Ventilation-perfusion relationships during anaesthesia

Göran Hedenstierna

Anaesthesia is given on approximately 60 000–70 000 occasions per million inhabitants in Western Europe and Scandinavia with more than half of these being general anaesthetics.

It has been well known for about a century that the oxygenation of arterial blood is impaired during anaesthesia; as early as 1943 Maier and Courmand found that the oxygen saturation of arterial blood was reduced after thoracotomy. In 1958, after the introduction of the blood gas electrodes, Campbell and coworkers showed that anaesthesia was often associated with an increased alveolar-arterial oxygen tension difference. Sometimes life threatening hypoxaemia can develop. It is generally held that the impairment of arterial oxygenation during anaesthesia is more severe in older subjects. Obesity is associated with a decrease in the oxygenation of blood, and smokers show more gas exchange impairment than non-smokers. The impairment in arterial oxygenation has made it routine to increase the inspired oxygen fraction during anaesthesia to 0.3–0.4 during an uncomplicated procedure, and even higher during anaesthesia in obese, bronchitic, or elderly patients. Despite numerous studies the causes of impaired gas exchange during anaesthesia have remained unclear; it is not until the last decade that a better understanding of the underlying mechanisms have been elucidated. The application of two advanced techniques in anaesthesia accounts for most of our new insight into gas exchange impairment in the anaesthetised subject—the multiple inert gas elimination technique (MIGET) and computed tomographic scanning (CT). However, before proceeding with the findings made with these techniques a short review of proposed mechanisms for impaired gas exchange during anaesthesia is presented.

ABSORPTION ATELECTASIS

Bendixen and coworkers published their “concept of atelectasis” 30 years ago. They noticed successive decreases in lung compliance and arterial oxygen tension (Pao2) which returned towards normal after deep inflation of the lungs. The authors proposed slow development of absorption atelectasis. Other groups were unable to reproduce their results, however, but found a rapid decrease in compliance and arterial oxygen tension on induction of anaesthesia. Moreover, atelectasis could not be shown on conventional chest radiographs. Atelectasis was therefore considered to be an unlikely cause of impaired oxygenation during anaesthesia.

AIRWAY CLOSURE

In 1966 Milic-Emili and coworkers demonstrated airway closure in dependent lung regions during a deep expiration in awake, healthy volunteers. In view of the reduced functional residual capacity (FRC) during anaesthesia the question arose as to whether airway closure was the cause of impaired gas exchange. Don et al found that gas was trapped in the lungs during anaesthesia and that it could be released only by deep inflations. A few years later direct evidence of airway closure was shown. Conflicting reports have, however, been presented and varying correlations between the magnitude of airway closure and the degree of impaired arterial oxygenation have been reported. Airway closure is therefore unlikely to be a major contributor to the impaired gas exchange during anaesthesia although it may be a factor.

HYPOXIC PULMONARY VASCONSTRICTION

In 1946 von Euler and Liljestrand observed that hypoxia produced pulmonary vasoconstriction and some 20 years later Thilenius showed that inhalational anaesthetics attenuated hypoxic vasoconstriction. In later studies Sykes and coworkers showed that most inhalational anaesthetics attenuate hypoxic vasoconstriction. Bjertnaes, on the other hand, found that intravenous barbiturates did not reduce hypoxic vasoconstriction. Results vary, however, presumably because of confounding factors obscuring the hypoxic vasoconstriction response. It should also be stressed that attenuation of hypoxic vasoconstriction does not cause impairment of the gas exchange unless an underlying disturbance of lung function causing a lowered Pao2...
is present. Thus, release of hypoxic vasoconstriction by the anaesthetic agent augments an already existing impairment of gas exchange, but does not lead to disturbances in an otherwise normally functioning lung.

**GAS DISTRIBUTION**

Hulands et al.\(^{21}\) and Rehder et al.\(^{22,23}\) using either an isotope technique or nitrogen washout, found decreased ventilation of the dependent lung regions in anaesthetised spontaneously breathing individuals, and during muscle paralysis and mechanical ventilation. Hulands et al.\(^{21}\) also found a small increase in perfusion of dependent lung regions with a subsequent

**Figure 1** Distributions of VA/Q in a 43 year old man with no cardiopulmonary disease before elective surgery (A) when awake, (B) during enflurane anaesthesia spontaneously breathing through a face mask (non-intubated, non-paralysed), and (C) after endotracheal intubation and muscle paralysis with mechanical ventilation. Inspired oxygen fraction was 0.21 during the awake recording and 0.40 during anaesthesia. Note the good matching of ventilation and blood flow in the awake situation and the presence of only a small shunt. Anaesthesia and spontaneous breathing caused some widening of the VA/Q distribution, an increase in shunt and dead space ventilation. Intubation and muscle paralysis caused a slight widening of the VA/Q distribution and reduced dead space ventilation to about the same level as when awake. From Tokics et al.,\(^{34}\) previously unpublished figure.

