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Pulmonary Atelectasis

A Pathogenic Perioperative Entity

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Atelectasis occurs in the dependent parts of the lungs of most patients who are anesthetized. Development of atelectasis is associated with decreased lung compliance, impairment of oxygenation, increased pulmonary vascular resistance, and development of lung injury. The adverse effects of atelectasis persist into the postoperative period and can impact patient recovery. This review article focuses on the causes, nature, and diagnosis of atelectasis. The authors discuss the effects and implications of atelectasis in the perioperative period and illustrate how preventive measures may impact outcome. In addition, they examine the impact of atelectasis and its prevention in acute lung injury.

IT has been known for decades that in patients with previously normal lungs, general anesthesia is associated with impaired oxygenation.[1] Pulmonary atelectasis was suspected as the major cause, based on the observation of a successive decrease in lung compliance and the partial pressure of arterial oxygen (Pa_{O_2}), both of which returned toward normal after deep inflations of the lung.[2] Bendixen *et al.*[2] thus demonstrated their concept of a progressive alveolar collapse during general anesthesia with mechanical ventilation. It is now known that atelectasis occurs in the most dependent parts of the lung of 90% of patients who are anesthetized and plays an important role in gas exchange abnormalities and reduced static compliance associated with acute lung injury (ALI).[3] This article reviews the causes, nature, and consequences of atelectasis, focusing on the role of atelectasis in development of perioperative morbidity, and illustrates how preventive measures could impact perioperative health. In addition, we discuss the impact of atelectasis and of its prevention in ALI.

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Etiology and Pathogenesis of Atelectasis

Three sets of mechanisms have been proposed that may cause or contribute to the development of atelectasis,[4] including compression of lung tissue, absorption of alveolar air, and impairment of surfactant function. This section describes these three underlying "physiologic" causes of atelectasis; clinical factors that can modulate the development of atelectasis are described in a subsequent section.

Compression Atelectasis

Compression atelectasis occurs when the transmural pressure distending the alveolus is reduced to a level that allows the alveolus to collapse. The diaphragm normally separates the intrathoracic and abdominal cavities and, when stimulated, permits differential pressures in the abdomen and chest. After induction of anesthesia, the diaphragm is relaxed and displaced cephalad and is therefore less effective in maintaining distinct pressures in the two cavities. Specifically, the pleural pressure increases to the greatest extent in the dependent lung regions (fig. 1) and can compress the adjacent lung tissue. This is termed *compression atelectasis*.[5]

Several lines of evidence support a role of the diaphragm in this setting. Froese and Bryan[6] used cineradiography to demonstrate a cephalad shift of the diaphragm during anesthesia and spontaneous breathing, which did not progress after muscle relaxation. However, a difference in the pattern of diaphragmatic movement was noted. In supine patients, during spontaneous breathing, the lower, dependent portion of the diaphragm moved the most, whereas with muscle paralysis, the upper, nondependent part showed the largest displacement. Two distinctly different patterns of diaphragmatic displacement were seen from the same new func-

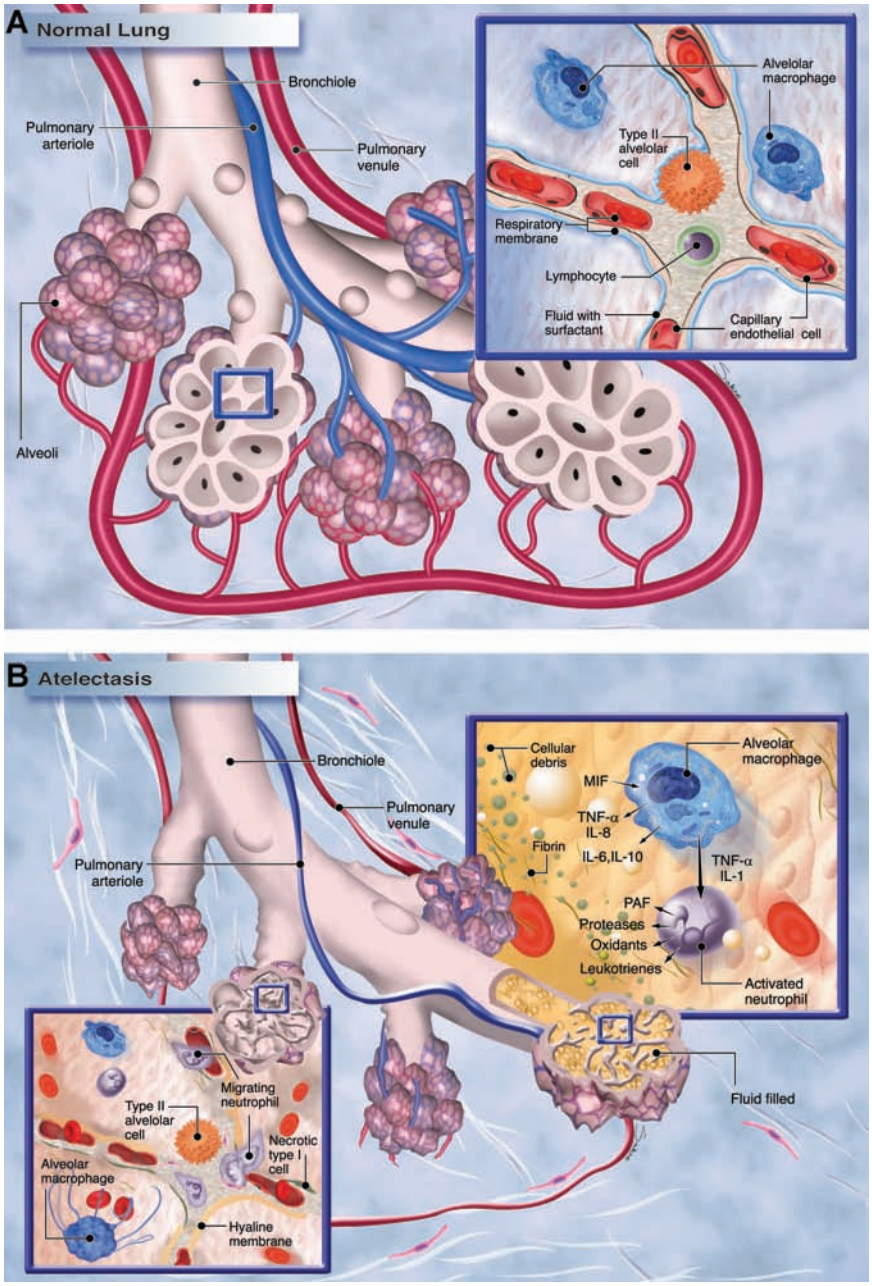

Fig. 1. (*A* and *B*) In normal lungs (*A*), the alveolar inflation and vascular perfusion are associated with low stress and are not injurious. Two separate barriers form the alveolar–capillary barrier, the microvascular endothelium, and the alveolar epithelium. In contrast, with atelectasis (*B*), alveolar inflation and deflation may be heterogeneous, and the resulting airway stress causes epithelial injury. Because the blood vessels are compressed, perfusion may be traumatic because of flow-induced disruption of the microvascular endothelium. Both epithelial and endothelial injury may initiate or propagate lung injury. This figure depicts the advanced stage of lung injury caused by atelectasis. The initial injury is simple collapse of alveoli. However, with time, this leads to an inflammatory reaction. As the derecruited lungs cause epithelial injury and loss of epithelial integrity, both type I and type II alveolar cells are damaged. Injury to type II cells disrupts normal epithelial fluid transport, impairing the removal of edema fluid from the alveolar space. In addition to collapse, derecruited lungs also become fluid filled. Neutrophils adhere to the injured capillary endothelium and migrate through the interstitium into the alveolar airspace. In the airspace, alveolar macrophages secrete cytokines, interleukin (IL)-1, -6, -8, and -10, and tumor necrosis factor (TNF)-α, which act locally to stimulate chemotaxis and activate neutrophils. IL-1 can also stimulate the production of extracellular matrix by fibroblasts. Neutrophils can release oxidants, proteases, leukotrienes, and other proinflammatory molecules, such as platelet-activating factor (PAF). MIF = macrophage inhibitory factor.

