Oxygen in neonatal anesthesia: friend or foe?
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Purpose of review
Clinical practices in oxygen administration are in need of change based on the increasing understanding of oxygen toxicity. Hypoxemia is due to many pathophysiological causes; avoiding hypoxemia is an important objective during neonatal anesthesia. Nevertheless, the only known cause for hyperoxemia is the excess and unnecessary administration of oxygen by healthcare providers. To avoid hyperoxemia is an important objective during neonatal anesthesia.

Recent findings
Neonatal exposure to 100% oxygen is almost never necessary. Much lower concentrations of inspired supplemental oxygen during the neonatal period can also lead to oxygen toxicity if oxygen is used when it is not necessary. Excess oxygen is associated with serious morbidities such as retinopathy of prematurity, bronchopulmonary dysplasia, injury to the developing brain, and childhood cancer. When providing supplemental oxygen, monitoring with modern SpO\textsubscript{2} technology and avoidance of SpO\textsubscript{2} values of 95–100% are less frequently associated with hyperoxemia.

Summary
Even brief neonatal exposures to pure oxygen must be avoided during neonatal anesthesia. When any dose of supplemental oxygen is given, a reliable pulse oximeter aiming to avoid hyperoxemia is necessary. Even though further research is essential, administration of oxygen by healthcare providers when it is not necessary is a foe and a neonatal health hazard.

Keywords
alveolar ventilation, injury to the developing brain, long-term outcomes, oxygenation, pulse oximetry saturation, retinopathy of prematurity

Introduction
Oxygen during neonatal anesthesia can really be a great ‘pal’, a ‘true friend’. Conversely, if used in excess or when not necessary, it can be one of the worst foes or antagonists for health, a true neonatal health hazard.

Ventilation with more than 21% oxygen (hyperoxic ventilation) is widely used in neonatal practice for resuscitation, acute interventions, and chronic supplementation, but it can accentuate problems, worse if there is increased alveolar ventilation.

The potential risks of unnecessary exposure to inspired oxygen are described in recent publications \cite{1**–4**,5–8, 9**,10*,11,12}. We have stressed that avoiding hypoxemia, as essential as it is, should not be equated with causing hyperoxemia \cite{1**,7,8,9**}.

Efforts aimed at avoiding unnecessary oxygen use lead to significant decreases in neonatal morbidities \cite{13,14,15*, 16–19,20**} and have not been associated with increases in mortality, short-term morbidity or long-term morbidity \cite{3**,14,18}. Furthermore, 100% oxygen during neonatal resuscitation is almost always unnecessary and potentially harmful \cite{6,11,19**}, stressing the need to ‘dose’ the oxygen as needed \cite{22}.

The use of oxygen during neonatal anesthesia has not been well studied \cite{5}. The percentage of all newborns that require surgery is very small, but they are usually tiny, immature, or critically ill infants.

The scope of this review is to evaluate physiologic concepts of neonatal oxygenation and recent information on morbidities associated with the use of excess oxygen and oxidant stress. Among the many systemic changes associated with hyperoxemia, which will not be discussed in this review, are increased plasma insulin and glucagon levels, and reduced myocardial contractility and relaxation.

My objective is to provide educational tools for clinical practice in neonatal anesthesia. Although it is essential to continue to zealously avoid hypoxemia and tissue hypoxia, we must avoid causing hyperoxemia, oxidant damage, and reperfusion injury.
Oxygen and oxidant stress
Supplemental oxygen allies with us as a friend in the struggle and cause to fight hypoxemia. A great friend who supports infants in bad times.

Tissue hypoxia is bad and should be avoided. There are more than 100 causes of hypoxemia and hypoxia and never a practice guideline has been designed to cause, or induce, hypoxemia.

On the contrary, there is absolutely no known pathophysiological cause of hyperoxemia in a living organism. The only known reason of neonatal hyperoxemia (and I do not mean oxidant stress) is us, the healthcare providers. Excess oxygen has no benefit in neonatal medicine and it is potentially harmful (Fig. 1, Table 1).

