

Physiology of apnoea and the benefits of preoxygenation

R Sirian FRCA
Jonathan Wills MA FRCA

Apnoea and the benefits of preoxygenation

What happens during apnoea?

This article will concentrate on factors that accelerate or delay the onset of severe hypoxaemia during apnoea (Fig. 1). In the anaesthetized patient, the oxygen consumption (VO_2) remains fairly constant at $\sim 250 \text{ ml min}^{-1}$. This is delivered to the tissues by haemoglobin whose oxygen is then replenished, on return to the pulmonary circulation, by the diminishing store of oxygen within the lungs. The alveolar partial pressure of oxygen (PA_{O_2}) decreases steadily, not only because the oxygen is being removed from the lungs but also because this oxygen removal generates a substantial negative intrathoracic pressure if the airway is obstructed.

Although the arterial partial pressure of oxygen (Pa_{O_2}) decreases in direct relation to the PA_{O_2} , the arterial haemoglobin oxygen saturation (Sa_{O_2}) remains $>90\%$ as long as the haemoglobin can be re-oxygenated in the lungs. The Sa_{O_2} only starts to decrease when the store of oxygen in the lungs is depleted and the PA_{O_2} is of the order of 6–7 kPa. Its subsequent decline is of a constant and rapid nature, about 30% every minute. At the start of this rapid decline, the Sa_{O_2} is still 90–95%. This inflection point we will define as ‘critical hypoxia’. It is for this reason that oximetry is not a good tool for predicting impending severe hypoxaemia.

However, because oximetry detects the decrease in Sa_{O_2} before any clinical signs are apparent, it has proved invaluable in detecting critical situations and has helped improve clinical practice to avoid these situations.

Various factors significantly influence the time period from the onset of apnoea to critical hypoxia.

Functional residual capacity

The functional residual capacity (FRC) is the most important store of oxygen in the body. The greater the FRC, the longer apnoea can be

tolerated before critical hypoxia develops. The alveolar fraction of oxygen (FA_{O_2}) is about 0.13 when breathing air. For an adult with a normal FRC and VO_2 , the oxygen content of the lungs will be consumed within $\sim 1 \text{ min}$ ($\approx 290 \text{ ml}$). This explains why critical hypoxia can be expected after 1 min of apnoea. Patients with reduced FRC (e.g. lung disease, kyphoscoliosis, pregnancy, and obesity) reach critical hypoxia more rapidly.

Preoxygenation

The aim of preoxygenation is to replace nitrogen in the FRC with oxygen; this process is also referred to as denitrogenation. This has a significant impact on body oxygen store and therefore increases tolerance to apnoea substantially.

A study¹ in 1984 when oximetry was still in its infancy revealed how quickly hypoxaemia developed in fit and healthy individuals 1 min after the induction of anaesthesia when preoxygenation was not performed. Mean Sa_{O_2} was 85.5% 1 min after induction. When preoxygenation was performed (even if only briefly and imperfectly), the Sa_{O_2} was found to be $>90\%$ in all individuals studied.

There has been much debate about the most efficient forms of preoxygenation.

An easy way to assess the efficacy of preoxygenation is to measure the end-tidal oxygen fraction (FE'_{O_2}), which will give an approximation of the alveolar oxygen fraction (FA_{O_2}). For an adult with a normal FRC and VO_2 , if the FA_{O_2} is >0.9 (i.e. as would be found after effective preoxygenation), the lungs would contain $\sim 2000 \text{ ml}$ of oxygen (i.e. 10 times VO_2).

Preoxygenation is a simple safety procedure. A possible reason for reluctance to preoxygenate patients is an overestimation of patients' discomfort. However, workers have found that most patients tolerate preoxygenation well.²

Maintenance of a patent airway

During steady-state respiration, a dynamic equilibrium exists between oxygen and CO_2 . The

Key points

Knowledge of those patients who will suffer early arterial desaturation during apnoea can allow careful preparation and early intervention. Examples include the critically ill, obese, parturient, and paediatric patients.

