Oxygenation is impaired in almost all subjects during anaesthesia, and hypoxaemia for shorter or longer periods is a common finding. Moreover, postoperative lung complications occur in 3–4% after elective surgery, and up to 20% in emergency operations. Rapid collapse of alveoli on induction of anaesthesia and more widespread closure of airways seem to explain the oxygenation impairment and may also contribute to postoperative pulmonary infection. Causative mechanisms to atelectasis and airway closure seem to be loss of respiratory muscle tone and gas resorption. Avoiding high inspired oxygen fractions during both induction and maintenance of anaesthesia prevents or reduces atelectasis, while intermittent ‘vital capacity’ manoeuvres, recruit atelectatic lung regions.

This review will examine the functional causes of impaired oxygenation and increase in venous admixture (shunt and perfusion of regions in excess of their ventilation, so called ‘low V\textsubscript{A}/Q regions’) that is regularly observed during anaesthesia. The morphological correlates (atelectasis and airway closure) to the functional impairment will then be discussed. Finally, measures that can be taken to prevent alveolar collapse and closure of airways are listed and their advantages and disadvantages are discussed.

**Oxygenation and venous admixture**

Calculation of the ‘shunt’ from arterial, mixed venous and alveolar PO\textsubscript{2} according to the ‘standard’ or Berggren shunt equation (Berggren, 1942) has shown that it is increased from 1 to 2% in the awake, healthy subject, to 8–10% in the anaesthetized patient (Nunn, 1993b). The standard shunt equation is based on the assumption of two populations of alveoli, those that are ‘ideally’ perfused in proportion to their ventilation and those that are perfused but not at all ventilated (the shunt). However, the lung does not contain two populations of alveoli only. There are a number of units with less ventilation than perfusion, with low V\textsubscript{A}/Q ratios (‘low V\textsubscript{A}/Q regions’), as well as units that are ventilated in excess of their perfusion (‘high V\textsubscript{A}/Q regions’). Perfusion of low V\textsubscript{A}/Q regions will also impede the oxygenation of blood and to a varying extent be included in the calculated ‘shunt’. The shunt, as measured by the standard oxygen technique, should therefore rather be called ‘venous admixture’ (Nunn, 1993b) (see Fig. 1).
A good correspondence between venous admixture and the sum of 'true' shunt and perfusion of 'low $V_a/Q$ regions' was seen in a study on 45 anaesthetized subjects (Gunnarsson et al., 1991a,b) (Fig. 1).

The magnitude of venous admixture will depend on the inspired oxygen fraction. During room air breathing the influence of low $V_a/Q$ regions on the calculated venous admixture will be the highest. If the subject is breathing, or is ventilated, with pure oxygen the influence of low $V_a/Q$ regions will be eliminated. This is because the low $V_a/Q$ units will have almost as high $P_aO_2$ as the more ventilated units, and the end-capillary blood will be oxygenated to almost the full extent (West, 1977). The minor difference, compared with normal lung units, is caused by the higher PCO$_2$ in the alveoli with low $V_a/Q$ ratios. Thus, venous admixture equals true shunt (perfusion of non-ventilated alveoli) during oxygen breathing. This fact has also been used for the recording of 'true' shunt. However, low $V_a/Q$ regions can be transformed to true shunt regions during oxygen breathing because of adsorption of gas so that atelectasis is produced. Alveoli become unstable at a certain inspired ventilation–perfusion ratio ($V_aU/Q$) that varies with the inspired oxygen fraction. Dantzker et al. (1975) made calculations and demonstrated that during the breathing of 100% $O_2$ alveoli can collapse at an inspired $V_a/Q$ of 0.08. This means that units that are not far from the normal range of $V_a/Q$ ratios can collapse during oxygen breathing! Thus, true shunt can be increased by the manoeuvre used for measuring it. Moreover, the calculation of shunt during oxygen breathing requires that the blood gas analyser is carefully calibrated for high arterial oxygen tensions. This may be more difficult than is thought of. Recording of a high $P_aO_2$ after standard calibration at normal $PO_2$ may result in underestimation of $P_aO_2$ and the calculation of an erroneously large shunt. Other methods, however, are available to measure shunt, as discussed below.