tional residual capacity (FRC) position. In an anesthetized patient breathing spontaneously, the active tension in the diaphragm is capable of overcoming the weight of the abdominal contents, and the diaphragm moves the most in the lower, dependent portion (because the lower or posterior diaphragm is stretched higher into the chest, it has the smallest radius of curvature and therefore contracts most effectively). In addition, the diaphragm is thicker posteriorly than anteriorly, and this may account for the disproportionate movement.[7] During paralysis and positive-pressure ventilation, the passive diaphragm is displaced by the positive pressure preferentially in the upper, nondependent portion (where there is least impedance to diaphragmatic movement). Subsequent studies confirmed these findings and, in addition, documented a reduction in the transverse area of the chest.[8] Using an advanced computed tomography (CT) scanner, Krayer *et al.*[9] demonstrated a reduced thoracic cross-sectional area in anesthetized subjects but had more variable results regarding shape and position of the diaphragm; some subjects showed a cranial shift of the diaphragm, but in other subjects, part of the diaphragm was unaffected or even moved caudally. Other investigators have also shown results inconsistent with the classic model of regional ventilation[10]; nevertheless, it can be concluded that FRC is reduced in the anesthetized subject, whether caused by loss of traction of the chest wall or compression of the lung. Loss of intercostal muscle function may also contribute to reduced FRC during anesthesia. Inhalation

agents decrease intercostal muscle activity, particularly in children.[11]

Hedenstierna *et al.*[8] also noted an additional source of lung compression in that there was a net shift of central blood volume from the thorax, which seemed to pool in the abdomen, resulting in additional dependent pressure arising from the abdomen and acting on the diaphragm. Finally, the displacement of the diaphragm has been studied under dynamic conditions, whereby increases in diaphragm tension through phrenic nerve stimulation have been shown to reduce the amount of atelectasis at isovolumic conditions in anesthetized patients.[12]

Therefore, compression atelectasis occurs during general anesthesia and is caused by chest geometry, overall cephalad diaphragm displacement, differential regional diaphragmatic changes, shift of thoracic central vascular blood into the abdomen, and altered diaphragmatic dynamics.

Gas Resorption

Resorption atelectasis—sometimes called *gas atelectasis*[4]—can occur by two mechanisms. After complete airway occlusion, a pocket of trapped gas is created in the lung unit distal to the obstruction. Because gas uptake by the blood continues and gas inflow is prevented by blocked airways, the gas pocket collapses.[13] Under these conditions, the rate of absorption of gas from an unventilated lung area increases with elevation of the fraction of inspired oxygen (F_{IO_2}).[14]

A somewhat different mechanism explains absorption atelectasis in the absence of airway occlusion. In this context, lung zones that have low ventilation relative to perfusion (low ventilation/perfusion [V_A/Q] ratio) have a low partial pressure of alveolar oxygen (P_{AO_2}) when air is breathed. When the F_{IO_2} is increased, P_{AO_2} increases, causing the rate at which oxygen moves from the alveolar gas to the capillary blood to increase greatly. The oxygen flux may increase so much that the net flow of gas into the blood exceeds the inspired flow of gas, and the lung unit becomes progressively smaller. Collapse is most likely to occur when the F_{IO_2} (and duration of exposure) is high or where the V_A/Q ratio (and mixed venous oxygen content) is low.[15,16]

Surfactant Impairment

Pulmonary surfactant that covers the large alveolar surface is composed of phospholipids (mostly phosphatidylcholine), neutral lipids, and surfactant-specific apoproteins (termed *surfactant proteins A*, *B*, *C*, and *D*). By reducing alveolar surface tension, pulmonary surfactant stabilizes the alveoli and prevents alveolar collapse. This stabilizing function of surfactant may be depressed by anesthesia, and such an effect has been confirmed *in vitro* by Woo *et al.*[17] The authors evaluated the effect of anesthetic agents on surfactant function using deflation pressure–volume curves in excised dog lungs. They found that the reduction in percent maximum lung volume was proportional to the concentration of both chloroform and halothane.[17] Wollmer *et al.*[18] also used pulmonary clearance of technetium-labeled diethylenetriamine pentaacetic acid to demonstrate that halothane anesthesia, in combination with high oxygen concentration, caused increased permeability of the alveolar–capillary barrier in rabbit lungs. The authors postulated that the increased rate of pulmonary clearance of technetium-labeled diethylenetriamine pentaacetic acid during anesthesia with halothane was likely to be caused by combined effects on the pulmonary surfactant or the alveolar epithelium or both.[18] In addition, it is known that the content of alveolar surfactant in isolated lungs is modified by mechanical factors. Hyperventilation by increased tidal volume,[19] sequential air inflations to total lung capacity,[20] or even a single cycle of increased tidal volume[19] all cause release of surfactant in isolated animal lungs. In rabbits, maintained increases in tidal volume increased the amount of total phospholipids recovered from bronchoalveolar lavages.[21,22] Supporting this is the report that the spontaneous occurrence of large gasping respirations increases the proportion of active forms of alveolar surfactant (phospholipids). Oyarzun *et al.*[23] examined the ventilatory variables of cats breathing spontaneously during anesthesia for 4 h. They found that the frequency of large gasps is directly correlated with the concentration of phospholipids in bronchoalveolar lavage fluid.[23]

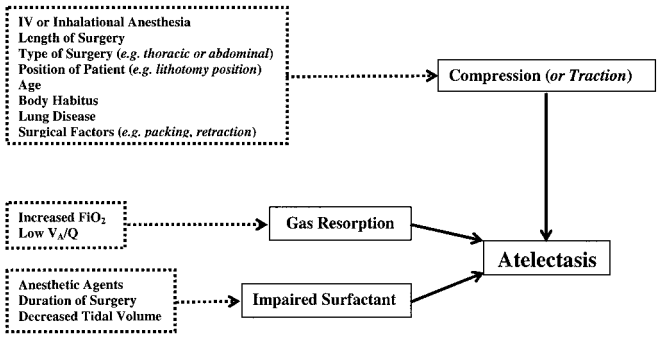

Fig. 2. This schematic outlines the probable pathogenic mechanisms underlying the development of atelectasis. F_{IO_2} = fraction of inspired oxygen; IV = intravenous; V_A/Q = ventilation/perfusion ratio.

All three mechanisms—compression, gas resorption, and surfactant impairment—may contribute to atelectasis formation during general anesthesia (fig. 2). However, given the surfactant reserve and the 14-h surfactant turnover time, it may be that primary changes in surface forces are less important; it is not known whether a collapsed alveolus can denature surfactant, and so the 14-h turnover time may not be relevant. Nonetheless, absorption and compression are considered to be the two mechanisms most implicated in perioperative atelectasis formation.[24]

Nature of Atelectasis

The following section reviews the characteristics of atelectasis in several clinical contexts and then reviews contemporary concepts regarding the nature of atelectasis.

Atelectasis due to Anesthesia. Anesthesia-induced atelectasis is traditionally thought of as collapse of alveoli. Brismar *et al.*[5] showed that within 5 min after induction of anesthesia, areas of increased density appeared in the dependent regions of both lungs on CT. The dense areas had an attenuation factor that corresponds to blood and connective tissue and indicates the absence of air. Injection of radiocontrast in the pleural space showed that the densities were located above the pleura, *i.e.*, within the lung.[25] Hedenstierna *et al.*[26] also found these densities in anesthetized sheep and confirmed histologically that the densities were collapsed lung regions and not fluid accumulation.

