during transport of the victim from a field setting to a medical facility (prehospital), during transport of the patient inside the hospital (intrahospital), and while the patient is transported from one hospital to another (interhospital). The ventilatory requirements of the individuals in each of these scenarios are different depending on the real or impending ventilatory failure and concurrent diseases and/or injuries.

Mechanical ventilation is used with varying frequencies in transport. Perez, Klofas, and Wise (2000) reported the results of a national survey where 250 air transport agencies were queried regarding method of ventilation of intubated individuals. Among the sample were various combinations of rotor-, fixed-wing, and critical care ground transport programs. About 40% of the responding programs used rotor-wing transportation alone. The survey response rate was 77%. Of the 193 surveys returned,

37.3% of the programs used manual ventilation for intubated individuals, 10.9% used a mechanical ventilator, and 45.5% used a combination of these techniques.

The individuals requiring mechanical ventilation in the prehospital setting include trauma victims and those who have suffered ventilatory arrest with or without cardiac arrest. This setting can be hostile in terms of temperature, noise, vibration, and moisture. Mechanical ventilators used in this setting must be particularly lightweight, robust, and relatively simple to operate (Branson, 1999). Electrical power and compressed gas supplies are limited, a situation which points to the need for efficient use of these perishable commodities.

The intrahospital transport of mechanically ventilated individuals includes transport between the emergency department and operating room, operating room and recovery room, recovery room and critical care unit, and the critical care unit and radiologic suite. A common reason for intrahospital transport of the mechanically ventilated patient is to allow for computerized tomography (CT) (Hurst et al., 1992; Indeck, Peterson, Smith, & Brotman, 1988). These transports can last over one hour, although transport to the CT suite could become less common with the introduction of a portable CT device (Mirvis, 1999). These individuals are often critically ill and suffer from pulmonary conditions such as acute respiratory distress syndrome (ARDS). In order to provide the same level of ventilatory support during transport, PVs used in this setting must be on par with CCVs. Requirements would include the ability to deliver an accurate tidal volume even within individuals with low pulmonary system compliance and high resistance as well as the ability to accomplish a variety of modes of ventilation and end-expiratory pressure while

imposing a minimal work of breathing.

Interhospital transport is usually accomplished to move the patient to a medical center that can provide level of care that is different than at the sending hospital. This care can be for trauma, obstetrics, neonatal intensive care, neurosurgery, and organ transplantation. As suggested by the findings by Pearl, Mihm, and Rosenthal (1987), most of these individuals have cardiovascular or pulmonary dysfunction.

The mode of transportation for these prehospital and interhospital transport include both rotor- and fixed wing aircraft. The cabin pressure in pressurized airplanes is usually equivalent to 8000 feet or 2400 meters. Rotor-wing aircraft are not usually pressurized and may have to fly at altitudes higher than 8000 feet. The consequences of the decrease of barometric pressure at higher altitudes include a lower ambient partial pressure of oxygen with a concomitant lower P_AO_2. If the patient is ventilated with an enriched oxygen mixture this is of little consequence. Other effects include the increase of the volume of closed spaces containing gas such as the cuff of an endotracheal or tracheostomy tube and in the middle ear. As the barometric pressure decreases, the density of gas diminishes which will affect the accuracy of the tidal volume delivered by a fluidically controlled ventilator (Branson, 1999). Mechanical ventilators used for interhospital transport, like those used during intrahosptial transport, must be able to approach the level of performance of a CCV for uninterrupted care. This includes functioning in modes that allow spontaneous breathing while imposing a minimal work of breathing. As will be seen in the following section, the military setting offers many of the same challenges as the transport setting.

Uniqueness of the Military Setting

Finally, PVs are used in military settings. Extremes in ambient temperature, noise, vibration, and limited sources of electrical power as well as compressed gases such as oxygen and air are some of the factors present in a military setting. In addition there exists the added possibility of incoming enemy fire, limited logistical support, and variable transport times (Farmer, 1996; Topley, 1998a & 1998b).

Changing Casualty Care Doctrine

From World War II through the Vietnam War and into the mid-1990's, United States Air Force (USAF) doctrine called for transportation of physiologically stabilized individuals. Despite the extensive use of air transport for patient movement during the Vietnam War as evidenced by approximately 55,000 patient movements during the first five months of 1969, the vast majority of these individuals were stable. This doctrine dictated the establishment of adequate medical assets near the combat zone where near-definitive surgery could be performed and individuals could recover to the point where they were stable enough to transport (Mabry et al., 1993).

Since the Vietnam War, this doctrine has proved problematic as the nature of military operations has not allowed for adequate placement of medical assets near the combat zone. In the 1983 bombing of the Marine barracks in Beirut, 88 casualties (19 of whom were critically injured) were flown to fixed medical facilities in Europe (Mabry et al., 1993). During Operation Just Cause in 1993, there was a logistical failure to transport the entire field hospital to Panama, resulting in the unexpected air evacuation to the United States of 192 fresh casualties during the first 24 hours of the operation (Dice, 1991).

Many of these individuals required manual ventilation and ongoing intravenous fluid resuscitation during transport. In both of these situations, wounded individuals were placed into an aeromedical transport system that was not staffed or equipped to meet their needs. Finally, in Operation Desert Storm insufficient in-theater medical assets to care for the anticipated number of casualties occurred and it was anticipated there would again be a need to transport critically ill individuals. A temporary fix of the aeromedical evacuation system was undertaken with the temporary assignment of personnel and equipment to these aeromedical evacuation units (Mabry et. al., 1993).

As a result of the 1991 conference on aeromedical evacuation, USAF doctrine covering the aeromedical transport now calls for the capability for the delivery of critical care, including mechanical ventilation, within the air evacuation system. This includes having these capabilities on-board aircraft and at patient transfer points (Mabry et al., 1993). Two case reports detail use of mechanical ventilation with critically ill trauma individuals during aeromedical evacuation by the United States Air Force (Topley, 1998a, 1998b).

Summary

PV use followed the use of ventilators in the critical care setting. The literature supports the use of PVs in the home, during transport, and in military settings. The overall challenge to the manufacturers of PVs is to produce a simple, robust, and affordable PV that performs to the level of a CCV. Part of that challenge is the PVs performance in modes that allow spontaneous breathing. Basic to performing in these modes is the resistance to airflow offered by PVs. The final section examines this issue

including the in vitro studies that have reported the WOB_I of PVs, recommendations of professional organizations regarding the use of PVs in spontaneous breathing modes, and recent investigations that have looked at the WOB_I of newer PVs.

Resistance to Airflow Through PVs and WOB When Used in Spontanesous Breathing Modes

Introduction

The American Society for Testing and Materials (ATSM) has established standards for electrically powered home care ventilators that includes PVs (ASTM, 1991). These standards address aspects of these ventilators including the external electrical power supply, battery requirements, controls, indicators, alarms, and delivered tidal volume. However these standards do not address resistance to inspiratory flow through these ventilators during spontaneous breathing.

In Vitro Studies Examining the WOB_I of Portable Ventilators

Kacmarek et al. (1990) used a model of spontaneous breathing to examine the imposed work of breathing produced by resistance to inspiratory flow through PVs during spontaneous breathing. This group tested five home care ventilators used in the SIMV or IMV modes with a variety of humidification devices. They found the WOB_I of these ventilators when set up according to the manufacturer's recommendations to range between 0.332 and 0.616 J/L. This essentially equals the work associated with moving the lung in a normal healthy adult (physiologic work of breathing), 0.3 to 0.6 J/L (Otis, 1964). Thus the total work of breathing for an adult breathing spontaneously through one of these ventilators would be approximately 0.632 to 1.2 J/L or double the physiologic work

of breathing. The cause of this WOB_I was suspected to be the method these ventilators employed to draw gas through the inspiratory circuit when the patient is spontaneously breathing. CCVs typically use a demand valve (opened by the patient's inspiratory effort) that provides a gas flow for the patient to breathe. To provide gas flow during spontaneous breathing these home care ventilators use methods such as drawing air through the air-intake valve of the piston chamber itself, through an anti-suffocation valve located within the device between the piston and exit port for gas flow from the ventilator, and via the exhalation valve of the ventilator circuit. The WOB_I was decreased to between 0.009 and 0.083 J/L by modifying the ventilators. The modification consisted of adding a one-way H-valve system distal to a pass-over humidifier or a humidity-moisture exchanger (HME). Gas for spontaneous breathing was drawn through this lower resistance system. Using these ventilators in spontaneous breathing modes imposed an excessive work of breathing that essentially doubled the total work of breathing. Kacmarek et al. recommended these home care ventilators should not be used in the SIMV/IMV modes unless an H-valve with a passover humidifier or HME is appropriately placed in the system.

Branson and Davis (1995) compared the imposed work of breathing produced by resistance to inspiratory flow through three home care ventilators, a CCV and a prototype ventilator designed for subacute care. The home care ventilators provided gas flow during spontaneous breathing using methods described by Kacmarek et al (1990). The CCV and the prototype ventilator both provided gas for spontaneous breathing using a demand valve opened by the subject's inspiratory effort. During simulated quiet breathing with a

tidal volume (V_T) of 0.2 L, and an inspiratory flow rate of 30 L/min, the WOB_I of the home care ventilators ranged between 0.09 to 0.14 J/L while the WOB_I of the CCV and prototype ventilator were 0.012 and 0.005 J/L, respectively. As simulated breathing demand increased (V_T = 0.6 L, inspiratory flow rate of 90 L/min) the WOB_I of the three home care ventilators ranged between 0.33 to 0.57 J/L while the WOB_I of the CCV and prototype ventilator were significantly less (0.04 and 0.03 J/L, respectively). Substantiating the findings of Kacmarek et al., the authors also recommended these home care ventilators not be used in IMV/SIMV modes without modification.

Recommendations of Professional Organizations Regarding the Use of PVs in Spontaneous Breathing Modes

The American Association for Respiratory Care (AARC) addressed these findings in their clinical practice guideline on Long-Term Mechanical Ventilation in the Home (Robart, Make, McInturff, Tureson, & Weimer, 1995). The authors of this guideline recommended not using home care ventilators in the SIMV or IMV modes without modifications described above which added to the size and weight of the PVs. The American College of Chest Physicians consensus statement regarding mechanical ventilation outside of the critical care unit (Make et. al., 1998) also states the method of delivering gas during spontaneous ventilation varies among home care ventilators and does not recommend using home care ventilators in the SIMV or IMV modes without the modifications previously described.

Recent In Vitro Investigations Examining the WOB_I Resulting From the Use of PVs

The findings of a recent study by Austin et al. (2001) suggested design changes in

home care ventilators have resulted in lower resistance during inspiration with a lower WOB_I during spontaneous breathing. These investigators used a model of spontaneous breathing to assess WOB_I of ten PVs, four of which are marketed as home care ventilators with the remainder marketed as transport ventilators. Three of these ventilators possessed a demand valve, which when opened by the patient's inspiratory effort delivered a flow of gas. The fourth (older) ventilator did not have a demand valve and required the patient to draw gas during spontaneous breathing through the air-intake valve of the piston chamber itself, through an anti-suffocation valve located within the device between the piston and exit port for gas flow from the ventilator, and via the exhalation valve of the ventilator circuit

During simulated breathing at a VT of 0.5 L with an inspiratory flow rate of 60 L/min, these three newer home care ventilators produced a WOB_I of 0.013 to 0.067 compared to a WOB_I of 0.386 J/L for the older home care ventilator. The WOB_I produced under these conditions by these newer home care ventilators was closer to the WOB_I produced by a CCV (Branson and Davis, 1995).

Summary

The work of breathing imposed by PVs when used in spontaneous breathing modes may be significant. This fact has lead to professional organizations recommending PVs be modified if used during spontaneous breathing. Findings of a recent study suggested the work imposed by newer generation PVs is insignificant Austin et al. (2001).

All of the investigations reported in the literature examining the flow-resistive forces of PVs and resulting WOB_I when used with spontaneous breathing were in vitro

studies. Examination of the flow-resistive forces and resultant WOB imposed by PVs using human subjects is the area most in need of investigation.

Mechanical models of spontaneous breathing are efficient in terms of time and risk to human subjects. However these models suffer two major drawbacks. The first is a mechanical model does not challenge the ventilator compared to actual human breathing. The mechanical models are driven by another mechanical ventilator (driving ventilator). While the tidal volume, inspiratory flow rate, and breathing rate can be set on the driving ventilator, what results is a monotonous breathing pattern that is predictably the same breath after breath. Thus the ventilator being studied is not challenged to make breath-by-breath changes in tidal volume, rate, and/or inspiratory flow.

The other major drawback of a mechanical model of spontaneous breathing is there is no way of evaluating the human response of breathing spontaneously through these devices. Nurses are concerned not only with the physiologic consequences of mechanical ventilation but also the individuals' response. As noted earlier there are few studies in the literature that report the breathing comfort of subjects while breathing through a ventilator and no investigations that report the breathing comfort of PVs.

The present investigation is the first to examine the WOB of humans when breathing through a PV. This investigation is also the first to examine the breathing comfort of these devices. By doing so, it adds to the body of knowledge addressing WOB_I and breathing comfort. Based on the findings of the in vitro studies examining WOB_I and PVs, this study is next logical step in this program of research. By quantifying the work imposed by PVs and the breathing comfort of subjects breathing spontaneously

with PVs, this study has the potential to improve the care of individuals whose breathing is supported with a PV. This study also has the potential to change the recommendations of professional bodies regarding the use of PVs with spontaneously breathing individuals.

CHAPTER III

METHOD

Purpose of the Study

The purpose of this study was to assess WOB_I, PTP_I, and breathing comfort of nonintubated healthy volunteers breathing through a sample of portable ventilators (PVs) and a critical care ventilator CCV in a controlled environment. A mouthpiece was attached to an endotracheal tube that will in turn was attached to the ventilator circuit.

By measuring the airway pressure at the tip of the endotracheal tube; the WOB and PTP imposed by the PV and endotracheal tube were examined. This represents a compromise between using no endotracheal tube and actually endotracheally intubating each participant. Actual intubation places a huge burden on the participant in terms of discomfort and risk as well as increases the expense and complexity of the investigation. On the other hand, having the participant breathe through the endotracheal tube attached to a mouthpiece adds resistance to the breathing circuit that is present in a real-world application.

Prior investigations examined the WOB_I (work that must be performed to overcome the resistance to flow through the PV) using a lung model of simulated breathing, however no other investigators have examined the WOB_I, PTP_I and breathing comfort of humans breathing spontaneously through PVs.

Portable Ventilators

A sample of three PVs (one of each model) were used: Achieva PS (Mallinckrodt, Inc., St. Louis, MO), LTV 1000 (Pulmonetic Systems, Inc., Colton, CA), and Univent

754 (Impact Instrumentation Corp., West Caldwell, NJ). These PVs were selected based on availability, their capability to self-generate compressed air, and their method of producing compressed air (Achieva PS, piston; LTV 1000, turbine; Impact 754, compressor). While the Achieva PS is substantially larger (about 15 kg) than the LTV 1000 and Univent 754 (about 6 kg), it represents a new generation of portable ventilators using a piston to generate compressed air used in the home. The CCV selected was the Puritan 7200ae (Mallinckrodt, Inc., St. Louis, MO). It would have been desirable to base the selection of the ventilators on investigations or surveys of users of PVs and CCVs. An exhaustive search of the literature failed to reveal such a publication. Therefore two experts in the field of mechanical ventilation, R. D. Branson, RRT and R. S. Campbell, RRT were interviewed and asked which modern PVs were popular and which CCV they would select as being widely used (personal communication, May 2, 2000). Together these individuals have over 75 publications in refereed journals with most covering aspects of mechanical ventilation. An additional reason for selecting the Univent 754 is it is the portable ventilator currently in the Department of Defense inventory. The 7200ae has been selected as a widely used CCV in past investigations (Branson & Davis, 1995). Finally the ventilators were selected based on their availability to the investigator.

These design characteristics are predicted to influence WOB_I, PTP_I and breathing comfort (see Table 1). For example, flow triggering has been suggested to be superior to pressure triggering and placing the exhalation valve in the breathing circuit may be inferior to placing it in the ventilator (Branson et al., 1994; Sassoon et al., 1989.

Research Hypotheses

Based on the design characteristics of the ventilators and prior in vitro investigations, when breathing through an 8.0 mm internal diameter endotracheal tube attached to a mouthpiece with an F_IO_2 of 0.4 across the following four combinations of pressure support and CPAP (0 cm H_2O and 0 cm H_2O, 10 cm H_2O and 0 cm H_2O, 0 cm H_2O and 5 cm H_2O, 10 cm H_2O and 5 cm H_2O):

1. The WOB_I with 7200ae < Achieva = LTV 1000 < Univent 754.
2. The PTP_I with 7200ae < Achieva = LTV 1000 < Univent 754.
3. The breathing comfort reported by subjects breathing with the 7200ae > Achieva = LTV 1000 > Univent 754.

Basic Study Design

This was a single blind 4 X 2 X 2 multi-factorial repeated measure design (Winer, 1962). The first factor is the ventilator type with four levels (Achieva, LTV 1000, Univent 754, 7200ae). The next factor is continuous positive airway pressure (CPAP) ventilation with two levels (0 and 5 H_2O). The final factor is pressure support ventilation (PSV) with two levels (0 and 10 H_2O). These are all fixed effects and there are a total of 16 treatment combinations. Table 2 illustrates these treatment combinations.

Table 2

4 X 2 X 2 Table Illustrating the Study Design with Factors and Levels

			Ventilator			
				LTV	Univent	
		PSV (cm H_2O)	Achieva	1000	754	7200ae
CPAP (cm H_2O)	0	0	X1	X2	X3	X4
		10	X5	X6	X7	X8
	5	0	X9	X10	X11	X12
		10	X13	X14	X15	X16

Note. CPAP = Continuous positive airway pressure, PSV = Pressure support ventilation. The Univent 754 does not offer PSV so a placebo of PSV = 0 cm H_2O was used when the design called for the Univent to deliver PSV = 10 cm H_2O

The Cook and Campbell (1979) diagram of the investigation is below.

$O_{1(Control)}$ X_1 X_2 X_3 X_4 $O_{2(Control)}$ X_5 X_6 X_7 X_8 $O_{3(Control)}$ 10 minute break $O_{4(Control)}$ X_9 X_{10} X_{11} X_{12} $O_{5\ (Control)}$ X_{13} X_{14} X_{15} X_{16} $O_{6(Control)}$

The issue of subject fatigue during the investigation was addressed by interspersing control observations throughout the investigation. The control observations ("O") represent measurement of peak negative inspiratory pressure ($P_i$max) and breathing comfort with the subject breathing through the endotracheal tube with hydroscopic heat and moisture exchanger filter and pneumotachograph. $P_i$max is an indicator of respiratory muscle fatigue (Black & Hyatt, 1969; Moxham, 1990).

The treatments ("X") represent a combination of ventilator, continuous positive airway pressure (CPAP) and pressure support ventilation (PSV). The four possible combinations of CPAP and PSV, in cm H_2O, are 0/0, 0/10, 5/0, 5/10. During each treatment, WOB_I, PTP_I, and breathing comfort data were gathered while the subject is breathing through the endotracheal tube attached to the mouthpiece, hydroscopic heat and moisture exchanger filter, and pneumotachograph attached to the ventilator.

Note one PV, the Univent 754, does not deliver PSV. When the Univent 754 was to deliver PSV, a placebo setting was used with PSV = 0 cm H_2O. The Univent 754 was not compared to the other ventilators when delivering PSV of 10 cm H_2O.

Design Advantages and Disadvantages

The chief advantage of the repeated measures design is economy of subjects. This is particularly important in the present investigation, as there is significant subject burden in terms of time and discomfort. Another advantage of the repeated measures design is control over individual differences between subjects, as the individual subject will serve as his/her own control.

Disadvantages include carry-over effects lessened by randomizing the sequence of treatments (ventilators, CPAP, PSV). Other chief disadvantages include history, maturation, statistical regression, testing, instrumentation, and attrition. History and maturation were addressed by randomization of the treatment sequence for each subject and measurement of maximal inspiratory pressure ($P_i max$) and breathing comfort prior to data collection and after 4, 12, and 16 data collection periods. Testing was addressed by randomization. Instrumentation was addressed by each subject acclimatizing to test equipment prior to the start of the investigation. Randomization of the sequence of treatments helped lessen carry-over effects between treatments (Cook and Campbell, 1979). All data was collected in one session, lessening subject attrition. In addition the subjects collected a payment of $50 only after they completed the study as an incentive to participate.

Randomization

The order of the ventilator was assigned to the subjects in a randomized fashion. Also the order of CPAP, PSV combinations were also completely randomized within subjects. Sixteen envelopes were prepared prior to starting the investigation. Contained

in these envelopes were the order of ventilators, CPAP, and PSV for that subject. A possible randomization schedule is located in Appendix B).

Description of Subjects

The subjects were healthy males and females recruited from the staff and faculty of the Colleges of Nursing and Medicine as well as staff members from University Hospital.

Inclusion Criteria

Nonobese (body mass index less than 30) healthy males and females between the ages of 18 and 65 years (National Heart, Lung, and Blood Institute, 1998). Participant height was measured using a steel height scale and weight was measured using a calibrated scale. Body mass index was calculated using the National Heart, Lung, and Blood Institute's body mass index calculator found at http://www.nhlbisupport.com/bmi.

Exclusion Criteria

History or Present Symptoms of Cardiopulmonary Disease

A participant with symptoms of cardiopulmonary disease may suffer dyspnea. The participant may perceive this dyspnea as breathing discomfort (Ingram & Braunwald, 2000). If the participant experiences dyspnea during the investigation, the breathing discomfort they rate may in fact not be due to the ventilator but due to intrinsic disease. Pulmonary function tests were not performed prior to the investigation as symptoms indicating significant pulmonary disease are likely revealed by questioning the subject (Smetana, 2000).

Symptoms of an Upper or Lower Respiratory Infection Either at the Time of the Study or in the 30 days Prior to the Study

A participant with a current or recent respiratory infection may suffer breathing discomfort due to inflammation of the pharyngeal and/or laryngeal mucosa (Brandenburg et al., 2000; Corey, Houser,& Ng, 2000). The breathing discomfort could be exacerbated by breathing the dry air/oxygen mixture.

Active Oral or Perioral Lesions

While the breathing filter is 99.99% efficient thus reducing the likelihood of breathing circuit contamination, it is likely a participant with active or perioral lesions would experience discomfort with the breathing apparatus (Chandrasekar, 1999).

Symptoms of Sinusitis Either at the Time of the Study in the 30 Days Prior to the Study

The participant with current or recent symptoms of sinusitis (facial pain, tooth pain, persistent cold-like symptoms) may perceive their symptoms as breathing discomfort produced by the ventilator (Brooks et al., 2000).

Recent Nasopharyngeal Surgery

Application of the noseclips could be painful to participants who have recently (in the last 30 days) had nasopharyngeal surgery.

Smoking

Smoking is an irritant to the airways. This irritation could be perceived by the subject as breathing discomfort. Subjects are excluded if they have smoked tobacco or other substances within eight weeks of the investigation (Smetana, 2000).

Number of Subjects

A power analysis was attempted based on investigations with a mechanical lung model. This was not successful due to the large difference in the WOB_I between the

ventilators and the small variance. For example, at a simulated tidal volume of 0.5 L with an inspiratory flow rate of 60 L/min, the WOB_I for the LTV 1000 was 0.004 J/L (SD 0.0007) while the WOB_I for the Univent 754 was 0.045 J/L (SD = 0.0171) (Austin et al., 2001). A power analysis based on these data suggests only two subjects are needed for a power of 0.8 with $p <$ or equal to 0.05. Therefore a power analysis (power 0.8, $p <$ or equal to 0.05) was done using the data gathered from the first sixteen subjects of the present study.

Methods of Measurement

Introduction

WOB_I, PTP_I, and $P_i max$ are biometric variables derived from measurements of flow, volume, and/or pressure. Breathing comfort is a supplemental subjective measure and is the sensation of satisfying breathing of the participants and was assessed using a visual analogue scale similar to the method used by Mols et al. in their 2000 investigation. The following describes how these variables were measured.

Flow

Flow was measured using a Fleisch type pneumotachograph (Hans Rudolph, Kansas City, MO) with a linear output between 0 and 400 L/min. Pneumotachographs are devices designed to produce a pressure drop when exposed to a given flow rate. It is the pressure drop that is actually measured and flow rate is then inferred from the pressure measurement (Sullivan, Peters, & Enright, 1984).

In a Fleisch type pneumotachograph, gas passes through a bed of capillary tubes and pressure is measured before the gas passes through the tubes and after exiting the

tubes. The basic principle behind a Fleisch type pnumotachograph is the tubes are of such small diameter that near their center flow is essentially one-dimensional and relatively steady. Poiseulle's Law for steady flow through a pipe shows the pressure drop is linearly related to the volume flow rate.

$$\Delta P = (8nl/\pi r^4)Q$$

In this equation, ΔP is the change in pressure, n is the viscosity of the fluid in the tube, , and l is the length of the tube, r is the radius of the tube, and Q is the volume flow (Sullivan et al., 1984).

The pressure drop across the pneumotachograph was measured using a differential pressure transducer (Special Instruments, Nördlingen, Germany). The analogue signal was converted to digital signal using a analogue to digital board (National Instruments, Austin, TX). The digital signal then will travel to a personal computer (WinBook, Hillard, OH) programmed with Labview software (National Instruments, Austin, TX). The program calculates flow from the pressure drop. Flow is graphically and digitally displayed on a breath-to-breath basis.

Volume

Volume is derived from flow. Here the flow signal is integrated with time resulting in volume (Sullivan et al., 1984). This is accomplished using the Labview Software (Austin, TX) and is displayed digitally and graphically on a breath-by-breath basis.

Pressure

Pressure was measured at the tip of the endotracheal tube (Mallinckrodt, St Louis, MO) using a pressure transducer (Special Instruments, Nördlingen, Germany). The pressure tubing consisted of nondistensible plastic tubing. Output from the transducer is linear between –80 and 80 cm H_2O. The analogue signal was converted to digital signal using an analogue to digital board (National Instruments, Austin, TX). The digital signal then traveled to a personal computer (WinBook, Hillard, OH) programmed with Labview software (National Instruments, Austin, TX). Pressure was graphically and digitally displayed on a breath-to-breath basis.

Calibration

Measurement error of the system is +/- 2% (Special Instruments, Nördlingen, Germany). Flow and volume calibration was assessed prior to gathering data on each participant using a 0.5 L calibration syringe (Hans Rudolph, Kansas City, MO). Pressure calibration was assessed using a U-tube water manometer (Hans Rudolph, Kansas City, MO). A measurement error of +/- 2% was accepted for these three parameters.

Frequency Response

The frequency response of the system was 100 Hz, well above maximum recommended frequency response of 60 Hz for pulmonary function instruments (Miller , Scacci, & Gast, 1987).

Calculation of WOB_I

By definition work (W) is performed when a force (F) moves its point of application over a given distance (D). This is described by the following equation:

$$W = F \times D$$

In a fluid system, such as the respiratory system, work (W) is performed when a pressure (P) changes the volume (V) of the system (Mador et al.,1993; Otis, 1964).

$$W = P \times V$$

This concept is used when examining work due to imposed resistances of artificial airways, ventilators, and other devices both in investigations using lung models and human subjects (Austin et al., 2001; Bolder et al., 1986; Branson et al., 1994; Branson, & Davis, 1995; Calzia et al., 1998; Kacmarek et al., 1990; Katz et al., 1985). In these studies as in the current investigation, WOB_I was determined using the pressure at the proximal airway (proximal to the endotracheal tube) which is distal to the resistance imposed by the endotracheal tube and mechanical ventilator rather than pleural pressure. This pressure is displayed on the X axis of the pressure-volume plot with volume displayed on the Y axis. Imposed work that area of the curve to the left of the baseline airway pressure as shown in Figure 2. This area was mathematically calculated using the LabView software (National Instruments, Austin, TX) and displayed digitally on a breath-by-breath basis as mJ/L.

Calculation of PTP_I

PTP_I was calculated using the method described by Calzia et al. (1998). PTP uses pressure measured in the esophagus during inspiration hence accounts for the effects on

this pressure of the compliance of the lungs and chest wall and the resistance of the airways, both physiologic and imposed. On the other hand, PTP_I uses pressure measured proximal to any imposed resistances, such as a ventilator and artificial airway. Thus PTP_I reflects the effect of imposed resistances on oxygen consumption of the respiratory muscles. Below is the formula for PTP_I. The calculations were performed using the LabView software (National Instruments, Austin, TX) and displayed on a breath-by-breath basis as cm H_2O/sec/min.

$$PTP_I = \int_0^{T_I} P * dt$$

Where P is the pressure measured at the tip of the endotracheal tube.

$P_i$max

$P_i$max is a measure of respiratory muscle fatigue (Moxham, 1990; Black & Hyatt, 1969). It is obtained by having the subject inspire near or at residual volume. $P_i$max was measured using the previously described pressure transducer.

Breathing Comfort

Breathing comfort was measured using a 100 mm horizontal visual analogue scale (VAS) (see Appendix C). Both horizontal and vertical VASs have been demonstrated to yield equally valid measures (Gift, 1989a). Results of clinical investigations by Scott and Huskisson (1976) using a VAS to measure pain and Gift (1989b) using a VAS to measure dyspnea suggest a vertical VAS may be easier for clinical subjects to use. Congruent with

the unipolar nature of the VAS, the anchor used on the left (low) end of the scale was "Breathing as uncomfortable as it could possibly be" and the anchor used on the right (high) end of the scale was "Breathing as comfortable as it could possibly be" (Gift, 1989a). A right angle stop was placed at each end of the 100 mm horizontal line and the anchors were placed beyond these right angle stops (Wewers & Lowe, 1990). Validity and reliability of the VAS was assessed as described below.

Pretest Investigations

Data from a pretest investigation supported the validity and reliability of the breathing comfort visual analogue scale. A blinded sample of 10 healthy non-intubated volunteers rated their breathing comfort when breathing spontaneously through a Hamilton Galileo ventilator (Hamilton Medical, Reno, NV) with the breathing circuit connected to breathing filter and hydroscopic heat and moisture exchanger.

A flow of air was triggered using a predicted comfortable setting (flow rate of 1 L/sec with a rise time of 25 msec) and a predicted uncomfortable setting (inspiratory pressure of -10 cm water with a rise time of 200 msec). An alpha level of 0.05 was used for all statistical tests. The breathing comfort score when using the predicted comfortable setting ($M = 8.1$, $SD = 1.27$) was significantly different statistically than when using the predicted uncomfortable setting ($M = 3.42$, $SD = 2.17$) when compared using a Student's T-test for paired data ($t = 6.65$, $df = 9$, $p = 0.0001$). These results support the validity of the instrument.

The investigation was repeated in 24 to 48 hours. There was a statistically significant correlation between day 1 and day 2 scores ($r = 0.93$, $p = 0.0001$). These

results supported the reliability of the breathing comfort visual analogue score. The interaction between ventilator setting and order of introduction was assessed using an analysis of variance. These results indicated a low likelihood of an interaction ($F = 1.34(1,39)$, $p = 0.69$).

Actual Study Procedure

1. Informed written consent was obtained from each subject. Body mass index was calculated using the National Heart, Lung, and Blood Institute's body mass index calculator found at http://www.nhlbisupport.com/bmi.

2. Subjects were instructed not to eat solid food within two hours of the investigation to lessen the likelihood of stomach distention. Subjects were instructed they may drink clear liquids as desired up to the start of the investigation.

3. The study was conducted in the Trauma/Critical Care Laboratory, first floor, Medical Science Building, University of Cincinnati Medical Center. Closing the door to a common hallway ensures the subjects' privacy. Air temperature was maintained between 21 and 27 degrees Celsius. Subjects were seated in a comfortable chair.

4. The pneumotachograph and pressure transducer were calibrated as previously described.

5. The order of devices is below:

Ventilator

Pneumotachograph

8.0 mm ID endotracheal tube (Mallinckrodt, St Louis, MO)

Pressure sensor

New hydroscopic heat and moisture exchanger filter (HumidVent Filter Compact Straight, (Hudson RCI, Temecula, CA). This hydroscopic heat and moisture exchanger filter is reported to be over 99% effective at filtering both viruses and bacteria and offers a resistance to flow less than 1.8 cm H_2O/L/sec at 1 L/sec (Package Insert, Hudson RCI, Temecula, CA). A new and sterile HumidVent was used for each subject, preventing cross-contamination between subjects. Also the hydroscopic heat and moisture exchanger filter reduces the likelihood of plugging of the capillary tubes of the pneumotachograph by condensation. While the hydroscopic heat and moisture exchanger filter does produce a resistance, this resistance is minimal and is constant between subjects. The benefits in terms of infection control are felt to outweigh the drawbacks of the breathing filter and hydroscopic heat and moisture exchanger filter.

New mouthpiece (Medical Graphics Corporation, St. Paul, MN)

See Figure 16 for a schematic diagram of this breathing apparatus.

