

**Editorial I****Just a little oxygen to breathe as you go off to sleep. . . is it always a good idea?**

Administration of oxygen 100% to patients before inducing anaesthesia provides a reserve of oxygen, mostly in the patient's functional residual capacity (FRC), to extend the time before hypoxia occurs, should there be difficulties achieving adequate ventilation after induction. Preoxygenation is now widely used, and in the operating theatres in which I work, the practice has extended beyond the anaesthetists to nursing staff and operating department practitioners, who now automatically apply a face mask to the patient while I administer the induction agents. An editorial in 2004 argued that routine preoxygenation 'could be recommended to the profession regardless of the experience, expertise or grade of the practitioner, and mandated for trainees'.<sup>1</sup> The author of this recommendation, and the enthusiastic theatre staff, all make the assumption that administering oxygen 100% is harmless. In his translation of the Hippocratic oath, Galen put great emphasis on the phrase *primum non nocere* (first, do no harm) and this tenet should be applied to the use of oxygen 100% before it becomes an accepted practice in all patients.

Oxygen toxicity has been known to occur for many decades. Despite ubiquitous and multiple cellular defence mechanisms, all mammals are sensitive to high concentrations of oxygen, with death occurring within a few days of exposure to oxygen 100%,<sup>2</sup> although among mammalian species humans tolerate hyperoxia relatively well. The likelihood of toxicity is a function of both oxygen partial pressure and duration of exposure. Breathing oxygen 100% at one atmosphere absolute pressure for <12 h has no known detrimental effects in humans. Beyond 12 h, the classic symptoms of an urge to take deep breaths, chest pain, and cough occur, and after 24 h forced vital capacity is reduced, indicating early lung injury. In terms of causing pulmonary oxygen toxicity, preoxygenation in the anaesthetic room for 3–5 min is, therefore, harmless.

Indirect adverse effects of breathing oxygen 100% are far more applicable to anaesthetic practice. Atelectasis, or collapse of small regions of lung, occurs in a majority of patients having a general anaesthetic involving muscle

relaxation and artificial ventilation.<sup>2</sup> This results from changes in the shape of the chest wall, spine, and diaphragm, causing a reduction in FRC and the volume of specific areas of the chest, particularly in the dependent areas of lung and behind the diaphragm. Three mechanisms contribute to lung collapse. First, compression atelectasis occurs when lung regions are reduced in volume to such an extent that the air is effectively squeezed out. Secondly, absorption atelectasis when airway closure is followed by absorption of the gases distal to the airway leading to complete collapse of the alveoli. Thirdly, atelectasis may occur when airways are extremely narrow, but not closed, when the rate at which alveolar gas is absorbed into the blood exceeds the rate at which gas can flow through the narrow airway to replace it, accelerating airway closure and alveolar collapse. When breathing oxygen 100%, this is likely to occur in lung regions with a  $\dot{V}/\dot{Q}$  ratio of <0.05.<sup>3</sup> Using the multiple inert gas elimination technique, areas of lung with  $\dot{V}/\dot{Q}$  ratios this low are easily demonstrated in the elderly when awake, and during general anaesthesia in patients of all ages. *In vivo* it is likely that all three mechanisms are at work simultaneously in different lung regions. In dependent regions behind the diaphragm, compression atelectasis will occur as a result of the weight of the abdominal contents in the absence of diaphragmatic muscle tone, a situation more likely to occur in obesity and in the presence of increased intra-abdominal pressure. In other dependent areas of the lung, the reduced FRC during anaesthesia will lead to resting lung volumes falling below the closing capacity, leading to airway closure and absorption atelectasis. In regions of lung bordering these dependent areas, airway narrowing will reduce the  $\dot{V}/\dot{Q}$  ratio below the threshold needed for collapse to occur.

Atelectasis during anaesthesia can be detected using computerized tomography (CT) scans, usually involving a single lung slice taken immediately cranial to the dome of the right diaphragm. The amount of atelectasis is quantified by measuring the cross-sectional area of the

atelectasis, expressed as a percentage of the total cross-section of lung on that CT slice. The percentages obtained by this technique seem small, but it must be remembered that each 1% of atelectasis on a cross-sectional CT scan represents around 3% of normally expanded lung volume. Surrogate measures of the amount of atelectasis during anaesthesia are often used, such as calculating the alveolar-arterial  $P_{O_2}$  difference or  $Pa_{O_2}:F_{I_{O_2}}$  ratio.