Preoxygenation is a simple safety procedure, which can have a significant influence on time to desaturation.

During apnoea, arterial oxygen saturation remains high until almost all of the body's reserves of oxygen have been used. Arterial oximetry is not a good predictor of impending hypoxaemia.

When severe hypoxaemia develops, the arterial oxygen saturation decreases rapidly, at a rate close to $30\% \text{ min}^{-1}$.

Increasing the oxygen fraction applied to the airway from 90% to 100% more than doubles the survival duration of open-airway apnoea.

It is important to maintain a patent airway if a patient is apnoeic, even if no ventilation is being attempted.

Time to critical hypoxaemia for an apnoeic obese patient is extended by preoxygenation in a head-up position.

R Sirian FRCA

Specialist Registrar in Anaesthesia
Queens Medical Centre
Derby Road
Nottingham
UK

Jonathan Wills MA FRCA

Consultant Anaesthetist
Department of Anaesthesia
Southmead Hospital
North Bristol Trust
Southmead Road
Westbury-on-Trym
Bristol BS10 5NB
UK

Tel: +44 1179505050
Fax: +44 1179595075

E-mail: jonathan.wills@nbt.nhs.uk
(for correspondence)

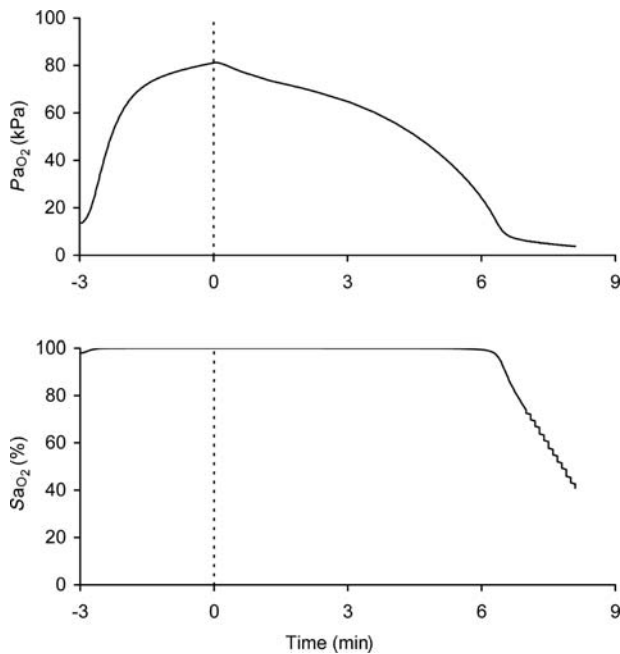


Fig 1 The simulated time course of changes to arterial partial pressure of oxygen and arterial haemoglobin oxygen saturation for a healthy individual who is preoxygenated for 3 min and then rendered apnoeic with an obstructed airway. These graphs are generated by the Nottingham Physiology simulator.

volume of CO₂ moving from the pulmonary circulation into the alveolar space is 80% of the volume of oxygen moving in the opposite direction.

The situation changes radically at the onset of apnoea. During apnoea, the rate of oxygen extraction from the alveoli remains unaffected, remaining ~250 ml min⁻¹. The amount of CO₂ entering the alveoli is considerably less. This is due to the fact that CO₂ is more water soluble than oxygen; therefore, only 10% (~20 ml) of the CO₂ produced every minute reaches the alveolar space. The remaining 90% remains dissolved in the tissues. The volume of gas within the lungs therefore decreases rapidly during apnoea, and if the airway is obstructed, the intrathoracic pressure decreases at a rate dependent upon oxygen consumption and the thoracic compliance.

Closed-airway apnoea commences with an intrathoracic pressure equal to or marginally greater than ambient pressure. The extraction of oxygen results in subatmospheric intrathoracic pressure almost immediately. During prolonged apnoea, intrathoracic pressure may be much lower than ambient pressure, substantially and dangerously reducing the alveolar partial pressure of oxygen.