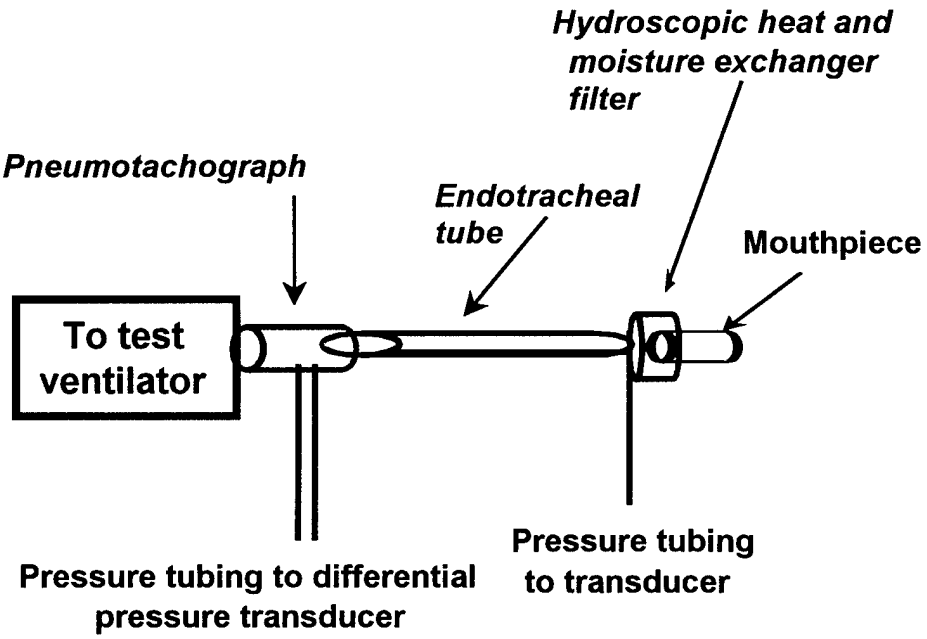


Figure 16. Breathing apparatus.

6. Each ventilator was prepared as per the manufacturer's specifications. The oxygen concentration of the inspired mixture was 0.4 This concentration as selected as it is commonly used in the clinical setting. Oxygen concentration was monitored with an oxygen analyzer.

The default inspiratory flow of the Univent 754 is a constant rate of 60 L/min. The other three ventilators have a variable inspiratory flow. During pilot testing, the default inspiratory flow of the Univent 754 was found to exceed a subject's normal inspiratory flow by about 30 L/min. With this default setting of 60 L/min, subjects consistently stated the inspiratory flow was too fast. Once the subjects triggered the inspiratory flow, the subjects often coughed and/or abruptly stopped their inspiratory flow. The subjects would quickly attempt to take another breath, however, the Univent 754 could not respond and a "Code 6 Error" would result from the subjects creating an airway pressure of greater than -10 cm H_2O and the Univent 754 would become inoperable. To overcome this problem, the inspiratory flow on the Univent 754 was set at 5 L/min greater than the subject's inspiratory flow during the initial control breathing period. Setting the inspiratory flow greater than 5 L/min more than the control inspiratory flow resulted in the same problem occurring when using the inspiratory flow default of 60 l/min. Five L/min was selected to help ensure the subject received at least an inspiratory flow equal to their inspiratory flow when breathing without a ventilator.

7. The order of the ventilators (including the critical care ventilator) and study conditions were randomized for each subject a priori. The study conditions were as

follows:

CPAP 0 cm H_2O, PSV 0 cm H_2O

CPAP 5 cm H_2O, PSV 0 cm H_2O

CPAP 0 cm H_2O, PSV 10 cm H_2O

CPAP 5 cm H_2O, PSV 10 cm H_2O

These conditions were selected as patients in the clinical setting are commonly ventilated using these ventilator settings. Since the Univent 754 does not offer PSV, a placebo setting of PSV of 0 cm H_2O was used in place of PSV 10 H_2O.

8. Headphones connected to a compact disk player were placed on the subject with a commercial recording of tropical rain forest sounds (Relax with Tropical Rain Forest, PILZ Entertainment, Concord, PA) to help mask auditory clues of the ventilator.

9. The ventilators and controls were out of the subject's view for the course of the investigation. Nose clips were placed to prevent nasal breathing.

10. The subject placed the mouthpiece in his/her mouth and establish a seal around mouthpiece. The 8.0 mm ID size was selected as this is a commonly used size of endotracheal tube for patients receiving mechanical ventilation as it is the minimal size to allow easy passage of a fiberoptic bronchoscope. The subject was asked to breathe normally for a 1-minute acclimatization period followed by the study period. The course of events were then:

Flow, volume, and pressure data were directly recorded onto the computer hard drive for five breaths over the two minute study period. Pilot work has shown that data from five breaths can be recorded over two minutes.

Before the data were saved, the baseline airway pressure was determined by examining the computer display. Baseline airway pressure, crucial to the calculation of the WOB_I and PTP_I, was determined for saved breath and manually entered into the computer program.

11. The subject were then asked to indicate their level of breathing comfort on the breathing comfort VAS.

12. $P_i$max was then obtained and recorded.

13. Steps 10, 11, and 12 constitute the control measurements and were repeated after each four study conditions.

14. The circuit of the first study ventilator with the study condition was attached to the flow sensor and the subject was instructed to breathe normally. No data were gathered for the first minute to aid in acclimatization to the ventilator. Data were recorded during the study period as described in Step 10. When indicating their breathing comfort on the VAS, the subject was asked to indicate breathing comfort on the VAS by comparing the recent phase of ventilator-supported breathing with normal breathing without ventilator support symbolizing maximal comfort at the right end of the VAS (Mols et al, 2000). This 2-minute study period was selected as Georgopoulos et al. (1996) and Puddy and Younes (1992) found ventilatory effort adapts rapidly to changes of support. In both of these investigations, the change in ventilatory effort was found to be complete within 2 breaths of changing the level of support.

15. The subject rested for 1 minute. The subject was allowed to wet his/her mouth with water and/or ice chips between ventilator runs.

16. Steps 14 and 15 was repeated for the remaining study conditions.

17. Half way through the study the subject had a 10 minute break. A control was done before and after the break.

Difficulties and Limitations of the Procedures and Alternative Approaches to Achieve the Aims of the Study

Subjects may have been reluctant to volunteer due to the time commitment (about 2 hours). This was addressed by providing payment to the subjects upon their completion of the study.

Another limitation is not recording the WOB_I and PTP_I for each breath. Due to limitations of the recording devices, this is not currently possible. However, saving the data from five breaths over the two minute study period is preferable to not recording any of these data.

The chief limitation is generalizing the findings to the population of interest, ventilator dependent individuals with artificial airways. Since actual endotracheal intubation represents an undue burden on the study subjects, breathing through an endotracheal tube attached to a mouthpiece represents an alternative to this uncomfortable and potentially morbid procedure. An alternative to using healthy volunteers would be to use ventilator dependent individuals. While this would increase the generalizability of the findings, this would place an additional burden on these already stressed individuals. Ventilator dependent individuals would likely add confounding variables. Thus use of healthy volunteers is an important first step. Future investigations could examine the WOB_I, PTP_I, and breathing comfort in ventilator dependent individuals.

Data Management and Quality Control

The flow, volume, and pressure data from the Labview program was downloaded directly to a spreadsheet (Excel, Microsoft, Redmond, WA). WOB_I and PTP_I, flow, volume, and pressure data was directly recorded onto the computer hard drive for five breaths over the two minute study period. Accuracy of the baseline airway pressure determined from examining the computer monitor was done post hoc by determining the baseline airway pressure from the pressure data captured for each breath. The difference between the baseline airway pressure determined post hoc and baseline airway pressure determined during the investigation was calculated for each breath. This difference was compared for each control period and each study breathing period. Breathing comfort scores were manually entered into the spreadsheet. After the data have been assessed for errors, statistical analysis was performed using a commercially available statistical program (Statistix, Analytical Software; Ft Lauderdale, FL). Data stored on all media will be stored in a locked drawer for up to five years after publication of the study. At that time the data will be destroyed.

Data Analysis

The subjects were described by the sex and mean height and weight.

Statistical analysis of the three study hypotheses was performed using repeated measures analysis of variance (ANOVA). Statistical significance was set a priori at an alpha level of 0.05. Tukey's method for comparison of means was selected as this method controls for experimentwise error rate yet retains good power (Analytical Software,

1998). The interaction of subject with the other sources (ventilator, CPAP, PSV, and combinations) was used as each main effect and interaction error term.

As this was a repeated measure design, attention was paid to changes occurring to the subjects over time that are independent of the independent variables (ventilator, CPAP, PSV). Therefore six control breathing periods were interspersed at regular intervals to assess for changes occurring to the subjects over time. These control breathing periods were at the beginning of the investigation, between the fourth and fifth testing period, after the eighth testing period, before the ninth testing period (after a 10 minute break), between the twelfth and thirteenth testing period and after the sixteenth testing period. During these control breathing periods, the subject breathed only through the testing apparatus and WOB_I, PTP_I, and breathing comfort were measured. In addition maximal inspiratory pressure was measured during these control breathing periods to assess subject fatigue.

The mean values of WOB_I, PTP_I, breathing comfort, and negative inspiratory pressure during the control breathing periods were compared using repeated measures ANOVA. Statistical significance was set a priori at an alpha level of 0.05. Tukey's method for comparison of means was used as this method controls for experimentwise error rate yet retains good power (Analytical Software, 1998).

Accurate and precise calculation of WOB_I and PTP_I was dependent on accurate and precise measurement of the baseline airway pressure (Calzia et al., 1998; Mador et al., 1994). The accuracy of the baseline airway pressure was assessed using a water manometer as per the manufacturer's directions.

The precision of the baseline airway pressure was assessed in the following fashion. The baseline airway pressure cursor was overlaid on the airway pressure tracing in real time on the cathode ray tube display. The baseline airway pressure value obtained in this manner was recorded. Flow, volume, and pressure data, as well as WOB_I and PTP_I measurements, were collected for five breaths during each two-minute study period at a rate of 100 Hz and examined retrospectively. The baseline airway pressure obtained in this retrospective manner for each breath was recorded. The difference between the baseline airway pressure obtained in real time from the tracing on the cathode ray tube was subtracted from the baseline airway pressure obtained by retrospectively examining the airway pressure during each breath. This difference (bias) was recorded for each breath and the mean values for each subject during each study condition was calculated.

The mean values of the difference in the baseline airway pressure obtained retrospectively and obtained in real time from examination of the cathode ray tube was compared using repeated measures ANOVA. Statistical significance was set a priori at an alpha level of 0.05. Tukey's method for comparison of means was selected as this method controls for experimentwise error rate yet retains good power (Analytical Software, 1998).

Human Subjects

The study was approved by the University of Cincinnati Medical Center Instutional Review Board (see Appendix D). IRB-approved notices were posted in approved locations (see Appendix E). An explanation of the entire procedure was offered to the

subject and written consent was obtained (see Appendix F). Inclusion and exclusion criteria are listed above. The subject was permitted to withdraw from the procedure at any time. Data was collected by a certified registered nurse anesthetist.

The risk of infection was reduced by using new mouthpieces and hydroscopic heat and moisture exchanger filters.

CHAPTER IV

RESULTS

Introduction

This chapter begins with a review of the statistical analyses we used in the investigation. Next, this chapter reports results of the study by addressing four areas: description of the sample, the three hypotheses, changes occurring to the subjects during the investigation not related to the independent variables, and precision of baseline airway pressure measurement.

The Three Study Hypotheses

This investigation sought to test the following hypotheses: Based on the design characteristics of the ventilators and prior in vitro investigations, when breathing through an 8.0 mm internal diameter endotracheal tube attached to a mouthpiece with an F_IO_2 of 0.4 across the following four combinations of pressure support and CPAP (0 cm H_2O and 0 cm H_2O, 10 cm H_2O and 0 cm H_2O, 0 cm H_2O and 5 cm H_2O, 10 cm H_2O and 5 cm H_2O):

1. The WOB_I with 7200ae < Achieva = LTV 1000 < Univent 754.
2. The PTP_I with 7200ae < Achieva = LTV 1000 < Univent 754.
3. The breathing comfort reported by subjects breathing with the 7200ae > Achieva = LTV 1000 > Univent 754.

The Univent 754 is not capable of delivering PSV therefore a placebo setting of 0 cm H_2O was used when subjects were to receive 10 cm H_2O of PSV from the Univent 754.

Description of Sample

The sample consisted of 16 healthy adults between the ages of 22 and 47 years. There were eight males and eight females. Inclusion criteria were non obese (body mass index less than 30) healthy males and females between the ages of 18 and 65 years (National Heart, Lung, and Blood Institute, 1998). Exclusion criteria included all subjects with a history or present symptoms of cardiopulmonary disease, symptoms of an upper or lower respiratory infection either at the time of the study or in the 30 days prior to the study, active oral or perioral lesions, symptoms of sinusitis either at the time of the study or 30 days prior to the study, recent nasopharyngeal surgery, and history of smoking any substance within 30 days of the study.

There was one African American male in the sample. The remainder of the subjects were European Americans. General characteristics of the study subjects are displayed in Table 3.

Table 3

General Characteristics of the Study Subjects

Characteristics	M	SD	Range
Age (years)	30.13	7.85	22 to 47
Height (inches)	67.50	2.70	64 to 73
Weight (pounds)	151.88	25.20	124 to 215
Body Mass Index	23.61	2.49	18.40 to 28.40

Note. N = 16

Study Hypotheses

Hypothesis Number One

The first hypothesis was based on the design characteristics of the ventilators and prior in vitro investigations: when breathing through an 8.0 mm internal diameter endotracheal tube attached to a mouthpiece with an F_IO_2 of 0.4 across the following tour combinations of pressure support and CPAP (0 cm H_2O and 0 cm H_2O, 10 cm H_2O and 0 cm H_2O, 0 cm H_2O and 5 cm H_2O, 10 cm H_2O and 5 cm H_2O) the WOB_I with 7200ae < Achieva = LTV 1000 <Univent 754. The mean WOB_I values for each combination of ventilator, CPAP, and PSV setting are located in Tables 4 to 7.

Overall, the mean WOB_I of female subjects breathing with the study ventilators across the conditions was 41.05 mJ/L (SD = 141.15 mJ/L) while the mean WOB_I of male subjects was 34.64 mJ/L (SD = 117.90).

Table 4

Imposed Work of Breathing, Imposed Pressure-Time Product, and Breathing Comfort with 0 cm water Continuous Positive Airway Pressure and 0 cm water Pressure Support Ventilation

Ventilator	Variable	M	SD	Min	Max
7200ae	WOB_I	24.92	26.37	0.03	111.88
	PTP_I	0.87	0.80	0.10	3.96
	BC	7.60	2.36	1.40	10.00
Univent 754	WOB_I	37.43	52.68	0.22	277.03
	PTP_I	8.86	38.50	0.16	230.73
	BC	3.44	1.99	0.60	6.5
Achieva	WOB_I	30.82	34.15	0.60	149.92
	PTP_I	1.37	1.27	0.14	7.10
	BC	6.50	2.44	1.30	9.6
LTV 1000	WOB_I	4.41	5.04	0.21	27.56
	PTP_I	0.47	0.36	0.05	1.86
	BC	7.09	2.34	1.80	9.60

Note. Min = minimum; Max = maximum; WOB_I = imposed work of breathing (mJ/L); PTP_I: imposed pressure-time product (cm water/s/L); BC: breathing comfort score (cm)

Table 5

Imposed Work of Breathing, Imposed Pressure-Time Product, and Breathing Comfort with 5 cm water Continuous Positive Airway Pressure and 0 cm water Pressure Support Ventilation

Ventilator	Variable	M	SD	Min	Max
7200ae	WOB_I	43.00	28.40	0.65	126.62
	PTP_I	1.15	0.74	0.19	3.05
	BC	6.09	2.42	0.90	9.50
Univent 754	WOB_I	171.70	209.38	1.86	1040.1
	PTP_I	6.08	7.69	0.65	40.41
	BC	1.60	1.71	0.50	6.3
Achieva	WOB_I	13.27	12.37	2.27	60.68
	PTP_I	1.41	0.98	0.23	4.73
	BC	5.85	2.25	2.50	9.20
LTV 1000	WOB_I	8.31	8.09	0.24	49.52
	PTP_I	0.70	0.55	0.003	3.65
	BC	5.91	2.93	1.2	9.8

Note. Min = minimum; Max = maximum; WOB_I = imposed work of breathing (mJ/L); PTP_I: imposed pressure-time product (cm water/s/L); BC: breathing comfort score (cm)

Table 6

Imposed Work of Breathing, Imposed Pressure-Time Product, and Breathing Comfort with 0 cm water Continuous Positive Airway Pressure and 10 cm water Pressure Support Ventilation

Ventilator	Variable	M	SD	Min	Max
7200ae	WOB_I	0.69	2.02	0.03	13.91
	PTP_I	0.33	0.28	0.02	1.63
	BC	6.56	2.43	1.50	10.00
Achieva	WOB_I	1.42	5.57	0.11	44.62
	PTP_I	0.55	0.58	0.15	5.05
	BC	5.61	2.54	1.20	9.70
LTV 1000	WOB_I	2.70	9.34	0.03	67.27
	PTP_I	0.35	0.36	0.04	2.04
	BC	5.94	2.18	2.4	9.5

Note. Min = minimum; Max = maximum; WOB_I = imposed work of breathing (mJ/L); PTP_I: imposed pressure-time product (cm water/s/L); BC: breathing comfort score (cm)

Table 7

Imposed Work of Breathing, Imposed Pressure-Time Product, and Breathing Comfort with 5 cm water Continuous Positive Airway Pressure and 10 cm water Pressure Support Ventilation

Ventilator	Variable	M	SD	Min	Max
7200ae	WOB_I	2.74	5.65	0.06	32.92
	PTP_I	0.46	0.41	0.09	1.86
	BC	3.93	3.09	0.40	9.20
Achieva	WOB_I	3.81	7.51	0.04	63.79
	PTP_I	1.26	1.88	0.10	13.58
	BC	4.48	2.47	1.10	8.30
LTV 1000	WOB_I	2.91	3.03	0.06	18.28
	PTP_I	0.47	0.66	0.06	5.37
	BC	5.37	2.83	0.80	9.40

Note. Min = minimum; Max = maximum; WOB_I = imposed work of breathing (mJ/L); PTP_I: imposed pressure-time product (cm water/s/L); BC: breathing comfort score (cm)

Statistical analysis of this hypothesis was performed using repeated measures ANOVA (see Table 8). Statistical significance was set a priori at an alpha level of 0.05. Sources of significance were ventilator, CPAP, and the interaction of ventilator and CPAP.

Ventilators were one source of significance: $\underline{F}$ (3,60) value of 13.12 with $\underline{p}$ = 0.0001. Tukey's method for comparison of means revealed the WOB_I obtained with the subjects breathing with the Univent 754 was different compared to the subjects breathing with the other ventilators (see Table 9).

Considering the CPAP setting alone, WOB_I obtained with 5 cm H_2O of CPAP was significantly higher compared to WOB_I obtained using 0 cm H_2O of CPAP: $\underline{F}(1,15) = 9.76$ with $\underline{p} = 0.0070$.

Finally, there was a significant interaction between the ventilators and CPAP setting: $\underline{F}(3,45) = 8.72$ with $\underline{p} = 0.0001$. Tukey's method for comparison of means revealed the WOB_I obtained with the Univent 754 with 5 cm H_2O of CPAP was significantly higher than the WOB_I obtained with the Univent 754 with 0 cm H_2O of CPAP and the other three ventilators regardless of CPAP setting (see Table 10).

Table 8

Repeated Measures ANOVA for Imposed Work of Breathing During Study Breathing Periods

Source	df	MS	F	p
Ventilator (A)	3	214318.00	13.12	0.0001
Subject (B)				
A X B	60	16340.00		
CPAP (C)	1	150410.00	9.76	0.0070
B X C	15	15404.50		
PSV (D)	1	14.12	0.00	0.9665
B X D	15	7722.87		
A X C	3	130547.00	8.72	0.0001
A X B X C	45	14970.10		
A X D	3	14475.30	1.91	0.1412
A X B X D	45	7570.32		
C X D	1	13238.00	1.24	0.2838
B X C X D	15	10712.10		
A X C X D	3	17311.90	1.55	0.2144
A X B X C X D	45	11160.3		
Total	255			

Note. CPAP = continuous positive airway pressure; PSV = pressure support ventilation

Table 9

Tukey's Test for Variable: Ventilator

Tukey Grouping	Ventilator	M
A	Univent 754	124.40
B	7200ae	14.26
B	Achieva	8.97
B	LTV 1000	3.74

Table 10

Tukey's Test for Variable: Ventilator by Continuous Positive Airway Pressure

Tukey Grouping	Ventilator	CPAP	M
A	Univent 754	5	216.24
B	Univent 754	0	32.57
B	7200ae	5	20.01
B	Achieva	0	10.55
B	7200ae	0	8.50
B	Achieva	5	7.39
B	LTV 1000	5	4.69
B	LTV 1000	0	2.79

Note. CPAP = continuous positive airway pressure (cm H_2O)

Hypothesis Number Two

The second hypothesis was based on the design characteristics of the ventilators and prior in vitro investigations, the PTP_I with 7200ae < Achieva = LTV 1000 < Univent 754. The mean PTP_I values for each combination of ventilator, CPAP, and PSV setting are located in Tables 4 to 7. Overall, the mean PTP_I of female subjects breathing with the study ventilators across the conditions was 1.72 cm water/s/L (SD = 4.60 cm water/s/L) while the mean WOB_I of male subjects was 1.60 cm water/s/L (SD = 4.90 cm water/s/L).

Statistical analysis of this hypothesis was performed using repeated measures ANOVA (see Table 11). The interaction of subject with the other sources (ventilator, CPAP, PSV, and combinations) was used as each main effect and interaction error term. Statistical significance was set a priori at an alpha level of 0.05. Sources of significance were ventilator, CPAP, and the interaction of ventilator and CPAP.

Ventilators were one source of significance: $F(3,60) = 8.71$ with $p = 0.0001$. Tukey's method for comparison of means revealed the PTP_I obtained with the subjects breathing with the Univent 754 was different compared to the subjects breathing with the other ventilators (see Table 12).

Considering the CPAP setting alone, PTP_I obtained with 5 cm H_2O of CPAP was significantly higher compared to PTP_I obtained using 0 cm H_2O of CPAP: $F(1,15) = 5.96$ with $p = 0.0275$.

Finally, there was a significant interaction between the ventilators and CPAP setting: $F(3,45) = 4.67$ with $p = 0.0064$. Tukey's method for comparison of means revealed the PTP_I obtained with the Univent 754 with 5 cm H_2O of CPAP was

significantly higher than the PTP_I obtained with the Univent 754 with 0 cm H_2O of CPAP and the other three ventilators regardless of CPAP setting (see Table 13).

Table 11

Repeated Measures ANOVA for Imposed Pressure Time Product During Study Breathing Periods

Source	df	MS	F	p
Ventilator (A)	3	268.37	8.71	0.0001
Subject (B)				
A X B	60	30.80		
CPAP (C)	1	124.15	5.96	0.0275
B X C	15	20.82		
PSV (D)	1	0.30	0.08	0.7815
B X D	15	3.81		
A X C	3	95.13	4.67	0.0064
A X B X C	45	20.39		
A X D	3	7.50	1.68	0.1851
A X B X D	45	4.47		
C X D	1	26.56	1.60	0.2258
B X C X D	15	16.65		
A X C X D	3	26.57	1.49	0.2310
A X B X C X D	45	17.88		
Total	255			

Note. CPAP = continuous positive airway pressure; PSV = pressure support ventilation

Table 12

Tukey's Test for Variable: Ventilator

Tukey Grouping	Ventilator	M
A	Univent 754	4.72
B	Achieva	0.90
B	7200ae	0.57
B	LTV 1000	0.45

Table 13

Tukey's Test for Variable: Ventilator by Continuous Positive Airway Pressure

Tukey Grouping	Ventilator	CPAP	M
A	Univent 754	5	7.24
B	Univent 754	0	2.19
B	Achieva	5	1.00
B	Achieva	0	0.80
B	7200ae	5	0.65
B	LTV 1000	5	0.53
B	7200ae	0	0.49
B	LTV 1000	0	0.38

Note. CPAP = continuous positive airway pressure (cm H_2O)

Hypothesis Number Three

The third hypothesis was based on the design characteristics of the ventilators and prior in vitro investigations, when breathing through an 8.0 mm internal diameter endotracheal tube attached to a mouthpiece with an F_IO_2 of 0.4 across the following four combinations of pressure support and CPAP (0 cm H_2O and 0 cm H_2O, 10 cm H_2O and 0 cm H_2O, 0 cm H_2O and 5 cm H_2O, 10 cm H_2O and 5 cm H_2O) the BC with 7200ae > Achieva = LTV 1000 > Univent 754. The mean BC values for each ventilator, CPAP, and PSV setting are located in Tables 4 to 7. Subject comments transcribed verbatim are located in Table 4 to 7.

Overall, the mean BC score of female subjects breathing with the study ventilators across the conditions was 4.73 cm (SD = 2.97 cm) while the mean WOB_I of male subjects was 5.59 cm (SD = 2.76 cm).

Table 14

Subject Comments with Setting of 0 cm H_2O Continuous Positive Airway Pressure and 0 cm H_2O Pressure Support Ventilation

Ventilator	
7200ae	Great when breathing passively but sluggish when I wanted more air to breath Very natural feel Very comfortable
Univent 754	Insp cycles off too soon on almost every breath Sometimes multiple breaths with each of my efforts Cuts off and back on Had to work harder overall Too noisy Too much vibration Choppy when inhaling Seems to stop insp prematurely Difficult to breathe in and out Significant rubbing on inspiration, increased effort to blow out I want to be able to exhale
Achieva	Mid insp slack in flow Some initial expiratory effort needed Fairly comfortable but could hear a click with every breath Very natural feel Rubbing on inspiration

LTV 1000	Inspiratory not bad at all but almost over vented my desired VT what at times was not comfortable Hard exhale Easy on exhalation, a lot of work to inhale

Table 15

Subject Comments with 5 cm H_2O Continuous Positive Airway Pressure and 0 cm H_2O Pressure Support Ventilation

Ventilator	
7200ae	Insp hardly any work. Early exhalation assoc with some effort Exhalation slightly not comfortable Difficult Exp Somewhat difficult to push air back out Lots resistance, inhale and exhale
Univent 754	About every 6th breath would cycle off too soon and that breath was bad Others were not too bad in terms of insp Breaths not in synch Discomfort mostly due to exhalation Inspiration not too bad Hyperventilation was close Very uncomfortable Would not let me exhale My ears popped Difficult to synchronize inhalation and exhalation Difficult to exhale Occasionally difficult to inhale Noticeably more uncomfortable Hard to exhale Difficult end expiration Sig rubbing on inspiration difficult to breathe in and push air back out Machine made breathing difficult

	Air was not in sync with my breathing
Achieva	Sl end exp push seemed required
	Too work to inhale
	Harder to exhale
	Slight time lag with insp effort
	Small amount of rubbing on inspiration, some what difficult
	to blow air back out
	Nice breathe inhaling, resistance exhaling
LTV 1000	Insp nearly effortless but required effort to exhale
	Felt a slight puff of air at the end
	Easy inspire, difficult expire
	Had to use a lot of abdominal muscles to exhale

Table 16

Subject Comments with 0 cm H_2O Continuous Positive Airway Pressure and 10 cm H_2O Pressure Support Ventilation

Ventilator	
7200ae	Easy somewhat pushy exhalation Very quick response to insp effort Could not fully exhale
Achieva	This feels great Insp is easy, exhalation hard to start Like breathing through a straw Thought I was suffocating Time lag
LTV 1000	A few jerks when exhaling Positive pressure noted Small amount forced air at end of inspiration This time was easier to blow air back out Breathing felt much more relaxed compared to last couple of sessions Hard to judge baseline

Table 17

Subject Comments with 5 cm H_2O Continuous Positive Airway Pressure and 10 cm H_2O Pressure Support Ventilation

Ventilator	
7200ac	Some over vent feeling, breath almost too big. No insp discomfort though Too much air pushed in Difficult to exhale A little hard to exhale against High pressure On inspiration puff of air is forced in, makes inspiration somewhat difficult I had to work very hard to exhale Felt like I was fighting vent to breath
Achieva	Sl initial trigger delay and feels like I have to blow out to stop inhalation Exhalation again very difficult, insp much easier than before Like breathing through a straw Thought I was suffocating Much more extra effort to open exp valve Noticably harder to exhale Felt as though I was getting too much air in on inspiration

LTV 1000	Smooth and easy Forced puff of air on inspiration Makes mouth dry. Somewhat difficult to push air back out Hard to exhale. I felt like I was fighting machine.

A repeated measures ANOVA was used to analyze the measurements of the BC for each combination of ventilator, CPAP, and PSV (see Table 18). The interaction of subject with the other sources (ventilator, CPAP, PSV, and combinations) was used as each main effect and interaction error term. Sources of significance were ventilator, CPAP, PSV, ventilator and CPAP interaction, and ventilator and PSV interaction. Following this analysis, Tukey's comparison of means was computed to examine where differences existed between these sources of significance.

Ventilators were one source of significance: $F(3,60) = 11.24$ with $p = 0.0001$. Tukey's method for comparison of means revealed the BC obtained with the subjects breathing with the Univent 754 was different compared to the subjects breathing with the other ventilators (see Table 19).

Considering the CPAP level alone, the BC with 5 cm H_2O of CPAP was significantly lower than with 0 cm H_2O of CPAP: $F(1,15) = 24.84$ with $p = 0.0002$.

Considering the PSV level alone, the BC with 10 cm H_2O of PSV was significantly lower than with 0 cm H_2O of CPAP: $F(1,15) = 8.11$ with $p = 0.0122$.

The interaction of ventilator and CPAP setting was a source of significance: $F(3,45) = 3.91$ with $p = 0.0144$. Tukey's method for comparison of means revealed numerous different combinations of ventilator and CPAP settings (Table 20).

Finally, the interaction of ventilator and PSV setting was a source of significance: $F(3,45) = 4.42$ with $p = 0.0083$. Tukey's post hoc test revealed numerous different combinations of ventilator and PSV settings (Table 21).

Table 18

Repeated Measures ANOVA for Breathing Comfort Score During Study Breathing Periods

Source	df	MS	F	P
Ventilator (A)	3	166.91	11.24	0.0001
Subject (B)				
A X B	60	14.85		
CPAP (C)	1	151.60	24.84	0.0002
B X C	15	6.10		
PSV (D)	1	31.92	8.11	0.0122
B X D	15	3.94		
A X C	3	9.42	3.91	0.0144
A X B X C	45	2.41		
A X D	3	10.79	4.42	0.0083
A X B X D	45	2.44		
C X D	1	3.85	1.67	0.2163
B X C X D	15	2.31		
A X C X D	3	3.42	2.00	0.1269
A X B X C X D	45	1.70		
Total	255			

Note. CPAP = continuous positive airway pressure; PSV = pressure support ventilation

Table 19

Tukey's Test for Variable: Ventilator

Tukey Grouping	Ventilator	M
A	7200ae	6.18
A	LTV 1000	6.08
A	Achieva	5.61
B	Univent 754	2.76

Table 20

Tukey's Test for Variable: Ventilator by Continuous Positive Airway Pressure

Tukey Grouping	Ventilator	CPAP	M
A	7200ae	0	7.34
A, B	LTV 1000	0	6.51
B, C	Achieva	0	6.05
B, C	LTV 1000	5	5.56
C	Achieva	5	5.17
C, D	7200ae	5	5.01
D, E	Univent 754	0	3.79
E	Univent 754	5	1.73

Note. CPAP = continuous positive airway pressure (cm H_2O)

Table 21

Tukey's Test for Variable: Ventilator by Pressure Support Ventilation

Tukey Grouping	Ventilator	PSV	M
A	7200ae	0	6.85
A, B	LTV 1000	0	6.50
A, B, C	Achieva	0	6.18
A, B, C	LTV 1000	10	5.65
B, C	7200ae	10	5.51
C	Achieva	10	5.04
D	Univent 754	10	3.01
D	Univent 754	0	2.52

Note. PSV = pressure support ventilation (cm H_2O)

Assessment of Changes to Subjects Occurring Over Time

During the six control breathing periods, the subject breathed only through the testing apparatus and WOB_I, PTP_I, and breathing comfort were measured. In addition, maximal inspiratory pressure was measured during these control breathing periods to assess subject fatigue. The means and standard deviations of these measurements are located in Table 22.

A repeated measures ANOVA was used to analyze the measurements of the WOB_I, PTP_I, BC score, and maximum inspiratory pressure during the control breathing periods (see Tables 23 to 26). The interaction of subject by control breathing period was used as each main effect and interaction error term.

The only significant difference found in all of these measurements among the six control periods was with maximum inspiratory pressure: $\underline{F}(5,75) = 2.54$ with $\underline{p} = 0.0355$ (see Table 26). However, Tukey comparison of means failed to reveal where the differences occurred in maximum inspiratory pressure between the six control breathing periods (see Table 27). Notable is the maximum inspiratory pressure achieved by the subjects did not decrease from the first to the sixth breathing period, but fell slightly between the first and the second breathing period and then increased, suggesting the subjects did not fatigue over the course of the investigation.