Oxygen causes tissue injury through formation of reactive oxygen intermediates that cause lipid peroxidation, directly damage DNA and cause protein sulfhydryl oxidation. No one knows how short an exposure to unnecessary oxygen can trigger this complex metabolic cascade in neonates, who have decreased antioxidant defenses and are highly susceptible to oxidative stress.

The evidence available over the past 15 years clearly suggests that oxygen toxicity is intimately involved in the damage that has been attributed to hypoxia [23**, 24–28]. Organ damage can occur when there is insufficient blood flow or oxygen. Many physicians assume that organ damage is caused by lactic acidosis. There are, however, few data to support this concept. Moreover, acidosis is protective, even during reperfusion when cellular damage may occur. Reperfusion is accompanied by generation of free radicals and other reactive species that cause damage, membranes, and nucleic acids [26]. Cellular proteins modified during reperfusion, in part by metal-catalyzed oxidation in which iron plays a key role, are involved in the pathogenesis of many severe disorders (Fig. 1, Table 1).

The problem is not just 100% oxygen but any amount of oxygen that is not necessary. For example, resuscitation of piglets for only 15 min with ‘just’ 40 or 60% oxygen causes increased oxidative stress and dose-dependent oxidation of DNA and phenylalanine. The increase in the hydroxyl attack may lead to a pro-oxidative status and risk of genetic instability [28]. Interestingly, it has been shown that insects breathe discontinuously to avoid oxygen toxicity and death [29]. Perhaps there is a lesson to be learned from all this that will lead to improved outcomes.

The present body of knowledge is important for routine clinical practice, so that we do not induce, initiate, or aggravate oxidant stress and the pathogenesis of many disorders, including cancer [30,31].

Table 1 Potential benefits and harms of excess oxygen during the neonatal period

<table>
<thead>
<tr>
<th>Potential benefit</th>
<th>Potential harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxidation</td>
<td>None</td>
</tr>
<tr>
<td>Oxidative stress</td>
<td>Serious and multisystemic: radicals damage proteins,</td>
</tr>
<tr>
<td>Reperfusion</td>
<td>membranes and DNA</td>
</tr>
<tr>
<td>Cell proliferation</td>
<td>None</td>
</tr>
<tr>
<td>Brain</td>
<td>Cancer</td>
</tr>
<tr>
<td>Lungs</td>
<td>None</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>BPD, edema, atelectasis</td>
</tr>
<tr>
<td>Lung compliance</td>
<td>Worsen with 100% oxygen</td>
</tr>
<tr>
<td>Apnea</td>
<td>None</td>
</tr>
<tr>
<td>Eyes</td>
<td>None</td>
</tr>
<tr>
<td>Long-term development</td>
<td>None</td>
</tr>
<tr>
<td>Survival</td>
<td>Worsen apnea, oxygen toxicity</td>
</tr>
</tbody>
</table>

BPD, bronchopulmonary dysplasia.

Anesthesia, oxygen, the developing brain, and long-term outcomes
The question arises whether modern anesthesia practices can harm the uniquely vulnerable developing brain [32**,33,34]. Their potential toxicity and risks/benefits have been reviewed [32**,35–41].

Why administer drugs that have never been well studied in neonates? Why give babies drugs that all available evidence suggests are a serious risk and potential danger for the developing brain?
One classic example is midazolam, a potent short-acting agent that has never been carefully studied in newborns, with high osmolality, benzyl alcohol, decreased clearance, and prolonged elimination half-life in neonates. Midazolam affects the developing brain and adds risk for poor outcomes. Poor neurological outcomes (neonatal death, severe intraventricular hemorrhage grade III or IV, or periventricular leukomalacia) were nine times more frequent with midazolam than with morphine in one randomized trial [42]. In another study, cerebral oxygenation, BP, and cerebral blood flow velocity decreased within 15 min after the loading dose in some ventilated premature infants [43]. Compared with placebo, midazolam has significant adverse effects and no apparent clinical benefit [44]. Animal studies showed that midazolam can trigger widespread apoptotic neurodegeneration in the developing brain and learning deficits for life [45,46]. Authors have asked whether ‘pediatric drugs cause developing neurons to commit suicide’ [47]? The answer seems to be ‘yes’ for midazolam. Finally, the Cochrane collaboration states that further research on the effectiveness and safety of midazolam in neonates is needed before it is used clinically [48]. If we give midazolam to neonates, we must know what motivates us to do so and be responsible for unnecessary and avoidable acute or long-term serious adverse effects.