Methods to restore normal FRC and various reexpansion maneuvers have been suggested. The application of positive end-expiratory pressure (PEEP) has been tested in several studies. Arterial oxygenation does not usually improve markedly, and atelectasis may persist.[27,28] Reopened units recollapse rapidly after discontinuation of PEEP. However, Rothen *et al.*[29,30] demonstrated in volunteers that peak inspiratory pressures of at least 40 cm H_2O were needed to fully reverse anesthesia-induced collapse of healthy lungs, and most of the reexpanded atelectatic lung tissue remains inflated for at least 40 min.

Direct Visualization of Atelectasis. Using a unique *in vivo* microscopic technique, Halter *et al.*[31] viewed alveoli in the living animal in real time during mechanical ventilation. In a surfactant deactivation model of acute respiratory distress syndrome (ARDS), they measured alveolar number and stability before, during, and after a recruitment maneuver with ventilation with either decreased or increased PEEP. They demonstrated that a recruitment maneuver opens atelectatic alveoli and that without adequate PEEP, alveoli are unstable and susceptible to derecruitment. Although associated with sampling limitations,[32] this elegant study was the first to directly demonstrate visual evidence of collapse of individual alveoli reflecting atelectasis and stabilization reflecting recruitment.[32]

Cyclic Lung Recruitment. Mechanical ventilation of areas of lung that are atelectatic is associated with repetitive collapse and reexpansion with each breath, often called *cyclic recruitment*. A conventional view of the effects of atelectasis on gas exchange conveys an image of mixed venous blood perfusing nonventilated or collapsed alveoli, resulting in a consistent and stable proportion of the pulmonary venous return that derives from deoxygenated blood.[33] This notional contribution (*i.e.*, deoxygenated blood added to oxygenated blood) is seen as the sum of two constant flow rates, resulting in a shunt fraction (Q_s/Q_t %)[7] that can be mathematically calculated.

However, we now know that the oxygen content of pulmonary venous blood varies significantly throughout the respiratory cycle as the shunt fraction changes with every breath. Baumgardner *et al.*[34] tested the hypothesis that cyclic collapse of alveoli in dependent lung regions with every breath should lead to large oscillations in Pa_{O_2} as shunt varies with the respiratory cycle. They placed a partial pressure of oxygen (P_{O_2}) probe in the brachiocephalic artery of rabbits after saline lavage. They found a significant effect of respiratory rate on the magnitude of oscillations; as the respiratory rate increased, the amplitude of oscillations became progressively smaller.[32] The higher respiratory rate avoided cyclic recruitment; *i.e.*, the shorter expiratory time allowed expiration without collapse. In practice, the beneficial effect of higher respiratory rates leading to improved oxygenation can be seen when ventilating pediatric patients and in particular neonates. This suggests that the dynamics of mechanical events leading to recruitment and derecruitment are important determinants of the amount of lung that is cyclically recruited.[34] A previous study by Williams *et al.*[35] also showed within-breath arterial P_{O_2} oscillations in an animal model of ARDS and confirmed that Pa_{O_2} oscillations occur in the atelectatic lung. The authors investigated the effect of PEEP on Pa_{O_2} oscillations. They found that as PEEP was increased, the amplitude of the Pa_{O_2} oscillation decreased and the mean Pa_{O_2} increased.[35] Several studies have evaluated the effects of various inspiratory-to-expiratory ratios on gas exchange, lung mechanics, and FRC; the inspiratory-to-expiratory ratio *per se* was not found to be a significant factor.[36–38]

Atelectasis: Volume Loss *versus* Fluid Filling. More recently, it has been argued that the dependent injured lung is derecruited, not because it is collapsed but because it is filled with fluid.[39] Work by Gattinoni *et al.*[40–42] had concluded that dependent portions of the injured lung are exposed to a compressive pressure from the increased weight of edematous lung and are collapsed. Such a "weight-of-the-lung" hypothesis has been studied, and it seems that the weight of the lung accounts for only approximately 20% of the vertical gradient in pleural pressure and alveolar volume in normal lungs.[43–45] Hubmayr[39] suggests an alternative view of the mechanics of injured lungs based on lung weight, shape matching, interpretation of CT images of the lung, and pressure–volume curves. For example, where edema fluid and foam fill dependent regions, high inflation pressures are required to inflate with air, as opposed to low pressures required for inflation with fluid. The pressure–volume characteristics of the former more closely display the classic findings associated with atelectasis, including the prominent "lower inflection point" reflecting opening pressure.[39] Evidence in support of edema as the source of regional impedance in ARDS

include parenchymal marker studies in oleic acid–injured lungs.[46] The parenchymal marker technique describes the topographic distribution of regional volume and ventilation in laboratory animals. The authors found that oleic acid injury did not produce collapse of dependent lung units in this model of ARDS.[46] They proposed an alternative mechanism for the topographic variability in regional impedances and lung expansion after injury, which was liquid or foam in alveoli and conducting airways.[46]

Factors Modulating the Formation of Atelectasis

It is important for clinicians to understand how atelectasis develops or worsens in the clinical context. Several important clinical events act as modifiers that influence the formation of atelectasis (fig. 2).

Type of Anesthesia. Atelectasis develops with both intravenous and inhalational anesthesia, regardless of whether the patient is breathing spontaneously or is paralyzed and mechanically ventilated.[47–49] Ketamine is the only anesthetic that does not produce atelectasis when used alone, although in conjunction with neuromuscular blockade, it does result in atelectasis.[50]

Ventilatory effects of regional anesthesia depend on the type and extension of motor blockade.[4] Neuroaxial blockade that has significant cephalad extension reduces inspiratory capacity by up to 20%, and expiratory reserve volume approaches zero[51]; less extensive blockade affects pulmonary gas exchange only minimally, and arterial oxygenation and carbon dioxide elimination are well maintained during most spinal and epidural anesthesia.[52,53] Closing capacity and FRC remain unchanged.[54]

Impact of Time. The maximum decrease in FRC seems to occur within the first few minutes of general anesthesia.[5,55] During anesthesia for surgical operations on the limb, FRC is not influenced further by depth or duration of anesthesia.[55,56] Don *et al.*[55] studied patients undergoing peripheral limb surgery who were free of cardiac and respiratory disease. Patients were divided into two groups, those breathing halothane in 100% oxygen and those breathing halothane in 30% oxygen in nitrogen. The FRC decreased comparably in both groups after induction of anesthesia, but this did not progress with time. However, other studies have found that during abdominal or thoracic surgery, pulmonary gas exchange deteriorates progressively during the course of the operation[57,58]; these studies were unable to determine the independent impact of time on atelectasis as opposed to surgical manipulation (*e.g.*, surgical packing, tissue retraction).

Effects of Position. In adults, changing from the upright to the supine position results in a decrease of 0.5 l in FRC to 1.0 l, even in the awake state.[7] After anesthesia, FRC is reduced by a further 0.5 l to 0.7 l.[49] The Trendelenburg position allows the abdominal contents to push the diaphragm further cephalad, resulting in a further decrease in FRC.[59] In the lateral decubitus position, the dependent lung is predisposed to atelectasis, whereas the nondependent lung may have an increased FRC. The overall result is usually a slight increase in total lung FRC, which, despite the differences in lung size, is independent of whether the right or the left lung is in the dependent position.[60] The prone position may increase FRC slightly,[61] although this may not decrease atelectasis. In fact, distribution of ventilation is more uniform in anesthetized patients in the prone position, in particular where the abdomen is not supported.[62] Prone positioning improves oxygenation in patients with ARDS.[63] Animal models have also demonstrated the benefit of prone positioning after oleic acid–induced lung injury as well as a model of lung injury induced solely by mechanical forces.[64,65] Prone positioning causes less extensive histologic injury and alters its distribution.[64,65]

Atelectasis is more prominent after cardiac surgery with cardiopulmonary bypass (CPB) than after other forms of surgery. Using a porcine model, Magnusson *et al.*[66] found that atelectasis is produced to a much larger extent after CPB than after anesthesia alone or with sternotomy. Furthermore, the CPB-associated atelectasis accounted for most of the marked post-CPB increase in shunt and hypoxemia.[66] Clinical experience is consistent with laboratory reports, and prominent atelectasis has been noted in the dorsal lung regions on the first postoperative day in cardiac surgery patients.[67] Other causes of gas exchange impairment after sternotomy and CPB have been investigated, including pulmonary endothelial permeability.[68] Macnaughton *et al.*[68] did not find any increase in pulmonary endothelial permeability, and they hypothesized that the major component of the deterioration in lung function was probably atelectasis occurring during bypass. Numerous studies have shown that a lung recruitment strategy and PEEP improves oxygenation in patients after CPB.[69,70] In addition, the application of PEEP of 10 cm H_2O during CPB to maintain lung inflation has been shown to be beneficial.[71] Many anesthetists intentionally inflate the patient's lungs before coming off CPB and directly visualize equal expansion of the lungs. This simple maneuver may detect significant obstruction from secretions or blood in the endotracheal tube.