When airway closure or narrowing occurs, absorption atelectasis is greatly influenced by the gas mixture present in the alveolus. When breathing air, the partial pressure of all gases present in mixed venous blood is about 87 kPa, compared with 95 kPa in the alveolar gas.<sup>2</sup> This difference of 8 kPa arises because water vapour is only present in alveolar gas, carbon dioxide carriage in the blood is mostly as dissolved bicarbonate rather than carbon dioxide gas in solution, and because of the small alveolar to arterial  $P_{O_2}$  difference caused by venous admixture. To keep the alveoli open in the normal healthy lung, this difference of 8 kPa must be countered by the elastic recoil of the respiratory system. When breathing oxygen 100%, the alveolar  $P_{N_2}$  will fall quickly, and for a short time nitrogen will diffuse from the blood into the alveolus and so mitigate against alveolar collapse. However, once blood  $P_{N_2}$  becomes negligible, the total partial pressure of gas in the mixed venous blood, even when breathing oxygen 100%, decreases to just 12.5 kPa ( $P_{O_2}$  of 6.4 kPa and  $P_{CO_2}$  of 6.1 kPa) whereas that of the alveolus remains unchanged, so introducing a pressure gradient of more than 80 kPa resulting in rapid transfer of oxygen across the alveolar-capillary barrier and alveolar collapse. Mathematical modelling of absorption atelectasis during anaesthesia has been used to predict the time taken for an area of unventilated lung to collapse after induction of anaesthesia.<sup>4</sup> This model supports the physiological principles already described by predicting that the rate at which collapse occurs is related to the  $F_{I_{O_2}}$  during anaesthesia and that preoxygenation for 3 min substantially reduces the time taken for collapse to occur irrespective of the  $F_{I_{O_2}}$  used after induction.

Do these physiological principles impact on clinical practice, in particular the role of oxygen 100% and absorption atelectasis? It is now more than a decade since CT studies first demonstrated that preoxygenation leads to greater areas of atelectasis after induction.<sup>5</sup> For example, if  $F_{I_{O_2}}$  before induction is 0.3, 0.6, 0.8, or 1.0, the mean percentage of atelectasis seen on CT scans post-induction is 0.2%, 0.2%, 1.3%, and 5.6% respectively.<sup>5, 6</sup> Re-expansion of atelectasis during anaesthesia (discussed later), usually provoked by falling oxygen saturation, is another time when oxygen 100% is often used. In a study, again using CT scanning, use of an  $F_{I_{O_2}}$  of 1.0 during the re-expansion manoeuvre led to recurrence of the atelectasis in 5 min whereas the lung remained expanded for more than 40 min when  $F_{I_{O_2}}$  was 0.4.<sup>7</sup> Finally, administering oxygen 100% before extubation also worsens atelectasis. CT scans

performed 20 min post-extubation in groups randomly assigned to be ventilated with an  $F_{I_{O_2}}$  of 0.4 or 1.0 before extubation were found to have 2.6% and 8.3% atelectasis, respectively.<sup>8</sup> The presence of more than 8% atelectasis immediately after operation is clinically very significant as re-expansion of this collapsed lung after major surgery may take some days.

Not all studies of atelectasis and anaesthesia have given such a clear link between  $F_{I_{O_2}}$  and atelectasis. Maintenance of anaesthesia with an  $F_{I_{O_2}}$  of either 0.3 or 0.8 found no significant difference in the amount of atelectasis 24 h after operation (2.5% vs 3.0%, respectively).<sup>9</sup> However, despite the lack of statistical difference between the groups in this small study, only four of 14 patients with an intraoperative  $F_{I_{O_2}}$  of 0.3 had more than 2% atelectasis after operation compared with 10 of 14 in the  $F_{I_{O_2}}$  of 0.8 group. These results also provide some reassurance that the atelectasis seen so commonly during anaesthesia may be partially resolved 24 h after the anaesthetic.

Collectively, these studies offer good evidence that the amount of atelectasis during anaesthesia increases significantly with increasing  $F_{I_{O_2}}$  and that the use of oxygen 100% at any stage of an anaesthetic is associated with significant pulmonary collapse. Reducing  $F_{I_{O_2}}$ , even by a small amount to 0.8, seems to be substantially better than using oxygen alone.