**Figure 2** Distribution of VA/Q in a 62 year old woman with no cardiopulmonary disease before cholecystectomy (A) when awake, (B) during anaesthesia and paralysis with mechanical ventilation, and (C) after addition of a PEEP of 10 cm H\(_2\)O. Note the good matching of ventilation and blood flow when awake with almost no shunt, and the considerable VA/Q mismatch during anaesthesia as well as appearance of shunt. With PEEP, further widening of the VA/Q distribution was seen with the appearance of high VA/Q mode and an increased shunt. From Tokics et al.,\(^{34}\) previously unpublished figure.
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Mean (SD) ventilation-perfusion relationships in subjects with no cardiopulmonary disease (normal, n = 45) and patients with severe chronic obstructive pulmonary disease (COPD, n = 10), awake and during general anaesthesia and muscle paralysis

<table>
<thead>
<tr>
<th></th>
<th>QMEAN</th>
<th>log SDQ</th>
<th>VMEAN</th>
<th>log SDV</th>
<th>Shunt (VA/Q)</th>
<th>Dead space (% VD)</th>
<th>PaO, (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0.76</td>
<td>0.68</td>
<td>1.11</td>
<td>0.52</td>
<td>0.5 (1-0)</td>
<td>0.5-1 (1-0)</td>
<td>34.8 (14-2)</td>
</tr>
<tr>
<td>Awake</td>
<td>0.65</td>
<td>1.38</td>
<td>0.76</td>
<td>0.8 (1-0)</td>
<td>4.8 (4-1)</td>
<td>35 (9-9)</td>
<td>21.4 (6-4)</td>
</tr>
<tr>
<td>COPD</td>
<td>0.64</td>
<td>1.37</td>
<td>0.80</td>
<td>0.7 (0-9)</td>
<td>43 (7-5)</td>
<td>9.6 (1-3)</td>
<td></td>
</tr>
<tr>
<td>Anaesthesia</td>
<td>0.61</td>
<td>1.03</td>
<td>1.0</td>
<td>1.0 (1-1)</td>
<td>32 (7-5)</td>
<td>16.8 (6-1)</td>
<td></td>
</tr>
</tbody>
</table>

QMEAN, VMEAN = mean VA/Q of the perfusion and ventilation distribution; log SDQ, log SDV = logarithmic standard deviation of the perfusion and ventilation distributions. Inspired oxygen fraction: awake 0.21, anaesthesia 0.40.

increase in the scatter of ventilation-perfusion ratios. However, no clear quantitative analysis was possible and the mechanism behind the increased scatter remained unknown.

Ventilation-perfusion relationships
Severinghaus and Stupfel showed that anaesthesia caused impaired elimination of carbon dioxide. Using a single breath washout technique, Nunn and Hill found that the anatomical (or series) dead space (mainly airways) was unchanged during anaesthesia, indicating that the alveolar (or parallel) dead space (ventilated but unperfused alveoli) was increased. Venous admixture, as calculated according to the standard oxygen "shunt" equation, is also increased during anaesthesia to approximately 10% of cardiac output. However, the elimination of carbon dioxide and oxygenation of blood allow no detailed analysis of the ventilation-perfusion relationships (VA/Q), and do not enable a clear separation of dead space and lung regions ventilated in excess of their perfusion (high VA/Q regions). Similarly, venous admixture includes not just perfusion of non-ventilated lung tissue (true shunt), but also regions which are poorly ventilated or perfused in excess of their ventilation ("low VA/Q regions"). The MIGET method, introduced in 1974, makes the construction of a virtually continuous distribution of ventilation-perfusion ratios possible. In young healthy volunteers studied by MIGET during anaesthesia with thiopentone and methoxyflurane both ventilation and perfusion were distributed to wider ranges of VA/Q ratios after induction of anaesthesia and muscle paralysis. Shunt, on the other hand, was little affected with a mean value of approximately 1%. This contrasted with the larger shunt found in subjects of the same age during halothane an-

Figure 3 Transverse computed tomographic (CT) scans of the chest and VA/Q distributions in a patient who was to undergo cholecystectomy (A) when awake, and (B) during anaesthesia and paralysis prior to surgery. When awake there were no densities in dependent lung regions on the CT scan and the VA/Q distribution was normal. During inhalational (enflurane) anaesthesia and paralysis dense regions are seen in dependent lung regions on the CT scan. Shunt increased with widening of the VA/Q distribution (increased log SDQ). From Gunnarsson et al.
aesthesia and muscle paralysis. A mean shunt of 8% was present with a range from 0% to 23%, as well as an increase in the scatter of VA/Q ratios, expressed as the logarithmic standard deviation of the perfusion distribution (log SDQ) which almost doubled from 0-43 when awake to 0-80 during anaesthesia.

