British Journal of Anaesthesia **91** (**1**): 81–91 (2003)
DOI: 10.1093/bja/aeg146

BJA

Novel aspects of pulmonary mechanics in intensive care

I. de Chazal and R. D. Hubmayr*

Room 8-62 Stabile Building, Mayo Clinic, Rochester, MN 55905, USA
**Corresponding author. E-mail: rhubmayr@mayo.edu*

Br J Anaesth 2003; **91**: 81–91

Keywords: intensive care; ventilation, mechanics

This review of the mechanical properties of the respiratory system is related to ventilator practice. As virtually all modern ventilators display traces of airway pressure (Paw), volume (V) and flow ($\dot{V}$) the necessary information is immediately available with no additional effort. This review interprets the information contained in ventilator waveforms. The review concentrates on three aspects where measurements are most useful, namely: (i) the diagnosis and management of patients with injured lungs; (iii) patients with airways obstruction; and (iii) the assessment of respiratory motor output. We will outline the precision and accuracy of the derived variables, discuss their scientific basis and review how decisions based on these measurements improve patient outcomes. We give a personal perspective even if it means taking sides in debates on controversial issues.

Basic principles

(For a full discussion of classic respiratory system mechanics the reader is referred to refs [6] and [47]). Classic respiratory mechanics is based on Newtonian physics as expressed in the equation of motion. The respiratory system is considered to be a resistive and elastic element in series. Any pressure applied to it is either stored as elastic pressure (Pel) or dissipated as resistive pressure (Pres)

$$P(t)=\mathrm{Pel}(t)+\mathrm{Pres}(t) \quad (1)$$

where t indicates a particular time.

In its simplest interpretation the elastic element represents lungs and chest wall, while the resistive element represents ventilator tubing, tracheal tube and airways (we will discuss the pitfalls and limitations of this simplistic model in the context of the specific applications). It follows that during inflation of the relaxed respiratory system Pel can be approximated by alveolar pressure (Palv) and Pres by the difference between proximal airway pressure (Paw) and Palv.

$$\mathrm{Pel}(t)=\mathrm{Palv}(t) \quad (2)$$

and

$$\mathrm{Pres}(t)=\mathrm{Paw}(t)-\mathrm{Palv}(t) \quad (3)$$

If flow is zero then Palv equilibrates with Paw so that Pel can be estimated from airway occlusion pressure. This is how a static recoil pressure–volume curve measurement is made.

As Pel is a function of volume and Pres a function of flow Equation 1 can be rewritten as

$$P(t)=\mathrm{Po}+\mathrm{E}V(t)+\mathrm{R}\dot{V}(t) \quad (4)$$

where Po is the elastic recoil pressure at relaxed end-expiration. In the clinical literature Po is often referred to as total PEEP. The constants E and R denote respiratory elastance and resistance and are the factors that scale volume and flow to yield Pel and Pres, respectively. Clinicians are more likely to use the term compliance (C), which is the inverse of E.

During relaxed expiration, flow is generated by Palv (relative to Paw), in that it is determined by the elastic recoil of the respiratory system and by the properties of the resistive element (i.e. properties of airway, tracheal tube and equipment). As both determinants vary with lung volume, so must passive expiratory flow. In normal lungs expiratory flow varies approximately linearly with volume and decreases exponentially with time.

Rearranging Equation 4 shows that the slope of the passive expiratory volume flow relationship equals R/E (or R*C), which has the units of time. This quantity is the time constant of the respiratory system and defines the time it takes for the elastic element to passively empty approximately 63% of its contents. Inspection of linearity and slope of the expiratory flow–volume curve can be useful when a

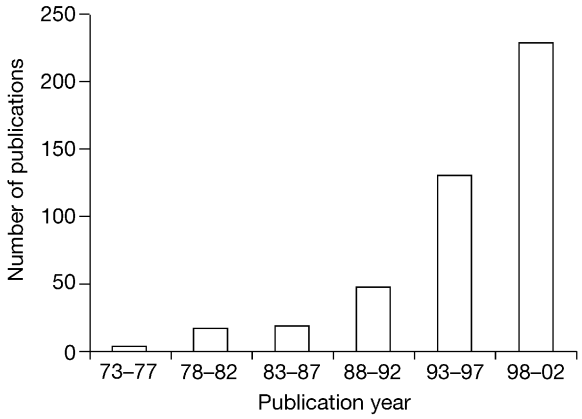

Fig 1 Results of a Medline search of the term 'respiratory mechanics' in association with ALI or ARDS.

diagnosis of airway or tracheal tube obstruction is suspected (see page 85).

Assessment of respiratory mechanics in the diagnosis and management of patients with injured lungs

The realization that the physical stress of mechanical ventilation can damage lungs or may amplify non-physical injury mechanisms has generated renewed interest in the mechanics of injured lungs.[21] Publications on this topic have increased exponentially in the last decade (Fig. 1). An International Consensus Conference held in 1993 defined acute lung injury (ALI) and adult respiratory distress syndrome (ARDS) as conditions characterized by abnormal pulmonary gas exchange in the presence of bilateral pulmonary infiltrates.[10] These features are non-specific, and must be related to the clinical setting and not attributed to left heart failure. ALI and ARDS differ only with respect to the severity of the gas exchange impairment and have a wide variety of causes.

Injury mechanisms and their consequences on lung mechanics

Irrespective of cause, injured lungs have an abnormal barrier function. The pulmonary capillaries are leaky and the alveolar epithelial cells cannot clear water and solute from the alveolar space properly,[11] with important consequences for the mechanical properties of the lung. Injury and oedema increase pulmonary elastance and resistance.[23 84] Numerous mechanisms have been proposed to explain this. Presently the most popular one is the 'baby lung' concept: alveolar flooding causes 'collapse' of the dependent lung so the greater lung elastance reflects the reduced number and smaller volume of near normal, non-dependent, and recruitable units.[28–30] Other proposed mechanisms include increased surface tension by inactivation of surfactant,[80] airway block by air–liquid interfaces and bubble formation in small airways,[16 18 54 92] reflex-broncho-constriction,[15 19] pneumo-constriction caused by release of inflammatory mediators[24] and peribronchial oedema.[18]

Susceptibility of injured lungs to VILI

Two attributes of the injured lung explain its susceptibility to additional ventilator induced lung injury: (i) the number of alveoli that can expand during inspiration is decreased and (ii) the distribution of liquid and surface tension varies in distal airspaces and hence the local impedances to lung expansion are heterogeneous.[5 42] The first attribute is the key abnormality in the 'baby lung concept'.[29] It explains the increased risk of lung injury from overdistension of aerated low impedance units. The second attribute, heterogeneity in regional impedances to lung expansion, has several consequences. One is a large shear stress between neighbouring, interdependent units that operate at different volumes. Tissue attachments between large aerated units and smaller neighbouring flooded or collapsed units carry a stress that is substantially greater than the average transpulmonary pressure.[56] Another consequence is injury to small airways and alveolar ducts caused by their repeated opening and collapse,[60 89] by energy dissipation during liquid bridge fracture or from the stress that is imposed on lining cells by the movement of air–liquid interfaces with respiration.[30 51] The relative contributions of these related injury mechanisms in different diseases is simply not known. Inferences from animal experiments with short-term endpoints are of interest but do not show which mechanism is important in which circumstance. Study of bubble and liquid flow in tubes, although constrained by simplifying assumptions (e.g. rigid tube of uniform diameter, smooth surface), are giving some quantitative data on this problem.[12 14 30]

Whole respiratory system mechanics: methods and mechanistic interpretation

Much literature now describes the static and dynamic pressure volume relationships of injured lungs, and the effects of interventions such as PEEP and recruitment manoeuvres.[23 37 46 50 53 55 76 91] A great deal of emphasis has been placed on methods and analytic approach,[27 36 68 72 77 94] but, there is little agreement how these measurements can be used clinically.