Inspired Oxygen. High oxygen concentration has been associated with atelectasis formation, and this is important because use of high F_{IO_2} (*i.e.*, approaching 1.0) represents standard practice among many anesthesiologists.[72] Previous studies suggested that inspired oxygen concentration may not be an important independent predictor of anesthesia-associated atelectasis.[5,55] However, one of these studies used the helium-dilution technique to measure FRC, which may not be as sensitive as the CT that was used in later studies.[55,73] In the absence of preoxygenation, atelectasis is not seen di-

rectly after induction of anesthesia; however, when F_{IO_2} is increased to 1.0 before intubation, development of atelectasis is a consistent finding.[74,75] Concerns about oxygen-induced atelectasis are not restricted to induction of anesthesia; increasing F_{IO_2} at the end of surgery to 1.0 before extubation also causes additional atelectasis, which persists into the postoperative period.[76] However, the use of lower F_{IO_2} may increase the risk of hypoxemia, should airway management subsequently prove difficult and ventilation be threatened.[77] One study investigated how different oxygen concentrations may affect the formation of atelectasis and the decrease in arterial oxygen saturation during apnea.[78] The authors found that during routine induction of general anesthesia, 80% oxygen caused minimal atelectasis, but the time margin before desaturation occurred was significantly shortened compared with that of 100% oxygen.[78] In addition, evidence suggests that administration of supplemental oxygen reduces the incidence of wound infection and could be beneficial during anesthesia and recovery.[79,80] Another possible benefit of supplemental oxygen during anesthesia includes a reduced incidence of postoperative nausea and vomiting after colorectal surgery,[81] although this was not found in patients undergoing gynecologic laparoscopy.[82]

The effects of nitrous oxide on lung volumes during anesthesia have also been studied.[83–85] There was no difference in the incidence of postoperative atelectasis if nitrous oxide in oxygen was used or if air in oxygen was used as the inspired gas.

In treating patients for induction of general anesthesia, anesthesiologists must trade off the very rare possibility of acute hypoxemia in the event of difficulty with airway management *versus* the common and predictable—but generally mild—impact of hyperoxia-induced atelectasis on later intraoperative gas exchange. Therefore, the use of a lower F_{IO_2} to replace preoxygenation has not been recommended as a new standard in clinical practice.[78]

Effects of Age. In adulthood, progressive age is not associated with increased propensity for development of atelectasis.[86] However, in young children (aged 1–3 yr) atelectasis seems to develop more readily than in adults,[87] possibly because of the far greater thoracic wall compliance resulting in less outwardly directed lung distension forces.[88] In infants, contraction of the diaphragm may cause paradoxical inward movement of the highly deformable chest wall, resulting in loss of lung traction. The resultant atelectasis could reduce ventilatory efficiency, increase diaphragmatic fatigue, and thereby further increase the tendency for atelectasis development. In addition, type I and II muscle fibers are not fully developed in children who are younger than 2 yr. This makes them prone to respiratory failure and fatigue when there is extra stress put on their respiratory system, not only during general anesthesia[89] but also in the presence of a respiratory tract infection, epiglottitis, or airway obstruction.

Closing volume is also greater in young children in whom the elastic supporting structure of the lung is incompletely developed. This puts the infant at greater risk for atelectasis because airway closure can occur even during tidal breathing.[24] The closing volume plus the residual volume constitutes the closing capacity. If FRC is decreased relative to closing capacity, this converts normal areas of lung to low V_A/Q areas and compounds the propensity for development of atelectasis.[90]

Body Habitus. Obesity worsens arterial oxygenation through multiple mechanisms,[91] of which development of atelectasis is an important contributor. This is because of a markedly reduced FRC promoting airway closure to a greater extent than in healthy-weight subjects.[92] As the weight of the torso and abdomen make diaphragmatic excursions more difficult—especially when recumbent or supine—the FRC decreases, and this is intensified in the setting of diaphragmatic paralysis associated with neuromuscular blockade. Don *et al.*[55] further clarified the effect of body size on gas exchange and showed that an individual with an increased weight/height ratio (*i.e.*, obese) would be at a particular disadvantage in the supine position because closing volume is increased in relation to FRC. Pelosi *et al.*[93] also investigated the effects of body mass index on FRC, respiratory mechanics, and gas exchange during general anesthesia. They found that with increasing body mass index (*i.e.*, ratio of body weight/surface area), FRC and lung compliance decreased, and the oxygenation index (Pa_{O_2}/P_{AO_2}) decreased exponentially.[93] Prone positioning, although difficult in obese patients, may improve oxygenation.[63] Consistent with the effects of obesity, the reduced FRC that occurs during pregnancy also potentiates atelectasis.[94]

Tidal Volume. The ARDSnet study recommends the use of low tidal volume in patients with ARDS.[95] Lower tidal volume reduces stretch-induced lung injury in patients with ARDS,[96] and this approach is translated into improved patient survival.[95,97] However, extrapolation of the low-tidal-volume approach to patients without lung injury (or ARDS) requires caution for two principal reasons. First, it has been long recognized that low tidal volume increases the development of atelectasis in the absence of lung injury.[2,98–100] Therefore, generalized adoption of low tidal volume in patients without preexisting lung injury (*e.g.*, during general anesthesia) could promote development of atelectasis. Second, in the presence of ARDS, the ARDSnet protocol is specific: The data stipulate 6 ml/kg (*vs.* 12 ml/kg) in the context of a precise ventilatory management protocol that stipulates many ventilatory parameters, in addition to tidal volume.[95] A recent study has suggested that the specific "low-tidal-volume" approach used in the ARDSnet study[95] was actually associated with the development of intrinsic PEEP,[97] raising the possibility that recruit-

ment—not simply low tidal stretch—played a protective role in these patients. Therefore, if a low tidal volume strategy is used that does not result in the development of intrinsic PEEP, the propensity for development of atelectasis might be significant. The use of low tidal volume in the absence of recruitment or PEEP in anesthetized patients without lung injury may lead to atelectasis and is not recommended.

Two practical points are important regarding mode of ventilation during general anesthesia. In contrast to volume-controlled ventilation, pressure-controlled ventilation results in smaller delivered tidal volumes when respiratory system compliance is decreased (*e.g.*, during surgical retraction or in the presence of abdominal packs). Smaller tidal volumes may lead to atelectasis and may go undiagnosed because there is no change in the peak airway pressure as pressure-controlled ventilation is being used. In addition, fresh gas flow may have an impact because with older volume-controlled ventilators, increased fresh gas flow results in increased delivered tidal volume.[101]

Preexisting Lung Disease. Smokers and patients with lung disease show more pronounced gas exchange impairment in the awake state than healthy subjects do, and this difference also persists during anesthesia.[102] However, only a small shunt and almost no atelectasis develops in these patients, but they may have severe V_A/Q mismatch. Hyperinflation of the lungs may make them resist collapse.[103] The chronic hyperinflated state of the lungs in chronic bronchitis changes the mechanical behavior of the lungs and the interaction with the chest wall so that the tendency to collapse is reduced. However, patients with chronic obstructive lung disease may have large regions with low V_A/Q ratios that can result, over time, in resorption atelectasis.[4]

Effects of Atelectasis

Development of atelectasis is associated with the development of several pathophysiologic effects, including decreased compliance, impairment of oxygenation, increased pulmonary vascular resistance, and development of lung injury.