An increase in shunt from 1-6% when awake to a mean of 8-6% during anaesthesia was recorded in other studies on older (37–64 years) surgical patients, and there was a widening of the VA/Q distribution (log SDQ 0-47 when awake, 1-01 during anaesthesia). An example of VA/Q distributions during different conditions is given in fig 1 and mean values are given in the table.

In elderly patients with more severe impairment of lung function, halothane anaesthesia with muscle paralysis, with or without nitrous oxide, caused considerable widening of the VA/Q distribution with log SDQ increasing from 0·87 when awake to 1·73 during anaesthesia. In addition, shunt increased to a mean of 15% but with a large range (0–30%). Thus, the most consistent findings during anaesthesia are an increased VA/Q mismatch, expressed as an increased log SDQ, and an increase in shunt.

During anaesthesia and mechanical ventilation regions with high VA/Q ratios develop, and the ratios further increase during ventilation with greater levels of PEEP (fig 2). The additional high VA/Q mode may be explained by the tiny perfusion of corner vessels in the interalveolar septa of lung tissue in upper lung regions where alveolar pressure may exceed pulmonary vascular pressure (zone I). Support for this hypothesis comes from a study on excised dog lungs, both artificially ventilated and perfused, so that a zone I was produced.

In the studies referred to above, anaesthesia was maintained with inhalational agents. Dueck and coworkers compared intravenous (pentobarbitone) and inhalational (halothane and nitrous oxide) anaesthetics in a sheep model and found no significant changes during intravenous anaesthesia in VA/Q relationships, blood gases, or in FRC. However, inhalational anaesthetics increased shunt from 1% when awake to 11% and 14% during anaesthesia with spontaneous and mechanical ventilation, respectively. FRC was reduced during inhalation anaesthesia and more so after muscle paralysis. In the sheep, therefore, inhalation anaesthesia produced VA/Q mismatch and shunt, possibly due to the decrease in FRC, whereas intravenous anaesthesia produced no changes. Similarly, small shunts were found during intravenous anaesthesia in 14 patients with a mean age of 59 years before pulmonary surgery, but log SDQ increased from 0·77 to 1·13. It may be that a better preserved hypoxic pulmonary vasoconstriction during barbiturate anaesthesia can explain the absence of, or the small increase in, shunt. An additional factor is the fractional inspired oxygen concentration (FIO2). Increasing FIO2 to 0·5 caused an increase in shunt of 3–4%. In elderly patients during halothane anaesthesia an increase in FIO2 from 0·53 to 0·85 caused shunt to increase from 7% to 10% of the cardiac output. Thus, a certain dependence on FIO2 exists, possibly explained by attenuation of hypoxic pulmonary vasoconstriction with increasing FIO2.

The patients studied by Anjou-Lindskog et al suffered from chronic bronchitis with abnormal spirometric parameters. Their log SDQ was also increased, on average well above the upper normal limit of 0·6. In a similar patient group of the same age with chronic bronchitis, studied during halothane anaesthesia before vascular reconstructive surgery on their legs, there was only a small increase in shunt during anaesthesia but an increased scatter of VA/Q ratios. These findings suggest that abnormal preoperative respiratory function may mod-
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Figure 6 Ventilation-perfusion distributions and computed tomographic (CT) scans in a patient with severe COPD (A) when awake and (B) during inhalational anaesthesia. Note the large transverse lung area on the CT scan when awake which is unchanged during anaesthesia (compare with fig 3). There is no atelectasis and practically no shunt either when awake or anaesthetised. "Low" VA/Q regions (0.005 < VA/Q < 1) appear during anaesthesia. From Gunnarsson et al.

ulate the anaesthesia-induced effects on the VA/Q distribution with less formation of shunt. This will be discussed further below.