The static respiratory system pressure–volume curve of patients with injured lungs has certain characteristics (Fig. 2): (i) an S-shaped inflation curve with an upper and lower inflection point (UIP and LIP, respectively); (ii) an increased recoil pressure at all lung volumes; and (iii) a reduced compliance defined by the slope of the inflation curve between LIP and UIP.

For many years the pressure at LIP was regarded as the critical opening pressure of collapsed lung units and was

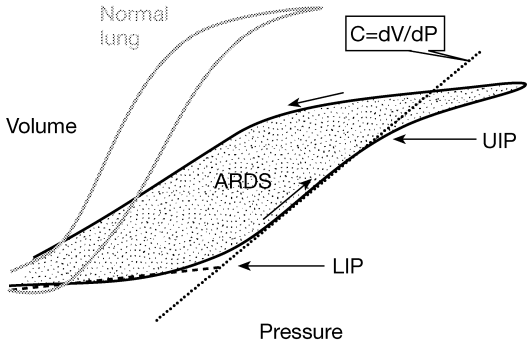

Fig 2 Cartoon of characteristic PV changes in injured lungs.

considered a target of 'best PEEP'. The pressure at UIP, in turn, was considered to indicate alveolar overdistension that should not be exceeded during mechanical ventilation.[75] These ideas have been challenged because most values from the PV curve have low specificity.[42 53] For example, when lungs are rinsed with mineral oils to increase surface tension, the LIP is prominent even though the lung units are 'open', that is aerated.[79 81] Similar characteristics are observed when saline filled lungs are inflated with air as happens during a newborn's first breath.[4] Attention is now on oedema, airway liquid and interfacial phenomena as causes of increased 'opening pressure' and lung impedance.[92 53] In some patients the LIP originates in the chest wall and not the lung.[57] This is likely in patients with small thoracic volumes because the chest wall PV curve is nonlinear in the low volume range.[67] Nevertheless, even in these patients the contribution of the chest wall to the pressure at LIP is quite small.

Because the chest wall may generate PV artifacts, some have advocated oesophageal pressure measurement to guide management in patients with injured lungs. Advocates usually emphasize that even in recumbent patients the change in oesophageal pressure (ΔPoes) reflects the average change in lung surface pressure or pleural pressure (ΔPpl). However, support for this statement is from experiments on normal animals.[34] Diseased lungs expand non-uniformly and non-uniform lung expansion is associated with non-uniform distributions of lung surface pressure.[1 43 52 62] This means that the position of the oesophageal balloon at which ΔPoes mirrors ΔPpl varies greatly with posture, mode of breathing and with the pattern of respiratory muscle activation. In other words, in injured lungs the calibration of the device with an occlusion test[7] does not guarantee that the signal, that is ΔPoes, will represent ΔPpl under the conditions under which the actual measurements are made. Any concern about erroneous conclusions from oesophageal manometry in patients with ARDS is speculative because it is not possible to measure Ppl without artifact in humans. However, we cite two examples in support of our arguments. Rich and colleagues measured lung mechanics in prone dogs.[71] During inhalation anaesthesia they observed looping and inversions of dynamic PV loops that suggested negative pulmonary resistances. They attributed this artifact to a halothane-related inhibition of intercostal muscles, ribcage instability, and chest wall distortion that changed the topographical distribution of ΔPpl. Another example is the apparent large decrease in chest wall compliance of ARDS patients in the prone posture.[63] The investigators defined chest wall compliance (Cw) as the ratio of tidal volume to ΔPoes. In 15 of 16 supine patients the Cw estimate was larger than the predicted norm (reaching values up to 0.45 litre cm H_2O^{-1}) and decreased dramatically upon the assumption of the prone posture. This suggests that in the supine posture the oesophageal balloon is near flooded derecruited lung, which does not expand during mechanical ventilation and therefore does not generate a local pressure swing. Paraspinal lung recruitment associated with the assumption of the prone posture dramatically increases volume and ventilation of perioesophageal lung regions, leading to a much smaller estimate of Cw.

While it is likely that some regions of the lungs approach their maximal volume at pressures near UIP,[48 55 74] the evidence that ventilating patients in this way causes injury provided tidal volume is kept low is circumstantial.[22 69 75] The pressures and volumes used to test this hypothesis in experimental animals were generally high and are nowadays rarely used in clinical practice. Therefore, the term overexpansion should be used with caution. We will return to this point in our discussion of clinical implications of mechanics measurements.

The effects of injury on recoil and on compliance need not be related. This is because abnormal surfactants with increased minimal surface tension and impaired dynamic properties (adsorption, spreading, and compression) cannot cause an appropriate change in surface tension with lung volume.[65 80] As a result both recoil and compliance of aerated units with abnormal surfactants must increase,[79 81 82] while the compliance of flooded and collapsed units must be more or less zero. This is just one of many examples why it is difficult to draw inferences about specific mechanisms from static whole lung PV curves. This would only be possible if the small-scale distributions of regional elastances were known.

In some patients there is a larger than anticipated recoil pressure difference between inflation and deflation, indicating PV hysteresis. There are several possible mechanisms for PV hysteresis: (i) the recruitment and derecruitment of lung units during the manoeuvre; (ii) the volume- and time-dependent molecular reorganization of surface active material which coats air–liquid interfaces in alveoli and conducting airways; (iii) stress relaxation and stress recovery of airways and lung parenchyma; (iv) spurious changes in lung volume on account of gas absorption during the PV measurement. The last is a well-described problem of the supersyringe technique.[83]

The clinical literature on ALI and ARDS has generally ignored mechanisms two and three and has attributed all volume- and time-related changes in PV characteristics to lung recruitment (i.e. the opening of previously closed units). While in injured lungs recruitment is undoubtedly an important cause of airway pressure and time-related changes in lung mechanics, it is certainly not the only one. In a series of classic papers Hildebrandt and colleagues studied the physiologic determinants of the PV loop.[39–41] In the normal lung, stress relaxation, stress recovery, and hysteresis are surfactant and surface tension phenomena, and they account for changes in lung volume with pressure and time. In other words 'recruitment manoeuvres' as they have been described in the critical care literature would be fully expected to alter volume and recoil of normal lungs by recruitment independent mechanisms. Compared with surface properties the fraction of elastic pressure that is lost because of tissue hysteresis is small.[25] However, it is not zero and as emphasized in studies of patients with asthma, can be an important source of relaxation in a lung which is actively constricted.[59]

The neglect of alternative mechanisms as explanations for PEEP induced changes in the volume of injured lungs is regrettable, because the reasoning behind the 'open lung approach' is largely based on putative benefits derived from recruitment. However, if PV measurements cannot distinguish between recruitment of new units and stress relaxation of already recruited units, then clinical decisions will be based on a mechanism (recruitment) that cannot be confidently assessed.

Role of respiratory mechanics testing in clinical decision-making

As pointed out, most of the recommendations using measurements of mechanics to guide ventilator management are based on physiologic reasoning and not on established clinical efficacy. We should consider factors that determine PV shape and lung mechanical properties, to assess the soundness of current practice. We will address two questions: (i) is there a single end-inspiratory pressure beyond which patients should not be mechanically ventilated? (ii) Do measurements of respiratory mechanics help in the choice of tidal volume and 'best PEEP'?

There is incontrovertible evidence that mechanical ventilation with large tidal volumes harms the lung.[2 21 85] In the single most definitive study trial on the topic, the ARDS network study, patients were randomized to receive mechanical ventilation with tidal volumes of either 6 or 12 cc kg^{-1} predicted body weight.[85] The designers of the study chose to ignore lung mechanics as a guide to ventilator management, and instead scaled tidal volume to predicted body weight, that is an estimate of the size of the normal lung. Because of this design choice, hypotheses about safety limits in end-inspiratory recoil pressure (also referred to as plateau pressure or end-inspiratory hold pressure) cannot be tested post hoc. Certainly, in each group in the study plateau pressure (Pplat) correlated with the severity of injury (the size of the baby lung) and with outcome (R. G. Brower, personal communication).[13] However, it is difficult to separate the effects of VT assignment and severity of lung impairment on Plat and outcomes.