A more detailed picture of the distribution of $V_a/Q$ ratios can be obtained by the multiple inert gas elimination technique (Wagner et al., 1974). This technique is based on the infusion of a number of inert gases (usually six) in a vein and the calculations of the retention (arterial/mixed venous concentration ratio) and excretion (mixed expired/mixed venous concentration ratio) of each gas. The ratios, together with the measured solubilities of the inert gases, enable the construction of a virtually continuous distribution of ventilation and perfusion against $V_a/Q$ ratios.

When this technique is applied to the anaesthesia setting, one major finding is an increased dispersion of $V_a/Q$ with the appearance of low $V_a/Q$ ratios. Thus, there is impaired matching of ventilation and perfusion during anaesthesia with regions that are poorly ventilated in relation to their perfusion. Another major observation is the appearance of true shunt of around 8%, but frequently exceeding 20% (Rehder et al., 1979; Prutow et al., 1982; Bindslev et al., 1981). Thus, there seem to be at least two major functional causes of impaired oxygenation during anaesthesia, low $V_a/Q$ and true shunt. The morphological correlates will be discussed in the following paragraphs.

**Atelectasis**

In their classic paper, Bendixen et al. (1963) proposed: ‘a concept of atelectasis’ as a cause of impaired oxygenation during anaesthesia. They observed a successive decrease in compliance of the respiratory system and a similar successive decrease in arterial oxygenation in both anaesthetized humans and in experimental animals. This was interpreted as formation of atelectasis. However, other research groups who were unable to reproduce their findings and noticed a more prompt fall in compliance and PaO$_2$ on induction of anaesthesia. Moreover, atelectasis could not be demonstrated on conventional chest X-ray. In the mid-1980s new observations were made that may explain the altered function of the lung during anaesthesia. Using computed tomography (CT) with transverse exposures of the chest, Brismar et al. (1985) demonstrated prompt development of densities in dependent regions of both lungs during anaesthesia. Similar densities had previously been observed in anaesthetized infants (Damgaard & Qvist, 1980). Morphological studies of these densities in various animals supported the diagnosis of atelectasis (Hedenstierna et al., 1989). An example of atelectasis as seen on a CT scan is shown in Fig. 2.

Atelectasis appears in around 90% of all patients who are anaesthetized (Gunnarsson et al., 1991a). It is seen during both spontaneous breathing and after muscle paralysis, whether intravenous or inhalational anaesthetics are used (Strandberg et al., 1986). The atelectatic area on a CT cut near the diaphragm is around 5–6% of the total lung area but can easily exceed
It should also be remembered that the amount of tissue that is collapsed is even larger, the atelectatic area comprising mainly lung tissue whereas the aerated lung consists only of 20–40% tissue, the rest being air. Thus, 15–20% of the lung is regularly collapsed at the base of the lung during uneventful anaesthesia, before any surgery has been performed! Abdominal surgery does not add much to atelectasis, but it can remain for several days in the postoperative period (Lindberg et al., 1992). It is rather likely that it is a focus of infection and that it can contribute to pulmonary complications. However, this has to be proved, or disproved, in larger studies. It may also be mentioned that after thoracic surgery and cardio-pulmonary bypass, more than 50% of the lung can be collapsed still several hours after surgery (Tenling et al., 1998). The amount of atelectasis decreases towards the apex, that is mostly spared (fully aerated). A three-dimensional reconstruction of the lung and atelectasis can be seen in Fig 3.

A comparison of the dynamics of atelectasis formation during nitrous oxide/oxygen ventilation with that of ventilating with nitrogen/oxygen (60/40% for both) during halothane anaesthesia resulted in some unexpected findings. Thus, no difference was observed between patients on the nitrogen (N2) and N2O regimes (Gunnarsson et al., 1989). This was at variance with established modelling, that suggests that nitrous oxide (N2O) should speed up the formation of atelectasis because of faster N2O absorption in poorly or non-ventilated lung regions (Dantzker et al., 1975; Joyce et al., 1993). However, Joyce & Williams (1999) critically reviewed the old ‘truths’. They noticed that they were based on steady, non-changing mixed venous gas tensions, an assumption that is not true during induction of anaesthesia. By adding a ‘peripheral tissue’ compartment they arrived at a more realistic dynamic model. With this model, there was no longer a difference in the formation of atelectasis whether N2O or N2 was used in addition to O2, a model thus in line with the results from the clinical experiments!