A patent airway will allow oxygen to diffuse into the apnoeic lung. Maintaining a patent airway and exposure to 100% oxygen produces ‘apnoeic mass-movement oxygenation’, which has been shown in animal and simulated human studies to maintain oxygen saturation for up to 100 min.

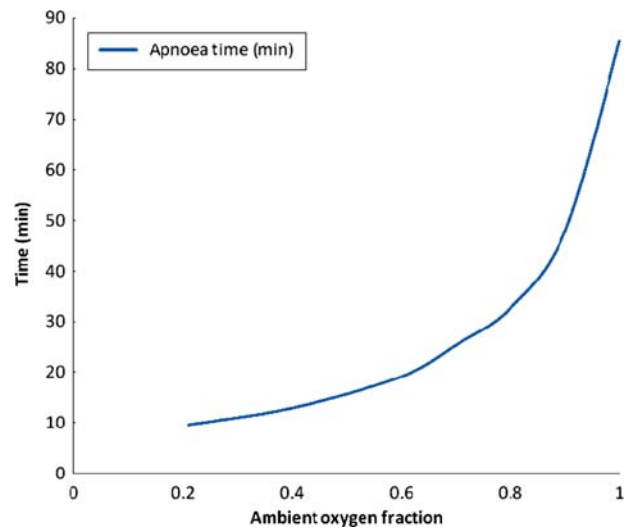


Fig 2 Time to severe desaturation after onset of apnoea for different ambient oxygen concentrations. Effective preoxygenation preceded the apnoea.

This passive diffusion of oxygen is more effective if the denitrogenation of the alveolar space is as complete as possible and a tight fitting-mask is used. It is important to ensure very high oxygen fraction $F_{I_{O_2}}$ to extend the safe duration of apnoea; increasing the oxygen fraction applied to the airway from 90% to 100% more than doubles the time to critical hypoxia with an open airway³ (Fig. 2). This has a much greater effect on time to critical hypoxia than increasing the $F_{I_{O_2}}$ applied to the airway from 21% to 90%.

Although the application of 100% oxygen to a patent airway in an apnoeic patient delays the onset of critical hypoxia, this approach will not reverse hypoxaemia that has already developed. Furthermore, it does not prevent the steady development of hypercapnia and associated acidosis, which over time becomes life threatening.

Re-oxygenation

When airway obstruction is relieved during apnoea, there is a rapid flow of gas into the depressurized thorax. Assurance of a high $F_{I_{O_2}}$ during this one-time passive inhalation may significantly extend the survivable duration of apnoea, buying time to rescue the airway. If oxygen 100% is supplied while the airway obstruction is relieved, the patient is likely to show a temporary reversal in their haemoglobin oxygen desaturation, even though tidal ventilation has not been resumed and the volume of oxygen inspired is small.

Haemoglobin concentration

The importance of haemoglobin is not in the storage of oxygen but in its effective transport from the lungs to the tissues. Anaemia will cause a small reduction in the time to critical hypoxia, although this effect will be more noticeable in patients who also have a reduced FRC.

Metabolic rate

Metabolic rate has a simple and predictable effect on the rate of oxygen consumption and therefore on the time to reach critical hypoxia. Increasing the oxygen consumption from 250 to 400 ml min⁻¹ reduces the time to 50% Sa_{o2} by ~40%.³

Physiological shunt and dead space

Venous admixture reduces the Pa_{o2} and Sa_{o2} predictably, but only when the accessible oxygen stores are depleted does severe hypoxaemia develop. However, many patients who present with 'shunting' of venous blood also have a reduced FRC (e.g. pulmonary oedema) and will for this reason have an accelerated onset of hypoxaemia.

