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REVIEW ARTICLE

# Positive pressure ventilation: what is the real cost?

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Positive pressure ventilation is a radical departure from the physiology of breathing spontaneously. The immediate physiological consequences of positive pressure ventilation such as haemodynamic changes are recognized, studied, and understood. There are other significant physiological interactions which are less obvious, more insidious, and may only produce complications if ventilation is prolonged. The interaction of positive pressure with airway resistance and alveolar compliance affects distribution of gas flow within the lung. The result is a wide range of ventilation efficacy throughout different areas of the lung, but the pressure differentials between alveolus and interstitium also influence capillary perfusion. The hydrostatic forces across the capillaries associated with the effects of raised venous pressures compound these changes resulting in interstitial fluid sequestration. This is increased by impaired lymphatic drainage which is secondary to raised intrathoracic pressure but also influenced by raised central venous pressure. Ventilation and PEEP promulgate further physiological derangement. In theory, avoiding these physiological disturbances in a rested lung may be better for the lung and other organs. An alternative to positive pressure ventilation might be to investigate oxygen supplementation of a physiologically neutral and rested lung. Abandoning heroic ventilation would be a massive departure from current practice but might be a more rationale approach to future practice.

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Positive pressure ventilation during the Copenhagen polio epidemic was the key to the reduction in mortality from 87% to 40%. It was achieved using medical students not sophisticated ventilators, with minimal understanding of the physiology of gas exchange, and with no real means of monitoring either oxygenation or carbon dioxide. It rapidly became obvious that its use could be extrapolated to the management of respiratory failure.[72 73 144] In the first edition of *Ventilation of the Lungs*, Mushin comments that 'positive pressure ventilation is a considerable deviation from the normal physiological mechanism of respiration'. Implicit in this statement is the notion that there will be a pathophysiological price to pay for disturbing the normal physiology of breathing. The immediate interactions, such as haemodynamic changes, are well delineated, but it is increasingly clear that not all the complications are either obvious or immediate. The ARDSnet study exposed previously concealed mortality suggesting the insidious and late impact of shear forces and other inflammatory reactions secondary to mechanical ventilation.[1]

The driving force of ventilatory techniques in the intensive care unit (ICU) is to achieve oxygenation which in severe lung injury may be both difficult and prolonged.

This review revisits the physiological cost involved in achieving oxygenation using positive pressure ventilation in the critically ill, and discusses some of the possible interactions (Table 1).

## Oxygenation and ventilation

Each ICU has rules as to what constitutes acceptable oxygenation and this varies with the patient and circumstances.[16] There are many examples of people functioning reasonably with far lower oxygenation indices than would be acceptable in an ICU. These range from high altitude residents and mountaineers to patients living with chronic airways disease.[98] In the ICU, monitoring of oxygenation still focuses on inspired oxygen concentration and arterial blood gases to indicate adequacy, whereas in other areas of practice, emphasis has moved to surrogates of tissue hypoxia such as $ScVO_2$ and lactate (Fig. 1). With

**Table 1** Some areas of potential physiological interaction with positive pressure ventilation

| |
|---|
| Positive pressure effects on intrathoracic pressures |
| Pressure and distribution of airflow into the alveoli |
| Pressure, stretch, and the lung |
| Surfactant functions |
| Positive pressure and cardiac output |
| Pulmonary capillary blood flow |
| Positive pressure and the lymphatics |
| Positive pressure and organ system function |

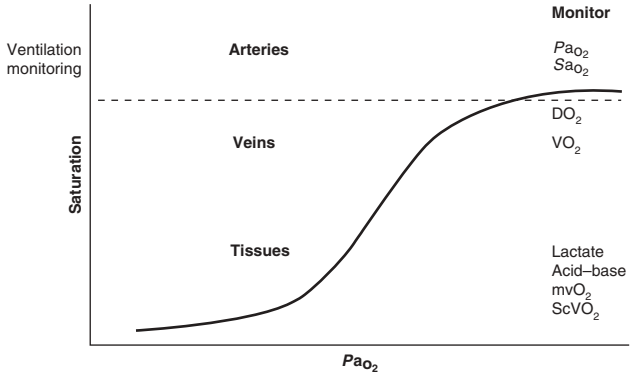


**Fig 1** Monitoring oxygenation. Based on arterial values which correlate poorly with adequacy of tissue oxygenation.

circulation, tissue and cell transport, and mitochondrial function interposed between lungand cell, the arterial values of oxygenation may not be the ideal monitoring parameters.