Oxygen by itself also causes cell death in the developing brain [27,49–51]; no study has addressed the combined effects of hyperoxemia and midazolam. It is likely that both combined are worse than each of them individually. Oxidative stress and reperfusion damage are implicated as two of the leading causes for delayed neuronal cell death and prorome changes in the developing brain. In animals, the greatest vulnerability to oxygen neurotoxicity is around the first 2 weeks of life, which in humans expands from 6 months of pregnancy to the third year of life. Damage by radical oxygen species and reperfusion is a potential serious problem for the developing brain [27,28,49–51]. Clinical studies are consistent with laboratory studies. Hyperoxemia is ‘a foe’. Oxygen toxicity has been identified as a contributing factor to the pathogenesis of cerebral palsy. In a large study of 1105 preterm infants [52], the risk of disabling cerebral palsy was double in those exposed to hyperoxia and eight-fold in the highest quintiles of oxygen exposure. Practicing to avoid hyperoxia does not produce poor outcomes [3**], actually the outcomes improved [14]. In a two-center prospective study, infants cared for with the aim of avoiding SpO2 values likely to cause hyperoxemia (i.e. SpO2 > 94–95% when breathing supplemental oxygen) had better long-term mental developmental index according to the Bayley scale [14].

The impact of clinical practices during the neonatal period on the developing brain cannot be ignored [53]. It has been over 45 years since Van Den Brenk and Jamieson [54] showed that, in mammals, there is potentiation by anesthetics of brain damage due to breathing high-pressure oxygen.

### Anesthesia, lung physiology, and oxygen

Fourteen healthy children aged 8–15 had brain functional magnetic resonance imaging (fMRI) while breathing pure oxygen. In 2 min (!), there were pronounced responses in brain areas that modify hypothalamus-mediated autonomic (sympathetic) and hormonal outflow, including the insula and hippocampus [55**]. Breathing 100% oxygen unleashes a cascade of ‘dastardly chemicals’ and quickly has potentially detrimental effects in humans.

During anesthesia or any neonatal ventilatory practice, alveolar pressures of carbon dioxide and oxygen can change in just a few seconds after ‘minimal’ modifications in care due to the simple but important alveolar gas equation. Therefore, PaO2 can change significantly and rapidly and lead to altered circulation and oxygenation, key processes in oxidative and reperfusion injury. Table 2

**Table 2 Alveolar gas equation: minimal increases in alveolar ventilation and oxygenation can rapidly change PACO2 and PAO2 and, therefore, neonatal blood oxygenation (Pao2)**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>PACO2, kPa (mmHg)</th>
<th>PAO2, kPa (mmHg)</th>
<th>Pao2, kPa (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Neonate in room air (warm humid gas)</td>
<td>5.3 (40)</td>
<td>14.6 (110)</td>
<td>9.3 (70)</td>
</tr>
<tr>
<td>(2) Modify ventilation (manual or respirator) increasing AV 10%</td>
<td>≤4.8 (35)*</td>
<td>≥15.2 (115)*</td>
<td>≥9.7 (74)*</td>
</tr>
<tr>
<td>(3) Modify ventilation (manual or respirator) increasing AV 10% + FiO2 from 0.21 to 0.30 (increased by about 0.1)</td>
<td>≤4.8 (35)</td>
<td>≥24 (180)</td>
<td>≥14.6 (110)</td>
</tr>
<tr>
<td>(4) Baseline on ventilation and FiO2 of 0.40</td>
<td>6.3 (47)</td>
<td>32.3 (242)</td>
<td>8 (60)</td>
</tr>
<tr>
<td>(5) Modify ventilation (manual or respirator) increasing AV 10% + an increase of ‘resting’ FiO2 (0.40) to 0.5</td>
<td>4.8 (35)</td>
<td>42.8 (321)</td>
<td>&gt;13.3 (100)</td>
</tr>
<tr>
<td>(6) 100% oxygen</td>
<td>8 (60)</td>
<td>80 (600)</td>
<td>As high as 60 (450) depending on V/Q and shunt</td>
</tr>
</tbody>
</table>

AV, alveolar ventilation.