Decreased Compliance. One of the first articles examining the effects of atelectasis was by Mead and Collier[99] in 1959. They noted that when anesthetized dogs were allowed to breathe spontaneously or were paralyzed and ventilated at tidal volumes of approximately 12.5 ml/kg, pulmonary compliance decreased progressively. They found that these changes were immediately reversed after forced inflations of the lungs, whereas forced deflations caused further compliance reductions. The appearance of the lungs as well as measurement of total and ventilatory lung volumes indicated that the lungs were atelectatic.[99]

These laboratory findings were translated into the perioperative context with the article by Bendixen *et al.*,[2] which reported that atelectasis caused a decrease in pulmonary compliance in surgical patients and was associated with a worsening in systemic oxygenation. The decreased compliance is conventionally considered to be due to a reduction in lung volume, such that inspiration–expiration cycles commencing from a lower FRC are completed on a less efficient section of the notional pressure–volume curve.[104] Therefore, greater energy is consumed because a given change in transpulmonary pressure results in a lesser tidal volume because of the sigmoid shape of the pressure–volume curve. An anatomical basis has been suggested for such atelectasis-associated decreased FRC in the context of general anesthesia (see Compression Atelectasis).[6]

The pressure–volume characteristics of the lung determine the work of breathing, and ventilatory work may be analyzed by plotting pressure against volume.[105] In the presence of increased airway resistance or decreased lung compliance, increased transpulmonary pressure is required to achieve a given tidal volume with consequent increase in the work of breathing.

Although the concept of altered compliance has been well established in the setting of "macroatelectasis" (*e.g.*, lobar or dependent atelectasis sufficiently large to be radiologically apparent), there are no data regarding whether microatelectasis (*e.g.*, after brief exposure to increased F_{IO_2} during preoxygenation[75]) has comparable effects on lung mechanics.

Impaired Oxygenation. In many situations, the most striking effect of atelectasis is impairment of systemic oxygenation. This was first identified in the context of general anesthesia[2] where the use of passive hyperinflations reversed the hypoxemia.[2] Others reported impairment of oxygenation during prolonged constant-volume ventilation using small tidal volumes in the absence of intermittent hyperinflations.[106–108]

Atelectasis can occur as a result of hyperoxia.[75,109] If high F_{IO_2} is continued, the effects may not be noted by observing pulse oximetry, but only if Pa_{O_2} is measured. In this situation, the impaired oxygenation can be expressed in terms of Pa_{O_2}. The cause of the impaired oxygenation has been shown, using the multiple inert gas technique, to result from increased mismatch of ventilation with perfusion.[75]

Two approaches have been shown to mitigate against the development of hypoxia. First, as demonstrated originally, intermittent hyperinflation maneuvers reverse the effect on gas exchange.[2] Maintenance of lung volume from the outset can prevent, as opposed to reverse, development of intraoperative atelectasis.[28] Second, although recognized as an issue for decades, the composition of the inspired gases used during induction of general anesthesia has been shown to directly impact the development of microatelectasis in healthy patients undergoing general anesthesia,[75] as well as in patients with lung injury.[110] Rothen *et al.*[75] found that very little

atelectasis occurred after the induction of general anesthesia in subjects whose lungs were ventilated with 30% oxygen in nitrogen. Furthermore, the increase in the amount of atelectasis was less rapid in the setting of 30% oxygen (in nitrogen) compared with 100% oxygen. This is consistent with the notion that a poorly absorbed gas such as nitrogen might prevent the early formation of atelectasis and, conversely, that use of a highly absorbed gas (*e.g.*, oxygen) would enhance the development of atelectasis.

Pulmonary Vascular Resistance. Early studies suggested that the pulmonary vascular resistance was minimal at FRC. Lung volume much above this notional value resulted in alveolar compression due to lung stretch, whereas lung volume falling below the FRC was thought to result in compression of extraalveolar vessels. Therefore, this notion explained the changes in pulmonary vascular resistance on the basis of physical alteration of the pulmonary blood vessels, either stretching or narrowing caused by increased lung volume or compression caused by decreased lung volume.[111–113] However, regional hypoxia develops in atelectatic lungs, and it has been shown that the mechanism of increased large vessel pulmonary vascular resistance in the lungs is due to hypoxic pulmonary vasoconstriction, due in turn to decreased alveolar and mixed venous oxygen tension.[114–116] Recent work by our group has demonstrated that this significant increase in vascular resistance can occur in previously normal lungs in an experimental setting, resulting in right ventricular dysfunction and increased microvascular leakage.[117]

Lung Injury. Extensive evidence has established the importance of maintenance of lung volume in the prevention of lung injury. The pivotal publication by Webb and Tierney[118] demonstrated that application of PEEP prevented the development of lung injury induced by extremely high tidal volume. The specific degree of atelectasis responsible for attenuation or prevention of high tidal volume–induced lung injury was explored by Sandhar *et al.*[119] and Muscedere *et al.*[120] using different experimental models over 5- and 2-h time periods, respectively. In isolated, nonperfused lungs that are ventilated with no or low PEEP, reductions in compliance and evidence of morphologically apparent lung injury occur. Permitting such atelectasis in the presence of high tidal volumes is associated with hyaline membrane formation, along with regional inhomogeneity of atelectasis and overdistension. Other articles have also demonstrated that repetitive lung collapse or atelectasis leads to increased neutrophil activation in previously injured lungs.[121,122] In addition to lung injury induced by extremely high tidal volumes, ventilation at low lung volumes worsens lung injury by repeated small airway closure.[123,124] The concept of permissive hypercapnia developed to avoid lung injury caused by high tidal volumes or high inflation pressures. Higher end-tidal carbon dioxide levels may be accepted to reduce volutrauma or barotrauma, particularly in pediatric patients.

Potentiation of lung injury by atelectasis has additional implications for inflammatory effects in the lung. Tremblay *et al.*[125] examined the effect of ventilation strategy on lung inflammatory mediators in the presence and absence of lung injury and demonstrated that in the absence of PEEP, an impairment in lung compliance was accompanied by increased cytokine concentrations (*e.g.*, tumor necrosis factor α, interleukin 1β) that were greatest in the groups pretreated with lipopolysaccharide.[125] These concepts were extended to the *in vivo* setting, where it was reported that maximal serum cytokine concentrations induced by high tidal volume occurred in the context of zero PEEP. In addition, atelectasis worsened the impairment of compliance induced by high tidal volume.[126] Perhaps of greatest concern in that publication was the high mortality (in the absence of cytokine alterations) observed in the *in vivo* combination of low-tidal-volume ventilation in the presence of atelectasis. These data suggest that in terms of the most meaningful outcome (*i.e.*, survival), the combination of low tidal volume and atelectasis may be the most adverse ventilation strategy and that the increased cytokines observed in the high-tidal volume groups may be of less importance.[126]

Recent work by our group, wherein rats without lung injury received ventilatory strategies with and without PEEP and recruitment maneuvers, may place these findings into perspective.[117] We found decreased survival in the zero-PEEP group and also demonstrated ultrastructural evidence of microvascular epithelial disruption in those animals. In addition, we demonstrated that right ventricular dysfunction, possibly secondary to increased pulmonary vascular resistance, occurred in the presence of reduced FRC.[117]

Clinical Impact of Atelectasis beyond the Operating Room. Development of atelectasis intraoperatively is associated with decreased lung compliance, impairment of oxygenation, increased pulmonary vascular resistance, and development of lung injury. The adverse effects of atelectasis persist in the postoperative period and can impact patient recovery. Atelectasis can persist for 2 days after major surgery.[127] Often, the lung dysfunction is transient, and normal lung function resumes soon after anesthesia and surgery. For example, atelectasis resolves within 24 h after laparoscopy in nonobese subjects.[128] Nevertheless, patients experience perioperative respiratory complications that may be related to reduction in FRC.[129,130]

Some pulmonary complications occur during or immediately after anesthesia—mainly hypoxemia. In a large study with more than 24,000 patients, 0.9% had a hypoxemic event in the postanesthesia care unit that necessitated a specific intervention other than only supple-

mental oxygen.[131] There is no clear evidence that atelectasis is the cause of all of these postoperative hypoxemic events; respiratory depression from residual anesthetic may be more likely.[24] However, it seems likely that preventing atelectasis formation during the whole perioperative period would increase the pulmonary oxygen reserve, potentially reducing the likelihood of late postoperative complications.