Those who argue that there is a safe threshold value of Pplat (often proposed as 30 cm H_2O), below which the choice of VT becomes less important, implicitly assume that the risk of injury increases as peak lung volume increases.[87] Normal lungs approach their total lung capacity, which may be viewed as their structural limit, at transpulmonary pressures between 30 and 35 cm H_2O. Thus, even in the heterogeneously affected injured lung the most normal and hence low impedance units would not exceed their capacity at Pplat less than 30 cm H_2O. Clinical evidence in support of this approach is the observation that in the ARDS Network trial the mortality of patients with the greatest respiratory system compliance was not influenced by VT assignment: that is, it was identical in the two study arms.[85]

However, there are powerful arguments against this reasoning. First, the lack of VT effect on mortality in the high compliance group has limited statistical power. Secondly, a post hoc analysis that focused on Pplat rather than compliance showed that the VT effect was preserved across all Pplat quartiles (R. G. Brower, personal communication). Thirdly, in spontaneously breathing animals experimentally induced hyperpnoea impairs lung barrier function.[49] And finally, fourthly, the large alveolar surface area change associated with high VT breathing inactivates surfactant irrespective of the peak lung volume reached.[45]

The clinical literature provides even less guidance to the question 'do respiratory mechanics measurements aid in the choice of best PEEP'? Most experimental studies on the topic have used measures of pulmonary gas exchange such as the $Pa_{O_2}/F_{I_{O_2}}$ ratio as surrogate outcome variables of clinical benefit. While there is no question that adjustments in PEEP guided by PV loops may be helpful in optimizing pulmonary gas exchange, it has also become clear that optimizing gas exchange need not convey outcome/survival benefit. Those patients randomized to the high tidal volume group, who ended up having an increased risk of dying, had more improvement in arterial oxygenation on day 1 than patients who were randomized to the low VT arm and who were more likely to survive.[85]

In summary, measurements of respiratory mechanics in patients with injured lungs can help to identify patients at risk for ventilator induced lung injury. Mechanical ventilation with airway pressures greater than 30–35 cm H_2O should make the clinician re-assess the settings of VT and PEEP. Until proven otherwise, patients with injured lungs should not receive a VT more than 8 cc kg^{-1} predicted bodyweight (some would argue 6 cc kg^{-1} predicted). Most experts agree that a routine PEEP setting of 5 cm H_2O is too little, but there is no evidence that setting PEEP guided by PV curves results in better outcomes.

Assessment of respiratory mechanics in patients with airflow obstruction

In contrast to ARDS/ALI, the mechanisms that govern patient/ventilator interactions in patients with airway obstruction are well understood. There is comparatively little controversy how to interpret and use information on lung mechanics in clinical decision-making. However, some care givers may not know or use the knowledge in their day to day practice. For example, in a recent survey one third of US senior medical residents were unable to manage auto-PEEP correctly at the end of their critical care training.[17] In this section of our review we will therefore focus on the bedside diagnosis of airflow obstruction and on the implications of this diagnosis for ventilator management.

Basic principles for identifying airway obstruction in a mechanically ventilated patient

Patients with obstructive lung disease cannot generate normal expiratory flow. In ambulatory patients this is shown by characteristic changes in the shape of the maximal expiratory flow–volume relationship. In mechanically ventilated patients, however, flow–volume curves are harder to interpret because: (i) one cannot assume a priori that expiratory flows are maximal; and (ii) absolute lung volume is not known. The critical care literature has therefore not paid much attention to flow–volume loops but has emphasized inadvertent PEEP and the recognition of dynamic hyperinflation as an important consequence of airflow obstruction.[32 33 64] Nevertheless, we find the flow–volume loop helpful to explain the mechanism of these features.

Dynamic hyperinflation occurs whenever the respiratory system cannot generate the necessary expiratory flow near FRC. In a ventilated patient the expiratory flow requirement is determined by tidal volume settings and breath timing (Fig. 3). It can be calculated from the ratio of tidal volume and expiratory time (V_T/T_E). Consider a paralysed patient who is being ventilated with a V_T of 0.8 litre, a mean inspiratory flow of 30 litre min^{-1} and a ventilatory frequency of 12 min^{-1}. At these settings the expiratory time (T_E) is 3.4 s and mean expiratory flow needed is 0.8/3.4 or approximately 0.25 litre s^{-1}. A patient with normal lungs can generate a mean expiratory flow of more than 0.25 litre s^{-1} during the normal tidal breathing and the lungs would therefore reach relaxation volume at end-expiration. The airway occlusion pressure at end-expiration would be atmospheric (or equal to extrinsic PEEP). In contrast, many patients with severe airways obstruction generate maximal flows between 25 and 75% of their vital capacity of no more than 0.1 litre s^{-1} (referred to MMEF or FEF 25–75 in the pulmonary function testing literature). If such patients were to be ventilated with the settings suggested in this example, they would 'dynamically hyperinflate' because they could not generate the necessary flow of 0.25 litre s^{-1} over most of their vital capacity range. In fact, the lung volume at which the respiratory system would reach a new steady state if these conditions were imposed is defined by the volume at which mean expiratory flow becomes 0.25 litre s^{-1}.

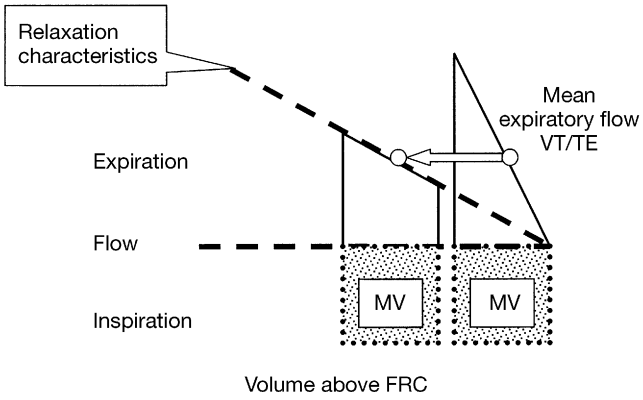

Fig 3 Factors that determine dynamic hyperinflation.

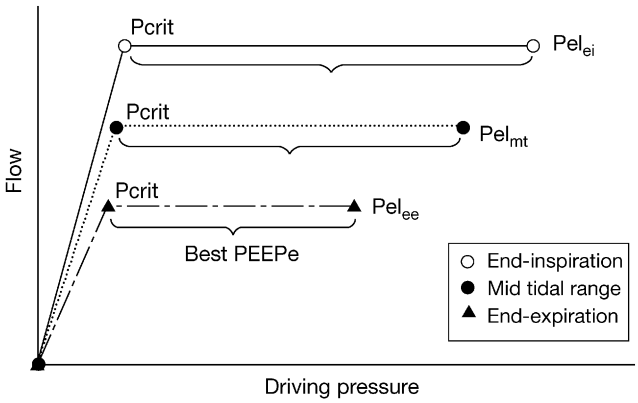

Fig 4 Iso-volume pressure flow curves.

Before discussing the clinical application of measurements of mechanics in obstructed patients, it is also helpful to recall the basic concepts of expiratory flow limitation. Figure 4 shows three hypothetical driving pressure–expiratory flow curves at three specific lung volumes (e.g. end-inspiration, mid-tidal range, and end-expiration). Note that the curves are non-linear, and that they have a pressure-dependent and a pressure-independent portion, that is separated by Pcrit, the critical driving pressure. Over 40 years ago Fry and Hyatt constructed such curves by asking volunteers to vary their expiratory efforts while they measured oesophageal pressure and expiratory flow.[26] Fry and Hyatt introduced the idea of dynamic airway collapse as the principal reason for effort independence of flow and provided a conceptual framework for examining flow–volume loops in pulmonary function testing.