Clinically relevant situations

Obesity

A morbidly obese patient has multiple pulmonary abnormalities, including decreased: vital capacity, expiratory reserve volume, inspiratory capacity, and FRC. The supine positioning of such a patient further decreases expiratory reserve volume and FRC and increases the possibility of the tidal volume decreasing within the closing capacity.⁴

The FRC is significantly reduced in obese patients, an average of 1.9 litre in obese adult males compared with 2.6 litre in lean subjects in the supine position.⁵

Jense and colleagues⁴ studied the effect of obesity on the time to develop hypoxaemia (Sa_{o2}=90%) after the onset of apnoea. First, preoxygenation was continued until expired nitrogen fraction (F_{E_{N2}}) was <0.05. After induction of anaesthesia and onset of muscle relaxation, no oxygen was administered and the airway was not supported. Time to desaturation for patients of normal weight was a mean of 6.06 min, but for those patients who were morbidly obese, this was only 2.72 min. Regression analysis of the data demonstrated a significant negative linear correlation between time to desaturation and increasing obesity.

In addition to these metabolic abnormalities and the reduced time to develop hypoxaemia, even with preoxygenation, obesity causes several problems during induction of anaesthesia. It is often more difficult to manage the airway with a face mask, intubation of the trachea is more frequently indicated, and there is a greater risk of failed intubation. For severely obese patients (BMI>40 kg m⁻²), preoxygenation of these patients in the 25° head-up position achieves oxygen tensions >20% higher than when preoxygenation is applied in the supine position.⁶ The increased risk of reflux and aspiration in these patients provides an additional reason for considering the head-up position.

Pregnancy

There are limited data on the time to critical hypoxia during apnoea in pregnant women. Baraka⁷ studied women undergoing

elective Caesarean section under general anaesthesia after 3 min preoxygenation and rapid sequence induction. During apnoea in the supine position, the average time to desaturation (Sa_{o2} 95%) was significantly reduced in the pregnant [173 (4.8) s] compared with the non-pregnant group [243 (7.4) s]. This would be expected as, during pregnancy, the FRC is reduced with further reductions occurring in the supine position, and the VO₂ is increased. The VO₂ steadily increases throughout pregnancy. At full term it is 15–30% greater than the normal non-pregnant values.

The same study also investigated the possible benefit of head-up positioning of 45° during preoxygenation. In the non-pregnant group, the time to reach Sa_{o2} of 95% was extended from 243 (7.4) s in the supine position to 331 (7.2) s by using the head-up position. Even though it has been shown that raising the awake pregnant mother to the upright position increases FRC and Pa_{o2} and reduces Pa_{co2}, while breathing air, there was no extension to the time to desaturation (Sa_{o2} 95%) in the pregnant women. This result may be explained if the gravid uterus prevents the descent of the diaphragm in the more upright position which would normally lead to an increase in FRC.

Critical illness

Critically ill patients suffer arterial desaturation more rapidly than healthy patients because of one or several of the following reasons: cardiopulmonary pathology, anaemia, low cardiac output, hyper-metabolic states, ventilation/perfusion imbalances, pain, airway obstruction, and depressed respiratory effort. Mort⁸ studied the effectiveness of preoxygenation in critically ill patients. In the unstable critically ill patient, not only was the initial Pa_{o2} lower but the benefit of 4 min of preoxygenation, as measured by the change in Pa_{o2}, was also decreased. During subsequent laryngoscopy and intubation, one in four of the unstable critically ill patients suffered some degree of desaturation. In comparison, patients who were stable but critically ill (ASA IV), the Pa_{o2} increased with preoxygenation and none of these patients suffered desaturation during intubation.

Rapid sequence induction of anaesthesia

It has been demonstrated that significant desaturation may occur before spontaneous recovery from succinylcholine apnoea. Heier and colleagues⁹ found that significant arterial haemoglobin desaturation (Sa_{o2}<80%) occurred in one-third of healthy volunteers following administration of succinylcholine 1 mg kg⁻¹ and thiopental 5 mg kg⁻¹. All subjects were preoxygenated for at least 3 min until end-tidal oxygen concentration was >90%, but the facemask was removed after the onset of paralysis to mimic complete airway obstruction. There was a clear correlation between the incidence of arterial desaturation and the duration of apnoea, with significant desaturation occurring when apnoea exceeded 5 min. It cannot be assumed therefore that a patient will remain well

oxygenated after a rapid sequence induction, if no active airway management is undertaken.