Either nitrogen or nitrous oxide may be used to reduce the  $F_{I_{O_2}}$ . Mathematical modelling predicts that the two gases should have similar effects on the time taken for gas to be absorbed from an unventilated lung unit.<sup>4</sup> However, this prediction over-simplifies the clinical situation, which will be influenced by the timing of the closure of the airway during the anaesthetic. If nitrous oxide is used immediately after induction and airway closure occurs in the first few minutes of the anaesthetic, when the alveolar to arterial  $P_{N_2O}$  gradient is large, then absorption of  $N_2O$  from the alveolus will be rapid and faster than the diffusion of any remaining nitrogen from the blood into the alveolus. Under this combination of circumstances, atelectasis is likely to occur. Should airway closure occur later in the anaesthetic when alveolar and arterial  $P_{N_2O}$  are similar, then little gas exchange will occur between the blood and alveolus beyond the closed airway, and the alveolus should remain expanded. Clinical support for these observations is sparse, with only one study comparing  $F_{I_{O_2}}$  of 0.4 in nitrogen or  $N_2O$ .<sup>10</sup> This study, which used  $Pa_{O_2}:F_{I_{O_2}}$  ratio to indirectly estimate the amount of atelectasis 30 min after induction, found that nitrous oxide at this early stage of an anaesthetic did indeed behave in a similar fashion to oxygen 100%. Thus, it seems that if  $N_2O$  is part of the anaesthetic technique from the outset, then atelectasis may be more frequent than when ventilation is with oxygen and air.

Re-expansion of atelectasis is possible for a patient who has a tracheal tube, and two techniques are described. The first involves increasing positive end-expiratory

pressure (PEEP) to 15 cm H<sub>2</sub>O, followed by an increase in tidal volume until peak inspiratory pressure reaches 40 cm H<sub>2</sub>O. This pattern of ventilation is then maintained for 10 breaths, before returning to standard ventilator settings.<sup>11</sup> The second involves a vital capacity manoeuvre to a sustained airway pressure of 40 cm H<sub>2</sub>O, which in the original studies was maintained for either 15 or 25 s.<sup>12, 13</sup> On the basis of subsequent CT scan studies, when using this technique half the atelectasis is re-expanded after just 2 s, and in three-quarters of patients all the atelectasis is re-expanded in 8 s.<sup>13</sup> At these high inflation pressures, there are benefits to minimizing the duration, particularly to reduce the cardiovascular effects of this prolonged and severe Valsalva manoeuvre and to minimize the small risk of pulmonary barotrauma. Prevention of atelectasis can be achieved with modest levels of PEEP, with 10 cm H<sub>2</sub>O preventing atelectasis formation even when high  $F_{I_{O_2}}$  is used.<sup>14</sup> Continuous positive airway pressure (CPAP) of 6 cm H<sub>2</sub>O applied via a tight fitting facemask before induction is also effective at preventing atelectasis formation, again despite using oxygen 100%, although this is a rather invasive technique to be used routinely.<sup>15</sup>

Use of oxygen 100% before and during anaesthesia will always be necessary in some patients. These include patients with a known difficult airway, a reduced FRC and therefore oxygen reserve (term pregnancy, obesity, abdominal distension, and lung pathology), an increased oxygen consumption (pregnancy, paediatrics, and sepsis), or pre-existing hypoxia from lung pathology. In these situations, an effective technique of preoxygenation<sup>16</sup> should continue to be used and should always be followed, whenever possible, by a properly administered re-expansion manoeuvre and PEEP then used to prevent atelectasis reforming. In patients who are hypoxic before induction, the use of CPAP before and during induction should be considered.

In other groups of patients, where the reasons for using oxygen 100% are less compelling but the anaesthetist wants the security provided by greater oxygen reserves than found when breathing air, use of  $F_{I_{O_2}}$  of 0.8 or 0.6 should be considered. Several minutes of protection from desaturation will still be obtained, and the possibility of atelectasis during anaesthesia and into the postoperative period will be reduced. In practice, the casual preoxygenation referred to at the start of this editorial usually involves a short exposure to an inadequate flow of oxygen with an ineffective seal between the mask and the patient. This type of preoxygenation will rarely achieve an  $F_{I_{O_2}}$  high enough to contribute to atelectasis formation, but neither will it significantly prolong the time to hypoxia if ventilation should prove impossible. If breathing additional oxygen is considered desirable before induction and the anaesthetist is content to avoid oxygen 100%, then the required  $F_{I_{O_2}}$  should still be delivered using the same technique as for preoxygenation<sup>16, 17</sup> but with some added air.

The same considerations should be applied to the use of oxygen 100% during re-expansion manoeuvres and before

extubation. Unfortunately, the groups of patients in whom atelectasis may be particularly detrimental are the same groups as listed above in whom use of oxygen 100% is more strongly indicated, so as usual clinicians must compromise between two opposing requirements.

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