There is a weak correlation between the size of atelectasis and body weight or body mass index (Strandberg et al., 1987), obese patients showing larger atelectatic areas than lean patients. While this was expected, it came as a surprise that atelectasis is independent of age, with children and young people showing as
much atelectasis as elderly patients (Gunnarsson et al., 1991a). Another unexpected observation was that patients with chronic obstructive lung disease showed less or even no atelectasis during the 45 min of anesthesia when they were studied (Gunnarsson et al., 1991b). The mechanism that prevents the lung from collapse is not clear. It may be airway closure before alveolar collapse, or it may be an altered balance between the chest wall and the lung that counters a decrease in the lung dimensions.

There is a good correlation between the amount of atelectasis and pulmonary shunt as measured by the multiple inert gas elimination technique. A regression equation, based on a total of 45 patients studied during inhalational anesthesia, has been calculated as: shunt \(= 0.8 \times \text{atelectasis} + 1.7 \ (r = 0.81, P<0.01)\), with atelectasis in percentage of the lung area just above the diaphragm on CT scan, and shunt in percentage of cardiac output. Interestingly, shunt did not increase with age (Gunnarsson et al., 1991a). By combining CT scanning and single photon emission CT, the distribution of shunt and its location within the atelectatic area was confirmed (Tokics et al., 1996) (Fig. 4).

### Airway closure

In addition to atelectasis, intermittent closure of airways can be expected to reduce the ventilation of dependent lung regions. Such lung regions may then become ‘low \(V_{A}/Q\)’ units (i.e. regions with a low ventilation/perfusion ratio) if perfusion is maintained or not reduced to the same extent as ventilation. Airway closure increases with age (Leblanc et al., 1970) as does the perfusion to ‘low \(V_{A}/Q\)’ regions (Gunnarsson et al., 1991a).

As anesthesia causes a functional residual capacity (FRC) reduction by 0.4–0.5 l, (Wahba, 1991), it may be anticipated that airway closure becomes even more prominent in the anesthetized subject. There is accumulating evidence that this is the case (Hedenstierna et al., 1976; Juno et al., 1978; Dueck et al., 1988; Rothen et al., 1998). The reduced ventilation in the lower half of the lung, just above the atelectatic region, that can be seen in Fig 4 is thus reasonably explained by airway closure. It can also be seen that ventilation is smaller than perfusion, causing ‘low \(V_{A}/Q\)’ regions. These contribute to impaired oxygenation during anesthesia.

As much as 74% of the impaired arterial oxygenation can be explained by atelectasis and airway closure taken together, according to the equation (Rothen et al., 1998): \(P_{a}O_{2} (\text{mmHg}) = 218 - 22 \ln \text{atelectasis} (\text{cm}^2) - 0.06 \ (\text{CV-ERV})\) (ml); \(r: 0.86, P<0.001\); where (CV-ERV) indicates the amount of airway closure occurring above FRC, and CV: closing volume, ERV: expiratory reserve volume. A simple three-compartment lung model can thus be constructed to explain oxygenation impairment during anesthesia. The model consists of one compartment with ‘normal’ ventilation and perfusion, one compartment with airway closure that impedes ventilation and a final compartment of collapsed lung with no ventilation at all. This is shown in Fig. 5 together with the subsequent impact on the \(V_{A}/Q\) distribution.

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**Figure 4** Transverse computed tomography scan with atelectasis visible in the dependent parts of both lungs (left panel) and corresponding vertical distributions of ventilation and lung blood flow by isotope technique (SPECT) (right panel) in an anesthetized subject. Note that ventilation is distributed preferentially to upper lung regions, contrary to what is normally observed in the waking subject. There is also decreasing ventilation in the lower part and the complete cessation of ventilation in the bottom, corresponding to the atelectatic area. Perfusion, on the other hand, increases down the lung, except for the bottom-most region where a decrease can be observed (so-called zone IV).