Table 22

Imposed Work of Breathing, Imposed Pressure-Time Product, Breathing Comfort, and Maximal Inspiratory Pressure During Control Breathing Periods

Control Breathing Period	Variable	M	SD	Min	Max
1	WOB_I	32.57	9.83	14.03	57.76
	PTP_I	0.74	0.09	0.61	0.94
	BC	7.14	2.25	2.20	9.90
	MIP	80.93	22.81	40.33	117.83
2	WOB_I	27.90	9.69	10.97	59.63
	PTP_I	0.72	0.10	0.61	0.93
	BC	7.56	2.27	2.60	10.00
	MIP	76.65	22.66	36.10	110.87
3	WOB_I	31.32	12.18	9.32	69.53
	PTP_I	0.79	0.27	0.57	1.69
	BC	7.45	2.70	1.10	10.00
	MIP	79.72	23.29	37.53	114.47
4	WOB_I	33.99	16.04	13.81	115.43
	PTP_I	0.75	0.12	0.64	

	BC	8.21	1.75	3.50	9.90
	MIP	83.42	23.86	36.73	117.90
5	WOB_I	31.61	11.46	17.35	88.91
	PTP_I	0.72	0.09	0.62	0.95
	BC	7.66	2.19	2.80	10
	MIP	84.43	24.25	40.03	117.27
6	WOB_I	30.14	11.02	11.02	64.32
	PTP_I	0.73	0.07	0.60	0.89
	BC	7.68	2.06	3.00	10.00
	MIP	84.11	23.59	36.03	117.23

Note. Min = minimum; Max = maximum; WOB_I = imposed work of breathing (mJ/L); PTP_I = imposed pressure-time product (cm water/s/L); BC: breathing comfort score (cm); MIP = maximal inspiratory pressure

Table 23

Repeated Measures ANOVA for Imposed Work of Breathing During Control Breathing Periods

Source	df	MS	F	p
Subject (A)	15	224.86	5.99	0.0000
Control Breathing Period (B)	5	69.95	1.86	0.1107
A X B	75	37.52		
Total	96			

Table 24

Repeated Measures ANOVA for Imposed Pressure Time Product During Control Breathing Periods

Source	df	MS	F	P
Subject (A)	15	0.04	2.26	0.0110
Control Breathing Period (B)	5	0.01	0.80	0.5534
A X B	75	0.02		
Total	96			

Table 25

Repeated Measures ANOVA for Breathing Comfort Score During Control Breathing Periods

Source	df	MS	F	p
Subject (A)	15	23.07	17.69	0.0000
Control Breathing Period (B)	5	2.02	1.55	0.1848
A X B	75	1.30		
Total	96			

Table 26

Repeated Measures ANOVA for Maximum Inspiratory Pressure During Control Breathing Periods

Source	df	MS	F	p
Subject (A)	15	2998.35	51.51	0.0000
Control Breathing Period (B)	5	147.67	2.54	0.0355
A X B	75	58.21		
Total	96			

Table 27

Tukey's Test for Variable: Control Breathing Period

Tukey Grouping	Control Breathing Period	M
A	1	80.93
A	2	76.65
A	3	79.72
A	4	83.42
A	5	84.43
A	6	84.11

Analysis of Baseline Airway Pressure Bias

The mean values of the difference in the baseline airway pressure obtained retrospectively and obtained in real time from examination of the display on the cathode ray tube were compared using repeated measures ANOVA for all data collected during the control and study breathing periods (see Tables 28 to 31). Statistical significance was set a priori at an alpha level of 0.05. The interaction of subject with the other sources was used as the error term for each main effect and interaction in Table 32 and the interaction of subject and control breathing period was used as the error term for each main effect and interaction in Table 33. No significant differences in baseline airway pressure bias were detected for the control or study breathing periods (see Tables 32 and 33).

Table 28

Difference Between Baseline Airway Pressure Determined Retrospectively and Baseline Airway Pressure Used in Imposed Work of Breathing and Imposed Pressure-Time Product Calculations, Continuous Positive Airway Pressure = 0 cm H_2O and Pressure Support Ventilation = 0 cm H_2O

Ventilator	M	SD	Min	Max
7200ae	-0.45	0.91	-4.5	0.58
Univent 754	-0.18	0.38	-1.26	0.89
Achieva	-0.22	0.33	-1.16	0.80
LTV 1000	-0.16	0.25	-0.92	0.42

Note. Min = minimum; Max = maximum

Table 29

Difference Between Baseline Airway Pressure Determined Retrospectively and Baseline Airway Pressure Used in Imposed Work of Breathing and Imposed Pressure-Time Product Calculations, Continuous Positive Airway Pressure = 5 cm H_2O and Pressure Support Ventilation = 0 cm H_2O

Ventilator	M	SD	Min	Max
7200ae	-0.31	0.29	-0.27	-0.50
Univent 754	-0.11	0.50	-0.86	2.6
Achieva	-0.18	0.30	-0.20	0.59
LTV 1000	-0.22	0.31	-0.90	0.87

Note. Min = minimum; Max = maximum

Table 30

Difference Between Baseline Airway Pressure Determined Retrospectively and Baseline Airway Pressure Used in Imposed Work of Breathing and Imposed Pressure-Time Product Calculations, Continuous Positive Airway Pressure = 0 cm H_2O and Pressure Support Ventilation = 10 cm H_2O

Ventilator	M	SD	Min	Max
7200ae	-0.21	0.20	-0.22	0.50
Univent 754	-0.17	0.32	-0.80	0.70
Achieva	0.19	0.32	-0.99	1.00
LTV 1000	-0.20	0.37	-0.86	0.96

Note. Min = minimum; Max = maximum

Table 31

Difference Between Baseline Airway Pressure Determined Retrospectively and Baseline Airway Pressure Used in Imposed Work of Breathing and Imposed Pressure-Time Product Calculations, Continuous Positive Airway Pressure = 5 cm H_2O and Pressure Support Ventilation = 10 cm H_2O

Ventilator	M	SD	Min	Max
7200ae	0.27	0.29	-1.39	0.33
Univent 754	-0.22	0.39	-1.24	1.14
Achieva	-0.20	0.35	-1.25	0.74
LTV 1000	-0.18	0.38	-2.04	0.78

Note. Min = minimum; Max = maximum

Table 32

Difference Between Baseline Airway Pressure Determined Retrospectively During Control Breathing Periods and Baseline Airway Pressure Used in Imposed Work of Breathing and Imposed Pressure-Time Product Calculations

Control Breathing Period	M	SD	Min	Max
1	0.07	0.03	0.04	0.12
2	0.07	0.03	0.01	0.12
3	0.06	0.02	0.02	0.10
4	0.06	0.02	0.02	0.10
5	0.06	0.03	0.02	0.11
6	0.06	0.02	0.02	0.12

Note. Min = minimum; Max = maximum

Table 33

Repeated Measures ANOVA for Baseline Airway Pressure Bias During Study Breathing Periods

Source	df	MS	F	P
Ventilator (A)	3	0.5124	1.67	0.1825
Subject (B)				
A X B	60	0.3064		
CPAP (C)	1	0.5552	2.58	0.1289
B X C	15	0.2150		
PSV (D)	1	0.0306	0.10	0.7615
B X D	15	0.3205		
A X C	3	0.0573	0.24	0.8651
A X B X C	45	0.2348		
A X D	3	0.2215	1.07	0.3707
A X B X D	45	0.2067		
C X D	1	0.1362	1.24	0.2838
B X C X D	15	0.1102		
A X C X D	3	0.1440	0.78	0.5103
A X B X C X D	45	0.1842		
Total	255			

Note. CPAP = continuous positive airway pressure; PSV = pressure support ventilation

CHAPTER V

DISCUSSION AND RECOMMENDATIONS

Discussion

The purpose of this investigation was to assess WOB_I, PTP_I, and breathing comfort of nonintubated healthy volunteers breathing through a sample of PVs and a CCV in a controlled environment. The hypotheses examined by this investigation were based on the design characteristics of the ventilators and prior in vitro investigations, when breathing through an 8.0 mm internal diameter endotracheal tube attached to a mouthpiece with an F_IO_2 of 0.4 across the following four combinations of pressure support and CPAP (0 cm H_2O and 0 cm H_2O, 10 cm H_2O and 0 cm H_2O, 0 cm H_2O and 5 cm H_2O, 10 cm H_2O and 5 cm H_2O):

1. The WOB_I with 7200ae < Achieva = LTV 1000 < Univent 754.
2. The PTP_I with 7200ae < Achieva = LTV 1000 < Univent 754.
3. The breathing comfort reported by subjects breathing with the 7200ae > Achieva = LTV 1000 > Univent 754.

WOB_I, PTP_I, and breathing comfort were assessed during six control breathing periods to assess changes occurring to the subjects extraneous to the effects of the independent variables. These control breathing periods were at the beginning of the investigation, between the fourth and fifth testing period, after the eighth testing period, before the ninth testing period (after a 10 minute break), between the twelfth and thirteenth testing period and after the sixteenth testing period. During these control

breathing periods the subjects breathed only through the testing apparatus and WOB_I, PTP_I, and breathing comfort were measured. In addition, maximal inspiratory pressure was measured during these control breathing periods to assess subject fatigue.

Accurate and precise calculation of WOB_I and PTP_I is dependent on accurate and precise measurement of the baseline airway pressure (Calzia et al., 1998; Mador, Walsh, & Tobin, 1994). The accuracy of the baseline airway pressure was assessed using a water manometer as per the manufacturer's directions. The precision of baseline airway pressure measurement during the control and study breathing periods was assessed by comparing the mean bias between the baseline airway pressure determined retrospectively and baseline airway pressure measured during real time.

This chapter will begin with a discussion of the study hypotheses, including possible explanations for the findings and how these findings compare to findings from previous investigations. A discussion will then be offered relating to the measurements obtained during the control breathing periods and the bias seen in baseline airway pressure. The nursing implications of the findings will be then be examined, followed by a discussion of how these findings related to the theoretical principles used in the investigation. This chapter will conclude with a summary of the findings, a discussion of the limitations of this study, and recommendation for further study.

Study Hypothesis Number One

Introduction

The first hypothesis was based on the design characteristics of the ventilators and prior in vitro investigations; under the standard condition of the study, we hypothesized

that the WOB_I with 7200ae < Achieva = LTV 1000 < Univent 754.

The findings did not fully support this hypothesis. Across the above combinations of CPAP and PSV, in subjects breathing with the 7200ae, Achieva, and LTV 1000 a lower WOB_I was measured compared to the Univent 754. However, there was no difference in the WOB_I when the subjects breathed with the 7200ae, Achieva, or LTV 1000. Methods of triggering and inspiratory flow generation are possible reasons why a greater WOB_I was measured with the Univent 754 compared to the other three ventilators. It was hypothesized WOB_I would be greater with the Achieva and LTV 1000 compared to the 7200ae as these two ventilator possess an external exhalation valve. The following paragraphs will discuss the effects of the following factors on WOB_I: the triggering variable, intrinsic positive end-expiratory pressure, inspiratory flow, and the location of the exhalation valve. The findings of the present investigation will then be compared to those of previous studies.

The Trigger Variable and WOB_I

The trigger variable is the variable that is manipulated to deliver inspiratory flow (Sassoon, 1992). Marini et al. (1985) found if the trigger variable is not set appropriately or if the ventilator is poorly designed, the individual's effort and inspiratory work increases. Trigger variables include a set time, pressure, volume, or flow. With time triggering, the ventilator delivers an inspiratory flow at a set frequency that is independent of the individual's effort. A ventilator delivering an inspiratory flow triggered by pressure delivers that inspiratory flow once the individual generates the set trigger pressure. A ventilator delivering an inspiratory flow triggered by volume delivers that inspiratory flow

once the individual generates the set trigger volume. A ventilator delivering an inspiratory flow triggered by flow delivers that inspiratory flow once the individual generates the set flow. Volume triggering is uncommonly used with pressure or flow triggering being the most common triggering variables (Sassoon, 1992). The following discusses the trigger variable in the context of the ventilators used in the present study.

Pressure triggering and the Univent 754.

With pressure triggering, the individual must generate a predetermined, or set negative pressure during inspiration for the ventilator to deliver a gas flow to the inspiratory limb of the breathing circuit. An increase in the sensitivity means an increase in this set value and a decrease in sensitivity means a decrease in this set value. Pressure can be measured at the patient end of the breathing circuit or at the inspiratory and/or expiratory ports of the ventilator. Pressure triggering is used with the Univent 754. Pressure is measured near the patient end of the breathing circuit. Once an inspiratory flow is triggered with the Univent 754, the ventilator delivers gas at a default rate of 60 L/min with the flow being adjustable in increments of 5 L/min down to 10 L/min. Flow is delivered with the Univent 754 until airway pressure rises to 5 cm H_2O above baseline airway pressure or three seconds have elapsed, which ever occurs first. Inspiratory flow is then cycled off (Impact Instrumentation, 1998).

Flow triggering and the 7200ae.

The method of flow triggering varies slightly between the 7200ae, Achieva, and LTV 1000. With the 7200ae, a baseline flow of fresh gas is continuously delivered to the inspiratory limb of the breathing circuit (called the base flow), at the same rate as the

nonadjustable base flow of the LTV 1000. In the present investigation this base flow was set at 10 L/min. Flow is measured at the exhalation port of the 7200ae. Flow sensitivity is computed as the difference in the set base flow and flow measured the exhalation port. Inspiratory flow is delivered when flow measured at the exhalation port of the 7200ae is equal to or greater than the flow sensitivity setting that in the present investigation was 3 L/min. Therefore when flow at the exhalation port equals 7 L/min or less, inspiratory flow was delivered by the 7200ae at a variable rate depending on the inspiratory demand (to maintain airway pressure at 0.5 cm above baseline) of the individual up to 180 L/min. Inspiratory flow is cycled off when flow measured at the expiratory port exceeds flow measured at the inspiratory port by 2 L/min (Mallinckrodt, Inc., 1998).

Flow triggering and the Achieva.

Flow triggering with the Achieva is accomplished in the following fashion. There is no base flow. Flow sensitivity can be set from 3 to 25 L/min with flow measured at the inspiratory port of the Achieva. In the present investigation flow sensitivity was set at 3 L/min. The Achieva delivers an inspiratory flow when the inspiratory flow of the individual is equal to or greater than the flow sensitivity. The Achieva delivers a variable inspiratory flow depending on the individual's inspiratory demand up to 150 L/min. Inspiratory flow is cycled off when flow measured at the inspiratory port is 17% of the peak inspiratory flow for that breath (Mallinckrodt, Inc., 1997; Dennis Tuerson, personal communication, April 5, 2001).

Flow triggering and the LTV 1000.

Flow triggering with the LTV 1000 is accomplished in a manner similar to the

Achieva. However, with the LTV 1000 there is a nonadjustable base flow of 10 L/min that is delivered into the inspiratory limb. A pneumotachograph is located at the patient end of the breathing circuit, however, the pneumotachograph is positioned such that it does not sense the base flow. Flow sensitivity is adjustable from 0 to 9 L/min. In the present investigation flow sensitivity was set at 3 L/min, the same setting as on the 7200ae and Achieva. When inspiratory flow measured by the pneumotachograph equals or exceeds the flow sensitivity, the LTV 1000 delivers a variable inspiratory flow up to 140 L/min depending on the individual's demand. Flow is cycled off when inspiratory flow measured by the pneumotachograph is 10% of the peak inspiratory flow for that breath. Inspiratory flow can also be pressure triggered with the LTV 1000 (Pulmonetic Systems, 2000).

Pressure versus flow triggering: Effects on WOB_I

Using both mechanical models and humans, investigators have generally reported a 25% reduction in inspiratory work of breathing with flow triggering compared to pressure triggering (Branson et al., 1994; Hirsch, Kacmarek, & Stanek, 1991; Sassoon et al., 1992). Sassoon (1992) posits with flow triggering there is a shorter delay time between the onset of inspiratory effort and the onset of inspiratory flow compared to pressure triggering. Branson suggests delay time is not the only trigger factor variable affecting WOB_I (Branson, 1994).

The triggering variable and delay time.

Sassoon (1992) explains factors that can affect the delay time between the onset of inspiratory effort and onset of inspiratory flow include errors due to the speed of the

pressure signal, errors due to digital sampling of the transducer, errors in the pressure-transducing circuit, discrepancies between the set and actual CPAP, and circuit noise. Pressure signals travel at a rate of about one foot per millisecond (ms) at sea level. This factor may affect delay time with the Univent 754 as the location of pressure sensing (patient end of the breathing circuit) is about four feet from the pressure transducer (located in the ventilator). Microprocessor-based systems, such as the Univent 754, operate in discrete time rather than continuous time. Therefore the pressure transducer is measuring (also called polling) the pressure in the breathing circuit a set number of ms (X ms) rather than continuously. The average increase in delay time is therefore X/2 ms. Transducers found in life support devices typically exhibit an error of described by the term +/- 0.1 + 3% of reading in cm H_2O. Thus when CPAP is zero, the transducer exhibits an error of +/- [0.1 + (3.0 * 0)] or 0.1 cm H_2O. A negative error shortens and a positive error lengthens delay time (Sassoon, 1992).

The presence of intrinsic positive end-expiratory pressure increases delay time as its presence increases the sensitivity relative to the set sensitivity. This was probably a major factor in increasing the delay time with the Univent 754. There was typically 2 cm H_2O of intrinsic positive end-expiratory pressure present when the subjects breathed with the Univent 754 (see Figures 17 and 18). Causes of noise in breathing circuit include compensatory flow or any other correction-based routine aimed at enhancing transducer sensitivity or accuracy. The Univent 754 does not possess these routines. The chief cause of the delay time increase of the Univent 754 in the present study was likely the presence of intrinsic positive end-expiratory pressure.

Figure 17
Pressure-Volume Curve
Representative for Breathing with Univent 754
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 0 cm water
Imposed Work of Breathing 29.92 mJ/L
Imposed Pressure Time Product 2.20 cm water/s/L

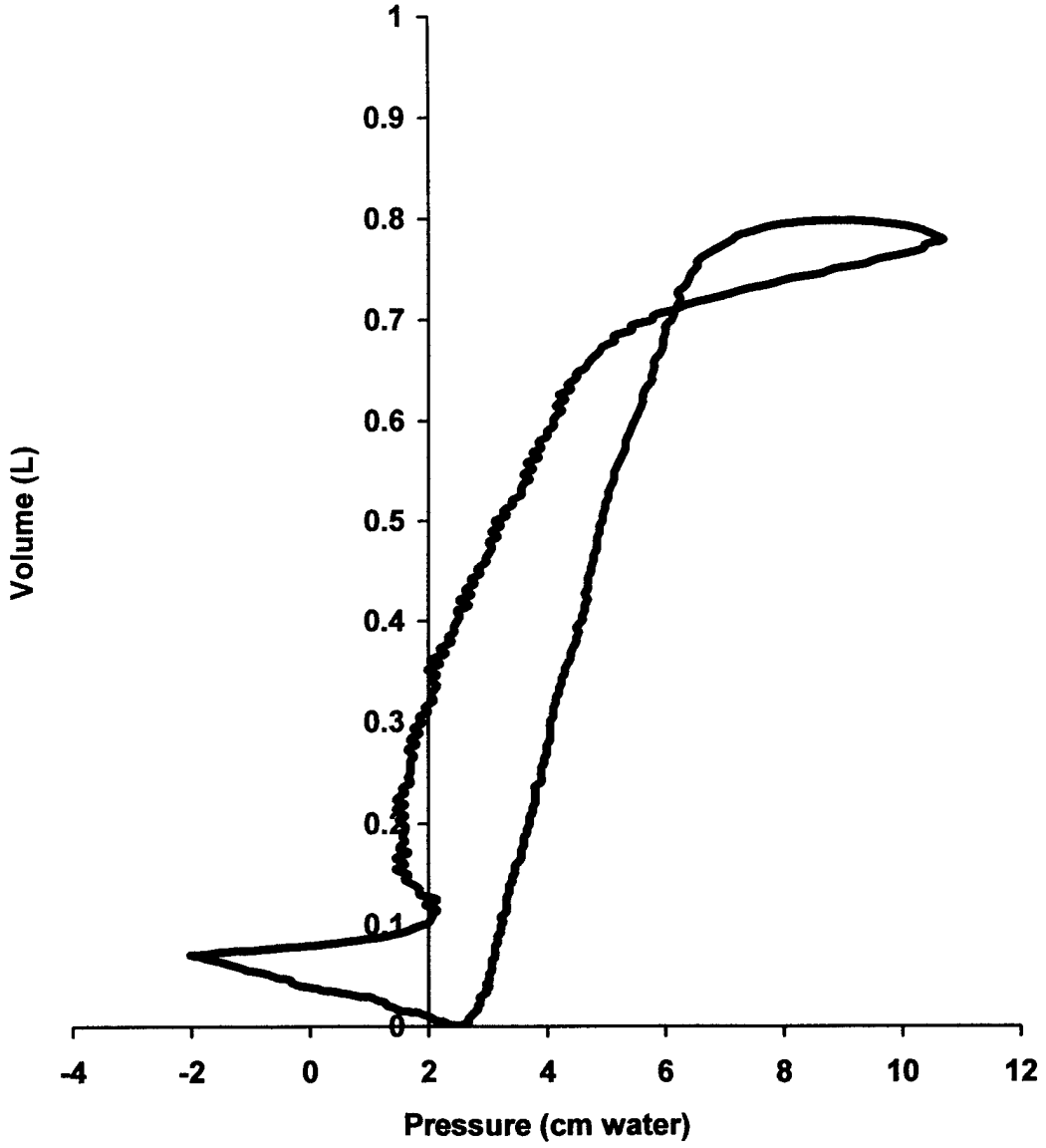
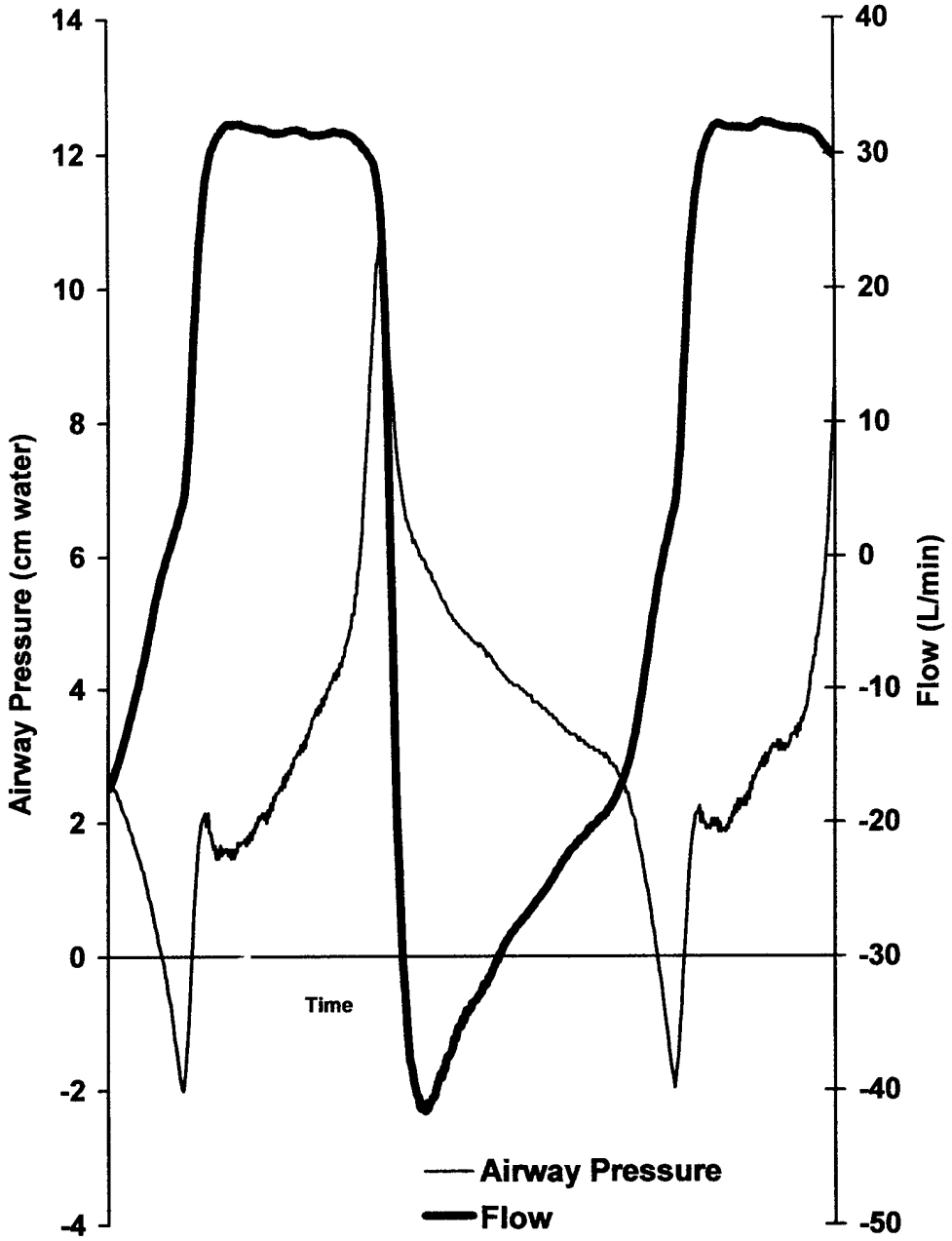


Figure 18
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with Univent 754
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 0 cm water
Duration of Tracing 9 seconds



The aggressiveness of inspiratory flow delivery and WOB_I

Branson (1994) suggests delay time increase is not the sole reason for decreases in inspiratory work of breathing with flow triggering compared to pressure triggering. He explains the aggressiveness of the delivery of flow is important when examining the WOB_I of individuals during spontaneous breathing with mechanical ventilators. WOB_I is a function of not only how far the airway pressure is below baseline airway pressure during inspiration but how long airway pressure remains below baseline airway pressure. The airway pressure with a ventilator that aggressively delivers flow will be below baseline airway pressure for a shorter period of time compared to a ventilator that delivers inspiratory flow less aggressively and airway pressure remains below baseline airway pressure for a longer period or time.

Effect of Variable Versus Nonvariable Inspiratory Flow on WOB_I

An examination of flow, volume, and pressure waveforms suggests another source increased WOB_I of subjects breathing with the Univent 754. The tracing in Figure 18 is airway pressure and flow plotted against time. Figure 17 contains a pressure-volume curve. Both were recorded from the same breath with the same subject breathing with the Univent 754 (CPAP and PSV = 0 cm H_2O). The WOB_I of this breath was 29.92 mJ/L, similar to the mean WOB_I for subjects breathing with the Univent 754 with CPAP and PSV = 0 cm H_2O (mean = 37.43 mJ/L). As can be seen in Figure 18, initially airway pressure decreases and inspiratory flow is triggered. Inspiratory flow rate is set at 35 L/min, 5 L/min greater than the subject's control inspiratory flow as explained in Chapter 4. However, this inspiratory flow was not adequate, as can be seen from the airway

pressure decreasing soon after peak inspiratory flow is attained. In Figure 17, the pressure-volume loop begins at the baseline airway pressure of about 2 cm H_2O. The subject begins the breath and airway pressure decreases to about –2 cm H_2O resulting in flow triggering and airway pressure begins to become positive and volume increases. However, there is a second negative deflection, representing the subject inspiring with an insufficient inspiratory flow. This contrasts to Figures 19 and 20, where a subject is breathing with the Univent 754 that is providing an adequate inspiratory flow. The other three ventilators provide a variable inspiratory flow. The tracings in Figures 19 and 20 are in contrast to the Figures 21 to 46, from subjects breathing with the other ventilators (CPAP and PSV = 0 cm H_2O).

Figure 19
Pressure-Volume Curve
Representative for Breathing with Univent 754
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 0 cm water
Imposed Work of Breathing 4.78 mJ/L
Imposed Pressure Time Product 0.70 cm water/s/L

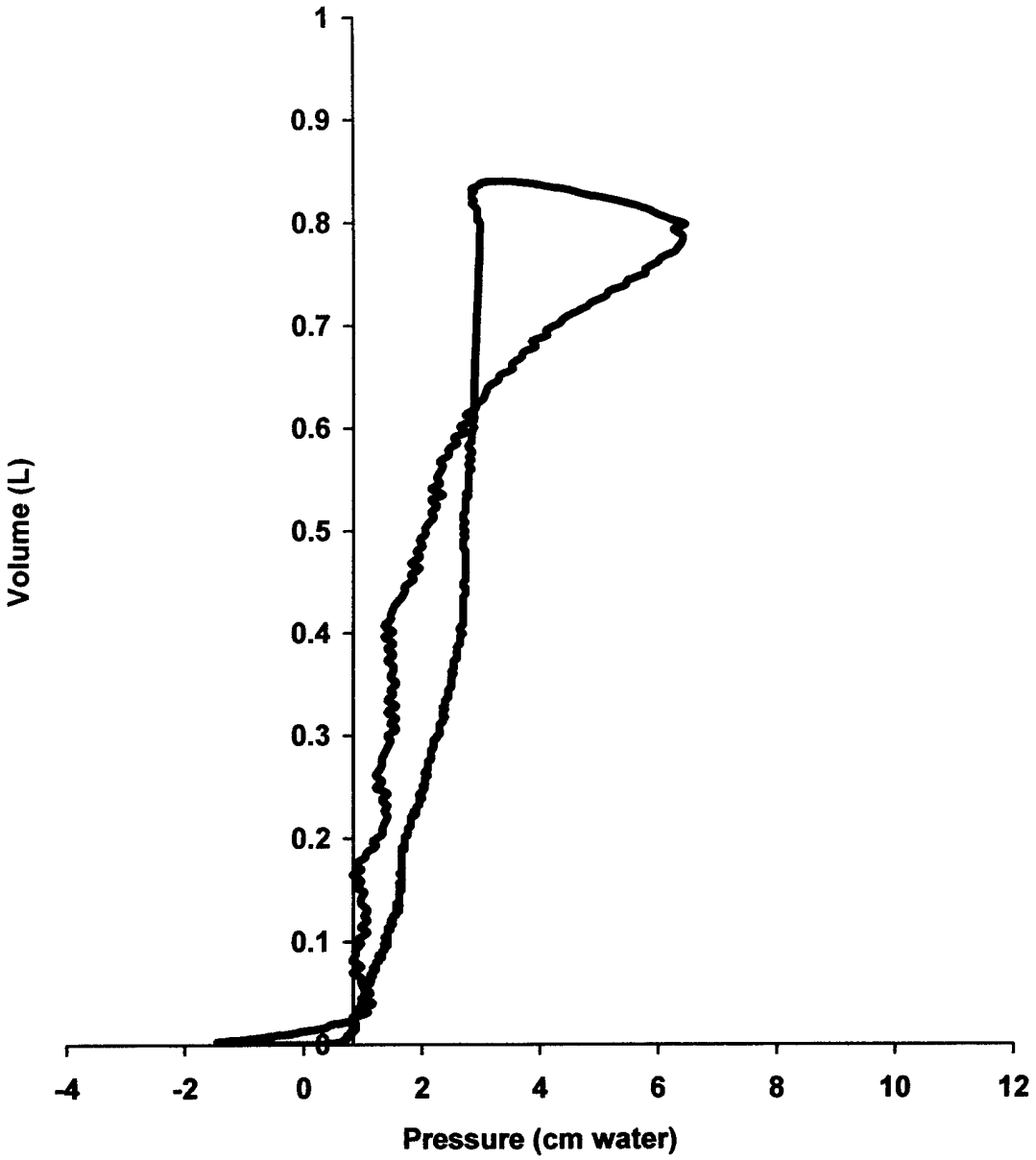


Figure 20
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with the Univent 754
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 0 cm water
Duration of Tracing 6 seconds

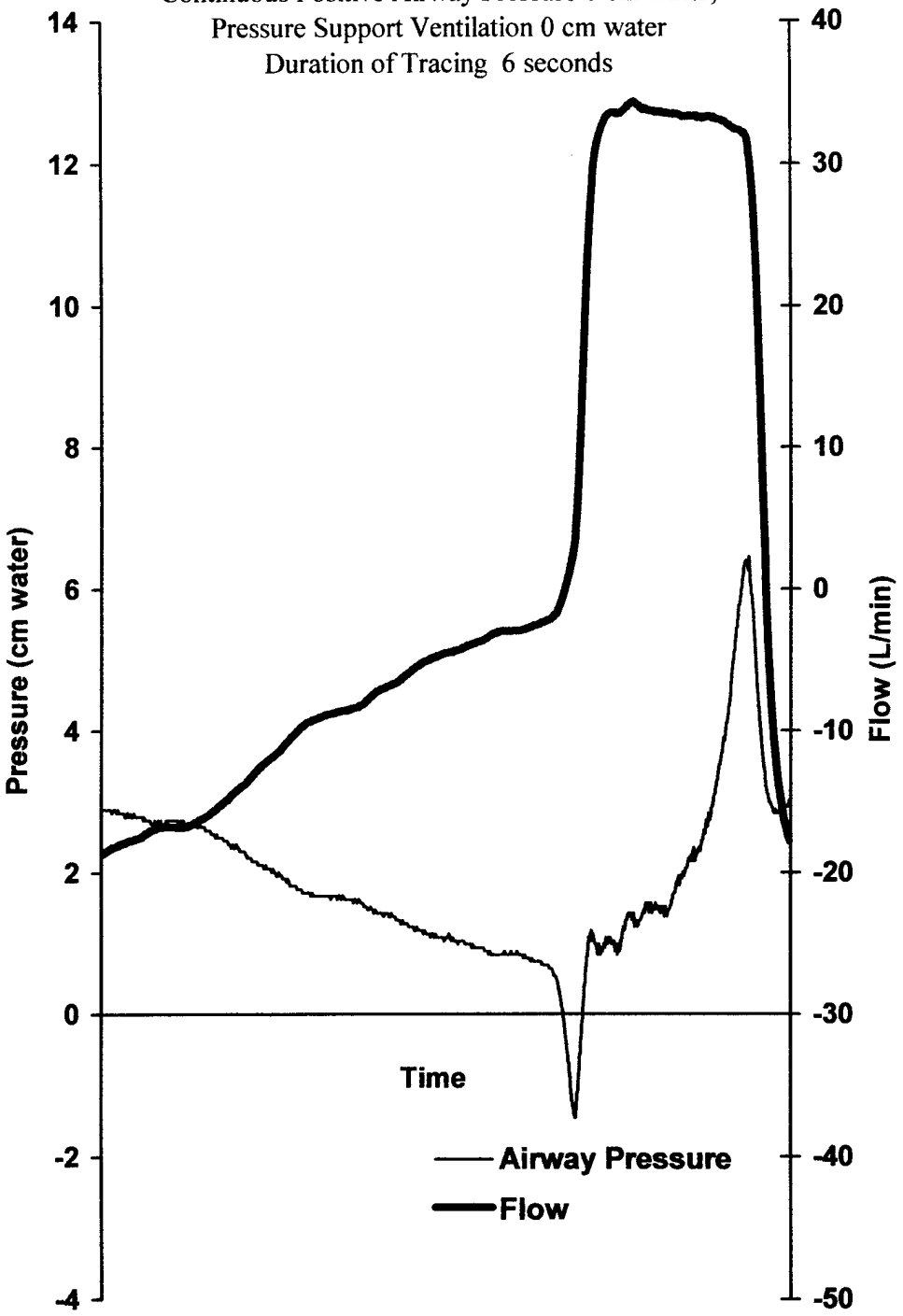


Figure 21
Pressure-Volume Curve
Representative for Breathing with 7200ae
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 0 cm water
Imposed Work of Breathing 25 mJ/L
Imposed Pressure Time Product 0.50 cm water/s/L