The characteristic postoperative mechanical respiratory abnormality after abdominal or thoracic surgery is a restrictive pattern with severely reduced inspiratory capacity, vital capacity, and FRC.[132–134] Patients breathe rapidly with small tidal volumes and are unwilling—or unable—to inspire deeply. Patients in whom postoperative pulmonary complications develop have a relatively greater reduction of FRC, vital capacity, and Pao_2 than those who do not.[132,134] The impact of postoperative pain control in preventing postoperative atelectasis has been the focus of much research effort. Although pain and muscle splinting in response to pain are traditionally assumed to be the principal causative factors, total relief of pain after upper abdominal surgery—using epidural analgesia—results in only partial restoration of vital capacity and has minimal effect on FRC.[135] However, a recent meta-analysis suggested that postoperative epidural opioids significantly decrease the frequency of atelectasis but not other pulmonary complications when compared with systemic opioids.[136] Other studies have found no difference in the incidence of pulmonary complications. Manikian *et al.*[137] demonstrated that thoracic epidural analgesia in 13 patients undergoing upper abdominal surgery caused a significant increase in forced vital capacity, but the FRC remained unchanged. Spence and Logan[138] reported no significant impact of postoperative epidural analgesia on oxygenation when compared with patients receiving systemic morphine, and Jayr *et al.*[139] reported that although the epidural provided superior postoperative analgesia, it did not affect the frequency of postoperative pulmonary complications, regardless of preoperative pulmonary status. Finally, a recent multicenter randomized trial of 915 high-risk surgical patients reported a slight reduction in postoperative pulmonary complications—but no impact on mortality or major morbidity—attributable to epidural *versus* systemic analgesia, although this study may have been underpowered to examine mortality.[140]

Two particular aspects of pulmonary defense mechanisms, coughing and removal of particulate matter, are adversely affected by the changes in lung mechanics and breathing pattern[135]; this may predispose to pulmonary infection. A number of studies examined the effects of halothane and thiopentone on mucociliary clearance and found that these agents may be responsible for reduced mucous clearance in the postoperative period.[141–143] A more recent study demonstrated that total intravenous anesthesia with propofol, alfentanil, and vecuronium depressed mucociliary flow in patients with healthy lungs.[144] Cervin and Lindberg[145] examined the effects of desflurane on mucociliary activity in the rabbit maxillary sinus *in vivo*. Desflurane increased mucociliary activity, and the authors concluded that desflurane is an airway irritating compound.[145] Atelectasis and pneumonia are often considered together because the changes associated with atelectasis may predispose to pneumonia.[146] Despite a direct lack of evidence of a correlation between atelectasis and pneumonia, reducing or avoiding atelectasis may diminish postoperative pulmonary complications[147] and thus improve outcome; however, this remains to be proven.

In a series of adults undergoing elective abdominal surgery, postoperative pulmonary complications occurred in 9.6% of cases.[148] Atelectasis and infectious complications account for the majority of reported pulmonary complications,[149] and the consequences include a significant burden in terms of morbidity[149] and additional healthcare costs.[150] In some series, pulmonary complications account for 24% of deaths within 6 days of surgery,[130,149] although the precise relation to atelectasis is unclear.

Experimental Evidence that Atelectasis Causes Lung Injury. The majority of studies examining the interactions of mechanical ventilation and nonventilatory lung injury have observed the effects of injurious mechanical ventilation strategy on preinjured lungs. However, several experimental studies have examined the effect of preemptive recruitment on the effects of subsequent lung injury.

Atelectasis Worsens Lung Injury Caused by Mechanical Stretch. Multiple studies have convincingly demonstrated that recruitment provides effective protection against lung injury that is either induced[118,151,152] or aggravated[120,125,153,154] by mechanical stretch. This may assume increasing importance as the role of tidal volume and plateau pressures in ARDS is debated.[95,155,156]

Atelectasis Worsens Lung Injury Not Caused by Mechanical Stretch. Most patients with severe lung injury require supportive mechanical ventilation. It is clear from multiple laboratory[157,158] and clinical[95,159] studies that stretch can cause or worsen lung injury. However, there is a vast spectrum of causes of ALI, and there are striking similarities—and few differences—in the pathogenesis, pathophysiologic dysfunction, and histologic appearance of ALI or ARDS, whether caused by stretch[158] or other etiologies.[160] Therefore, because recruitment is effective in reducing stretch-induced injury and because so many pathogenic and morphologic features are shared between stretch-induced *versus* other forms of injury, it may be that the protective effects of recruitment could be applicable to lung injury that is not caused by increased tidal stretch.

Additional specific lines of evidence exist. Inflation of a lung graft before reimplantation, as opposed to main-

tenance of the lung in a deflated state, confers increased viability.[161–163] The importance of inflation in lung protection has been confirmed in *in vivo*[162,163] and *ex vivo*[161] models and may be mediated either *via* reduction in pulmonary vascular resistance[161] (potentially decreasing endovascular shear injury) or through prevention of surfactant inactivation.[163] Finally, early application of mechanical ventilation may, through maintenance of lung volume (FRC), reduce mortality in experimental porcine sepsis[164] and in experimental hemorrhagic shock.[165]

Detection of Atelectasis

Atelectasis is usually suspected when alterations in lung physiology consistent with the development of atelectasis (*e.g.*, decreased compliance, impaired oxygenation) occur in a setting where atelectasis is likely. However, confirmation of atelectasis is possible through a variety of means.

Conventional Chest Radiography. Lobar or segmental atelectasis is classically represented as opacification of the lobe or lobar segment in question. General signs of atelectasis relate to volume loss. The most direct and reliable sign is the displacement of the interlobar fissure. Other signs of volume loss, such as increase of the hemidiaphragm and mediastinal shift, are maximal nearest the point of volume loss. Compensatory overinflation of the remaining aerated segments in the affected lobe is present, and the collapsed portion of the lung is of increased opacity and often triangular in at least one projection.[166] For example, when atelectasis results from proximal bronchial occlusion, an obstruction may be identifiable in the proximal bronchial tree, beyond which the tree is not aerated. If atelectasis results from absorption, the features are similar to consolidation, where the atelectatic lung parenchyma is opacified, and contrasts with the patent bronchial airway.

In addition to airway characteristics, other features of atelectasis are important. The "silhouette" sign allows identification of the lobe or segment of the lung that is affected. It is based on the principle that apposition of densely atelectatic lung with an additional contiguous structure, such as the diaphragm or the heart, results in obliteration of the boundary between the lung and the adjacent structure. For example, opacification of part of an atelectatic lung in conjunction with obliteration of the ipsilateral hemidiaphragm suggests lower lobar atelectasis; in contrast, preservation of the hemidiaphragm indicates that the ipsilateral lower lobe is not atelectatic.

A cardinal characteristic of atelectasis is volume loss of the affected lobe. This is associated with secondary changes in adjacent structures, in an attempt to "fill the gap" created by the loss of lung volume, and results in alterations including shift of the mediastinum or the hilum towards the affected area, elevation of the ipsilateral hemidiaphragm, and secondary (or "compensatory") emphysema in the adjacent nonatelectatic lung.