**Figure 5** Three compartment lung model (to the left) and the corresponding \(V_{A}/Q\) distribution (to the right) during anesthesia. The lung model consists of one well-ventilated and perfused compartment (A), causing the major \(V_{A}/Q\) mode that is centred upon a \(V_{A}/Q\) ratio of approximately 1, of another compartment further down the lung that has an impeded ventilation because of intermittent airway closure (compartment B), producing a low \(V_{A}/Q\) mode within ratios of 0.01 – 0.1, and, finally, in the bottom of the lung a compartment with collapse of alveoli (atelectasis) causing shunt (\(V_{A}/Q\) ratio of = 0)(compartment C).
Mechanisms of atelectasis formation during anaesthesia

Three possible mechanisms may cause atelectasis (Rahn & Farhi, 1963):
- Compression
- Absorption of gas behind occluded airways
- Loss of surfactant.

Compression atelectasis

The diaphragm separates two spaces with different pressures as well as vertical pressure gradients. Thus, the end-expiratory intrathoracic pressure is normally lower than the abdominal pressure. The vertical pressure gradient in the pleural space of the awake subject is 0.2–0.4 cm H2O per cm (see above) whereas this gradient approximates 1 cm H2O per cm in the abdomen. If the diaphragm no longer acts as a rigid wall between these two spaces, the abdominal pressure will be transmitted into the thoracic cavity, increasing in particular the pleural pressure in dependent lung regions. This could result in compression atelectasis. Indirect evidence of this is the fact that no atelectasis developed during ketamine anaesthesia (Tokics et al., 1987b), a drug known to maintain respiratory muscle function. More direct support for the role of the diaphragm is shown by tensing the diaphragm by phrenic nerve stimulation that reduces the amount of atelectasis at iso-volumic conditions (Hedenstierna et al., 1994).

Gas resorption

The relationship between the reduction in FRC and atelectasis development is frequently put forward. However, chest strapping, resulting in a reduction of FRC by about 0.7 l, did not produce any atelectasis (as assessed by CT) during a 20-min period of spontaneously breathing air (Tokics et al., 1988). However, short periods of breathing 100% oxygen near residual volume may cause atelectasis (Burger & Macklem, 1966). Thus an increased inspiratory fraction of oxygen may promote atelectasis formation if there is a concomitant reduction in FRC.

Surfactant

The function of surfactant may be impeded by anaesthesia (Wollmer et al., 1990). Furthermore, a lack of intermittent deep breaths, as is usually the case during mechanical ventilation, may result in a decreased content of active forms of alveolar surfactant (Otis et al., 1993). A decreased function of surfactant results in reduced alveolar stability, may contribute to liquid bridging in the airway lumen, and thereby cause airway closure (Oyarzun et al., 1991). However, little is known about the details of these mechanisms.

Prevention of atelectasis during anaesthesia

There are several interventions that can help prevent atelectasis or even reopen collapsed tissue. Some of these have already been introduced in the paragraph on mechanisms of atelectasis. The interventions that will be discussed are:
- Positive end-expiratory pressure (PEEP)
- Maintenance or restoration of respiratory muscle tone
- Recruitment manoeuvres
- Minimization of pulmonary gas resorption.

Positive end-expiratory pressure

The application of 10 cm H2O PEEP has been tested in several studies and will consistently reopen collapsed lung tissue. This is more likely an effect of increased inspiratory airway pressure than of PEEP per se (Brismar et al., 1985; Tokics et al., 1987a). However, some atelectasis persists in most patients. Whether further increase in the PEEP level reopens this tissue was not analysed in these studies. PEEP, however, appears not to be the ideal procedure. First, shunt is not reduced proportionately, and arterial oxygenation may not improve significantly. Hewlett et al. (1974) warned of the ‘indiscriminate use of PEEP in routine anaesthesia’. The persistence of shunt may be explained by a redistribution of blood flow towards more dependent parts of the lungs when intrathoracic pressure is increased by PEEP. Under such circumstances, any persisting atelectasis in the bottom of the lung receives a larger share of the pulmonary blood flow than without PEEP (West et al., 1964). Also, an increased intrathoracic pressure will impede venous return and decrease cardiac output. This results in a lower venous oxygen tension for a given oxygen uptake and reduces arterial oxygen tension (West, 1977). Secondly, the lung re-collapses rapidly after discontinuation of PEEP. Within 1 min after cessation of PEEP the collapse is as large as it was before the application of PEEP (Brismar et al., 1985).