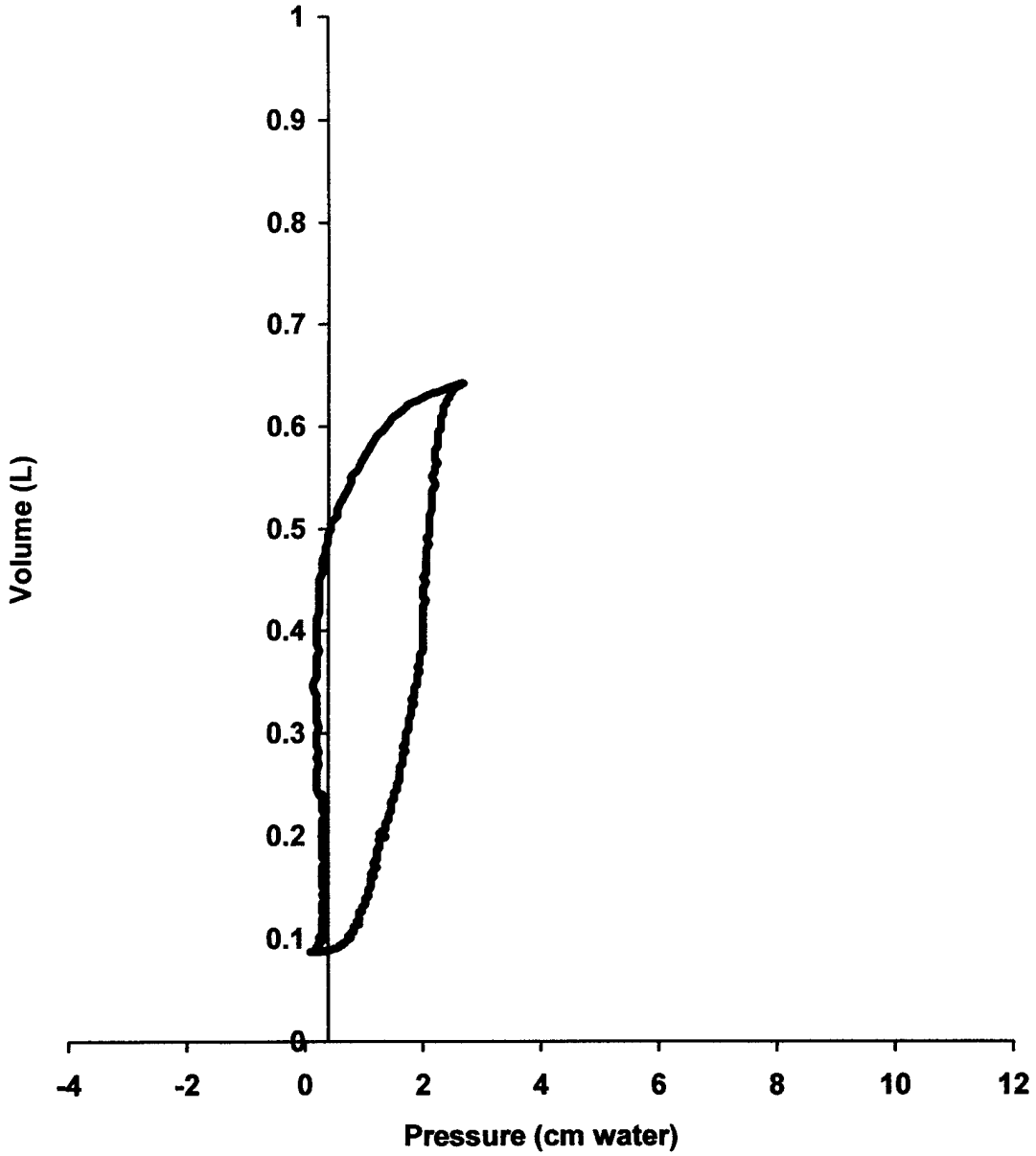


Figure 22
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with 7200ae
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 0 cm water
Duration of Tracing 9 seconds

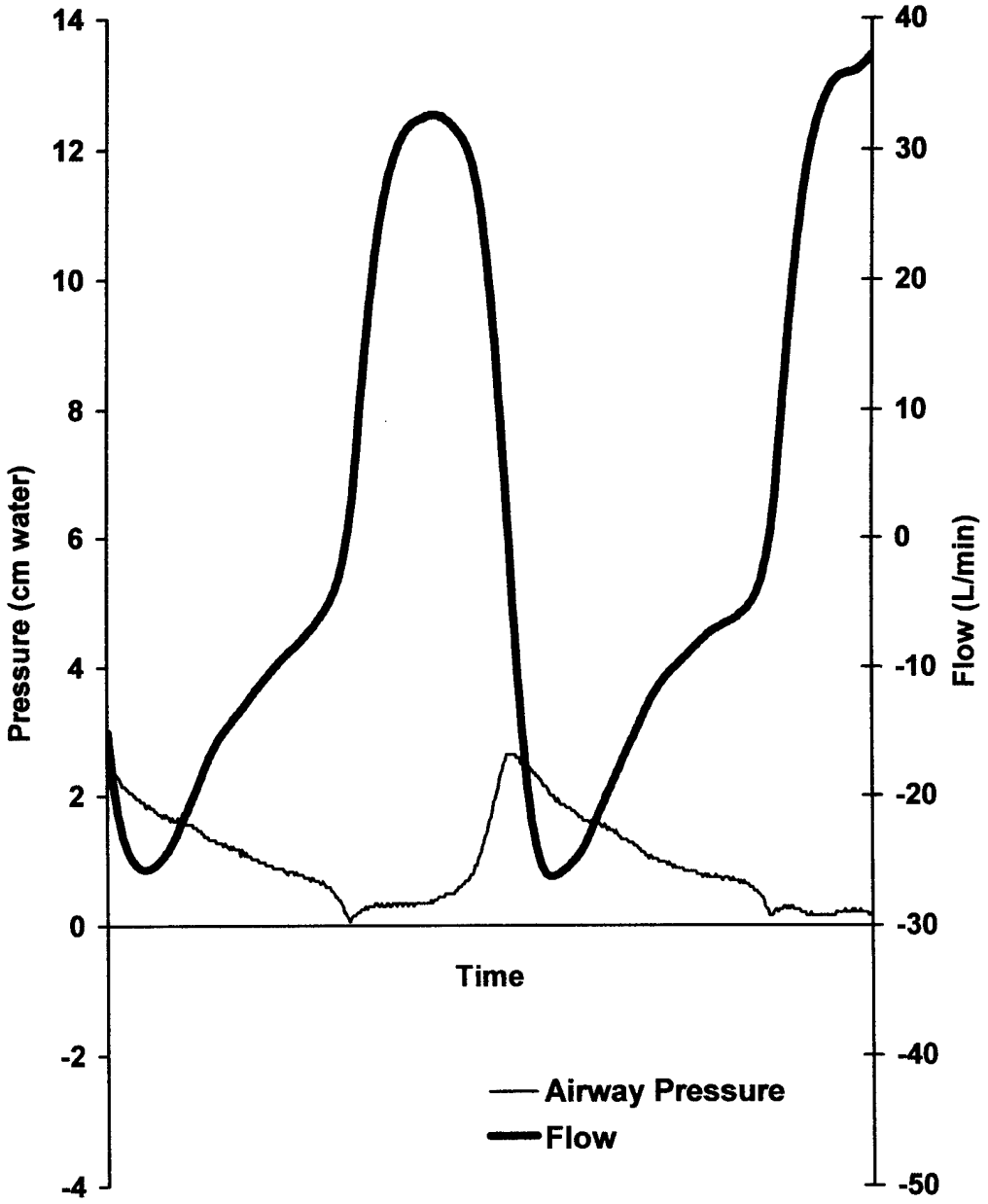


Figure 23
Pressure-Volume Curve
Representative for Breathing with Achieva
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 0 cm water
Imposed Work of Breathing 30 mJ/L
Imposed Pressure Time Product 1.14 cm water/s/L

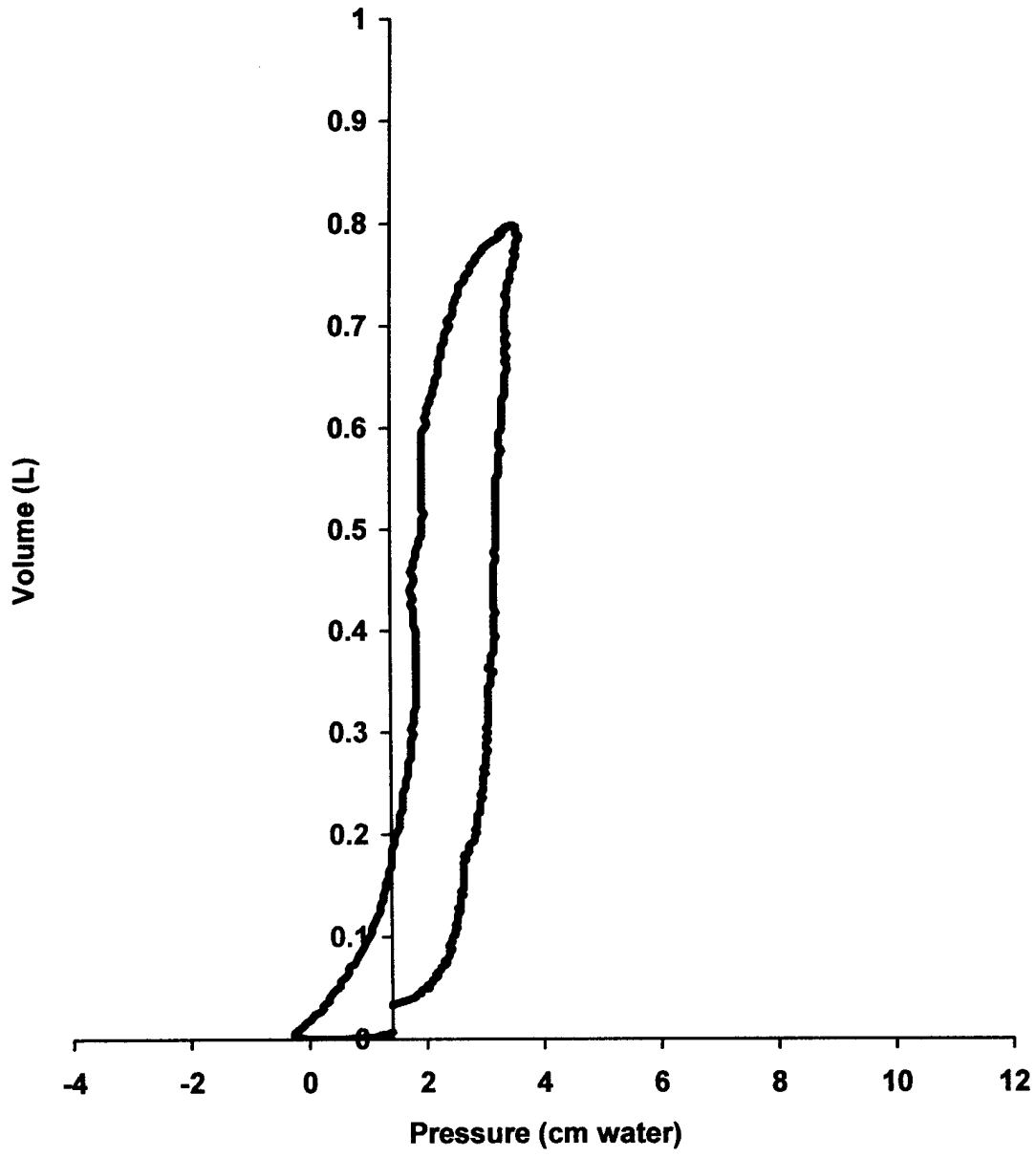


Figure 24
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with Achieva
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 0 cm water
Duration of Tracing 9 seconds

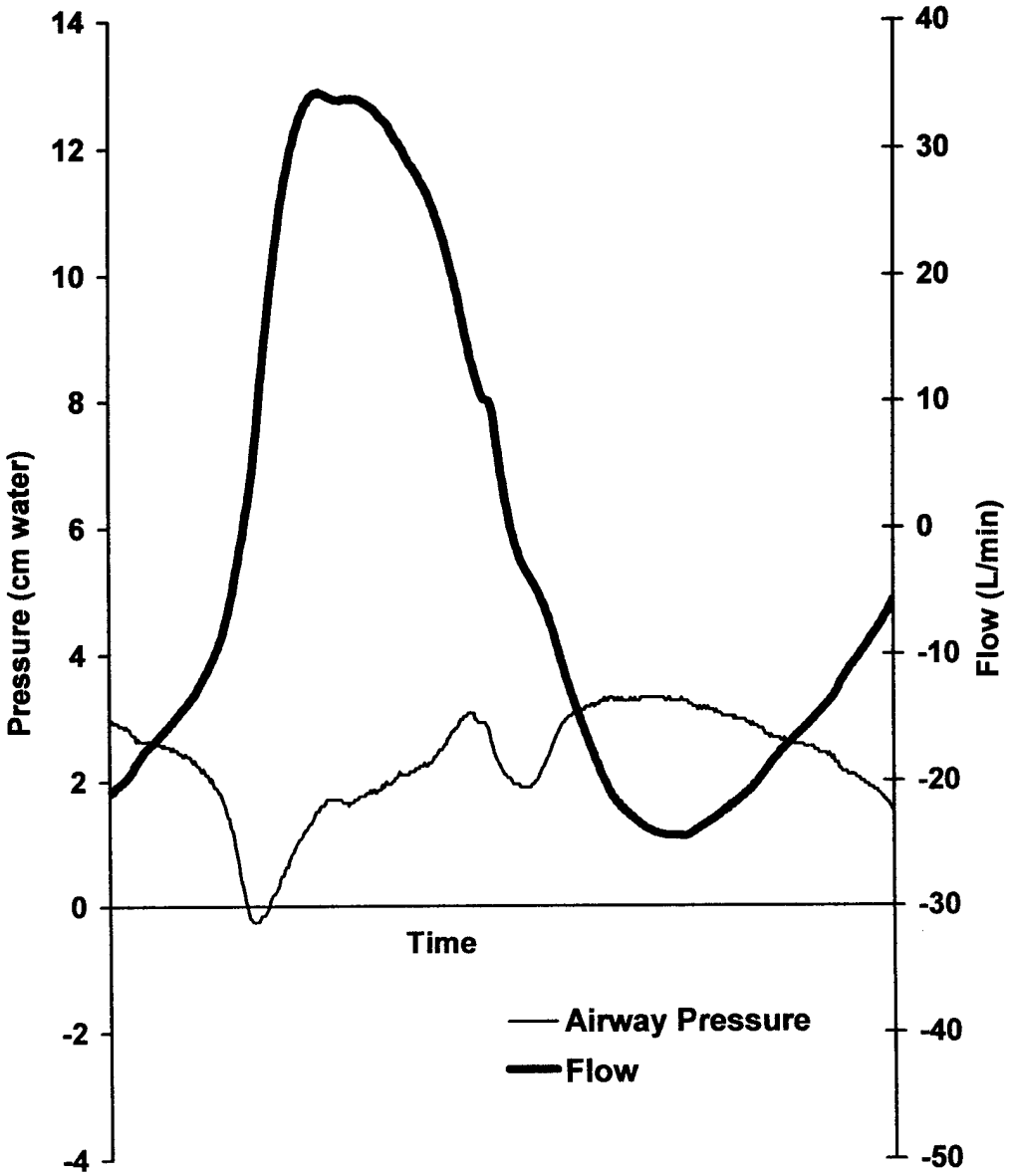


Figure 25
Pressure-Volume Curve
Representative for Breathing with LTV 1000
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 0 cm water
Imposed Work of Breathing 4 mJ/L
Imposed Pressure Time Product 0.45 cm water/s/L

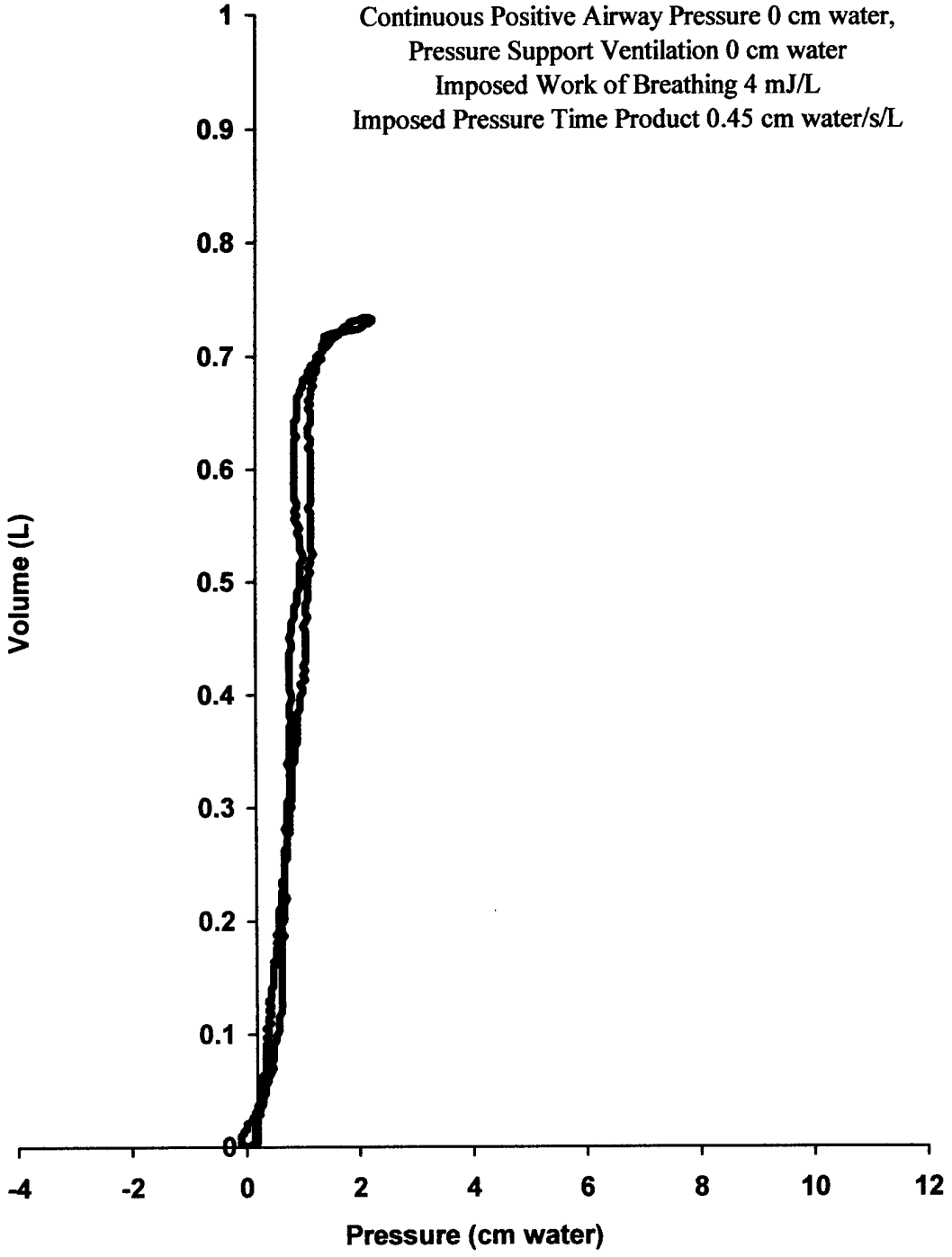


Figure 26
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with LTV 1000
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 0 cm water
Duration of Tracing 9 seconds

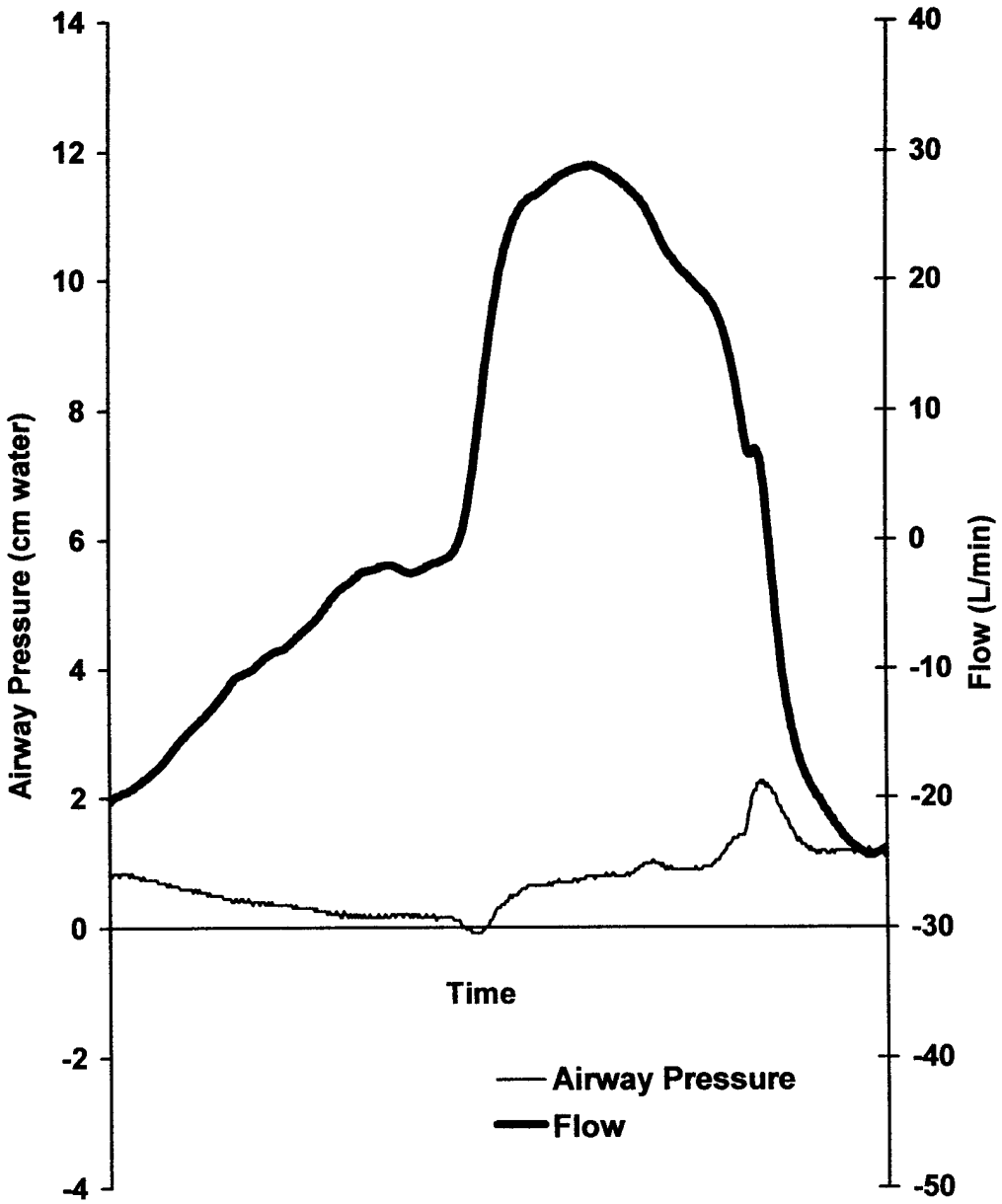


Figure 27
Pressure-Volume Curve
Representative for Breathing with 7200ae
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 10 cm water
Imposed Work of Breathing 0.7 mJ/L
Imposed Pressure Time Product 0.68 cm water/s/L

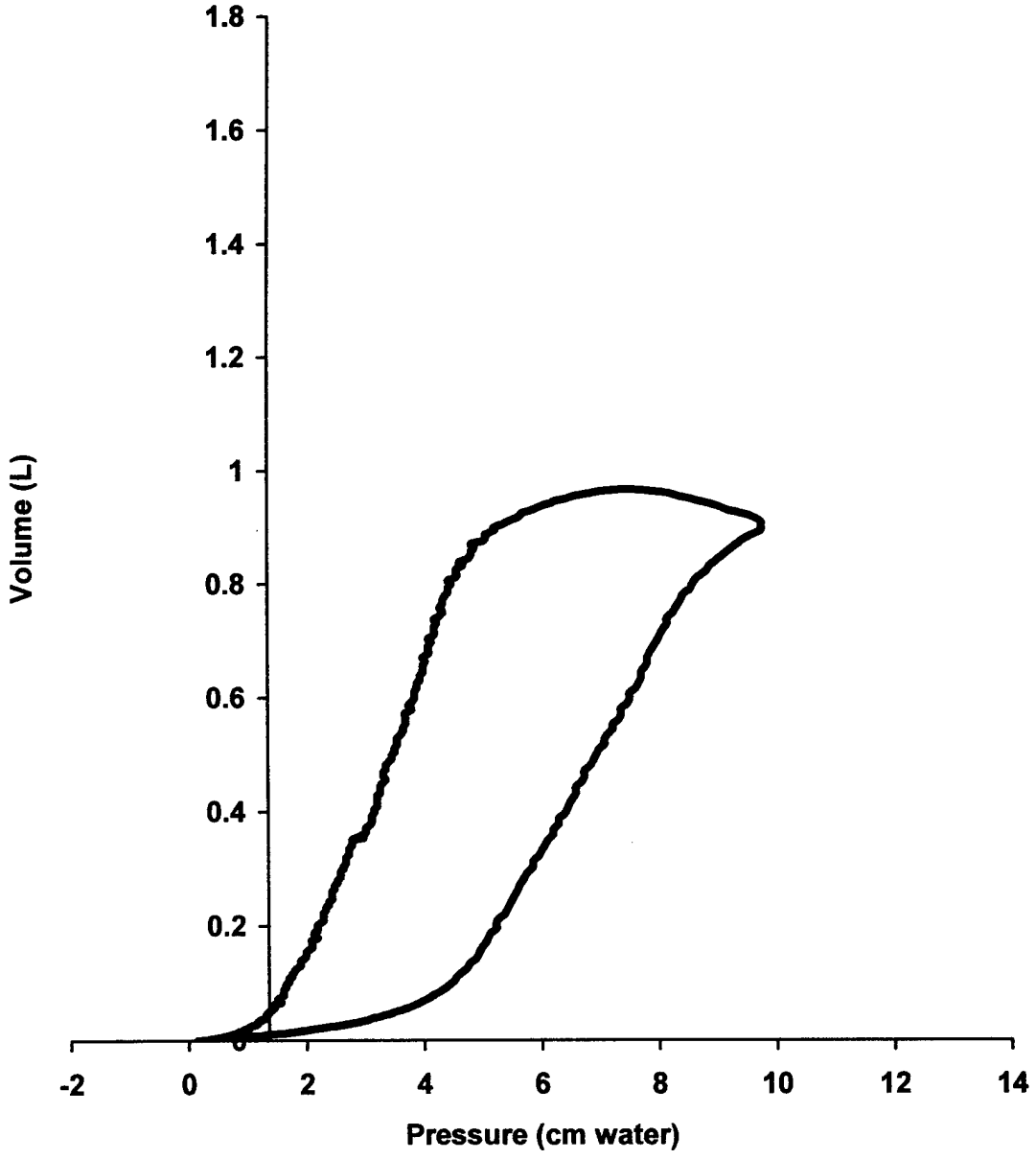


Figure 28
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with 7200ae
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 10 cm water
Duration of Tracing 3.38 seconds

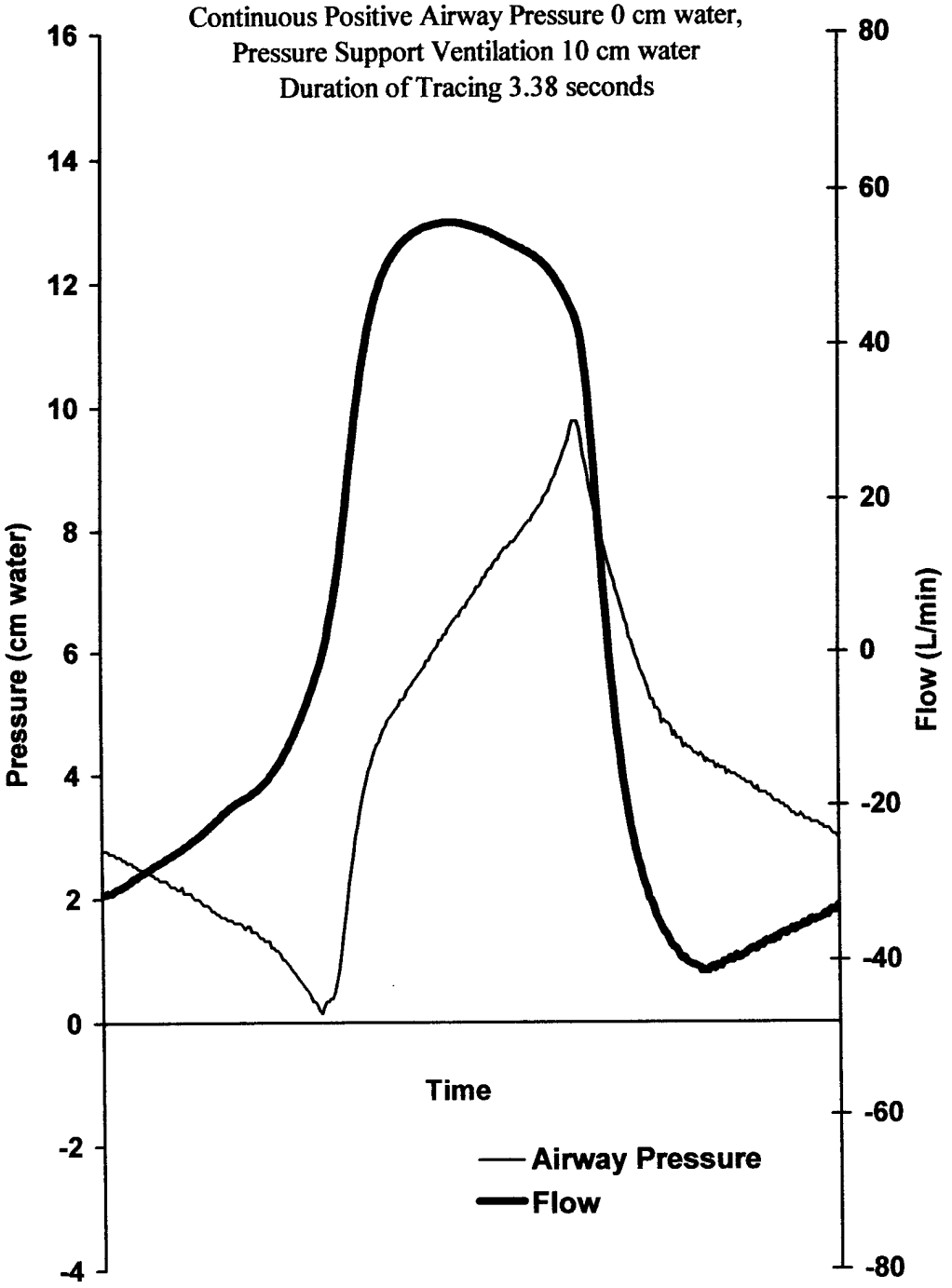


Figure 29
Pressure-Volume Curve
Representative for Breathing with Achieva
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 10 cm water
Imposed Work of Breathing 1.42 mJ/L
Imposed Pressure Time Product 0.77 cm water/s/L