Iso-volume pressure flow curves can be measured in relaxed or paralysed mechanically ventilated patients.[33] We are not suggesting that this be done clinically, but find it

useful for reviewing important principles. In a paralysed mechanically ventilated patient the maximal driving pressure for expiratory flow is the respiratory system recoil pressure at the lung volume in question (denoted by $Pel_{ei,\ mt,\ ee}$ in Fig. 4). As shown on page 81, Pel is the airway occlusion pressure at the volume under consideration. The driving pressure for flow will be reduced relative to Pel by applying extrinsic PEEP (PEEPe). The resulting changes in flow at a given lung volume can be measured and after repeating this process over many PEEPe settings a set of iso-volume pressure–flow curves can be constructed. If one were to do this in a young person with normal lungs one would discover that any application of PEEPe, no matter how small, reduces isorecoil flow. In other words, normal lungs do not reach maximal expiratory flow when they empty passively. The same procedure in a patient with severe emphysema would show that Pel is already greater than the pressure needed to reach maximal flow. Hence, applying a small PEEPe will not affect flow. Instead of reducing driving pressure with PEEPe one could just as well increase it by applying a negative airway pressure.[58] If there were no corresponding flow change one would have to conclude that expiratory flow limitation is present and that driving pressure is greater than Pcrit.

The bedside diagnosis of obstruction in mechanically ventilated patients

It is easy to confirm airflow obstruction and test for expiratory flow limitation in a patient who makes little to no spontaneous respiratory efforts.[7 35] Therefore, the best time to assess patients for airway disease is shortly after intubation when most are heavily sedated or have received relaxants. We can assess: (i) inadvertent PEEP by airway occlusion at endexpiration; (ii) the shape of the expiratory flow–volume curve, looking for non-linearity and end expiratory flow transients; (iii) the shape of the Paw tracing during volume preset mechanical ventilation including the decrease from the peak to the plateau airway pressure; and (iv) the inspection of the peak Paw response to small step changes in PEEP.

Inadvertent PEEP

Inadvertent (or intrinsic) PEEP (PEEPi) is defined as the difference between the respiratory system recoil pressure at end-expiration (end-expired airway occlusion pressure or total PEEP as it is sometimes referred to) and the end-expired airway pressure during mechanical ventilation (i.e. PEEPe). In a relaxed, mechanically ventilated patient the presence of inadvertent PEEP indicates dynamic hyperinflation and shows that end-expired lung volume is greater than relaxation volume. While virtually all patients with COPD have some degree of dynamic hyperinflation during mechanical ventilation, PEEPi and dynamic hyperinflation are not specific to this condition. Mechanical ventilation with high minute volumes often causes dynamic hyperinflation irrespective of the patient's lung mechanics. Furthermore, the presence of PEEPi and dynamic hyperinflation do not mean that end-expired lung volume is increased in absolute terms. Many recumbent patients with obesity or ascites breathe at lung volumes near residual volume because of mass loading of their chest wall.[61] As even a normal lung will suffer limitation of flow at low volumes, dynamic hyperinflation must occur. Because of the increased recoil and weight of the chest wall even small increases in end-expired lung volume above relaxation volume will generate large amounts of PEEPi (at times in excess of 15 cm H_2O). Therefore PEEPi must be obtained in the clinical context if it is to be used to diagnose airways disease.

Many mechanical ventilators have automated the measurement of PEEPi by imposing an appropriately timed end-expired occlusion. However, in most cases this measurement is not reliable in patients with spontaneous respiratory muscle activity.

Inspection of expiratory flow–volume and flow-time tracings

As pointed out on page 81, the slope of the passive expired flow–volume relationship has the units of time and defines the time constant (τ) of the relaxed respiratory system. It is determined by the product of R and C and defines the time after which approximately two-thirds of end-inspired lung volume will be expelled. Factors such as the use of neuromuscular blocking agents, intubation, anaesthesia, and mechanical ventilation alter respiratory system mechanics. Depending on tracheal tube size the resistance may be as great as 10 cm H_2O litre^{-1} s^{-1} while compliance may be as small as 0.06 litre cm H_2O^{-1}.[20] This means that 'normal' intubated patients should be able to empty a tidal breath without trapping in less than 1 s.

Even without measuring the slope of the expired flow–volume curve there is a lot to be learnt from simple pattern recognition. Many patients with lung disease, particularly if flow is limited during passive expiration, have a non-linear curve. Unless ventilator tubing and other apparatus dampens the signal, dynamic airway collapse is associated with a large flow transient (flow spike) at the beginning of expiration. This is because gas residing in the collapsing airways is being expelled at a high rate before flow limitation sets in. The persistence of expiratory flow immediately before the transition from expiration to inspiration is another sign that the lung has not completely emptied in the time available for expiration and that PEEPi is present.

The same events may be seen in relation to time that is by inspecting the expiratory flow-time tracing. However, expiratory flow is not expected to vary linearly with time. As is true for the PEEPi measurement, flow tracings must be interpreted with caution in patients who breathe with the ventilator. The expiratory flow transient that can show dynamic airway collapse may be blunted by inspiratory muscle activity that extends into the early expiratory phase

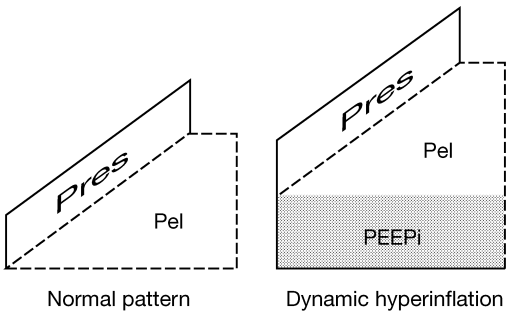

Fig 5 An airway pressure–time tracing during inflation of the respiratory system with constant inspiratory flow.

of the machine cycle. Phasic expiratory muscle activity will amplify flow transients between end-expiration and the beginning of inspiration and when present should not be viewed as evidence of dynamic hyperinflation.

Inspection of the Paw tracing (Fig. 5)

Recalling Equations 1 and 4 on page 81, Paw is the sum of an elastic and resistive pressure. If a constant (square wave) inspiratory flow is used to inflate the relaxed respiratory system (i.e. during volume preset mechanical ventilation) and the inspiratory resistance is constant in the tidal breathing range, then the resistive pressure must remain constant except during flow transients at the beginning and end of inflation. The pressure transients corresponding to these flow transients define a resistive pressure (Pres). In the absence of patient effort Pres can therefore be estimated from the initial step increase in pressure at the beginning of lung inflation or from the pressure decrease at the end of the breath (i.e. from the difference between peak and plateau pressure). The two estimates of Pres ought to be very similar (see Fig. 5). If they are not, that is if the early step increase in pressure is obviously greater than the pressure decrease at the end of inspiratory flow, one can conclude: (i) inspiratory resistance decreased significantly with volume; or more likely (ii) the initial step change in pressure is not only because of Pres but also reflects PEEPi. Recall that PEEPi is a pressure that drives expiratory flow and that it must be counter balanced before flow can be antagonized in the inspiratory direction.

This method of estimating PEEPi has certain advantages over the end-expiratory airway occlusion method because it is not as sensitive to artifacts from spontaneous muscle activity. Most patients relax at end-inflation because lung inflation inhibits inspiratory activity. This means that the decrease in pressure from the end-inspiratory peak to the plateau pressure can be usually measured unencumbered by respiratory artifact. On the other hand even in patients who trigger each machine breath it is usually possible to estimate the early inspiratory pressure transient by back extrapolation.