Maintenance of muscle tone

The use of an anaesthetic that allows maintenance of respiratory muscle tone will prevent formation of atelectasis. Ketamine does not impair muscle tone and does not cause atelectasis. This is the only anaesthetic so far tested that does not cause collapse. However, if muscle relaxation is required, atelectasis will appear as with other anaesthetics (Tokics et al., 1987b).

Another attempt is to restore respiratory muscle tone by pacing of the diaphragm. This was tested by applying phrenic nerve stimulation that did reduce the atelectatic area (Hedenstierna et al., 1994). The effect, however, was small, and this technique is certainly too complicated to be used as a routine during anaesthesia and surgery.

Recruitment manoeuvres

The use of a sigh manoeuvre, or a double tidal volume, has been advocated to reopen any collapsed lung tissue (Nunn,
However, atelectasis is not decreased by a tidal volume, or by a sigh up to an airway pressure of 20 cm H₂O (Rothen et al., 1993). Not until an airway pressure of 30 cm H₂O is reached does the atelectasis decrease to approximately half the initial size. For a complete reopening of all collapsed lung tissue, an inflation pressure of 40 cm H₂O is required (Rothen et al., 1993). Such a large inflation and subsequent expiration down to −20 cm H₂O corresponds to a vital capacity measured during spontaneous breathing with the patient awake.

As the vital capacity manoeuvre, as described above, may result in adverse cardiovascular events, the dynamics in resolving atelectasis during such a procedure was analysed (Rothen et al., 1999). It was found that in adults with healthy lungs, inflation of the lungs to +40 cm H₂O maintained for no more than 7–8 s may re-expand all previously collapsed lung tissue (Fig. 6).

**Minimizing gas resorption**

Ventilation of the lungs with pure oxygen after a vital capacity manoeuvre that had reopened previously collapsed lung tissue, resulted in a rapid reappearance of atelectasis (Rothen et al., 1995a). If 40% O₂ in nitrogen is used for ventilation of the lungs, atelectasis reappeared slowly, and 40 min after the vital capacity manoeuvre only 20% of the initial atelectasis had reappeared. Thus, ventilation during anaesthesia should be carried out with a moderate fraction of inspired oxygen (FIO₂, e.g., 0.3–0.4) and be increased only if arterial oxygenation is compromised.

The striking effects of oxygen during anaesthesia raised the question whether the preoxygenation during induction of anaesthesia had an effect on atelectasis formation. The breathing of 100% O₂, just for a few minutes before and during the commencement of anaesthesia, increases the safety margin in the event of a difficult intubation of the airway with prolonged apnoea. However, there turned out to be a prize for it. Avoidance of the preoxygenation procedure (ventilation with 30% O₂) eliminated atelectasis formation during the induction and subsequent anaesthesia (Rothen et al., 1995b). In a recently finished study, 12 patients were breathing 100% O₂ during the induction of anaesthesia, another 12 were breathing 80% O₂ and still another 12 breathed 60% O₂ (Edmark et al., 2003). Atelectasis appeared in all patients on 100% O₂ and was much smaller in the 80% O₂ group, and almost absent in the 60% O₂ group (Fig. 7). The findings call for a re-evaluation of the present standard preoxygenation procedures for inducing anaesthesia.

In summary, rapid collapse of alveoli on induction of anaesthesia and more widespread closure of airways seem to explain oxygenation impairment during anaesthesia. They may also contribute to postoperative pulmonary infection, the causative mechanisms of which seem to be loss of respiratory muscle tone and gas resorption. Avoiding high inspired oxygen fractions during both induction and maintenance of anaesthesia prevents or reduces atelectasis, while intermittent ‘vital capacity’ manoeuvres, recruit atelectatic lung regions.

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