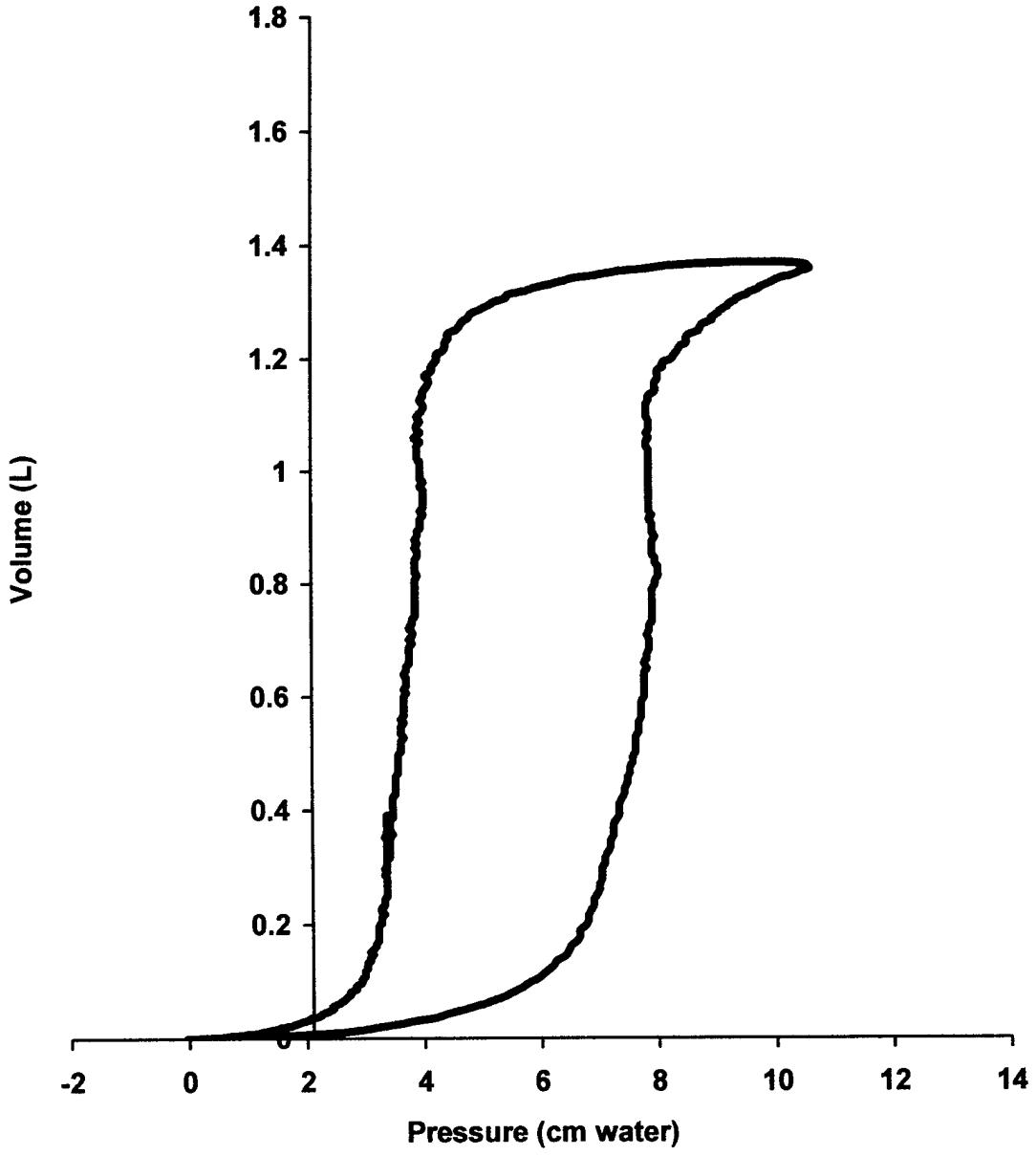


Figure 30
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with Achieva
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 10 cm water
Duration of Tracing 3.38 seconds

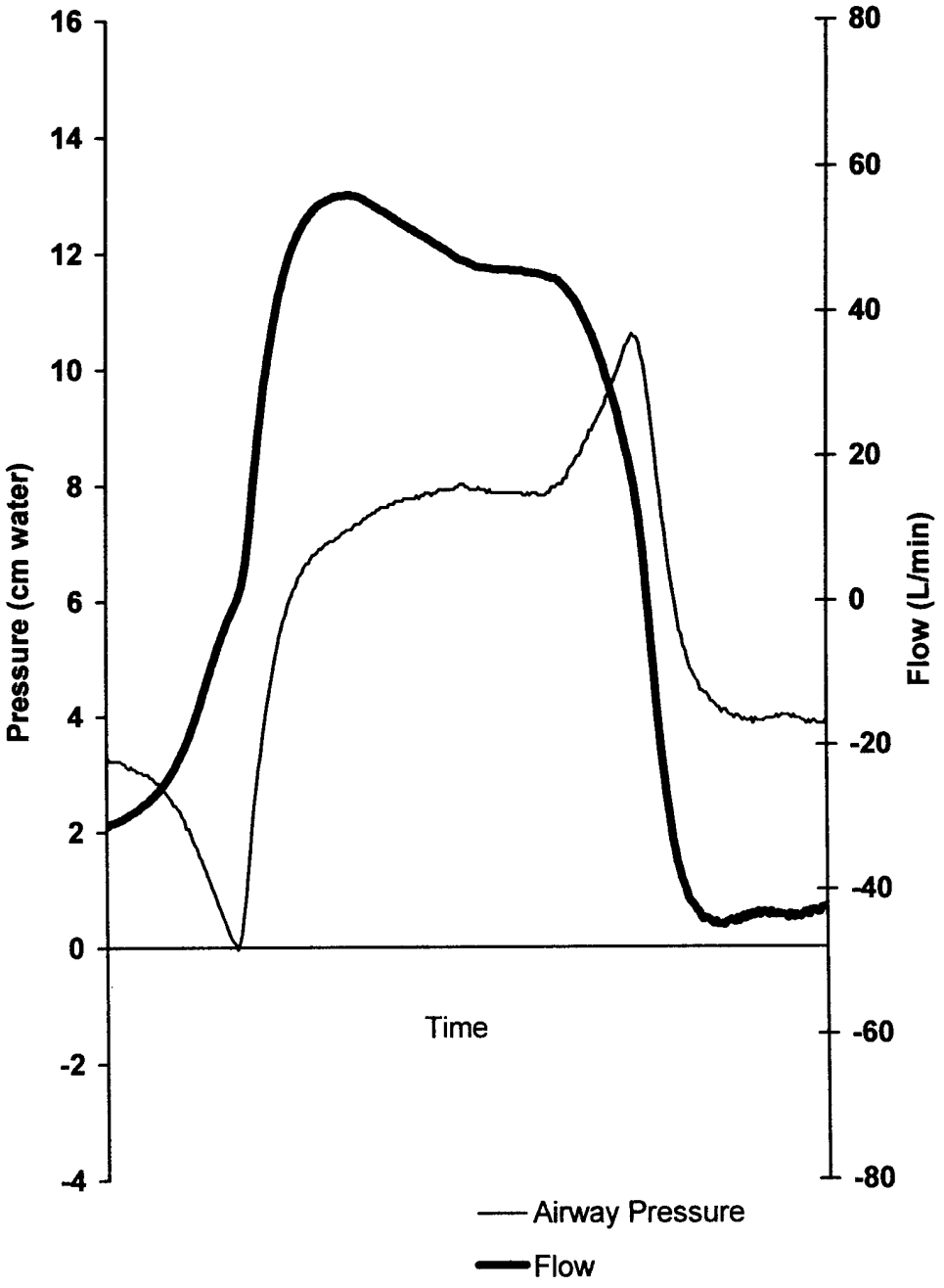


Figure 31
Pressure-Volume Curve
Representative for Breathing with LTV 1000
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 10 cm water
Imposed Work of Breathing 2.7 mJ/L
Imposed Pressure Time Product 0.44 cm water/s/L

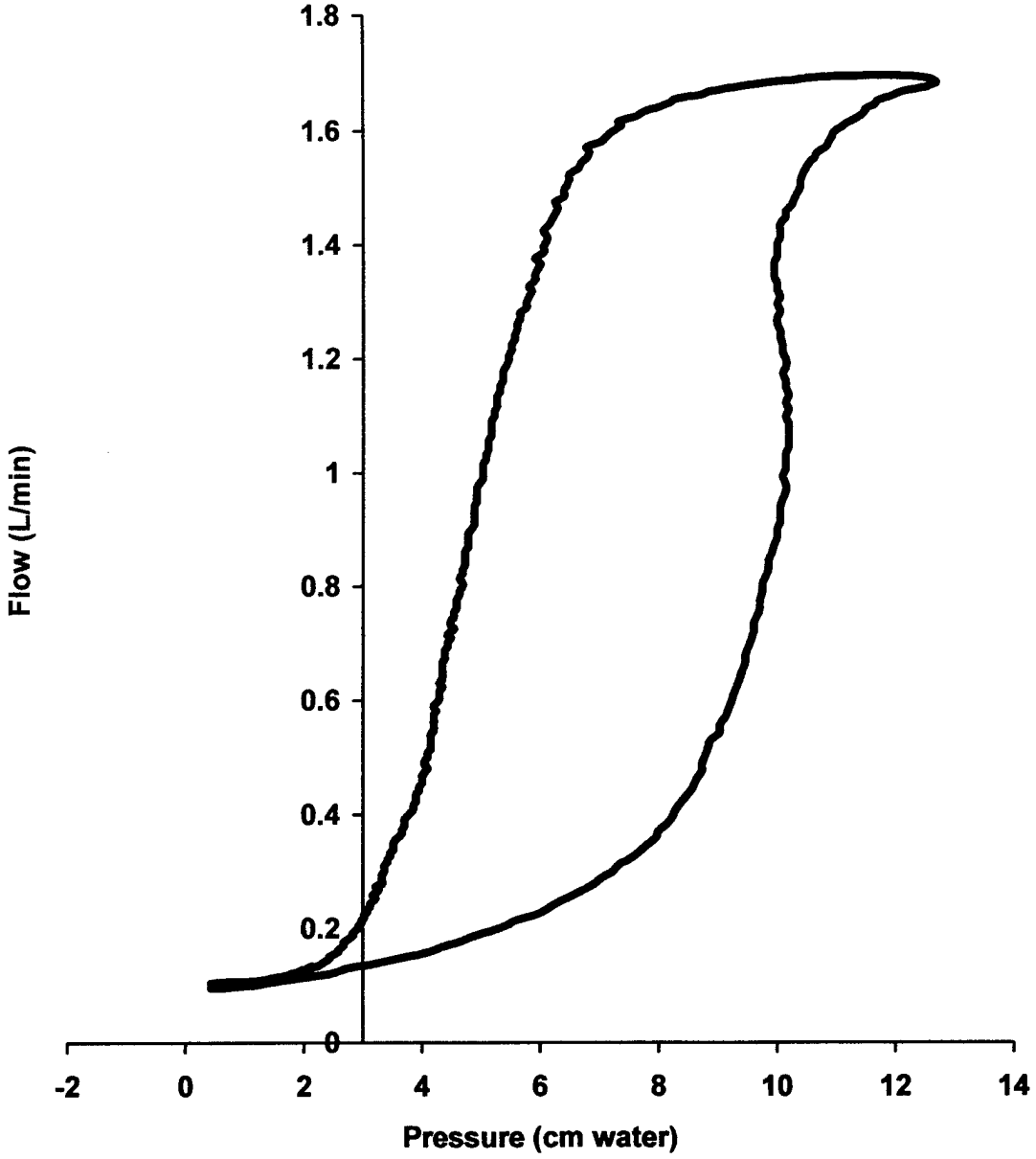


Figure 32
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with LTV 1000
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 10 cm water
Duration of Tracing 3.38 seconds

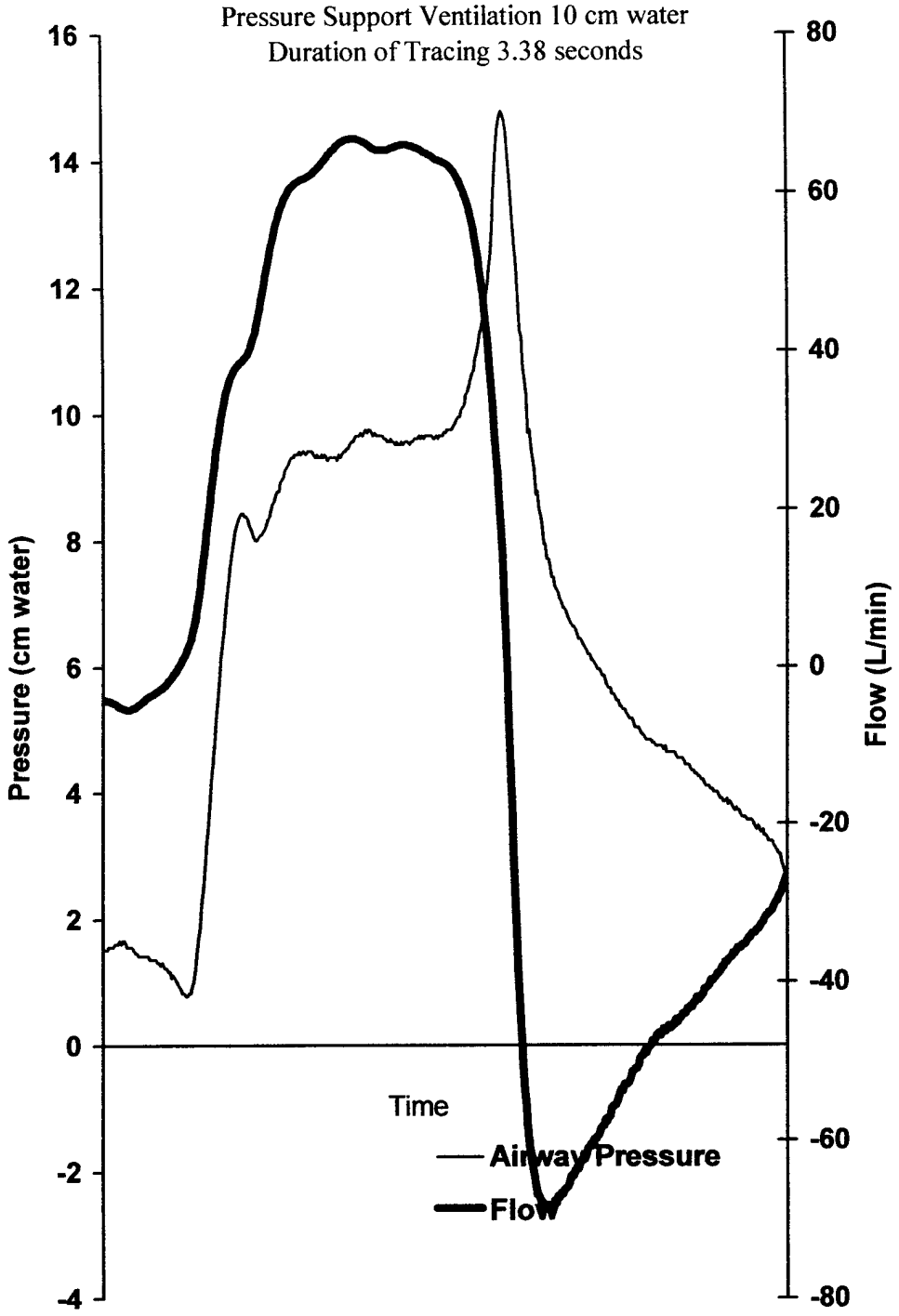


Figure 33
Pressure-Volume Curve
Representative for Breathing with 7200ae
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 0 cm water
Imposed Work of Breathing 43 mJ/L
Imposed Pressure Time Product 0.80 cm water/s/L

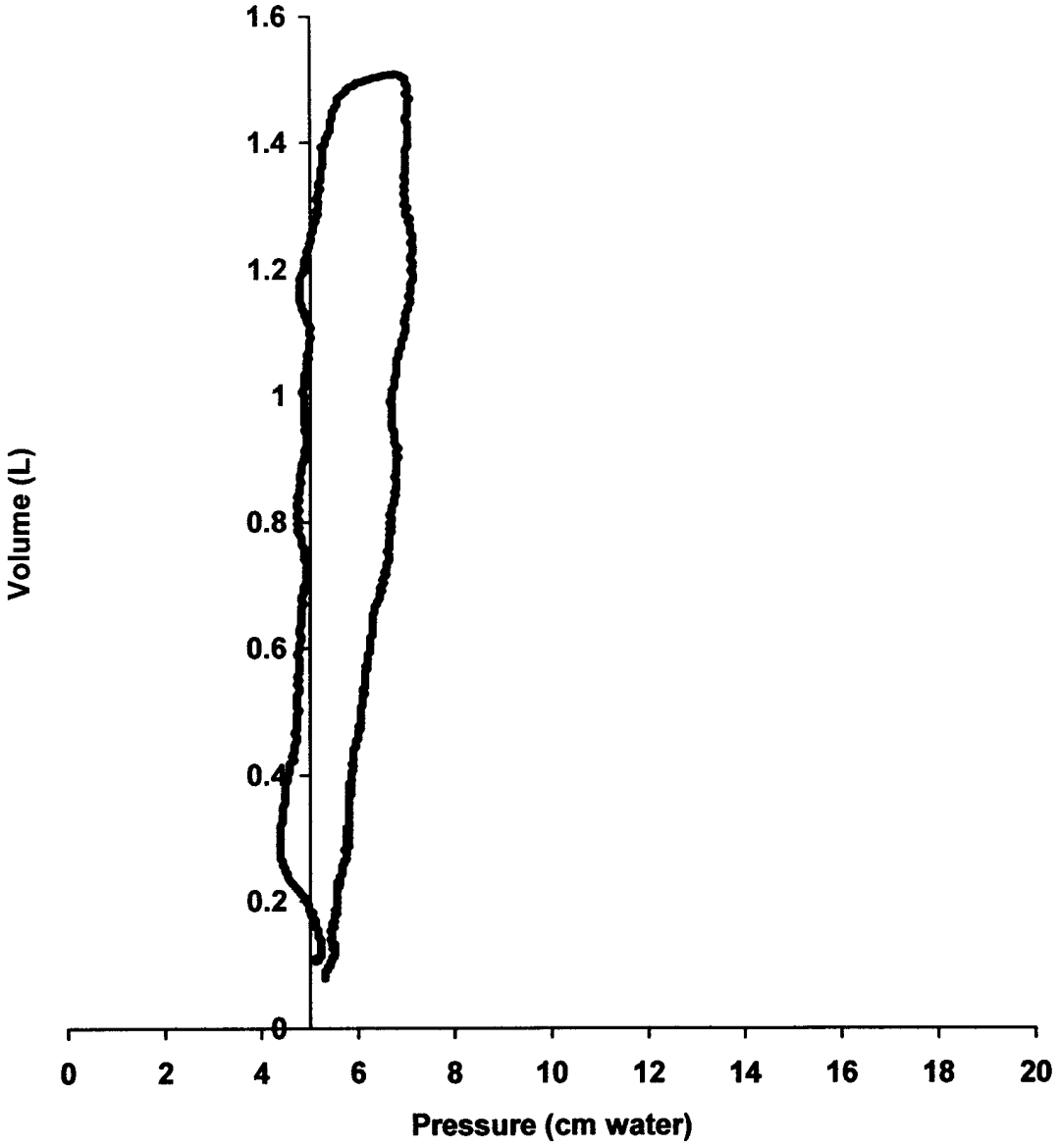


Figure 34
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with 7200ae
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 0 cm water
Duration of Tracing 6 seconds

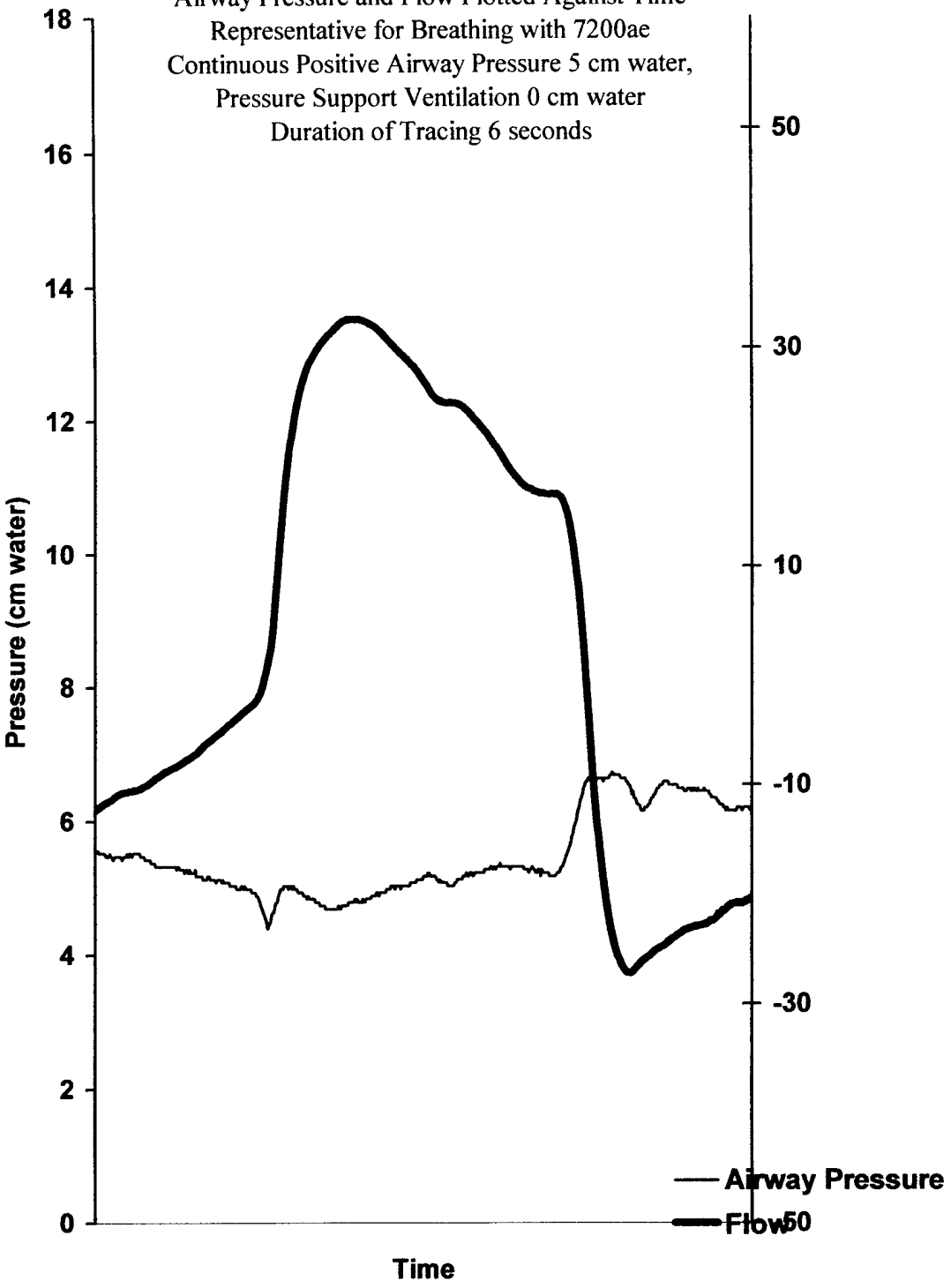


Figure 35
Pressure-Volume Curve
Representative for Breathing with Univent 754
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 0 cm water
Imposed Work of Breathing 170 mJ/L
Imposed Pressure Time Product 3.7 cm water/s/L

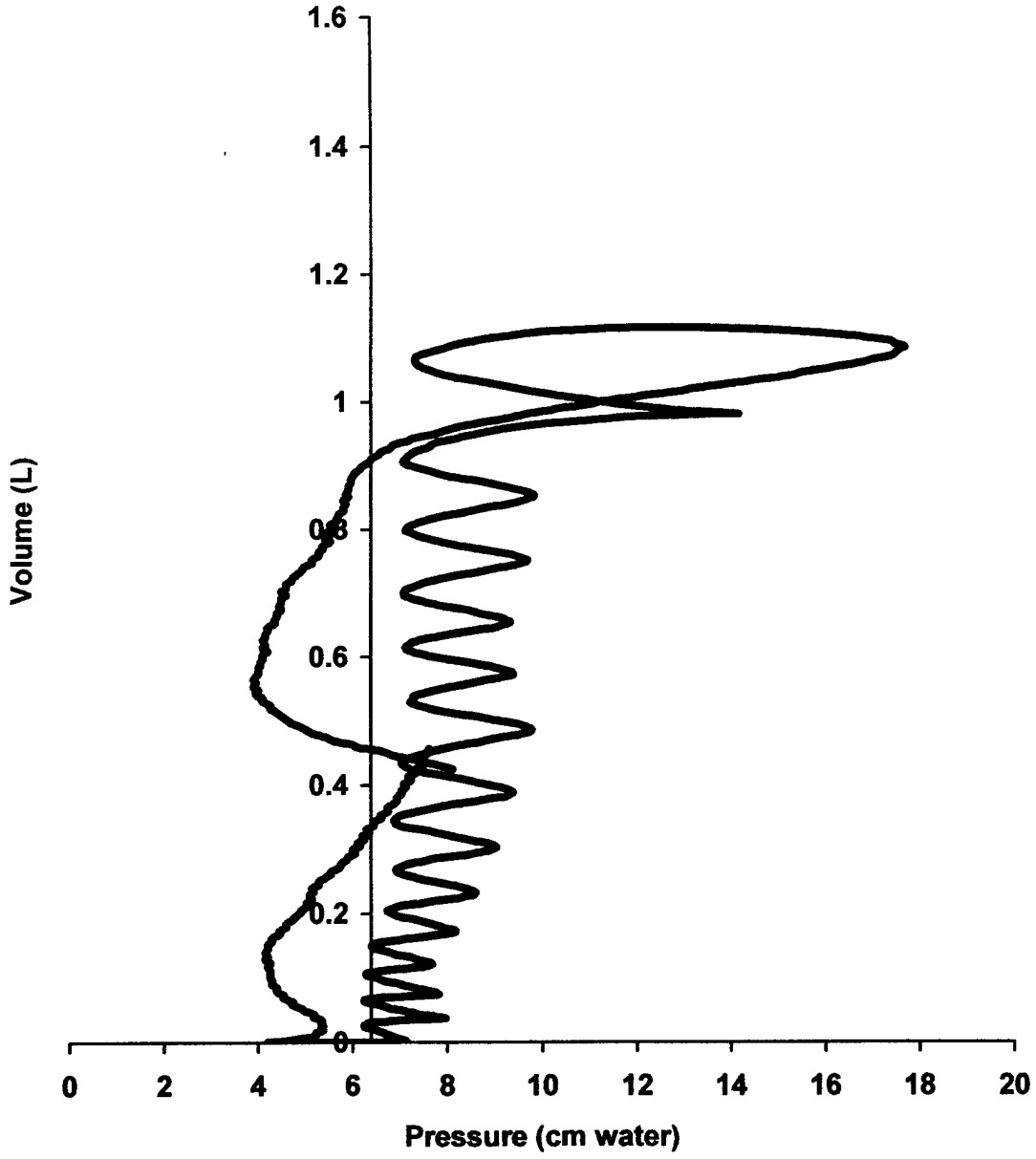


Figure 36
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with Univent 754
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 0 cm water
Duration of Tracing 6 seconds

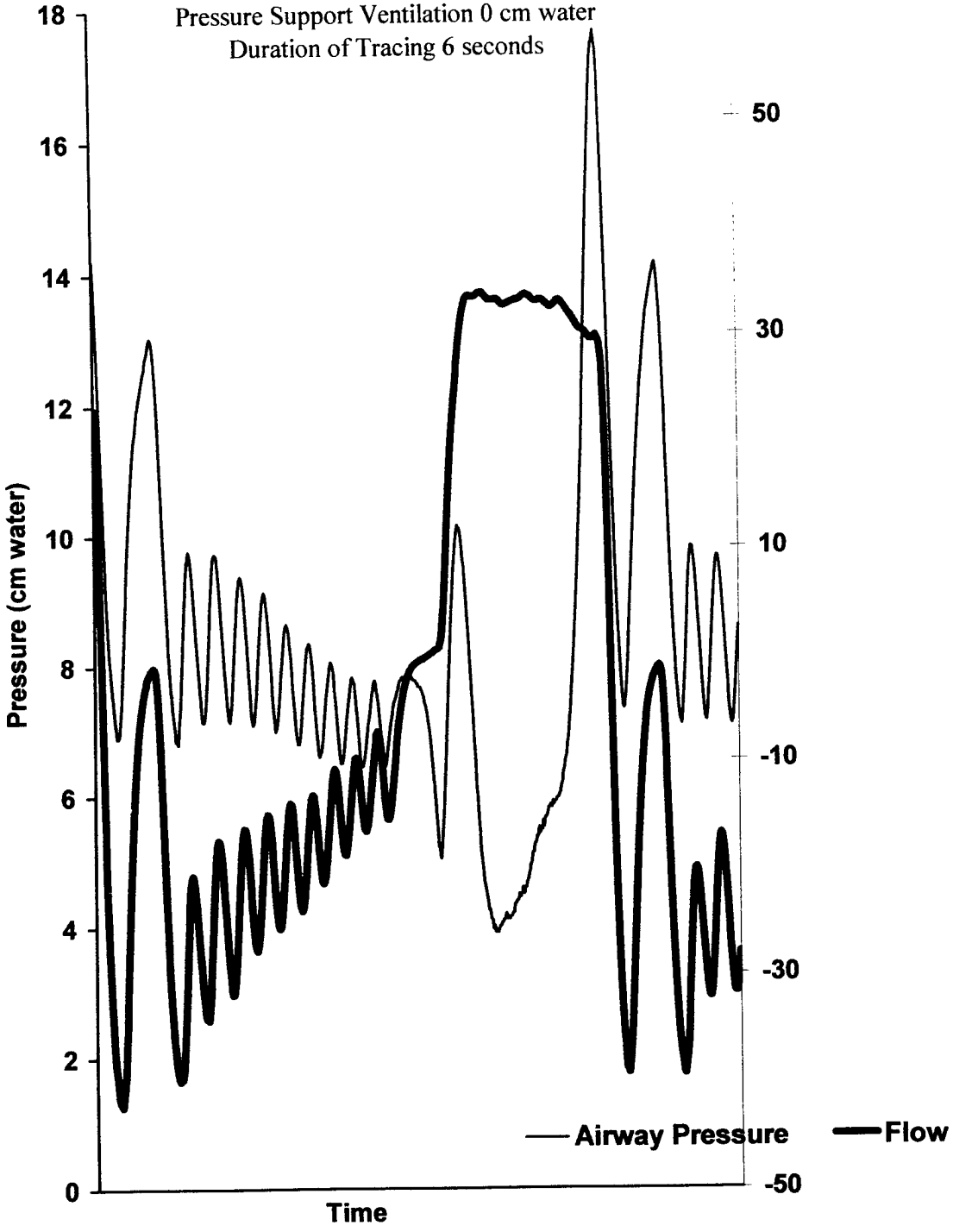


Figure 37
Pressure-Volume Curve
Representative for Breathing with Achieva
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 0 cm water
Imposed Work of Breathing 13 mJ/L
Imposed Pressure Time Product 1.00 cm water/s/L

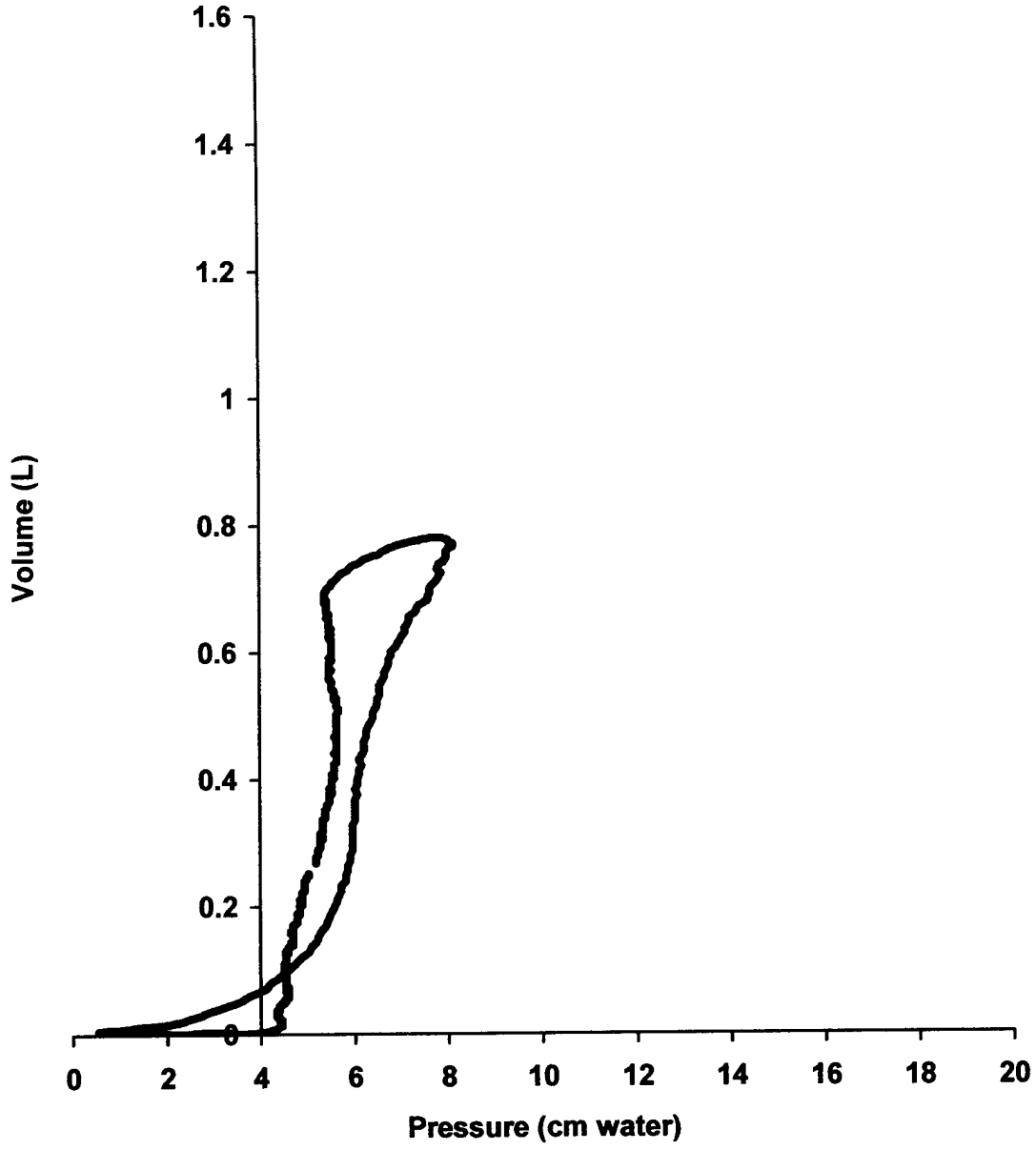


Figure 38
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with Achieva
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 0 cm water
Duration of Tracing 6 seconds