By dividing Pres and inspiratory flow one can compute an ohmic resistance, which if it is large (>15 cm H_2O litre^{-1} s^{-1}), suggests a problem with a tracheal tube or the airways. The pitfalls of this measurement are that it depends on the flow setting. Tracheal tubes have very non-linear pressure/flow characteristics, so resistance is very flow dependent. The use of correction factors determined *in vitro*, to adjust for tube size, may not help as inspissated secretions and 'tube biting' can cause high inspiratory resistance. With inspiratory flow values less than 1 litre^{-1} s^{-1} and tracheal tubes greater than 7 mm internal diameter, Pres is usually less than 10 cm H_2O. As a rule of thumb, unless there are other indicators of intrinsic airways disease such expiratory flow limitation, increases in Pres above this value should be attributed to tube and ventilator apparatus problems. However, a normal inspiratory resistance does not preclude the presence of severe expiratory airflow obstruction for example from emphysema.

The peak Paw response to small step changes in PEEP (Fig. 6)

As explained in Figure 4, if PEEP does not affect expiratory flow, then expiratory flow limitation is present. It is neither feasible nor necessary to construct iso-volume pressure flow curves at the bedside. Nevertheless, the mechanisms depicted in Figure 4 explain why measuring airway pressure responses to PEEPe is an easy way to check for expiratory flow limitation. In a patient who is ventilated in a volume preset mode any reductions in iso-volume flow range must decrease expired volume (the integral of all iso-volume flows with respect to time), cause gas trapping, raise PEEPi and the Pel at end-expiration (total PEEP). As the delivered inspired gas volume is kept constant the peak airway pressure of the subsequent breath must increase by an amount equal to the change in PEEPi. In other words changes in peak airway pressure indicate changes in lung volume (Figs 5 and 6). To the extent that changes in PEEPe do not affect respiratory muscle activity at end-inflation, this test for flow limitation remains valid even in patients who trigger the ventilator.

Similar inferences can be made during pressure preset mechanical ventilation, provided peak airway pressure is kept constant during the PEEPe adjustment. In that instance PEEPe induced increases in PEEPi and total PEEP would reduce respiratory system inflation pressure (Ppeak minus total PEEP) and consequently lower peak inspiratory flows. In other words, during bilevel pressure ventilation to constant end-inflation pressures, if there are no changes in peak inspiratory flow when PEEPe was adjusted, expiratory flow limitation is likely. However, such an inference cannot be made in patients who trigger the ventilator because any change in inspiratory effort would also affect peak inspiratory flow.

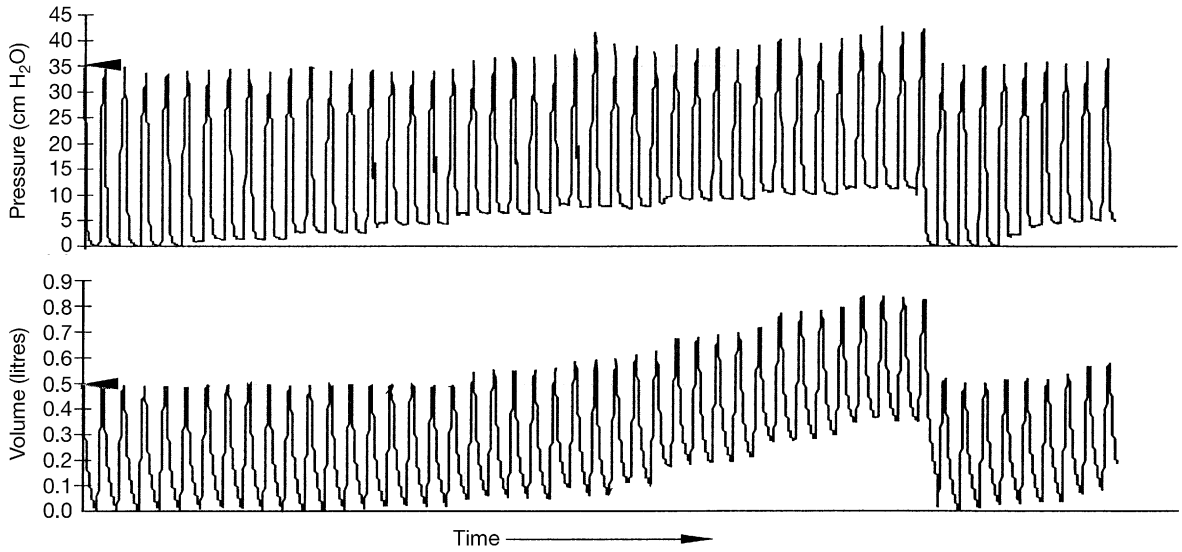

Fig 6 PEEP and the detection of expiratory flow limitation.

Clinical implications of respiratory mechanics measurements in patients with obstruction

A detailed discussion of the ventilatory management of the patient with airway obstruction is beyond the scope of this review, but we will make a few specific comments. With few exceptions patients with dynamic hyperinflation and flow limitation during passive expiration in the mid vital capacity range (i.e. over a range of recoil pressures between approximately 10 and 20 cm H_2O) will prove to have severe COPD when they are later tested in a pulmonary function laboratory.[70] Therefore, there is no reason why severe COPD should remain unsuspected and undiagnosed in any mechanically ventilated patient. Dynamic hyperinflation and gas trapping to high lung volumes increases the work of breathing and can reduce cardiac output.[64] The increased work of breathing (the work to trigger a machine assisted breath) may be reduced by careful application of PEEPe. Figures 4 and 6 help to know how one arrives at the 'best PEEP' for this objective. Assuming the patient is flow limited, the maximum PEEPe that can be applied without affecting iso-volume flow and hence worsen trapping is given by the difference between Pel_{ee} (total PEEP) and Pcrit of the pressure flow curve near end-expiration. It follows that best PEEP is the maximum amount of PEEPe that can be applied without raising peak airway pressure during volume preset mechanical ventilation (Fig. 6).

Patients who are hypotensive because of dynamic hyperinflation should be given fluids and the ventilator settings adjusted to minimize PEEPi. This usually requires a reduction in tidal volume and treatment such as sedation to reduce the ventilatory frequency. Increasing inspiratory flow in the hope of prolonging TE is rarely effective in patients, who trigger the ventilator, because increases in flow tend to increase ventilatory frequency by a Breuer Hering reflex-related mechanism.[66 86]

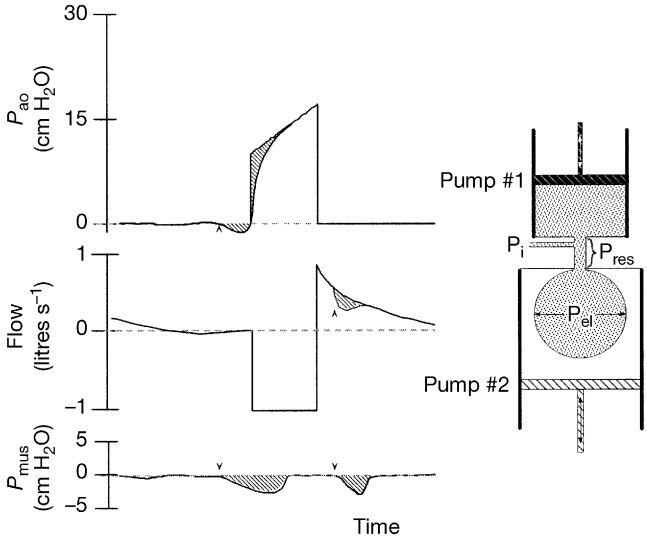

Fig 7 Schematic of inspiratory muscle activity (Pmus) on airway pressure and flow during mechanical ventilation in a volume preset mode.