In the critically ill, several observations regarding oxygenation can be made.

(i) Even with relatively low arterial saturations, there may be adequate tissue oxygenation.
(ii) When tissue oxygenation is in jeopardy, it is very often due to problems not related directly to the lungs.
(iii) Saturation and $Pa_{O_2}$ below the acceptable normal range correlate poorly with tissue oxygenation.
(iv) When patients are difficult to oxygenate, tolerance of lower values develops rapidly, provided there are no markers of tissue hypoxia.
(v) It is often stated that 'few patients with lung injury die of hypoxaemia'. Clearly, some do but often death is due to acquired complications.

Margins of safety for oxygenation are essential, but difficulty arises when it is necessary to use aggressive ventilation to achieve margins that may be far in excess of actual requirement. If this is associated with late complications, then methods of assessing adequacy of oxygenation may need to be reconsidered.

## Breathing, ventilation, and intrathoracic pressures

In inspiration, small negative intrapleural, interstitial, and alveolar pressures are generated allowing the lung to inflate. On expiration, intrapleural pressure returns towards atmospheric, but remains negative, whereas interstitial and alveolar pressures return towards atmospheric or slightly positive pressure.

Positive pressure ventilation reverses this cycle with high intrathoracic pressures on inspiration which are transmitted, to the alveoli and the interstitial tissues, following the path of least resistance to inflate the alveoli. The intrapulmonary and interstitial pressures remain positive throughout inspiration but will return towards atmospheric pressure on expiration, unless PEEP is added when the pressures remain positive throughout.

## Ventilation, alveolar ventilation, and recruitment

During spontaneous breathing, the negative pressure gradient generates air distribution which is locally influenced by the state of the airways, alveoli, and interstitium. Surfactant modifies the effects of Laplace's law at these low pressures so that small alveoli are both relatively easy to inflate and have less tendency to collapse on expiration. Despite these effects, there is regional variation in gas volume distribution even in volunteers breathing normally.[89] The same factors influence flow with positive pressure ventilation, but the forces acting are different. In the tracheal tube, a single pressure applied over a specific time produces a waveform which forces gas through the airways. The state of the airways, in particular their resistance, and the alveolar compliance determine the effect of that pressure in different regions of the lung. These factors combined can be considered as the individual 'time constants' of the lung regions or of individual alveoli. In damaged lung, the range of different time constants between regions will increase even if the surfactant was normal. Positive pressure will preferentially aerate high compliance areas at the expense of lower compliance areas, whereas collapsed alveoli may require high sustained pressure to force them open, but this may be ineffective. It is a daily observation in the operating theatre that re-inflation of a collapsed but previously normal lung requires sustained high positive pressure and it is a gradual and far from uniform process (Fig. 2).

Recruitment is the opening and maintaining open potentially under ventilated areas. The fundamental concept behind recruitment is to use the physics of inflation judiciously, to increase the number of alveoli and hence alveolar surface area involved in gas exchange. The central tenet is that this will improve oxygenation. A wide range of strategies aimed to 'recruit' alveoli have been advocated, but the problem with any of these techniques is that the variation in time constants between alveoli and lung regions precludes a single pressure or waveform being suitable for all lung regions.

CT scanning and electrical impedance tomography (EIT) have revolutionized the ability to 'see' what actually happens to lung inflation with positive pressure ventilation.

Using EIT, the inferred pressure–volume curve clearly shows a lower and upper inflection point (increased/reduced conductivity). The lower inflection point is thought to represent recruitment whereas the upper inflection point represents over-distension, although this is contentious (Fig. 3). Physiologically, this methodology has clearly shown not only regional variation in both recruitment and over-distension but that pathology in the lung increases the diversity of these changes.[34] EIT indicates a huge regional variation in both recruitment and over-inflation, in injured lungs, both within and between lungs.[18 58–60 133] It also demonstrates that whole lung inflection points do not represent individual areas.