There is no doubt that conventional chest radiographs can reveal collapse in a segmental or lobar distribution. However, the ability of chest radiographs to detect atelectasis that occurs during general anesthesia or during mechanical ventilation of recumbent critically ill patients is less certain.[167]

Computed Tomography. Computed tomography is emerging as the preferred method for imaging the lung because of the widespread availability, resolution, high signal/noise ratio for lung tissue, and speed. From conventional CT images, it is possible to measure whole and regional lung volumes, distribution of lung aeration, and recruitment behavior under various clinical conditions and interventions.[168] In the 1980s, atelectasis was shown by CT in anesthetized patients.[5,169]

Since then, atelectasis has been studied extensively. Atelectasis on a CT scan has been defined as pixels with attenuation values of −100 to +100 Hounsfield units.[3] Hounsfield units quantify attenuation or density seen on CT. In this study, Lundquist *et al.*[3] studied patients undergoing elective abdominal surgery with CT of the thorax during anesthesia. Attenuation values in histograms of the lung and atelectasis were studied using two methods of calculating the atelectatic area. On the basis of the CT findings, atelectasis occurs in the most dependent parts of the lungs and occurs in almost 90% of patients who are anesthetized. The extent of the atelectasis in the dependent regions can be reduced by PEEP.[5]

The lung in ARDS is characterized by a marked increase in lung tissue and a massive loss of aeration.[170] Gattinoni *et al.*[40,41,171,172] have extensively investigated the distribution of tidal volume and recruitment in patients with ARDS using CT scans. They concluded that PEEP makes the gas distribution more homogenous in patients with ARDS, stretching the upper levels and recruiting the lower ones, and thereby reduces the atelectatic tissue in dependent regions. Rouby[173] has assessed PEEP-induced lung overdistension using CT. Rouby determined the threshold to differentiate PEEP-induced alveolar recruitment from PEEP-induced lung overdistension. The threshold of 900 Hounsfield units allows a reliable determination of PEEP-induced alveolar overdistension. A number of human studies have clearly reported the simultaneous onset of alveolar recruitment and lung overinflation in patients receiving PEEP levels of 10 and 20 cm H_2O.[174–177] These recent approaches have important implications in the diagnosis as well as the management of atelectasis because they point clearly to the propensity for injurious regional overinflation occurring as a result of efforts to reverse atelectasis (*e.g.*, increased PEEP, recruitment maneuvers) in the setting of ARDS.

Magnetic Resonance Imaging. Magnetic resonance imaging allows three-dimensional imaging without the

use of ionizing radiation. Unfortunately, the lung is not well suited to magnetic resonance imaging. On spin-echo images in healthy subjects, little signal is obtained from lung parenchyma. Areas of consolidation and masses can be identified, but the degree to which they can be differentiated has yet to be fully established. This technique has been used in preterm neonates to study pulmonary dysfunction.[178] The authors compared lung water content and distribution between preterm and term infants and concluded that lung water content is higher in preterm infants, consistent with dependent atelectasis.[178] Xenon-enhanced CT is a method for noninvasive measurement of regional pulmonary ventilation, determined from the wash-in and wash-out rates of the radiodense, nonradioactive xenon gas, measured by serial CT scans.[179] This may provide a valuable tool for noninvasive measurement of regional lung function and atelectasis in the future. Although magnetic resonance has several advantages over CT (*e.g.*, contrast material is not necessary, possibility for multiple planar imaging), it is not apparent that magnetic resonance offers any distinct advantages over CT in the evaluation of atelectasis at the current time.[180]

Ultrasonography. Although more commonly used in assessment of pleural collections or in the context of echocardiography, thoracic ultrasonography has been used in assessment of lung parenchyma.[181] It has been suggested as a useful aid to the rapid diagnosis of atelectasis[182] and, in the context of ARDS, seems to be useful for the assessment of regional consolidation.[183] Recently, use of a specific ultrasonographic detection of the cardiac impulse, termed the *lung pulse*, has been reported to be a highly sensitive early indicator of the presence of atelectasis.[184] The use of ultrasonography may offer significant advantages for patients in the operating room or in the intensive care unit in terms of rapidity and ease of examination, without the disadvantages of patient transport and radiation exposure. However, its role in clinical practice remains to be determined.[185]

Intravital Microscopy. Intravital microscopy applied to the pleural surface enables experimental visualization of atelectasis and examination of its role in the pathogenesis of lung injury (see Direct Visualization of Atelectasis).[31] In addition to access issues, there are limitations to interpretation,[32] including the fact that visualization is restricted to lung tissue that is immediately below the pleural surface, with deeper parenchyma beyond the range of the instrument.

Cytokine Profile. There are other methods of detecting atelectasis in the preclinical setting, including lung lavage levels of cytokines.[125] Tremblay *et al.*[125] examined the effect of ventilation strategy on lung inflammatory mediators in the presence and absence of lung injury using an isolated rat model. Lung lavage cytokine concentrations were greatest in the groups ventilated without PEEP in both the control intravenous lipopolysaccharide–treated groups. Zero PEEP in combination with high volume ventilation had a synergistic effect on cytokine concentrations. This finding that atelectasis worsens stretch-induced lung injury resulting in increased lung and systemic cytokine concentrations was confirmed by Chiumello *et al.*[126] However, it is important to note that experimental atelectasis—even when lethal—is not associated with increased cytokines in the absence of high tidal volumes.[126] The measurement of lung lavage levels of cytokines in the clinical situation is impractical.

Prevention or Reversal of Atelectasis

The factors important in the prevention or reversal of atelectasis differ considerably, depending on whether the lungs are injured or uninjured. Because of the adverse pathophysiology associated with the development of atelectasis and the preclinical findings that recruitment of atelectatic lung may reduce the propensity toward subsequent injury,[161–163] it is important to examine how recruitment may be achieved.

Prevention or Reversal of Atelectasis in Healthy Lungs. Progressive pulmonary atelectasis (and the associated impairment of oxygenation) may occur during constant ventilation whenever periodic hyperinflation is lacking; it is reversible by passive hyperinflation (*i.e.*, three successive inflations: first, with a pressure of 20 cm H_2O for 10 s; second, with a pressure of 30 cm H_2O for 15 s; and third, with a pressure of 40 cm H_2O sustained for 15 s).[2] This was taken as evidence that atelectatic alveoli are reopened by the deep breaths, and that conclusion was supported by the reduction in pulmonary compliance occurring during ventilation and the return of compliance to control values after hyperinflation.

Nunn *et al.*[107] examined arterial oxygenation in patients during routine anesthesia. They found that arterial oxygenation increased when a pressure of 40 cm H_2O was maintained for 40 s; lower pressures, even with modest levels of PEEP, were not effective.[107] A more recent study by Tusman *et al.*[28] examined an "alveolar recruitment" strategy in healthy lungs during general anesthesia. The authors hypothesized that because atelectasis occurs during general anesthesia, an initial increase in pressure would be required to open collapsed alveoli, and if this inspiratory recruitment was combined with sufficient end-expiratory pressure, alveoli would remain open. They allocated patients to one of three groups: no PEEP; an initial control period without PEEP followed by PEEP of 5 cm H_2O; and PEEP of 15 cm H_2O with high tidal volume (18 ml/kg, or peak inspiratory pressure 40 cm H_2O) maintained for 10 breaths, followed by stepwise reduction of PEEP and tidal volume. The third group, receiving the alveolar recruitment strategy, had a significant increase in arterial oxygenation during general anesthesia. Treatment with PEEP of 5 cm

H_2O alone did not have the same effect on oxygenation. The authors concluded that high initial pressures are needed to overcome the anesthesia-induced collapse and that PEEP of 5 cm or more is required to prevent the newly recruited alveoli from collapsing. In addition, there was no evidence of barotrauma or pulmonary complications as a result of the high initial airway pressures.[28]

Prevention or Reversal of Atelectasis in Injured Lungs. It has become evident that a number of ventilatory strategies can produce or worsen lung injury.[157] The use of large tidal volumes,[153] high peak airway pressures,[186] and end-expiratory alveolar collapse with cyclic reopening[120] have all been proposed as deleterious when ventilating injured lungs. Several studies have shown that lung injury secondary to ventilation with large tidal volume is attenuated if end-expiratory volume is maintained by the use of PEEP.[118,126,152] In addition, ventilation at low FRC worsens lung injury, possibly by repeated small airway closure, and PEEP markedly attenuates this injury.[120,126] Therefore, recruitment of atelectatic lung reduces the injurious effects of mechanical ventilation with both low and high tidal volumes and protects against development of ventilator-induced lung injury.