Value of respiratory mechanics in the assessment of respiratory drive and timing

In most cases, when ventilator waveforms are measured, concurrent activity of the respiratory pump is a confounding signal. However, as shown with a simple mechanical analogue (Fig. 7) inspection of ventilator waveforms can indicate the performance of the ventilatory pump. Figure 7 shows a resistive and elastic element (the respiratory system) connected to two pressure generators (the mechanical ventilator, pump 1 and the respiratory muscles, pump 2). In the absence of phasic respiratory muscle activity, the airway pressure and flow patterns reflect the choice of ventilator mode and the relaxation characteristics of lungs

and chest wall. During lung inflation with constant inspiratory flow, the production of muscle pressure (Pmus) by the respiratory pump alters the shape of the inspiratory Paw tracing (shaded area in Fig. 7). In contrast during lung inflation with constant pressure (not shown) Pmus would alter the shape of the inspiratory flow profile. Activation of respiratory muscles during lung deflation distorts the expiratory flow profile. Significant differences from the expected pressure volume and flow patterns indicate a large Pmus output, which is a large patient effort. In comparison, minor departures indicate decreased respiratory muscle pressure on account of low drive, abnormal neuro-mechanical coupling, muscle weakness, muscle fatigue, or hyperinflation.

A great deal has been written about patient–ventilator interactions and the reader is referred to several reviews of this topic.[44 88] Here we consider the clinical context in which this information can be used. Ventilator waveforms can show if respiratory efforts (and hence drive) are increased and if respiratory muscle output is synchronous with machine inflations. Based on this assessment, the care giver must decide if an intervention is required. This depends on the assessment of patient comfort and on the judgment whether the work of breathing is excessive and potentially harmful. Harm may arise either because: (i) the task is fatiguing (a state that has proven difficult to define and document in the clinical setting); (ii) is uncomfortable; or (iii) causes a dangerous stress response that jeopardizes the balance between oxygen supply and demand in vulnerable tissues. Once the decision to intervene has been made, therapy consists of a change in ventilator settings with or without the judicious use of sedatives. Changes in ventilator settings can affect respiratory drive and timing through several pathways: (i) by alleviating shortness of breath (cortical/behavioural feedback); (ii) by correcting hypercapnia and hypoxaemia (chemoreceptive feedback); and (iii) by affecting amplitude and rate of lung and chest wall expansion (neuromechanical feedback). Behavioural and chemoreceptive pathways will influence effort and drive while neuromechanical feedback is more likely to affect breath timing. Failure to reduce excessive patient efforts through increases in ventilator support is usually an indication for sedatives.

Patient–ventilator dys-synchrony is exceedingly common and if patient discomfort or efforts are not judged excessive, may not require specific therapy. Predisposing factors include all the conditions associated with reduced muscle pressure output and impaired neuro-mechanical feedback. Without careful inspection of pressure volume or flow tracings it is often very difficult to appreciate that a patient generates inspiratory efforts far in excess of machine rate. It may also become apparent that there is no appreciable temporal relationship between efforts and machine breaths. Such patients are often encephalopathic, hypermetabolic, and critically ill. They may be easy to ventilate because they are too weak or their drive is too suppressed to 'fight the ventilator'. Nevertheless, recognition of 'silent tachypnoea' is useful because it is the respiratory controller's manifestation of a stress response, predicts futile weaning attempts and guides the use of sedatives, narcotics and paralytics. Although, to our knowledge, this hypothesis has not been formally tested, we contend that respiratory waveform analysis is a more effective way of monitoring the dosing of neuromuscular blocking agents than monitoring neuromuscular transmission.

Acknowledgements

Supported by National Institute of Health grants HL 57364 and HL 63178.

References

1 Agostoni E. *Handbook of Physiology, The Respiratory System*, Chapter 30. Baltimore, MD: Waverly Press, 1986

2 Amato, MB, Barbas CS, Medeiros DM, *et al.* Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med* 1998; **338**: 347–54

3 Artigas A, Bernard GR, Carlet J, *et al.* The American-European Consensus Conference on ARDS, part 2: ventilatory, pharmacologic, supportive therapy, study design strategies, and issues related to recovery and remodeling. Acute respiratory distress syndrome. *J Respir Crit Care Med* 1998; **157**: 1332–47

4 Avery ME. The aeration of the lung at birth. In: Schaffer AJ, ed. *The Lung and Its Disorders in the Newborn Infant.* Philadelphia, PA: WB Saunders, 1968; 24–30

5 Bachofen H, Schürch S, Michel RP, Weibel ER. Experimental hydrostatic pulmonary edema in rabbit lungs: morphology. *Am Rev Respir Dis* 1993; **147**: 989–96

6 Bates JHT. Assessment of mechanics. In: Lenfant C, Marini JJ, Slutsky AS, eds. *Physiological Basis of Ventilatory Support. Lung Biology in Health and Disease Series*, Vol 118, Chapter 7. New York: Marcel Dekker, Inc., 1998; 231–56

7 Bates JH, Rossi A, Milic-Emili J. Analysis of the behavior of the respiratory system with constant inspiratory flow. *J Appl Physiol* 1985; **58**: 1840–48

8 Baydur A, Behrakis PK, Zin WA, Jaeger M, Milic-Emili J. A simple method for assessing the validity of the oesophageal balloon technique. *Am Rev Resp Dis* 1982; **126**: 788–91

9 Behrakis PK, Higgs BD, Bevan DR, *et al.* Partitioning in respiratory mechanics in halothane-anesthetized humans. *J Appl Physiol* 1985; **58**: 285–9

10 Bernard GR, Artigas A, Brigham KL, *et al.* Report of the American-European consensus conference on ARDS: definitions, mechanisms, relevant outcomes and clinical trial coordination. The Consensus Committee. *Am J Respir Crit Care Med* 1994; **149**: 818–24

11 Berthiaume Y, Folkesson HG, Matthay MA. Lung edema clearance: 20 years of progress: invited review: alveolar edema fluid clearance in the injured lung. *J Appl Physiol* 2002; **93**: 2207–13

12 Bilek AM, Dee KC, Gaver DP 3rd. Mechanisms of surface-tension-induced epithelial cell damage in a model of pulmonary airway reopening. *J Appl Physiol* 2003; **94**: 770–83

13 Brower RG. Mechanical ventilation in acute lung injury and ARDS—tidal volume reduction. *Crit Care Clin* 2002; **18**: 1–13

14 Cassidy KJ, Gavriely N, Grotberg JB. Liquid plug flow in straight and bifurcating tubes. *J Biomech Eng* 2001; **123**: 580–9

15 Chung KF, Keyes SJ, Morgan BM, Jones PW, Snashall PD.

Mechanisms of airway narrowing in acute pulmonary edema in dogs: influence of the vagus and lung volume. *Clin Sci* 1983; **65**: 289–96

16 Cook CD, Mead J, Schreiner GL, Frank NR, Craig JM. Pulmonary mechanics during induced pulmonary edema in anesthetized dogs. *J Appl Physiol* 1959; **14**: 177–86

17 Cox CE, Shannon S, Carson E, *et al*. Effectiveness of medical resident education in mechanical ventilation. *Am J Respir Crit Care Med* 2003; **167**: 32–8

18 Delaunois L, Sergysels R, Martin RR. Acute effects on airways mechanics of pulmonary edema induced by intravenous oleic acid in dogs. *Bull Eur Physiopath Respir* 1980; **16**: 47–55

19 Derks CM, D'Hollander AA, Jacobovitz-Derks D. Gas exchange and respiratory mechanics in moderate and severe pulmonary oedema in dogs. *Bull Eur Physiopath Respir* 1981; **17**: 163–77