Children

Children have smaller FRC and greater VO_2 per unit weight than healthy adults. Critical hypoxia develops more quickly after the onset of apnoea and this is more pronounced in younger children. During apnoea in a 1-month-old child, the rate of decline of Pa_{O_2} is three times more rapid than that of an adult,¹⁰ the Sa_{O_2} of 90% is reached in 0.25 min if there is no preoxygenation and the airway is closed. Preoxygenation for 1 min extends the time to Sa_{O_2} of 90% to 1.5 min.¹⁰ This is valuable extra time to manage a patient who may have a difficult airway.

In an older child of 8 yr, the time after the onset of apnoea to Sa_{O_2} of 90% is 0.47 min. However, the benefit of preoxygenation is greater than that for a younger child (time to 90% Sa_{O_2} extended to 5.11 min).¹⁰

Therefore, although successful preoxygenation of paediatric patients is more difficult than in adults, it is even more valuable in gaining time to achieve definitive control of the airway.

Conclusion

If ventilation is not possible after the onset of apnoea, the factors that will have the greatest effect on the time until critical hypoxia is reached are the FRC, the alveolar concentration of oxygen, and the metabolic rate. Haemoglobin concentration and degree of circulatory shunt are less important factors.

The anaesthetist can help delay the onset of critical hypoxia by optimizing preoxygenation. Until definitive control of the airway is possible, the anaesthetist can apply oxygen 100% to a patent

airway so as to allow passive oxygen influx into the lungs and help prevent the development of subatmospheric intrathoracic pressures.

References

1. Drummond GB, Park GR. Arterial oxygen saturation before intubation of the trachea—an assessment of techniques. *Br J Anaesth* 1984; **56**: 987–92
2. Heck Z, Stegmann JU, Lorenz C, Heck M, Schlack W. Acceptance of preoxygenation in clinical routine by patients and by anaesthesiologists. *Anesthesiol Intensivmed Notfallmed Schmerzther* 2001; **36**: 471–5
3. Hardman JG, Wills JS, Aitkenhead AR. Factors determining the onset and course of hypoxaemia during apnoea: an investigation using physiological modelling. *Anesth Analg* 2000; **90**: 619–24
4. Jense HG, Dubin SA, Silverstein PI, O'Leary-Escolas U. Effect of obesity on safe duration of apnoea in anesthetized humans. *Anesth Analg* 1991; **72**: 89–93
5. Tucker DH, Sieker HO. The effect of change in body position on lung volumes and intrapulmonary gas mixing in patients with obesity, heart failure and emphysema. *Am Rev Resp Dis* 1960; **82**: 787–91
6. Dixon BJ, Dixon JB, Carden JR, et al. Preoxygenation is more effective in the 25° head-up position than in the supine position in severely obese patients. *Anesthesiology* 2005; **102**: 1110–5
7. Baraka AS. Preoxygenation during pregnancy in the head-up versus the supine position. *Anesthesiology* 2006; **104**: 1110–5
8. Mort TC. Preoxygenation in critically ill patients requiring emergency tracheal intubation. *Crit Care Med* 2005; **33**: 2672–5
9. Heier T, Feiner JR, Lin J, Brown R, Caldwell JE. Hemoglobin desaturation after succinylcholine-induced apnea. *Anesthesiology* 2001; **94**: 754–9
10. Hardman JG, Wills JS. The development of hypoxaemia during apnoea in children: a computational modelling investigation. *Br J Anaesth* 2006; **97**: 564–70

Please see multiple choice questions 1–4