The "open-lung" approach to ventilating patients with ARDS consists of a recruitment maneuver with high sustained airway pressures to open atelectatic alveoli followed by application of PEEP to maintain alveolar patency. This approach was among the interventions performed in a study that showed an improvement in oxygenation and reduced mortality in patients with ARDS.[159] The researchers calculated the inflection point from a pressure–volume curve (corresponding to an upward shift in the slope of the curve), and PEEP was preset at 2 cm H_2O above the inflection point in the protective ventilation group. If the inflection point could not be determined on the pressure–volume curve, PEEP of 16 cm H_2O was used. Recruiting maneuvers were frequently used and consisted of continuous positive airway pressures of 35–40 cm H_2O for 40 s followed by a return to previous PEEP levels.[159]

Gattinoni *et al.*[40] also showed that with increasing PEEP from 0 to 20 cm H_2O, gas distribution became more homogenous in sedated and paralyzed patients with ARDS and reduced the reopening–collapsing tissue. Suter *et al.*[187] suggested that the optimum end-expiratory pressure in patients with acute respiratory failure was the PEEP level that resulted in the greatest total static compliance. This maximum compliance produced by PEEP resulted in optimum overall cardiopulmonary interaction to ensure maximal global oxygen delivery. In patients with low FRC values at zero end-expiratory pressure, maximum oxygen transport was achieved at higher levels of PEEP than in patients with normal or high FRC values.

The timing of recruitment maneuvers was examined by Grasso *et al.*[188] in patients with ARDS who were ventilated with a lung-protective ventilatory strategy (low tidal volumes of 6 ml/kg). They defined a recruiting maneuver as continuous positive airway pressure of 40 cm H_2O for 40 s. Measurements of Pao_2/Fio_2 ratio, volume–pressure curve, and respiratory mechanics were obtained 2 and 20 min after application of a recruiting maneuver. The authors classified the patients as responders and nonresponders. Recruitment maneuvers increased the Pao_2/Fio_2 ratio significantly more in responders—who had been ventilated for a longer period of time—than in nonresponders. The authors concluded that application of recruiting maneuvers improves oxygenation only in patients with early ARDS who do not have impairment of chest wall mechanics and with a large potential for recruitment.[188]

Treating Atelectasis in the Postoperative Period. Postoperative pulmonary complications are increasingly recognized as an important perianesthetic issue.[146] Determination of the frequency and clinical impact of postoperative pulmonary complications is hampered by the lack of a uniform definition of a postoperative pulmonary complication among studies. Included in the definition are pneumonia, severe respiratory failure (usually defined as the need for mechanical ventilation), bronchospasm, and atelectasis (often not defined). Most studies referring to postoperative atelectasis do not directly measure FRC.

Reversing or preventing atelectasis is possible in many patients in the perioperative period[146,189] and is of proven benefit in preventing pulmonary complications.[146] Techniques or devices that either encourage or force patients to inspire deeply are of most clinical importance.[190–192] The aim is to produce a large and sustained increase in transpulmonary pressure distending the lung and reexpanding collapsed lung units. Several methods have been studied, including intermittent positive-pressure breathing, deep-breathing exercises, incentive spirometry, and chest physiotherapy. A meta-analysis suggests that all regimens studied are equally efficacious in reducing the frequency of postoperative pulmonary complications after upper abdominal surgery.[193]

The beneficial effect on gas exchange of a simple posture change from supine to seated has been demonstrated, both in healthy subjects[90] and after upper abdominal surgery.[91] Identification of FRC as the single most important lung volume in postoperative patients provides a specific goal of therapy.[189] FRC can be measured by a number of techniques. Gas dilution techniques (*e.g.*, helium equilibration, nitrogen washout) have been used.[93,194] One disadvantage of these methods is that the tracer gas may not mix with all gas in the lungs because of occluded airways; this source of error can be overcome by using body plethysmography.

Finally, early work reported the use of thoracic or sternal traction[195,196] as well as the use of intravenous aminophylline[197] as successful treatments of atelectasis in a number of case reports, but given the impracticalities and adverse effects of these therapies, they have no clinical application today.

Recruitment of Atelectatic Lung Is Easier to Achieve in the Absence of Injury. Although the pressure–volume relation in ARDS—and the ability to recruit lung—may depend on the etiology,[171] it is always easier to recruit lung when injury is absent or mild, compared with when significant injury is established.[42,188,198] This is because the uninjured lung is highly compliant, and its inflection point (opening pressure) on the inflation pressure–volume curve is either low or not detectable. In contrast, the inflection point is significantly greater when injury has been established; in fact, elevation of the inflection point increases in proportion to the extent of injury.[194] Such impaired compliance (and difficulty with recruitment) has a pathophysiologic basis in established injury. The causes include surfactant dysfunction due to impairment of large aggregate formation,[199] direct inhibition by plasma proteins that have exudated into the air space,[200–202] and the progression of cellular infiltration and edema in the pulmonary interstitium and alveoli.[203,204] Increases in pulmonary vascular resistance, which characteristically parallel the progression of the lung injury,[205] may decrease lung compliance further.[206] Finally, when recruitment has been achieved, less airway pressure is required to prevent derecruitment than is required to achieve recruitment.[207]

Summary and Future Implications

In the future, clinicians may be able to predict the subsequent development of ALI. In an optimal setting, this would be after recognition of the identifiable etiology and before its initiation (*e.g.*, before major surgery or before reperfusion during transplantation surgery). Alternatively, early institution of prophylactic recruitment after identification of an etiologic event, particularly when associated with a worrisome predictive stratification (*e.g.*, pancreatitis with elevated cytokine profile), would be ideal. The eventual prospect of predicting (or early detection of) ALI and ARDS makes "prophylactic lung recruitment" (to maintain or recover normal resting lung volume) increasingly tenable, and if validated by clinical studies, this could become integrated into the perioperative care of patients who are at risk of developing critical illness.

Atelectasis occurs in almost all patients undergoing general anesthesia. We have reviewed the causes, effects, nature, identification, and prevention of atelectasis in the perioperative period. Unless restoration of FRC takes place, atelectasis can have detrimental consequences. Current literature indicates that intraoperative and postoperative lung recruitment improves intermediate physiologic outcomes (*e.g.*, oxygenation, work of breathing); however, the benefits might have more significant implications for lung injury and ARDS. Low stretch ventilation can achieve, at best, attenuation of stretch-induced injury; at worst, it can cause loss of lung volume, potentially contributing to or worsening injury. Prophylactic recruitment however, could reduce or prevent lung injury that results from a variety of primary etiologies, as well as reducing injury resulting from mechanical stretch. If proven in the clinical setting, this approach could reduce the development of critical illness in many general medical and surgical patient populations.

Note Added in Proof

Since acceptance of this manuscript, Squadrone *et al*. have demonstrated that reversing atelectasis with noninvasive continuous positive airway pressure in high-risk postoperative patients who are hypoxic results in reduced need for reintubation and a lower incidence of pneumonia and sepsis (Squadrone V, Coha M, Cerutti E, Schellino MM, Biolino P, Occella P, Belloni G, Vilianis G, Fiore G, Cavallo F, Ranieri VM; Piedmont Intensive Care Units Network [PICUN]: Continuous positive airway pressure for treatment of postoperative hypoxemia: A randomized controlled trial. JAMA 2005; 293:589–95).

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