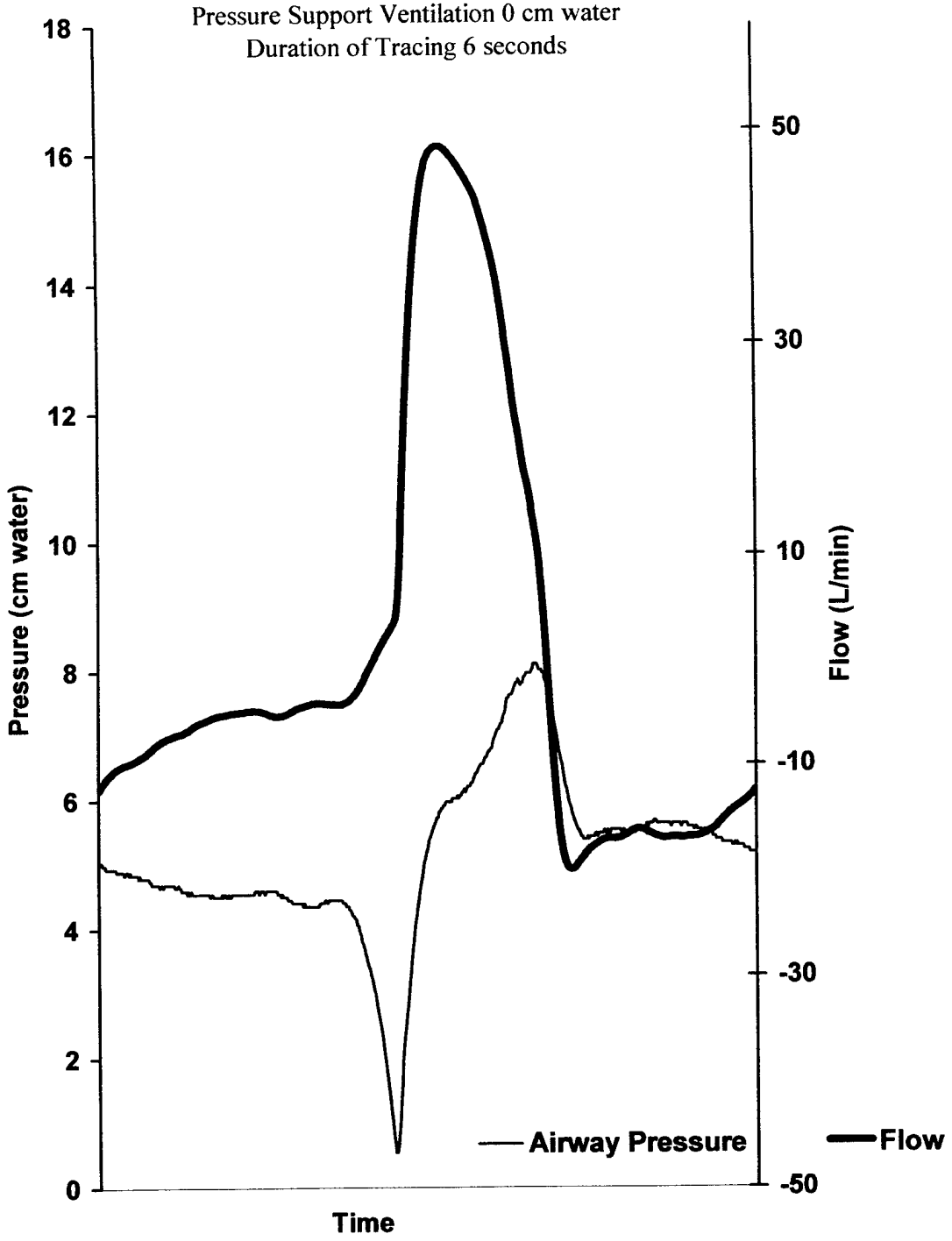


Figure 39
Pressure-Volume Curve
Representative for Breathing with LTV 1000
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 0 cm water
Imposed Work of Breathing 9 mJ/L
Imposed Pressure Time Product 0.40 cm water/s/L

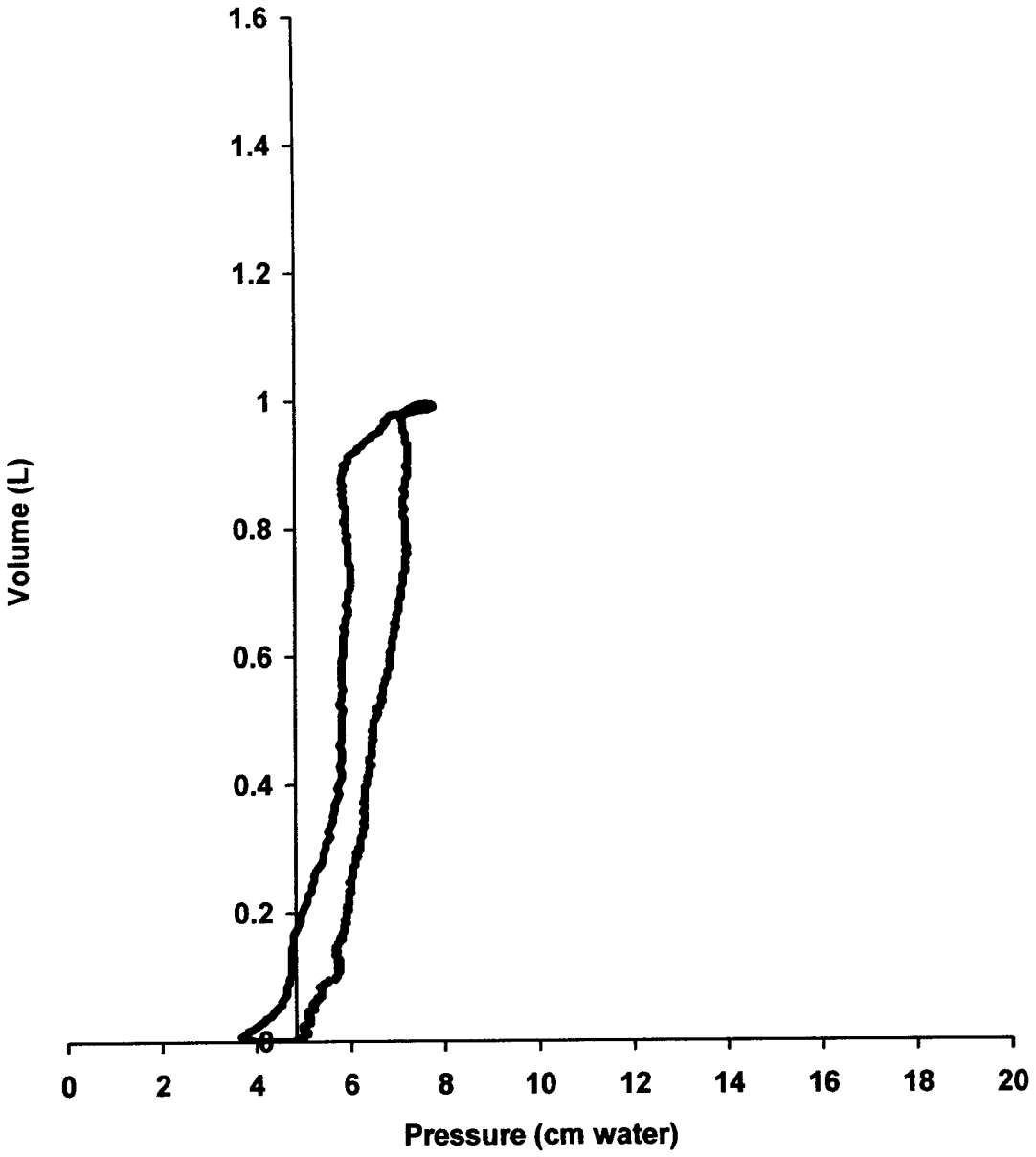


Figure 40
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with LTV 1000
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 0 cm water
Duration of Tracing 6 seconds

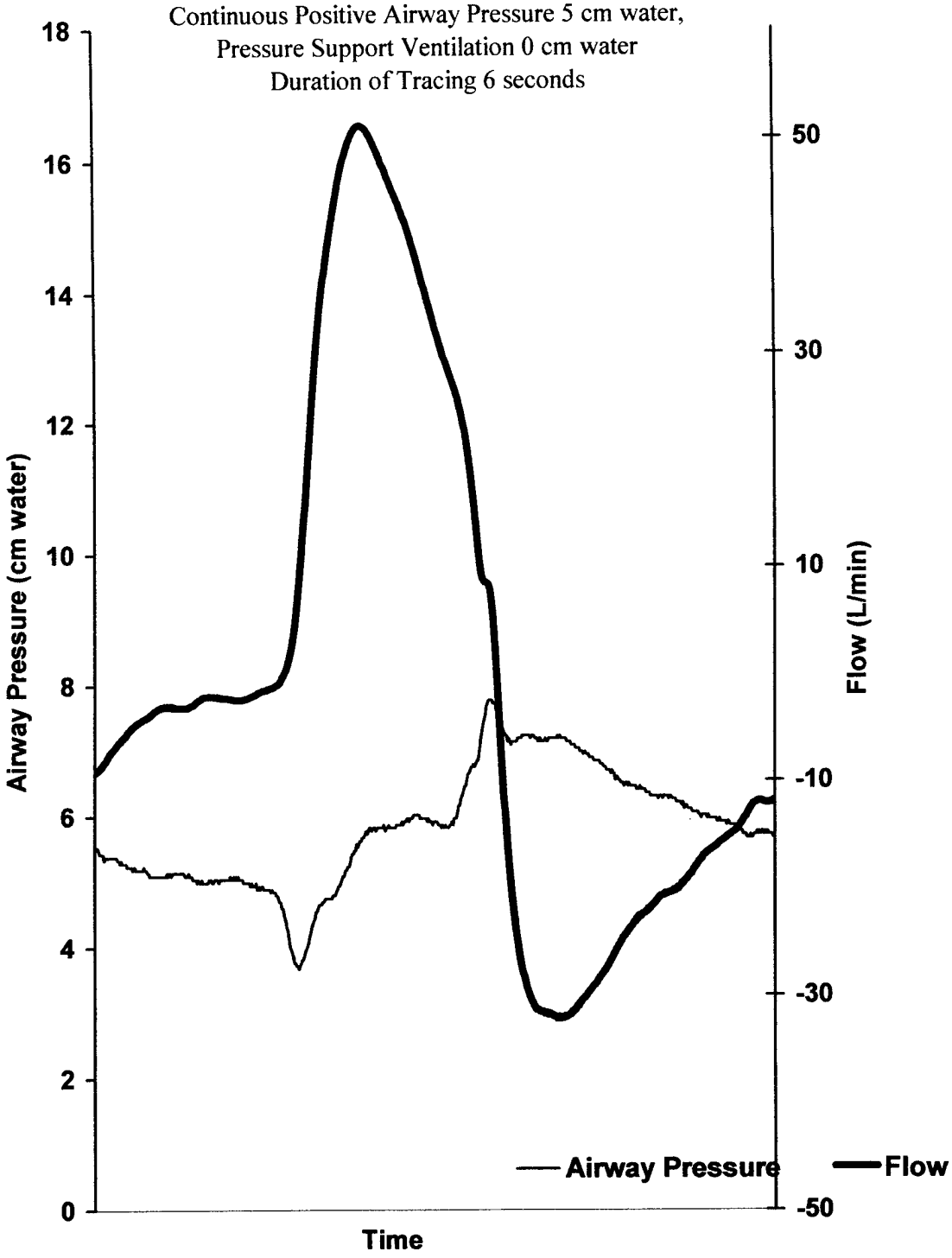


Figure 41
Pressure-Volume Curve
Representative for Breathing with 7200ae
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 10 cm water
Imposed Work of Breathing 2.7 mJ/L
Imposed Pressure Time Product 0.53 cm water/s/L

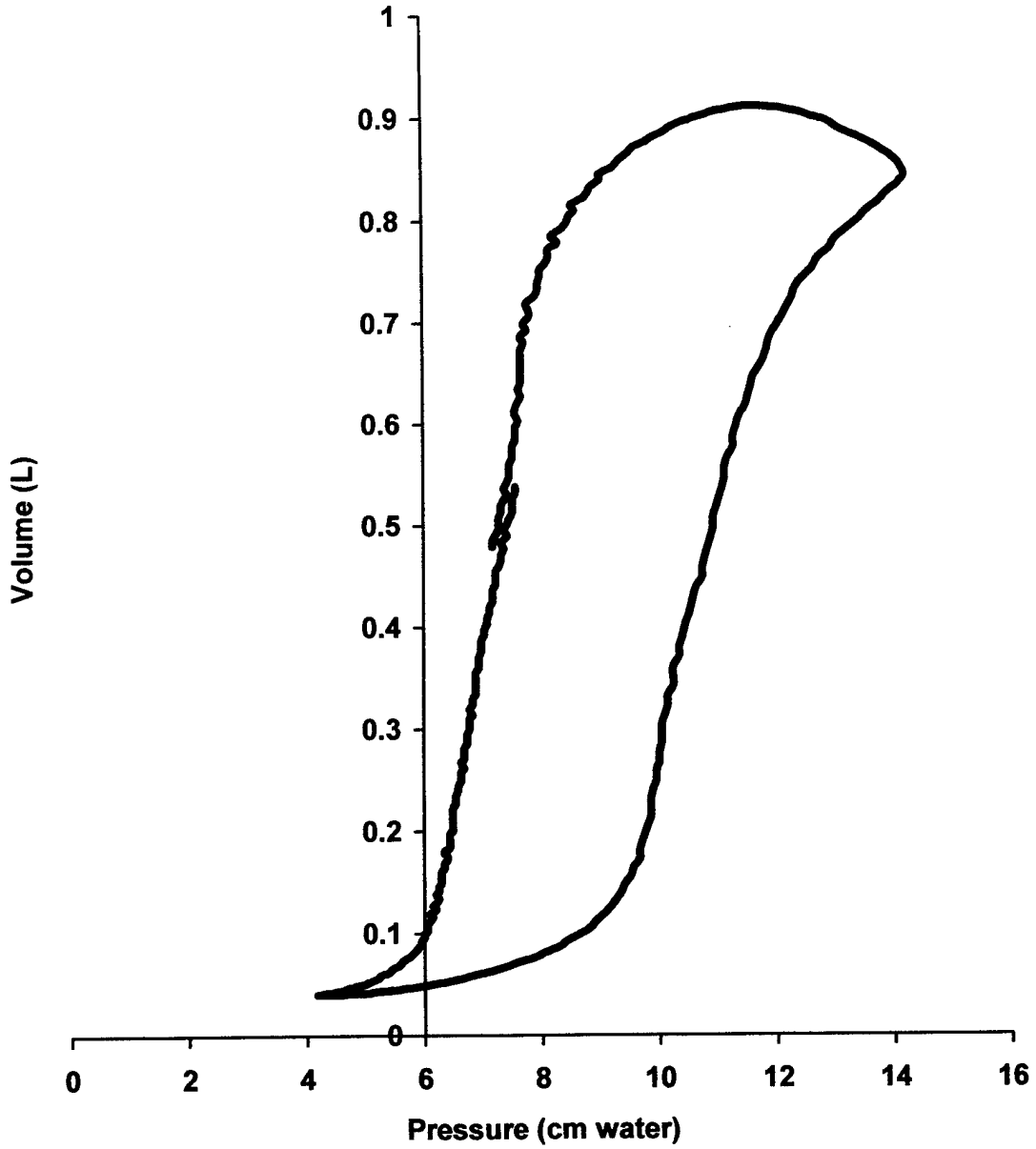


Figure 42
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with 7200ae
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 10 cm water
Duration of Tracing 3.13 secs

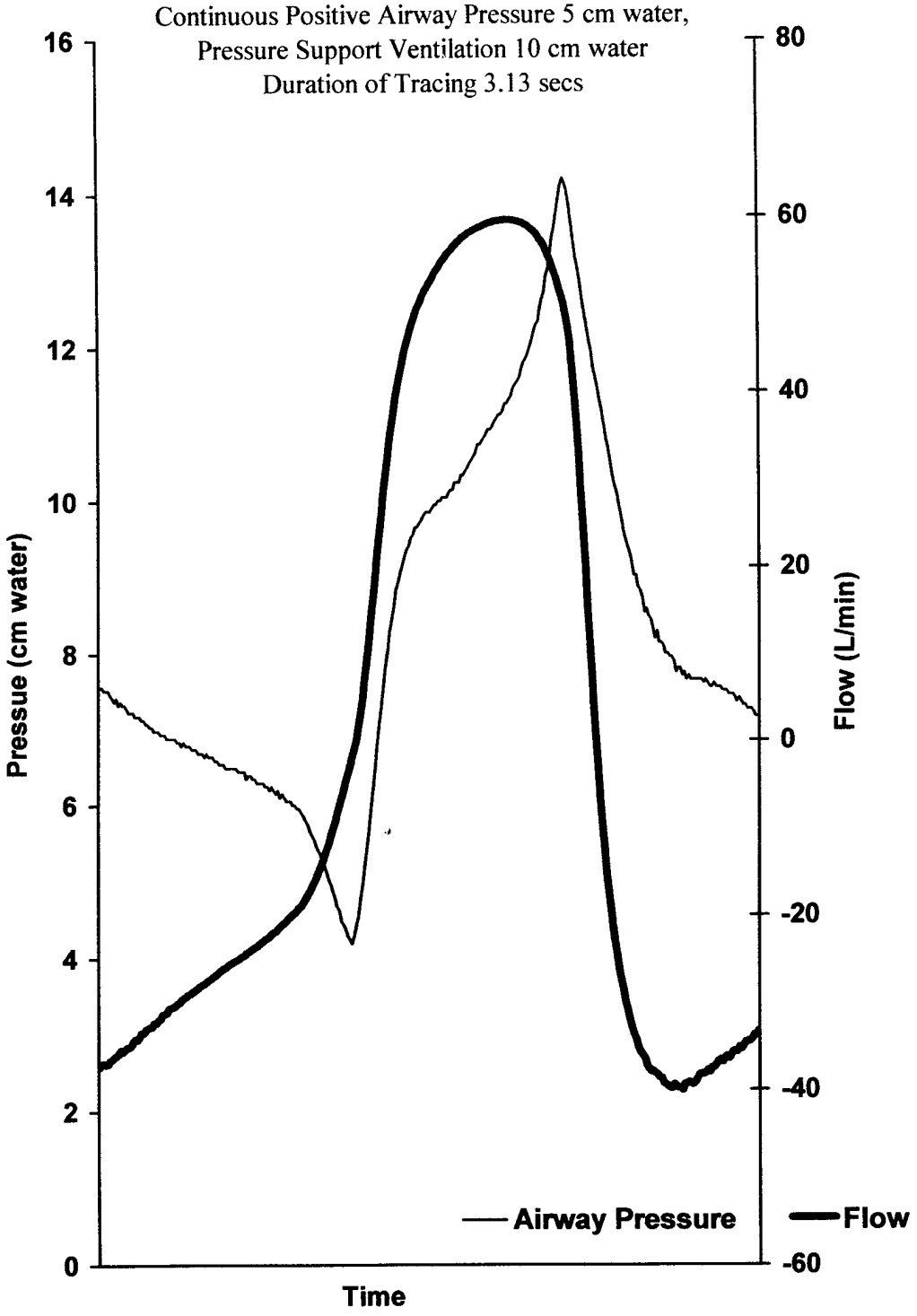


Figure 43
Pressure-Volume Curve
Representative for Breathing with Achieva
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 10 cm water
Imposed Work of Breathing 3.81 mJ/L
Imposed Pressure Time Product 0.77 cm water/s/L

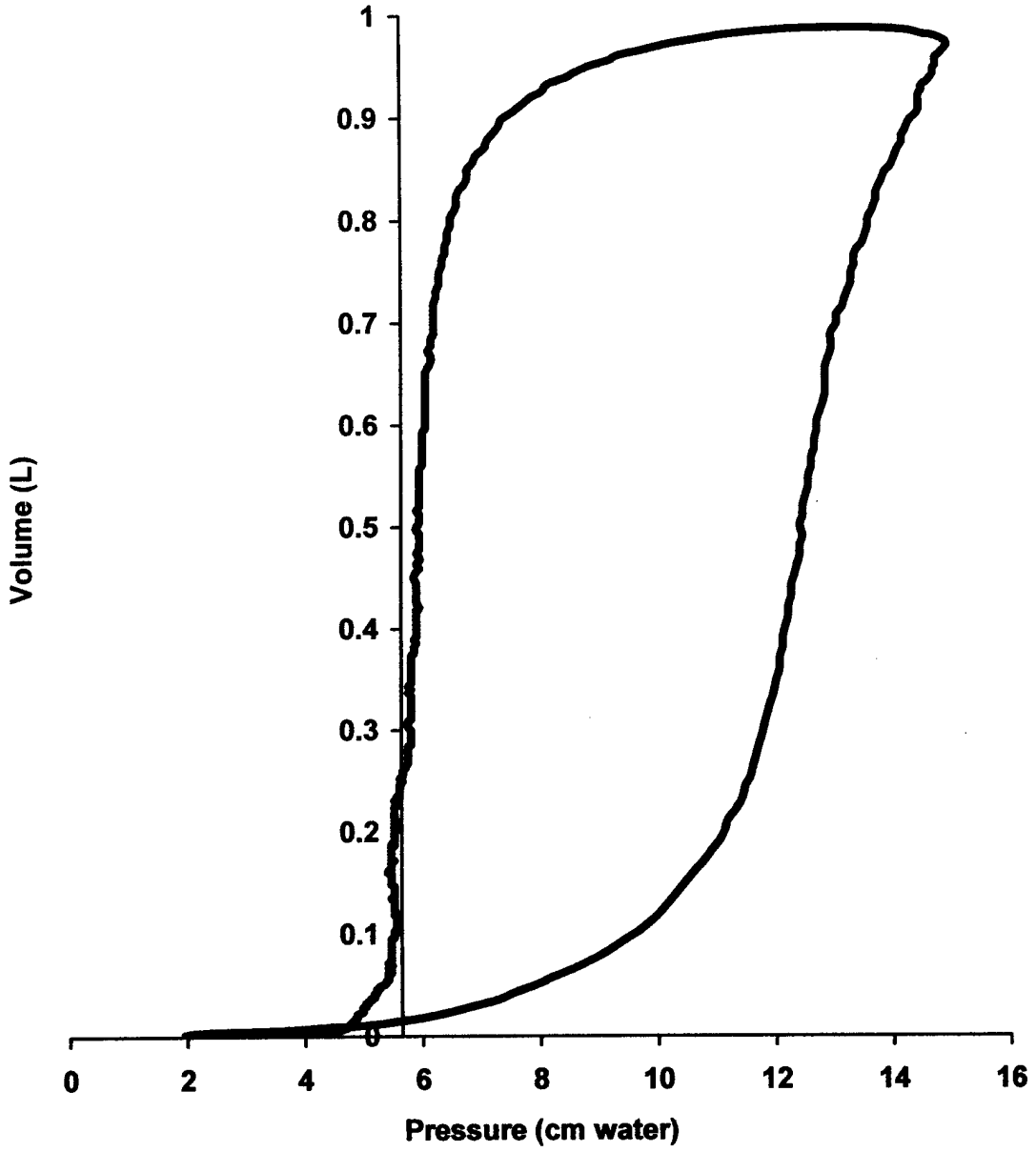


Figure 44
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with Achieva
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 10 cm water
Duration of Tracing 3.13 secs

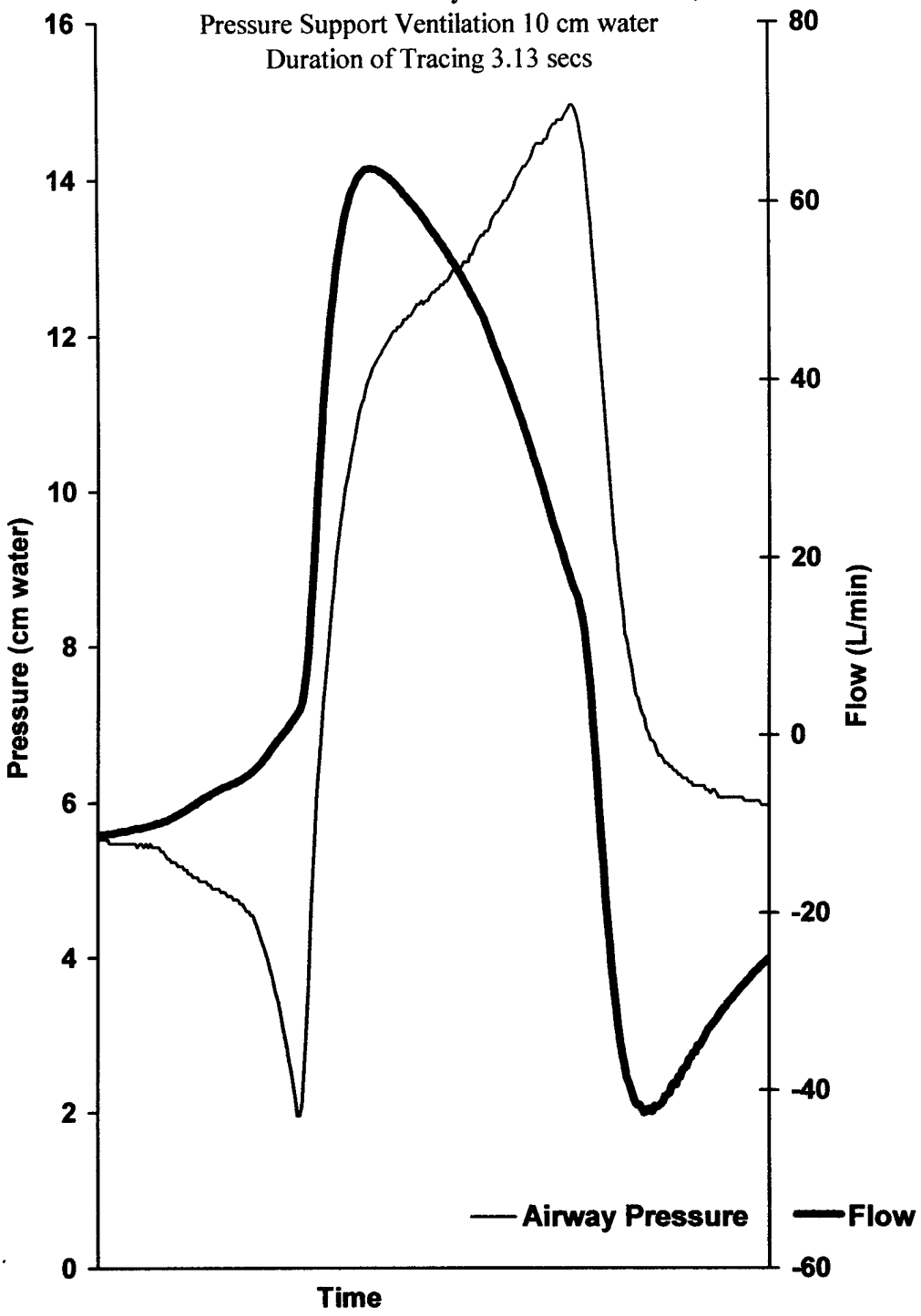


Figure 45
Pressure-Volume Curve
Representative for Breathing with LTV 1000
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 10 cm water
Imposed Work of Breathing 2.88 mJ/L
Imposed Pressure Time Product 0.80 cm water/s/L

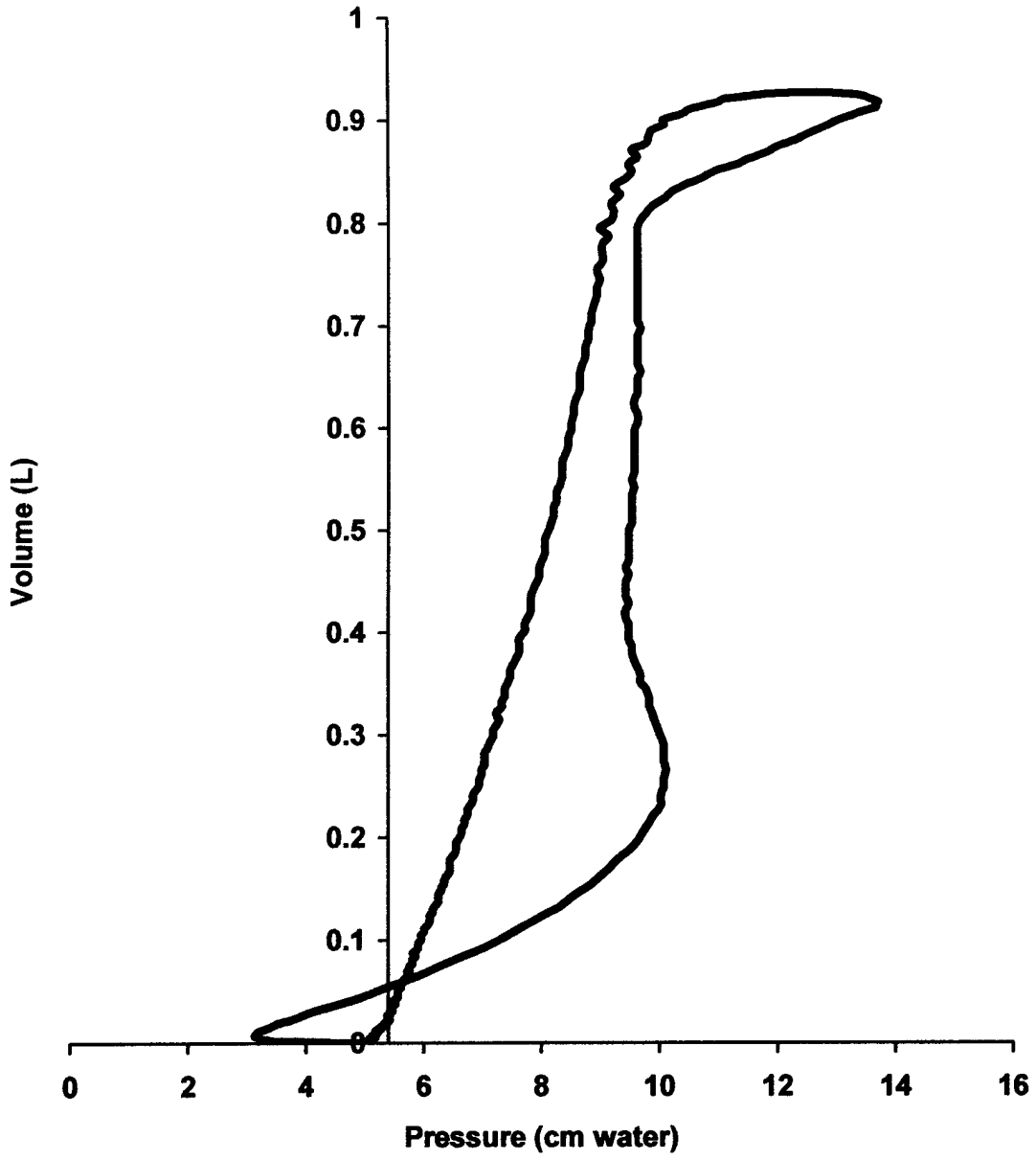
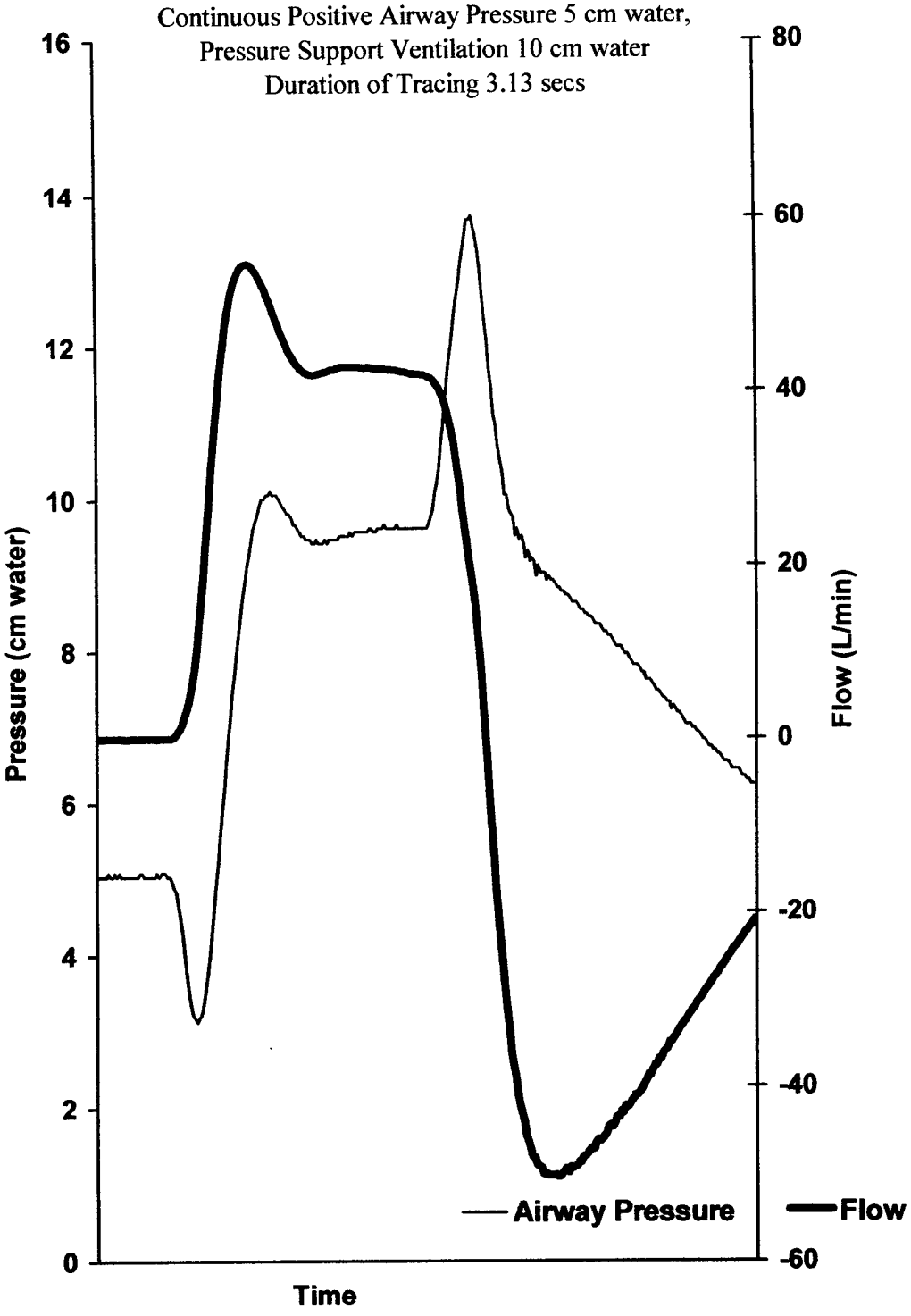


Figure 46
Airway Pressure and Flow Plotted Against Time
Representative for Breathing with LTV 1000
Continuous Positive Airway Pressure 5 cm water,
Pressure Support Ventilation 10 cm water
Duration of Tracing 3.13 secs



The alternative was to increase the inspiratory flow with the Univent 754. We attempted this procedure, but increasing the flow resulted in subjects coughing and halting inspiration. Thus setting the inspiratory flow of the Univent 754 to 5 L/min above the subjects resting inspiratory flow represents a compromise.