*The lower the PACO2 the higher will be the PAO2 and the Pao2. Numbers 2–3 and 5–6 (with rounded numbers) show what happens when modifications are made. As can be easily understood, this must be avoided when not necessary.
Inhaled gas should always be warm and humid.

If airway narrowing is present, absorption atelectasis occurs 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. The gas mixture we give infants influences atelectasis in these cases.

Known physiological principles very accurately predict the rate at which absorption atelectasis occurs during anesthesia. High FiO2 worsens compliance and pure oxygen results in reabsorption atelectasis shortly after its application [57,58,59] (Table 3). The alveolar to venous pressure gradient must be countered by the respiratory elastic recoil to keep alveoli open, but this gradient is too high with 100% oxygen (Table 3). With just 3 min of ‘preoxygenation’, the higher the FiO2, the greater the areas of atelectasis [4**,60] and the shorter the time required for collapse to occur, irrespective of the FiO2 used after induction. Interestingly, nitrous oxide, which is discussed in detail in this same issue, behaves at an early stage in a similar fashion to oxygen, increasing the risk of atelectasis.

Alveolar recruitment maneuvers are useful [56,57,58–62], more so if done with low FiO2. When an FiO2 of 1.0 is used, there is rapid recurrence of the atelectasis [61], and decreased FRC and ventilation homogeneity. One recruitment technique, effective to maintain FRC and ventilation distribution, is positive end-expiratory pressure (PEEP) of 6 cmH2O [56]; the other may be a vital capacity maneuver with a sustained inspiratory pressure. When they are used with high FiO2, this is detrimental because of atelectasis and because the PaO2 will increase to very high levels immediately upon recruitment (Table 2), with potentially serious toxicity. This same occurs with an FiO2 of 1.0 before extubation, which also increases the risk for postoperative atelectasis (Table 4). Therefore, FiO2 should be titrated with an oxygen:air blender to try to avoid hypoxemia and hyperoxemia (i.e. Spo2 not less than 85–88% and not above 94–95%).

More oxygen than necessary in the postoperative period can, paradoxically, aggravate central hypoventilation and apnea (Tables 1 and 4). Adequate monitoring is mandatory but pure oxygen should not be used in the recovery room. If saturation is normal in room air (95–100%), the FiO2 used should be 0.21; otherwise, it should be dosed to maintain the Spo2 within the ranges mentioned above. The treatment of apnea, including postoperative apnea, is to ventilate the alveoli, to breathe, and not to give supplemental oxygen.

In an editorial a question was posed: ‘Is it always a good idea to get ‘just a little oxygen’ to breathe as you go off to sleep [4**]? My answer is definitely not. It is never a good idea to get ‘just a little oxygen’ to breathe, unless there are clear clinical indications. More than 57 years ago Comroe et al. [63] described mental changes during oxygen therapy, and, in 1975, it was clearly described that lung units with low VA/Q ratios become more unstable with oxygen breathing [64]. Comroe, in his elegant book, discusses ‘how to delay progress without even trying’ [65]. Another editorial [66], arguing that routine preoxygenation could be recommended, fits well into that category. The body of knowledge showing potential adverse effects of providing unnecessary oxygen has expanded exponentially. To decrease the gap between knowledge and practice clinicians should not turn their back on it.