CT has also been used to assess recruitment. In ARDS, a recruitment technique using an initial sustained high pressure with subsequent PEEP at various levels to maintain recruitment only achieved an estimated mean recruitment of 13%, and showed that a large part of the lung was not recruitable.[48 65] It did indicate that high levels of PEEP, 15 mm Hg, are more effective than lower levels, 5 mm Hg, both in maintaining alveolar patency and improving oxygenation. PEEP is also effective in preventing collapse and derecruitment.[43 87 130] All these techniques result in sustained increase in intrathoracic pressure.

A further consideration is that pressure is effectively distributed across compliant lung but dampened by poorly compliant areas. Paradoxically, the techniques used to open closed airways, probably results in increased gas distribution not to the abnormal areas but rather to the functional areas over-inflating them and potentially impairing their function.[17 127] The result of recruitment is therefore unpredictable.

In summary, the physics of the lung inflated by a single pressure waveform will result in unpredictable gas distribution due to variable regional compliance. There will be over-distension of normal alveoli, and although there will be some recruitment, it may be very limited, especially in areas of collapse or consolidation. The combination of high inspiratory pressures and high levels of PEEP will result in sustained pressures throughout the respiratory cycle.

Recruitment in the short term with relatively normal lungs works well but in damaged lungs, and particularly over time, recruitment techniques may exacerbate problems while apparently improving oxygenation indices.

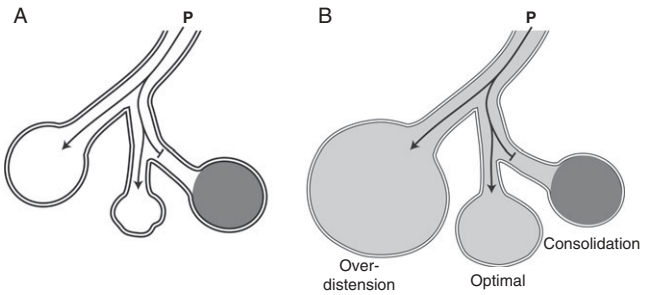


**Fig 2** Alveolar inflation. (A) Represents the beginning of inspiration. Pressure P acts on a consolidated alveolus, a normal alveolus and a distended alveolus. (B) End inspiration. Pressure P produces a broad spectrum of effects.

## Ventilation pressure and stretch

The reduction in mortality highlighted by the ARDSnet study was associated with lower peak pressure ventilation, but it also appears that the shear forces that occur particularly in initiating inflation may cause injury.[1 20 24 36 49 85 121 122 124 149]

Stress and shear forces exerted during the cyclic opening and closing of alveoli result in increased cytokine production and white cell sequestration, as does over-distension of alveoli.[19 20] These effects are seen over a range of ventilatory patterns and it may predispose to injury and infection.[78 128 143] Repetitive identical ventilation exerts different

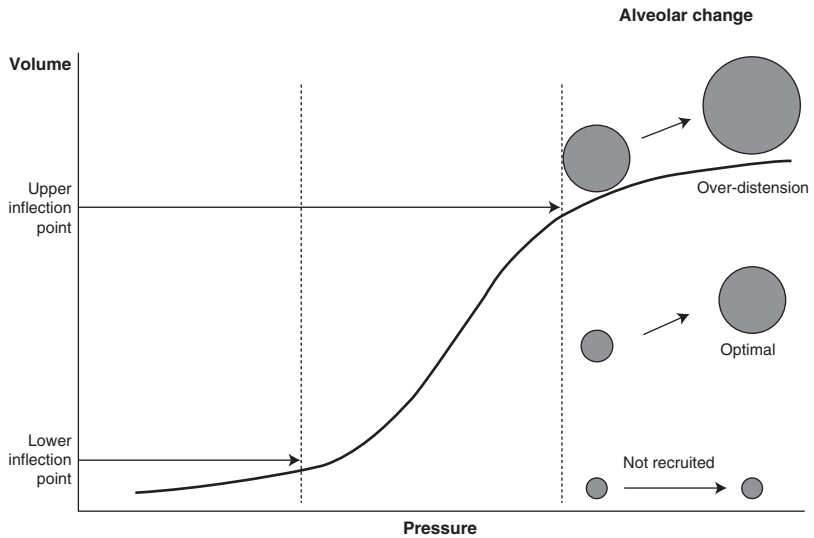


**Fig 3** Pressure–volume curve and the effects on alveoli.

and more damaging shear forces than variable ventilation where both volume and duration are varied.[13 95] These inflammatory effects originating in the lung may cause secondary inflammatory problems in other organs.[35 38 68 84 92]

In recruitment, manoeuvres the lowering of the peak pressure is important whereas the use of higher PEEP maintains alveolar patency and reduces the shear forces. The net effect is high pressure throughout the ventilatory cycle.