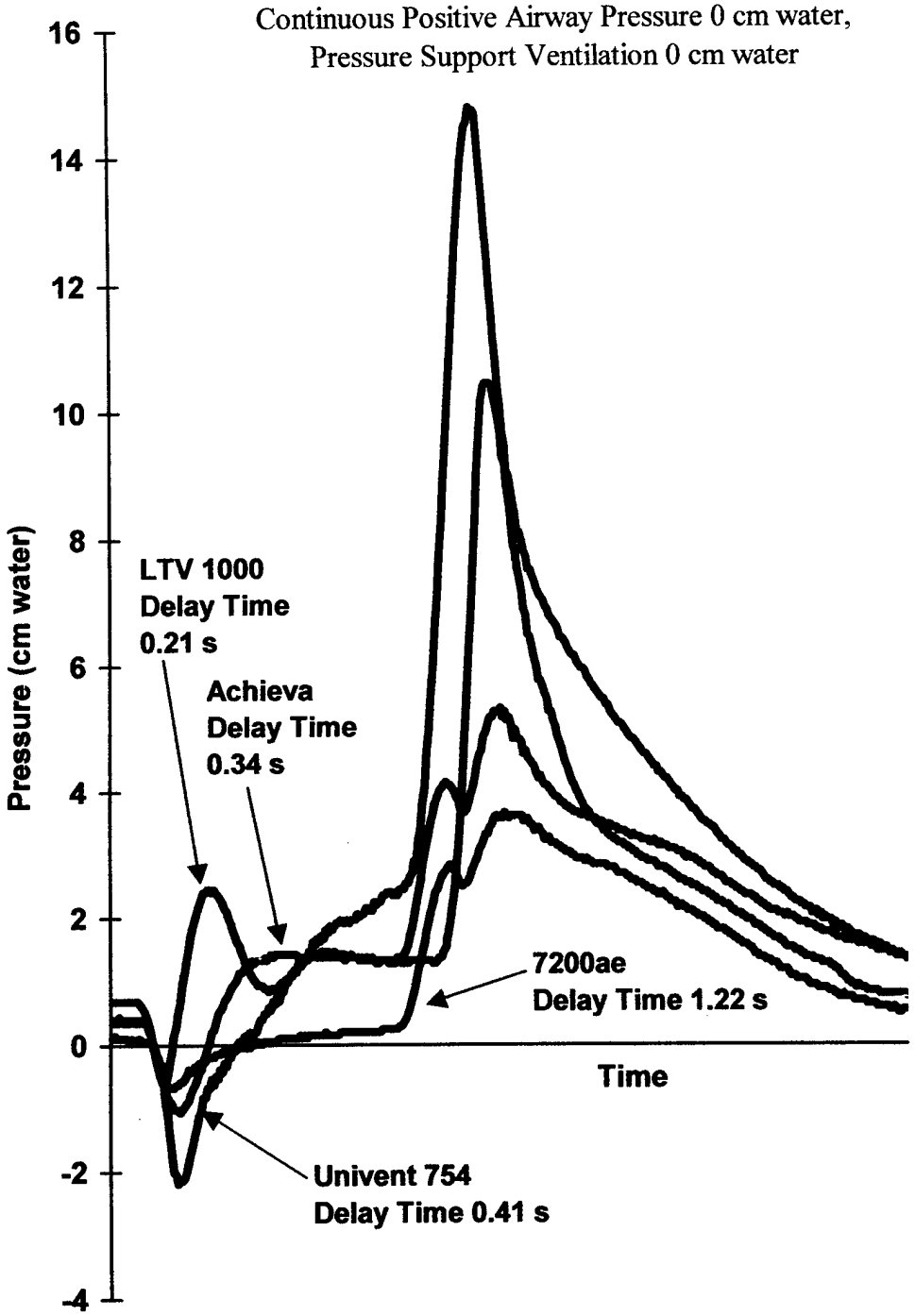
In summary, the presence of pressure triggering, intrinsic positive end-expiratory pressure, and the occasionally insufficient fixed flow output of the Univent 754 likely accounted for the significantly increased WOB_I, increased PTP_I and decreased breathing comfort of the subjects breathing with this ventilator.

Location of the Exhalation Valve and WOB_I

In contrast to the 7200ae, all of PVs in the present study have an external exhalation valve. PVs often possess an external exhalation valve to enable these ventilators to use a more convenient single limb breathing circuit. The control of the external exhalation valve is accomplished in the following manner. The individual triggers inspiratory flow via flow or pressure triggering as described above. The external exhalation valve is closed by gas pressure carried in an accessory small bore tubing that runs parallel to the inspiratory limb of the patient circuit. Thus the pressure must travel from the ventilator down this path, about four feet in length, to close the exhalation valve. Pressure travels at the speed of sound at sea level, about 1 foot per ms (Sassoon, 1992). The breathing circuits used with the PVs were about 4 feet in length. Thus the external exhalation valve is predicted to be about 4 ms slower in closing compared to the internal exhalation valve on the 7200ae.

High quality pressure waveforms that allow examination of such short intervals are difficult to obtain using human subjects. The pressure waveforms using these ventilators with a mechanical model of spontaneous breathing with a tidal volume, inspiratory flow, resistance, and compliance similar to the subjects in the present investigation reveals the delay time, time from the pressure tracing leaving baseline to returning to baseline, of 1.22 seconds for the 7200ae, 0.41 seconds for the Univent 754, 0.34 seconds for the Achieva, and 0.21 seconds for the LTV 1000 (see Figure 47). These were constructed using a previously described simulator of spontaneous breathing (Katz et al., 1985). Despite the presence of an external exhalation valve, the response time of the PVs was less than the CCV, contributing to the low WOB_I of the PVs. This indicates the electronic control algorithm of the PVs and the gas delivery mechanism of the PVs overcomes the drawback of the external exhalation valve.

Figure 47
Simulated Spontaneous Breathing
Tidal Volume 1L, Inspiratory Flow 30 L/min
Airway Pressure Plotted Against Time
Continuous Positive Airway Pressure 0 cm water,
Pressure Support Ventilation 0 cm water



Comparison of the Present Findings with Previous Studies: WOB_I

No other studies could be identified that examined WOB_I, PTP_I, and breathing comfort of subjects breathing with a portable ventilator. Comparison of the WOB_I and PTP_I of subjects in this investigation with the WOB_I reported in investigations using models of spontaneous breathing is problematic. Models of spontaneous breathing typically use a ventilator as the breathing "muscles" supplying monotonous breaths of a fixed inspiratory flow, tidal volume, and rate. There are also differences between studies as some use a resistor to impose natural airway resistance while others use a resistor imposing the resistance of an endotracheal tube. In addition, these models simply passively inflate with the inspiratory flow. As was seen in the present study, a person may find the inspiratory flow too brisk resulting in coughing and halting the inspiratory flow. Finally, investigations using spontaneous breathing models usually have little or no intrinsic positive end-expiratory pressure, as the breathing rate is low enough to prevent air trapping. One of the most important drawbacks of using models of spontaneous breathing is there is no subject who can volunteer their subjective comments.

Austin et al. (2001) used a model of spontaneous breathing to compare characteristics of various portable ventilators during spontaneous breathing under three conditions (VT = 0.3 L with VI = 30 L/min, VT = 0.5 L with VI = 60 L/min, VT = 0.8 L with VI = 80 L/min). The Univent 754 and LTV 1000 were included in that investigation. Examining the condition most similar to the present investigation (VT = 0.3 L with VI = 30 L/min) with CPAP and PSV = 0 cm H_2O, the mean WOB_I using the Univent 754 and LTV 1000 were similar: 16.67 mJ/L versus 37.43 mJ/L and 3.0 mJ/L versus 4.41 mJ/L,

respectively. Under the same condition with CPAP = 5 cm H_2O and PSV = 0 cm H_2O, the mean WOB_I using the Univent 754 was less with the lung model study (130 mJ/L versus 171.70 mJ/L) while using the LTV 1000 the mean WOB_I was greater with the lung model study (16.67 mJ/L versus 8.32 mJ/L). The WOB_I using the LTV 1000 with PSV = 10 cm H_2O and CPAP = 0 cm H_2O was less in the lung model study (0.33 mJ/L versus 2.70 mJ/L). Finally the WOB_I using the LTV 1000 of PSV with PSV = 10 cm H_2O and CPAP = 5 cm H_2O was greater in the lung model study (6.67 mJ/L versus 2.91 mJ/L).

Miyoshi, Fujino, Mashimo, and Nishimura (2000) reported the results of another study using a spontaneous breathing lung model. Here they evaluated the spontaneous breathing characteristics of four portable ventilators (Mallinkrodt 740, Tbird, Espirit, LTV 1000) and a CCV (7200ae). These investigations did not measure WOB_I directly, rather they measured such parameters as delay time and peak negative inspiratory pressure. They reported the PVs tested performed at the same level as the CCV.

Branson and Davis (1995) also used a spontaneous breathing lung model to compare the spontaneous breathing characteristics of four portable ventilators (Aquitron LP 6 and LP 10, Tbird, PLV 102) and a CCV (7200ae). These investigators reported the WOB_I resulting from the use of the PVs that did not have a demand valve (LP 6 and 10, PLV 102) was significantly higher (90 to 140 mJ/L) compared to the PV that had a demand valve (Tbird, 7200ae, 5 to 12 mJ/L) under similar breathing conditions as found with the subjects in the present study.

The WOB_I found with the use of the PVs in present study was significantly lower than that found by Kacmarek et al. (1990) in their study of older PVs. These investigators

also used a spontaneous breathing lung model. Under breathing conditions similar to those seen with the subjects in the current study, these investigators reported the WOB_I ranging from 133 to 215 mJ/L. None of these ventilators possessed a demand valve. The WOB_I decreased with the retrofitting of these ventilators with a demand system (4 to 83 mJ/L). These investigators concluded PVs that did not have a demand valve should not be used with spontaneous breathing individuals.

Summary

The WOB_I of subjects breathing with the Univent 754 was significantly higher than when the subjects breathed with the other three ventilators, supporting the first hypothesis. Pressure triggering rather than flow triggering along with the presence of intrinsic positive end-expiratory pressure are likely explanations. In addition the inspiratory flow of the Univent 754 defaults to a nonvariable flow of 60 L/min. This was found to be too brisk for the subjects and was lowered to 5 L/min greater than the subject's inspiratory flow. However intermittently this flow was outstripped by the subject's inspiratory demand, resulting in a diminution of airway pressure and an increase in the inspiratory work of breathing. The presence of an external exhalation valve did not appear to affect WOB_I. The WOB_I measured with subjects breathing with the Achieva and LTV 1000, both of which have an external exhalation valve, was not significantly different than the WOB_I measured when they breathed with the 7200ae with its internal exhalation valve.

Study Hypothesis Number Two

The second hypothesis was based on the design characteristics of the ventilators and prior in vitro investigations of the PTP_I with 7200ae < Achieva = LTV 1000 <

Univent 754. The findings regarding PTP_I mirrored those of WOB_I. Across the above combinations of CPAP and PSV, in subjects breathing with the 7200ae, Achieva, and LTV 1000 a lower PTP_I was measured compared to the Univent 754, supporting the hypothesis. However, there was no difference in the PTP_I when the subjects breathed with the 7200ae, Achieva, or LTV 1000. This section will discuss PTP_I as a supplemental measure of energy expenditure, the significantly increased PTP_I measured in subjects breathing with the Univent 754, the lack of a significant difference in WOB_I measured in subjects breathing with the 7200ae, Achieva, and LTV 1000, and will conclude with a comparison of the PTP_I found in the present study and that found in previous investigations.

PTP_I as a Supplemental Measure of Energy Expenditure

PTP_I is a supplemental measure of the energy expended to overcome the resistance imposed by a device (Calzia et al., 1998; Otis, 1964). There must be a volume change in order to measure work. If negative inspiratory pressure is generated but there is change in volume, by definition no work is performed however energy is still expended. PTP_I overcomes this drawback of using work to measure the energy expended to overcome the resistance imposed by a device. PTP_I varies directly with the magnitude of the airway pressure drop below baseline airway pressure during inspiration and how long the airway pressure remains below baseline airway pressure.

Significantly Increased PTP_I Measured in Subjects Breathing with the Univent 754

Across the range of study conditions, the PTP_I of subjects breathing with the Univent 754 was approximately five to ten times greater than when the subjects were

breathing with the 7200ae, Achieva, or LTV 1000. Examining the pressure-volume curves of typical breaths offers reasons for these findings.

Figures 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, and 45 are representative pressure-volume curves across the range of conditions. As pointed out in the discussion of WOB_I, subjects breathing with Univent 754 had to generate a greater negative airway pressure to trigger inspiratory flow. Airway pressure remained below baseline longer when the subjects breathed with the Univent 754. This duration was due to magnitude of the negative inspiratory pressure seen with the Univent 754 and the briskness of the inspiratory flow response of the Univent 754. Factors leading to the greater negative inspiratory pressure seen with subjects breathing with the Univent 754 include pressure triggering, the presence of intrinsic positive end expiratory pressure, and the presence of nonvariable inspiratory flow with the Univent 754.

The pressure-volume curve in Figure 17 is from a subject where there is about +2 cm H_20 of intrinsic positive end expiratory pressure and the subject's inspiratory flow demand is greater than the inspiratory flow output of the Univent 754. The WOB_I and PTP_I is much greater in this subject compared to the subject with a lower intrinsic positive end-expiratory pressure and whose inspiratory demand is met by the inspiratory flow output of the Univent 754 (see Figure 19).

Lack of a Significant Difference in PTP_I Measured in Subjects Breathing with the 7200ae, Achieva, and LTV 1000

As with WOB_I, there were no significant differences measured in the PTP_I of subjects breathing with the 7200ae, Achieva, or LTV 1000 across the range of conditions.

The PVs, the Achieva and LTV 1000 both responded with inspiratory flow at negative inspiratory pressure and times comparable to the CCV, the 7200ae. The control algorithm and control of the exhalation valve of these two ventilators likely account for these findings.

Previous Studies Examining PTP_I of Subjects Breathing with PVs

Austin et al. (2001) reported the PTP_I found with seven PVs using a spontaneous breathing lung model. With CPAP and PSV = 0 cm H_2O and tidal volume of 0.3 L, inspiratory flow of 30 L/min, the PTP_I ranged from 0.13 to 6.69 cm H_2O /s/L. The WOB_I found with the Univent 754 under these conditions was 1.0 cm H_2O /s/L compared to 8.86 cm H_2O /s/L in the present investigation. The increased PTP_I seen with the Univent 754 in the present study may be accounted for by the use of pressure triggering, presence of intrinsic positive end-expiratory pressure, and the occasional undersupply of inspiratory flow. In the lung model study, the model will not halt inspiration and attempt to restart inspiration but rather will passively inflate with inspiratory flow. In the present study an F_IO_2 of 0.4 was used while the lung model study used an F_IO_2 of 1.0.

In the study discussed above, Branson and Davis (1995) also examined the PTP_I of the four PVs and the CCV. They found for the PVs with no demand valve the PTP_I ranged from 3.15 to 5 cm H_2O /s/L compared to 0.30 cm H_2O /s/L for the PV with a demand valve. These were measured under conditions similar to those in the present study. The PTP_I reported for the subjects breathing with the 7200ae was 0.55 cm H_2O /s/L, similar to that found in the present study for the 7200ae.

Summary

The increased PTP_I of subjects breathing with the Univent 754 across the study conditions was likely due to its mechanism that uses pressure triggering rather than flow triggering and the occasional presence of intrinsic positive end-expiratory pressure and insufficient inspiratory flow output. Across the range of conditions there were no significant differences in PTP_I of subjects breathing with the 7200ae, Achieva, and LTV 1000 reflecting the likelihood the control algorithm and control of the exhalation valve on the PVs is comparable to that seen with the CCV.

Hypothesis Number Three

The third hypothesis was based on the design characteristics of the ventilators and prior in vitro investigations the breathing comfort of subjects breathing with the 7200ae > Achieva = LTV 1000 > Univent 754.

The findings did not fully support this hypothesis. Across the above combinations of CPAP and PSV, subjects breathing with the Univent 754 did report a lower breathing comfort than when breathing with the 7200ae, Achieva, and LTV 1000. However there were no statistical differences between the breathing comfort of subjects breathing with the 7200ae, Achieva, and LTV 1000. The section will discuss the basis for the hypothesis; the factors that may account for the significantly lower breathing comfort seen reported for subjects breathing with the Univent 754; breathing comfort reported by subjects breathing with the 7200ae, Achieva, and LTV 1000; breathing comfort during inspiration, expiration, and transitions; and a comparison of the findings of the present study with those of previous investigations.

Basis of the Hypothesis

This hypothesis was based on clinical observations as well as the findings of validation of the breathing comfort visual analogue scale discussed in Chapter 3. That is breathing comfort decreases as the subject has to generate more negative inspiratory pressure to trigger inspiratory flow. It was predicted subjects would indicate a ventilator was more less comfortable if he/she had to expend more work to trigger inspiratory flow.

Factors that may Account for the Significantly Lower Breathing Comfort Reported by Subjects Breathing with the Univent 754

Indeed in subjects breathing with the Univent 754, a higher WOB_I and PTP_I was measured and these subjects indicated breathing was less comfortable with this ventilator. However other factors may have contributed to this perception. The subjects' comments provide clues as to what contributed to breathing comfort (see Tables 14 to 17). First, the compressor integral to the Univent 754 transmitted sharp vibrations to the subject via the breathing circuit. Second, unlike the other three ventilators tested, the Univent 754 has a nonvariable inspiratory flow. As discussed earlier, once inspiratory flow is triggered with the Univent 754 the subject receives inspiratory flow at the set rate or at the default of 60 L/min. Sixty liters per minute was too fast for the subjects of this investigation and the inspiratory flow rate was adjusted down to 5 L/min above the subject's resting inspiratory rate. This adjustment overcame the problem of excessive inspiratory flow. However, this inspiratory flow was not always sufficient for the subjects on a breath-by-breath basis. On breaths where the inspiratory flow was not sufficient, subjects entrained ambient air via the antisuffocation valve resulting in a greater work of breathing. The antisuffocation valve is

a mechanical valve that allows an individual, if they are able to spontaneously breathe, to entrain ambient air into the breathing circuit in cases of failure of the mechanical ventilator or in cases where the inspiratory flow provided by the ventilator does not meet the individual's inspiratory needs. In addition, during the control breathing periods the subjects exhibited a descending inspiratory flow pattern. The inspiratory flow pattern of the Univent 754 is a fixed square wave pattern (see Figures 18 and 20). Finally there is a solenoid integral to the Univent 754 that controls the CPAP level. As can be seen from the tracings in Figures 35 and 36, this solenoid opens and closes repeatedly to maintain the desired CPAP level.

Breathing Comfort: Inspiration, Expiration, Transitions

The subjects were not asked specifically to rate inspiration, expiration, or the transition between inspiration and expiration, or the transition between expiration and inspiration. The subjects were asked only to rate breathing comfort.

The subjects were asked to write down any comments they after each breathing period. These comments were brief however do provide additional insight into the subjects' experience. For example, the subjects' comments indicate that inspiratory time was only a part of the contribution to breathing comfort. Of the 97 comments offered by the subjects; 34 referred to inspiration, 35 referred to expiration, and 28 referred to neither specifically to inspiration or expiration. Overall the subjects were more likely to provide negative compared to positive comments.

Breathing Comfort and the 7200ae, Achieva, and LTV 1000

There was no difference in breathing comfort scores between the 7200ae, Achieva,

and LTV 1000. This is not surprising as there was no difference in WOB_I or PTP_I of subjects breathing with these ventilators across the range of test conditions. Notable is the difference in methods these three ventilators use in generating inspiratory flow. Both the 7200ae and Achieva use a piston to generate flow while the LTV 1000 uses a turbine. The results indicate across the range of study conditions subjects find these methods of flow generation equally comfortable.

Comparison of the Present Findings with Results of Past Investigations

An exhaustive review of the literature failed to reveal other studies examining the breathing comfort of PVs. Russell and Greer (2000) used a 10 cm visual analog scale to measure the breathing comfort of 24 healthy nonintubated subjects to compare three ventilation modes: synchronized intermittent mandatory ventilation, biphasic positive airway pressure, and assisted spontaneous ventilation. They concluded assisted spontaneous breathing was the most comfortable mode of ventilation. The same CCV was used to deliver these three modes. No PV was used in this study.

Mols et al. (2000) reported the results of a study where they measured breathing comfort of 10 nonintubated healthy volunteers breathing with two spontaneous breathing modes: PSV an automatic tube compensation delivered by the same CCV. They asked volunteers to rate the transition between ventilation modes as better, the same, or worse compared to the previous mode. They reported subjects preferred automatic tube compensation over PSV.

Manning et al. (1995) found subjects rated breathing as less comfortable if the inspiratory flow rate increased (200%, 300%) or decreased (70%) from their normal

inspiratory flow rate. There were 10 subjects in this study using assist-control ventilation and a 40 cm visual analogue scale. These investigators concluded there are different mechanisms likely responsible for breathing discomfort at high and low flow rates. With high flow rates they suggested the mechanism is related to localized upper airway discomfort. At low flow rates the mechanism offered was unrelated to chemical or mechanical factors and may be due to afferent mismatch. The decrease in breathing comfort seen in the present investigation associated with the Univent 754 may be due to a decreased inspiratory flow with some of the breaths.

Summary

The breathing comfort of subjects breathing with the Univent 754 was less than when subjects breathed with the 7200ae, Achieva, and LTV 1000 across the range of study conditions. Subjects breathing with the Univent 754 did also exhibit a higher WOB_I and PTP_I, supporting the hypothesis. The use of a fixed inspiratory flow on the Univent 754 appeared to contribute to the decreased breathing comfort. There were no significant differences in breathing comfort for subjects breathing with the 7200ae, Achieva, and LTV 1000 across the range of study conditions. No studies could be identified that examined the breathing comfort of subjects.

Measurements During Control Periods

During the six control breathing periods the subject breathed only through the testing apparatus and WOB_I, PTP_I, and breathing comfort were measured. In addition, maximal inspiratory pressure was measured during these control breathing periods to assess subject fatigue. Comparing the mean values of these measures with ANOVA

revealed there was only a statistically significant difference in the maximum inspiratory pressure (see Tables 23 to 26). A Tukey comparison of means failed to detect where these differences occurred between means (see Table 27). If the subjects had fatigued during the course of the investigation, we would expect to see a progressively decreasing maximum inspiratory pressure. Rather, inspiratory pressure decreased slightly between the first and second breathing period then increased during the course of testing. Possible explanations for these findings include the subjects slightly fatiguing between the first and second control periods. This is unlikely as one would expect the subjects to continue to fatigue during the course of the investigation. Another possible explanation is the subjects became more comfortable with the instrument during the course of the investigation, that is, learning occurred during the course of the investigation. A third explanation is the subjects became more motivated during the course of the investigation increasing their effort. A fourth explanation is the precision of the measuring device was altered during the course of the investigation in a systematic fashion.

Precision of Measuring Baseline Airway Pressure

A determinant of the accuracy and precision of the calculation of the WOB_I and PTP_I is identification of the baseline airway pressure. The WOB_I is the area of the pressure-volume curve to the left of the baseline airway pressure. The PTP_I pressure measured proximally to any imposed resistances is integrated over the duration of inspiration. Thus, a falsely increased baseline airway pressure will result in a falsely increased WOB_I and PTP_I. Conversely, a falsely low baseline airway pressure will result in the calculation of a falsely low WOB_I and PTP_I.

The accuracy of the pressure transducer was assessed using a water manometer. Assessing the precision of the baseline airway pressure offered a greater challenge. The baseline airway pressure was visually identified from the computer monitor during the data collection. Retrospectively, we determined the baseline airway pressure by examining the airway pressure data gathered and recorded each 100 ms. The difference in these values, retrospectively determined baseline airway pressure and airway pressure determined during real time, was calculated. The mean difference was calculated for each ventilator and control period. The mean differences were compared using ANOVA. There were no statistically significant differences detected between the means of these differences during either the control or study breathing periods.

Implications for Nursing Practice

Nurses care for mechanically ventilated patients in locations outside of the acute care hospital. These locations include during intrahospital transport for diagnostic and/or therapeutic procedures. These locations also include interhospital transport, usually from an outlying hospital to a larger center for definitive care. Finally, nurses care for ventilator dependent individuals in austere military settings, long-term settings and the home. With PVs supporting the life-sustaining function of breathing in individuals in these settings, nurses should have a solid knowledge of their function and capabilities.

Investigators performing earlier work with a spontaneous breathing model suggested many portable ventilators imposed an excessive WOB_I that may result in respiratory muscle fatigue (Branson & Davis, 1995; Kacmarek et al., 1990). The results of these studies suggested the PVs included in these studies did not perform to the level of

critical care ventilators (CCVs) when used in spontaneous breathing modes. If the individual was in a critical care unit and ventilated in a spontaneous breathing mode, then the mode should be changed to a positive pressure breathing mode such as assist-control if ventilation is supported with a portable ventilator. If the change in mode of ventilation resulted in ventilator asynchrony and/or decreased comfort, the individual required increased amounts of sedation (Bergbom-Engberg, 1989). Ventilation and oxygenation could also be altered during this transition. If the individual was cared for in the home or long-term care facility, investigators recommended if a PV was used with a spontaneous breathing individual, the PV should be modified to reduce the imposed work and lessen the chance of the individual suffering respiratory muscle fatigue. This added complexity and expense to the PV.

Recent work, including the studies by Miyoshi et al. (2000) and Austin et al. (2001), all using a spontaneous breathing lung model, suggest newer PVs offer a lower WOB_I during spontaneous breathing modes compared to their older counterparts. The implications of these studies include the increased safety and comfort when using these newer PVs in spontaneous breathing modes. Their findings suggested individuals ventilated with CCVs with spontaneous breathing modes could be supported during transport with a newer PV while not altering the ventilation mode. Also these findings suggested individuals in the home or long-term care facilities could be supported with spontaneous breathing modes with one of these newer PV. Until now this investigation was not repeated with human subjects.

As suggested by the results of laboratory studies examining the function of PVs

during spontaneous breathing and the results of this study, not all approved and commonly used PVs function at the same level during spontaneous breathing. The fact the device is approved does not mean its performance is equal to another device offering the same features. Nurses caring for ventilator dependent individuals should have not only an understanding of the modes of ventilation but also of the capability of the ventilator. The nurse may incorrectly treat anxiety rather than increased work of breathing when an individual is being ventilated with a PV used in a spontaneous breathing mode.

These results suggest mechanically ventilated individuals who require ventilator support outside of the critical care unit can experience a WOB_I, PTP_I, and breathing comfort similar to if their ventilation was supported with a CCV. However, this depends on the performance of the PV. When breathing with the Achieva and LTV 1000 subjects in the present study experienced WOB_I, PTP_I, and breathing comfort similar to that experienced while breathing with the 7200ae, a CCV. These results indicate to practitioners, including nurses, that actual performance of a PV is variable.

The work imposed by these ventilators is often evaluated using a model of spontaneous breathing. The results of this investigation point to the need for nurses to insist evaluation of work imposed by ventilators include human testing. The evidence for this includes the finding of subjects breathing with Univent 754. The drawbacks of a fixed inspiratory flow and problems when attempting to adjust the inspiratory flow of the Univent 754 were made apparent during human testing.

PVs are becoming increasingly sophisticated, as evidenced by the findings of this investigation that suggests there is no difference between the work imposed by and the

breathing comfort of the Achieva and LTV 1000 (PVs) and the 7200ae (CCV). As case managers and members of multidisciplinary teams caring for mechanically ventilated individuals, nurses should be aware of the level of performance of these PVs. Nurses should be aware these less expensive and easier to use PVs are available, facilitating caring for mechanically ventilated individuals outside of traditional critical care settings.

The results of this investigation also indicate the need for the nurse to understand breathing comfort when patients are supported by mechanical ventilation. We found comfort is not related solely to the resistance to inspiratory flow but a more complex phenomenon. The results of this study, supported by the comments of the subjects, indicate that the phenomenon of breathing comfort may include velocity of inspiratory flow, the characteristics of inspiratory flow (fixed versus variable), and expiratory characteristics. Nurses should be familiar with the alternations in breathing caused by mechanical ventilators as these sensations, such as the vibration during inspiration caused by the Univent 754, contribute to breathing comfort as suggested by the results of this investigation.

Application of Theoretical Perspectives

The physiological framework guiding this investigation included the concepts of spontaneous breathing, work of breathing and breathing comfort.

Spontaneous Breathing

During spontaneous breathing, the volume of gas inspired is dependent on the negative pressure generated by the person's inspiratory effort. As the diaphragm contracts and the chest wall enlarges, air will move down the pressure gradient into the lungs. The

forces that must be overcome by the respiratory muscles to allow this to occur include the elastic forces that develop in the tissues of the lungs and chest when a change in volume occurs, flow-resistive forces offered by the airways to the flow of gas and by the nonelastic deformation of tissue, inertial forces that depend on the mass of tissues and gases, gravitational forces that can be considered part of the inertial forces but in practice are included in the measurement of elastic forces, and distorting forces of the chest wall observed at relatively high rates of ventilation or when breathing through resistances (Rousso & Campbell, 1986).

In this investigation, we examined a sixth force, the imposed resistive force that exists if the individual is spontaneously breathing through an apparatus such as an artificial airway and/or ventilator with associated breathing circuit (Banner et al., 1994). We found that the force imposed by the Univent 754 across the range of CPAP and PSV settings was significantly greater than the force imposed by the 7200ae, Achieva, and LTV 1000. The causes of this increased imposed force includes pressure triggering, presence of intrinsic positive end-expiratory pressure, and the fixed inspiratory flow of the Univent 754. The presence of the external exhalation valve on the Achieva and LTV 1000 did not seem to result in a greater WOB_I, PTP_I and lower breathing comfort compared to the subjects breathing with the 7200ae.

Work of Breathing

Work of breathing can be divided into groups corresponding with the forces that must be overcome for the individual to inspire: work to overcome the elasticity of the lungs and chest, work to overcome the flow-resistive forces offered by the airways to the

flow of gas and by the nonelastic deformation of tissue, work to overcome the inertial forces, work to overcome gravitational forces (usually considered part of the inertial forces but in practice are included in the measurement of elastic forces), and work to overcome the distorting forces of the chest wall observed at relatively high rates of ventilation or when breathing through resistances (Rousso & Campbell, 1986).

Specifically, in this study we examined work to overcome the resistive forces imposed by breathing apparatus, PVs and a CCV. This is termed inspiratory imposed work of breathing, which is measured as the area to the left of the baseline airway pressure on the pressure-volume curve. Because energy is still expended when inspiratory pressure is generated but a change of volume does not result, this measure was supplemented with pressure time product, which examines airway pressure during inspiration and the duration of that inspiratory airway pressure.