### Oxygen and retinopathy of prematurity

A 32-week-gestation infant without cardiopulmonary disease and severe retinopathy of prematurity (ROP) was described in 1977 [67]. Oxygen was given only on the fourth day for 4 h, during and after general anesthesia. FiO2 varied between 1.0 and 0.5; no PaO2 was measured. Prior to extubation, with FiO2 1.0, the PaO2 was 325 torr (41.4 kPa) and, 30 min post extubation with FiO2 0.28, the PaO2 was 104 torr (13.8 kPa). After 30 min and 6 h in room  

| Table 3 Absorption atelectasis is greatly influenced by the gas mixture present in the alveolus |
|-----------------------------------------------|-----------------------------------------------|
| Room air                                      | 100% oxygen                                   |
| Alveolar pressure of gases (minus water vapor pressure) | About 95 kPa (713 mmHg)                       |
| Alveolar pressure of nitrogen                 | Normal 69.8 kPa (523 mmHg)                    |
| Blood nitrogen pressure                       | Normal                                        |
| Total mixed venous blood gases pressure       | About 87 kPa (652 mmHg)                       |
| Alveolar to venous pressure gradient          | 8 kPa (80 mmHg)                               |
| Rapid alveolar–capillary transfer of O2       | No                                            |
| Absorption atelectasis                        | No                                            |
| If airway narrowing is present                | The same                                      |
|                                              |                                              |

Inhaled gas should always be warm and humid.
The PaO₂ as 70 and 64 torr, respectively. Phibbs [68] warned clinicians that this case was not unique and that susceptible infants can be blinded by brief exposure to high PaO₂. He recommended, 30 years ago, that FiO₂ always be adjusted to maintain normal neonatal PaO₂ using an oxygen:air blender that reliably delivers FiO₂ between 0.21 and 1.0.

The risk of ROP persists until the retinal vasculature has matured. In general terms, the retina of a 2–3-month-old infant who was 24 weeks, gestation at birth or of a 5–8-week-old infant born at 26–30 weeks, gestation may still be highly susceptible to hyperoxemia.

Interestingly, wide, rapid fluctuations in oxygenation may cause more derangement of vascular responses than persistent hyperoxia, and must be avoided [7,8,9**,13]. A practice aiming to avoid hyperoxemia and fluctuations is associated with lower rates of severe ROP and laser surgery [13,14,15*,16–18]. Only one small retrospective study [69], from the University of North Carolina, shows no significant improvement in ROP rates. In an editorial, the same author [70] states that he will continue to inform that data suggest that lowering oxygen saturation reduces severe ROP but the risk to overall development is not yet known. As shown here, however, knowledge and evidence of practices that aim to avoid hyperoxemia demonstrate benefits for ROP and for prevention of potential harm to the developing brain, long-term development and other morbidities (Table 1, Fig. 1).

Excess oxygen is risky for newborns [1**,2***]. More oxygen than necessary, even for a short time, serves to oppose or impede health objectives and is associated with injury, fitting perfectly the definition of ‘foe’, being hostile to the purposes or interests of healthcare providers (Fig. 1).

### Monitoring of oxygenation during anesthesia
Owing to space limitations I cannot cover this in detail. More than 90 publications have addressed SpO₂ monitors. Table 5 summarizes a few [7,8,9**,71,72–78].

Cellular oxygenation is complex [9**]; one day we may be able to monitor this clinically. With the aim of avoiding hypoxemia and hyperoxemia and oxidant stress, we have shown [71**] that when the SpO₂ is more than 94%, in neonates who are receiving supplemental O₂, there is hyperoxemia in 60% of the samples.

Fortunately, for the well being of many newborns, the history of neonatal O₂ monitoring is ‘coming of age’ after the past 10–12 years of extensive research and education.

### Summary
Oxygen should never be denied when necessary. An adequate state-of-the-art SpO₂ monitor serves as a guide to increase FiO₂ and by how much. Pure oxygen is almost never necessary.