## Ventilation and surfactant

Surfactants modify the surface tension and hence the law of Laplace. The denser the molecules, the lower the surface tension which enables small alveoli, with dense surfactant, to remain open but also facilitates inflation during inspiration. In larger alveoli during inflation, the density of surfactant decreases as the surface area increases and the influence on the surface tension decreases, so that the surface tension increases. This is highly efficient in spontaneous breathing at low pressures as it facilitates effective gas distribution throughout the lung. With positive pressure ventilation, air is forced into the lung under pressure and the resultant pressure waveform may generate wave formation in the surfactant layers altering the uniformity of spread. This is known in surfactant technology, but there is little or no information relating to surfactant wave behaviour in the lung. A fundamental difference in the performance of surfactant between spontaneous and positive pressure ventilation may be due to distortion of surfactant spread. This is unlikely to be uniform across the lung due to wide variation in pressure and therefore of flow.

Positive pressure also influences the production and function of surfactant. In lung injury, type II pneumocytes are reduced in number and surfactant production is reduced.[99] Function is altered by the mix of cholesterol and protein which then affects the ability of the surfactant to form surface structures.[83 99 137] This is exacerbated by inflammation which releases protein and other materials that mix with the surfactant, mediators that directly affect surfactant, membrane permeability changes that allow fluid dilution of surfactant, and polymerizing fibrin that adsorbs these surface active compounds, effectively removing them.[115 116 126 129 131 138] Infection is implicated, with evidence that both pseudomonas and pneumocystis pneumonias alter surfactant function, although it is uncertain whether it is due to the disease or the ventilation. It is likely other infections do likewise.[40 113 136] Medical intervention such as lavage effectively removes surfactant impairing regional and whole lung compliance.[29] Surfactant dysfunction changes compliance and exaggerates heterogeneous lung inflation necessitating ventilation patterns which may cause further damage.[11 30 69 123]

Surfactant has a role in the immune defences of the lung. The lung provides more than 50 $m^2$ of contact across a fine membrane and is therefore a potential site for invasion. Not only does surfactant influence inflammatory response, but it has a substantial role in mucosal immunity and at least two surfactants have activity as collectins (molecules that bind to foreign particles such as bacteria, fungi, and viral particles and assist in their phagocytosis).[21 50 53 54 67]

In conclusion, both positive pressure and lung injury alter the production and function of surfactant. Changes in surface tension and loss of immunocompetence both predispose to lung injury and infection. A vicious cycle ensues where the disease and the supportive treatment may be synergistic in producing deleterious effects and will make positive pressure ventilation both more difficult and more prone to cause further injury.

## Effect on the cardiovascular system

The effects of positive pressure ventilation on the cardiovascular system are well known. In normal breathing, the negative pressure phase of inspiration assists venous return, alleviates pressure on the pulmonary capillaries, and encourages flow. With positive pressure ventilation, the intrathoracic pressure increases during inspiration causing a decrease in venous return, right ventricular output, and pulmonary blood flow. Paradoxically, there may be a reduction in right ventricular impedance, but whether this offsets the decrease in venous return is unknown.[90] There is some evidence to show that as PEEP increases, right ventricular outflow tends to decrease, reducing return to the left ventricle.[91 134] This effect may be partially offset by the increased intrathoracic–extrathoracic gradient assisting left ventricular output. This may be beneficial in cardiac failure but is not usually relevant in other circumstances where raised intrathoracic pressure reduces output.[102]

On expiration, the intrathoracic pressure returns towards zero so that venous return will increase. If PEEP is applied, positive intrathoracic pressure continues to inhibit venous return through expiration. The reduced collapsibility of the inferior vena cava often seen with ventilation and PEEP is a clear indicator of a degree of venous stasis.[91] Fluid administration improves venous return and cardiac output but at the cost of increased central venous pressures (CVP) and hence increased end-capillary pressures in the lungs and other organs.