The mean WOB_I and PTP_I of subjects was greater with the Univent 754 compared to the other three ventilators across the range of CPAP and PSV settings used in this study. The mean WOB_I and PTP_I of subjects breathing with the other two PVs, the Achieva and LTV 1000, were not significantly different compared to the CCV, the 7200ae. The cause of the increased flow resistive forces seen with the Univent 754 are probably due to its use of pressure triggering, presence of intrinsic positive end-expiratory pressure, and fixed inspiratory flow. The other three ventilators appeared to offer a similar imposed inspiratory forces as evidenced by lack of significant differences between WOB_I and PTP_I when subjects breathing with these ventilators.

Breathing Comfort

We measured breathing comfort with a 10 cm visual analogue scale. Across the range of CPAP and PSV settings, there was a significantly higher WOB_I and PTP_I measured when subjects breathed with the Univent 754 compared to the other three ventilators. The breathing comfort was significantly lower, across the range of CPAP and PSV settings, with subjects breathing with the Univent 754 compared to the other three ventilators. There were no significant differences in WOB_I, PTP_I, and breathing comfort of subjects breathing with the 7200ae, Achieva, and LTV 1000. These findings support the increase in inspiratory effort, measured by the WOB_I and PTP_I, results in a decrease in breathing comfort. However the decrease in breathing comfort reported by subjects breathing with the Univent 754 might be due to its fixed inspiratory flow and vibration generated during inspiration.

Summary of the Findings

The results of this study partially supported the three hypotheses. Regarding the first and second hypotheses, there were no significant differences in the WOB_I and PTP_I of subjects breathing with the 7200ae, Achieva and LTV 1000. However, congruent with the first and second hypotheses, the WOB_I and PTP_I of these three ventilators was significantly lower compared to the Univent 754 across the range of CPAP and PSV settings at an F_IO_2 of 0.40. The third hypothesis addressed breathing comfort and was only partially supported. There were no significant differences in the breathing comfort of subjects breathing with the 7200ae, Achieva and LTV 1000 754 across the range of CPAP and PSV settings at an F_IO_2 of 0.40. However the breathing comfort of

subjects breathing with the 7200ae, Achieva, and LTV 1000 was significantly greater than when the subjects breathed with the Univent 754.

There were no significant differences in WOB_I, PTP_I, and breathing comfort of the subjects during the six control breathing periods indicating the changes seen during the study breathing periods were likely due to the effects of the study ventilators. The slight decrease in maximal inspiratory pressure seen during the second and third breathing period suggests the subject experienced fatigue then recovered. Alternatively it may represent the subject learning over time. Another explanation is it represents systematic measurement error.

There was no difference in the bias of the baseline airway pressure within the study and within the control breathing periods suggesting the precision in the measuring WOB_I and PTP_I.

Limitations

Sample and threats to internal and external validity are limitations of this study (Rubin, 1987).

Limitations: Sample

The number of subjects participating in this study was first determined by the number of cells in this 4 X 2 X 2 design, which is 16 subjects. This sample size was the minimum number of subjects necessary to perform an analysis of power for this design. The initial plan was to perform a power analysis to predict the number of subjects needed to attain a power of 0.80. However on examination of the data and reflecting on the comments of the subjects, to continue the investigation would place undo burden on

future subjects. Regardless of the CPAP and PSV settings, the WOB_I and PTP_I of subjects breathing with the Univent 754 was significantly higher compared to the subjects breathing with the other three ventilators. The subjects rating their breathing with the Univent 754 as significantly less comfortable than breathing with the other three ventilators confirmed these findings. The subject's comments also indicated breathing with the Univent 754 was less comfortable compared to breathing with the other three ventilators.

There were other main effects and interactions that were not statistically significant at $p < \text{or} = 0.05$. These are summarized in Tables 34 and 35. Having an inadequate sample size increases the likelihood of a Type II error, not rejecting the null hypothesis when it is actually false. However in the present investigation the hypotheses addressed the main effect of ventilator and not the main effects of CPAP, PSV, or the interactions.

The subjects comprised a convenience sample of health care workers in the southwestern Ohio region. These subjects may not be representative of the total population since they were from one geographic area and had a healthcare background.

Table 34

Power of Main Effects and Interactions That Were Not Statistically Significant ($p < or = 0.05$) with N = 16 Subjects

	PSV (D)	Ventilator (A) * PSV (D)	CPAP (C) * PSV (D)	Ventilator (A) * CPAP (C) * PSV (D)
Imposed Work of Breathing	0.05	0.46	0.18	0.38
Pressure-Time Product	0.06	0.41	0.22	0.37
Breathing Comfort	NA	NA	0.23	0.48

Note. PSV = pressure support ventilation; CPAP = continuous positive airway pressure, NA = not applicable

Table 35

Number of Subjects Needed to Attain a Power of 0.80 for Main Effects and Interactions That Were Not Statistically Significant ($p < or = 0.05$)

	PSV (D)	Ventilator (A) * PSV (D)	CPAP (C) * PSV (D)	Ventilator (A) * CPAP (C) * PSV (D)
Imposed Work of Breathing	> 5000	32	105	39
Pressure-Time Product	1600	36	81	41
Breathing Comfort	NA	NA	78	31

Note. PSV = pressure support ventilation; CPAP = continuous positive airway pressure, NA = not applicable

Limitations: Internal Validity

The internal validity determines the extent to which the measurements of WOB_I, PTP_I, and breathing comfort reflect the true variables (Rubin, 1987). The research protocol and measurement instruments were the largest threat to the investigation's internal validity. The truth of the observation of the signal (accuracy) and the consistency of the observation of the signal (precision) are two important aspects of the instrumentation (Rubin, 1987). The strategies used to assess the accuracy and precision of the measurement instruments were carried out by the investigator as outlined in the investigation's procedure.

Limitations: Internal Validity –Accuracy

Accurate calculation of WOB_I and PTP_I are dependent on accurate measurement of flow, volume, and pressure. We assessed the accuracy of the pneumotachograph to measure flow and volume using a calibrated syringe prior to use on each subject. We also assessed the accuracy of the pressure transducer using a calibrated water manometer prior to use on each subject. The formulas used to calculate WOB_I and PTP_I are standard formulae (Calzia et al., 1998).

The greatest threat to the accuracy of the calculation of WOB_I and PTP_I was the identification of baseline airway pressure. Both of these parameters require baseline airway pressure to be identified with WOB_I referring to the volume change per inspiratory pressure change and PTP_I referring to the inspiratory pressure change per inspiratory time. The inspiratory pressure is identified as the negative pressure deflection below baseline

airway pressure. Baseline airway pressure was identified on the computer display during real time and entered into the program that calculated WOB_I and PTP_I. During data analysis, baseline airway pressure was identified by examining the airway pressure data gathered each 100 ms. The difference between the baseline airway pressure identified retrospectively and that identified in real time and used for calculation of WOB_I and PTP_I was calculated for each study and control breathing period.

During the study breathing periods, this mean difference across the range of study conditions was –0.14 to –0.33. Thus the baseline airway pressure used for calculating WOB_I and PTP_I was slightly less than the true baseline airway pressure. The result was the calculated WOB_I and PTP_I was slightly less than the true WOB_I and PTP_I.

During the control breathing periods this mean difference was 0.06 to 0.07 cm H_2O. Thus the baseline airway pressure used for calculating WOB_I and PTP_I was slightly more than the true baseline airway pressure. The result was the calculated WOB_I and PTP_I was slightly more than the true WOB_I and PTP_I.

The accuracy of the 10 cm visual analog scale was assessed a priori with a sample of $\underline{N} = 10$ subjects. A flow of air was triggered using a predicted comfortable setting (flow rate of 1 L/s with a rise time of 25 ms) and a predicted uncomfortable setting (inspiratory pressure of -10 cm water with a rise time of 200 m). An alpha level of 0.05 was used for all statistical tests. The breathing comfort score when using the predicted comfortable setting ($\underline{M} = 8.1$, $\underline{SD} = 1.27$) was significantly different statistically than when using the predicted uncomfortable setting ($\underline{M} = 3.42$, $\underline{SD} = 2.17$) when compared using a Student's T-test for paired data ($\underline{t} = 6.65$, $\underline{df} = 9$, $\underline{p} = 0.0001$). These results support the

validity of the instrument. The inspiratory pressure was about five times that of the ventilators in the present investigation. While the instrument measured differences in breathing comfort with subjects breathing with ventilators requiring these high inspiratory pressures, the instrument may not be sensitive enough to measure breathing comfort of subjects breathing with ventilators requiring less inspiratory pressure.

Due to limitations of the measuring instrument, the WOB_I and PTP_I was measured for five breaths rather than continuously during each two minute breathing period. These five breaths represent only a snap shot of the subject's breathing during the breathing periods. It would have been preferable to measure the parameter continuously to gather a more accurate representation of the subject's breathing.

Limitations: Internal Validity – Precision

The precise measurement of WOB_I and PTP_I require precise measurement of flow, volume, and pressure. The same pneumotachograph and pressure transducers were used throughout the study. The same investigator operated all of the devices. The same investigator used the same steel rule to measure breathing comfort on the visual analog scale. The greatest threat to precision was the measurement of baseline airway pressure.

Precise calculation of WOB_I and PTP_I was dependent on precise identification of the baseline airway pressure. As discussed above, baseline airway pressure was identified during real time by the same investigator. The difference between the baseline airway pressure identified retrospectively and in real time and used for calculation of WOB_I and PTP_I was calculated for each study and control breathing period. We examined the difference between these mean differences was examined using a repeated measures

ANOVA.

There were no significant differences ($p < \text{or} = 0.05$) detected between the mean bias values when examined by the main effects of ventilator, CPAP, PSV, or any of the interactions (see Table 33). This finding supports the precision of the identification of baseline airway pressure during the study breathing periods. The same technique was used to examine the control breathing periods for differences between the baseline airway pressure identified during data analysis and identified during real time. Again there were no statistically significant differences noted in these mean differences during the control breathing periods (see Table 32).

We used measurement of WOB_I, PTP_I, breathing comfort, and maximal inspiratory pressure to assess for changes in the subjects not due to the ventilators. There was no difference in the mean values of these parameters among subjects over the course of the investigation except for maximal inspiratory pressure. We used this parameter to assess subject fatigue. The maximal inspiratory pressure measured during the second control period was significantly less than the maximal inspiratory pressure measured during the first, third, fourth, fifth, and sixth breathing periods. This may represent the subject experiencing fatigue then recovering. Alternatively it may represent the subject learning over time. Another explanation is it represents systematic measurement error.

Limitations: External Validity

These findings are limited to healthy nonobese volunteers between the ages of 18 and 65 years. The findings should not be generalized to other populations. This study centered on the assessment of WOB_I, PTP_I, and breathing comfort of healthy nonobese

volunteers breathing with one of three PVs and a CCV. The sample ($\underline{N}$ = 16 subjects) of healthcare workers from southwestern Ohio limits the ability to generalize the findings of this investigation. The findings of no significant differences in the WOB_I, PTP_I, and breathing comfort of subjects breathing with the 7200ae, a CCV, and the Achieva and LTV 1000, PVs across the range of study conditions raised questions for research in this and other populations.

The generalizability of these findings are also limited to the ventilators used in the investigation. As was supported in the investigation, the performance of ventilators vary within modes of ventilation. However the findings regarding pressure triggered (Univent 754) versus flow triggered (7200ae, Achieva, LTV 1000) could be cautiously applied to other pressure and flow triggered ventilators.

Recommendations for Further Study

Replication of the current investigation with changes in the research method based on the aforementioned limitations could result in different findings. Suggested measurement instrument changes include using an instrument that will continuously measure WOB_I and PTP_I as well as will identity baseline airway pressure in real time. Future subjects could find a vertical VAS easier to use. Based on the information gleaned from the subjects' comments, future investigations should include these comments. A qualitative investigation could even be conducted on the subjects' experience while breathing with a ventilator. This change will help overcome the accuracy limitations of the method of measuring WOB_I of only five breaths during the study breathing period as well as identifying baseline airway pressure. Other suggested changes to the protocol include

repeating the investigation with other CCVs and PVs. In addition the study should be replicated using a range of F_IO_2's and various size endotracheal tubes. Also a greater range of CPAP and PSV could be included in future protocols. Regarding sample composition, the investigation should be repeated with subjects from diverse geographic areas and of diverse ethnicity. Actually endotracheally intubating healthy subjects places more burden on the subjects, however, doing so more closely approximates clinical conditions. Finally, repeating the study on intubated ventilator dependent individuals would greatly increase the external validity of the findings.

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APPENDIX A

MODES OF MECHANICAL VENTILATION

APPENDIX A

Modes of Mechanical Ventilation

A mechanical ventilator is a machine. By definition a machine is designed to transform energy to perform work (Proctor, 1995). A mechanical ventilator uses the electrical energy (energy = volts x amps x time) or pneumatic energy (energy = pressure x volume) to augment or replace an individual's muscles in performing the work of breathing. The work of breathing is the desired output. The basic functions of a mechanical ventilator include power input, power transmission or conversion, control scheme, and output (pressure, volume, and flow waveforms). The control scheme and ventilator output (pressure, volume, and flow) determine what are commonly referred to as the modes of ventilation delivered by a mechanical ventilator (Chatburn, 1991). Understanding of the control scheme of a mechanical ventilator starts with an examination of the mechanics of ventilation.

Basics of Mechanical Ventilation

In physiology, force is measured as pressure, displacement is measured as volume and relevant rate of change is measured as flow. These concepts are illustrated by the equations below.

$$\text{Pressure} = \text{force} \div \text{area}$$

$$\text{Volume} = \text{area} \times \text{displacement}$$

$$\text{Average flow} = \Delta\text{volume} \div \Delta\text{time}$$

$$\text{Instantaneous flow} = dv/dt \text{ (the derivative of volume with respect to time)}$$

A pressure difference (P_{tot}) must be applied across the respiratory system to overcome the elastic recoil of the lung and chest wall (P_{el}) and the resistance of the anatomical and artificial airways (P_{res}). A simplified form of a linear differential equation referred to as the equation of motion for the respiratory system describes this relationship.

$$P_{tot} = P_{el} + P_{res}$$

If the patient is breathing spontaneously, this equation can be written as

Respiratory muscle pressure = volume/compliance + flow x resistance

Respiratory muscle pressure is the transrespiratory pressure (airway pressure – body surface pressure) generated by the muscles of respiration to expand the thoracic cage and lungs. This pressure is not directly measurable.

If there is no spontaneous breathing effort with the ventilator supplying all of the ventilation demands, the equation is written as

Ventilator pressure = volume/compliance + flow x resistance

Ventilator pressure is the transrespiratory pressure produced by the ventilator during inspiration.

Finally if there is a combination of spontaneous and ventilator-supplied breaths, the equation is written as:

Respiratory muscle pressure + ventilator pressure = volume/compliance + flow x resistance

These equations ignore the small amounts of pressure required to overcome inertia and distorting forces of the chest wall observed at relatively high breathing rates or when breathing through high resistances. Inertia forces are those forces opposing starting the flow of gas. These equations also assume P_{tot} represents the change of pressure from baseline. The P_{tot} then is the pressure applied across the respiratory system above the applied positive end-expiratory pressure.

If the phenomenon of dynamic hyperinflation is present where there is insufficient expiratory time for the lung to deflate to its resting volume, then end-expiratory alveolar pressure will be positive relative to airway opening pressure. This positive pressure is termed alternatively auto-positive end-expiratory pressure (auto-PEEP), intrinsic PEEP, or occult PEEP. With the presence of auto-PEEP,

$$P_{tot} = P_{el} + P_{res}$$

becomes:

$$P_{tot} = P_{el} + P_{res} + \text{auto-PEEP}$$

The variables in the above equations are pressure, volume, and flow as these change with time. The parameters are compliance and resistance as these are assumed to remain constant (Chatburn, 1994).

Chatburn's Classification of Ventilation Modes

Chatburn (1991) offered a systematic method of classifying ventilation modes as a replacement for one first published by Mushin in 1959 with the latest modification published in 1980 (Mushin, Rendell-Baker, Thompson, & Mapelson, 1980). The disadvantages of this older classification system included its use of outmoded mechanical mechanisms, contradictory terms, lack of definitions for terms, and lack of appropriate detail.

Chatburn noted that a classification system should be based on a theoretical framework (Chatburn, 1991). He selected a mathematical model (equation of motion) that can be applied to all ventilator types. In addition he felt the classification system should be consistent, specific, and provide appropriate detail. He used the variables discussed above (pressure, volume, and flow) to classify the modes of mechanical ventilation. These variables are used as control, phase, and conditional variables.

Control variables are the variables (pressure, volume, flow, time) that the ventilator varies to cause inspiration. Despite changes in the ventilatory load (changes in compliance and/or resistance of the respiratory system), the ventilator will keep the control variable constant while changing all the other preset variables.

Phase variables are the variables measured and used to initiate a phase of the ventilatory cycle. These phases are trigger, limit, and cycle. The trigger variable causes the ventilator to begin inspiration. Typically the ventilator delivers the breath in response to a fall in pressure measured in the breathing circuit or a decrease in flow measured in the breathing circuit. Rarely is a drop in volume in the ventilator circuit used to trigger the delivery of a breath. If the breath is time triggered, the breath is termed machine-triggered or mandatory.

Inspiration is terminated when the cycle variable is met. For example if the breath is volume cycled, attainment of the preset volume will terminate inspiration.

The limit variable is the variable with a preset maximum value. Thus during inspiration this preset maximum will not be exceeded. For example, if the breath is volume cycled and pressure limited, the ventilator will create a pressure forcing a gas mixture into the patient's lungs while not exceeding this limit variable. Inspiration will terminate when the cycle variable is met, in this case when the preset tidal volume is delivered.

Conditional variables are additional variables coming into play when the ventilator delivers two or more different breath types. For example, if there is a minimum mandatory minute ventilation the patient must attain while breathing in a ventilation mode that allows him/her to breathe spontaneously while also receiving mandatory breaths, the ventilator will deliver additional mandatory breaths if this preset mandatory minute ventilation is not met with the patient breathing spontaneously.

The scheme proposed by Chatburn describing the ventilator modes uses specific

combinations of control, phase, and conditional variables defined for both mandatory and spontaneous breaths.

Mandatory Versus Spontaneous Breaths

The distinction between mandatory and spontaneous breaths is important to understanding the various modes of ventilation. A mandatory breath is a breath that is not initiated or terminated by the patient but rather is initiated and terminated by the ventilator. A time-triggered and/or time cycled breath are both *mandatory breaths*. A breath the patient initiates and terminates is a termed *spontaneous breath*.

Common ventilator modes where solely mandatory breaths are delivered are controlled mechanical ventilation (CMV), pressure controlled ventilation (PCV), and pressure controlled inverse ratio ventilation (PCIRV). Ventilator modes where solely spontaneous breaths are delivered include continuous positive airway pressure (CPAP), pressure support ventilation (PSV), and assisted mechanical ventilation (AMV). Finally ventilator modes delivering a combination of mandatory and spontaneous breaths include assist/control ventilation (A/C), intermittent mandatory ventilation (IMV), and synchronized mandatory ventilation (SIMV). This investigation will use PVs with CPAP (0 and 5 cm H_2O) and PSV mode (0 and 10 cm H_2O).

APPENDIX B

POSSIBLE RANDOMIZATION SCHEDULE

Contingency table illustrating the factors and levels for the present investigation and a possible order of ventilators, continuous positive airway pressure (CPAP, in cm H_2O), and pressure support ventilation (PSV, in cm H_2O) combinations for a subject.

Ventilator	Achieva				LTV 1000				Univent 754				7200 ae			
PEEP	CPAP 0		PEEP 5		CPAP 0		PEEP 5		CPAP 0		PEEP 5		CPAP 0		PEEP 5	
PSV	PSV 0	PSV 10	PSV 0	PSV 10	PSV 0	PSV 10	PSV 0	PSV 10	PSV 0	PSV 10	PSV 0	PSV 10	PSV 0	PSV 10	PSV 0	PSV 10
Trial 1						X										
Trial 2												X				
Trial 3	X															
Trial 4					X											
Trial 5															X	
Trial 6			X													
Trial 7		X														
Trial 8				X												
Trial 9						X										
Trial 10														X		
Trial 11										X						
Trial 12									X							
Trial 13													X			
Trial 14											X					
Trial 15																X
Trial 16								X								

Note: Univent 754 does not offer PSV therefore PSV of 0 cm H_2O will be used as a placebo when randomization calls for PSV of 10 cm H_2O.

APPENDIX C

VISUAL ANALOGUE SCALE

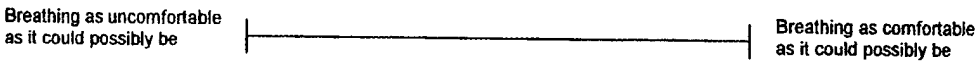
Subject number _____

Date

Breathing condition

Breathing Comfort Visual Analogue Scale

How comfortable was your breathing when breathing with the last ventilator? Please indicate by marking the line.



Note. Not to scale. Reduced for publication.

APPENDIX D

INSTITUTIONAL REVIEW BOARD APPROVAL AND ADDENDUM:

University of Cincinnati Medical Center

UNIVERSITY OF CINCINNATI MEDICAL CENTER
INSTITUTIONAL REVIEW BOARD
NOTIFICATION FORM

PRINCIPAL INVESTIGATOR: Paul N. Austin, C.R.N.A., M.S.

CO-INVESTIGATOR(S): Marilyn Sommers, Ph.D., R.N.
Jay Johannigman, M.D.
Theresa Beery, Ph.D., R.N.
Paul Succop, Ph.D.

PROTOCOL : 01-01-30-04-EE - "Spontaneous Breathing and Mechanical Ventilators"

XXX *APPROVED - Initial__x__ Full Board___ Expedited__X__
(Approval includes informed consent document and advertising, if applicable)

Sponsor:

DATE: February 7, 2001
The approval for this research activity expires on: February 7, 2002

1 If the study involves a drug, you must complete the Pharmacy Committee Drug Information Sheet (available at the In-Patient Pharmacy, University Hospital).

2. You are required to immediately report any adverse reactions or complications of the project to the Institutional Review Board.

3. The period of approval of this research project is stated above. A progress report form must be filed with the Institutional Review Board on at least an annual basis, and sometimes more frequently at the discretion of the Board. If the progress report is not returned by the specified date, your department head will be notified.

4. There may be no change or addition to the project, or changes of the investigators involved, without prior approval of the IRB.

5. If this protocol has not been initiated within two years of this date, you will be required to resubmit the study for reconsideration by the Institutional Review Board. However, this regulation is not intended to negate the requirement that a progress report be filed with the IRB office on at least an annual basis.

6. Notification of approval by the Institutional Review Board does not necessarily indicate approval by other committees of the Medical Center with the exception of Radiation Safety.

7 You are required to modify this study, subject to IRB approval, if subsequent information regarding any drug, device or procedure utilized in the study is received from the manufacturer or any other reliable source, that could reasonably increase or alter potential harm to subjects. The informed consent statement must be modified to include this new information or an addendum must be prepared as a means to assure subject notification. In cases where the subject has completed the study, the modification or addendum is only necessary if the additional information received could impact the subjects in the future.

Chairperson, Institutional Review Board

DHHS Assurance No. M1138
Identification No. 01

*The attached consent has been approved by the IRB. Please copy this ICS document and use for all subjects entered into the study.

University of Cincinnati
Medical Center

College of Medicine
Institutional Review Board
University of Cincinnati
PO Box 670567
Cincinnati OH 45267-0567
Eden and Bethesda Avenues
Phone (513) 558-5259

MEMORANDUM

Paul Austin, CRNA, MS
ML 0558

FROM: Peter T. Frame, M.D., Co-chairperson
University of Cincinnati Medical Center
Institutional Review Board

DATE: February 21, 2001

#01-01-30-04 – "Spontaneous Breathing and Mechanical Ventilators"

Please be advised that the University of Cincinnati Medical Center Institutional Review Board reviewed and approved the modification to the above referenced study as outlined in your letter of February 12, 2001. We have attached a copy of the revised informed consent documents stamped with the IRB date of approval and date the approval expires. To avoid confusion, the expiration date corresponds to the end of the current IRB approval period. Please use a copy of this stapled and dated version of the consent when new subjects are enrolled in the protocol. This action took place at today's meeting.

Thank you for your continued cooperation with the Board's regulations with regard to changes in your research activities.

APPENDIX E

NOTICE SEEKING VOLUNTEERS

Call for Volunteers

If you are interested in participating in a study that seeks to assess the work performed by and the breathing comfort of nonintubated healthy volunteers breathing through three portable ventilators and a critical care ventilator, please call Paul Austin at 558-3850.

Participants will spend about 3 hours for one day in the Trauma/Critical Care Research Laboratory in the Surgical Research Unit.

Please note the inclusion and exclusion criteria below.

Inclusion Criteria:
Nonobese (body mass index less than 30) healthy males and females between the ages of 18 and 65 years.

Exclusion Criteria:
History or present symptoms of cardiopulmonary disease, symptoms of an upper or lower respiratory infection either at the time of the study or in the 30 days prior to the study, active oral and/or perioral lesions, sinusitis, recent nasopharyngeal surgery, smoking of any substance within eight weeks of the investigation.

Participants will be paid $50 for their participation.

APPENDIX F

INFORMED CONSENT

UNIVERSITY OF CINCINNATI

Consent to Participate in a Research Study

"Spontaneous Breathing and Mechanical Ventilators"

Protocol# 01-1-30-4

INVESTIGATOR INFORMATION:

Paul N. Austin, CRNA MS
Principal Investigator Name

513-558-3850, Pager 937-637-3489
Telephone Number 24 hr/day-work

and

Marilyn Sommers, PhD, RN; Jay Johannigman, MD; Teresa Beery, PhD RN; Paul Succop, PhD
Co-investigators

INTRODUCTION
Before agreeing to participate in this study, it is important that the following explanation of the proposed procedures be read. It describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes alternative procedures available and the right to withdraw from the study at any time. I have been told that no guarantee or assurance can be made as to the results. I have also been told that refusal to participate in this study will not influence standard treatment available to me.

I, _____ have been asked to participate in the research study under the direction and medical supervision of Jay Johannigman, MD. Other professional persons associated with the study may assist or act for him/her.

This research is not sponsored by a corporation.

will be one of approximately 50 subjects to participate in this trial.

PURPOSE
I understand that the purpose of this research study is to determine the work performed by and the comfort of a person who is spontaneously breathing through a ventilator (breathing machine).

DURATION
My participation in this study will last for approximately three hours for one day.

PROCEDURES
My participation in this study will require one visit to the study location, the Trauma/Critical Care Research Laboratory. I will be asked not to eat any food during the two hours before the study but I can drink liquids at any time before the study and water and/or ice chips during the study. I will be weighed and my height will be measured. I will be seated and nose clips will be placed on my nose to prevent breathing through my nose. I will be assigned a clean and new breathing filter that is more than 99.99% efficient in filtering viruses and bacteria. This filter will be changed after every subject. I will also be assigned a clean mouthpiece that will be

sterilized between uses. I will place the mouthpiece in my mouth and maintain an airtight seal. The mouthpiece and filter will be attached to a measuring device and ventilator. I will not be able to see the ventilator. I will wear earphones connected to a compact disk player. I will listen to music of my choice during the study. I will breathe for one minute to get used to breathing this way. I will then breathe for between three and five minutes. At the end of that three to five minute period I will rate my breathing comfort by placing a mark on a line. I will then rest for one minute and during this time I may have a sip of water and/or ice chips. The procedure will then be repeated twenty one times with different ventilator settings using four different ventilators. I understand there will be a ten minute break halfway through the study. I understand I must notify the investigator if I want additional breaks. I understand the display of a computer will be continuously videotaped but I will not be videotaped or photographed at any time. I understand no medications will be used during this study. I understand no specimens will be collected during this study. I understand no procedures or test articles to be used in this study are investigational.

EXCLUSION

I should not participate in this study if any of the following apply to me:

- I am under 18 or over 65 years of age
- My body mass index is less than 30
- I have a history or present symptoms of heart or lung disease, symptoms of a cold or lung infection either at the time of the study or in the 30 days prior to the study
- I have sores in or around my mouth, a sinus infection, or recent nose or throat surgery
- I have smoked any substance within eight weeks of the study

RISKS/DISCOMFORTS

I have been told that the study described above may involve the following risks and/or discomforts and safeguard and or precautions to avoid them: Breathing discomfort including shortness of breath, nasal discomfort due to use of the nose clips, and mouth discomfort due to the mouthpiece. All of these are relieved by stopping the study. The nose clips and mouthpiece are made of soft plastic which will help prevent discomfort. The risk of infection is reduced by using new breathing filter with each subject and sterilizing the mouthpiece between subjects. The breathing filter is more than 99.99% efficient in filtering viruses and bacteria. There also may be risks and discomforts which are not yet known.

PREGNANCY

If I am a woman and I am or should be come pregnant, there is no risk to me or my fetus by participation in this study

BENEFITS

I have been told that I will receive no direct benefit from my participation in this study, but my participation may help health care practitioners better understand how to measure breathing discomfort.

ALTERNATIVES

I understand the alternative to participating in this study is to refuse to participate or withdraw from the study.

NEW FINDINGS

I have been told that I will receive any new information during the course of the study concerning significant treatment findings that may affect my willingness to continue my participation.

CONFIDENTIALITY

Every effort will be made to maintain the confidentiality of my study records. Agents of the United States Food and Drug Administration and the University of Cincinnati Medical Center will be allowed to inspect sections of my medical and research records related to this study. The data from the study may be published; however, I will not be identified by name. My identify will remain confidential unless disclosure is required by law.

FINANCIAL COSTS TO THE SUBJECT

Funds are not available to cover the costs of any ongoing medical care and I remain responsible for the cost of

non-research related care. Tests, procedures or other costs incurred solely for purposes of research will not be my financial responsibility. If I have questions about my medical bill relative to research participation, I may contact Paul N. Austin, CRNA MS.

COMPENSATION IN CASE OF INJURY
If I am injured as a result of research, I will contact Paul N. Austin, CRNA MS at 513-558-3850 or the Chairman of the Institutional Review Board at 513-558-5259. The University of Cincinnati Medical Center makes decisions concerning reimbursement for medical treatment for injuries occurring during or caused by participation in biomedical or behavioral research. In the event I become ill or injured as a direct result of my participation in the research study, necessary medical care will be made available to me and the University, at its discretion, will pay medical expenses necessary to treat such injury (1) to the extent I am not otherwise reimbursed by my medical or hospital insurance, or by third party or governmental programs providing such coverage, and (2) provided I have used the breathing machine as directed by the study doctor in accordance with the study protocol. Financial compensation for such things as lost wages, disability or discomfort due to injury during research is not routinely available."

PAYMENTS TO PARTICIPANTS:
I have been told that I will receive $50 my participation in this study.

RIGHT TO REFUSE OR WITHDRAW
It has been explained to me that my participation is voluntary and I may refuse to participate, or may discontinue my participation **AT ANY TIME**, without penalty or loss of benefits to which I am otherwise entitled. I have also been told that the investigator has the right to withdraw me from the study **AT ANY TIME**. I have been told that my withdrawal from the study may be for reasons related solely to me (e.g. not following study-related directions from the Investigator; a serious adverse reaction) or because the entire study has been terminated. I have been told that the sponsor has the right to terminate the study or the investigator's participation in the study at any time.

OFFER TO ANSWER QUESTIONS
This study has been explained to my satisfaction by _____ and my questions were answered. If I have any other questions about this study, I may call Paul N. Austin, CRNA MS at 513-558-3850.

If I have any questions about my rights as a research subject, I may call the Chairman of the Institutional Review Board at 513-558-5259.

IF RESEARCH RELATED INJURY OCCURS, I WILL CALL Paul N. Austin, CRNA MS at 513-558-3850.

PARTICIPATION IN ANOTHER STUDY:

Is the subject participating in another study? If yes, please provide the principal investigator's name and title of the study.

TITLE OF STUDY: _____

INSTITUTIONAL STUDY NUMBER

SPONSOR STUDY NUMBER _____

LEGAL RIGHTS
Nothing in this consent form waives any legal rights I may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

I HAVE READ THE INFORMATION PROVIDED ABOVE. I VOLUNTARILY AGREE TO PARTICIPATE IN THIS STUDY. AFTER IT IS SIGNED, I WILL RECEIVE A COPY OF THIS CONSENT FORM.

_____ _____
Subject Signature Date

☐ **If verbal assent/consent was obtained, please check box and create a witness signature line which the witness must sign and date.**

_____ _____
Legal Representative Parent Date

_____ _____
Signature and Title of Person Obtaining Consent and Identification of Role in the Study Date

_____ _____
Signature of Investigator Date

PI. Paul Austin
PROTOCOL NO. 01-01-30-04
RECEIVED 2/13/01
REVISED 2/12/01
APPROVED 2/21/01
EXPIRES ON 2/7/2002
SIGNED _____
Chairperson/Designee
University of Cincinnati
Medical Center IRB

APPENDIX F

VISUAL ANALOGUE SCALE

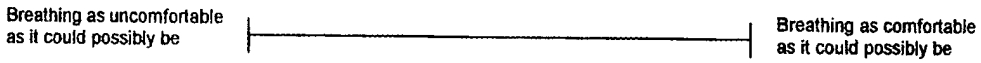
Subject number _____

Date

Breathing condition

Breathing Comfort Visual Analogue Scale

How comfortable was your breathing when breathing with the last ventilator? Please indicate by marking the line.



Note. Not to scale. Reduced for publication.