---

**Table 4** Several practices that increase potential for risk before, during, and after neonatal anesthesia

<table>
<thead>
<tr>
<th>Problems</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>Developing brain</td>
</tr>
<tr>
<td>Manual ventilation</td>
<td>Hypocarbia</td>
</tr>
<tr>
<td>Manual ventilation – no humidified warm gas</td>
<td>Inadequate gas conditioning</td>
</tr>
<tr>
<td>Lack of air:oxygen blender</td>
<td>‘We see no problems’; ‘Cannot allow hypoxia’; ‘We have always done this’; ‘Baby looks good (or pink)’; ‘SpO₂ is great’; (other)</td>
</tr>
<tr>
<td>100% oxygen</td>
<td>Many risks (described in text)</td>
</tr>
<tr>
<td>Excess oxygen, any FiO₂</td>
<td>‘We see no problems’; ‘Cannot allow hypoxia’; ‘We have always done this’; ‘Baby looks good (or pink)’; ‘SpO₂ is great’; (other)</td>
</tr>
<tr>
<td>Preoxygenation (even 2–3 min)</td>
<td>‘We see no problems’; ‘Cannot allow hypoxia’; ‘We have always done this’; ‘Baby looks good (or pink)’; ‘SpO₂ is great’; (other)</td>
</tr>
<tr>
<td>Insufficient PEEP</td>
<td>Decrease FRC</td>
</tr>
<tr>
<td>Alveolar recruitment maneuvers</td>
<td>Risk if too high pressures</td>
</tr>
<tr>
<td>Apnea</td>
<td>High PaO₂ and systemic damage</td>
</tr>
<tr>
<td>Wide rapid fluctuations in oxygenation</td>
<td>Giving unnecessary oxygen; hyperventilating</td>
</tr>
<tr>
<td>SpO₂ &gt;95% when breathing supplemental O₂</td>
<td>Care providers still do not quite understand how bad this is</td>
</tr>
</tbody>
</table>

FRC, functional residual capacity; PEEP, positive end-expiratory pressure; ROP, retinopathy of prematurity.
Table 5 Practical concepts on saturation monitoring, based on peer-reviewed publications and reports

<table>
<thead>
<tr>
<th>Statement</th>
<th>Comments</th>
<th>Clinical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>SpO₂ monitors are valuable to detect hypoxemia</td>
<td>Monitors vary in the ability to accurately detect hypoxemia</td>
<td>See below</td>
</tr>
<tr>
<td>SpO₂ is not a measurement of tissue oxygenation</td>
<td>A low SpO₂ does not necessarily mean that there is tissue hypoxia</td>
<td>We do not have a tool to measure tissue oxygenation</td>
</tr>
<tr>
<td>Six type of noise can ‘confuse’ the monitor, when it is most needed</td>
<td>Medications, shock, venous desaturation and stasis, anesthesia, surgery,</td>
<td>‘Confusion’ leads to falsely low SpO₂ readings, data drop out, false bradycardia,</td>
</tr>
<tr>
<td></td>
<td>motion, cold extremities, light and others</td>
<td>holding periods and false alarms</td>
</tr>
<tr>
<td>SpO₂ monitors are different according to the manufacturer</td>
<td>‘One monitor is not the same as another monitor’</td>
<td>Those with greatest accuracy are more valuable in caring for sick patients</td>
</tr>
<tr>
<td>Signal extraction technology is extremely useful</td>
<td>Extraction of the arterial signal from all other noises and motion</td>
<td>Provides more accuracy in readings</td>
</tr>
<tr>
<td>Sensors are also different according to the manufacturer</td>
<td>Low noise optical probes (LNOP) act as a ‘shock absorber’</td>
<td></td>
</tr>
<tr>
<td>Normal SpO₂ in room air</td>
<td>Not an adequate SpO₂ target when neonates receive supplemental O₂</td>
<td></td>
</tr>
<tr>
<td>SpO₂ cannot detect hypoxemia</td>
<td>SpO₂ 96–100% when giving supplemental O₂</td>
<td>Avoiding ‘normal’ SpO₂ when breathing O₂ decreases risk of oxidant damage</td>
</tr>
<tr>
<td>During resuscitation time to stable SpO₂</td>
<td>Mean of 22 s for Masimo SET and 64 to 74 s for two other monitors</td>
<td>Better guided administration of the needed dose of oxygen</td>
</tr>
<tr>
<td>Relative risk reduction of severe ROP is associated with the technology</td>
<td>Two-center study; 40% reduction with Masimo SET; P = 0.02</td>
<td>Education, alarm limits, targets, implementation of practice guidelines and adequacy of technology are all necessary</td>
</tr>
<tr>
<td>No one knows what the ‘best’ or ‘ideal’ saturation range is at all times</td>
<td>Eradicating some bad practices is not the same as implementing routinely</td>
<td>Paying attention to ‘details’ we can accomplish a clinical difference and improve outcomes</td>
</tr>
<tr>
<td></td>
<td>outdated practices in a rigid way</td>
<td></td>
</tr>
<tr>
<td>SpO₂ &gt;95% when breathing supplemental O₂</td>
<td>Is of high risk for high PaO₂</td>
<td>Risk of inducing oxidant stress</td>
</tr>
</tbody>
</table>