Atelectasis formation

Prompt development of densities in dependent regions of both lungs has been demonstrated during anaesthesia by computed tomographic scanning, and similar densities have been seen in anaesthetised infants. The densities appear both during spontaneous breathing and after muscle paralysis, and during both inhalational and intravenous (barbiturate) anaesthesia. In anaesthetised sheep and horses similar densities in dependent lung regions were seen, and subsequent morphological analysis showed them to be atelectasis with little or no interstitial oedema or vascular congestion. If these findings are extrapolated to humans it can be concluded that anaesthesia causes atelectasis. The rapid appearance of the densities following induction of anaesthesia and after discontinuation of PEEP of 10 cm H₂O is against slow resorption of gas as a cause of atelectasis, and another as yet unidentified mechanism remains to be found. This may be relaxation of the respiratory muscles, in particular the diaphragm, permitting the transmission of the higher intra-abdominal pressure into the intrathoracic cavity. Preliminary findings during phrenic nerve stimulation during anaesthesia show reduction of the atelectasis.

More recently, the VA/Q distribution has been correlated with CT findings during anaesthesia. The major VA/Q disturbance was once again shunt and very little low VA/Q (fig 3), and a good correlation between the magnitude of shunt and the size of atelectasis was seen (fig 4). PEEP can reduce the atelectatic area but the effect on shunt varies; in some patients it falls and in others it increases. The continuing shunt despite PEEP can probably be explained by a redistribution of blood flow towards dependent, atelectatic regions. The intravenous anesthetic agent ketamine, which does not reduce muscle tone, did not produce atelectasis or shunt as assessed by MIGET, whereas both were seen when the same patient was paralysed with a muscle relaxant.

Atelectasis and shunt did not increase with age of the patients when data from several studies were pooled. Thus, the worsening of arterial oxygenation in the elderly needs another explanation. Figure 5 shows the dependence of shunt (probably caused by atelectasis) and perfusion of low VA/Q regions on age. In the awake state shunt is negligible and perfusion of low VA/Q regions is also small, although it increases with age. During anaesthesia shunt is much larger, but still essentially independent of age. Perfusion of low VA/Q regions increases both with anaesthesia and age. It can be said that anaesthesia worsens the match of ventilation and blood flow by as much as 20 years of aging. Why the VA/Q match deteriorates during anaesthesia
still remains to be established. One possibility is the previously discussed airway closure that is known to become more important with age in the awake subject.\(^{46}\)

**Chronic bronchitis and anaesthesia**

In a recent study\(^ {50}\) patients with chronic bronchitis were studied whilst awake and during anaesthesia by both MIGET and CT scanning. Surprisingly, they developed no, or very little, atelectasis during anaesthesia, with only minimal shunt. On the other hand, severe Va/Q mismatch occurred with a large percentage of perfusion going to lung regions with low Va/Q ratios (fig 6). This agrees with other studies\(^ {47,48}\) which found minor shunt but a varying degree of Va/Q mismatch in patients with chronic bronchitis (table).

The cause of low Va/Q can only be speculated upon, but it is assumed that chronic hyperinflation may alter the mechanical behaviour of the lungs and that airways close during expiration before alveolar collapse, thus preventing prompt formation of atelectasis. However, ventilation is also reduced in relation to perfusion which causes low Va/Q regions. During prolonged anaesthesia the low Va/Q regions may become atelectatic and shunt develops due to a faster uptake of gases by the blood than is delivered to alveoli via the airways.

**Conclusion**

Calculations from carbon dioxide elimination and oxygenation of blood have demonstrated increased dead space and venous admixture during anaesthesia. With the use of MIGET, a more detailed insight into the impairment of gas exchange during anaesthesia has emerged. Thus, dead space is unchanged or increased modestly, whereas regions with high Va/Q ratios develop, usually in upper non-dependent lung regions with poor perfusion of alveoli. Shunt—that is, perfusion of regions with Va/Q ratios <0.005—is increased in most patients and correlates with the formation of atelectasis as assessed by CT scanning. In addition, anaesthesia increases or causes Va/Q mismatch with increased dispersion of Va/Q ratios by a mechanism that has not yet been fully established, but may be airway closure. Shunt and perfusion of low Va/Q regions correlate well with the amount of anaesthetic as determined by the standard oxygen shunt equation. Atelectasis and shunt are independent of age, whereas the Va/Q mismatch increases with age, explaining the worsening of oxygenation of blood that occurs in the elderly. Finally, the abnormal gas exchange in patients with obstructive lung disease during anaesthesia appears to be explained mainly by increased Va/Q mismatch, whereas shunt and atelectasis formation is minimal.

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Contribution of multiple inert gas elimination technique to pulmonary medicine. 6. Ventilation-perfusion relationships during anaesthesia.

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