20 Diehl JL, El Atrous S, Touchard D, Lemaire F, Brochard L. Changes in the work of breathing induced by tracheotomy in ventilator-dependent patients. [Article]. *Am J Resp Crit Care Med* 1999; **159**: 383–8

21 Dreyfuss D, Saumon G. Ventilator-induced lung injury: lessons from experimental studies. *Am J Respir Crit Care Med* 1998; **157**: 294–323

22 Dreyfuss D, Soler P, Basset G, *et al*. High inflation pressure pulmonary edema: respective effects of high airway pressure, high tidal volume and positive end expiratory pressure. *Am J Resp Crit Care Med* 1988; **137**: 1159–64

23 Eissa NT, Ranieri VM, Corbeil C, *et al*. Analysis of behavior of the respiratory system in ARDS patients: effects of flow volume and time. *J Appl Physiol* 1991; **70**: 2719–29

24 Esbenshade AM, Newman JH, Lams PM, Jolles H, Brigham KL. Respiratory failure after endotoxin infusion in sheep: lung mechanics and lung fluid balance. *J Appl Physiol* 1982; **53**: 967–76

25 Fredberg JJ, Stamenovic D. On the imperfect elasticity of the lung. *J Appl Physiol* 1989; **67**: 2408–19

26 Fry DL, Hyatt RE. Pulmonary mechanics. A unified analysis of the relationship between pressure, volume and gasflow in the lungs of normal and diseased human subjects. *Am J Med* 1960; **29**: 672–89

27 Ganzert S, Guttmann J, Kersting K, *et al*. Analysis of respiratory pressure–volume curves in intensive care medicine using inductive machine learning. *Artif Intelligence Med* 2002; **26**: 69–86

28 Gattinoni L, D'Andrea LI, Pelosi P, Vitale G, Fumagalli R. Regional effects and mechanism of positive end expiratory pressure in early adult respiratory distress syndrome. *JAMA* 1993; **269**: 2122–7

29 Gattinoni L, Pesenti A, Avalli L, *et al*. Pressure–volume curve of total respiratory system in acute respiratory failure: computed tomographic scan study. *Am Rev Respir Dis* 1987; **136**: 730–6

30 Gattinoni L, Pelosi P, Suter PM, Pedoto A, Vercesi P, Lissoni A. Acute respiratory distress syndrome caused by pulmonary and extrapulmonary disease: different syndromes? *Am J Respir Crit Care Med* 1998; **158**: 3–11

31 Gaver DP III, Kute SM. A theoretical model study of the influence of fluid stresses on a cell adhering to a microchannel wall. *Biophys J* 1998; **75**: 721–33

32 Gay PC, Rodarte JR, Tayyab M, Hubmayr RD. The evaluation of bronchodilator responsiveness in mechanically ventilated patients. *Am Rev Respir Dis* 1987; **136**: 880–5

33 Gay PC, Rodarte JR, Hubmayr RD. The effects of positive expiratory pressure on isovolume flow and dynamic hyperinflation in patients receiving mechanical ventilation. *Am Rev Respir Dis* 1989; **139**: 621–6

34 Gillespie DJ, Lai YL, Hyatt RE. Comparison of esophageal and pleural pressures in the anaesthetized dog. *J Appl Physiol* 1973; **35**: 709–13

35 Gottfried SB, Rossi A, Higgs BD, *et al*. Noninvasive determination of respiratory system mechanics during mechanical ventilation for acute respiratory failure. *Am Rev Respir Dis* 1985; **131**: 414–20

36 Harris SR, Hess DR, Venegas JG. An objective analysis of the pressure–volume curve in the acute respiratory distress syndrome. *Am J Resp Crit Care Med* 2000; **161**: 432–39

37 Hermle G, Mols G, Zugel A, *et al*. Intratidal compliance–volume curve as an alternative basis to adjust positive end-expiratory pressure: a study in isolated perfused rabbit lungs. *Crit Care Med* 2002; **30**: 1589–97

38 Hickling, K. Reinterpreting the pressure–volume curve in patients with acute respiratory distress syndrome. *Curr Opin Crit Care* 2002; **8**: 32–8

39 Hildebrandt J. Pressure–volume data of cat lung interpreted by a plastoelastic, linear viscoelastic model. *J Appl Physiol* 1970; **28**: 365–72

40 Horie T, Hildebrandt J. Dynamic compliance, limit cycles, and static equilibria of excised cat lung. *J Appl Physiol* 1971; **31**: 423–30

41 Horie T, Hildebrandt J. Volume history, static equilibrium, and dynamic compliance of excised cat lung. *J Appl Physiol* 1972; **33**: 105–12

42 Hubmayr RD. Perspective on lung injury and recruitment: a skeptical look at the opening and collapse story. *Am J Respir Crit Care Med* 2002; **165**: 1647–53

43 Hubmayr RD, Margulies SS. Effects of unilateral hyperinflation on the interpulmonary distribution of pleural pressure. *J Appl Physiol* 1992; **73**: 1650–54

44 Hubmayr RD, Simon PM. Assessment of drive/muscle function. In: Lenfant C, Marini JJ, Slutsky AS eds. *Physiological Basis of Ventilatory Support. Lung Biology in Health and Disease Series*, Vol 118, Chapter 4. New York: Marcel Dekker, Inc., 1998; 153–75

45 Ito Y, Veldhuizen RAW, Yao L-Y, McCaig L, Bartlett AJ, Lewis JF. Ventilation strategies affect surfactant aggregate conversion in acute lung injury. *Am J Respir Crit Care Med* 1997; **155**: 493–9

46 Jonson B, Richard JC, Straus C, Mancebo J, Lemaire F, Brochard L. Pressure–volume curves and compliance in acute lung injury: evidence of recruitment above the lower inflection point. *Am J Respir Crit Care Med* 1999; **159**: 1172–8

47 Loring SH. Mechanics of the Lung and Chest Wall. In: Lenfant C, Marini JJ, Slutsky AS (eds). *Physiological Basis of Ventilatory Support. Lung Biology in Health and Disease series*, Vol 118, Chapter 5. New York: Marcel Dekker, Inc., 1998; 177–205

48 Malbouisson LM, Muller JC, Constantin JM, Lu Q, Puybasset L, Rouby JJ. Computed tomography assessment of positive end-expiratory pressure-induced alveolar recruitment in patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2001; **163**: 1444–50

49 Mascheroni D, Kolobow T, Fumagalli R, Moretti MP, Chen V, Buckhold D. Acute respiratory failure following pharmacologically induced hyperventilation: an experimental animal study. *Intensive Care Med* 1988; **15**: 8–14

50 Matamis D, Lemaire F, Harf A, Brun-Buisson C, Ansquer JC, Atlan G. Total respiratory pressure–volume curves in the adult respiratory distress syndrome. *Chest* 1984; **86**: 58–66

51 Marini JJ. Ventilator-induced airway dysfunction? *Am J Respir Crit Care Med* 2001; **163**: 806–7

52 Martin CJ, Young AC, Ishikawa K. Regional lung mechanics in pulmonary disease. *J Clin Invest* 1965; **44**: 906–13

53 Martin-Lefèvre L, Ricard JD, Roupie E, Dreyfuss D, Saumon G. Significance of the changes in the respiratory system pressure–volume curve during acute lung injury in rats. *Am J Respir Crit Care Med* 2001; **164**: 627–32

54 Martynowicz MA, Minor TA, Walters BJ, Hubmayr RD. Regional

expansion of oleic acid-injured lungs. *Am J Respir Crit Care Med* 1999; **160**: 250–58

55 Martynowicz MA, Walters BJ, Hubmayr RD. Mechanisms of recruitment in oleic acid injured lungs. *J Appl Physiol* 2001; **90**: 1744–53

56 Mead J, Takashima T, Leith D. Stress distribution in lungs: a model of pulmonary elasticity. *J Appl Physiol* 1970; **28**: 596–603