Oxidant stress is a ‘part of life’, but the only neonatal cause for PaO₂ greater than normal are treatments administered by healthcare providers. To avoid hypoxemia, without permitting hypoxemia, is neither easy nor simple. Understanding oxygen toxicity leads to new ways of interrupting pathologic sequences. We can neither simplify complex matters nor take one good friend for granted. The dual nature of oxygen is clear: therapeutically beneficial and potentially toxic, a great friend or the worst foe.

Inducing brief, prolonged and/or widely fluctuating hypoxemia is a potentially bad and high-risk practice for newborn babies, despite lack of a randomized trial. Absence of evidence is not evidence of absence [79], and this well applies to the risks of hypoxemia and oxidant stress in neonates.

On the basis of evidence and knowledge and on more than 10 years of studying this topic and observing practices and resistance to change, my opinion is that oxygen is not really the foe. Just as for art (‘Art hath an enemy called Ignorance’, Ben Johnson), some infants have an enemy in ignorance and/or guidelines, strict rules, or practices that may induce hypoxemia. Therefore, without even trying, we are the real foes, not oxygen, putting the well being of some infants at high risk, by not refining the use and indications of oxygen. Maybe, the coming of age for neonatal oxygen therapy will be reached when we diminish or eliminate the gap between knowledge and practice, and we implement the aim of never administering unnecessary oxygen and of trying to avoid SpO₂ more than 95%, to decrease episodes or periods of hypoxemia and its associated risks.

You can now move on to something else, relax and ‘take a (deep) breath, but do not add oxygen if it is not needed’, as Ola Saugstad wrote [27].

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:
• of special interest
•• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 417).

4. Lumb AB. Just a little oxygen to breathe as you go off to sleep . . . is it always a good idea? Br J Anaesth 2007; 99:769–771.
Pediatric anesthesia


9 Sola A, Pérez Saldería Y, Favareto V. Clinical practices in neonatal oxygenation - Where have we failed? What can we do? J Perinatol (in press).

10 Description of current and salient aspects on oxygenation. Excellent description of current and salient aspects on oxygenation.


16 Oxygen toxicity and effects of practices that aim to prevent hyperoxemia seem to be different in boys than in girls. Oxygen toxicity and effects of practices that aim to prevent hyperoxemia seem to be different in boys than in girls.


21 New information and wonderful insight, both for scientists and for clinicians. New information and wonderful insight, both for scientists and for clinicians.


31 Excellent description of the current situation and the need for further research. Excellent description of the current situation and the need for further research.


56 Very original study in 14 children showing rapid adverse effects of pure oxygen on the brain and how carbon dioxide affects the response.


59 Important findings for clinical practice.
Oxygen in neonatal anesthesia

Sola 339


70 Castillo A, Sola A, Baquero H, et al. Pulse oximetry saturation levels and arterial oxygen tension values in newborns receiving oxygen therapy in the neonatal intensive care unit: is 85% to 93% an acceptable range? Pediatrics (in press).

71 When neonates are receiving supplemental oxygen and the Spo2 is more than 94%, there is hyperoxemia in 60% of the samples. We also describe salient clinical issues regarding Spo2 monitoring.


A comprehensive and simple analysis of what is really ‘evidence’ and what is not.