Positive pressure ventilation is associated with salt and water retention. While classically this is due to increased secretion of anti-diuretic hormone mediated through the reduced atrial distension seen with positive pressure ventilation, more recently atrial natriuretic peptide has been implicated.[4 42 66] Correction of this by intravascular fluid administration results in further fluid retention.[5 7 139]

## The pulmonary capillary and blood flow

The mean capillary pressure is usually 7–10 mm Hg, a value derived from the gradient between the pulmonary

artery pressure and the venous outflow pressure in the pulmonary vein. Intrathoracic pressure will act uniformly across the capillary and should not directly influence gradient, unless the capillary is physically compressed by the raised interstitial pressure along its course.

During normal breathing, the pressures in the interstitium and the alveoli are small relative to the capillary perfusion pressure. This low pressure system enables the hydrostatic and oncotic pressures to facilitate fluid and substrate movement between compartments but also ensures unimpeded blood flow. Furthermore, the pressures within the lung generally are lower than capillary pressure in all phases and do not influence capillary flow. The exceptions being areas higher than the atrium where the pressure gradients are lower, and in the dependent areas where, theoretically, lung tissue weight may press on capillaries. These effects are small and transient. In disease, this can be different. Patients with chronic obstructive pulmonary disease with hyperinflation have a high intrathoracic pressure on expiration which compresses the interstitium and the capillaries, thus increasing capillary resistance and modifying blood flow.[88] On inspiration, as the intrathoracic pressures decrease, flow can recover.

Positive pressure ventilation in a critically ill patient, even with peak inspiratory pressures limited to 30 mm Hg, produces interstitial pressures considerably in excess of capillary pressure and will tend to compress the capillary and impede flow. In expiration, PEEP of 15 mm Hg may still exceed capillary pressure and prevents recovery of normal flow.[97] Compensatory mechanisms will also be modified. Hypoxic vasoconstriction, which is pre-capillary and which is highly effective in diverting blood flow during spontaneous breathing at low pressures, may be offset by the magnitude of the external pressures being applied.[140] The capillary pressure itself increases minimally with pre-capillary vasoconstriction, probably in the order of 1 mm Hg; hence, the capillary will remain susceptible to external pressure.[23 120] At high altitude, some individuals respond to hypoxia by a more generalized, albeit still regionally heterogeneous, increase in pulmonary artery pressure which influences flow, presumably diverting it to appropriate areas.[32 64] During positive pressure ventilation, compliant inflatable lung regions readily transmit pressure and in these areas the pressure will impede capillary flow whereas non-compliant damaged or infected lung will dampen pressure transmission and may have better perfusion. Compensatory diversion is unlikely to overwhelm the effects of this magnitude. Perfusion–ventilation mismatch is inevitable.

The high venous pressures, secondary to positive pressure ventilation, will also adversely affect the pressure gradients affecting Starling's forces and encouraging fluid flux, leading to interstitial fluid retention.

In the critically ill, increasing pulmonary artery pressures, high inflation pressures, and persistently high venous pressures probably damage the integrity of the capillary endothelium. 'Capillary stress failure' or disruption of the capillary is seen in extreme exercise in racehorses and is probably also seen in humans with high pulmonary artery pressures, high alveolar pressure, and in altitude hypoxia.[64 132 143]

Capillary perfusion pressure is of central importance to lung function. The consequences of persistently raised intrathoracic pressure are altered flow by compression of the capillary, modified Starling's forces, and raised end-capillary pressures. Compensatory mechanisms are unlikely to be effective and may aggravate ventilation–perfusion mismatch.

## Lymphatics

The lymphatics subserve at least two functions, drainage and defence. The lung has a massive surface area continuously exposed to a large volume of poorly filtered air. Fluid is drained from the interstitium by the reticuloendothelial system that removes extraneous material before it reaches the circulation.

The lung lymphatics consist of thin, single cell, conduits within the interstitium with valves to assist unidirectional flow. During inspiration, the negative pressure in the lung is transmitted to the interstitium and to the lymphatics and a gradient allows fluid to drain into the lymphatics. This is highly efficient and lymph flow can increase considerably if needed.[9 41 51 52 76] As the lymphatics fill, pressure increases and elasticity increases forward flow aided by muscle activity in the limbs or by ventilatory movement.[2] Towards the hilum, smaller channels coalesce into larger ones and they end in the thoracic duct or large lymphatics which drain into central veins.[112]

The pressure in the peripheral lymphatics reaches a maximum around 4 mm Hg, at which flow is maximal but if the pressure continues to increase the walls overstretch and leak. This pressure of around 4 mm Hg is adequate to provide a hydrostatic gradient between the lymphatics and the central veins which have very low pressures during the inspiration. The collecting ducts are slightly more robust and contain smooth muscle. This helps the lymphatics compensate for some outflow resistance, but they are still easily compressed. Flow will be relatively easily impeded both by external pressure on the lymphatic walls or by outflow resistance.