57 Mergoni M, Martelli A, Volpi A, Primavera S, Zuccoli P, Rossi A. Impact of positive end-expiratory pressure on chest wall and lung pressure–volume curve in acute respiratory failure. *Am J Respir Crit Care Med* 1997; **156**: 846–54

58 Milic-Emili J. Expiratory flow limitation—detection and clinical implications—Roger S. Mitchell Lecture. *Chest* 2000; **117** (Suppl. 1): 219S–223S

59 Mitzner W, Brown RH. Potential mechanism of hyperresponsive airways. *Am J Respir Crit Care Med* 2000; **161**: 1619–23

60 Muscedere JG, Mullen JB, Gan K, Slutsky AS. Tidal ventilation at low airway pressures can augment lung injury. *Am J Respir Crit Care Med* 1994; **149**: 1327–34

61 Pankow W. Podszus T. Gutheil T. Penzel T. Peter JH. Vonwichert P. Expiratory flow limitation and intrinsic positive end-expiratory pressure in obesity. *J Appl Physiol* 1998; **85**: 1236–43

62 Pelosi P, Goldner M, McKibben A, *et al.* Recruitment and derecruitment during acute respiratory failure: an experimental study. *Am J Respir Crit Care Med* 2001; **164**: 122–30

63 Pelosi P, Tubiolo D, Mascheroni D, *et al*. Effects of the prone position on respiratory mechanics and gas exchange during acute lung injury. *Am J Respir Crit Care Med* 1998; **157**: 387–93

64 Pepe PE, Marini JJ. Occult positive end-expiratory pressure in mechanically ventilated patients with airflow obstruction: the auto-PEEP effect. *Am Rev Respir Dis* 1982; **126**: 166–70

65 Pison U, Bock JC, Pietschmann S, Veit S, Slama K (1995) The adult respiratory distress syndrome: pathophysiological concepts related to the pulmonary surfactant system. In: Robertson B, HW Tauesch, eds. *Lung Biology in Health and Disease. Vol 84: Surfactant Therapy for Lung Disease*. New York: Marcel Dekker, 169–197

66 Puddy A, Younes M. Effect of inspiratory flow rate on respiratory output in normal subjects. *Am Rev Respir Dis* 1992; **146**: 787–9

67 Ranieri VM, Brienza N, Santostasi S, *et al*. Impairment of lung and chest wall mechanics in patients with acute respiratory distress syndrome: role of abdominal distention. *Am J Respir Crit Care Med* 1997; **156**: 1082–91

68 Ranieri VM, Giulani R, Fiore T, Dambrosio M, Milic-Emili J. Volume–pressure curve of the respiratory system predicts effects of PEEP in ARDS: 'occlusion' versus 'constant flow' technique. *Am J Respir Crit Care Med* 1994; **149**: 19–27

69 Ranieri VM, Zhang H, Mascia L, *et al.* Pressure–time curve predicts minimally injurious ventilatory strategy in an isolated rat lung model. *Anesthesiology* 2000; **93**: 1320–8

70 Reinoso MA, Gracey DR, Hubmayr RD. Interrupter mechanics of patients admitted to a chronic ventilator dependency unit. *Am Rev Respir Dis* 1993; **148**: 127–31

71 Rich CR. Rehder K. Knopp TJ. Hyatt RE. Halothane and enflurane anesthesia and respiratory mechanics in prone dogs. *J Appl Physiol Respir Environ Exercise Physiol* 1979; **46**: 646–53

72 Rodriguez L, Lemaire F, Marquer B, *et al*. A new simple method to perform pressure–volume curves obtained under quasi-static conditions during mechanical ventilation. *Intensive Care Med* 1999; **25**: 173–9

73 Rosi A, Polese G, Milic-Emili J. Monitoring respiratory mechanics in ventilated patients. In: Tobin MJ, ed. *Principles and Practice of Intensive Care Monitoring*. New York: McGraw-Hill, 1998; 553–95

74 Rouby JJ. Lu Q. Goldstein I. Selecting the right level of positive end-expiratory pressure in patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2002; **165**: 1182–6

75 Roupie E, Dambrosio M, Servillo G, *et al.* Titration of tidal volume and induced hypercapnia in acute respiratory distress syndrome. *Am J Resp Crit Care Med* 1995; **52**: 121–8

76 Servillo G, De Robertis E, Maggiore S, Lemaire F, Brochard L, Tufano R. The upper inflection point on the pressure–volume curve. *Intensive Care Med* 2002; **28**: 842–9

77 Servillo G, Svantesson C, Beydon L, *et al.* Pressure–volume curves in acute respiratory failure. Automated low flow inflation versus occlusion. *Am J Respir Crit Care Med* 1997; **155**: 1629–36

78 Slutsky A, Scharf S, Brown R, Ingram RH Jr. The effects of oleic acid-induced pulmonary edema on pulmonary and chest wall mechanics in dogs. *Am Rev Respir Dis* 1980; **121**: 91–6

79 Smith JC, Stamenovic D. Surface forces in lungs. I. Alveolar surface tension–lung volume relationships. *J Appl Physiol* 1986; **60**: 1341–50

80 Spragg RG, Lewis JF. Pathology of the surfactant system of a mature lung: Second San Diego Conference. *Am J Resir Crit Care Med* 2001; **163**: 280–2

81 Stamenovic D, Smith JC. Surface forces in lungs. II. Microstructural mechanics and lung stability. *J Appl Physiol* 1986; **60**: 1351–7

82 Stamenovic D, Smith JC. Surface forces in lungs. III. Alveolar surface tension and elastic properties of lung parenchyma. *J Appl Physiol* 1986; **60**: 1358–62

83 Sydow M. Burchardi H. Zinserling J. Ische H. Crozier TA. Weyland W. Improved determination of static compliance by automated single volume steps in ventilated patients. *Intensive Care Med* 1991; **17**: 108–14

84 Tantucci J, Corbeil C, Chassé M, *et al.* Flow and volume dependence of respiratory system resistance in patients with adult respiratory distress syndrome. *Am Rev Respir Dis* 1992; **145**: 355–60

85 The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; **342**: 1301–8

86 Tobert DG, Simon PM, Stroetz RW, Hubmayr RD. The determinants of respiratory rate during mechanical ventilation. *Am J Respir Crit Care Med* 1997; **155**: 485–92

87 Tobin MJ. Medical progress—advances in mechanical ventilation. *N Engl J Med* 2001; **344**: 1986–96

88 Tobin MJ. Jubran A. Laghi F. Patient–ventilator interaction. *Am J Respir Crit Care Med* 2001; **163**: 1059–63

89 Tremblay LN, Slutsky AS. Ventilator-induced injury: barotrauma and biotrauma. *Proc Assoc Am Physician* 1998; **110**: 482–8

90 Vieira SR, Puyabasset L, Lu Q, *et al*. Scanographic assessment of pulmonary morphology in acute lung injury: significance of the lower inflection point detected on the lung pressure–volume curve. *Am J Respir Crit Care Med* 1999; **159**: 1612–23

91 Ward NS, Lin DY, Nelson DL, *et al*. Successful determination of lower inflection point and maximal compliance in a population of patients with acute respiratory distress syndrome. *Crit Care Med* 2002; **30**: 963–8

92 Wilson TA, Anafi RC, Hubmayr RD. Mechanics of edematous lungs. *J Appl Physiol* 2001; **90**: 2088–93

93 Yan S, Kayer B, Tobias M, *et al*. Comparison of static and dynamic positive end expiratory presure using the Campbell diagram. *Am J Resp Crit Care Med* 1996; **154**: 938–44

94 Younes M, Webster K, Kun J, Roberts D, Masiowski B. A method for measuring passive elastance during proportional assist ventilation. *Am J Respir Crit Care Med* 2001; **164**: 50–60