Positive pressure ventilation will push fluid from alveolus towards the interstitium and potentially towards and into the lymphatics. The positive pressure on the interstitium may compress some peripheral lymphatics potentially aiding flow, but it may also compress these thin-walled vessels impeding flow.[93 100] A second effect is that high CVPs associated with ventilation will form a significant hydrostatic barrier to flow, given that the lymphatic pressure is usually in single figures.[15 70 71 125] Lymph flow is again impeded.[147]

During expiration, lower intrathoracic pressure and decreasing CVPs may allow resumption of flow, but the use of PEEP, especially high PEEP, may obviate this recovery[112] (Fig. 4). Positive pressure ventilation

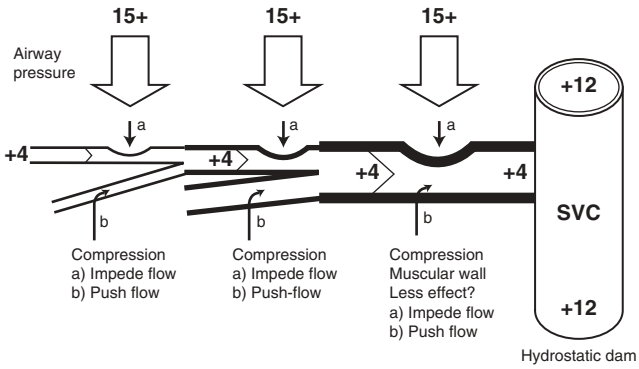


**Fig 4** Airway pressure and the lymphatics. Peak flow at a pressure of 4 mm Hg. Airway pressure of 15 mm Hg or higher compresses thin-walled collapsible lymphatics. The lymphatics drain into the central veins characterized by the superior vena cava (SVC). If the SVC pressure is high, 12 mm Hg in this example, drainage will be impeded. Hence both airway pressures and venous pressures will potentially impede drainage.

increases lung water as does PEEP.[3 12 44 45 55 57 74 86 135] PEEP helps remove fluid from alveoli, but the reduction in thoracic duct drainage results in fluid retention in the interstitium.[45 55 70 82 86]

In the deliberately injured lung, PEEP increases lymph production but impairs lymph flow.[55 93 111 135] Measuring flow in the thoracic duct using a fistula shows that both positive pressure ventilation and PEEP then increase flow but, as the fistula bypasses the hydrostatic barrier of the central veins, this might be expected. Anaesthetized, ventilated animals on PEEP with high atrial pressures had less pulmonary oedema and reduced formation of pleural effusion if they had thoracic duct drainage.[3 55] A similar mechanism was inferred in ventilated patients with pancreatitis where thoracic duct drainage was associated with an improvement in lung function.[37] The information available is limited, but at present there is no clear explanation of how a very low pressure system can drain effectively if there is high CVP.[148] The net effect of impaired drainage over time would be fluid accumulation in the lung and pleural spaces and potentially increased susceptibility to lung infection.[28]

In the lung, there is no direct evidence linking impaired lymphatic drainage to infection risk but elsewhere, such as with chronic lymphoedema there is both fluid sequestration and predisposition to infection.[28 79 108 117 147]

Circumstantial associations include the observation that in the critically ill nosocomial lung infection usually starts some days after commencing ventilation even in otherwise fit individuals and that time interval is commensurate with the effects of lymphatic obstruction. After lung transplant, the infection rate in the first few days is high and antibody responses are minimal.[142] In these patients, lymphatic drainage re-establishes itself as early as the second week.[107] There is also an adverse relationship between a CVP >7 mm Hg and outcome in ventilated lung transplant patients.[101]

Ventilation impairs lymphatic drainage and chronic lymphatic obstruction predisposes to infection in other situations, but there is limited evidence for these statements.[2 9 28]

## Organ systems and positive pressure ventilation

The obvious immediate effects of positive pressure ventilation on other organs relate to a decrease in cardiac output (Fig. 5). The predominant effects on the kidney are a decrease in glomerular filtration rate and diversion of intra-renal blood flow both due to reduced cardiac output and both readily corrected either by fluid administration or by changing to a spontaneous mode of ventilation.[5 47 103 139]

Some of the effects of PEEP on the hepato-splanchnic circulation can be reversed by fluid administration, implying a primary role for cardiac output. However, this does not apply to reduced portal blood flow or increased hepatic blood volume both of which are secondary to venous congestion, nor the reduced hepatosplanchnic lymphatic drainage.[6 14 39 46 80 104 114 141 146] Hepatic metabolic function is impaired by PEEP of 10 mm Hg in sepsis but is less significant after cardiac surgery.[61 114] PEEP has been shown to increase transcapillary fluid flux peripherally, thereby increasing interstitial fluid, and it also influences microcirculatory flow.[10 57 77 96]

The sustained increases in CVP secondary to positive pressure ventilation lead to venous congestion, increased end-capillary pressure and altered fluid dynamics within organs with potentially deleterious effects.[14 94 106 118 119] It also affects lymphatic function. In the kidney, venous congestion compresses lymphatic collecting ducts impeding drainage and a similar mechanism is postulated for both mesenteric and peritoneal drainage.[74 75 105] Raised intra-abdominal pressure impairs lymphatic drainage and affects organ function.[81] High thoracic duct pressure increases interstitial fluid in both liver and kidneys and has measurable effects on renal function.[110] This may provide linkage to the increasing evidence that excess fluid itself may delay recovery in areas as diverse as lower gastrointestinal surgery, free flap surgery, and ventilation of acute lung injury, although this is contentious.[22 56 62 63 109 145]

The evidence for the effects of venous and lymphatic congestion impairing organ function is as yet rudimentary, but the physics is hard to dismiss.

## Conclusions

Ventilation with PEEP is a proven, effective modality in both anaesthesia and ICU, despite the immense physiological derangement it causes. The true costs incurred cannot be assessed until these physiological derangements are recognized and evaluated. The redistribution of alveolar ventilation and the associated altered capillary

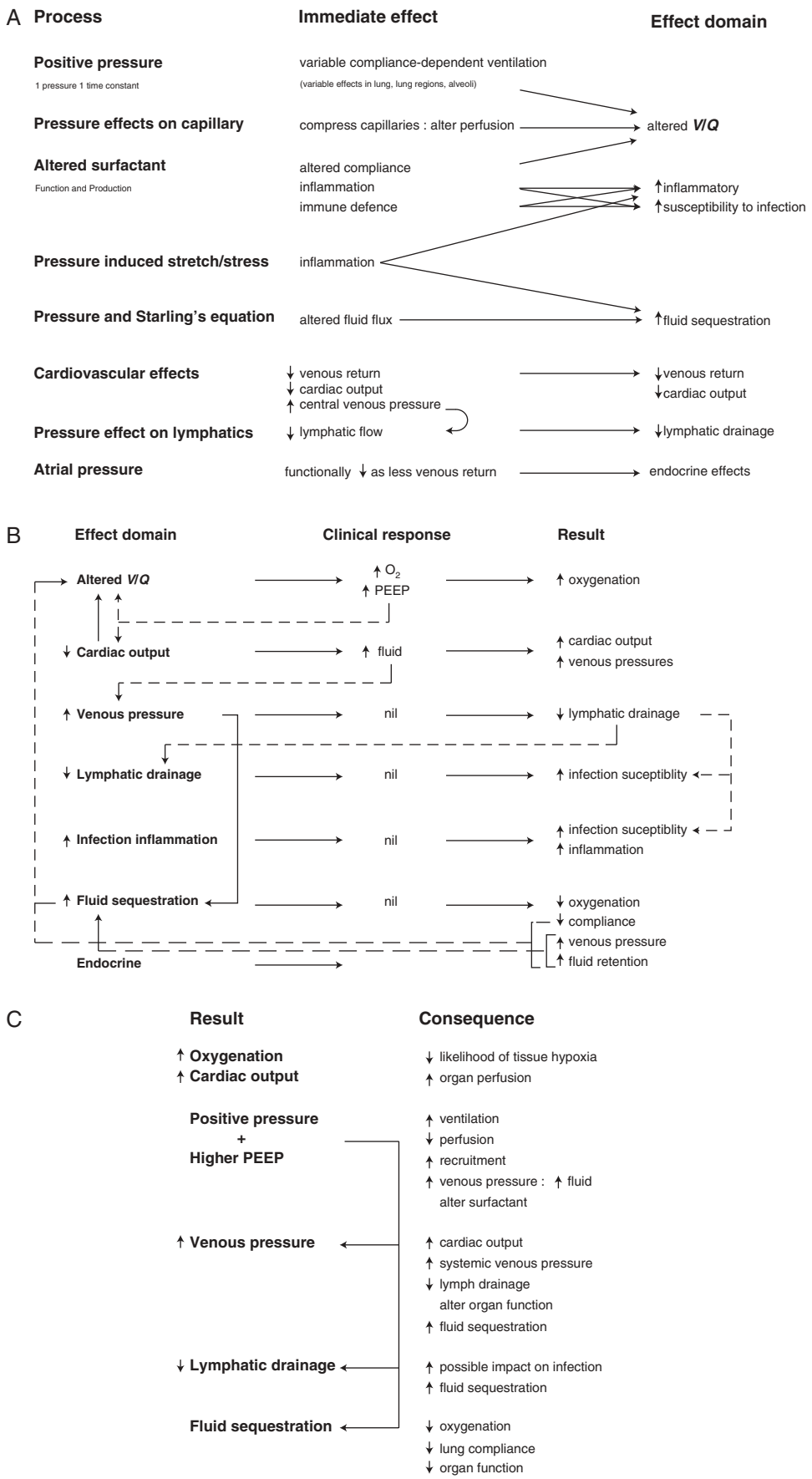


**Fig 5** Flow diagram illustrating the physiological interactions of positive pressure ventilation. (A) leads to (B) leads to (C)

perfusion, the functional changes in surfactant, the transcapillary fluid shifts, the impaired lymphatic drainage, and impeded venous return all contribute to wet, harder to ventilate lungs. This necessitates more aggressive ventilation, while impeded lymphatic drainage predisposes to stasis and infection. Correction of the immediate problem of reduced cardiac output by fluid administration increases central and systemic venous pressures further. The recently recognized complications of ventilation have been attributed to barotrauma and inflammation, but the other physiological mechanisms outlined here may have been ignored. Prolonged ventilation is associated with lung injury, infection, and multi-organ system dysfunction and if these may, even in part, be attributable to the physiological derangements described, then the real cost of ventilation, or oxygenation, is and has always been higher than was realized. (See Fig. 5)

There are other reasons why ventilation should be reassessed. Genuine developments in positive pressure ventilation are constrained by physics. The simple fact that only one pressure and one time-related waveform can be delivered at the tracheal tube precludes the potential for genuine technological advance. Is ventilation as a modality at an evolutionary dead end? Are there potential alternatives? It would seem logical in severe illness to avoid physiological derangement and to rest the lung. Tank or cuirasses could use the thorax to generate a negative inspiratory pressure, and maintain near-normal gradients that are fundamental to alveolar, capillary, and lymphatic function while minimizing haemodynamic disturbance. In severe illness, oxygen supplementation would inevitably be required to meet tissue requirements. Fundamental to this would be a new approach to defining tissue oxygen requirements divorced from the current approach based on measurement of arterial content. Does the technology to supplement oxygen exist? The same technological principles that revolutionized critical care dialysis from 'high tech' to bedside haemofiltration should allow the development of bedside extracorporeal oxygenation using the heart as the pump. Lung assist devices already exist, but are in their infancy.[8 31 33 150 151]

Will maintenance of 'normal' ventilatory patterns assist recovery? The evidence from non-invasive ventilation and the occasional study using an iron lung provides circumstantial encouragement.[25–27]

There are many unanswered questions, but for future progress there are three preliminary steps to be taken:

(i) recognition of the full range of physiological derangement and its potential consequences;
(ii) accepting the physical and physiological constraints in the further evolution of positive pressure ventilation;
(iii) acknowledgment that while positive pressure ventilation, a technology now more than 50 yr old, serves an immensely useful function, it may be time to consider alternatives in the critically ill.

What is the real cost of ventilation? We will not know until we evaluate the role of physiological derangement on late complications. It is likely the cost is high.

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